# Integrating New Advances into Community Oncology Practice

*CME/MOC, NCPD and ACPE Accredited*

**Saturday, October 17, 2026**
**7:15 AM – 12:00 PM ET**

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# Agenda

**Module 1 — Breast Cancer:** *Drs Geyer, Lustberg, Nanda and Wander*

**Module 2 — Prostate Cancer:** *Drs Agarwal and Antonarakis*

**Module 3 — Multiple Myeloma:** *Drs Lonial and Richardson*

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# Prostate Cancer Faculty



**Neeraj Agarwal, MD, FASCO**
Faculty Medical Oncologist
Dana-Farber Cancer Institute
Co-Director, Prostate Cancer Program
Harvard Cancer Consortium
The Lank Center for Genitourinary Oncology
Boston, Massachusetts



**Emmanuel S Antonarakis, MD**
Clark Endowed Professor of Medicine
Division of Hematology, Oncology and Transplantation
University of Minnesota
Minneapolis, Minnesota

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# Consulting General Medical Oncologists



**Susmitha Apuri, MD**
Florida Cancer Specialists & Research Institute
Inverness and Lecanto, Florida



**Mamta Choksi, MD**
Florida Cancer Specialists & Research Institute
Trinity, Florida



**Sunil Gandhi, MD**
Florida Cancer Specialists & Research Institute
Lecanto, Florida



**Shaachi Gupta, MD, MPH**
Florida Cancer Specialists & Research Institute
West Palm Beach, Florida



**Maen Hussein, MD**
Florida Cancer Specialists & Research Institute
The Villages, Florida



**Renjitha Ignatius, MD**
Florida Cancer Specialists & Research Institute
Sun City Center, Florida



**Shachar Peles, MD**
Florida Cancer Specialists & Research Institute
Lake Worth, Florida



**Syed F Zafar, MD**
Florida Cancer Specialists & Research Institute
Fort Myers, Florida

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# Agenda

Introduction: ESMO 2026; Recent FDA Approvals

Selection of Endocrine Therapy – Dr Antonarakis

Utility of PARP Inhibitors – Dr Agarwal

AKT Inhibition for PTEN-Deficient Disease – Dr Antonarakis

Radiopharmaceuticals – Dr Agarwal

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# Agenda

**Introduction: ESMO 2026; Recent FDA Approvals**

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# Select ESMO 2026 Abstracts

## Prostate Cancer

| | |
|---|---|
| Abstract LBA4 | Darolutamide with androgen deprivation therapy (ADT) and definitive or salvage locoregional radiation therapy (RT) for localised, very high-risk prostate cancer: Interim analysis of an international, placebo-controlled, randomised phase 3 trial (DASL-HiCaP; ANZUP1801). Niazi T et al. |
| Abstract LBA53 | Perioperative apalutamide (APA) plus androgen deprivation therapy (ADT) with radical prostatectomy plus pelvic lymph node dissection (RP + PLND) vs RP + PLND alone in patients (pts) with high-risk localized or locally advanced prostate cancer (HR LPC/LAPC): PROTEUS substudy. Briganti A et al. |
| Abstract LBA56 | Capivasertib (capi) + abiraterone (abi) vs placebo (pbo) + abi in patients (pts) with PTEN-deficient metastatic hormone sensitive prostate cancer (mHSPC): Updated overall survival (OS) from CAPItello-281. Fizazi K et al. |

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# Select ESMO 2026 Abstracts

## Prostate Cancer

| | |
|---|---|
| Abstract 2215O | Long-term overall survival with abiraterone acetate plus prednisone in the PEACE-1 phase 3 trial for de novo metastatic castration-sensitive prostate cancer (mCSPC).<br>Fizazi K et al. |
| Abstract 2219RO | Utility of ctDNA tumor fraction (TF) as a prognostic biomarker in TALAPRO-3: Phase 3 study of talazoparib (TALA) + enzalutamide (ENZA) vs placebo (PBO) + ENZA in patients (pts) with homologous recombination repair (HRR) gene–mutated metastatic castration-sensitive prostate cancer (mCSPC).<br>Azad A et al. |
| Abstract 2222RO | Patient-reported outcomes (PROs) in men with metastatic castration-sensitive prostate cancer (mCSPC) and homologous recombination repair (HRR) gene alterations receiving talazoparib (TALA) + enzalutamide (ENZA) vs placebo (PBO) + ENZA: Results from the Phase 3 TALAPRO-3 study.<br>Azad A et al. |

