Idecabtagene vicleucel (ide-cel, bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): initial KarMMa results

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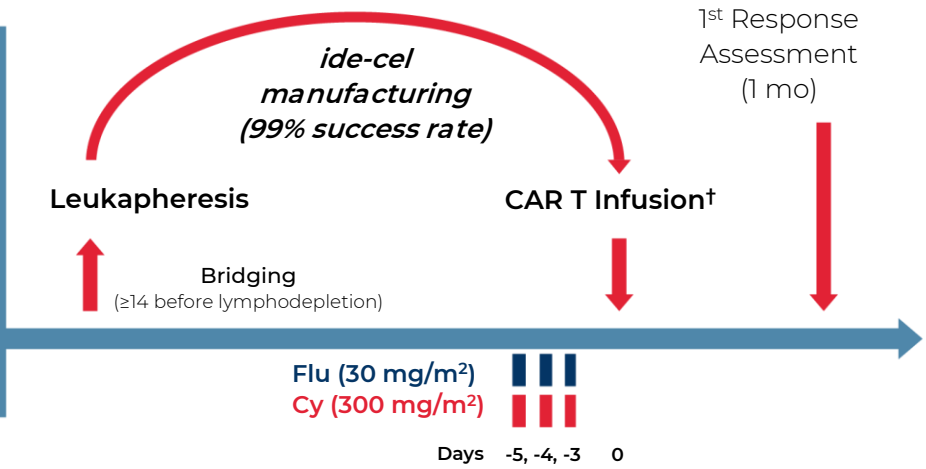
HEMA NEWS

Presented on: EHA 25 Virtual Congress, June 11-14, 2020

Phase II Pivotal KarMMa Study

- RRMM
- ≥3 prior regimens with ≥2 consecutive cycles each (or best response of PD)
- Previously exposed to:
  - IMiD agent
  - Proteasome inhibitor
  - Anti-CD38 antibody
- Refractory to last prior therapy per IMWG*



Study Status as of Jan 14, 2020§

Screened N=158	
Leukapheresed N=140	
Treated N=128 (Target Dose CAR+ T cells)	
150 × 10^6	n=4
300 × 10^6	n=70
450 × 10^6	n=54
Median Follow-up (mo)	
150 × 10^6	18.0
300 × 10^6	15.8
450 × 10^6	12.4
Total	13.3

Endpoints

- Primary: ORR (null hypothesis ≤50%)
- Secondary: CRR (key secondary; null hypothesis ≤10%), Safety, DOR, PFS, OS, PK, MRD‡ , QOL, HEOR
- Exploratory: Immunogenicity, BCMA expression/loss, cytokines, T cell immunophenotype, GEP in BM

EudraCT: 2017-002245-29
ClinicalTrials.gov: NCT03361748

BCMA, B-cell maturation antigen; CRR, complete response rate; Cy, cyclophosphamide; DOR, duration of response; Flu, fludarabine; GEP in BM, gene expression profile in bone marrow; HEOR, health economics and outcomes research; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; QOL, quality of life.
*Defined as documented disease progression during or within 60 d from last dose of prior antimyeloma regimen. †Patients were required to be hospitalized for 14 d post-infusion. Ide-cel retreatment was allowed at disease progression for best response of at least stable disease. ‡By next-generation sequencing. §Cutoff is with a minimum follow-up of 13 mo after the last patient received ide-cel.

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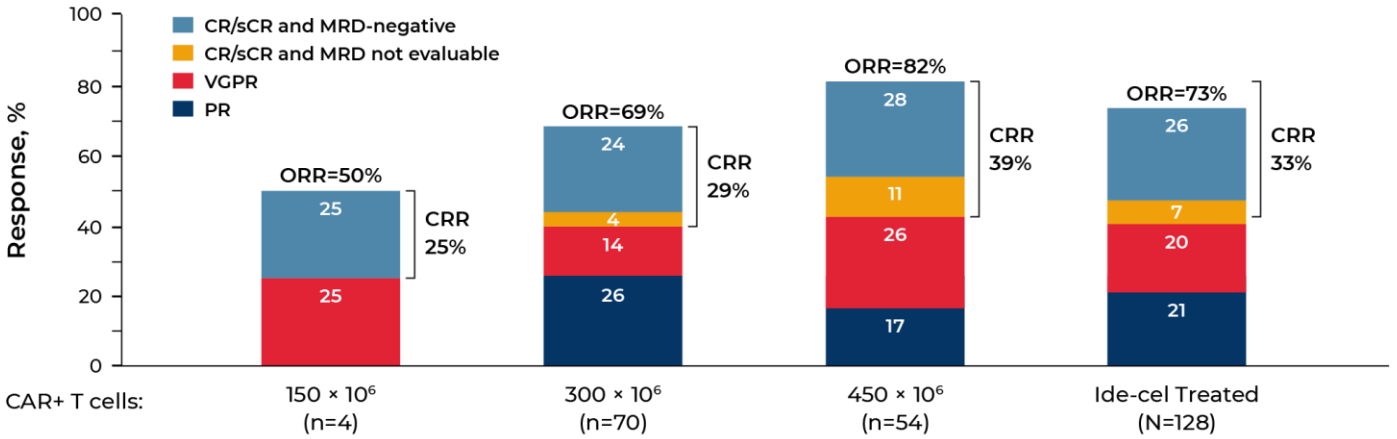
Best Overall Response



