THE IMPACT OF FIRST-LINE DARATUMUMAB ON LIGHT-CHAIN AMYLOIDOSIS SURVIVAL: A REAL-WORLD ANALYSIS OF 70 PATIENTS

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INTRODUCTION

Daratumumab-based induction therapy has become the standard of care for light-chain (AL) amyloidosis following the landmark ANDROMEDA trial [1]. However, important clinical questions remain, including the optimal combination partners, treatment duration, and dexamethasone dosing. Furthermore, strategies for managing suboptimal responses are still debated. Real-world evidence is needed to address these gaps and refine clinical practice.

AIM

To evaluate the real-world impact of daratumumab-based frontline therapy on survival and organ responses in patients with AL amyloidosis treated at our institution.

METHOD

We retrospectively analyzed 70 patients with AL amyloidosis treated between 2013 and 2025 at our institution. Daratumumab became available in 2022, although its use was partially limited by reimbursement restrictions. Clinical characteristics, treatment regimens, survival outcomes, and organ responses were analyzed. Survival endpoints included overall survival (OS) and major organ deterioration progression-free survival (MOD-PFS).

CONCLUSIONS

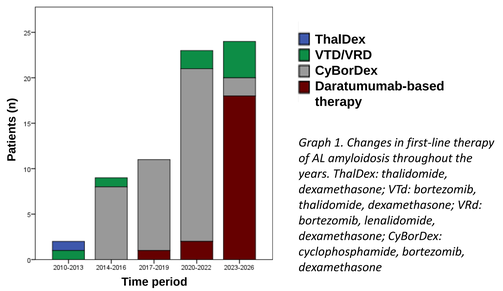
These real-world findings support the use of front-line daratumumab in AL amyloidosis. De-escalated dexamethasone dosing and a limited number of treatment cycles may be sufficient to achieve favorable clinical outcomes while maintaining treatment efficacy.

RESULTS

Patient Characteristics and First-Line Treatment

Characteristic	All patients (N=70)	ANDROMEDA-eligible patients (N=48)
Male/Female — no.	26/44	30/28
Median age (range) — yr.	66.4 (44.3–85.7)	63.8(44.3– 84.6)
AL isotype kappa/lambda — no.	20/50	16/32
Median dFLC (range) — mg/liter	240(4–5391)	191(4–1879)
Cardiac stage I /II /III /IV — no.	15/26/23/6	7/14/10/4
European modified Mayo Clinic stage I /II /IIIa /IIIb — no.	5/17/26/22	5/17/26/-

Table 1. Patient characteristics



Graph 1. Changes in first-line therapy of AL amyloidosis throughout the years. ThalDex: thalidomide, dexamethasone; VTd: bortezomib, thalidomide, dexamethasone; VRd: bortezomib, lenalidomide, dexamethasone; CyBorDex: cyclophosphamide, bortezomib, dexamethasone

Major Organ Deterioration Progression-Free Survival

The ANDROMEDA trial introduced the concept of major organ deterioration–progression-free survival (MOD-PFS)*, demonstrating a significant survival benefit with daratumumab compared with the control arm.

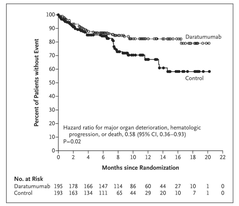
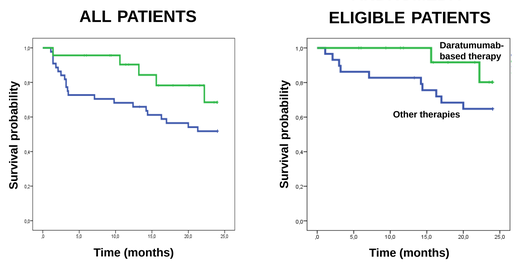


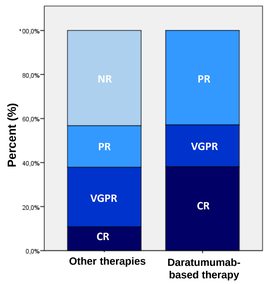
Image 1. Results of the ANDROMEDA trial[1]

In our real-world cohort, we observed a similar trend, with daratumumab showing a borderline significant benefit in MOD-PFS (p=0.09). Interestingly, among patients who met the ANDROMEDA eligibility criteria, the association was less pronounced and did not reach statistical significance.



*Graph 2. and 3. Kaplan–Meier Estimates of Survival Free from Major Organ Deterioration or Hematologic Progression (MOD-PFS)**
**Major organ deterioration was defined as end-stage cardiac or renal failure.*

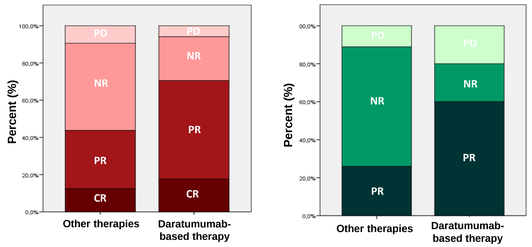
Therapeutic response



Regarding hematologic response, we observed a significantly higher rate of complete responses in the daratumumab group (p=0.001). Notably, there were no patients in this group who failed to achieve any hematologic response.

Graph 4. Hematologic response rate between patients treated with daratumumab-based treatment vs. other therapies. CR: complete remission; VGPR: very good partial response; PR: partial response; NR: no response

In contrast, the difference in organ response between the two groups did not reach statistical significance, which may partly be explained by the shorter follow-up period (p=0.35 and p=0.2).



Graph 5. and 6.: Cardiac and renal response rate between patients treated with daratumumab vs. other therapies. CR: complete remission; VGPR: very good partial response; PR: partial response; PD: progressive disease

De-escalation

In our institutional practice, cyclophosphamide was not included in induction, dexamethasone was given at only 8 mg weekly, and, mainly due to funding constraints, patients received a median of 8 cycles of daratumumab instead of the 24-month maintenance used in the ANDROMEDA trial.
Despite this less intensive approach, our outcomes were comparable to ANDROMEDA, raising the question of whether the clinical and financial burden of intensive induction and prolonged maintenance can be reduced without compromising outcomes.

CONTACT INFORMATION

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REFERENCES

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