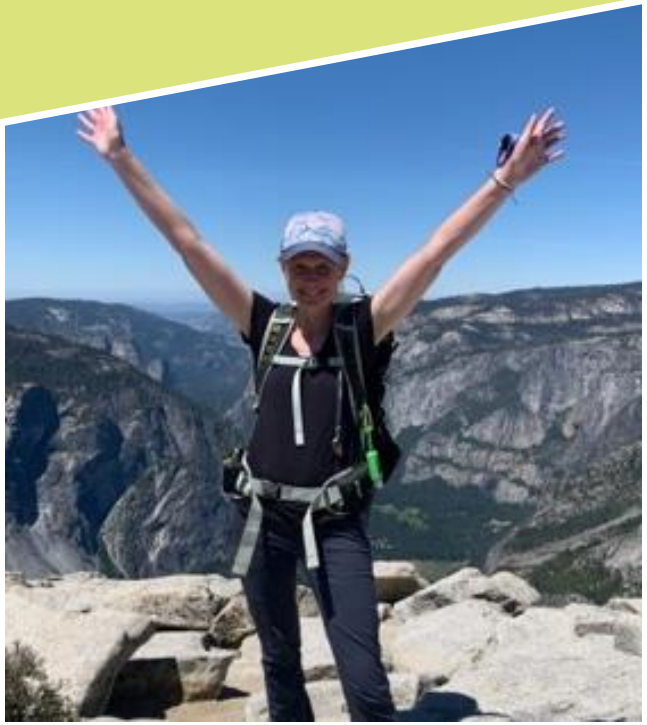


Unleash Time

2seventy bio company presentation

November 2024

2seventybio

Cautionary note regarding forward-looking statements

These slides and the accompanying oral presentation may contain “forward-looking statements”. These statements include, but are not limited to: statements about our plans, strategies, timelines and expectations with respect to the development and commercialization of Abecma (ide-cel); statements about the discontinuation of the ongoing Phase 3 KarMMa-9 study, including the potential cost savings; expectations as to the market size for Abecma; the progress and results of our commercialization of *Abecma*; anticipated revenues resulting from sales of *Abecma*; statements about the efficacy and perceived therapeutic benefits of *Abecma*; and expectations regarding our use of capital, expenses and other future financial results, including our net cash spend and cash runway. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, the risk that the market opportunities for our approved product or any future approved product are smaller than we believe they are; the risk that BMS, upon whom we rely for the successful development and commercialization of *Abecma* does not devote sufficient resources thereto, is unsuccessful in its efforts, or chooses to terminate its agreements with us; the risk that *Abecma* will not be as commercially successful as we may anticipate; and the risk that we are unable to manage our operating expenses or cash use for operations. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled “Risk Factors” in the information statement contained in our most recent Form 10-K and most recent quarterly reports any other filings that we have made or will make with the Securities and Exchange Commission in the future. All information in this presentation is as of the date of the release, and 2seventy bio undertakes no duty to update this information unless required by law. This presentation has been prepared by 2seventy bio for the exclusive use of the party to whom 2seventy bio delivers this presentation. This presentation does not constitute an offer to sell or the solicitation of an offer to buy any securities of the Company. The information contained herein is for informational purposes and may not be relied upon in connection with the purchase or sale of any security. Neither 2seventy bio nor any of its affiliates or representatives makes any representation or warranty, expressed or implied, as to the accuracy or completeness of this presentation or any of the information contained herein, or any other written or oral communication transmitted or made available to the you or your affiliates or representatives. 2seventy bio and its affiliates and representatives expressly disclaim to the fullest extent permitted by law any and all liability based, in whole or in part, on the presentation or any information contained herein or any other written or oral communication transmitted or made available to you or your affiliates or representatives, including, without limitation, with respect to errors therein or omissions therefrom.

Unlocking *Abecma* Value in 2024

Abecma™ (idecabtagene vicleucel) SUSPENSION FOR IV INFUSION

- First-in-class CAR T treatment for 3L+ r/r multiple myeloma
- $358M total US commercial revenue in 2023; $183M Q3 2024 YTD
- ~7 months into the launch of *Abecma* in earlier lines in partnership with BMS

***Abecma* opportunity to see sustainable growth**	FDA approval in April in 3L+ setting, supported by robust KarMMa-3 ph. 3 data	Continue to invest in additional studies to generate data and further optimize real world use of *Abecma*
Strong cash and path to profitability	~$192M cash balance as of Sept 30; runway beyond 2027	Recent strategic re-alignment generates cost savings of ~$150 million in 2024 and ~$200 million in 2025
Lean, fit-for-purpose structure	Tuned organization with sole focus on *Abecma* growth	Streamlined cost structure and financial profile; 3Q24 YTD operating expenses reduced approx. 52% (~$140M) vs. same period prior year

Strategic realignment successfully executed in 1H 2024: sale of R&D assets to Regeneron and Novo Nordisk

Completed sale of R&D business to Regeneron in April 2024: sold oncology and autoimmune research and development programs

Completed sale of R&D program to Novo Nordisk in June 2024: sold Hemophilia A program and gene editing technology for up to $40 million

2seventy focused exclusively on development and commercialization of *Abecma*, creating path to financial sustainability

New company structure and leadership aligns with go-forward business needs; streamlined team of ~60-70 employees

Transactions maximize value for shareholders and best positions Abecma to deliver for patients

KarMMa-3 supports the totality of *Abecma*'s competitive profile in a population of patients with high unmet need

Abecma is now available for the treatment of adult patients with relapsed or refractory multiple myeloma earlier in their treatment journey

SUPERIOR EFFICACY VS. STANDARD REGIMENS

3x longer mPFS

8x higher percentage of ≥CR

20.7-mos mPFS in bridged patients with reduced tumor burden[1]

ESTABLISHED SAFETY PROFILE

Generally predictable CRS & NT

No parkinsonism or Guillain-Barre syndrome in registration trials[2]