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# Recent FDA Approvals

| | |
|---|---|
| **FDA APPROVAL**<br>**June 12, 2026** | **Capivasertib with abiraterone and prednisone for PTEN-deficient androgen pathway modulation-naïve or -sensitive prostate cancer** |
| **FDA APPROVAL**<br>**July 31, 2026** | **Lutetium Lu 177 vipivotide tetraxetan with androgen receptor pathway inhibitor therapy for metastatic androgen pathway modulation-naïve or -sensitive prostate cancer** |

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# Agenda

**Introduction: ESMO 2026; Recent FDA Approvals**

**Selection of Endocrine Therapy – Dr Antonarakis**

- Endocrine Treatment for Localized Disease
- Treatment for M0 Disease
- First-Line Endocrine Treatment

**Utility of PARP Inhibitors – Dr Agarwal**

**AKT Inhibition for PTEN-Deficient Disease – Dr Antonarakis**

**Radiopharmaceuticals – Dr Agarwal**

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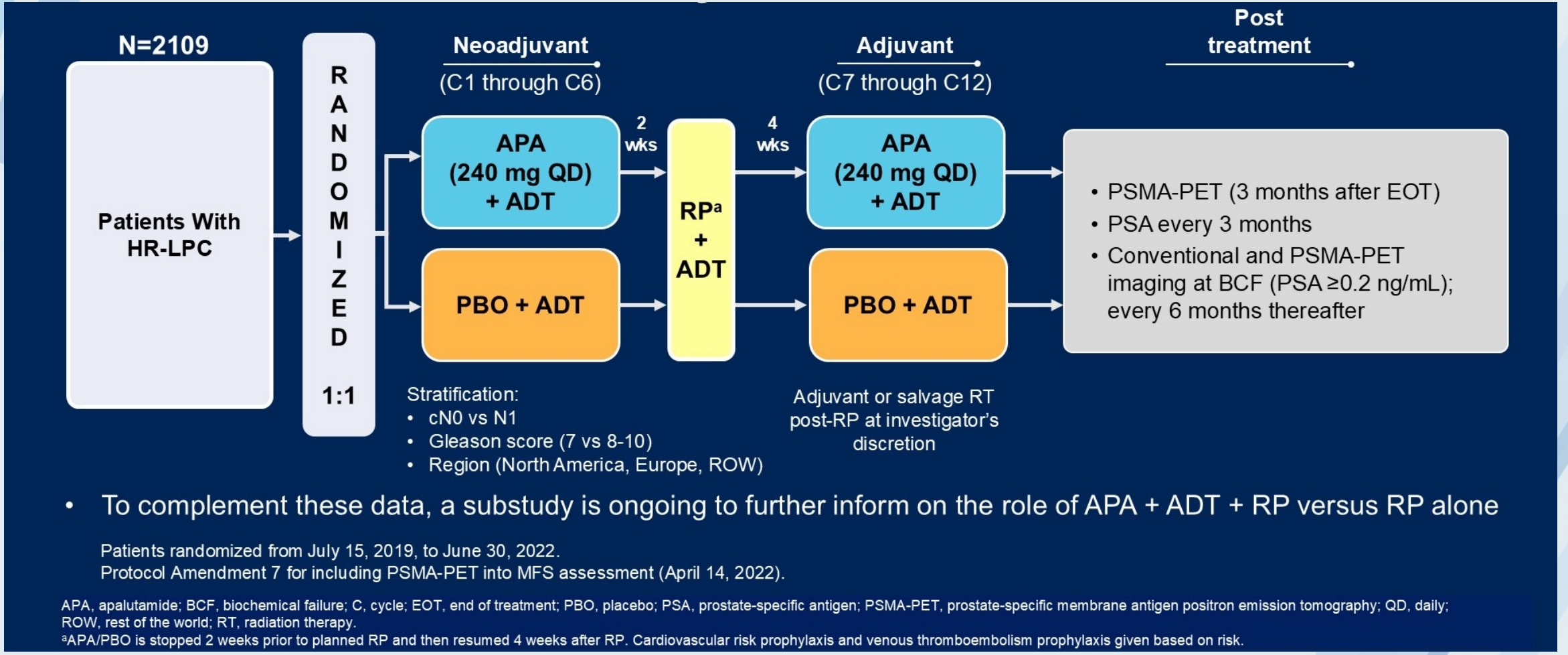
# Endocrine Treatment for Localized Disease

**Select Datasets**

- Taplin ME et al. Perioperative (neoadjuvant and adjuvant) apalutamide (APA) + androgen deprivation therapy (ADT) vs placebo (PBO) + ADT with radical prostatectomy (RP) in high-risk localized or locally advanced prostate cancer (HR LPC/LAPC): Final analysis of the PROTEUS phase 3 study. ASCO 2026;Abstract LBA1.
- Taplin ME et al. Perioperative apalutamide in high-risk localized prostate cancer. *N Engl J Med* 2026;395(6):546-60.

