Abstract: [FR-OR057] Eculizumab (ECU) Inhibits Thrombotic Microangiopathy (TMA) and Improves Renal Function in Adult Atypical Hemolytic Uremic Syndrome (aHUS) Patients (Pts)

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Background: aHUS is a rare, severe, genetic, life-threatening disease of chronic complement-mediated TMA. ECU, a terminal complement inhibitor, is approved for the treatment of aHUS. Here, we report safety and efficacy results of ECU in adult pts from the largest prospective study performed in aHUS.

Methods: This was a single-arm, Phase 2 trial of ECU in adult pts (≥18 yrs) with aHUS and platelets <LLN at screening. Prior plasma exchange or infusion (PE/PI) was not required for inclusion. The primary endpoint was the proportion of pts with complete TMA response at 26 wks.

Results: 41 pts enrolled and 38 (93%) received 26 wks of treatment. 30 pts (73%) were newly diagnosed (median duration to treatment initiation of 2 weeks). Six pts had no PE/PI during the current clinical manifestation. At wk 26, 30 pts (73%) achieved the primary endpoint.

Table: Wk 26 ITT Results (N=41)	
Baseline Demographics and Disease Characteristics	
Age (years) – mean (SD)	40.3 (15.3)
Female sex – n (%)	28 (68)
Identified complement regulatory protein mutation or auto-antibody – n (%)	21 (51)
Time from aHUS diagnosis until screening (months) – median (range)	0.8 (0–311)
Newly diagnosed pts – n (%)	30 (73)
Duration of current clinical manifestation of aHUS (months) – median (range)	0.5 (0.0–19.1)
PE/PI during current clinical manifestation of aHUS – n (%)	35 (85)
Dialysis at baseline – n (%)	24 (59)
Prior renal transplant – n (%)	9 (22)
Platelet count <150x10⁹/L – n (%)	27 (66)
LDH >ULN – n (%)	32 (78)
eGFR ≤60 mL/min/1.73 m² – n (%)	41 (100)
Efficacy Outcomes	
Complete TMA response – n (%)	30 (73)
Hematologic normalization– n (%)	36 (88)
Platelet count normalization – n (%)	40 (98)
Platelet count increase (x10⁹/L) – mean (95% CI)	119 (94; 145) *P*<0.0001
eGFR increase from baseline ≥15 mL/min/1.73 m² – n (%)	22 (54)
eGFR increase from baseline (mL/min/1.73 m²) – mean (95% CI)	26.1 (19.8; 32.4) *P*<0.0001
CKD improvement ≥1 stage from baseline – n (%)	26 (63)
Complete TMA response: normalization of platelets and LDH, and <25% increase in serum Cr from baseline on 2 consecutive measurements ≥4 wks apart. **Hematologic normalization:** platelet and LDH normalized for ≥2 consecutive measurements ≥4 wks apart. **Platelet count normalization:** platelet count ≥150x10⁹/L ≥2 consecutive measurements ≥4 wks apart.	

24/41 pts (59%) were on dialysis at BL, 20 of whom discontinued by wk 26. Mean (95% CI) eGFR increase from baseline was 26.1 mL/min/1.73 m^2 (19.8; 32.4: $P<0.0001$). Two pts who were not on dialysis at baseline initiated during the treatment period and remained on dialysis through 26 wks. QoL significantly improved. ECU was generally safe and well tolerated. Two pts had meningococcal infections; one pt continued ECU. No pts died. **Conclusions:** ECU normalized hematologic parameters and significantly improved renal function and QoL. 83% of pts on dialysis at baseline were able to discontinue by wk 26. The results of this prospective study confirm that ECU inhibits complement-mediated TMA in adult aHUS pts. The study is ongoing.
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Session: Glomerular Diseases: New Approaches to Prognosis and Treatment
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Location: Room 206

Individual author disclosures are available in the Kidney Week 2013 *Disclosure Digest* which is available to each meeting participant or upon request in November.