

4. SPECIAL CONDITIONS

BISPECIFIC ANTIBODIES IN RELAPSED/REFRACTORY AL AMYLOIDOSIS: CLINICAL EXPERIENCE IN TWO ACADEMIC BELGIAN CENTERS

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Background. Patients diagnosed with systemic AL amyloidosis benefit from plasma cell-directed therapies similar to those used in multiple myeloma (MM). The goal of therapy is to rapidly and significantly reduce free light chains, in order to prevent further organ damage and enhance survival. The current first-line of care combines daratumumab with VCD. In the absence of approved options for relapsed/refractory (RR) disease, we conducted a retrospective review of cases who had progressed after daratumumab and were treated with an anti-BCMA bispecific antibody in two academic Belgian centers.

Results. The cohort included ten patients with RRAL amyloidosis (median age 66, range 43-79). The involved light-chain was lambda in 8. Half of them had an associated MM. Cytogenetics revealed 1q amplification in 3 patients, t(11;14) in 3 others and was unknown for the others. The organ involvement was as follows: heart in 6, kidney in 6, liver in 4 (one of which required orthotopic liver transplantation), soft tissue in 2, peripheral nervous system in 2 and GI in 2. Mayo 2012 staging system was as follows: stage I in 4, II in 2, IIIA in 2 and IIIB in 2. All patients had received extensive prior therapy (median of two prior lines, range 1-5), all had been exposed to the 3 major classes of MM drugs, were refractory to daratumumab, as well as IMiDs in eight cases and venetoclax in two cases. At the time of anti-BCMA initiation, all patients had a progressive disease, marked by new organ involvement or worsening of pre-existing organ impairment. The median interval from initial diagnosis to an-

ti-BCMA injection was 40 months (range 3-50). The median number of cycles administered was 2 (range 1-6). Eight patients achieved a complete hematological response within the first cycle. The remaining 2 patients could not be evaluated. An early renal response was observed in 5 patients and an improvement in cardiac or liver function was seen in 2 of them. In terms of safety, CRS occurred in all patients (grade 1-2 in 8) within the first 3 days and resolved after one dose of tocilizumab. With the exception of one patient who developed a grade 3 neurotoxicity, no patient experienced an ICANs. Infectious complications were observed in 4 patients, all of whom required IVIg substitution. One patient presented a grade 4 rotavirus gastroenteritis, related to its prior liver transplant immunosuppression. One patient experienced subclinical pulmonary oedema related to cardiac arrhythmia, and another developed neurological complications that led to therapy discontinuation. As of January 20th 2026, all patients are alive except for two, the first of whom died of multiple organ failure despite achieving a CR, and the second as a result of multiple episodes of septicemia.

Conclusions. Anti-BCMA bispecific immunotherapy induces a rapid complete hematological response in heavily pretreated RRAL amyloidosis, with manageable toxicities, particularly low-grade CRS and almost no ICANs. Organ responses remain difficult to evaluate in view of the short follow-up period. However, early indications are encouraging and should be confirmed on a longer follow-up. These findings emphasize the potential of anti-BCMA bispecifics as a promising therapeutic option for RRAL amyloidosis patients.