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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Phase I Clinical Study of Humanized BCMA-Single-Domain Antibodies-Targeting CAR T (BCMA-CART) in Patients with Relapsed/Refractory Multiple Myeloma

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Background: The CAR structure adopted by CART-BCMA is composed of a single-domain antibody targeting BCMA, CD8 hinge region, transmembrane region, 4-1BB co-stimulatory domain, and CD3-ζ T cell activation domain. In the phase I clinical study (NCT05346198) carried out in China, the safety and efficacy of CART-BCMA were initially evaluated through the dose escalation + dose expansion design, and the recommended dose (RD dose) for follow-up studies was determined as well.
Method: Enrolled patients with relapsed and/or refractory multiple myeloma (RRMM) had previously received at least 3 lines of therapy including at least one proteasome inhibitor and one immune modulator. After lymphatic preconditioning chemotherapy (program: fludarabine 30mg/m ^{2}/d and cyclophosphamide 300mg/m ^{2}/d, -5, -4, -3, for 3 consecutive days), all patients received a single dose of CART-BCMA at 2.5×10 ^{6}, 5×10 ^{6} and 7.5×10 ^{6} CAR-positive T cells/kg (subject body weight), according to the dose level in which they were enrolled.
R esults : Up to June 26, 2023, a total of 15 cases of RRMM received 2.5×10 ^{6} CAR-positive T cells/kg (n=3), 5×10 ^{6} CAR-positive T cells/kg (n=11) or 7.5×10 ^{6} CAR-positive T cells/kg (n=1) dose level of CART-BCMA cell infusion therapy on the basis of the dose level in which they were enrolled. The median follow-up time was 14.42 months (range: 10.2-26.6 months). The median age of the subjects was 63.0 years old (range: 36-73 years old) (Table 1), 73.3% of the subjects (n=11) had previously received ≥4 lines of multiple myeloma therapy, and the median line of treatment was 5 lines (range: 3-9 lines), among which, 2 subjects (13.3%) had previously received autologous hematopoietic stem cell transplantation, and 4 subjects (26.7%) had relapsed/refractory diseases after previous treatment with proteasome inhibitors, immune modulators and CD38 monoclonal antibodies (three-drug relapsed/refractory). Nine subjects (60.0%) had high-risk cytogenetic abnormalities according to sMART 3.0 criteria, and 6 subjects (40.0%) had extramedullary plasmacytoma.
The most common grade ≥3 adverse events were hematological toxicity, including decreased neutrophil count (n=13, 86.7%), decreased white blood cell count (n=12, 80.0%), decreased lymphocyte count (n=10, 66.7%), anemia (n=8, 53.3%), decreased platelet count (n=4, 26.7%). The first patient in the 7.5×10 ^{6} CAR-positive T cells/kg dose group had a dose-limiting toxicity (DLT) event of grade 4 platelet count decrease, and no DLT event occurred in the other low-dose groups (2.5 and 5×10 ^{6} CAR-positive T cells/kg). All 15 patients (100.0%) developed grade 1-2 cytokine release syndrome (CRS), no grade ≥3 CRS occurred, and the median time to CRS was 2.0 days (range: 1-13 days) , with a median duration of 7.0 days (range: 2 to 17 days). After the occurrence of CRS, all patients recovered without sequelae after supportive treatment, and 6 patients (40%) received tocilizumab (3 subjects received 2 doses, 3 subjects received 1 dose), 4 patients (26.7%) used glucocorticoids. There was no event of immune effector cell-associated neurotoxicity syndrome (ICANS), and no death event occurred.
The median time to the first response (TTR) of the patients was 0.953 months (range: 0.92 to 2.23 months). All 15 patients who received CART-BCMA infusion achieved remission, and the overall remission rate (ORR) (At least achieve PR or better efficacy) was 100% (95%CI, 78.20%-100.00%), as shown in Figure 1, among which, the best response of 9 patients (60%) was strict complete remission (sCR), 5 patients (33.3%) achieved very good partial response (VGPR), and 1 patient (6.7%) achieved PR. All sCR patients achieved MRD negativity. The ORR of 6 patients with extramedullary plasmacytoma was 100%, of which 2 achieved sCR and 4 achieved VGPR. Notably, gradual deepening of remission was observed in 12 patients (80%), of which 10

patients (66.7%) further deepened the depth of remission on days 60-90 after infusion, and 2 patients (13.3%) were assessed sCR at day 360.

