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ASH 2020 Data Review

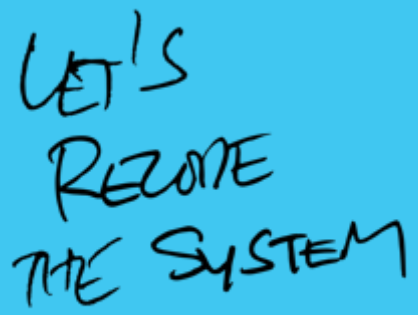
Dec 7, 2020

LET'S RECODE THE STORY

NASDAQ: BLUE

forward-looking statements

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements we make regarding the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our ability to advance product candidates into, and successfully complete, clinical studies, the timing or likelihood of regulatory filings and approvals, and the timing and likelihood of entering into contracts with payors for value-based payments over time or reimbursement approvals, and our commercialization plans for approved products are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties that are described in our most recent quarterly report on Form 10-Q, as well as our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.



today's agenda

welcome	Nick Leschly *chief bluebird*
LentiGlobin for TDT and SCD data	Richard Colvin, M.D. PhD, *head of SGD clinical research*
CRB-401 (ide-cel) data	Liviu Niculescu, M.D. PhD, *head of clinical development for multiple myeloma*
CRB-402 (bb21217) data	Philip Gregory, D. Phil., *chief scientific officer*
Q&A to include	Chip Baird, *chief financial officer* Dave Davidson, M.D. *chief medical officer*

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Must Beat the Odds.

Period.

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Compelling data across programs

LentiGlobin SCD	Complete elimination (100%) of severe VOEs
LentiGlobin TDT	Up to 6 years of TI across all ages and genotypes; 87% TI in pediatric patients
CRB-401 (ide-cel)	34.2 months median overall survival
CRB-402 (bb21217)	84% ORR with 32% CR at the recommended 450 dose; 17 months mDOR at all doses

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Sickle Cell Disease

Resolution of Serious Vaso-Occlusive Pain Crises and Reduction in Patient-Reported Pain Intensity: Results from the Ongoing Phase 1/2 HGB-206 Group C Study of LentiGlobin for Sickle Cell Disease (bb1111) Gene Therapy

Improvements in Health-Related Quality of Life for Patients Treated with LentiGlobin for Sickle Cell Disease (bb1111) Gene Therapy

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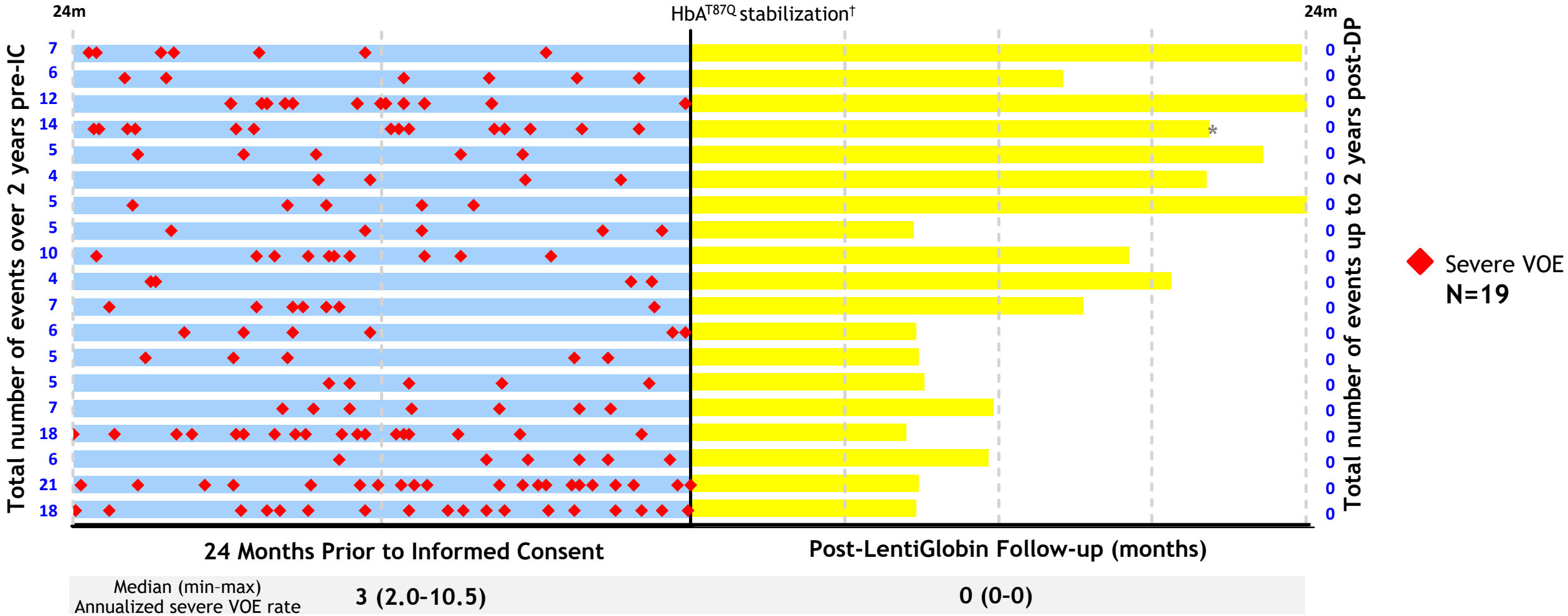
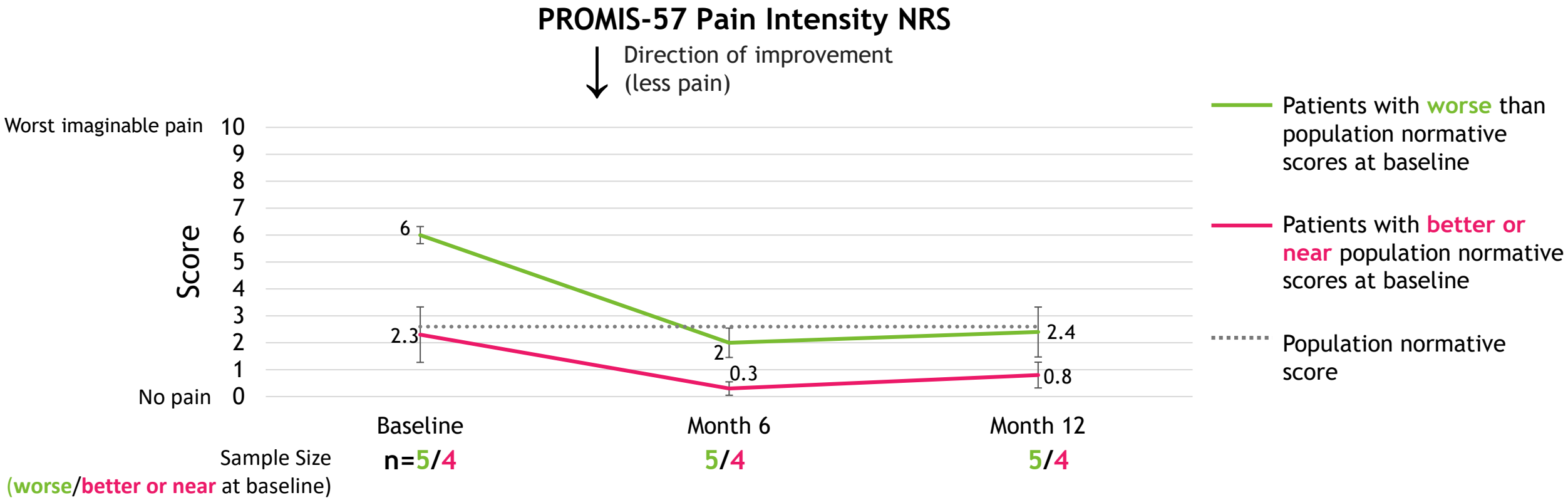
HGB-206 Group C: Complete resolution of severe VOEs post-LentiGlobin treatment



Protocol sVOEs are shown; Patients with ≥ 4 sVOE at baseline before IC and with ≥ 6 months of follow-up post-DP infusion are included. A severe VOE is as an event with no medically determined cause other than a vaso-occlusion, requiring a ≥24-hour hospital or emergency room observation unit visit or at least 2 visits to a day unit or ER over 72 hours with both visits requiring intravenous treatment for the following: acute episodes of pain, acute chest syndrome, acute hepatic sequestration, and acute splenic sequestration; †HbA^{T87Q} stabilizes within 6 months; *One death, unlikely related to LentiGlobin, > 18 months post treatment in a patient with significant baseline SCD-related cardiopulmonary disease.
Note: In the last datacut, one patient had a non-serious VOCexpression at Day 107. This event is recorded as an investigator reported VOE but does not meet the definition of a protocol VOE
DP, drug product; ER, emergency room; IC, informed consent; max, maximum; min, minimum; sVOEs, severe VOEs; VOE, vaso-occlusive event; VOC, vaso-occlusive crises.

