Dr. Kaya Video Transcript

Narrator:

INDICATION

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.

Dr. Kaya:

Hello. I am Dr. Hakan Kaya.

It is an interesting time to be treating patients who have multiple myeloma. As more and more therapies are available for multiple myeloma, I, along with many of my colleagues, face the clinical challenge of determining where and when to use them. In such a complex treatment paradigm, I like having options, but they definitely add to the complexity. One thing I am certain of is that I need a therapy that would offer my patients an opportunity to have a positive outcome, especially after relapse. So, for each one of my patients, I need to strategize and plan for both near- and long-term solutions that I believe will provide them the most benefit.

Many patients are getting triplet therapies or even quad therapies in the first and second line. So once patients relapse, it is likely they will already have been exposed to multiple classes of drugs, including an IMiD, a PI, and an anti-CD38 antibody like daratumumab. As a result, we are finding that we're re-challenging patients with these classes even earlier than before. I'm having success in introducing XPOVIO, a different class, in third and sometimes second line.

Narrator:

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. Kaya:

XPOVIO is the first and the only FDA-approved oral therapy in a unique class called XPO1 inhibitors. It acts by inhibiting the nuclear export of tumor suppressor proteins and growth regulators, leading to their accumulation in the nucleus, causing cell cycle arrest and apoptosis.

I have been using it extensively in appropriate adult patients since it was approved in 2019 and have treated 22 patients to date with positive results.

I would say that my experience with XPOVIO has been positive. I've been using XPOVIO in a range of patient types and have seen responses.

Recently, I used it in a patient in the third line, who had just relapsed on a daratumumab-based regimen. The patient was a 62-year-old male who had been given RVd in the first line, followed by a stem cell transplant and lenalidomide maintenance. After relapse, he was on DPd for 14 months before relapsing again. Having exhausted all other commonly used classes at that point, I took the opportunity to introduce a different class with XPOVIO, an XPO1 inhibitor. I used XPOVIO in combination with bortezomib and dexamethasone. The efficacy data and the generally manageable safety profile of XVd from the BOSTON trial encouraged me to use it in the third line.

It has been over 8 months since he started on XVd and he continues to respond well. As with all multiple myeloma therapies, you have to balance out the clinical efficacy with adverse events. When treated proactively, some, such as nausea, resolve after the first month.

Narrator:

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.

Dr. Kaya:

My optimal approach in managing patients on XPOVIO includes educating patients on what to expect and providing clear directives to my staff. Based on my experience, there are three steps that I always follow when treating patients with XPOVIO.

First, before starting XPOVIO, I always provide my patients with two prophylactic antiemetics to mitigate potential GI adverse events.

Second, I monitor adverse events and potentially reduce the dose during therapy. Interestingly, I found that patients tolerate XPOVIO well at lower doses while efficacy is maintained.

Finally, my staff and I proactively monitor for adverse events including fatigue, dehydration, and weight loss and take appropriate measures when needed. This level of supportive care has been effective in helping to optimize my experience and my patients' experience and our staff's experience as well. Our nursing staff has been essential in keeping patients on treatment when addressing potential management issues.

Narrator:

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.

Dr. Kaya:

When trying to generate positive outcomes, the healthcare team needs to keep in touch regularly with the patient, especially during the first 4 to 6 weeks of treatment initiation. Keeping communication lines open helps patients proactively discuss any possible adverse events that they may be experiencing. We're making sure that even though XPOVIO is an oral medication, they're still coming to the office once a week for the first month so that we can monitor them closely. With XPOVIO's known, generally manageable, and reversible adverse event profile, we have gotten very skilled at identifying potential issues like fatigue and GI toxicities. It is also important to monitor routine labs such as CBC. At the end of the day, it is really motivating to see the positive experiences our patients are having while on XPOVIO.

Narrator:

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.

Dr. Kaya:

My clinical experience with XPOVIO has been consistent with the XVd trial data. With the lower dose and proactive adverse event management, you can keep patients on XPOVIO longer now. It has given our patients another treatment option that they did not have before, a different class of therapy which works in a unique way. As of today, I have treated 22 patients with XPOVIO and it is going to remain part of my treatment algorithm for multiple myeloma. I am hoping that my experience with XPOVIO can inspire others to use it with their appropriate patients.

Narrator:

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.