IASO206 Clinical Development Plan (CDP) for Multiple Myeloma (MM)

2026.06.23 Medical team of clinical development department

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IASO206 多发性骨髓瘤（MM）临床研发计划示意图

BCMA靶向 in vivo CAR-T | 全生命周期开发路径

单次静脉给药 | 无需单采 | 无需体外制备 | 无需清淋预处理 | 提升可及性与治疗便利性

1 早期临床 / FIH
- 剂量递增 + 扩展
- 验证安全性、药效
CAR-T全程与初步疗效

2 ≥4L RRMM
全球单臂
关键性研究

3 2-4L RRMM
随机III期
确证研究

4 NDMM 适合移植（TE）
ASCT后
巩固/强化

5 NDMM 不适合移植（TI）
诱导后一次性
深度清除

6 注册与生命周期管理
全球准入 /
上市后扩展

1 ≥4L RRMM：全球单臂关键性研究

★ 首个注册路径

- 研究类型：全球、多中心、开放标签、单臂
- 目标人群：≥4线RRMM， ECOG 0–1
- 入组人群：既往接受过BCMA靶向治疗 / 未接受过BCMA靶向治疗
- 关键终点：ORR、CR/sCR、MRD阴性（NGS）、DOR/PFS、安全性
- 注册价值：支持特条件 / 加速批准

2 2-4L RRMM：随机III期确证研究

★ 全球核心确证研究

- 设计：多中心、随机、开放标签、优效性研究
- 随机：1:1（IASO206 vs 研究者选择SOC）
- 目标人群：Len-refractory, BCMA-naive，ECOG 0–1
- SOC示例：DPd、PVd、DVd、Dkd/Kd，Isa-Pd
- 共同主要终点：MRD阴性（NGS，10^{-5}；技术可行拘10^{-6}）+ PFS（IRC/IMWG 2016）
- 样本量：450–500例

3 NDMM-TE：适合移植人群

诱导治疗 4–6周期 → ASCT → 1:1随机

- IASO206*来那度胺维持（增注后约1个月开始）
- 来那度胺持续维持至PD

- 入组要点：完成诱导 + ASCT；PR/VGPR或更好；未进展；ECOG 0–1
- 共同主要终点：PFS + 9个月MRD阴性CR率
- MRD：xNGS检测

4 NDMM-TI：不适合移植人群

诱导治疗 4–6周期 → 1:1随机

- IASO206单次输注
- 标准基线治疗/维持直至PD

- 入组要点：TI-NDMM；诱导后≥PR；未进展； ECOG 0–1
- SOC示例：DRd、VRd-lite、D-VMP维持或一线SOC
- 共同主要终点：PFS + 9个月MRD阴性CR率
- MRD：xNGS检测

关键开发原则

A. 先关键注册，再向早线前移

B. MRD阴性 + PFS为关键疗效证据

C. 全球开发覆盖 NMPA / FDA / EMA / PMDA

D. 强调一次性治疗，低治疗负担与长期可及性

总体路径： FIH建立安全性与可行性 → ≥4L RRMM单臂研究争取早期批准 → 2-4L RRMM随机III期确证 → 向NDMM适合/不适合移植人群前移 → 上市后扩展

IASO206 Injection: China IIT Study Design

- **Objective: To assess first-in-human safety/tolerability, PK/PD and preliminary efficacy across three planned dose levels to support Phase Ib dose selection.**

First-in-human dose-escalation IIT

- Design: **single-center, open-label, 3+3 dose-escalation**
- Key Inclusion Criteria : **18 to 75 years old; R/R multiple myeloma after ≥2 prior lines; BCMA-targeted therapy–naïve ; ECOG PS ≤2**
- **Single administration; total 9–18 subjects**

AEs, adverse events; BCMA, B-cell maturation antigen; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IIT, investigator-initiated trial; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK/PD, pharmacokinetics/pharmacodynamics; R/R, relapsed/refractory; TTR, time to response; TU, transducing units.

IASO206 Injection: Phase Ib Plan

- **Objective:** To confirm and further evaluate the two proposed dose levels, low and high, previously explored in the China IIT study

Dose-confirmation phase

- Key Inclusion Criteria : **18 to 75 years old; R/R multiple myeloma after ≥3 prior lines; naïve to BCMA-targeted therapy and TCEs ； ECOG PS ≤2**
- Open-label “3+3” dose-confirmation design
- 3–6 subjects per Dose level; **total 6–9 subjects**

Dose-expansion phase

- Select one dose cohort for expansion based on dose-confirmation findings
- Planned enrollment: **15–20 subjects**
- Further evaluate the proposed RP2D in R/R multiple myeloma after ≥3 prior lines : safety, efficacy, PK/PD and other endpoints to support Phase II

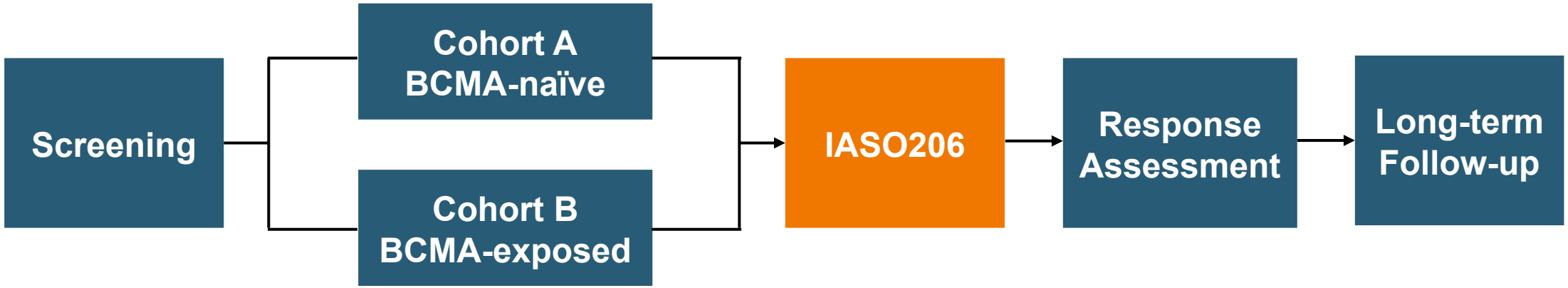
Phase 1b Timeline (10 Sites)

Dec 2026	Apr 2027	Sep 2027	Dec 2027	Mar 2028
US IND Approval	FPI First Patient In	Dose-confirmation End (RP2D)	LPI Last Patient In	**Data cut-off & completion**

AEs, adverse events; BCMA, B-cell maturation antigen; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IIT, investigator-initiated trial; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK/PD, pharmacokinetics/pharmacodynamics; R/R, relapsed/refractory; TTR, time to response; TU, transducing units.

IASO206 Late-Line Clinical Development Strategy

Option 1: Two-Cohort Balanced Study



Key Inclusion Criteria：

- Age ≥18 years with MM
- Prior ≥3 LoT
- Triple-exposed (PI, IMiD, anti-CD38 mAb)
- ECOG PS 0–1

Study Design：

- Two cohorts;
- Cohort A: BCMA-naïve, Cohort B: Prior BCMA-exposed
- Sample size: 60-90 pts in cohort A, 60 pts in cohort B

Primary Endpoint

- ORR by IRC

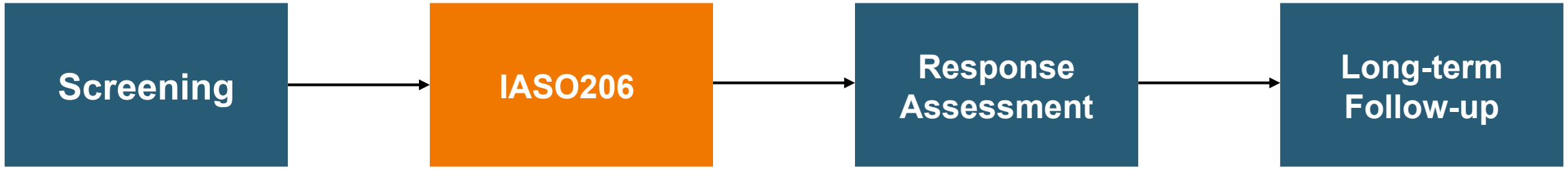
Key Secondary Endpoints

- DOR, CR/sCR, TTR, PFS, OS, MRD negativity rate, AEs, PK/PD

AEs, adverse events; CR/sCR, complete response/stringent complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMiD, immunomodulatory drug; LoT, line of therapy; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteosome inhibitor.

IASO206 Late-Line Clinical Development Strategy

Option 2: Single-Arm Trial



Key Inclusion Criteria：
- Age ≥18 years with MM
- **Prior ≥4 LoT**
- Triple-exposed (PI, IMiD, anti-CD38 mAb)
- Prior BCMA-targeted therapy (CAR-T, T-cell engager, or ADC)
- ECOG PS 0–1

Study Design：
- Open label
- Sample Size: 60

Primary Endpoint
- ORR by IRC

Key Secondary Endpoints
- DOR, CR/sCR rate, PFS, OS, MRD negativity rate, AEs, PK/PD

AEs, adverse events; CR/sCR, complete response/stringent complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMiD, immunomodulatory drug; LoT, line of therapy; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteosome inhibitor.

