Transcript Details
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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Bispecific Antibody Treatment in Relapsed or Refractory Multiple Myeloma

Announcer:

You're listening to *Project Oncology* on ReachMD.

This medical industry feature, titled "Bispecific Antibody Treatment in Relapsed or Refractory Multiple Myeloma" is sponsored by Janssen Oncology.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:

Welcome to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me to discuss an emerging treatment class in multiple myeloma is Dr. Leo Shunyakov, medical oncologist and hematologist at Central Care Cancer Center.

Dr. Shunyakov, thank you so much for being here today.

Dr. Shunyakov:
Thank you so much, Dr. Caudle. It's a great pleasure to be here.

Announcer:

The consultants are paid speakers for Janssen Biotech, Inc. The speakers are presenting on behalf of Janssen and must present information in compliance with FDA requirements.

Dr. Caudle:

Well, we're happy that you're here, and to start us off Dr. Shunyakov, can you share a bit about your experience with multiple myeloma?

Dr. Shunyakov:

Of course. I have been treating multiple myeloma for over 20 years, and it's very encouraging to see the progress that has been made, specifically, the continuous innovation to provide patients with additional treatment options. Advancements have been made in frontline and relapsed or refractory treatment options, and multiple myeloma patients are living longer, with age-adjusted death rates falling at an average of 1.3% annually, between 2011 and 2020. Part of it is due to numerous additional options for patients to switch to, upon relapse. Despite there being more options available to treat this disease, age-adjusted rates for new myeloma cases have not changed significantly, and deaths from multiple myeloma are projected to make up 2.1% of all cancer deaths in 2023. Looking ahead, I think bispecific T-cell engaging antibodies may provide additional opportunities to treat multiple myeloma patients.

Dr. Caudle:

You know, with that being said, can you tell us more about the bispecific T-cell engaging antibodies?

Dr. Shunyakov:

Sure. This is an emergent therapeutic class, and the first bispecific antibody in relapsed or refractory multiple myeloma was approved by the FDA in October of 2022. This off-the-shelf subcutaneous injection called TECVAYLI®, or teclistamab, is for adult patients who have

received 4 or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. TECVAYLI® binds to the CD3 receptor expressed on the surface of T-cells, and B-cell maturation antigen, or BCMA, expressed on the surface of multiple myeloma cells and some healthy B-lineage cells. In vitro, teclistamab activated T-cells caused the release of various proinflammatory cytokines, and result in the lysis of multiple myeloma cells.

Dr. Caudle:

Thank you so much for breaking that down for us, Dr. Shunyakov. And before we continue our discussion, let's take a moment to review some important safety information for TECVAYLI®.

Announcer:

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TECVAYLI®. Initiate treatment with TECVAYLI® step-up dosing schedule to reduce risk of CRS. Withhold TECVAYLI® until CRS resolves or permanently discontinue based on severity.
- Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious and life-threatening reactions, can occur in patients receiving TECVAYLI®. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment. Withhold TECVAYLI® until neurologic toxicity resolves or permanently discontinue based on severity.
- TECVAYLI® is available only through a restricted program called the TECVAYLI® and TALVEY™ Risk Evaluation and Mitigation Strategy (REMS).

Please listen to the full Important Safety Information and Indication presented at the end of this podcast. Additionally, please read the full Prescribing Information, including Boxed WARNING.

And now, back to the podcast.

Dr. Caudle:

For those just tuning in, you're listening to *Project Oncology* on ReachMD.

I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Shunyakov about the treatment option TECVAYLI® for relapsed or refractory multiple myeloma.

Now, Dr. Shunyakov, if we zero in on this treatment option, what were the data that led to its approval?

Dr. Shunyakov:

Thank you. The MajesTEC-1 clinical trial was the basis of the FDA approval, and it evaluated the safety and efficacy profile in patients with relapsed or refractory myeloma. In this trial, treatment with TECVAYLI® provided an overall response rate of 61.8% in patients.