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# Phase III PROTEUS Study Design

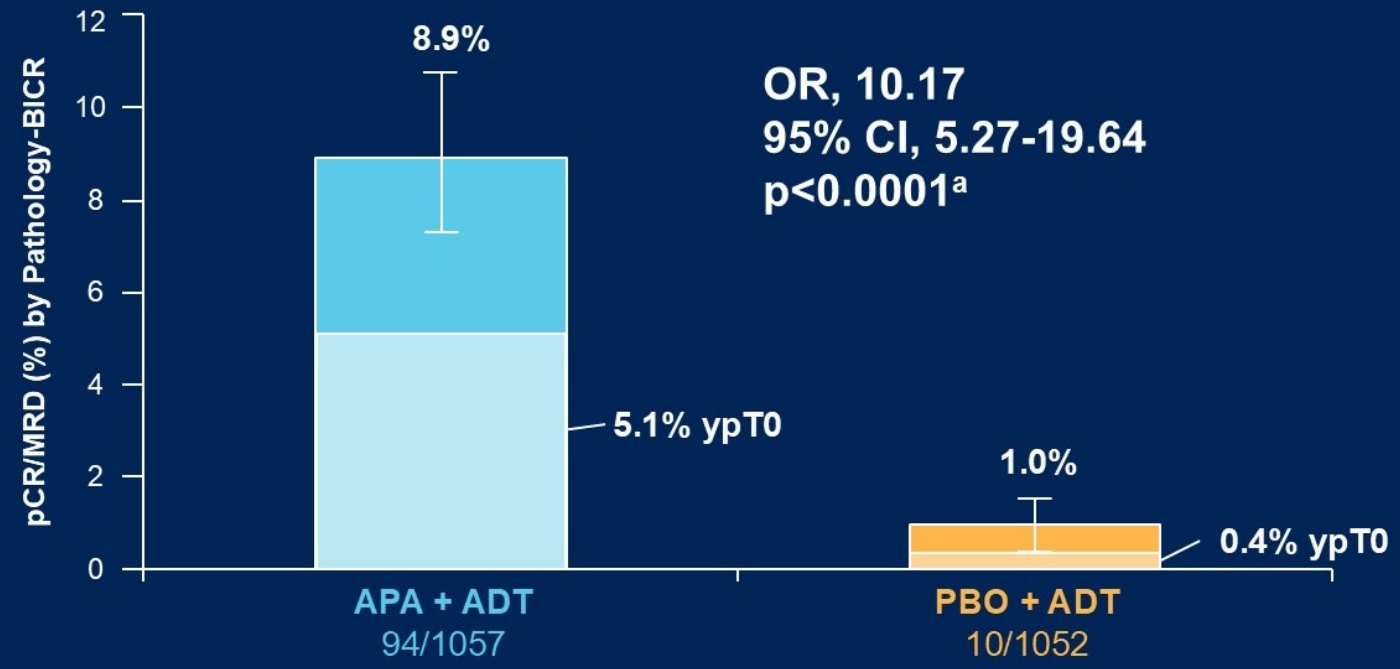



Dual primary endpoints: pathologic complete response/minimal residual disease, metastasis-free survival

Taplin ME et al. ASCO 2026;Abstract LBA1.
Taplin ME et al. *N Engl J Med* 2026;395(6):546-60.

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# Phase III PROTEUS Dual Primary Endpoint: Pathologic Complete Response (pCR)/Minimal Residual Disease (MRD)




**OR, 10.17**
**95% CI, 5.27-19.64**
**p<0.0001[a]**

**9-fold improvement in pCR/MRD at RP after 6-cycle neoadjuvant APA + ADT vs PBO + ADT**

**Exploratory end point of RCB (≤ypT2, N0, ≤0.25 cm$^3$) corroborates pCR/MRD:**

- APA + ADT vs PBO + ADT, 30.6% vs 11.7%
- OR, 3.36; 95% CI, 2.67-4.23; p<0.0001

pCR/MRD: Minimal residual tumor ≤5 mm (greatest dimension of largest tumor lesion) in prostate-confined disease (≤ypT2, N0) or no tumor identified (ypT0)
RCB: Residual cancer burden ≤0.25 cm$^3$ in prostate-confined disease (≤ypT2, N0)

