Key Safety Risks With Xaluritamig: A Guide for Study Staff

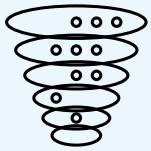
Monitor and counsel your patients on xaluritamig for these key safety risks. Risk mitigation measures are outlined in Protocol Section 6.2.1.1.

Key Safety Risks

Key safety risks are based on biological mechanisms, nonclinical toxicity studies, and clinical experience with xaluritamig.

Cytokine release syndrome (CRS)

CRS is characterized by a release of cellular cytokines. Clinical hallmarks of CRS may include the following:



- Constitutional – fever, rigors, fatigue, malaise
- Neurologic – headache, mental status changes, dysphasia, tremors, dysmetria, gait abnormalities, seizure
- Respiratory – dyspnea, tachypnea, hypoxia
- Cardiovascular – tachycardia, hypotension
- Gastrointestinal – nausea, vomiting, transaminitis, hyperbilirubinemia
- Hematological – bleeding, hypofibrinogenemia, elevated D-dimer
- Skin – rash

Infusion reactions may be clinically indistinguishable from manifestations of CRS.

Localized inflammatory events

Events observed during administration of xaluritamig include myalgia, myofascitis, myositis, muscle weakness, arthralgia, pain in extremity, soft tissue swelling, orbital edema, periorbital edema, and genital edema (including scrotal edema), oropharyngeal pain, mucosal inflammation, stomatitis, and pharyngeal swelling. Vasculitis has been observed but there is insufficient evidence for association, therefore is considered a potential risk.

Immune effector cell-associated neurotoxicity syndrome (ICANS)

Administration of xaluritamig has been associated with ICANS which may be serious. Adverse events that may be associated with ICANS include encephalopathy and neurotoxicity. Patients should be closely monitored for signs and symptoms of ICANS during xaluritamig treatment.

Increased liver enzymes and bilirubin

Aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyl transferase increased, hypertransaminasemia, hyperbilirubinemia, and liver function test increased have been observed during administration of xaluritamig.

Rash

The most frequently reported events were rash, macular rash, and maculopapular rash.

Potential Safety Concerns

Other potential safety concerns are based on preclinical studies and experience with other STEAP1-targeting agents.

Inflammatory response involving organs with epithelial lining

There is the potential for an inflammatory response resulting in organ system toxicities such as the following:

- Gastrointestinal tract – eg, colitis, esophagitis, gastritis, duodenitis, ileitis
- Pulmonary – eg, pneumonitis, tracheitis
- Dermatologic – eg, rash, dry skin, erythema, pruritus
- Renal – eg, cystitis, nephritis
- Hepatobiliary – eg, cholecystitis

Other neurologic events

A wide range of commonly observed neurological symptoms have been associated with the use of the bispecific anti-CD3/CD19 T-cell engager blinatumomab in patients with acute lymphoblastic leukemia. However, the spectrum of neurologic events has not been observed in clinical studies for other CD3 bispecific molecules, and the neurotoxicity may in part be associated with targeting CD19.

Tumor lysis syndrome (TLS)

While rare in prostate cancer, TLS is a severe, life-threatening disorder that can occur in highly proliferative malignancies or with debulking of extensive tumor burden.

Signs and symptoms may include: hyperkalemia, hyperphosphatemia, hyperuricemia, hyperuricosuria, and hypocalcemia, potentially causing lethal cardiac arrhythmias, seizures, and/or renal failure.

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