Safety and efficacy data from Nexicart-2, the first US trial of CAR-T in R/R light chain (AL) amyloidosis, Nxc-201.

Heather Jolie Landau, Charlotte Hughes, Aaron Seth Rosenberg, Mehrdad Abedi, Shahzad Raza, Jeffrey A. Zonder, Eugene Brailovski, Sergio Giralt, Sham Mailankody, Jae H. Park, Miguel-Angel Perales, Saad Z. Usmani, David Marks, Raymond Comenzo, Sridevi Rajeeve, Jennifer Liu; Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan Kettering, New York, NY; UC Davis Comprehensive Cancer Center, Sacramento, CA; University of California Davis, Davis, CA; Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; Barbara Ann Karmanos Cancer Institute, Detroit, MI; Immix Biopharma, Los Angeles, CA; Department of Hematology-Oncology, Tufts Medical Center, Boston, MA; Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Background: No FDA approved treatments exist for relapsed/refractory (RR) AL Amyloidosis. Chimeric antigen receptor T-cell (CAR-T) is a novel approach to treating RR AL Amyloidosis. In this study, we report safety and efficacy data from NEXICART-2, the first U.S. clinical trial of any CAR-T in RR AL Amyloidosis. **Methods:** NEXICART-2 (NCT06097832) is a single-arm, multi-site U.S. Phase 1b/2 dose escalation and expansion trial of autologous BCMA-targeted CAR-T NXC-201 in RR AL Amyloidosis. It will enroll 40 patients (pts) with a 6 patient safety run-in, that has now completed. Pts must have been exposed to bortezomib and anti-CD-38 antibody with persistent or relapsed disease. Lymphodepletion was with fludarabine and cyclophosphamide. The primary endpoint is complete hematologic response (CR) rate (Palladini. 2012). **Results:** 7 pt (4 F, 3 M), median age 66 years (range: 56-82) were included. Median follow-up 97 days (range 7-209). Median prior lines 4 (range: 2-9); including 4(57%) with prior autologous stem cell transplant; 6/7 had gain 1q. Median dFLC at enrollment were 5.4 mg/dL (range: 2.4-12.1). 57% (4/7) had cardiac involvement (Mayo stage I (N =2), II (N=4) and IIIa (N=1) with median NT-proBNP 909 pg/mL (range: 146 – 2,532)); 2/7 had New York Heart Association (NYHA) class II heart failure, 5/7 class I. 2 pts had kidney involvement, with 4.5 and 10.0gm of proteinuria in 24h. 3 pts received 150 million and four 450 million CAR+T cells. CRS was observed in 5 pts (grade 1 (N=4), grade 2 (N=1)); onset day 1 (N=3) or 3 (N=2), lasting <24 hours following 1 dose of tocilizumab in all pts. No pt had neurotoxicity. Adverse events included neutropenia (grade 3 (N=3), grade 4 (N=2). 1 pt with pre-existing stage 4 chronic kidney disease prior to enrollment had Grade 4 acute on chronic kidney injury. There was no febrile neutropenia, treatment-related infections, cardiac toxicity, and no deaths. All pts (7/7, 100%) normalized pathological disease markers after NXC-201. Pts 1, 2, 4, 5, 6, 7 normalized FLCs at median 7 days (range 7-14) following NXC-201, all with reduction of dFLC to <1 mg/dL. Pts 1, 2, 4, 5, 6 had MRD negativity in bone marrow by flow cytometry (10^{-6} sensitivity) at day 25 or 26 (Pt 7 was not MRD evaluable as of the cut-off date). Pt 3 had a renal organ response per AL criteria (reduction in albuminuria) and resolution of the m-spike 15 days following NXC-201 (0.79g/dl at enrollment). As of the data cutoff, all pts are in VGPR/CR, with no relapses recorded. Improvement in NYHA class from II to I occurred in 1 pt 14 days following NXC-201 treatment. 15 pts are expected to have been treated at presentation time. **Conclusions:** In this first reported U.S. CAR-T clinical trial experience in RR AL Amyloidosis, we demonstrate that NXC-201 can be given safely and resulted in rapid and deep hematologic responses in all pts treated. Our data suggests that the novel anti-BCMA CAR-T NXC-201 may become a valuable treatment option for RR AL pts. Clinical trial information: NCT06097832. Research Sponsor: Immix Biopharma; MSK Cancer Center Support Grant/Core Grant (P30 CA008748).