Data as of 20 August 2020

HGB-206 Group C: Decrease in patient-reported pain intensity

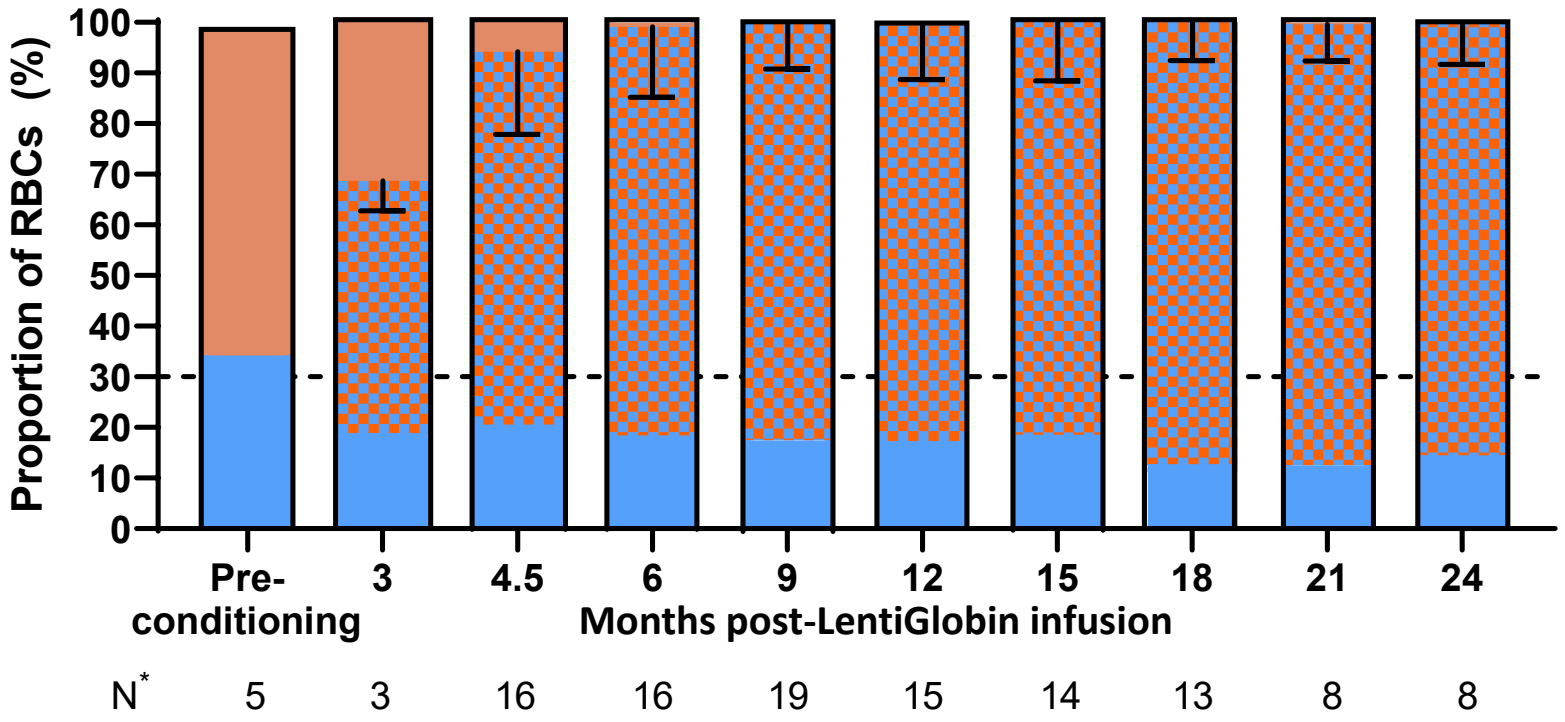


Patients with baseline values (n):	At Month 12
Worse than population normative values (n=5)	All 5 patients reported improvement, including clinically meaningful improvement in 4 patients
Better or near population normative values (n=4)	Patients either remained stable (n=2) or reported clinically meaningful improvement (n=2)

Average pain (0-10) over the past 7 days

NRS, Numeric Rating Scale; PROMIS, Patient Reported Outcomes Measurement Information System

HGB-206 Group C: Near pancellular expression of HbA^{T87Q} ≥ 6 months post-LentiGlobin treatment



RBCs with β^A only (Source: transfused blood)

RBCs positive for $\beta^{A\text{-}T87Q}$ by single cell Western (RBCs with detectable $\beta^{A\text{-}T87Q}$ in addition to β^S)

RBCs with β^S only

- Median (min–max) HbA^{T87Q}/RBC was 15.3 (11.7–20)† pg in patients with ≥ 6 months follow-up, which is comparable to the 13–18 pg of HbA/RBC in individuals with sickle cell trait‡ and higher than 10 pg of HbF/RBC in those with HPFH§

Mean & SD are depicted; Reducing HbS to < 30% is recommended by guidelines for exchange RBC transfusions for patients with SCD (indicated by dashed line); *Number of patients with data available; †Calculated as (% HbA^{T87Q} of total Hb/% RBCs containing $\beta^{A\text{-}T87Q}$) x MCH; ‡Calculated to 13–18 pg HbA/RBC using 50% HbA/RBC for the lower end of the range and 60% HbA/RBC for the upper end of the range; §Estimated in Steinberg MH et al., Blood 2014.
Hb, hemoglobin; HPFH, hereditary persistence of fetal hemoglobin; max, maximum; MCH, mean corpuscular hemoglobin; min, minimum; pg, picogram; RBCs, red blood cells; SD, standard deviation.

Data as of 20 August 2020

ß-thalassemia

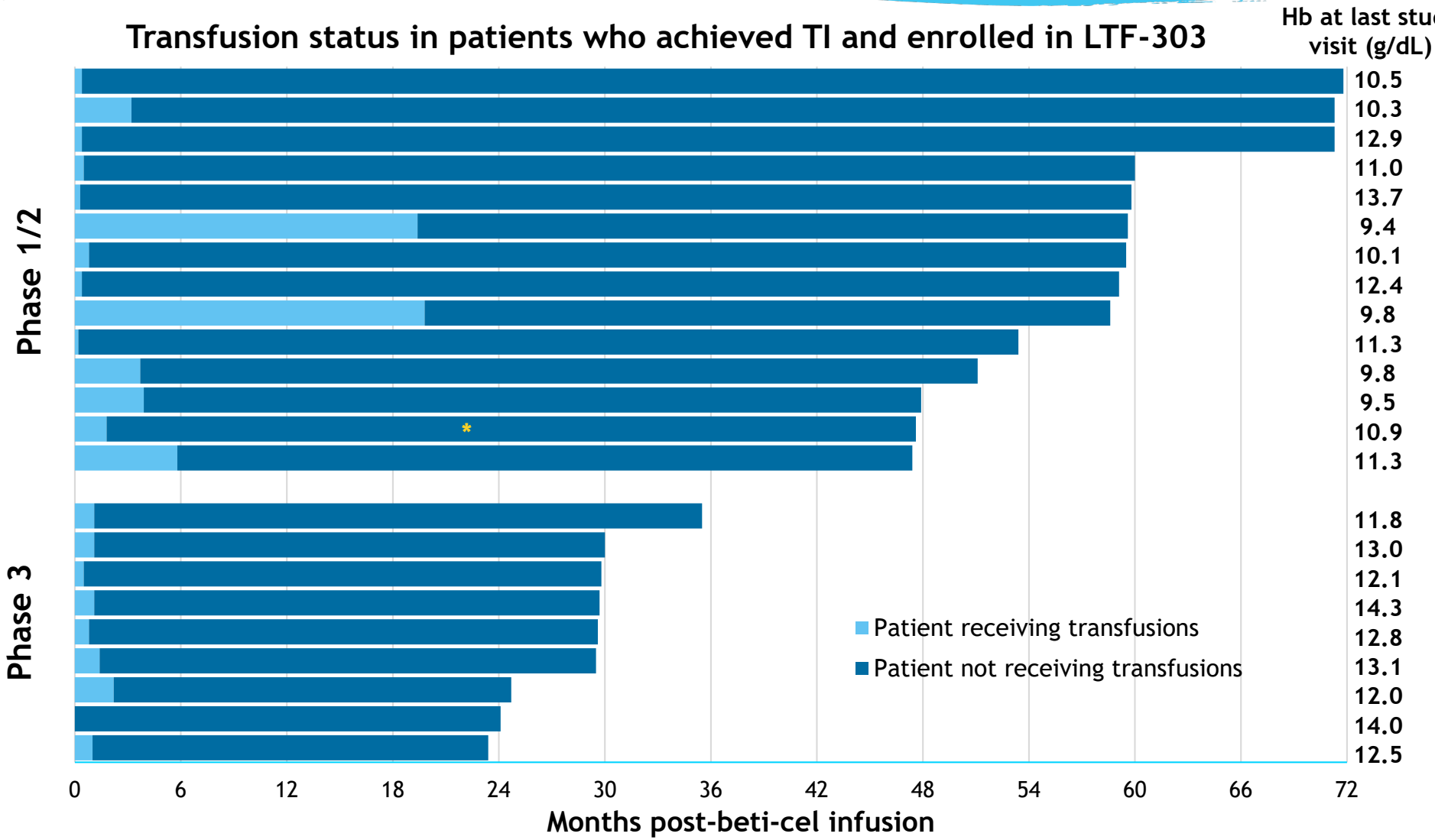
Transfusion dependent thalassemia Long-Term Efficacy and Safety of Betibeglogene Autotemcel (beti-cel) Gene Therapy for the Treatment of Transfusion-Dependent ß-Thalassemia: Results in Patients with up to 6 Years of Follow-up