IASO206 Late-Line Clinical Development Strategy

Option 3: Randomized Confirmatory Trial

Key Inclusion Criteria：
- Age ≥18 years with MM
- Prior ≥3 LoT
- Triple-exposed (PI, IMiD, anti-CD38 mAb)
- BCMA-naïve
- ECOG PS 0–1

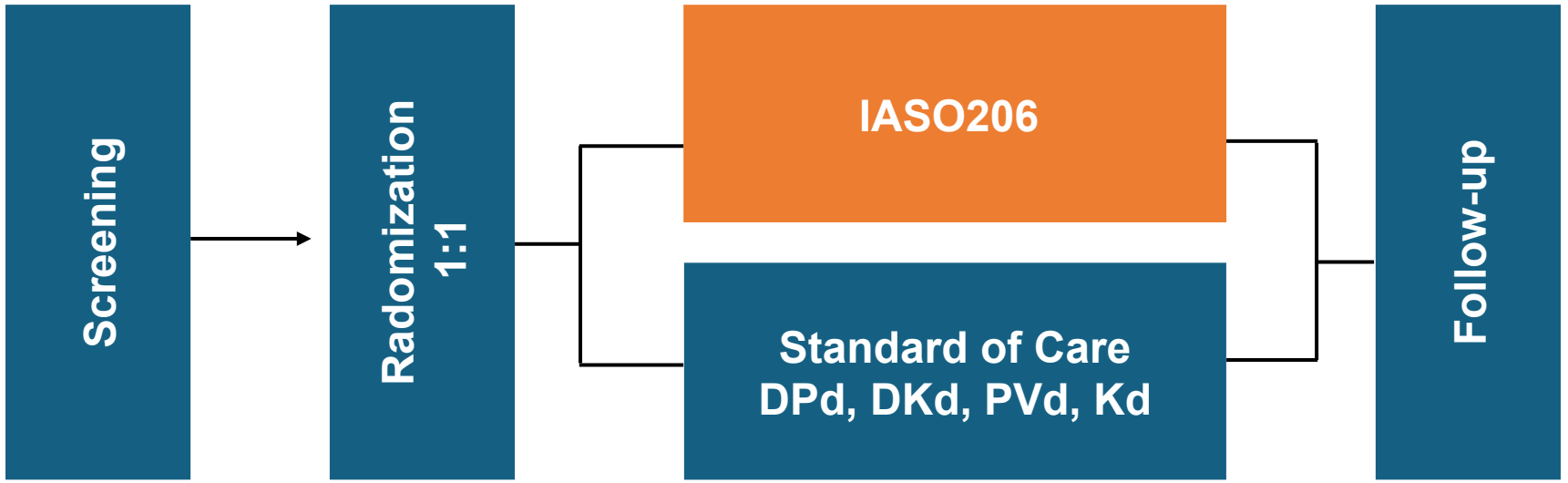
Study Design：
- Open label, randomized study;
- 1:1 ratio
- Sample size: 120

Primary Endpoint
- MRD negativity CR Rate
- PFS assessed by IRC

Key Secondary Endpoints
- DOR, CR/sCR rate, PFS, OS, MRD negativity rate, AEs, PK/PD

AEs, adverse events; CR/sCR, complete response/stringent complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMiD, immunomodulatory drug; LoT, line of therapy; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteosome inhibitor.

IASO206 early line Clinical Development Strategy



Study design:

- 1:1 randomization
- n=approximately 450~500, 100+ sites globally

Endpoint:

- **Co-primary: MRD[a] negativity CR rate at 9m and PFS**
- Key secondary： ORR, DOR, OS, CR rate, Safety

Key Inclusion Criteria:

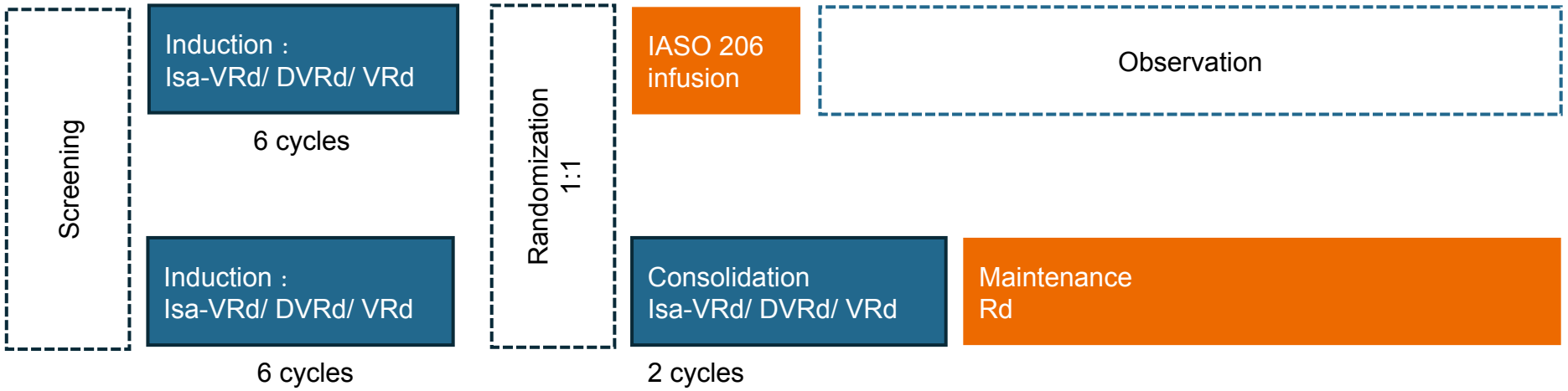
- Age ≥ 18 years
- Prior 1-3 LoT
- Triple-exposed (PI, IMiD, anti-CD38 mAb)
- ECOG PS 0 to 1

Key Exclusion Criteria:

- Prior B-cell maturation antigen (BCMA)-targeted therapy
- Prior T-cell engager therapy
- Prior CAR therapy or other genetically modified T-cell therapy

a.MRD was assessed by next-generation sequencing (NGS) using the clonoSEQ® assay (Adaptive Biotechnologies), with analytical sensitivity thresholds of 10^{-5} and 10^{-6}.
CR, complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMiD, immunomodulatory drug; LoT, line of therapy; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PI, proteosome inhibitor.

NDMM Patients (Transplant-ineligible)



Eligibility:

- NDMM patients
- Not considered for high-dose chemotherapy with ASCT due to ineligibility or deferral
- Measurable disease
- ECOG 0-1

Study Design:

- 1:1
- Sample size: ~700

Primary Endpoints:

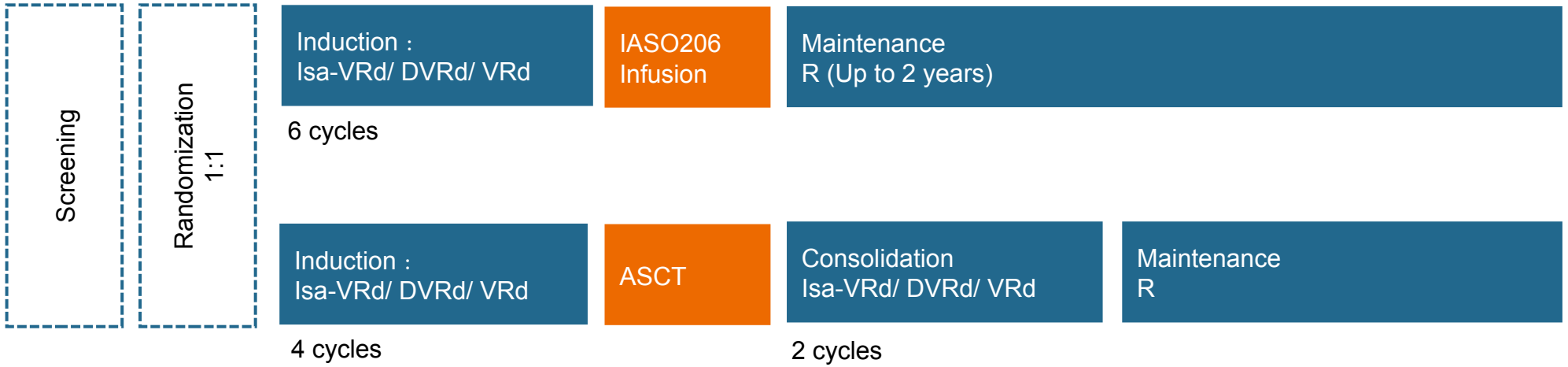
- PFS
- MRD-/CR at 9m after randomization

Secondary Endpoints:

- ORR, CRR, OS
- Overall MRD- rate, Sustained MRD- CR
- Time to subsequent therapy, PFS2, Safety

CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ORR, overall response rate;

NDMM Patients (Transplant-eligible)



Eligibility:
- NDMM patients
- ASCT eligible
- Measurable disease
- ECOG PS 0-1

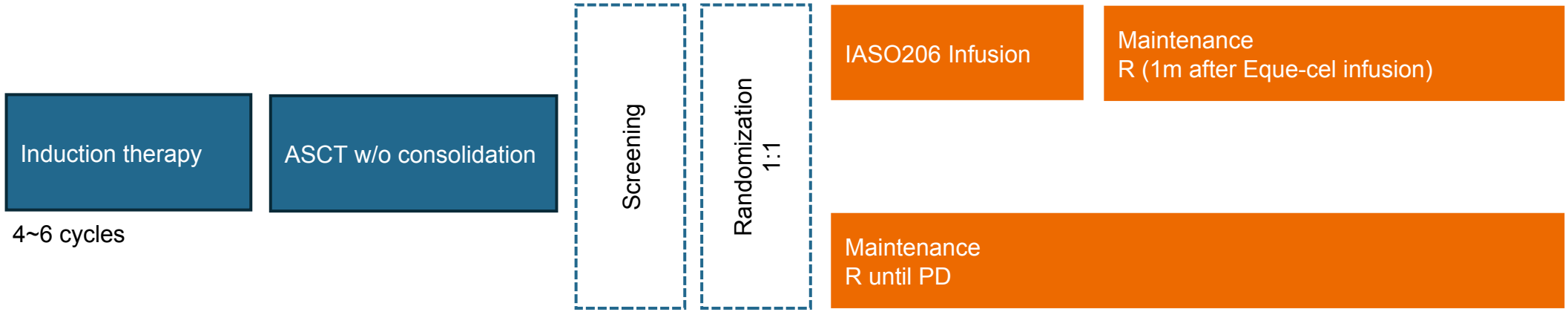
Study Design:
- 1:1
- Sample size: ~800

Primary Endpoints:
- PFS
- MRD-/CR at 12m after randomization

Secondary Endpoints:
- ORR, CR, OS
- Overall MRD- rate, MRD- CR
- Time to subsequent therapy, PFS2, Safety

CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS2, progression-free survival 2;

NDMM Patients (suboptimal response post ASCT)



Eligibility:
- Received 4~6 cycles of induction therapy;
- Double-exposed;
- With or without prior anti-CD38 mAb;
- Have received a single ASCT 80~120 days prior to ICF;
- Achieved **PR or VGPR** as the best response;
- No PD after initiating induction therapy;

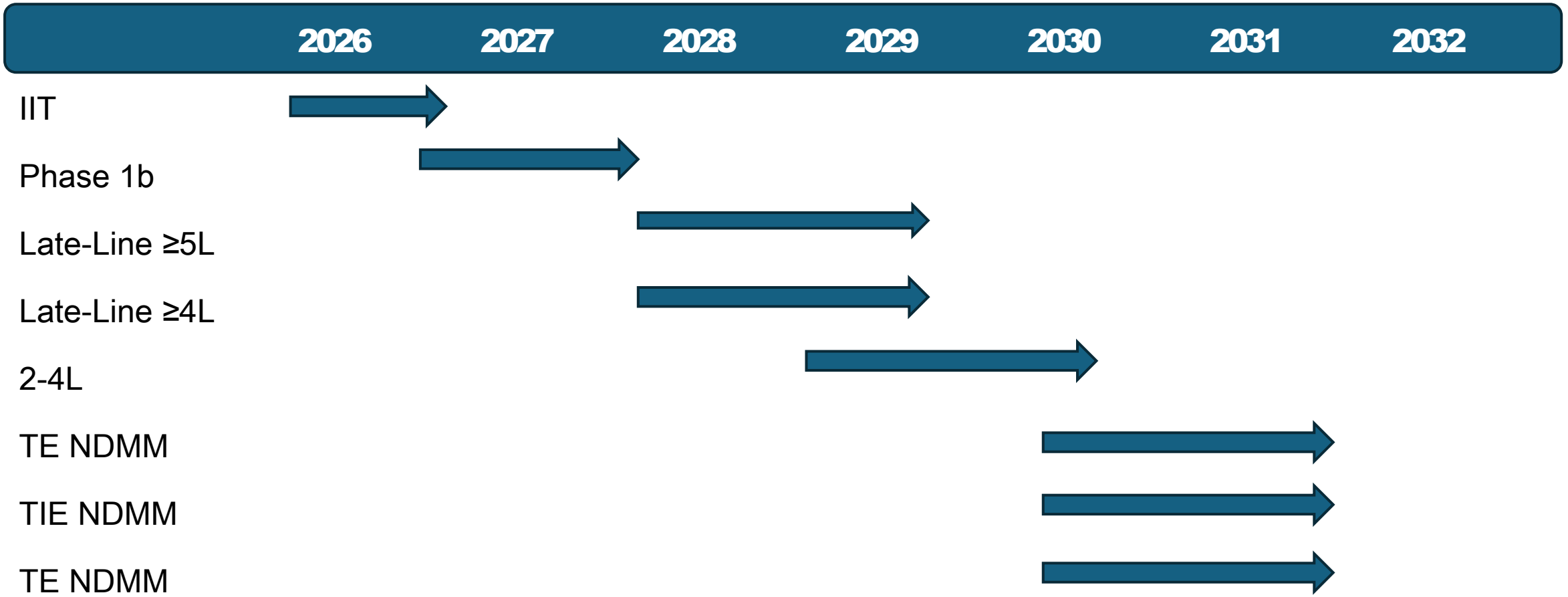
Study Design:
- 1:1
- Sample size: ~700

Primary Endpoints:
- PFS
- MRD-/CR at 9m after randomization

Secondary Endpoints:
- ORR, CR, OS
- Overall MRD- rate, MRD- CR
- Time to subsequent therapy, PFS2, Safety

CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS2, progression-free survival 2;

Study Duration



IASO BIOTHERAPEUTICS

THANK YOU

Efficacy of teclistamab in patients with RRMM after BCMA-targeting therapies

Median follow-up: 28.0 months (range, 0.7-31.1)

- Pts with prior CAR-T: 29
- Pts with Prior ADC: 15
- Pts with both: 4

Median duration of teclistamab treatment: 6.0 months (0.2-29.8)

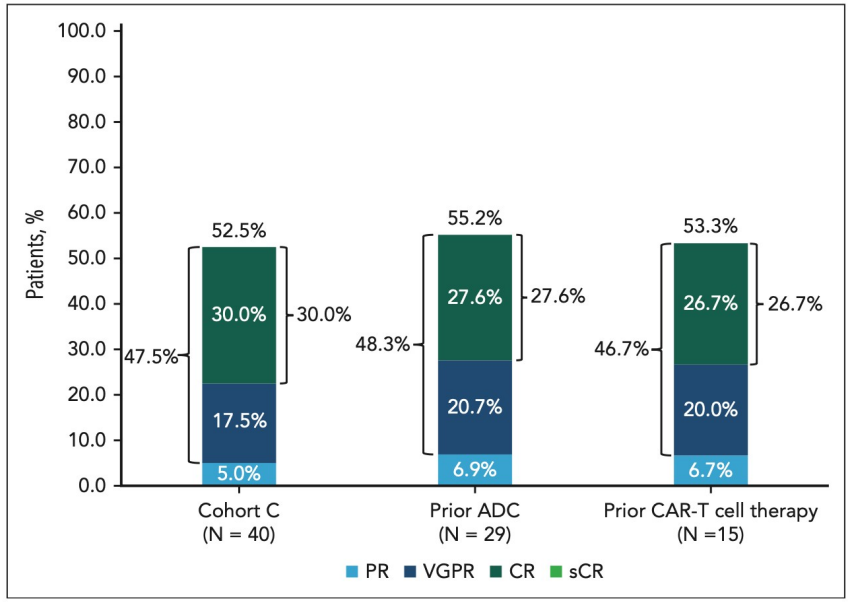


Figure 1. Response to teclistamab in patients with R/RMM who had prior BCMA-targeted therapy (ADC or CAR-T therapy).

