Systematic Literature Review and Network Meta-Analysis of Crovalimab Compared With Eculizumab, Ravulizumab and Best Supportive Care in Paroxysmal Nocturnal Hemoglobinuria

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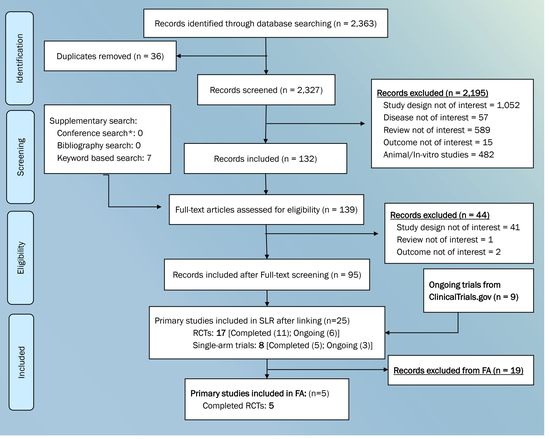
Introduction

- C5 inhibitors including eculizumab (ECU) and ravulizumab (RAV) are the standard of care (SoC) for paroxysmal nocturnal hemoglobinuria (PNH).
- Crovalimab (CRO) is a novel anti-C5 antibody approved for the treatment of PNH and administered subcutaneously every 4 weeks. In the randomized, Phase III COMMODORE 2 (C5 inhibitor-naive) study,[1] crovalimab demonstrated non-inferior efficacy outcomes vs. eculizumab. These findings were supported by results from the randomized, Phase III COMMODORE 1 (C5 inhibitor-pretreated) study.[2]
- This research aims to investigate the relative effectiveness of crovalimab vs. eculizumab, ravulizumab, and best supportive care (BSC) in patients with PNH.

Prisma Flow Diagram of Included Studies

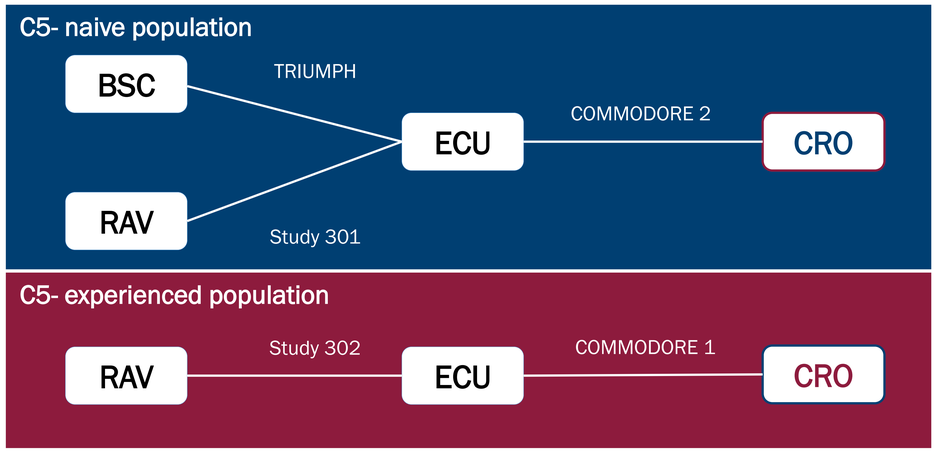


Methods

- A systematic literature review was conducted to identify randomized clinical trials investigating complement inhibitors for patients with PNH.
- The main endpoints were the proportions of patients with transfusion avoidance (TA) and breakthrough hemolysis (BTH) as well as the change in FACIT-Fatigue score from baseline.
- Data from trials with C5 inhibitor-naive and pre-treated patients were pooled for the base case and analyzed separately for subgroup analyses.
- Five studies with relevant data were eligible, informing a Bayesian Network Meta-Analysis (NMA) to estimate the effectiveness of crovalimab vs eculizumab, ravulizumab and BSC using informative priors for the between study heterogeneity.
- Mean differences and the probability of crovalimab being non-inferior (20% margin) were calculated using simulated data from random effects models (base case) and fixed effects models (sensitivity analysis).

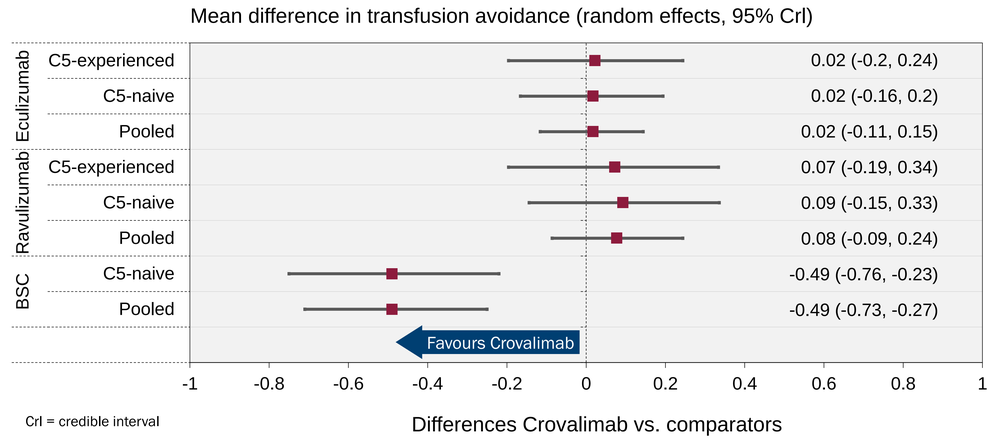
Results

1 Network of Connected Randomized Controlled Trials



Background: The network was based on a small set of studies with a small sample size. Patients enrolled in TRIUMPH were transfusion dependent (potential effect modifier). Therefore, the comparison vs. BSC should be interpreted accordingly.