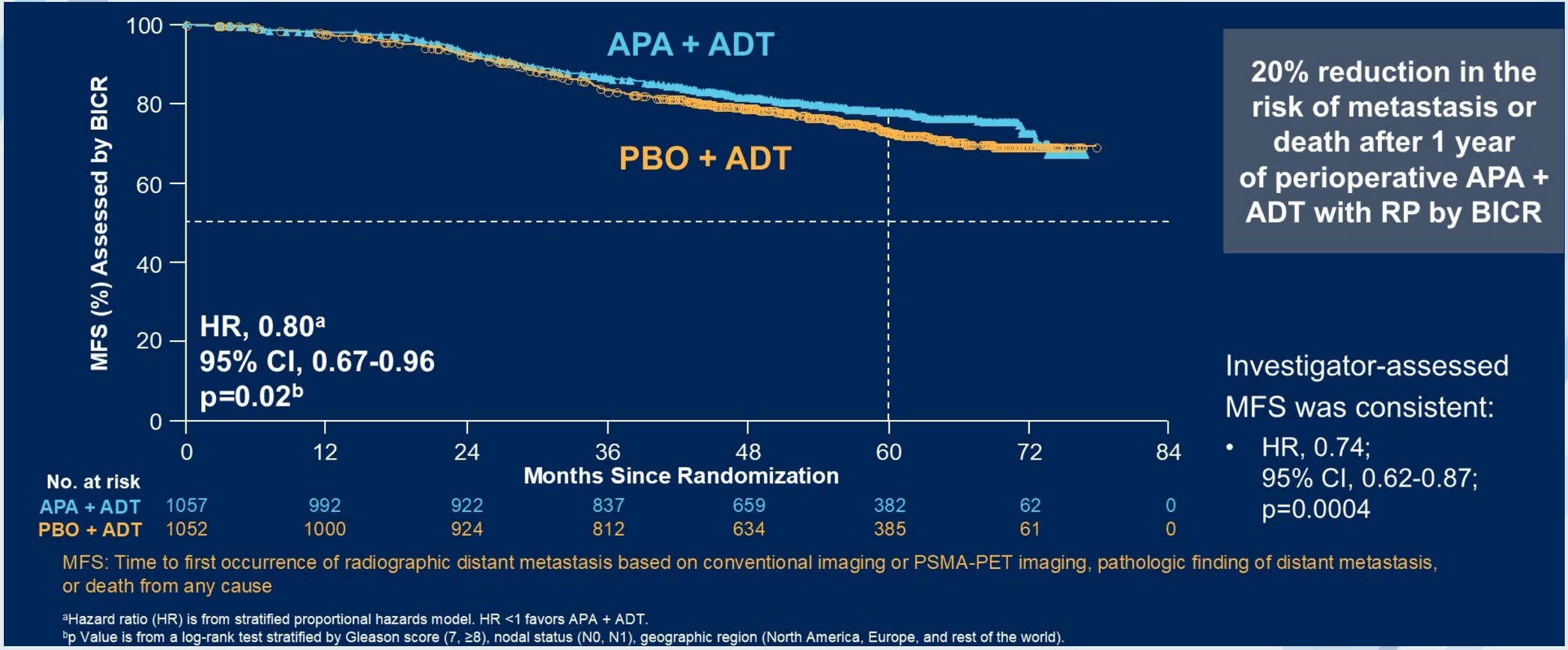
Error bars indicate 95% confidence intervals (CIs). Odds ratio (OR) is from a logistic regression adjusted for stratification factor; OR >1 favors APA + ADT.
[a]p Value is based on Cochran-Mantel-Haenszel test stratified by Gleason score (7, ≥8), nodal status (N0, N1), geographic region (North America, Europe, and rest of the world).

BICR = blinded independent central review; RCB = residual cancer burden


Taplin ME et al. ASCO 2026;Abstract LBA1.
Taplin ME et al. *N Engl J Med* 2026;395(6):546-60.


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# Phase III PROTEUS Dual Primary Endpoint: Metastasis-Free Survival (MFS)




Taplin ME et al. ASCO 2026;Abstract LBA1.
Taplin ME et al. *N Engl J Med* 2026;395(6):546-60.

