National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Updated 6/1/2020

Positive Quality Intervention: Zanubrutinib Patient Selection and Management in Mantle Cell Lymphoma

Description:

The purpose of this PQI is to identify differentiating characteristics which would indicate zanubrutinib (Brukinsa) as a preferred treatment option in Mantle Cell Lymphoma as well as discussing key counseling and monitoring criteria to improve patient outcomes.

Background:

Zanubrutinib is a potent, highly specific, and irreversible inhibitor of Bruton's tyrosine kinase (BTK) and is an investigational treatment for B-cell malignancies including chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), and Waldenström macroglobulinemia (WM)[1]. Zanubrutinib received FDA breakthrough therapy designation for the treatment of adult patients with MCL following at least one prior therapy on November 14, 2019 based on data from a phase I and a phase II trial. [3,5]

Zanubrutinib has shown greater selectivity for BTK with fewer off-target receptor interactions compared to the currently approved agents in the class.[2] Potential side effects seen with BTK inhibitors are likely related to off-target interaction with other receptors including epidermal growth factor receptor (EGFR) and interleukin-2-inducible T-cell kinase (ITK). [3-5] A phase I/II trial evaluated zanubrutinib 160 mg twice daily or 320 mg once daily in 144 patients with various B-cell malignancies. Safety analysis in these patients showed a less than 2% incidence of both Atrial fibrillation (Afib) and major hemorrhage which are potential grade 3/4 adverse effects seen with other BTK inhibitors.[5]

PQI Process:

Upon receipt of an order for zanubrutinib:

- Ensure patient is appropriate candidate for zanubrutinib based on indication
  - Patient comorbidities may make zanubrutinib a safer option (i.e., history of Afib, recent hemorrhage, hypertension, concomitant PPI or H2R antagonists)
- Dose of zanubrutinib is either 160 mg twice daily or 320 mg once daily based on patient preference/ability to adhere to twice daily medication
- Reduce zanubrutinib dose accordingly if co-administered with:
  - Strong CYP3A inhibitor – 80 mg once daily
  - Moderate CYP3A inhibitor – 80 mg twice daily
  - Moderate or strong CPY3A inducer – avoid concomitant use
- Reduce zanubrutinib dose to 80 mg twice daily in patients with severe hepatic impairment (Child-Pugh Class C)
- Consider prophylaxis for herpes simplex virus, *Pneumocystis jirovecii* pneumonia, and other infections according to standard of care in patients at increase risk for infections. Grade 3 or higher infections occurred overall in 23% of patients on zanubrutinib with pneumonia being the most common infection.

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PQI Process continued:

- Verify monitoring parameters:
  - CBC with differential, hepatic function
  - Signs/symptoms of Afib/flutter, bleeding, or infections including opportunistic infections

Patient Centered Activities:

- Provide Oral Chemotherapy Education (OCE) sheet
- Counsel to administer orally
  - Review once a day vs. twice a day dosing
- Review baseline labs and chronic medications – dose adjustment needed with concomitant CYP3A4 inhibitors
- Proper sign/symptom monitoring
- Evaluate if patients have missed any doses between cycles to determine if interventions are needed such as reminders, calendars, pill box, etc.
- See full prescribing information for dose modifications with Grade 3 or worse adverse effects

References:

1. BeiGene Presents Updated Head to Head Results from Phase 3 Trial of Zanubrutinib vs. Ibrutinib in Patients with Waldenström's Macroglobulinemia at the 2020 American Society of Clinical Oncology (ASCO) Virtual Scientific Program [news release]: BeiGene. Published May 29, 2020. http://ir.beigene.com/news-releases/news-release-details/beigene-presents-updated-head-head-results-phase-3-trial?loc=US
2. Flinsenberg TWH, et al. *Differential effects of BTK inhibitors ibrutinib and zanubrutinib on NK cell effector function in patients with mantle cell lymphoma*. Haematologica. June 6, 2019. Epub ahead of print.
3. Song Y, Zhou K, Zou D, et al. Safety and activity of the investigational Bruton tyrosine kinase inhibitor zanubrutinib (BGB-3111) in patients with mantle cell lymphoma from a phase 2 trial. In: Proceedings from the 2018 ASH Annual Meeting; December 1-4, 2018; San Diego, CA. Abstract 148.
4. Tam CS, et al. *A head-to-head Phase III study comparing zanubrutinib versus ibrutinib in patients with Waldenström macroglobulinemia.* Future Oncol. 2018 Sep;14(22):2229-2237.
5. Tam CS, et al. *Phase I study of selective BTK inhibitor zanubrutinib in B-cell malignancies and safety and efficacy evaluation in CLL*. Blood. July 24, 2019. Epub ahead of print.

Supplemental Information:

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