Favorable outcomes in pediatric patients in the phase 3 HGB-207 (Northstar-2) and HGB-212 (Northstar-3) studies of betibeglogene autotemcel gene therapy for the treatment of transfusion-dependent ß-thalassemia

Response of patients with transfusion-dependent ß-thalassemia (TDT) to betibeglogene autotemcel (beti-cel; LentiGlobin for ß-thalassemia) gene therapy based on HBB genotype and disease genetic modifiers

Improvement in erythropoiesis in patients with transfusion-dependent ß-thalassemia following treatment with betibeglogene autotemcel (LentiGlobin for ß-thalassemia) in the Phase 3 HGB-207 study

Maintained durable transfusion independence with long term follow-up



All patients who achieved TI, maintain TI

64% (14/22) of patients in Phase 1/2 achieved TI†

Duration of ongoing TI:
51.2 (28.1 – 69.4) months

Weighted average Hb:
10.4 (9.4 – 13.3) g/dL

90% (9/10) of patients in Phase 3 achieved TI†

Duration of ongoing TI:
26.1 (19.4 – 31.4) months

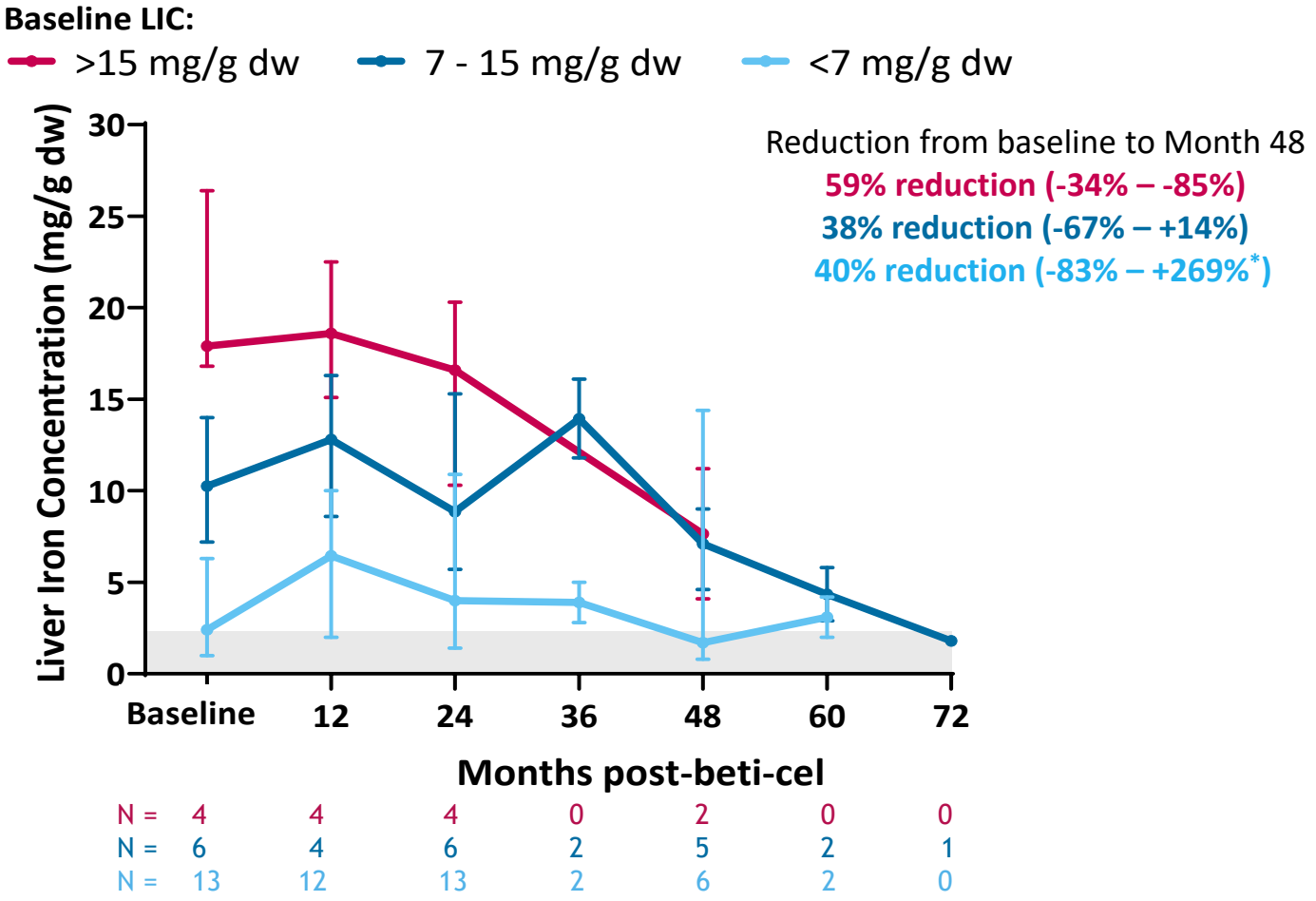
Weighted average Hb:
12.5 (11.9 – 13.5) g/dL

*Patient had a single transfusion for an acute event of Bartonella infection; †Includes patients of all genotypes/ages who entered LTF-303.
Hb, hemoglobin; TI, transfusion independence (defined as weighted average Hb ≥ 9 g/dL without packed red blood cell transfusions for ≥ 12 months).

Data as of 3 March 2020

Reduced iron burden over time in transfusion independent patients

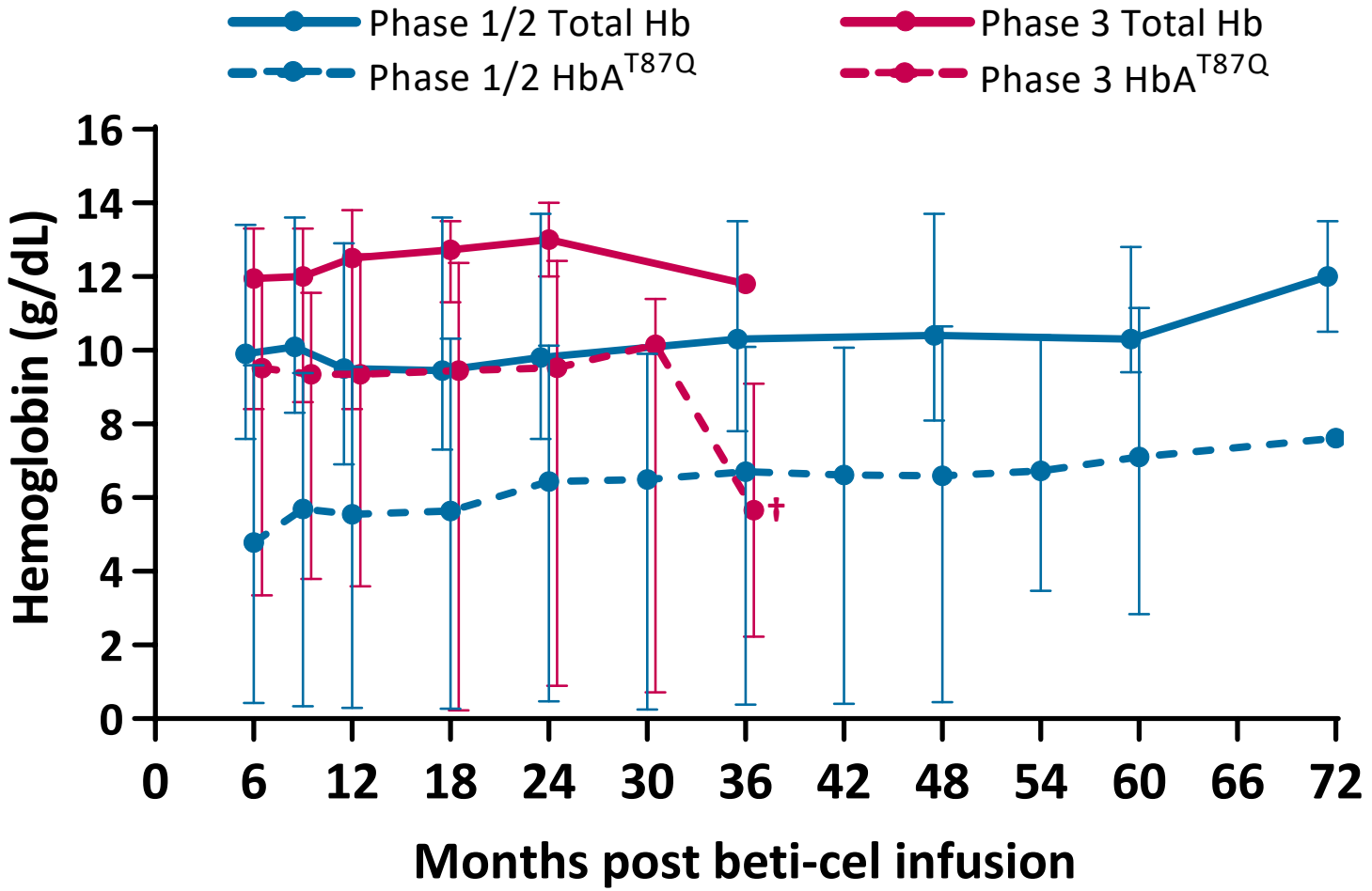
Liver iron content in patients who achieved TI



*The patient with a 269% increase at Month 48 had an LIC over time of 3.9 mg/g dw (baseline), 3.6 mg/g dw (Month 24), 2.8 mg/g dw (Month 36), 14.4 mg/g dw (Month 48), 4.2 mg/g dw (Month 60).
Median (min – max) depicted. Gray bar indicates reference range. LIC, liver iron concentration; TI, transfusion independence.