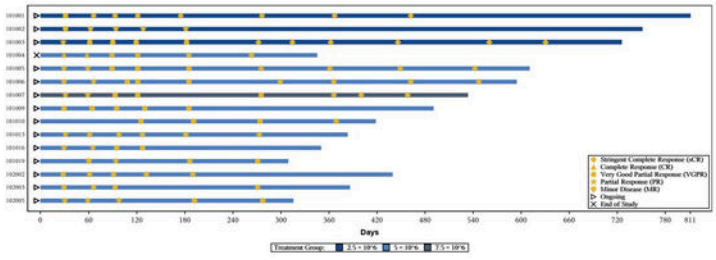
Conclusion:Data from this phase 1 clinical study showed that CART-BCMA is well tolerated and highly efficacious in patients with RRMM. Patients with extramedullary plasmacytoma had the comparable response to those without extramedullary diseases. Notably, 12 patients (80%) patients elicted deeper response after 3 months of CART-BCMA infusion

Disclosures No relevant conflicts of interest to declare.

Table 1： Demographic and disease baseline characteristics of 15 RRMM patients treated with CART-BCMA

	CART-BCMA dose（CAR positive T cell /kg）			total
	2.5×10^6 （N = 3）	5×10^6 （N = 11）	7.5×10^6 （N = 1）	（N = 15）
Median age (range) (years)	63.0（58-64）	62.0（36-73）	64.0（64-64）	63.0（36-73）
female，n（%）	2(66.7%)	5(45.5%)	1(100%)	8(53.3%)
Median time since diagnosis (range) (months)	52.83（38.9-53.6）	47.61（3.8-82.7）	56.80（56.8-56.8）	52.83（3.8-82.7）
Extramedullary plasmacytoma，n（%）	0	6(54.5%)	0	6(40.0%)
Proportion of plasma cells >30% in bone marrow，n（%）	0	3(27.3%)	1(100%)	4(26.7%)
ECOG，n（%）				
0	1(33.3%)	2(18.2%)	0	3(20.0%)
1	2(66.7%)	9(81.8%)	1(100%)	12(80.0%)
R-ISS stage，n（%）				
I	2(66.7%)	1(9.1%)	0	3(20.0%)
II	1(33.3%)	8(72.7%)	0	9(60.0%)
III	0	1(9.1%)	1(100%)	2(13.3%)
Abnormal cytogenetic，n（%）				
High risk	3(100%)	6(54.5%)	0	9(60.0%)
Del(17p)	1(33.3%)	1(9.1%)	0	2(13.3%)
T(4;14)	1(33.3%)	1(9.1%)	0	2(13.3%)
T(14;16)	0	0	0	0
T(14;20)	0	0	0	0
1q21	2(66.7%)	5(45.5%)	0	7(46.7%)
Bridging Therapy，n（%）	1(33.3%)	3(23.1%)	0	4(23.5%)
Previous ⩾4-line therapy，n（%）	2(66.7%)	8(72.7%)	1(100%)	11(73.3%)
Median number of prior treatment lines (range)，n（%）	5（3-5）	5（3-9）	4（4-4）	5（3-9）
Previous three-drug relapsed /refractory ，n（%）	0	4(36.4%)	0	4(26.7%)

Figure 1: Swimlane plot of response duration for different dose groups (FAS analysis set responders)



Note: The length of the swim lane chart represents the number of days from the start of the infusion to the cut-off day (2023-06-26) or EOS, whichever occurs first. 101009, 1010010, 101013, 101016, 102002, and 102005 are baseline with extramedullary lesions.

Figure 1

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