Key Breast Cancer Trials Open at Allegheny Health Network

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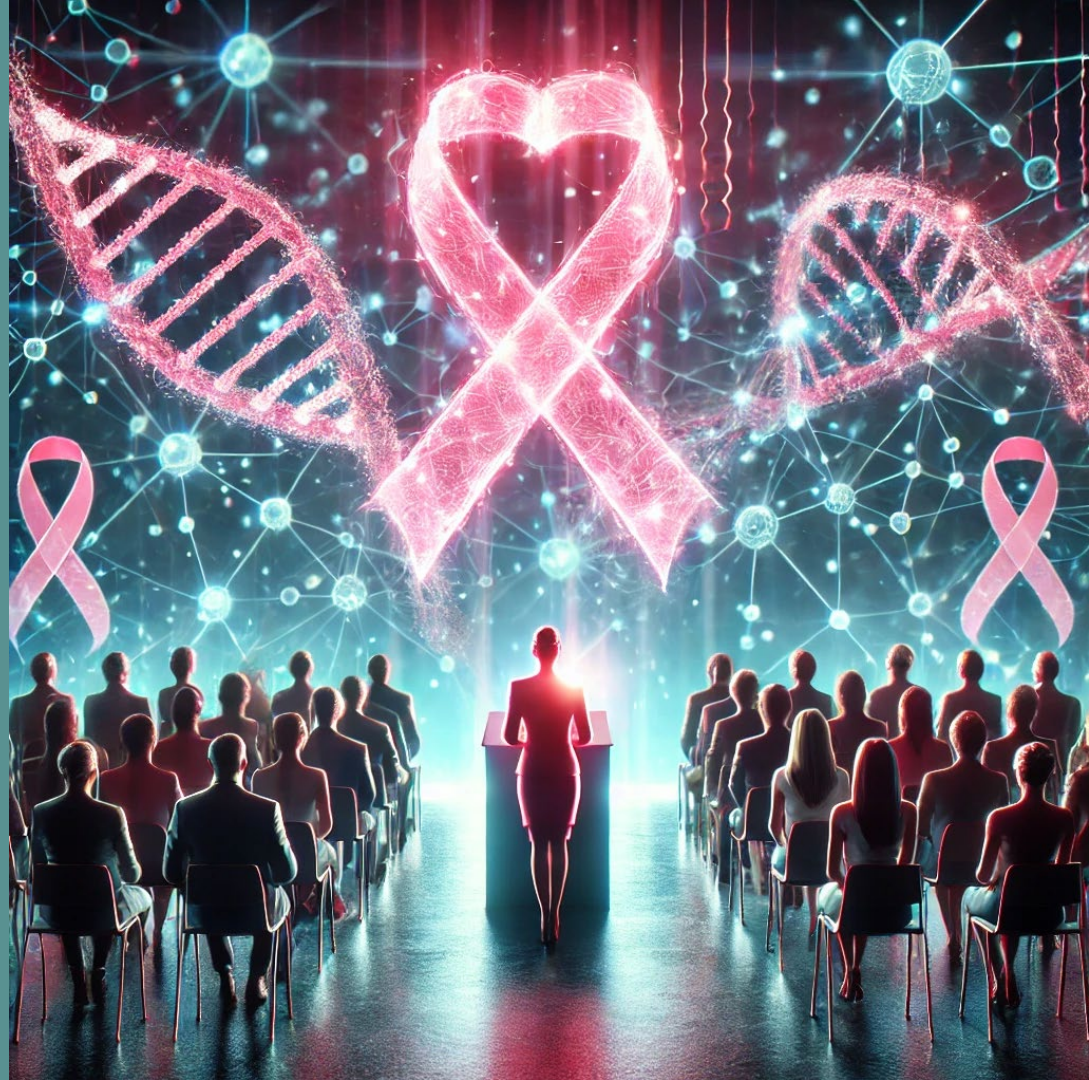