Data as of 3 March 2020

Durable HbA^{T87Q} support stable total Hb



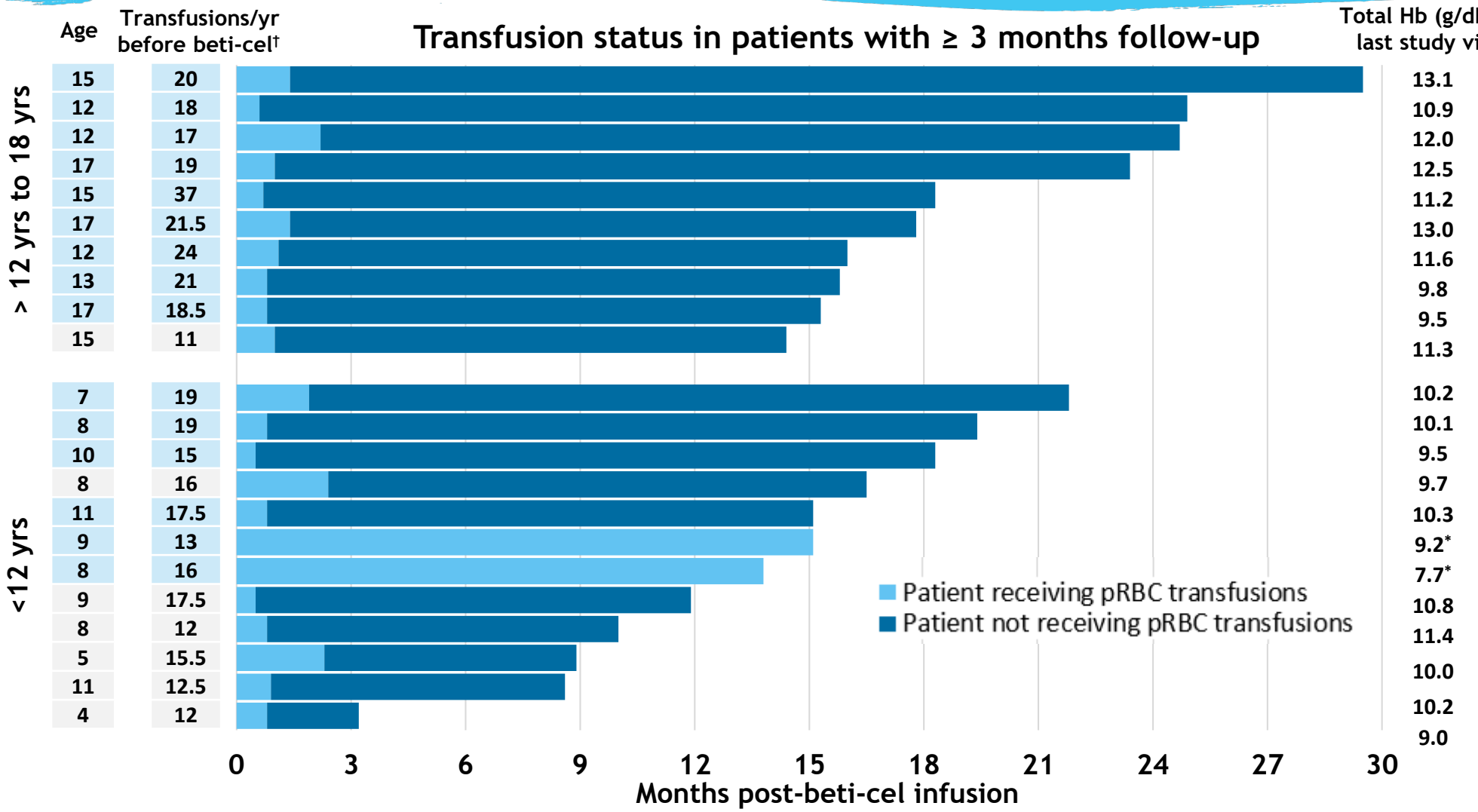
Total Hb represents unsupported Hb without pRBC transfusions in the prior 60 days

† The change in peripheral blood VCN and HbA^{T87Q} levels in phase 3 at Month 36 are the result of a change in sample size. The 2 patients had HbA^{T87Q} levels at Month 30 and 36 of 9.9 and 9.1 g/dL and 0.7 and 2.2 g/dL, respectively. Median (min – max) depicted.

n* = number of pts with HbA^{T87Q} evaluation; Hb, hemoglobin.

Data as of 3 March 2020

87% (13/15) of evaluable pediatric patients achieved transfusion independence



9/9 patients ≥12 to <18 yrs achieved TI

- **Duration of ongoing TI: 14.9** (12.2 – 21.6) months
- **Weighted average Hb during TI: 11.4** (9.5 – 12.8) g/dL

4/6 patients <12 yrs achieved TI

- **Duration of ongoing TI: 15.2** (12.3 – 17.7) months
- **Weighted average Hb during TI: 10.1** (9.4 – 10.3) g/dL

Grey boxes indicate patients not evaluable for TI; †Annualized transfusion episodes within 2 yrs of enrollment. *Hb supported by pRBC transfusions
The two patients who continue to receive transfusions received drug product with 61% and 58% vector-positive cells; peripheral blood vector copy number at last study visit was 0.19 copies/diploid genome (c/dg) and 0.22 c/dg.
TI, transfusion independence (defined as weighted average hemoglobin (Hb) ≥ 9 g/dL without packed red blood cell (pRBC) transfusions for ≥ 12 months).

Data as of 3 March 2020

CRB-401

Idecabtagene vicleucel (ide-cel, bb2121), a BCMA-directed CAR T cell therapy, in patients with relapsed and refractory multiple myeloma: updated results from phase 1 CRB-401 study

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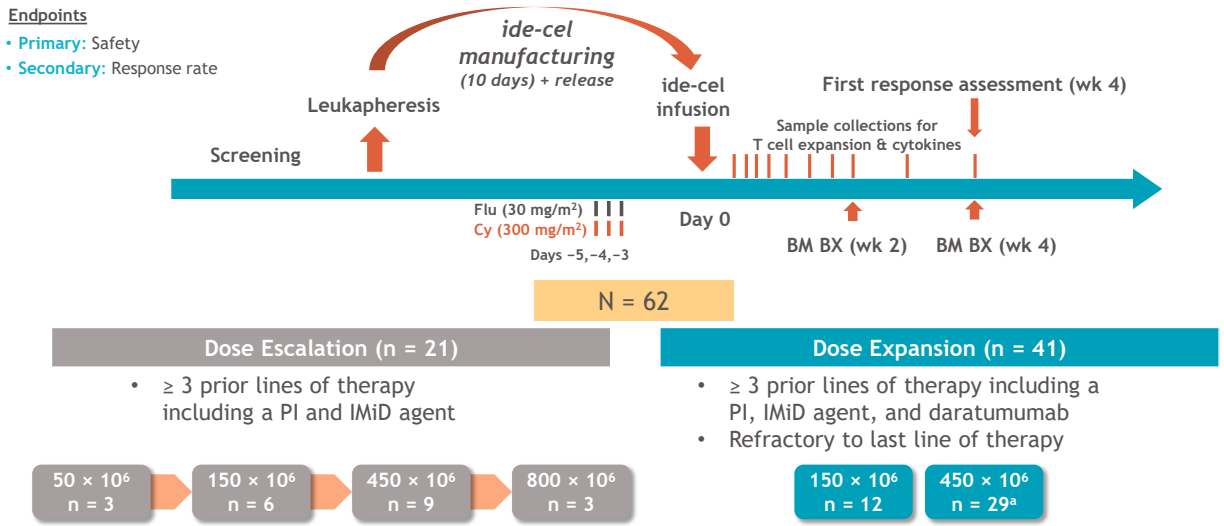
Ide-cel: a BCMA-directed CAR T cell therapy

- Patients with RRMM previously exposed to IMiD agents, PIs, and anti-CD38 antibodies have poor outcomes with subsequent regimens[1-3]
  - Deep and durable responses are uncommon[1]
  - Median PFS 2-6 months[1]
  - Median OS < 12 months[1]
- Ide-cel demonstrated tolerability and promising efficacy in patients with RRMM in early results from the first-in-human phase 1 CRB-401 study[4]

Objective: to present long-term results from CRB-401, including additional dose-expansion data

CRB-401 study design



11 patients (17.7%) ongoing with an 18.1-month median duration of follow-up in all patients
Manufacturing success rate of 100%

Data cutoff: April 7, 2020.
[a]One patient who received 205 × 10⁶ CAR+ T cells and 1 who received 305 × 10⁶ CAR+ T cells are included under the 450 × 10⁶ target dose.

