
# EDUCATION UPDATE

from
Allegheny Health Network Oncology

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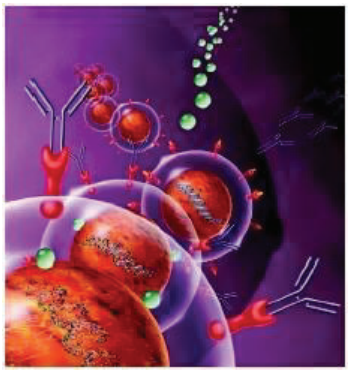
# AHNCI FUNDAMENTALS ANTICANCER THERAPY COURSE – 2026



**Didactic: March 12, 19, 26**
**Outpatient RN and APP Simulation: March 30**
**Inpatient RN and APP Simulation: March**
**Exam: April 9, 2026**
**Administration Practicum: (completed by May 22)**

# Allegheny Health Network Cancer Institute
# Fundamentals of Anticancer Therapy Course

This course is intended for novice clinicians (physicians, nurses, pharmacists, and allied health care professionals) who practice in hematological-medical units, skilled nursing facilities, home care, hospice, radiation oncology, and/or cellular transplant. This course content is appropriate for new as well as experienced clinicians who will be handling antineoplastic anticancer therapies. This course is designed to provide the oncology clinicians with a comprehensive review of knowledge required to administer anticancer therapies.

Course Faculty: This course uses a multidisciplinary approach from the knowledge, skills, and expertise of physicians, nurses, advanced practice practitioners, and oncology clinical pharmacy specialists to provide a comprehensive overview of anticancer therapy.

**Criteria for completion to earn contact hours**

Course Materials: Course materials are distributed at the beginning of each course with additional handouts as necessary throughout the course. Materials include the course schedule, objectives, evaluation form, and content outlines. This course also requires additional simulated videos, standard of practice (SOP) manual with post assessment, and weekly assignments.

Course Evaluation: Participants are requested to complete an evaluation for each speaker/lecture. The evaluations are collected at the conclusion of each day. Feedback is utilized for subsequent course evaluations. Pathways for the course are **role** dependent as follows:

- Didactic + SOP with post assessment + simulation with videos + practicum + exam
- Didactic + SOP with post assessment + simulation with videos + exam
- Didactic + SOP with post assessment + exam
- Didactic + SOP with post assessment
- Didactic only
- SOP with post assessment + exam
- SOP with post assessment + simulation with videos + practicum + exam
- Simulation with videos + practicum + exam
    - Experienced clinicians may attend any portion for NCPD or CME. Final NCPD and CME pending
    - Participants are eligible for continuing education (CEs) based on the sections they attend. Contact hours are only offered on the scheduled course dates attended.
    - Special consideration for contact hours may be awarded accordingly

ACT examination requirements:

a. Individuals who pass anti-cancer therapy exams with an initial passing score of 85%:
    i. incorrect questions are retaken, then reviewed with the employee

b. Individuals who do not pass anti-cancer therapy exams with an initial score of less than 85%:
    i. incorrect questions are reviewed with the employee and study notes are taken by the employee
    ii. the employee retakes the exam within a week, unless determined by the manager/director/professional development team otherwise for an extension
    iii. if the retake score is greater than or equal to 85%:
        a. incorrect questions are retaken, then reviewed with the employee
    iv. if the retake score is less than 85%:
        a. the employee retakes a course and retests upon course completion

**Presence/absence of any conflict of interest for any planner or speaker**

- The planners and presenters have no conflicts of interest to disclose for this activity
- There is no commercial support or sponsors for this educational activity.

**The provider approval statement this program was awarded**

- Allegheny General Hospital is accredited by the Accreditation Council for Continuing Medical Education to provide continuing education for physicians.
- Allegheny General Hospital designates this live activity. *AMA PRA Category Credits*™ pending.
- West Penn Hospital is approved as a provider of nursing continuing professional development by Pennsylvania State Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.
- You may attend any portion of the course for NCPD or CME.
- Final CE and CME pending.
- Pharmacotherapeutics CE and CME:
    - Cell-Cycle Specific Agents
    - Cell-Cycle Non-Specific Agents
    - Hormone Therapy
    - Myelosuppression and Growth Factors
    - Molecular Targeted Therapies
    - Immunotherapy
- All disclosures relevant conflicts have been mitigated.

# Allegheny Health Network Cancer Institute

## *ANTICANCER THERAPY FUNDAMENTALS COURSE*

## COURSE LEARNING OUTCOMES

Upon completion of this course, the participant will be able to:

1. Explain the staging impact on treatment modality decisions.
2. Describe historical advances in oncology, including the FDA approval process and clinical trials.
3. Discuss principles of cancer treatments.
4. Identify the importance of the cell cycle and cellular kinetics as they relate to the anticancer therapies.
5. Explain the mechanism of action for each of the major drug classifications.
6. Calculate anticancer therapy doses based on the BSA and Calvert formulas.
7. Recognize drugs that can cause tissue necrosis.
8. Demonstrate management strategies of an extravasation.
9. Match acute, subacute, and chronic toxicities along with side effects associated with anticancer therapies.
10. Formulate a comprehensive plan of care, including side effects and toxicities for a patient receiving anticancer therapy.
11. Review financial concepts related to anticancer therapy.
12. Perform the steps required in the anticancer therapy administration process.
13. Demonstrate management of an anticancer therapy spill.
14. Manage hypersensitivity and/or anaphylactic reactions.
15. Incorporate anticancer therapy standards of practice into clinical practice.

# Allegheny Health Network Cancer Institute

***ANTICANCER THERAPY COURSE – Day 1***

| | |
|---|---|
| 7:30 a.m. | *Registration & Welcome*<br>Mary E. Kern, MSN, RN, OCN, CHSE |
| 8:00 a.m. | *Overview of Anticancer Therapies*<br>Mary E. Kern, MSN, RN, OCN, CHSE<br>**scientific basis, diagnosis, staging* |
| 10:00 a.m. | Break |
| 10:15 a.m. | *Myelosuppression and Overview of Growth Factors*<br>Danielle Roman, Clinical Pharmacist Specialist, BCOP<br>**treatment/symptom management* |
| 11:45 am | Lunch |
| 12:30 p.m. | Cell-Cycle Specific Agents<br>*Plant Alkaloids, Antimetabolites, Miscellaneous Agents and Nursing Implications*<br>Mary E. Kern, MSN, RN, OCN, CHSE<br>**treatment/symptom management* |
| 2:00 p.m. | Break |
| 2:15 p.m. | *Toxicity Assessments*<br>Marcia Almiron-Wolbert, MSN, RN, OCN<br>**treatment/symptom management* |
| 3:15 p.m. | Wrap-up and Evaluations<br>*Self-Study Completion - Standard of Practice (SOP) Review Booklet and ACT Videos<br>*Complete Weekly Homework<br>**professional* |
| 3:45 p.m. | Adjourn |

# Anti-Cancer Therapy (ACT) Guidelines and Recommendations for Practice

Mary E. Kern, MSN, RN, OCN, CHSE

Professional Development Specialist AHNCI

Mary.KERN@ahn.org

*No disclosures*

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## Learning Outcomes

- Discuss principles of cancer treatments
- Describe historical advances in oncology, including the FDA clinical trial and approval process
- Apply pharmacokinetic and pharmacodynamic principles to safely administer anti-cancer therapies relative to staging
- Assess patient-specific factors including stage, co-morbidities, risk and performance status to individualized treatment plans

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# STATISTICS

- Greater than 2 million new cases were expected to be diagnosed in the US in 2024 (excludes basal and squamous cell skin cancer)
- Cancer is the 2nd most common death in the US (heart disease #1)
- As much as 42% of new cases are potentially avoidable with lifestyle changes (smoking = 19%, excess body weight, alcohol, poor nutrition and physical inactivity= 18%)
- Cancer death rate has dropped 1.6% per year from 2012-2021
- Overall survival rates have increased substantially from 39% in the 1960's to 69% in more recent years

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Cancer Statistics 2025

## Estimated number of new cancer cases in the US in 2025

| Male | | | Female | | |
|---|---|---|---|---|---|
| Prostate | 313,780 | 30% | Breast | 316,950 | 32% |
| Lung & bronchus | 110,680 | 11% | Lung & bronchus | 115,970 | 12% |
| Colon & rectum | 82,460 | 8% | Colon & rectum | 71,810 | 7% |
| Urinary bladder | 65,080 | 6% | Uterine corpus | 69,120 | 7% |
| Melanoma of the skin | 60,550 | 6% | Melanoma of the skin | 44,410 | 4% |
| Kidney & renal pelvis | 52,410 | 5% | Non-Hodgkin lymphoma | 35,210 | 4% |
| Non-Hodgkin lymphoma | 45,140 | 4% | Pancreas | 32,490 | 3% |
| Oral cavity & pharynx | 42,500 | 4% | Thyroid | 31,350 | 3% |
| Leukemia | 38,720 | 4% | Kidney & renal pelvis | 28,570 | 3% |
| Pancreas | 34,950 | 3% | Leukemia | 28,170 | 3% |
| All sites | 1,053,250 | | All sites | 988,660 | |

Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.
Source: Cancer Facts & Figures 2025.

Cancer Statistics 2025

## Estimated number of new cancer deaths in the US in 2025

American Cancer Society

| Male | | | Female | | |
|---|---|---|---|---|---|
| Lung & bronchus | 64,190 | 20% | Lung & bronchus | 60,540 | 21% |
| Prostate | 35,770 | 11% | Breast | 42,170 | 14% |
| Colon & rectum | 28,900 | 9% | Pancreas | 24,930 | 8% |
| Pancreas | 27,050 | 8% | Colon & rectum | 24,000 | 8% |
| Liver & intrahepatic bile duct | 19,250 | 6% | Uterine corpus | 13,860 | 5% |
| Leukemia | 13,500 | 4% | Ovary | 12,730 | 4% |
| Esophagus | 12,940 | 4% | Liver & intrahepatic bile duct | 10,840 | 4% |
| Urinary bladder | 12,640 | 4% | Leukemia | 10,040 | 3% |
| Non-Hodgkin lymphoma | 11,060 | 3% | Non-Hodgkin lymphoma | 8,330 | 3% |
| Brain & other nervous system | 10,170 | 3% | Brain & other nervous system | 8,160 | 3% |
| All sites | 323,900 | | All sites | 294,220 | |

Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.
Source: Cancer Facts & Figures 2025.


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# SURVIVORSHIP

- Focuses on the health and well-being of a person with cancer from diagnosis until end of life.
- Includes physical, psychosocial and economic issues
- Includes family, friends and caregivers

- The most reported social issue reported after diagnosis and treatment is "financial toxicity"

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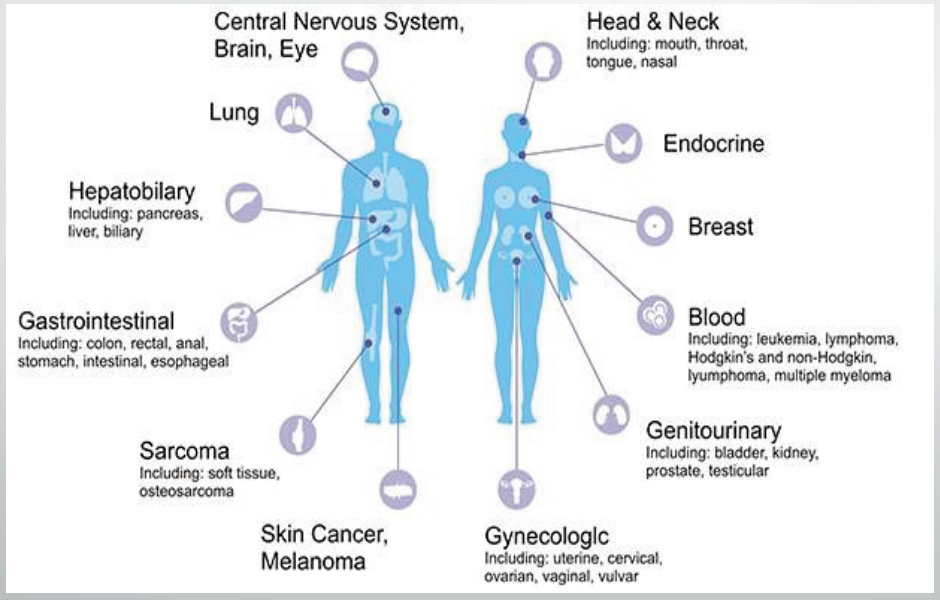


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# ROUTES OF ADMINISTRATION

IV (peripheral or central line)

Oral

SQ

IM

Intra-arterial/ Intrahepatic Intrathecal (LP)

Intraventricular (Ommaya)

Intraperitoneal (Abdominal )

Intra-pleural (sclerosis/malignant pleural effusions)

Intravesical (bladder)

Procedural (HIPEC/HIPOC, TACE)

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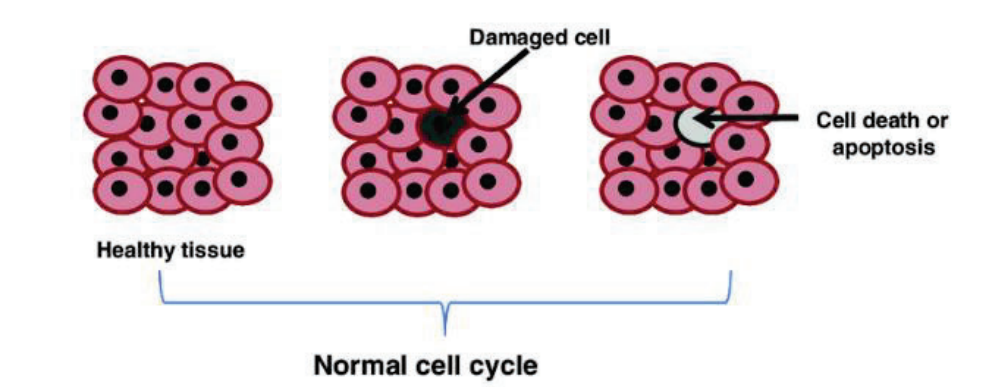
# Normal cell cycle

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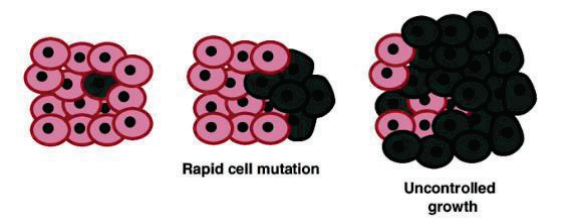
# CANCER CELLS

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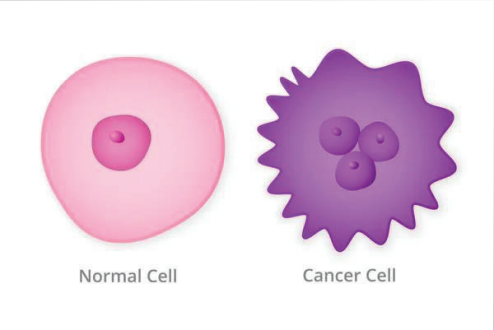
# Cancer cells and why we hate them…




- Abnormal cell structure and proliferation
- Hyperchromatic – nuclei stain darker
- Pleomorphism- cells vary in size and shape
- Polymorphism – nucleus varies in size and shape

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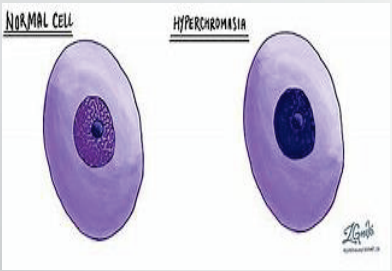
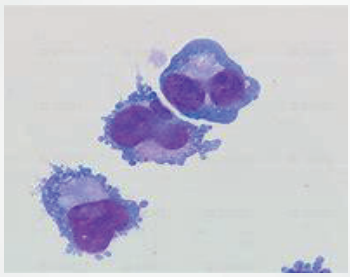
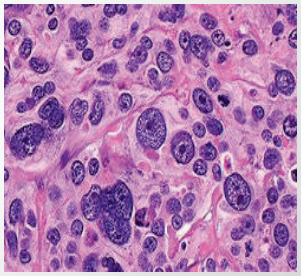



Hyperchromatic



Pleomorphic



Polymorphic

Cancer cells and why we hate them…

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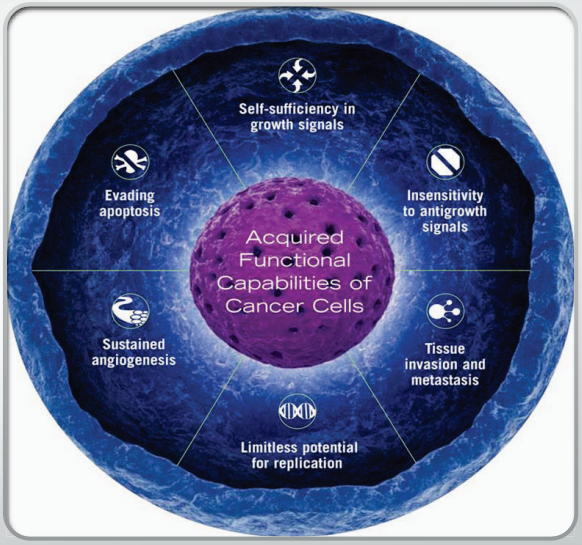
## 7 Deadly Sins of Cancer Cells

1. Uncontrolled growth and division
2. Genetic instability
3. Ability to evade apoptosis
4. Sustained angiogenesis
5. Invasion and metastasis
6. Reprogramming of energy metabolism
7. Immune evasions

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## Uncontrolled growth and division

- Cancer cells have lost their ability to self-regulate
- They bypass checkpoints that normally detect errors which leads to rapid proliferation
- Telomeres normally shorten with each cell division eventually signaling cell senescence (aging) or apoptosis (cell death).
- Cancer cells re-activate telomerase, an enzyme that maintains the telomere length and allows them to divide indefinitely

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## Genetic Instability

- Cancer cells accumulate genetic mutations that affect the genes that regulate cell growth, division, repair and apoptosis (cell death)
- Frequently display chromosomal abnormalities like translocation, deletions, and amplifications
- Often have defects in their DNA repair mechanisms that lead to additional mutations and genomic instability.

- **Translocations** (ie: t 9;22)
- **Deletions** (ie: q 5 with MDS)
- **Inversions** (ie: i 11,13)
- **Amplifications** (more copies of DNA sequence)
- **Aneuploidy** (abnormal number chromosomes)
- **Transcription** errors of DNA when transcribed into messenger RNA

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## Genetics vs. Epigenetics

### Genetics

- What genes you have
- DNA sequence itself
- Changes in the DNA (mutations)
- Largely inherited
- Relatively stable
- Permanent changes to code

### Epigenetics

How those genes are used

- Expression without altering DNA
- Changes in gene activity
- Can be inherited but also environmentally influenced and are potentially reversible
- Changes in gene activity, impacting phenotype

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# Ability to evade apoptosis

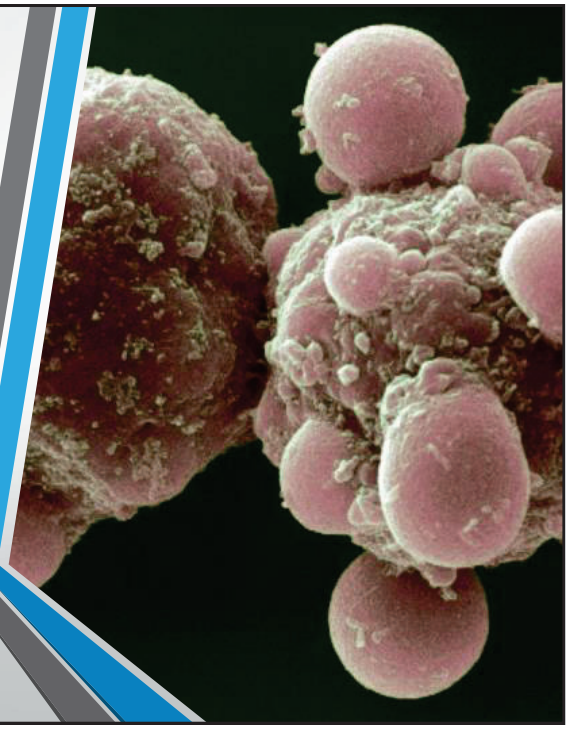
Cancer cells inactivate pro-apoptotic proteins preventing the cell from undergoing programmed death

**Or**

Cancer cells over express anti-apoptotic proteins which block the pathway for apoptosis to occur

**Or**

Deregulate signaling pathways or alter mitochondrial function



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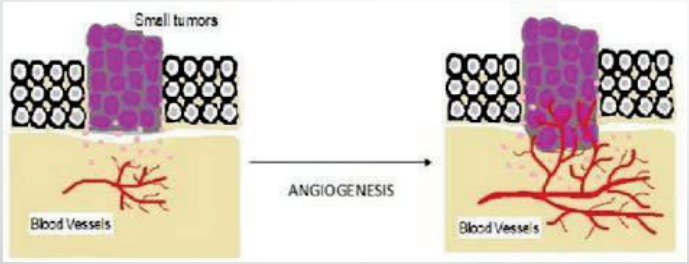
# Sustained angiogenesis

- In order to grow and metastasize, cancer cells can initiate the production of new blood vessels




- Cancer cells recruit normal cells in the vicinity to assist

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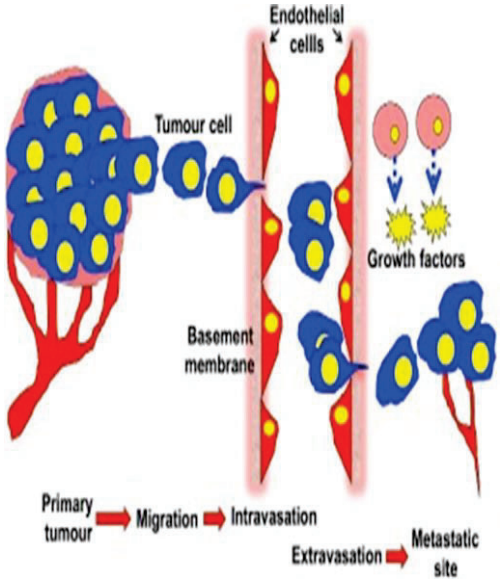
# Invasion and Metastasis

Cancer cells have increased motility and invasiveness allowing them to break away from the primary tumor

They produce enzymes that degrade the scaffolding that holds cells together allowing them to travel freely

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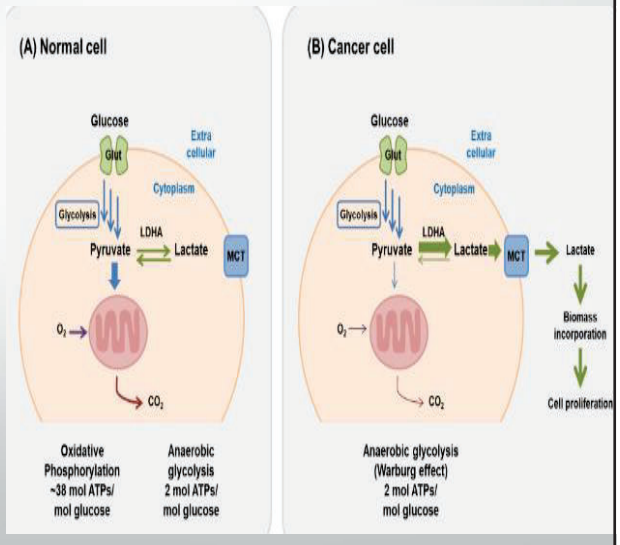
# Reprogramming of Energy Metabolism

Cancer cells RELY on glucose to produce energy even in the presence of oxygen.

Warburg Effect:

- Inefficient energy production
- Provides building blocks
- It allows the cancer cells to grow rapidly.

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# Immune Evasion

Cancer cells develop mechanisms to evade detection and destruction by the immune system

1. Loss of expression of tumor-associated antigens
2. Immune checkpoint upregulation
3. Secretion of immunosuppressive factors
4. Recruitment of immunosuppressive cells
5. Alteration of the tumor microenvironment
6. Antigenic variation and heterogeneity

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# An Immune Heist

- They dress up in disguise
- They bribe the guards
- They build a fortress
- They keep changing their clothes
- They recruit their own security team






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# Cell Signaling in a normal cell

How all cells receive, process and respond to information vital to growth, proliferation and cellular death

- Message is sent through a chemical signal
- Another cell has a specific receptor designed to receive that specific message
- It is passed along within the cell activating a chain of events
- The signal is amplified to ensure the message gets to the right proteins and genes within the cell
- The cell acts based on each message
- Once complete, the message is destroyed so the cell doesn't keep doing the same thing indefinitely

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# Cell Signaling in a cancer cell

- They ignore all the stop signs
- The signal that tells the cell to self-destruct no longer functions properly
- They send signals to build new roads (angiogenesis) and throw out the "bat sign" to attract other cells
- They send out misleading signals to trick the immune system

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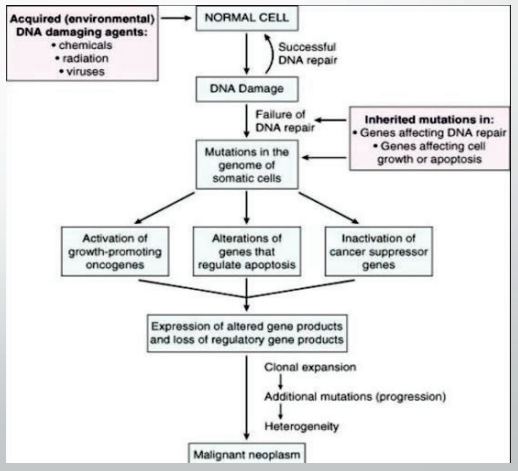
# Molecular basis of cancer

## Involved Genes

- Proto-oncogenes
- Tumor suppressor genes
- Genes regulating apoptosis
- DNA repair genes
- PDL-1 & PDL-2 pathways

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# Theories of Causation

Genetic damage and instability of somatic cells (non-reproductive cells)

Proto-oncogenes are normal genes that regulate growth and repair

- when working normally they signal cell division and regulate cell death. Gas pedal
- when mutated or overexpressed they morph into oncogenes leading to uncontrolled growth/proliferation. Gas pedal is stuck

Results of this dysfunction:

- Proteins are formed where they are not normally
- Proteins can be in the appropriate cells, but in excessive amounts
- Proteins form unusually and can not be regulated by normal methods

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| Oncogene | Type of cancer | Gene Modification |
|---|---|---|
| Abl | Chronic Myeloid leukemia | Translocation |
| Myc | Burkitt's Lymphoma | Translocation |
| L-Myc | Small cell lung cancer | Amplification |
| N-Myc | Neuroblastoma | Amplification |
| Ras | Bladder Cancer | Mutation |
| K-Ras | Colon cancer | Mutation |
| N-Ras | Acute myeloid leukemia | Mutation |

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# RAS

| RAS Oncogene | Characteristics | Associated Cancers |
|---|---|---|
| **KRAS** | Most frequently mutated RAS gene; Located on chromosome 12. Relatively difficult to target therapeutically. | Pancreatic cancer (most common), colorectal cancer, lung cancer (adenocarcinoma), bladder cancer, ovarian cancer, thyroid cancer, cholangiocarcinoma |
| **HRAS** | Located on chromosome 11. Relatively less common in solid tumors compared to KRAS; some response to targeted therapies | Bladder cancer, head and neck squamous cell carcinoma, leukemia (rare), melanoma |
| **NRAS** | Located on chromosome 1; Mutations less frequent than KRAS; some response to targeted therapies | Melanoma, hematologic malignancies (e.g., leukemia, myeloma), colorectal cancer, lung cancer (adenocarcinoma), thyroid cancer |

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# Tumor Suppressor Genes

Built in brakes and repair kits working to:

- Stop cell growth
- Repair DNA damage
- Control cell death (aka apoptosis)

A mutation of the TSG allows all of these functions to go unchecked and unbalanced.

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# P53 – one of the most mutated TSG

- ✓ This is a tumor suppressor gene
- ✓ Located on 17p13, first discovered in 1979
- ✓ Located in almost all normal tissues
- ✓ Unstable and degrades very quickly
- ✓ Is one of the most mutated gene in cancer

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# Proto-oncogenes to Oncogenes

This is Gene. Gene is out for a Sunday drive living his best life!

Every car has a gas pedal, right?

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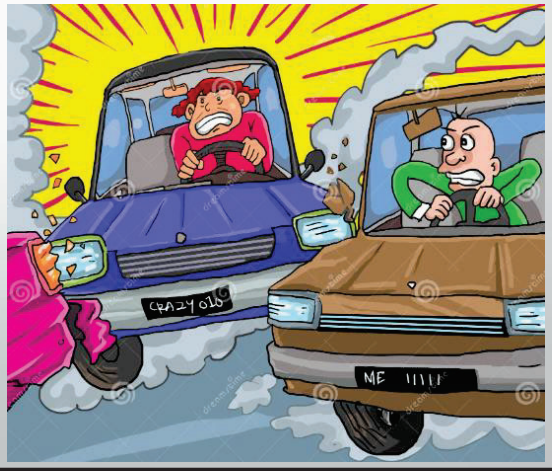
# Oncogene

What if that pedal gets stuck???

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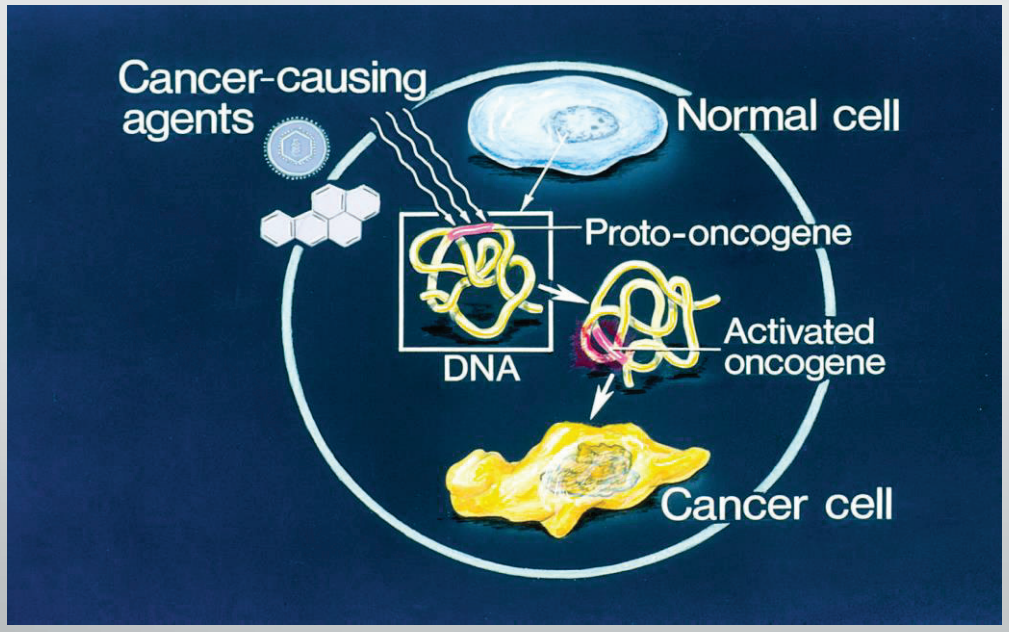


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# Examples of oncogenes

| Oncogene Family | Specific Oncogene(s) | Cancer Types Frequently Implicated | Mechanism of Action | Therapeutic Challenges |
|---|---|---|---|---|
| Receptor Tyrosine Kinases (RTKs) | ERBB (EGFR, HER2) | Lung, Breast, others | Constitutive activation of growth signaling pathways | Some (like EGFR and HER2) are targetable, others not |
| | VEGF Receptor | Various | Promotes angiogenesis (blood vessel formation) | |
| Non-receptor Tyrosine Kinases | ABL | Leukemia (CML) | Constitutive activation of growth signaling pathways | Targetable with tyrosine kinase inhibitors (TKIs) |
| RAS Family | KRAS, HRAS, NRAS | Pancreatic, Colorectal, Lung | Constitutive activation of growth signaling pathways | Often difficult to target therapeutically |
| Serine/Threonine Kinases | B-RAF | Melanoma, other cancers | Constitutive activation of MAPK pathway | Targetable with BRAF inhibitors, but resistance can occur |
| MYC Family | MYC | Lymphomas, Leukemias, Lung | Overexpression drives uncontrolled cell growth and division | |
| Cyclin-Dependent Kinases (CDKs) | CDK4/6 | Breast, Melanoma | Uncontrolled cell cycle progression | |
| PI3K/AKT/mTOR Pathway | PIK3CA | Breast, Colorectal, Lung | Uncontrolled cell growth, survival, and metabolism | |

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# Staging per the American Joint Committee on Cancer (AJCC)

## Why do we do it?

- Determine the extent of disease
- Determine prognosis
- Determine a plan

### Tumor Registry

- Collects and aggregates data

### American College of Surgeons

- Biopsy
- Pathology
- Re-staging for recurrence

## How do we do it?

- Diagnostic testing
- Biopsies
- Blood tests (tumor markers)
- Imaging (CT, MRI, PET)
- Nuclear med

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| Staging System | Cancer Type(s) | Key Staging Factors | Stage Description Style |
|---|---|---|---|
| TNM | Most solid tumors | T (Tumor size/extent), N (Lymph node involvement), M (Metastasis) | Numerical (I, II, III, IV) or alphanumeric (e.g., IIA, IIIB |
| FIGO | Gynecological cancers (cervix, uterus, ovary, vulva, vagina) | Tumor size, spread to nearby organs, lymph node involvement, distant metastasis | Roman numerals (I, II, III, IV) |
| HEME | Hematological malignancies (leukemia, lymphoma, myeloma) | Bone marrow involvement, peripheral blood involvement, lymph node involvement, extramedullary disease, cell type, cytogenetics | Descriptive categories |
| VA Stage (VALSG) | Small-cell lung cancer | Extent of disease | Limited vs. Extensive |
| Brain | Brain tumors (gliomas, meningiomas, etc.) | Tumor location, size, infiltration, edema, CNS spread, grading (I-IV) | Varies by tumor type |

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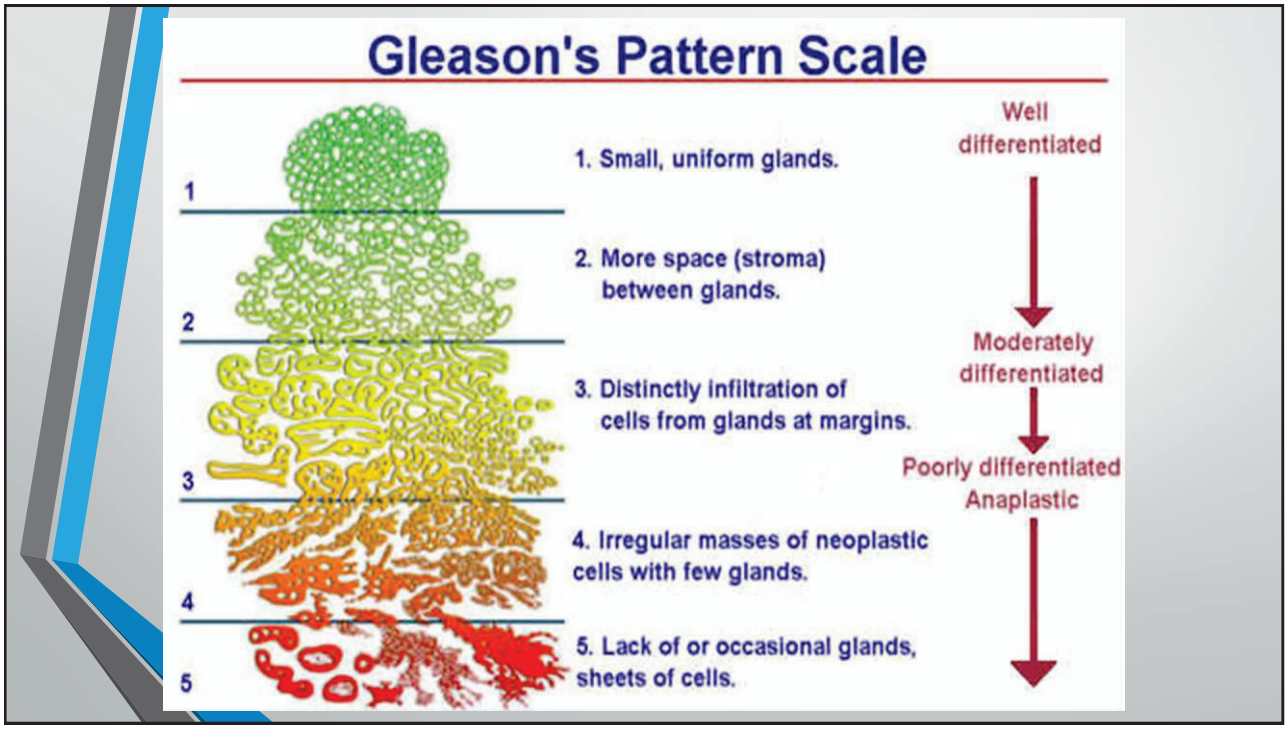


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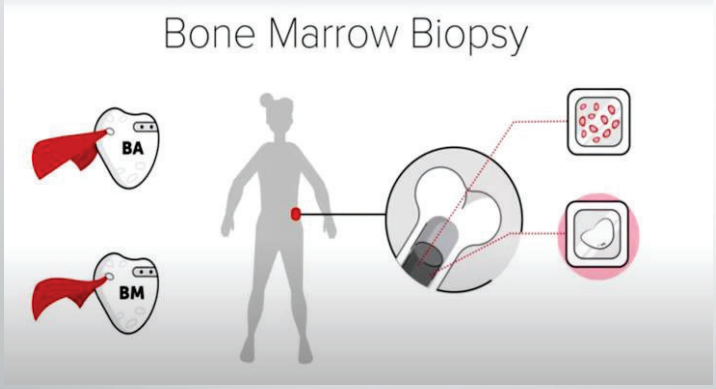
## Bone marrow biopsy & aspirate (Heme)




Aspirate examines the liquid
- Cytogenetics/FISH
- Immunophenotyping/Flow Cytometry
- Morphological review

BM biopsy examine a small piece of the bone
- Cellularity
- Overall health of the cells

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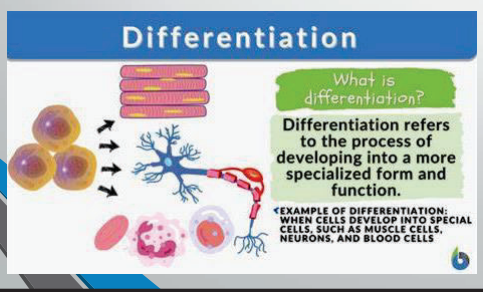
# Differentiation & Proliferation

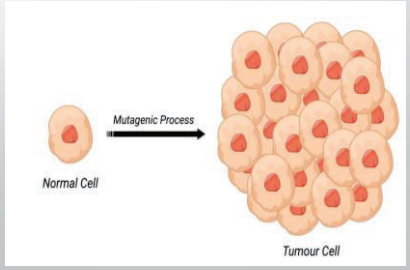
Differentiation

- Maturation or rate of growth
- Slow growth vs, rapid growth




Proliferation

- Cell division and multiplication
- Normal for growth and repair
- Uncontrolled in cancer

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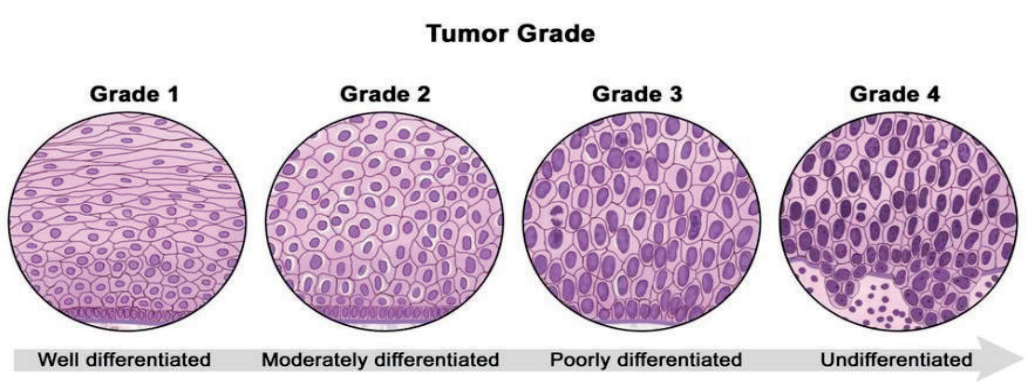
# Grading and Differentiation

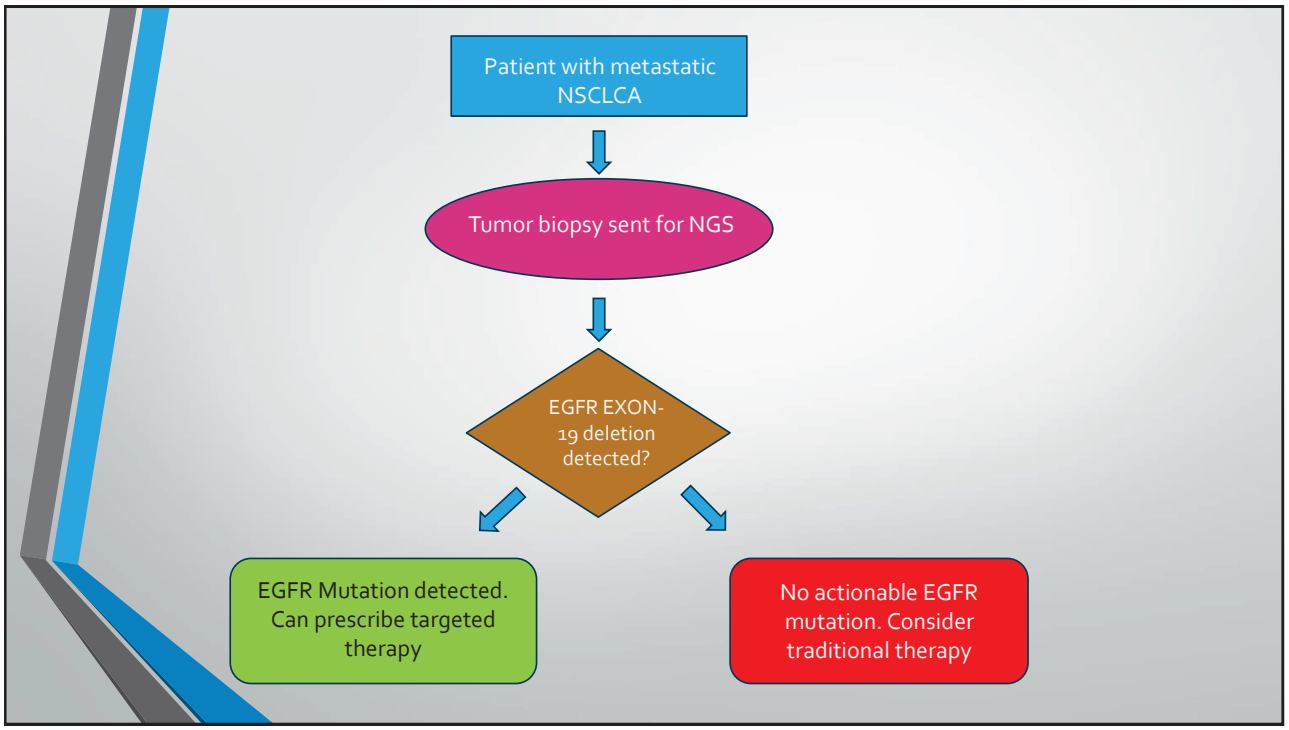



40

# Molecular Testing

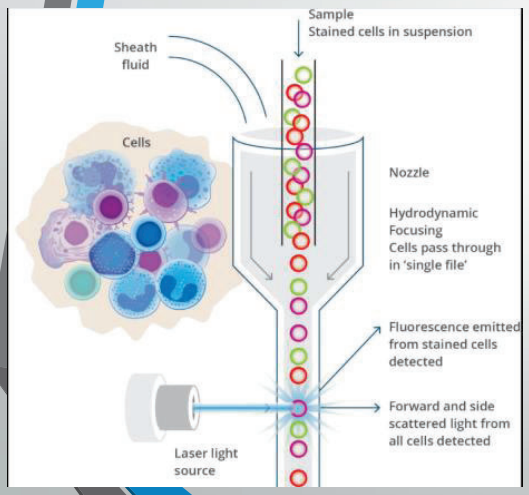
- Gene-Based
- Karyotyping/cytogenetics
- Deletions - q
- Inversions - i
- Translocations – t
- PCR
- Amplification
- FISH (Florescence In Situ Hybridization)
- Uses fluorescent probes
- NGS (Next Gen Sequencing)
- Allows for errors to be found quickly
- Can track how cancer is changing over time

41




42

# Molecular testing




## Flow Cytometry

- Laser-based technology
- Provides rapid analysis of qualitative and quantitative characteristics
- Fluorescent antibodies are added to the suspension allowing for multiple markers to be detected simultaneously
- Each cell is analyzed for size, texture, and antibodies
- Identifies "clusters of differentiation" or CD.

Example: CD20 – found on the surface of B-cells

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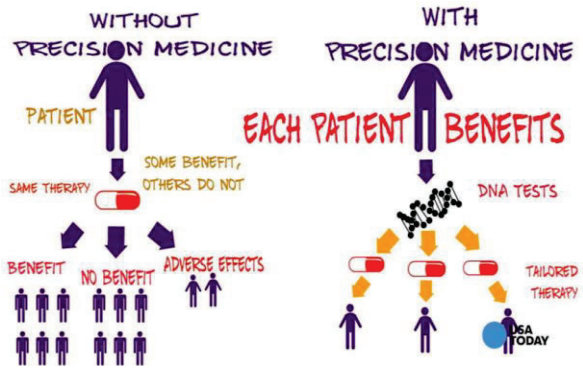
# Precision Medicine

- Moving beyond "one size fits all"
- Understanding the tumor's blueprint with genetic testing
- Targeted therapies based on the genetic profile

The right patient, the right treatment, at the right time to maximize efficacy and reduce side effects.