- Primary (ORR >50%) and key secondary (CRR >10%) endpoints were met in the ide-cel treated population
  - *ORR of 73% (95% CI, 65.8–81.1; P<0.0001*) and CRR (CR/sCR) of 33% (95% CI, 24.7–40.9; P<0.0001)*
  - *Both ORR and CRR increased with higher target dose*
- Median time to first response of 1.0 mo (range, 0.5–8.8); median time to CR/sCR of 2.8 mo (range, 1.0–11.8)
- Median follow-up of 13.3 mo across target dose levels

Data cutoff: 14 Jan 2020. MRD-negative defined as $<10^{-5}$ nucleated cells by next generation sequencing. Only MRD values within 3 mo of achieving CR/sCR until progression/death (exclusive) were considered. Values may not add up due to rounding. CR/sCR, complete response/stringent CR; CRR, CR rate; MRD, minimal residual disease; ORR, overall response rate (≥PR); PR, partial response; VGPR, very good PR. **P* value from the primary analysis (data cutoff: 16 Oct 2019) with same ORR and 95% CI.

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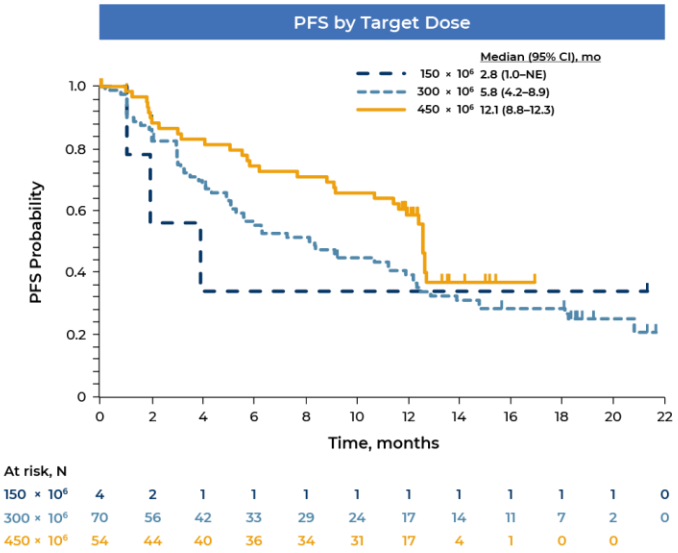
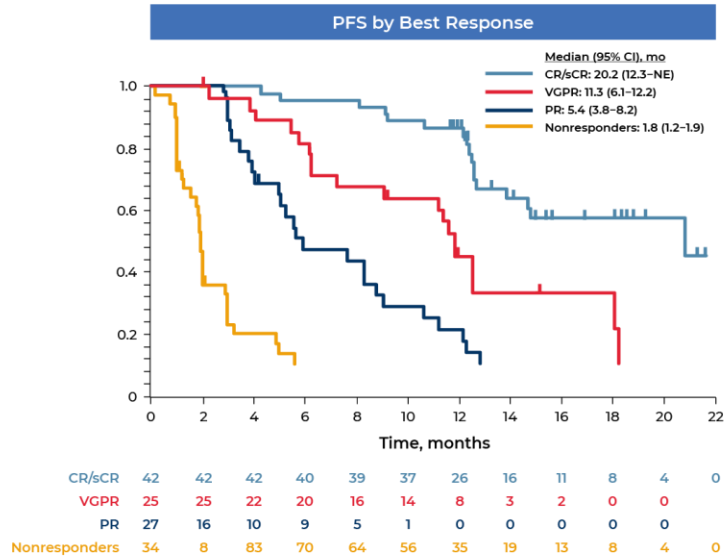
Progression-Free Survival By Target Dose and Best Response



- PFS increased with higher target dose; median PFS was 12 mo at 450 × 10^6 CAR+ T cells



- PFS increased by depth of response; median PFS was 20 mo in patients with CR/sCR

Data cutoff: 14 Jan 2020. NE, not estimable; PFS, progression-free survival.