Lin Y, et al. ASH 2020. Abstract 131.

1. Davies F, et al. EHA 2020 [abstract EP1033]; 2. Jagannath S, et al. ASCO 2020 [abstract 8525];
3. Gandhi UH, et al. *Leukemia* 2019;33:2266-2275; 4. Raje N, et al. *N Engl J Med* 2019;380:1726-1737.
Lin Y, et al. ASH 2020. Abstract 131.

Safety

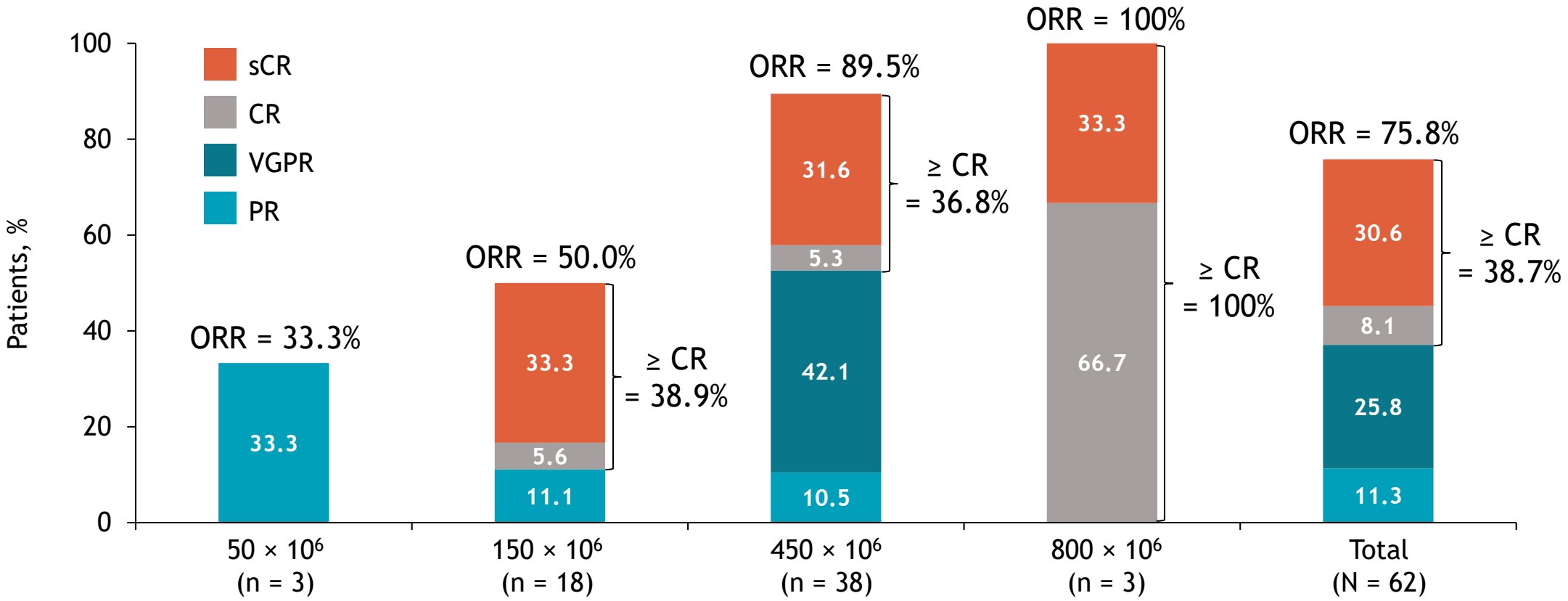
AEs of special interest, n (%)	Any grade N = 62	Grade 3/4 N = 62
Any AE	62 (100)	61 (98.4)
Neutropenia	57 (91.9)	55 (88.7)
Febrile neutropenia	10 (16.1)	8 (12.9)
Anemia	47 (75.8)	35 (56.5)
Infection[a]	47 (75.8)	14 (22.6)
CRS[b]	47 (75.8)	4 (6.5)
Thrombocytopenia	46 (74.2)	35 (56.5)
Leukopenia	40 (64.5)	38 (61.3)
Lymphopenia	23 (37.1)	22 (35.5)
Neurologic toxicity[c]	22 (35.5)	1 (1.6)

- Median time to recovery of grade 3/4 neutropenia and thrombocytopenia (in patients without recovery by month 1) was 1.9 and 2.2 months, respectively[d]
- 1 (1.6%) death within 8 weeks of infusion
  - Grade 2 CRS events on days 1 and 8 resolved on days 4 and 12, respectively
  - MR on day 31; persistent cytopenias requiring transfusions
  - Withdrew from care and died in hospice of unknown cause 51 days after infusion
- 7 (11.3%) additional deaths within 6 months
  - 1 (1.6%) due to AE (cardiopulmonary arrest not attributable to ide-cel)
  - 6 (9.7%) due to myeloma

[a]Includes the SOC infections and infestations. [b]CRS uniformly graded per Lee DW, et al. *Blood* 2014;124:188-195. [c]Grouped term; events reported ≤ 8 weeks after infusion. Excludes 1 patient with grade 1 insomnia lasting 251 days. [d]Time from first ide-cel infusion to the first grade ≤ 2 event after day 32.

Lin Y, et al. ASH 2020. Abstract 131.

Best response



All 15 patients with ≥ CR who had a qualified assessment were MRD negative by NGS[a]

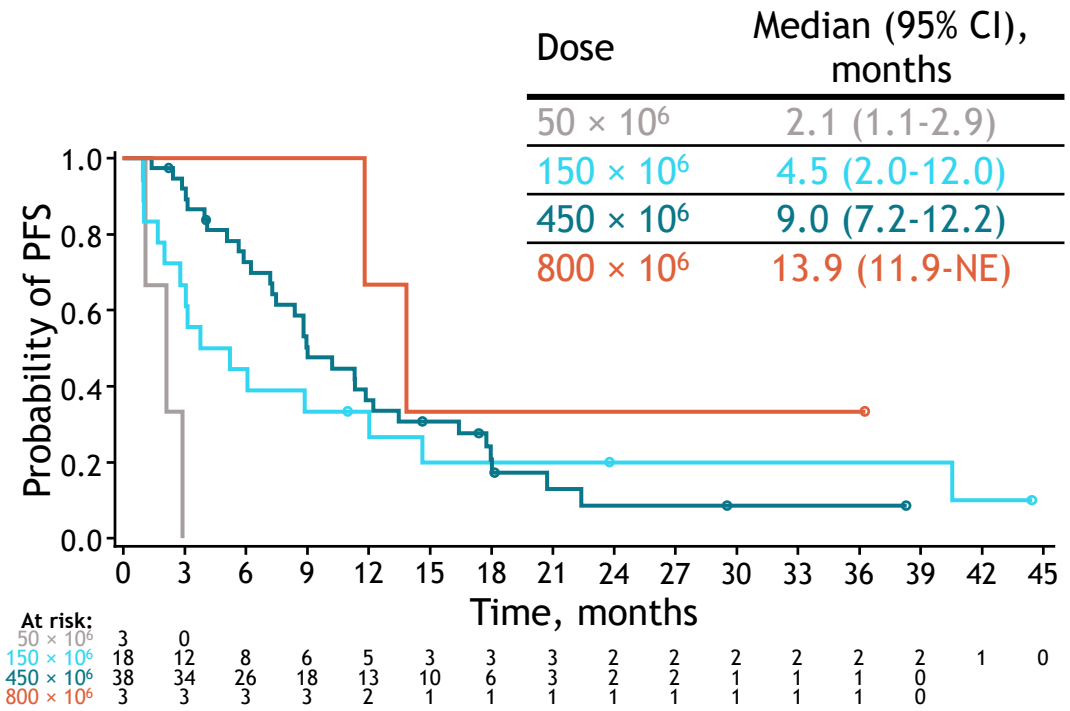
[a]Of 24 patients with ≥ CR, 8 had no MRD assessment and 1 had an assessment outside of the 3-month window; 10^{-4} sensitivity.

Lin Y, et al. ASH 2020. Abstract 131.