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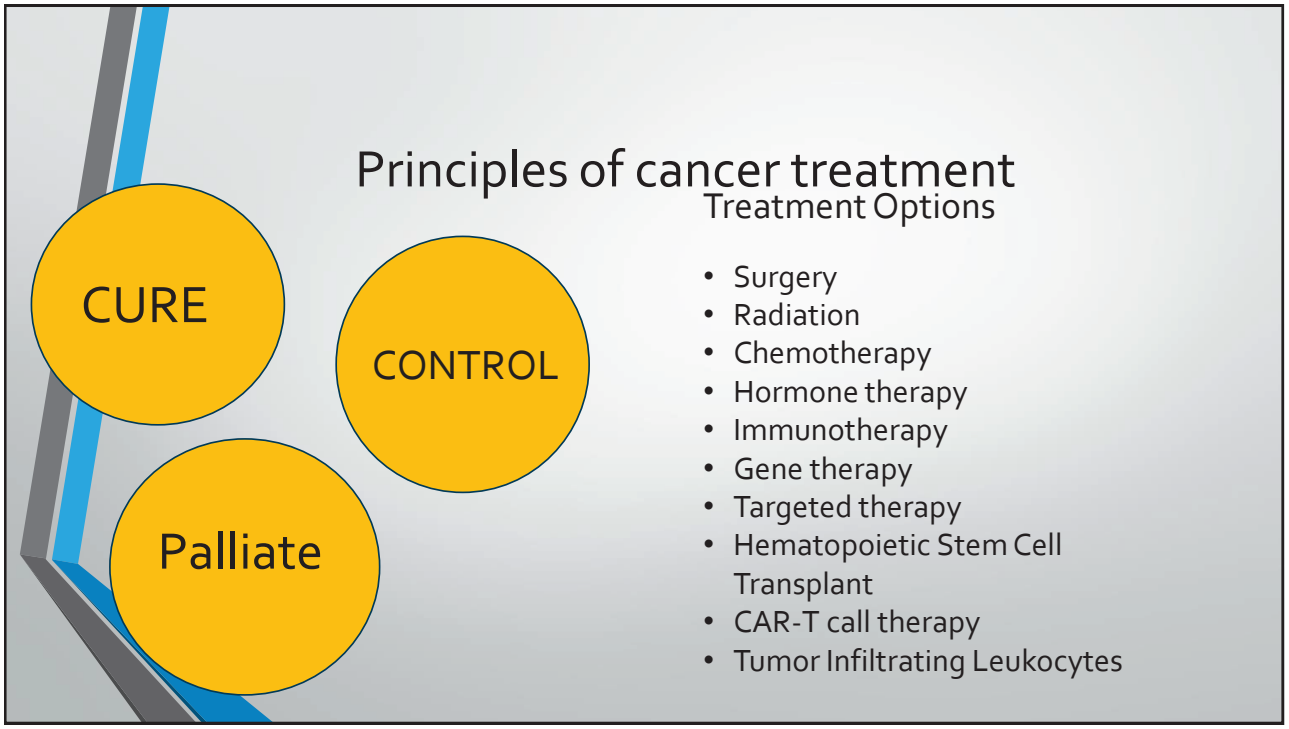
Principles of cancer treatment
CURE
CONTROL
Palliate
Treatment Options
• Surgery
• Radiation
• Chemotherapy
• Hormone therapy
• Immunotherapy
• Gene therapy
• Targeted therapy
• Hematopoietic Stem Cell Transplant
• CAR-T call therapy
• Tumor Infiltrating Leukocytes

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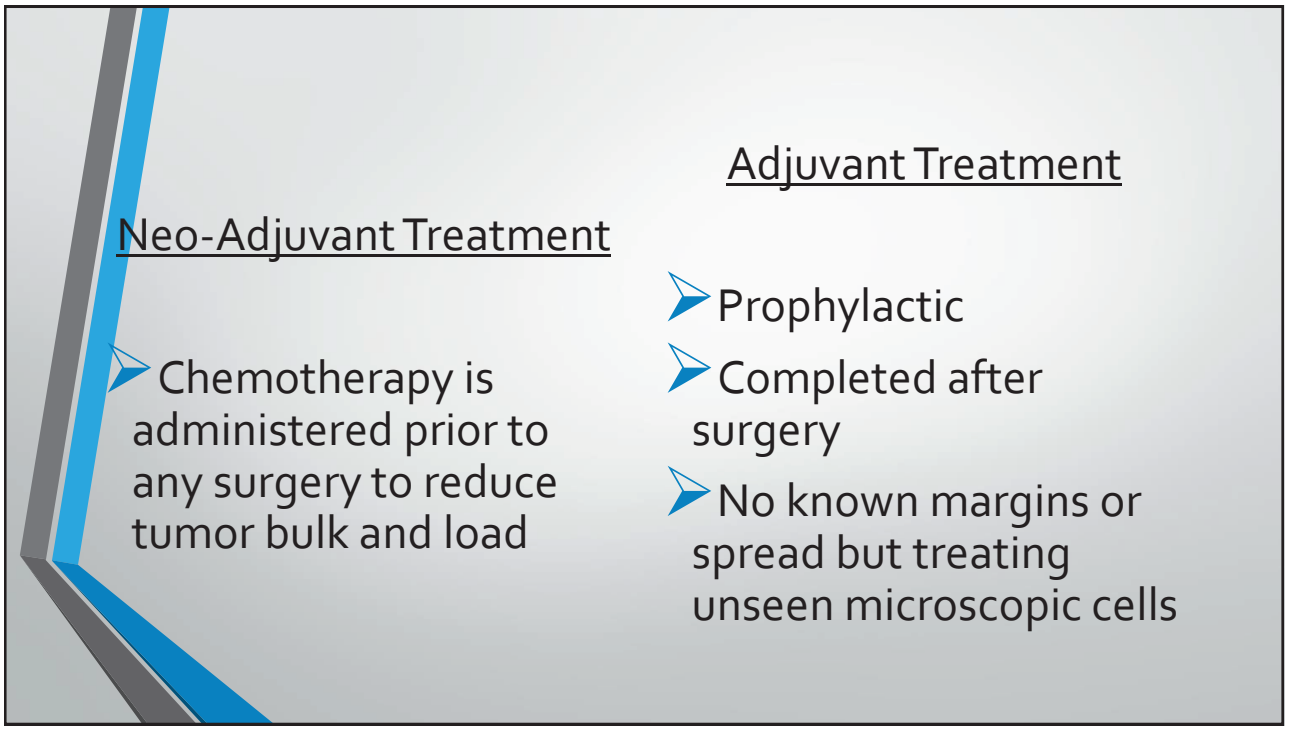
Neo-Adjuvant Treatment
Chemotherapy is administered prior to any surgery to reduce tumor bulk and load
Adjuvant Treatment
Prophylactic
Completed after surgery
No known margins or spread but treating unseen microscopic cells

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American Cancer Society. *Cancer Facts & Figures 2025*. Atlanta: American Cancer Society; 2025.

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# HISTORY OF CANCER AND TREATMENT MODALITIES

Mary E. Kern, MSN, RN, OCN, CHSE
Professional Development Specialist AHNCI
Mary.KERN@ahn.org
* No disclosures*

1

The History of Cancer Therapy, an Interactive Timeline

2

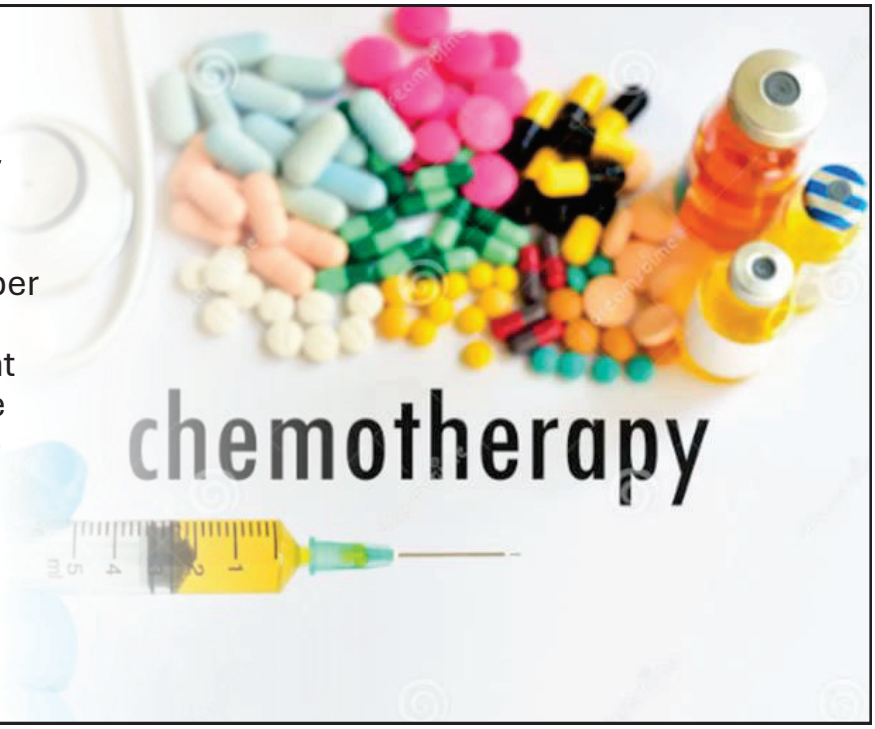
## What is chemotherapy?

- Cytotoxic drugs that interfere with a cancer cell's ability to grow and divide.
- Targets rapidly dividing cells
- Cannot differentiate between healthy cells and cancer cells
- Leads to side effects

3

## Goal of chemotherapy

To reduce the number of cells to a small enough number that can theoretically be taken care of by the immune system.

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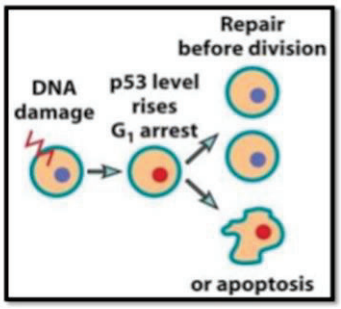
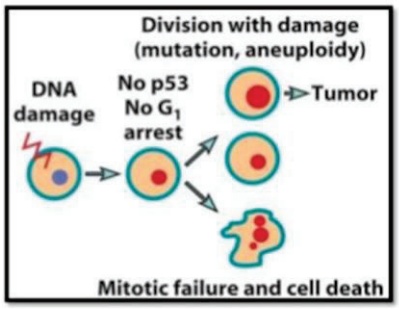
# Chemotherapy drugs are categorized based on how they affect the way cells reproduce


5

## Cell Cycle And Cancer



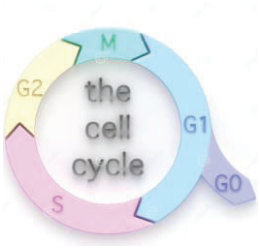




https://www.slideshare.net/ileshkucha/cell-cycle-and-tumor-kinetics

6

# Cell Cycle

- G0 (Gap 0): The resting phase
- G1 (Gap1): The cell is growing and carrying out its normal duties
- S (Synthesis): The cell replicates its DNA
- G2 (Gap 2): the cell prepares for division, grows, checks for errors
- M (Mitosis) The cell divides into 2 daughter cells
  - Prophase
  - Metaphase
  - Anaphase
  - Telephase

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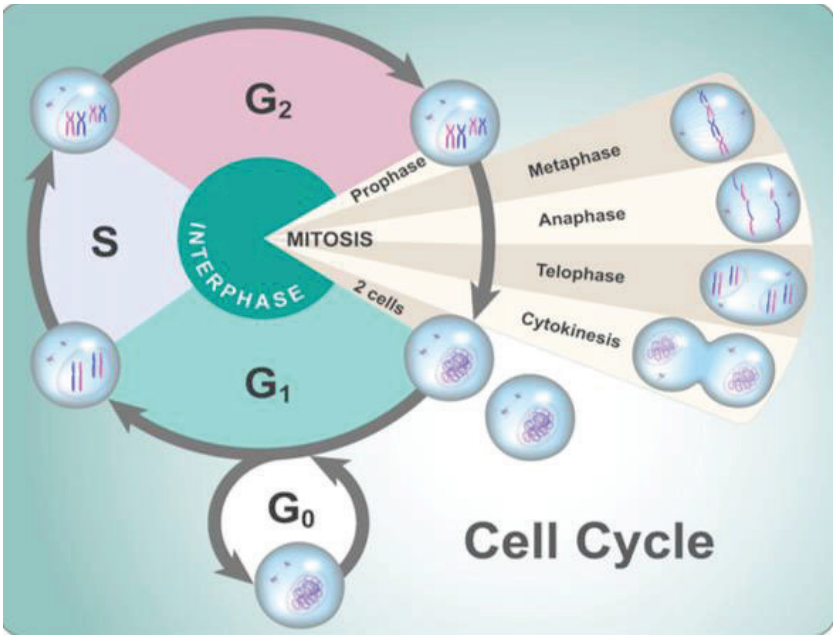



8

## G0 (Gap 0): Resting

- Not linear to the process of cell division
- Cells can enter and exit the resting stage at any point
- Because cells are not dividing, they are considered protected from exposure to most chemotherapeutic agents

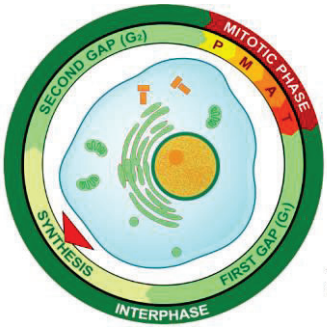


## G1 (Gap 1)

- Cells are growing and functioning in their specific capacity
- Preparing for DNA replication
- Cellular contents (except chromosomes) are duplicated
- 1st check point for errors

## Synthesis (S)

- Cellular blueprints are made
- Exact duplication occurs
- Highly regulated process
- Errors have serious consequences at this stage
- Mirrors DNA replication (chromosomes are replicated)




*Cell duplicates its DNA

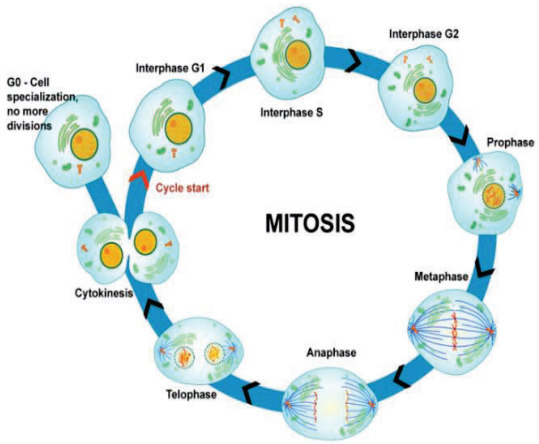


## Gap 2 (G2)

- The cell meticulously checks for errors in the replicated DNA
- If errors are detected, the process ceases allowing for repair or apoptosis
- The final quality control

# Mitosis (M)

- Divided into 4 phases (Prophase, Metaphase, Anaphase, Telephase
- Cell divides into 2 identical daughter cells
- Both daughter cells enter resting phase
- Cycle begins again

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# Check Points

G1 (Restriction point)
- Most critical
- Cell size
- Nutrient availability
- Growth factors
- DNA damage

G2
- DNA Replication complete?
- DNA damage?
- Cell size

M (Spindle Checkpoint)
- Chromosome alignment
- Spindle fiber attachment

All these things must occur to maintain genome stability

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# Cell-Cycle Regulatory Components

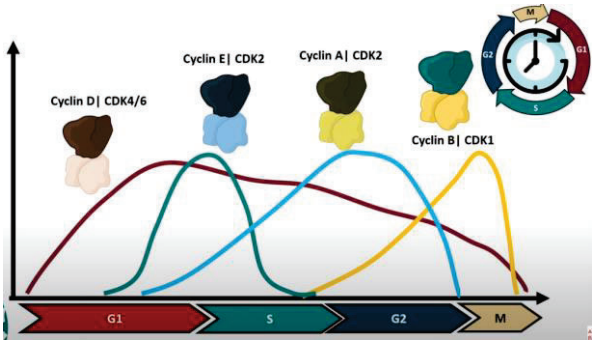
## Cyclins

Regulatory proteins that act like "project managers" showing up at specific times in the cell cycle to do specific things

**Cyclin-CDK complex** is essentially a project manager with the appropriate tools

## Cyclin-dependent kinases (CDK)

- Always present in the cells but inactive unless bound to a cyclin
- Complex that drives the cell



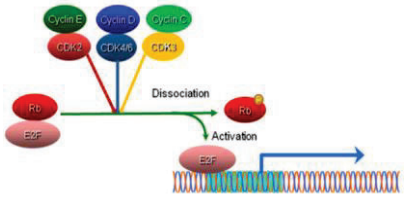

Cyclin and CDK in cell cycle progression | How Cyclin CDK works?. YouTube. (n.d.). https://youtu.be/Lxylidj-3Ts?si=T-iL4dAaoEBXBwaJ



# Cyclin-CDK complexes

### Normal cell

- Regulate cell cycle progression
- Control cell-cycle checkpoints




### Cancer cell

- Dysregulation
- Leads to mutations
- Bypassing checkpoints
- Creating genomic instability
- Evading apoptosis

## Cell-cycle specific agents (PAM)

- Primarily affect cells actively dividing during a particular phase
- More effective against rapidly proliferating cells
- Can have SOME effect on cells outside of their target phase
- Treatment in divided doses or continuous infusions
- Important to stay on regular schedule

### Plant Alkaloids

- Derived from plants
- Interfere with cell division

### Antimetabolites

- Mimic naturally occurring metabolites
- Leads to faulty DNA, RNA replication (S phase)

### Misc, Agents

- Actions unknown or re-classified

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## Cell-cycle non-specific = (AAN)

- Affects cells in all phases
- More effective on slow growing cells
- Often used in combination with cell-cycle specific agents
- Associated with greater myelosuppression
- Cumulative toxicities

**Alkylating Agents**

- Targets both dividing and resting cells
- Causes abnormal linking of DNA
- Inaccurate replication and cellular death

**Antitumor Antibiotics**

- Bind/react with DNA and inhibit RNA synthesis

**Nitrosourea Agents**

- Crosses the blood/brain barrier

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## Cell Cycle Specific

- Work in specific cell-cycle phase
- Most effective in divided doses or continuous infusions with short intervals in between cycles
- Acts on rapidly growing/dividing cells
- Important to stay on schedule
- Impacts all rapidly growing cells i.e. hair, GI
- Earlier myelosuppression (7-day onset)

## Cell Cycle Non-specific

- Works on all phases including G0 (resting phase)
- More effective on slower growing cells
- Cell kill is directly proportional to the amount of drug administered
- Very dose dependent with acceptable deferment to give the highest dose possible
- More organ toxic
- Later and sometimes more severe myelosuppression (10 days onset)

**Often used in combination**

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# Rationale for Combination Chemotherapy

- Synergistic effect (one may increase permeability of the cell making it susceptible to another drug)
- Different mechanisms of action
- Reduce drug resistance
- Improved disease control
- Reduced overall toxicities at lower doses


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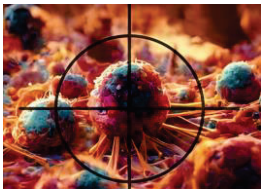
# Chemotherapy OR Targeted Therapies

## Cytotoxic Agents

- Kills all rapidly dividing cells
- Side effects reflect those areas (N/V/D, alopecia, fatigue, risk of infection, anemia)
- Dosages based on BSA


## Target Therapies

- Designed to attack specific molecules &/or pathways that are involved in tumor growth
- Fewer, less severe side effects
- Dosed in mg and m2



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# Targeted Therapy Pathways (Anti-Cancer Therapy)

- Anaplastic lymphoma kinase (ALK)
- BCR-ABL
- BRAF V600E and MEK inhibitors
- B-cell receptor pathway inhibitors
- CDK inhibitors
- Epidermal Growth Factor Receptor (EGFR) inhibitors
- Epigenetic DNA hypomethylation and histone modification
- Fm-like tyrosine kinase 3 (FLT3) inhibitors
- Hedgehog pathway inhibitors
- Janus kinase-2 (JAK2) inhibitors
- Mammalian target of rapamycin (mTOR)
- Mediators of apoptosis Bcl-2
- Multiple kinase pathways (MKIs)
- Poly (ADP-ribose)polymerase (PARP) inhibitors
- Proteasome inhibitors
- Protein kinase inhibitors
- Tyrosine kinase inhibitors (TKIs)
- Vascular endothelial growth factor (VEGF)/Anti-angiogenesis

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# Hormonal Therapies

## Breast Cancer

- Selective Estrogen Receptor Modulators (SERMS)-tamoxifen
- Aromatase Inhibitors (Ais)-Arimidex, Letrozole, Aromasin
- Estrogen receptors antagonists-Faslodex

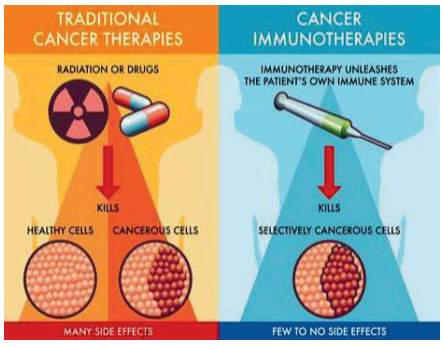
## Prostate Cancer

- Anti-androgens-Casodex, Xtandi, eulexin, nilandron
- Androgens-testosterone
- CYP17 inhibitors-Zytiga
- LHRH agonists-zoladex, Lupron, trelstar



# Immunotherapy

- Cytokines
- Immunomodulators
- Monoclonal Antibodies (MABs)
- Chimeric Antigen Receptor-T (CAR-T)
- Immunotherapy
  - Checkpoint inhibiotrs
    - CTLA-4
    - PD-1 & PD-L1



# Dose-Dense Chemotherapy

- Researched in Breast and Lymphoma
- Allows delivery of standard doses over shorter intervals
- Shortened cycle: 14 days instead of 21
- Developed as a means of eradicating micro-metastases and drug resistance
- Stricter patient selection
- Supportive measures are crucial to success

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| **Hazard Precautions** | **Attention** **Read and Follow all Instructions** |
|---|---|

**See the Nurse Before Entering Room**

1. If you are **pregnant, suspect you are pregnant, breast feeding, or trying to conceive** please stop at nurse's station for further instructions.
2. Double glove with **nitrile/protective gloves** when **handling body fluids or when cleaning room.**
3. Wear impervious gowns and double nitrile gloves when handling linens soiled with body fluids.
4. Wear masks and goggles when there is a risk for splashing.
5. Use disposable underpads whenever possible for incontinence.
6. Provide male patient with urinal with tight fitting lid.
7. Flush toilet twice after using to dispose of body fluids/excreta
8. Place all contaminated linens in yellow ACT linen bags
9. Discard diapers and pads in yellow ACT container.
10. For incontinent patients, apply skin barrier to area to avoid chemical burns. Keep clean and change frequently.

Reviewed and Revised December 2023 –AHNCI ACT Council & Hema/Onc P&T Subcommittee

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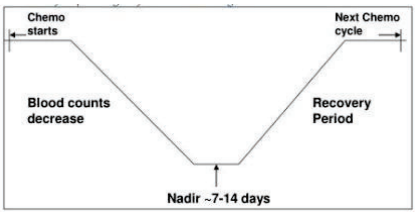
## Toxicities associated with rapidly dividing cells

Myelosuppression
- Depression of bone marrow
- Expressed as Nadir

Emetogenicity = Level 1-5
Level 1 = <10% incidence
Level 2 = 10-30%
Level 3 = 30-60%
Level 4 = 60-90%
Level 5 = >90%

**Nadir**
- Lowest point of bone marrow suppression
- Typically, 7-14 days from the start of treatment






## Measure of Tumor Response

- **Complete Response (CR)** = undetectable disease
- **Partial Response** = 30% or more significant reduction
- **Stable Disease** = unchanged/no growth or reduction
- **Progressive Disease** = advancing disease 20% or more in the presence of therapy
- **Relapse** = after complete response, new tumor or original tumor reappears
- **MRD** (measurable residual disease & minimal residual disease) = used in hematological malignancies for amount of cancer cells present after treatment

# Key Factors Affecting Response

- Age and overall comorbidities
- Performance status including lifestyle factors
- Tumor biology including type, genetics, burden and metastases
- Hormone receptor status
- Treatment factors including drug, dose, combination therapies
- **ADHERENCE**

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# Measurement Scales and Criteria

- Performance Scale
  - ECOG (0-5)- the higher the score the worse the performance status with 5 being deceased
  - Karnofsy (100%-0%)- the lower the score, the worse the performance status with 0 being deceased
- Tumor assessment
  - Scans
  - Assays
  - Tumor markers


- Survival data
  - **OS**-Overall survival
  - **PFS**-Progression-Free survival
  - **DSS**-Disease-Specific survival
  - **RFS-** Relapse-Free survival

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Questions???

# Understanding Clinical Trials

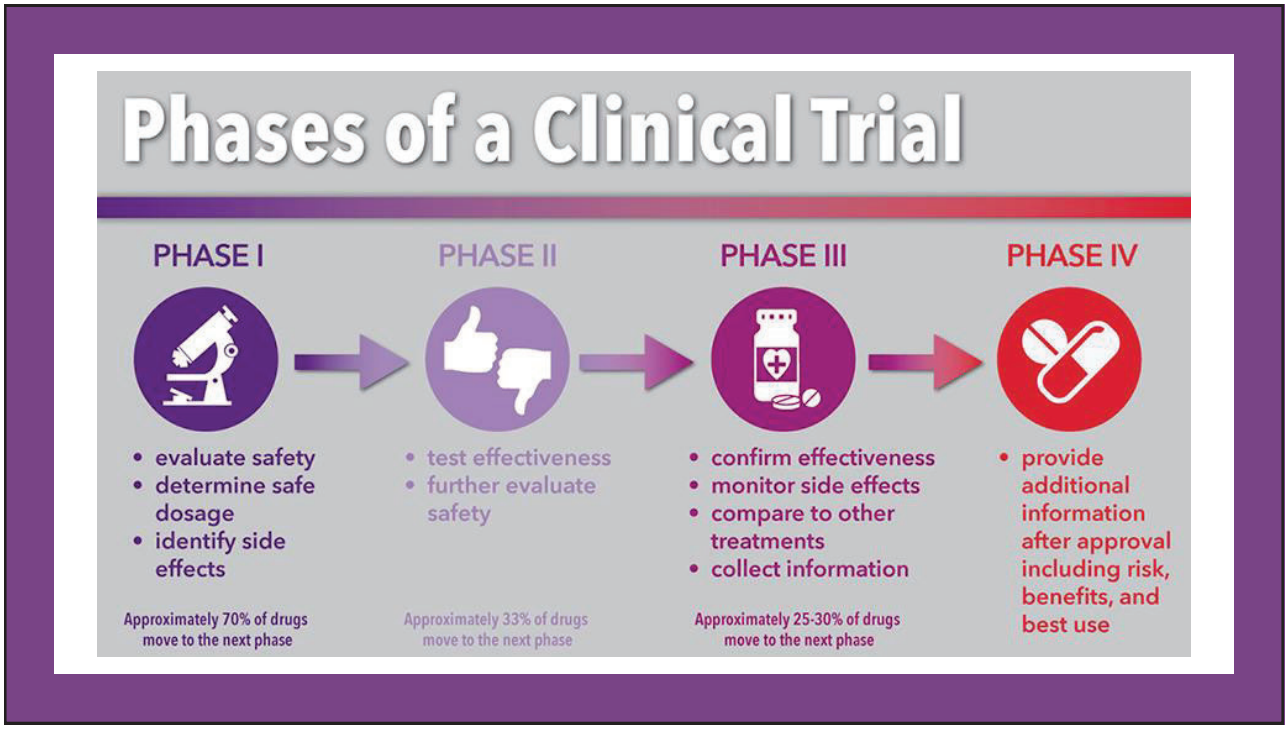
Mary E. Kern, MSN, RN, OCN, CHSE
Professional Development Specialist AHNCI
mary.KERN@ahn.org
* No Disclosures*

1

## Testing New Treatments Safely

- Clinical trials are research studies that test new medical approaches (drugs, devices, therapies).
- Goal: Determine if a new treatment is safe and effective.
- Involve people (participants) with a specific medical condition.
- Conducted in phases to carefully assess safety and efficacy.

2

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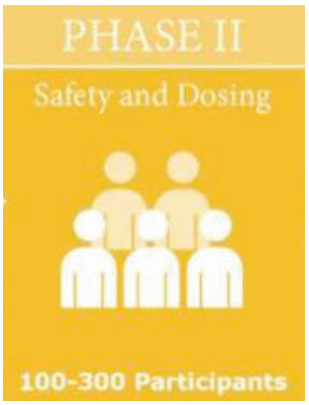
## Phase 1: Safety First


- Small number of healthy volunteers or patients.
- Primary goal: Assess safety, identify side effects, determine safe dosage.
- Focus is on pharmacokinetics (how the body processes the drug).
- Does not evaluate effectiveness.

4

## Phase 2: Does it Work?

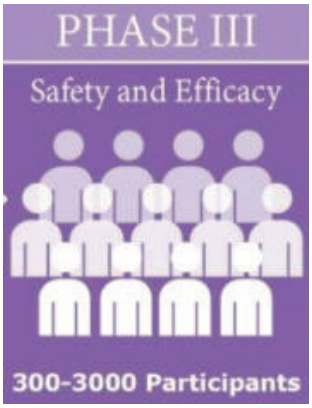
- Larger group of patients with the target condition.
- Primary goal: Evaluate effectiveness and further assess safety.
- Start to look at optimal dosage.
- Refines treatment approach based on Phase 1 results.






## Phase 3: Large-Scale Benefits

- Large number of patients with the target condition, often at multiple sites.
- Primary goal: Confirm effectiveness, monitor side effects, compared to standard treatments.
- Provides strong evidence of the treatment's benefits and risks.




# Phase 4: Long-Term Effects

- Post-market surveillance after treatment approval.
- Monitors long-term effects, rare side effects, and real-world effectiveness.
- Identifies any unexpected problems.
- May include additional studies to explore further benefits or uses.

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# Supporting Clinical Trial Participants

- Patient education and consent process.
- Monitoring for side effects and adverse events.
- Accurate data collection and reporting.
- Maintaining patient confidentiality.
- Supporting patient well-being throughout the trial.

8

| Feature | Trade Name | Generic Drug | Biosimilar Drug |
|---|---|---|---|
| **Name** | Proprietary and often complex | May vary, but must demonstrate bioequivalence | Complex, similar but not identical to the reference product |
| **Development** | Extensive research & development; patented | No new research & development; relies on existing data | Extensive research & development; demonstrates biosimilarity to a reference product |
| **Approval Process** | Rigorous clinical trials demonstrating safety and efficacy | Abbreviated New Drug Application (ANDA) showing bioequivalence to the trade drug | Biologics License Application (BLA) demonstrating biosimilarity to a reference product |
| **Patent Protection** | Yes, typically for a period of 20 years from the date of patent application | No patent protection | No patent protection on the reference product, but patents may exist on the biosimilar itself |
| **Pricing** | High, reflects R&D costs and marketing | Significantly lower than trade drugs | Usually lower than the reference product, but typically higher than small molecule generics |
| **Active Ingredient** | Same as generic and biosimilar | Identical to the trade drug (chemically) | Very similar but not identical to the reference product (biologically) |
| **Interchangeability** | Not interchangeable with generics or biosimilars (unless specifically approved) | Generally interchangeable with other generics of the same drug | Interchangeability is determined on a case-by-case basis by the FDA, may or may not be interchangeable with the reference product. |

9

QUESTIONS???

10

# Myelosuppression and Growth Factors

Danielle Roman, PharmD, BCOP
Manager, Oncology Clinical Pharmacy
danielle.roman@ahn.org

1

# Objectives

- Formulate a comprehensive plan of care, including side effects and toxicities for a patient receiving anticancer therapy – (myelosuppression and growth factors)

No Disclosure

2

# Myelosuppression

Reduction in bone marrow function that results in reduced production of red blood cells (RBC), white blood cells (WBC), and platelets

↓ RBC = anemia

↓ WBC = neutropenia

↓ platelets = thrombocytopenia

3

# Chemotherapy-Induced Myelosuppression

- Most common dose-limiting toxicity
- Nadir is the lowest point of blood count fall to after a cycle of chemotherapy

4

# ⬇ WBC = Neutropenia

- WBC normal range = 4.8 – 10.8 x $10^3/mm^3$
- Neutrophils are 1st line of body's defense against bacterial infection
- Monitor absolute neutrophil count (ANC)
  - Normally 50 – 60% of total WBC
- Severe neutropenia
  - ANC < 500 x$10^3/mm^3$ or < 1000 with predicted decline to < 500 x$10^3/mm^3$ within 48 hours
  - Rate of decline and duration of neutropenia are critical factors

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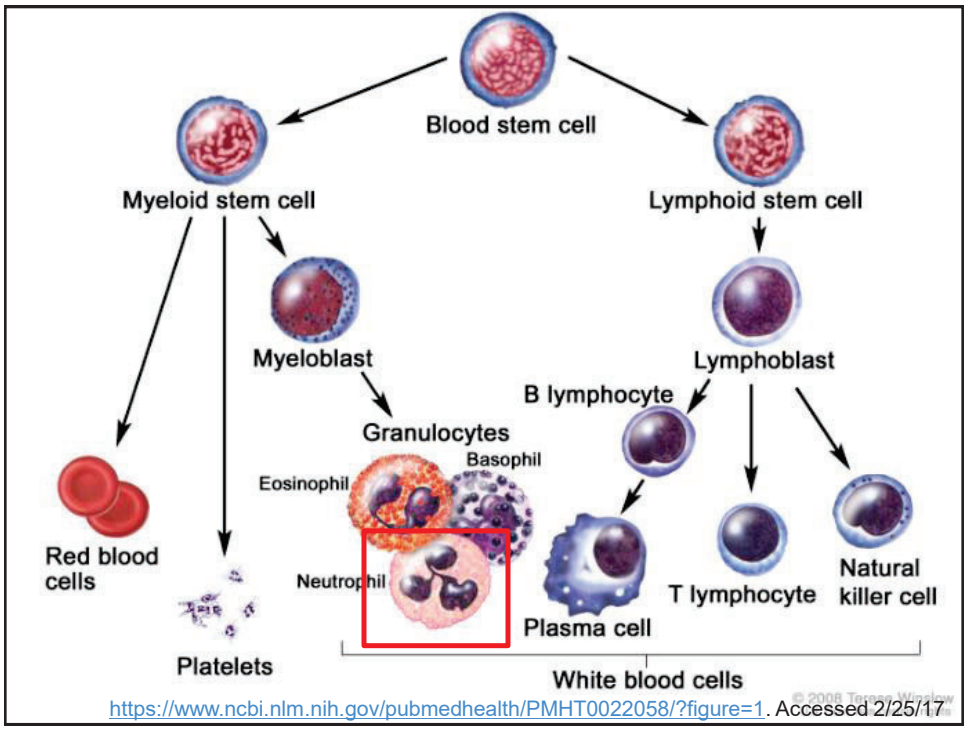
# Febrile Neutropenia

- Single temperature ≥ 38.3° C (101 F) orally or ≥ 38° C (100.4 F) over 1 hour AND
- Neutropenia: < 500 neutrophils/mcL or < 1000 neutropils/mcL and a predicted decline to ≤ 500 over the next 48 hours

NCCN Guidelines. Hematopoietic Growth Factors. Version 3.2026.

6




https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0022058/?figure=1. Accessed 2/25/17



# Calculating ANC

$$ANC = \frac{(\%\ \text{neutrophils} + \%\ \text{bands})}{100} \times WBC$$

Infection Risk:

| | |
|---|---|
| ANC = 1500 – 2000 | Not significant |
| ANC = 1000 – 1500 | Minimal |
| ANC = 500 – 1000 | Moderate |
| ANC < 500 | Severe |

# Reporting of Neutrophils

- Can be reported as mature and immature neutrophils
  - Mature neutophils are also known as neutrophils, segmented neutrophils, polys, segs, granulocytes
  - Immature neutrophils are also known as banded neutrophils, bands, segmented bands
- Must add mature and immature neutrophils to get total neutrophils



# Example: Calculating ANC

Total WBC count = 1800 (1.8 x $10^3/mm^3$)

Polys = 45%

Bands = 5%

Add polys and bands: 45% + 5% = 50%

Convert percent to decimal by dividing by 100

50/100 = 0.5

Multiple total WBC count and (polys+ bands)

1800 x 0.5 = 900

# Patient Case: MC

MC is a 73-year-old female who is scheduled to receive her 1st cycle of paclitaxel and carboplatin for metastatic ovarian cancer.

Labs pre-chemotherapy:

WBC = 4.2 x $10^3/mm^3$

Neutrophils (aka polys)= 42%

Bands= 5%

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# Risk Factors for Neutropenia: Patient Factors

- ⬆ age
- Tumor invasion of bone marrow
- Prior treatment with chemo, radiation, or multimodal therapy
- Diseases (ex/ aplastic anemia)
- Interruption of integrity of normal barriers

Itano and Taoka. Core Currriculum for Oncology Nursing.1998

12

# Risk Factors for Neutropenia: Treatment-Related Factors

- Chemotherapy
  - Destruction of rapidly dividing hematopoietic cells
- Radiation
  - Treatment fields that receive ≥ 20 Gy that involve the major bone marrow production sites
- Steroids
  - Typically don't cause neutropenia but prevent migration of neutrophils to the bacteria and the process of phagocytosis

Itano and Taoka. Core Currriculum for Oncology Nursing.1998

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# Assessment of Neutropenia

- Patient history
  - Previous cancer therapy
  - Current antibiotics
  - Current use of WBC growth factors
- Physical exam
  - Access device for drainage, erythema, tenderness
  - Vital signs – fever may be only response to infection
  - Oral cavity
  - Abnormal breath sounds

Itano and Taoka. Core Currriculum for Oncology Nursing.1998

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## Monitoring and Education

- Monitoring: CBC/differential, ANC
  temperature, signs and symptoms of infection
- Education: awareness of nadir, temperature
  signs of infection,
  avoid large crowds,
  ill people/children,
  use good hygiene,
  hand-washing techniques,
  avoid meds that can mask fever

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## Clinical Consequences of Neutropenia

- ⬆ risk of infection
- Delay in therapy
  - Must have adequate neutrophils prior to treatment
  - Most providers require > 1000 – 1500 cells/$mm^3$ prior to retreatment
- Dose reduction

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## Management of Neutropenia

- Dose reduction of chemotherapy
- Delay chemotherapy until count recovery
- Prophylaxis with WBC growth factors

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## WBC Growth Factors

- Also known as granulocyte colony stimulating factors (G-CSFs) or myeloid growth factors
- Promote proliferation and differentiation of hematopoietic progenitor cells along multiple pathways
- Use
  - Shorten duration and depth of neutropenia
  - Reduce incidence of febrile neutropenia (FN), length of hospitalization
  - Decrease infection-related mortality

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# G-CSFs

| Short Acting |
| --- |
| • Filgrastim (Neupogen)<br>• Tbo-filgrastim (Granix)<br>• Filgrastim-sndz (Zarxio)*<br>• Filgrastim-aafi (Nivestym)*<br>• Filgrastim-ayow (Releuko)* AHN inpatient preferred product<br>• Sargramostim (Leukine) (GM-CSF) |
| **Long-Acting** |
| • Pegfilgrastim (Neulasta, Neulasta Onpro)<br>• Pegfilgrastim-jmdb (Fulphila)* AHN inpatient preferred product (with restrictions)<br>• Pegfilgrastim-cbqv (Udenyca)*<br>• Pegfilgrastim-apgf (Nyvepria)*<br>• Pegfilgrastim-fpgk (Stimufend)*<br>• Pegfilgrastim-bmez (Ziextenzo)*<br>• Eflapegrastim-xnst (Rolvedon)<br>• Efbemalenograstim alfa-vuxw (Ryzneuta) |

* biosimilar

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# Filgrastim and Biosimilars

- Short acting
- Dosing
  - Myelosuppressive chemo: 5 mcg/kg daily until post-nadir ANC recovery (typically recommend 10 – 14 days)
  - Higher doses may be used in bone marrow transplant and mobilization
- Route: SQ (recommended route) or IV
- If used as prophylaxis, start 24 – 96 hours after completion of chemo
- Do not administer in period 24 hours before or after cytotoxic chemo
- Usually round dose to nearest 300 mcg or 480 mcg

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# Pegfilgrastim and Biosimilars

- Long acting
- Dosing: 6 mg x 1, given 24 – 96 hours after completion of myelosuppressive chemo
- Route: SQ
- Should be at least 12 days between dose of pegfilgastim and next dose of chemo
  - Do not use with weekly chemo
- Neutrophil – mediated clearance that depends on ANC
- **Only approved for use as prophylaxis**
- May impact PET/CT assessment and interpretation
  - Increases bone marrow and spleen FDG uptake



# Neulasta® Onpro® Kit

- Includes prefilled syringe (6 mg) for use with on-body injector (SQ)
- Applied to back of upper arm or abdomen on the same day as chemotherapy
  - Use back of arm only if there is caregiver available to monitor the status
- Delivers dose 27 hours after placement
- Dose delivered over 45 minutes
- Keep device at least 4 inches away from electrical equipment (cell phones, microwaves)
- Should not be worn during radiation or MRI, CT scan
- If device fails or leaks, administer the regular pegfilgrastim injection ASAP

https://www.neulasta.com/stay-at-home-with-neulasta-onpro

## Another Long-Acting G-CSF: eflapegrastim-xnst (Rolvedon)

- Dosing: 13.2 mg once per chemo cycle
  - Pre-filled syringe
- Route: SQ
- Administer ~24 hours after cytotoxic chemo
- Do not administer within 14 days before to 24 hours after chemo

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## Patient Case: DS

Gemcitabine 1000 mg/$m^2$ on day 1 and 8

Docetaxel 75 mg/$m^2$ on day 8

Every 21 days

Her insurance requires use of a pegfilgrastim biosimilar product (not an on body).

When would you schedule her pegfilgrastim injection in relationship to her chemotherapy doses?

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# G-CSF Adverse Effects

- Bone pain – mainly long bones
- Musculoskeletal pain
- Fever
- Injection site reactions
- Peripheral edema
- Rash
- Splenic rupture (long-term administration)

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# G-CSF– Induced Bone Pain

- Reported incidence varies
  - ~20% reported in clinical trials
  - 59% reported in clinical practice
  - Higher incidence in younger patients and patients receiving taxanes
- Proposed mechanism
  - Bone marrow expansion
  - Stimulation of peripheral nerve fibers
  - Cause release of inflammatory cytokines
  - Direct effect on bone metabolism
    - Activate osteoclasts and osteoblasts to cause break down of bone

Lambertini et al. Crit Rev Oncol Hematol 2014;89:112-28.

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# Treatment Options for Bone Pain

- Data is limited
- 1st line treatment
  - Acetaminophen
  - NSAIDS

  } Caution: may suppress fever

    - Naproxen 500 mg BID (or similar NSAID) x 5 – 7 days after G-CSF administration
- 2nd line treatment
  - Opioids
  - Antihistamines
    - Loratadine 10 mg daily (or similar antihistamine) x 5 – 7 days after G-CSF administration
  - G-CSF dose reduction (typically not recommended)

Lambertini et al. Crit Rev Oncol Hematol 2014;89:112-28

NCCN Guidelines. Hematopoietic Growth Factors. Version 3.2026.

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# WHEN TO GIVE G-CSF?

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# G-CSF Uses

- Prophylaxis
  - Options: filgrastim, tbo-filgrastim, filgrastim-sndz, or pegfilgrastim
  - Primary and secondary prophylaxis
  - Start administering 24 – 96 hours post chemo
    - Less benefit if start > 96 hours
  - Give filgrastim and sargramostim daily until ANC recovery (usually approximately 10 days)
- Therapeutic use
  - Options: filgrastim, tbo-filgrastim, filgrastim-sndz, or sargramostim (NOT pegfilgrastim)
  - Continue until ANC recovery

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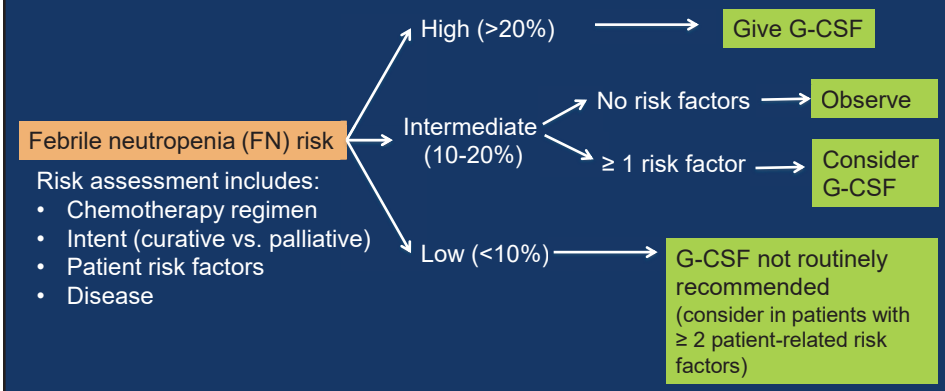
# Primary Prophylaxis




Patient-related risk factors:
- Prior chemo or radiation
- Persistent neutropenia
- Bone marrow involvement by tumor
- Recent surgery and/or open wound
- Liver dysfunction (bilirubin >2)
- Renal dysfunction (CrCl < 50)
- Age >65 years receiving full chemo dose
- HIV infection (low CD4 count)
- Poor performance status

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# FN Risk - Regimen Examples

- High risk (>20%)
  - Dose-dense AC → dose-dense paclitaxel (Breast)
  - TC (docetaxel and cyclophosphamide) (Breast)
  - Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine (Hodgkin lymphoma)
  - Dose-adjusted EPOCH (NHL)
  - HyperCVAD (NHL)
  - Topotecan (SCLC)
- Intermediate risk (10 – 20%)
  - Paclitaxel every 21 days (breast)
  - FOLFIRINOX (colorectal and pancreatic)
  - CHOP (NHL)
  - Carboplatin/etoposide (SCLC)
  - Sacituzumab govitecan (breast)

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# Secondary Prophylaxis

Evaluation prior to 2nd and subsequent cycles:

Febrile Neutropenia or Dose-limiting neutropenic event

- Prior use of G-CSF → Consider chemo dose reduction or switch regimen
- No prior G-CSF → Consider G-CSF

Dose-limiting neutropenic event = nadir count or day of treatment count that could otherwise impact planned dose of chemo

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# Revisit Patient Case: MC

MC is a 73-year-old female who is scheduled to receive her 1st cycle of paclitaxel and carboplatin for metastatic ovarian cancer.

Risk of febrile neutropenia with this chemotherapy is 10 – 20%

Labs pre-chemotherapy:

WBC = 4.2 x $10^3/mm^3$

Neutrophils (or segs) = 42%

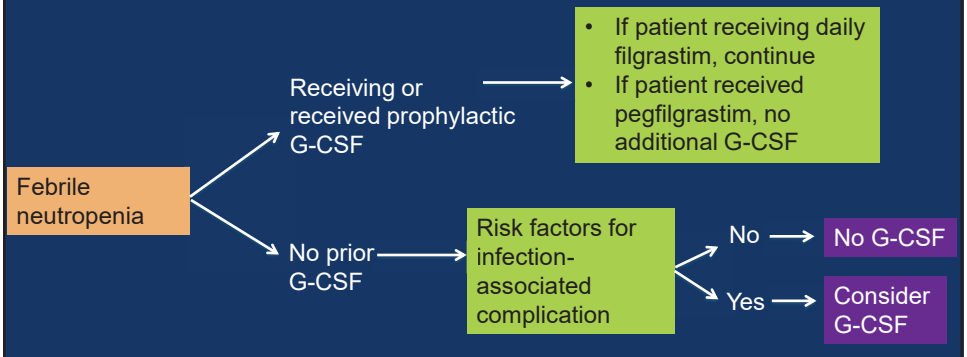
Bands= 5%



# Patient Case: MC

- Should MC receive primary prophylaxis with pegfilgrastim?
- What are important patient counseling points regarding neutropenia?

# Therapeutic Use




- Continue therapeutic growth factor until post-nadir ANC recovery to normal or near-normal

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# Risk factor for Infection-Related Complication

- Sepsis syndrome
- Age >65 years
- Severe neutropenia (ANC < 100 or anticipated duration > 10 days)
- Pneumonia or other clinically documented infection
- Invasive fungal infection
- Hospitalization at the time of fever
- Prior episode of FN

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## Considerations with G-CSF in AML and MDS

- G-CSF may increase risk of AML and MDS
  - Increase risk of AML 0.41% and MDS 1.92%
- MDS
  - Not recommended for routine infection prophylaxis
  - Consider use in neutropenic patient with recurrent or resistant infections
  - G-CSF 1- 2 mcg/kg 1 – 2 x /week may be combined with an ESA for patients with ring sideroblasts (RS) ≥ 15% (or RS ≥ 5% with *SF3B1* mutation) and serum epoetin level ≤ 500 mU/mL if no response to luspatercept-aamt
- AML
  - Consider for post-remission therapy
  - Patients should be off G-CSF for at least 7 days before obtaining BM to document remission

NCCN Guidelines. Acute Myeloid Leukemia. V 3.2026
NCCN Guidelines. Myelodysplastic Syndromes. V.3.2026
NCCN Guidelines. Hematopoietic Growth Factors. Version 3.2026.

