SCRIP
CITELINE COMMERCIAL

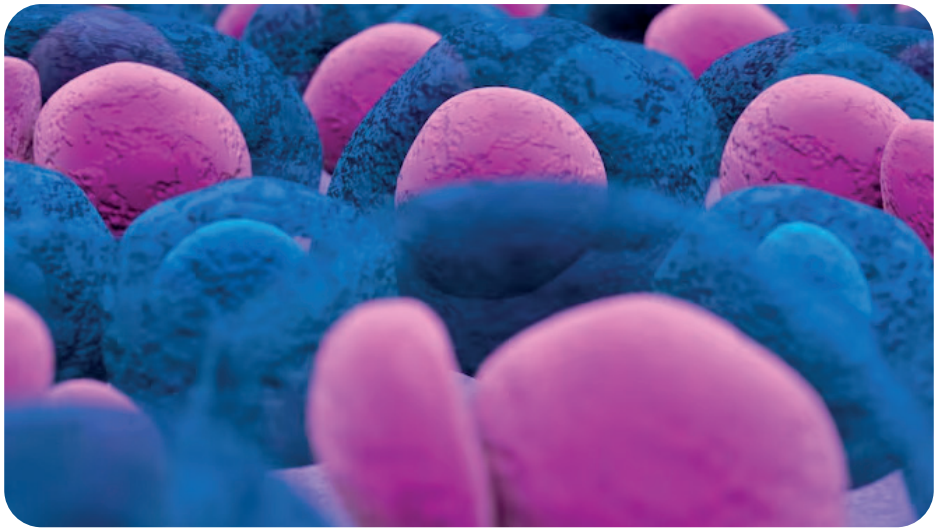
With Plethora Of New Myeloma Treatments, MMRF Study Aims To Better Guide Use

CITELINE
a norstella company

With Plethora Of New Myeloma Treatments, MMRF Study Aims To Better Guide Use

By Alaric DeArment

The MMRF aims to incorporate a variety of new bispecific antibodies, cell therapies, checkpoint inhibitors and novel small molecules into the Horizon study.



The dizzying array of new treatments for multiple myeloma is set to become even more complex in the near future, and a new platform trial aims to get a better handle on how the variety of drugs with different modalities and targets can fit into treatment.

The Multiple Myeloma Research Foundation (MMRF) announced 4 December that it enrolled the first patient in the Horizon Clinical Trials Program, an adaptive platform trial taking place across academic medical centers and community cancer clinics that make up the Multiple Myeloma Research Consortium. Horizon will include multiple arms that will enable the testing of various treatments for relapsed/refractory, newly diagnosed and smoldering myeloma, with the first one testing Johnson & Johnson's BCMAxCD3-directed bispecific antibody Tecvayli (teclistamab-cqyv).

The Phase II study, which has an estimated completion date of 31 July 2030, will enroll 300 patients. The announcement comes just days before the American Society of Hematology meeting kicks off in San Diego.

"We're in an interesting kind of time for multiple myeloma overall, where we've had a lot of successes over the past 25, 26 years, and patients now have more options than ever before," MMRF CEO Michael Andreini told *Scrip*. "There are 15-plus approved therapies to treat multiple myeloma – and that's great progress and great news – but with that comes a whole set of new questions that need to be answered."

OPTIMIZING MYELOMA THERAPY

For many years, the backbone treatments for myeloma comprised proteasome inhibitors, immunomodulating drugs and anti-CD38 monoclonal antibodies. But in recent years, there has been an explosion of new immunotherapy options, particularly bispecific antibodies and CAR-T cell therapies that target BCMA and, more recently, bispecifics and CAR-Ts against GPRC5D.

"It's really about what are the right optimal treatment approaches amongst those various agents, so what are the right combinations; what are right sequencing approaches; what are the optimal dosing schedules for patients – so that all patients can get the most out of these great agents that we have," Andreini said.

At present, most of the newer therapies are approved for later lines of treatment. For example, Tecvayli and J&J's GPRC5DxCD3-directed bispecific Talvey (talquetamab-tgvs) have approval for fifth-line and later disease. The same is true of Pfizer's BCMAxCD3-directed Elrexfio (elranatamab-bcmm) and likely other players coming down the pike like Regeneron Pharmaceuticals'

linvoseltamab. Regeneron's drug has been delayed due to a complete response letter from the US Food and Drug Administration in August related to issues with the third-party manufacturer.

The BCMA-directed CAR-T cell therapies have been on the market longer and thus had more time to move up in treatment, with Bristol Myers Squibb and 2seventy bio's Abecma (idecabtagene vicleucel) having FDA approval in the third-line and later setting, while J&J and Legend Biotech's Carvykti (ciltacabtagene autoleucel) has approval in the second line, though it is also being studied in the first line.

And that's not including all of the other investigational therapies, such as BMS's GPRC5D-targeted CAR-T therapy BMS-986393 – which is currently in a pivotal Phase II study – as well as iberdomide and mezigdomide, which belong to the new CELMoD class that BMS intends to be successors to the immunomodulating drugs like Pomalyst (pomalidomide) and Revlimid (lenalidomide).

Andreini said the arm with Tecvayli will enable the evaluation of different dosing schedules of the drug in order to balance efficacy, safety and tolerability. "So the first arm is informing an important treatment-related question for patients," he said.

But more is to come, and the aim is for Horizon to incorporate a variety of approved and investigational agents.

"We're in active discussions with really all the major biopharma companies in this space, evaluating bringing in different agents, some of which will be other bispecifics, cell therapies, newer small molecule therapies being developed, potentially checkpoint inhibitors as well," Andreini said, adding that the idea is to work with the major players in myeloma in order to help them with their development path and to help them understand the optimal uses of their drugs in the space.

Checkpoint inhibitors are a class that has historically not performed well in multiple myeloma, particularly PD-1 and PD-L1 inhibitors. In 2017, the FDA slapped a clinical hold on Merck & Co.'s program to develop Keytruda (pembrolizumab) for multiple myeloma after Phase III trials showed excess deaths among patients receiving the drug.

But Andreini pointed to some of the more novel immune checkpoints as having some promise in myeloma. In particular, there was the MMRF-sponsored MyCheckpoint study, published in August in *Nature Cancer*, in which three of six patients receiving an anti-TIGIT antibody and two of six receiving an anti-LAG3 antibody showed durable clinical responses.

Ultimately, the goal is to have a significant effect on the standard of care, given the current one-size-fits-all approach to treatment.

"There isn't really a ton of nuance in terms of which patients, for what reasons might get different combinations and sequences at different points in time, and so that's really lacking in the multiple myeloma space, and we know that one-size-fits-all approach to treatment is not going to achieve long, durable remissions and cures for patients," Andreini said. "The results and insights generated from these studies that we're doing, we hope, will be very instrumental in informing the standard of care going forward."