RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Tazverik (tazemetostat) Tablets
Clinical Update

Clinical update: FDA Accelerated Approval of Tazverik (tazemetostat) for Relapsed/Refractory Follicular Lymphoma.
FDA approval date: June 18, 2020

Tazverik 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 complete resection.
- Adult patients with relapsed or refractory follicular lymphoma with EZH2 mutation positive tumors as detected by an FDA-approved test and who have received at least 2 prior systemic therapies.
- Adult patients with relapsed or refractory follicular lymphoma with no satisfactory alternative treatment options.

These indications were approved under accelerated approval with a priority review, based on overall response rate and duration of response in the company's Phase 2 clinical trial cohorts of FL patients with EZH2 mutations and wild-type EZH2.

The efficacy of Tazverik was evaluated in an open-label, single-arm, multi-center Phase 2 clinical trial (Study E7438-G000-101, NCT01897571) in patients with histologically confirmed FL whose disease had progressed following at least two prior systemic treatment regimens. Patients were enrolled into two cohorts: one cohort enrolled 45 patients with EZH2 activating mutations and a second cohort enrolled 54 patients with wild-type EZH2. All patients were treated with 800 mg of tazemetostat, administered orally twice a day. The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR) according to the International Working Group Non-Hodgkin Lymphoma (IWG-NHL) criteria (Cheson 2007) as assessed by Independent Review Committee. Median duration of follow-up was 22 months for patients with EZH2 activating mutations and 36 months for patients with wild-type EZH2.
Among the 45 FL patients with an EZH2 activating mutation who received Tazverik, the median age was 62 years (range 38 to 80); 42% were male; 42% had early progression following front-line therapy (POD24); and all had an ECOG performance status (PS) of 0 or 1. The median number of lines of prior systemic therapy was 2.0 (range 1 to 11); 49% were refractory to rituximab and 49% were refractory to their last therapy. In the 42 patients treated with at least 2 prior systemic therapies, the ORR (95% confidence interval) was 69% (53%, 82%), with 12% of patients achieving a complete response and 57% achieving a partial response. The median DOR was 10.9 months and ongoing.
Among the 54 FL patients with wild-type EZH2 who received Tazverik, the median age was 61 years (range 36 to 87); 63% were male; 59% had POD24; and 91% had an ECOG PS of 0 or 1. The median number of lines of prior systemic therapy was 3.0 (range 1 to 8); 59% were refractory to rituximab and 41% were refractory to their last therapy. In the 53 patients treated with at least 2 prior systemic therapies, the ORR (95% confidence interval) was 34% (22%, 48%), with 4% of patients achieving a complete response and 30% achieving a partial response. The median DOR was 13.0 months.
The most common (≥20%) adverse reactions are fatigue, upper respiratory tract infection, musculoskeletal pain, nausea and abdominal pain.