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J&J Hits Another Myeloma Milestone With FDA Approval Of Talvey

First Approved GPRC5D-Directed Therapy

by Alaric DeArment

The approval gives the company's products a key presence in the myeloma space from the point of diagnosis and into later lines of disease.

Johnson & Johnson's *Janssen Pharmaceutical Cos.* has further strengthened its market position in the treatment of multiple myeloma with the US Food and Drug Administration accelerated approval of Talvey (talquetamab-tgvs) as the first approved GPRC5DxCD3-targeting bispecific antibody to treat the disease. In addition to being the third first-in-class myeloma drug from Janssen to win approval, Talvey also means the drug maker has options for treatment from the time of diagnosis all the way through later lines of therapy.

The FDA granted Talvey accelerated approval on 9 August, based on results from the Phase II MonumenTAL-1 trial among patients who had at least four prior lines of therapy – including a proteasome inhibitor, an immunomodulatory drug and an anti-CD38 antibody – and received subcutaneous Talvey at 0.4mg/kg weekly or 0.8mg/kg biweekly. Janssen told *Scrip* that Talvey's list price is $45,000 per month, or a range of $270,000-$360,000 per year based on typical average treatment duration of six to eight months in the trial.

With Talvey carrying a list price in the six figures – in common with the other newer myeloma drugs – experts have pointed to potential payer concern about growing cost. But in an interview with *Scrip*, Tyrone Brewer, US president for Janssen Oncology, expressed confidence about coverage based on conversations with payers thus far.

"What I will say is that at least initial feedback would certainly suggest that we fully anticipate that Talvey will have broad coverage similarly to what we see with [J&J's BCMA bispecific] Tecvayli, so both by Medicare as well as most … commercial payers," he said.

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Janssen was the first company to win approval for an anti-CD38 antibody, Darzalex (daratumumab) as well as the subcutaneous Darzalex Faspro (daratumumab and hyaluronidase-fihj), which are now approved and widely used in first-line disease, and was the first with a BCMA-directed bispecific antibody, Tecvayli (teclistamab-cqyv), and Carvykti (ciltacabtagene autoleucel) was the second anti-BCMA CAR-T cell therapy. (Also see "*J&J Advances Myeloma Domination Plan With Bispecific Tecvayli Approval*" - Scrip, 26 Aug, 2022.) Darzalex/Darzalex Faspro in particular is a key backbone therapy often used in combination with other agents in various lines of therapy.

"We feel that we'll have the opportunity to be able to treat patients from diagnosis through the progression of disease," Brewer told *Scrip*.

With the approval of Tecvayli and now Talvey, along with Darzalex and Carvykti, Janssen has become one of the dominant players in the multiple myeloma space, alongside *Bristol Myers Squibb Company*. BMS's portfolio includes immunomodulatory drugs like the recently generically available Revlimid (lenalidomide), Pomalyst/Imnovid (pomalidomide) and the seldom used Thalomid (thalidomide), the *2seventy Bio, Inc.*-partnered anti-BCMA CAR-T Abecma (idecabtagene vicleucel) and a deep pipeline that includes additional BCMA- and GPRC5D-directed candidates and the new cereblon E3 ligase modulator (CELMoD) class.

Myeloma Market Snapshot: New Drug Classes On The Way, But Cost Could Be A Problem

By Alaric DeArment

29 Jul 2023
More BCMA-directed therapies are in development, as well as ones targeting GPRC5D and FcRH5, along with CELMoDs. The question is how to bring those into therapy and pay for them.

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Company Strengthens Presence In Myeloma

The pivotal portion of MonumenTAL-1 included 187 fifth-line patients who had not received prior T-cell redirection therapy. Among those receiving the drug biweekly at 0.8mg/kg, the overall response rate (ORR) was 73.6%, with 58% achieving a very good partial response (VGPR) or better and 33% achieving a complete response (CR) or better. In the 0.4mg/kg weekly dosing cohort, the ORR was 73%, with 57% achieving VGPR or better and 35% achieving CR or better. Median duration of response (DoR) was not reached in the 0.8mg/kg cohort – with about 85% of responders maintaining response for at least nine months – while in the 0.4mg/kg cohort median DoR was 9.5 months.

GPRC5D is one of the more novel therapeutic targets in multiple myeloma. BCMA has been

around a bit longer, with Tecvayli, Carvykti and BMS/2seventy's Abecma (idecabtagene vicleucel) already on the market, with several additional agents on the way. Others coming down the pike include FcRH5 – the target of *Roche Holding AG*'s Phase I/II cevostamab – and cereblon E3 ligase, for which BMS is developing the CELMoD drugs iberdomide and mezigdomide.

On the GPRC5D front, potential competitors to Talvey include Roche's Phase I bispecific forimtamig and BMS's Phase I CAR-T BMS-986393.

The question that remains is how GPRC5D-directed agents like Talvey will be sequenced in the clinic, especially relative to anti-BCMA therapies.

Talvey's labeling specifies that the drug is for fifth-line and later disease among patients with prior proteasome inhibitor, immunomodulator and anti-CD38 exposure, though the clinical trials section also incorporates a cohort of 32 patients from MonumenTAL-1 who had previously received a BCMA-directed bispecific or CAR-T. Among those patients, ORR was 72%, with 59% of responders maintaining response for at least nine months, but the company did not disclose a breakdown of depth of response or the median DoR.

But Brewer said sequencing of therapies would not be a simple matter of Talvey coming before or after BCMA-directed therapy.

"There's going to be a lot of things that are going to go into consideration," he said. "So for instance, you may have patients that you feel may be at high risk of infection, and that would be a concern if you want to do a BCMA agent – this is where Talvey becomes a great option, you may have patients that have already been exposed to a BCMA agent – this is where Talvey becomes an important option."

In terms of the dosing schedule, Brewer emphasized that using 0.8mg/kg versus 0.4mg/kg would be the physician's decision, but he added the patients who would be more likely candidates for biweekly dosing would be those with better performance status who had better responses to prior therapy and thus did not need to see the physician on such a regular basis, whereas the less fit patients would likely be better candidates for the weekly dosing schedule.

Combined targeting of GPRC5D and BCMA is another potential option, and Brewer highlighted early results presented at the American Society of Clinical Oncology meeting June from the Phase I/II RedirecTT-1 study of Tecvayli/Talvey showing that among 63 patients with a median five prior lines of therapy, the ORR across all dose levels was 84%, with 34% achieving a CR or better, while among 13 patients receiving the recommended Phase II dose, the ORR was 92%, with a 31% rate of CR or better. High response rates were also observed among patients with extramedullary disease, where clonal plasma cells grow outside the bone marrow and which is associated with poorer outcomes.

Janssen is not alone in testing combination strategies involving bispecific antibodies. ClinicalTrials.gov lists a Phase Ib study that Roche's Genentech launched on 31 July combining cevostamab with *Pfizer Inc.*'s BCMA-directed bispecific antibody, elranatamab, which is due for a decision from the FDA soon.