Abstract: P865

Title: TECLISTAMAB IN COMBINATION WITH LENALIDOMIDE IN PREVIOUSLY TREATED PATIENTS WITH MULTIPLE MYELOMA IN THE PHASE 1B MULTICOHORT MAJESTEC-2 STUDY

Abstract Type: Poster Presentation

Session Title: Myeloma and other monoclonal gammopathies - Clinical

Background:

Teclistamab (tec) is the first B-cell maturation antigen (BCMA)–directed bispecific antibody approved for the treatment of relapsed/refractory multiple myeloma (MM). Tec redirects CD3+ T cells to mediate T-cell activation and subsequent lysis of BCMA-expressing MM cells. The immunomodulatory drug (IMiD) lenalidomide (len), an established backbone of MM treatment, induces tumor cell apoptosis and stimulates immune cell activity. The cytotoxic and immunomodulatory actions of each drug in a fully immune-based regimen of tec + len may potentially contribute to enhanced efficacy of this combination.

Aims:

We report preliminary safety (primary objective), efficacy, and PK data for tec + len in pts with triple-class exposed MM from the phase 1b MajesTEC-2 study (NCT04722146).

Methods:

Eligible pts with MM had received ≥2 prior lines of therapy (LOT) including a proteasome inhibitor, IMiD, and anti-CD38 antibody. All pts provided informed consent. Pts received weekly subcutaneous tec 0.72 mg/kg + len 25 mg, or tec 1.5 mg/kg + len 15 mg, preceded by the approved tec step-up dosing schedule. Adverse events (AEs) were graded by CTCAE v5.0; cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded per ASTCT. Responses were assessed per IMWG.

Results:

As of Feb 6, 2023, 31 pts had received tec + len (0.72 mg/kg + 25 mg, n=12; 1.5 mg/kg + 15 mg, n=19). Median follow-up was 9.9 months (range, 1.1–15.4). Median age was 71.0 years (range, 54–84); pts had received a median of 4 prior LOT (range, 2–9), 61.3% of pts had received >3 prior LOT, 64.5% were IMiD-refractory, and 41.9% were len-refractory (100.0% were len-exposed). The most common AEs in pts across both dose levels were neutropenia (74.2% [grade (gr) 3/4 67.7%]; febrile neutropenia, 6.5% [all gr 3/4]), diarrhea (48.4% [gr 3/4 3.2%]), anemia (38.7% [gr 3/4 19.4%]), thrombocytopenia (38.7% [gr 3/4 16.1%]), fatigue (32.3% [gr 3/4 3.2%]), and constipation (32.3% [no gr 3/4]). CRS occurred in 67.7% of pts, with median time to onset 2.0 days (range, 1–4) and median duration 2.0 days (range, 1–15); all but 1 CRS event occurred during cycle 1 (1 [subsequent] event in cycle 2). CRS was gr 1/2 except for 1 gr 3 case (with associated gr 3 hypotension). ICANS occurred in 2 pts (6.5%; both gr 1). Infections occurred in 25 pts (80.6%) overall (gr 3/4 45.2%), most commonly pneumonia (22.6% [all gr 3/4]), COVID-19 (19.4% [gr 3/4 3.2%]), and sepsis (16.1% [all gr 3/4]). AEs led to treatment discontinuation in 5 pts and death in 3 pts (sepsis, COVID-19, and acute renal failure associated with progressive disease). In 31 evaluable pts, overall response rate (ORR) was 74.2% (≥ complete response [CR] 35.5%). Among responders, median follow-up was 10.1 months (range, 3.9–15.4), median time to first response was 1.2 months (range, 0.8–4.4), and median duration of response was not reached. The PK profile of tec + len was generally within the range for tec monotherapy.

Summary/Conclusion:

Promising efficacy (ORR 74.2%, ≥CR 35.5%) was observed with an immune-based doublet regimen of tec + len in a len-exposed population including 41.9% of pts who were len-refractory. The safety profile was consistent with tec and len individually, with no new safety signals, no dose-limiting toxicities, and an infection rate consistent with

tec alone, supporting the potential of this combination. Tec + len as maintenance therapy after autologous stem cell transplant in pts with newly diagnosed MM will be evaluated in the randomized phase 3 MajesTEC-4 study (NCT05243797).

Keywords: B-cell maturation antigen, Multiple myeloma, Phase I, Bispecific