SWOG S2206

Phase III Trial of

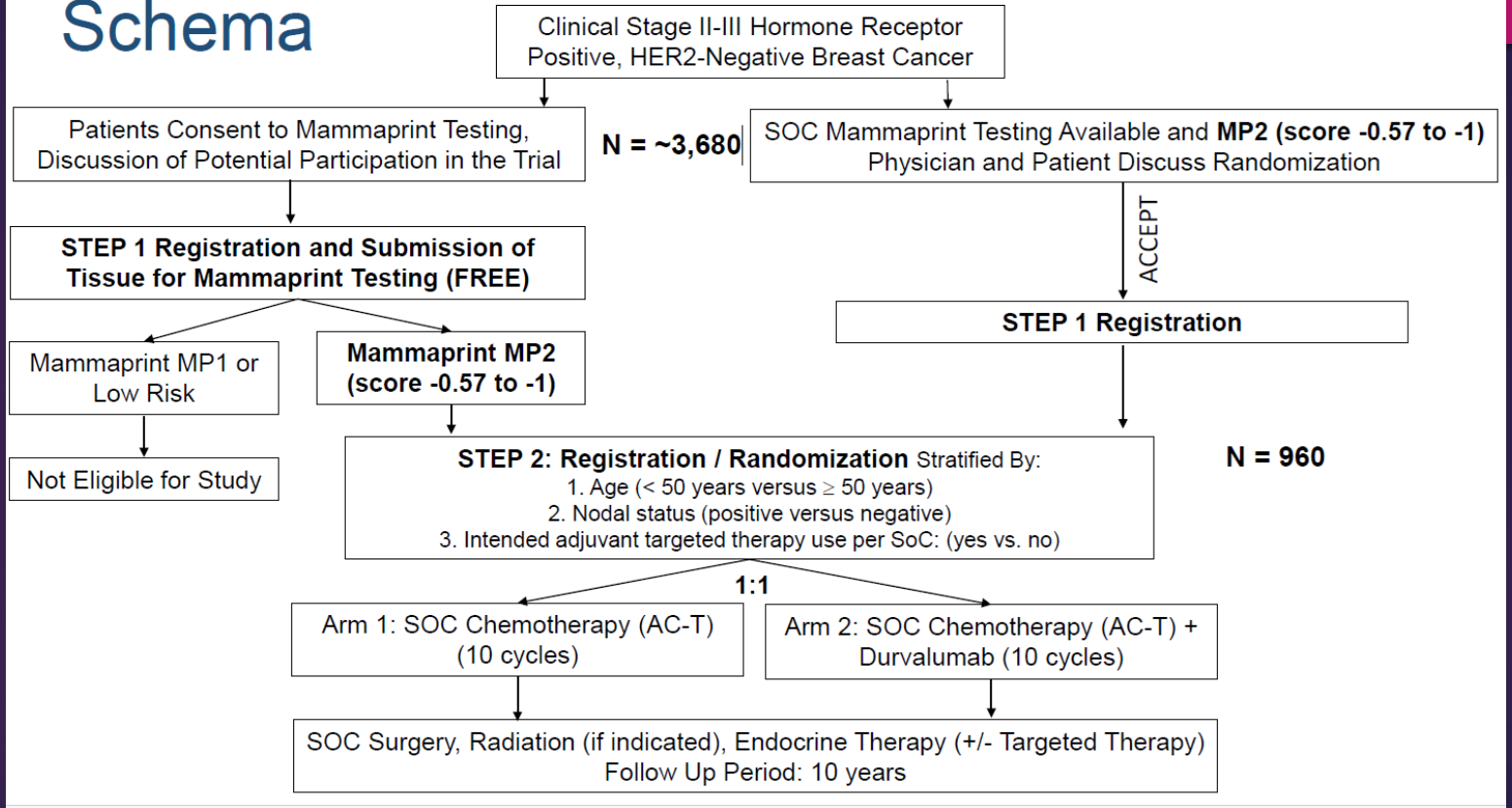
Neoadjuvant Durvalumab Plus Chemotherapy

versus

Chemotherapy Alone

for Adults with MammaPrint High 2, HR Positive / HER2 Negative Stage II-III Breast Cancer