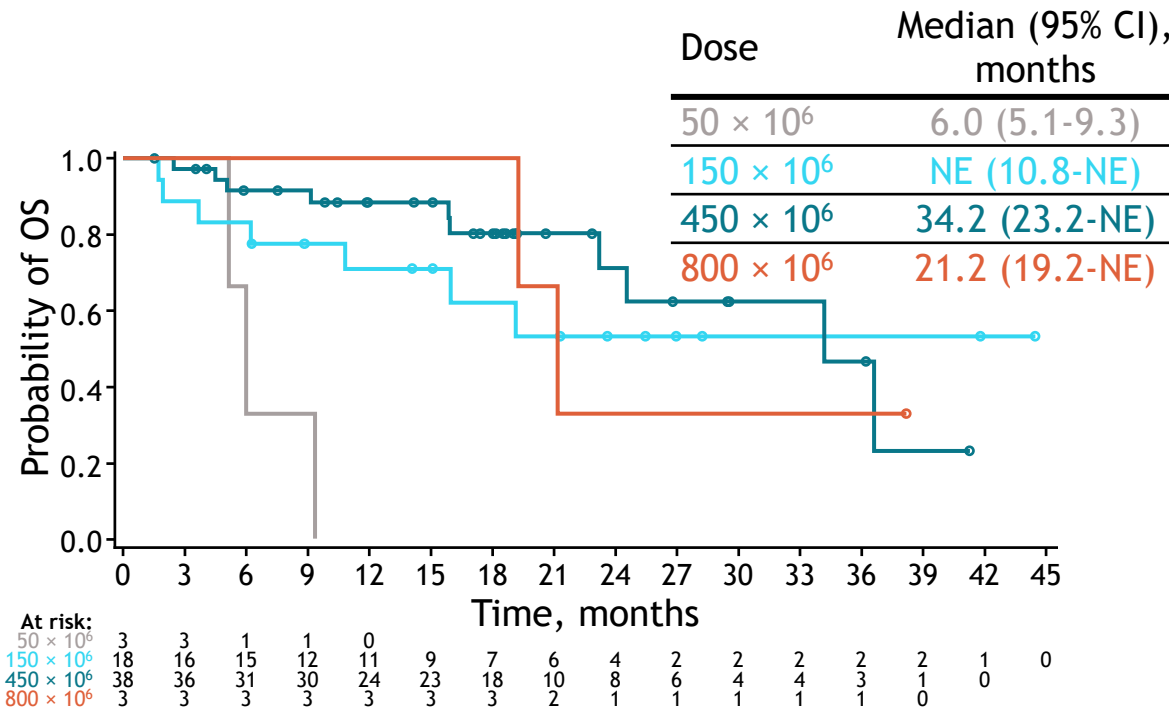
Data as of 7 April 2020

PFS and OS

PFS by target dose



OS by target dose



Median PFS 8.8 months
(95% CI, 5.9-11.9 months) across all treated patients

Median OS 34.2 months
(95% CI, 19.2-NE months) across all treated patients

Median and 95% CI from Kaplan-Meier estimate. NE, not estimable.

Lin Y, et al. ASH 2020. Abstract 131.

Data as of 7 April 2020

Conclusions

- Efficacy and safety reflect prior reports and support a favorable clinical benefit-risk profile for ide-cel at target dose levels ≥ 150 × 10^6 CAR+ T cells, with a median OS of 34.2 months in a highly triple-class- exposed population and half of ongoing responders achieving DOR > 2 years
- In the pivotal phase 2 KarMMa trial, ide-cel treatment resulted in favorable risk/benefit profile in triple-class exposed RRMM[1]
  - ORR 73% (including CR rate 33%)
  - Median DOR 10.7 months, median PFS 8.8 months, median OS 19.4 months
- Ide-cel is under review by FDA (PDUFA: March 27, 2021) and is being explored in several ongoing clinical trials:

KarMMa-2	Phase 2 study of ide-cel in triple-class-exposed patients and patients with high-risk MM (PD within 18 months of 1L or inadequate response to ASCT); NCT03601078
KarMMa-3	Phase 3 study of ide-cel vs standard regimens in triple-class-exposed patients with 2-4 prior lines of therapy; NCT03651128[2]
KarMMa-4	Phase 1 study of ide-cel in patients with high-risk NDMM (R-ISS stage III disease per IMWG criteria); NCT04196491[3]

1. Munshi NC, et al. *J Clin Oncol* 2020;38(suppl) [abstract 8503]; 2. Delforge M, et al. ASH 2020 [abstract 2323]; 3. Usmani SZ, et al. ASH 2020 [abstract 1418].
Lin Y, et al. ASH 2020. Abstract 131.

Data as of 7 April 2020

CRB-402

Updated Results from the Phase 1 CRB-402 Study of Anti-BCMA CAR-T Cell Therapy bb21217 in Patients with Relapsed and Refractory Multiple Myeloma: Correlation of Expansion and Duration of Response with T-Cell Phenotypes

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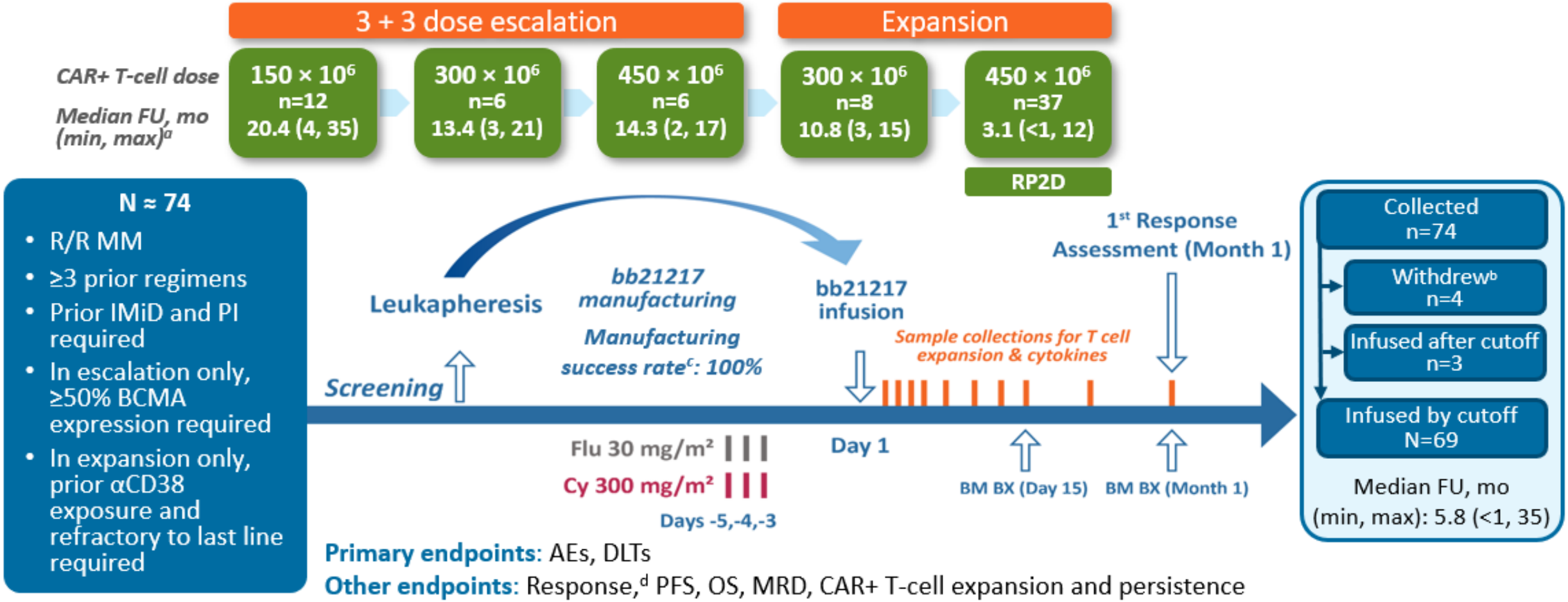
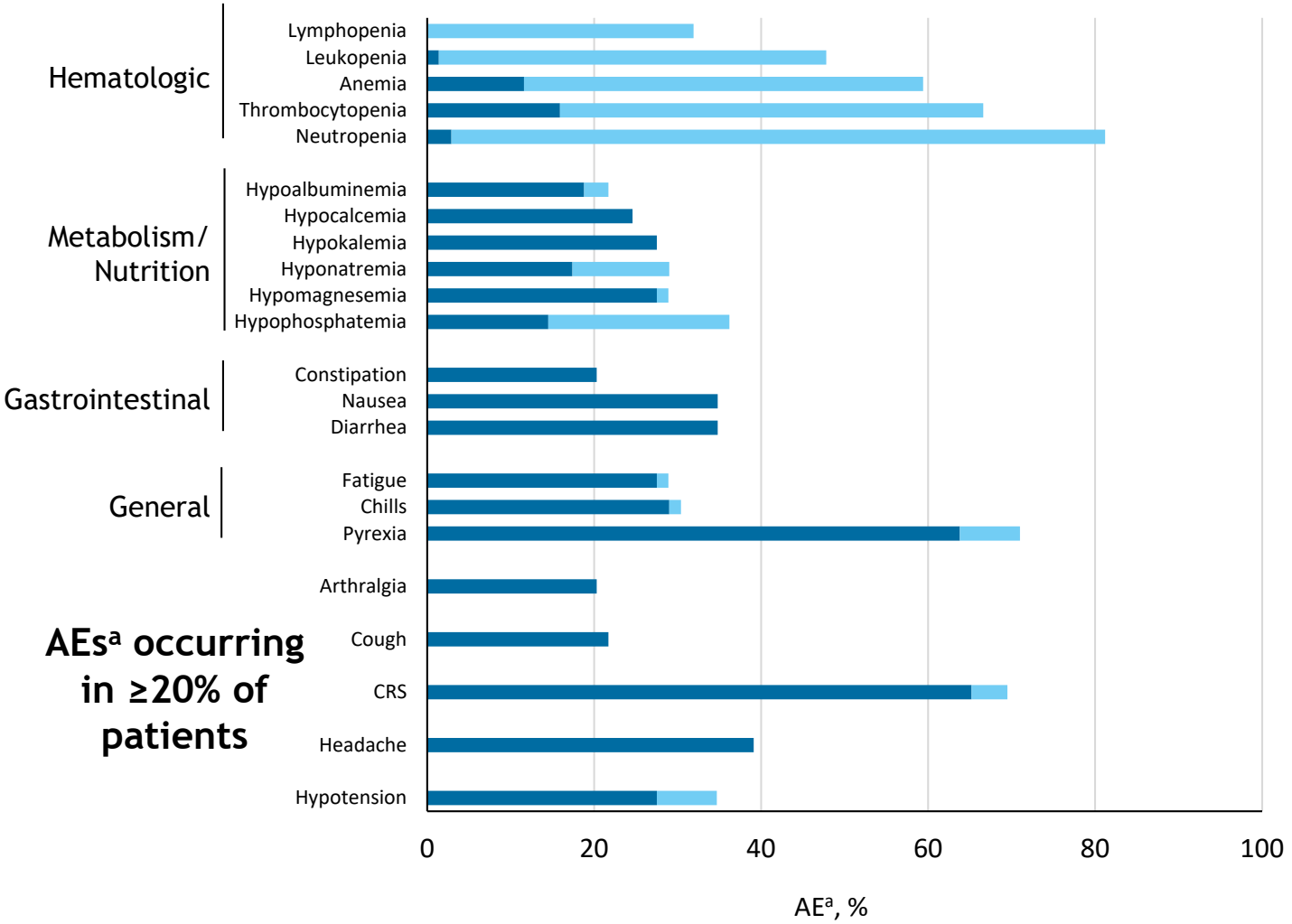
CRB-402 Phase 1 Study Design and Status