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## Patient Case: GB

GB is a 56-year-old male who received cycle 1 of R-CHOP for a diagnosis of diffuse-large B-cell lymphoma (DLBCL). He did not receive primary prophylaxis with growth factor since he did not have any high risk factors for febrile neutropenia.

Selected labs from Cycle 1 Day 15:

CBC: WBC 1.5 x $10^3$

segmented neutrophils: 25%

band neutrophils: 0%

GB denies any signs or symptoms of infection

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## Patient Case: GB

- What is his ANC on Cycle 1 Day 15?
- Is a WBC growth factor indicated on Cycle 1 Day 15?
- What changes do you recommend for Cycle 2 R-CHOP?

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## ⬇ RBC = Anemia

- Often measured by level of hemoglobin (Hgb)
- Normal Hgb 12 – 16 g/dL
- Evaluate anemia when Hgb ≤ 11 g/dL
- Occurs in 30 – 90% of patients receiving chemo
- ↑ risk of hypoxia, fatigue, CHF exacerbation

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## Anemia Toxicity Scale

| Grade | Severity | NCI/WHO Hgb scale (g/dL) |
|---|---|---|
| 0 | None | Normal* |
| 1 | Mild | 10 - normal |
| 2 | Moderate | 8 - < 10 |
| 3 | Severe | 6.5 - < 8 |
| 4 | Life-threatening | < 6.5 |

*14-18 g/dL (Men); 12-16 g/dL (Women)

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## Etiology of Anemia

- ↓ Erythropoietin stores
- ↓ vitamin b12, folic acid, iron
- Blood loss
- Hemolysis
- Infiltration of tumor into blood marrow
- Chemotherapy-induced
- Radiation-induced
- Combination of any of the above

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# Management of Anemia

- Treat underlying cause
- Observation
- Packed red blood cell (PRBC) transfusion
  - 1 unit PRBC = ↑ Hgb by 1 g/dL
- Erythropoetin stimulating agents (ESA)
  - Epoetin alfa *(Procrit)*
  - Darbepoetin alfa *(Aranesp)*
  - Epoetin alfa-epbx *(Retacrit)**

*Biosimilar



# ESAs

- Recombinant erythropoetin
- Indication: chemotherapy-induced anemia (also used for other indications such as chronic kidney disease, MDS)
- Discontinue following completion of chemo
- Adverse effects include hypertension, thrombosis, arthralgias, headache pure red cell aplasia
- Monitor Hgb, iron stores, blood pressure, signs/symptoms of thrombosis

# ESA Starting Dosing for Chemo-Induced Anemia

- Consider initiating when Hgb< 10 g/dL
- Epoetin alfa initial dosing
  - 150 units/kg SQ 3 times per week
  - 40,000 units SQ weekly
- Darbepoetin alfa initial dosing
  - 2.25 mcg/kg SQ weekly
  - 500 mcg SQ every 3 weeks

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# Dose Titration

- Titrate subsequent doses based on Hgb response
- If Hgb reaches level needed to avoid transfusions or increases by > 1 g/dL in any 2 week period, ⬇ dose by 25% for epoetin and 40% for darbepoetin
  - Refer to product insert for specific recommendations
- No response = Hgb ⬆ by < 1 g/dL in 1st 4 weeks of epoetin or 1st 6 weeks of darbepoetin
- Discontinue if no response within 8 weeks

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# ESA Black Box Warning

- ESAs may ↓ survival and/or ↑ tumor progression

  (breast, NSCLC, head & neck, lymphoid, cervical cancer trials)
- **Not to be used in curative setting**
- Only for cancer patients receiving concomitant chemotherapy
- Use lowest dose for gradual response

  Gradual = ↑ hgb of 1 g/dL/month

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# Risks and Benefits: ESAs versus RBC Transfusions

| ESAs | | RBC Transfusions | |
|---|---|---|---|
| Risks | • ↑ thrombotic events<br>• ↓ survival<br>• ↓ time to tumor progression | Risks | • Transfusion reactions<br>• Congestive heart failure<br>• Viral transmission<br>• Bacterial contamination<br>• Iron overload |
| Benefits | • Transfusion avoidance<br>• Gradual improvement in fatigue | Benefits | • Rapid ↑ Hgb and Hct<br>• Rapid improvement in fatigue |

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## ↓Platelets = thrombocytopenia

- Normal range 150,000 – 440,000 cells/$mm^3$
- Thrombocytopenia = platelet count < 100,000 cells/$mm^3$
- ↑ bleeding risk if platelets < 20,000 cells/$mm^3$
- Clinical presentation
  - Bleeding (gums, nosebleed, etc)
  - Bruising easily
  - Petechiae = red/purple spots caused by minor hemorrhage

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## Disease-related Risk Factors

- Immune thrombocytopenia purpura (ITP)
- Thrombotic thrombocytopenia purpura (TTP)
- Hypocoagulation disorders
- Tumor invasion of bone marrow

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## Treatment-related Risk Factors

- Chemotherapy
  - Usually see platelet drop after WBC drop
  - Recovery in 2 – 6 weeks
- Radiation therapy
- Medications (ex/ valproic acid, digoxin, heparin, phenytoin, sulfonamides)

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## Patient Considerations

- Avoid activities that increase bleeding (ex. contact sports)
- Avoid concomitant medications that affect platelet function
  - Aspirin, NSAIDs,
- Monitoring parameters
  - Platelet count ≥ 100,000 cells/$mm^3$ prior to chemo
  - Bleeding

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## Management of Thrombocytopenia

- Platelet transfusion (per American Association of Blood Banks guidelines)
  - Life span of transfused platelet is 2 – 6 days
- Chemo dose reduction or change in treatment regimen
- Pharmacotherapy
  - Romiplostim

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## Thrombopoetin (TPO) Agonists

- FDA approved for ITP in patients who had insufficient response to steroids, IVIG, or splenectomy
- Agents
  - Romiplostim *(Nplate)*
  - Eltrombopag *(Promacta)*

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# Romiplostim for ITP

- Use lowest dose necessary to achieve and maintain platelet count ≥ 50,000
- Starting dose = 1 mcg/kg subQ once weekly (based on actual body weight)
- Monitoring: CBC baseline and weekly until stable x 4 weeks then monthly
- Adverse reactions
  - Headache, fatigue, arthralgia, rebound thrombocyopenia, bone marrow reticulin formation, thromboembolism



# Romiplostim for CIT

- Purpose = maintain dose schedule and intensity of chemo
- No standard dose strategy
  - Consider weekly dosing starting at 2 – 4 mcg/kg
  - Increase by 1 – 2 mcg/kg/week to target platelet count of 100,000 – 150,000/mcL
  - Max dose = 10 mcg/kg/week

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# Eltrombopag

- Use: ITP
- Guidelines also recommend as a treatment option for thrombocytopenia post-hematopoietic cell transplant
- Use lowest dose necessary to maintain platelet count ≥ 50,000
- Starting dose = 50 mg PO once daily on empty stomach
  - Starting dose of 25 mg for patients with moderate-to-severe hepatic impairment and patients of East-Asian ethnicity
- Maximum dose = 75 mg PO once daily
- Monitor: CBC weekly until stable then monthly, LFTs every 2 weeks during dose titration then monthly
- Adverse events
  - Hepatotoxicity, rash, rebound thrombocytopenia, bone marrow reticulin formation, thromboembolism



# Patient Case: JK

JK is a 50-year-old female receiving gemcitabine + nab-paclitaxel on days 1 and 15 every 28 days for metastatic pancreatic cancer. Her platelets prior to cycle 3 day 1 are 40,000. All other labs WNL.

What do you recommend?

# Questions

Mary E. Kern, MSN, RN, OCN, CHSE

Professional Development Specialist AHNCI

mary.KERN@ahn.org

*No Disclosures*

# Cell-cycle Specific Agents

1

## Learning Outcomes

- Identify the importance of the cell cycle and cellular kinetics as they relate to the various anticancer therapies
- Explain the mechanism of action for each of the major drug classifications. – (cell cycle specific agents - plant alkaloids, antimetabolites, miscellaneous agents)

2

# Cell-cycle specific agents (PAM)

| |
|---|
| Primarily affect cells actively dividing during a particular phase |
| More effective against rapidly proliferating cells |
| Can have SOME effect on cells outside of their target phase |
| Treatment in divided doses or continuous infusions |
| Important to stay on regular schedule |

## Plant Alkaloids
- Derived from plants
- Interfere with cell division

## Antimetabolites
- Mimic naturally occurring metabolites
- Leads to faulty DNA, RNA replication (S phase)

## Misc, Agents
- Actions unknown or re-classified

3

# Plant Alkaloids- Cellular saboteurs

**Vinca Alkaloids**: Periwinkle Plant
- Vincristine (Oncovin)
- Vinblastine (Velban)
- Vinorelbine (Navelbine)
- Vincristine Liposome (Marquibo)

**Epipodophyllotoxins**: Mandrake Plant
- Etoposide (Vespid) VP-16
- Teniposide (Vumon) VM-26

**Taxanes**: Yew Tree
- Paclitaxel (Taxol)
- Docetaxel (Taxotere)
- Paclitaxel protein-bound particles/albumin-bound (Abraxane)
- Cabazitaxel (Jevtana)

**Camptothecins** Happy Tree
- Topotecan (Hycamtin)
- Irinotecan (Camtosar/CPT-11)

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## Plant Alkaloids-Major dose limiting toxicities

- Neuropathy
- Numbness/tingling
- Paresthesia
- Ataxia
- Autonomic nervous system dysfunction
- Orthostasis
- Constipation
- Diminished reflexes

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## Vinca Alkaloid-**Vincristine** (Oncovin)

**Side Effects:**

- Neurotoxicity
- Vesicant/Extravasation
- Myelosupression
- Constipation

- **Indications**:
  - ALL
  - Hodgkin's and Non-Hodgkin's
  - Sarcomas
  - Neuroblastomas

- **Dosage Range:**
  - Vary between 0.5 and 1.4 mg/m2
  - Total dose should be limited to 2 mg to prevent neurotoxicity

- **Administration:**
  - IV administration over 5 minutes – not on a pump (free-flow only)
  - NEVER given intrathecally

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## Vinca Alkaloid- **Vinorelbine Tartrate**(Navelbine)

- **Indications:**
  - Solid tumors – NSCLCA ; advanced breast
- **Dosage Range:**
  - Single agent or combination therapy
  - Weekly IV doses of 30 mg/m2
  - Oral doses of 80 mg/m2
  - Dose adjustments according to ANC
  - Dose reductions with hepatic dysfunction
- **Administration:**
  - IV over 5 minutes- **free-flow only**
  - Oral administration on an empty stomach as a single ingestion at bedtime to minimize side effects

**Side Effects:**

- Vesicant/Extravasation
- Neurotoxicity
- Myelosuppression

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## Podophyllotoxins- **Etoposide (VP-16)**

- **Indications:**
  - Testicular
  - Small cell lung cancer
  - Off label lymphomas and HSCT
- **Dosage Range:**
  - Variable
  - Oral doses doubled due to 50% bioavailability in gelatin capsules
  - Dose reductions with renal dysfunction
- **Administration:**
  - Oral, intravenous, intrapleural and intraperitoneal
  - Concentrated solutions will precipitate

**Side Effects:**

- Neuropathies
- Drops BP if administered too quickly and in transplant
- Myelosuppression in high doses
- Alopecia
- Increased incidence of radiation recall
- Higher doses (PSCT) = Palmar Plantar Erythrodysesthesia (PPE) and severe skin sloughing

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## Mitotic Inhibitors- **Paclitaxel** (Taxol)

- **Indications:**
- Breast, Prostate, Bladder, NSCLCA, Ovarian
- Many off label uses in solid tumors

- **Dosage Range:**
- Variable
- Extensive plasma protein binding (> 90%)

- **Administration:**
- IV or intraperitoneal
- Mix in either glass or polyolefin containers with 0.22 µM filter and polyethylene-lined administration sets (PVC causes leaching)
- *Use non-pvc tubing

**Side Effects:**

Myelosupression
- Neurotoxicity
- Vesicant/Extravasation
- Bradycardia
- Alopecia (cold cap)
- Hypersensitivity Reactions:
  - Occurs in 20% to 40% of patients
  - **Premedications:**
  - Decadron 20 mg at 12 hours, 6 hours and pre-dose
  - Tylenol 650 mg pre-dose
  - Benadryl 50 mg pre-dose
  - Famotidine 40 mg pre-dose

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## Mitotic Inhibitors- **Docetaxel** (Taxotere)

Semi-synthetic taxane derived from the needles of the European yew tree

**Indications:**
Breast cancer
Gastric adenocarcinoma
Prostate
NSCLCA
Head and neck

**Administration:**
Mix in either glass or polyolefin containers with 0.22 µM filter and polyethylene-lined administration sets (PVC causes leaching)
Requires Non-PVC bag, does not require a filter

**Side Effects**:
- Vesicant/Extravasation
- Myelosuppression
- GI toxicities
- Rash
- Alopecia (cold cap)
- Capillary leak/Fluid retention syndrome:
  - Premedicate with Decadron*

**Hypersensitivity**
- Premedication:
- Decadron 8 mg PO BID for 3 days beginning 1 day prior to administration
- Pulmonary edema
- Indirectly assists with CLS

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# Mitotic Inhibitor

**Taxol (Paclitaxel)**

- Given IV over 1 or more hours
- More common and severe HSR
- Pre-medications
- Moderate to severe myelosuppression (especially neutropenia)
- N/V
- Fatigue
- Mucositis
- Peripheral neuropathy (cumulative)
- Alopecia

**Taxotere (Docetaxel)**

- Given IV over 1 hours
- Less frequent and severe
- Pre-meds for HSR and fluid retention
- Myelosuppression (severe neutropenia)
- N/V
- Fatigue
- Stomatitis
- More pronounced edema (Decadron)
- Peripheral neuropathy (less severe)
- Alopecia

**For both, DO NOT TREAT with a bili over 1.5 without a proceed to treat order**

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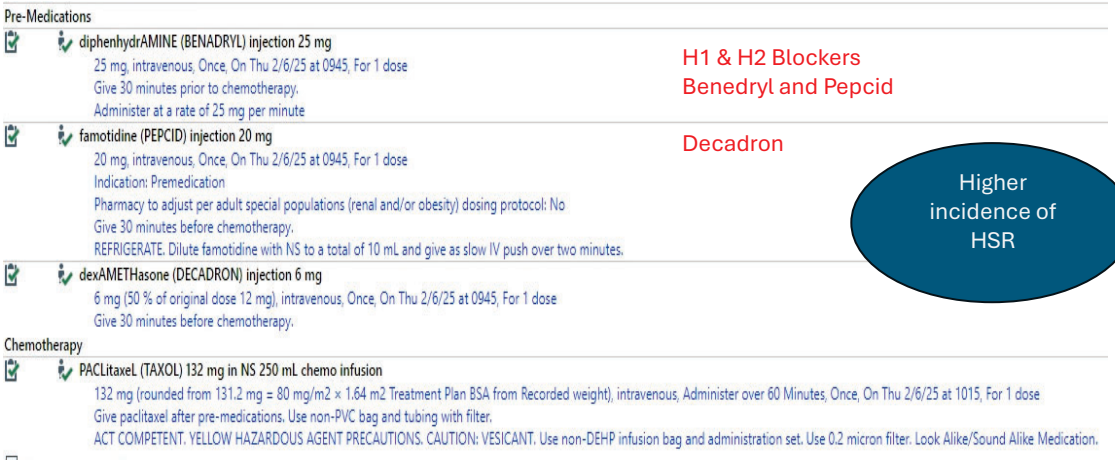
# Hypersensitivity Potential Taxol

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# Hypersensitivity Potential Taxotere


Pre-Medications

dexAMETHasone (PF) (DECADRON) 12 mg/20 mL in NS syringe

12 mg, intravenous, Once as needed, give if patient forgot to take any of home doses, Starting at treatment start time, for 1 dose

Chemotherapy

DOCEtaxeL (TAXOTERE) 80 mg in NS 150 mL chemo infusion

50 mg/m2 (66.7 % of original dose 75 mg/m2), intravenous, Administer over 60 Minutes, Once, Starting 30 minutes after treatment start time

Give docetaxel after pre-medication.

CAUTION: VESICANT. ACT COMPETENT. HAZARDOUS AGENT PRECAUTIONS. Protect from light. Dispense with non-PVC bag and Tubing. Look Alike/Sound Alike Medication.

Less risk of HSR

Premedicate with Decadron

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# Symptom of Hypersensitivity Reaction

**Mild**

- Itching, hives
- Rash, redness
- Mild swelling
- Runny nose
- Mild cough
- Mild abdominal cramps
- Nausea

**Moderate**

- Worsening hives
- Angioedema eyes, lips, throat
- Wheezing, increased cough
- SOB
- Moderate abd cramping
- Vomiting

**Severe (anaphylaxis)**

- Extensive angioedema, affecting airway
- Severe SOB, stridor
- Rapid, weak pulse
- Drop in BP
- Cardiac arrest

Arthralgias, myalgias, fever also often reported/observed


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# Mitotic Inhibitors
## Paclitaxel Protein/Albumin-Bound (Abraxane)

**Indications**:
- Metastatic breast cancer
- Locally advanced or metastatic non-small cell lung cancer (NSCLC):
- Metastatic pancreatic cancer: Often a first-line treatment option.
- Advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction
- Locally recurrent or metastatic triple-negative breast cancer:

**Side Effects:**
- Infusion site skin reaction-Vesicant
- Myelosuppression
- Neurotoxicity- CIPN
- GI toxicity

**NO Pre-meds**

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# Camptothecins
## Irinotecan (CPT-11/Camstar)

**Indications**
- Colorectal
- Ovarian
- SCLCA

**Side effects**
- Myelosuppression
- GI Toxicity
  - DOSE LIMITING DIARRHEA

  **Grade 3**
  - 7-9 Stools per day
  - Incontinence
  - Severe cramping

  **Grade 4**
  - 10 stools per day
  - Bloody stools
  - Need for parental support

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# Treating Irinotecan-related GI Toxicity

**Early diarrhea syndrome**

- Occurs during or within 24 hours of infusion
- Due to cholinergic effect
- Treat with atropine 0.25mg-1mg IV
- No laxatives during treatment

**Late diarrhea syndrome**

- Starts 24 or more hours after infusion
- Loperamide 4 mg PO as a loading dose immediately with first episode
- Loperamide 2mg PO every 2 hours ATC
- Loperamide can be discontinued after 12 hour with no diarrhea
- If diarrhea persists >24 hours, hospitalization with supportive hydration is warranted

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# Anti-Metabolites


**Pyrimidine Analogues**

- Fluoruracil (Flouracil/ Efudex/Fluoroplex) 5-FU
- Capecitabine (Xeloda)
- Cytarabine (Cytosar) ARA-C

**Folic Acid Antagonists**

- Methotrexate (MTX)
- Pemetrexed (Alimta)

**Purine Analogues**

- Fludarabine Phosphate (Fludara)
- Gemcitabine (Gemsar)

**Hypomethylating**

- Azacitidine (Vidaza)
- Decitabine (Dacogen

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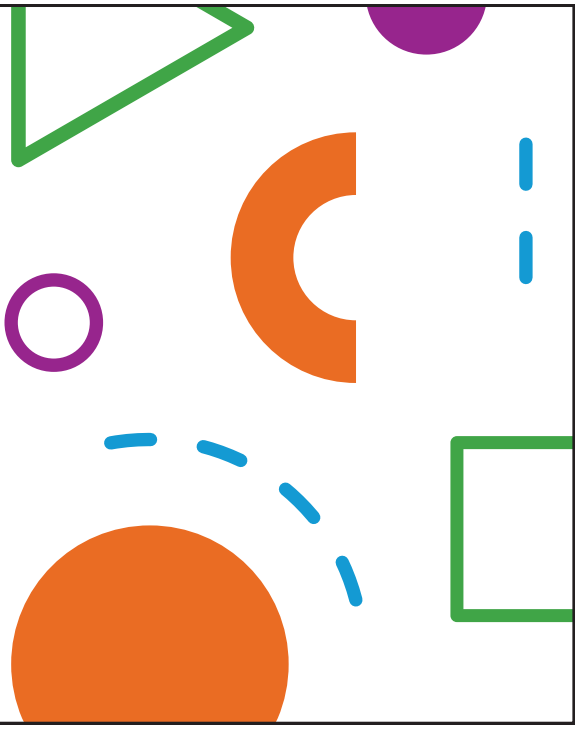
# Mechanism of Action

- Cell cycle specific for S phase (DNA Synthesis)
- Cytotoxicity is time and dose dependent
- Duration of exposure is important
- Most effective against tumors that have a high growth fraction
- Toxicities due to damage of normal cells with a high growth fraction
- Heavy Metal derivatives
- Metallic Taste
- GI toxicities (mouth - to - butt)



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# Pyrimidine Analogs - 5-Fluorouracil (Flouracil; Adrucil) (IV, Topical)

**Dose and Administration**
- Many varying schedules
- IVP, IV continuous infusion, topical cream
- Daily, weekly, monthly
- Intra arterial FUDR

Uridine triacetate overdose antidote within 96 hours

**Leucovorin given to enhance efficacy**

**Indications:**
- Breast
- Head and Neck
- GI (esophageal, colon, gastric, pancreatic)

**Side Effects:**
- GI (increased with continuous infusion)
  - Ice chips pre/post infusion
  - 10-15 minutes pre and post infusion
- Myelosuppression increased with IVP weekly
- Cardiovascular - MI
- Dermatologic-alopecia, dermatitis, dry thin skin, photosensitivity, hyperpigmentation, nail changes, hand foot syndrome
- Vesicant

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# Pyrimidine Analogs- Capecitabine (Xeloda)

**Dose and Administration**

- Pharmacology – oral 5-FU
- Results in higher concentrations of 5 FU within tumor tissues and lower concentration in normal cells and plasma
- Oral – consistent GI absorption
- 2500mg/m2/day (in 2 divided doses)
- 14 days on and 7 days off is one cycle
- Uridine triacetate overdose antidote within 96 hours

**Side Effects:**

- Increased therapeutic index and decrease in systemic toxicities
- Similar to 5 FU
- Greater incidence of hand – foot syndrome – PPE
- Increases Warfarin effects
- Take with food and water to minimize toxicities

**Indications:**
**Met breast**
**Colon and rectal**

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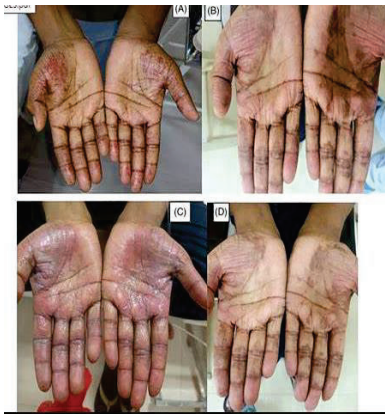
# Palmar-Plantar Erythrodysesthesia (PPE)/Hand-Foot Syndrome – HFS)

- A disorder characterized by redness, marked discomfort, swelling, and tingling in the palms of the hands or the soles of the feet
- Also known as Hand-Foot Syndrome
- Symmetric erythema and edema in palms and soles
- Palmoplantar dysesthesia
- Tingling sensation → burning pain
- Pain and temperature sensation reduced
- Erythema and edema with onset of neuropathic symptoms
- Erythema → blistering → desquamation, erosion, ulceration
- Symptoms recur with repeated exposure
- Occurs in 60% patients receiving fluorouracil, capecitabine. docetaxel, liposomal doxorubicin
- May lose fingerprints (not permanent)

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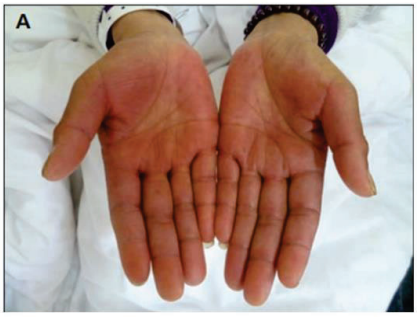
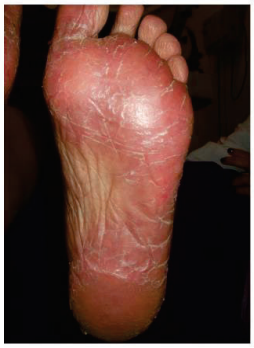
# Integumentary – PPE/HFS Grading

| Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|
| Minimal skin changes or dermatitis (e.g., erythema, edema, or hyperkeratosis) without pain | Skin changes (e.g., peeling, blisters, bleeding, fissures, edema, or hyperkeratosis) with pain; limiting instrumental ADL | Severe skin changes (e.g., peeling, blisters, bleeding, fissures, edema, or hyperkeratosis) with pain; limiting self care ADL | --- |



Qiao J, Fang H. *CMAJ.* 2012;184(15):E818. Miller KK, et al. *J Am Acad Dermatol.* 2014;71(4):787-94.

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# Treatment for PPE/HFS

- Most effective - dose interruption or modification
- Symptoms typically improve within 1-2 weeks
- Grades 2-3 = dose interruption
- Grade 3 = dose reduction

**Important Considerations:**
- Avoid direct sunlight and use sunscreen SPF ≥ 30
- Avoid hot baths/showers
- Avoid alcohol-based or fragranced skin care products
- Do not treat like acne!
- Moisturize


**Supportive measures:**
- topical corticosteroids, wound care, emollients and topical keratolytic, analgesics
- Hydrocortisone 1% + moisturizer + sunscreen + doxycycline BID x 6 weeks
- Oral Tetracyclines
  - Prevention vs treatment
  - Doxycycline
  - Minocycline – less photosensitizing

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## Pyrimidine Analogs- Cytosine Arabinoside/ARA-C (Cytarabine) -(IV, SQ, IT)

**Dose and Administration**

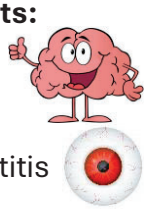
- IVP, IV continuous infusion, SQ, IT
- Low dose 100-400mg/m2
- Intermediate dose 1gm/m2
- High dose 2 or 3 gm/m2
- Neuro check before each dose
- Hold drug if neuro assessment changes from baseline
- **Steroid eye gtts** (start prior to first dose and 48 hours after last dose)

**Side Effects:**

- GI
- Myelosuppression
- Dermatological

**High Dose side effects:**

- Neurological – Cerebellar (ataxia)
- Ocular – conjunctivitis, keratitis



**Indication: Leukemia**

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## Folic Acid Antagonist
## Methotrexate (PO, IV, IM, IT)

**Indications:**

- Leukemia
- Lymphoma
- CNS mets
- Lung
- Breast
- Head and Neck
- Osteosarcoma
- Rheumatoid arthritis
- Ectopic Pregnancy

**Dose and Administration**

- PO, IVP, IV infusion, IM, IT
- Wide range of doses

**Intrathecal Administration**

- Immediate acute chemical arachnoiditis, headache, neck/back pain, fever, nuchal rigidity.
- Progressive neurotoxicity's, confusion, irritability, ataxia, dementia

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# Folic Acid Antagonist
## Methotrexate

**Side Effects**

- Hematological
- GI (including mucositis)
- Renal
- Uric acid nephropathy (prevent with vigorous hydration and alkalinization of urine)
- Pulmonary – interstitial pneumonitis
- Dermatological – rash, photosensitivity, alopecia, acne, pigment changes
- Widely distributed to body tissues
- Caution in patients with abnormal fluid collections (effusions, blisters, ascites)
- AVOID PPI'S (prilosec, pepcid etc.)
- Must take folic acid

High –Dose Rescue

- Leucovorin Rescue **required to salvage normal cells***
- Folinic acid enters and rescues normal cells from the toxic effects of folic acid antagonists (taken up by normal cells)
- Must be given within 24 hours of MTX
- Usually high does, 5-8-grams / m2
- Follow MTX levels to decide when to stop LCV
  - **Urine PH >7.0 until serum MTX <0.05- 0.1 mcmol./L**

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# Folic Acid Antagonist
## Pemetrexed (Alimta)

**Indications:**

- Mesothelioma
- NSCLCA
- Bladder, breast, cervical, colorectal, esophageal, gastric, head and neck, ovarian, pancreatic, and renal

**Dosing and Administration**

- Infuse over 10 minutes

NSCLCA

- 500 mg / m2 on day 1 of a 21-day cycle

Mesothelioma

- 500-600 mg / m2 on day one of a 21-day cycle

**Side Effects:**

- Hematologic
- GI (including mucositis)
- Dermatological
- Edema
- Administer B12 (1000 mcg IM 1 week prior to first cycle and repeat every 9 weeks until treatment completed)
- Administer **Folic Acid** (400-1000mcg daily starting 1 week prior to first cycle and daily for 3 weeks after final cycle)

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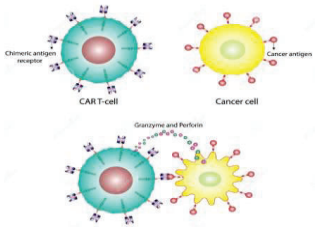
# Purine Analogs
## Fludarabine (Fludara)

**Indications:**
- CLL
- Transplant
- CAR-T

**Dose and Administration**
- 25 mg / m2 over 30 minutes daily x 5 days given every 28 days.




**Side Effects:**
- Myelosuppression
- Increased T cell susceptibility –depletes T cells (lympho-depleting)
- B-cell aplasia
- GI
- Pulmonary
  - Pneumonia, cough, dyspnea
- Metabolic – Tumor Lysis
  - Hyperkalemia, hypophosphatemia, hypocalcemia, metabolic acidosis, renal failure
- Neurotoxicity
  - Weakness, agitation, confusion, visual changes
    - (More common with higher doses no longer given)

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# Hypomethylating Agents

Works at a level above the DNA, manipulating gene expression. This makes it a relatively gentler approach compared to some other therapies that directly target DNA. Hypomethylating Agents are considered epigenetic therapy.

**Azacitidine (Vidaza)**
- MDS and AML
- Subcutaneous or IV
- SQ- roll in palms prior to administering
- Stable 1 hour unrefrigerated
- IV only in saline or LR

**Side Effects**
- Myelosuppression
- GI
- Misc. – fever, injection site reaction (give 2 inches apart)

*Azacitidine (Onureg) – oral version

**(Decitabine)Dacogen**
- MDS
- 5q deletion
- Stable 4 hours cold and 15 minutes if prepared at room temperature

**IV**
- Myelosuppression
- There are 2 dosing regimens for DACOGEN: 3-day and 5-day dosing

*Decitabine and Cedazuridine (Inqovi)– oral version

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# Miscellaneous Agents

**Hydroxyurea** (Hydrea)
**Arsenic** (Trisenox)
**Transretonoic** Acid
**Procarbazine** (Matulane)

**Mechanism of Action**
- Cell-cycle specific
- Act in various stages of the cell cycle
- Specific to each agent
- Typically, G-phases of cycle

**HDAC**
Histone deacetylases are a class of enzymes that remove acetyl groups from an ε-N-acetyl lysine amino acid on a histone, allowing the histones to wrap the DNA more tightly

- Vorinostat (Zolinza)- T cell lymphoma
- Istodax (Romidepsin) – cutaneous t-cell lymphoma (CTCL)
- Panobinostat (Farydak) – multiple myeloma
- Belinostat (Beleodaq) – peripheral t-cell lymphoma (CTCL)

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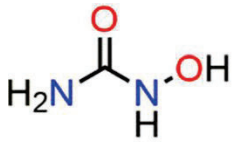
# Hydroxyurea (Hydrea)

**Therapeutic Uses:**
- CML, Leukemia, Squamous Head & Neck Cancer, Polycythemia vera
- Myeloprolifertive Neoplasms (MPN)

- Usual oral doses range from 10-30 mg/kg/day or 500-3000 mg/day
- If WBC count falls to <2500 cells/mm3, or the platelet count to <100,000/mm3, therapy should be stopped for at least 3 days and resumed when values rise toward normal

- **Side Effects:**
- Headaches
- Dermatological
- Hyperuricemia
- GI
- Myelosuppression
- Do not open capsules



Hydroxyurea

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# Procarbazine (Mutulane)

**Lymphomas, Brain**

**Mechanism of Action:**
Cell-cycle phase nonspecific antineoplastic agent which inhibits protein and nucleic acid synthesis and suppresses mitosis

**Acute side effects:**
N&V, diarrhea, anorexia, fevers, chills, sweating, lethargy, myalgias, arthralgias, pruritus, dizziness, ataxia, headaches

**Chronic:**
myelosuppression, alopecia, rash, nightmares, depression, nervousness, hallucinations, diplopia

****tyramine restricted diet must be instituted while taking this drug**

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# Arsenic Trioxide (Trisenox)


**Indications:** Acute Promyelocytic Leukemia (APL)

**Dosing and Administration:**

**Induction:** 0.15 mg/kg/day; administer daily until bone marrow remission; maximum induction: 60 doses

**Consolidation:** 0.15 mg/kg/day starting 3-6 weeks after completion of induction therapy; maximum consolidation: 25 doses over 5 weeks

Administer as I.V. infusion over 1-2 hours.
If acute vasomotor reactions occur, infuse over a maximum of 4 hours

Side Effects:
**APL differentiation syndrome**
- dyspnea, fever, weight gain, pulmonary infiltrates, and pleural or pericardial effusions)in patients with APL

**Hyperleukocytosis:**
- leukocytes ≥10,000/mm3)

**QT prolongation**
- May lead to torsade de pointes or complete AV block.

Hypokalemia or hypomagnesemia
- Correct QTc >500 msec prior to treatment
- hospitalize patient if QTc >500 msec, syncope, or arrythmia develop during therapy
- do not reinitiate until QTc <460 msec

****Any empty or partial vial/bag must be disposed of in a designated black bin****

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# Tretinoin/All-trans-retinoic acid/ATRA

Induces maturation of acute promyelocytic
leukemia (APL) cells in cultures and decreases proliferation of APL cells

Administered with Arsenic (Trisenox)
PO dosing
45mg/m2/day with daily dosing in split doses

Take with food


**Acute side effects:**

- H/A, dry skin and mucous membranes, erythema, xerostomia, desquamation of skin, lip inflammation
- bone pain,
- somnolence, insomnia, weakness, fatigue, dizziness,
- anxiety, and depression

**Chronic side effects:**

- arthralgias, myalgias
- hepatic toxicity

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# Retinoic acid syndrome (Differentiation Syndrome)

**Differentiation Syndrome is a rare but serious side effect:**

Symptoms often arise due to the release of cytokines by maturing leukemia cells, causing an inflammatory response and endothelial damage, leading to capillary leak syndrome

- Flu-like symptoms (fever)
- Leukocytosis
- Fluid retention
- Edema
- Pulmonary infiltrates
- Pleural and pericardial effusions
- Hypotension
- Cerebral HTN

Manage with high dose steroids and temporarily discontinue drug

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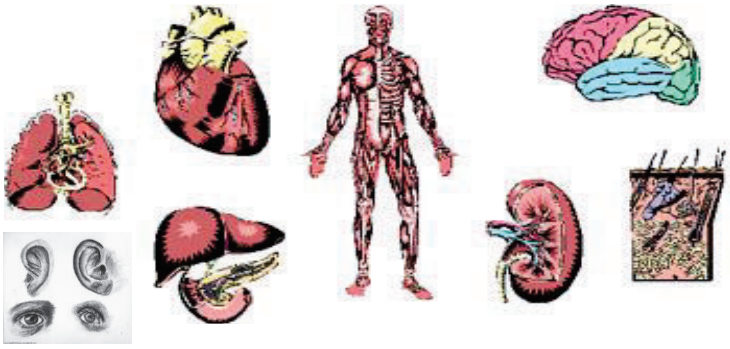
# Toxicity Assessment Overview



Marcia Almiron Wolbert, MSN, RN, OCN
Professional Development Specialist AHNCI
Marcia.ALMIRONWOLBERT@ahn.org

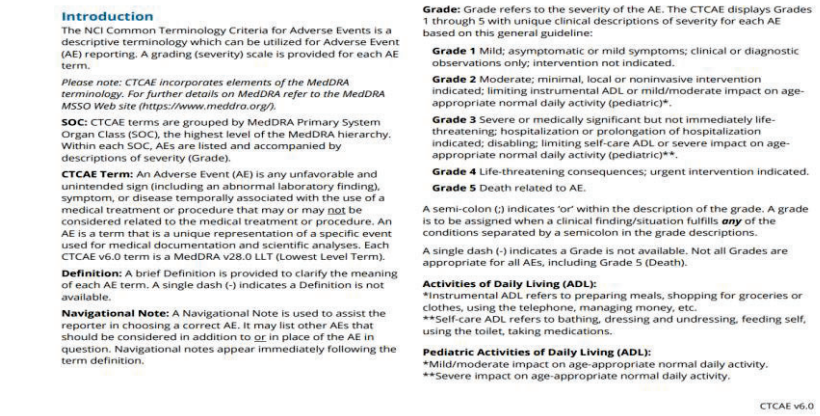
*No Disclosures*



# Learning Outcomes

- Describe the subjective and objective physical assessment of an adult patient for the review of systems
- Formulate a comprehensive plan of care, including side effects and toxicities for a patient receiving anticancer therapy.

# Common Terminology Criteria for Adverse Events (CTCAE)



**Introduction**

The NCI Common Terminology Criteria for Adverse Events is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term.

*Please note: CTCAE incorporates elements of the MedDRA terminology. For further details on MedDRA refer to the MedDRA MSSO Web site (https://www.meddra.org/).*

**SOC:** CTCAE terms are grouped by MedDRA Primary System Organ Class (SOC), the highest level of the MedDRA hierarchy. Within each SOC, AEs are listed and accompanied by descriptions of severity (Grade).

**CTCAE Term:** An Adverse Event (AE) is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure. An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses. Each CTCAE v6.0 term is a MedDRA v28.0 LLT (Lowest Level Term).

**Definition:** A brief Definition is provided to clarify the meaning of each AE term. A single dash (-) indicates a Definition is not available.

**Navigational Note:** A Navigational Note is used to assist the reporter in choosing a correct AE. It may list other AEs that should be considered in addition to or in place of the AE in question. Navigational notes appear immediately following the term definition.

**Grade:** Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

**Grade 1** Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.

**Grade 2** Moderate; minimal, local or noninvasive intervention indicated; limiting instrumental ADL or mild/moderate impact on age-appropriate normal daily activity (pediatric)*.

**Grade 3** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL or severe impact on age-appropriate normal daily activity (pediatric)**.

**Grade 4** Life-threatening consequences; urgent intervention indicated.

**Grade 5** Death related to AE.

A semi-colon (;) indicates 'or' within the description of the grade. A grade is to be assigned when a clinical finding/situation fulfills ***any*** of the conditions separated by a semicolon in the grade descriptions.

A single dash (-) indicates a Grade is not available. Not all Grades are appropriate for all AEs, including Grade 5 (Death).

**Activities of Daily Living (ADL):**
*Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
**Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications.

**Pediatric Activities of Daily Living (ADL):**
*Mild/moderate impact on age-appropriate normal daily activity.
**Severe impact on age-appropriate normal daily activity.

CTCAE v6.0

Grades 3 and 4 – require 'Proceed to Treat'

AHN





# ECOG - Performance Status

| Grade | Definition |
|---|---|
| 0 | Fully active, able to carry on all pre-disease performance without restrictions |
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light nature |
| **2** | **Ambulatory and capable of all self care but unable to carry out work activities. Up and about more than 50% of waking hours** |
| 3 | Capable of only limited self care, confined to bed or chair >50% of waking hours |
| 4 | Completely disabled. Cannot carry on any self care. Totally confined to bed or chair. |
| 5 | Dead |

ECOG higher than 2 – require 'Proceed to Treat'

# Karnofsky - Performance Status

| Grade | Definition |
|---|---|
| 100 | Normal, no complaints, no evidence of disease |
| 90 | Able to carry on normal activity, minor signs/symptoms of disease |
| 80 | Normal activity with effort, some signs/symptoms of disease |
| 70 | Cares for self, Unable to carry on normal activity or do active work |
| 60 | Requires occasional assistance, but is able to care for most needs |
| **50** | **Requires considerable assistance and frequent medical care** |
| 40 | Disabled, requires special care and assistance |
| 30 | Severely disabled, hospitalization is indicated although death is not imminent |
| 20 | Hospitalization necessary, very sick, active supportive treatment necessary |
| 10 | Moribund, fatal processes progressing rapidly |
| 0 | Dead |

**Karnofsky lower than 50 – require "Proceed to Treat"**

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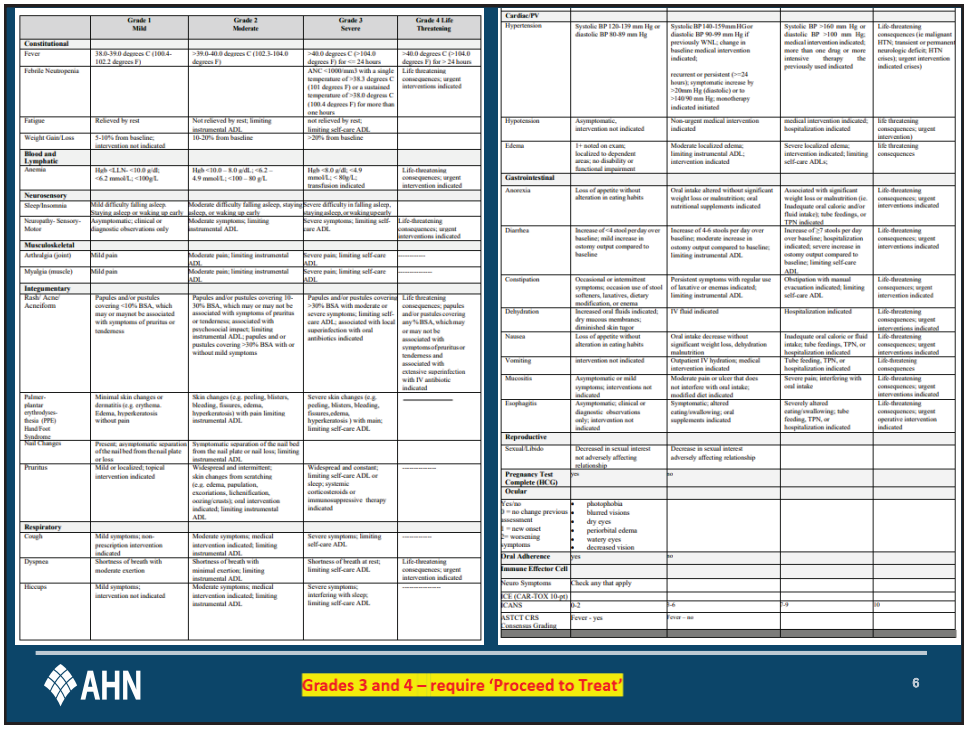


| | Grade 1 Mild | Grade 2 Moderate | Grade 3 Severe | Grade 4 Life Threatening |
|---|---|---|---|---|
| **Constitutional** | | | | |
| Fever | 38.0-39.0 degrees C (100.4-102.2 degrees F) | >39.0-40.0 degrees C (102.3-104.0 degrees F) | >40.0 degrees C (>104.0 degrees F) for <= 24 hours | >40.0 degrees C (>104.0 degrees F) for > 24 hours |
| Febrile Neutropenia | | | ANC <1000/mm3 with a single temperature of >38.3 degrees C (101 degrees F) or a sustained temperature of >38.0 degrees C (100.4 degrees F) for more than one hours | Life threatening consequences; urgent interventions indicated |
| Fatigue | Relieved by rest | Not relieved by rest; limiting instrumental ADL | not relieved by rest; limiting self-care ADL | |
| Weight Gain/Loss | 5-10% from baseline; intervention not indicated | 10-20% from baseline | >20% from baseline | |
| **Blood and Lymphatic** | | | | |
| Anemia | Hgb <LLN- <10.0 g/dl; <6.2 mmol/L; <100g/L | Hgb <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 – 80 g/L | Hgb <8.0 g/dL; <4.9 mmol/L; < 80g/L; transfusion indicated | Life-threatening consequences; urgent intervention indicated |
| **Neurosensory** | | | | |
| Sleep/Insomnia | Mild difficulty falling asleep. Staying asleep or waking up early | Moderate difficulty falling asleep, staying asleep, or waking up early | Severe difficulty in falling asleep, staying asleep, or waking up early | |
| Neuropathy- Sensory-Motor | Asymptomatic, clinical or diagnostic observations only | Moderate symptoms, limiting instrumental ADL | Severe symptoms; limiting self-care ADL | Life-threatening consequences; urgent interventions indicated |
| **Musculoskeletal** | | | | |
| Arthralgia (joint) | Mild pain | Moderate pain; limiting instrumental ADL | Severe pain; limiting self-care ADL | ---------- |
| Myalgia (muscle) | Mild pain | Moderate pain; limiting instrumental ADL | Severe pain; limiting self-care ADL | ---------- |
| **Integumentary** | | | | |
| Rash/ Acne/ Acneiform | Papules and/or pustules covering <10% BSA, which may or maynot be associated with symptoms of pruritus or tenderness | Papules and/or pustules covering 10-30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL; papules and or pustules covering >30% BSA with or without mild symptoms | Papules and/or pustules covering >30% BSA with moderate or severe symptoms; limiting self-care ADL; associated with local superinfection with oral antibiotics indicated | Life threatening consequences; papules and/or pustules covering any%BSA, whichmay or may not be associated with symptomsofpruritusor tenderness and associated with extensive superinfection with IV antibiotic indicated |
| Palmer-plantar erythrodyses-thesia (PPE) Hand/Foot Syndrome | Minimal skin changes or dermatitis (e.g. erythema. Edema, hyperkeratosis without pain | Skin changes (e.g. peeling, blisters, bleeding, fissures, edema, hyperkeratosis) with pain limiting instrumental ADL | Severe skin changes (e.g. peeling, blisters, bleeding, fissures,edema, hyperkeratosis ) with main; limiting self-care ADL | ---------- |
| Nail Changes | Present, asymptomatic separation of the nail bed from the nail plate or loss | Symptomatic separation of the nail bed from the nail plate or nail loss; limiting instrumental ADL | | |
| Pruritus | Mild or localized; topical intervention indicated | Widespread and intermittent; skin changes from scratching (e.g. edema, papulation, excoriations, lichenification, oozing/crusts); oral intervention indicated; limiting instrumental ADL | Widespread and constant; limiting self-care ADL or sleep; systemic corticosteroids or immunosuppressive therapy indicated | ---------- |
| **Respiratory** | | | | |
| Cough | Mild symptoms; non-prescription intervention indicated | Moderate symptoms; medical intervention indicated; limiting instrumental ADL | Severe symptoms; limiting self-care ADL | ---------- |
| Dyspnea | Shortness of breath with moderate exertion | Shortness of breath with minimal exertion; limiting instrumental ADL | Shortness of breath at rest; limiting self-care ADL | Life-threatening consequences; urgent intervention indicated |
| Hiccups | Mild symptoms; intervention not indicated | Moderate symptoms; medical intervention indicated; limiting instrumental ADL | Severe symptoms; interfering with sleep; limiting self-care ADL | ---------- |

| | | | | |
|---|---|---|---|---|
| **Cardiac/PV** | | | | |
| Hypertension | Systolic BP 120-139 mm Hg or diastolic BP 80-89 mm Hg | Systolic BP 140-159mmHGor diastolic BP 90-99 mm Hg if previously WNL; change in baseline medical intervention indicated;<br><br>recurrent or persistent (>=24 hours); symptomatic increase by >20mm Hg (diastolic) or to >140/90 mm Hg; monotherapy indicated initiated | Systolic BP >160 mm Hg or diastolic BP >100 mm Hg; medical intervention indicated; more than one drug or more intensive therapy the previously used indicated | Life-threatening consequences (ie malignant HTN; transient or permanent neurologic deficit; HTN crises); urgent intervention indicated crises) |
| Hypotension | Asymptomatic, intervention not indicated | Non-urgent medical intervention indicated | medical intervention indicated; hospitalization indicated | life threatening consequences; urgent intervention) |
| Edema | 1+ noted on exam; localized to dependent areas; no disability or functional impairment | Moderate localized edema; limiting instrumental ADL; intervention indicated | Severe localized edema; intervention indicated; limiting self-care ADLs; | life threatening consequences |
| **Gastrointestinal** | | | | |
| Anorexia | Loss of appetite without alteration in eating habits | Oral intake altered without significant weight loss or malnutrition; oral nutritional supplements indicated | Associated with significant weight loss or malnutrition (ie. Inadequate oral caloric and/or fluid intake); tube feedings, or TPN indicated | Life-threatening consequences; urgent interventions indicated |
| Diarrhea | Increase of <4 stool per day over baseline; mild increase in ostomy output compared to baseline | Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL | Increase of ≥7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL | Life-threatening consequences; urgent interventions indicated |
| Constipation | Occasional or intermittent symptoms; occasion use of stool softeners, laxatives, dietary modification, or enema | Persistent symptoms with regular use of laxative or enemas indicated; limiting instrumental ADL | Obstipation with manual evacuation indicated; limiting self-care ADL | Life-threatening consequences; urgent intervention indicated |
| Dehydration | Increased oral fluids indicated; dry mucous membranes; diminished skin turgor | IV fluid indicated | Hospitalization indicated | Life-threatening consequences; urgent interventions indicated |
| Nausea | Loss of appetite without alteration in eating habits | Oral intake decrease without significant weight loss, dehydration or malnutrition | Inadequate oral caloric or fluid intake; tube feedings, TPN, or hospitalization indicated | Life-threatening consequences; urgent interventions indicated |
| Vomiting | intervention not indicated | Outpatient IV hydration; medical intervention indicated | Tube feeding, TPN, or hospitalization indicated | Life-threatening consequences |
| Mucositis | Asymptomatic or mild symptoms; interventions not indicated | Moderate pain or ulcer that does not interfere with oral intake; modified diet indicated | Severe pain; interfering with oral intake | Life-threatening consequences; urgent interventions indicated |
| Esophagitis | Asymptomatic; clinical or diagnostic observations only; intervention not indicated | Symptomatic; altered eating/swallowing; oral supplements indicated | Severely altered eating/swallowing; tube feeding, TPN, or hospitalization indicated | Life-threatening consequences; urgent operative intervention indicated |
| **Reproductive** | | | | |
| Sexual/Libido | Decreased in sexual interest not adversely affecting relationship | Decrease in sexual interest adversely affecting relationship | | |
| **Pregnancy Test Complete (HCG)** | yes | no | | |
| **Ocular** | | | | |
| Yes/no<br>0 = no change previous assessment<br>1 = new onset<br>2= worsening symptoms | • photophobia<br>• blurred visions<br>• dry eyes<br>• periorbital edema<br>• watery eyes<br>• decreased vision | | | |
| **Oral Adherence** | yes | no | | |
| **Immune Effector Cell** | | | | |
| Neuro Symptoms | Check any that apply | | | |
| ICE (CAR-TOX 10-pt) | | | | |
| ICANS | 0-2 | 3-6 | 7-9 | 10 |
| ASTCT CRS Consensus Grading | Fever - yes | Fever – no | | |