RELIABLE MANUFACTURING

Unlimited slot availability

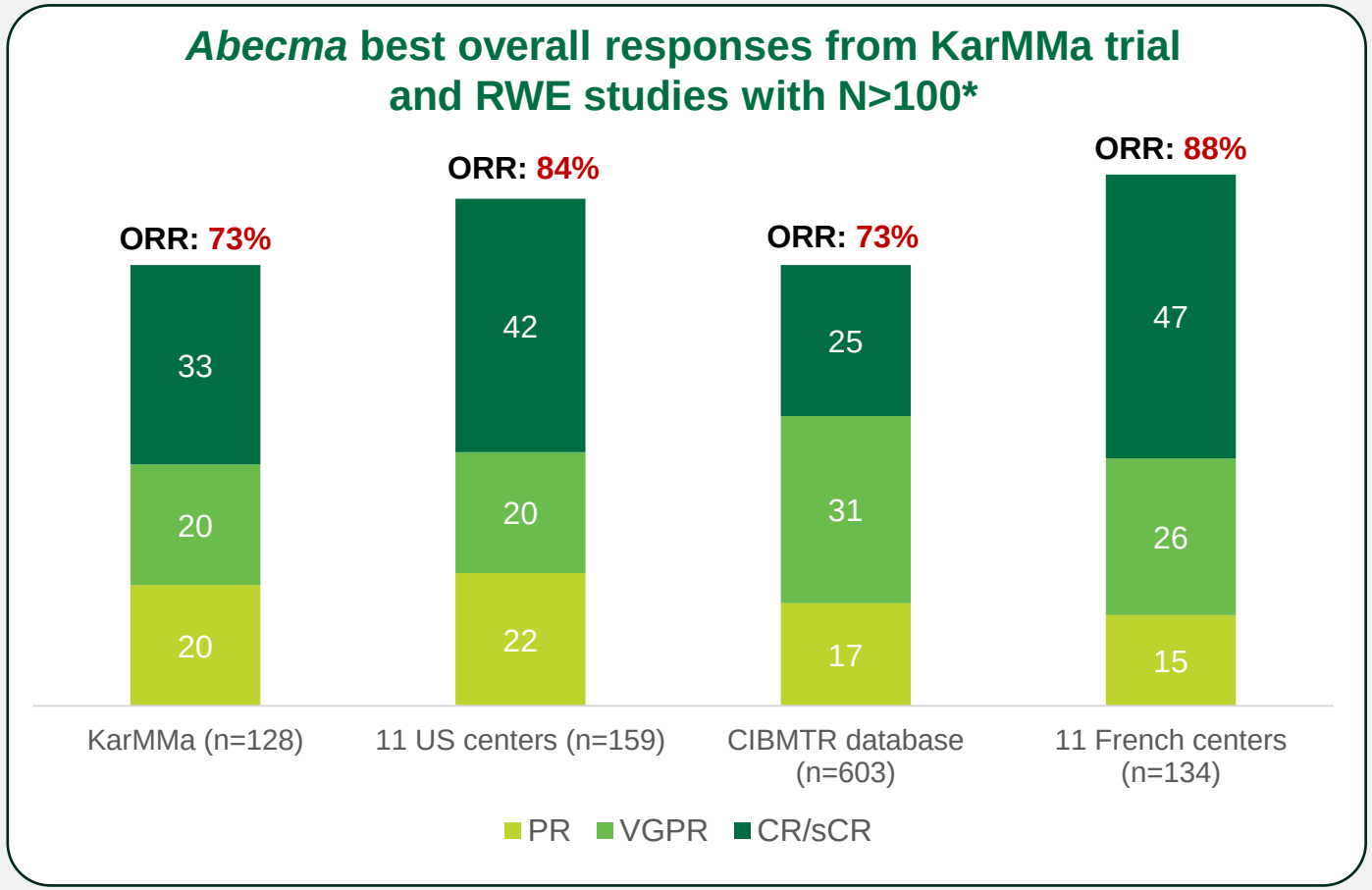
Highest number of locations

94% US commercial manufacturing success rate

[1]While in an unpowered subgroup where these findings should be interpreted with caution

[2]Grade 3 myelitis and Grade 3 parkinsonism mentioned in USPI have occurred after treatment with *Abecma* in another study in multiple myeloma

Abecma real world experience shows consistent outcomes with the KarMMa pivotal study despite sicker patient population

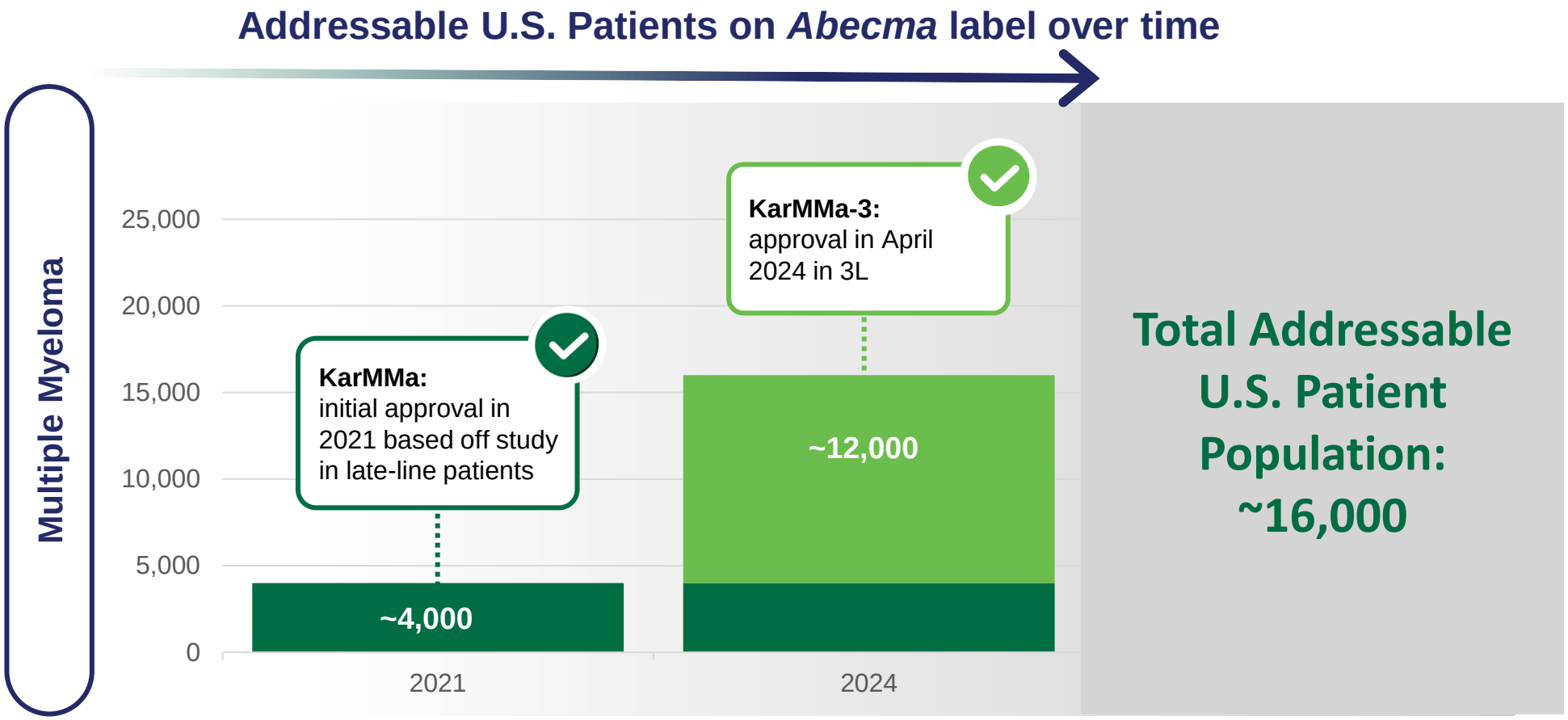


- Several large global studies show *Abecma* efficacy in the real world is consistent or better than the KarMMa study
- Many RWE patients across all studies would not have met the eligibility criteria for KarMMa
- Safety data similar to KarMMa with no new safety signals; limited Parkinsonism and Guillain-Barre and low non-relapse mortality*