Dr. Shunyakov:

Additionally, 32 patients, or 29.1% treated with TECVAYLI® achieved a very good partial response or better. 31 patients, or 28.2%, showed a complete response or better, median time to first confirmed response was 1.2 months, with a range of 0.2 to 5.5 months, and the overall response rate was 61.8%, totaling 68 patients. With a median follow-up, of 7.4 months among responders, the estimated duration of response rate was 90.6% with a 95% confidence interval, range 80.3% to 95.7% at 6 months, and 66.5% with a 95% confidence interval, range 38.8% to 83.9% at 9 months.

Dr. Caudle:

Thank you for that. And as a follow-up to that, what was found regarding its safety?

Dr. Shunyakov:

In addition to the boxed warning information presented earlier, warnings and precautions include hepatotoxicity, infections, neutropenia, hypersensitivity and other administration reactions, and embryo-fetal toxicity. Adverse reactions greater than or equal to 20% in MajesTEC-1 were pyrexia, cytokine release syndrome, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea.

Dr. Shunyakov:

The most common Grade 3 to 4 laboratory abnormalities, affecting 20% or more of patients, were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

Dr. Caudle:

You know, Dr. Shunyakov, now that we know more about TECVAYLI®, let's frame this in a larger context. Why is it so important to continue to expand treatment options in multiple myeloma?

Dr. Shunyakov:

Innovating in this space is important, because these patients with relapsed or refractory disease have already exhausted several treatment options available to them, and giving an additional option may mean providing these patients with an opportunity to better manage their disease.

Dr. Caudle:

Thank you for that. And before we close, Dr. Shunyakov, let's look ahead for just a moment. Where do you see the future of multiple myeloma treatments headed?

Dr. Shunyakov:

The treatment landscape is constantly evolving, which is great for healthcare professionals and patients, and I hope to see this continue in the future. Increasing the arsenal of available treatments means patients have more choices along their multiple myeloma treatment journeys, and I believe that bispecifics are important clinical options for the multiple myeloma community.

Dr. Caudle:

Well, with those thoughts in mind, I'd like to thank my guest, Dr. Shunyakov, for joining me to discuss the treatment option TECVAYLI®. Dr. Shunyakov, it was great having you on the program.

Dr. Shunyakov:

Thank you very much for this opportunity to share information about Tecvayli.

Dr. Caudle:

Thank you. I'm your host, Dr. Jennifer Caudle, and please stay tuned for the full important safety information, including box warning and indication for Tecvayli.

Announcer:

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TECVAYLI®. Initiate treatment with TECVAYLI® step-up dosing schedule to reduce risk of CRS. Withhold TECVAYLI® until CRS resolves or permanently discontinue based on severity.
- Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious and life-threatening reactions, can occur in patients receiving TECVAYLI®. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment. Withhold TECVAYLI® until neurologic toxicity resolves or permanently discontinue based on severity.

TECVAYLI® is available only through a restricted program called the TECVAYLI® and TALVEY™ Risk Evaluation and Mitigation Strategy (REMS).

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome - TECVAYLI® can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 72% of patients who received TECVAYLI® at the recommended dose, with Grade 1 CRS occurring in 50% of patients, Grade 2 in 21%, and Grade 3 in 0.6%. Recurrent CRS occurred in 33% of patients. Most patients experienced CRS following step-up dose 1 (42%), step-up dose 2 (35%), or the initial treatment dose (24%). Less than 3% of patients developed first occurrence of CRS following subsequent doses of TECVAYLI®. The median time to onset of CRS was 2 (range: 1 to 6) days after the most recent dose with a median duration of 2 (range: 1 to 9) days. Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

Initiate therapy according to TECVAYLI® step-up dosing schedule to reduce risk of CRS. Administer pretreatment medications to reduce risk of CRS and monitor patients following administration of TECVAYLI® accordingly. At the first sign of CRS, immediately evaluate patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold or permanently discontinue TECVAYLI® based on severity.

TECVAYLI® is available only through a restricted program under a REMS.

Neurologic Toxicity including ICANS - TECVAYLI® can cause serious or life-threatening neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS).