AHN

**Grades 3 and 4 – require 'Proceed to Treat'**

6

6

| CHEMOTHERAPY AND TARGETED THERAPY TOXICITIES | |
|---|---|
| General | Fatigue |
| Neurological | Encephalopathy; peripheral neuropathies; seizures; cognitive changes |
| Ocular | Keratitis; conjunctivitis; visual changes; color blindness; photophobia |
| Pulmonary | Pneumonitis; pulmonary fibrosis; pulmonary edema; bronchospasm |
| Cardiovascular | Dysrhythmias, myocardial; hyper/hypo-tension; pericardial effusions; QT prolongation |
| Renal /Nephrotoxicity | Nephritis; SIADH, electrolyte abnormalities; acute kidney injury |
| Gastrointestinal | Nausea; vomiting; anorexia; diarrhea; constipation; mucositis; GI fistula/perforation |
| Pancreatic | Pancreatitis |
| Hepatic | Elevated LFTs; jaundice |
| Musculoskeletal | Arthralgias; muscle cramps |
| Integumentary | Alopecia; nail changes; pigment changes; rash; photosensitivity |
| Hematological | Neutropenia; anemia; thrombocytopenia |
| Reproductive | Infertility |

7

| IMMUNOTHERAPY ('ITIS') TOXICITIES | |
|---|---|
| Neurological | Encephalitis; neuritis; aseptic meningitis |
| Ocular | Uvelitis; iritis; conjunctivitis |
| Pulmonary | Pneumonitis |
| Cardiovascular | Myocarditis |
| Renal /Nephrotoxicity | Nephritis |
| Gastrointestinal | Colitis; enteritis; mucositis; nausea; diarrhea; constipation |
| Pancreatic | Pancreatitis; hyperglycemia |
| Hepatic | Hepatitis |
| Musculoskeletal | Joint swelling /pain |
| Integumentary | Rash; vitiligo |
| Hematological | Neutropenia; anemia; thrombocytopenia; CRS |
| Hormonal | Thyroiditis; autoimmune diabetes; adrenal insufficiency; hypophysitis |

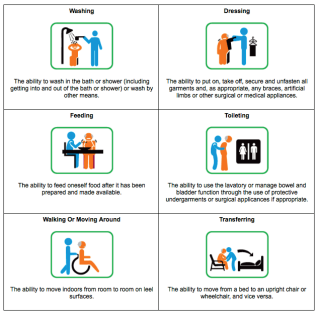
8

| HORMONAL THERAPY TOXICITIES | |
|---|---|
| General | Hot flashes, mood fluctuations, fatigue, gynecomastia, decreased libido |
| Ocular | Visual field changes |
| Neurologic | Seizures |
| Cardiac | Hypertension, edema, fluid retention, ischemic heart disease, dysthymias |
| Skeletal | Bone mineral density changes |
| Hematologic | Venous thrombus embolism (VTE) |
| Integumentary | Dryness, pruritus, rash, nail changes |
| Hepatic | Hypertriglyceridemia, transaminitis, hypercholesterolemia, hypokalemia |
| Gastrointestinal | Nausea, diarrhea, constipation |

9

# Performance Status and Toxicities

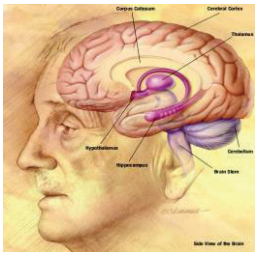
- Measures level of functioning (ADLs)
- Determines treatment decisions
  - Hold
  - Delay
  - Stop
  - Adjustments
- Assesses quality of life

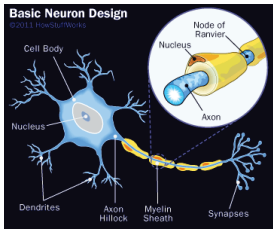


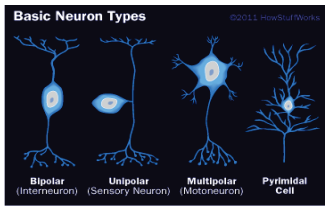

10

# Neurological Toxicity

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| **Neurosensory** | | | | |
| Sleep/Insomnia | Mild difficulty falling asleep. Staying asleep or waking up early | Moderate difficulty falling asleep, staying asleep, or waking up early | Severe difficulty in falling asleep, staying asleep, or waking up early | |
| Neuropathy- Sensory-Motor | Asymptomatic; clinical or diagnostic observations only | Moderate symptoms; limiting instrumental ADL | Severe symptoms; limiting self-care ADL | Life-threatening consequences; urgent interventions indicated |






11

# Neurological Toxicity

Nervous system

(destroys the axons and myelin sheath)

- Central nervous system (CNS) (hallucinations confusion, seizures)
  - Brain
  - Spinal cord
- Peripheral nervous system (PNS)
  - Peripheral nerves

- Encephalopathy/Encephalitis
- Leukoencephalopathy
- Aseptic meningitis

Parts of the brain

- Brain stem – controls reflexes and autonomic functions (cardiorespiratory center)
  - Medulla
  - Pons
  - Midbrain
- Hypothalamus – controls hunger/thirst, sleep, and temperature
- Cerebellum – coordination and movement, balance, speech, gait, handwriting, ataxia
- Cerebrum (cerebral cortex) – memory and thought processes

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# Neurological Assessment

Motor
- Balance
- Foot drop/atrophy
- Reflexes
- Ototoxicity (CNVIII)

Sensory
- Numbness
- Tingling
- Burning sensation
- Sensitivity to temperature
- Limb "falling asleep"
- "Stocking and glove" feeling
- "Electric shock" pain

Autonomic
- Orthostatic hypotension, Bowel and bladder dysfunction (paralytic ileus, constipation, urinary retention), , erectile dysfunction,

Cognitive
(destroys grey and white matter)
- Attention span
- Comprehension
- Following directions
- Distractions
- Processing information
- Numbers or finances
- Details, names, or dates
- Manual dexterity or walking
- Recognizing familiar objects
- Multitasking
- Short-term memory
- Behavior, especially in social settings

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# Neurological Toxicity Management

Pharmacologic
- Dose modification of the neurotoxic agent is the 'gold standard'
- Opioid and NSAID analgesics are ineffective
- Strongest evidence for duloxetine (Cymbalta)
- Consider use of TCAs, gabapentin, pregabalin, topical gel containing baclofen, tricyclic antidepressants, amitriptyline, and ketamine, serotonin and norepinephrine reuptake inhibitors (SNRIs), anti-epileptics

Non-pharmacologic
- Psychological, physical, and/or occupational therapy
- Relaxation
- Massage
- Acupuncture
- Audiogram

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# Cardiovascular Toxicity

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| **Cardiac/PV** | | | | |
| Hypertension | Systolic BP 120-139 mm Hg or diastolic BP 80-89 mm Hg | Systolic BP 140-159 mm HG or diastolic BP 90-99 mm Hg if previously WNL; change in baseline medical intervention indicated;<br><br>recurrent or persistent (>=24 hours); symptomatic increase by >20mm Hg (diastolic) or to >140/90 mm Hg; monotherapy indicated initiated | Systolic BP >160 mm Hg or diastolic BP >100 mm Hg; medical intervention indicated; more than one drug or more intensive therapy the previously used indicated | Life-threatening consequences (ie malignant HTN; transient or permanent neurologic deficit; HTN crises); urgent intervention indicated crises) |
| Hypotension | Asymptomatic, intervention not indicated | Non-urgent medical intervention indicated | medical intervention indicated; hospitalization indicated | life threatening consequences; urgent intervention) |
| Edema | 1+ noted on exam; localized to dependent areas; no disability or functional impairment | Moderate localized edema; limiting instrumental ADL; intervention indicated | Severe localized edema; intervention indicated; limiting self-care ADLs; | life threatening consequences |

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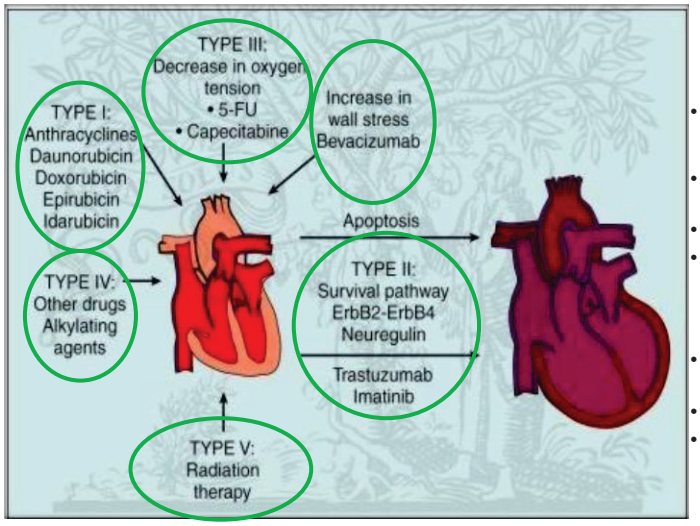
# Cardiotoxicity




- **Cardiomyopathy**
  - **heart failure/left ventricle dysfunction**
- **Myocardial ischemia/infarction**
- **Hypertension**
- **Arrhythmias**
  - **QT prolongation, bradycardia, atrial fibrillation**
- **Pericarditis, pericardial effusion**
- **CHF**
- **Thromboembolism**

Abeloff et al. Cardiac Effects of Cancer Therapy Page: 985

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# Cardiovascular Assessment and Management

- Prior to beginning therapy: baseline Echo or MUGA
  - EF greater than or equal to 50%
- Baseline ECG
  - Repeat about every 3 months
- Cardiac toxicity suspected if >10-20% decrease in LVEF
- Complications can occur at the time of treatment or any time after therapy
- Assess for signs and symptoms of toxicity before each treatment/visit
- Assess for electrolyte abnormalities on routine labs
  - KCL, magnesium, phosphorous,calcium
- Monitor renal function
  - BUN, creatinine
- Blood Pressure, edema, dyspnea on exertion, orthopnea, JVD, weight gain, fatigue, cough, dullness at the lung bases

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# Thromboembolism (PE, VTE)

- **Cancer induces hypercoagulable state-** 7 to 10-fold increased risk
- Risk depends on disease status, use of steroids, use of proper thromboprophylaxis, patient mobility etc.
- Unknown clear cause
- Some meds may induce platelet aggregation and also cause interaction between platelets and the endothelium

**Chemotherapy**
Some agents can cause chemical phlebitis, inhibit synthesis of coagulation factors)

**Targeted Therapy**
Thalidomide -Lenalomide
Palomide -Bevacizumab

**Growth Factors**
Epoetin alpha
Darbopoetin

**Hormonal Therapy**

**Combination Regimens**

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**Table 5.** Predictive Model for Chemotherapy-Associated VTE in the Ambulatory Setting

| Patient Characteristic | Points |
|---|---|
| Site of cancer | |
| Very high risk (stomach, pancreas, primary brain tumor) | 2 |
| High risk (lung, lymphoma, gynecologic, bladder, testicular, renal tumors) | 1 |
| Prechemotherapy platelet count ≥ 350,000/μL | 1 |
| Hemoglobin level < 10 g/dL or use of red-cell growth factors | 1 |
| Prechemotherapy leukocyte count > 11,000/μL | 1 |
| Body mass index ≥ 35 kg/m$^2$ | 1 |
| Calculate total score, adding points for each criterion in the model | |
| Interpretation: | |
| High risk ≥ 3 points | |
| Intermediate risk, 1 to 2 points | |
| Low risk, 0 points | |

NOTE. Data adapted.[88]
Abbreviation: VTE, venous thromboembolism.

**Unfractionated Heparin**

- **5,000 units/SubQ Q8H (prophylaxis)**

**LMWH**

- **Enoxaparin**
  - **30 mg sq bid/40 mg sq daily**
  - **1mg/kg sq bid, 1.5mg/kg sq daily**
- **Tinzaparin**
  - **175 units/kg sq daily**
- **Dalteparin**
  - **5000 units sq daily, then 2500 units in subacute setting**
- **Fondaparinux**
- **Warfarin**
  - **Avoid in malignancies**

**Platelet-inhibitors**

- **ASA, NSAIDS etc.**

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# Respiratory

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| **Respiratory** | | | | |
| Cough | Mild symptoms; non-prescription intervention indicated | Moderate symptoms; medical intervention indicated; limiting instrumental ADL | Severe symptoms; limiting self-care ADL | ---------- |
| Dyspnea | Shortness of breath with moderate exertion | Shortness of breath with minimal exertion; limiting instrumental ADL | Shortness of breath at rest; limiting self-care ADL | Life-threatening consequences; urgent intervention indicated |
| Hiccups | Mild symptoms; intervention not indicated | Moderate symptoms; medical intervention indicated; limiting instrumental ADL | Severe symptoms; interfering with sleep; limiting self-care ADL | ---------- |

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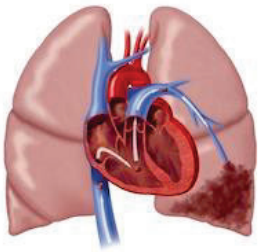
# Pulmonary Toxicity

- Range from reversible short-term airway disease to diffuse permanent fibrosis and structural destruction
- Interstitial Lung Disease (ILD)
- Pneumonitis
- Acute
  - Within minutes to a few months
    - Bronchospasm
    - Hypersensitivity
    - Pneumonitis
    - Alveolar hemorrhage
    - Differentiation/retinoic acid syndrome
    - Interstitial pneumonitis
- Chronic
  - Months to years after
    - Progressive pneumonitis
    - Pulmonary fibrosis
    - Interstitial lung disease (ILD)
- Indeterminate
  - Undefined and unclear



21

# Pulmonary Assessment and Management

- PMH
  - Age
  - Tobacco
  - Occupation
  - Deteriorating creatinine clearance
  - Prior lung disease
  - Autoimmune disease
  - COPD
  - GVHD
  - Thoracic radiation
- Tachypnea
- Crackles
- Cough +/- hemoptysis
- Pleuritic pain
- ABGs – respiratory alkalosis
- Chest X-ray and CT
- PET
- Bronchoscopy

- Bronchodilator
- Strict I&O
- PFT's baseline an every 3 months
- Steroid treatment
- Oxygen
- CXR
- Educate on toxicity, HOB>30, opioids

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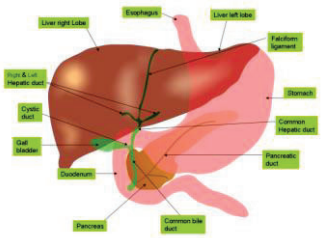
# Hepatic Toxicity

- Usually transient and asymptomatic
- Caused by direct toxic effect to the liver resulting from drug metabolism
- Disruption of hepatocytes with apoptosis of the hepatocytes
- Fatty changes, hepatocellular necrosis, parenchymal cell damage, cholestasis, hepatic fibrosis
- Disruption of transport proteins
- Cytotoxic T-cell activation
- Bile duct injury
- CYP protein
- Race has variable toxicities
- More common in females
- Comorbidities (obesity, diabetes, malnutrition )
- History transplant, alcohol, infections, hepatitis
- Veno Occlusive Disease/Sinusoidal Obstruction Syndrome






# Hepatic Assessment and Management

Assessment

- Elevated aminotransferases = hepatocellular injury/portal hypertension
- Elevated bilirubin and alkaline phosphatase = cholestasis
- Jaundice
- Pruritus
- Dark urine
- Hepatomegaly
- Coagulopathy
- Hepatic encephalopathy
- GI symptoms, ascites, nausea, RUQ pain

Management

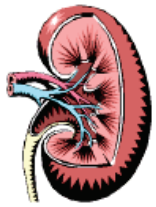
- LFT's (TB <1.2mg/100dl)
- LDH
- DIC screens/CBC/Diff/Plt
- Amylase/Lipase levels
- Educate on U/S, lab work, avoid alcohol

**Elevated LDH (140 units per liter (U/L) to 280 U/L)**

- levels are the product of enhanced glycolytic activity of the tumor and tumor necrosis due to hypoxia, the latter being associated with high tumor burden

# Genitourinary Toxicities – Nephrotoxicity

- Direct damage to glomerulus, renal blood vessels, and/or nephrons (tubular atrophy)
- Damage may be irreversible and lead to necrosis – no new nephrons – (born 1 million)
- Precipitation of metabolites in acid environment of urine and causes obstructive nephropathy (esp with tumor lysis syndrome
- Impaired water excretion or water intoxication (SIADH)
- Decreased renal perfusion



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# Genitourinary Toxicities – Nephrotoxicity

Assessment and Management

- Age (increased age = decreased kidney size and function)
- Nutritional status
- Other medications
- Serum BUN>22 and creatinine >1.5mg/dL
- Creatinine clearance decreased (>60ml/min)
- ARF
- Tumor lysis
- Daily electrolytes magnesium, calcium decreased
- Chronic comorbidities
- Hematuria
- Edema
- Hypertension
- Weight gain
- Renal ultrasound

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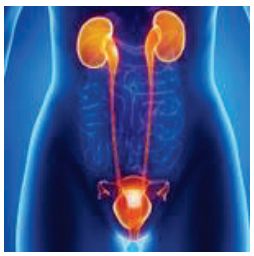
# Genitourinary Toxicities – Bladder

- Hemorrhagic cystitis
- BK virus
- Urinalysis
- Mesna
- Bladder irrigations
- Hydration
- Urine alkalization



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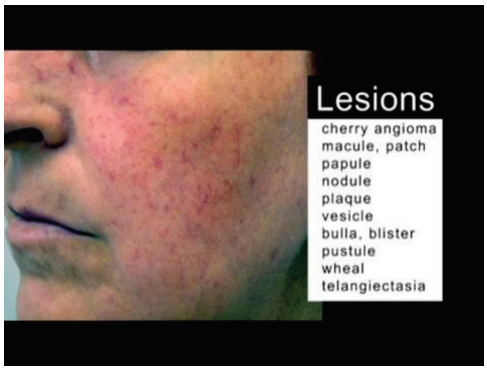
# Integumentary Toxicities

- Risk factors:
  - Age, gender, fair skin, UV exposure, smoking, combination with chemo
- Acneiform rash
- Papules
- Blisters
- Lesions
- Wounds
- Color
- Texture
- Moisture
- Integrity
- Skin turgor
- Moles
- Petechiae
- Hyperpigmentaiton
- Nail changes




https://www.google.com/search?q=integumentary+assessment&safe=active&source=lnms&tbm=isch&sa=X&ved=2ahUKEwj-2NKAzb36AhVlGVkFHUQiAplQ_AUoAXoECAIQAw&biw=1280&bih=577&dpr=1.5#imgrc=mzwGVbtg277BtM

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# Integumentary
# Papulopustular (Acneiform) Rash

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| **Integumentary** | | | | |
| Rash/ Acne/ Acneiform | Papules and/or pustules covering <10% BSA, which may or maynot be associated with symptoms of pruritus or tenderness | Papules and/or pustules covering 10-30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL; papules and or pustules covering >30% BSA with or without mild symptoms | Papules and/or pustules covering >30% BSA with moderate or severe symptoms; limiting self-care ADL; associated with local superinfection with oral antibiotics indicated | Life threatening consequences; papules and/or pustules covering any % BSA, which may or may not be associated with symptoms of pruritus or tenderness and associated with extensive superinfection with IV antibiotic indicated |

- Occurs in up to 80% of patients
- Presents in skin with high density of sebaceous glands
  - Scalp, face, upper chest, back
- May include pain, pruritus, irritation, stinging
- Risk factors:
  - Age, gender, fair skin, UV exposure, smoking, combination with chemotherapy
- Initial pustules sterile, may develop secondary bacterial infection
- May be surrogate marker for efficacy
- Resolution within 4 weeks of treatment discontinuation
- May wax and wane, and improve or resolve spontaneously without stopping treatment

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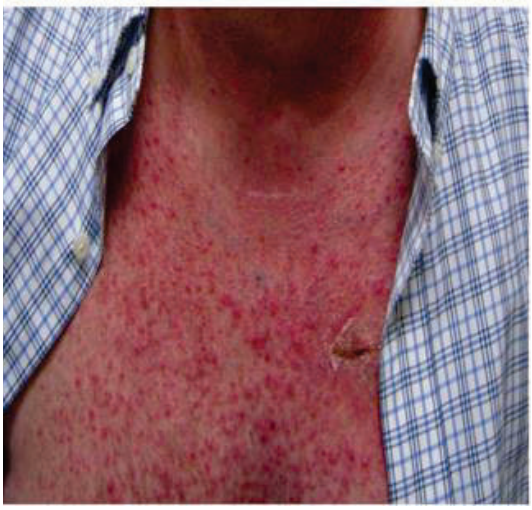
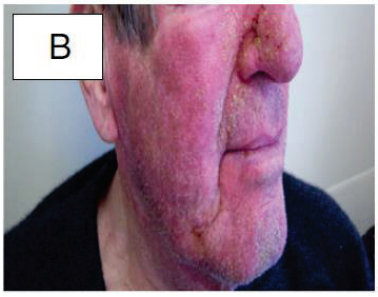
# Integumentary
# Papulopustular Rash



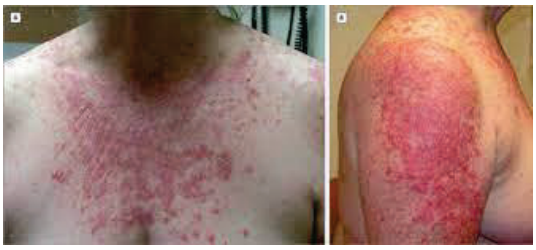


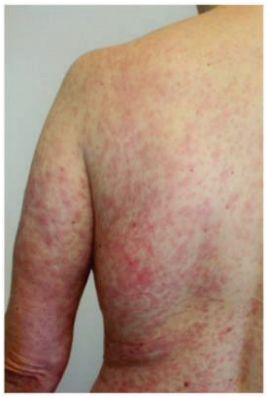

Lacouture ME, et al. *Support Care Cancer.* 2011;19:1079-1095.

30

# Integumentary
# Immune-Mediated Maculopapular

- Maculopapular rash – also most common
  - Characterized by macules (flat) and papules (elevated)
  - Also known as morbilliform rash
  - Frequently affects upper trunk





Brahmer JR, et al. *J Clin Oncol*. 2018; 36(17):1714-1768.
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Management of Immunotherapy-Related Toxicities. Version 1.2020. nccn.org
Kähler KC, et al. *J Dtsch Dermatol Ges*. 2016;14(7):662-81.



# Integumentary -Maculopapular Rash

| Grade | Presentation | Management |
|---|---|---|
| 1 | Macules/papules covering < 10% BSA +/- symptoms | • Continue immunotherapy<br>• Topical emollient<br>• Oral antihistamine for pruritus<br>• Moderate potency topical steroids to affected area |
| 2 | Macules/papules covering 10-30% BSA +/- symptoms; limiting instrumental ADLs | • Continue immunotherapy and monitor weekly<br>• Topical emollient<br>• Oral antihistamine for pruritus<br>• Moderate – high potency topical steroids to affected areas AND/OR<br>• Prednisone 0.5-1 mg/kg/day |
| 3-4 | Macules/papules covering > 30% BSA +/- symptoms; limiting self-care ADLs | • Hold immunotherapy<br>• High potency topical steroids to affected areas<br>• Prednisone 0.5-1 mg/kg/day (may ↑ up to 2 mg/kg/day if no improvement)<br>• Urgent dermatology consult; consider biopsy<br>• Consider inpatient care |

- Symptoms may include pruritus, burning, tightness
- Taper steroids over at least 4 weeks
- Avoid skin irritants and sun exposure
- For grade 2 steroid use – treat until symptoms improve to grade 1 or less and then taper over 4-6 weeks

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Management of Immunotherapy-Related Toxicities. Version 1.2020. nccn.org

# Integumentary
# Palmar-Plantar Erythrodysesthesia (PPE)/Hand-Foot Syndrome – HFS)

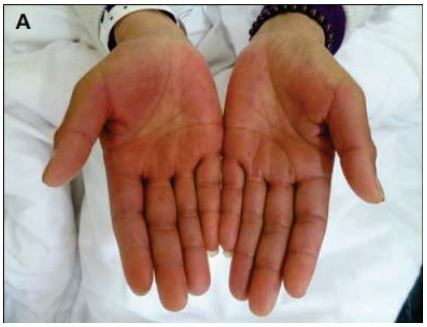
- A disorder characterized by redness, marked discomfort, swelling, and tingling in the palms of the hands or the soles of the feet
- Also known as Hand-Foot Syndrome (HFS)
- Symmetric erythema and edema in palms and soles
- Palmoplantar dysesthesia
  - Tingling sensation → burning pain
  - Pain and temperature sensation reduced
  - Erythema and edema with onset of neuropathic symptoms
    - Erythema → blistering → desquamation, erosion, ulceration
- Symptoms recur with repeated exposure
- Occurs in 60% patients receiving fluorouracil, capecitabine. docetaxel, liposomal doxorubicin
- May lose fingerprints (not permanent)

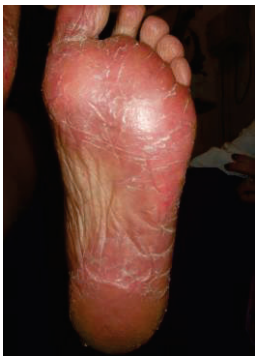
CTCAE Version 5.0



# Integumentary – PPE/HFS Grading

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| Palmer-plantar erythrodyses-thesia (PPE) Hand/Foot Syndrome | Minimal skin changes or dermatitis (e.g. erythema. Edema, hyperkeratosis without pain | Skin changes (e.g. peeling, blisters, bleeding, fissures, edema, hyperkeratosis) with pain limiting instrumental ADL | Severe skin changes (e.g. peeling, blisters, bleeding, fissures,edema, hyperkeratosis ) with main; limiting self-care ADL | _____ |

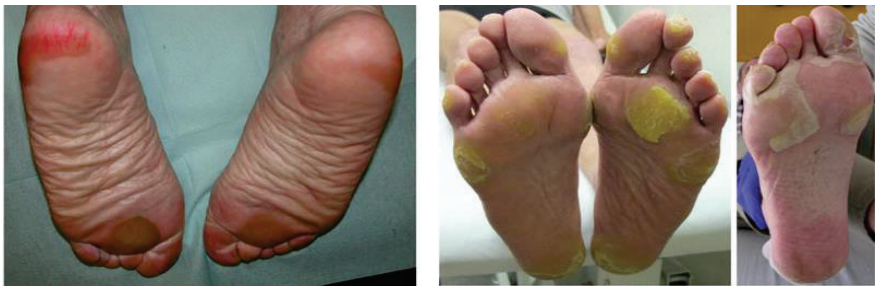


Qiao J, Fang H. *CMAJ.* 2012;184(15):E818. Miller KK, et al. *J Am Acad Dermatol.* 2014;71(4):787-94.

# Integumentary – Hand Foot Skin Reaction (HFSR)

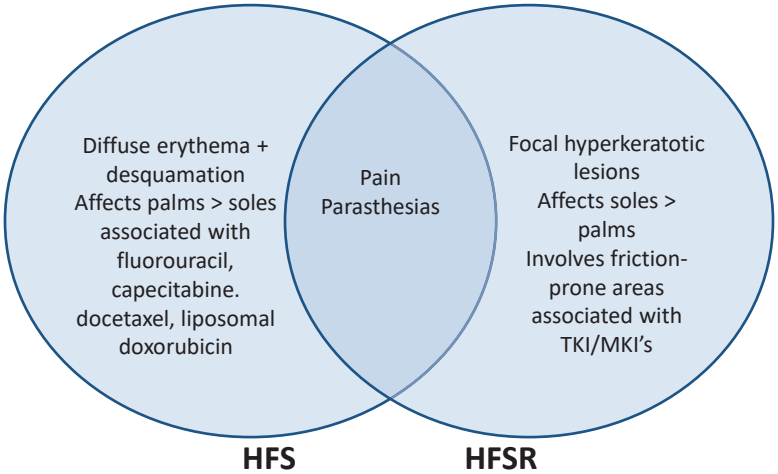
- Hand-foot skin reaction (HFSR) most common cutaneous AE with Tyrosine Kinase Inhibitors (TKIs)
- Dose-dependent and characteristically localizes to areas of **pressure or friction** on the skin, such as on the heels, metatarsal heads, and areas of friction caused by shoes or manual labor - localized, tender lesions over areas subject to friction/trauma
- Incidence varies by drug, up to 62-92%
- Occurs in initial 2-6 weeks of treatment
- Lesions usually painful, may include paresthesia, tingling, burning, soreness of palms and soles, and ↓ tolerance of contact with hot objects – then blisters and hyperkeratotic skin



McLellan B, et al. *Ann Oncol.* 2015;26:2017-2026.
Miller KK, et al. *J Am Acad Dermatol.* 2014;71(4):787-94.

35

# Integumentary HFS vs. HFSR




Miller KK, et al. *J Am Acad Dermatol.* 2014;71(4):787-94.

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# Integumentary – HFS/HFSR Treatment

- Most effective - dose interruption or modification
- Symptoms typically improve within 1-2 weeks
- Grades 2-3 = dose interruption
- Grade 3 = dose reduction

- Avoid direct sunlight and use sunscreen SPF ≥ 30
- Avoid hot baths/showers
- Avoid alcohol-based or fragranced skin care products
- Do not treat like acne!
- Moisturize

- Supportive measures:
  - topical corticosteroids, wound care, emollients and topical keratolytics, analgesics
- Hydrocortisone 1% + moisturizer + sunscreen + doxycycline BID x 6 weeks
- Oral Tetracyclines
  - Prevention vs treatment
    - Doxycycline
    - Minocycline – less photosensitizing
- Systemic steroids not typically used

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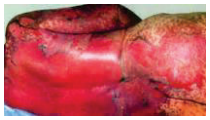
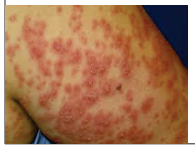
# Severe Cutaneous Adverse Reactions (SCAR)

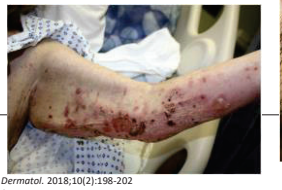
- thought to be T-cell mediated delayed hypersensitivity reactions
- can be caused by autoimmunity and a number of allergens, including bacteria and viruses
- Types:
  - Bullous dermatitis (most common bullous pemphigoid)
  - Stevens-Johnson Syndrome (SJS)
  - Toxic epidermal necrolysis (TEN)
  - Acute generalized exanthematous pustulosis
  - Drug Reaction with Eosinophilia and System Symptoms (DRESS)/Drug induced hypersensitivity syndrome (DIHS)

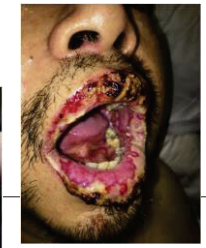


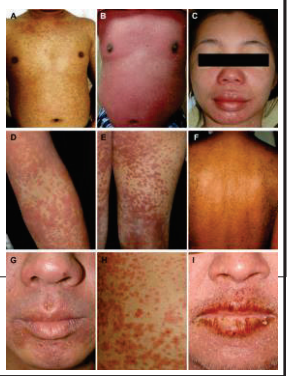
**Management**:

- Urgent dermatology, ophthalmology, and urology consultation (skin biopsy)
- Permanently discontinue immunotherapy
- Prednisone/methylprednisolone 1-2 mg/kg/day
- Consider IVIG
- Inpatient care necessary









Chirasuthat P, Chayavichotsilp P. *Case Rep Dermatol.* 2018;10(2):198-202
Coleman EL, et al. *Clin Dermatol.* 2020;38(1):94-104.

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# Sexual and Reproductive Functioning

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| **Reproductive** | | | | |
| Sexual/Libido | Decreased in sexual interest not adversely affecting relationship | Decrease in sexual interest adversely affecting relationship | | |

- assess decreased libido, sleep disturbances, hot flashes (hormonal changes), irritability, difficulty reaching orgasm, erectile dysfunction, vaginal dryness and stenosis, retrograde ejaculation
- concurrent sedatives, anti-hypertensives, narcotics, antidepressants
- age, stress
- XRT
- educate on sperm banking, ovary banking, water based lubricants, discuss pregnancy and contraception

**PLISSIT – (permission, limited information, specific suggestions, intensive therapy)**
**BETTER – (bring up, explain, tell, timing, educate, record)**

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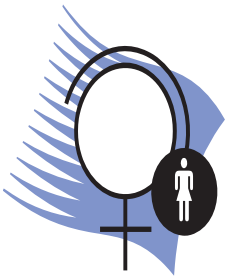
# Sexual and Reproductive Functioning



- Sterility
- Impotence
- Testicular atrophy
- Premature menopause
- Libido

- Caused by biological process of cancer, effects of treatment, psychological issues
- Women <35 can tolerate higher doses with continues menses
- Alkylating agents have 80-90% irreversible infertility
- 40-100% patients report some dysfunction
- Frequently unreported

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# Sexual and Reproductive Functioning

- Male infertility occurs with depletion of epithelium lining of seminiferous tubules
- Testicular volume decreases resulting in oligospermia or azoospermia and infertility

- Female infertility occurs with hormonal changes or direct effects that cause ovarian fibrosis and follicular destruction
- Premature ovarian failure
- FSH and LH are elevated with estradiol decreased causing menopausal symptoms

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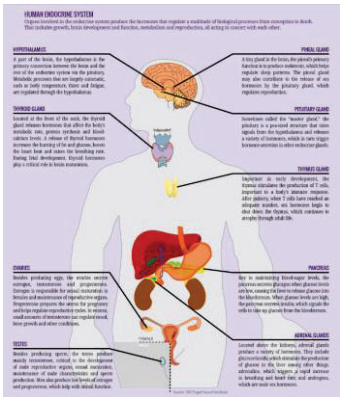
# Endocrine Toxicities

- Adrenal, thyroid, pituitary
- Hyperthyroidism
- Hypothyroidism
- Hypophysitis
  - fatigue and headache
- Hyperglycemia
- Adrenal insufficiency
- Thyroiditis

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# Ocular Toxicities

- Blepharitis – inflammation of eyelids
- Trichomegaly – abnormal growth of eyelashes
- Ectropion – lower lid pulls away from the eye
- Dysfunctional tears
- Corneal tears
- Conjunctivitis – damage to epithelial layer of lining of sclera
- Diplopia – double vision
- Keratitis – inflammation of the cornea
- Photophobia
- Uveitis – inflammation of the iris
- Epiphora – watery eyes
- Optic neuritis
- Periorbital/eyelid edema
- Serious retinal detachment
- Retinal vein occlusion and/or detachment
- Maculopathy- disease or damage to macula or retina

Management

- Warm and/or cool compresses
- Eyelid scrubs
- Artificial tears
- Steroid eye drops
- Antihistamine eye drops
- Baby shampoo
- Topical antibiotic ointment and/or steroids
- Sunglasses
- Low sodium diet
- Sleep with head elevated
- Ophthalmologist

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# Alopecia

- Hair cells have high mitotic and metabolic rate
- Damage is to shaft (thinning and breakage)
- Damage to roots (complete alopecia)
- Loss begins about 2 weeks after treatment
- Re-growth may take up to 3-5 months after treatment- average daily growth of shaft is 0.35mm

- Assess for chemotherapy medications (most all have some degree)
- Educate when to expect loss and re-growth, refer to "Look Good/Feel Better“
- Instruct on gentle hair care, no permanent waves, coloring, dryers, irons, ice caps, or hypothermia
- All hair
- Scalp cooling

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# Fatigue

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| Fatigue | Relieved by rest | Not relieved by rest; limiting instrumental ADL | not relieved by rest; limiting self-care ADL | |

- 50-100% patients (most common and distressing symptom of cancer patients)
- Related to disease, biochemical imbalance, deconditioning, stress, treatment, quality of rest/sleep, nutrition, functional status
- Altered sleep patterns, depression, anxiety, environmental factors
- Assess nutrition, pain, nutrition, sleep
- Obtain PT/OT consults
- Educate and encourage exercise, rest, imagery, nutrition

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# Hypersensitivity and Anaphylaxis

**Taxanes**

- Primarily due to the release of pro-inflammatory cytokines (IL-2 and TNFa)
- More solvent related reactions and mast cell activation to the solvents
- Pre-meds are a **MUST**
  - H1 – diphenhydramine (suppress antihistamine release)
  - H2- famotidine (suppress gastric acid)
  - Steroids – dexamethasone
- Usually occur within first 15 minutes, but can be delayed

**Monoclonal Antibodies**

- Antigen/antibody reaction that is IgE mediated
- Premeds help
- Can be immediate or delayed

**Platins**

- Premedication is not helpful
- Patients react to the platin salts
- These are IgE medicated reactions therefore most patients react after few doses
  - Carboplatin typically with 4th -6th doses
  - Oxaliplatin has 2 peaks
    - 1st with 3rd cycle
    - Then 6th cycle
- Patient may require desensitization protocols

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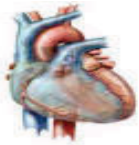
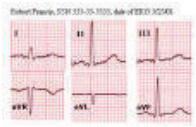
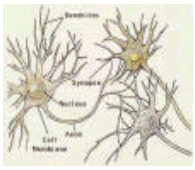
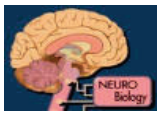
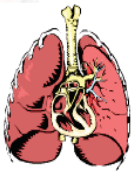
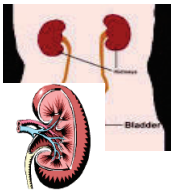
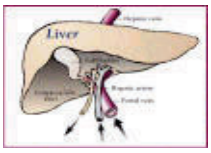
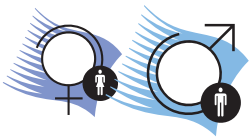







# LATE EFFECTS





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## Hypersensitivity and Anaphylaxis

**Risk Factors**

- history skin reactions
- respiratory dysfunction
- overweight/obesity
- menopausal/post-menopausal
- females more than males
- allergies to other drugs
- LDH levels
- higher neutrophil counts and lower monocyte counts
- higher during second line treatments
- recurrent drug exposure
- history IV contrast reaction
- older age (rituximab)
- younger age (oxaliplatin)
- more than 12 months exposure for Carboplatin
- verify beta blocker - yes/no – med assessment – take/not take what about the day?
- bring meds to visit

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| Types of Reactions – Pathways of Anaphylaxis | | | | |
|---|---|---|---|---|
| **Triggers** | Environmental allergens; Food allergens; Chemotherapy; MABs; Other Drugs | Chemotherapy MABs | Chemotherapy MABs | Contrast Dyes; Dyalisis membranes; glycosaminogly cans |
| **Phenotype** | Type I IgE/non IgE | Cytokine release | Mixed | Complement |
| **Endotypes** | Mast cells, basophils | T-cells, macrophages, monocytes; | T-cells, macrophages, monocytes; Basophils, mast cells, | Mast cell, basophils |
| **Biomarkers** | histamine, tryptase | IL, TNF | IL, TNF histamine, tryptase | histamine, tryptase |
| **Symptoms** | Flushing, pruritis, urticaria, throat tightness, SOB, back pain, N/V/D, CV collapse | Fever, chills, rigors, nausea, pain, headache, hypotension, O2 desaturation | Fever, chills, rigors, nausea, pain, headache, Flushing, pruritis, urticaria, throat tightness, SOB, back pain, N/V/D, CV collapse | Hypotension, oxygen desaturation |
| **Treatment** | **Epinephrine** | | | |

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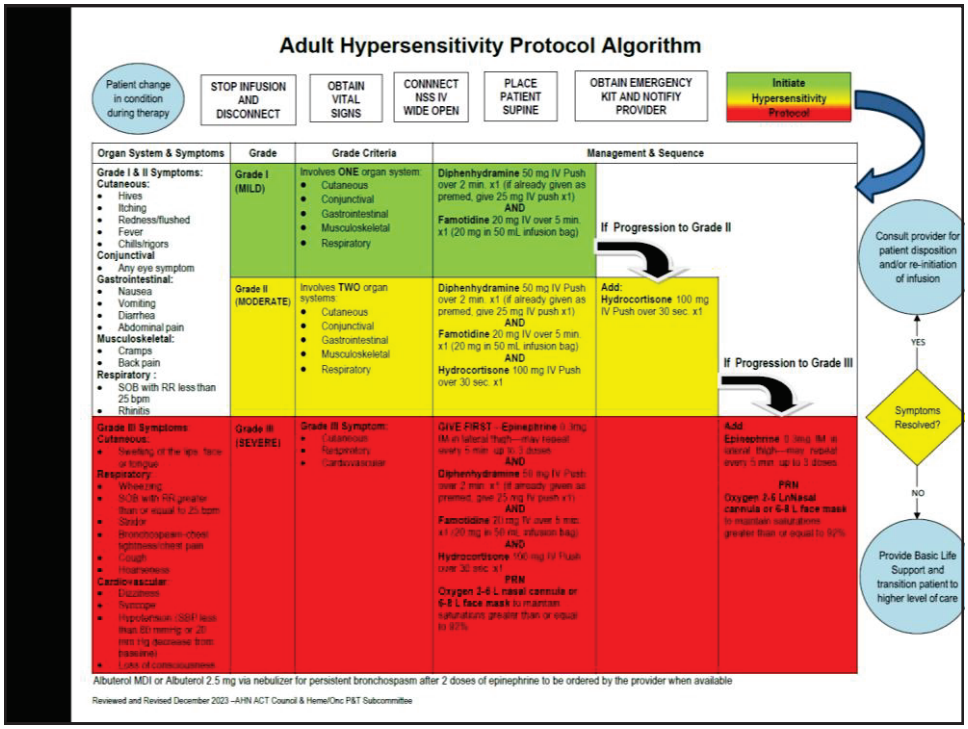


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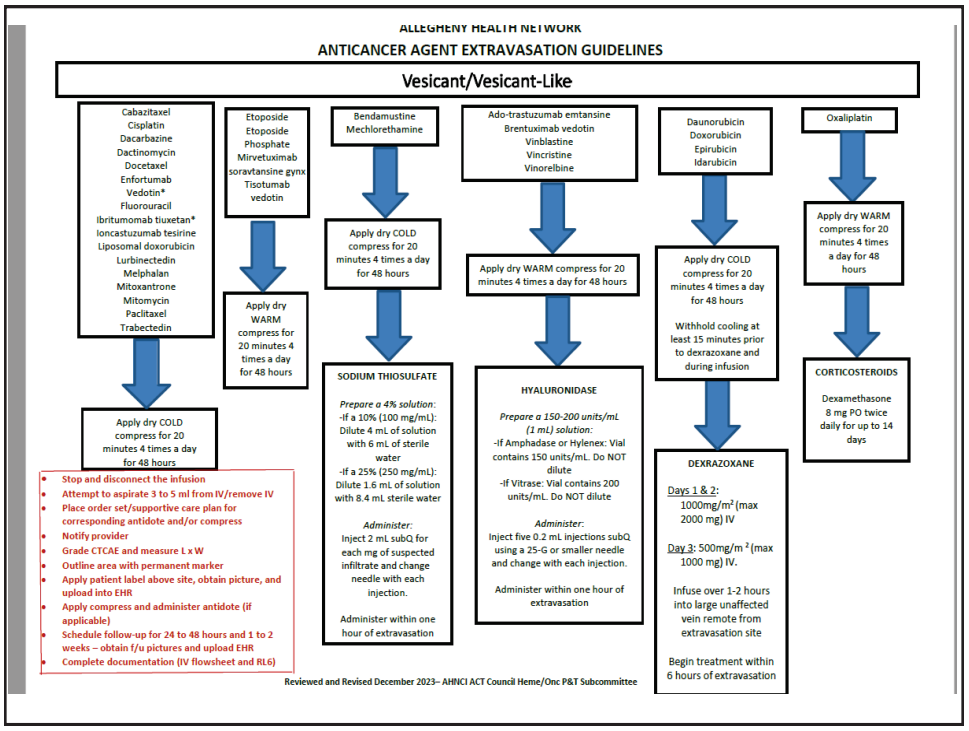
ALLEGHENY HEALTH NETWORK
ANTICANCER AGENT EXTRAVASATION GUIDELINES
Vesicant/Vesicant-Like
Cabazitaxel
Cisplatin
Dacarbazine
Dactinomycin
Docetaxel
Enfortumab Vedotin*
Fluorouracil
Ibritumomab tiuxetan*
Ioncastuzumab tesirine
Liposomal doxorubicin
Lurbinectedin
Melphalan
Mitoxantrone
Mitomycin
Paclitaxel
Trabectedin
Apply dry COLD compress for 20 minutes 4 times a day for 48 hours
Etoposide
Etoposide Phosphate
Mirvetuximab soravtansine gynx
Tisotumab vedotin
Apply dry WARM compress for 20 minutes 4 times a day for 48 hours
Bendamustine
Mechlorethamine
Apply dry COLD compress for 20 minutes 4 times a day for 48 hours
SODIUM THIOSULFATE
Prepare a 4% solution:
-If a 10% (100 mg/mL): Dilute 4 mL of solution with 6 mL of sterile water
-If a 25% (250 mg/mL): Dilute 1.6 mL of solution with 8.4 mL sterile water
Administer:
Inject 2 mL subQ for each mg of suspected infiltrate and change needle with each injection.
Administer within one hour of extravasation
Ado-trastuzumab emtansine
Brentuximab vedotin
Vinblastine
Vincristine
Vinorelbine
Apply dry WARM compress for 20 minutes 4 times a day for 48 hours
HYALURONIDASE
Prepare a 150-200 units/mL (1 mL) solution:
-If Amphadase or Hylenex: Vial contains 150 units/mL. Do NOT dilute
-If Vitrase: Vial contains 200 units/mL. Do NOT dilute
Administer:
Inject five 0.2 mL injections subQ using a 25-G or smaller needle and change with each injection.
Administer within one hour of extravasation
Daunorubicin
Doxorubicin
Epirubicin
Idarubicin
Apply dry COLD compress for 20 minutes 4 times a day for 48 hours
Withhold cooling at least 15 minutes prior to dexrazoxane and during infusion
DEXRAZOXANE
Days 1 & 2: 1000mg/m² (max 2000 mg) IV
Day 3: 500mg/m² (max 1000 mg) IV.
Infuse over 1-2 hours into large unaffected vein remote from extravasation site
Begin treatment within 6 hours of extravasation
Oxaliplatin
Apply dry WARM compress for 20 minutes 4 times a day for 48 hours
CORTICOSTEROIDS
Dexamethasone 8 mg PO twice daily for up to 14 days
Stop and disconnect the infusion
Attempt to aspirate 3 to 5 ml from IV/remove IV
Place order set/supportive care plan for corresponding antidote and/or compress
Notify provider
Grade CTCAE and measure L x W
Outline area with permanent marker
Apply patient label above site, obtain picture, and upload into EHR
Apply compress and administer antidote (if applicable)
Schedule follow-up for 24 to 48 hours and 1 to 2 weeks – obtain f/u pictures and upload EHR
Complete documentation (IV flowsheet and RL6)
Reviewed and Revised December 2023– AHNCI ACT Council Heme/Onc P&T Subcommittee

