CB-011, an allogeneic anti-BCMA CAR-T cell therapy with immune cloaking, in patients with relapsed/refractory Multiple Myeloma (r/r MM)

Dose escalation results from the CaMMouflage phase 1 trial

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Disclosures

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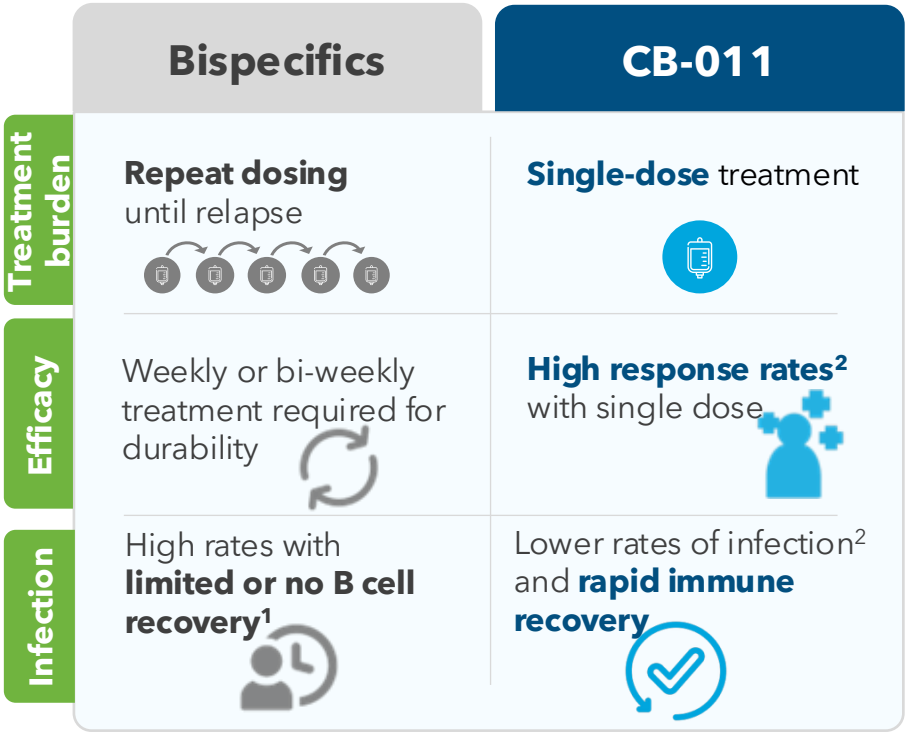
- Consultant
  - JNJ, BMS, Caribou Biosciences, Kite, Karyopharm

Allogeneic CAR-T cell therapy can fill unmet need in MM



[1]Frerichs, KA, et al. Blood Adv. 2024 Jan 9;8(1):194-206; Jelinek T, et al. Blood 144 (2024) 1934-1936; Schreiber S, et al. Mol. Therapy 3 (9) 4130-4134; 2025; [2]Based on Grade 3+ infections, at recommended dose for expansion as seen in results from dose escalation portion of the CaMMouflage clinical trial
MM: multiple myeloma; r/r: relapsed or refractory

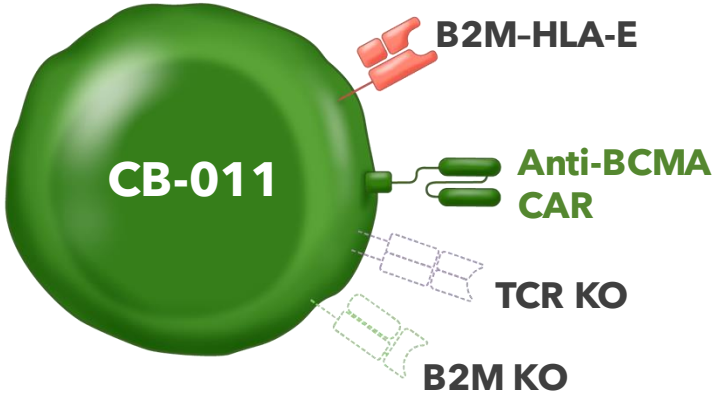
Allogeneic CAR-T cell therapy can fill unmet need in MM

	Bispecifics	CB-011	Auto CAR-T	
Treatment burden / Access	**Repeat dosing** until relapse	**Single-dose** treatment	Overcomes access challenges to **treat more patients**	**1 of 10 MM patients** receive auto CAR-Ts[3]
Efficacy / Speed	Weekly or bi-weekly treatment required for durability	**High response rates**[2] with single dose	**No wait** needed between eligibility and lymphodepletion	**Weeks to months** from eligibility to lymphodepletion[4]
Infection / Scale	High rates with **limited or no B cell recovery**[1]	Lower rates of infection[2] and **rapid immune recovery**	Potential for **50-100 doses** per manufacturing batch at commercial launch	**1 dose** per manufacturing batch

[1]Frerichs, KA, et al. Blood Adv. 2024 Jan 9;8(1):194-206; Jelinek T, et al. Blood 144 (2024) 1934-1936; Schreiber S, et al. Mol. Therapy 3 (9) 4130-4134; 2025; [2]Based on Grade 3+ infections, at recommended dose for expansion as seen in results from dose escalation portion of the CaMMouflage clinical trial; [3]Gilead Q3 2024 earnings call transcript; Poseida Therapeutics International Myeloma Society Meeting data call 2024; [4]Kourelis, T. et al. Transplant Cell Ther 2023 29(4):255-258
MM: multiple myeloma; r/r: relapsed or refractory

