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Xpovio(Selinexor) Tablets
Clinical Update

Clinical Update: FDA approved Xpovio(Selinexor) for treatment of Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma (DLBCL).

FDA approval date: June 22, 2020

Xpovio is a first-in-class, oral Selective Inhibitor of Nuclear Export (SINE) compound. Xpovio functions by selectively binding to and inhibiting the nuclear export protein exportin 1 (XPO1, also called CRM1). Xpovio blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell. The forced nuclear retention of these proteins can counteract a multitude of the oncogenic pathways that, unchecked, allow cancer cells with severe DNA damage to continue to grow and divide in an unrestrained fashion. It is indicated for the treatment of adult patients with multiple myeloma (RRMM) and relapsed or refractory diffuse large B-cell lymphoma (DLBCL).

The accelerated FDA approval of XPOVIO is based on the results from the multi-center, single-arm Phase 2b SADAL (Selinexor Against Diffuse Aggressive Lymphoma) study (NCT02227251), which evaluated 134 patients (median of 2 prior systemic therapies with a range of 1-5) with relapsed or refractory DLBCL. Patients were administered a fixed 60 mg dose of XPOVIO given orally twice weekly for a four-week cycle. Patients with germinal center B-cell (GCB) or non-GCB subtypes of DLBCL were included in enrollment. The SADAL study met its primary endpoint of overall response rate (ORR) with an ORR of 29%, including 18 (13%) complete responses (CRs) and 21 (16%) partial responses (PRs) All 134 patients were included in the safety analyses. The most common treatment-related adverse events (AEs) were cytopenias along with gastrointestinal and constitutional symptoms and were generally reversible and managed with dose modifications and/or standard supportive care. The most common non-hematologic AEs were fatigue (63%), nausea (57%), decreased appetite (37%), and diarrhea (37%), and were mostly Grade 1 and 2 events. Grade 3 and 4 laboratory abnormalities in ≥15% of patients included thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia. Grade 4 laboratory abnormalities in ≥5% of patients were thrombocytopenia (18%), lymphopenia (5%), and neutropenia (9%).

As part of the FDA accelerated approval, the FDA has agreed that the XPORT-DLBCL-030 study could serve as the confirmatory trial for evaluating selinexor in DLBCL. This trial will assess the effect of selinexor or placebo added to a standard backbone immunochemotherapy of rituximab-gemcitabine-dexamethasone-platinum (R-GDP) in patients with 1-3 prior treatments for DLBCL. The rationale for this study is based on data from the ongoing Phase 1B study being conducted by the French Lymphoma