National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Updated 5/29/20

Positive Quality Intervention: Tucatinib Management

Description:

The purpose of this PQI is to highlight tucatinib and its usage and management in advanced unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2-based regimens in the metastatic setting.

Background:

Tucatinib is an oral tyrosine kinase that is highly selective for HER2, a growth factor receptor over-expressed in various types of cancers. Tucatinib binds to the HER2 protein, inhibiting its role in signaling pathways and ultimately the growth of HER2-expressing cells.

Tucatinib, in combination with trastuzumab and capecitabine, is being studied in the HER2CLIMB trial that enrolled patients with locally advanced unresectable or metastatic HER2 positive breast cancer who had previously been treated with trastuzumab, pertuzumab, or trastuzumab emtansine. Patients received either tucatinib 300 mg orally twice daily or placebo in addition to trastuzumab and capecitabine.

	Tucatinib Group	Placebo Group
PFS at 1 year	33.1%	12.3%
Median PFS duration	7.8 months	5.6 months
OS at 2 years	44.9%	26.6%
Median OS duration	21.9 months	17.4 months

Additionally, researchers analyzed the subgroup of patients with brain metastases and found significantly increased PFS with tucatinib in this patient population as well, reporting primary results of PFS at one year of 24.9% in the tucatinib group compared to 0% in the placebo group. Presented at the 2020 ASCO Annual Meeting, an exploratory analysis in the HER2CLIMB trial of intracranial efficacy in patients with brain metastases who received tucatinib combination versus placebo group: a 42% reduction in the risk of death, a 68% reduction in the risk of CNS disease progression or death, and an increase in intracranial response rate (47% vs. 20%) for patients who had active measurable intracranial lesions at baseline.[5]

PQI Process:

- Identify eligible HER2 positive patients as potential candidates for tucatinib

When receiving a prescription for tucatinib

Dose adjustments:

Dose Reduction	Recommended Dose	How to Supply
1st dose reduction	250 mg PO BID	One 150 mg tablet + two 50 mg tablets BID
2nd dose reduction	200 mg PO BID	One 150 mg tablet + one 50 mg tablet BID
3rd dose reduction	150 mg PO BID	One 150 mg tablet BID

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PQI Process continued:

- When to adjust which agent:
  - All side effects should be assessed for relationship to tucatinib, capecitabine, and/or trastuzumab
  - Liver function abnormalities: tucatinib dose should be adjusted, regardless of relationship to drug
  - Left ventricular dysfunction: tucatinib should be held if ≥ 16% reduction from baseline, ejection fraction (LVEF) below institutional limits of normal and ≥ 10% reduction from baseline, or LVEF < 40%
  - QTc prolongation: tucatinib dose should be adjusted, regardless of relationship to drug
- Drug interactions:
  - Avoid concomitant strong CYP3A4 and CYP2C8 inhibitors and inducers

Patient Centered Activities:

- Provide Oral Chemotherapy Education Sheet
- Administration: can be taken with or without food at the same time twice each day. Can be taken at the same time as the capecitabine in the regimen
- Storage: store at room temperature in the original bottle; do not remove desiccant from bottle. Once the bottle is opened, medication should be used within 3 months
- Recommend antidiarrheal agents to have on hand when starting tucatinib

Financial Assistance:

- Can call **855.4SECURE** or visit **SeaGenSecure.com**
- Patient Assistance Program, Claims Appeal and Patient Assistance, and Commercial Out-of-Pocket Assistance are available

Supplemental Information:

Common side effects reported the HER2CLIMB trial:

- Diarrhea (80.9%; reported to be manageable with short courses of antidiarrheals)
- Palmar-plantar erthrodysethesia syndrome (63.4%)
- Nausea (58%), vomiting (35.9)
- Fatigue (45%)
- Increased liver transaminases (20%; reported to be transient and reversible)
- Stomatitis, headache, decreased appetite also reported

References:

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3. Tucatinib. Seattle Genetics. Available at https://www.seattlegenetics.com/pipeline/tucatinib. Accessed March 27, 2020.
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5. Lin NU, Borges V, Anders C, et al. Intracranial Efficacy and Survival With Tucatinib Plus Trastuzumab and Capecitabine for Previously Treated HER2-Positive Breast Cancer With Brain Metastases in the HER2CLIMB Trial. *JCO*. 2020, JCO2000775. doi: 10.1200/JCO.20.00775.