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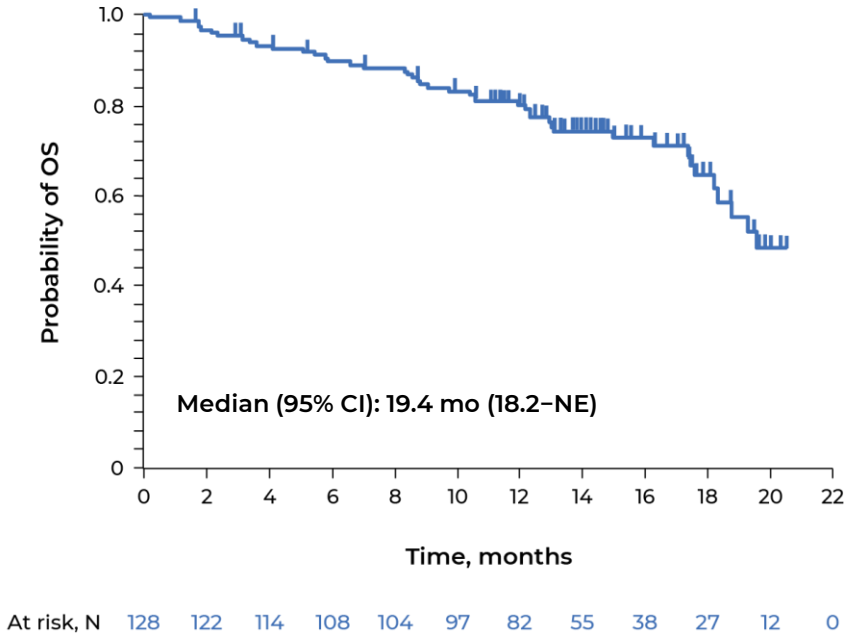
Overall Survival



- 78% of all ide-cel treated patients were event-free at 12 mo
- Survival data are immature with 66% of patients censored overall; 72% at target dose of 450 × 10^6 CAR+ T cells

Data cutoff: 14 Jan 2020. NE, not estimable; OS, overall survival.

- *Munshi et al. Idecabtagene vicleucel (ide-cel; bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): Initial KarMMa results. Presentation at American Society of Clinical Oncology (ASCO) meeting, 2020; May 29-31, 2020. Abs. 8503.*

Most Common Adverse Events

AE,* n (%)	Ide-cel Treated (N=128)	
	Any Grade	Grade ≥3
Hematologic		
Neutropenia	117 (91)	114 (89)
Anemia	89 (70)	77 (60)
Thrombocytopenia	81 (63)	67 (52)
Leukopenia	54 (42)	50 (39)
Lymphopenia	35 (27)	34 (27)
Gastrointestinal		
Diarrhea	45 (35)	2 (2)
Nausea	37 (29)	0
Other		
Hypokalemia	45 (35)	3 (2)
Fatigue	43 (34)	2 (2)
Hypophosphatemia	38 (30)	20 (16)
Hypocalcemia	34 (27)	10 (8)
Pyrexia	32 (25)	3 (2)
Hypomagnesemia	30 (23)	0
Decreased appetite	27 (21)	1 (<1)
Headache	27 (21)	1 (<1)
Hypogammaglobulinemia	27 (21)	1 (<1)
Cough	26 (20)	0
CRS†	107 (84)	7 (5)

- Cytopenias were common; not dose related
- Median time to recovery of grade ≥3 neutropenia and thrombocytopenia was 2 mo (95% CI, 1.9–2.1) and 3 mo (95% CI, 2.1–5.5), respectively‡
- Delayed recovery (>1 mo) of grade ≥3 neutropenia in 41% of patients and thrombocytopenia in 48%§
- Infections (including bacterial, viral, fungal) were common (69%); not dose-related
- 5 deaths (4%) within 8 wk of ide-cel infusion
  - 2 following MM progression
  - 3 from AEs (CRS, aspergillus pneumonia, GI hemorrhage)
- 1 additional death from AE (CMV pneumonia) within 6 mo, in the absence of MM progression

‡Recovery determined by laboratory values. §Includes patients with grade 3/4 cytopenia at 1 mo post-infusion.

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