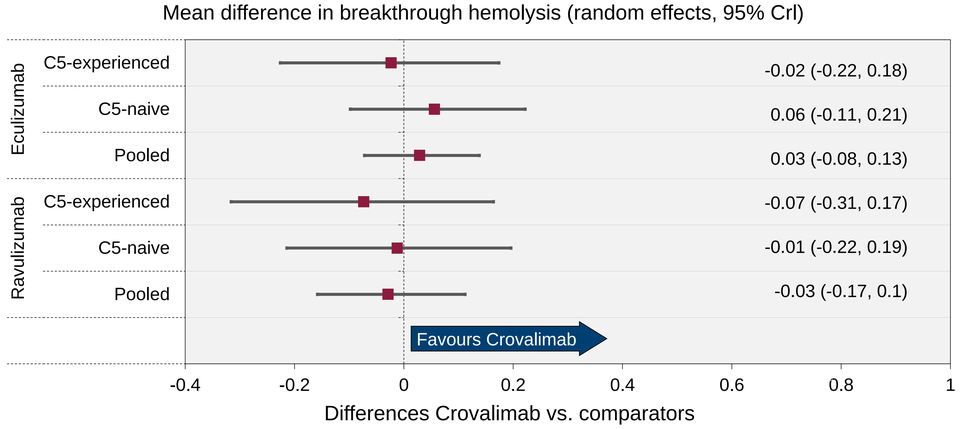
2 Comparable Outcomes in Achieving Transfusion Avoidance for C5-inhibiting Treatments



CrI = credible interval

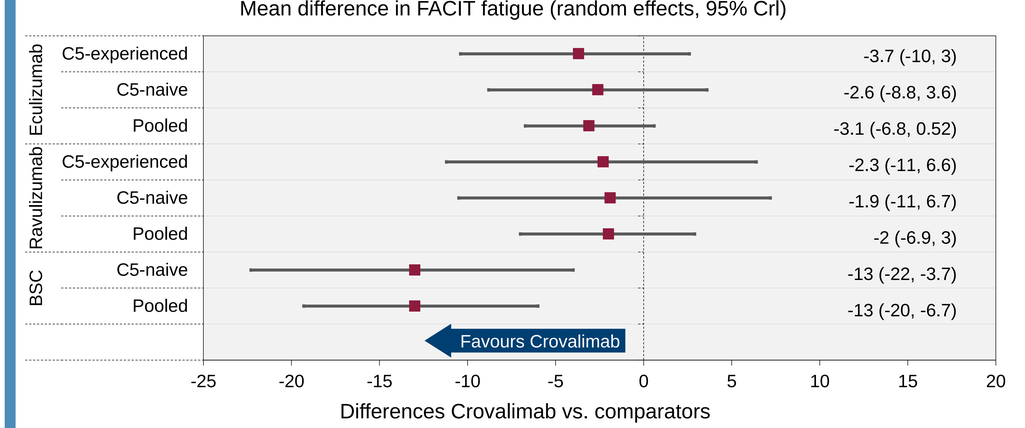
Background: Prior transfusion rates were slightly higher in COMMODORE 1 vs Study 302 and more balanced between COMMODORE 2 and Study 301. The results suggest similar transfusion outcomes for C5 treatments with a non-inferiority probability ≥ 82%.

3 Comparable Outcomes in Avoiding Breakthrough Hemolysis for C5-inhibiting Treatments



Background: LDH and Hb levels as well as aplastic anaemia rates were broadly balanced at baseline between the COMMODORE studies and the respective Studies 301/302. The results suggest similar breakthrough hemolysis outcomes for anti-C5 treatments with a non-inferiority probability ≥ 88%.

4 Comparable or Numerically Better Outcomes for Crovalimab as Measured by the FACIT-Fatigue Score



Background: The results suggest that crovalimab is associated with numerically better FACIT-Fatigue outcomes vs. eculizumab & ravulizumab and statistically better outcomes vs. BSC. These findings are consistent with the evaluation by the German GBA, which identified a benefit in FACIT-Fatigue responders (C5-experienced).[3]

Conclusions

The results indicate that crovalimab is non-inferior vs. ravulizumab across multiple key clinical endpoints. The results also suggest that crovalimab is associated with statistically better outcomes vs. best supportive care without C5 inhibitors.

The results suggest that quality of life measured by FACIT-Fatigue score was numerically better for crovalimab vs ravulizumab and eculizumab and statistically better vs. best supportive care.

Crovalimab is a next-generation C5 treatment, consistently delivering highly effective and sustained disease control as current SoC, but with unique SC dosing from home or in a clinic every 4 weeks. In COMMODORE 1 & 2, the majority of patients preferred crovalimab over eculizumab.[4]

References

1. Phase 3 randomized COMMODORE 1 trial: Crovalimab versus eculizumab in complement inhibitor-experienced patients with paroxysmal nocturnal hemoglobinuria, Scheinberg et al (2024), American Journal of Hematology, https://doi.org/10.1002/ajh.27413.
2. Phase 3 randomized COMMODORE 2 trial: Crovalimab versus eculizumab in patients with paroxysmal nocturnal hemoglobinuria naive to complement inhibition, Röth et al (2024), American Journal of Hematology, https://doi.org/10.1002/ajh.27412.

References (continued)

3. https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1127/.
4. Patient Preferences and Treatment Satisfaction in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Treated with Crovalimab and Approved C5 Inhibitors in the Phase III Randomized COMMODORE 1 and COMMODORE 2 Trials, Kulasekararaj et al (2023), blood, https://doi.org/10.1182/blood-2023-178610.

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