Parameter	Results
Median time to first response	1.2 (0.2-4.9)
Median time to best response	2.9 (1.1-12.3)
DOR	14.8 (95% CI, 8.0−22.6)
Prior CAR-T	14.4 (95% CI, 2.6-NE)
Prior ADC	14.8 (95% CI, 6.2-22.6)
PFS	4.5 (95% CI, 1.3-11.6)
OS	15.5 (95% CI, 8.3-27.9
12m event-free rate	61.2% (95% CI, 37.1-78.4)
MRD	8 evaluable pts; 7 achieved MRD- at 10^{-5}

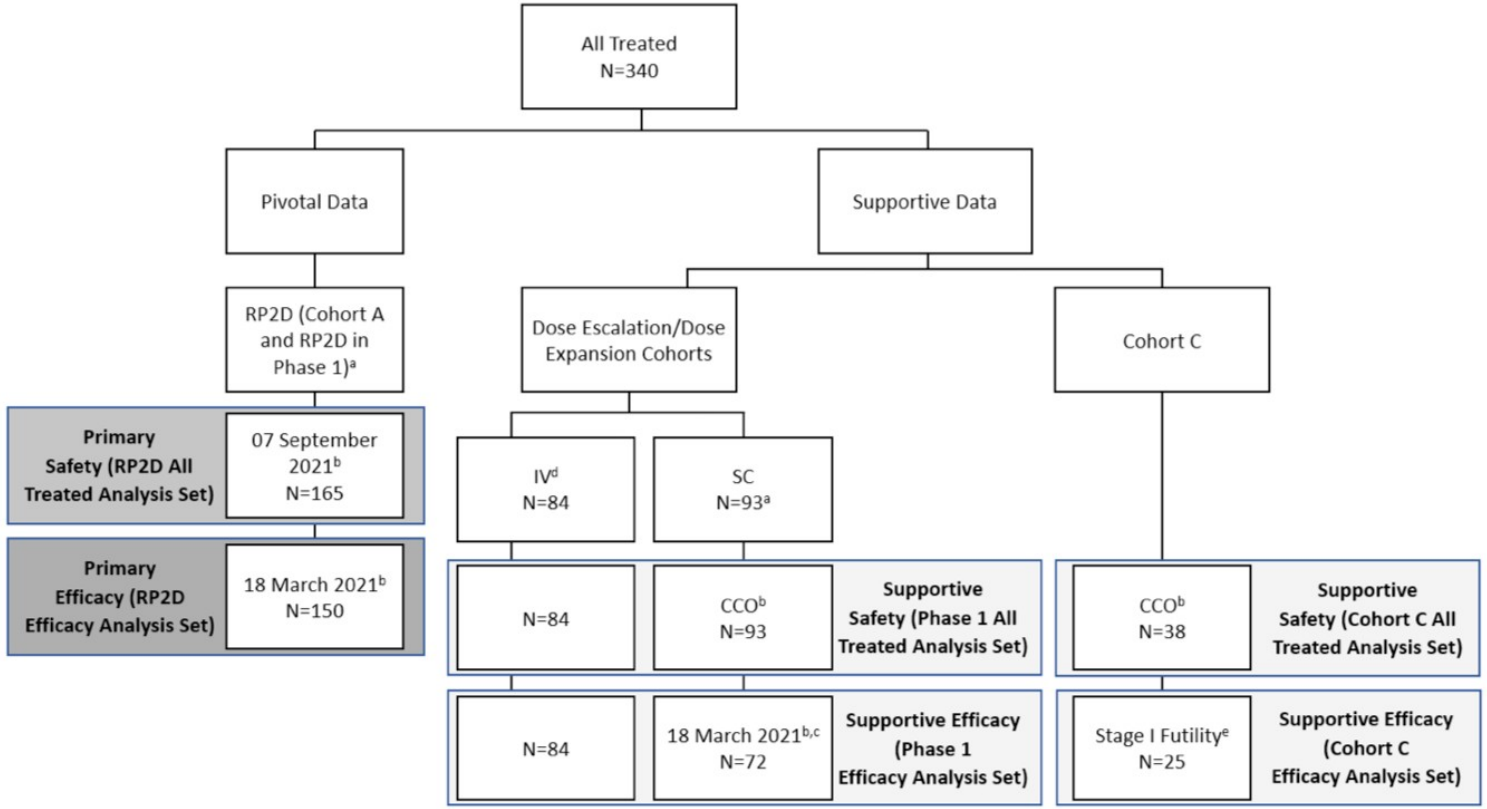
https://doi.org/10.1182/blood.2023023616

Eligible patients for phase 2 Cohort A were patients with RRMM with at least 3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb. Patients with prior BCMA-directed therapy (CAR T-cells or antibody drug conjugate) were excluded from Cohort A. Cohort C enrolled patients with RRMM with at least 3 prior lines of therapy, including a PI, an IMiD, an anti-CD38 mAb, and a BCMA-directed therapy. However, Cohort C is not relevant to this BLA because the proposed indication does not include patients with prior BCMA-directed therapy and the sample size of Cohort C is too small to draw any conclusions regarding safety and efficacy of teclistamab in patients with prior BCMA-directed therapy. FDA otherwise concurs with the information presented in the Applicant's Table 3.

The FDA's Assessment:

The size of the safety database of 165 patients who received the RP2D of teclistamab and the extended safety database, which included a total of 340 patients who received teclistamab monotherapy, is considered adequate based on teclistamab being a product that is intended to treat a life-threatening disease in a circumstance where there is no alternative satisfactory treatment. However, the assessment of safety is limited by the MajesTEC-1 single arm trial design, and there is currently no randomized data available comparing teclistamab to either placebo or standard of care therapy. FDA's analysis did not include the 38 patients from phase 2 Cohort C due to the limited number of patients and limited duration of follow up in this cohort precluding an adequate assessment of safety in patients with prior BCMA-directed therapy. FDA does not agree with the Applicant's statement that no additional safety issues were observed following long-term treatment. The 120-day safety update included two additional serious neurological TEAEs (Grade 4 seizure and Grade 5 (fatal) Guillain-Barré syndrome) that occurred with longer follow-up. Therefore, the current safety database may represent an underestimate of cumulative neurological toxicity. A PMR will be issued to further characterize neurologic toxicity with longer follow-up and in a randomized setting.

Figure 1: Analysis Populations; MajesTEC-1



CCO=clinical cutoff; IV=intravenous(ly); RP2D=recommended Phase 2 dose, SC=subcutaneous(ly)

a. Subjects treated at RP2D in Phase 1 are presented in both pivotal RP2D data and Phase 1 (dose escalation/dose expansion) data.
b. A subject must have received the first dose of teclistamab on or before this date to be included in the indicated population.
c. One subject in the 6 mg/kg SC cohort who received their first step-up dose on 17 March 2021 was excluded from the efficacy analyses for Phase 1 (dose escalation/dose expansion) because the cohort was incomplete at the time of the data cutoff for inclusion in efficacy analysis and the only subject enrolled in it had not yet received a treatment dose.
d. All subjects treated with teclistamab IV received their first dose prior to 18 March 2021.
e. As described in this section, subjects evaluated in Stage 1 of the analysis for Cohort C were included in the efficacy analysis, all of whom received at least 1 dose of teclistamab on or before 23 March 2021.

The primary analysis for all efficacy endpoints was performed separately by cohort and based on the BICR assessment of disease status using the safety analysis set (same as the final analysis evaluable set, N=123 for Cohort A and N=64 for Cohort B), which is all enrolled participants who received ≥1 dose of study drug. All enrolled participants received at least one dose of study drug.

The primary endpoint was ORR, defined as the proportion of subjects who achieved a PR or better according to the IMWG response criteria (Kumar et al, 2016), as assessed by BICR. The ORR and its 2-sided 95% Clopper-Pearson exact confidence interval (CI) were presented, with the

corresponding null ORR ≤30% for Cohort A and null ORR ≤15% for Cohort B. The study was to be considered successful if the lower bound of the 95% confidence interval exceeds 30% and 15%, respectively. Sensitivity analyses of ORR were performed using disease response based on a computerized algorithm according to the IMWG response criteria (Kumar et al, 2016).

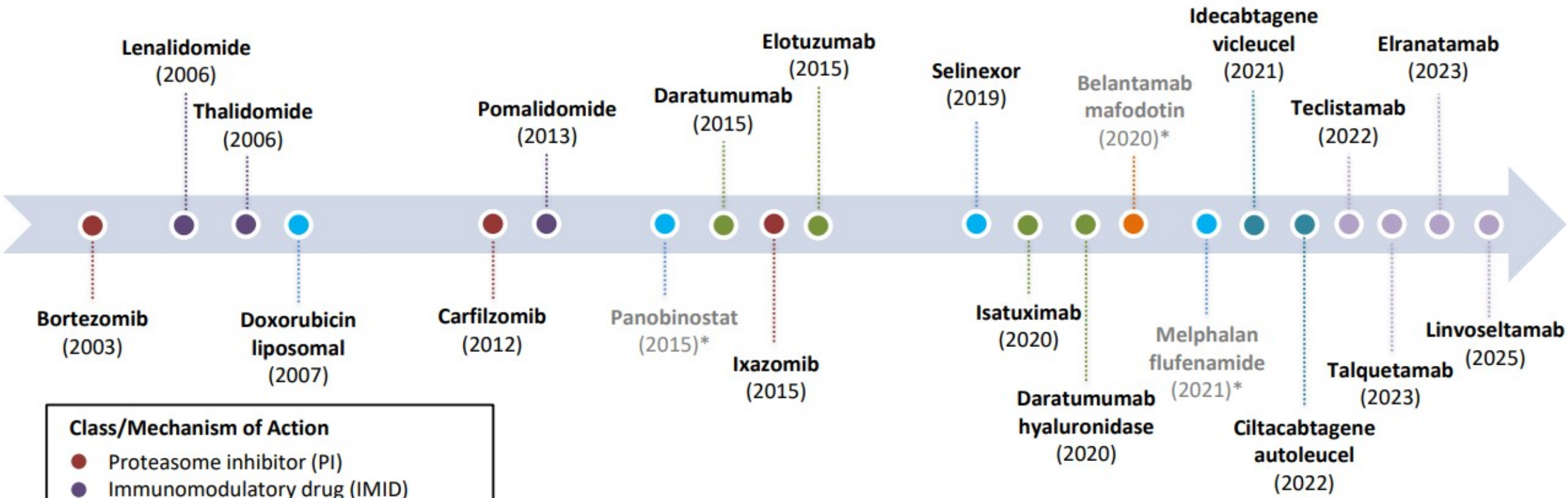
The secondary endpoints of CR or better rate and MRD negativity rate were analyzed similarly. DOR was estimated using the Kaplan-Meier method. Time to response was analyzed using descriptive statistics. Subgroup analyses for ORR included (but were not limited to) age, gender, and race.

