SUN-226

Safety and Efficacy of Eculizumab in Adult and Pediatric Patients With aHUS, With or Without Baseline Dialysis

Jan Menne,[1] Nicole C.A.J. van de Kar,[2] Johan Vande Walle,[3] Christophe M. Legendre,[4] John F. Kincaid,[5] Maryvonne Hourmant[6]

[1]Klinik für Nieren- und Hochdruckerkrankungen, Hannover, Germany; [2]Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands; [3]Ghent University Hospital, Ghent, Belgium; [4]Université Paris Descartes & Hôpital Necker, Paris, France; [5]Alexion Pharmaceuticals, Inc., Cheshire, CT, USA; [6]Department of Nephrology and UMR 643, CHU de Nantes, Nantes, France

INTRODUCTION

- Atypical hemolytic uremic syndrome (aHUS) is characterized by chronic, uncontrolled complement activation and thrombotic microangiopathy (TMA), leading to renal and other end organ damage[1,2]
- Despite management with plasma exchange/plasma infusion (PE/PI), 29% of pediatric and 56% of adult patients with aHUS progress to end-stage renal disease or die within the first year of diagnosis as a result of TMA manifestations[2]
  - In addition, complications of central venous catheters inserted for PE/PI occur in one third of children with aHUS[3]
- Eculizumab, a terminal complement inhibitor, is a humanized monoclonal antibody that binds with high affinity to the human C5 complement protein, blocking the generation of pro-inflammatory C5a and C5b-9[4]
  - It is the first and only approved treatment for aHUS in pediatric and adult patients[5,6]
- In a previous prospective trial of adults with aHUS and clinical evidence of progressing TMA treated with eculizumab (C08-002), 80% of patients who were receiving dialysis at the beginning of the study were able to discontinue dialysis during the treatment period[4]
  - Results from a subanalysis showed that eculizumab was well tolerated, inhibited TMA, and significantly increased estimated glomerular filtration rate (eGFR) after 2 years in patients with and without baseline dialysis[7]
- In study C10-003,[8] the first-ever prospective study of pediatric patients with aHUS, and study C10-004,[9] the largest prospective trial in an adult-only population with aHUS, eculizumab inhibited TMA and improved renal function
  - Notably, 82% and 79% of patients on dialysis at baseline, respectively, were able to discontinue dialysis during sustained treatment with eculizumab[8,9]

OBJECTIVE

- Here, we report the results of 2 post hoc subanalyses of studies C10-003 (US National Institutes of Health www.ClinicalTrials.gov identifier NCT01193348) and C10-004 (US National Institutes of Health www.ClinicalTrials.gov identifier NCT01194973) to characterize the efficacy and safety of eculizumab in pediatric and adult aHUS patients, respectively, with or without use of dialysis at baseline

METHODS

- The study designs and endpoints for trials C10-003 and C10-004 are shown in **Table 1**
- In trial C10-003, fixed doses of eculizumab were administered intravenously based on prespecified body weight cohorts
- In trial C10-004, eculizumab was administered as per the following schedule: 900 mg intravenously once weekly for 4 weeks, 1200 mg at week 5, then 1200 mg every 2 weeks

Table 1. Trial Designs for C10-003 and C10-004

	Trial C10-003 Pediatric Patients (N=22)	Trial C10-004 Adult Patients (N=41)
Study Design	• Open-label, single-arm, multicenter, multinational, interventional clinical trials	
	• Pediatric patients with aHUS aged 1 month to <18 years with body weight ≥5 kg • No PE/PI for >5 weeks prior to enrollment • Platelet count at screening and baseline visit <150 x 10^9/L • Signs or symptoms of hemolysis at start of current aHUS[a] • SCr ≥97th percentile for age at screening	• Adult patients with aHUS aged ≥18 years with the following at screening: – Platelet count <150 x 10^9/L – Hemoglobin concentration ≤LLN – LDH ≥1.5 x ULN – SCr ≥ULN
	• No requirement for identified complement mutation or antibody	
	• Required vaccination against *Neisseria meningitidis* ≥14 days prior to receiving the first dose of eculizumab, or have been vaccinated and received prophylactic antibiotics for 14 days after vaccination[b]	
Primary Outcomes	• Proportion of patients who achieved complete TMA response at 26 weeks[c] defined as platelet count normalization (≥150 x 10^9/L), LDH <ULN, and improvement in renal function (≥25% decrease in SCr from baseline)	• Proportion of patients who achieved complete TMA response at 26 weeks[c] defined as platelet count normalization (≥150 x 10^9/L), LDH <ULN, and preservation of renal function (≤25% decrease in SCr from baseline) • Modified complete TMA response[c] (a secondary endpoint) was defined as platelet count normalization (≥150 x 10^9/L), LDH <ULN, and improvement in renal function (≥25% decrease in SCr from baseline)
Secondary Outcomes	• TMA event-free status (no decrease in platelet count >25% from baseline, no PE/PI, and no new dialysis) • Hematologic normalization (platelet count normalization[c] [≥150 x 10^9/L] and LDH normalization[c] [LDH ≤ ULN]) • Platelet count normalization[c] • LDH normalization[c] • Renal function measures – eGFR increase from baseline – eGFR increase ≥15 mL/min/1.73^2 from baseline[c] – ≥25% decrease in SCr from baseline[c] – CKD improvement ≥1 stage from baseline • Improvement in health-related quality of life[d] • Safety parameters, including TEAEs determined to be related to eculizumab	