CB-011 key attributes

First allogeneic anti-BCMA CAR-T cell therapy with immune cloaking
Manufactured using Cas12a chRDNA genome-editing technology



- Immune cloaking implemented through:
  - *B2M* gene KO to slow down T cell-mediated rejection
  - B2M–HLA-E-peptide fusion insertion to blunt NK cell-mediated rejection
- Removal of HLA class I surface expression mimics a 6 of 12 HLA match
- Designed for functional persistence

chRDNA: CRISPR hybrid RNA-DNA

CB-011 CaMMouflage Phase 1 trial (NCT05722418)

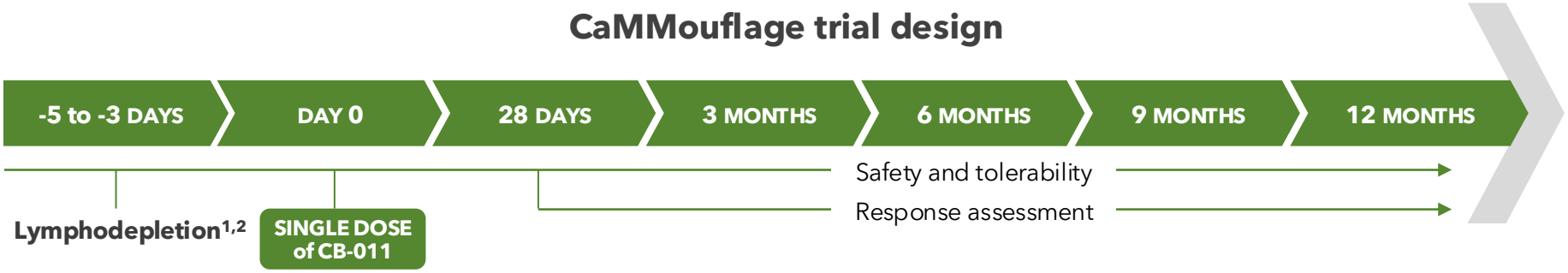
Eligibility
- ≥3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 antibody

Exclusion
- Prior CAR-T cell therapy and/or BCMA-targeted therapy within the last 3 months

Lymphodepletion regimens evaluated
- 300 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days
- 500 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days

CB-011 dose levels evaluated
- 50M, 150M, 300M, 450M, 800M CAR-T cells

CaMMouflage trial design



Off-the-shelf product, no manufacturing wait time, promising deep and durable responses observed with CB-011 are key reasons why investigators enrolled patients in CaMMouflage trial[3]

[1]300 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days; [2]500 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days
[3]Based on survey results from CaMMouflage investigators asking why patients were treated with CB-011 vs other treatment options
cy: cyclophosphamide; flu: fludarabine; IMiD: immunomodulatory drug; PI: proteasome inhibitor

48 patients treated in dose escalation of CaMMouflage trial

Initial LD regimen (N=13)

LD: 300 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days
CB-011 dose levels evaluated: 50M, 150M, 450M CAR-T cells
Outcomes:
- No DLTs observed
- Minimal cell expansion and efficacy observed
- 1 patient had robust cell expansion with depth of lymphodepletion and achieved sCR with sustained MRD negativity beyond 21 months

cy dose increased in LD regimen for optimal engraftment of CB-011

Selected LD regimen (N=35)

LD: 500 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days
CB-011 dose levels evaluated: 150M, 300M, 450M, 800M CAR-T cells
Outcomes:
- No DLTs observed
- Improved cell expansion and efficacy observed

Recommended dose for expansion (RDE)

LD: 500 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days
CB-011 dose level: 450M CAR-T cells

DLT: dose-limiting toxicity; LD: lymphodepletion; cy: cyclophosphamide; flu: fludarabine
sCR: stringent complete response; MRD: minimal residual disease

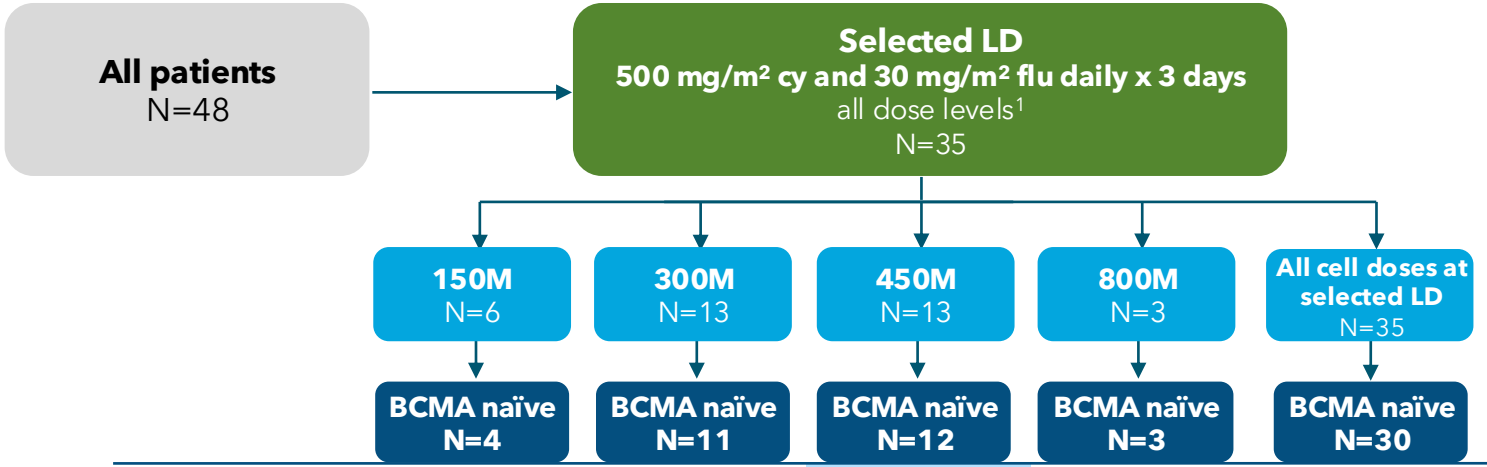
CaMMouflage trial: baseline and disease characteristics

