Background:

The efficacy of ravulizumab (intravenous [IV] formulation; administered every 8 weeks) for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) has been demonstrated in several randomized trials (NCT02946463, NCT03056040, NCT03406307). In study 303 (NCT03748823), subcutaneous (SC) ravulizumab, administered weekly via an on-body delivery system, showed pharmacokinetic non-inferiority to IV ravulizumab in adult patients with PNH who were clinically stable on prior IV eculizumab treatment. Here, we report results from the first 1 year of SC treatment, starting at day 15 for patients who continued SC ravulizumab during the extension period (SC/SC) and day 71 for patients who switched from IV ravulizumab to SC ravulizumab (IV/SC).

Aims: To evaluate the efficacy, treatment administration satisfaction and safety of SC ravulizumab through the first 1 year (day 351) of treatment in adult patients with PNH previously treated with eculizumab.

Methods:

Patients (≥ 18 years) with clinically stable PNH (lactate dehydrogenase [LDH] levels ≤ 1.5 × upper limit of normal [246 U/L]) and ≥ 3 months prior eculizumab treatment were enrolled in the study, which consisted of a screening period (day -1 to day -30), a 10-week randomized treatment period and an extension period of up to 172 weeks. During the randomized treatment period, patients were assigned (2:1 ratio) to receive either SC ravulizumab or IV ravulizumab; all patients received SC ravulizumab during the extension period. Efficacy endpoints included: change in LDH from baseline; incidence of breakthrough hemolysis; transfusion avoidance; and stabilized hemoglobin (avoidance of a ≥ 2 g/dL decrease in hemoglobin in the absence of transfusion). Treatment administration satisfaction was assessed via the Treatment Administration Satisfaction Questionnaire (TASQ), which has been validated in a PNH population. Safety, including adverse events (AEs), serious AEs (SAEs) and adverse device effects (ADEs), were also assessed up to the 1-year data cut-off.

Results: In total, 128 patients received SC ravulizumab (SC/SC: n = 84; IV/SC: n = 44; mean [range] duration of SC treatment: 486.4 [37–709] days). Efficacy endpoints (SC/SC and IV/SC) remained stable over time through 1 year of SC ravulizumab treatment. Mean (standard deviation [SD]) percentage change in LDH from baseline to SC day 351 was 0.9% (20.5%). Breakthrough hemolysis events were infrequent: 5/128 patients (3.9%); no event was considered free C5-related. Transfusion avoidance was maintained in 83.6% of patients during SC treatment, and 79.7% achieved stabilized hemoglobin. Improvement in total TASQ score with SC ravulizumab (compared with baseline IV eculizumab) was apparent at the first post-SC treatment assessment (SC day 29) and maintained until data cut-off.
The most common AEs (reported by ≥ 10% of patients, excluding ADEs related to device product issues) during SC treatment were headache (14.1%, all grade ≤ 2), COVID-19 (14.1%, one death) and pyrexia (10.9%); injection site reaction (4.7%) was the most common non-device related ADE. Treatment-emergent SAEs were experienced by 21.1% of patients through to data cut-off. Although many patients had ≥ 1 device issue ADE, full SC dose administration was achieved in 99.9% of attempts. ADE incidence decreased over time.

**Summary/Conclusion:**
The SC method of administration provides an additional treatment option for patients with PNH receiving ravulizumab therapy. Patients may be switched from IV eculizumab or IV ravulizumab to SC ravulizumab without loss of efficacy.