



Positive Quality Intervention: Tazemetostat (Tazverik) management in Relapsed/Refractory Follicular Lymphoma

Description:

This PQI will discuss the initiation and management of tazemetostat in the treatment of relapsed or refractory (r/r) follicular lymphoma (FL)

Background:

Tazemetostat is a methyltransferase inhibitor indicated for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for completed resection and adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test, such as via the cobas® EZH2 Mutation Test, and who have received at least 2 prior systemic therapies or who have no satisfactory alternative treatment options. For r/r follicular lymphoma, mutation status was determined using the cobas EZH2 mutation test to detect: Y646X [S,H,C], y646F, Y646N, A682G, and A692V. Patients in trials received 800mg of tazemetostat orally twice daily until disease progression or unacceptable toxicity with tumor assessments every 8 weeks. For EZH2 mutant FL patients the ORR was 69% (n=42) with a CR of 12% and PR of 57%. EZH2 wild-type FL patients had an ORR of 34% (n=53) with a CR of 4% and PR of 30%^{1,2}.

In trial the median PFS was 13.8 months by both investigator and an independent review committee (IRC) assessment in patients with *EZH2* mutations. In the *EZH2* wild-type group, the median PFS was 5.6 months by investigator review and 11.1 months by IRC review. Main usage is currently within 3rd or greater line treatment with mutation typically seen in 2nd/3rd line r/r. Mutation is identified in 2nd or 3rd line if patient is positive. The treatment is fairly well tolerated; the most common adverse reactions (≥20%) in patients with r/r FL were fatigue, upper respiratory tract infection, musculoskeletal pain, nausea, and abdominal pain¹. Only 8% of patients permanently discontinued therapy due to adverse events, and 9% of patients required dose reductions. A well tolerated medication such as tazemetostat can be considered without testing for mutation if other alternatives are deemed too intolerable^{2,3}.

PQI Process:

- Confirm acceptable diagnosis and associated indication. EZH2 testing may not be required for all patients
 - Patient who has received 2 systemic therapies
 - Consider testing patient for EZH2, if positive, would be considered eligible candidate
 - No satisfactory alternative treatment options
 - Patient that has received 2 previous lines of therapy, and is evaluated to not to be a good candidate for additional chemoimmunotherapy or other treatments, testing for an EZH2 mutation would not be necessary
 - Speak with provider as a potential alternative treatment to current pathway
- Recommended dosage of Tazverik is 800mg orally twice daily with or without food
- Dose modifications for adverse reactions
 - First Dose Reduction -> 600mg orally twice daily
 - Second Dose Reduction -> 400mg orally twice daily
 - Patients unable to tolerate 400mg orally twice daily should permanently discontinue tazemetostat

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PQI Process Continued¹:

- Cytopenia dose modifications
 - Neutropenia (Neutrophil count less than $1 \times 10^9/L$)
 - Withhold until neutrophil count is greater than or equal to $1 \times 10^9/L$ or baseline
 - First occurrence, resume at same dose
 - Second and third occurrence resume at reduced dose
 - Permanently discontinue after third occurrence
 - Thrombocytopenia (Platelet count less than $50 \times 10^9/L$)
 - Withhold until platelet count is greater than or equal to $75 \times 10^9/L$ or baseline
 - First and second occurrence, resume at reduced dose
 - Permanently discontinue after third occurrence
 - Anemia (Hemoglobin less than 8 g/DL)
 - Withhold until improvement to at least Grade 1 or baseline, then resume at same or reduced dose.
- Other adverse reactions (Grades 3 and 4)
 - Grade 3
 - Withhold until improvement to at least Grade 1 or baseline
 - For first and second occurrence, resume at reduced dose
 - Permanently discontinue after third occurrence
 - Grade 4
 - Withhold until improvement to at least Grade 1 or baseline
 - For first occurrence, resume at reduced dose
 - Permanently discontinue after second occurrence

Patient Centered Activities¹:

- Provide Oral Chemotherapy Education Sheet and counsel patient on potential drug interactions with tazemetostat
- Counsel patient on common side effects (>20%) including pain, fatigue, nausea, decreased appetite, vomiting, and constipation
- Monitor patient's laboratory values for decreased hemoglobin and decreased lymphocytes and increased glucose in r/r follicular lymphoma patients

Supplemental Information:

- Information on FDA-approved tests for detection of EZH2 mutation in r/r follicular lymphoma: FDA.gov/CompanionDiagnostics

Patient Support:

- Quick Start, Bridge Supply, Patient Assistance and Co-Pay Assistance Programs available for eligible patients
- EpizymeNOW Patient & Product Support Website: www.tazverik.com/hcp/follicular-lymphoma/resources
- Patient Support Contact: Monday-Friday (9 am to 6 pm ET) at: 1-833-4EPINOW (437-4669)

References:

1. TAZVERIK™ (tazemetostat) [prescribing information]. Cambridge, MA: Epizyme, Inc.; July 2020.
2. Morschhauser F, Tilly H, Chaidos A, et al. Phase 2 multicenter study of tazemetostat, an EZH2 Inhibitor, in patients with relapsed or refractory follicular lymphoma. *Blood*. 2019;134(suppl 1):123. doi:10.1182/blood-2019-128096
3. Burke, JM, Bucholtz, E, et al. New Developments in Follicular Lymphoma: Treatment Guidance and Clinical Resources. *Clinical Care Options Oncology*. 2020.

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