700 Lenalidomide, Bendamustine, and Rituximab As First-Line Therapy for Patients > 65 Years with Mantle Cell Lymphoma: Results From the Phase I Portion of the Nordic Lymphoma Group MCL4 (LENA-BERIT) Trial

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Background: Mantle cell lymphoma is a disease of the elderly, with a median age of 70 years. Younger patients may be treated with potentially curative treatment including high dose chemotherapy. For elderly patients, however, no standard therapy has been defined. In a randomized comparison between R-CHOP and R-bendamustine (R-B) by the German StiL Group, R-B was associated with less toxicity and improved outcomes, making R-B a preferable first-line treatment option. Lenalidomide (LEN) is another active agent in MCL, with a response rate of 53% as a single agent in relapsed/refractory MCL. In the current trial, we investigate if the addition of lenalidomide to R-B may enhance efficacy, with manageable toxicity, for the older population of MCL patients. **Methods:** In phase I, the MTD of LEN was to be determined, starting with 5 mg/day increasing up to 25 mg/day in a sequential dose escalation using a 3+3 design. LEN, bendamustine and rituximab are given in 6 cycles/28 days. LEN D1-21, B 90 mg/m^2 D1-2 and R 375 mg/m^2 D1. The maintenance phase consists of LEN 25 mg/day, D1-21, for 7 cycles. Eligibility criteria are age > 65 years or ≤ 65 years, unable to tolerate high dose chemotherapy, with stage II-IV untreated mantle cell lymphoma,.**Results:** The trial was commenced in October 2009.The phase I portion initially recruited 12 pts according to the original protocol design in 3 cohorts with LEN dose from 5-15 mg d 1-21. Median age was 72.5 years, range 66-85. MIPI high risk n=8, intermediate risk n=4. Response after 6 cycles: CR/CRu n=9/10, PR n=1/10 (ORR 100%). Molecular remission in BM: 5/9 pts. Toxicity was more profound than expected, mostly during cycle 1 (SAE n=9, AE Grade III/IV n=14). Notable was a high incidence of cutaneous and allergic AE. No patients could receive more than 10 cycles, median 6.5. A dose limiting toxicity (DLT) was noted at the dose of 15 mg. This led to a modification of the phase I protocol: Cohort A: No LEN in cycle 1, cycles 2-6: 10 mg LEN days 1-14. During maintenance, cycles 7-8: LEN 10 mg days 1-21, cycles 9-13: LEN 15 mg days 1-21. Cohort B: Same as Cohort A, but reducing B to 70 mg/m2 in cycles 2-6. Cohort C: as Cohort B, but reducing LEN to 5 mg days 1-14 cycles 2-6. In Cohort A, 2 of 6 patients experienced a DLT. Evaluation of Cohort B (6 pts) is ongoing.
Conclusions: The addition of LEN to the R-B regimen leads to increased toxicity in elderly patients with MCL. Early data indicate a high response rate