

Good News: FDA Panel Votes to Approve Belantamab Mafodotin

July 16, 2020

On Tuesday, July 14, the U.S. Food & Drug Administration's ODAC ([the Oncologic Drugs Advisory Committee](#)) voted 12-0 in favor of approving belantamab mafodotin (Bela) for the treatment of relapsed/refractory myeloma. Patients must have received at least four previous therapies, including an IMiD (such as lenalidomide or pomalidomide), a proteasome inhibitor (such as bortezomib or carfilzomib), and an anti-CD38 monoclonal antibody (such as daratumumab or isatuximab).

The Bela therapy is a first-in-class therapy directed against a BCMA (B-cell maturation antigen) strongly expressed on the surface of myeloma cells. Bela is a monoclonal antibody drug conjugate. The drug, mafodotin, enters the myeloma cell with antibody binding and enhances the anti-myeloma efficacy. (I describe the drug in [this episode](#) of "Ask Dr. Durie.")

Purpose of ODAC hearing

The FDA can approve new agents without holding an ODAC hearing. However, in this case the hearing was scheduled to determine whether the risk of an unusual eye toxicity had been adequately evaluated and did not seriously negatively impact the benefit-risk profile. The eye issue is called a keratopathy and occurred in 71% of patients in the pivotal [DREAMM-2 trial](#). The keratopathy can cause blurred vision and/or dry eyes and may be progressive without dose or schedule adjustments. With these adjustments, treatment can be continued, and the eye issues will resolve over time. To evaluate the benefit-risk ratio, the ODAC team needed to understand full details for both efficacy and adverse events.

Treatment Benefit

The ODAC chairperson, Dr. Philip C. Hoffman, said, "It seems clear this is an active agent."

This conclusion was based upon the overall response rate (ORR) of 31% in this heavily previously treated population of patients. The 196 patients in the DREAMM-2 trial were randomized to receive either a 2.5mg/Kg dose or

a 3.4mg/Kg dose. The results in the two arms turned out to be rather similar, with a 31% ORR in the 2.5mg /Kg cohort and 34% in the 3.4mg/Kg cohort.

Deep response achieved were also similar at the VGPR (very good partial response) or better level in 19% and 20% respectively. Overall response rates (ORRs) were similar in patients with and without high-risk cytogenetics. These responses were sustained despite required treatment adjustments. Median duration of response estimates were 11 months. Thus, as noted, clear evidence of benefit!

Eye Toxicity

Eye toxicity or keratopathy was the major focus of attention for the reviewers. One aspect of concern was that the eye toxicity could occur without the patient experiencing symptoms. That is why the ocular risk evaluation and mitigation strategy (REMS) proposed by GlaxoSmithKline to provide education to all physicians administering Bela and their patients regarding the risk of keratopathy (corneal adverse reactions) was so important.

It was evident that careful discussions with patients to obtain informed consent prior to starting treatment would be essential. The eye examinations required prior to receiving treatment intravenously every three weeks will, unfortunately, be cumbersome, but manageable, and absolutely required to avoid any ongoing damage to the eyes.

The Bottom Line:

ODAC panel member Dr. Heidi D. Klepin echoed the feelings of the group: “I think the efficacy and toxicity remains favorable in the highly pretreated patient population.”

It is highly likely that the FDA will endorse this ODAC opinion. It is extremely encouraging to see this first-in-class anti-BCMA therapy moving toward approval. There are many additional therapies targeting the attractive BCMA receptor and it will be important to monitor outcomes as this first agent enters clinical practice. Others to follow, such as anti-BCMA CAR T-cell therapy, will not be so broadly accessible for patients across the U.S. and, subsequently, globally. The many ongoing [DREAMM trials](#) illustrate that combinations with other agents will certainly provide added benefits for patients. (The IMWG is currently planning to implement a registry for all anti-BCMA therapies, which will gather and collate all of the patient outcomes.)

All in all, good news indeed about this first step in the anti-BCMA immune therapy portfolio!