P903 DARATUMUMAB PLUS BORTEZOMIB AND DEXAMETHASONE IN NEWLY DIAGNOSED PATIENTS WITH MAYO 2004 STAGE 3 LIGHT-CHAIN AMYLOIDOSIS: A PROSPECTIVE PHASE 2 STUDY

Topic: Myeloma and other monoclonal gammopathies - Clinical

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Background:
Patients with systemic light-chain (AL) amyloidosis at the advanced cardiac stage exhibit extremely poor survival. Although daratumumab has shown superior outcome in treatment of AL amyloidosis according to the result of ANDROMEDA trial, whether these feeble patients can benefit from daratumumab therapy need further investigation.

Aims:
To prospectively explore the value of daratumumab plus bortezomib and dexamethasone in patients with AL amyloidosis at the advanced heart-stage.

Methods:
This is a phase 2, open-label, single center clinical trial planning to include 40 newly diagnosed patients with Mayo 2004 stage 3a and 3b AL amyloidosis at Peking Union Medical College Hospital (Beijing, China). Eligible patients should have measurable hematological disease (baseline dFLC >50mg/L). Initiation treatment includes daratumumab (intravenously at 16 mg/kg weekly during cycles 1-2, once every two weeks during cycles 3-6 and once every 4 weeks thereafter for up to 12 cycles), bortezomib (at 1.3mg/m² subcutaneously weekly during cycles 1-6) and dexamethasone (20mg weekly during cycles 1-6). Each cycle consists of 4 weeks. Treatment responses are evaluated every week during the first cycle and at the end of each cycle since cycle 2. Termination of the therapy is considered when patients have progressed disease, serious side effects related to treatment or initiation of the second-line treatment. (ClinicalTrials.gov identifier: NCT04474938)

Results:
From 28th May, 2021 to 28th January, 2022, 38 patients were enrolled. Twenty-nine (76.3%) patients were male and the median age was 59 years (range 41-77). The median NT-proBNP was 10665 pg/ml (range 803 ~ >35000) and the median cTnI was 0.17ug/L (range 0.07-3.07). Twenty-one patients (55.3%) were stage 3b. Median dFLC was 265 mg/L (range 72-2966). Twenty-four patients (63.2%) had NYHA class III or IV heart function. The median number of organs involved was 2 (range 0-4). Fourteen (36.8%) patients had kidney involvement and nine (23.7%) patients had liver involvement.

The median number of treatment cycles was 3.25 (range 0.25-9). For the best hematologic response, 34 of 38 patients (89.5%) reached ≥PR, including 18 patients (47.4%) with CR and 8 (21.1%) patients with VGPR. At the end of the first cycle, 8 patients (22.9%) achieved CR; 12 patients (34.3%) reached VGPR; 9 patients (25.7%) had PR and 6 patients (17.1%) were NR. The hematological ORR was 74.1% at 3 months (40.7% with CR and 18.5% with VGPR). The median time to the first hematologic remission was 7 days (range 7-21) and the median time to ≥VGPR was 14 days (range 7 days – 3 months). The cardiac response rate was 18.5% at 3 months and 23.5% at 6 months. After the median follow-up time of 4.5 months (range 0.7-8.6), the median OS was not reached. The 6-month survival rate of all patients was 76.6%, with 84.7% for stage 3a and 69.0% for stage 3b.
The most common grade 3 or 4 adverse events were infection (n=8, 21.1%). Infusion reaction was recorded in 5 patients (13.2%) and only 1 patient was categorized as grade 3 reaction. All of them occurred during the first time of infusion. Other serious adverse effects included grade 3 diarrhea (n=3), pneumothorax (n=1), bone fracture (n=1), deep venous thrombosis (n=1), hematuresis (n=1), gastrointestinal bleeding (n=1), ischemic stroke (n=1) and intestinal obstruction (n=1). No patients withdrew due to adverse events.

Summary/Conclusion:

Our results showed that daratumumab plus bortezomib and dexamethasone had favorable safety and potential advantage among patients with AL amyloidosis presenting severe cardiac involvement.