Schema


Clinical Stage II-III Hormone Receptor Positive, HER2-Negative Breast Cancer
Patients Consent to Mammaprint Testing, Discussion of Potential Participation in the Trial
N = ~3,680
SOC Mammaprint Testing Available and MP2 (score -0.57 to -1) Physician and Patient Discuss Randomization
ACCEPT
STEP 1 Registration and Submission of Tissue for Mammaprint Testing (FREE)
STEP 1 Registration
Mammaprint MP1 or Low Risk
Mammaprint MP2 (score -0.57 to -1)
Not Eligible for Study
STEP 2: Registration / Randomization Stratified By:
1. Age (< 50 years versus ≥ 50 years)
2. Nodal status (positive versus negative)
3. Intended adjuvant targeted therapy use per SoC: (yes vs. no)
N = 960
1:1
Arm 1: SOC Chemotherapy (AC-T) (10 cycles)
Arm 2: SOC Chemotherapy (AC-T) + Durvalumab (10 cycles)
SOC Surgery, Radiation (if indicated), Endocrine Therapy (+/- Targeted Therapy)
Follow Up Period: 10 years

Key Eligibility – Step 1: Screening

- Histologically confirmed **ER-positive and/or PR positive and HER2-negative** (as per ASCO CAP) breast cancer. HER2 equivocal cases eligible (per ASCO CAP)
- **Clinical stage II-III disease** (inflammatory breast cancer is eligible)No metastatic disease. No locally recurrent breast cancer.
- **MammaPrint High 2 (MP2) status: score -0.57 to -1.02** mechanisms to enroll:
  - MammaPrint testing was ordered as standard of care test (billed to patient's insurance) within 12 weeks prior to registration to Step 1.
  - Consent to screening. Must have at least 10 unstained FFPE slides available from initial tumor biopsy. Agendia will perform testing (cost covered by the study)
- No contraindications to immunotherapy
- No prior treatment for current breast cancer. Pts. must be candidates for doxorubicin, paclitaxel, and durvalumab therapy.

Key Eligibility – Step 2: Randomization

- Pts. must meet Step 1 criteria.
- Pts. must be registered within 84 days (12 wks) after receiving an MP2 status.
- Within 2 years prior to registration: Pts. must not have history of non-infectious pneumonitis that required steroid treatment or evidence of active pneumonitis
    - Pts. must not have active autoimmune disease that required systemic treatment. Replacement therapy (e.g. thyroxine for pre-existing hypothyroidism, insulin for type I diabetes mellitus, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
- Within 28 days prior to registration: Pts. must have:
    - adequate bone marrow, kidney, and cardiac function
    - Pts. must not have uncontrolled diabetes
    - Pts must have had a complete H&P

Cryo-Prevent BC Study: Cryotherapy to Prevent Peripheral Neuropathy from Taxane Chemotherapy Regimens in Early-Stage Breast Cancer

- **Funder**: Claude-Worthington Benedum Foundations Award
- **Clinical Phase**: Phase 3
- **Study Rationale**: We hypothesize that breast cancer patients using cold therapy / cryotherapy gloves and socks prior to, during and after the taxane administration portion of their neoadjuvant/adjuvant chemotherapy will report less frequency and severity of CIPN leading to completion of more cycles of treatment without delays or dose reductions compared to the control arm.

Cryo-Prevent BC Study: Study Design

- This is a prospective, randomized, single institution study looking at prevention of CIPN in early-stage breast cancer patients.
- The study will enroll 74 patients with early-stage breast cancer defined as stage I-III who are eligible for the described taxane based chemotherapy.
- Patients will be randomized (1:1) to either utilize frozen SuzziPad cryotherapy / cold therapy gloves and socks or no intervention (no cryotherapy). The gloves and socks will be put on the patient for up to 30 minutes during the taxane infusion.

Cryo-Prevent BC Study: Study Objective(s)

Primary:

- The primary objective of the study is to compare the rate of development and severity of CIPN (sensory and motor) based on CTCAE v 5.0 scoring for peripheral neuropathy.