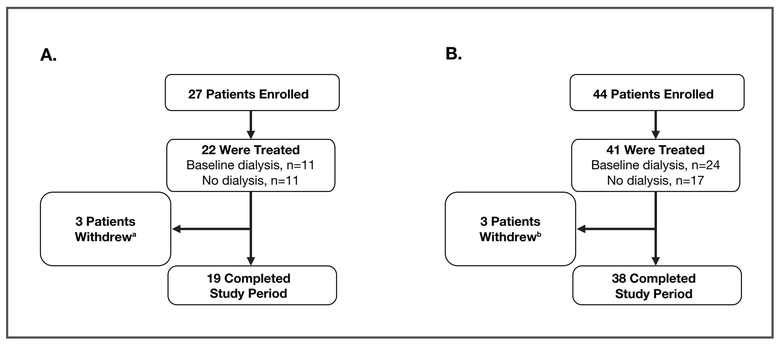
aHUS, atypical hemolytic uremic syndrome; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FACIT-F, Pediatric Functional Assessment of Chronic Illness Therapy–Fatigue; LDH, lactate dehydrogenase; LLN, lower limit of normal; PE/PI, plasma exchange/plasma infusion; SCr, serum creatinine; TEAE, treatment-emergent adverse event; TMA, thrombotic microangiopathy; ULN, upper limit of normal.
[a]LDH ≥1.5 x ULN, hemoglobin concentration ≤LLN, fragmented red blood cells with a negative Coombs test.
[b]In trial C10-003, patients were also vaccinated against pneumococcus and *Haemophilus influenzae*. Due to lack of availability of a vaccine for patients aged <2 years, patients in this age group received antibiotic prophylaxis throughout treatment.
[c]Confirmed by ≥2 consecutive measurements obtained ≥4 weeks apart.
[d]Measured by the Pediatric FACIT-F questionnaire in trial C10-003 and the FACIT-F questionnaire in trial C10-004.

RESULTS

Patients

- Patient disposition in trials C10-003 and C10-004 are shown in **Figure 1**
- Baseline demographics and clinical characteristics for both trials are summarized in **Table 2**

Figure 1. Patient Disposition in the Intent-to-Treat Populations of: A) C10-003 and B) C10-004



[a]During the 26-week study period, due to confirmed diagnosis of Shiga toxin-producing *E. coli* hemolytic uremic syndrome (n=1), serious adverse event of agitation (n=1), and family request (n=1).
[b]During the 26-week study period, due to a serious adverse event of meningococcal meningitis (n=1), lack of efficacy (n=1), and pregnancy (n=1).