Hansen et al, J Clin Oncol (2023), Sidana et al, oral presentation 1027 ASH 2023; Cayla et al, abstract 2139 ASH 2023

*Source: FAERS database. RWD analyses are observational in nature and reflect data outside of the controlled clinical trial setting. These analyses are not tested for statistical significance and are not intended to be compared to clinical trial data

KarMMa-3 study has the potential to drive label expansion into broad U.S. market opportunity



Key questions on *Abecma* in earlier lines

What did we learn from KarMMa-3 in terms of OS?	• OS was confounded by patient-centric design, which allowed for crossover. Imbalance in early deaths driven by patients untreated with ide-cel • No difference between *Abecma* and SOC in ITT; when adjusted for crossover, OS favors *Abecma* arm
What does this mean for *Abecma* in the 3L+ commercial setting?	• 3x mPFS benefit over standard of care in heavily pretreated, triple class exposed* patient population • Importance of bridging therapy, especially in high-risk patients
What are you doing to shift the dynamics in the market?	• Educating market on *Abecma's* competitive profile • BMS driving education on KarMMa-3 label including patient population, real world evidence, treatment sequencing and use of bridging
What other evidence generation strategies are you pursuing?	• KarMMa-2 cohort 2c data demonstrate the potential of *Abecma* in NDMM. Of note, **all patients who received maintenance with lenalidomide are still in response. ISRs with maintenance post *Abecma* are underway.** • New cohort in KarMMa-2 is investigating optimized bridging strategy

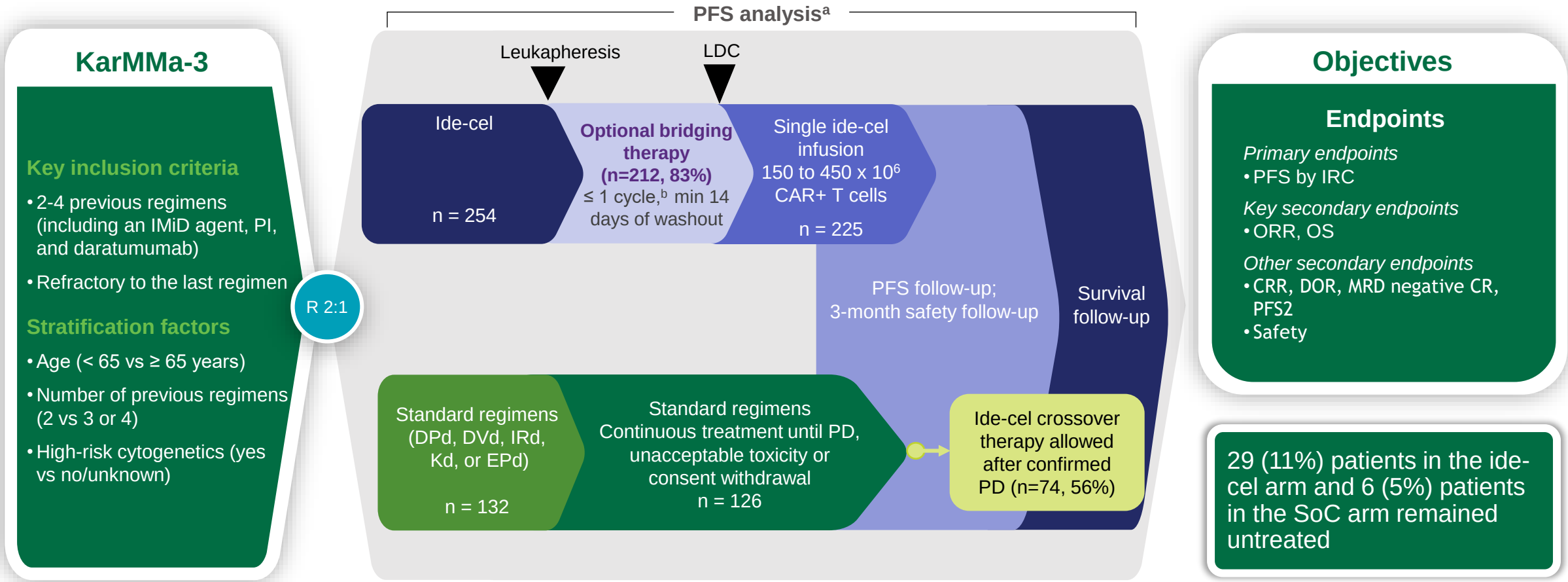
*Patients who received an immunomodulatory agent, a PI, and an anti-monoclonal antibody. ISR = Investigator sponsored research

KarMMa-3

2seventybio

Rodríguez-Otero P, et al. ASH 2023 Abstract 1028

KarMMa-3 study design (NCT03651128)



Objectives

Endpoints

Primary endpoints
- PFS by IRC

Key secondary endpoints
- ORR, OS

Other secondary endpoints
- CRR, DOR, MRD negative CR, PFS2
- Safety

29 (11%) patients in the ide-cel arm and 6 (5%) patients in the SoC arm remained untreated

[a]Time from randomization to the first occurrence of disease progression or death from any cause according to IMWG criteria; [b]Up to 1 cycle of DPd, DVd, IRd, Kd, or EPd may be given as bridging
AE, adverse event; DPd, daratumumab/pomalidomide/dexamethasone; DVd, daratumumab/bortezomib/dexamethasone; EPd, elotuzumab/pomalidomide/dexamethasone; IRC, Independent Response Committee; IRd, ixazomib/lenalidomide/dexamethasone; Kd, carfilzomib/dexamethasone; LDC, lymphodepleting chemotherapy; min, minimum; MRD, minimal residual disease; PD, progressive disease; PFS2, progression-free survival on next line of therapy; PROs, patient-reported outcomes; PS, performance status; R, randomization