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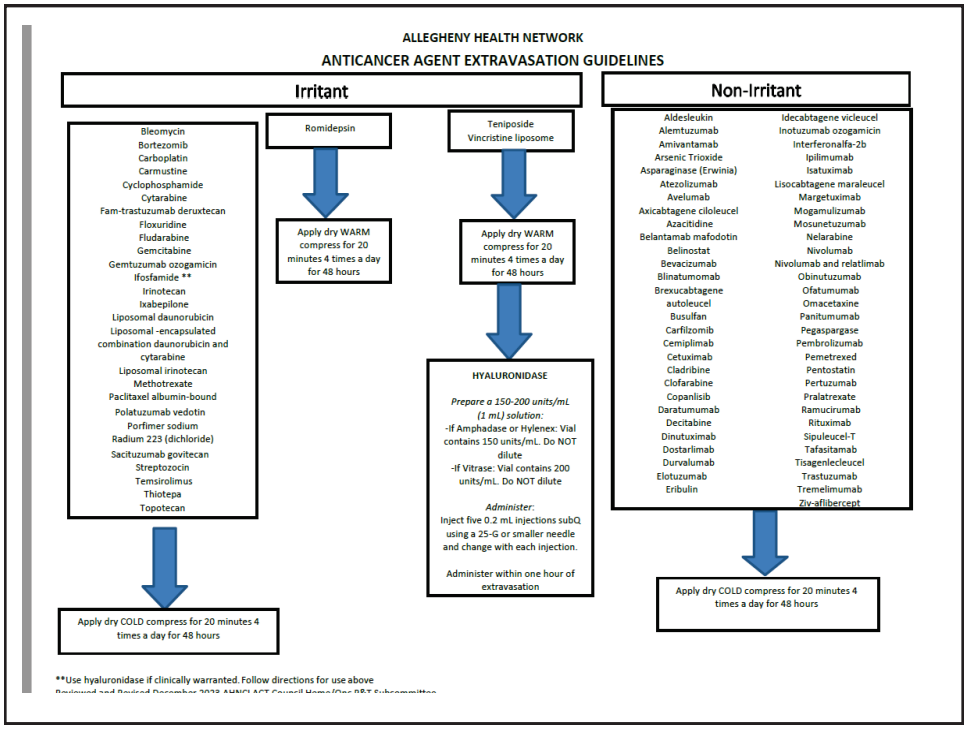
ALLEGHENY HEALTH NETWORK
ANTICANCER AGENT EXTRAVASATION GUIDELINES
Irritant
Bleomycin
Bortezomib
Carboplatin
Carmustine
Cyclophosphamide
Cytarabine
Fam-trastuzumab deruxtecan
Floxuridine
Fludarabine
Gemcitabine
Gemtuzumab ozogamicin
Ifosfamide **
Irinotecan
Ixabepilone
Liposomal daunorubicin
Liposomal -encapsulated combination daunorubicin and cytarabine
Liposomal irinotecan
Methotrexate
Paclitaxel albumin-bound
Polatuzumab vedotin
Porfimer sodium
Radium 223 (dichloride)
Sacituzumab govitecan
Streptozocin
Temsirolimus
Thiotepa
Topotecan
Apply dry COLD compress for 20 minutes 4 times a day for 48 hours
Romidepsin
Apply dry WARM compress for 20 minutes 4 times a day for 48 hours
Teniposide
Vincristine liposome
Apply dry WARM compress for 20 minutes 4 times a day for 48 hours
HYALURONIDASE
Prepare a 150-200 units/mL (1 mL) solution:
-If Amphadase or Hylenex: Vial contains 150 units/mL. Do NOT dilute
-If Vitrase: Vial contains 200 units/mL. Do NOT dilute
Administer:
Inject five 0.2 mL injections subQ using a 25-G or smaller needle and change with each injection.
Administer within one hour of extravasation
Non-Irritant
Aldesleukin
Alemtuzumab
Amivantamab
Arsenic Trioxide
Asparaginase (Erwinia)
Atezolizumab
Avelumab
Axicabtagene ciloleucel
Azacitidine
Belantamab mafodotin
Belinostat
Bevacizumab
Blinatumomab
Brexucabtagene autoleucel
Busulfan
Carfilzomib
Cemiplimab
Cetuximab
Cladribine
Clofarabine
Copanlisib
Daratumumab
Decitabine
Dinutuximab
Dostarlimab
Durvalumab
Elotuzumab
Eribulin
Idecabtagene vicleucel
Inotuzumab ozogamicin
Interferonalfa-2b
Ipilimumab
Isatuximab
Lisocabtagene maraleucel
Margetuximab
Mogamulizumab
Mosunetuzumab
Nelarabine
Nivolumab
Nivolumab and relatlimab
Obinutuzumab
Ofatumumab
Omacetaxine
Panitumumab
Pegaspargase
Pembrolizumab
Pemetrexed
Pentostatin
Pertuzumab
Pralatrexate
Ramucirumab
Rituximab
Sipuleucel-T
Tafasitamab
Tisagenlecleucel
Trastuzumab
Tremelimumab
Ziv-aflibercept
Apply dry COLD compress for 20 minutes 4 times a day for 48 hours
**Use hyaluronidase if clinically warranted. Follow directions for use above

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# The Experience of Financial Toxicity

- 42% of insured patients with cancer express a significant or catastrophic financial burden
- A survey of patients with breast cancer showed that 94% of this population wanted to discuss cost of treatment but only 14% of them reported having that conversation
- A 2015 study showed a direct correlation between cancer-related financial burden (CRFB) and qualify of life; higher CRFB scores correlated with lower qualify-of-life scores
- 27% of insured adult patients with cancer reported medication nonadherence due to cost
- An estimated 42% of patients aged 50 years or older diagnosed with cancer depleted their entire life's assets

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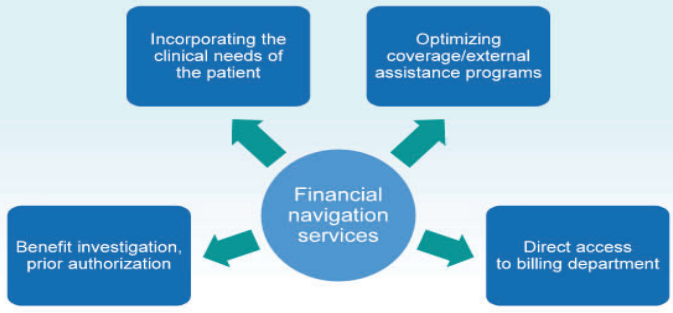
# Part of the Multidisciplinary Team

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Allegheny Health Network

## Models of Financial Advocacy Programs

**Financial counselors**
- Medicaid enrollment
- Charity programs

**Social worker/financial advocate**
- Copay and patient assistance program (PAP) help
- Basic needs

**Financial navigation**
- Insurance optimization
- Part of multidisciplinary team
- Involved with treatment plan
- Navigates our complex health insurance landscape

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## Summary Slide

- CTCAE
- Anticancer Toxicity
  - Chemotherapy and targeted therapy
  - Immunotherapy
  - Hormonal
- Performance Status
  - ECOG
  - Karnofsky

- Neurological
- Cardiovascular
- Peripheral Vascular/VTE/PE
- Pulmonary
- Respiratory
- Hepatic
- Genitourinary
- Integumentary
- Reproductive/Sexual
- Endocrine
- Ocular
- Alopecia
- Fatigue
- Hypersensitivity/Anaphylaxis
- Extravasation
- Late/long term effects

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# Spring 2026 Fundamentals of Anticancer Therapy Day 1

# Allegheny Health Network Cancer Institute

## *ANTICANCER THERAPY COURSE – Day 2*

| | |
|---|---|
| 8:00 a.m. | *Review Take- Home Work*<br>Mary E. Kern, MSN, RN, OCN, CHSE<br>**treatment/symptom management* |
| 8:30 a.m. | *Molecular Targeted Therapies and Immunotherapy*<br>Jeremy Pappacena, PharmD, BCOP<br>Jennifer Niccolai, PharmD, BCOP<br>**treatment/symptom management* |
| 10:00 a.m. | Break |
| 10:15 a.m. | *Hormone Therapy*<br>Heather Kennihan MSN, RN, OCN<br>**treatment/symptom management* |
| 11:30 a.m. | Lunch |
| 12:15 p.m. | *GI Toxicities and Assessment*<br>Mary E. Kern, MSN, RN, OCN, CHSE<br>**treatment/symptom management* |
| 1:15 p.m. | Break |
| 1:30 p.m. | *Treatment - BSA, ANC, Calvert, Mosteller*<br>Mary E. Kern, MSN, RN, OCN, CHSE<br>**treatment* |
| 3:00 p.m. | Wrap-up and Evaluations<br>*Self-Study Completion - Standard of Practice (SOP) Review Booklet and ACT Videos<br>*Weekly Homework<br>**professional* |
| 3:15 p.m. | Adjourn |

PRESENTED BY: Jennifer Niccolai, PharmD, BCOP and Jeremy Pappacena, PharmD, BCOP

03/19/26

# Targeted and Immunomodulating Therapies in Oncology


1

## Learning Objectives

- Describe the general mechanistic differences of conventional chemotherapy compared to targeted and immunomodulating therapies
- Recall the common class adverse effects of targeted and immunomodulating therapies based on their mechanism of action
- Identify potential drug-drug and drug-food interactions that can negatively impact a patient's treatment
- Recommend appropriate management of adverse effects for a patient experiencing adverse effects of these treatments

2

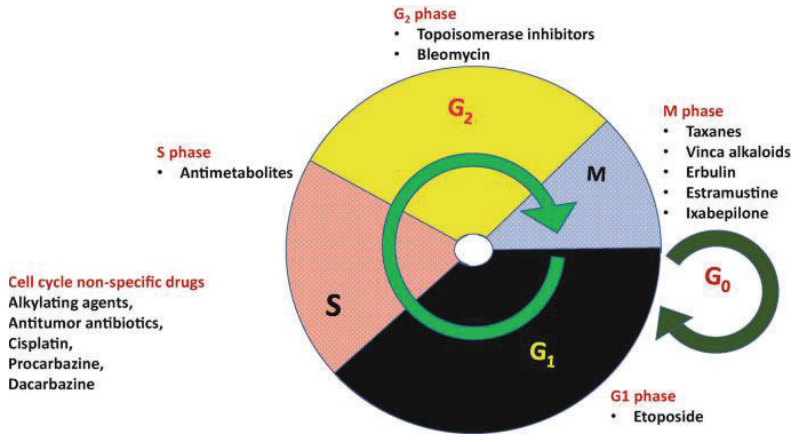
# Definitions

- Conventional Chemotherapy
  - Standard cytotoxic therapy that directly kills or prevents division of rapidly dividing cells
    - Can affect any actively dividing cell in the body
- Targeted Therapy
  - Directed towards a specific molecule or marker that cancer cells need to grow and survive
    - Tend to be overexpressed in certain malignancies, but can also be present in healthy cells
- Immunomodulating Therapy
  - Alters the body's own immune system to help attack cancer cells
- Antibody-Drug Conjugates
  - Consists of a monoclonal antibody targeting a specific molecule or marker with a cytotoxic "payload" delivering conventional chemotherapy directly to cancer cells

Chemotherapy to treat cancer - nci. April 29, 2015. Accessed February 6, 2026.
Https://www. Cancer.gov/publications/dictionaries/cancer-terms/def/targeted-therapy. February 2, 2011. Accessed February 6, 2026.
Https://www. Cancer.gov/publications/dictionaries/cancer-terms/def/immunomodulating-agent. February 2, 2011. Accessed February 6, 2026.
Https://www. Cancer.gov/publications/dictionaries/cancer-terms/def/antibody-drug-conjugate. February 2, 2011. Accessed February 6, 2026.

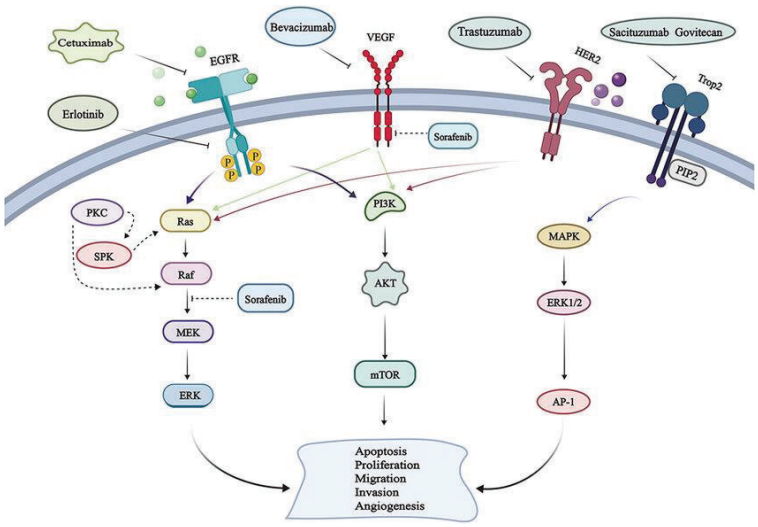


# Conventional Chemotherapy




Priyadarshini R. Springer Nature; 2021:1049-1076.

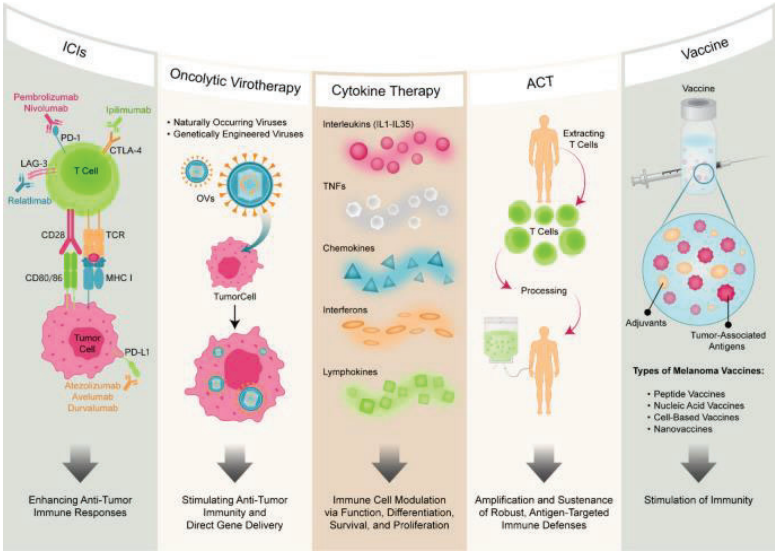
# Targeted Therapy




Duan, Huaiyu, et al. International Journal of Nanomedicine. 18. 3973-3988.

5

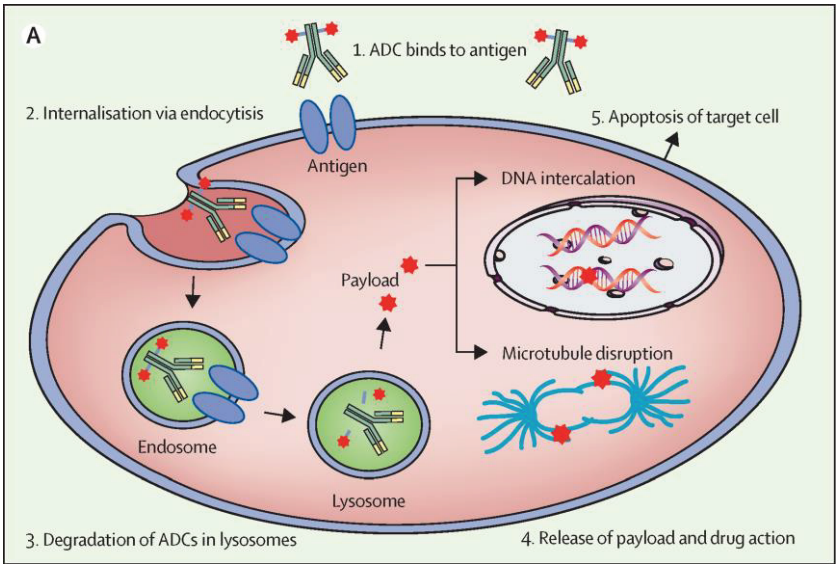
# Immunomodulating Therapy




Karimi H, et al. Med Oncol. 2026;43(3):133.

6

# Antibody-Drug Conjugates




Chau CH, et al. The Lancet. 2019;394(10200):793-804.

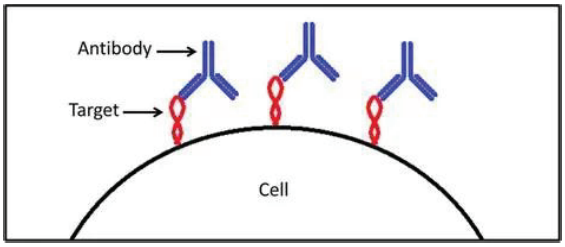
7

# Monoclonal Antibodies

8

# Monoclonal Antibodies (mAbs)

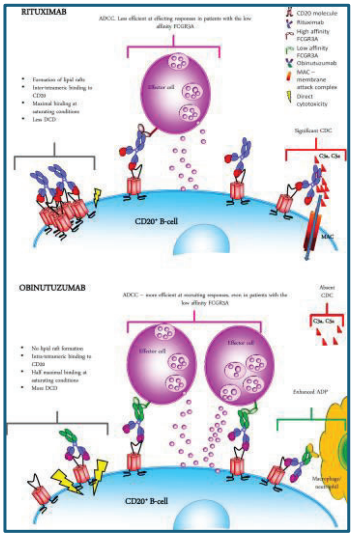
- Lab-made antibodies (type of immune protein)
- Designed to specifically target a certain antigen, such as one found on cancer cells
- They are made from a single clone of a B cell, a type of white blood cell and part of the immune system.




9

# Anti-CD20 Monoclonal Antibodies

- Mechanism




- Agents
  - Obinutuzumab
  - Rituximab
  - Rituximab and hyaluronidase
- Indications
  - Acute lymphoblastic leukemia (ALL)
  - B Cell lymphomas
    - Burkitt's lymphoma
    - Diffuse large B cell lymphoma (DLBCL)
    - Follicular lymphoma
    - Mantle cell lymphoma
    - Marginal zone lymphoma
  - Chronic lymphocytic leukemia (CLL)

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# Anti-CD20 Monoclonal Antibodies

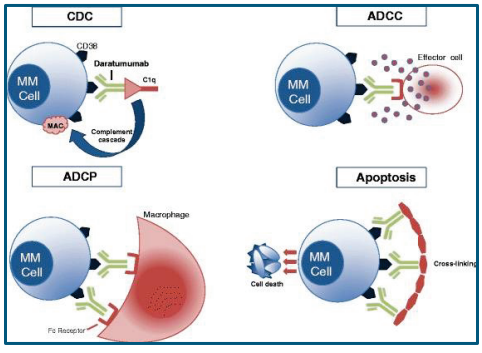
- Common Adverse Effects
  - Infusion reactions
    - Rigors
    - Potentially serious reactions (angioedema, bronchospasm, hypotension, hypoxia, acute respiratory distress syndrome, myocardial infarction, shock)
    - Risk factors
      - First infusion
      - Higher tumor burden
      - History of cardiac or pulmonary conditions
  - Infection
  - Hepatitis B reactivation

- Monitoring/Considerations
  - Hepatitis B panel (core antibody and surface antigen) pre-testing
  - Titrated infusion
  - Rituximab and hyaluronidase subcutaneous injection has lower risk of administration-related reactions
  - Rigors may require meperidine for resolution



# Anti-CD38 Antibodies

- Mechanism




- Agents
  - Daratumumab
  - Daratumumab and hyaluronidase
  - Isatuximab
- Indications
  - Multiple Myeloma

# Anti-CD38 Antibodies

- Common Adverse Effects
  - Fatigue
  - Myelosuppression
  - Upper respiratory tract infections
- IV products only
  - Infusion reactions
  - Pulmonary toxicity
- Isatuximab only
  - Hypertension
  - GI toxicity

- Monitoring/Considerations
  - Type and screen prior to therapy initiation (false positive indirect Coombs' test)
  - Daratumumab and hyaluronidase post-injection monitoring
    - 1 hour after first injection (D1C1)
    - 30 minutes after second injection (D8C1)
    - No monitoring after third injection and beyond (D15C1 and subsequent)
  - IV infusions are titrated

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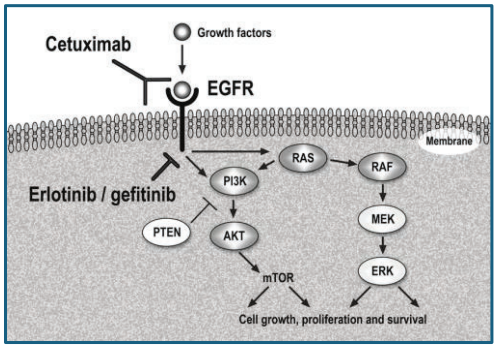
# EGFR Inhibitors

- Mechanism




| Agent | Indications |
|---|---|
| Cetuximab | Colorectal cancer (*KRAS/NRAS wild type*) Head and Neck cancer |
| Panitumumab | Colorectal cancer (*KRAS/NRAS* wild type) |
| Amivantamab<br>Amivantamab and hyaluronidase | Non-small cell lung cancer (*EGFR* mutation) |
| Necitumumab | Non-small cell lung cancer |

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# EGFR Inhibitors

| Agents | Common Side Effects | Monitoring/Considerations |
|---|---|---|
| Cetuximab and Panitumumab | Acneiform Rash<br>Diarrhea<br>Low magnesium levels | Rash responds well to typical acne treatments such as topical antibiotics (clindamycin lotion), systemic antibiotics (doxycyline, minocycline), short-term topical corticosteroids<br><br>Magnesium level prior to each treatment<br><br>H1-RA (diphenhydramine) prior to first cetuximab dose, monitor for one hour following infusion |
| Amivantamab<br>Amivantamab and hyaluronidase | Edema<br>Electrolyte changes<br>Infusion reactions (IV)<br>Muscle/bone pain<br>Nail changes<br>Ocular toxicity<br>Pulmonary toxicity<br>Venous thromboembolic events | IV – weeks 1 and 2 must be administered via peripheral line to reduce risk of reaction<br>Pre-medications required<br><br>Subcutaneous- lower risk of infusion reactions<br>Pre-medications still required (diphenhydramine and acetaminophen prior to all in infusions, glucocorticoid initial dose only and subsequent doses if reaction occurs) |
| Necitumumab | Hypocalcemia<br>Hypomagnesemia<br>Hypophosphatemia<br>Rash<br>Rare/serious cardiovascular events (warning for cardiopulmonary arrest)<br>Rare/serious thromboembolism (warning for VTE/ATE) | |

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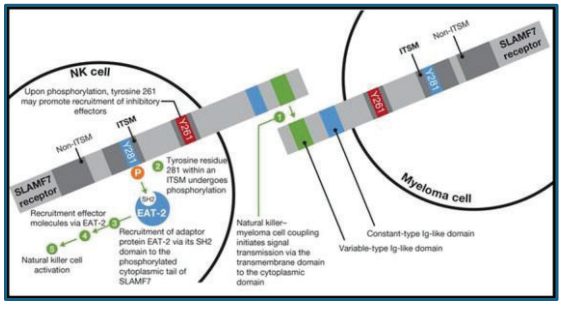
# Elotuzumab

- Mechanism: Anti-SLAMF7 Monoclonal Antibody




- Indication
  - Multiple Myeloma
- Adverse Effects
  - Cardiovascular
  - Electrolyte changes
  - Herpes zoster infection
  - Myelosuppression
  - Peripheral neuropathy
  - Upper respiratory tract infections
- Administration
  - Titrated infusion
  - All infusion related reactions were grade 3 or lower
  - Most infusion reactions occurred during first dose
  - HSV/VZV prophylaxis required

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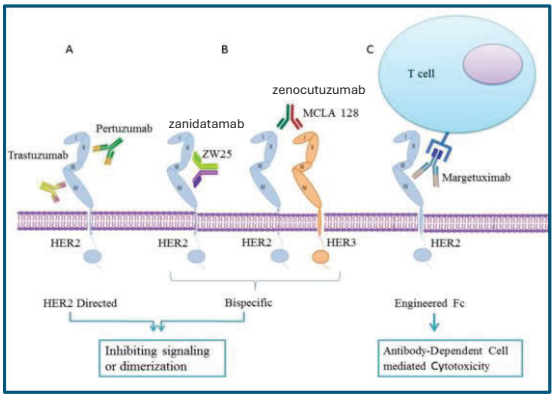
# HER2 Targeted Monoclonal Antibodies

- Mechanism




- Agents
  - Margetuximab
  - Trastuzumab
  - Trastuzumab and hyaluronidase
  - Pertuzumab
  - Pertuzumab, trastuzumab, and hyaluronidase
  - Zanidatamab
  - Zenocutuzumab
- Indications
  - Breast cancer
  - Biliary tract cancer
  - Colorectal cancer
  - Endometrial cancer
  - Gastric/Gastroesophageal adenocarcinoma
  - *requires certain degree of HER2- positivity or expression
  - NSCLC and pancreatic cancer NRG1 fusion positive (Zenocutuzumab)

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# HER-2 Targeted Monoclonal Antibodies

- Common Adverse Effects
  - Infusion related reactions
  - Pulmonary toxicity
  - Reversible cardiomyopathy
  - Skin reactions
  - Edema (Zenocutuzumab)
  - Elevated LFTs (Zenocutuzumab)

- Monitoring and considerations
  - Cardiac monitoring (MUGA or ECHO during therapy and after completion)
  - Infusion considerations
    - Loading doses for first doses of trastuzumab and pertuzumab, longer infusions
    - Pre-medications required for zanidatamab, longer infusion times for doses 1-4
    - Monitor for 1 hour post zenocutuzumab infusion
    - Longer infusion time for first margetuximab dose
  - Subcutaneous products exist
    - Herceptin and hyaluronidase
    - Herceptin, pertuzumab, and hyaluronidase

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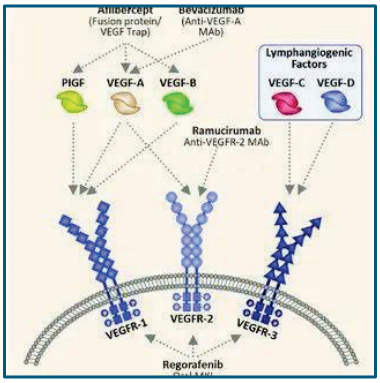
# VEGF Inhibitors

- Mechanism




- Agents
  - Bevacizumab
  - Ramucirumab
  - Ziv-aflibercept
- Indications
  - Colorectal cancer
  - Gastric/Gastroesophageal junction adenocarcinoma
  - Glioblastoma
  - Gynecologic malignancies
  - Hepatocellular carcinoma
  - Mesothelioma
  - Non-small cell lung cancer
  - Renal cell carcinoma

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# VEGF Inhibitors

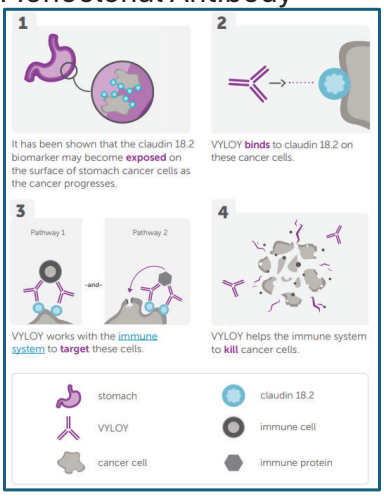
- Common Adverse effects
  - Bleeding
  - GI perforation
  - Hypertension
  - Nephrotic syndrome
  - Proteinuria
  - Venous/Arterial thromboembolism
  - Wound healing complications

- Monitoring/Considerations
  - Monitor blood pressure prior to each infusion
  - Monitor for protein in urine with urinalysis
    - May require 24-hour urine collection if POC UA protein $\geq$ 2+
  - Hold medication before and after surgery to allow for wound healing
  - Ramucirumab requires diphenhydramine pre-medication

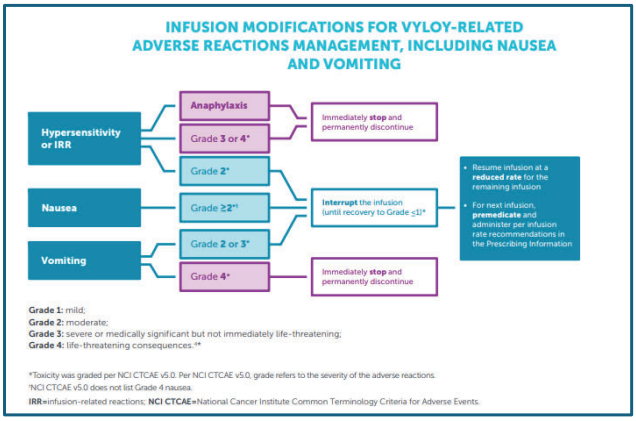
20

# Zolbetuximab

- Mechanism: Anti-CLDN18.2 Monoclonal Antibody




- Indication
  - Gastric or gastroesophageal adenocarcinoma, CLDN18.2 positive
- Adverse reactions
  - Acute nausea vomiting
  - Hypersensitivity reactions/anaphylaxis

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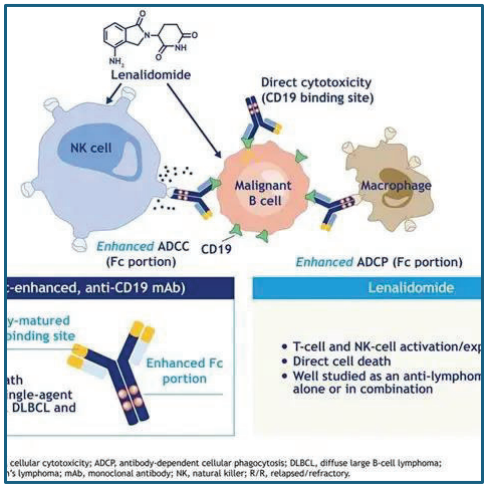
# Tafasitamab

- Mechanism: Anti-CD19 Monoclonal antibody




- Indications
  - Diffuse large B-cell lymphoma
  - Follicular lymphoma
- Adverse effects
  - Fatigue
  - Infections
  - Infusion related reactions
  - Myelosuppression
  - Respiratory tract infections
- Considerations
  - Pre-medications required prior to first three infusions (acetaminophen, H1-RA, H2-RA, dexamethasone).
  - Pre-medications optional for subsequent infusion if previous infusions tolerated
  - Initial infusion is titrated

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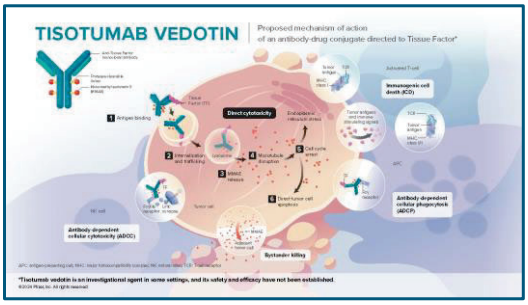
# Antibody-Drug Conjugates



## Anti-c-MET ADC

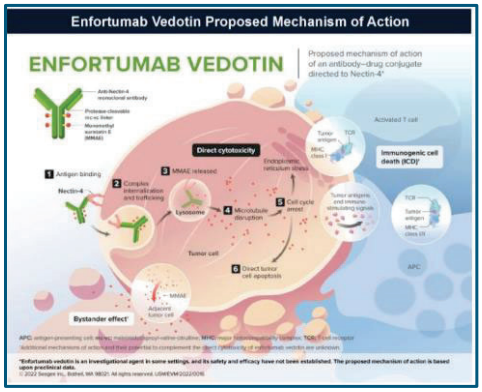
- Telisotuzumab Vedotin
- Mechanism




- Indication
  - NSCLC (c-Met protein expression)
- Adverse Effects
  - Electrolyte changes
  - Infusion reactions
  - Myelosuppression
  - Ocular toxicity
  - Peripheral edema
  - Peripheral neuropathy
  - Pulmonary toxicity
- Monitoring/Considerations
  - Only if prior infusion reaction, pre-medicate with acetaminophen, H1-/H2-RA, methylprednisolone
  - Dosing cap for patients ≥ 100kg

# Anti-Nectin-4 ADC

- Enfortumab Vedotin
- Mechanism



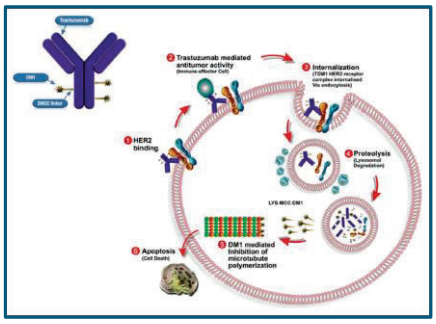

- Indications
  - Bladder/Urothelial cancer
- Adverse effects
  - Alopecia
  - Diarrhea
  - Hyperglycemia (hold if blood glucose ≥ 250)
  - Peripheral neuropathy
  - Pneumonitis
  - Ocular toxicity (dry eye, keratitis)
  - Skin rash
- Monitoring/Considerations
  - Irritant
  - Monitor blood glucose
  - May use lubricating eye drops for ocular toxicity
  - Dosing cap for patients ≥ 100kg

25

# HER-2 ADCs

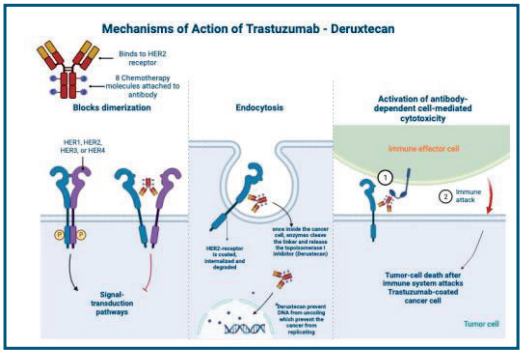
**Ado-Trastuzumab Emtansine (TDM-1)**

- Mechanism




**Fam-Trastuzumab Deruxtecan (T-DXd)**

- Mechanism




26

# Her-2 ADCs

| Agents | Indications | Side Effects | Monitoring/ Considerations |
|---|---|---|---|
| Ado-trastuzumab emtansine | Breast cancer | • Cardiotoxicity (decreased ejection fraction)<br>• Elevated liver function tests<br>• Myelosuppression<br>• Neuropathy<br>• Skin rash | • Use requires HER2 positivity<br>• Echocardiogram every 3 months<br>• Longer initial infusion |
| Fam-Trastuzumab Deruxtecan | Breast cancer<br>Gastric cancer<br>NSCLC<br>Metastatic solid tumors | • Cardiotoxicity (decreased ejection fraction)<br>• Myelosuppression<br>• Nausea/vomiting (high risk)<br>• Pulmonary toxicity | • Use requires HER2 positivity or HER2 mutation positivity (lung only)<br>• Echocardiogram every 3 months<br>• Longer initial infusion |

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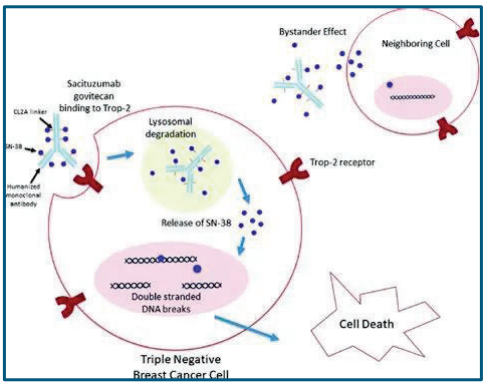
# Anti-Trop-2 ADCs

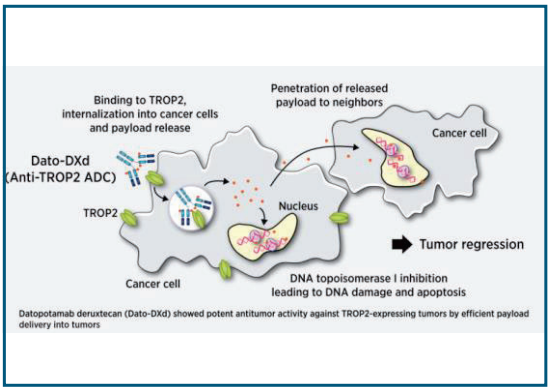
**Sacituzumab Govitecan**

- Mechanism




**Datopotamab Deruxtecan**

- Mechanism




28

# Anti-Trop-2 ADCs

| Agents | Indications | Adverse Effects | Monitoring/ Considerations |
|---|---|---|---|
| Sacituzumab Govitecan | Breast cancer | • Alopecia<br>• Diarrhea<br>• Electrolyte changes<br>• Fatigue<br>• Hyperglycemia<br>• Hypersensitivity reactions<br>• Myelosuppression | • Initial infusion over 3 hours, subsequent over 1 hour<br>• Pre-medicate with acetaminophen and H1/H2-RA<br>• Can consider atropine pre-medication<br>• Loperamide for diarrhea following treatment |
| Datopotamab Deruxtecan | Breast Cancer<br>NSCLC | • Constipation<br>• Fatigue<br>• Infusion reaction<br>• Nausea<br>• Ocular toxicities (dry eye, keratitis)<br>• Stomatitis | • Administration<br>  • Initial infusion over 90 minutes, observe for 60 minutes post infusion<br>  • Second infusion over 30 minutes, observe for 60 minutes post infusion<br>  • Subsequent infusions 30 minutes, observe for 30 minutes post infusion<br>  • Pre-medicate with acetaminophen, H1-RA +/- corticosteroid<br>• Ocular toxicity<br>  • Ophthalmic exam baseline, yearly while on treatment, end of treatment<br>  • Patient should use lubricant eye drops four times a day and as needed<br>• Stomatitis<br>  • Patient should use steroid-containing mouthwash four times a day and as needed (dexamethasone oral solution)<br>  • Patient should hold ice chips or ice water in the mouth throughout infusion |

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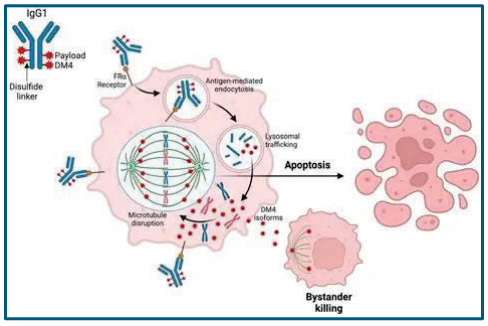
# Anti-Folate Receptor Alpha ADC

- Mirvetuximab Soravtansine
- Mechanism

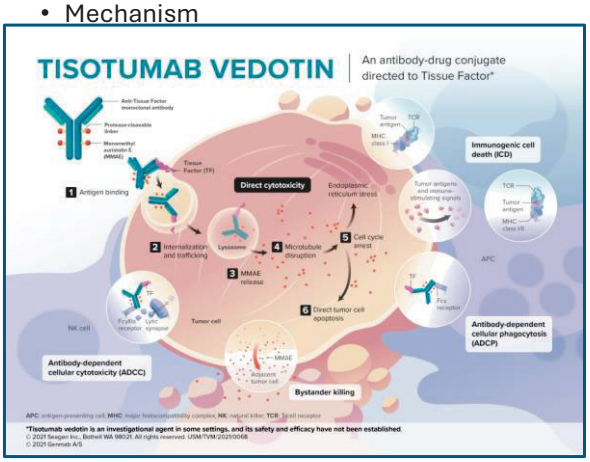



- Indication
  - Ovarian cancer
- Adverse Effects
  - Elevated liver function tests
  - Fatigue
  - Ocular toxicity
  - Peripheral neuropathy
  - Pneumonitis
- Monitoring/Considerations
  - Requires folate receptor alfa positivity for use
  - Has unique dosing (uses Adjusted ideal body weight)
  - Pre-medicate with acetaminophen, H1-RA, antiemetics
  - Ocular toxicity
    - Ophthalmic exam at baseline, every other cycle for the first 8 cycles and then as clinically indicated
    - Patients should use prophylactic artificial tears and ophthalmic topical steroids

30

# Anti-Tissue Factor ADC

- Tisotumab vedotin
- Mechanism




- Indication
  - Cervical cancer
- Adverse Effects
  - Bleeding
  - Fatigue
  - Ocular toxicity (keratitis, conjunctivitis)
  - Peripheral neuropathy
  - Pulmonary toxicity
  - Skin rash
- Monitoring/Considerations
  - Ocular toxicity
    - Ophthalmic exam at baseline, prior to every cycle for the first 9 cycles and then as indicated
    - Patient to administer topical ophthalmic corticosteroids, topical vasoconstrictor ophthalmic drops (only prior to infusion), and lubricating eye drops.
    - Patient to sue cooling eye pads during infusion

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# ADCs for Hematologic Malignancies

| Agents | Mechanism | Indications | Adverse Effects | Monitoring/ Considerations |
|---|---|---|---|---|
| Belantamab Mafadotin | Anti-BCMA monoclonal antibody + microtubule-disrupting agent (mcMMAF) | Multiple myeloma | • Myelosuppression<br>• Ocular toxicity<br>• Diarrhea<br>• Elevated liver function tests<br>• Fatigue<br>• Increased CPK<br>• Increased serum creatinine<br>• Upper respiratory tract infections | • Ocular toxicity<br>  • Ophthalmic exam at baseline and within 10 days of each subsequent dose<br>  • Artificial tears at least four times a day |
| Brentuximab Vedotin | Anti-CD30 monoclonal antibody + microtubule-disrupting agent (MMAE) | Hodgkin lymphoma<br>Anaplastic large cell lymphoma<br>Primary cutaneous anaplastic large cell lymphoma<br>Diffuse large B-cell lymphoma | • Myelosuppression<br>• Skin rash<br>• Hyperglycemia<br>• Peripheral neuropathy<br>• Pulmonary toxicity<br>• Elevated liver function tests<br>• Acute pancreatitis (rare) | • Consider PJP prophylaxis |
| Gemtuzumab Ozogamicin | Anti-CD33 monoclonal antibody + cytotoxic calicheamicin derivative (induces DNA double-strand breaks) | Acute myeloid leukemia | • Cardiotoxicity<br>• Bleeding<br>• Hepatotoxicity (SOS/VOD)<br>• Infection<br>• Fatigue<br>• Fever | • Pre-medications:<br>  • Acetaminophen<br>  • Diphenhydramine<br>  • Methylprednisolone<br>  • Can administer additional diphenhydramine and methylpred PRN<br>• Monitor 1-hour post-infusion |

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# ADCs for Hematologic Malignancies

| Agents | Mechanism | Indications | Adverse Effects | Monitoring/ Considerations |
|---|---|---|---|---|
| Inotuzumab Ozogamicin | Anti-CD22 monoclonal antibody + cytotoxic calicheamicin derivative (induces DNA double-strand breaks) | Acute lymphoblastic leukemia | • Hepatotoxicity (SOS/VOD)<br>• Myelosuppression<br>• Infection<br>• Bleeding<br>• Infusion reactions | • Pre-medicate with acetaminophen, H1-RA, corticosteroid<br>• Monitor 1-hour post-infusion |
| Loncastuximab Tesirine | Anti-CD19 monoclonal antibody + alkylating agent (SG3199) | Diffuse large B-cell lymphoma | • Myelosuppression<br>• Cutaneous reactions<br>• Edema, effusions<br>• Hyperglycemia<br>• Elevated liver function tests<br>• Fatigue | • Premedication: dexamethasone 4 mg twice daily for 3 days starting day before infusion<br>• Specific adjusted body weight dosing for patients with BMI $\geq$ 31<br>• Irritant with vesicant-like properties |
| Polatuzumab Vedotin | Anti-CD78B monoclonal antibody + mmicrotubule-disrupting agent (MMAE) | Diffuse large B-cell lymphoma | Myelosuppression<br>Peripheral neuropathy<br>Infusion reactions<br>Hepatotoxicity<br>Diarrhea<br>Fatigue<br>Increased serum creatinine | • Requires PJP prophylaxis<br>• Administration<br>  • Pre-medicate with acetaminophen and H1-RA (often given in combination with rituximab)<br>  • Infuse initial dose over 90 minutes and monitor for 90 minutes post-infusion<br>  • Infuse subsequent doses over 30 minutes and monitor 30 minutes post-infusion |



# Targeted Therapies

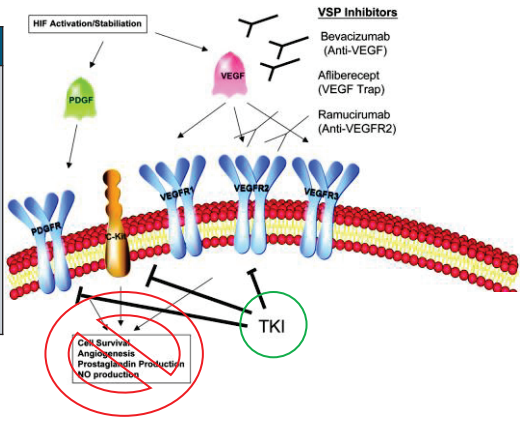
# Targeted Therapies

- Numerous cellular pathways identified in tumorigenesis
- Targeting these pathways can “halt” cellular transcription and proliferation leading to apoptosis
- Agents targeting the same pathway tend to have similar adverse effects
- Frequently given as oral therapy



# VEGF Tyrosine Kinase Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits tumor growth via inhibition of angiogenesis | Axitinib<br>Cabozantinib<br>Fruquintinib<br>Lenvatinib<br>Pazopanib<br>Regorafenib<br>Sorafenib<br>Sunitinib<br>Vandetanib | Endometrial Cancer<br>Colon Cancer<br>Renal Cell Carcinoma<br>Sarcoma<br>Thyroid Carcinoma |