AE, adverse event; BCMA, B-cell maturation antigen; BM BX, bone marrow biopsy; CAR, chimeric antigen receptor; Cy, cyclophosphamide; DLT, dose-limiting toxicity; Flu, fludarabine; FU, follow-up; IMiD, immunomodulatory drug; MM, multiple myeloma; mo, month; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; R/R, relapsed/refractory.
[a]Calculated as the interval between bb21217 infusion and date of discontinuation or data extract date if subject is ongoing; [b]One patient who required remanufacture withdrew prior to bb21217 infusion; [c]Three patients required one re-manufacturing run; [d]Per International Myeloma Working Group criteria.

Overall Safety and Tolerability

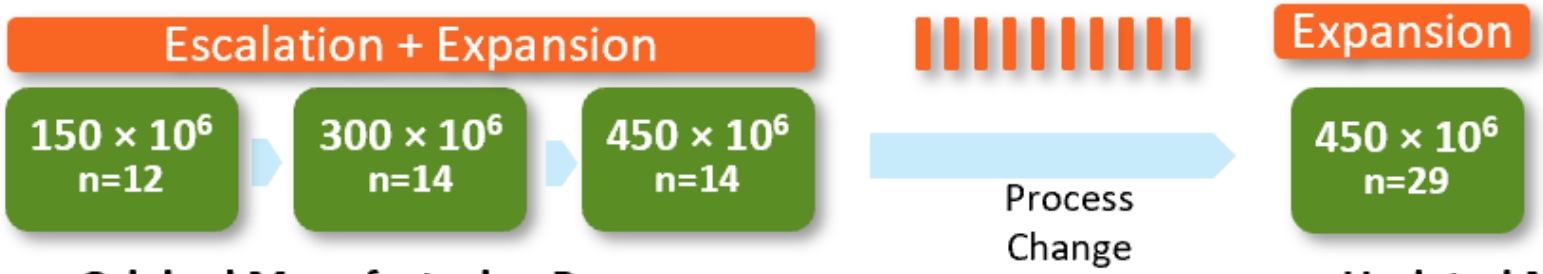


- Cytopenias were common and not dose related
  - Median time to recovery of Gr 3/4 neutropenia and Gr 3/4 thrombocytopenia was 2.0 mos and 2.2 mos
- Grade 3/4 infections were reported in 18 patients (26%)[b]
  - One death from infection within 6 months, in the absence of MM progression
- Two deaths within 8 weeks of bb21217 infusion, both due to CRS

AE, adverse event; CRS, cytokine release syndrome; MM, multiple myeloma.
[a]AEs after first documented progressive disease are excluded. [b]iinfections included pneumonia, bacteremia and other

Data as of 1 September 2020

Tumor Response and Manufacturing Process Change



Original Manufacturing Process

CAR+ T-Cell Dose:	150 × 10⁶ (n=12)	300 × 10⁶ (n=14)	450 × 10⁶ (n=14)	Total (N=40)
Median follow-up (min, max), mo	20 (4, 35)	11 (3, 21)	9 (<1, 17)	12 (<1, 35)
Tumor response,[a] n/N (%)				
ORR	10/12 (83)	6/14 (43)	8/14 (57)	24/40 (60)
sCR/CR	5 (42)	2 (14)	4 (29)	11 (28)
VGPR	5 (42)	3 (21)	3 (21)	11 (28)
PR	0	1 (7)	1 (7)	2 (5)

Updated Manufacturing Process

CAR+ T-Cell Dose:	450 × 10⁶ (N=29)
Median follow-up (min, max), mo	2 (<1, 6)
Tumor response,[a] n/N (%)	
ORR	16/19 (84)[b]
sCR/CR	6 (32)
VGPR	4 (21)
PR	6 (32)

The overall response rates across all target dose levels 150-450 x 10^6 cells of the 69 patients treated was 68% with 29% achieving a CR or higher

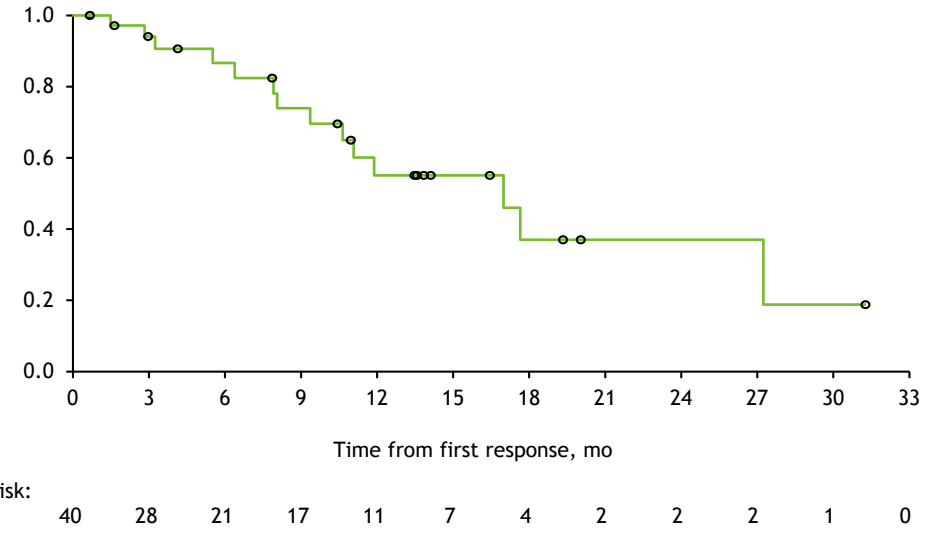
CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; Gr, Grade; ORR, objective response rate; PD, progressive disease; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
[a]Patients with ≥2 months of follow-up or PD/death within 2 months; response confirmed by a consecutive response of the same category or better. [b]One of the three non-responding patients had unconfirmed PR at Month 2.