The prespecified analysis population in Cohort A, as stated in the protocol, included all enrolled participants who received at least one dose of the study intervention. However, FDA modified efficacy population to include the indicated patient population from study C1071003 Cohort A, which included patients who had received at least 4 prior lines of therapy including a PI, IMiD, and an anti-CD38 antibody.

In Cohort A, the study was planned to test the null hypothesis that the ORR by BICR as defined by IMWG is ≤30% versus the alternative hypothesis that the ORR by BICR as defined by IMWG is >30%. In Cohort B, the study was planned to test the null hypothesis that the ORR by BICR as defined by IMWG is ≤15% versus the alternative hypothesis that the ORR by BICR as defined by IMWG is >15%.

The protocol stated that the sample size for Cohort A and Cohort B was calculated to provide adequate power for testing the statistical hypotheses regarding the primary endpoint of ORR independently in the two cohorts using a two-stage design based on exact binomial distribution. A total of 120 participants enrolled and treated in Cohort A provides approximately 98% power to detect a true ORR by BICR of 48% to reject the null hypothesis, with a 1-sided significance level of 0.025. Similarly, a total of 60 participants enrolled and treated in Cohort B provides approximately 91% power to detect a true ORR by BICR of 34% to reject the null hypothesis, with a 1-sided significance level of 0.025. FDA notes these terms of "hypotheses testing" for the single-arm trial were for sample size calculation purposes. In a single- arm trial, FDA does not consider any inferential procedures to evaluate the trial results. Instead, the efficacy decision is based on the lower limit of a 95% confidence interval to exceed a clinically relevant response rate. Comparison of response rate from single-arm trials against a historical rate is challenging because the historical benchmark is difficult to verify. Due to difference in population, trial design and other possible unknown confounders, the historical estimation is likely subject to biases which cannot be resolved.

Approvals for MM (2003 – 2025)



Class/Mechanism of Action

- Proteasome inhibitor (PI)
- Immunomodulatory drug (IMID)
- Monoclonal antibody (mAb)
- Antibody drug conjugate (ADC)
- Chimeric antigen receptor T-cell (CAR T)
- Bispecific antibody (bsAb)
- Other

*Approval withdrawn

Abbreviations: MM=multiple myeloma

Source: FDA

ABBV products in MM

合作产品	合作方	靶点 / 机制	开发状态	合作模式
ABBV-383 / TNB-383B	TeneoOne / Teneobio	BCMA × CD3 双抗	Phase 3	先合作，后 AbbVie 收购 TeneoOne
SIM0500	先声再明 / Simcere Zaiming	GPRC5D × BCMA × CD3 三特异性抗体	Phase 1	AbbVie 获得 option-to-license 权利
ABBV-2001 / ISB 2001	Ichnos Glenmark Innovation / IGI	CD38 × BCMA × CD3 三特异性抗体	Phase 1	AbbVie 获得全球独家授权
Venetoclax	Roche / Genentech	BCL-2 抑制剂	MM 未获批，曾开展 Phase 3	共同开发 / 商业化背景
Surzetoclax (ABBV-453)		BCL-2 inhibitor	1	

NCT	Phases	Start Date	Study Design	
NCT05650632	1	2023-03-21		

ABBV products in MM

Study	Link
KarMMa-9	https://clinicaltrials.gov/study/NCT06045806

2. **Type of Participant and Target Disease Characteristics**
   a. Participant with NDMM who has received induction therapy followed by high-dose chemotherapy and ASCT, without subsequent maintenance. **EXCEPTION**: Participant received ≤ 7 days of LEN maintenance therapy and the investigator documents that there is no impact to the overall benefit/risk assessment due to the temporary interruption of LEN.

   b. Participant must have received a minimum of 4 cycles of induction therapy that includes an IMiD and a PI (with or without anti-CD38 monoclonal antibody) prior to a single ASCT. A maximum of 6 cycles is permitted (which can include up to 2 cycles of post-ASCT consolidation).
      i. For participants who have not received post-ASCT consolidation therapy, the participant must be within 80 to 120 days post transplant at the time of consent.
      ii. For participants treated with post-ASCT consolidation therapy, the participant must be within 60 days of the last dose of consolidation therapy at the time of consent and within 180 days post transplant at the time of consent.

      Note: Participant must not have confirmed progression since commencing induction. When screening results are suggestive of progression, repeat assessments must be performed to exclude PD per IMWG.

   c. Participant must have documented best overall response of PR or VGPR per IMWG post ASCT (or post consolidation, if applicable) at time of randomization.

   d. Per investigator's assessment, participant must be a candidate for single-agent LEN maintenance.

Number of Participants:

Not applicable as of Protocol Amendment 05:

A total of 618 NDMM participants who achieved suboptimal response, defined as PR or VGPR post ASCT, will be randomly assigned in a 1:1 ratio to the experimental group (Arm A) or the control group (Arm B).

To obtain the targeted sample size of 618, approximately 687 participants will be screened assuming a screen failure rate of 10%.

While LEN maintenance has demonstrated progression-free survival (PFS) and overall survival (OS) improvement over observation or placebo post ASCT, the magnitude of this benefit is still different in patients who achieve deep responses post ASCT versus those who do not. In the CALGB study, at a median follow-up of 34 months, participants who achieved a CR post ASCT did not reach median time to progression (mTTP) while those who did not achieve a CR had a mTTP of 43 months.

Changes per Protocol Amendment 05:

As of September 2024, the CA0891043 study had achieved 10% of target enrollment after the first year since the first participant had been enrolled. Based on this enrollment rate, the study will not meet its scientific objectives within a timeline that would be clinically relevant. As a result, on 25-Sep-2024 (Dear Investigator Letter; Approved v1.0 930230293), a decision was made to discontinue enrollment for new participants in the trial. As of 24-Oct-2024, the last participant was consented and enrollment into the study was fully closed. After further careful consideration of the study objectives, a decision was made to close the study. The decision was not due to safety concerns associated with the study treatment of idecabtagene vicleucel (ide-cel) or lenalidomide for the participants with multiple myeloma.

As of 04-Dec-2024 (Dear Investigator Letter; Approved v1.0 930234081), the following measures were put into effect:

- Participants currently on treatment, or planned to initiate treatment, were allowed to continue study treatment through to End of Treatment (EOT).
- Redefinition of EOT by arm.
- Reduction in assessments, retaining those focused on safety.
- Long Term Follow Up (LTFU) instructions provided, with details outlined by arm.

A Study to Compare the Efficacy and Safety of Idecabtagene Vicleucel With Lenalidomide Maintenance Therapy Versus Lenalidomide Maintenance Therapy Alone in Adult Participants With Newly Diagnosed Multiple Myeloma Who Have Suboptimal Response After Autologous Stem Cell Transplantation (KarMMa-9)

Active, not recruiting

No longer looking for participants

ClinicalTrials.gov ID NCT06045806

Sponsor Celgene

Information provided by Celgene (Responsible Party)

Last Update Posted 2026-03-05

- Part 3 (Phase 2 dose expansion): teclistamab has anti-myeloma activity and demonstrates acceptable safety in 1 or more cohorts of subjects with relapsed or refractory multiple myeloma with unmet medical need, that differ by previous therapy:
  - Cohort A: treatment with teclistamab will have significant anti-myeloma activity (ie, the lower limit of two-sided 95% confidence interval [CI] for ORR is greater than 30%).
  - Cohort B: treatment with teclistamab will have significant anti-myeloma activity (ie, the lower limit of two-sided 95% CI for ORR is greater than 25%).
  - Cohort C: treatment with teclistamab will result in an ORR >15% (ie, based on Simon's 2-stage design).

