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Efficacy and safety of the long-acting C5-inhibitor ravulizumab in adult patients with Atypical Hemolytic Uremic Syndrome (aHUS)

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Background: Ravulizumab was engineered to achieve extended complement C5 inhibition, given every 8 weeks, while retaining the proven efficacy and safety of eculizumab. Here we evaluate the efficacy and safety of ravulizumab in adults with aHUS.

Methods: This was a phase 3, single arm study (NCT02949128). Complement inhibitor-naïve patients (pts) aged ≥18 years who fulfilled diagnostic criteria for aHUS (exclusion of ADAMTS13 <5% activity and Shiga toxin-producing Escherichia Coli) and active thrombotic microangiopathy (TMA) received ravulizumab at 8-week intervals during the maintenance phase. The primary endpoint was complete TMA response during the initial 183-day evaluation period. Secondary endpoints included time to complete TMA response, components of complete TMA response over time, CKD stage, dialysis-free status over time and time to dialysis-free status.

Results: Fifty-six eligible pts were analyzed. Median age at baseline was 40 (range, 20–77) years and 36 (66%) were female. Complete TMA response was achieved in 30 pts (54%). 17/29 (59%) pts stopped dialysis (at a median time of 30 days). Primary endpoint and TMA parameter response over time is shown in the figure. Improvement in CKD stage from baseline was observed in 32/47 (68%) pts at Day 183. The most frequent serious adverse events were hypertension and pneumonia, each reported in 3 (5%) pts; 4 deaths not attributed to treatment occurred. No meningococcal infections were reported.

Conclusions: 8-weekly ravulizumab dosing produced immediate, sustained and complete complement inhibition resulting in rapid hematologic and renal response with no unexpected safety concerns.