Nicholas Kuypers, PhD | nicholas.kuypers@novartis.com

Poster# **MDS-848**

Cost per responder analysis of iptacopan versus eculizumab and ravulizumab in treatment of paroxysmal nocturnal hemoglobinuria: implications for decision-making

Kyi-Sin Than,[1] Jason Shafrin,[2] Sanjana Muthukrishnan,[1] Nicholas Kuypers,[3] Jincy Paulose,[3] Ver Bilano,[4] Glorian Yen[3]

[1]Center for Healthcare Economics and Policy, FTI Consulting, Washington, DC, USA; [2]Center for Healthcare Economics and Policy, FTI Consulting, Los Angeles, CA, USA; [3]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [4]Novartis Pharmaceuticals Limited, London, UK

KEY FINDINGS & CONCLUSIONS

- Iptacopan treatment leads to a lower cost to achieve a response among PNH patients compared with eculizumab, ravulizumab, and eculizumab biosimilar
- Among treatment responders, iptacopan has a lower cost per responder in the trial treatment duration of 24 weeks which might be sustained through a period of one year
- Iptacopan is a cost-effective alternative to standard C5is among C5i-experienced and complement inhibitor–naive patients, with higher response rates and lower cost per responder
- The results of this study supplement the existing evidence on the economic value of iptacopan by providing an understanding of the value of the PNH treatments for those who respond to treatment

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BACKGROUND

- Paroxysmal nocturnal hemoglobinuria (PNH) is a genetic, progressive bone marrow failure disorder, characterized by hemolytic anemia, hemoglobinuria, thrombosis, peripheral blood cytopenia, and somatic symptoms, imposing a lifelong burden on patients with unmet needs[1-3]
- From 2007, complement 5-inhibitors (C5is) eculizumab, and ravulizumab (2018), have been used to treat PNH.[2,4] In 2024, two eculizumab biosimilars (ABP 959, eculizumab-aagh), with comparable safety and efficacy to eculizumab, received FDA approval[5,6]
- While C5i therapies suppress intravascular hemolysis (IVH), patients may have a suboptimal response and extravascular hemolysis (EVH), which may lead to anemia and transfusion-dependence[7]
- In December 2023, iptacopan, a first-in-class oral factor B inhibitor monotherapy, was approved for treatment of adults with PNH.[8,9] Despite multiple PNH treatment options, pharmacists, physicians, and payers may be uncertain whether the improved efficacy of newer treatments provides sufficient economic value compared to existing C5is

OBJECTIVE

- To compare the average cost per responder in the US for iptacopan vs C5is (ravulizumab, eculizumab, eculizumab biosimilar) among patients with PNH who are either (i) C5i-experienced with hemoglobin <10 g/dL or (ii) complement inhibitor naive

METHODS

- *Overview:* A cost per responder comparison was conducted using data from prescribing information, clinical trials, and wholesale acquisition drug cost, and response was defined as the share of patients achieving red blood cell (RBC) transfusion independence due to treatment. The model framework (**Table 1**) is described below
- *Data:* C5i-experienced response was obtained from the APPLY-PNH trial (NCT04558918)[10] for iptacopan and ravulizumab/eculizumab, and complement inhibitor–naive response from the APPOINT-PNH trial (NCT04820530)[11] and the external C5i control arm of the real-world APPEX cohort (NCT05842486).[12] The eculizumab biosimilar was assumed to have the same efficacy as eculizumab and, due to unavailability of prices, a 20% discounted drug cost
- *Discontinuation:* Given sustained response with iptacopan in the 48-week APPLY-PNH trial extension phase, 24-week efficacy was assumed to be maintained for one year. Discontinuation rate was obtained from the APPLY-PNH for iptacopan and the C5is, and an annual rate was calculated assuming a constant hazard for each cycle (4-weeks). The discontinuation was assumed to be the same in the complement inhibitor–naive population
- *Costs:* Drug and administration costs were calculated for the treatment duration of 24-weeks and extrapolated to one year based on labeled dosing and estimated discontinuation, and did not include medical cost offsets.
- *Primary outcomes:* number needed to treat (NNT) to achieve response compared to no treatment "(" $1/[response]_tx$ ")"; average cost per responder