Patient and disease characteristics	All patients[1] (N=48)	Patients treated with initial LD regimen[2] (N=13)	Patients treated with selected LD regimen[3] (N=35)
Age, years, median (range)	68.5 (49-84)	68.0 (49-84)	69 (53-82)
Male, n (%)	33 (68.8)	9 (69.2)	24 (68.6)
ECOG performance status, n (%)			
0	13 (27)	6 (46)	7 (20)
1	35 (73)	7 (54)	28 (80)
R-ISS disease stage, n (%) at diagnosis			
I	6 (13)	2 (15)	4 (11)
II	17 (35)	5 (39)	12 (34)
III	12 (25)	4 (31)	8 (23)
Unknown	13 (27)	2 (15)	11 (31)
High risk cytogenetics[4], n (%)	27 (56)	8 (62)	19 (54)
Extramedullary disease (EMD)[5], n (%)	17 (35)	5 (39)	12 (34)
Prior lines of therapy, median (range)	4 (3-11)	4 (3-9)	4 (3-11)
Median time since diagnosis (years)	5.3 (1-15)	5.3 (2-10)	5.3 (1-15)
Prior stem cell transplant, n (%)	30 (63)	10 (77)	20 (57)
Prior exposure to BCMA therapy, n (%)	8 (17)[6]	3 (23)	5 (14)

[1]All patients treated with a single dose of CB-011 and a LD regimen of either 300 mg/m^2 cy (initial LD) or 500 mg/m^2 cy (selected LD) with 30 mg/m^2 flu daily x 3 days
[2]300 mg/m^2 cy with 30 mg/m^2 flu daily x 3 days; [3]500 mg/m^2 cy with 30 mg/m^2 flu daily x 3 days
[4]High-risk cytogenetics include t(4;14), del(17/17p), t(14;16), t(14;20), and amplification/gain (1q) at any time from diagnosis to screening
[5]EMD defined as: soft tissue plasmacytoma noncontiguous with bone or lytic lesion with paramedullary extension
[6]4 patients received belantamab (ADC) one of whom also received elranatamab (bispecific), 3 patients received teclistamab (bispecific), and 1 patient received NK trispecific (CC-92329 (BCMAXNKG2D/CD16))
Data cutoff 24Sept2025
ADC: antibody-drug conjugate; cy: cyclophosphamide; ECOG: Eastern Cooperative Oncology Group; flu: fludarabine; NK: natural killer; R-ISS: Revised International Staging System