Data as of 1 September 2020

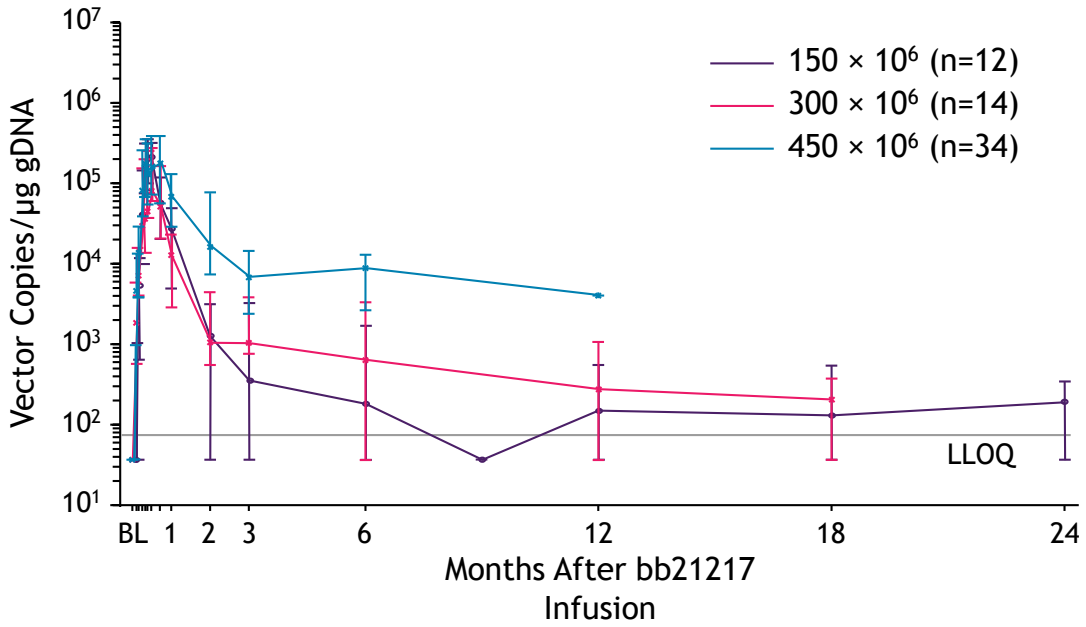
Duration of Response and CAR T-Cell Persistence

Duration of Response

N	Events	Censored	Median (min, max) follow-up, mo	Median DOR (95% CI), mo
40	14	26	7 (1, 31)	17.0 (9.4- NE)



Median VCN by Dose



	Month				
	3	6	12	18	24
Detectable vector,[a] n	27	20	6	3	2
No. at risk[b]	30	23	11	6	2

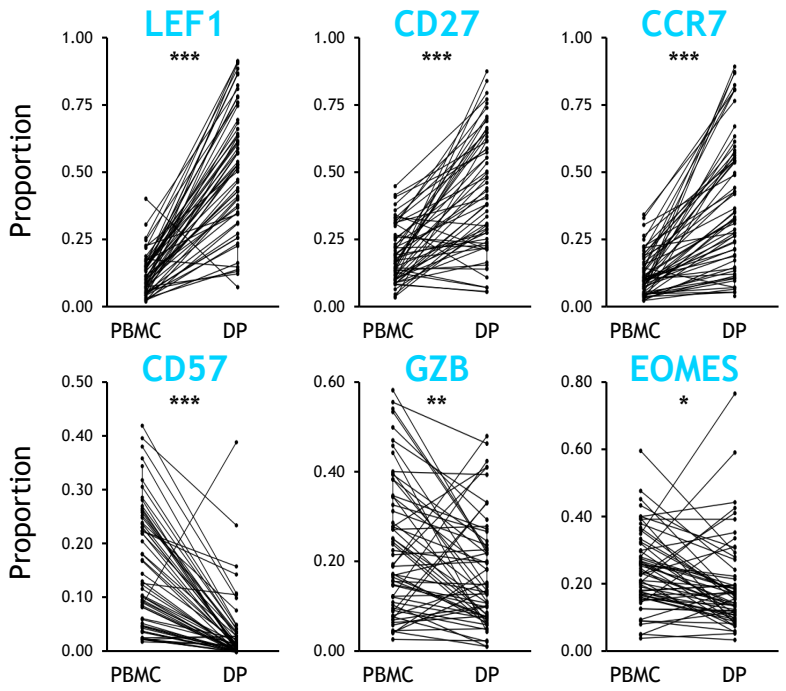
CI, confidence interval; DOR, duration of response; mo, month; NE, not estimable
BL, baseline; gDNA, genomic DNA; LLOQ, lower limit of quantification; PD, progressive disease; VCN, vector copy number.
[a]Includes detectable but not measurable; [b]Includes VCN data for patients until PD, includes one patient who received subsequent chemotherapy before progression and one subject treated in the Expansion part dosed at 544 x 10^6 cells is included under target dose of 450 x 10^6 cells. Error bars for median VCN represent interquartile range.

Data as of 1 September 2020

Enrichment for Memory-Like T Cells Associated with Peak CAR T Expansion and Response

- Patients with a higher proportion of memory-like T cells in bb21217 drug product have significantly better peak expansion
- A higher proportion of memory-like T cells is associated with numerically less disease progression

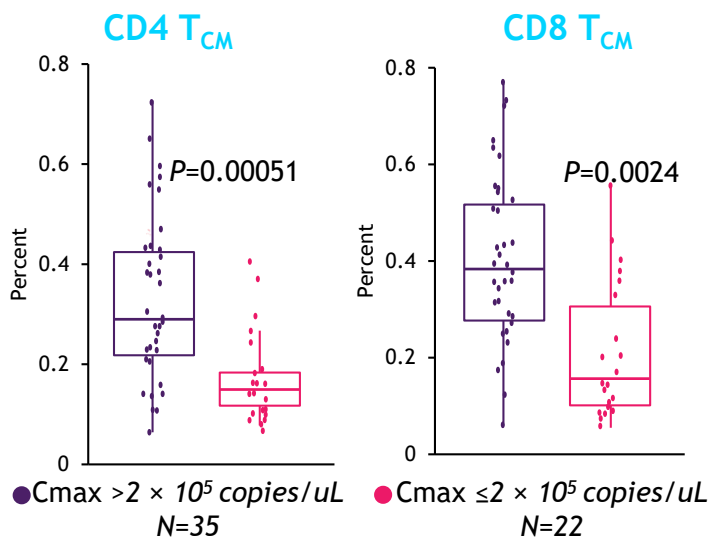
bb21217 Process Enriches for Memory-Like Markers



N=59

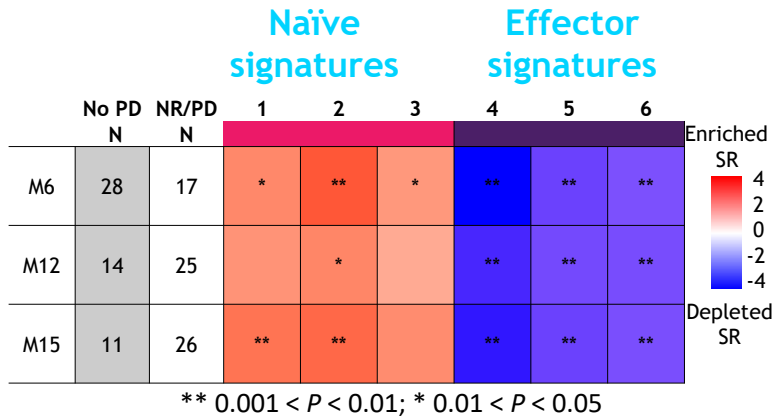
*** P<0.001; ** 0.001 < P < 0.01; * 0.01 < P < 0.05

Memory-Like T Cells Correlate with Peak Expansion



Poster 1401
Molecular and Phenotypic Profiling of Drug Product and Post-infusion Samples from CRB402, an Ongoing Phase I Clinical Study of bb21217 a BCMA-directed CAR T Cell Therapy

Memory-Like T Cells Correlate with Sustained Response



** 0.001 < P < 0.01; * 0.01 < P < 0.05

- Patients with sustained response (No PD) are more likely to have drug product enriched for naïve gene signatures and depleted of effector gene signatures compared to patients without a sustained response (NR/PD)

1. Goldrath_Naive_vs_Eff_CD8_Tcell_Up
2. GSE11057_Naive_Vs_Eff_Memory_CD4_Tcell_Up
3. GSE9650_Naive_vs_Eff_CD8_Tcell_Up
4. GSE11057_Naive_vs_Eff_Memory_CD4_Tcell_Dn
5. GSE9650_Naive_vs_Eff_CD8_Tcell_Dn
6. Kaech_naive_vs_Day8_Eff_CD8_Tcell_Dn

AUC, area under the curve; CCR7, C-C chemokine receptor type 7; Cmax, maximum concentration; DP, drug product; EM, effector memory; EOMES, eomesodermin; GZB, granzyme B; LEF1, lymphocyte enhancer-binding factor 1; M, month; NR, non-responder; PBMC, peripheral blood mononuclear cell; PD, progressive disease; pts, patients, SR, sustained response; T_{CM}, central memory T cell; T_{SCM}, stem cell memory T cell.

Summary: bb21217 Phase 1 study in R/R MM

- ✓ Consistent and tolerable safety profile with low rates of Grade ≥3 CRS and neurotoxicity
- ✓ Promising ORR, CR and MRD negative rates at the recommended Phase 2 dose
- ✓ Supportive of the mechanistic hypothesis that enriching drug product for memory like T cells may translate to improved DOR and PFS
- ✓ The Phase 1 CRB-402 study has completed enrollment; follow-up is ongoing



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