Sensitivity Analysis:

- *Deterministic sensitivity analysis:* Varied cost and response parameters by +/- 20%
- *24-week scenario:* Estimated iptacopan cost per responder compared to C5is for clinical trial treatment duration of 24 weeks
- *Eculizumab biosimilar discount:* Applied discounts of 10% and 30% to test robustness of results

Table 1. Cost Per Responder Model Framework

Criteria	Description
Population	• Patients with PNH experienced with treatment and hemoglobin <10 g/dL • Patients with PNH naive to treatment with complement inhibitors
Intervention	Iptacopan
Comparator	Ravulizumab; eculizumab; eculizumab biosimilar
Treatment Response Definition	Share of patients achieving red blood cell (RBC) transfusion independence due to treatment
Time Frame/ Treatment Duration	• 1 Year, accounting for discontinuation • Sensitivity Analysis: 24 weeks
Outcomes	**Clinical:** Number Needed to Treat (NNT) to achieve response **Economic:** Treatment cost, including drug acquisition and administration cost; Cost per responder, the ratio of the total cost to the total number of responders or response rate
Setting	US Payer

RESULTS

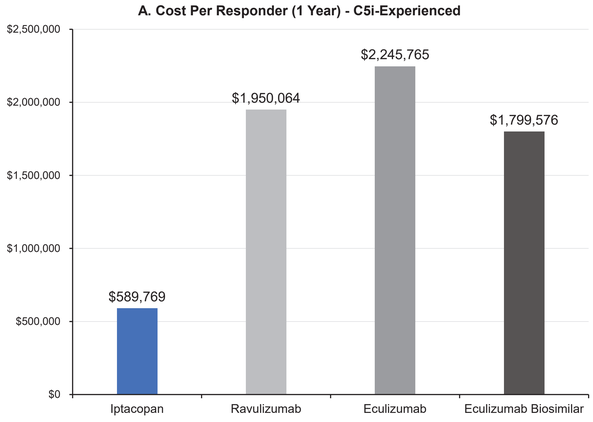
C5i-Experienced Patients

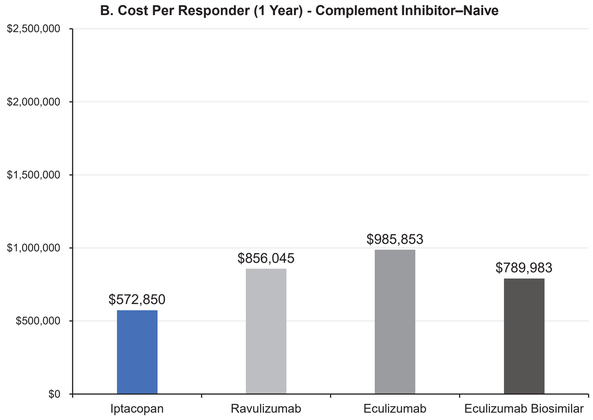
- To achieve 1 more patient with response, 1.1 additional patients need to be treated with iptacopan (vs no treatment), compared to 4.0 additional patients with C5is (vs no treatment)
- The one-year cost per responder with iptacopan was $589,769, $1,950,065 with ravulizumab, $2,245,765 with eculizumab, and $1,799,575 with the biosimilar. Thus, iptacopan cost per responder was $1,360,296 less than ravulizumab, $1,655,996 less than eculizumab and $1,209,807 less than the biosimilar (**Figure 1A**)

Complement Inhibitor–Naive Patients

- To achieve 1 more patient with response, 1.1 additional patients need to be treated with iptacopan (vs no treatment), compared to 1.7 additional patients with C5is
- The one-year cost per responder was $572,849 with iptacopan, $856,045 with ravulizumab, $985,853 with eculizumab, and $789,983 with the biosimilar. Thus, iptacopan cost per responder was $283,197 less than ravulizumab, $413,004 less than eculizumab and $217,134 less than the biosimilar (**Figure 1B**)