CaMMouflage trial: efficacy

Responses observed at all CB-011 doses with selected LD



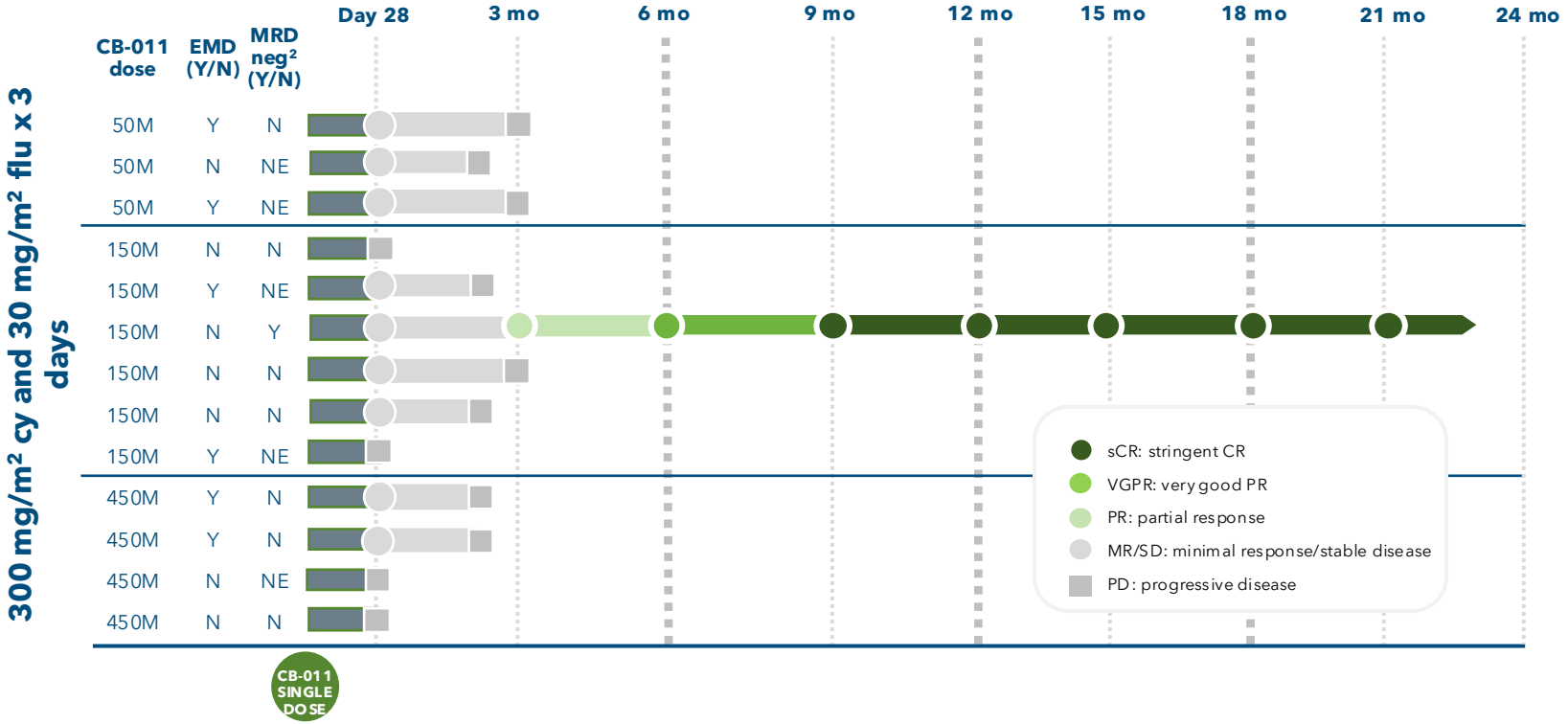
ORR	75%	55%	**92%**	33%	70%
CR/sCR	50%	18%	**75%**	0%	43%
≥VGPR	50%	27%	**83%**	0%	50%
MRD-negative rate[2]	50% (2/4)	0% (0/3)[3]	**91% (10/11)[4]**	0% (0/3)	57% (12/21)

[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

Initial LD regimen[1]: longest responder remains in stringent CR with sustained MRD negativity beyond 21 months



[1]300 mg/m² cy and 30 mg/m² flu daily x 3 days
[2]MRD negative at ≤10^{-5}. MRD results in non-responders are based on local report
EMD: extramedullary disease; NE: Not evaluable
Data cutoff: 24Sept25

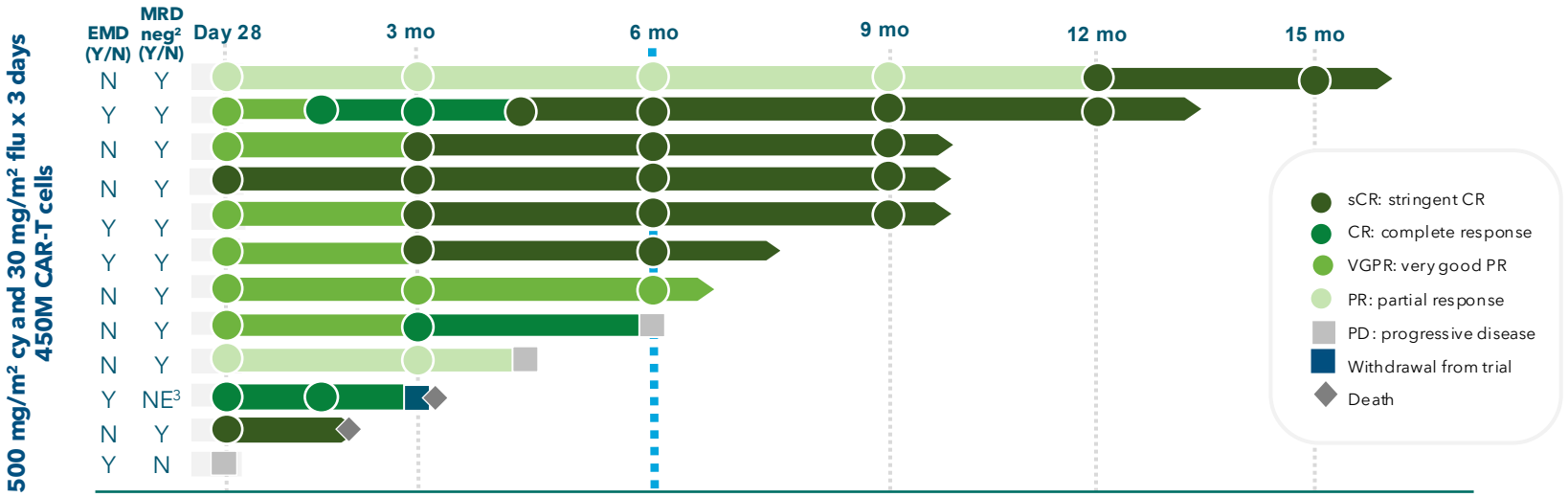
CB-011 induces deep and durable responses at recommended dose for expansion in BCMA-naïve patients[1]

