The UK Experience of Daratumumab Monotherapy in Relapsed Systemic AL Amyloidosis

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INTRODUCTION / METHODS

- Whilst patient survival in AL amyloidosis [1] is improving, most patients still relapse thus there is a need to develop new novel agents for use in this setting.
- Daratumumab is a monoclonal antibody, which targets CD38; an antigen expressed on malignant plasma cells in AL amyloidosis thus providing a rationale for its use [2].
- Fifty-three patients treated with daratumumab monotherapy (2016-2019) for relapsed / refractory systemic AL amyloidosis were identified from the database at the UK National Amyloidosis Centre.

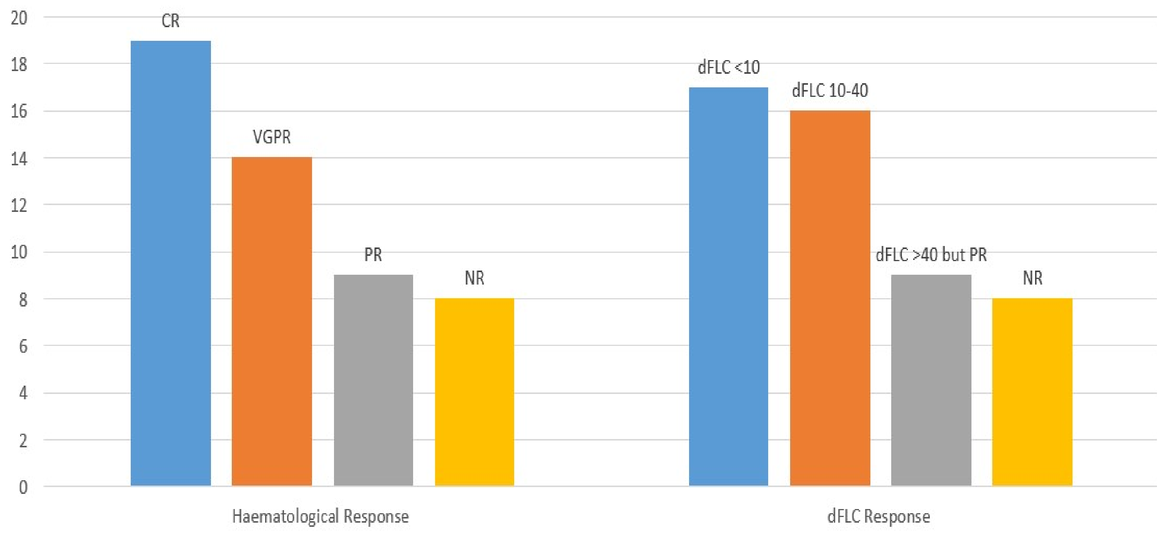
RESULTS

Median age 68 (42-85) years; 34 (64.2%) male.
Prior lines of therapy: Bortezomib: 92.5%, Lenalidomide 83.0%, Autologous stem cell transplantation 24.5%.
Organ involvement in AL amyloidosis: Cardiac: 73.6%, Renal: 56.6%, Liver: 26.4%

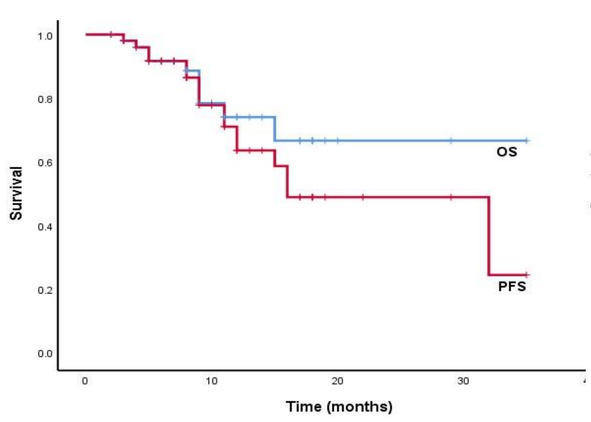
Haematological Response:

- Median time from diagnosis to commencing daratumumab was 32 (3-115) months
- Median time to response was 1 (1-6) month. Beyond 3 months, only 2 patients, who had not yet responded, achieved a haematological response.

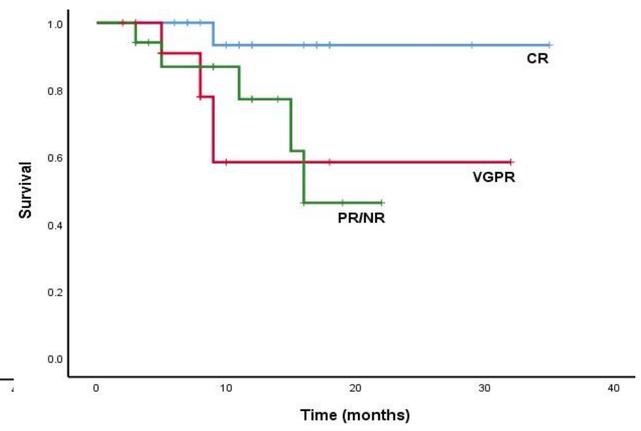
- <u>Six month organ response</u>:
  Cardiac: 16 assessable. 7/16 responded, 4/16 progressed.
  Renal: 8 assessable. 2/8 responded, 1/8 progressed.
  Hepatic: 8 assessable. No responders, 3/8 progressed.



Overall (OS) and Progression-free Survival (PFS)



OS by Haematological Response



- Median follow up 9 (2-35) months during which, 66.0% continue on daratumumab, 18.9% died, 7.5% stopped therapy and 7.5% moved to next line therapy.
- Median PFS: 19.9 (95% CI: 8.2-31.8) months
- Median OS: Not reached
- Median OS in patients achieving complete haematological response (CR) (not reached) vs. lesser haematological response (median 22.7 [95% CI: 17.0-28.4] months (p=0.04)
- Patients achieving rapid response (at 1 month) had a longer median PFS (not reached) than those who responded later (9 [95% CI: 5.8-12.2] months) (p=0.013).

Adverse event	Any grade, n (%)	Grade 3-4, n (%)
Infusion Reaction	7 (13.2)	0
Fatigue	6 (11.3)	0
Thrombocytopenia	6 (11.3)	0
Infection	5 (9.4)	0
Anaemia	5 (9.4)	1 (1.9)
Fluid Overload	4 (7.5)	2 (3.8)
Diarrhoea	3 (5.7)	0
Fall	2 (3.8)	2 (3.8)
Nausea	2 (3.8)	0
Insomnia	2 (3.8)	0
Hypertension	1 (1.9)	0

CONCLUSIONS

Daratumumab monotherapy is a safe, effective therapy in patients with multiply-relapsed systemic AL amyloidosis

Responses are rapid, seen in 84% patients and long lasting, especially in rapid-responders (within a month)

Furthermore, 43.8% of evaluable patients with cardiac involvement demonstrate an organ response making daratumumab an attractive option in this subgroup

Disclosures: No conflicts of interest to declare

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[1] Quock TP, Yan T, Chang E, et al. Epidemiology of AL amyloidosis: a real-world study using US claims data. Blood Adv. 2018;22(10):1046-1053.
[2] Seckinger A, Hillengass J, Emde M, et al. CD38 as Immunotherapeutic Target in Light Chain Amyloidosis and Multiple Myeloma-Association With Molecular Entities, Risk, Survival, and Mechanisms of Upfront Resistance. Front Immunol. 2018;9:1676.

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