Table 2. Patient Demographics and Baseline Clinical Characteristics

Parameter	Trial C10-003 Pediatric Patients (N=22) Dialysis (n=11)	Trial C10-003 Pediatric Patients (N=22) No Dialysis (n=11)	Trial C10-003 Pediatric Patients (N=22) *P* Value[a]	Trial C10-004 Adult Patients (N=41) Dialysis (n=24)	Trial C10-004 Adult Patients (N=41) No Dialysis (n=17)	Trial C10-004 Adult Patients (N=41) *P* Value[a]
Age at first infusion, mean (range), years	5.5 (0.0–17.0)	7.7 (1.0–17.0)	0.25	35.2 (18.0–65.0)	47.6 (27.0–80.0)	0.01
Female gender, n (%)	4 (36.4)	6 (54.6)	0.67	17 (70.8)	11 (64.7)	0.74
Patient-reported family history of aHUS, n (%)	3 (27.3)	3 (27.3)	NE	4 (16.7)	2 (11.8)	NE
Identified complement abnormalities, n (%)			1.00			0.35
Factor H autoantibody (+)	1 (9.1)	1 (9.1)		1 (4.2)	0	
C3 (gain-of-function mutation)	1 (9.1)	0		1 (4.2)	3 (17.6)	
Factor H mutation	2 (18.2)	0		8 (33.3)	1 (5.9)	
Factor H mutation + *factor H* mutation	0	0		1 (4.2)	0	
Factor H mutation + *MCP* mutation	0	0		0	1 (5.9)	
Factor I mutation	1 (9.1)	1 (9.1)		0	2 (11.8)	
MCP mutation	0	3 (27.3)		2 (8.3)	0	
Identified *DGKE* mutation, n (%)	NE	NE	NE	NE	NE	NE
No identified mutation, n (%)	6 (54.5)	5 (45.5)	NE	10 (41.7)	10 (58.8)	NE
Duration from aHUS diagnosis until screening, median (range), days	6.9 (3.9–5740.2)	62.1 (0.9–1738.5)	0.22	NE	NE	NE
Duration of aHUS clinical manifestation to baseline, median (range), days	6 (0.9–40.2)	5.4 (0.9–127.8)	0.50	12.9 (0.9–26.7)	29.4 (0.9–574.5)	0.06
First clinical TMA manifestation, n (%)	10 (90.9)	6 (54.5)	0.15	23 (95.8)	7 (41.2)	0.0002
No PE/PI during current manifestation, n (%)	6 (54.5)	6 (54.5)	1.00	2 (8.3)	4 (23.5)	0.21
Prior renal transplant, n (%)	1 (9.1)	1 (9.1)	1.00	3 (12.5)	6 (35.3)	0.13
Platelet count x 10^9/L, mean (SD)	105.6 (34.2)	69.4 (43.3)	0.09	108.2 (74.5)	134.7 (50.0)	0.06
Patients with platelet count <150 x 10^9/L, n (%)	11 (100.0)	11 (100.0)	1.00	18 (75.0)	9 (52.9)	0.19
LDH (U/L), mean (SD)	1357.2 (1138.3)	2530.2 (2222.1)	0.15	572.3 (627.8)	380.7 (194.3)	0.20
LDH >ULN, n (%)	8 (72.7)	11 (100.0)	0.65	19 (79.2)	13 (76.5)	0.25
Hemoglobin concentration (g/L), mean (SD)	77.6 (17.5)	83.1 (13.0)	0.60	81.9 (13.8)	96.7 (17.0)	0.01
Serum creatinine (µmol/L), mean (SD)	212.0 (146.1)	107.4 (57.2)	0.09	527.2 (280.4)	253.8 (129.9)	0.001
eGFR[b] mL/min/1.73 m^2, mean (SD)	11.2 (3.9)	54.2 (30.0)	<0.0001	10.2 (3.2)	27.3 (12.9)	<0.0001
eGFR (mL/min/1.73 m^2), n (%)			<0.0001			<0.0001
<15	10 (90.9)	0		23 (95.8)	4 (23.5)	
15–29	1 (9.1)	3 (27.3)		1 (4.2)	5 (29.4)	
30–44	0	2 (18.2)		0	6 (35.3)	
45–59	0	2 (18.2)		0	2 (11.8)	
60–89	0	2 (18.2)		0	0	
≥90	0	2 (18.2)		0	0	
Duration of dialysis during current manifestation prior to first eculizumab dose, median (range), days	7 (1.0–36.0)[c]	N/A	NE	13 (2.0–26.0)[d]	N/A	NE

aHUS, atypical hemolytic uremic syndrome; *DGKE*, diacylglycerol kinase ε; eGFR, estimated glomerular filtration rate; LDH, lactate dehydrogenase; MCP, membrane cofactor protein; N/A, not applicable; NE, not evaluated; PE/PI, plasma exchange/plasma infusion; SD, standard deviation; TMA, thrombotic microangiopathy; ULN, upper limit of the normal range.
[a]*P* values were generated by statistical comparisons between subgroups.
[b]In C10-003, the eGFR was calculated using the Schwartz formula: eGFR (mL/min/1.73 m^2) = [0.4136 x height (cm)] / SCr (mg/dL)]. In C10-004, the eGFR was calculated using the Modification of Diet in Renal Disease equation.
[c]n=10. One patient receiving dialysis at baseline was not included in the calculation of pretreatment dialysis duration due to receipt of dialysis outside of the specified range from day -7 to day 14.
[d]n=18. Of the initial 24 patients on dialysis, 4 patients began dialysis between days 0 and 14, and another 2 patients had no dialysis records between their current clinical manifestation and day 0.