The end of study (study completion) is defined as 2 years after the last subject has received his or her initial dose of teclistamab. For Part 3, the primary analysis may be done separately for each cohort. Analysis of the primary endpoint for Part 3, ORR (PR or better), will be conducted approximately 6 months after the 100th subject in Cohort A and 90th in Cohort B (if applicable) received his or her initial dose of teclistamab. Cohort C will use Simon's 2-stage design as detailed in Section 11.13.

An updated analysis for efficacy will be conducted at approximately 8 to 12 months after the 100th subject in Cohort A received his or her initial dose of teclistamab and at the end of the study, as defined above. Additional updated analyses for efficacy may be conducted as determined based on emerging data.

In Part 3, subjects with relapsed or refractory myeloma will be enrolled into cohorts based on prior therapy exposures. Cohort A and Cohort C are ongoing; Cohort B is not planned to be enrolled.

- Cohort A will enroll approximately 100 subjects with multiple myeloma who are triple class exposed (PI, IMiD, and anti-CD38 monoclonal antibody) and have previously received treatment with ≥3 prior lines of therapy.
- Cohort B was planned to enroll approximately 90 subjects who are more heavily pretreated (≥4 prior lines of therapy) and considered penta-drug refractory (ie, refractory to ≥2 PIs, ≥2 IMiDs, and an anti-CD38 monoclonal antibody). This cohort will not be opened for enrollment.
- Cohort C will enroll approximately 38 subjects who have previously received ≥3 prior lines of therapy that included a PI, an IMiD, an anti-CD38 monoclonal antibody, and an anti-BCMA treatment (with CAR-T cells or an ADC).
- **Cohort A**: With approximately 100 subjects treated with teclistamab, there will be >85% power to declare the ORR is higher than 30% at the one-sided significance level of 0.025 with the assumption that ORR among those treated with teclistamab will be at least 45%. Subjects treated with teclistamab who have a non-evaluable response will be counted as non-responders in the ORR assessment.
- **Cohort B:** With approximately 90 subjects treated with teclistamab, there will be approximately 85% power to declare the ORR is higher than 25% at the one-sided significance level of 0.025 with the assumption that ORR among those treated with teclistamab will be at least 40%. Subjects treated with teclistamab who have a non-evaluable response will be counted as non-responders in the ORR assessment.
- **Cohort C:** Simon's 2-stage design will be used to test the null hypothesis that the ORR is at most 15%, against the alternative that the ORR is at least 35%. With one-sided significance level of 0.025 and a power of 80%, Cohort C needs 34 response-evaluable subjects. Assuming a non-evaluable rate of 10%, a total sample size required for Cohort C is 38 subjects.

  The Stage 1 analysis will be performed when the first 21 subjects are enrolled and have been followed for at least 2 cycles to be evaluable for response. Further enrollment may be terminated if 3 or fewer responses are observed in the first stage. Otherwise, an additional 17 subjects will be enrolled to ensure there is a total 34 response-evaluable subjects with 2 stages combined.

PRIMARY THERAPY FOR HCT CANDIDATES[a-d]
Preferred • Daratumumab/Lenalidomide/Bortezomib/Dexamethasone (category 1) • Isatuximab-irfc/Bortezomib/Lenalidomide/Dexamethasone (category 1)
Other Recommended • Bortezomib/Lenalidomide/Dexamethasone (category 1) • Carfilzomib/Lenalidomide/Dexamethasone • Daratumumab/Carfilzomib/Lenalidomide/Dexamethasone • Isatuximab-irfc/Carfilzomib/Lenalidomide/Dexamethasone
Useful in Certain Circumstances • Bortezomib/Cyclophosphamide/Dexamethasone • Carfilzomib/Cyclophosphamide/Dexamethasone[e] • Daratumumab/Bortezomib/Cyclophosphamide/Dexamethasone • Dexamethasone/Thalidomide/Cisplatin/Doxorubicin/Cyclophosphamide/Etoposide/ Bortezomib[f] (VTD-PACE)

MAINTENANCE THERAPY[g]
Preferred • Lenalidomide[h] (category 1)
Other Recommended • Carfilzomib/Lenalidomide[h] • Daratumumab/Lenalidomide[h]
Useful in Certain Circumstances • Bortezomib ± Lenalidomide[h] • Daratumumab • Ixazomib (category 2B)

[a] Selected, but not inclusive of all regimens. The regimens under each preference category are listed by order of NCCN Category of Evidence and Consensus alphabetically.
[b] Supportive Care Treatment for Multiple Myeloma (MYEL-I).
[c] See MYEL-F for considerations for myeloma therapy and for specific populations (eg, Black/African American individuals).
[d] Management of Renal Disease in Multiple Myeloma (MYEL-L).
[e] Treatment option for patients with renal insufficiency and/or peripheral neuropathy.
[f] Generally reserved for the treatment of aggressive MM.
[g] Two-drug maintenance recommended for high-risk MM.
[h] There appears to be an increased risk for secondary cancers, especially with lenalidomide maintenance following transplant. The benefits and risks of maintenance therapy versus secondary cancers should be discussed with patients.

Note: All recommendations are category 2A unless otherwise indicated.

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PRIMARY THERAPY IF HCT-DEFERRED[i] OR IF HCT IS NOT INDICATED[a-d,j]	
In general, continue primary therapy until progression with de-escalation of therapy (modification of dose and duration) as needed.	
Preferred • Daratumumab/Lenalidomide/Dexamethasone (category 1) • Daratumumab/Bortezomib/Lenalidomide/Dexamethasone (for patients <80 years old who are not frail) (category 1) • Isatuximab-irfc/Bortezomib/Lenalidomide/Dexamethasone (for patients <80 years old who are not frail) (category 1)	
Other Recommended • Carfilzomib/Lenalidomide/Dexamethasone • Bortezomib/Lenalidomide/Dexamethasone (category 1) • Isatuximab-irfc/Lenalidomide/Dexamethasone	
Useful In Certain Circumstances • Lenalidomide/Low-Dose Dexamethasone (category 1) • Bortezomib/Cyclophosphamide/Dexamethasone • Bortezomib/Dexamethasone • Bortezomib/Lenalidomide/Dexamethasone (VRD-lite) for patients assessed as being frail	• Carfilzomib/Cyclophosphamide/Dexamethasone[e] • Daratumumab/Cyclophosphamide/Bortezomib/Dexamethasone[k] • Isatuximab-irfc/Carfilzomib/Lenalidomide/Dexamethasone (category 2B) • Ixazomib/Lenalidomide/Dexamethasone • Lenalidomide/Cyclophosphamide/Dexamethasone

RRMM after 1-3 prior lines of therapy

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THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,l-o]
Relapsed/Refractory Disease After 1–3 Prior Therapies

Preferred*
Order of regimens does not indicate comparative efficacy

Anti-CD38 Refractory	Bortezomib-Refractory	Lenalidomide-Refractory
• Carfilzomib/Lenalidomide/Dexamethasone (category 1) • Carfilzomib/Pomalidomide/Dexamethasone • Pomalidomide/Bortezomib/Dexamethasone (category 1) ***After two prior therapies including lenalidomide and a proteasome inhibitor (PI)*** ▸ Elotuzumab/Pomalidomide/Dexamethasone ***After two prior therapies including an IMiD and a PI and with disease progression on/within 60 days of completion of last therapy*** ▸ Ixazomib/Pomalidomide/Dexamethasone	• Carfilzomib/Lenalidomide/Dexamethasone (category 1) • Daratumumab/Carfilzomib/Dexamethasone (category 1) • Daratumumab/Lenalidomide/Dexamethasone (category 1) • Isatuximab-irfc/Carfilzomib/Dexamethasone (category 1) • Carfilzomib/Pomalidomide/Dexamethasone ***After one prior therapy including Lenalidomide and a PI*** ▸ Daratumumab/Pomalidomide/Dexamethasone (category 1) ▸ Daratumumab/Teclistamab-cqyv (category 1) ***After two prior therapies including Lenalidomide and a PI*** ▸ Isatuximab-irfc/Pomalidomide/Dexamethasone (category 1) ▸ Elotuzumab/Pomalidomide/Dexamethasone	• Daratumumab/Bortezomib/Dexamethasone (category 1) • Daratumumab/Carfilzomib/Dexamethasone (category 1) • Isatuximab-irfc/Carfilzomib/Dexamethasone (category 1) • Pomalidomide/Bortezomib/Dexamethasone (category 1) • Carfilzomib/Pomalidomide/Dexamethasone ***After one prior therapy including Lenalidomide and a PI*** ▸ Daratumumab/Pomalidomide/Dexamethasone (category 1) ▸ Daratumumab/Teclistamab-cqyv (category 1) ***After two prior therapies including Lenalidomide and a PI*** ▸ Isatuximab-irfc/Pomalidomide/Dexamethasone (category 1) ▸ Elotuzumab/Pomalidomide/Dexamethasone ***After two prior therapies including an IMiD and a PI and with disease progression on/within 60 days of completion of last therapy*** ▸ Ixazomib/Pomalidomide/Dexamethasone