92% ORR (11/12)

75% ≥CR rate (9/12)

91% MRD neg (10/11 evaluable patients)

7 of 12 ≥VGPR at ≥6 months



[1]Selected LD with 450M CAR-T cells; [2]MRD negative at ≤10^{-5}; [3]Sample was not evaluable
One patient who had previously withdrawn from the trial died on day 90 of treatment-related ICAHT; one patient died of pneumonia on day 50 (not treatment related)
Median follow up for all patients in 450M cohort is 8.3 months
Data cutoff 24Sept2025
CR: complete response; cy: cyclophosphamide; flu: fludarabine; LD: lymphodepletion; M: million; mo: month;
MRD: minimal residual disease; NE: not evaluable; ORR: overall response rate

CaMMouflage trial: safety and tolerability

No GvHD, IEC-EC, parkinsonism, or cranial nerve palsies observed at any dose level

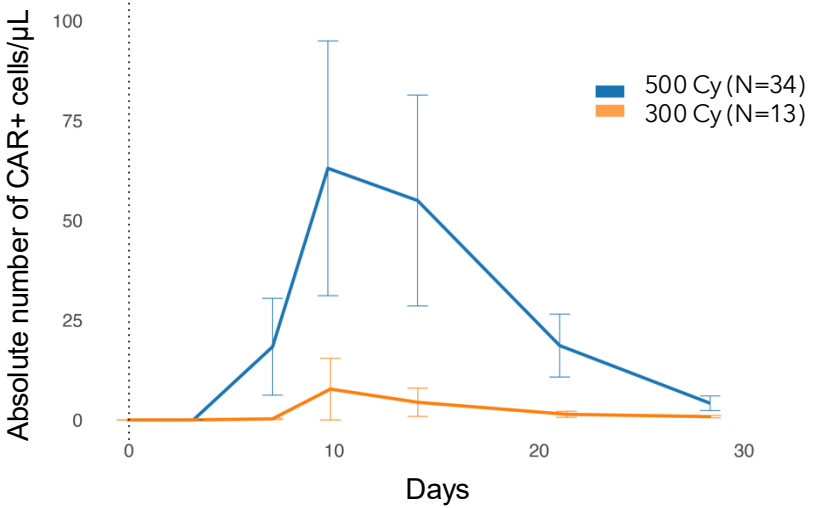
	All at selected LD[1] (N=35)		**BCMA-naïve 450M at selected LD[1]** (N=12)	
Adverse events	Any grade n (%)	Grade ≥3 n (%)	Any grade n (%)	Grade ≥3 n (%)
Infections, n (%)	17 (49)	5 (14)	8 (67)	3 (25)
CRS, n (%)	11 (31)	1 (3)	4 (33)	1 (8)
ICANS, n (%)	3 (9)	--	3 (25)	--
IEC-HS, n (%)	3 (9)	1 (3)	1 (8)	1 (8)
IEC-EC	--	--	--	--
GvHD	--	--	--	--
Prolonged cytopenias[2]	NA	11/33 (33)	NA	5/12 (42)

- Notable AEs are manageable
- 3 events of note at 450M dose level:
  - 1 grade 5 ICAHT (CB-011-related) on day 90[3]
  - 1 grade 5 pneumonia (unrelated to CB-011) on day 50
  - 1 grade 4 Guillain-Barré Syndrome (CB-011-related) on day 129, resolving
- 1 event of note at 300M dose level:
  - 1 grade 5 RSV (unrelated to CB-011) on day 73[4]
- Prophylactic measures for cytopenias and infections and early intervention for IEC-HS have been successfully implemented in the protocol

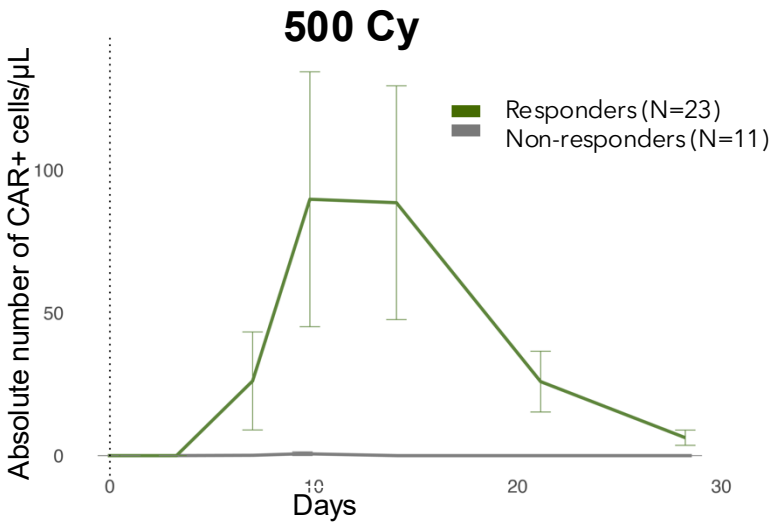
[1]LD regimen of 500 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days.
[2]Any continued ≥ grade 3 cytopenia based on laboratory data at ≥ day 35; denominator is those evaluable at day 35 (+/-5 days).
[3]This patient also experienced a Grade 3 IEC-HS event (reported in table above)
[4]Grade 5 RSV event occurred after data cutoff date of 24Sept2025 and is reflected in data table
Data cutoff 24Sept2025

