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Pfizer Touts Elrexfio's Potential For Community Oncology Use In Myeloma

Second Approval Of BCMA-Directed Bispecific Antibody

by Alaric DeArment

The drug maker is pointing to potential biweekly dosing as raising the possibility for the bispecific's use in community oncology, though an expert had said it could take some time for that to happen.

The number of BCMA-directed therapies for treating multiple myeloma grew as the US Food and Drug Administration gave accelerated approval to Elrexfio (elranatamab-bcmm), *Pfizer Inc.*'s anti-BCMAxCD3 bispecific antibody. Given its flat dosing, dosing schedule and adverse event profile, the company sees the potential for the drug to gain traction in the community oncology setting rather than staying relegated to academic cancer centers, as BCMA-directed therapies have generally been to date.

The FDA gave the green light to Elrexfio on 14 August for patients who have received at least four prior lines of therapy that include a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, based on results from the Phase II MagnetisMM-3 clinical trial. Elrexfio is one of the key pipeline drugs Pfizer expects will help drive company growth in the second half of the decade despite the upcoming loss of exclusivities of several top-selling drugs. (Also see "*Pfizer Anticipates A 'Bolus Of Revenue' From RSV, Prevnar 20 Launches This Year*" - Scrip, 2 May, 2023.)

Pfizer told *Scrip* the wholesale acquisition cost (WAC) for Elrexfio is $7,556 for a 44mg vial and $13,051 for a 76mg vial and that while the company expects the average annualized WAC to be $41,500 per month, it anticipates the monthly price to be lower – around $26,000 – as patients potentially switch to biweekly dosing.

Elrexfio is the second BCMA-directed bispecific antibody to win FDA approval, after the approval

in October 2022 of *Johnson & Johnson*'s Tecvayli (teclistamab-cqyv). (Also see "*J&J Adds Second Anti-BCMA Myeloma Therapy In US With Tecvayli Approval*" - Scrip, 26 Oct, 2022.) It is also the fourth BCMA-directed therapy overall, after J&J's CAR-T Carvykti (ciltacabtagene autoleucel); *Bristol Myers Squibb Company*/*2seventy Bio, Inc.*'s CAR-T Abecma (idecabtagene vicleucel); and *GSK plc*'s antibody-drug conjugate (ADC) Blenrep (belantamab mafodotin-blmf), which is currently off the market.

It also comes fresh on the heels of the 10 August FDA approval of J&J's Talvey (talquetamab-tgvs), as the first GPRC5D-approved myeloma therapy. (Also see "*J&J Hits Another Myeloma Milestone With FDA Approval Of Talvey*" - Scrip, 10 Aug, 2023.)

The approval of Elrexfio was based on data from MagnetisMM-3, which also appeared in *Nature* on 15 August. Cohort A, comprising 123 patients, showed a 61% overall response rate (ORR), including 35% who had a complete response (CR) or better. Median duration of response (DOR), progression-free survival (PFS) and overall survival (OS) were not reached at a median follow-up of 14.7 months. Fifteen-month rates for those secondary endpoints were 71.5%, 50.9% and 56.7%, respectively.

Cohort B, which included 64 patients, showed an ORR of 33% among patients who had received prior BCMA-directed CAR-T or ADC therapy, with 84% of responders maintaining response for at least nine months.

Aiming For The Community Setting

The increasingly crowded anti-BCMA marketplace will make it important for the various players to stand out. In addition to Elrexfio, other bispecific antibodies directed to BCMA candidates are on the way, including *Regeneron Pharmaceuticals, Inc.*'s Phase II linvoseltamab and BMS's Phase I alnuctamab.

One of the selling points that Pfizer is looking to use for Elrexfio is its dosing schedule, which starts with 12mg and 32mg step-up doses on days 1 and 4, followed by a 76mg treatment dose on day 8, once-weekly dosing at 76mg through week 24 and then biweekly dosing at 76mg starting at week 25.

Tecvayli is dosed at 0.3mg/kg on days 1 and 4, 1.5mg/kg on day 7 and then 1.5mg/kg each week thereafter.

"What we see here is differentiation around being the first and only biweekly BCMA option," Pfizer multiple myeloma development head Sriram Krishnaswami told *Scrip*. "I think that's something that we see as being important."

Regeneron has touted linvoseltamab using the same arguments, pointing to its flat 200mg dose

and a dosing schedule that starts out weekly before becoming biweekly and finally – if patients achieve a very good partial response (VGPR) or better – monthly.

Krishnaswami said flat dosing can also be of benefit for clinics from an efficiency standpoint.

"I think often we see with body surface area-based or weight-based dosing potential for wastage during the ongoing treatment phase," he told *Scrip*.

But potentially the most ambitious goal is to potentially bring use of Elrexfio into the community oncology setting, which Krishnaswami said flat dosing could enable by eliminating "any complexities and confusions."

The adverse event profile and associated monitoring requirements are another factor, said Pfizer vice president of hematology Akos Czibere. He noted that while patients require hospitalization for 48 hours for the first step-up dose and for 24 hours after the second dose, they do not require it afterward.

"Patients only need to stay a couple of days for the first dose, a day for the second, and then after that they're free, if needed, to go home," Czibere told *Scrip*.

In other words, the lack of need for extensive hospitalization would allow patients to receive the drug at community oncology centers rather than large cancer centers. That, Czibere said, is because there is limited incidence of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).

"We do see very little repeat CRS and very little … after the first full dose," he said, adding that physicians can be assured that whatever CRS and ICANS does happen will be mostly low-grade and will have occurred during step-up and primary dosing.

But at the American Society of Clinical Oncology meeting in June, MagnetisMM-3 lead investigator and Emory University myeloma specialist Ajay Nooka told *Scrip* it would be some time – at least a year – before use of use of Elrexfio took hold in the community setting, given that physicians there would need time to receive education and develop familiarity with the drug before becoming comfortable using it. (Also see "*Regeneron, Pfizer Tout Potential BCMA Bispecific Advantages At ASCO*" - Scrip, 6 Jun, 2023.)

Given that bispecific antibodies can increase the risk of infections due to the incidence of cytopenias, that presents another consideration on top of CRS and ICANS. However, Czibere said myeloma physicians are familiar with monitoring for and treating infections, and it would not likely be a major issue impeding use of the drug in the community setting. Indeed, the risk of infections from BCMA-directed therapies in general is one of the reasons why the emerging class

of GPRC5D-directed therapies might be more attractive for some patients. (Also see "*Multiple GPRC5D Agents For Myeloma Raise Questions On Positioning*" - Scrip, 20 Dec, 2022.)

Earlier this month, *Blood Cancer Journal* published consensus recommendations from an expert panel on monitoring, prophylaxis and treatment of infections in patients receiving bispecific antibody therapy for multiple myeloma. Key recommendations included universal herpes simplex and varicella zoster virus prophylaxis, screening for hepatitis B virus reactivation risk in all patients, use of immunoglobulin and colony-stimulating factors in certain patients and other measures.