Secondary objectives include:

- Evaluate skin and nail toxicity (nail separation, nail discoloration, paronychia, skin pain) utilizing CTCAE v5.0.
- Evaluate total amount of taxane given in mg.
- Evaluate total number of chemotherapy delays in days due to any adverse side effect.
- Safety analysis (based on any adverse events reported utilizing CTCAE v5.0 during their standard of care medical oncology toxicity assessment).

Cryo-Prevent BC Study

Inclusion Criteria

- Women and men (ages 18-70)
- Diagnosed with stage I-III early-stage breast cancer.
- Planned to receive curative treatment with neoadjuvant or adjuvant chemotherapy utilizing Taxotere and Cyclophosphamide (TC) for four cycles or Adriamycin and Cyclophosphamide (AC) for four cycles followed by Paclitaxel (T) for (twelve weekly cycles or four cycles dosed every twenty-one days) or the keynote 522 regimen (Paclitaxel (T) plus Carboplatin (C) for (twelve weekly cycles or four cycles dosed every twenty-one days) plus Pembrolizumab every 3 weeks followed by Adriamycin and Cyclophosphamide and Pembrolizumab every 3 weeks for four cycles).

Cryo-Prevent BC Study

Exclusion Criteria

- Subjects with pre-existing peripheral neuropathy (grade 1 or higher)
- Metastatic Breast Cancer
- History of receiving chemotherapy in the past
- Participant is allergic to the glove/sock material.
- Participants with Reynaud's disease
- Participants with any open wounds or rashes on their hands or feet.
- Participants with skin or nail conditions that the treating physicians determines to be ineligible for use of cryotherapy gloves.

Cambria-1 Protocol (Global) V2.0 dated 14-Dec-2022

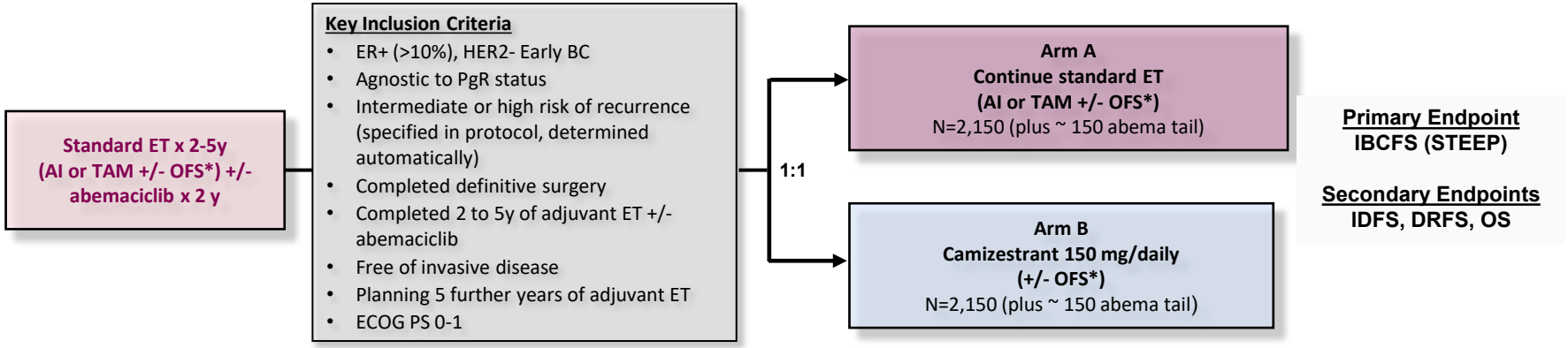
Study Title:

A Phase III, Open-Label, Randomized Study to Assess the Efficacy and Safety of Extended Therapy With Camizestrant versus Standard Endocrine Therapy (Aromatase Inhibitor or Tamoxifen) in Patients with ER+/HER2- Early Breast Cancer and an Intermediate or High Risk of Recurrence Who Have Completed Definitive Locoregional Therapy and at Least 2 Years of Adjuvant Endocrine-Based Therapy Without Disease Recurrence

