



## Positive Quality Intervention: Management of Infigratinib (Truseltiq™) in Cholangiocarcinoma

**Description:** This PQI will discuss the role of infigratinib in cholangiocarcinoma treatment along with prescribing specifics and adverse effects.

**Background:** Infigratinib belongs to the class of agents which target the fibroblast growth factor receptor 2 (FGFR2). FGFR2 fusions and rearrangements play a key role in cholangiocarcinoma.<sup>1</sup> Cholangiocarcinomas are a heterogeneous group of rare malignancies of the biliary tree and are divided based on anatomic location to intrahepatic, extrahepatic, and hilar.<sup>2</sup> Each encompass intricacies in presentation and management. FGFR2 fusions and rearrangements are more commonly (~15%) seen in those with intrahepatic cholangiocarcinoma which often present in the advanced incurable setting due to vague symptoms. Intrahepatic cholangiocarcinomas carry a poor prognosis. Following front-line treatment, second-line treatment lacks a standard across all advanced cholangiocarcinoma patients and traditional chemotherapy approach has proven to have minimal to no benefit (5% objective response rate and median PFS of 4 months).<sup>3</sup> Best practice is to molecularly profile all intrahepatic cholangiocarcinoma tumors to determine actionable targetable mutations such as that seen with FGFR2 fusions and rearrangements.<sup>2</sup> In May 2021, infigratinib was granted accelerated FDA approval based on results of a phase 2 trial.<sup>1</sup> Javle et al performed a multicenter, open-label, single arm study of infigratinib 125 mg po daily for 21 days and 7 days off in previously treated advanced or metastatic cholangiocarcinoma patients with FGFR2 fusions or rearrangements.<sup>4</sup> One hundred and eight patients received at least one dose of infigratinib. Objective response rate was 23.1% with one complete response reported and 24 partial responses. Another 61% showed stable disease. Median PFS was 7.3 months. Grade 3 adverse events that occurred in  $\geq 10\%$  were hyperphosphatemia (10%), stomatitis (15%), hypophosphatemia (12%), and hyponatremia (13%). FGFR inhibitor class adverse effects include hyperphosphatemia, hypophosphatemia, nail changes, alopecia, myalgias/arthralgias, dry eye, taste changes, and rare retinal pigment epithelial detachment.<sup>1</sup>

**Helsinn Therapeutics (U.S.), Inc. will discontinue distribution of TRUSELTIQ® (infigratinib) capsules as of March 31, 2023.**

### PQI Process:<sup>1</sup>

- Confirm diagnosis for advanced cholangiocarcinoma with FGFR2 fusion or rearrangement
- Confirm progression on at least one prior line of therapy
- Verify dosing: recommended starting dose is 125 mg po daily x 21 days then 7 days off on an empty stomach (1 hour before or 2 hours after food)
  - Dose modifications for renal and hepatic dysfunction
- Check for drug-drug interactions as strong and moderate CYP3A4 inhibitors and inducers should be avoided and acid-reducing agents should be avoided
  - If unavoidable, dosing of histamine-2 antagonist or antacids should be staggered to avoid co-administration with infigratinib (2 hours before or after antacids; 2 hours before or 10 hours after histamine-2 antagonists)
- Monitoring includes ophthalmic exam at baseline, 1 month, at 3 months, and every 3 months while on therapy and phosphorus monitoring
- Dose modifications:

1 <sup>st</sup> dose reduction	2 <sup>nd</sup> dose reduction	3 <sup>rd</sup> dose reduction
100 mg po daily for 21 days then 7 days off	75 mg po daily for 21 days then 7 days off	50 mg po daily 21 days with 7 days off

**IMPORTANT NOTICE:** NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual's sole responsibility to seek guidance from a qualified healthcare professional. Updated 3.22.23

- Dose modifications for hyperphosphatemia:

Hyperphosphatemia Severity	Dose modifications & recommendations
Serum phosphate >5.5 - 7.5 mg/dL	<p>Continue infigratinib at the current dose and start/adjust a phosphate binder</p> <ul style="list-style-type: none"> <li>Dosing for phosphate binder should be held during the week off infigratinib therapy each cycle (Days 22-28) and during any dose interruptions for infigratinib non-hyperphosphatemia adverse events</li> </ul>
<p>Serum phosphate &gt;7.5 mg/dL <b>or</b> Single serum phosphate &gt;9 mg/dL regardless of duration or dose of phosphate lowering therapy</p>	<p>Hold infigratinib until serum phosphate <math>\leq</math> 5.5 mg/dL Resume infigratinib as below, with maximal phosphate binder dosing:</p> <ul style="list-style-type: none"> <li>If serum phosphate &gt;7.5 mg/dL occurred for &lt; 7 days: Restart infigratinib at the same dose</li> <li>If serum phosphate &gt;7.5 mg/dL for &gt;7 days or if patient had a one-time serum phosphate of &gt;9 mg/dL: Resume infigratinib at the next lower dose level</li> </ul>
Serum phosphate with life threatening consequences; urgent intervention indicated (ex. dialysis)	Permanently discontinue infigratinib

### Patient-Centered Activities:<sup>1</sup>

- Provide [Oral Chemotherapy Education](#) Sheet
- Instruct patient to take at the same time a day on an empty stomach for 21 days then 7 days off
- Educate patient that if a dose is missed greater than 4 hours skip the medication for that day
- Counsel patient on [phosphate lowering diet](#) and the importance of following up with healthcare professional for routine lab monitoring
- Educate patient to review any new medications with healthcare team prior to starting given the potential for drug-drug interactions
- Discuss avoidance of grapefruit and grapefruit juice due to drug-food interaction
- Instruct patients to use effective contraception during treatment and for one month after final dose
- Counsel patient on signs of retinal pigment detachment and the importance of following up at specific time intervals with ophthalmologist exams

### References:

1. [TRUSELTIQ™ \(infigratinib\) \[prescribing information\]](#).
2. National Comprehensive Cancer Network. Hepatobiliary Cancers.
3. Lamarca A, Palmer DH, Wasan HS, et al. Second-line FOLFOX chemotherapy versus active symptom control for advanced biliary tract cancer (ABC-06): a phase 3, open-label, randomised, controlled trial. Lancet Oncol. 2021 may, 22(5): 690-701.
4. Javle M, Roychowdhury S, Kelley RK, et al. Infigratinib (BGJ398) in previously treated patients with advanced or metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements: mature results from a multicentre, open-label, single-arm, phase 2 study. Lancet Gastroenterol Hepatol. 2021; 6: 803-815.