Efficacy Outcomes

Primary Outcome: Complete TMA Response at 26 Weeks

C10-003

- Complete TMA response was achieved in 6 of 11 patients (54.5%) with and 8 of 11 patients (72.7%) without baseline dialysis (*P*=0.66) (**Figure 2A**)
  - Median (range) time to complete TMA response was 103.0 (35.0–153.0) and 36.5 (7.0–83.0) days, respectively (*P*=0.01)

C10-004

- Complete TMA response was achieved in 17 of 24 patients (70.8%) with and 13 of 17 patients (76.5%) without dialysis at baseline (*P*=0.74) (**Figure 2B**), after a median (range) of 66.0 (28.0–147.0) and 56.0 (2.0–85.0) days, respectively (*P*=0.13)
- Modified complete TMA response was achieved in 15 of 24 (62.5%) and 8 of 17 patients (47.1%) with and without dialysis, respectively

TMA and Hematologic Outcomes at 26 Weeks

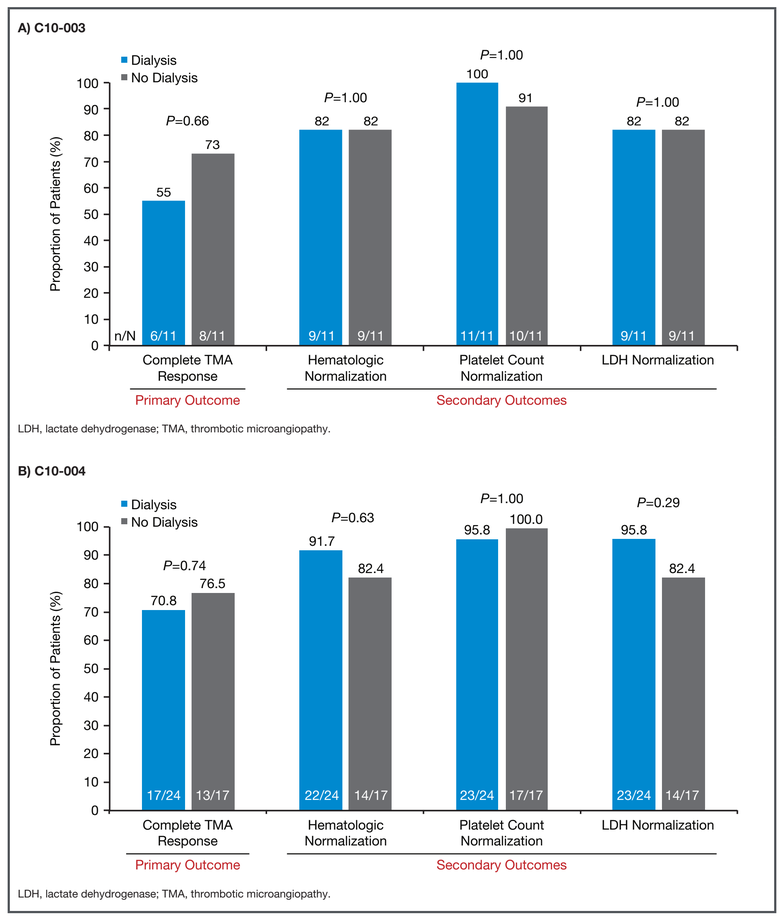
C10-003

- Eleven of 11 (100.0%) and 10 of 11 patients (90.9%) with and without baseline dialysis, respectively, achieved TMA event-free status
- Hematologic normalization, platelet count normalization, and lactate dehydrogenase normalization were achieved by similar proportions of patients with and without baseline dialysis (*P*=1.00) (**Figure 2A**)
  - Median (range) time to platelet count normalization was 7.0 (1.0–80.0) in patients with and 7.0 (6.0–19.0) days in patients without baseline dialysis (*P*=0.97)
- Eculizumab significantly improved mean platelet count change from baseline in patients with and without baseline dialysis (*P*=0.94) (**Figure 3A**)
- Of 10 patients on PE/PI at baseline (5 in each subgroup), all (100.0%) discontinued by week 26

