2023–2024 Drug Updates in Hematologic Malignancies

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Presenter's disclosures of conflicts of interest are found at the end of this article.

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Abstract

At the highly anticipated session at JADPRO Live 2024, Oxana Megherea, PharmD, BCOP, covered several newly approved therapies for patients with multiple myeloma, leukemia, lymphoma, and other hematologic malignancies, including their mechanisms of action and strategies for managing adverse events.

The field of hematologic malignancies continues to evolve rapidly. At the latest JADPRO Live conference, Oxana Megherea, PharmD, BCOP, a hematology-oncology clinical pharmacy specialist at the Abramson Cancer Center, provided an in-depth review of the latest drug approvals and expanded indications in the hematologic space over the past year.

MULTIPLE MYELOMA

One of the newly approved agents, motixafortide (Aphexda), is a CXCR4 inhibitor used for stem cell mobilization in multiple myeloma patients undergoing autologous stem cell transplantation. The drug is administered subcutaneously as a slow push following 4 days of G-CSF therapy, with a second dose administered if mobilization goals are unmet.

Adverse Event Management

The main toxicity concerns include hypersensitivity reactions, flushing, paresthesia, and injection site reactions. Premedication with diphenhydramine, acetaminophen, montelukast, and famotidine is recommended, with 1-hour post-administration monitoring.

"If patients experience reactions despite premedication, corticosteroids like dexamethasone or methylprednisolone can be added to their regimen," Dr. Megherea noted.

MYELODYSPLASTIC SYNDROME

A first-in-class telomerase inhibitor, imetelstat (Rytelo), received approval for transfusion-dependent anemia in patients with low to intermediate-1 risk myelodysplastic syndrome (MDS) who have failed or are intolerant to erythropoiesis-stimulating agents (ESAs). The drug is administered intravenously every 4 weeks.

Adverse Event Management

Hematologic toxicities were common, including the rate of grade 3 and

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higher toxicities. Neutropenia (74%) and thrombocytopenia (75%) at all grades were the most notable toxicities reported.

"This highlights the need for close monitoring, implementing antimicrobial prophylaxis per institutional guidelines, and administering transfusions or growth factors as needed," Dr. Megherea said.

Advanced practitioners should also monitor for infusion-related reactions, which, although low in incidence, require premedication with diphenhydramine and hydrocortisone.

CHRONIC GVHD

Axatilimab (Niktimvo), a CSF-1 receptor inhibitor, was approved for chronic graft-vs.-host disease (GVHD) after at least two prior lines of therapy. The agent works by preventing macrophage-driven inflammation and fibrosis. It is administered intravenously every 2 weeks.

Adverse Event Management

Common laboratory abnormalities include elevations in liver function tests (LFTs), creatine phosphokinase (CPK), lipase, and amylase. While these abnormalities are generally low-grade, baseline and periodic monitoring are essential. Infection risk is not dose-dependent, emphasizing the need for close monitoring.

The rate of infusion-related reactions is generally low. Premedication with an antihistamine and acetaminophen is recommended only in patients who have a previous reaction to axatilimab.

LYMPHOMAS

The fusion protein denileukin diftitox (Lymphir) was re-approved for relapsed/refractory cutaneous T-cell lymphoma. It demonstrated clinical efficacy and meaningful benefit in these heavily pretreated patients. This agent delivers diphtheria toxin directly to IL-2 receptor-expressing cancer cells, leading to apoptosis.

Lisocabtagene maraleucel (Breyanzi), a CD19-directed CAR T-cell therapy, was granted expanded indications for follicular lymphoma and mantle cell lymphoma. The therapy is administered as a one-time infusion following lymphodepleting chemotherapy.

Epcoritamab (Epkinly) is a bispecific CD20-directed CD3 T-cell engager that was previously approved for diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma but recently gained approval for follicular lymphoma after two or more prior lines of therapy. The dosing regimen differs slightly from its use in DLBCL, incorporating an additional dose to the step-up schedule to reduce the risk of cytokine release syndrome (CRS) and neurotoxicity.

Zanubrutinib (Brukinsa), another BTK inhibitor, was granted approval for relapsed/refractory follicular lymphoma in combination with obinutuzumab (Gazyva). The combination significantly improved overall response rates (70%) and progression-free survival compared to obinutuzumab alone.

"This marks the first BTK inhibitor with meaningful activity in follicular lymphoma, providing a new treatment option," Dr. Megherea commented.

Adverse Event Management

Infusion reactions were common with denileukin diftitox, so it is recommended to premedicate and administer intravenous hydration prior to each dose in cycles 1 to 3. Capillary leak syndrome (CLS) occurred in 27% of patients, typically within the first two cycles. Advanced practitioners should monitor for hypotension, edema, and hypoalbuminemia. Hepatotoxicity was seen in over 50% of patients, and therefore frequent LFT assessments are recommended.

"Baseline ophthalmologic exams are recommended due to the risk of visual impairment, which was reversible in most patients," Dr. Megherea noted.

As expected with CAR T-cell therapies, cytokine release syndrome (CRS), neurotoxicity (including ICANS), cytopenias, and infections were common in patients receiving lisocabtagene maraleucel. Given these risks, supportive care measures are important, including antimicrobial prophylaxis per institutional guidelines, premedications, and intravenous immunoglobulin (IVIG) as needed for hypogammglobulinemia.

For epcoritamab, premedications including corticosteroids, acetaminophen, and diphenhydramine, are recommended to mitigate the risk of CRS. Other notable side effects included injection site reactions, neutropenia, and thrombocytopenia, highlighting the need for antiviral

and anti-*Pneumocystis jirovecii* pneumonia prophylaxis and close monitoring by clinicians.

Compared to other BTK inhibitors, zanubrutinib is associated with increased cytopenias, particularly neutropenia and thrombocytopenia. Advanced practitioners should implement routine CBC monitoring and early antimicrobial prophylaxis. Atrial fibrillation (3%) and bleeding risk require additional monitoring.

CHRONIC LYMPHOCYTIC LEUKEMIA

Pirtobrutinib (Jaypirca), a non-covalent (reversible) BTK inhibitor, was approved for chronic lymphocytic leukemia (CLL) after two prior lines of therapy, including a covalent BTK inhibitor and a BCL2 inhibitor. Unlike other BTK inhibitors, pirtobrutinib retains activity against BTK C481 mutations, which commonly drive resistance. "This therapy shows promising activity in this heavily pretreated patient population after they have progressed on a covalent BTK inhibitor," Dr. Megherea said.

Adverse Event Management

Compared to first-generation BTK inhibitors, pirtobrutinib has a lower incidence of atrial fibrillation (1%), although bleeding risk remains a concern. Patients undergoing procedures should have the therapy held 3 to 7 days before and after surgery depending on the type of surgery and risk of bleeding. Prophylaxis, including vaccinations and antimicrobial prophylaxis, should be considered in patients who are at increased risk for infections, including opportunistic infections.

Disclosure

Dr. Megherea has served on an advisory board for BioLineRx.