4. SPECIAL CONDITIONS

DARATUMUMAB IN PATIENTS WITH AL AMYLOIDOSIS: A PORTUGUESE MULTICENTER REAL-WORLD STUDY

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Introduction. Light-chain (AL) amyloidosis remains a plasma cell dyscrasia with limited therapeutic options and challenging management. Daratumumab (DARA), an anti-CD38 monoclonal antibody, has demonstrated high efficacy in clinical trials, changing the treatment paradigm of AL. However, real-world data are scarce but essential, particularly in frail and unselected patients.

Methods. A multicenter retrospective study in Portugal including AL patients treated with daratumumab in first line (1L) or at relapse, assessing baseline characteristics, treatments, responses, and progression-free survival (PFS) and overall survival (OS).

Results. A total of 67 patients were included, median age 65 years (39–84), 55% male, 89.6% ECOG PS 1–2. Median time from symptom onset to diagnosis was 5 months (m) (1–25 m), with 41.8% having 1–2 organs involved and 16.6% ≥3 organs, most frequently heart (73%) and kidney (72%). Mayo 2012 stages were I (16.4%), II (26.9%), III (29.9%), and IV (26.9%). Daratumumab was used in 1L in 68.7% and at relapse in 31.3% of patients. In 1L, DARA achieved superior hematologic responses compared with non-DARA regimens: CR 54% vs. 10%, ≥VGPR 91% vs. 43%, and PD 0% vs. 24%. Organ response was also more frequent in the DARA group (kidney 48% vs. 19%; heart 63% vs. 38%). Regarding toxicity, grade 3–4 hematologic events occurred in 9% (DARA) vs. 10% (non-DARA), cardiovascular events in 17% vs. 10%, and infections in 11% vs. 5%. With a median follow-up of 25 months (2–180), 3-year PFS was 80% vs. 40% (p=0.004) in 1L with and without DARA, respectively, and median OS was not reached in either group (OS 80% at 8 years for the whole cohort). In multivariate analysis, ≥VGPR (HR 0.27; p=0.023), ECOG PS 0–1 (HR 0.17; p=0.018), and use of DARA in 1L (HR 2.56; p=0.04) were independently associated with prolonged PFS, while NT-proBNP ≥8500 ng/mL was associated with inferior OS (HR 4.15; p=0.034).

Conclusions. This real-world study confirms the efficacy of DARA in AL, with superior hematologic and organ responses in 1L, albeit with higher cardiovascular and infectious toxicity. Depth of response (≥VGPR), ECOG PS 0–1, and first-line use were associated with longer PFS, whereas elevated NT-proBNP was associated with poorer OS. These data support the use of DARA-based combinations as an early first-line standard therapy and highlight the need for, and importance of, real-world studies.