Abstract: P2097

Title: SUBCUTANEOUS CM355, A NOVEL BISPECIFIC CD20/CD3 ANTIBODY SHOWED PROMISING EFFICACY AND FAVORABLE SAFETY PROFILE IN RELAPSED/REFRACTORY B-CELL NON-HODGKIN LYMPHOMA

Abstract Type: e-Poster Presentation

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

CM355 is a novel CD20xCD3 bispecific IgG4 antibody that induces T cell dependent cellular cytotoxicity to eliminate malignant B-cells. Asymmetric affinity binding to CD20 and CD3 reduces antibody trapping in T-cell-containing tissues, and no Fc gamma receptors (FcγR) binding is designed to mitigate the risk of cytokine release. We report results **of** an ongoing single arm, open label, multicenter phase I/II study evaluating CM355 in relapsed/refractory (R/R) B-cell Non-Hodgkin Lymphoma (B-cell NHL) (NCT05210868).

Aims:

To evaluate the safety,tolerability,efficacy,pharmacokinetics (PK)/ pharmacodynamics (PD) of CM355 in R/R B-cell NHL.

Methods:

Eligible patients must have progressed on or after at least 1 prior line of systemic therapy and received CD20-directed therapy. Standard 3+3 method was adopted. Treatment-emergent adverse events (TEAEs) were evaluated and graded according to CTCAE v5.0. Cytokine release syndrome (CRS) were graded according to ASTCT 2019 consensus criteria. Responses were assessed by Lugano 2014.

Results:

As of Dec 25, 2023, a total of 9 patients (aggressive, aNHL, n=2; indolent, iNHL, n=7) were enrolled to receive CM355 subcutaneously (SC). Two dose cohorts (0.5/1.5/6.0mg, n=3; 1.0/3.0/15.0mg, n=6) were completed, while the dose escalation up to higher dose was still ongoing. Median age was 59 years (range, 36-72) and median number of prior systemic therapies was 2 (range, 1-6).

Among the 9 patients, the most common treatment-related adverse events (TRAEs) were interleukin level increased (n=8, 88.9%), CRS (n=6, 66.7%), blood immunoglobulin M decreased (n=5, 55.6%), all of the events were Gr1-2. All CRS events were Gr1-2 and most of them occurred during the first cycle. The most common Gr ≥ 3 TRAEs/TEAEs were neutrophil count decreased (n=2, 22.2%) and anemia (n=2, 22.2%). No injection site reactions reported and no TEAEs led to treatment discontinuation. One DLT event of Grade (Gr) 4 anemia occurred in the 1.0/3.0/15.0mg cohort, and the Safety Monitoring Committee (SMC) evaluated this dose cohort was safe and tolerable. MTD was not reached.

As of 28 Feb 2024, 9 patients were evaluable for efficacy, including 3 patients receiving dose of 0.5/1.5/6.0mg and 6 patients receiving dose of 1.0/3.0/15.0mg. CM355 exhibited anti-tumor activity at dose levels ≥ 0.5/1.5/6.0 mg. The overall response rate (ORR) was 100.0% (9/9) with complete response rate (CRR) was 77.8% (7/9). Both of the two aNHL patients, including one transformed DLBCL and one DLBCL NOS, achieved complete response (CR). Among 7 iNHL patients, including Gr1-3a FL, the ORR was 100.0% (7/7) with CRR of 71.4% (5/7). Most of the responders were still under treatment with sustained response.

CM355 demonstrated a favorable PK profile, which was characterized by a slow absorption rate and reduced Cmax supporting the use of subcutaneous dosing for mitigating the risk of CRS. Based on PopPK simulation, predicated bioavailability of SC is around 68.2%. A sustained depletion of circulating peripheral B-cells was observed after SC dosing.

Summary/Conclusion:

At the doses evaluated, CM355 SC demonstrated favorable safety profile and promising efficacy in patients with R/R B-cell NHL. All CRS events were manageable with minimal intervention. Rapid and deep responses, as well as the convenience of SC formulation, support further clinical development for treatment of B-cell NHL.

Keywords: Antibody, NHL, Bispecific, CD20