#3377: ANTI-CD3/B-CELL MATURATION ANTIGEN BISPECIFIC ANTIBODY CM336 IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: AN OPEN-LABEL, PHASE I/II STUDY

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INTRODUCTION

- Multiple myeloma is an incurable malignancy characterized with high relapse rates.[1] Therapeutic options to improve clinical outcomes remain limited for patients with relapsed/refractory multiple myeloma (RRMM).[2]
- CM336 is a novel B-cell maturation antigen (BCMA) × CD3 bispecific antibody, redirecting T cells to BCMA-expressing myeloma cells.

AIM

This phase I/II trial aims to evaluate the safety and efficacy of CM336 in RRMM patients (NCT05299424).

METHOD

A first-in-human, open-label, phase I/II trial (**Figure 1**).

Primary endpoints

- **Does escalation (Part A):** incidences of AEs, DLT
- **Dose expansion (Part B):** ORR by IMWG 2016 (sCR, CR, VGPR, PR)

RESULTS

Patients

- Of the 68 enrolled pts, 22% had extramedullary plasmacytoma.
- As of October 30, 2024, 11 pts in Part A and 40 pts in Part B remained on treatment.

Table 1: Demographics and baseline characteristics

	Part A (n=25)	Part B (n=43)
Age, years	63 (41-76)	65 (40-76)
Female	18 (72%)	18 (42%)
ECOG PS		
0-1	23 (92%)	38 (88%)
2	2 (8%)	5 (12%)
Time since diagnosis, years	4.3 (1.4-12.3)	3.7 (0.5-12.6)
ISS stage at screening		
Stage I/II	21 (84%)	34 (79%)
Stage III	4 (16%)	9 (21%)
High-risk cytogenetics [a, b]	5 (42%)	18 (44%)
Extramedullary plasmacytomas	5 (20%)	10 (23%)
No. of prior lines of therapy	4 (2-15)	4 (2-13)
Prior MM therapy		
Triple-class exposed [c]	25 (100%)	43 (100%)
Penta-class exposed [d]	10 (40%)	21 (49%)

Data cutoff date: October 30, 2024. Data are presented as n (%) or median (range). [a] Refers to any positive result for p53 deletion (17p-), t(4;14), or t(14;16). [b] Being analyzed in 12 and 41 pts, respectively. [c] Includes ≥1 IMiD, ≥1 PI, and ≥1 anti-CD38 antibody. [d] Includes ≥2 IMiDs, ≥2 PIs, and ≥1 anti-CD38 antibody. [e] Being analysed based on all 5, 25, 26, 50 pts in the ≤1.0 mg cohorts, Part A, 3/20/80/160 mg cohorts in Part A+B, and the combined doses of 3/20/80 mg and 3/20/80/160 mg cohorts, respectively. [f] Two pts in the ≤1.0 mg cohorts and one pt in the 3/20/80/160 mg cohort had not undergone post-treatment imaging evaluation.
Abbreviations: *BOR, best overall response; ICANS, immune effector cell associated neurotoxicity syndrome; IQR, interquartile range; ISS, International Staging system; MRD, minimal residual disease; NE, not evaluable; NR, not reached; TRAEs, treatment-related adverse events; TTR, time to response*

Safety

- In Part A, maximum tolerated dose was not reached.
- In the overall population (n=68),
  - The most common TEAEs were CRS, lymphocyte count decreased, and anaemia (**Table 2**).
  - TRAEs leading to treatment discontinuation (3%) were infrequent.
  - No drug-related death occurred.
  - Five pts (7%) developed grade 2 CRS. All CRS events were resolved completely.
  - No ICANS was reported.

Efficacy

- In Part A, with a median follow-up of 12.1 months, 12 of 23 (52%) response-evaluable pts (≥1 post-treatment scan) achieved sCR or CR (**Table 3**).
- In the combined cohorts of 3/20/80 mg and 3/20/80/160 mg, the ORR was 71% (**Figure 2**).
- In total 68 pts, 19 pts with sCR or CR were evaluable for MRD. MRD negativity rate was 95%, and median time to MRD-negative response was 2.1 months.

Figure 2: ORR

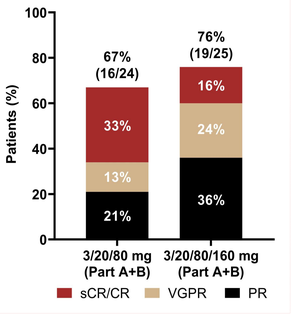


Table 2: TEAEs occurring in ≥30% of overall population

	Part A (n=25)		Part B (n=43)		Total (n=68)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
CRS	17 (68%)	1 (4%)	29 (67%)	0	46 (68%)	1 (1%)
Lymphocyte count decreased	16 (64%)	14 (56%)	26 (60%)	23 (53%)	42 (62%)	37 (54%)
Anaemia	17 (68%)	10 (40%)	24 (56%)	9 (21%)	41 (60%)	19 (28%)
Neutrophil count decreased	16 (64%)	12 (48%)	17 (40%)	13 (30%)	33 (49%)	25 (37%)
White blood cell count decreased	11 (44%)	5 (20%)	21 (49%)	9 (21%)	32 (47%)	14 (21%)
Pyrexia	11 (44%)	1 (4%)	18 (42%)	0	29 (43%)	1 (1%)
Hypokalaemia	10 (40%)	2 (8%)	17 (40%)	3 (7%)	27 (40%)	5 (7%)
Platelet count decreased	9 (36%)	3 (12%)	17 (40%)	4 (9%)	26 (38%)	7 (10%)
Pneumonia	13 (52%)	9 (36%)	13 (30%)	8 (19%)	26 (38%)	17 (25%)

