Abstract: P925

Title: PHASE 1 TRIAL OF ANTI-CD38 MONOCLONAL ANTIBODY CM313 IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA OR LYMPHOMA

Abstract Type: Poster Presentation

Session Title: 14. Myeloma and other monoclonal gammopathies - Clinical

Background:

Relapsed/refractory multiple myeloma (RRMM) and relapsed/refractory lymphoma are malignancies that pose significant therapeutic challenges. CM313, an anti-CD38 monoclonal antibody, has demonstrated preclinical anti-tumor activity in both MM and lymphoma through antibody-dependent cellular cytotoxicity, complement-dependent cytotoxicity, and antibody-dependent cellular phagocytosis.

Aims:

To characterize the safety and preliminary efficacy of CM313 in adult patients (pts) with RRMM or relapsed/refractory lymphoma (mainly limited to Waldenstrom's macroglobulinemia and marginal zone lymphoma [MZL]).

Methods:

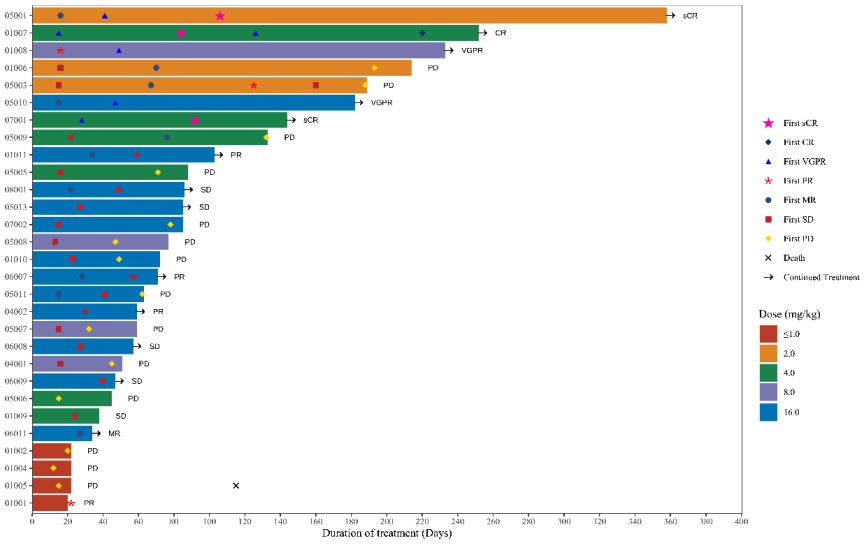
This open-label, multicenter, phase 1 trial (NCT04818372) consisted of a modified dose-escalation phase (Part A) and a dose-expansion phase (Part B). Eligible patients (aged 18-75 years) had a relapse or become refractory to prior therapies and were required to have measurable disease. In Part A, pts were treated with CM313 at doses of 0.006, 0.06, 0.3, 1.0, 2.0, 4.0, 8.0, 16.0, and 24.0 mg/kg. Dose-limiting toxicities (DLTs) were assessed over a 21-day cycle following the first infusion. The recommended doses of CM313 for Part B were 4.0, 8.0, and 16.0 mg/kg. CM313 was administered intravenously once weekly for the first 8 cycles, then every 2 weeks for 8 cycles (cycles 9-16), and then every 4 weeks onwards until disease progression or unacceptable toxicity. The primary endpoints were safety and tolerability for Part A and overall response rate (ORR) for Part B.

Results:

As of October 10, 2022, 34 pts were enrolled in the trial, with 17 in Part A (all RRMM) and 17 in Part B (14 RRMM and 3 MZL). Median age was 59 years (range 39-74). Pts had received a median of 3 prior lines of therapies (range 1-10). The maximum tolerated dose was not reached, and no DLTs were observed. Grade 3 or higher treatment-emergent adverse events (TEAEs) were reported in 15/34 (44.1%) pts (8 [23.5%] were considered drug related); there were no grade 5 TEAEs. 5 (14.7%) pts experienced at least one serious adverse event (2 [5.9%] were considered drug related). The most frequent drug-related TEAEs (≥20% of pts) were infusion-related reaction (IRR; 50.0%), lymphocyte count decreased (35.3%), white blood cell count decreased (32.4%), and neutrophil count decreased (20.6%). All IRRs were grade 1/2 and occurred during the first and/or second infusions.

Among the 29 out of 31 RRMM pts (93.5%) who had at least one post-baseline efficacy assessment, ORR was 34.5% (95%CI: 17.94-54.33; 10 of 29), with an ORR of 33.3% in 16.0 mg/kg cohort (Figure). At a median follow-up of 6 months (range 0.4-17.5), the median progression free survival for the 29 RRMM pts was 132 days (95%CI: 49.0-193.0), and the median overall survival was not reached yet.

Figure. Swimmer plot of disease responses in 29 RRMM patients



≤1.0 mg/kg group includes 0.006 mg/kg, 0.06 mg/kg, 0.3 mg/kg and 1.0 mg/kg group.
RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; CR, complete response; VGPR, very good partial response; PR, partial response; MR, minimal response; SD, stable disease; PD, progressive disease.

Summary/Conclusion:

CM313 monotherapy demonstrated preliminary promising clinical efficacy with tolerable and manageable safety profile. Further studies are ongoing and planned.