MP161

INCREASED UNDERSTANDING OF ATYPICAL HAEMOLYTIC URAEMIC SYNDROME (aHUS): CHARACTERISTICS OF PATIENTS RECRUITED INTO THE GLOBAL aHUS REGISTRY

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INTRODUCTION

- Capturing epidemiological and treatment data on rare conditions is challenging and this can be compounded by geographic dispersion of the relatively small numbers of patients.[1]
  - The establishment of registries is a critical component of advancing rare disease research.[1]
- Atypical haemolytic uraemic syndrome (aHUS) is a rare genetic disease that affects both children and adults.[2-5] It is a progressive, life-threatening condition that results from chronic, uncontrolled complement activation in most patients.[3-5]
  - It is characterised by systemic thrombotic microangiopathy (TMA) leading to severe renal and other end-organ damage.[3-5]
- Plasma exchange and infusion (PE/PI) has been the treatment of choice for aHUS;[3] however, evidence suggests that PE/PI only transiently maintains normal levels of hematologic markers and does not treat the underlying condition.[4]
- Eculizumab (Soliris®; Alexion Pharmaceuticals, Inc., Cheshire, CT, USA) is a terminal complement inhibitor,[6] and the first approved treatment for aHUS in paediatric and adult patients.[6-7]
- The Global aHUS Patient Registry (NCT01522183) was initiated following approval of eculizumab at the request of the European and US regulatory authorities.
  - The registry was implemented in April 2012 and prospectively captures effectiveness and safety data on patients treated with eculizumab.
  - The registry records information on the progression of disease in all aHUS patients (whether treated with eculizumab or with other disease-management strategies).

OBJECTIVE

- To report the characteristics of patients enrolled in the aHUS registry from its inception (April 2012) through to September 2013.

METHODS

Patient Eligibility Criteria

- Male or female patients of any age with a clinical diagnosis of aHUS.
  - With or without an identified complement regulatory factor genetic abnormality or anticomplement factor antibody (if tested).
  - ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) >5%, if performed.
- Patients were excluded if they had haemolytic uraemic syndrome due only to Shiga toxin-producing *Escherichia coli*.
- All patients (or legal guardians) provided written informed consent to take part.

Primary Outcome Measures Collected

- Proportion of patients who experience specified events and time to first and subsequent occurrence of specified events.
- Long-term manifestations of TMA complications of aHUS.
- Safety and efficacy of eculizumab.
- Other clinical outcomes, including morbidity and mortality in patients receiving eculizumab or managed differently.

Data Collection

- The following data are collected at study enrolment and every 6 months thereafter:
  - Demographics
  - Medical and disease history
  - Symptomatology
  - Targeted laboratory results (including genetic results)
  - TMA complications
  - Associated treatments and concomitant medications
  - Clinical and patient-reported outcomes
  - Safety of eculizumab and other aHUS treatments.
- Each patient will be followed for a minimum of 5 years; data are stored anonymously.

Registry Support

- The registry is supported by Alexion Pharmaceuticals, Inc., with governance by an independent scientific advisory board and national coordinators representing each participating country.

RESULTS

Patient Recruitment

- Between inception and 09 April 2014, 441 patients from 14 countries worldwide were enrolled in the Global aHUS Patient Registry.
- In Europe, 295 (66.9%) patients were recruited from 10 countries (**Figure 1**).
- Outside of Europe, 100 (22.7%), 26 (5.9%), 16 (3.6%) and 4 (0.9%) patients were enrolled in the USA, Australia, Israel and Canada, respectively.

Characteristics of Enrolled Patients

- **Tables 1–4** provide information on demographics, aHUS diagnosis, baseline clinical characteristics and eculizumab treatment characteristics for the 211 patients enrolled at last data cutoff (18 September 2013).