C10-004

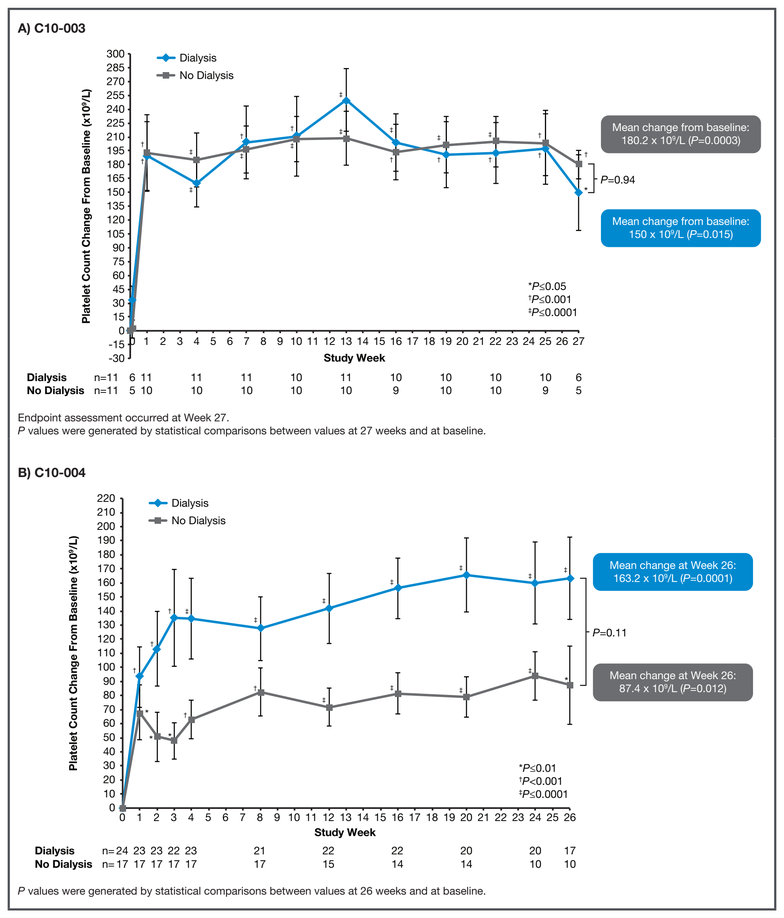
- Twenty-two of 24 patients (91.7%) with baseline dialysis and 15 of 17 (88.2%) without dialysis achieved TMA event-free status
- Similar proportions of patients with and without baseline dialysis met criteria for improvements in hematologic parameters (*P*≥0.29) (**Figure 2B**)
  - Median (range) time to platelet count normalization was 14.0 (6.0–84.0) in patients with and 8.0 (0.0–82.0) days in patients without baseline dialysis (*P*=0.14)
- Eculizumab significantly improved mean platelet count change from baseline in both subgroups (*P*=0.11) (**Figure 3B**)
- Of 24 patients with baseline dialysis, 22 also had history of PE/PI at baseline; during the study, all discontinued PE/PI (including 17 before eculizumab initiation and 5 by week 26)
- Of 17 patients without baseline dialysis, 13 had history of PE/PI at baseline; all discontinued PE/PI during the study (including 9 before eculizumab initiation and 4 by week 26)
- Four of the 6 patients not receiving PE/PI at baseline received PE/PI during the study period; of these, 2 were patients with and 2 were patients without dialysis at baseline
- No patients received PE/PI at week 26

Figure 2. Proportion of Patients in Each Subgroup Achieving Complete TMA Response, and Hematologic, Platelet Count, and LDH Normalization at 26 Weeks



LDH, lactate dehydrogenase; TMA, thrombotic microangiopathy.

Figure 3. Mean Platelet Count Improvement Over 26 Weeks



Endpoint assessment occurred at Week 27.
P values were generated by statistical comparisons between values at 27 weeks and at baseline.

P values were generated by statistical comparisons between values at 26 weeks and at baseline.

