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Ash 2022 – toxicity still looms large for Regeneron's bispecific

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Another five treatment-related deaths, despite a dose regimen change, raise questions about whether odronextamab will be able to compete.

At Ash 2020 presentation of data on Regeneron's CD20-targeting bispecific odronextamab was marred by five treatment-related deaths. Two years later, the company has reported five more fatalities – and this time with a dosing regimen that was meant to reduce toxicity.

Regeneron was already behind Abbvie and Genmab's similarly acting epcoritamab and Roche's glofitamab, and facing questions about how it might compete. The latest disclosure might make it all but impossible for Regeneron to gain a foothold in this space.

All the aforementioned projects are T-cell recruiting CD20xCD3 bispecifics. Epcoritamab looks like the project to beat in terms of efficacy, and in aggressive lymphoma it is also ahead with the regulators: the project has a Pdufa date of May 21, 2023.

Roche is not too far behind – glofitamab impressed at this year's Asco and the company has filed it with the FDA, a spokesperson told *Evaluate Vantage*. Data from the project's pivotal phase 1/2 trial were presented at Ash today and published in the New England Journal of Medicine.

And another contender is Johnson & Johnson/Xencor's plamotamab; an Ash poster on Monday showed an ORR of 52% in DLBCL, putting this project in line with glofitamab, but behind epcoritamab.

Roche has a separate anti-CD20 bispecific, Lunsumio, that is approved in the EU and expecting a US decision by December 29, though this targets the less aggressive disease follicular lymphoma.

Playing catch-up

It was in this context that data on odronextamab were presented today, from a cohort of patients in the phase 2 Elm-2 trial with second-line or later diffuse large B-cell lymphoma (DLBCL).

The study was put on partial clinical hold in December 2020 over concerns about cytokine release syndrome in the phase 1 Elm-1 study; the hold was lifted in May 2021 and a longer step-up dosing regimen introduced to try and reduce this side effect. Notably, the regimen in Elm-2 was modified again during the trial to mitigate this risk even further.

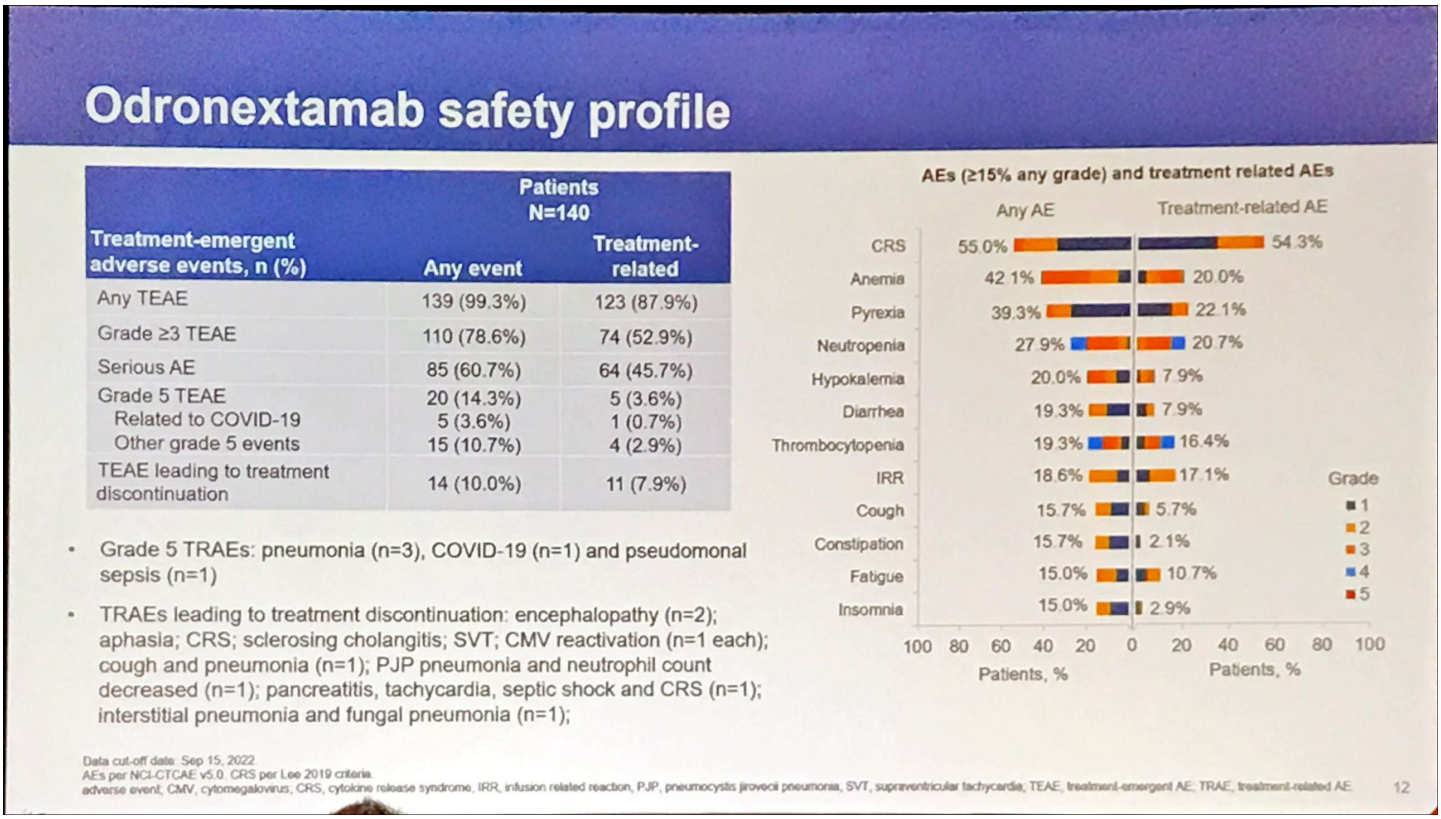
Although cytokine release syndrome rates did look slightly better in Elm-2, this is not the end of concerns over odronextamab's toxicity. Among 140 patients there were five treatment-related deaths in the study, caused by pneumonia in three cases, Covid and pseudomonal sepsis.

Despite this the presenter, Dr Won Seog Kim of the Samsung Medical Center in Seoul, described odronextamab's toxicity profile as "manageable".

There was some good news: among 130 evaluable patients the overall response rate, as assessed by central review, was 49%, and 31% of patients had a complete response. This looks better than the 40% ORR seen in DLBCL in Elm-1.

The question now is whether this will matter with epcoritamab and glofitamab looking at least as good, if not better, in terms of efficacy – and with no treatment-related deaths.

This story has been updated to clarify the regulatory status of glofitamab and Lunsumio, and to include details on plamotamab.



Source: Dr Won Seog Kim & Ash