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Positive Quality Intervention: Zanubrutinib (Brukinsa®) Patient Selection and Management in Mantle Cell Lymphoma

Description: The purpose of this PQI is to identify differentiating characteristics which would indicate zanubrutinib 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). 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.[2,4] Since that time, zanubrutinib has gained approval in marginal zone lymphoma (MZL), and Waldenström macroglobulinemia (WM). It is still an investigational treatment for B-cell malignancies including chronic lymphocytic leukemia (CLL). Zanubrutinib has shown greater selectivity for BTK with fewer off-target receptor interactions compared to the currently approved agents in the class.[1] 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).[2-4] 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.[4]

PQI Process:[5] 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 (ex. history of Afib, recent hemorrhage, hypertension, concomitant PPI or H2R antagonists)
- Dose of zanubrutinib: 160 mg twice daily or 320 mg once daily
- 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 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 infections occurred in 23% of patients with pneumonia being the most common
- Verify monitoring parameters:
  - CBC with differential, hepatic function
  - Signs/symptoms of Afib/flutter, bleeding, or infections including opportunistic infections
- See full prescribing information for dose modifications with Grade 3 or worse adverse effects

Patient Centered Activities:

- Provide Oral Chemotherapy Education (OCE) sheet
- Counsel to administer orally, review once a day vs twice a day dosing
- Proper sign/symptom monitoring
- Evaluate if patients have missed any doses between cycles; consider reminders, calendars, pill box, etc
- Patient Assistance: NCODA Financial Assistance Tool

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References:

1. Flinsenberg TWH, et al. Differential effects of BTK inhibitors ibrutinib and zanubrutinib on NK-cell effector function in patients with mantle cell lymphoma. Haematologica. 2020 Jan 31;105(2):e76-e79.
2. Song Y, et al. Treatment of Patients with Relapsed or Refractory Mantle–Cell Lymphoma with Zanubrutinib, a Selective Inhibitor of Bruton's Tyrosine Kinase. Clin Cancer Res. 2020 Aug 15;26(16):4216-4224.
3. Tam CS, et al. A randomized phase 3 trial of zanubrutinib vs ibrutinib in symptomatic Waldenstrom macroglobulinemia: the ASPEN study. Blood. 2020 Oct 29;136(18):2038-2050.
4. Tam CS, et al. Phase I study of selective BTK inhibitor zanubrutinib in B-cell malignancies and safety and efficacy evaluation in CLL. Blood. 2019 Sep 12;134(11):851-859.
5. Brukinsa (zanubrutinib) [package insert].