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In Competitive DLBCL Setting, Pfizer Goes Old School With Adcetris

by Alaric DeArment

The ECHELON-3 trial in third-line diffuse large B-cell lymphoma showed positive topline results regardless of CD30 expression, and the drug maker intends to take the data to the FDA.

While multiple new biologics for treating diffuse large B-cell lymphoma (DLBCL) have come onto the market in recent years, *Pfizer Inc.* is highlighting data in the disease for Adcetris (brentuximab vedotin), a drug that originally received US Food and Drug Administration approval over a decade ago and was part of the drug maker's acquisition of its original developer, Seagen.

On 12 March, Pfizer announced topline results from the Phase III ECHELON-3 trial, which showed the combination of Adcetris with the anti-CD20 monoclonal antibody rituximab (*Roche Holding AG*'s Rituxan and biosimilars) and the immunomodulating drug lenalidomide (*Bristol Myers Squibb Company*'s Revlimid and generics) yielded statistically significant and clinically meaningful improvement on the primary endpoint of overall survival (OS) as well as positive results on the key secondary endpoints of progression-free survival (PFS) and overall response rate (ORR), compared with rituximab/lenalidomide and placebo. The 230 patients in ECHELON-3 had received two or more prior lines of therapy and were not eligible to receive stem cell transplant or CAR-T cell therapy.

Notably, the results showed an improvement in patients irrespective of expression of CD30, the antigen target of Adcetris, which has high levels of expression in Hodgkin lymphoma and other indications the antibody-drug conjugate (ADC) has FDA approval for, dating back to its original approval in

Key Takeaways

- Pfizer announced positive topline results for Adcetris – which it acquired when it

2011. ([#ASC148549])

Pfizer said it plans to share the ECHELON-3 data with the FDA to potentially support a regulatory filing.

Adcetris Jumps Into Competitive 3L DLBCL Space

The latest results build on prior Phase I and Phase II data supporting the use of Adcetris in DLBCL. According to a publication of Phase I data in the journal *Blood* in March 2022, although Adcetris works in Hodgkin and T-cell non-Hodgkin lymphomas by directing its cytotoxic payload to CD30-expressing cells, researchers also believe that it has immune cell stimulation and bystander effects that augment its cytotoxicity. The publication pointed to Phase II data that showed an ORR of 44% in relapsed/refractory DLBCL that, as in the latest Phase III results, exhibited no correlation between CD30 expression and response.

bought Seagen last year – in third-line and later DLBCL.

- Consistent with prior studies, the results from ECHELON-3 showed responses independent of CD30 antigen expression.
- Pfizer plans to apply for FDA approval, though the third-line and transplant-ineligible settings have multiple agents with a variety of antigen targets.

ECHELON-3's enrollment of patients ineligible for stem cell transplant or CAR-T cell therapy likely eliminates competition with CAR-T therapies, assuming the results lead to a label consistent with the trial population.

However, a number of newer agents for DLBCL have come onto the market in recent years that could be competitors to the Adcetris triplet combination in the third-line and transplant-ineligible settings, should Pfizer secure approval in that indication.

In June 2019, the FDA approved Roche's CD79b-targeting ADC Polivy (polatuzumab vedotin piiq) for third-line DLBCL, in combination with bendamustine and rituximab. (Also see "*Roche's Polivy ADC Is Approved As Another New Option For R/R DLBCL* " - Scrip, 11 Jun, 2019.)

Incyte Corporation and *MorphoSys AG*'s Monjuvi (tafasitamab) is a potential non-CAR-T therapy option that also targets CD19 and has had accelerated approval since August 2020 for relapsed/refractory DLBCL patients who are not eligible for stem cell transplant. The label does not specify the prior number of therapies required, though patients in the pivotal Phase II L-MIND trial had one to three prior lines. (Also see "*Morphosys/Incyte's Monjuvi Wins Early US FDA Approval In Second-Line DLBCL*" - Scrip, 4 Aug, 2020.)

In April 2021, the FDA gave accelerated approval to *ADC Therapeutics SA*'s Zylonta (loncastuximab tesirine-lpyl), a CD19-directed ADC, for patients with third-line and later

DLBCL. (Also see "*Keeping Track: US FDA Says Yes To AZ's Farxiga In CKD And ADC's Zynlonta, But No To Leo's Tralokinumab, Chiesi's Pegunigalsidase*" - Pink Sheet, 30 Apr, 2021.)

More recently, the FDA has given accelerated approval to CD20xCD3-targeting bispecific antibodies for third-line and later DLBCL. *AbbVie Inc.* and *Genmab A/S*'s Epkinly (epcoritamab-bysp) received accelerated approval in May 2023. (Also see "*Genmab Geared Up To Launch Epkinly With AbbVie*" - Scrip, 22 May, 2023.). Roche's Columvi (glofitamab-gxbm) got accelerated approval a month later. (Also see "*FDA Nod For Roche's Columvi Brings Third Anti-CD20 Bispecific To Market*" - Scrip, 16 Jun, 2023.)

[*Editor's note: A previous version of this article misstated Polivy's antigen target and listed among bispecifics for DLBCL an additional Roche product, Lunsumio (mosunetuzumab-axgb), which is approved for relapsed/refractory follicular lymphoma.*]