CAR T-Cell Therapy
After one prior line of therapy including IMiD and a PI, and refractory to lenalidomide
▸ Ciltacabtagene autoleucel (category 1)

After two prior lines of therapies including an IMiD, an anti-CD38 monoclonal antibody and a PI
▸ Idecabtagene vicleucel (category 1)

* For Other Recommended regimens and for regimens Useful in Certain Circumstances for Relapsed/Refractory Disease After 1–3 Prior Therapies, see MYEL-G 4 of 5

EHA–EMN Evidence-Based Guidelines

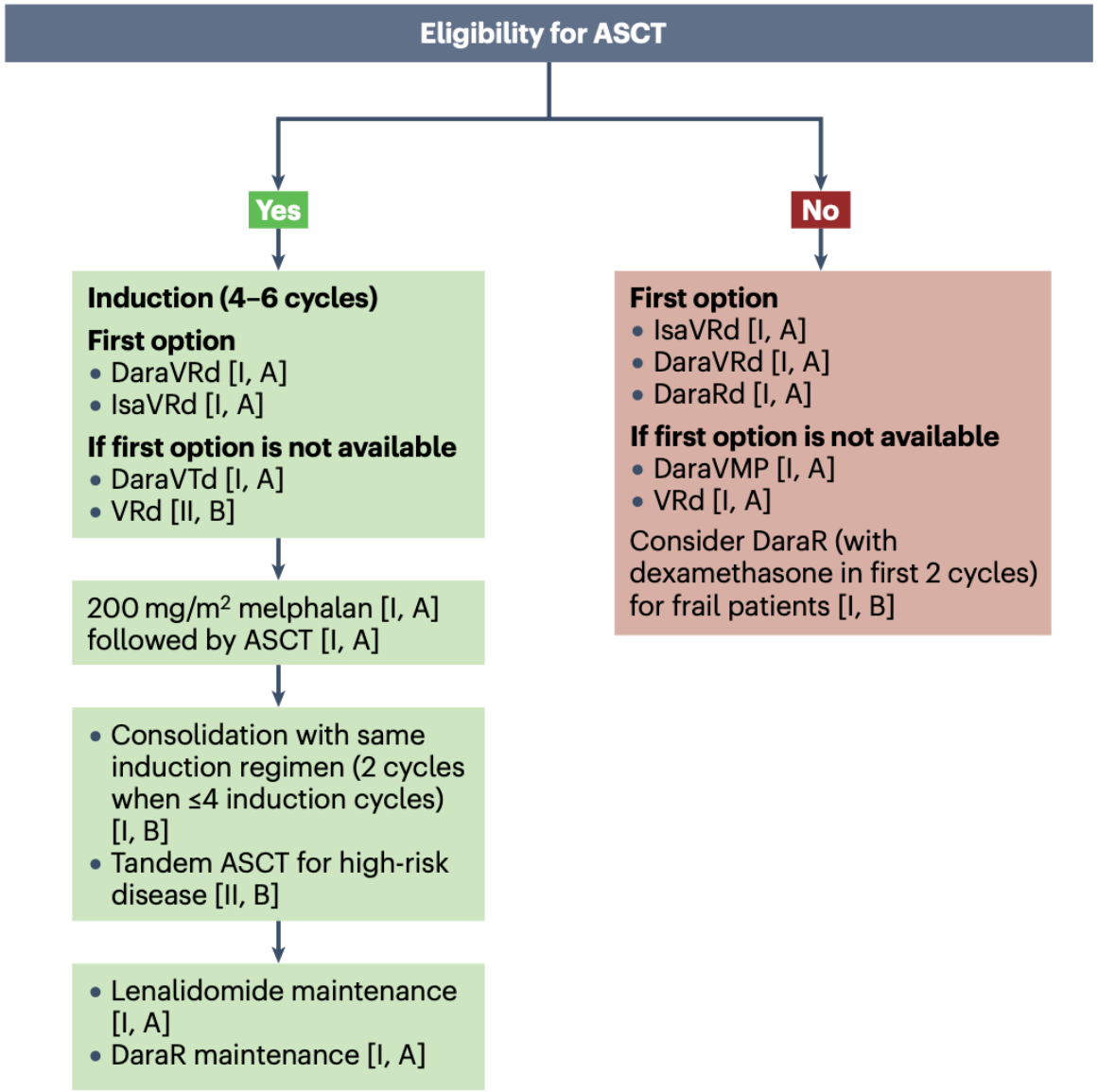


Fig. 1 | Recommendations for the treatment of patients with newly diagnosed multiple myeloma. Recommendations include supporting levels of evidence and have been graded[170] (Supplementary Table 1). ASCT, autologous stem cell transplantation; d, dexamethasone; Dara, daratumumab; Isa, isatuximab; M, melphalan; P, pomalidomide; R, lenalidomide; T, thalidomide; V, bortezomib.

Source: https://doi.org/10.1038/s41571-025-01041-x

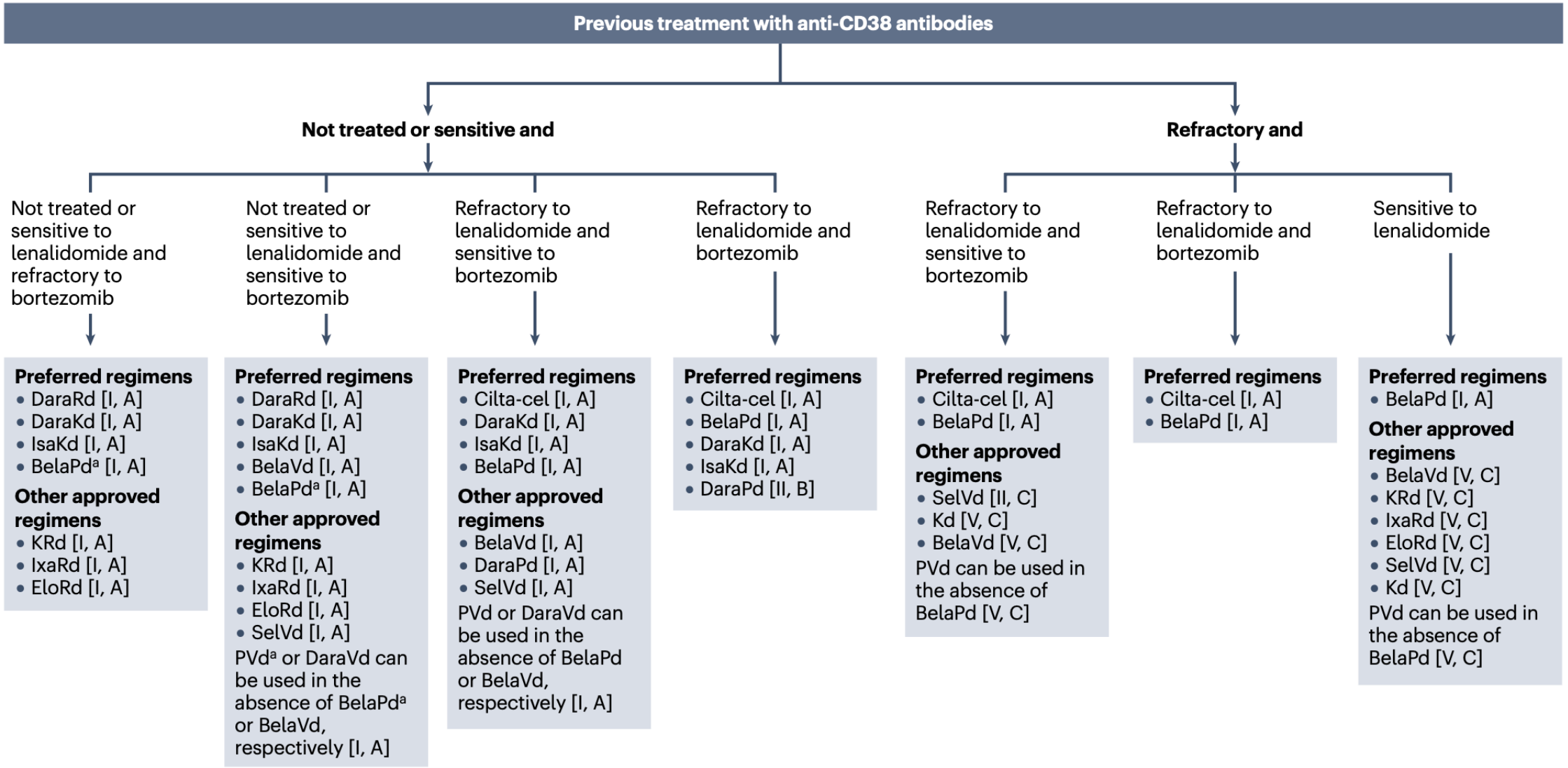
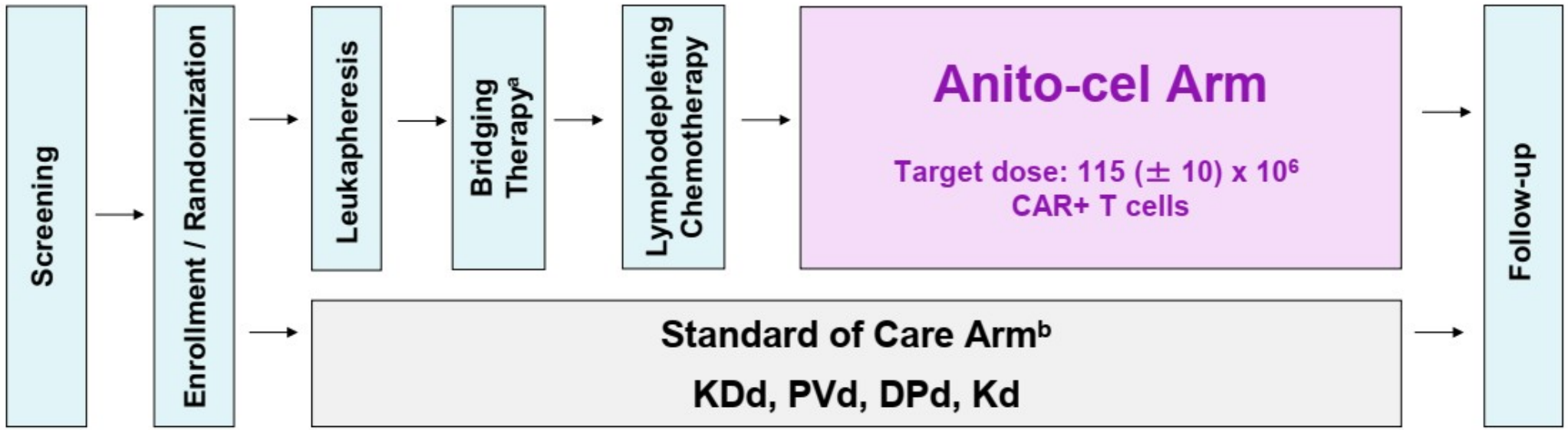


