Daratumumab for Refractory and Frequently Relapsing Immune Thrombotic Thrombocytopenic Purpura – a Case Series with Long-Term Follow-up –

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INTRODUCTION

- Immune thrombotic thrombocytopenic purpura (iTTP) is a life-threatening thrombotic microangiopathy (TMA) caused by inhibitory autoantibodies to ADAMTS13.
- Management of acute iTTP consists of daily therapeutic plasma exchange (TPE), administration of the anti-VWF nanobody caplacizumab, and immunosuppression with corticosteroids.
- Despite this, 30% of patients relapse with some patients being refractory to treatment with persistence of ADAMTS13 deficiency and inhibitor, and some showing a frequently relapsing course (r/r iTTP).
- Management of r/r iTTP patients is challenging and no consensus guidelines currently exist.
- Daratumumab, an anti-CD38 antibody, has emerged as an efficacious and safe therapeutic option for a variety of autoimmune diseases, including single patients with iTTP.

METHODS

- Retrospective analysis from 3 Swiss centres.
- 8 treatment episodes with daratumumab in 5 patients (4 treatments in 3 patients, University Hospital Zürich; 3 in 1 patient, University Hospital Bern; 1, University Hospital Basel).
- Patient-level data from January 1st, 2014 through July 1st, 2024 included disease course, treatment with response and adverse reactions, ADAMTS13 activity and inhibitor levels.
- ADAMTS13 recovery following treatment was defined as partial (ADAMTS13 activity >20%) and complete (>50%).

CONCLUSION & OUTLOOK

- Following daratumumab, most patients that responded achieved complete ADAMTS13 recovery. At 12 months this was maintained in the majority of patients and at 24 months in some of these.
- Only mild adverse reactions occurred
- Our retrospective evaluation indicates that daratumumab could be an efficacious and safe option for r/r iTTP patients failing to respond to rituximab.
- Prospective studies are warranted to confirm the long-term efficacy and safety of daratumumab treatment in such patients.

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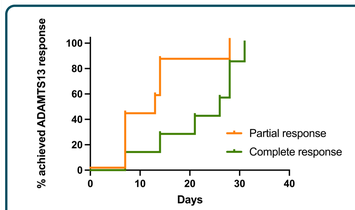
AIM OF THE STUDY

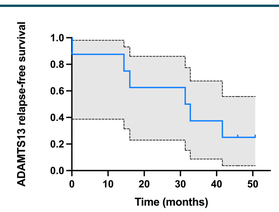
Highlight the efficacy of daratumumab therapy in the setting of refractory and frequently relapsing iTTP (r/r iTTP) by illustrating five real-life cases from our centres.

RESULTS

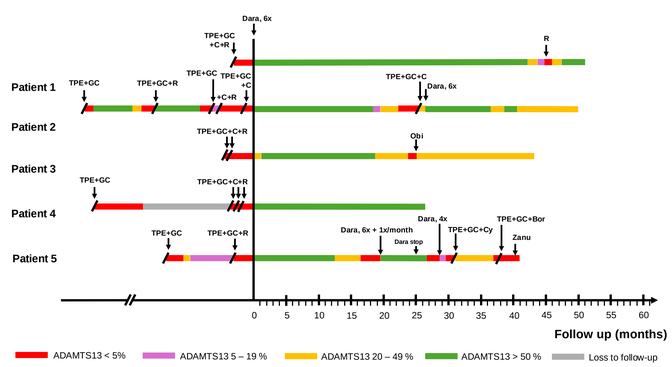
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age at diagnosis (years)	31	26	32	19	28
Sex	Female	Male	Female	Female	Male
# of daratumumab cycles (applications per cycles)	1 (6)	2 (6, 6)	1 (6)	1 (6)	3 (6, 6, 4)
# of previous iTTP episodes	0	2	1	3	3
Associated disease	Hypothyroidism	none	none	none	Metabolic syndrome
Median # of prior lines of treatment	2	5	2	4	2
Type of episode treated	Primary refractory	Frequently relapsing	Primary refractory	Primary refractory	Frequently relapsing
Treatments (days)					
TPE	15	22	11	24	23
GC	101	816	432	384	412
Caplacizumab	121	30	37	30	0
Rituximab	4	8	8	4	6
Obinutuzumab	0	0	1?	0	1
Daratumumab	6	12	6	6	22
ADAMTS13 at daratumumab initiation	< 5%	< 5%	< 5%	< 5%	< 5%

	Results (range)
Median # of infusions	6 (4 - 22)
Response rates	
Partial (ADAMTS13 activity 20 – 50 %)	0
Complete (ADAMTS13 activity > 50 %)	7
None	1
ADAMTS13 activity at response, median (%)	
max.	78 (53 – 102.2)
at 6 weeks	67 (43 – 100)
Time to reach response, median (days)	
Partial	14 (7 – 28)
Complete	26 (7 – 31)
ADAMTS13 relapse after initial daratumumab response	5
Time to next treatment, median (months)	19 (9 – 40)
Follow-up, median (months)	44 (27 – 52)
Daratumumab-associated adverse events (#)	2





In all cases with response, daratumumab treatment led to the rapid eradication of ADAMTS13 inhibitor and recovery of ADAMTS13 activity. The estimated median time to partial and complete ADAMTS13 response was 13 and 26 days, respectively. With a median follow-up of 44 months (27 - 50), median ADAMTS13 RFS was 32 months; 12-month ADAMTS13 RFS was 85.7%.



Abbreviations: TPE, total plasma exchange; GC, glucocorticoids; C, caplacizumab; R, rituximab; Dara, daratumumab; Obi, Obinutuzumab; Cy, cyclophosphamide; Bor, bortezomib; Zanu, zanubrutinib.

Of eight treatment episodes with daratumumab, 7 achieved complete ADAMTS13 activity recovery > 50% (87.5%). Mean ADAMTS13 activity at response was 70% (n=7, SD 23.1%). One episode (12.5%) was unsuccessful to improve ADAMTS13 activity. Of special note, daratumumab was not only able to achieve durable remission rates in patients with frequently relapsing disease off-label treatment was surprisingly efficient in even those patients with severely refractory disease. Exposure to daratumumab in these cases lead to rapid eradication of ADAMTS13 inhibitors.