GvHD: graft-versus-host disease; ICANS: immune effector cell-associated neurotoxicity syndrome; ICAHT: immune effector cell-associated hematotoxicity; IEC-EC: immune effector cell-associated enterocolitis; IEC-HS: immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; LD: lymphodepletion; M: million; NA: not applicable; RSV: respiratory syncytial virus

CB-011 expansion is associated with LD regimen and clinical outcome



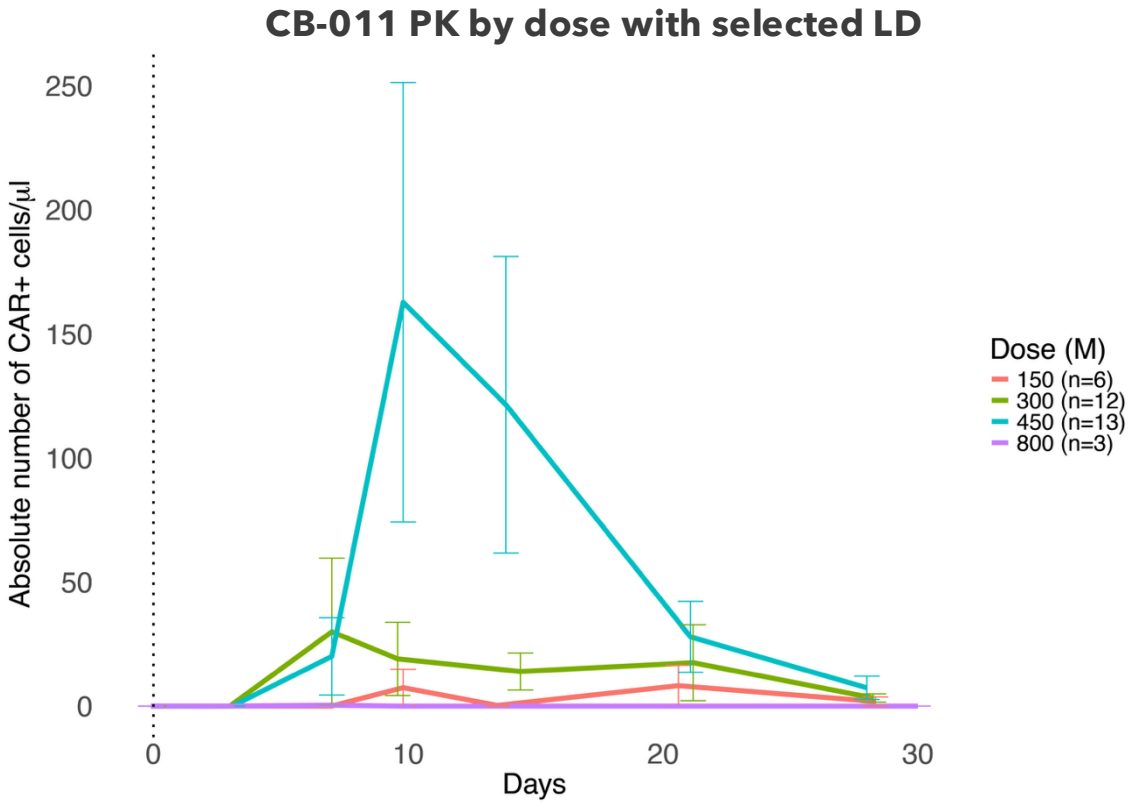
Measurement	500 Cy	300 Cy
Tmax (median)	Day 10	Day 14
Cmax (mean)	71 cells/µL	8 cells/µL
AUC (mean) 0-week 4	662 cells/µL	65 cells/µL



Measurement	Responders	Non-responders
Tmax (median)	Day 14	Day 8
Cmax (mean)	104 cells/µL	1 cells/µL
AUC (mean) 0-week 4	976 cells/µL	4 cells/µL