Heavily Pretreated, Triple Class Exposed* Patient Population

Characteristic	Ide-cel (n = 254)	Standard regimens (n = 132)
Median (range) age, years	63 (30–81)	63 (42–83)
Median (range) time from diagnosis to screening, years	4.1 (0.6–21.8)	4.0 (0.7–17.7)
Previous autologous HSCT	214 (84)	114 (86)
R-ISS disease stage		
I	50 (20)	26 (20)
II	150 (59)	82 (62)
III	31 (12)	14 (11)
EMP	61 (24)	32 (24)
High tumor burden[a]	71 (28)	34 (26)
High-risk cytogenetics[b]	166 (65)	82 (62)
del(17p)	66 (26)	42 (32)
t(4;14)	43 (17)	18 (14)
t(14;16)	8 (3)	4 (3)
1q gain/amplification	124 (49)	51 (39)
Ultra-high–risk cytogenetics[c]	67 (26)	29 (22)
Median (range) time to progression on last prior antimyeloma therapy, months	7.1 (0.7–67.7)	6.9 (0.4–66.0)
Daratumumab refractory	242 (95)	123 (93)
Triple-class–refractory[d]	164 (65)	89 (67)

Baseline characteristics were generally balanced between treatment arms

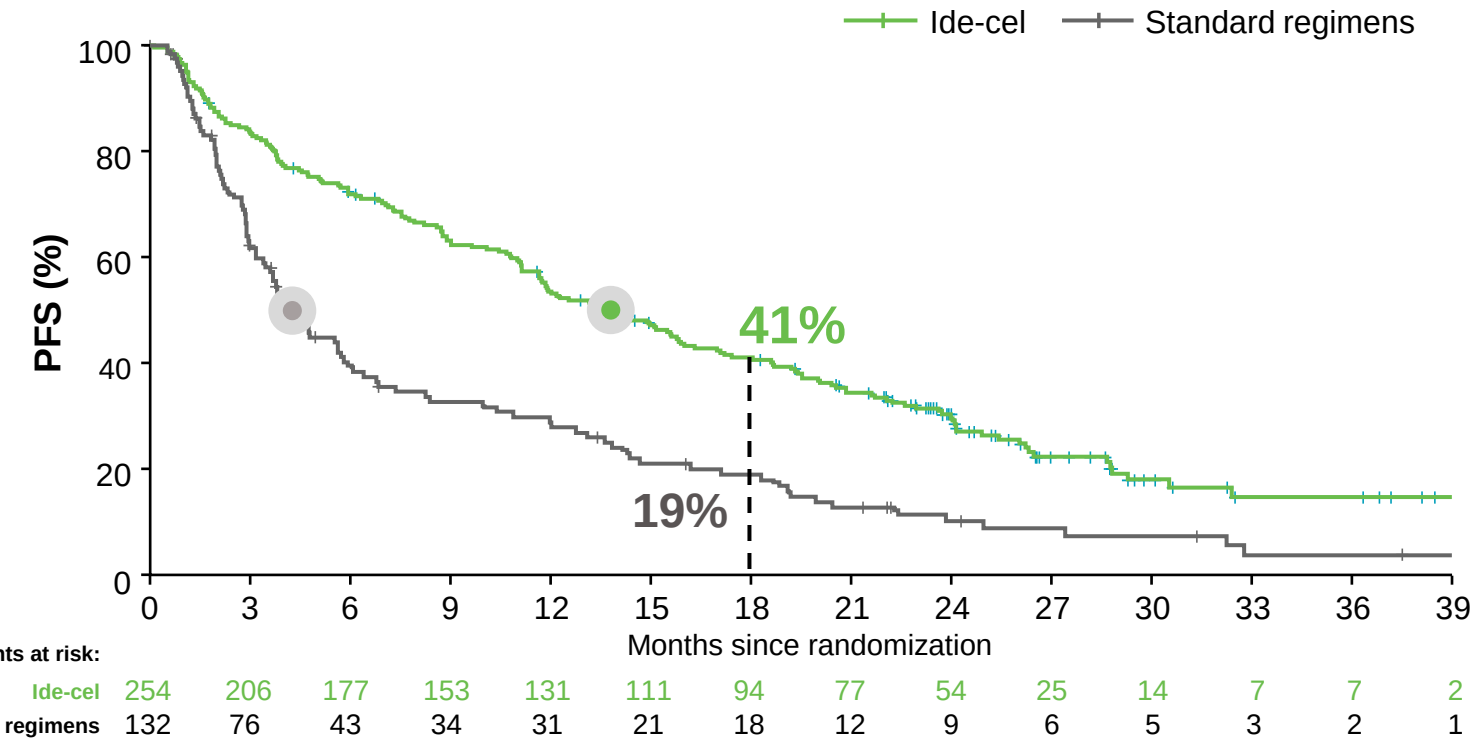
Overall, 66% of patients had triple-class refractory RRMM and 95% were daratumumab refractory, indicating a difficult-to-treat patient population

Adapted from Rodríguez-Otero P, et al. *N Engl J Med* 2023;388:1002–1014.
Data are n (%) unless otherwise stated. [a]≥ 50% CD138+ plasma cells in bone marrow; [b]Included del(17p), t(4;14), t(14;16), or 1q gain/amplification; [c]≥ 2 of del (17p), t(4;14), t(14;16), t(14;20), or 1q gain/amplification; [d]Refractory to ≥ 1 each of an IMiD agent, a PI, and an anti-CD38 antibody. EMP, extramedullary plasmacytoma; HSCT, hematopoietic stem cell transplantation; R-ISS, revised International Staging System.

*Patients who received an immunomodulatory agent, a PI, and an anti-monoclonal antibody

Rodríguez-Otero P, et al. ASH 2023 Abstract 1028

Significant benefit with ide-cel at final PFS analysis (ITT population)



Median PFS[a]

13.8 months

4.4 months

Hazard ratio[b]

HR 0.49

(95% CI, 0.38–0.63)

