# Utility Analysis of Crovalimab and Eculizumab in Paroxysmal Nocturnal Hemoglobinuria

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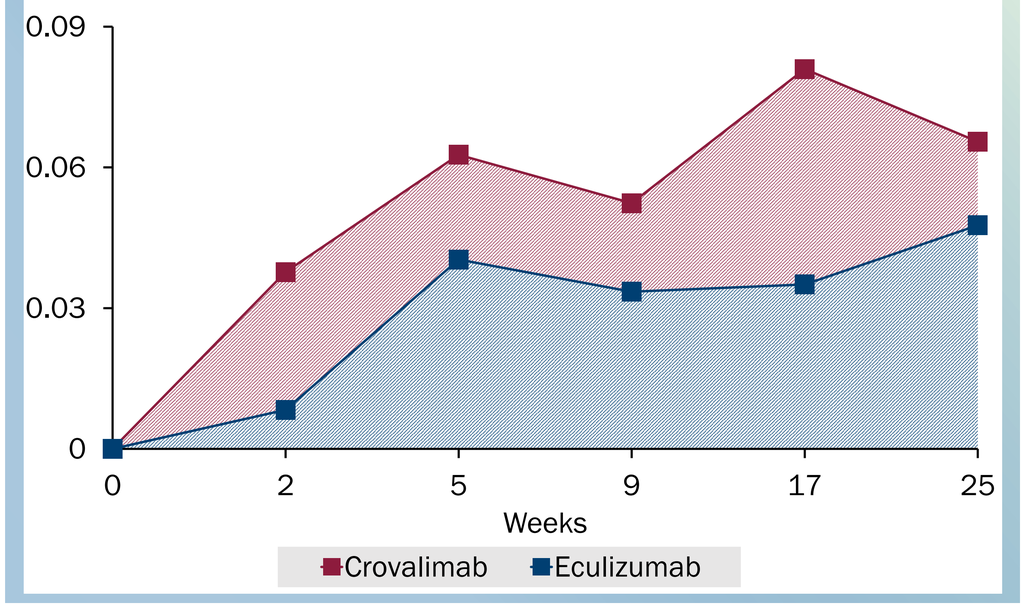
## Introduction

- Crovalimab is a novel anti-C5 antibody for the treatment of paroxysmal nocturnal hemoglobinuria (PNH).
- In the randomized Phase III COMMODORE 2 (C5 inhibitor-naive) study, crovalimab demonstrated non-inferior efficacy outcomes vs eculizumab.[1] These results were supported by results from the randomized Phase III COMMODORE 1 (C5 inhibitor-pretreated) study.[2]
- Crovalimab is the first monthly subcutaneous treatment for people with PNH approved in the EU and Japan. Crovalimab is also approved in the US and China.
- This research aims to investigate the health status of patients as measured by EQ-5D-5L translated into utility scores for the UK, US and Japan.[3,4,5]

