Abstract: S206

Title: EQUE-CEL, A NOVEL FULLY HUMAN BCMA-TARGETING CAR-T THERAPY IN PATIENTS WITH HIGH RISK NEWLY DIAGNOSED MULTIPLE MYELOMA

Abstract Type: Oral Presentation

Session Title: CAR T cell therapy for the treatment of Multiple Myeloma

Background:

Eque-cel, a fully human BCMA-specific CAR structure, has been approved for marketing in treating relapsed and refractory multiple myeloma (RRMM) patients with at least 3 lines of prior therapy in China. The data was previously reported in the 20th IMS Annual Meeting (abstract P-290). Here, we report efficacy and safety data of Eque-cel in transplant-ineligible patients with high-risk newly diagnosed multiple myeloma in FUMANBA-2 study (NCT05181501).

Aims:

The objective is to evaluate the safety, efficacy, and PK/PD of Eque-cel.

Methods:

FUMANBA-2, a multicenter, open-label, phase 1, single-arm study, is currently evaluating Eque-cel in newly diagnosed MM (NDMM) patients with high risk features (defined as RISS stage Ⅲ , double-hit, or triple-hit per mSMART 3.0 criteria).Patients would receive 4 cycles of induction therapy (recommended regimens include Bortezomib-Lenalidomide-Dexamethasone, Bortezomib-Cyclophosphamide-Dexamethasone or Bortezomib-Adriamycin-Dexamethasone) before Eque-cel infusion. After the third cycle of induction therapy, the patients who were evaluated not eligible for Autologous Stem Cell Transplant (ASCT) underwent T cell collection via leukapheresis for Eque-cel manufacture. After lymphodepletion with Fludarabine-Cyclophosphamide, patients received a single infusion of Eque-cel at the dose of 1.0 x 106 CAR-T cells/Kg. Primary efficacy endpoint was the proportion of minimal residual disease (MRD)-negative subjects (MRD−; sensitivity <10-5) and progression-free survival (PFS). Secondary endpoints included overall response rate, duration of response, safety, pharmacokinetics, and pharmacodynamics (soluble BCMA level and cytokinetics).

Results:

As of the January 25th, 2024, 16 patients (68.8% male; median aged 58.5 years [range, 51-69]) received Eque-cel with a median follow-up of 13.1 (range, 7.9-24.3) months. High-risk cytogenetics were detected in 100% patients, including 62.5% (10/16) double-hit and 12.5% (2/16) triple-hit. 25% (4/16) patients had extramedullary disease. 37.5% (6/16) patients had R-ISS stage Ⅲ disease, among whom 6.3% (1/16) with double-hit cytogenetics and 6.3% (1/16) with triple-hit cytogenetics. Only one patient received lenalidomide as maintenance therapy at the investigator’s discretion from day 92 post Eque-cel infusion and discontinued on day 96 due to allergy.

With median follow-up 7.46 (range, 2.8-18.1) months post Eque-cel infusion, all patients achieved MRD negativity, and 71.4% (95% CI: 25.8-92.0) patients achieved sustained MRD negativity over 6 months. A 100% ORR was observed, with 93.8% (15/16) ≥ CR. Median DOR and median PFS have not reached. The 6-month PFS rate was 93.8% (95% CI: 63.23-99.10) and the 12-month PFS rate was 84.4% (95% CI: 49.31-96.00).

Grade 1-2 CRS occurred in 68.8% (11/16) patients. No Grade ≥3 CRS and no ICANS or neurotoxicity was observed. The most common ≥ grade 3 treatment-related AEs were neutropenia (81.3%), lymphopenia (68.8%), leukopenia (62.5%). Grade ≥3 infection diseases occurred in 25.0% (4/16) patients, and only one patient with grade 3 respiratory infection was related to Eque-cel. One death due to Covid-19 infection was reported which was considered not related to Eque-cel by the investigator.

The expansion of Eque-cel reached the median peak level of 79681.30 copies/μg gDNA at a median of 10

(range, 7-21) days. The median persistence of Eque-cel was 75 (range, 29-283) days after infusion. Soluble BCMA was cleared within 1 month post-infusion in 81.25% (13/16) patients. Induction of inflammatory cytokines was observed with median peak levels of 64.28 (range, 9.12-3017.83) pg/mL for IL-6, 49.30 (range, 3.66-117.30) mg/L for CRP, and 553.35 (range, 68.10-2349.00) ng/mL for Ferritin.

Summary/Conclusion:

Eque-cel achieved deep responses in transplant-ineligible patients with high-risk NDMM. Lower incidence and severity of CRS showed more favorable safety profile in high-risk NDMM than that in RRMM. These results support a favorable clinical benefit–risk profile of Eque-cel in transplant-ineligible NDMM.

	1.0×10^6 CAR$^+$ cells/kg (N=16)
mPFS (95%CI)	- (10.842, -)
PFS rate, % (95%CI)	
3-month	100.0 (-)
6-month	93.8 (63.23,99.10)
12-month	84.4 (49.31,96.00)
MRD negative at any time point, %	100
Sustained MRD negative for ≥3 months, % (95%CI)	100 (100,100)
Sustained MRD negative for ≥6 months, % (95%CI)	71.4 (25.8,92.0)
Sustained MRD negative for ≥12 months, % (95%CI)	71.4 (25.8,92.0)
Response, n (%)	
ORR	16 (100%)
≥VGPR	16 (100%)
≥CR	15 (93.8%)
CRS, n (%)	
Any grade	11 (68.8%)
Grade 1	8 (50.0%)
Grade 2	3 (18.8%)
Median time to the first onset of CRS, d (range)	7 (2,9)
Median duration of CRS, d (range)	3 (1,8)
ICANS	0
Pharmacokinetic parameters, median	
C_{max}, copies/μg (%geometric CV)	79681.299 (133.144)
T_{max}, d (range)	10 (7,21)
$AUC_{0\text{-}28days}$, copies/μg (%geometric CV)	691468.75 (176.63)

At January 25,2024 cutoff.
$AUC_{0\text{-}28days}$, area under the curve of the transgene level from time of dose to 28 days post-infusion; CI, Clopper-Pearson confidence interval ; C_{max}, peak serum concentration; CR, complete response ; CRS, cytokine release syndrome ; CV, coefficient of variation; d, days ; DOR, duration of response ; MRD, minimal residual disease; ORR, overall response rate; PFS, progression free survival; pts, patients; T_{max}, time to peak concentration; VGPR, very good partial response.

***** Correspondence: chenbing2004@126.com

Keywords: B-cell maturation antigen, Multiple myeloma, High risk, CAR-T