18-month PFS rate

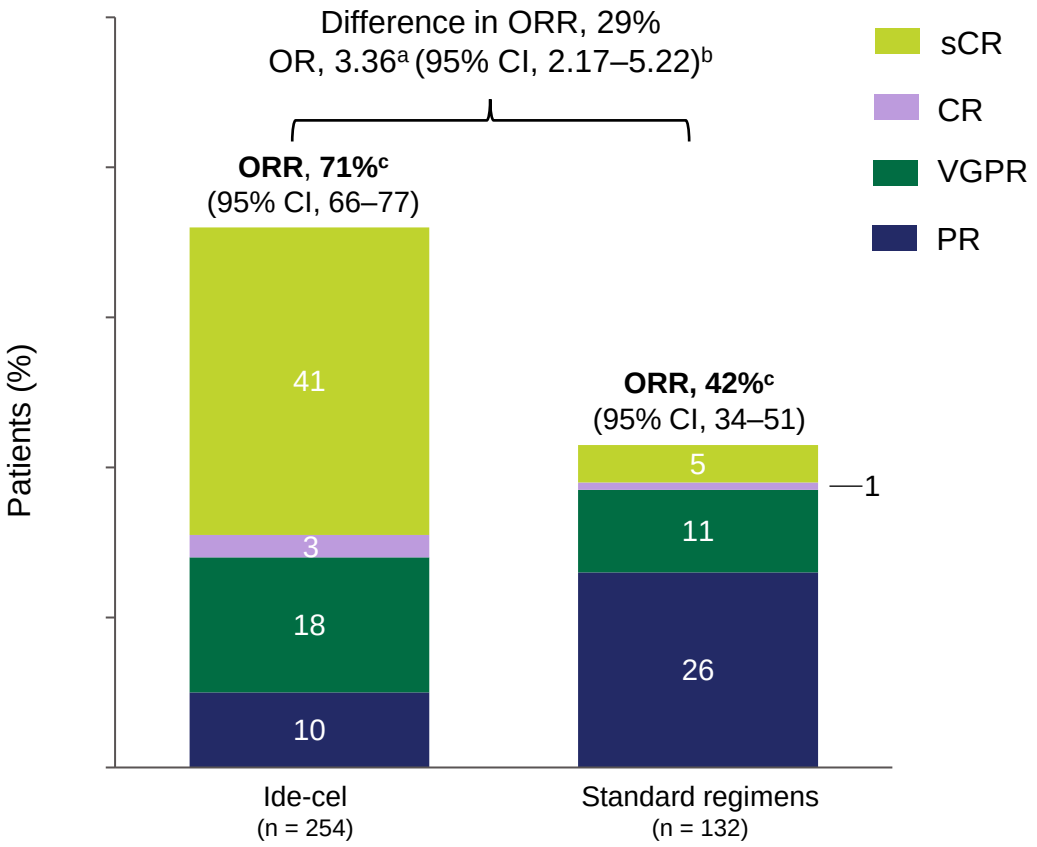
41% | **19%**

- Ide-cel continued to show longer PFS than standard regimens, with a 51% reduction in risk of PD or death, consistent with the KarMMa-3 interim analysis[1]
- With extended follow-up, the safety profile of ide-cel was consistent with prior reports with no new safety signals identified[2-4]

PFS was analyzed in the ITT population of all randomized patients in both arms and included early PFS events occurring between randomization and ide-cel infusion. PFS based on IMWG criteria per IRC. [a]Based on Kaplan-Meier approach; [b]Statified HR based on univariate Cox proportional hazard model. CI is two-sided. IMWG, International Myeloma Working Group; mITT, modified intent-to-treat; SE, standard error.

1. Rodríguez-Otero P, et al. *N Engl J Med* 2021;384:705-716. 2. Rodríguez-Otero P, et al. N Engl J Med 2021;384:705-716; 3. Munshi NC, et al. N Engl J Med 2021;384:705-716; 4. Raje N, et al. N Engl J Med 2019;380:1726-1737.

Statistically significant, deep and durable responses with ide-cel



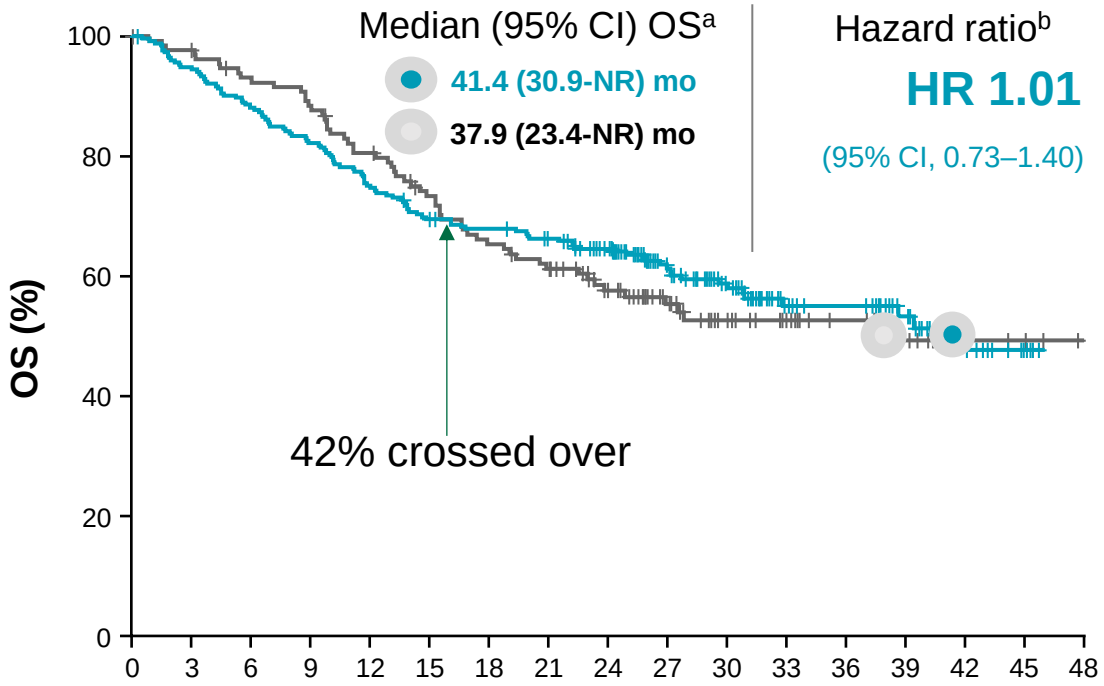
	Ide-cel (n = 254)	Standard regimens (n = 132)
CR rate, % (95% CI)[d]	44 (38–50)	5 (2–9)
MRD-negative CR rate, n/N (%) (95% CI)[e]	57/163 (35) (28–42)	1/54 (2) (0–5)
Median (95% CI) DOR, months	16.6 (12.1–19.6)	9.7 (5.5–16.1)
Median PFS2, months	23.5	16.7
HR (95% CI)	0.79 (0.60–1.04)	

- With extended follow-up, ide-cel continued to demonstrate higher ORR versus standard regimens[1]
- CR rate increased by 5% in the ide-cel arm but was unchanged for standard regimens
- Ide-cel continued to demonstrate durable, statistically significant and clinically meaningful improvements in patient-reported outcomes[2]

Per IMWG criteria. Individual responses may not sum to ORR due to rounding.
[a]OR is for ORR, calculated based on the observed response rate with two-sided Wald CI; [b]Two-sided Wald interval; [c]Patients with ≥ PR; [d]Patients with CR or sCR; [e]≥ 1 negative MRD value within 3 months prior to achieving ≥ CR until PD or death. MRD was assessed by NGS at a sensitivity of 10^{-5} per IMWG Uniform Response Criteria and as specified by the protocol. 95% CI was calculated using 2-sided Wald interval. OR, odds ratio; NGS, next generation sequencing; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
1. Rodríguez-Otero P, et al. *N Engl J Med* 2021;384:705-716. 2. Hansen et al, ASH 2023

