Preliminary Results Of A Phase 1 Dose Escalation Study Of The First-In-Class Anti-CD74 Antibody Drug Conjugate (ADC), STRO-001, In Patients With Advanced B-Cell Malignancies. Abstract PS1071

Background

CD74 is expressed on B cells throughout differentiation and is an attractive target for treatment of multiple myeloma (MM) and non-Hodgkin's lymphoma (NHL). Sutro's cell-free protein synthesis (XpressCF™) and site-specific conjugation (XpressCF+™) platform technologies were used to generate STRO-001, a novel CD74-targeting aglycosylated ADC. STRO-001 contains a potent maytansinoid warhead conjugated to two specific sites (drug-antibody ratio of 2) using a stable non-cleavable linker.

Aims

This first-in-human Phase 1, open-label, multicenter, dose escalation study was designed to evaluate the safety, tolerability, and preliminary anti-tumor activity of STRO-001 in adults with B-cell malignancies.

Methods

Patients with advanced, relapsed/refractory MM and NHL are eligible for enrollment. STRO-001 is administered as a 60-minute IV infusion on Days 1 and 15 of a 28-day cycle until disease progression or dose-limiting toxicity (DLT). Two cohorts, one for MM and one for NHL patients, with an initial accelerated dose titration design (N of 1) are being enrolled and analyzed independently with 3+3 dose escalation being triggered by pre-specified safety events.

Results

14 patients (7 MM and 7 NHL), have been treated at 7 dose levels: .05, .075, .15, .27, .43, .65 and .91 mg/kg. NHL subtypes include: 2 follicular lymphoma (FL), 1 marginal zone lymphoma, 2 diffuse large B-cell lymphoma (DLBCL), 1 Burkitt's lymphoma and 1 composite DLBCL/FL. 4 females and 10 males have been treated to date. Median age is 67 (r 21-82). Median ECOG performance – 1 (r 0-2). Median number of prior systemic therapies is 5 (range 2-12). Two patients (1-MM and 1-NHL) had received CAR-T therapy. Based on a related, grade 2 non-hematologic adverse event (fever, chills, vomiting), the 3+3 dose escalation design was triggered at the 0.91 mg/kg dose level in the NHL cohort. Median number of STRO-001 doses administered is 4 (r 1-12). 11 patients have completed at least one cycle (two doses) of STRO-001 and are evaluable for safety and for dose escalation recommendation. No grade ≥ 3 treatment-related adverse events (TRAEs) have been observed. The most common grade 1-2 TRAEs are fatigue, nausea, chills and infusion reaction occurring in 2 out of 11 patients. All treatment discontinuations have been secondary to disease progression. One patient with localized recurrence of DLBCL achieved a complete response (CR) after 2 cycles and progressed with new sites of disease after 12 doses (6 cycles). 3 patients remain on treatment and dose escalation is ongoing. Preliminary PK analysis showed maximum serum concentrations of ADC (0.39-8.2 µg/mL) and total antibody (0.41-9.1 µg/mL) increased after single IV doses of STRO-001 (0.05-0.65 mg/kg). The terminal phase half-life estimated for total antibody in 3 patients ranged 37-47 hours. STRO-001

did not exhibit evidence of accumulation with the 2 week dose interval. There is no evidence of anti-STRO-001 antibodies.

Conclusion

STRO-001 is the first ADC generated with novel cell-free protein synthesis technology and site-specific conjugation with the non-natural amino acid pAMF to be tested in the clinic. STRO-001 has been well-tolerated, and the absence of immunogenicity is encouraging. No ocular toxicity or DLTs have been observed and MTD has not been reached. Preliminary anti-tumor activity (CR) has been observed in a patient with recurrent DLBCL. The study continues to enroll patients in dose escalation with single patient MM cohorts and 3+3 NHL cohorts. This study is registered with clinicaltrials.gov identifier NCT03424603.