

Positive Quality Intervention: Tucatinib (Tukysa®) 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 inhibitor that is highly selective for HER2, a growth factor receptor over-expressed in various types of cancers.¹ 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.²

	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. Upon receiving a prescription for tucatinib:

- Verify appropriate starting dose: typically 300 mg by mouth two times daily
- Confirm orders for capecitabine and trastuzumab
- Drug interactions: avoid concomitant strong CYP3A4 and CYP2C8 inhibitors and inducers
- 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
 - Left ventricular ejection fraction (LVEF): tucatinib should be held if $\geq 16\%$ reduction from baseline, LVEF below limits of normal and $\geq 10\%$ reduction from baseline, or LVEF $< 40\%$
 - QTc prolongation: tucatinib dose should be adjusted, regardless of relationship to drug

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PQI Process Continued:

Dose adjustments:

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

Patient Centered Activities:

- Provide [Oncology Chemotherapy Education \(OCE\)](#) sheet
- Provide [Tucatinib Patient Guided Resource](#)
- Administration: can be taken with or without food at the same time twice each day and at the same time as the capecitabine in the regimen
- Counsel patient on common side effects
 - Diarrhea (80.9%)
 - Provide [Oral Chemotherapy Education Supplemental Sheet](#)
 - Reported to be manageable with short courses of antidiarrheals
 - Recommend antidiarrheal agents to have on hand when starting tucatinib
 - Palmar-plantar erythrodysesthesia syndrome (63.4%)
 - See [Medication Induced Hand-Foot Syndrome](#) PQI and provide [Oral Chemotherapy Education Supplemental Sheet](#)
 - Nausea (58%), vomiting (35.9%)
 - See [Chemotherapy Induced Nausea and Vomiting](#) PQI, [CINV Assessment Tool](#), and provide [Oral Chemotherapy Education Supplemental Sheet](#)
 - Fatigue (45%)
 - Increased liver transaminases (20%)
 - Reported to be transient and reversible
 - Stomatitis, headache, decreased appetite also reported
- 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
- 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

References:

1. English DP, Rogue DM, Santin AD. HER2 expression beyond breast cancer: therapeutic implications for gynecologic malignancies. *Mol Diagn Ther.* 2013;17(2):85-99.
2. Murthy RK, Loi S, Okines A, et al. Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. *NEJM.* 2020; 382:597-609.
3. Tucatinib. Seattle Genetics. Available at <https://www.seagen.com/science/pipeline/tucatinib>.
4. Tucatinib combination extends survival in HER2- positive metastatic breast cancer, including patients with brain metastases. The ASCO Post. Available at: <https://www.ascopost.com/issues/january-25-2020/tucatinib-combination-extends-survival-in-her2-positive-metastatic-breast-cancer/>. Published JAN 25, 2020.
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.

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