OS analysis confounded by substantial crossover

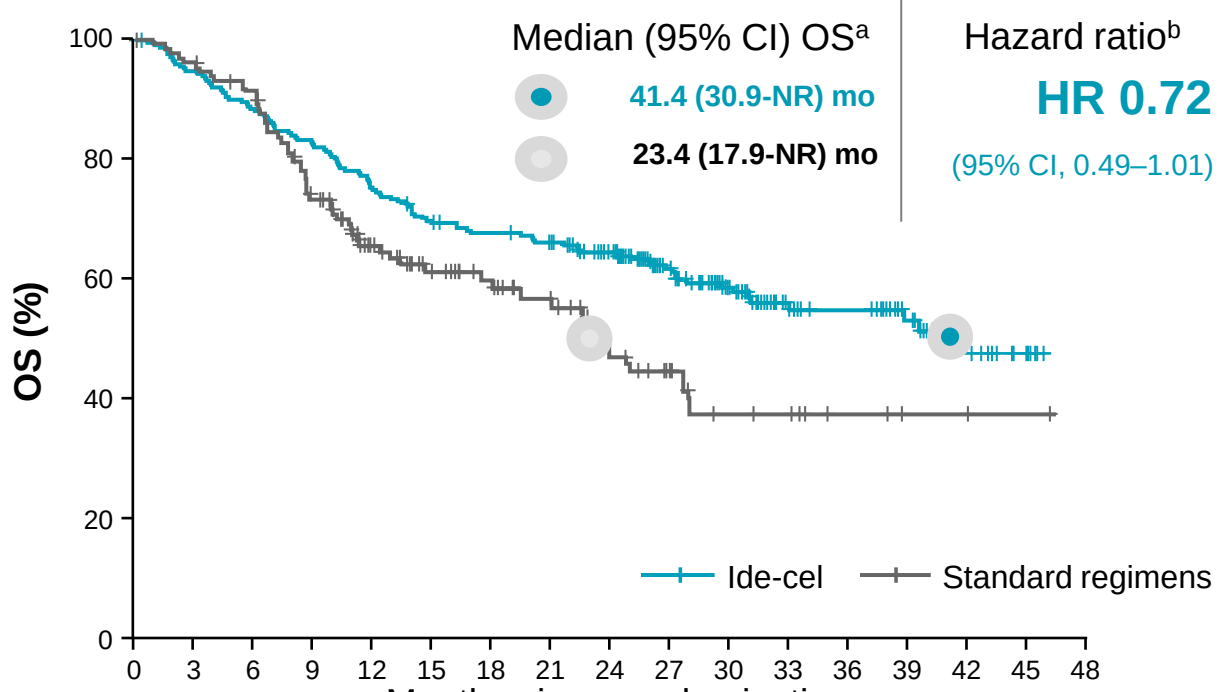
ITT population



Patients at risk

Ide-cel	254	240	223	208	190	175	169	161	143	103	75	48	44	30	13	4	0
Standard regimens	132	128	120	114	103	91	81	75	59	45	32	24	18	11	4	3	0

Sensitivity analysis adjusted for crossover[c]



254	240	223	208	190	175	169	161	143	103	75	48	44	30	13	4	0
132	126	118	93	67	50	42	34	21	14	9	8	4	2	1	1	0

More than half of patients in standard regimens arm received ide-cel as subsequent therapy upon confirmed PD and the majority received ide-cel within 3–16 months of randomization

Prespecified crossover-adjusted analysis shows OS benefit of ide-cel

Information fraction for OS was 74% (n = 164/222 required events). [a]Based on Kaplan–Meier approach; [b]Stratified HR is based on the univariate Cox proportional hazards model. CI is 2-sided and calculated by bootstrap method; [c]Two-stage Weibull model without recensoring (prespecified analysis). NR, not reached.

Rodríguez-Otero P, et al. ASH 2023 [Abstract 1028]

Patients who never received ide-cel drive imbalance in early OS events

Patients who died ≤6 months from randomization, n (%)	Ide-cel (n = 254)	Standard regimens (n = 132)
Patients who died	**30 (12)**	**9 (7)**
Did not receive study treatment	**17 (7)**	**0**
Received study treatment	**13 (5)**	**9 (7)**
Primary cause of death		
AEs	8 (3)	3 (2)
Myeloma progression	18 (7)	6 (5)
Other causes[a]	4 (2)	0

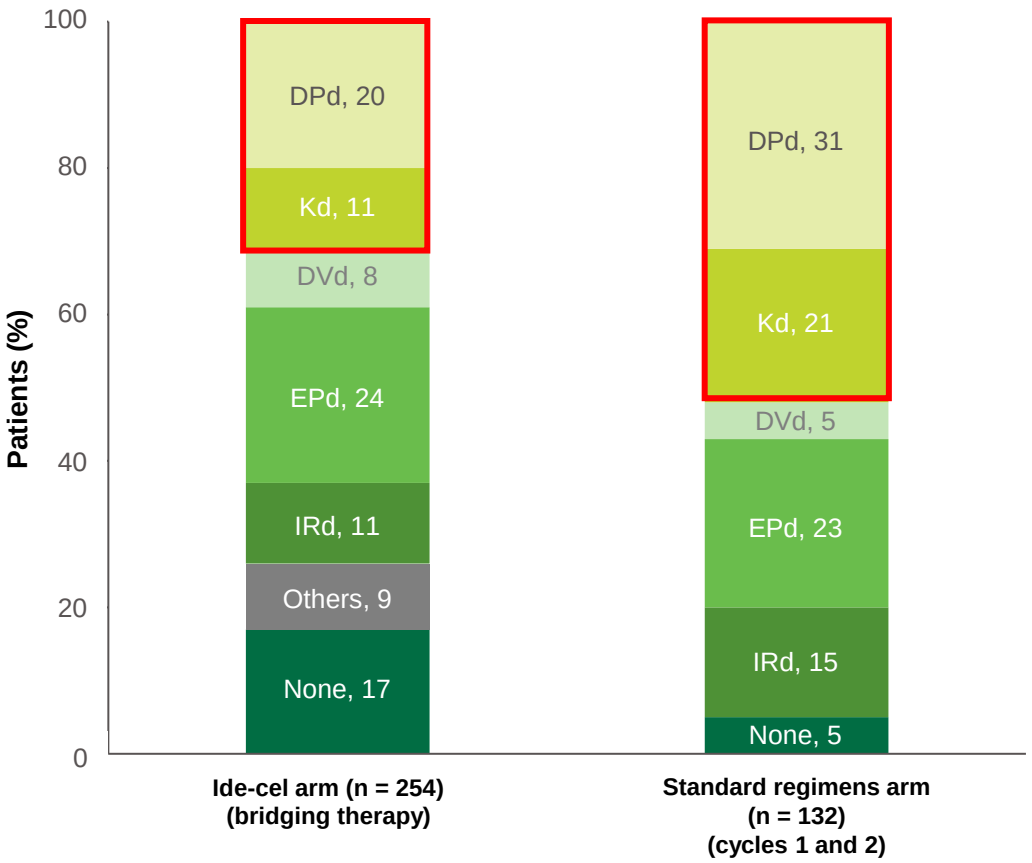
	Ide-cel		Standard regimens	
Baseline characteristic, n (%)	Deaths ≤ 6 months from randomization (n = 30)	ITT population (n = 254)	Deaths ≤ 6 months from randomization (n = 9)	ITT population (n = 132)
R-ISS stage III	9 (30)	31 (12)	2 (22)	14 (11)
High-risk cytogenetic abnormalities[b]	21 (70)	107 (42)	6 (67)	61 (46)
EMP	12 (40)	61 (24)	3 (33)	32 (24)
High tumor burden[c]	14 (47)	71 (28)	2 (22)	34 (26)

