(S201) CB-011, AN ALLOGENEIC ANTI-BCMA CAR-T CELL THERAPY WITH IMMUNE CLOAKING, FOR PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (CAMMOUFLAGE PHASE 1 TRIAL)

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background

CB-011 is an allogeneic anti-BCMA CAR-T cell therapy with immune cloaking manufactured from healthy donor T cells. It features 4 genome edits made with the CRISPR-Cas12a chRDNA genome-editing technology: (1) insertion of a BCMA-specific CAR, (2) *TRAC* gene KO to reduce risk of GvHD, (3) knockout (KO) of *B2M* to reduce T cell-mediated rejection, and (4) B2M–HLA-E fusion insertion to blunt NK cell-mediated rejection.

Aims

CaMMouflage is a Phase 1 trial (NCT05722418) composed of 3+3 dose escalation and dose expansion to evaluate the safety and efficacy of CB-011 in patients (pts) with r/r MM and determine the recommended Phase 2 dose (RP2D).

Methods

Pts received ≥3 prior lines of therapy (including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody). Pts received lymphodepletion (LD) for 3 days of either 300 cyclophosphamide (cy) or 500 cy (300 mg/m^2 or 500 mg/m^2 of cy, respectively) with 30 mg/m^2 of fludarabine followed by a single infusion of CB-011 at doses of 50 million (M), 150M, 300M, 450M, or 800M CAR-T cells.

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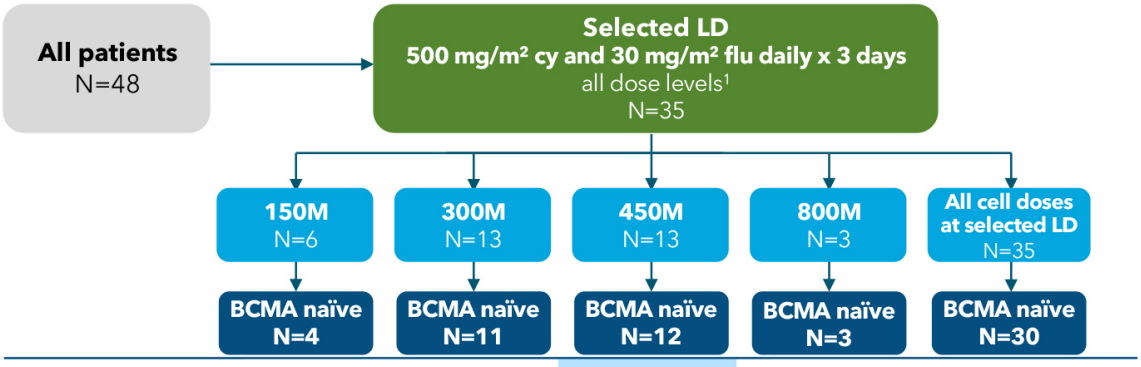
Results

As of Sep 24, 2025, a total of 48 pts received CB-011. The median age was 68.5 years (49-84). Pts received a median of 4 prior lines of therapy (3-11), and 17% received prior BCMA-targeted therapy. 56% of pts had high-risk cytogenetics and 35% had extramedullary disease. Of the 13 pts dosed in the 300 cy LD cohort, one experienced CAR-T cell expansion and achieved an MRD-negative sCR ongoing at 21 months post dosing; therefore, the 500 cy LD regimen was implemented to optimize CAR-T cell expansion. In pts who received the 500 cy LD regimen (N=35), infections occurred in 49% of pts (14%, grade ≥3), CRS occurred in 31% of pts (3%, grade ≥3), ICANS occurred in 9% of pts (no grade ≥3), immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome occurred in 9% of pts (3%, grade ≥3), and prolonged grade ≥3 cytopenias occurred in 33% of pts. No cases of GvHD, immune effector cell-associated enterocolitis, parkinsonism, or cranial nerve palsies were observed at any dose level. One grade 4 event of Guillain-Barré syndrome (GBS) occurred and is resolving. Three deaths occurred [pneumonia (unrelated), RSV (unrelated), ICAHT (related)], and have resulted in prophylactic measures/early intervention being implemented. For BCMA-naïve pts who received the recommended dose for expansion (RDE; 500 cy LD and 450M CAR-T cell dose) of CB-011 (N=12), the ORR was 92% and the [3] CR rate was 75% (see figure 1). At a median follow-up of 8.3 months, 7/12 (58%) pts were in a VGPR or better at ≥6 months. Of the MRD-evaluable pts, 10/11 (91%) achieved MRD negativity at 10^{-5} threshold. CB-011 exhibits a central memory CD8 T cell phenotype at peak of expansion. CB-011 expansion directly correlated with clinical responses and was higher in pts treated with 500 cy compared with 300 cy LD. Rapid recovery of endogenous T and NK cells was observed with endogenous B cells recovering within 6 months regardless of clinical response. Updated data will be presented.

Summary/Conclusion

In a high-risk, heavily pretreated r/r MM pt population, CB-011 drove deep and durable responses with a manageable safety profile. Based on these results, the RDE is 450M CB-011 CAR-T cells after 500 cy LD. The dose expansion phase of CaMMouflage is enrolling BCMA-naïve and prior BCMA therapy-exposed r/r MM patients.

Figure 1: Responses observed at all CB-011 doses with selected LD



	150M N=6	300M N=13	450M N=13	800M N=3	All cell doses at selected LD N=35
	BCMA naïve N=4	BCMA naïve N=11	BCMA naïve N=12	BCMA naïve N=3	BCMA naïve N=30
ORR	75%	55%	**92%**	33%	70%
CR/sCR	50%	18%	**75%**	0%	43%
≥VGPR	50%	27%	**83%**	0%	50%
MRD-negative rate[2]	50% (2/4)	0% (0/3)[3]	**91% (10/11)[4]**	0% (0/3)	57% (12/21)

[1]150M, 300M, 450M, or 800M CAR-T cells; [2]MRD negative at ≤10^{-5}; [3]MRD available for 3 patients at the time of the data cut; [4]MRD not evaluable in one patient. Data cutoff 24Sept2025
CR: complete response; cy: cyclophosphamide; flu: fludarabine; LD: lymphodepletion; M: million; MRD: minimal residual disease; ORR: overall response rates; sCR: stringent complete response; VGPR: very good partial response