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A Retrospective Chart Review Study to Evaluate the Clinical Outcome according to Treatment in Atypical Hemolytic Uremic Syndrome Patients in South Korea: A interim analysis

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Objectives: Atypical hemolytic uremic syndrome (aHUS) is a rare disease caused by thrombotic microangiopathy (TMA) due to uncontrolled activation of the complement immune system. Eculizumab that was approved in 2016 is a humanized monoclonal antibody that blocks terminal complement C5 activation. We aim to identify the clinical characteristics of patients in Korea who were diagnosed as aHUS, and the clinical prognosis in patients treated with or without eculizumab.

Methods: In this retrospective, non-interventional, multi-center, chart review study, 57 patients who were clinically diagnosed with aHUS from 1 January 2013 to 31 December 2021 were enrolled at 15 sites in Korea. Of these, 52 patients were included in the analysis set; 12 (23%) in the eculizumab treated group, 40 (77%) in the non-eculizumab treated group. As the primary endpoint we compared the end-stage kidney disease (ESKD)-free survival rate and overall survival rate as markers to evaluate long-term survival rate according to eculizumab treatment, by using the cox-proportional hazard model.

Results: The age of diagnosis of aHUS in patients at baseline was 47.04 years. 55.77% of patients were diagnosed with TMA triggering events and 17.31% had multiple TMA. There was no significant difference between two group except for extra-renal manifestations in various baseline characteristics. The ESKD-free survival probability (78.75% vs 52.03%) and overall survival probability rate (100.00% vs 69.82%) were relatively high in the eculizumab treated group compared to the non-treated group, respectively. However, this effect was not statistically proven due to the small number of enrolled patients.

Conclusions: The results of this interim report support the characteristics of Korean aHUS patients. Furthermore, although not statistically significant, it suggests that eculizumab has the potential to improve survival in patients with aHUS. More data of patients will be collected and evaluated in future planned reports, and the effectiveness of eculizumab will be analyzed from various clinical perspectives.

Figure 1. ESKD-free survival and overall survival by eculizumab treated and non-eculizumab treated groups

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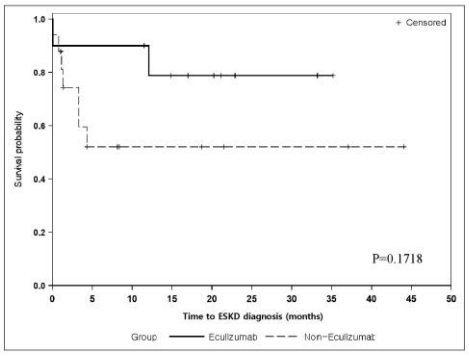
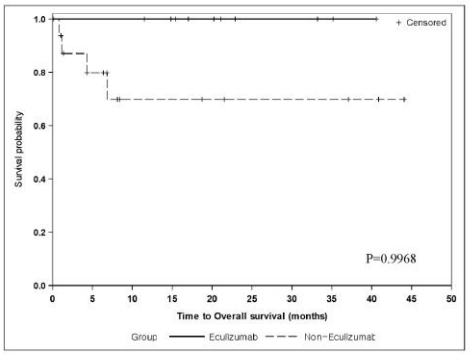
(A)



ESKD = end-stage kidney disease
ESKD-free survival: (Date of event (or censored) - first onset date of TMA diagnosed of aHUS + 1)/30.4375
- Date of event: The date of ESKD diagnosis or death of any cause, whichever comes first
- Date of censored: The last follow-up date or Eculizumab discontinued date in Eculizumab patients, and the last follow-up date in non-Eculizumab patients
Patients with 1) TMA onset diagnosed of aHUS since 2018-01-01, 2) had date of event/censored and 3) ESKD after TMA onset diagnosed of aHUS were included.

(B)



Overall survival: (Date of event (or censored) - first onset date of TMA diagnosed of aHUS + 1)/30.4375
- Date of event: The date of death of any cause
- Date of censored: The last follow-up date or Eculizumab discontinued date in Eculizumab patients, and the last follow-up date in non-Eculizumab patients
Patients with 1) TMA onset diagnosed of aHUS since 2018-01-01, 2) had date of event/censored and 3) ESRD after TMA onset diagnosed of aHUS were included.

Table 1. Demographics and baseline characteristics

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	Eculizumab (N=12)	Non-Eculizumab (N=40)	Analysis Set (N=52)	p-value
Sex, n(%)				
Male	5(41.67)	26(65.00)	31(59.62)	0.1884*
Female	7(58.33)	14(35.00)	21(40.38)	
Age at time of TMA diagnosed with aHUS (years)				
n	12	40	52	
mean(SD)	35.92(21.25)	50.38(22.38)	47.04(22.77)	0.0527**
Triggering event of TMA diagnosed of aHUS, n(%)[1]				
Patient with triggering event of TMA diagnosed of aHUS	8(66.67)	21(52.50)	29(55.77)	0.3862***
Multiple TMA, n(%)[1]				
Yes	1(8.33)	8(20.00)	9(17.31)	0.6655*
Extra-renal manifestations due to TMA diagnosed with aHUS, n(%)[1]				
Patient with extra-renal manifestations	11(91.67)	17(42.50)	28(53.85)	0.0027***
Laboratory test at TMA diagnosed of aHUS				
WBC(109/L), n	12	37	49	
median	8.92	9.22	9.22	0.8799****
Platelet(PLT) (109/L), n	12	38	50	
median	55.50	77.00	75.00	0.4331****
Hemoglobin(Hb) (g/dL), n	12	37	49	
mean(SD)	8.60(1.78)	8.44(2.03)	8.48(1.96)	0.8094**
Schistocytes, n(%)				
Yes	7(100.00)	19(79.17)	26(83.87)	0.5622*
LDH (IU/L), n	12	33	45	
median	612.50	650.00	650.00	0.8074****
BUN (mg/dL), n	12	37	49	
median	58.00	57.00	57.00	0.9815****
Serum Creatinine(SCr) (mg/dL), n	12	33	45	
median	3.42	3.10	3.11	0.5636****
eGFR (mL/min/1.73m2), n	12	31	43	
median	14.08	15.00	15.00	0.6550****
Renal biopsy, n(%)	8(66.67)	10(25.00)	18(34.62)	
With TMA	7(87.50)	7(70.00)	14(77.78)	0.5882*

min = minimum, max = maximum, SD = standard deviation

1Denominator of percentage is the number of analysis set in each treatment method.

* p-value comparing the difference between groups using Fisher's exact test
** p-value comparing the difference between groups using independent t-test
*** p-value comparing the difference between groups using Chi-square test
**** p-value comparing the difference between groups using Wilcoxon rank sum test

One patient may have 2 or more than treatment type.