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Positive Quality Intervention: Ibrutinib (Imbruvica®) Expansion with Obinutuzumab (Gazyva®)

Description: The purpose of this PQI is to expand on therapy management of ibrutinib (Imbruvica®) when used in combination with obinutuzumab (Gazyva®).

Background: Ibrutinib in combination with obinutuzumab has been approved for adult patients with previously untreated chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). This indication is a non-chemotherapy option for treatment naïve patients diagnosed with CLL/SLL which may further help reduce the need for chemotherapy. As an oral and IV combination therapy, coordination of the medically integrated pharmacy team is critical. The iLLUMINATE trial found ibrutinib and obinutuzumab to be efficacious as a first-line, non-chemotherapy regimen in CLL/SLL patients regardless of age or disease status. The median follow-up was 31.3 months and the most common Grade 3 or 4 adverse effects were neutropenia and thrombocytopenia. After a median follow-up of 31.3 months (IQR 29.4–33.2), median progression-free survival was significantly longer in the ibrutinib plus obinutuzumab group (median not reached [95% CI 33.6–non-estimable]) than in the chlorambucil plus obinutuzumab group (19.0 months [15.1–22.1]; hazard ratio 0.23; 95% CI 0.15–0.37; p<0.0001). Estimated 30-month progression-free survival was 79% (95% CI 70–85) in the ibrutinib plus obinutuzumab group and 31% (23–40) in the chlorambucil plus obinutuzumab group.

PQI Process: Upon receiving a new prescription for ibrutinib for specific use in combination with obinutuzumab:

- Verify an established CLL/SLL diagnosis (independent of patient's del(17p) status, comorbidities and age) in the treatment naive patient and relevant dosing
- Assess risk for tumor lysis syndrome (tumor burden, baseline kidney dysfunction, abnormalities of potassium, uric acid, phosphate, calcium) which commonly occurs during the first cycle
- Dosing:
    - Ibrutinib 420 mg by mouth once daily with:
        - Obinutuzumab 100 mg IV on Day 1
        - then obinutuzumab 900 mg IV on Day 2
        - then obinutuzumab 1000 mg IV on Day 8 and Day 15 every 28 days for 1 Cycle
    - Followed by ibrutinib 420 mg by mouth once daily with:
        - Obinutuzumab 1000 mg IV on Day 1 every 28 Days for 5 Cycles
- Consider administering ibrutinib prior to obinutuzumab when given on the same day
- Consider modification in ibrutinib dose if warranted due to hypertension, dermatologic toxicities, evidence of bleeding, hepatic impairment, fluid retention, or cardiac arrhythmias
- Verify scheduling of pre-medications for obinutuzumab:
    - Acetaminophen 650 mg - 1000 mg at least 30 minutes prior
    - Antihistamine (diphenhydramine 50 mg) at least 30 minutes prior
    - IV glucocorticoid (dexamethasone 20 mg) at least 60 minutes prior
- Review CBC, CMP, hepatic function, and LDH monthly and as indicated
- Verify recommended antiviral (herpes and varicella virus) and pneumocystis prophylaxis are initiated
- Review Ibrutinib (Imbruvica®) Management PQI
- Confirm baseline EKG has been obtained

Patient-Centered Activities:

- Provide ibrutinib Oral Chemotherapy Education (OCE) sheet and written education for obinutuzumab
- Counsel patient on disease state, treatment regimen, what to expect and verify patient understanding
- Ibrutinib should be taken at the same time each day, swallowed whole, with a glass of water and prior to obinutuzumab infusion when given on the same day
- Avoid grapefruit and Seville orange products
- Advise patient to take a missed dose as soon as possible on the same day and to resume normal dosing schedule for the next day
- Patient Assistance: NCODA Financial Assistance Tool

References:

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5. U.S National Library of Medicine (clinicaltrials.gov). Ibrutunib in Treating patients with Relapsed Hairy Cell Leukemia. Assessed at: https://clinicaltrials.gov/ct2/show/NCT01841723. 6-28-19.
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