# VEGF Tyrosine Kinase Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Hypertension<br>Bleeding<br>Thromboembolism<br>Proteinuria<br>Wound Healing Impairment<br>Gastrointestinal Perforation<br>Hand Foot Syndrome (regorafenib)<br>Hair color changes (pazopanib)<br>Stomatitis (regorafenib) | Blood pressure<br>Signs of VTE<br>Urine protein every 3 months<br>Non-healing wounds | Subject to numerous drug interactions including acid suppressive therapies.<br><br>HFS managed with unscented moisturizers (urea, Udderly Smooth®). Severe cases can necessitate topical steroids.<br><br>Consult clinical pharmacist for any questions. |

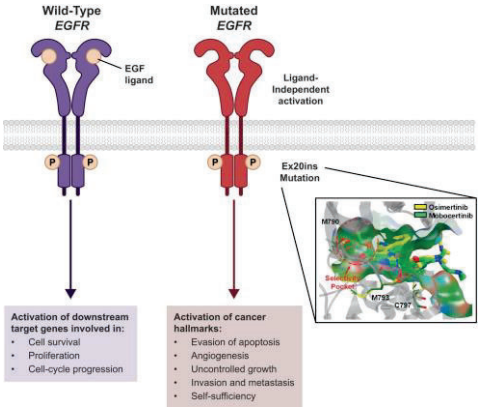
37

# RAS-RAF Pathway

38

# EGFR Tyrosine Kinase Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to select mutant forms of EGFR | Afatinib<br>Dacomitinib<br>Erlotinib<br>Gefitinib<br>Lazertinib<br>Osimertinib | EGFR-Mutated Non-Small Cell Lung Cancer |




39

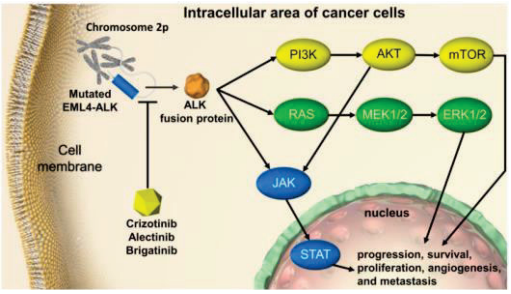
# EGFR Tyrosine Kinase Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Acneiform Rash<br>EKG Changes<br>Decreased LVEF (Osimertinib)<br>Diarrhea | EKG and ECHO (if needed) at baseline and periodically throughout treatment<br><br>Dermatologic events<br><br>Palpitations<br><br>Bowel movements and hydration status | Subject to numerous drug interactions.<br><br>Requires specific EGFR mutation(s) for use.<br><br>Acneiform rash managed with topical or systemic antibiotics / steroids.<br><br>Consult clinical pharmacist for any questions. |

40

# Anaplastic Lymphoma Kinase (ALK) Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to ALK-rearranged oncogenic fusion proteins | Alectinib<br>Brigatinib<br>Ceritinib<br>Crizotinib<br>Lorlatinib | ALK-Rearranged Non-Small Cell Lung Cancer |




41

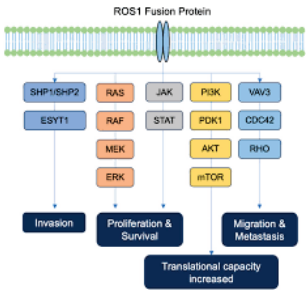
# ALK Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Edema<br>Bradycardia<br>Metabolic Derangements<br>Hepatotoxicity<br>Nephrotoxicity<br>Myalgia<br>Visual Disturbances<br>Mood Disorders (lorlatinib) | Complete Metabolic Panel<br><br>Creatinine Kinase levels at therapy initiation<br><br>Heart rate and blood pressure<br><br>Fluid status / weight gain | Subject to numerous drug interactions.<br><br>Requires specific ALK-rearrangement for use.<br><br>Consult clinical pharmacist for any questions. |

42

# ROS Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to and inhibiting the proto-oncogene ROS1 | Repotrectinib<br>Taletrectinib | ROS1-Mutated Non-Small Cell Lung Cancer |



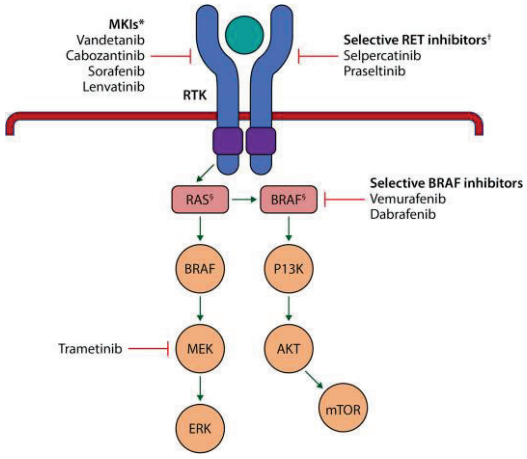



# ROS1 Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Cognitive Disorders (repotrectinib)<br>Ataxia (repotrectinib)<br>Mood Disorders (repotrectinb)<br>Hepatotoxicity<br>Myalgia<br>Metabolic Derangements<br>Fractures<br>EKG Changes | Complete Metabolic Panel<br><br>Creatinine Kinase levels at therapy initiation<br><br>Signs/symptoms of skeletal fracture<br><br>EKG at baseline and as indicated | Subject to numerous drug interactions.<br><br>Requires specific ROS1 rearrangement for use.<br><br>Consult clinical pharmacist for any questions. |

# RET Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to and inhibiting oncogenic RET mutated fusion proteins | Pralsetinib<br>Selpercatinib | RET-Fusion Positive Non-Small Cell Lung and Thyroid Cancers |




45

# RET Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Bleeding/Hemorrhage<br>Hepatotoxicity<br>Hypertension<br>EKG Changes<br>Impaired Wound Healing | Complete Metabolic Panel<br><br>Signs/symptoms of bleeding<br><br>EKG and blood pressure at baseline and as indicated<br><br>Non-healing wounds | Subject to numerous drug interactions.<br><br>Requires specific RET fusion protein positivity or mutation for use.<br><br>Consult clinical pharmacist for any questions. |

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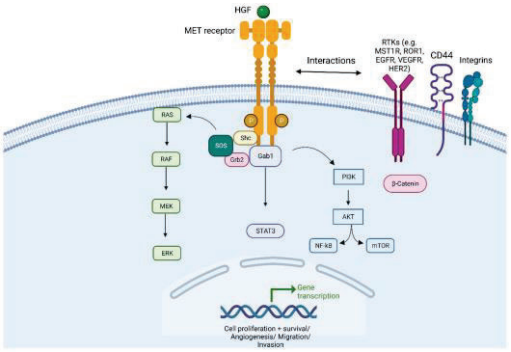
# MET Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to and inhibiting oncogenic MET mutation | Capmatinib<br>Tepotinib | MET exon 14 skipping mutation positive Non-Small Cell Lung and Thyroid Cancers |




47

# MET Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Photosensitivity<br>Edema<br>Increased Serum Creatinine<br>Hepatotoxicity<br>Pancreatic Toxicity<br>Metabolic Derangements | Complete Metabolic Panel<br><br>Amylase/Lipase<br><br>Cholesterol Panel<br><br>Fluid status / weight gain | Subject to numerous drug interactions.<br><br>Requires specific MET mutation for use.<br><br>Patients should be assessed for any abdominal pain, especially with eating.<br><br>Consult clinical pharmacist for any questions. |

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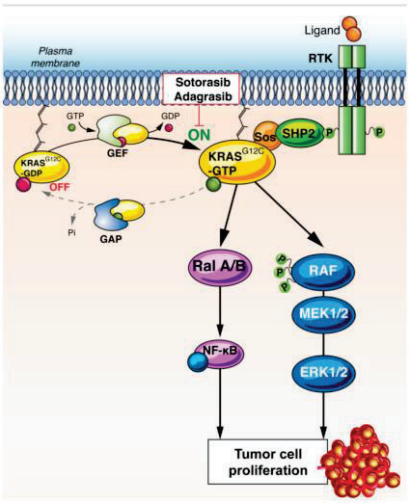
# KRAS Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to and inhibiting oncogenic KRAS mutation | Adagrasib<br>Sotorasib | KRAS-Mutated Non-Small Cell Lung, Colorectal, and Pancreatic Cancers |




49

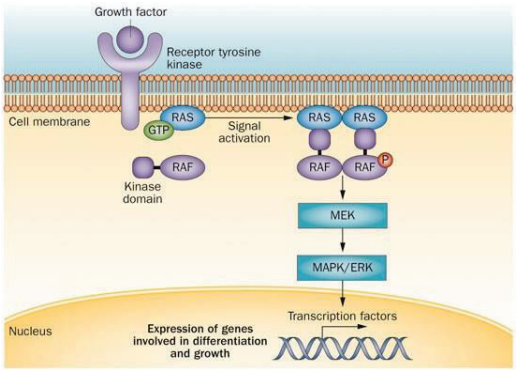
# KRAS Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Diarrhea<br>Nausea/Vomiting<br>Hepatotoxicity<br>Myelosuppression | Complete Metabolic Panel<br><br>CBC with Differential | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Requires specific KRAS mutation for use.<br><br>Consult clinical pharmacist for any questions. |

50

# BRAF Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to and inhibiting oncogenic BRAF mutation | Dabrafenib<br>Encorafenib<br>Vemurafenib | BRAF V600E mutated melanoma, non-small cell lung, and colorectal cancers (encorafenib only) |




51

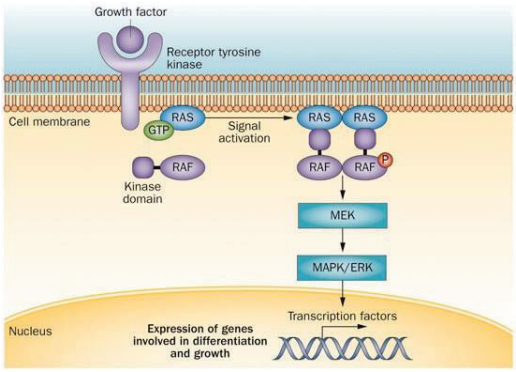
# BRAF Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Fevers<br>Cardiomyopathy<br>Dermatologic Toxicity<br>Ocular Toxicity<br>EKG Changes | Fevers >103 F<br>ECHO<br>EKG<br>Periodic dermatologic and ocular exams | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Requires specific BRAF mutation for use.<br><br>Fevers managed with antipyretics (APAP and NSAIDs).<br><br>Often given with MEK inhibitors to reduce the risk of developing cutaneous squamous cell carcinoma.<br><br>Consult clinical pharmacist for any questions. |

52

# MEK Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to and inhibiting MEK in the EGFR pathway | Binimetinib<br>Cobimetinib<br>Trametinib | BRAF V600E mutated melanoma and non-small cell lung cancer |




53

# MEK Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Fevers<br>Cardiomyopathy<br>Dermatologic Toxicity<br>Diarrhea<br>Ocular Toxicity<br>EKG Changes | Fevers >103 F<br>ECHO<br>EKG<br>Periodic dermatologic and ocular exams | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Often requires specific BRAF mutation for use<br><br>Fevers managed with antipyretics (APAP and NSAIDs).<br><br>Binimetinib paired with encorafenib<br>Cobimetinib paired with vemurafenib<br>Trametinib paired with dabrafenib<br><br>Consult clinical pharmacist for any questions. |

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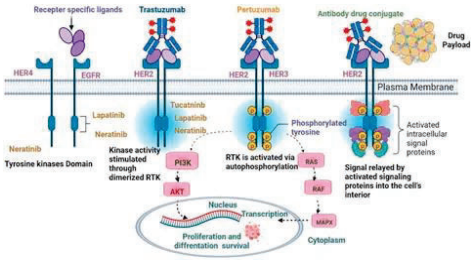
# HER2 Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits HER2 activation of downstream signaling of pro-survival pathways | Tucatinib<br>Neratinib<br>Lapatinib<br>Zongertinib | HER2-overexpressed breast cancer<br><br>HER2-overexpressed colorectal cancer (tucatinib and lapatinib)<br><br>HER2-overexpressed biliary tract cancers (tucatinib)<br><br>HER2-mutated non-small cell lung cancer (zongertinib) |




55

# HER2 Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Cardiomyopathy (less than IV HER2 inhibitors)<br>**Diarrhea**<br>Hand-foot syndrome<br>Hepatoxicity | CBC<br>CMP<br><br>Echocardiogram | Subject to numerous drug interactions.<br><br>Optimize anti-diarrheal use<br>- Loperamide<br>- Diphenoxylate/atropine<br><br>Consult clinical pharmacist for any questions. |

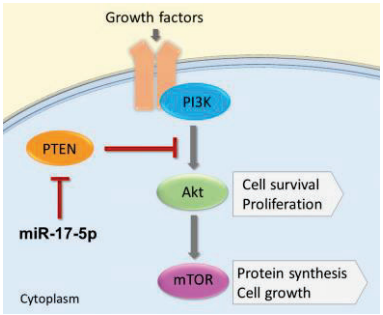
56

# PI3K-AKT Pathway

57

## mTOR Inhibitors

| Mechanism | Agents | Common Uses |
|---|---|---|
| Inhibits mTOR signaling, halting the cell cycle at the G1 phase | Everolimus (PO)<br>Temsirolimus (IV) | Breast Cancer<br>Endometrial Cancers<br>Neuroendocrine Cancers<br>Renal Cell Carcinoma |




58

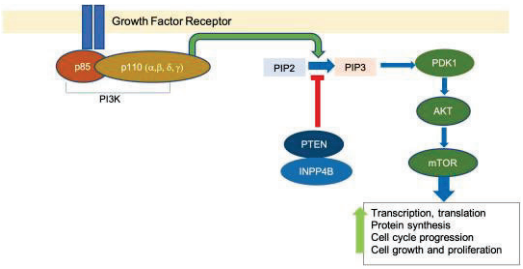
# mTOR Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Mucositis/Stomatitis<br>Hypercholesterolemia<br>Hyperglycemia | Cholesterol panel<br>Fasting glucose | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Alcohol-free dexamethasone solution to prevent stomatitis.<br><br>Consult clinical pharmacist for any questions. |

59

# PI3KCA Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cellular proliferation / survival by binding to phosphatidylinositol 3-kinase (PI3K) and inhibiting the AKT pathway | **Breast**<br>Alpelisib<br>Capivasertib<br>Inavolisib<br><br>**CLL**<br>Duvelisib<br>Idelalisib<br>Umbralisib | Hormone positive, PI3KCA mutated breast cancer<br><br>Chronic Lymphocytic Leukemia |




60

## PI3KCA Inhibitors

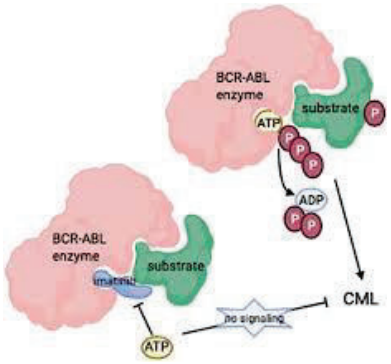
| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Mucositis/Stomatitis<br>Diarrhea<br>Infection (CMV and PJP – CLL only)<br>Myelosuppression<br>Hepatotoxicity<br>Hypercholesterolemia<br>Hyperglycemia | Fasting glucose<br>Cholesterol panel<br>CBC<br>CMP<br><br>CMV serologies as needed for patients with CLL | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Requires specific PI3KCA mutation for use in breast cancer<br><br>PJP prophylaxis recommended for CLL patients.<br><br>Alcohol-free dexamethasone solution to prevent stomatitis.<br><br>Consult clinical pharmacist for any questions. |



# Agents for Hematologic Malignancies

# BCR-ABL Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits the proto-oncogenic driver BCR-abl fusion protein encoded by the Philadelphia chromosome t(9;22) | Imatinib<br>Dasatinib<br>Nilotinib<br>Bosutinib<br>Ponatinib<br>Asciminib | CML<br><br>Philadelphia-chromosome positive ALL |




63

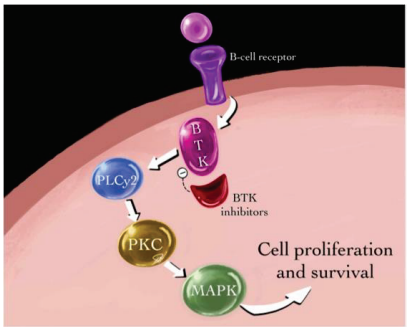
# BCR-ABL Inhibitors

| Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Bone Marrow Suppression<br>Pancreatitis<br>Periorbital edema – imatinib<br>Pleural effusion – dasatinib<br>Cardiac abnormalities – nilotinib<br>Diarrhea – bosutinib<br>Heart failure, hepatotoxicity, arterial occlusion, VTE – ponatinib | EKG (nilotinib)<br><br>Edema<br><br>Abdominal pain<br><br>CMP and serum phosphorus<br>CBC<br>BCR-ABL PCR | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Adherence is extremely important. Missing 3 doses per month can affect long term outcomes and lead to resistance.<br><br>Consult clinical pharmacist for any questions. |

64

# BTK Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits the Bruton's tyrosine kinase activity which is constitutively active on malignant B-cells | Ibrutinib<br>Acalabrutinib<br>Zanubrutinib<br>Pirtobrutinib | Various B-cell malignancies<br>- CLL<br>- Mantle Cell<br>- Marginal Zone<br>- Follicular Lymphoma<br>- Waldenstrom Macroglobulinemia |




65

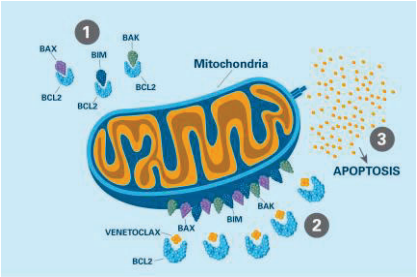
# BTK Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Upper respiratory tract infections<br>Bone marrow suppression<br>Bleeding<br>Hypertension<br>Atrial fibrillation<br>Rash<br>Hepatotoxicity<br>Tumor Lysis Syndrome | Tumor Lysis Syndrome Labs<br>CBC<br>CMP<br><br>EKG as indicated<br>Blood pressure | Subject to numerous drug interactions.<br><br>In CLL, WBC will initially increase and is NOT a sign of disease progression.<br><br>Consult clinical pharmacist for any questions. |

66

# BCL-2 Inhibitor

| Mechanism | Agent (PO) | Common Uses |
|---|---|---|
| Inhibits the anti-apoptotic protein BCL-2 which is overexpressed in various hematologic malignancies | Venetoclax | AML<br>CLL<br>Mantle Cell Lymphoma<br>Multiple Myeloma |




67

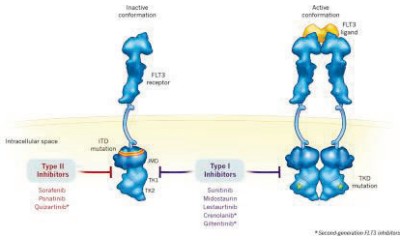
# BCL-2 Inhibitor - Venetoclax

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Upper respiratory tract infections<br>Bone marrow suppression<br>**Tumor Lysis Syndrome**<br>Rash | Tumor Lysis Syndrome labs<br>CBC<br>CMP | Subject to numerous drug interactions.<br><br>Patients may require admission or frequent outpatient lab draws for tumor lysis syndrome monitoring.<br><br>Consult clinical pharmacist for any questions. |

68

# FLT3 Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits FLT3 receptor signaling and cell proliferation, inducing apoptosis in FLT3-mutated leukemic cells | Midostaurin<br>Quizartinib<br>Gilteritinib | FLT3 mutated acute myeloid leukemia |



69

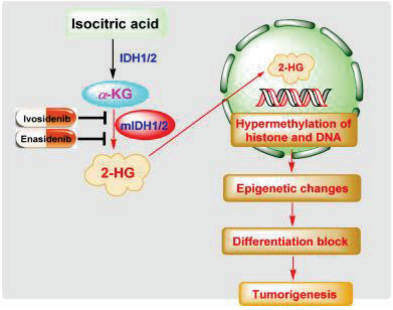
# FLT3 Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| QTc prolongation<br>Bone marrow suppression<br>Edema<br>Diarrhea<br>Hepatotoxicity | CBC<br>CMP<br><br>EKG at baseline and periodically throughout treatment | Subject to numerous drug interactions.<br><br>Requires specific FLT3 mutation(s) for use.<br><br>Consult clinical pharmacist for any questions. |

70

# IDH Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits mutant IDH enzyme. Mutant IDH leads to accumulation of 2-hydroxyglutarate in leukemic cells, preventing normal stem cell differentiation. | Enasidenib (IDH2)<br>Ivosidenib (IDH1)<br>Olutasidenib (IDH1) | IDH mutated MDS/AML<br><br>IDH mutated CNS tumors |




71

# IDH Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| QTc prolongation<br>Bone marrow suppression<br>Edema<br>Diarrhea<br>Rash<br>Hepatotoxicity<br>**Differentiation syndrome** | CBC<br>CMP<br><br>EKG at baseline and periodically throughout treatment<br><br>Signs/symptoms of differentiation syndrome: Fever, unexplained weight gain, peripheral edema, dyspnea, low blood pressure, hypoxemia, and renal/kidney failure | Subject to numerous drug interactions.<br><br>Requires specific IDH mutation(s) for use.<br><br>Differentiation syndrome managed with dexamethasone.<br><br>Consult clinical pharmacist for any questions. |

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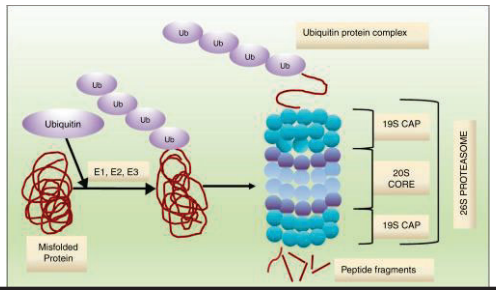
# Proteasome Inhibitors

| Mechanism | Agents | Common Uses |
|---|---|---|
| Inhibits proteasomes which are responsible for regulating protein homeostasis within the cell. Inhibition leads to cell-cycle arrest and apoptosis | Bortezomib (IV, SC)<br>Carfilzomib (IV)<br>Ixazomib (PO) | Multiple myeloma |

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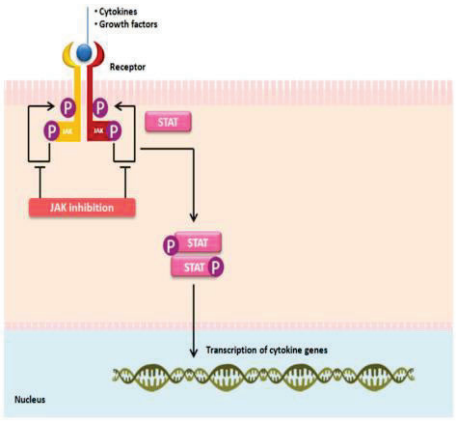
# Proteasome Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Neuropathy<br>Rash<br>Diarrhea<br>Upper respiratory tract infection<br>Myelosuppression<br>Heart failure (carfilzomib)<br>Renal toxicity (carfilzomib)<br>Tumor Lysis Syndrome (carfilzomib) | CBC<br>CMP<br><br>Signs and symptoms of heart failure or decreased pulmonary function | Ixazomib subject to numerous drug interactions.<br><br>Neuropathy is highest with IV bortezomib.<br><br>Pre-hydration commonly given with initial doses of carfilzomib to mitigate risk of TLS.<br><br>Consult clinical pharmacist for any questions. |

74

# JAK2 Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits activation of the JAK2-STAT pathway, decreasing cytokine and growth factor production responsible for hematopoiesis | Ruxolitinib<br>Pacritinib<br>Momelotinib<br>Fedratinib | Myeloproliferative neoplasms<br>- Myelofibrosis<br>- Polycythemia Vera |




75

# JAK2 Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Myelosuppression<br>Diarrhea<br>Infection<br>Bleeding | CBC<br>CMP<br><br>Signs and symptoms of infection | Subject to numerous drug interactions.<br><br>Patients should not abruptly discontinue treatment due to rebound effects.<br><br>Consult clinical pharmacist for any questions. |

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# Miscellaneous Agents

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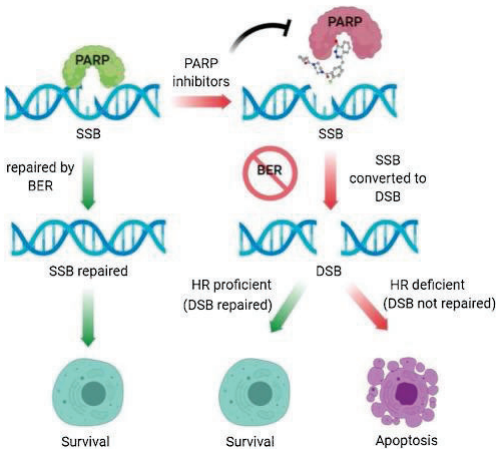
## PARP Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Prevents repair of double-stranded DNA breaks which leads to disruption of cellular homeostasis and cell death | Olaparib<br>Niraparib<br>Rucaparib<br>Talazoparib | BRCA mutated breast cancers<br><br>HRD or BRCA mutated ovarian, pancreatic, and prostate cancers |

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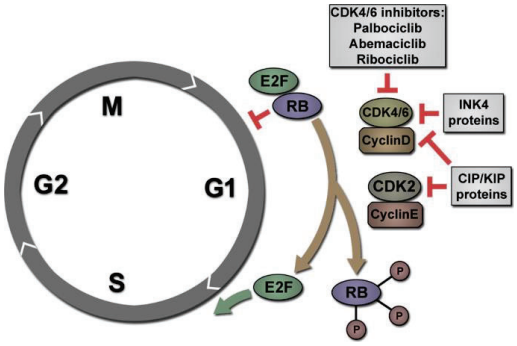
# PARP Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Myelosuppression<br>• Niraparib – thrombocytopenia<br>• Olaparib – anemia<br>Nausea/Vomiting<br>Diarrhea<br>Fatigue | Signs/symptoms of interstitial lung disease<br><br>CBC<br>CMP | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Prolonged use can increase the risk of developing MDS/AML.<br><br>Myelosuppression, fatigue, and GI adverse effects tend to be self-limiting after 4-8 weeks.<br><br>Initial niraparib dosing may be modified based on weight and/or platelet count.<br><br>Consult clinical pharmacist for any questions. |

79

# CDK4/6 Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits cyclin-dependent kinases 4 and 6 preventing progressing through the cell cycle, resulting in arrest at the G1 phase | Abemaciclib<br>Palbociclib<br>Ribociclib | Hormone positive breast cancers |




80

# CDK4/6 Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Diarrhea – abemaciclib (90%)<br>EKG Changes – ribociclib<br>Neutropenia – palbociclib, ribociclib<br>Hepatotoxicity | CBC – should be done during off-week of ribociclib and palbociclib<br><br>EKG monitoring for ribociclib prior to treatment and one week after initiation | Subject to numerous drug interactions including acid suppressive therapies.<br><br>ANC > 1,000 prior to cycle initiation for ribociclib and palbociclib<br><br>Provide antidiarrheals for as needed use with abemaciclib<br><br>Consult clinical pharmacist for any questions. |

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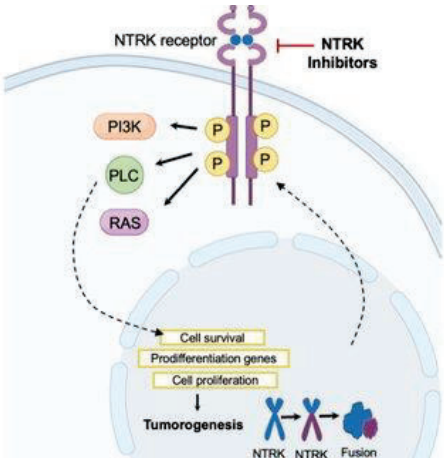
# NTRK Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits the proto-oncogenic drivers encoded by NTRK chromosomal rearrangements | Entrectinib<br>Larotrectinib | NTRK Gene Fusion positive solid tumors |

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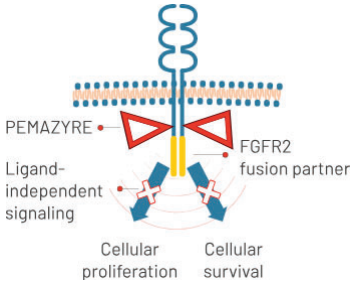
# NTRK Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Cognitive Impairment<br>Mood Disorders<br>Hepatotoxicity<br>Myelosuppression<br>Myalgia/Arthralgia | Monitor for memory changes, sleep disturbances, and other cognitive issues<br><br>CMP<br>CBC | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Requires specific NTRK gene fusion(s) for use.<br><br>Consult clinical pharmacist for any questions. |



# FGFR Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits the proto-oncogenic drivers encoded by FGFR altered enzyme activity | Futibatinib<br>Pemigatinib<br>Erdafitinib | FGFR altered solid tumors |



# FGFR Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Hyperphosphatemia<br>Ocular Toxicity<br>Nail Changes<br>Myelosuppression<br>Hepatotoxicity<br>Rash | Ophthalmological exams at baseline and periodically throughout treatment<br><br>CMP and serum phosphorus<br>CBC | Subject to numerous drug interactions including acid suppressive therapies.<br><br>Evaluate patient for signs/symptoms of keratitis, dry eye, and retinal pigment epithelial detachment.<br><br>Consult clinical pharmacist for any questions. |

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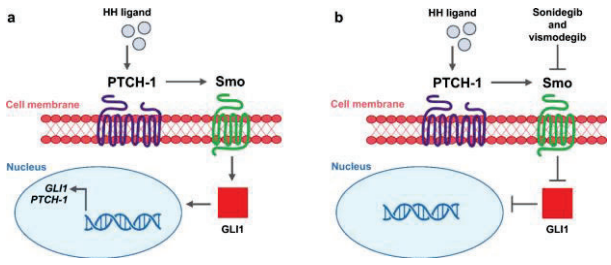
# Hedgehog Inhibitors

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits Smoothened homologue, the transmembrane protein involved in Hedgehog signal transduction | Glasdegib<br>Sonidegib<br>Vismodegib | Relapsed/refractory AML – glasdegib<br><br>Cutaneous basal cell carcinoma – sonidegib and vismodegib |

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# Hedgehog Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Dermatologic toxicity<br>Myalgia/Arthralgia<br>Alopecia<br>Dysgeusia<br>Nausea/vomiting<br>QTc prolongation | CBC<br>CMP<br>CK levels<br><br>EKG | Subject to numerous drug interactions.<br><br>Consult clinical pharmacist for any questions. |

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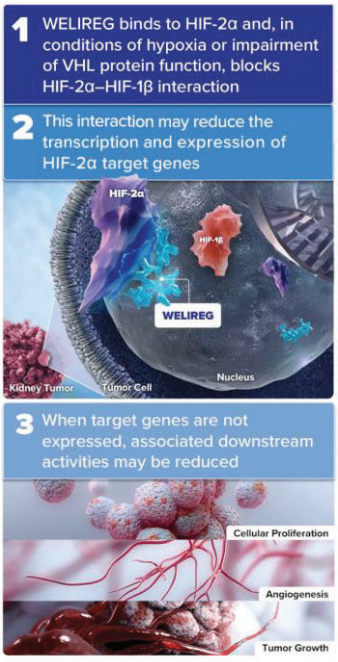
# HIF-2a Inhibitor

| Mechanism | Agents (PO) | Common Uses |
|---|---|---|
| Inhibits hypoxia-inducible factor 2-alfa, which plays a role in promoting cellular adaptation to hypoxia. | Belzutifan | Renal Cell Carcinoma |

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## HIF-2a Inhibitors

| Common Adverse Effects | Monitoring | Clinical Considerations |
|---|---|---|
| Anemia<br>Hypoxia<br>Hepatotoxicity<br>Musculoskeletal Pain | CBC<br>O2 Sat <88% | Subject to numerous drug interactions.<br><br>Consult clinical pharmacist for any questions. |



## Targeted Therapies – Take Home Points

- Understanding the mechanism of agents can help determine potential adverse effects
- Targeted therapies have allowed for more tailored medicine
- Oral therapies, while convenient, are subject to more drug-drug and drug-food interactions
  - Intestinal and systemic cytochrome inhibition
  - Acid suppression

# Immunomodulating Therapies

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## Immunotherapy

- Cytotoxic T-lymphocyte associated protein 4 (CTLA) inhibitors
  - Ipilimumab, tremilimumab
- Programmed-death (ligand)-1 (PD(L)-1) inhibitors
  - PD-1 inhibitors: cemiplimab, dostarlimab, nivolumab, pembrolizumab, penpulimab, retifanlimab, tislelizumab, toripalimab
  - PDL-1 inhibitors: atezolizumab, avelumab, cosibelimab, durvalumab
- Lympohocyte-activation gene 3 (LAG-3) inhibitor
  - Relatlimab
- Interleukin (IL-2) Products
  - Aldesleukin

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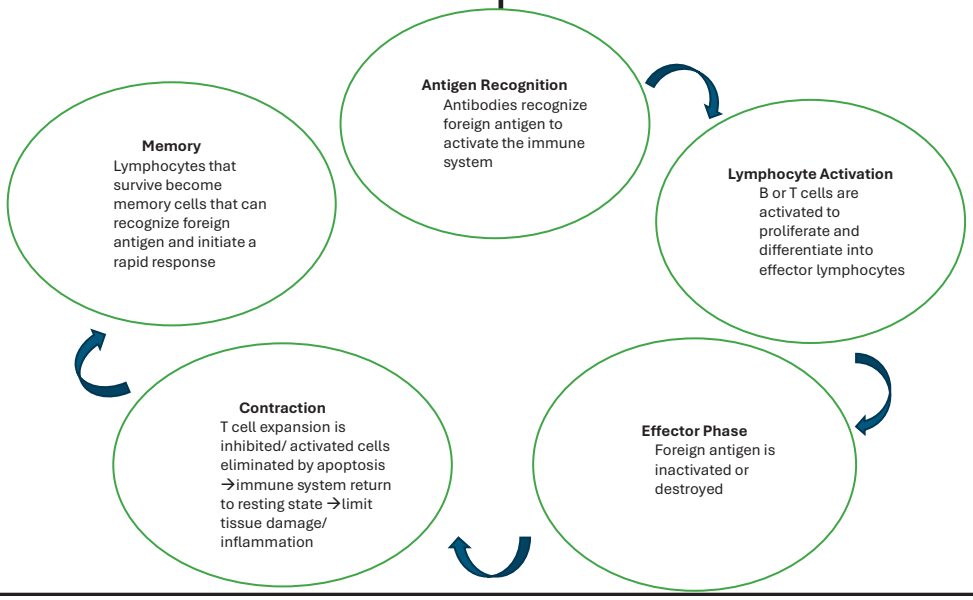
# Phases of Immune Response

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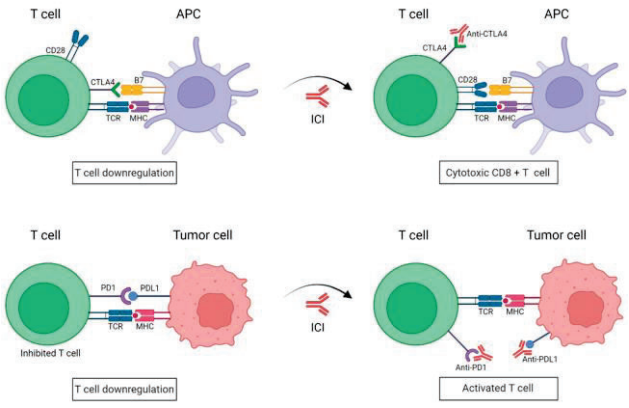
# Checkpoint Inhibitors (ICI) Mechanism of Action

- Inhibitory and stimulatory pathways and checkpoints regulate the identification and elimination of abnormal cells
- Cancer cells disrupt these pathways and avoid recognition
- ICIs block the prevent T-lymphocytes from recognizing and killing cancer cells
- Once blocked, T-cells are released and can elicit an immune response against cancer cells

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# CTLA-4 Inhibitors

- Agents
  - Ipilimumab
  - Tremelimumab
- Indications
  - Colorectal
  - Esophageal
  - HCC
  - Melanoma
  - Mesothelioma
  - Merkel cell
  - NSCLC
  - RCC
- Most commonly given in combination with PDL-1/PD-1 inhibitor
  - Ipilimumab + nivolumab
  - Tremelimumab + durvalumab

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# PDL-1/PD-1 Inhibitors

- Agents
  - Atezolizumab
  - Avelumab
  - Cemiplimab
  - Cosibelimab
  - Dostarlimab
  - Durvalumab
  - Nivolumab
  - Nivolumab + Relatlimab
  - Pembrolizumab
  - Penpulimab
  - Retifanlimab
  - Tislelizumab
  - Toripalimab
- Indications
  - Everything??
  - 22+ indications and counting
  - Some indications require biomarker testing
    - PDL-1, CPS, TPS, etc.
    - MSI-H/dMMR
    - TMB-H

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# Immune Checkpoint Inhibitor Adverse Effects

- Common Adverse Effects
  - Cardiomyopathy
  - CNS toxicity (including demyelinating disease)- extremely rare
  - Colitis
  - Dermatitis/skin rash
  - Endocrine changes
    - Hypo-/hyperthyroid
    - Hypophysitis (CTLA-4 inhibitors)
    - Adrenal insufficiency (CTLA-4 inhibitors)
  - Hepatitis
  - Nephritis
  - Pneumonitis
  - Ophthalmic toxicity
  - Pancreatitis

- Monitoring/Considerations
  - Lab monitoring
    - CMP (LFTs, BUN, SCr)
    - TSH/Free T4
    - ACTH, AM Cortisol (CTLA-4 agents only)
  - Cardiac monitoring (intuition-specific)
  - Symptom monitoring
    - Chest pain
    - Cough/shortness of breath
    - Diarrhea
    - Headache
    - Rash
    - Severe fatigue
    - Severe muscle weakness/pain
    - Vision changes/eye pain

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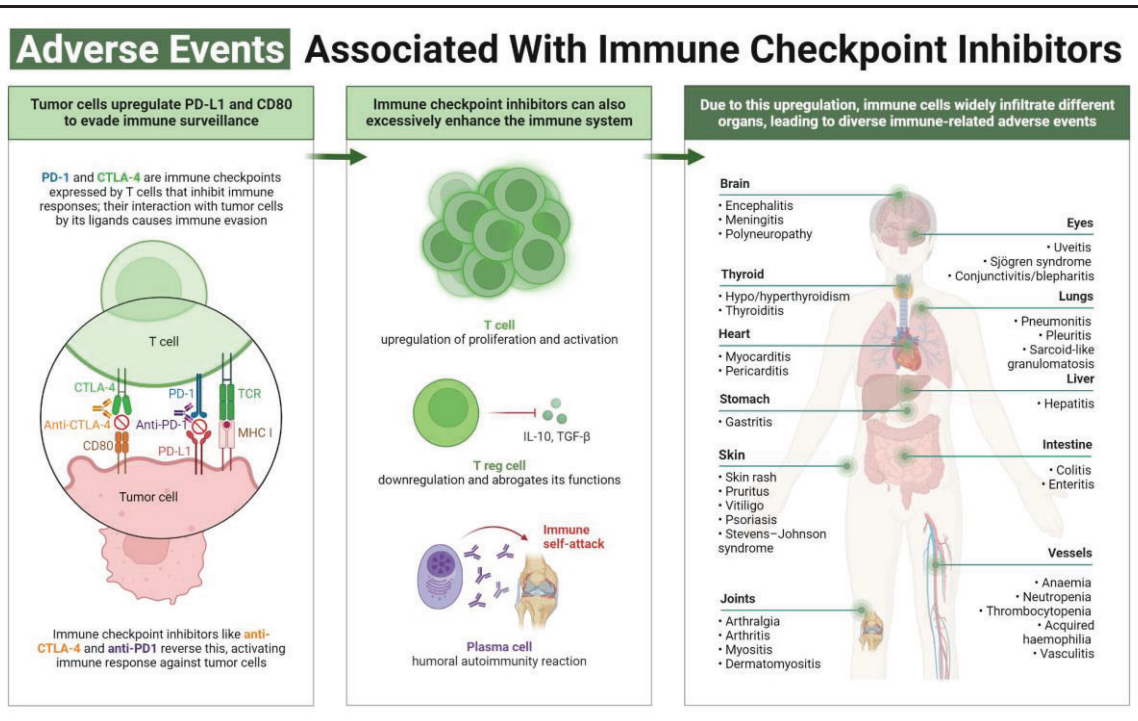


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# Treatment of Immune Mediated-AEs

- Organ system and grade specific
  - Hold IO
  - Corticosteroids oral (prednisone 0.5-1mg/kg/day) or IV (methylprednisolone 1-2 mg/kg/day)
    - Infection prophylaxis: Prednisone ≥ 20 mg/day for 4 weeks or longer requires PJP prophylaxis
    - GI prophylaxis: consider PPI
    - Osteoporosis/bone loss: increased risk of vertebral fractures if prednisone ≥ 30 mg for 30 days or longer; recommend calcium/vitamin D supplementation
  - Steroid refractory: additional immunosuppressants may be indicated
    - Colitis: infliximab or vedolizumab
    - Pneumonitis: IVIG or tocilizumab

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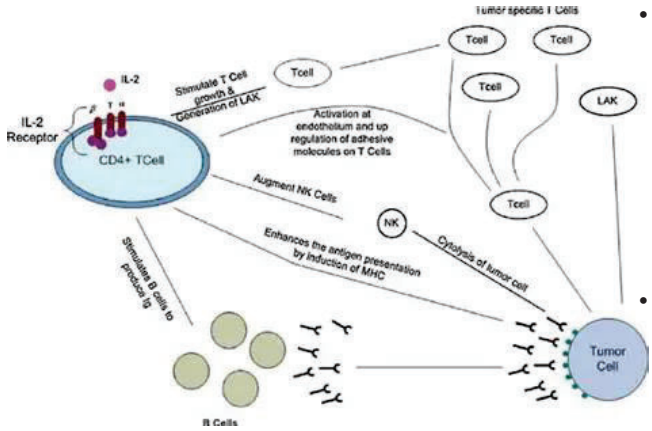
# Interleukin Therapy




- Agent
  - Aldesleukin
- Indications
  - Melanoma
  - Renal cell carcinoma
- Adverse effects
  - Capillary leak syndrome (hypotension, oliguria, hypoxia, edema)
  - CNS toxicity
  - Dermatologic toxicity
  - Flu-like symptoms
  - GI toxicity
  - Hepatotoxicity
  - Hyperglycemia/DM
  - Hypersensitivity/infusion reactions,
  - Infection
- Monitoring/Considerations
  - Pretesting: CBC/CMP, LVEF (ECHO), PFTs
  - Monitoring during therapy: CBC/CMP, TFTs
  - Pre-medications required
  - CLS monitoring: hypotension, dyspnea, edema, hypoalbuminemia
  - Administered inpatient with cardiac monitoring

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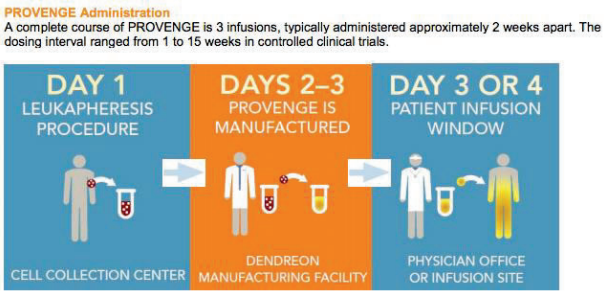
# Genetically Engineered Therapies

- Sipuleucel-T
- Chimeric antigen receptor T-cell therapy (CAR-T)
  - T cells are taken from blood and genetically changed in the lab to have a receptor called a CAR on their outer surface
  - Helps the T cells attach to a specific cancer cell antigen
  - CAR T cells are then returned to individual.
  - Since different cancers have different antigens, each CAR is made for a specific cancer's antigen
    - Tisa-cel, axi-cel, brexu-cel, liso-cel, ide-cel, cilta-cel, obe-cel
- Tumer Infiltrating Lymphocytes (TILs)
  - Helps immune system fight cancer by using own TILs
  - Cells are collected from tumor, multiplied in a lab, and then returned to the body in large numbers to help target and destroy cancer cells
  - Lifileucel



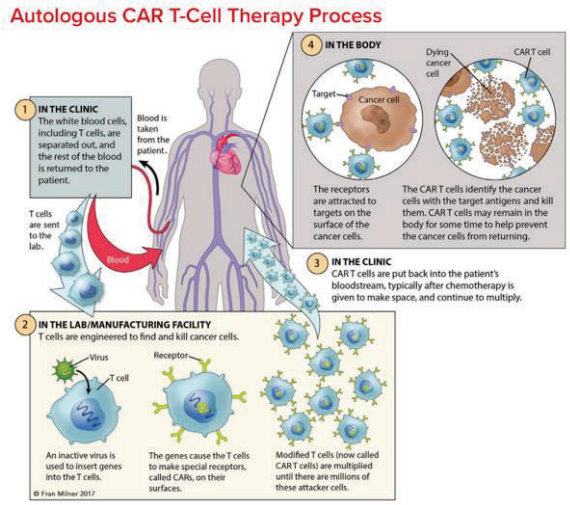
# Sipuleucel-T

- Autologous cellular immunotherapy
- Designed to induce an immune response targeted against PAP, an antigen expressed in most prostate cancers
- Indication: metastatic prostate cancer




- Adverse effects
  - Bone/muscle pain
  - Flu like symptoms/fever
  - Infusion reactions
  - Cerebrovascular/cardiovascular events (post-marketing reports)
  - Thromboembolic events (post-marketing reports)
- Administration
  - Administer over 60 minutes
  - Pre-medicate with acetaminophen and diphenhydramine
  - Product has 3-hour room temperature BUD

# CAR-T Cell Therapy




| Agent | | Indication |
|---|---|---|
| Tisagenlecleucel | Tisa-cel | ALL, DLBCL, FL |
| Axicabtagene ciloleucel | Axi-cel | DLBCL, FL |
| Brexucabtagene autoleucel | Brexu-cel | ALL, mantle cell lymphoma |
| Lisocabtagene maraleucel | Liso-cel | CLL, DLBCL, FL, mantle cell lymphoma, MZL |
| Idecabtagene vicleucel | Ide-cel | Multiple myeloma |
| Ciltacabtagene autocleucel | Cilta-cel | Multiple myeloma |
| Obecabtagene autoleucel | Obe-cel | ALL |

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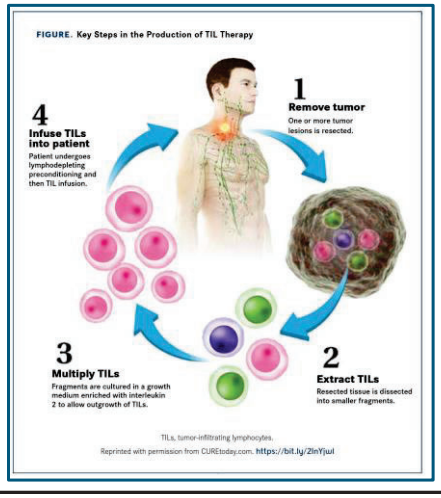
# Lifileucel

- TILs




- Indication
  - Melanoma
- Adverse effects
  - Capillary leak syndrome
  - CRS
  - Edema (including cerebral, pulmonary)
  - Hypotension
  - Tachycardia
  - Diarrhea
  - Nausea/vomiting
  - Myelosuppression
  - Fever/chills
  - Fatigue

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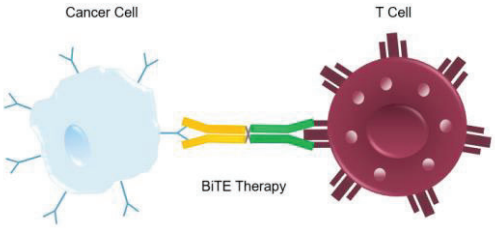
# Bispecific T-Cell Engager (BiTE) Therapy

- A substance made in the laboratory that can bind to two target proteins on the surface of different cells.
  - May bind to a certain protein on healthy T and to a different protein on cancer cells
  - Brings the T cells and cancer cells close together so the T cells can more effectively kill the cancer cells

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| | Indications | CRS | ICANS |
|---|---|---|---|
| **Talquetamab** | Multiple myeloma | Risk: 76% of patients<br>Median time to onset: 2 days<br>Median duration: 2 days | Risk: ~10% of patients<br>Median time to onset: 2.5 days<br>Median duration: 2 days |
| **Elranatamab** | multiple myeloma | Risk: 58% of patients (43.2% with dose one)<br>Median time to onset: 2 days<br>Median duration: 2 days | Risk: 3.3% of patients (2.7% after 1st dose)<br>Median time to onset: 3 days<br>Median duration: 2 days |
| **Teclistamab** | Multiple myeloma | Risk: 72% of patients<br>Median time to onset: 2 days (1-6 days)<br>Median duration: 2 days (1-9 days) | Risk: 6% of patients<br>Median time to onset: 4 days (2-8 days)<br>Median duration: 3 days (1-20 days) |
| **Linvoseltamab** | Multiple myeloma | Risk: 46% of patients<br>Median time to onset: 11 hours (-1-184 hours)<br>Median duration: 17 hours (1-76 hours) | Risk: 8% of patients<br>Median time to onset: 1 day (1-4 days)<br>Median duration: 2 days (1-11 days) |
| **Glofitamab**<br><br>12 cycles | DLBCL | Risk: 70% of patients<br>Median time to onset: 14 hours (5-74 hours)<br>Median duration: 2 days (1-14 days) | Risk: 4.8% of patients |
| **Epcoritamab**<br><br>Indefinite | DLBCL and FL | Risk: 49-51% of patients<br>Median time to onset: 24-59 hours<br>Median duration: 2 days | Risk: 6% of patients<br>Median time to onset: 16.5-21.5 days (median from most recent admin, 3 days)<br>Median duration: 2-4 days |
| **Mosunetuzumab** | FL | Risk: 39% of patients<br>Median time to onset: 5 hours (1 hour-3 days)<br>Median duration: 3 days (1-29 days) | Risk: 1% of patients<br>Median time to onset: 17 days (1-48 days)<br>Median duration: 3 days (1-20 days) |
| **Blinatumomab** | ALL | Risk: 7-16% depending on indication<br>Median time to onset: 2 days<br>Median duration: 5 days | Risk: 7.5% |
| **Tarlatamab** | SCLC | Risk: 73% of patients<br>Median time to onset: 16 hours<br>Median duration: 4 days | Risk: 6%<br>Median time to onset: 16 days |

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# BiTE and CAR-T Cell Therapy AEs

## Cytokine Release Syndrome (CRS)

- **Presentation**
  - Fever (≥38.0°C) must be present at the onset of CRS
  - May include fatigue, headache, rash, diarrhea, arthralgia, diarrhea
  - Can progress to hypotension, SIRS, vascular leakage, peripheral/pulmonary edema, renal failure, cardiac dysfunction, multiorgan failure
- **Treatment**
  - Tocilizumab
  - Corticosteroids

## Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

- **Presentation**
  - Encephalopathy with confusion/behavior changes
  - Visual and auditory hallucination
  - Language dysfunction
  - Headache, fatigue, tremors
  - Dysgraphia, fine motor impairment
  - Seizures
  - Cerebral edema and death (rare)
- **Treatment**
  - Corticosteroids

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# Immunomodulators

| Class | Agents | Indications | Adverse effects | Monitoring/ Considerations |
|---|---|---|---|---|
| **iMids** | Lenalidomide<br>Pomalidomide<br>Thalidomide | Multiple myeloma, other hematologic malignancies | • Diarrhea<br>• infection<br>• Myelosuppression<br>• Neuropathy (thalidomide)<br>• Skin rash<br>• VTE | • Renal dosing adjustments<br>• REMS program (embryofetal toxicity) |
| **Interferons** | Ropeginterferon Alfa-2b | Polycythemia vera | • Arthralgia/<br>• Musculoskeletal pain<br>• Diarrhea<br>• Flu-like symptoms<br>• Pruritis<br>• Infection<br>• Injection site reaction<br>• Depression<br>• Sleep disorder | • Subcutaneous injection every 2 weeks<br>• Consider pre-medicating with acetaminophen |

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# Questions?

