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POSTER ABSTRACTS

653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

Low-Dose Venetoclax-Dexamethasone in t(11;14) Positive Relapsed and Refractory Multiple Myeloma; Interim Results from the Ongoing, Danish, Investigator-Initiated, Open Label, Phase 2 Victoria Study

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Background
Venetoclax (VEN) is an oral BCL-2 inhibitor that is effective for the treatment of multiple myeloma (MM) with t(11;14), expressing high levels of BCL-2. In a previous phase 1 study, VEN was given to 66 patients [30 with t(11;14)] with relapsed and refractory MM (RRMM) at 300, 600, 900 or 1200 mg in dose-escalation cohorts and 1200 mg in the expansion cohort, without reaching a maximum tolerated dose; the overall response rate (ORR) in t(11;14) positive patients was 40% (Kumar et al. 2017). Later, in a phase 1-2 study, 800 mg VEN with 40/20 mg weekly dexamethasone (DEX) was explored in 51 patients with RRMM and t(11;14) with an overall response rate (ORR) of 48-60% (Kaufman et al. 2021). Here, we report the interim results of an ongoing, Danish, investigator-initiated, open label, phase 2 study which is testing the safety and efficacy of low-dose VEN-DEX in RRMM.
Methods
Patients with RRMM, at least one prior line of therapy and t(11;14) were included in the study between 1 st July 2020 and data cutoff in 31 st July 2022. VEN was administered orally, once daily at a dose of 400 mg. DEX was administered orally, once weekly at a dose of 20 mg. Treatment continued until progressive disease or unacceptable toxicity. After discontinuation of treatment, patients were followed for 24 months. The primary endpoint of the study was ORR, key secondary endpoints were progression-free survival (PFS) and overall survival (OS). Grade three or higher adverse events (AE) were recorded.
Results
Patient characteristics
At the time of data cutoff in July 2023, twenty-six patients were included in the study. The median (IQR) age was 74 (63-82) years. The median time from diagnosis was 4 (1-7) years. The median (IQR) number of prior lines of therapy was 3 (2-5). 46% of patients were males. At screening, 56% had anemia, 7% had renal failure, 15% had hypercalcemia according to the CRAB criteria. Performance status was 0 in 40% and 1-2 in 60% of patients. 47% of patients had ISS I, 19% had ISS II, 33% had ISS III. Besides t(11;14), present in all patients, 7% of patients had high-risk cytogenetic abnormalities, defined as the presence of t(4;14), t(14;16) or del(17p). 55% of patients had been treated with high dose melphalan and autologous stem cell transplantation, 92% had been exposed to an IMiD, 96% to a proteasome inhibitor, 70% to daratumumab. 29% were triple class-refractory, 15% were penta-drug refractory.
Safety
One patient had a grade 4 ventricular ulcer, besides this there were no grade 4 or 5 AEs. The most frequent grade 3 AE was infection, detected in 9 (35%) patients. Of these, there were 3 cases of pneumonia, 3 cases of COVID-19, 1 case of influenza, 1 case of gastroenteritis, and 1 case of fever of unknown focus. Other grade 3 AEs related to venetoclax were dehydration in 2 patients, thrombocytopenia in 1 patient, and nausea in 1 patient. The dose of venetoclax was reduced in 3 patients, to 200 mg daily in each case.
Efficacy
Ten of 25 evaluable patients had partial response or better, resulting in an ORR of 40% (Figure 1A). Four percent of patients achieved stringent complete response, 16% very good partial response and 20% partial response. In subgroup analysis, worse responses were observed in patients with creatinine >177 μmol/L (n=2), high-risk cytogenetics (n=2), triple-class refractory (n=7) and penta-drug refractory (n=3) disease. In responding patients, the median duration of response (DOR) was

not reached. The estimated percentage of patients still responding to therapy was 74% after one year and 55% after two years. The median (95% CI) PFS in the intention-to treat population was 5.5 (3.7; not available) months (Figure 1B). Median OS was not reached. The estimated percentage of patients still alive was 90% after one year.

Conclusion:

Based on this interim analysis, low-dose VEN-DEX in patients with RRMM and t(11;14) has a convenient safety profile and an efficacy comparable to previously tested VEN and VEN-DEX regimens with higher VEN doses.

Updated results will be presented at the meeting.

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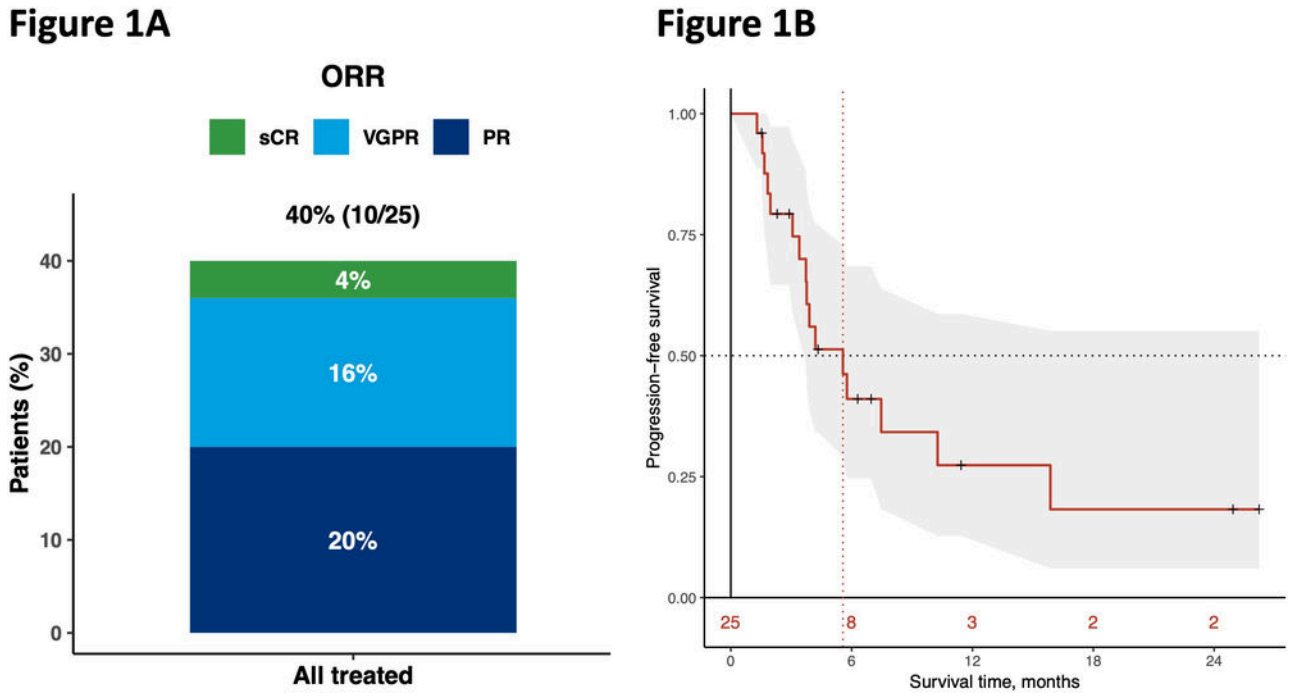

Figure 1

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