Lead Coordinating Investigator:

Erika Hamilton, MD, Sarah Cannon Research institute, Nashville, USA

CAMBRIA1 Study Design



* Pre-menopausal women and men will receive ovarian function suppression (OFS) mandatory in Camizestrant arm, per local guideline in control arm

Stratification Factors

• Risk	High[a]	Intermediate[b]
• Duration of prior adjuvant ET	24 to <42 mo	≥ 42 to 63 mo
• Menopausal status	Pre, Peri, Men	Post
• Prior ET	Tamoxifen	AI
• Prior adjuvant CDK4/6i	Yes	No

[a]**High-Risk** = T4, T3 N+, ≥ 4+ LN, T1c-T2, 1 LN+ with G3 or Ki67 >= 20%, or high-risk gen sig, T1a-T2, 2-3 LN+ with G3 or Ki67 >=20% or high-risk gen sig

[b]**Intermediate-Risk** = T3N0, T1c-T2 N0 with G3 or Ki67 >= 20%, or high-risk gen sig or prior chemotherapy, T1a-T2, 2-3 LN+ without G3, Ki67 >=20%, or high-risk gen sig

Based on Clinical Study Protocol v2.0 dated 14-Dec-2022

Inclusion Criteria

I.C. #4 Pre-, peri-, and post-menopausal women, and men, with at least one of the following:

(a)

T4 tumours

(tumour of any size with direct extension to the chest wall and/or the skin ulceration or macroscopic nodules)

regardless of nodal status

(b)

Pathological primary invasive tumour

size >5 cm

regardless of nodal status

For patients who received neoadjuvant systemic therapy (chemotherapy and/or ET), primary tumour size >5 cm on breast imaging is allowed

(c)

Pathological tumor of any size with involvement in ≥2 ipsilateral lymph nodes

For patients who have suspected involvement of locoregional lymph nodes, confirmation of nodal disease by pathology, cytology, immunohistochemistry, and/or one-step nucleic acid amplification is required

For this study, locoregional lymph nodes include ipsilateral lymph nodes:

- axillary
- intraclavicular and supraclavicular
- internal mammary

- Intramammary LN not counted in N staging
- If contralateral lymph nodes +, pt is not eligible

Inclusion Criteria

(d)

Pathological primary invasive tumor size >1 cm and ≤5 cm

with involvement of 1 positive lymph node

(or only micrometastatic disease)

if at least one of the following features is present:

- Pathological grade 3
- Pre-existing high risk of recurrence per genomic signature assessment from medical record if in compliance with local regulations and conducted in accordance with intended use
- Centrally assessed Ki-67 ≥20% via an AstraZeneca-provided laboratory test using archival sample **where country-specific in vitro diagnostic approvals are available**, as required.

(e)

Pathological primary invasive tumor size >1 cm and ≤5 cm

without involvement of any ipsilateral lymph nodes

if at least one of the following features is present:

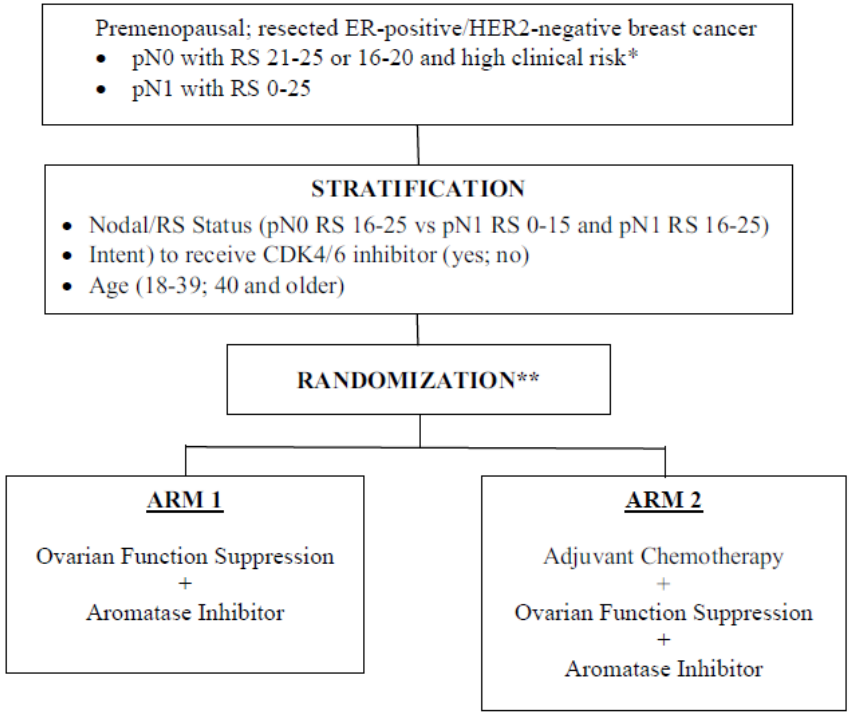
- Pathological grade 3
- Pre-existing high risk of recurrence per genomic signature assessment from medical record if in compliance with local regulations and conducted in accordance with intended use
- Centrally assessed Ki-67 ≥20% via an AstraZeneca-provided laboratory test using archival sample **where country-specific in vitro diagnostic approvals are available**, as required
- Prior cytotoxic chemotherapy for the current diagnosis of breast cancer

NRG-BR009 OFSET

A Phase III Adjuvant Trial Evaluating the Addition of Adjuvant Chemotherapy to Ovarian Function Suppression plus Endocrine Therapy in Premenopausal Patients with pN0-1, ER- Positive/HER2-Negative Breast Cancer and an Oncotype Recurrence Score <25

Schema

Figure 1. NRG-BR009 Schema



* **High clinical risk defined as:**
1) low histologic grade with primary tumor size > 3 cm, OR
2) intermediate histologic grade with primary tumor size > 2 cm, OR
3) high histologic grade with primary tumor size > 1 cm

** Randomization is 1:1.

Patient Population

Key Inclusion:

- Patients must be premenopausal
- ECOG of 0,1, or 2
- Must have undergone surgery with axillary staging
- Must be pT1-3, N0-1
  - If N0, Oncotype must be 21-25 or 16-20 with tumor size >3cm, tumor size >2cm with intermediate histologic grade, or tumor size >1cm with high histologic grade
  - If N1-3, Oncotype must be <26
- ER and/or PR+ (greater than 1% staining) and HER2-

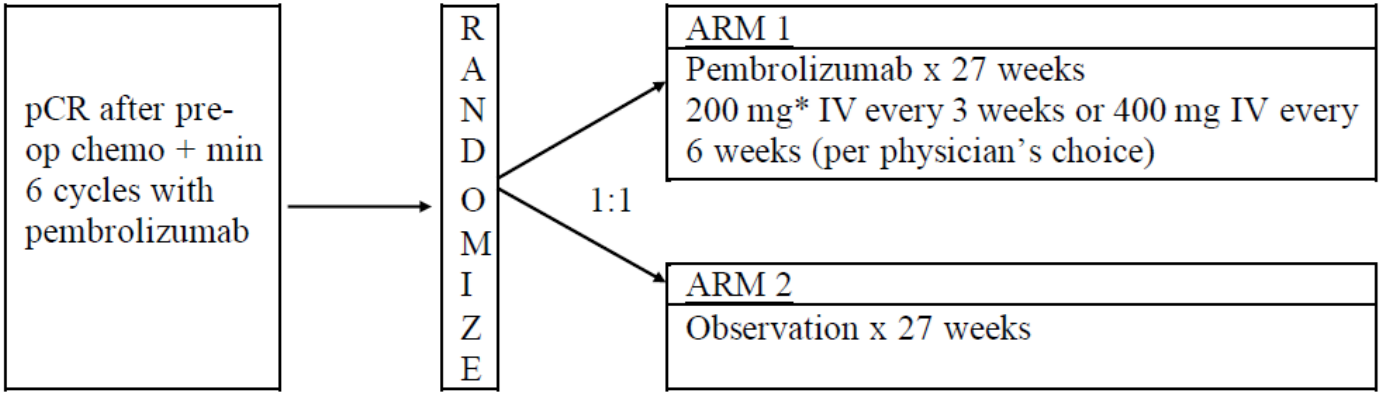
Key Exclusion:

- Surgery was greater than 16 weeks prior to pre-entry
- Short course of ET greater than 6 weeks
- History of ipsilateral or contralateral breast cancer (excluding prior DCIS/LCIS)
- Life expectancy <10 years
- Any XRT, chemotherapy, or biotherapy administered for the currently diagnosed breast cancer (short course excepted). Prior TAM for prevention is allowed

A012103 OptimICE-pCR

De-Escalation of Therapy in Early-Stage TNBC Patients Who Achieve pCR After Neoadjuvant Chemotherapy with Checkpoint Inhibitor Therapy

Schema



*For Canadian sites only: Pembrolizumab 2 mg/kg (maximum dose to 200 mg) IV is alternative dosing permitted at CCTG sites.

Treatment or observation is to continue for 27 weeks or until unacceptable adverse event. Patients will be followed for 5 years after registration or recurrence. Thereafter, patients will be followed annually (+/- 3 months) for overall survival for a total of 10 years after registration.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

Key Eligibility

- ECOG 0-2
- cT1cN1-2, or cT2-4cN0-2
  - Clinical stage II or stage III at diagnosis (AJCC 8th edition)
- pCR after completing neoadjuvant therapy (residual DCIS is allowed; $pN0_i$ is considered pN0)
  - Neoadjuvant therapy comprised of a chemotherapy with pembrolizumab for at least 6 cycles
  - If patients are cN0 but surgical pathology shows pN1, patients are not eligible
  - If patients are cN1 and SLNB is positive, they must have an ALND
- ER and PR ≤10%, HER2- (IHC and FISH) by ASCO/CAP
- If patients undergo BCS but do not plan on adjuvant XRT, they are not eligible

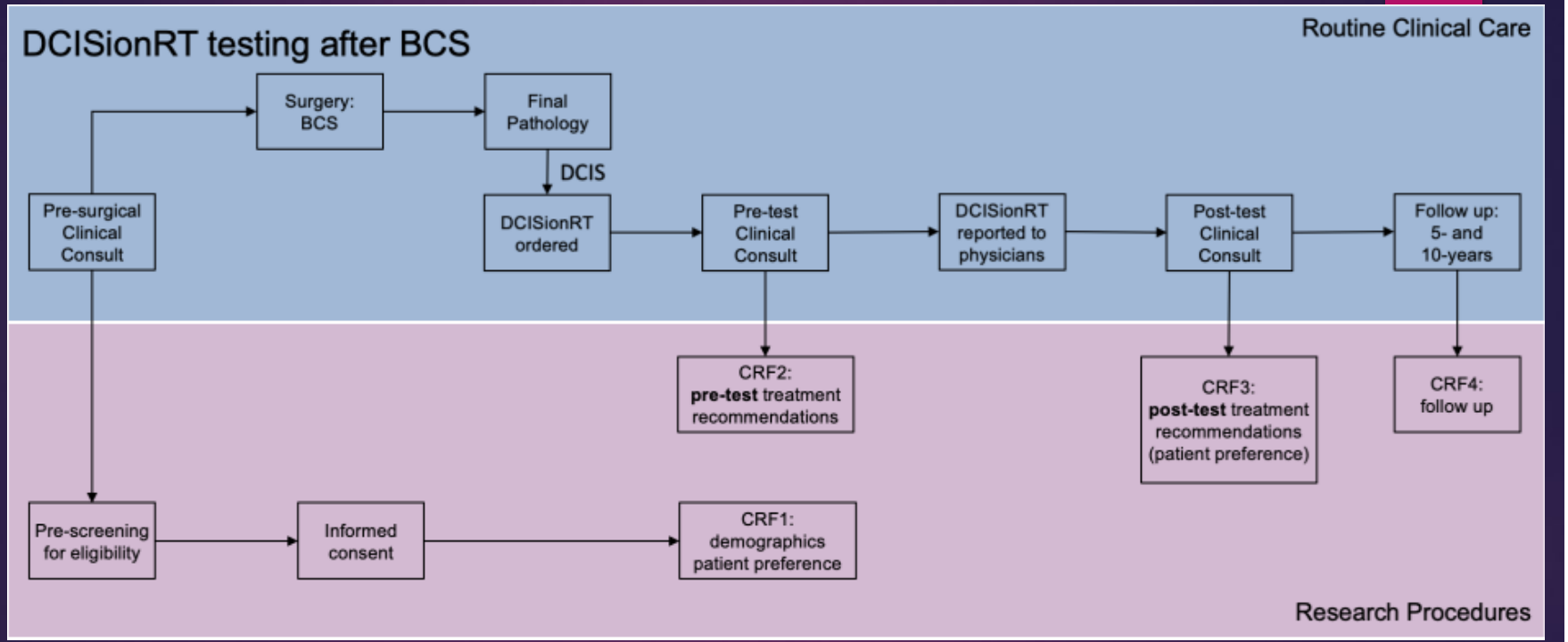
Refer to Protocol Section 3.2 for complete eligibility criteria