AHN





# Targeted and Immunomodulating Therapies in Oncology

AHN

Spring 2026

# Hormonal Therapy in Cancer Treatment

Heather Kennihan MSN, RN, OCN
AHN Cancer Institute
Professional Development Specialist
Heather.Kennihan@ahn.org

*I have nothing to disclose

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## Learning Outcomes

- Identify hormonal functions within the body
- Review cell cycle and cellular kinetics related to hormonal anticancer therapies
- Discuss the mechanism of action for hormonal therapy
- Describe side effects of hormonal anticancer therapy

2

# What are hormones?

The body's means of regulating various functions via chemical messages which aid in:

- Digestion
- Growth and development, including sexual and reproduction
- Nutrient metabolism and storage

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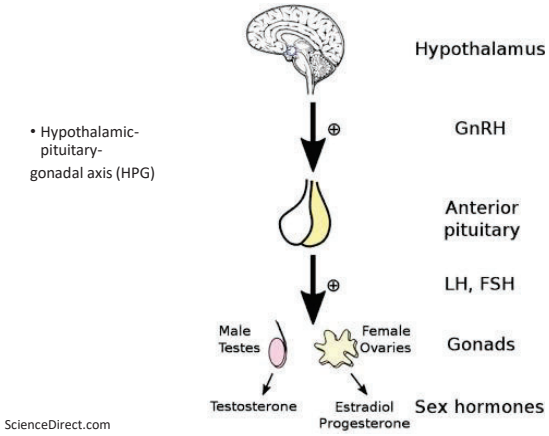
# How are hormones produced?

- Hypothalamic-pituitary-gonadal axis (HPG)

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# Estrogen

**Where does estrogen come from?**

- Steroid hormone derived from cholesterol
- Fat cells
- Adrendal glands
- Produced by the ovaries and testes
- Passively crosses the cell membrane - and eventually exerts its function in the nucleus of the cell
- Androgens can be changed to estrogens in peripheral tissues, especially adipose tissue.
- mediated by an enzyme called **aromatase**

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# Estrogen

**What does estrogen do?**

- Primary and secondary sexual characteristics
- Growth of long bones and reduction in bone resorption
- Impacts function of ovaries, cervical secretions, endometrial lining, and vaginal tissue
- Stimulate breast changes
- Cardiac, lipid, and vascular effects

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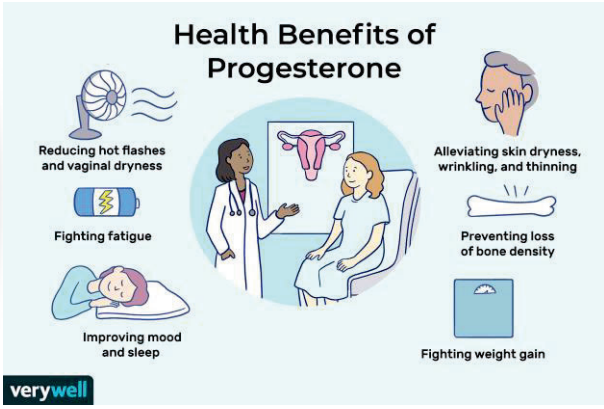
## What is progesterone?

- Steroid hormone
- Secreted by the corpus luteum following ovulation and by the adrenal cortex
- Functions include:
  - Breast tissue development
  - Action on the renal tubule
  - Smooth muscle relaxation

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## Testosterone

- Secreted by the testes and adrenal cortex under the influence of luteinizing hormone (LH)
  - Can be converted peripherally to estrogens
- Majority circulates bound to proteins, only 2% is unbound and therefore able to function
- Affect development of primary and secondary male characteristics and play a part in sperm production
  - Promotes protein metabolism and MSK growth
  - Influences fat distribution
  - Stimulates erythropoiesis

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# Important Definitions

**Agonist**: a substance that acts like another substance and produces the same or similar effect (works together)

**Antagonist**: a substance that acts like another substance, but binds to a receptor and prevents activation by the natural substance (blocker)

**Upregulation**: increased number of cell receptors

**Downregulation**: decreased number of cell receptors

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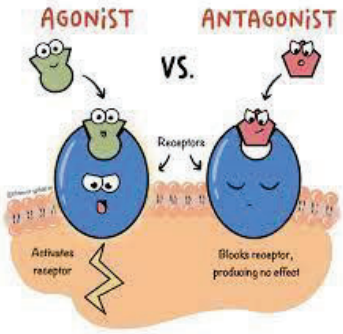
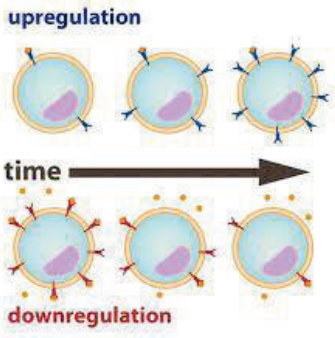
## What's the difference?

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## Hormonal Therapies for Breast Cancer

### Anti-estrogens:

***Estrogen Receptor Antagonist***

- Toremifene (Fareston)
- Fulvestrant (Faslodex)
- Elacestrant (Orserdu)

***SERMS (Selective Estrogen Receptor Modulators)***

- Tamoxifen (Nolvadex)
- Raloxifene (Evista)

***Aromatase Inhibitors (AIs):***

- Aminoglutethamide (Cytraden)
- Anastrozole (Arimidex)
- Exemestane (Aroamasin)
- Letrozole (Femara)

***Ovarian Suppression (agonist):***

- Leuprolide (Lupron)
- Goserelin (Zoladex)

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## Hormonal Therapy-Breast Cancer

### Background

- Development and growth of breast cancer is often driven by hormones, 80% of breast cancers are estrogen positive, or ER+.
- Breast cancer that is ER+ is seen as fuel.

### Uses

- Chemoprevention
  - High risk and less than 50 years of age, atypical hyperplasia
- Maintenance treatment for curative intent
- Palliative treatment for metastatic cancer

### Hormonal therapy can be done in three ways:

- Ovarian ablation
- Blocking production of estrogen
- Blocking effects of estrogen

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# Hormonal Therapy-Breast Cancer

- **Pre-menopausal**
  - Females have multiple sources of estrogen: ovaries, adrenal cortex, peripheral tissues
  - Ovarian suppression or ovarian ablation

    ***Permanent***:
    - By removal of the ovaries or external beam radiation

    ***Temporary***:
    - Administration of GnRH agonists
    - Interferes with the typical HPG axis by causing desensitization of the pituitary cells
    - Lupron and Zoladex -given by depot injection in monthly intervals

- **Post-menopausal**
  - females no longer have ovarian function, thus only produce estrogen in the adrenal cortex and peripheral tissues. Men also fall into this category

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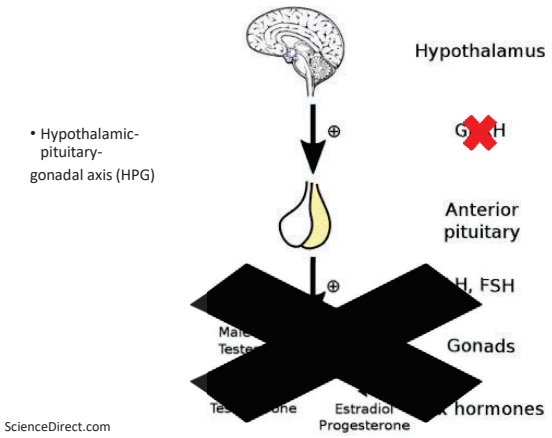
# How are hormones stopped and blocked?




- Hypothalamic-pituitary-gonadal axis (HPG)

ScienceDirect.com

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## Selective Estrogen Receptor Modudulators (SERMS)

### Tamoxifen (Nolvadex)

- Dose is 20mg PO daily
- Acts as an estrogen antagonist in most tissues
  - However, has some estrogen agonist properties on specific tissues
    - uterus, bone, vasculature

### Raloxifene(Evista)

- Dose is 60mg PO daily

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## Reduction of Estrogen into the Nucleus

- These drugs interfere with estrogen's ability to affect change on a cell
  - estrogen is still produced, but it cannot work
- Occurs because they bind to the intracellular estrogen receptor
  - Prevents estrogen from binding to the receptor
  - Binds to the receptor, no space for estrogen
  - Receptor cannot be "turned on"
  - Used pre-menopausal, but can also be used post menopausal
- Typical drugs include tamoxifen and toremifene
- Faslodex also falls into this category, but its action is slightly different

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## Side Effects

- Hot flashes
- Fatigue
- Edema
- Mood changes
- Depression
- Rash
- Nausea
- Vaginal discharge
- Arthralgia
- Elevated liver enzymes
- Blood clots- Including DVT, PE, CVA
- Uterine malignancy (endometrial cancer)

**MULTIPLE drug interactions**

- Must be very cautious with SSRIs (particularly fluoxetine, **paroxetine**, and sertraline), warfarin

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## Fulvestrant (Faslodex)

- Given as an IM injection Day 1, Day 15, Day 29, then every 4 weeks
- Dose is 500mg, split into two (5mL) syringes
- MUST be given in the gluteal area – not simultaneously
- Indicated only for metastatic or recurrent breast cancer

***Side Effects***:

- Fatigue
- Hot flashes
- Headaches
- Nausea
- Diarrhea
- Abdominal pain
- Decreased appetite
- Increases transaminases

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# Elacestrant (Orserdu)

- Given orally 345mg daily- take with food to reduce nausea
- Dose reduce for toxicities- (have 86mg tablets)
- Indicated only for metastatic or recurrent breast cancer that is ESRI-mutated and have failed one line of endocrine therapy

***Side Effects***:

- Arthralgias
- Fatigue
- Hot flashes
- Headaches
- Nausea
- Increased cholesterol
- Increased AST
- Diarrhea, constipation
- Abdominal pain
- Decreased appetite

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# What happens during menopause?

- Cessation of ovarian function
- Generally occurs between the ages of 48 and 55
- Lack of menstruation for a full year or persistently elevated FSH levels
- Adrenal estrogens are unable to sustain form and function like ovarian estrogen
- Results in vasomotor dysfunction
- Long term, rates of osteoporosis and risk for cardiovascular disease increase
- Decreased amount of Estrogen

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## Reduction in Estrogen by blocking Aromatase

**Aromatase-** Enzyme that mediates all steps of the conversion of testosterone to estrogen

- Produced in the ovaries, breasts, and other peripheral tissues, such as adipose tissue
- Role for AIs
  - Lowers estrogen levels by stopping the aromatase enzyme in fat tissue from changing other hormones into estrogen
  - These drugs do not stop the ovaries from making estrogen
  - These drugs targeting estrogen production-aromatase inhibitors-are used in post-menopausal women
  - Used in pre-menopausal women is possible, but they require ovarian suppression first

Most common drugs include Arimidex, Letrozole, and Exemestane

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## Aromatase Inhibitors

- Anatrozole (Arimidex)
  - Dose: 1mg PO q day
- Letrozole (Femara)
  - Dose: 2.5mg PO q day
- Exemestane (Aromasin)
  - Dose: 25mg PO q day

### Side Effects

- Arthralgias
- Myalgias
- Hot flashes
- Vaginal dryness
- Vaginal atrophy
- GI distress
- Edema
- Venous thrombosis
- Decreased bone density

22

## Length of Therapy

**Minimum of 5 years for curative intent, early stage patients to prevent recurrence**

- at least 5 years of adjuvant endocrine therapy
- can also be given as a sequential regimen following tamoxifen administration

**Until disease progression for patients with metastatic disease**

23

## Side Effect Management

- Real world data tells us that development of intolerable side effects is the primary reason for non-adherence and treatment discontinuation in patients on these medications.
  - This has direct implications on disease free intervals AND overall survival

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# Side Effect Management

## Vasomotor symptoms

-Lifestyle modification

-Antidepressants (venlafaxine, paroxetine, citalopram, and desvenlafaxine)

-Anticonvulsants (gabapentin, pregabalin)

-Oxybutynin

-No data to support use of supplements (phytoestrogens, black cohosh, vitamin E, evening primrose oil, etc)

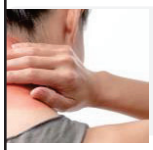
## Gynecologic effects

-Mainly vaginal dryness and decreased libido

-Interventions include vaginal lubricants and some patients may be candidates for local estrogen therapy (creams/gels)

25

# Aromatase Inhibitor-Induced Musculoskeletal Symptoms (AIMSS)



Symptom pattern including arthralgias, myalgias, tendonitis, carpal tunnel syndrome

½ Almost 50% of those on an AI report musculoskeletal symptoms after starting treatment and approximately 20% of those on who are on these medications will eventually discontinue them due to these symptoms (Henry et al., 2012)

Musculoskeletal symptoms are also reported by patients on tamoxifen, but at a significantly lower rate

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# AIMSS Treatment

- Acetaminophen and NSAIDs may be useful for short term symptom management,
- Local therapy (wrist splints, steroids for trigger finger)
- Omega-3 Fatty Acids: 3.3g/day has shown to decrease AIMSS symptoms, but results were only clinically significant for those with a BMI ≥ 30 $kg/m^2$
- Acupuncture: 18 sessions over 12 weeks has shown to produce a "clinically meaningful" response to acupuncture (over half of the patients experienced at least a 30% reduction in pain scores)
- Duloxetine: 30-60mg daily has been shown to decrease AIMSS in 70% of women
- Vitamins/Supplements: most data is either equivocal or negative

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# AIMSS Treatment (continued)

- Exercise/Yoga
  - Some of the best data is here
  - In randomized clinical trials, aerobic exercise, resistance/weight training, yoga, and combinations of these have all been shown to lower pain scores and increase quality of life assessment scores
  - No specific form of exercise seems to be more effective than another, but few comparative studies exist
  - In general, 150 minutes per week should be the goal. However, benefit is seen at smaller amounts of time

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# AIMSS Treatment (continued)

Switch Therapy

- Those who are intolerant of one AI may be able to better tolerate a different AI
- Mechanism of action for the three AIs is generally the same, this phenomenon is likely due to individual differences
- We will ask a patient to hold their AI for a period of time and then restart the new medication once musculoskeletal symptoms have improved
- Numbers vary significantly between studies, but in general, many patients are able to eventually tolerate one of the AIs

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## Ovarian Suppression

***Goserelin (Zoladex)***

- Given as a subcutaneous injection at 28 day (3.6mg) or 12 week intervals (10.8mg).
  - If being used to suppress ovarian function in pre-menopausal women, monthly dosing more reliable

***Lupreolide (Lupron)***

- Several dosing options available, all given IM.
  - 3.75 mg every 28 days
  - 11.25 mg every 12 weeks

30

## Side Effects

- Hot flashes
- Decreased bone density
- Emotional lability
- Edema
- Headache
- Depression
- Fatigue
- Weight changes
- Vaginal atrophy
- Pain at injection
- Local site reaction

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## Case Study

Patient has estrogen and progesterone positive breast cancer and is a candidate for hormonal therapy. What additional information would we need to determine what therapy would be best ?

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## Hormonal Therapies for Prostate Cancer

***Gonatropin releasing hormone (Gn-RH agonists):***

- Leuprolide (Lupron)
- Goserelin (Zoladex)
- Provenge (Sipuleucel)

***Gonatropin releasing hormone (Gn-RH antagonist):***

- Firmagon(degarelis)

***Anti-androgens (androgen antagonists):***

- Bicalutamide (Casodex)
- Flutamide (Eulexin)
- Nilutamide (Nilandron)

***CYP17 inhibitor:***

- Zytigia (abiraterone)

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## Hormonal Therapy-Prostate Cancer

### Background

- Androgens stimulate growth of prostate cells
- ALL prostate tumors are considered hormone positive
- ALL patients with prostate cancer are candidates for hormonal based therapy

### Hormonal therapy purpose

- Lower androgen levels
- Stop androgens from working

### Surgical Castration

- Removal of the testicles

### Medical Castration

- GnRH agonsists –Lupron(leuprolide), Zoladex(goserelin), Trelstar(triptorelin)
  - must also have patients on anti-androgen therapy prior to starting due risk of tumor flare from initial increase in testosterone
- GnRH antagonist – Firmagon (degarelix), Orgovyx (relugolix)
- CYP17 inhibitor – Zytigia (abiraterone)

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# GnRH Agonists

**Leuprolide (Lupron IM, Eligard SQ)**

7.5mg monthly

22.5mg every 12 weeks

30mg every 16 weeks

45mg every 24 weeks

**Goserelin (Zoladex)**

**SQ**

3.6 mg every 28 day

10.8mg every 12 weeks

***Side Effects:***

Tumor flare

Headache

Fatigue

Depression

Dizziness

Insomnia

Hot flashes

Weight change

Edema

Emotional lability

Testicular atrophy

Sexual dysfunction

Pain at injection site

Local site reaction

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# GnRH Antagonists

**Degarelix (Firmagon)**

loading dose: 240mg (split into 2 syringes)

maintenance: 80mg every 28 days

**Given as deep SQ**

**Needle is inserted at 45 degrees**

**Does not cause initial increase in testosterone**

Faster drop in testosterone levels (7 days vs. 28 days)

No concern for tumor flare

*Side Effects:*

- Fatigue
- Hot flashes
- Weight change
- Increased transaminases
- Injection site reactions (up to 40%)

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# CYP17 Inhibitor

**Abiraterone (Zytiga)**

- dose: 1000mg PO q day
- mechanism of action:
  - inhibits the enzyme CYP17, which catalyzes the formation of precursors to testosterone

- Drug lowers levels of other hormones, so patients must also take prednisone (usually 5mg PO BID).

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# Side Effects

- Hypertension
- Edema
- Fatigue
- Insomnia
- Electrolyte abnormalities (K+)
- Increased triglycerides
- Constipation
- Diarrhea
- Increased transaminases
- Myalgias
- Arthralgias
- Joint swelling
- Cough
- Increased blood sugars

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# Anti-androgens

All anti-androgens are still given with a GnRH agonist/antagonist – except Nilutamide

**Nilutamide (Niladron)**
- Dose: 300mg PO q day for first 30 days, then 150mg PO q day

**Apalutamide (Erleada)**
- Dose: 240mg PO q day

**Bicalutamide (Casodex)**
- Dose: 50mg PO q day

**Darolutamide (Nubeqa)**
- Dose: 600mg PO BID

**Enzalutamide (Xtandi)**
- Dose: 160mg PO q day

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# Side Effects Anti-androgens

| |
|---|
| Hot flashes |
| Fatigue |
| Neutropenia |
| Rash |
| Diarrhea |
| Nausea |
| Constipation |
| Edema |
| Pain |
| Gynecomastia |
| Genital atrophy |

- Decreased libdo
- Hypertension
- Peripheral edema
- Electrolyte abnormalities
- Hyperglycemia
- Headache
- Pelvic pain
- Hematuria
- Decreased appetite
- Increased liver enzymes
- Falls/bone fracture***

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## Case Study

Patient is newly diagnosed prostate cancer starting his first injection of a GnRH Agonist. He is also instructed to take a Anti-androgen.

- Which drugs could he get for GnRH agonist?
- What anti-androgen could he take?
- What are some topics we would want to discuss prior to his injection and starting an oral agent?

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| HORMONAL THERAPY TOXICITIES | |
|---|---|
| General | Hot flashes, mood fluctuations, fatigue, gynecomastia, decreased libido |
| Ocular | Visual field changes |
| Neurologic | Seizures |
| Cardiac | Hypertension, edema, fluid retention, ischemic heart disease, dysthymias |
| Skeletal | Bone mineral density changes |
| Hematologic | Venous thrombus embolism (VTE) |
| Integumentary | Dryness, pruritus, rash, nail changes |
| Hepatic | Hypertriglyceridemia, transaminitis, hypercholesterolemia, hypokalemia |
| Gastrointestinal | Nausea, diarrhea, constipation |

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# Key Points

**Hormonal therapy can be broken down into three basic modalities**

- centralized (gonad ablation)
- extracellular (AI)
- intracellular (SERMs, anti-androgens)

**Breast**

- Aromatase inhibitors (AIs) – post menopausal, if used premenopausal need ovarian suppression
  - arthralgias, myalgias, decreased bone density, vaginal dryness and atrophy, venous thrombosis
- Selective estrogen receptor modulators (SERMs) – premenopausal, but can be used post menopausal
  - uterine malignancies, venous thrombosis

**Prostate**

- GnRH agonists
  - testicular atrophy, pain and local injection site reactions, tumor flare, hot flashes
- GnRH antagonists
  - injection site reactions, no initial increase in testosterone levels
- CYP17 inhibitor
  - lowers other hormones, so need prednisone

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# References


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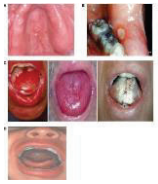
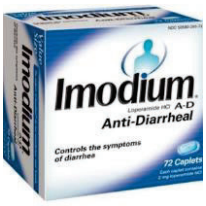
# GI Toxicities

Mary E. Kern, MSN, RN, OCN, CHSE
Professional Development Specialist, AHNCI
Mary.KERN@AHN.org
* No Disclosures*

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## Learning Outcomes

- Formulate a comprehensive plan of care, including side effects and toxicities for a patient receiving anticancer therapy – (gastrointestinal toxicities )

2

# Background

- GI toxicity manifestation ➡ Reduction in mucosal barrier integrity

| Morphologic changes to the mucosa | Effect |
|---|---|
| Changes in the regulation of tight junctions | -Intestinal permeability<br>-Destruction of the intestinal |
| Immunoreactive antigens and endotoxin release | -Aggravate inflammatory process<br>-Mucosal damage |
| Disturbances of enterocytes | -Impair the ability to combat free oxygen radicals |

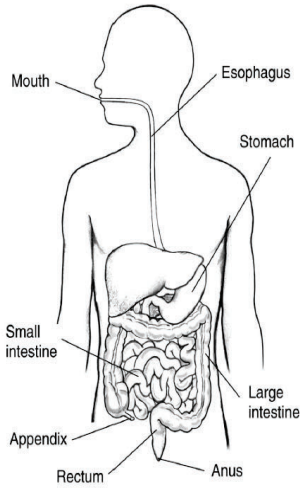
- Effect of GI related toxicities:
  - Dose reduction
  - Dose delays
  - Cessation of cancer treatment
  - Compromised nutritional intake
  - Malabsorption
  - Electrolyte imbalance
  - Reduced quality of life
  - Ulcerations/infection
  - Ulcerations/bleeding
  - Pain

Mitchell E , et al. Seminars in Oncology (2006) 3. 106-120.
Fre´de´ric et al. Best Practice & Research Clinical Gastroenterology 23 (2009) 113–124.

3

# Common GI Toxicities

- Mouth:
  - Mucositis
- Esophagus:
  - Mucositis
- Stomach:
  - Nausea and vomiting
- Lower GI tract:
  - Constipation
  - Diarrhea



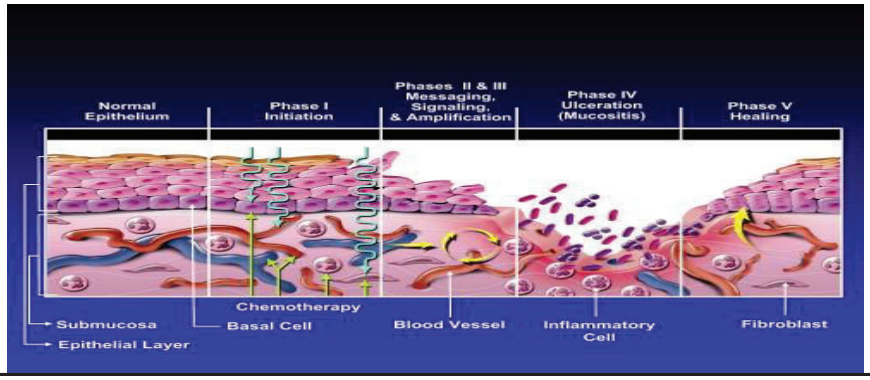

Mitchell E , et al. Seminars in Oncology (2006) 3. 106-120.
Fre´de´ric et al. Best Practice & Research Clinical Gastroenterology 23 (2009) 113–124.

4

# Mucositis

Complex interaction between epithelial and connective tissue compartments

| Phase 1 | Generation of oxidative stress |
|---|---|
| Phase 2 | DNA damage and epithelial layer cellular death; cytokine production leading to tissue injury and apoptosis |
| Phase 3 | Amplification leading to biological alteration of mucosal tissue |
| Phase 4 | Ulceration cause by inflammation and overgrowth – pain and bacteremia |
| Phase 5 | Healing with renewal epithelial proliferation and differentiation |

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# Incidence

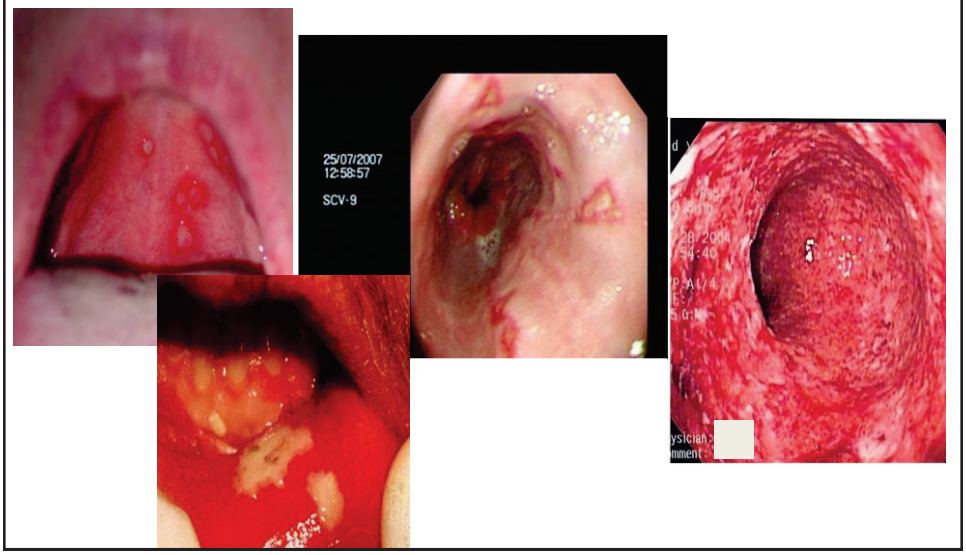
Generally: 40-75% of patients

- **Systemic cytotoxic therapy**
  - **Antimetabolites**
    - **5-FU**
    - **Methotrexate/Pemetrexed**
    - **Melphalan**
    - **Cytarabine**
  - **Anti-tumor antibiotics**
  - **Plant alkaloids**
  - **Alkylating agents**
- **Targeted therapy**
  - **EGFR**
  - **TKI/MKI**
  - **mTOR inhibitors**
  - **Immunotherapy**
    - **PD-L1**
- **Radiation therapy**

- Disease
  - GI malignancies
  - Head and Neck
  - Leukemia
  - Lymphoma
  - HSCT
  - GVHD
- Medications
  - Anticholinergics
  - Steroids
  - Phenytoin
- Age
- Poor Oral Hygiene
  - Dentures
- Poor Nutrition
- Alcohol/Tobacco

6

# Clinical manifestations- What to look for…

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# Prevention and Management Oral and GI Mucositis

**Oral Mucositis**

- Oral Hygiene
  - Soft toothbrush and flossing 2-3 times daily
  - Saline rinses
  - Remove dentures
  - Regular dental exams
  - Increase high-protein foods and fluid intake
- **Oral Cryotherapy (15 minutes prior and 30 minutes after for up to 2 hours)**
  - **5-Fu**
  - **Melphalan**
- Others
  - Palifermin with HSCT
  - Low level laser therapy
  - Benzydamine mouthwash for H&N cancer on XRT therapy
  - Zinc supplements
  - Magic swizzle (lidocaine, diphenhydramine, Mylanta)
  - Nystatin
  - Fluconazole
  - Antiviral ( acyclovir)
  - Mucosal coating agents

**GI Mucositis**

- Amifostine
- Octreotide
- Sulcarafate enema
- Probiotics
- Cryotherapy

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# Mucositis Case Study

A patient undergoing treatment for stage II small cell lung cancer is currently receiving combination chemotherapy EC with thoracic radiation. The patient is in the clinic for cycle 3 of the treatment.

Assessment reveals:

- decrease saliva
- slight redness of mucosa
- 3 ulcerations oral mucosa- each 0.3cm located buccal, soft palate & tongue
- able to eat soft foods and tolerate room temperature liquids
- weight loss of  2 kg since last office visit

1. What are the drugs in this regimen? Acronym: EC

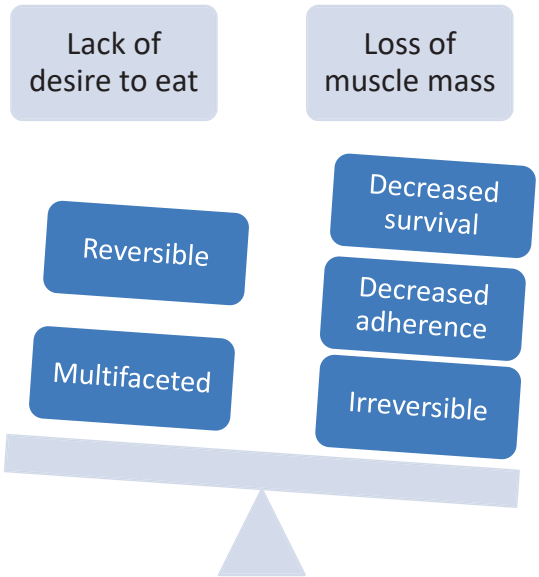
2. What grading would you give for the mucositis?

3. List 2 key teaching points specific to mucositis.

4. Would you anticipate a change in the patient's treatment today? Why/Why Not?

9

# Anorexia/Cachexia

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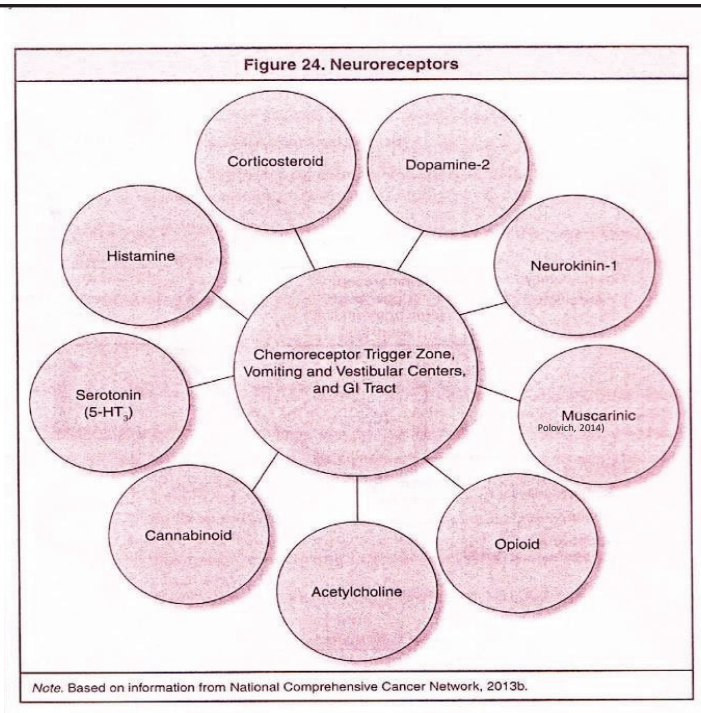
# Chemotherapy Induced Nausea/ Vomiting (CINV)

- Experienced by up to 80% of patients
- With new agents has decreased to less than 35%
- Nausea
  - Subjective experience "wavelike" feeling in stomach or back of throat
- Retching
  - Rhythmic contractions involving esophagus, diaphragm, and abdominal muscles
- Vomiting
  - Forceful expulsion of gastric contents
- these can be independent phenomena or sequential





Polovich, 2014)

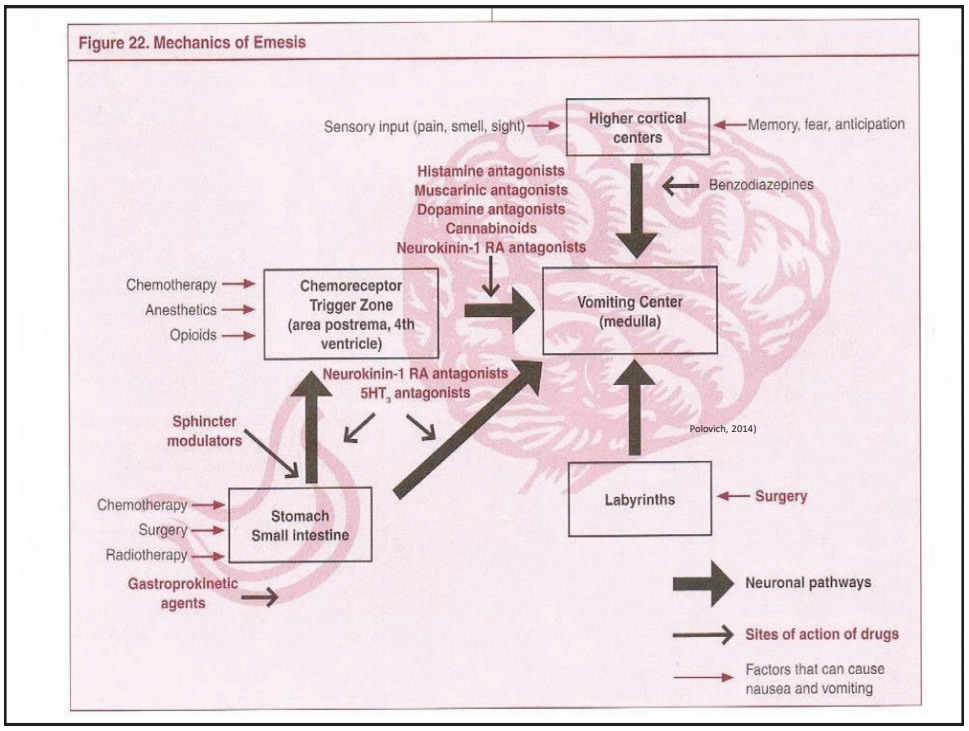


Figure 22. Mechanics of Emesis
Sensory input (pain, smell, sight)
Higher cortical centers
Memory, fear, anticipation
Histamine antagonists
Muscarinic antagonists
Dopamine antagonists
Cannabinoids
Neurokinin-1 RA antagonists
Benzodiazepines
Chemotherapy
Anesthetics
Opioids
Chemoreceptor Trigger Zone (area postrema, 4th ventricle)
Vomiting Center (medulla)
Neurokinin-1 RA antagonists
5HT3 antagonists
Sphincter modulators
Polovich, 2014)
Chemotherapy
Surgery
Radiotherapy
Stomach Small intestine
Gastroprokinetic agents
Labyrinths
Surgery
Neuronal pathways
Sites of action of drugs
Factors that can cause nausea and vomiting

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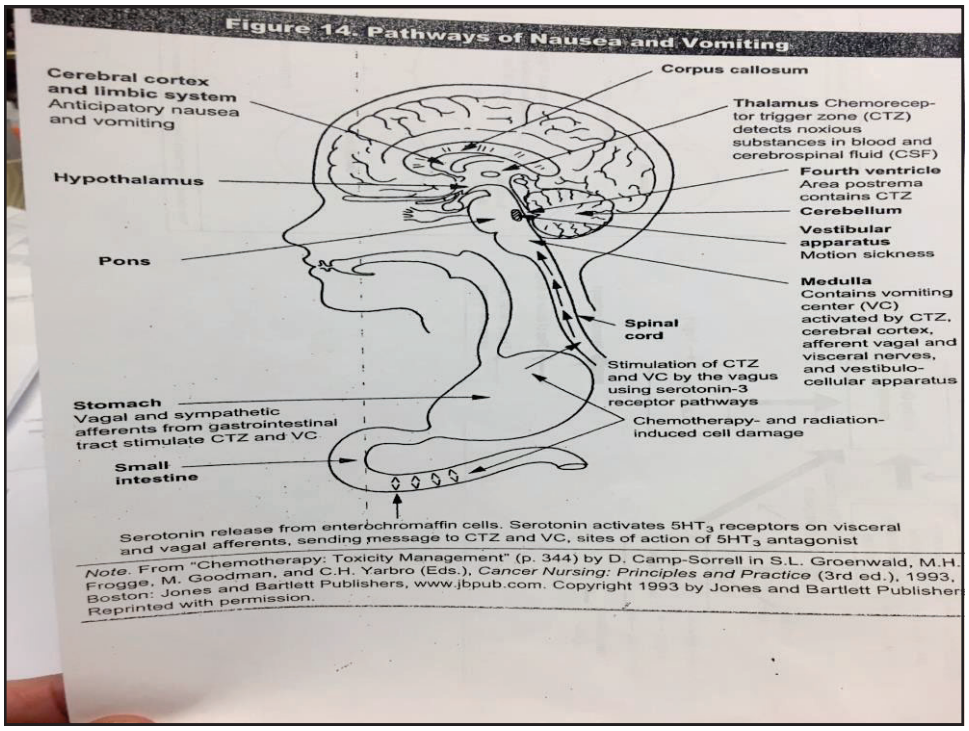
Figure 14. Pathways of Nausea and Vomiting
Cerebral cortex and limbic system
Anticipatory nausea and vomiting
Corpus callosum
Thalamus Chemoreceptor trigger zone (CTZ) detects noxious substances in blood and cerebrospinal fluid (CSF)
Hypothalamus
Fourth ventricle
Area postrema contains CTZ
Cerebellum
Vestibular apparatus
Motion sickness
Pons
Medulla
Contains vomiting center (VC) activated by CTZ, cerebral cortex, afferent vagal and visceral nerves, and vestibulocellular apparatus
Spinal cord
Stimulation of CTZ and VC by the vagus using serotonin-3 receptor pathways
Stomach
Vagal and sympathetic afferents from gastrointestinal tract stimulate CTZ and VC
Chemotherapy- and radiation-induced cell damage
Small intestine
Serotonin release from enterochromaffin cells. Serotonin activates 5HT3 receptors on visceral and vagal afferents, sending message to CTZ and VC, sites of action of 5HT3 antagonist
Note. From "Chemotherapy: Toxicity Management" (p. 344) by D. Camp-Sorrell in S.L. Groenwald, M.H. Frogge, M. Goodman, and C.H. Yarbro (Eds.), Cancer Nursing: Principles and Practice (3rd ed.), 1993, Boston: Jones and Bartlett Publishers, www.jbpub.com. Copyright 1993 by Jones and Bartlett Publishers. Reprinted with permission.

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# Causes CINV

| High >90% | Moderate 30-90% | Low (10-30%) |
|---|---|---|
| **Anthracycline/ Cytoxan combo**<br>Carmustine (BCNU)<br>Carboplatin (AUC greater than 4)<br>**Cisplatin**<br>Cytoxan >1500 mg/m2<br>Dacarbazine<br>Doxorubicin >60mg/m2<br>Epirubicin >90mg/m2<br>Ifosfamide >2g/m2<br>Melphalan<br>Procarbazine<br>Streptozocin<br>Sacituzumab-povitecan-hzly | Aldesleukin (>12-15 MIU/m2)<br>Azacitidine<br>Bendamustine<br>Bulsulfan<br>Bosutinib<br>Carboplstin<br>Carmustine<br>Clofarabine<br>Cyclophosfamide(1500mg/m2 and PO)<br>Cytarabine (>200 mg/m2)<br>Dactinomycin<br>Daunorubicin<br>Doxorubicin<br>Daunorubicin and cytarabine liposome<br>Epirubicin<br>Fam-trastuzumab deruxtecan-nxki<br>Idarubicin<br>Ifosfamide <2g/m2)<br>Interferon alpha<br>Irinotecan<br>Irinotecan liposomal<br>Lurbinectdin<br>Imatinib<br>Lenvatinib<br>Melphalan<br>Methotrexate<br>Oxaliplatin<br>Temozolomide<br>Trabectiden | Alemtuzumab<br>Afatinib<br>Axatinib<br>Alectinib<br>Arsenic trioxide<br>Belinostat<br>Blinatunomab<br>Brentuximab<br>Bortezomib<br>Cabazitaxel<br>Carfilzomib<br>Cytarabine (100-200 mg/m2)<br>Cetuximab<br>Capecitibine<br>Cobimetinib<br>Docetaxel<br>Doxorubicin (liposomal)<br>Dabrafenib<br>Dasatinib<br>Eribulin<br>Everolimus<br>Etoposide<br>Elotozumab<br>Fludarabine<br>5-Fluorouracil<br>Gemcitibine<br>Ipilimumab<br>Ixabepilone<br>Methotrexate<br>Mitomycin<br>Mitoxantrone<br>Necitumumab<br>Olaratumab<br>Olanarib<br>Paclitaxel<br>Pemetrexed<br>Palbocinib<br>Regorafenib<br>Sunitunib<br>Temsirolimus<br>Thalidomide<br>Venetoclax<br>Vorinostat |

- Brain metastases
- Side effects other medications
- Excessive secretions
- Gastroparesis
- Electrolyte imbalance
- Uremia
- Anxiety
- Vestibular dysfunction
- Malignancy ascites
- Age
- Younger more than older
- Gender (female more than male)
- Alcoholics experience less N/V

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# Types of CINV

**Anticipatory**

- Conditioned response
- 18-57%
- Anxiety
- History N/V
- Less than 50
- Females
- Motion sickness
- Pregnancy induced N/V

**Acute**

- Occurs within few minutes
- Peaks 5-6 hours
- Resolves within 24 hours
- Highly emotogenic = more than 90% patients
- Moderate = 30-90%
- Low = 10-30%
- Minimal = les than 10%

**Delayed**

- More than 24 hours after administration up to several days
- **Carboplatin. Cisplatin, Cyclophosphamide, Doxorubicin, Melphalan, targeted therapies, oral agents**

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# Emetogenic Regimens

| Highly | Moderate | Minimal |
|---|---|---|
| 5HT3 antagonist: Palonosetron 0.25 mg IVP<br>AND<br>Dexamethasone 12 mg in in 20 ml NS (PF) IVP over 5 minutes (8 mg po daily days 2-4)<br>AND<br>Nki antagonist: Fosaprepitant 150 mg in 150 ml NSSS IV over 20 minutes<br><br>With/Without<br>Diphenhydramine 25 mg in 10 ml IVP over 2 minutes<br><br>Rescue meds (script):<br>Prochlorperazine 10 mg PO every 6 hours PRN<br>Lorazepam 0.5 mg PO every 6 hours PRN | 5HT3 antagonist: Palonosetron 0.25 mg IVP<br>AND<br>Dexamethasone 12 mg in in 20 ml NS (PF) IVP over 5 minutes (8mg po daily days 2-3)<br><br>With/Without<br>Fosaprepitant 150 mg in 150 ml NSSS IV over 20 minutes<br><br>Diphenhydramine 25 mg in 10 ml IVP over 2 minutes<br><br>Rescue meds (script):<br>Prochlorperazine 10 mg PO every 6 hours PRN<br>Lorazepam 0.5 mg PO every 6 hours PRN | Palonosetron 0.25 mg IVP<br><br>OR<br><br>Dexamethasone 12 mg in in 20 ml NS (PF) IVP over 5 minutes<br><br>Rescue meds (script):<br>Prochlorperazine 10 mg PO every 6 hours PRN<br>Lorazepam 0.5 mg PO every 6 hours PRN |

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# CINV Clinical Pearls

| Class | Mechanism of Action | Examples | Side Effects | Clinical Pearls |
|---|---|---|---|---|
| 5-$HT_3$ Receptor Antagonist | Serotonin receptor antagonist Inhibits 5-$HT_3$ receptors in vomiting centers | Palonosetron (Aloxi), Granisetron (Kytril), Ondansetron (Zofran), Dolasetron (Anzemet) | Headache, Constipation, QT prolongation | Palonosetron approved for 7-day dosing. Approved for delayed N/V. Granisetron can be given rapid IV bolus. |
| Neurokinin-1 Antagonist | Neurokinin-1 receptor antagonist | Aprepitant (orsl emend)<br>Fosaprepitant (Emend)<br>Cinvanti (injectable emulsion)<br>Rolapitant (Varubi)<br>Netupitant (Akynzeo) | Constipation, Hiccups, Loss of appetite, Diarrhea, Fatigue, Decreased INR, decreases effectiveness of contraceptives | Given in combination with 5$HT_3$ and corticosteroids on day1. Increases AUC of steroids-may need dose reduction of steroids. |
| Dopamine Antagonist/Phenothiazides | Blocks dopamine receptors | Haloperidol (Haldol)<br>Metoclopramide (Reglan)<br>Prochloperazine (Compazine)<br>Promethazine (Phenergan) | Sedation, extra pyramidal symptoms (EPS), dystonia, dizziness, orthostasis, diarrhea | Administering haloperidol with diphenhydramine (25-50mg) prevents extrapyramidal symptoms. |
| Corticosteroid | Antiprostaglandin synthesis activity | Dexamethasone (Decadron) | Insomnia, acne, anxiety<br>Perineal burning (rapid IV administration) | Increases efficacy 15-25% - Administer slowly over at least 10 minutes |
| H2 Blockers | Histamine blocker | Famotidine (Pepcid)<br>Ranitidine (Zantac) | Headaches, dizziness, diarrhea | ---------- |
| Proton Pump Inhibitors | Blocks gastric acid secretion by irreversibly binding to and inhibiting the hydrogen-potassium ATPase pump | Prilosec<br>Pantoprazole (Protonix) | May lower mag levels | Monitor renal function |
| Cannabinoid | Interacts with cannabinoid receptors | Dronabinol<br>Nabilone | Sedation, vertigo, euphoria, dysphoria, dry mouth, tachycardia, orthostasis | Caution in patients with psychiatric history. |
| Anxiolytic | Benzodiazepine<br>CNS Depressant | Lorazepam (Ativan)<br>Alprazolam (Xanax) | Sedation, confusion, hyperactivity, agitation, dizziness, lightheadedness, hallucinations | Older patients decreased starting dose assess for comorbidities, i.e. hepatic or renal dysfunction, advanced liver disease. |
| Antipsychotics | Binds to alpha-1, dopamine, histamine H-1, muscarinic, and serotonin type 2 (5-HT2) receptors | Olanzapine (Zyprexa) | Dry mouth, sedation | ---------- |

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# Non – Pharmacologic Management

**Dietary management:**

- Small frequent meals
- Healthful foods
- Avoid overeating
- Medicate prior to eating
- Avoid fatty, spicy foods
- Eat cold or room temp food
- Cook between TX
- Eat favorite food when not nauseated
- Ginger preference
- Papaya

**Behavior Interventions:**

- Music therapy
- Acupressure – useful in nausea
- Acupuncture –under study
- Progressive muscle relaxation
- Guided imagery

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# Complications CINV

- Discomfort
- Treatment delay or withdrawal
- Impaired quality of life
- Dehydration
- Anorexia, weight loss, nutritional depletion
- Physical and mental deterioration
- Increase intracranial pressure
- Aspiration
- Cost
- Caregiver strain
- Loss productivity and work

20

# CINV Case Study

A patient with stage 2 breast cancer is receiving adjuvant AC. The first treatment was last Friday. Patient reports episodes of nausea since Saturday. The patient was able to take occasional sips of fluids and eat some soup. The patient also reports 3 episodes of vomiting in the past 24 hours.

