INTRODUCTION

- Consolidation therapy post autologous stem cell transplant (ASCT) with combinations of bortezomib with an IMiD (either thalidomide or lenalidomide) and dexamethasone (Dexa) has been evaluated in patients with multiple myeloma (MM) in an attempt to deepen responses and to improve survival.
- Bortezomib, IMiDs and steroids (mainly VTD or VRD) have been administered in various combinations. However, it is not clear if the use of Dexa is needed in consolidation regimens.
- The primary endpoint of this prospective study was to explore the efficacy of VR consolidation without Dexa in newly-diagnosed MM patients who received induction therapy with bortezomib-based regimens and then they underwent high dose melphalan (HDM) and ASCT.
- Secondary endpoints include: safety, time to progression (TTP), time to next treatment (TNT), and the effects of VR on bone metabolism in the absence of bisphosphonates administration.

PATIENTS - METHODS

- Between January 2010 and November 2013, 59 consecutive patients (30/29F; median age 54 year, range 37-68 years) who achieved at least stable disease post-ASCT were entered into this study.
- Consolidation consisted of 4 cycles of VR, which started on day 100 post-ASCT.
- Bortezomib was given at a dose of 1.3 mg/m², iv (or sc when it was available), on days 1, 4, 8 and 11 of a 21-day cycle.
- Lenalidomide was given at a dose of 25 mg, p.o., daily on days 1-14.
- Patients did not receive any bisphosphonate during or post-ASCT as well as throughout the period of VR consolidation.
- Bone remodeling was studied by the measurement of the following serum indices on the day of stem cell collection prior to ASCT and then before and after VR consolidation (3 measurements for each patient):
  - i) osteoclast regulators [soluble receptor activator of nuclear factor kappaB ligand (RANKL) and osteoprotegerin],
  - ii) osteoblast inhibitors dickkopf-1 (Dkk-1) and sclerostin,
  - iii) bone resorption markers (CTX and TRACP-5b) and
  - iv) bone formation markers [bone-specific alkaline phosphatase (bALP) and osteocalcin (OC)].

EFFICACY OF VR CONSOLIDATION

- Before HDM, one (1.7%) patient had achieved a stringent complete remission (sCR), one (1.7%) was in CR, 30 (50.8%) were in very good partial remission (vgPR), 22 (37.3%) were in PR, while 5 (8.5%) patients had stable disease (Fig.1).
- After ASCT, 34 (57.6%) patients improved their status of response; in total, 14 (23.7%) patients achieved a sCR, one (1.7%) CR, 35 (59.3%) vgPR and 9 (15.3%) PR.
- After VR consolidation, 25/39 (64%) patients further improved their status of response; overall, 30 (50.8%) patients achieved a sCR, one (1.7%) CR, 26 (44.1%) vgPR and two (3.4%) PR.

THE COMBINATION OF BORTEZOMIB AND LENALIDOMIDE (VR) CONSOLIDATION POST-ASCT, IN THE ABSENCE OF Dexamethasone and Bisphosphonates, IMPROVES RESPONSE RATES AND BONE METABOLISM IN NEWLY DIAGNOSED PATIENTS WITH MULTIPLE MYELOMA

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RESULTS

- The most important adverse events (>10% of the patients, Fig.2) included neutropenia (68%, grade 3/4 23%), thrombocytopenia (59%, grade 3/4 7%), peripheral neuropathy (56%, grade 3/4 2%), anemia (50%, grade 3/4 4.5%), skin rash (34%, grade 3/4 9%), infections (34%, no grade 3/4), fatigue (20%, no grade 3/4), diarrhea (16%, no grade 3/4) and constipation (14%, 2% grade 3/4).
- No patient developed deep vein thrombosis.
- Fifteen patients (34.1%) experienced at least one infectious episode (grade 1 and 2); the majority included viral or bacterial infections of the upper respiratory tract.

TOXICITY

- The median follow-up after the ASCT was 31 months (range: 7-49 months) and 14 of 44 (31.8%) patients have progressed.
- The median TTP and TNT after the ASCT have not been reached yet (Fig.5-6).
- The probability of 4-year without progression was 55%.

CONCLUSIONS

- We conclude that 4 cycles of VR consolidation without dexamethasone is an effective regimen which improves the quality of response in approximately 40% of patients and produces long TTP.
- In the absence of bisphosphonates, VR consolidation has beneficial effects on bone metabolism and is related with the absence of SREs.