Figure 1. Cost Per Responder Among (A) C5i-*Experienced* Patients and (B) Complement Inhibitor–*Naive* Patients

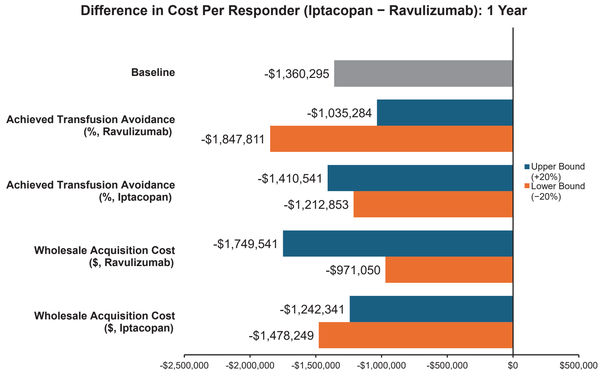




Sensitivity Analysis

- In both populations, the difference in cost per responder with iptacopan compared to C5is was most sensitive to changes in the proportion of responders in the comparator cohort, and comparator wholesale acquisition cost (WAC) (vs ravulizumab shown in **Figure 2**), and least impacted by changes in the treatment discontinuation rate (not shown). In all cases, iptacopan still has a lower cost per responder
- The cost per responder for iptacopan was lower compared to all three C5i comparators over 24 weeks. Among C5i-experienced, 24-week cost per responder with iptacopan was $264,337, $975,298 with ravulizumab, $1,060,511 with eculizumab, and $849,877 with the biosimilar. Among complement inhibitor–naive patients, the 24-week cost per responder outcomes were $256,754 (iptacopan), $428,139 (ravulizumab), 465,546 (eculizumab), and $373,082 (biosimilar)
- Among C5i-experienced patients, the 1-year cost per responder for the eculizumab biosimilar assuming 10% and 30% discount was $2,022,670 and $1,576,481 (vs $589,769 for iptacopan), respectively. Among complement inhibitor–naive patients, the cost per responder was $887,918 and $692,048 (vs $572,850 for iptacopan)

Figure 2. Deterministic Sensitivity Analysis of Difference in Cost Per Responder Comparing Iptacopan and Ravulizumab Among C5i-Experienced Patients



DISCUSSION

- The cost per responder analysis provides a comparison of the costs of achieving transfusion avoidance. It accounts for different dosing schedules and pricing structures across multiple PNH treatment options and standardizes the cost relative to achieving a meaningful clinical endpoint and thus is a useful economic metric for clinicians to assess the value of different PNH treatment options
- Results were most sensitive to changes in the proportion of responders in the comparator cohort, and comparator cost. Cost per responder for iptacopan was lower than C5is even over a 24-week treatment period

LIMITATIONS

- This study assumes a 20% eculizumab biosimilar discount in the base case due to limited data at the time of analysis. Emerging ABP 959 and eculizumab-aagh pricing suggests 10% and 30% discounts, respectively, even with which iptacopan has a lower cost per responder
- The one-year extrapolation assumes sustained 24-week treatment efficacy, based on the sustained outcomes in the 48-week follow-up of the APPLY-PNH trial, but discontinuation and adherence are accounted for based on rates observed in the long-term follow-up of the APPLY-PNH trial
- Cost per responder does not account for medical cost offsets such as cost savings to the healthcare system due to response achieved

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Disclosures

Kyi-Sin Than, Jason Shafrin, and Sanjana Muthukrishnan are employees of FTI Consulting, Inc., a consulting firm to health care, life sciences, government, and non-governmental entities. Nicholas Kuypers, Jincy Paulose, Ver Bilano, and Glorian Yen are employees of Novartis, the sponsor of this study.

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