Figure 1. European Distribution of Patient Enrolment April 2014

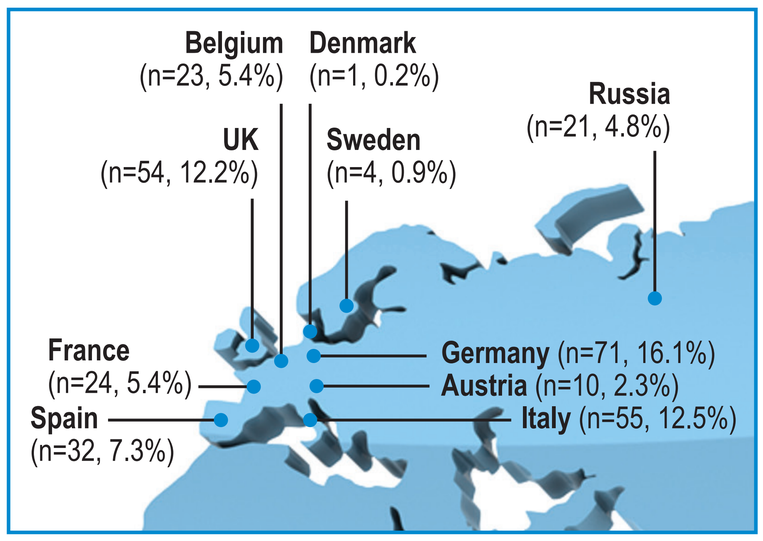

Table 1. Patient Demographics

	Ever treated with eculizumab (n=104)	Never treated with eculizumab (n=107)	Total (N=211)
Mean age at registry enrolment (SD), years	n=100 24.9 (21.0)	n=98 25.0 (17.2)	n=198 25.0 (19.2)
Age at registry enrolment, n (%)			
<2 years	17 (16.3)	2 (1.9)	19 (9.0)
≥2 to <5 years	8 (7.7)	7 (6.5)	15 (7.1)
≥5 to <12 years	15 (14.4)	18 (16.8)	33 (15.6)
≥12 to <18 years	5 (4.8)	16 (15.0)	21 (10.0)
≥18 years	55 (52.9)	55 (51.4)	110 (52.1)
N/A	4 (3.8)	9 (8.4)	13 (6.2)
Sex, n (%)			
Female	58 (55.8)	45 (42.1)	103 (48.8)
Male	46 (44.2)	54 (50.5)	100 (47.4)
N/A	0	8 (7.5)	8 (3.8)

N/A, not available; SD, standard deviation

Table 2. aHUS Diagnosis Characteristics

	Ever treated with eculizumab (n=104)	Never treated with eculizumab (n=107)	Total (N=211)
Mean age at initial symptoms (SD), years	n=93 23.8 (21.4)	n=76 17.1 (16.4)	n=169 20.8 (19.5)
Mean age at diagnosis (SD), years	n=94 23.9 (21.4)	n=75 17.1 (16.8)	n=169 20.9 (19.8)
Stated family history of aHUS			
Yes	16 (15.4)	20 (18.7)	36 (17.1)
No	88 (84.6)	87 (81.3)	175 (82.9)
Any identified complement genetic mutation or autoantibody, or CFHR1/3 deletion, n/N screened (%)			
Yes	47/88 (53.4)	45/69 (65.2)	92/157 (58.6)
No	41/88 (46.6)	24/69 (34.8)	65/157 (41.4)

N/A, not available; SD, standard deviation

Table 3. Baseline Clinical Characteristics

	Ever treated with eculizumab (n=104)	Never treated with eculizumab (n=107)	Total (N=211)
Management history prior to enrolment, n (%)			
Kidney transplant	14 (13.5)	20 (18.7)	34 (16.1)
Dialysis	58 (55.8)	33 (30.8)	91 (43.1)
Plasma exchange/infusion	59 (56.7)	31 (29.0)	90 (42.7)
Mean baseline eGFR (SD), mL/min/1.73 m^2	n=39 42.8 (48.1)	n=29 76.0 (63.8)	n=68 57.0 (57.3)

SD, standard deviation

Table 4. Characteristics of Patients Treated with Eculizumab

	Ever treated with eculizumab (n=103)
Mean age at eculizumab treatment initation (SD), years	n=99 24.9 (21.1)
Mean time on eculizumab (SD), years	n=100 1.2 (0.89)
Any discontinuation of eculizumab, n (%)	
No	86 (83.5)
Yes	17 (16.5)
Restarted eculizumab (among those who discontinued), n (%)	
No	14 (82.4)
Yes	3 (17.6)

SD, standard deviation

CONCLUSIONS

- The Global aHUS Patient Registry will contribute towards increasing the understanding and awareness of aHUS disease history and progression.
- Data collected via the registry will also improve knowledge of the safety and efficacy of eculizumab in aHUS.
- As of 18 September 2013, 211 patients were enrolled
  - Mean age at diagnosis was 21 years
  - Family history of aHUS was reported by 36 (17%) patients
  - Of those screened, 59% had an identified complement mutation
  - 34 (16.1%) patients had previously received a renal transplant.
- In April 2014, 441 patients had been enrolled.
- Results of analyses from collected data will ultimately provide the opportunity to optimise care and improve quality of life for patients with aHUS.

Presented at the 51st ERA-EDTA congress, 31 May – 03 June 2014, Amsterdam, Netherlands

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ACKNOWLEDGEMENTS

The authors would like to acknowledge Bioscript Medical, which provided editorial support with funding from Alexion Pharma Intl.