Renal Outcomes at 26 Weeks

C10-003

- Nine of 11 (81.8%) and 10 of 11 patients (90.9%) with and without baseline dialysis had eGFR improvement ≥15 mL/min/1.73 m^2 from baseline to week 26 (**Table 3**, **Figure 4A**)
- Of the 11 patients on dialysis at baseline, 9 (81.8%) discontinued during the study after a mean (range) of 7 (4.0–15.0) days; the remaining 2 patients were on dialysis at week 26 (**Table 3**)
- Of the 11 patients not on dialysis at baseline, all 11 (100.0%) remained dialysis-free during 26 weeks
- Thus, 2 (9%) of pediatric patients, who received dialysis for 7 and 36 days before initiation of eculizumab, remained on dialysis at 26 weeks

C10-004

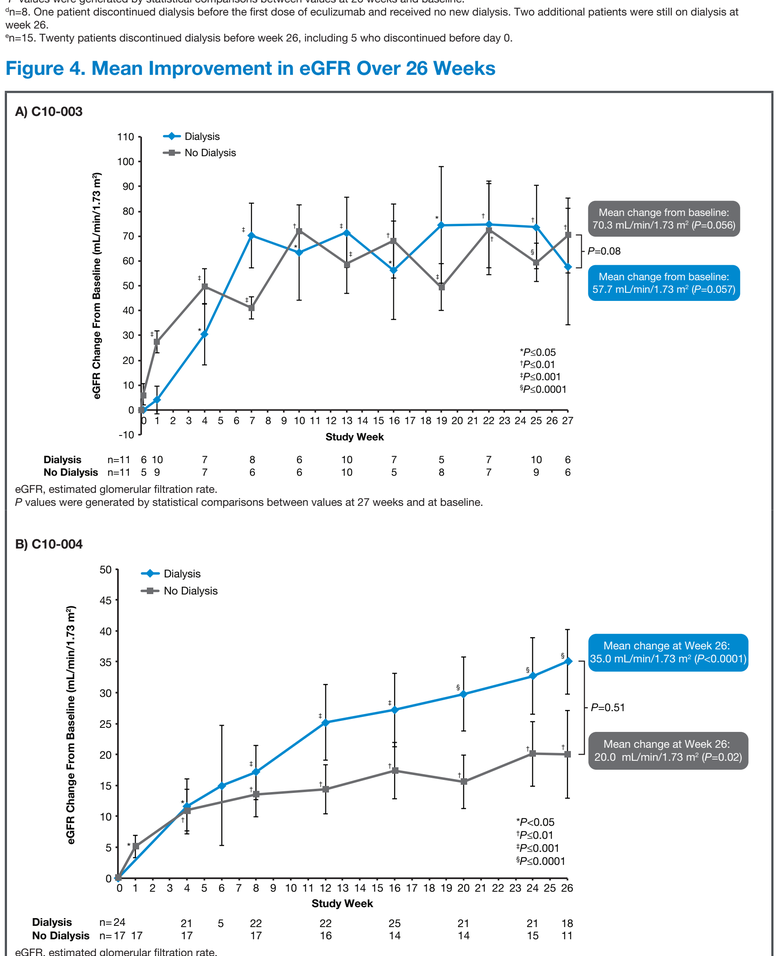
- Eculizumab significantly improved mean (SD) eGFR (mL/min/1.73 m^2) from baseline in patients with (35.0 [22.3], *P*<0.0001) and without (20.0 [23.5], *P*=0.018) baseline dialysis (*P*=0.50) (**Table 3**; **Figure 4B**)
- Of the 24 patients with baseline dialysis, 20 (83.3%) discontinued dialysis during the 26-week study period (**Table 3**)
  - Of these, 5 discontinued before the first eculizumab dose and 15 of the remaining 19 (79%) discontinued dialysis before week 26
  - Four of 19 patients (16.7%) continued dialysis at week 26
- Of the 17 patients without dialysis at baseline, 4 (23.5%) initiated new dialysis during the treatment period
  - Two patients received a mean (range) of 3.5 (2–5) days of new dialysis and subsequently discontinued dialysis; the remaining 2 continued dialysis at week 26
- Thus, a total of 6 of 41 patients (14.6%) were on dialysis at week 26