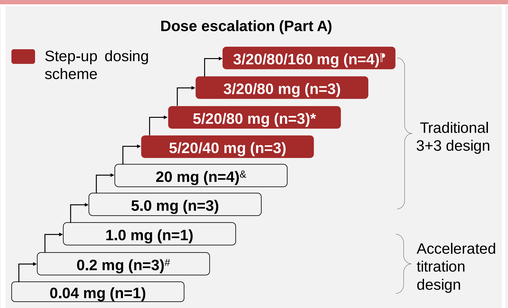
Table 3: Efficacy outcomes

	Part A								Part A+B		
	≤1.0 mg (n=3) [f]	5.0 mg (n=3)	20 mg (n=4)	5/20/40 mg (n=3)	5/20/80 mg (n=3)	3/20/80 mg (n=3)	3/20/80/160 mg (n=4)	Total (n=23) [f]	3/20/80 mg (n=24)	3/20/80/160 mg (n=25) [f]	Total (n=49) [f]
BOR											
sCR/CR	0	1 (33%)	3 (75%)	2 (67%)	2 (67%)	3 (100%)	1 (25%)	12 (52%)	8 (33%)	4 (16%)	12 (24%)
VGPR	0	0	0	0	0	0	1 (25%)	1 (4%)	3 (13%)	6 (24%)	9 (18%)
PR	0	0	0	0	0	0	1 (25%)	1 (4%)	5 (21%)	9 (36%)	14 (29%)
MR	0	0	1 (25%)	0	0	0	0	1 (4%)	1 (4%)	0	1 (2%)
SD	1 (33%)	2 (67%)	0	1 (33%)	0	0	1 (25%)	5 (22%)	2 (8%)	4 (16%)	6 (12%)
NE	0	0	0	0	0	0	0	0	2 (8%)	1 (4%)	3 (6%)
PD	2 (67%)	0	0	0	1 (33%)	0	0	3 (13%)	3 (13%)	1 (4%)	4 (8%)
ORR	0	1 (33%)	3 (75%)	2 (67%)	2 (67%)	3 (100%)	3 (75%)	14 (61%)	16 (67%)	19 (76%)	35 (71%)
Median follow-up (IQR), mo [e]	16.6 (12.1-18.3)	13.8 (13.2-16.2)	14.5 (13.9-15.0)	11.9 (11.6-13.4)	11.9 (9.2-12.1)	9.9 (9.9-10.5)	5.9 (4.9-7.4)	12.1 (9.9-14.1)	2.8 (2.0-4.0)	3.2 (2.1-4.3)	3.1 (2.1-4.2)
TTR, mo	0	0.7	1.6 (1.4-3.8)	0.9 (0.7-1.0)	1.5 (1.3-1.6)	1.6 (1.4-2.2)	1.0 (0.9-2.1)	1.4 (0.7-3.8)	1.4 (0.6-2.2)	1.4 (0.7-3.4)	1.4 (0.6-3.4)
MRD negativity rate, n/N (%)	0	1/1 (100%)	3/3 (100%)	2/2 (100%)	2/2 (100%)	2/3 (67%)	1/1 (100%)	11/12 (92%)	6/7 (86%)	4/4 (100%)	10/11 (91%)
Time to MRD-negative response, mo	0	1.6	12.0 (8.0-12.0)	2.8 (1.0-4.6)	10.4 (10.1-10.8)	4.1 (3.7-4.5)	1.2	4.6 (1.0-12.0)	1.8 (1.2-4.5)	1.9 (1.2-2.3)	1.9 (1.2-4.5)

Figure 1: CM336 dosing schedule

Key Eligibility
- 18 years or older
- ECOG PS score of ≤2
- Measurable MM
- ≥2 prior lines of therapy with exposure to a PI, an IMiD, and an anti-CD38 antibody.

Subcutaneous injection once weekly (21-day cycle)



[#] Expanded to 3 pts due to incomplete DLT observation period and early dropout due to PD.
[&] Expanded to 4 pts due to incomplete scheduled administration caused by COVID-19 during DLT observation period.
* One DLT (grade 3 CRS) occurred; and then 3/20/80 mg was given for the next 3 pts.
[β] Expanded to 4 pts due to early withdrawal without undergoing DLT evaluation.

Abbreviations: AEs, adverse events; CR, complete response; CRS, cytokine release syndrome; DLT, dose-limited toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; ORR, objective response rate; PD, progressive disease; PI, proteasome inhibitor; PR, partial response; pts; patients; sCR, stringent complete response; VGPR, very good partial response.

CONCLUSIONS

- CM336 was well-tolerated, with a manageable safety profile.
- CM336 demonstrated promising preliminary clinical efficacy in RRMM patients.

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