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POSTER ABSTRACTS

654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

High Responses Rates with Single Agent Belantamab Mafodotin in Relapsed Systemic AL Amyloidosis

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Introduction:
Systemic AL amyloidosis, a rare incurable plasma cell disorder, has no approved treatments at relapse. Belantamab mafodotin is an antibody-drug conjugate which targets BCMA antigen approved for relapsed refractory myeloma. We report our results using belantamab mafodotin monotherapy for the treatment of patients with relapsed refractory AL amyloidosis including those traditionally excluded from clinical trials (eGFR<30 ml/min/1.73m ^{2} and cardiac Mayo stage IIIb disease).

Methods:
All patients treated with belantamab mafodotin monotherapy at standard dose (2.5 mg/kg) or dose reduction between April 2021 - July 2023. Standardised assessments including measurement of cardiac biomarkers, clonal parameters and imaging were performed and disease assessment was reported as per International Society of Amyloidosis consensus criteria.

Results:
Twenty-seven patients were included. The median age at was 65 years (range 41-76) and eight (30%) patients were aged >70 years. Eighteen (67%) had λ AL-type and nine (33%) κ AL-type. A median of two organs were involved at baseline (range 1-4) with renal and cardiac involvement in 20 (74%) and 15 (56%) respectively (3 each for Mayo stage IIIa and stage IIIb).
The median time from AL amyloidosis diagnosis to first administration of belantamab mafodotin was 69 (range 5-174) months (~6 years) with a median of 3 prior lines of treatment (range 2-6). Prior drug class exposure included proteasome inhibitors (100%), immunomodulatory drugs (81%) and anti-CD38 antibody (81%) therapy. Ten patients (37%) had undergone prior melphalan-conditioned autologous stem cell transplantation.
At the time of first belantamab mafodotin dose, the median involved free light chain concentration was 118mg/l (range 31-1778), eGFR was 40 ml/min (range 7 - 120) and a third (9/27) with an eGFR <30 ml/min/1.73m ^{2}. NT-proBNP was 845 ng/l (range 99-70,000).

At data cut-off, a median of 5 (range 1-11) doses of belantamab mafodotin were delivered. Of those with evaluable disease, best haematological overall response rate (partial response or better) was 80% (20/25) at a median time to best haematological response of 2 months (95% CI 1-4, range 1-17). Complete response (CR) or very good partial response (VGPR) was achieved in 64% (16/25). Two patients have only had 1 cycle and too early to perform response assessment.
Reasons for treatment discontinuation (n=12) were: inadequate response/progression (n=7), keratopathy (n=1), grade 3 thrombocytopenia (n=1), physician choice (n=3: discontinued due to treatment for unrelated metastatic squamous cell carcinoma but remains in CR; facilitation of renal transplant; prior to BCMA-directed CAR-T in VGPR).
At a median follow-up of 13 months follow-up (95% CI 4-18, range 1-27) from belantamab mafodotin initiation, 15 patients (56%) remain on therapy. Two patients died (1 due to progressive disease, 1 unrelated) and seven patients progressed and had subsequent line of therapy at a median time of 6 months (95% CI 2-4) in those that had a next line of therapy. Median treatment-free survival or death was 27 months (10-NR), and 1-year treatment-free survival/death was 69% (95% CI 41-86). Median overall survival (OS) is not reached. 1-year OS is 88% (95% CI 59-97).
Bilateral microcystic corneal keratopathy, the most frequent adverse event, was seen in 19 (70%) patients (5%; 1/19 grade 4).Ocular adverse events improved in all patients after treatment delay. Only one patient required treatment cessation due to ocular toxicity (despite achieving PR after one dose). Thrombocytopenia was reported in 3 (11%) (grade 3: 1; grade 2: 1). Only two patients remained on the standard dose of 2.5mg/kg for >3 cycles. Nine patients had eGFR <30ml/min and 6/9 started at a dose of 1.25mg/kg with no unexpected side effects (1 patient had grade 3 keratopathy). One patient post-renal transplantation (on tacrolimus and mycophenolate) had no significant toxicity and achieved a CR after cycle 3. No treatment-related deaths, cardiac or renal toxicities observed in our cohort.

Conclusion:

Belantamab mafadotin has high efficacy and good tolerability in multiply relapsed AL amyloidosis including efficacy in patients otherwise excluded from clinical trials. Treatment-emergent adverse events (especially keratopathy) do not preclude delivery of drug with appropriate dose reductions.

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