Light-Chain Amyloidosis Patients Treated With Daratumumab: A Single-Center Experience

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Introduction

Light chain (AL) amyloidosis is an extreme form of systemic amyloidosis, causing organ dysfunction, mainly affecting the heart and kidneys.Current treatment AL amyloidosis based on anti-plasma cell therapies.

The achievement of a deep haematologic response is the first goal of therapy, since it associates with organ response and improved overall survival.

Background

Daratumumab was the first monoclonal CD38 antibody approved for the treatment of AL amyloidosis.

The use of daratumumab has demonstrated significant effectiveness and tolerability in patients with AL amyloidosis.

There are few real-world data about the use of Daratumumab in patients with AL amyloidosis from Latin America.

Objective

Describe the hematological and organ response in patients with AL amyloidosis treated with daratumumab.

Materials & Methods

A retrospective cohort of adult patients (≥18 years of age), diagnosed with AL amyloidosis treated with Daratumumab at the Hospital Italiano de Buenos Aires from January 2018 to April 2022.

Daratumumab was administered intravenously with low-dose dexamethasone alone or in combination with cyclophosphamide, bortezomib, and dexamethasone.

In patients with cardiac compromise, the dose of daratumumab was divided over two days and bortezomib was also adjusted to reduce toxicities. Data was obtained from the Institutional Registry of Amyloidosis.

Results

Twelve patients were included. One patient died during the first cycle of daratumumab, and the remaining 11 patients completed a median of 11 (IQR, 2-30) cycles. Overall, ten (83%) patients presented a hematologic response after a median of 1.5 cycles of treatment. Median time-to-hematologic response was 1.5 months.

Four of the evaluable patients achieved a cardiac response, with a median time to response of 8 months. Two of the evaluable patients achieved a renal response, with a median response time of 16 months.

After a median follow-up of 21 months, one patient underwent a successful cardiac transplant and autologous stem cell transplantation (ASCT), while two other patients were in preparation for ASCT.

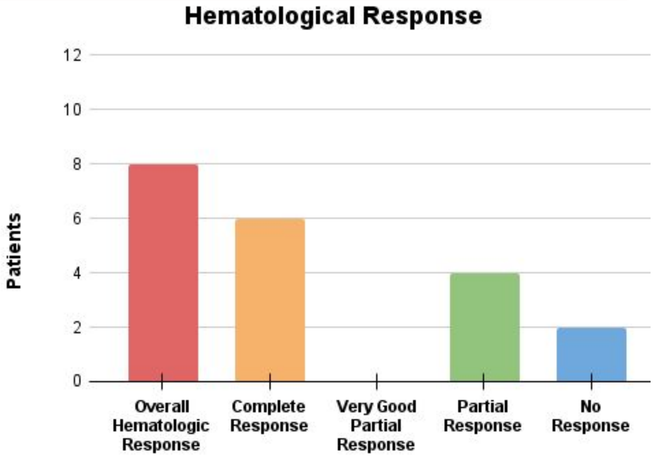
Seven patients remained on daratumumab at the last follow-up.

Regarding tolerability, there were no unexpected toxicities,although more than half of our patients had advanced cardiac stage.

Table 1. Baseline (at the start of daratumumab) characteristics of the patients (n=12).

Variable	Median (IQR)/n (%)
Age (years) median (IQR)	64 (IQR, 43-77)
Male/Female (n/n)	4/8
Newly diagnosed/Relapsed or refractory disease (n/n)	5/7
Time from diagnosis (months) median (IQR)	16 (IQR, 2-39)
Prior lines of treatment	2 (IQR, 1-4)
Prior Bortezomib	7 (100%)
Prior IMiD	2 (29%)
Prior ASCT	3 (29%)
Best prior response VGPR	1 (14%)
Best prior response < VGPR	5 (72%)
Refractory to last treatment	1 (14%)
Number of organs involved	2 (IQR, 1-3)
Cardiac involvement	9 (75%)
NT-ProBNP (pg/mL)	4430 (IQR, 171-11086)
Mayo 2012 stage	
I	2 (17%)
II	2 (17%)
III	3 (25%)
IV	4 (33%)
Unknonw	1 (8%)
Kidney involvement	6 (50%)
Proteinuria >5 g/24 h	2 (17%)
dFLC (mg/L)	282 (IQR, 23-1556)
Plasma cells in bone marrow (%), median (IQR)	20 (IQR, 5-40)

ASCT: autologous stem-cell transplant; dFLC: difference between involved/uninvolved free light chain; IMiDs: immunomodulatory drugs; IQR: interquartile range; NT-ProBNP:N-terminal prohormone of brain natriuretic peptide.



Conclusions

Daratumumab induces deep and rapid hematologic response in newly diagnosed and previously treated AL amyloidosis patients. Intravenous administration is tolerated, even in patients with advanced heart disease.

Patients reached a rapid normalisation of serum FLC without relevant toxicity.

Understanding the effective treatment strategies and adapting to a patient-tailored approach is of paramount importance.

References

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