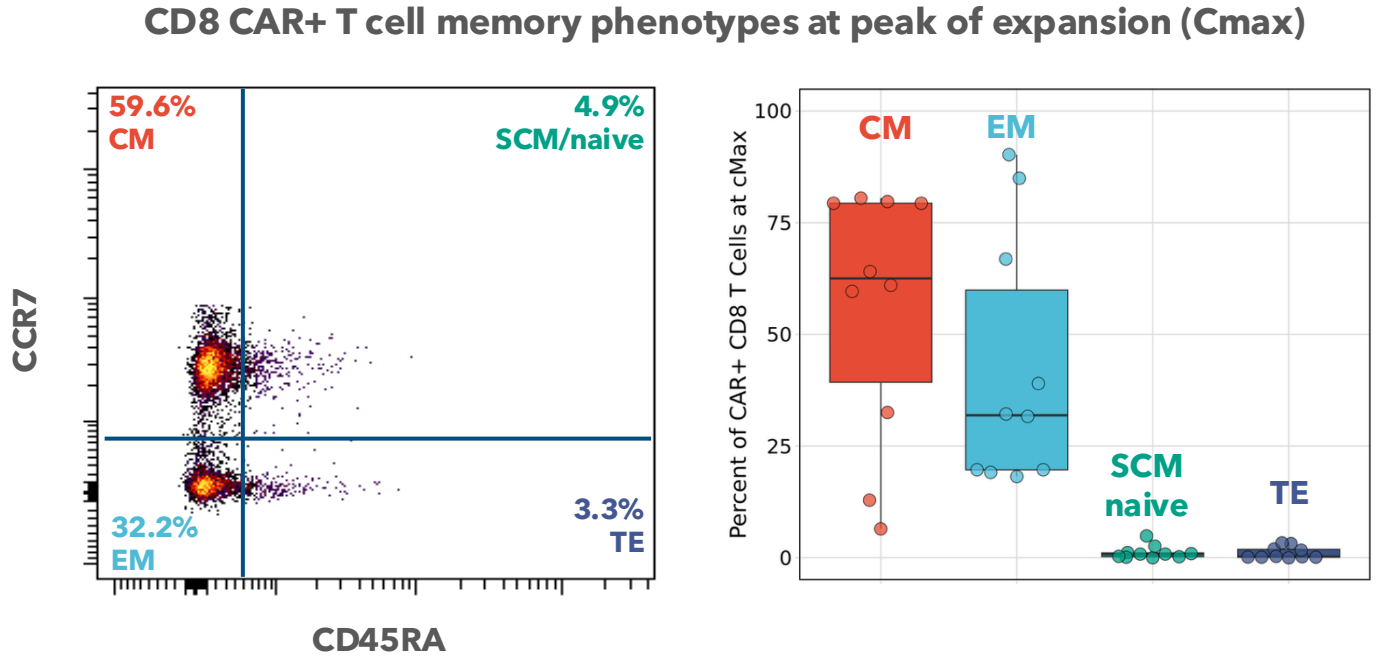
Flow PK data up to Day 28 visit from 34 of 35 patients. Mean with SE shown; Data cutoff 24Sept2025
AUC: area under the curve; Cmax: maximum concentration; Tmax: time to maximum concentration;
LD: lymphodepletion; PK: pharmacokinetic; SE: standard error average

Highest cell expansion at 450M dose level with selected LD



Flow PK data up to Day 28 visit from 34 of 35 patients treated with 500 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days; arithmetic mean with SE shown by dose level
Data cutoff 24Sept2025

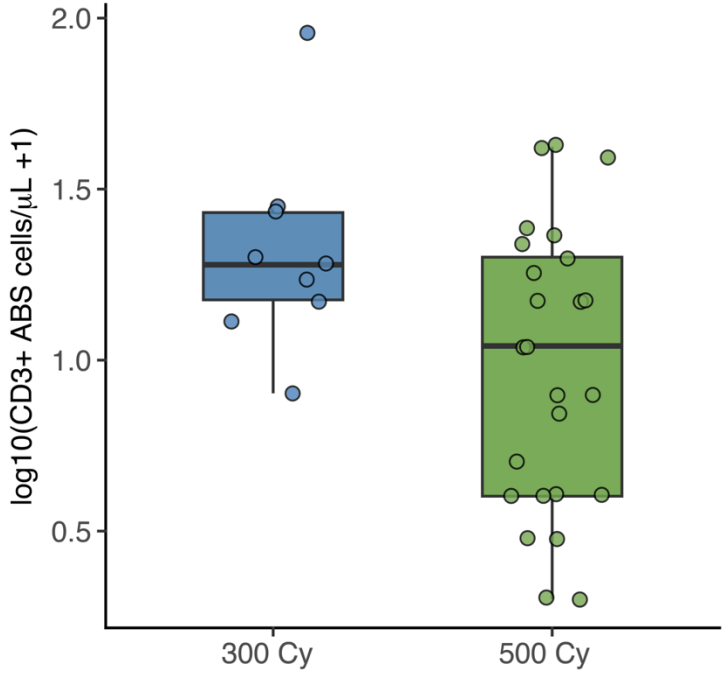
CB-011 exhibits central memory CD8 T cell phenotype at peak of expansion



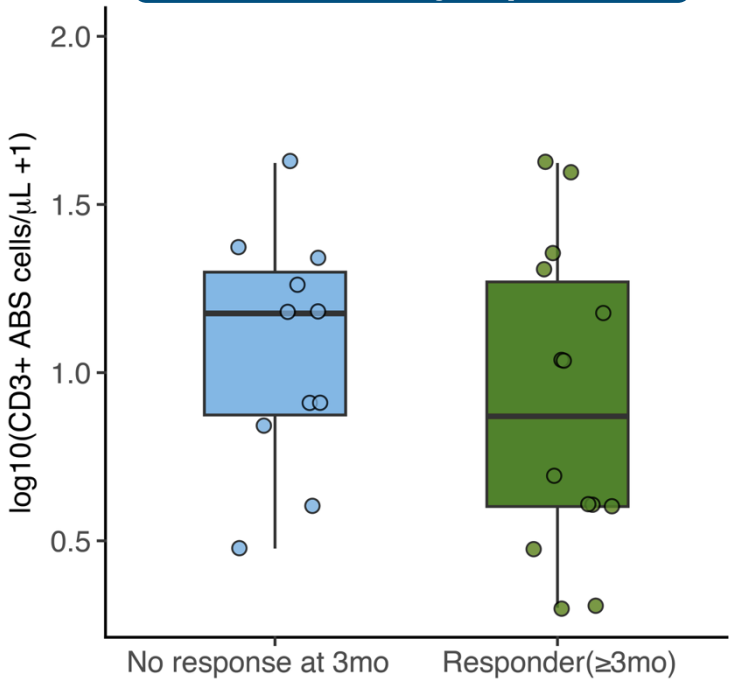
Data shown for 450M dose with selected LD patients with at least 100 CAR+ CD8 T cell events by flow cytometry. (10/13 evaluable patients)
Data cutoff of 24Sept2025
cMax for each patient defined as timepoint with highest CAR+ ABS cells/uL between D0-D28 (Median D14, Range D10-D21)
CM: central memory (CD45RA-CCR7+); EM: effector memory (CD45RA-CCR7-); SCM/naïve: stem cell memory/naïve (CD45RA+CCR+); TE: terminal effector (CD45RA+CCR7-)