Key Eligibility

- No prior history of breast cancer. Prior DCIS is allowed
  - "Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial."
- No known active liver disease
- Cardiac disease (must be 2B or better)
- No history of intolerance to pembrolizumab or its components (includes Grade 3 or Grade 4 infusion reactions or hypersensitivity)
  - Prior irAEs are allowed if resolved to ≤grade 1 and did not require chronic steroids with subsequent therapy
- Chronic systemic steroids or immunosuppressive medications
  - Replacement therapy (thyroxine, insulin, corticosteroids for adrenal/pituitary insufficiency are not considered systemic therapy)

Prelude DCISion-RT PREDICTII

- A Prospective Study to Evaluate the Effect of the DCISionRT Test on Treatment Decisions in Patients with DCIS Following Breast-Conserving Therapy


DCISionRT testing after BCS
Routine Clinical Care
Surgery: BCS
Final Pathology
DCIS
Pre-surgical Clinical Consult
DCISionRT ordered
Pre-test Clinical Consult
DCISionRT reported to physicians
Post-test Clinical Consult
Follow up: 5- and 10-years
CRF2: pre-test treatment recommendations
CRF3: post-test treatment recommendations (patient preference)
CRF4: follow up
Pre-screening for eligibility
Informed consent
CRF1: demographics patient preference
Research Procedures

Key Eligibility

- 1. Patient must have histologically confirmed ductal carcinoma in situ (DCIS) in a single breast (presence of lobular carcinoma in situ (LCIS) or other benign breast disease in addition to DCIS is acceptable).
- 2. Patient must have the DCISionRT test ordered during routine patient care.
- 3. Patient must be eligible for or have recently completed breast conserving surgery.
- 4. Patient must be eligible to receive radiation and/or systemic treatment. 5. Patient must be 30 to 85 years old.
- 6. Patient must have tumor size of less than 6 cm.
- 7. Patient must have been diagnosed with DCIS within 120 days of consent

Key Eligibility

- 1. Patient tissue is insufficient to generate DCISionRT test results or required DCISionRT inputs (age, tumor size, margin status, palpability) are missing.
- 2. Patient has evidence of invasive breast cancer, including microinvasion, lymph node involvement, or Paget's disease of the nipple or suspicious mammogram findings in the lymph nodes or contralateral breast.
- 3. Patient has been surgically treated with an ipsilateral mastectomy for primary DCIS.
- 4. Patient has had any prior ipsilateral or contralateral breast DCIS or invasive breast cancer.
- 5. Patient has a prior history of in-field radiation in the ipsilateral breast.
- 6. Patient has had prior systemic endocrine or chemotherapy prior to testing.
- 7. Patient is pregnant.

Questions?