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A Phase III Study Of ASCT Vs Cyclophosphamide-Lenalidomide-Dexamethasone and Lenalidomide-Prednisone Maintenance Vs Lenalidomide Alone In Newly Diagnosed Myeloma Patients

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Abstract

Background High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) improves survival in multiple myeloma (MM). The introduction of novel agents challenged the role of ASCT at diagnosis. We conducted a multicenter 2X2 randomized trial comparing conventional chemotherapy plus lenalidomide with ASCT followed by maintenance with lenalidomide-prednisone (RP) or lenalidomide (R) alone in newly diagnosed young MM (NDMM) patients.

Methods Eligible patients with NDMM ≤ 65 years were enrolled. All patients received Rd induction (four 28-day cycles of lenalidomide 25 mg day 1-21 and low-dose dexamethasone 40 mg day 1,8,15,22) followed by stem cell mobilization. Patients were randomized to receive consolidation with CRD [six 28-day cycles of cyclophosphamide (300 mg/m^2 day 1,8,15), dexamethasone

(40 mg days 1,8,15,22) and lenalidomide (25 mg days 1-21)] or MEL200-ASCT (melphalan 200 mg/m^2 with stem-cell support). Patients were randomly assigned to receive subsequent maintenance with RP (28-day cycles of lenalidomide 25 mg days 1-21 plus prednisone 50 mg every other day) or R alone (28-day cycles of lenalidomide 25 mg days 1-21). Primary study endpoint was progression-free survival (PFS); secondary endpoints included safety, responses and overall survival (OS). Data cut off was May 30th, 2013.

Results Three-hundred and eighty-nine patients were enrolled in the trial. Patient characteristics were well balanced between CRD (n=194) and MEL200-ASCT (n=195), and between R (n=195) and RP (n=194) arms. Median follow-up was 31 months. In the intent to treat (ITT) analysis, the median PFS was not reached with MEL200-ASCT and 28 months with CRD (the respective 3-year PFS was 60% vs. 38%, HR=0.62, 95%CI: 0.49-0.85, P=0.003). Median time from enrolment to maintenance was 14 months. In the population of patients eligible for maintenance, 2-year PFS from the start of maintenance was 73% for RP and 56% for R patients (HR= 0.57, 95%CI: 0.34-0.93; P=0.03). In the subgroup of patients who received MEL200-ASCT, 2-year PFS from the start of maintenance was 83% for patients who received RP and 64% for those who received R alone (HR=0.36 95%CI: 0.15-0.87, P=0.02). In the subgroup of patients who received CRD, 2-year PFS from the start of maintenance was 64% for patients who received RP and 47% for those who received R alone (HR=0.75, 95%CI: 0.40-1.39, P=0.36). At present, no differences in OS were noticed between patients randomised to received CRD or MEL200-ASCT, and between patients who received RP or R maintenance. As expected, the rates of grade 3-4 hematologic (85% vs. 26%, P<0.001) and non-hematologic (35% vs. 19%, P=0.003) adverse events (AEs) were higher in the MEL200-ASCT arm compared with the CRD arm. The main non-hematologic AEs were infections (18% vs. 5%, P=0.001) and gastrointestinal AEs (18% vs. 3%, P<0.001). Rates of grade 3-4 hematologic (8% vs. 7%, P=0.85) and non-hematologic (12% vs. 13%, P=0.88). AEs were similar in the RP and R arms. The main non-hematologic AEs in both RP and R groups were infections (3% vs. 3%). At present, 6 second primary malignancies and 3 cases of cutaneous basalioma have been reported.

Conclusions MEL200-ASCT significantly prolonged PFS in comparison with CRD. At present no difference in OS was reported, this may be due to the low number of events and to the length of follow-up. The increase in toxicity with MEL200-ASCT did not adversely impact on efficacy. The addition of prednisone to lenalidomide maintenance significantly reduced the risk of progression in comparison with lenalidomide alone, without increasing the toxicity. Updated data with longer follow-up will be presented at the meeting.

Disclosures: Palumbo: *Amgen:* Consultancy, Honoraria; *Bristol-Myers Squibb:* Consultancy, Honoraria; *Celgene:* Consultancy, Honoraria; *Janssen Pharmaceuticals:* Consultancy, Honoraria; *Millenium:* Consultancy, Honoraria; *Onyx:* Consultancy, Honoraria. **Gay:** *Celgene:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Spencer:** *Celgene:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Larocca:** *Celgene:* Honoraria. **Caravita:** *Celgene:* Honoraria, Research Funding. **Petrucci:** *Celgene:* Honoraria. **Hajek:** *Celgene:* Honoraria; *Celgene:* Consultancy. **Boccadoro:** *Celgene:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding.

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