Depth of lymphodepletion associated with improved patient outcomes

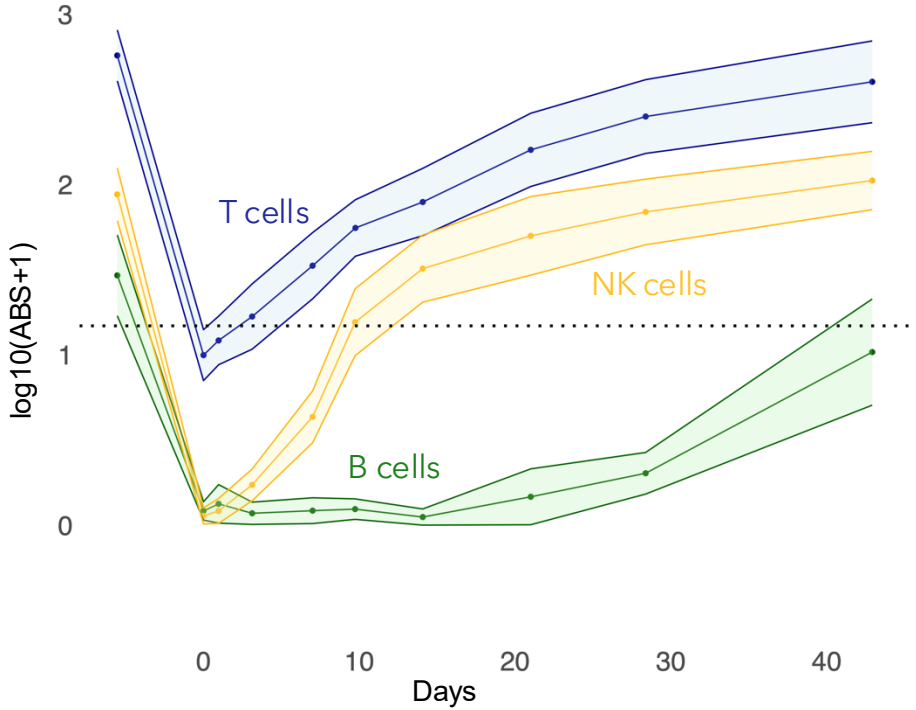
Endogenous T cells at Day 0 by LD dose of cytoxan



Endogenous T cells at Day 0 for selected LD by response



Rapid recovery of endogenous T and NK cells may contribute to the manageable safety profile



- Patient T cell depletion enables CAR-T cell expansion
- Fast recovery of T and NK cells quickly reinstates the patient's natural immunity, likely contributing to the favorable safety profile[1,2]

Average of log transformed values shown with ribbons reflecting standard error; dotted line is lower limit of quantification (LLOQ) for B cells. N=34 (no data collected for n=1). Data through week 6 for 34 patients who received CB-011 with LD regimen of 500 mg/m^2 cy and 30 mg/m^2 flu daily x 3 days.
Data cutoff 24Sept2025

[1]van de Donk N et al. 21st IMS (Annual Meeting, Brazil), 2024, P-090.
[2]Tabbara N, et al. Hematology Am Soc Hematol Educ Program. 2024;(1):116-125

CaMMouflage trial conclusions and next steps

- Deep, durable responses observed with CB-011 in heavily pre-treated r/r MM patients
  - Longest responder remains in sCR with sustained MRD negativity beyond 21 months
- **92% ORR, 75% ≥ CR rate, 91% MRD negativity, and 7 of 12 ≥VGPR at ≥6 months** at the recommended dose for expansion (RDE) of 450M CAR-T cells with selected LD
- **Manageable safety profile** observed with no GvHD, colitis, or parkinsonism
  - Rapid hematologic and immunologic recovery observed after CB-011 infusion
- **Enrollment ongoing in dose expansion** at 450M CAR-T cell dose with selected LD
  - Prior BCMA therapy exposed and BCMA naïve r/r MM patients are eligible
  - Outpatient administration allowed

MRD negative at $\leq 10^{-5}$
Data cutoff 24Sept2025
CR: complete response; GvHD: graft-versus-host disease; M: million; MM: multiple myeloma; MRD: minimal residual disease; ORR: overall response rate; r/r: relapsed or refractory; VGPR: very good partial response.

Gratitude for patients, caregivers, investigators, and site staff