# EP1009 IDECABTAGENE VICLEUCEL (IDE-CEL, BB2121), A BCMA-DIRECTED CAR T CELL THERAPY, IN PATIENTS WITH RELAPSED AND REFRACTORY MULTIPLE MYELOMA: UPDATED KARMMA RESULTS

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## Background

Patients with relapsed and refractory multiple myeloma (RRMM) previously exposed to immunomodulatory agents, proteasome inhibitors (PIs), and anti-CD38 monoclonal antibodies (mAbs) have poor outcomes with subsequent treatments. In the pivotal KarMMa trial, ide-cel, a BCMA-directed CAR T cell therapy, showed frequent, deep, and durable responses in heavily pretreated patients with RRMM (Munshi NC, et al. *N Engl J Med* 2021;384:705-716).

## Aims

To report updated efficacy and safety data from the phase 2 KarMMa trial (NCT03361748).

## Methods

Eligible patients had received ≥ 3 prior regimens (including an immunomodulatory agent, a PI, and an anti-CD38 mAb) and were refractory to their last regimen per IMWG criteria. After 3 days of lymphodepletion (cyclophosphamide 300 mg/m$^2$ + fludarabine 30 mg/m$^2$), patients received 150–450 × $10^6$ CAR+ T cells (target dose levels). The primary endpoint was overall response rate (ORR). The key secondary endpoints included complete response (CR) rate (CR + stringent CR [sCR]). Other secondary endpoints included duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety.

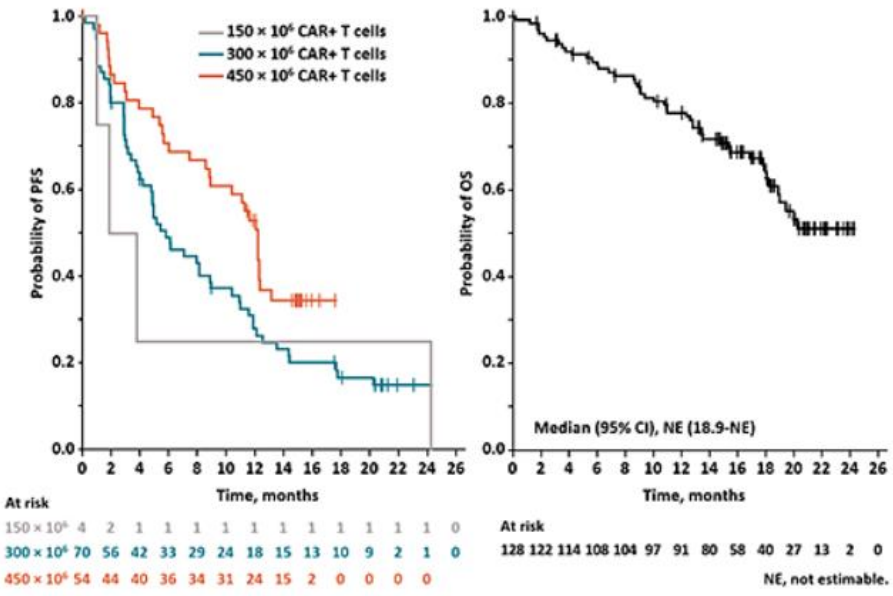
## Results

Of the 140 patients enrolled in KarMMa, 128 received ide-cel. Data are presented for the treated patients, who had a median age of 61 years and had received a median of 6 (range, 3-16) prior regimens; 84% were triple-class refractory, and 26% were penta-refractory (lenalidomide, pomalidomide, bortezomib, carfilzomib, and daratumumab). Most patients (88%) had received bridging therapy. At the data cutoff (7 April 2020), the median follow-up was 15.4 months. The ORR was 73% and the median PFS was 8.8 months; both increased with

higher dose (**Table**). At the highest target dose (450 × $10^6$ CAR+ T cells), the ORR was 81%, the CR rate was 39%, and the median PFS increased to 12.2 months with longer follow-up. Responses were observed in all subgroups, including difficult-to-treat subsets (eg, high tumor burden [ORR, 71%], extramedullary disease [70%], and R-ISS stage III disease [48%]). OS continues to mature, and the median has not been reached (**Figure**); the estimated 15-month OS rate was 71%. The most common any-grade toxicities were cytopenia (97%) and cytokine release syndrome (CRS; 84%). CRS was mostly grade 1/2; 5 patients (4%) had grade 3, 1 had grade 4 (at 300 × $10^6$), and 1 had grade 5 (at 300 × $10^6$) events. Investigator-identified neurotoxicity was reported in 23 patients (18%); 4 patients (3%) had grade 3 and 0 had grade ≥ 4 events. Tocilizumab was used in 67 and 3 patients with CRS and neurotoxicity, respectively. Similarly, steroids were used in 19 and 10 patients with CRS and neurotoxicity, respectively.

| Dose, × $10^6$ CAR+ T cells | 150 (n = 4) | 300 (n = 70) | 450 (n = 54) | 300-450 (n = 124) | Total (N = 128) |
|---|---|---|---|---|---|
| ORR, n (%) | 2 (50) | 48 (69) | 44 (81) | 92 (74) | 94 (73) |
| CR/sCR, n (%) | 1 (25) | 20 (29) | 21 (39) | 41 (33) | 42 (33) |
| Median DOR, mo* | † | 9.9 | 11.3 | 10.7 | 10.7 |
| Median PFS, mo* | † | 5.8 | 12.2 | 8.8 | 8.8 |

*Kaplan-Meier estimate. †Not reported due to small n.




## Conclusion

Updated results from the KarMMa trial continue to demonstrate deep, durable responses with ide-cel in heavily pretreated, triple-class–exposed patients with RRMM. Efficacy and safety reflect prior reports and support a favorable clinical benefit-risk profile for ide-cel across the target dose levels.

**Keyword(s):** CAR-T, Myeloma, Refractory, Relapse