1. What are the drugs in this regimen? Acronym: AC

2. What grading would you give for the nausea?

3. What grading would you give for the vomiting?

4. How would you proceed with this patient?

5. State 2 teaching points for this patient for the next cycle.

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# Diarrhea

Acute
- Lasting 1-2 days
- Typically resolves on own

Persistent
- Lasting 2-4 weeks

Chronic
- Lasts as least 4 weeks with potentially transient symptoms

Uncomplicated
- Grade 1 or 2 without additional signs or symptoms

Complicated
- Grade 3 or 4
- Grade 1 or 2 accompanied by cramping, nausea, vomiting, fever, bleeding, dehydration, sepsis, neutropenia, decreased performance status

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# Colitis

- Characterized by the inflammation of the colon
  - Neutropenic entercolitis (typhilitis)
  - C-diff colitis
  - Immune-mediated colitis (block anti-inflammatory mechanisms)
    - Cytotoxic T-Lymphocyte antigen 4 (CTLA-4)
    - Programmed cell-death protein (PD-L)
    - P13K inhibitors

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# Pathophysiology

| Osmotic | Secretory | Exudative | Inflammatory | Dysentery |
|---|---|---|---|---|
| Water drawn into intestinal lumen<br>• Gut injury<br>• Dietary factors<br>• Digestion<br>• Lactose intolerance<br>• Large stool volumes | Small & large intestines secrete more fluids and electrolytes than absorbed<br>• Infection<br>• Inflammation<br>• Chemo<br>• Targeted therapies<br>• Radiation<br>• GVHD<br>• Endocrine tumors | Alterations mucosal integrity, epithelial loss, enzyme destruction, defective absorption colon<br>• Cancer<br>• Inflammatory diseases<br>• Cancer treatment | Invasive or toxin producing bacteria<br><br>Causes impaired mucosal integrity that results in tissue damage<br>• Targeted therapies<br>• Checkpoint inhibitors | Characterized by blood in the stool |

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# Incidence

| Chemotherapy | Targeted and Immunotherapy |
|---|---|
| – As high 80%<br>– Chronic up to 49%<br>– **Antimetabolites**<br>– **Irinotecan** | – 60%<br>– **TKIs**<br>– **MABs**<br>– **Checkpoint inhibitors** |

Others
- Carcinoid syndrome
- Colon cancer
- Lymphoma
- Pancreatic
- Thyroid
- Radiation therapy
- GVHD
- Anxiety/Stress

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## Contributing Factors

- Diet
  - High fiber diet
  - Lactose intolerance
- Nutritional supplements
  - Vitamin C excess
  - Vitamin A and zinc deficiency
- GI inflammation
  - Crohn's disease
  - Diverticulitis
  - Irritable bowel syndrome
  - Radiation proctitis
  - Ulcerative colitis
- Neuroendocrine
  - Diabetes
  - Hyperthyroidism
  - Neuroendocrine tumors
- GI Malabsorption
  - Bowel wall edema
  - Celiac disease
  - Motility disturbances
  - Partial bowel wall obstruction
  - Protein losing enteropathy
  - Short bowel
- Pshycological factors
  - Anxiety
  - Stress
- Therapy related
  - Chemotherapy
  - Multimodality therapy
  - Radiation therapy
  - GVHD
- Infection- Clostridium difficile infections

Stein A., et al. Therapeutic Advances in Medical Oncology. (2010) 2(1) 5163

- History
- Diet
- Quality and character
- Medications
- Vitals
- Weight
- Skin integrity
- Labs
  - C-diff
  - CMP
  - Albumin
  - CBC
  - Lactic acid
- Endoscopy
- CT TAP

*** Alison Tokarchic Pharm.D.

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# Management

| Pharmacologic | Non-Pharmacologic |
|---|---|
| • Fluids and Electrolytes<br>**Medications**:<br>Antimotility Agents<br>• Lomotil 10mg →5 mg QID max 20mg/day<br>• Immodium 4mg →2mg after each stool max 16 mg/day<br>Late onset irinotecan induced 2 mg Q 2hours<br><br>Somatostatin Analogs<br>• Octreotide 100-150mcg TID up to 500 mcg TID or continuous IV 25-50 mcg/hr.<br><br>Anticholinergics<br>• Atropine 0.25-1mg for early onset irinotecan induced<br><br>Bulk forming laxatives<br>• Questran<br><br>***Corticosteroids added for targeted therapy/immunotherapy induced | • Diet-BRAT<br>• Fluids PO and IV replacement<br>• ⦸ Milk, sorbitol<br>• Watch Supplements-Ensure<br>• Eat food room temp<br>• Clean area with soap and water<br>• Moisture barrier<br>• Know when to call/come in<br>• Probiotics |

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# Diarrhea Case Study

A patient with metastatic colon cancer has been admitted for diarrhea. The patient is currently receiving IFL. Last treatment was 1 week ago. Reports having 8 BMs over the past 24 hours.

Appetite is poor and reports not eating or drinking much.
"I took Imodium but it didn't seem to help."

1. What are the drugs in this regimen? Acronym: IFL

2. What toxicity grading would you give for this assessment?

3. What interventions specific to diarrhea would you implement?
(Give at least 1 pharmacological and 1 non-pharmacological intervention.)

4. What treatment would be indicated for patient on a TKI, CTLA-4, PD-1, or P13K with the same symptoms?

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# Constipation

- Decreased passage of stool, bloating, cramping, hard stool, straining, ileus, hemorrhoids
- 40-60%
- Primary
  - Lack physical activity, decreased fiber
- Secondary and Iatrogenic
  - Pathologic process –autonomic nervous system dysfunction opioids, chemo, psychotropic meds, anticonvulsants, metabolic, endocrine
- **Which drug classificaiton has the highest incidence of constipation and potential ileus?**

_____

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## Causes of Constipation

| | | | |
|---|---|---|---|
| **Disease (Malignancy) Related** | | | |
| Intestinal obstruction | Hypercalcemia | Decreased activity | Bowel surgery |
| **Gastrointestinal** | | | |
| Anorexia | Inadequate dietary fiber intake | Decreased abdominal muscle tone | Intestinal obstruction by tumor in the bowel wall |
| **Neurologic** | | | |
| Autonomic neuropathy | Depression | Spinal cord compression | Weakness |
| **Metabolic and Endocrine** | | | |
| Dehydration | Diabetes | Hypokalemia | Hypothyroidism |
| **Therapy Related** | | | |
| Decreased activity | Post-surgical | Radiation therapy | Chemotherapy/ Medications |

J Support Oncol 2006;4:213-8 Support Care Cancer 2006;14:890-900

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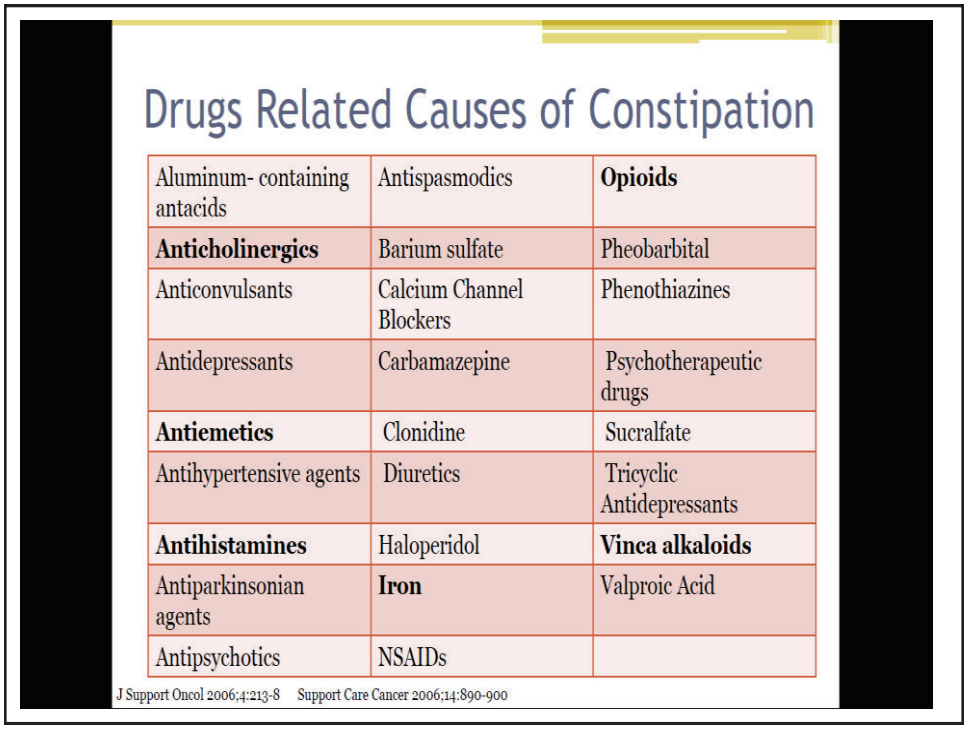


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# Constipation Clinical Pearls

| Class | Mechanism of Action | Examples | Clinical Pearls |
|---|---|---|---|
| Bulk Agents | Increase stool bulk and water content (Mancici & Bruera, 1998). | cellulose or psyllium | Require adequate concomitant fluid intake and may not be appropriate for many patients with cancer. The risk of intestinal obstruction may be present for certain patients with underlying delayed GI transit times (Xing & Soffer, 2001). |
| Osmotic Laxatives | Increase the fluid content in the bowel and may increase peristalsis (Mancici & Bruera, 1998). | sorbitol, lactulose, polyethylene glycol (PEG) 3350 | Some may have an unpalatable sweet taste and lead to potential abdominal cramping, flatulence, and distention (Bisanz et al., 2009). Polyethylene glycol should be mixed with adequate fluid. |
| Saline Laxatives | Increase water absorption into the bowel and increase intestinal transition time. | magnesium hydroxide, magnesium citrate, sodium phosphate | Use with caution in patients with underlying cardiac or renal disease (Lembo & Camilleri, 2003). |
| Stimulant Laxatives | Increase GI motility (Heitkemper & Wolff, 2007). | biscodyl, castor pil, docusate, senna, cascara (Wald, 2003) | Appear to be safe for chronic use (Wald, 2003); docusate may be used in combination with other stimulants, such as senna. |
| Prokinetic Agents | Serotonin agonist properties as well as antidopaminergic ones (Tack, 2008) | metoclopramide | Side effects include drowsiness, extrapyramidal effects, dizziness, and hypertension. |
| Periperal Opioid Antagonists | Selectively block the mu-opioid Seceptors involved in opioid induced constipation (Yuan, 2007) | methylnaltrexone, alvimopan | Methylnaltrexone relieves opioid-induced constipation in patients with advanced illness, including cancer, without comproming the efficacy of opioid therapy and works quickly with a median time to laxation of slightly more than six hours (Thomas et al., 2008). Only available subcutaneously, which is costly.<br>Side effects include abdominal pain and flatulence (Thomas et al., 2008).<br>Alvimopan is oral, but only indicated to accelerate postoperative GI recovery in patients who have undergone bowel resection surgery. |
| Chloride Channel Activators | Increases the release of chloride-rich fluid into the intestine, subsequently increase intestinal motility (Sucampo Phamaceuticals, 2011) | Lubiprostone | Side effects include nausea, headache, and diarrhea (Johanson & Ueno, 2007) |
| Suppositories and Enemas | Stimulate laxation | glycerin, mineral oil, phosphate, and bisacodyl | Effectiveness has not been established in patients with cancer (Bisanz et al., 2009).<br>Additionally, rectal manipulation typically is contraindicated in patients who are neutropenic or thrombocytopenic. |

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# Summary Slide

- Mucositis
  - Antimetabolites, anti-tumor antibiotics, plant alkaloids, alkylating agents, radiation therapy
  - EGFR, TKI/MKI, mTOR inhibitors, immunotherapy
- CINV
  - -highly emetic – Carbo, Cisplatin, cyclophosphamide, doxorubicin, melphalan, nitrogen mustard, targeted therapies
  - 5HT3 inhibitors cause headaches and constipation
  - NK1 cause hiccups
  - Phenothiazine's cause extrapyramidal effects
- Diarrhea
  - Assess if ACT or immunotherapy
  - ACT (anti-metabolites, irinotecan)– can be managed with Imodium or lomotil, octreotide, atropine
  - Immunotherapy (TKI, MABs, checkpoint inhibitors) requires steroids (can develop colitis, enterocolitis, typhilitis)
- Constipation
  - Vincas
  - Bowel obstructions

# Spring 2026 Fundamentals of Anticancer Therapy Day 2

## Allegheny Health Network Cancer Institute

### *ANTICANCER THERAPY COURSE – Day 3*

| | |
|---|---|
| 8:00 a.m. | *Review Take- Home Work*<br>Mary E. Kern, MSN, RN, OCN, CHSE<br>**treatment/symptom management* |
| 8:30 a.m. | Cell- Cycle Non-Specific Agents<br>*Alkylating Agents, Antitumor Antibiotics, Nitrosoureas and Nursing Implications*<br>Heather Kennihan, MSN, RN, OCN<br>**treatment/symptom management* |
| 9:30 a.m. | Break |
| 9:45 a.m. | Cell- Cycle Non-Specific Agents<br>*Alkylating Agents, Antitumor Antibiotics, Nitrosoureas and Nursing Implications*<br>Heather Kennihan, MSN, RN, OCN<br>**treatment/symptom management* |
| 10:45 a.m. | *Toxicity Case Studies (con't)*<br>Mary E. Kern, MSN, RN, OCN, CHSE<br>Marcia Almiron-Wolbert, MSN, RN, OCN<br>**treatment/symptom management* |
| 11:30 a.m. | Lunch |
| 12:15 p.m. | *Toxicity Case Studies*<br>Mary E. Kern, MSN, RN, OCN, CHSE<br>**treatment/symptom management* |
| 1:45 p.m. | Final review of content/Workbook |
| 2:30 p.m. | Wrap-up and Evaluations<br>*Self-Study Completion - Standard of Practice (SOP) Review Booklet and ACT Videos<br>*Weekly Homework<br>**professional* |
| 2:45 p.m. | Adjourn |

# Cell Cycle Non-Specific Anti-cancer Therapy

Heather Kennihan MSN, RN, OCN
AHN Cancer Institute
Professional Development Specialist
Heather.Kennihan@ahn.org

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## Learning Outcomes

- Identify function of cell cycle non-specific anti-cancer therapy drugs
- Explain the mechanism of action for anti-tumor antibiotics, alkylating agents, and nitrosoureas
- Discuss side effects of each drug

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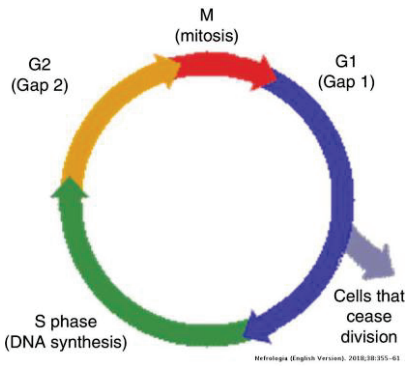
## Cell-Cycle Non-Specific

- Effects all phases of cell cycle – even G0 (resting phase)
- More effective in slower growing cells
- Very dose dependent
- Side effects directly proportional to amount drug given
- All have some degree of bone marrow suppression
  - Alkylating Agents
  - Antitumor Antibiotics
  - Nitrosourea Agents



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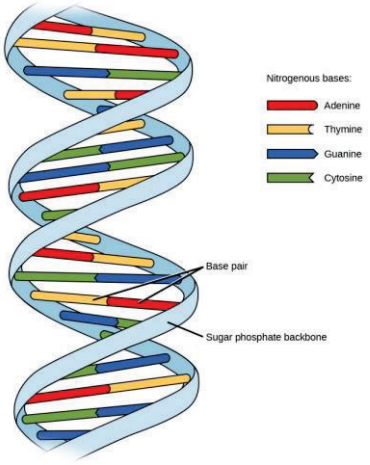
## How Alkylating Agents Work

- Disrupts structure of DNA
- Cross-linking of DNA strands; also intra-strand cross-links
  - DNA strands are therefore unable to separate during DNA replication
- Interfere with cellular replication of DNA, transcription of RNA, translation into protein
  - Miscoding during replication and genetic mutations



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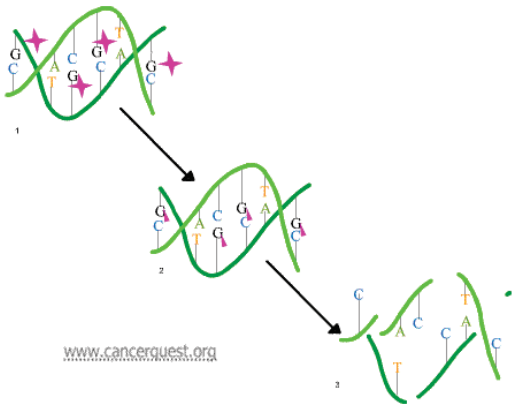
## What the changes in cells look like in the DNA strands.

Alkylating agents attaches to the alkyl group (H+ ion) to the DNA base. Makes the DNA fragmented by doing this. Prevents DNA synthesis and RNA transcription.

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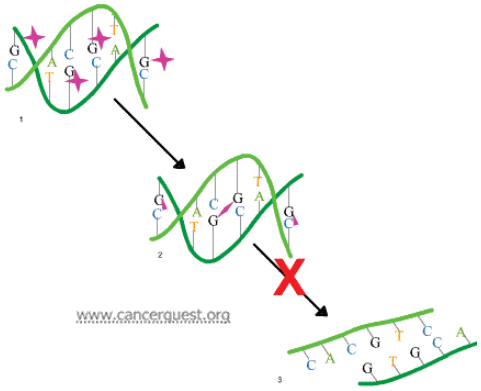
## Forming Cross Bridges/Links




May cause damage by the formation of cross bridges. These cross bridges prevent DNA from being separated for synthesis or transcription.

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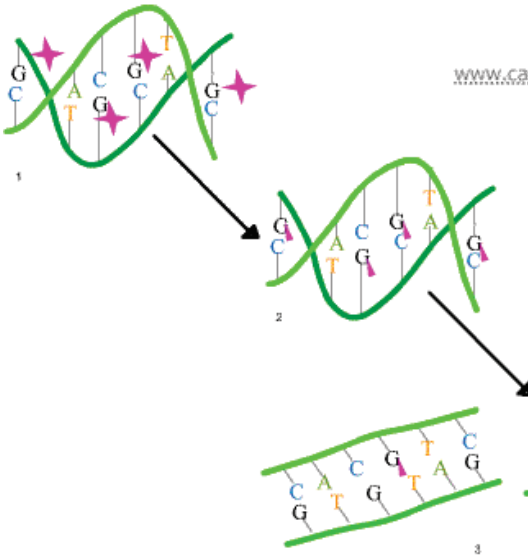
## Mis-paring of nucleotides

Alkylating agents can also induce the mispairing of nucleotides leading to cell mutation. Normally the cells pair with A-T and G-C. Altered pairing occurs as seen here with the G-T pairing.

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## Nursing Considerations

- Can be given as bolus, short infusion or over 24 hours.
- Many side effects include:
  *myelosuppression
  *N/V
- *infertility

**Secondary Malignancies and Fertility**

- Occur after being treated with Alkylating Agents
- Unrelated to first cancer diagnosis
- Highest risk in Hodgkin, followed by breast
- More common in younger patients
- Develop Acute Leukemia or skin cancers related to radiation and chemotherapy treatments
- Can take 1-30 years to develop

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# Alkylating Agents

| **Most Common**: |
|---|
| Cyclophosphamide (Cytoxan) |
| Ifosfamide (Ifex) |
| Cisplatin (Platinol) |
| Carboplatin (Paraplatin) |
| Bendamustine (Treanda) |
| Melphalan (Alkeran) |
| Busulfan (Myleran) |
| Temozolamide (Temodar) |
| Oxaliplatin (Eloxatin) |
| Thiotepa (Thioplex) |

Less Common:
- Chlorambucil (Leukeran)
- Altretamine (Hexalen)
- Trabectedin (Yondelis)
- Dacarbazine
- Lurbinectedin (Zepzelca)
- Streptozocin (Zanosar)

- Mustargen (Nitrogen Mustard) - Developed in the 1940s for war
  - Extreme N/V, vesicant (antidote is sodium thiosulfate-not used)

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# Ifosfamide (Ifex) –Alkylating Agent

- Causes cross linking of DNA Strands
- Hepatic metabolism -excreted in urine and needs **Mesna**

Acute SE - **CNS penetration** of metabolites (lethargy, hallucinations, nightmares, encephalopathy, coma, seizures)
  - Methylene blue antidote and thiamine
  - Daily Uas

Delayed SE- Hemorrhagic cystitis in 20-40% of patients and renal failure (usually need phosphorus replacement)
- Mesna should be given for 12-24 after infusion complete. (can be IV or PO mix in OJ)

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# Cyclophosphamide (Cytoxan) (PO, IV, Intrapleural)- Alkylating Agent

- Causes cross-linking DNA strands
- Hepatic metabolism and excreted in urine

***Mesna*** *is frequently given to prevent hemorrhagic cystitis/Can also place 3-way Foley for CBI****

Acute SE- N&V, SIADH– high dose can result in nasal stuffiness, dizziness

Daily UAs

Delayed SE- pancytopenia, myocardial depression, hemorrhagic cystitis, alopecia, rhinorrhea and mucositis; cardiomyopathy (high dose)

- Should have pre-and post hydration for doses > 500mg/m2
- Infused typically over 1 hour

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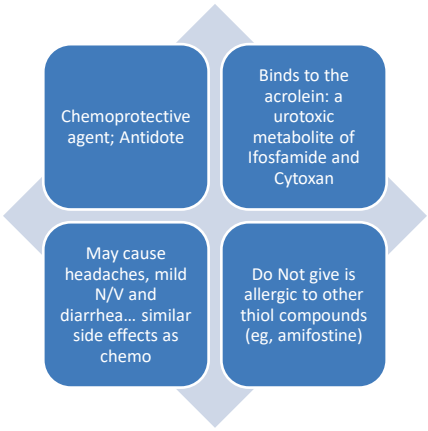
# Mesna (IV or PO)




Ifosfamide dosing:

- 60 % of Ifos. dose divided into 3 Mesna doses- typically 15 min. prior, at 4 and 8 hours

Cyclophosphamide dosing:

- 1:1 ratio to Mesna
- Continuous Mesna over 24 hours until 6 hours after last dose or intermittent infusions

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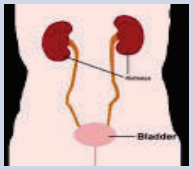
# Hemorrhagic Cystitis

| Causative Agents | Hemorrhagic cystitis | Management (Mesna) |
|---|---|---|
| Contact with Acrolein metabolic by-product of Ifosfamide and Cyclophosphamide<br><br>**Cytoxan**<br>Low dose (<1000mg) 6-10% toxicity<br>High dose (1-4gm/m2 or 60mg/kg) at 40% incidence<br><br>**Ifosfamide**<br>18-40% incidence | Bladder mucosal irritation/damage/ inflammation/ulceration from binding of drug metabolites or by-products to the bladder mucosa<br><br>  | Detoxifies and inactivates metabolites and flushes from bladder<br><br>Oral in orange juice or cola<br><br>Administer Mesna (cryoprotectant that binds to Acrolein in bladder and inactivates it and flushes from system)<br><br>Stop drug immediately for cystitis or hematuria, 3-way foley for clots and administer Amicar to promote clotting |

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# Platin Family Hypersensitivity/Anaphylaxis

- Premedication is not helpful
- Patients react to the platin salts
- These are IgE medicated reactions therefore most patients react after few doses
  - Carboplatin typically with 4th -6th doses
  - Oxaliplatin has 2 peaks
    - 1st with 3rd cycle
    - Then 6th cycle
- Patient may require desensitization protocols

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# Cisplatin (Platinol)- Alkylating Agent

- Break DNA strands and cause cross linking/bridging of DNA bases
- High concentration in liver, intestine, and kidneys
  - Serum creatinine <1.5mg/dl, renal tubular necrosis, increases toxicity of amphotericin, vancomycin, aminoglycosides, and methotrexate.
  - Check 24 hour creatinine clearance must be >50
  - May administer Mannitol
  - Depletes magnesium
- Administer after Taxol to prevent delayed Taxol excretion and subsequent bone marrow depression
- Vesicant esp. in higher doses

Acute SE- Severe N&V, almost immediate and can be delayed, diarrhea, hypersensitivity

Delayed SE- peripheral neuropathies, ARF, Tinnitus (oto-toxicity - consider baseline audiogram - high frequency loss)

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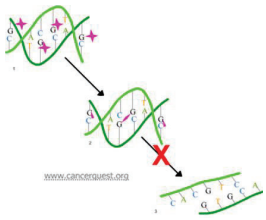
# Carboplatin (Paraplatin)
## Alkylating Agent




Hypersensitivity/ ANAPHYLAXIS Common after 4-6 doses

- Produces Interstrand DNA cross – links/bridging
- More water soluble and a slower reaction with DNA and a slower clearance
- Ordered as AUC (area under the curve [1-6])

Acute SE- N&V, abnormal LFT's, decreased creatinine clearance, mild paresthisias

Delayed SE- Dose-limiting effects esp. delayed thrombocytopenia (days 18-28)

- Administer after Taxol to maximize cell kill and to limit myelosuppression

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# Oxaliplatin (Eloxatin) - Alkylating Agent

- Binds to the DNA forming cross links
- 3rd generation platinum analogue
- Do not prepare or infuse with NSS. ONLY dextrose solutions recommended

Acute SE- vesicant, transient parethesia, dysesthesia, or hypoesthesia in hands, feet, or throat, pharyngolaryngeal dysesthesia (feeling unable to breathe)

  - 1-48 hours lasting up to 14 days

Delayed SE- chronic sensory neurotoxicity precipitated by cold exposure

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# Patient Education

- Post Signage
- 1st day and at least 7 days after treatment keep hands and feet warm
- Wear gloves into freezer or refrigerator
- Drink warm fluids
- Avoid straws
- Avoid A/C on high
- Warm car in winter time

Keep hands, feet, throat and mouth warm!!!

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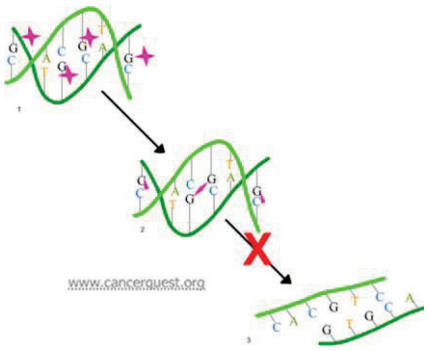
# Bendamustine (Treanda) (IV)

## Alkylating Agent -

- Induces durable DNA damage through single and double strand cross linking.
- Acute SE- N/V; monitor for infusion reactions (esp in second and subsequent cycles); increase risk of severe skin toxicity with concomitant allopurinol
- Delayed SE- Manageable myelosuppression, N/V, diarrhea, pruritis, rash, fever, chills, vesicant/extravasation, fatigue, headache, dizziness, mouth sores

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## Melphalan (Alkeran) - (PO/IV) -Alkylating Agent

- Inhibits RNA and DNA synthesis and creates cross-links in DNA strands
- Needs to be administered within 60 minutes of reconstitution if IV

Acute SE – Severe N/V esp. in PSCT; ice chips 15 minutes before, during, and 15 minutes after infusion

Delayed SE - Myelosupression may be delayed 4-6 weeks, N/V, musositis/stomatitis (ice chips 15-minutes pre and up to 48 hours after)

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## Busulfan (Myleran) - (PO/IV)- Alkylating Agent

- Effects myeloid cells most by interfering with DNA replication and RNA transcription.
- Causes cell death by cross links of DNA strands
- Take on empty stomach if PO
- Usually given IV – better tolerated
- Pre –med with Dilantin but AHN uses Ativan

Acute SE – emesis, seizures

Delayed SE – diarrhea, N/V, mouth sores, extremely myelosuppressive, VOD/HSOS , pulmonary fibrosis, and hyperpigmentation of skin

NO Tylenol or IBUPROPHEN for at least 72 hours - interferes with absorption of Bulsulfan

**WPH follows 24 hours*

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## Temozolamide (Temodar) - (PO/IV)

- High blood brain barrier penetration
- Give orally with full glass of water on empty stomach
- Do not crush or dissolve capsule

Acute SE - N/V, headache, fatigue, photosensitivity

Delayed SE - severe myelosuppression as dose-limiting factor, (platelets nadir 21-40 days), (WBC nadir 1-44 days)

- Recently available in IV form over 90 minutes 0.9% saline only
- PCP (pneumocytis pneumonia) prophylaxis trimeththoprim-sulfamethoxazole with concurrent radiation

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Thiotepa (Tepandina)- Alkylating Agent

Produces cross-linking of DNA strands –causes cellular death

Cellular transplant and primary CNS

Acute SE: skin rash, N/V

Delayed SE: myelosuppression, H/a, drowsiness, CNS toxicity, VOD/SOS

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# Anti-tumor Antibiotics

Anthracyclines = "CIN"

- Doxorubicin (Adriamycin)
- Daunorubicin (Cerubidine)
- Idarubicin (Idamycin)
- Epirubicin (Ellence)
- Valrubicin (Valstar)
- Dactinomycin(Cosmegen®) (mcq or mg)

Liposomal Anthracyclines

Doxil (liposomal doxorubicin)

Daunoxome (liposomal daunorubicin)

Vyxeos (liposome-encapsulated daunorubicin/cytarabine)

Anti-tumor Antibiotics:

Bleomycin (Blenoxane)

Mitoxantrone (Novantrone)

Mitomycin-C (Mutamycin)

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## *Anti-tumor Antibiotics - Anthracyclines*

- Composed of atetracyclic chromophores (usually red, orange, yellow, blue, purple) linked to a sugar
- Disrupts DNA transcription and inhibits DNA and RNA synthesis
- DNA binding (break the double helix of DNA)
- Interacts/inhibits topoismerase II (enzymes that unwind the coils)
- Secreted through the hepatic system (check bilirubin)

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## Lifetime doses and Colors

Mitomycin-C- <20mg/m2 per dose

Idarubicin - Total dose <150 mg/m2

Doxorubicin and Daunorubicin - total dose 550mg/m2 (400 mg/m2 with concurrent radiation)

Mitoxantrone- Total dose <140mg/m2

Epirubicin-Total dose 800-900mg/m2

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# Side Effects

- Alopecia
- G.I. Toxicity
- Myelosupression
- Arrhythmia
- Cardiotoxicity
- Vesicants/Extravasation
- Liver toxicity (TBili)
- Total cumulative doses
- MUGA scans

(LVEF greater than 50%)

- ECHOs
- Hyperuricemia
- Photosensitivity
- Radiation recall
- Local Flares
- Urine discoloration-pink to red – for 48hrs
  - Except-mitoxantrone
    - blue

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# 5 "Cins" of Anthracyclines

- Color
  - Purple, orange, red or blue
- Cardiac
  - CHF
- Cold (vesicant/extravasation)
  - Can cause tissue necrosis if leaked outside the vein
- Cremaphor (urine and LFTs)
  - Excreted in urine-changes colors
- Cumulative doses
  - Needs monitored and tracked prior to each dose



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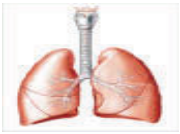
# Bleomycin (IVP, IV infusion, IM, SC, pleural effusions)



- Single and double strand breaks in DNA
- Free radical formation with oxygen
- ***Pulmonary toxicity***, fever and chills, and above side effects
- PFTs at initiation and every 1-2 months thereafter (fibrosis)
- Treats lung, H&N, cervical, testicular, Hodgkins, NHL, malignant pleural effusions, melanoma
- Higher incidence of infusion reaction with lymphoma (may do test dose)

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# Liposomal Anthracyclines Daunoxome (Doxil and Daunorubicin)

- Encapsulated in long-circulating STEALTH liposomes
- Approved for AIDS related Kaposi's (also ovarian, multiple myeloma)
- Above noted side effects and also palmar-plantar erythrodysestheses (PPE) and infusion related reactions
- Only compatible in D5W and should shake every 30 minutes to mix during infusion
- Start infusion at 1mg/minute over at least 60 minutes

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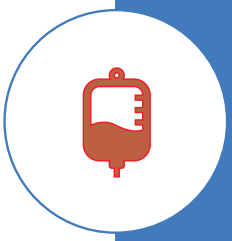
# Vyxeos (liposome-encapsulated daunorubicin/cytarabine)

- IV infusion over 90 minutes
- Approved for AML
- Contains copper
- bleeding, fever, rash, swelling, nausea, mouth or throat sores, diarrhea, constipation, muscle pain, tiredness, stomach pain, difficulty breathing, headache, cough, decreased appetite, irregular heartbeat, pneumonia, blood infection, chills, sleep disorders



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# Nitrosoureas (Brain and CNS tumors)

- High lipid solubility and crosses the blood-brain barrier and metabolized in liver
- Inhibits DNA & RNA synthesis
- Breaks DNA helix and interferes with DNA replication
- **Severe N&V, cumulative myelosuppression 4-6 weeks**, **pulmonary fibrosis**, and chronic renal dysfunction

<u>Carmustine (BCNU):</u>

IV ethanol infusion and administered in glass or non-pvc tubing

1400 mg/m2 cumulative dose

<u>Lomustine (CCNU):</u>

PO version of BCNU

One dose every 6 weeks

Take on empty stomach

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| CHEMOTHERAPY AND TARGETED THERAPY TOXICITIES | |
|---|---|
| General | Fatigue |
| Neurological | Encephalopathy; peripheral neuropathies; seizures; cognitive changes |
| Ocular | Keratitis; conjunctivitis; visual changes; color blindness; photophobia |
| Pulmonary | Pneumonitis; pulmonary fibrosis; pulmonary edema; bronchospasm |
| Cardiovascular | Dysrhythmias, myocardial; hyper/hypo-tension; pericardial effusions; QT prolongation |
| Renal /Nephrotoxicity | Nephritis; SIADH, electrolyte abnormalities; acute kidney injury |
| Gastrointestinal | Nausea; vomiting; anorexia; diarrhea; constipation; mucositis; GI fistula/perforation |
| Pancreatic | Pancreatitis |
| Hepatic | Elevated LFTs; jaundice |
| Musculoskeletal | Arthralgias; muscle cramps |
| Integumentary | Alopecia; nail changes; pigment changes; rash; photosensitivity |
| Hematological | Neutropenia; anemia; thrombocytopenia |
| Reproductive | Infertility |

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# Alkylating Agents Summary

Cisplatin (IV):
- Ototoxicity
- Nephrotoxicity
- Creatinine clearance>50
- Daily creatinine <1.5
- Administer magnesium
- Mannitol administration
- Severe N/V
- Vesicant >55mg/m2

Carboplatin(IV):
- Delayed thrombocytopenia (18-28 days) dose limiting toxicity
- Anaphylaxis with increased doses

Oxaliplatin(IV):
- Larynegeal spasms
- Keep warm
- Drink warm fluids
- No straws

Cytoxan(IV):
- Mesna-hemorrhagic cystitis
- Myocardial

Ifosfamide(IV):
- CNS toxicities
- Hemorrhagic cystitis-Mesna

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# Alkylating Agents Summary

**Melphalan**-prolonged 4-6 weeks myelosuppression, N/V, severe mucositis/stomatitis

**Busulafan(Myleran)**-seizures, VOD, pulmonary toxicities, N/V high

**Temodar (PO):**

- Orally on empty stomach
- Do not crush or dissolve
- Severe myelosuppression

**Thiotepa (IV):**

- Used in children/BMT
- Dermatologic effects

**Bendamustine (IV):**

- Approved for B-cell NHL & Indolent NHL
- Skin reactions, rash, prutitutis
- Delayed myelosuppression

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## Anti-tumor Antibiotics-Anthracyclines-Summary

Composed of atetracyclic chromophores (usually red, orange, blue, purple) linked to a sugar

- Check Bilirubin
- Cardio toxic-MUGA or ECHO
- Total cumulative doses
- Vesicant- Central line preferred

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# Case Study

Mr. Arthur Jenkins, 68 years old newly diagnosed with Diffuse Large B-Cell Lymphoma. Retired school teacher. PMH of HTN, DM type 2, Osteoarthritis

- Imaging: CT scan of the chest, abdomen, and pelvis showed widespread lymphadenopathy, splenomegaly, and a mediastinal mass.
- Biopsy: Excisional biopsy of the supraclavicular lymph node confirmed the diagnosis of Diffuse Large B-Cell Lymphoma (DLBCL), a high-grade non-Hodgkin lymphoma.
- Bone Marrow Biopsy: Negative for lymphoma involvement.
- PET scan: Showed metabolically active disease in multiple lymph node regions and the spleen

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# Chemotherapy regimen R-CHOP

- Rituximab IV (dose based on body surface area)
- Cyclophosphamide IV (dose based on body surface area)
- Doxorubicin IV (dose based on body surface area)
- Vincristine IV (dose based on body surface area, max dose 2mg)
- Prednisone 100 mg PO (daily for 5 days, starting today)

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# Let's apply what we learned today

1. **Acute Infusion Reactions:** What are the immediate concerns during and immediately after administration of these agents? How would you monitor for and manage them?
2. **Myelosuppression:** What are the expected nadir times for each blood cell line? What are the signs and symptoms of neutropenia, anemia, and thrombocytopenia? What interventions would be put in place?
3. **Nausea and Vomiting:** Given the emetogenic potential of CHOP, what antiemetic strategies are crucial? How would you assess the effectiveness of these interventions?
4. **Cardiotoxicity :** What are the long-term and acute risks associated with Doxorubicin? What monitoring is essential?
5. **Neuropathy :** What are the common manifestations of vincristine-induced neuropathy? How would you assess for this, and what patient education is important?

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# And more questions

**6. Hemorrhagic Cystitis :** What is the mechanism and prevention strategy for this complication?

**7. Tumor Lysis Syndrome (TLS):** Given his diagnosis and disease burden, what are the risk factors and signs/symptoms of TLS? How is it prevented and managed?

**8. Infection Risk:** What patient education is critical regarding infection prevention? When should Mr. Jenkins seek immediate medical attention?

**9. Psychosocial Support:** How would you address Mr. Jenkins' anxiety and ensure his wife feels supported and informed?

**10. Patient Education:** What key information needs to be reinforced with Mr. Jenkins and his wife before discharge after his first cycle?

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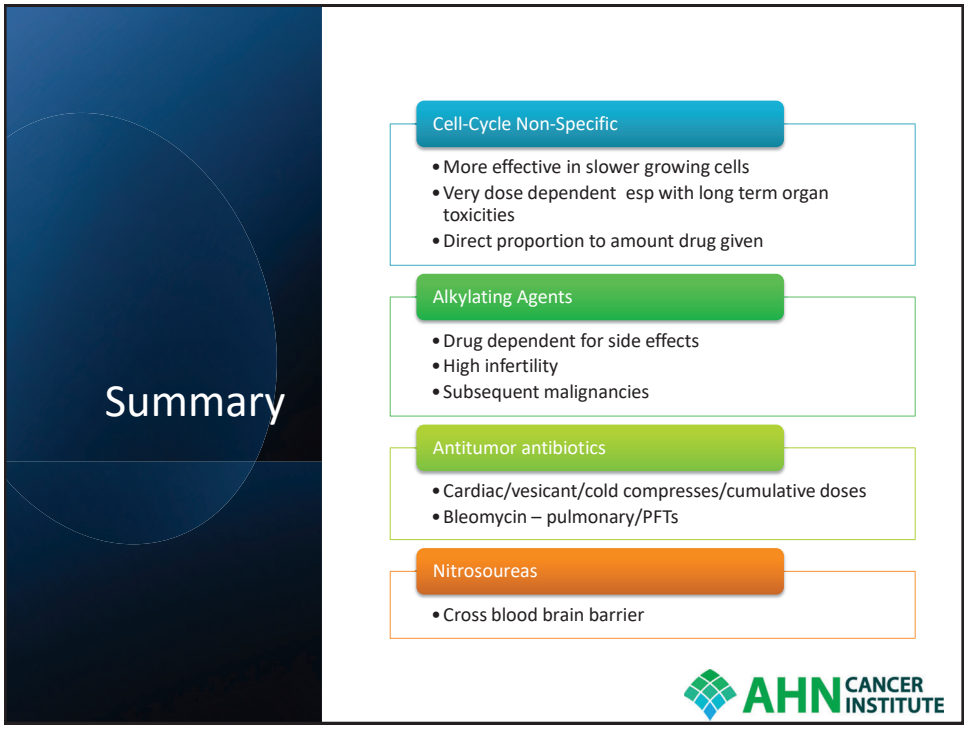
Summary
Cell-Cycle Non-Specific
• More effective in slower growing cells
• Very dose dependent esp with long term organ toxicities
• Direct proportion to amount drug given
Alkylating Agents
• Drug dependent for side effects
• High infertility
• Subsequent malignancies
Antitumor antibiotics
• Cardiac/vesicant/cold compresses/cumulative doses
• Bleomycin – pulmonary/PFTs
Nitrosoureas
• Cross blood brain barrier
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Cell Cycle Non-Specific Anti-cancer Therapy
Heather Kennihan MSN, RN, OCN
AHN Cancer Institute
Professional Development Specialist
Heather.Kennihan@ahn.org
412-285-0478
AHN CANCER INSTITUTE

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# References


- UpToDate Lexidrug (2025). Retrieved January 10-February 11, 2025. https://online.lexi.com/lco/action/home

# Spring 2026 Fundamentals of Anticancer Therapy Day 3

# Allegheny Health Network Cancer Institute

***ANTICANCER THERAPY COURSE – Day 4***

**Vignettes and Practice – View Prior to Attending**

**treatment/symptom management/professional*

1. To maintain rules of social distancing here are the stations:
    a. ACT exam review
    b. ACT releasing medication
    c. Administration (infusion and IVP, CSTD, alternate routes, on-pro, SQ, IM, procedural, OACT)
    d. Hypersensitivity
    e. Extravasation
    f. Spills

| **OUT – PATIENT ONLY – March 30, 2026**<br>**AM SESSION** | **IN-PATIENT ONLY – March 31, 2026**<br>**AM SESSION** |
|---|---|
| 7:30-8:15 – Exam, SOP, and HW review | 7:30-8:15 – Exam, SOP, and HW review |
| 8:15-8:45 – Station 1 | 8:15-8:45 – Station 1 |
| 8:45-9:00 – Break | 8:45-9:00 – Break |
| 9:00-9:30 – Station 2 | 9:00-9:30 – Station 2 |
| 9:30- 10:00 – Station 3 | 9:30- 10:00 – Station 3 |
| 10:00-10:30 – Station 4 | 10:00-10:30 – Station 4 |
| 10:30 – 11:00 – Station 5 | 10:30 – 11:00 – Station 5 |
| 11:00 – 11:45 – Debrief | 11:00 – 11:45 – Debrief |
| | |
| **OUT – PATIENT ONLY – March 30**<br>**PM SESSION (if needed)** | **IN-PATIENT ONLY – March 31**<br>**PM SESSION (if needed)** |
| 12:00 -12:45 - Exam, SOP, and HW review | 12:00 -12:45 - Exam, SOP, and HW review |
| 12:45- 1:15 – Station 1 | 12:45- 1:15 – Station 1 |
| 1:15- 1:30 - Break | 1:15- 1:30 - Break |
| 1:30 -2:00 –Station 2 | 1:30 -2:00 –Station 2 |
| 2:00 – 2:30 – Station 3 | 2:00 – 2:30 – Station 3 |
| 2:30 - 3:00 – Station 4 | 2:30 - 3:00 – Station 4 |
| 3:00 – 3:30 – Station 5 | 3:00 – 3:30 – Station 5 |
| 3:30 – 4:15 – Debrief | 3:30 – 4:15 – Debrief |
| | |

## Allegheny Health Network Cancer Institute

***ANTICANCER THERAPY COURSE – Day 5***

**scientific basis/diagnosis/staging/treatment/symptom management*

| | |
|---|---|
| 8:00 a.m. | Exam |
| 9:30a.m. | Break |
| 10:00 a.m. | Exam Review |
| 11:00 a.m. | Wrap-up and Evaluation |

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## Allegheny Health Network Cancer Institute

***ANTICANCER THERAPY COURSE – Day 6***

**Administration Practicum Day (TBD)**

**treatment/symptom management/professional*