Table 3. Summary of Renal Outcomes

Parameter	Trial C10-003 Pediatric Patients (N=22) Dialysis (n=11)	Trial C10-003 Pediatric Patients (N=22) No Dialysis (n=11)	Trial C10-003 Pediatric Patients (N=22) *P* Value[a]	Trial C10-004 Adult Patients (N=41) Dialysis (n=24)	Trial C10-004 Adult Patients (N=41) No Dialysis (n=17)	Trial C10-004 Adult Patients (N=41) *P* Value[a]
eGFR change from baseline (mL/min/1.73 m^2), mean (SD)	+57.7 (57.3)[b] *P*=0.057[c]	+70.3 (37.1)[b] *P*=0.006[c]	0.08	+35.0 (22.3) *P*<0.0001[c]	+20.0 (23.5) *P*=0.0179[c]	0.50
eGFR (mL/min/1.73 m^2) at 26 weeks, mean (SD)	69.8 (59.1)	124.6 (24.6)	NE	44.5 (22.5)	51.2 (27.7)	NE
eGFR improvement from baseline ≥15 mL/min/1.73 m^2, n (%)	9 (81.8)	10 (90.9)	1.00	15 (62.5)	7 (41.2)	0.22
Serum creatinine decrease ≥25%, n (%)	7 (63.6)	9 (81.8)	0.64	15 (62.5)	9 (52.9)	0.75
CKD improvement ≥1 stage from baseline, n (%)	9 (81.8)	8 (88.9)	1.00	15 (62.5)	11 (64.7)	1.00
Patients with dialysis at baseline who discontinued dialysis during the study, n (%)	9 (81.8)	N/A	N/A	20 (83.3)	N/A	N/A
Time to discontinuation of dialysis after eculizumab initiation, median (range), days	7 (4.0–15.0)[d]	N/A	N/A	29 (1.0–180.0)[e]	N/A	N/A

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; N/A, not applicable; NE, not evaluated; SD, standard deviation.
[a]*P* values were generated by statistical comparisons between subgroups.
[b]Endpoint assessment occurred at Week 27.
[c]*P* values were generated by statistical comparisons between values at 26 weeks and baseline.
[d]n=8. One patient discontinued dialysis before the first dose of eculizumab and received no new dialysis. Two additional patients were still on dialysis at week 26.
[e]n=15. Twenty patients discontinued dialysis before week 26, including 5 who discontinued before day 0.

Figure 4. Mean Improvement in eGFR Over 26 Weeks



eGFR, estimated glomerular filtration rate.
P values were generated by statistical comparisons between values at 27 weeks and at baseline.

Health-Related Quality of Life

- In C10-003, the Pediatric Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score mean change from baseline to 27 weeks was 28.66 (range, 16.91–45.00; *P*=0.06) for patients with baseline dialysis and 20.50 (range, 2.00–32.00; *P*=0.13) for patients without a history of dialysis (*P*=0.24 between subgroups)
- In C10-004, FACIT-F score mean change from baseline to 26 weeks was statistically significant: 18.75 (range, 2.00–43.00; *P*=0.0002) for patients with baseline dialysis, and 15.28 (range, 1.00–40.00; *P*=0.002) for patients without dialysis (*P*=0.20)

Safety

- In both studies, treatment-emergent adverse events (TEAEs) were mild or moderate (**Table 4**)
- In C10-003, serious TEAEs occurring in ≥2 patients included fever, hypertension, upper respiratory tract infection, and viral gastroenteritis
  - One patient (on baseline dialysis) discontinued due to agitation, a serious TEAE
  - One patient (on baseline dialysis) had a human anti-human antibody response, and continued eculizumab treatment without apparent adverse effect and with no apparent impact on clinical response to eculizumab treatment
- In C10-004, 2 patients had meningococcal infections
  - One patient (without baseline dialysis; transplanted; serogroup unknown) discontinued eculizumab treatment on day 120 due to meningococcal meningitis, was hospitalized, and later recovered
  - The second patient (with baseline dialysis; not transplanted; serogroup B) developed meningococcal sepsis on day 133 and was hospitalized; eculizumab treatment was not interrupted, and the patient recovered without sequelae
  - Both patients had been vaccinated (quadrivalent conjugate vaccine and polysaccharide vaccine, respectively); neither received prophylactic antibiotics
- No new safety concerns or deaths occurred in either study