Early deaths occurred most commonly in patients with multiple high-risk features, mostly due to myeloma progression, and mostly in patients in the investigational arm who never received ide-cel

No differences in death rates due to AEs were observed between treatment arms

[a]All 4 cases of "death from other cause" in the ide-cel arm were reported verbatim as "unknown", which was coded under the system organ class of "general disorder and administration site condition"; [b]Included del17p13 (reflective of del[17p]), t(14;16), or t(4;14); [c]Determined by the higher value between bone marrow aspiration and bone marrow biopsy CD138+ plasma cell. Low tumor burden: < 50%, high tumor burden: ≥ 50%.

Suboptimal bridging therapy



Lower use of effective bridging regimens

- Less use of DPd and Kd in ide-cel arm—the 2 regimens with the most disease burden reduction during bridging therapy[1]

Lower dose intensity bridging therapy in ide-cel arm

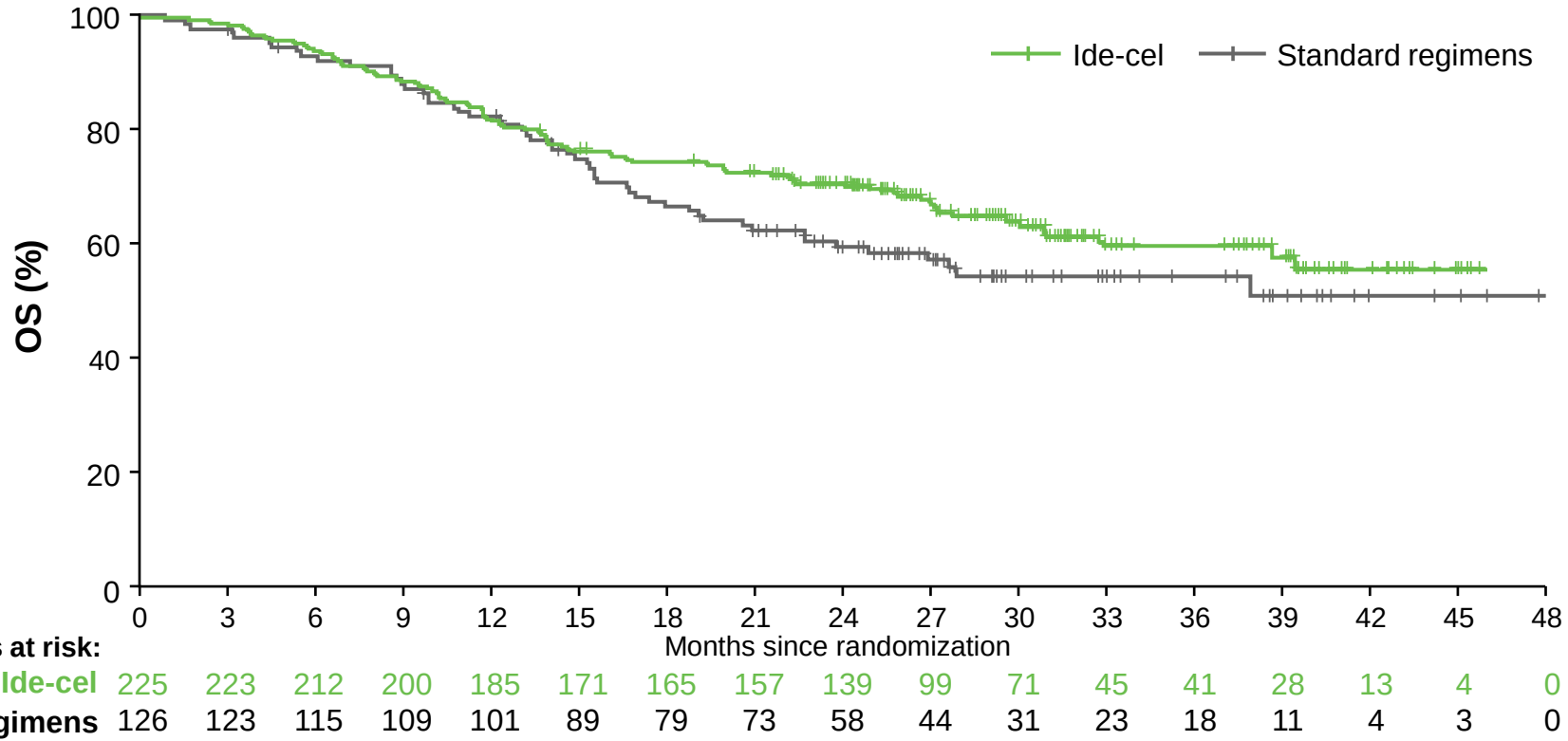
- 17% had no bridging; median 24 day washout period before ide-cel

Median (range) time without therapy within first 60 days

- Ide-cel arm: 26 (1–60) days
- Standard regimens arm: 6 (0–60) days

Cumulative dose during bridging therapy for the ide-cel arm and cycles 1 and 2 for the standard regimens arm was defined as the sum of all doses taken in mg. Dose intensity was defined as the cumulative dose divided by total days. [a]For patients in the ide-cel arm, bridging therapy was considered in the dose intensity calculation: total days in denominator = (earliest date of infusion, death, off-study, last alive, or start of subsequent therapy) − randomization date. For patients in the standard regimens arm, only the cycle 1 and cycle 2 dose were considered in dose intensity calculation. Einsele H et al. IMS 2023.

Trend of OS benefit with ide-cel among treated patients



Median OS[a]

NR

NR

Hazard ratio[b]

HR 0.83

(95% CI, 0.58–1.18)

In the treated population of patients who received the study treatment to which they were randomly assigned, there was a trend toward OS benefit with ide-cel versus standard regimens

[a]Based on Kaplan–Meier approach; [b]Stratified HR based on the univariate Cox proportional hazards model. CI is two-sided.