Fig. 2 | Recommendations for the treatment of patients with relapsed and/or refractory multiple myeloma at second line. Recommendations include supporting levels of evidence and have been graded[170] (Supplementary Table 1). [a]Only in patients exposed to lenalidomide. Bela, belantamab mafodotin; cilta-cel, ciltacabtagene autoleucel; d, dexamethasone; Dara, daratumumab; Elo, elotuzumab; Isa, isatuximab; Ixa, ixazomib; K, carfilzomib; P, pomalidomide; R, lenalidomide; Sel, selinexor.

Source: https://doi.org/10.1038/s41571-025-01041-x

iMMagine-3 Global Phase 3 Randomized Study of Anti-CD38 + IMiD Exposed Patients



STUDY DESIGN

- 1:1 Randomization
- n = Approximately 450, ~130 sites globally

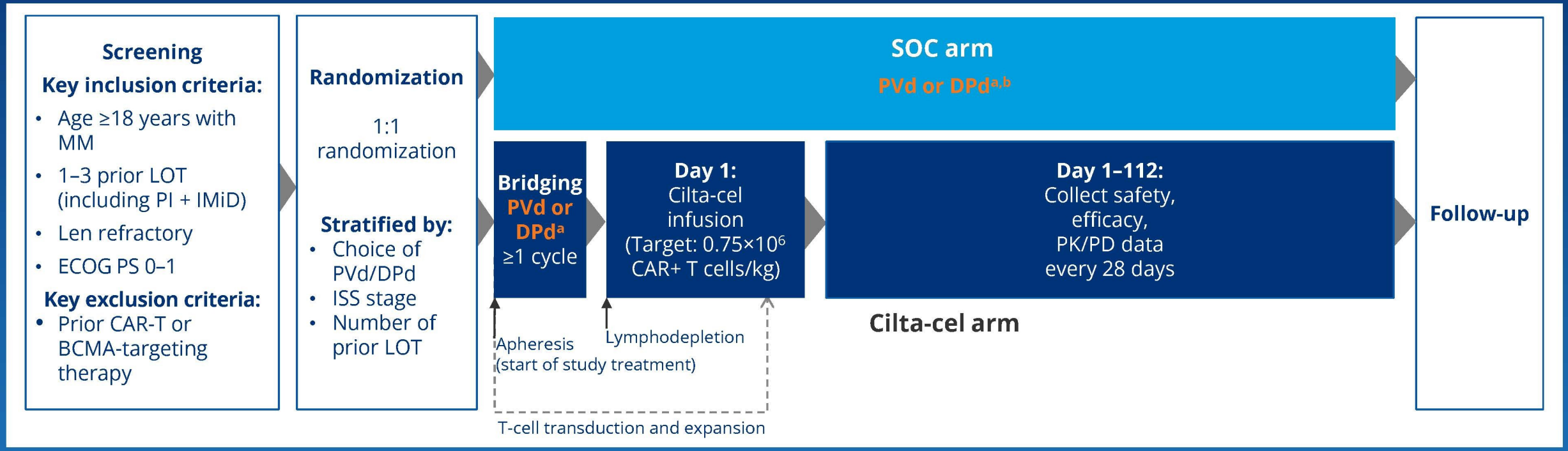
STUDY ENDPOINTS

- Dual Primary Endpoints: PFS and MRD negativity
- Key Secondary Endpoints: CR rate, MRD, OS, safety

[a] Optional Bridging therapy will be the SOC regimen selected prior to randomization
[b] Cycles will continue until unacceptable toxicity, progression as per IMWG criteria, or patient withdrawal of consent

Source : Study Details | NCT06413498 | A Study Comparing Anitocabtagene Autoleucel to Standard of Care Therapy in Participants With Relapsed/ Refractory Multiple Myeloma | ClinicalTrials.gov

CARTITUDE-4: Study Design and Endpoints



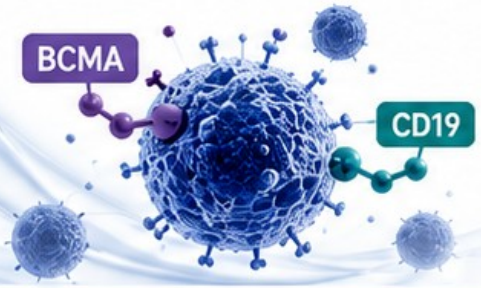
Primary endpoint

- PFS[c]

Secondary endpoints

- Efficacy: ≥CR, ORR, MRD negativity, OS
- Safety
- PROs

[a]Physicians' choice. [b]Administered until disease progression. [c]Time from randomization to disease progression/death.
BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; len, lenalidomide; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PVd, pomalidomide, bortezomib, and dexamethasone; SOC, standard of care.



DURGA-4 | NCT07391657 临床研究概览

AZD0120（BCMA×CD19 双靶点自体 CAR-T）在复发/难治性多发性骨髓瘤中的关键 III 期研究

1 研究基本信息

- ClinicalTrials.gov ID: NCT07391657
- 链接: https://clinicaltrials.gov/study/NCT07391657
- 研究阶段：Phase III
- 计划样本量：508例
- 申办方：AstraZeneca

2 研究设计

- 开放标签
- 随机
- 多中心
- 全球对照研究

3 目标人群

- R/R MM（复发/难治性多发性骨髓瘤）
- 1–3线既往治疗
- 用于较早线复发/难治人群的关键研究

4 对照方案（研究者选择 SOC）

- DKd
- DPd
- PVd
- Kd

SOC = standard of care

5 研究定位与关键看点

1. AZD0120 在较早线 R/R MM 中的关键注册型研究
2. 直接对比强标准治疗方案

6 主要研究终点

- **主要终点 1：** 无进展生存期（PFS）
- **主要终点 2：** 9个月 MRD 阴性率

目标为证明 AZD0120 相较研究者选择 SOC 的优效性

7 主要入排标准

主要入选标准

- 年龄 ≥18岁
- 符合 IMWG 诊断标准的多发性骨髓瘤
- 具有可测量病灶
- 依据 IMWG 2016 标准证实疾病进展（PD）
- 既往接受 1–3 线治疗，且包含 IMiD 和 PI 或 anti-CD38
- 研究者判断可接受至少 1 种 SOC 方案（DKd / DPd / PVd / Kd）
- ECOG 0–1，血液学及肝肾功能充分

主要排除标准

- 已知活动性或既往中枢神经系统 / 脑膜 MM 受累
- 原发性淀粉样变、活动性浆细胞白血病、Waldenström 巨球蛋白血症或 POEMS 综合征
- 原发难治性 MM
- 显著神经系统或精神疾病
- 其他导致治疗相关风险不可接受的严重合并症

核心要点： DURGA-4 是 AZD0120 在 1–3线 R/R MM 中开展的全球随机 III 期研究，计划入组 **508例**，主要终点包括 **PFS** 和 **9个月 MRD 阴性率**，并与研究者选择的 SOC 方案直接比较。

注：本图基于 ClinicalTrials.gov 及 AstraZeneca 公布信息整理。