Abstract: P772

Title: LONG-TERM RAVULIZUMAB TREATMENT IN COMPLEMENT INHIBITOR-EXPERIENCED PATIENTS WITH PNH PROVIDES DURABLE CONTROL OF INTRAVASCULAR HEMOLYSIS WITH LOW INCIDENCE OF MAJOR ADVERSE VASCULAR EVENTS AND DEATH.

Abstract Type: Poster Presentation

Session Title: Bone marrow failure syndromes incl. PNH - Clinical

Background:

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare chronic hematologic disorder characterized by uncontrolled terminal complement activation, major adverse vascular events (MAVEs, including thrombosis) and increased morbidity and mortality. Where available, ravulizumab is considered the standard of care for patients with PNH, supported by pivotal studies of adult complement inhibitor-naïve and complement inhibitor-experienced patients with PNH (studies 301 and 302, respectively). Published data are available for the primary evaluation period (26 weeks) and up to 18 months of the open-label extension (OLE) period for both studies.

Aims:

To report the clinical efficacy and safety of ravulizumab maintenance treatment for up to 4 years in complement inhibitor-experienced patients with PNH.

Methods:

Study 302 (NCT03056040) is a phase 3 randomized open-label active-controlled non-inferiority multicenter study comparing the efficacy and safety of ravulizumab with eculizumab in clinically stable adult patients with PNH who had received eculizumab treatment for ≥6 months and had lactate dehydrogenase (LDH) levels ≤1.5 × upper limit of normal (ULN; 246 U/L) at screening. After the primary evaluation period, patients continued ravulizumab maintenance treatment or switched from eculizumab to receive ravulizumab for the OLE. During the OLE, patients received weight-based dosing of ravulizumab every 8 weeks. Outcomes of interest included change in LDH level from baseline, proportion of patients experiencing breakthrough hemolysis (BTH; as previously defined), MAVEs and patient survival.

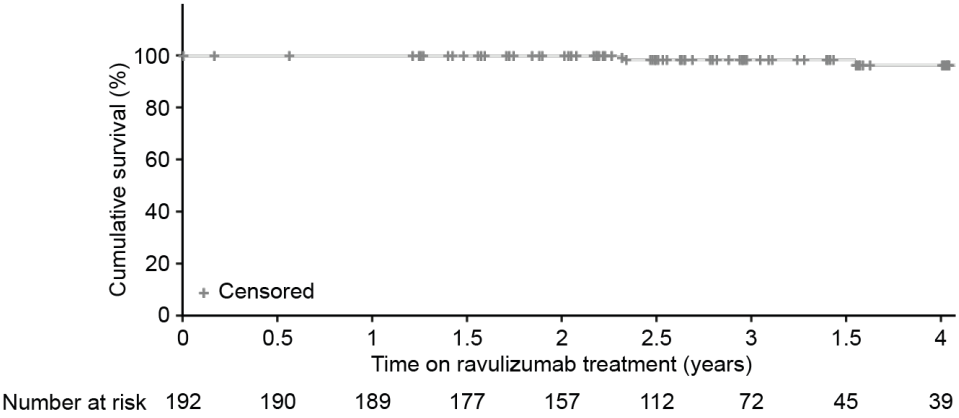
Results:

Overall, 195 patients were randomly assigned to receive treatment. Baseline patient demographics and clinical characteristics are available in the literature. Overall, patient sex distribution was relatively equal (50.3%, male), mean (standard deviation; SD) baseline LDH level was 231.6 (49.2) U/L, 50 (25.6%) patients had a history of MAVEs and mean (SD) years on eculizumab before first infusion of study drug was 5.8 (3.5) years. In the OLE, 96 patients assigned to ravulizumab continued treatment and 95 patients assigned to eculizumab switched to ravulizumab. During ravulizumab treatment, patient LDH levels remained <1.5 × ULN, and patient serum C5 concentrations were <0.5 µg/mL up to data cut. Instances of BTH during ravulizumab treatment were low, with 13/191 patients (6.8%) experiencing BTH; of these events, one (7.6%) was associated with a thrombotic event (cerebral infarction). Incidence of treatment-related MAVEs was low, with three patients (1.6%, including one patient with a history of MAVEs) reporting 4 MAVEs (event rate: 0.8; deep vein thrombosis, n = 1; thrombophlebitis, n = 1; cerebral infarction [two events], n = 1). Of the 192 patients who received ravulizumab, 11 (5.7%) discontinued and three (1.6%) died during the study period, with an overall incidence of 0.6 per 100 patient-years (98.4% survival rate; **Figure 1**). Of these deaths, one was associated with *Escherichia* sepsis and two were associated with neoplasms (urothelial carcinoma of the kidney and lung cancer). All deaths were considered not related to ravulizumab treatment.

Summary/Conclusion:

To date, this study reports the longest duration of ravulizumab treatment exposure in C5 inhibitor-experienced patients with PNH (527.04 patient-years). Effective control of intravascular hemolysis with ravulizumab was reflected by LDH levels being maintained at <1.5 × ULN and the low incidence of MAVEs and maintained patient survival throughout the 4-year long-term study period.

Figure 1: Overall survival of patients with paroxysmal nocturnal hemoglobinuria who received ravulizumab (N = 192)



Number at risk	192	190	189	177	157	112	72	45	39

Keywords: Paroxysmal nocturnal hemoglobinuria (PNH), Complement