## Descriptive mean change from baseline in utility

COMMODORE 2, Japanese tariff

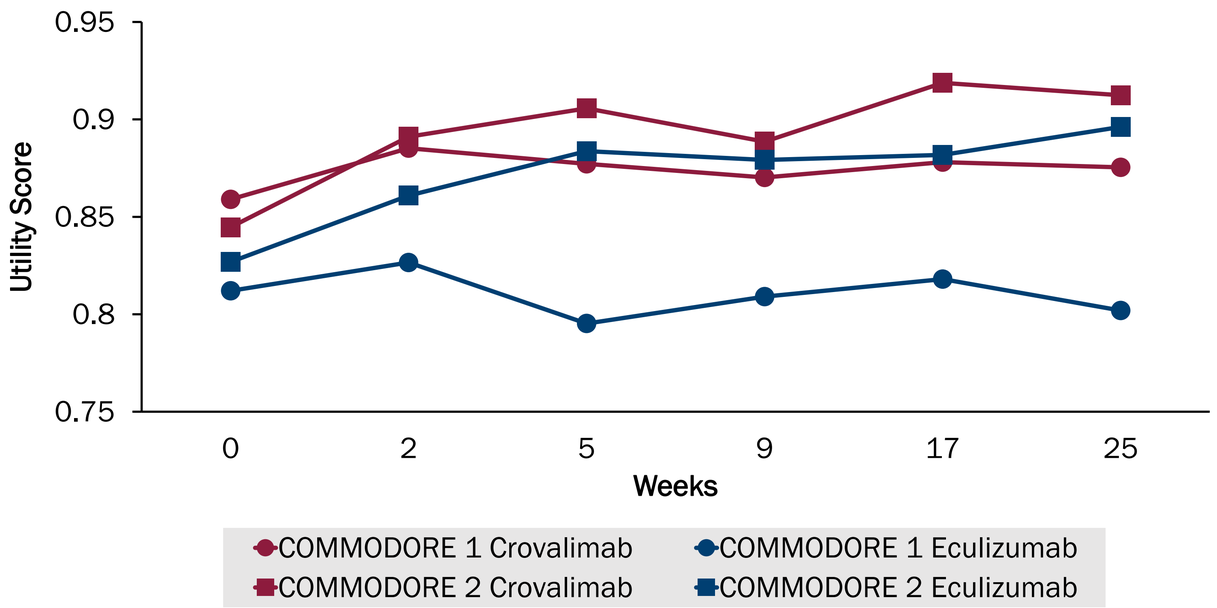



## Methods

- EQ-5D-5L results from pooled randomized COMMODORE 1 and 2 study arms were mapped to recommended value sets for the UK, US and Japan to derive utility scores (see on the left for descriptive change from baseline and below for absolute values).
- Economic evaluations in PNH are typically based on health states differentiated by a breakthrough hemolysis (BTH) event. Therefore, the objective was to adjust for the presence of a BTH event.[6]
- Further relevant covariates were included in an iterative approach evaluating the statistical contribution of parameters and the overall model fit.
- Following this approach, utility scores were estimated using a linear mixed-effects model with a final set of covariates controlling for study treatment, the presence of a BTH event and baseline utility across timepoints.

## Results

### Absolute utility scores (US tariff) by treatment and study




**Summary:**
Utility of patients pretreated with a C5 inhibitor was stable while the utility of naïve patients increased on both study treatments.

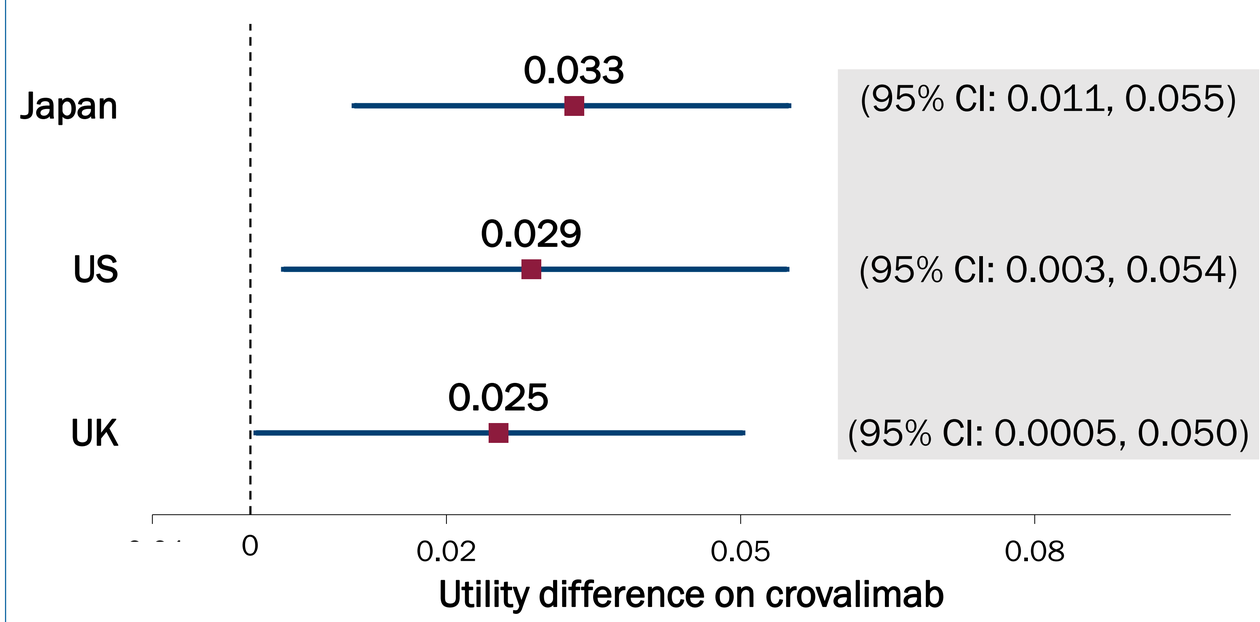
### Parameter estimates of the statistical model by tariff

