Disclosures

- None

Objectives

- Review data on the use of oral paclitaxel with encequidar in patients with metastatic breast cancer
- Identify the potential role of oral paclitaxel with encequidar as well as clinical considerations
- Discuss the mechanism of action of tucatinib and compare to currently approved small molecular tyrosine kinase inhibitors used in breast cancer
Oral paclitaxel with encequidar (OPE): The first orally administered paclitaxel shown to be superior to IV paclitaxel on confirmed response and survival with less neuropathy: A Phase III clinical study in metastatic breast cancer


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Metastatic Breast Cancer and Paclitaxel

- Taxanes remain a foundation of breast cancer treatment.
  - IV Paclitaxel FDA-approved schedule for mBC: 175 mg/m² Q 3 weeks
  - IV Paclitaxel (oral clinical practice): 60 mg/m² Q 2 weeks (capsules by viva, Q 2–4 weeks)
- Benefits of an oral mode of administration include patient convenience, home treatment, lack of IV access, removal of the risk of infusion hypersensitivity reactions and the need for prophylactic corticosteroids.
- Paclitaxel is not orally absorbed because it is secreted by the P-glycoprotein (P-gp) pump.
- Encequidar (HMR3081A) is a highly specific, potent inhibitor of P-gp and increases the absorption of oral paclitaxel.
- Oral paclitaxel and encequidar (OPE) is composed of 30 mg capsules of solubilized paclitaxel and a 15 mg tablet of encequidar.

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Dose Justification for OPE

Phase I PK Study (N=36) vs. Phase II Study in pre-treated mBC (N=26)

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Conclusions

- Oral pacitaxel and encorudier is the first oral taxane in a Phase III trial to demonstrate a significant improvement in confirmed overall response rate compared to IV pacitaxel.
- In the modified intent-to-treat population, centrally confirmed ORR increased from 25.6% with IV pacitaxel to 40.4% with OPE (P=0.005).
- Response with OPE was durable with 33.7% of patients responding for >200 days.
- Although PFS was similar, oral pacitaxel and encorudier was associated with improved overall survival in the modified intent-to-treat population.
- Oral pacitaxel and encorudier was associated with a lower incidence of neuropathy and alopecia but a higher incidence of low-grade gastrointestinal adverse events compared to IV pacitaxel.
- Oral pacitaxel and encorudier provides an important oral therapeutic option for patients with metastatic breast cancer, representing a meaningful improvement in the clinical profile of pacitaxel.

Tucatinib
Tucatinib MOA

- Oral reversible tyrosine kinase inhibitor
  - Selectively inhibits HER2
  - Minimal inhibition of EGFR
    - ↓ rates of diarrhea

- Crosses BBB


Pharmacology Updates
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