KarMMa-3 Data Supports the Potential of *Abecma* in 3L+

- KarMMa-3 demonstrates a **significantly longer** and **clinically meaningful improvement** of **PFS** with ide-cel versus standard regimens in patients with early line relapse and triple-class exposed* (TCExp) RRMM across all subgroups[1]
  - 51% reduction in risk of disease progression or death with ide-cel
- Patient-centric KarMMa-3 design allowed crossover, which confounds the OS interpretation
  - 56% of patients in the standard regimens arm crossed over to receive ide-cel
  - A prespecified analysis adjusting for crossover showed **improved OS with ide-cel** versus standard regimens
- Bridging therapy was suboptimal for patients with multiple high-risk features and rapidly progressing disease
  - This highlights the importance of **effective bridging therapy**
- The safety profile of ide-cel was manageable and consistent with previous studies[1-3]
- KarMMa-3 shows a favorable benefit-risk profile with ide-cel, and supports the use of ide-cel in patients with TCExp RRMM, a population with poor survival outcomes with conventional therapies

1. Rodríguez-Otero P, et al. N Engl J Med 2023;388:1002–1014; 2. Munshi NC, et al. N Engl J Med 2021;384:705–716; 3. RajeN, et al. N Engl J Med 2019;380:1726–1737.

*Patients who received an immunomodulatory agent, a PI, and an anti-monoclonal antibody

KarMMa-2c and KarMMa-9

Update on KarMMa-9 Study

The initiation of KarMMa-9 in a NDMM population was based on the positive data generated in **KarMMa-2 cohort 2c** in a similar patient population.

Since that time, NDMM treatment landscape has improved considerably:

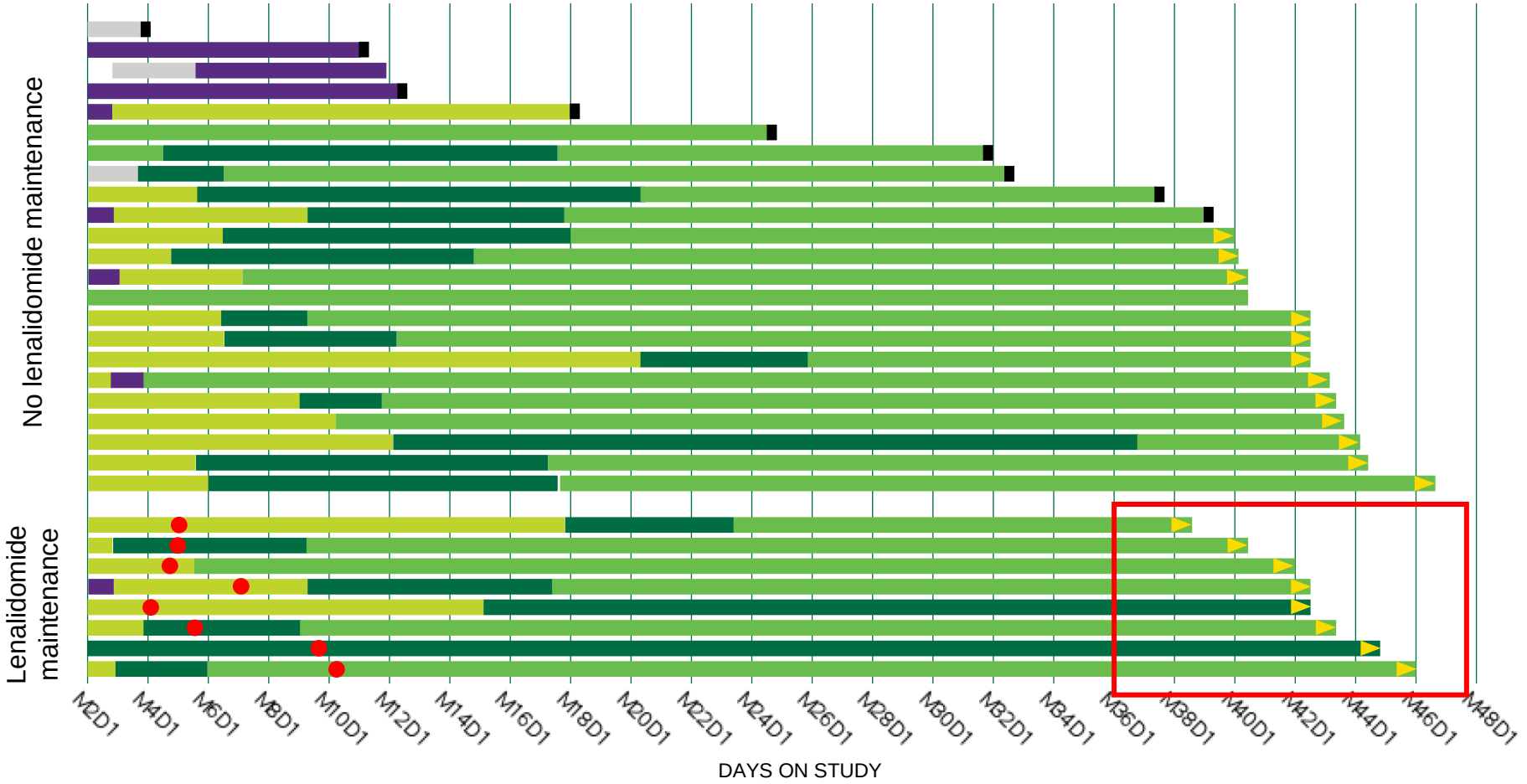
- Increasing use of quadruplet therapy induction
- Incorporation of more aggressive consolidation therapies
- Ongoing optimization of maintenance therapy regimens

As a result, there are considerably fewer eligible patients.

We, along with our study sponsor BMS, will **discontinue enrollment in the Phase 3 KarMMa-9 study** and continue to focus on serving patients with a high unmet need who will benefit most from *Abecma*.

With our focus on capital allocation and creating value for all stakeholders, we anticipate this decision will conserve over $80 million in near-term expenditures and accelerates our path to breakeven.

KarMMa-2c: Deepened responses in patients with inadequate response to frontline ASCT (less than VGPR)



- All treated patients alive at data cut-off with median follow up of 39.4 months; no new safety signals
- ORR: 87.1%; CRR: 77.4%
- At 36 months, DOR was 80.9% and PFS was 76.8%
- Of the 8 patients that received lenalidomide maintenance, progression events have not been observed

CR/sCR
VGPR
PR
MINIMAL RESPONSE
STABLE DISEASE
PD
LEN Maintenance
Ongoing

The bar starts at month 2, day 1 (equivalent to 1 month post ide-cel infusion) and continues to later of last response assessment date or data cutoff date (May 3, 2023). Response was defined as ≥ PR based on IMWG criteria by investigator assessment.
D, day; LEN, lenalidomide; M, month.

Rodríguez-Otero P, et al. ASH 2023 Abstract 1028

THANK YOU