Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/what-are-the-data-supporting-first-line-c5-inhibitor-treatment-of-pnh/16112/

Released: 09/22/2023
Valid until: 09/22/2024
Time needed to complete: 41m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

What Are the Data Supporting First Line C5 Inhibitor Treatment of PNH?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Broome:
Hi, I'm Dr. Catherine Broome, Associate Professor of Medicine at MedStar Georgetown University Lombardi Cancer Center in Washington DC. And we're going to talk today about the Data Supporting First Line C5 Inhibitor Treatment of PNH.

So as you all remember, the natural history of PNH prior to C5 inhibition demonstrated a significant mortality compared with age and sex match controls. Two clinical trials evaluating the efficacy of C5 inhibitors were TRIUMPH and SHEPHARD. These trials both enrolled patients who had PNH with evidence of hemolysis and transfusion requirements. For a very rare disease, both of these trials had robust numbers, including 87 patients in TRIUMPH and 97 patients and SHEPHARD. SHEPHARD was an open-label trial, TRIUMPH was a randomized, multicenter, double-blind, placebo-controlled trial. And the primary endpoints were stabilization of hemoglobin levels, transfusion independence, and hemolysis assessed by LDH.

As we can see here, the patients who received the C5 inhibition had a significant improvement in their lactate dehydrogenase level compared to placebo patients. Those patients also had an increase in the number of type III erythrocytes, as one might expect from the protection afforded by the C5 inhibition. Before treatment, we looked at median number of transfusions. And we can see that during treatment, patients received no transfusions, which was a statistically significant improvement over the placebo group. Patients who had a stabilized hemoglobin level were about 50% in the C5 group, as compared to the placebo group. By week 26, the median number of units of packed cells which were transfused per patient was 0 in the C5 inhibitor group, and 10 in the placebo group. Patients in the C5 inhibitor group also had a mean increase or an improvement in FACIT-Fatigue scores, where the placebo group, the mean FACIT-Fatigue score decreased during the period study.

In SHEPHARD, 89 of 97% patients maintained complete inhibition of serum hemolysis activity with every-14-day dosing throughout the duration of the treatment period. Every patient that was treated with C5 inhibition with eculizumab had a substantial reduction in hemolysis as measured by LDH. And you can see that, graphed here, change from baseline with regards to FACIT-Fatigue was also significant in SHEPHARD, which was a single-arm, non-controlled trial.

The 301 study actually looked at a longer-acting C5 inhibitor, it assessed non-inferiority of ravulizumab compared to eculizumab in complement inhibitor-naive adult patients with PNH. Co-primary efficacy endpoints were the proportion of patients remaining transfusion free and LDH normalization. And in this trial, ravulizumab was non-inferior to eculizumab for both the primary, co-primary endpoints and all of the secondary endpoints. And here you can see the 301 study results, transfusion avoidance, LDH normalization, percent change in LDH, change in FACIT-Fatigue score, breakthrough hemolysis, or hemoglobin stabilization; all favored ravulizumab, some more significantly than others. But you can see that this definitely demonstrates non-inferiority for the longer-acting C5 inhibitor ravulizumab when compared to eculizumab.

I think one of the most important things to think about in C5 inhibition in PNH is that C5 inhibition has a major impact on survival. And we saw that curve at the beginning of the talk. As we look at the age and sex match normal population compared to an eculizumab treated population with PNH, we can see that treatment with C5 has basically normalized the survival curve so that it matches age and sex match normal population.

Thank you for joining. I hope you enjoyed this talk.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, LLC. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.