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P898 A PROSPECTIVE PHASE 2 STUDY TO ASSESS MINIMAL RESIDUAL DISEASE AFTER IXAZOMIB, LENALIDOMIDE, DEXAMETHASONE (IRD) TREATMENT FOR NEWLY DIAGNOSED TRANSPLANT ELIGIBLE MULTIPLE MYELOMA PATIENTS

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background:

Autologous stem cell transplantation (ASCT) proceeded by induction with proteasome inhibitor, immunomodulatory agent, +/- CD38 monoclonal antibody and dexamethasone is the standard of care (SOC) for eligible patients with multiple myeloma. Despite novel drugs, the outcome of high-risk patients is poor. This phase 2 Nordic Myeloma Study Group (NMSG) trial, NCT03376672, investigates the response to ixazomib (I), lenalidomide (R) and dexamethasone (D) (IRD) induction followed by IRD consolidation and risk-based maintenance either with R alone in non-high-risk patients (NHR) or IR in high-risk patients (HR). Here we present the preplanned results for all patients after 2 years on maintenance.

Aims:

The primary endpoint is the minimal residual disease (MRD) $<10^{-4}$ (positive or negative) by flowcytometry at any time during treatment compared to the historical Finnish Myeloma Group (FMG) trial (RVD+ASCT+R maintenance). The secondary endpoints include flow-MRD negativity $<10^{-5}$, overall response rate (ORR), safety, progression-free survival (PFS), results between NHR and HR patients and overall survival (OS). MRD was assessed every 6 months in patients achieving CR.

Methods:

A written informed consent was obtained from all patients. Altogether 120 patients were included in the study which consisted of 4 IRD cycles as induction, ixazomib 4 mg on days (d) 1, 8, 15, lenalidomide 25 mg on d 1-21, dexamethasone 40 mg weekly in 28-day cycles. Mobilization and single ASCT were performed according to the SOC. Three months post-ASCT patients received 2 IRD consolidation cycles followed by risk stratified maintenance. Patients with del17 (cut of 60%), t(4;14), t(14;16), t(14;20) or +1q were included in HR group and they received ixazomib 4 mg on d 1, 8, 15 and lenalidomide 10 mg on d 1-21/28. If well tolerated, lenalidomide was

increased to 15 mg after 3 cycles. At inclusion 52.5% of patients belonged to NHR and 47.5% to HR group.

Results:

The ORR, at least PR, with induction, was 84%. Forty-three percent (51/120) of patients were MRD $<10^{-4}$ at any time during protocol treatment versus 45% of historical control. At 2 years on maintenance 40/120 (33%) were ≥ CR and 18/40 (45%) also flow-MRD neg $<10^{-5}$. At 2 years on maintenance 82% of NHR and 74% of HR patients were progression-free (p= 0.395). In the high-risk group, patients with +1q with other HR aberration had the shortest median PFS, 24 (6-48) months.

Sustained flow-MRD negativity $<10^{-5}$ in at least two consecutive samples was detected in 12 patients in the HR group (21%) compared to 12 in the non-HR group (19%), p=0.778. Median PFS for patients with sustained flow-MRD negativity was not reached and was 38 (20-48) months for patients who lost the negativity and 29 (0-47) months for flow-MRD positive patients. OS at 3 year was 92% in NHR and 86% in HR group, p=0.573.

Treatment related mortality was 1.7% Pneumonia was the most common grade 3 SAE. Two (1.7%) secondary malignancies were diagnosed: one lung and one pancreas cancer.

Summary/Conclusion: The ORR was 84% for IRD induction and 43% had MRD $<10^{-4}$ at any time during treatment. After 2 years of maintenance 33% of patients were in ≥ CR and 45% of those were also flow-MRD negative $<10^{-5}$. There was no difference in sustained MRD negativity $<10^{-5}$ or PFS between HR and NHR patients. The 3-year OS was comparable between NHR and HR groups, 92% vs 86%, respectively. Ixazomib plus lenalidomide maintenance seemed to overcome the worse prognosis for HR in regard to PFS and OS.

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