Table 4. Safety of Eculizumab Treatment and Summary of TEAEs

Category	Trial C10-003 Pediatric Patients (N=22) Dialysis (n=11)	Trial C10-003 Pediatric Patients (N=22) No Dialysis (n=11)	Trial C10-004 Adult Patients (N=41) Dialysis (n=24)	Trial C10-004 Adult Patients (N=41) No Dialysis (n=17)
TEAEs (frequency ≥15%), n (%)				
Abdominal pain	3 (27.3)	4 (36.4)	–	–
Acute tonsillitis	–	2 (18.2)	–	–
Alopecia	–	–	4 (16.7)	–
Anemia	–	–	4 (16.7)	3 (17.6)
Anxiety	–	–	4 (16.7)	–
Arthralgia	–	–	–	4 (23.5)
Asthenia	–	–	–	5 (29.4)
Catheter site infection	3 (27.3)	–	–	–
Cough	4 (36.4)	4 (36.4)	–	3 (17.6)
Dermatitis diaper	2 (18.2)	–	–	–
Diarrhea	3 (27.3)	4 (36.4)	7 (29.2)	6 (35.3)
Dyspepsia	2 (18.2)	–	–	–
Dyspnea	–	–	4 (16.7)	–
Edema (peripheral)	–	–	–	4 (23.5)
Headache	3 (27.3)	–	8 (33.3)	7 (41.2)
Hypertension	3 (27.3)	–	–	4 (23.5)
Hypophosphatemia	–	–	–	3 (17.6)
Hypotension	–	–	5 (20.8)	–
Leukopenia	–	–	4 (16.7)	–
Lymphadenopathy	–	2 (18.2)	–	–
Muscle spasms	–	3 (27.3)	–	–
Myalgia	–	–	–	3 (17.6)
Nasopharyngitis	2 (18.2)	4 (36.4)	4 (16.7)	3 (17.6)
Nausea	–	–	4 (16.7)	–
Neck pain	–	2 (18.2)	–	–
Oropharyngeal pain	–	3 (27.3)	–	–
Pleural effusion	2 (18.2)	–	–	–
Proteinuria	–	–	4 (16.7)	–
Pyrexia	6 (54.5)	5 (45.5)	4 (16.7)	3 (17.6)
Rash	2 (18.2)	–	–	–
Renal impairment	–	–	–	3 (17.6)
Upper respiratory tract infection	4 (36.4)	3 (27.3)	–	–
Urinary tract infections	3 (27.3)	–	4 (16.7)	3 (17.6)
Vitamin D deficiency	–	–	–	3 (17.6)
Vomiting	3 (27.3)	3 (27.3)	–	3 (17.6)
Patients with any serious TEAE, n (%)	9 (81.8)	4 (36.4)	12 (50.0)	6 (35.3)
Possible relationship to eculizumab treatment, n (%)	3 (27.3)	0 (0)	5 (20.8)	2 (11.7)

TEAEs, treatment-emergent adverse events.

CONCLUSIONS

- In these post hoc analyses, eculizumab treatment resulted in clinically meaningful improvements in hematologic and renal parameters in pediatric and adult patients with aHUS, with and without dialysis at baseline
- Approximately 80% with baseline dialysis discontinued dialysis in both trials, consistent with a prior trial in adolescents and adults[4]
  - No patient started new dialysis in the pediatric trial
- Rates of adverse events were similar between the subgroups in both studies, and no new or unexpected safety concerns were reported
- Together, these data provide additional support that sustained treatment with eculizumab is effective and well tolerated in both pediatric and adult patients with aHUS, regardless of dialysis status at baseline

REFERENCES

1. Noris M, et al. *Clin J Am Soc Nephrol*. 2010;5(10):1844-59.
2. Fremeaux-Bacchi V, et al. *Clin J Am Soc Nephrol*. 2013;8(4):554-62.
3. Johnson S, et al. *Pediatr Nephrol*. 2014;29(10):1967-78.
4. Legendre CM, et al. *N Engl J Med*. 2013;368(23):2169-81.
5. US Food and Drug Administration. Soliris (eculizumab) [prescribing information], Cheshire, CT: Alexion Pharmaceuticals, Inc.; 2014.
6. European Medicines Agency. Soliris (eculizumab) [summary of product characteristics], Paris, France: Alexion Europe SAS; 2014.
7. Legendre C, et al. Poster MP035. Presented at: European Renal Association-European Dialysis and Transplant Association; May 18-21, 2013; Istanbul, Turkey.
8. Greenbaum LA, et al. *J Am Soc Nephrol*. 2013;24:821A-2A.
9. Fakhouri F, et al. *J Am Soc Nephrol*. 2013;24:49A-50A.

ACKNOWLEDGMENTS

Editorial and medical writing assistance was provided by Peloton Advantage, LLC, funded by Alexion Pharmaceuticals, Inc.

Presented at the International Society of Nephrology (ISN) World Congress of Nephrology (WCN) 2015, March 13–17, 2015, Cape Town, South Africa