In the clinical trial, neurologic toxicity occurred in 57% of patients who received TECVAYLI® at the recommended dose, with Grade 3 or 4 neurologic toxicity occurring in 2.4% of patients. The most frequent neurologic toxicities were headache (25%), motor dysfunction (16%), sensory neuropathy (15%), and encephalopathy (13%). With longer follow-up, Grade 4 seizure and fatal Guillain-Barré syndrome (one patient each) occurred in patients who received TECVAYLI®.

In the clinical trial, ICANS was reported in 6% of patients who received TECVAYLI® at the recommended dose. Recurrent ICANS occurred in 1.8% of patients. Most patients experienced ICANS following step-up dose 1 (1.2%), step-up dose 2 (0.6%), or the initial treatment dose (1.8%). Less than 3% of patients developed first occurrence of ICANS following subsequent doses of TECVAYLI®. The median time to onset of ICANS was 4 (range: 2 to 8) days after the most recent dose with a median duration of 3 (range: 1 to 20) days. The most frequent clinical manifestations of ICANS reported were confusional state and dysgraphia. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold or permanently discontinue TECVAYLI® based on severity per recommendations and consider further management per current practice guidelines.

Due to the potential for neurologic toxicity, patients are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI® step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves.

TECVAYLI® is available only through a restricted program under a REMS.

TECVAYLI® and TALVEY™ REMS - TECVAYLI® is available only through a restricted program under a REMS called the TECVAYLI® and TALVEY™ REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Hepatotoxicity - TECVAYLI® can cause hepatotoxicity, including fatalities. In patients who received TECVAYLI® at the recommended dose in the clinical trial, there was one fatal case of hepatic failure. Elevated aspartate aminotransferase (AST) occurred in 34% of patients, with Grade 3 or 4 elevations in 1.2%. Elevated alanine aminotransferase (ALT) occurred in 28% of patients, with Grade 3 or 4 elevations in 1.8%. Elevated total bilirubin occurred in 6% of patients with Grade 3 or 4 elevations in 0.6%. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TECVAYLI® or consider permanent discontinuation of TECVAYLI® based on severity.

Infections - TECVAYLI® can cause severe, life-threatening, or fatal infections. In patients who received TECVAYLI® at the recommended dose in the clinical trial, serious infections, including opportunistic infections, occurred in 30% of patients, with Grade 3 or

4 infections in 35%, and fatal infections in 4.2%. Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI® and treat appropriately. Administer prophylactic antimicrobials according to guidelines. Withhold TECVAYLI ® or consider permanent discontinuation of TECVAYLI® based on severity.

Monitor immunoglobulin levels during treatment with TECVAYLI® and treat according to guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

Neutropenia - TECVAYLI® can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI® at the recommended dose in the clinical trial, decreased neutrophils occurred in 84% of patients, with Grade 3 or 4 decreased neutrophils in 56%. Febrile neutropenia occurred in 3% of patients.

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local institutional guidelines. Monitor patients with neutropenia for signs of infection. Withhold TECVAYLI® based on severity.

Hypersensitivity and Other Administration Reactions - TECVAYLI® can cause both systemic administration-related and local injection-site reactions. Systemic Reactions - In patients who received TECVAYLI® at the recommended dose in the clinical trial, 1.2% of patients experienced systemic-administration reactions, which included Grade 1 recurrent pyrexia and Grade 1 swollen tongue. Local Reactions - In patients who received TECVAYLI® at the recommended dose in the clinical trial, injection-site reactions occurred in 35% of patients, with Grade 1 injection-site reactions in 30% and Grade 2 in 4.8%. Withhold TECVAYLI® or consider permanent discontinuation of TECVAYLI® based on severity.

Embryo-Fetal Toxicity - Based on its mechanism of action, TECVAYLI® may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TECVAYLI® and for 5 months after the last dose.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common Grade 3 to 4 laboratory abnormalities (≥20%) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

INDICATION AND USAGE

TECVAYLI® (teclistamab-cqyv) is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Please read full Prescribing Information, including Boxed WARNING, for TECVAYLI®.

This medical industry feature was brought to you by Janssen Oncology. If you missed any part of this discussion, visit reachmd.com/project-oncology, where you can Be Part of the Knowledge.

Thanks for listening.