| UK | Estimate | Standard error | t value | 2.5% lower CI | 97.5% upper CI |
|---|---|---|---|---|---|
| Intercept | 0.86 | 0.008 | 108.40 | 0.846 | 0.878 |
| BTH event | -0.06 | 0.031 | -1.85 | -0.112 | 0.015 |
| Baseline utility | 0.01 | 0.000 | 15.57 | 0.005 | 0.006 |
| Eculizumab treatment | -0.03 | 0.013 | -1.96 | -0.050 | -0.0005 |
| **Japan** | | | | | |
| Intercept | 0.85 | 0.007 | 121.30 | 0.838 | 0.866 |
| BTH event | -0.03 | 0.029 | -1.17 | -0.085 | 0.034 |
| Baseline utility | 0.01 | 0.000 | 16.09 | 0.005 | 0.007 |
| Eculizumab treatment | -0.03 | 0.011 | -2.90 | -0.055 | -0.011 |
| **US** | | | | | |
| Intercept | 0.89 | 0.008 | 110.20 | 0.875 | 0.907 |
| BTH event | -0.07 | 0.031 | -2.24 | -0.125 | 0.003 |
| Baseline utility | 0.01 | 0.000 | 15.62 | 0.004 | 0.006 |
| Eculizumab treatment | -0.03 | 0.013 | -2.18 | -0.054 | -0.003 |

**Summary:**
BTH events are associated with a statistically insignificant decrease in utility. Baseline utility has a statistically significant positive influence and patients on crovalimab have a statistically significantly higher utility.

## Results

### Treatment effect for crovalimab




**Summary:**
Results of the model indicate that patients on crovalimab have a statistically higher utility compared to eculizumab regardless of the tariff.

### Absolute utility estimates by BTH health state and treatment

| UK | Treatment | Estimate | Standard error | 2.5% lower CI | 97.5% upper CI |
|---|---|---|---|---|---|
| No BTH | Crovalimab | 0.86 | 0.01 | 0.85 | 0.88 |
| | Eculizumab | 0.84 | 0.01 | 0.82 | 0.86 |
| BTH | Crovalimab | 0.81 | 0.03 | 0.75 | 0.87 |
| | Eculizumab | 0.78 | 0.03 | 0.72 | 0.85 |
| **Japan** | | | | | |
| No BTH | Crovalimab | 0.85 | 0.01 | 0.84 | 0.86 |
| | Eculizumab | 0.82 | 0.01 | 0.80 | 0.84 |
| BTH | Crovalimab | 0.82 | 0.03 | 0.77 | 0.88 |
| | Eculizumab | 0.79 | 0.03 | 0.73 | 0.85 |
| **US** | | | | | |
| No BTH | Crovalimab | 0.89 | 0.01 | 0.87 | 0.91 |
| | Eculizumab | 0.86 | 0.01 | 0.84 | 0.89 |
| BTH | Crovalimab | 0.82 | 0.03 | 0.77 | 0.89 |
| | Eculizumab | 0.79 | 0.03 | 0.73 | 0.86 |

**Summary:**
Utility estimates by health state range between 0.78 for patients on eculizumab who experience a BTH event, and 0.89 for patients on crovalimab without a BTH event.

## Conclusions

Results from the utility analysis show that patients with PNH treated with C5 inhibitors in general can achieve a quality of life like that of the general population.

The results of the statistical model indicate that patients on crovalimab have a statistically higher utility than patients on eculizumab.

Patient utility was higher for patients receiving crovalimab compared to eculizumab regardless of the value set being used.

Pharmacoeconomic evaluations in PNH are typically based on models using health states differentiated by BTH event. Health state utility values estimated in this analysis may serve to inform future cost utility analyses that use this approach.

### References

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### Financial Disclosures

All authors are employees of F. Hoffmann-La Roche Limited or Genentech, Inc. and may own stock of Roche

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