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CHRONIC KIDNEY DISEASE. PATHOPHYSIOLOGY, PROGRESSION & RISK FACTORS - 2

SP283 RISK OF THROMBOTIC MICROANGIOPATHY IN PATIENTS WITH ATYPICAL HAEMOLYTIC URAEMIC SYNDROME DISCONTINUING FROM CHRONIC ECULIZUMAB THERAPY

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Introduction and Aims: Atypical haemolytic uraemic syndrome (aHUS) is a rare, genetic life-threatening disorder characterised by thrombotic microangiopathy (TMA) and end organ damage. Clinical manifestations of TMA are seen throughout disease progress and, historically, outcomes have been poor. Prospective clinical trials (100 patients [pts]) have shown eculizumab (Ecu), a monoclonal antibody blocking terminal complement, to inhibit complement-mediated TMA and be well tolerated in pts with aHUS. Life-long treatment with Ecu is indicated for pts with aHUS due to risk of TMA, but discontinuation of treatment has been attempted.
Methods: A retrospective analysis of a series of selected cases of 6 pts with aHUS where Ecu therapy was discontinued or altered from the indicated dosing regimen.
Results: Pt details including genetic mutation, duration of Ecu treatment and outcomes post Ecu discontinuation are described in the table. During Ecu treatment, all pts demonstrated improvement or normalisation of haematological parameters and no new TMA manifestations. Four pts had improved renal function, while 2 remained on dialysis. The median time on indicated Ecu dose was 5.2 (range 1–14) months and the median time to new TMA post-discontinuation was 3 (range 2–12) months. Two pts have not had any new TMA manifestations following alteration or discontinuation of the approved dosing regimen. Pt 4 has continued to receive Ecu at a reduced dose (900 mg/month) for 12 months and pt 6 discontinued Ecu and has been followed-up for 19 months.
Conclusions: Discontinuation of chronic Ecu treatment in this case series of pts with aHUS led to new TMA manifestations in 4/6 pts (2 without identified mutations, 1 with an MCP mutation and 1 with a C3 mutation) requiring re-initiation of Ecu. These findings highlight the importance of sustained complement blockade in pts with aHUS.

Table. Patient case series

	1	2	3	4	5	6
Age(years) and gender	37, F	22, M	16, F	37, F	38, F	39, M
Complement mutation	MCP	No mutation identified	C3	MCP, homozygous CFH risk haplotype	No mutation identified	No mutation identified, homozygous CFH risk haplotype
Previously transplanted	N	N	N	Y	Y	N
Time on Ecu (months)	4.5	6	6	3	14	1
Time to new TMA event after discontinuation (months)*	3	2	3	N/A	12	N/A
Reason for new TMA event	Unknown	Unknown	Upper airway infection	N/A	Influenza vaccination	N/A

*Pt 4 did not discontinue but received a reduced dose of Ecu (900 mg/month) for 12 months
CFH, complement factor H; Ecu, eculizumab; N/A, not applicable; TMA, thrombotic microangiopathy