Transcript for Dr. Vij Video

Narrator:

XPOVIO® (selinexor) is a prescription medicine approved:

In combination with bortezomib and dexamethasone (XVd) to treat adult patients with multiple myeloma who have received at least one prior therapy.

IMPORTANT SAFETY INFORMATION

Thrombocytopenia: XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma.

Thrombocytopenia is the leading cause of dosage modifications. Monitor platelet counts at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Monitor patients for signs and symptoms of bleeding. Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Dr. Vij:

Hello, I'm Dr. Ravi Vij, Professor of Medicine in the Division of Medical Oncology, Section of Stem Cell Transplant and Leukemia at Washington University School of Medicine in St Louis, Missouri.

Over the past decade, treating multiple myeloma with triplet therapies combining IMiDs, proteasome inhibitors, and/or monoclonal antibodies has steadily increased as is in line with ASCO and CCO Joint Clinical Practice Guidelines. This means that as early as second relapse, many patients will have already been exposed to at least three different drug classes.

According to data from 2021, nearly 80% of patients with multiple myeloma have been exposed to an anti-CD38 monoclonal antibody by the second line of therapy. This is in line with what I typically see in patients with multiple myeloma in my clinical practice.

Due to the clonal evolution of multiple myeloma, patients inevitably relapse. With each relapse, drug-resistant clones are more likely to emerge and proliferate across subsequent lines of therapy, leading to a more treatment-resistant disease. Utilizing triplet therapies with different mechanisms of action earlier in the treatment is aimed at inducing deeper responses and potentially preventing the development of treatment resistance.

For healthcare providers who want to try an option with a different mechanism of action for patients already triple class exposed and/or refractory, XPOVIO in combination with bortezomib and dexamethasone, also known as XVd, may be an option to consider. XPOVIO is the first and only FDA-approved XPO1 inhibitor that helps restore the body's own tumor suppressor pathways to fight multiple myeloma as early as first relapse. Oral, once-weekly selinexor, or XPOVIO, in combination with bortezomib and dexamethasone (XVd) is recommended by the National Comprehensive Cancer Network (NCCN) as a Category 1 therapeutic option in previously treated multiple myeloma with 1-3 prior lines of therapy. XPOVIO is a reversible nuclear export inhibitor blocking exportin 1, also known as XPO1. By

blocking XPO1, it leads to an accumulation of tumor suppressor proteins, like p53, in the nucleus and causes cell cycle arrest and apoptosis by inhibiting the export of oncoprotein mRNAs like c-Myc and cyclin-D1.

In the XVd trial, XVd demonstrated an early and sustained PFS benefit over Vd with deep and durable responses. Three out of four patients experienced a response to XVd, and of the XVd patients who responded, the median duration of response was 20.3 months. Importantly, XVd was not associated with serious organ toxicities of the cardiac, pulmonary, renal, or liver systems. Warnings and precautions include thrombocytopenia, neutropenia, gastrointestinal toxicity, hyponatremia, serious infection, neurological toxicity, embryo-fetal toxicity, and cataract. As mentioned before, XPOVIO has been approved by the FDA in combination with bortezomib and dexamethasone for the treatment of multiple myeloma as early as first relapse.

For patients who have already been exposed to multiple drug classes, once-weekly XPOVIO with Vd may provide an early and sustained PFS with deep and durable responses. The most common adverse reactions in over 20% in patients with multiple myeloma who received XVd were fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract, and vomiting.

Narrator:

Important Safety Information

Neutropenia: XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection.

Monitor more frequently during the first 3 months of treatment. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients.

Nausea/Vomiting/Diarrhea: Provide prophylactic antiemetics or treatment as needed.

Anorexia/Weight Loss: Monitor weight, nutritional status, and volume status at baseline and throughout treatment and provide nutritional support, fluids, and electrolyte repletion as clinically indicated.

Hyponatremia: XPOVIO can cause severe or life-threatening hyponatremia. Monitor sodium level at baseline and throughout treatment.

Serious Infection: XPOVIO can cause serious and fatal infections. Atypical infections reported after taking XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.

Neurological Toxicity: XPOVIO can cause life-threatening neurological toxicities.

Coadministration of XPOVIO with other products that cause dizziness or mental status changes may increase the risk of neurological toxicity.

Advise patients to refrain from driving and engaging in hazardous occupations or activities until the neurological toxicity fully resolves. Institute fall precautions as appropriate.

Embryo-Fetal Toxicity: XPOVIO can cause fetal harm when administered to a pregnant woman.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with a female partner of reproductive potential to use effective contraception during treatment with XPOVIO and for 1 week after the last dose.

Cataracts: New onset or exacerbation of cataract has occurred during treatment with XPOVIO. The incidence of new onset or worsening cataract requiring clinical intervention was reported.

ADVERSE REACTIONS

The most common adverse reactions (ARs) (≥20%) in patients with multiple myeloma who received XVd were fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract, and vomiting.

Grade 3-4 laboratory abnormalities (≥10%) were thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia.

Fatal ARs occurred in 6% of patients within 30 days of last treatment. Serious ARs occurred in 52% of patients. Treatment discontinuation rate due to ARs was 19%. The most frequent ARs requiring permanent discontinuation in >2% of patients included fatigue, nausea, thrombocytopenia, decreased appetite, peripheral neuropathy and vomiting. Adverse reactions led to XPOVIO dose interruption in 83% of patients and dose reduction in 64% of patients.

USE IN SPECIFIC POPULATIONS

No overall difference in effectiveness of XPOVIO was observed in patients >65 years old when compared with younger patients. Patients ≥65 years old had a higher incidence of discontinuation due to an adverse reaction (AR) and a higher incidence of serious ARs than younger patients.

The effect of end-stage renal disease (CLCR <15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

Please see full Prescribing Information.

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.