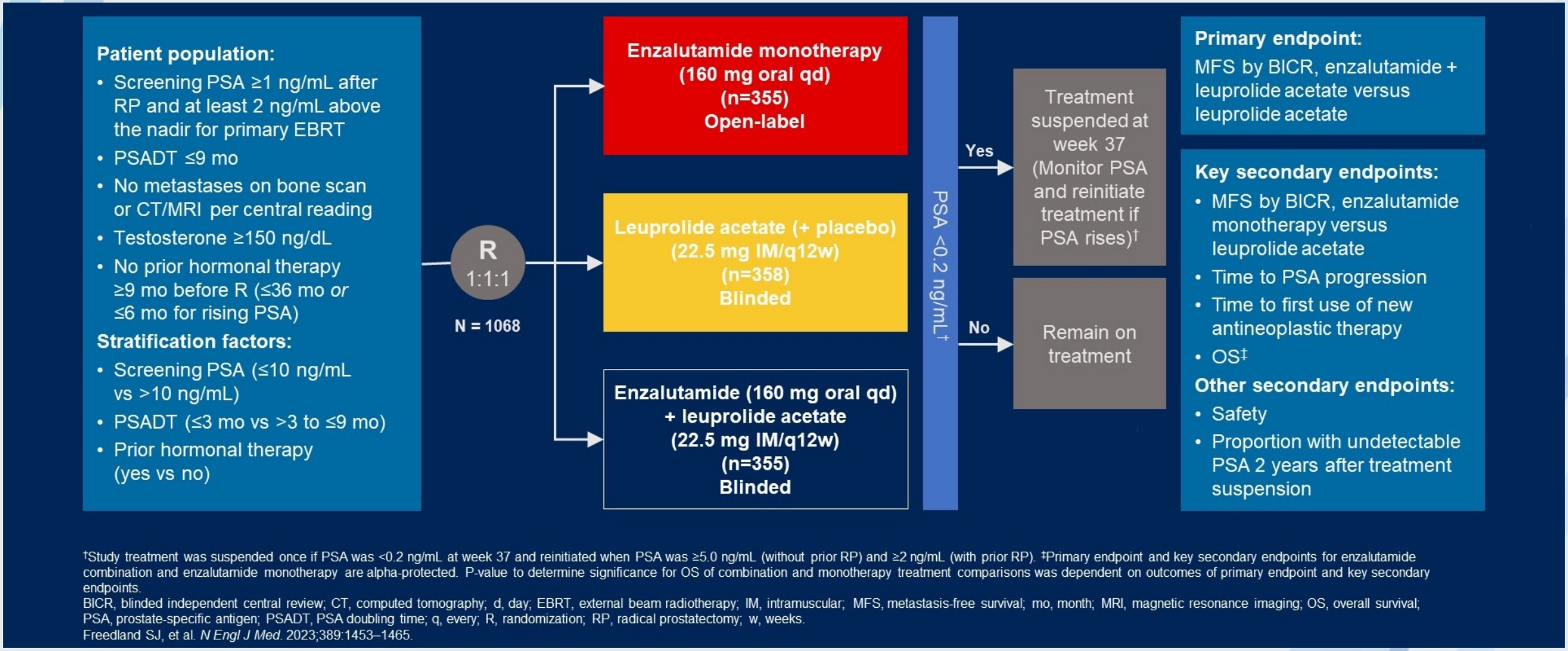
# Treatment for M0 Disease

**Select Datasets**

- Shore ND et al. Outcomes of men with high-risk biochemically recurrent prostate cancer who suspended enzalutamide monotherapy treatment in the phase 3 EMBARK study. Genitourinary Cancers Symposium 2024;Abstract 15.
- Freedland SJ et al. Improved outcomes with enzalutamide in biochemically recurrent prostate cancer. *N Engl J Med* 2023;389(16):1453-65.
- Shore ND et al. Improved survival with enzalutamide in biochemically recurrent prostate cancer. *N Engl J Med* 2026;394(6):563-75.

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# Phase III EMBARK Study Design




†Study treatment was suspended once if PSA was <0.2 ng/mL at week 37 and reinitiated when PSA was ≥5.0 ng/mL (without prior RP) and ≥2 ng/mL (with prior RP). ‡Primary endpoint and key secondary endpoints for enzalutamide combination and enzalutamide monotherapy are alpha-protected. P-value to determine significance for OS of combination and monotherapy treatment comparisons was dependent on outcomes of primary endpoint and key secondary endpoints.

BICR, blinded independent central review; CT, computed tomography; d, day; EBRT, external beam radiotherapy; IM, intramuscular; MFS, metastasis-free survival; mo, month; MRI, magnetic resonance imaging; OS, overall survival; PSA, prostate-specific antigen; PSADT, PSA doubling time; q, every; R, randomization; RP, radical prostatectomy; w, weeks.

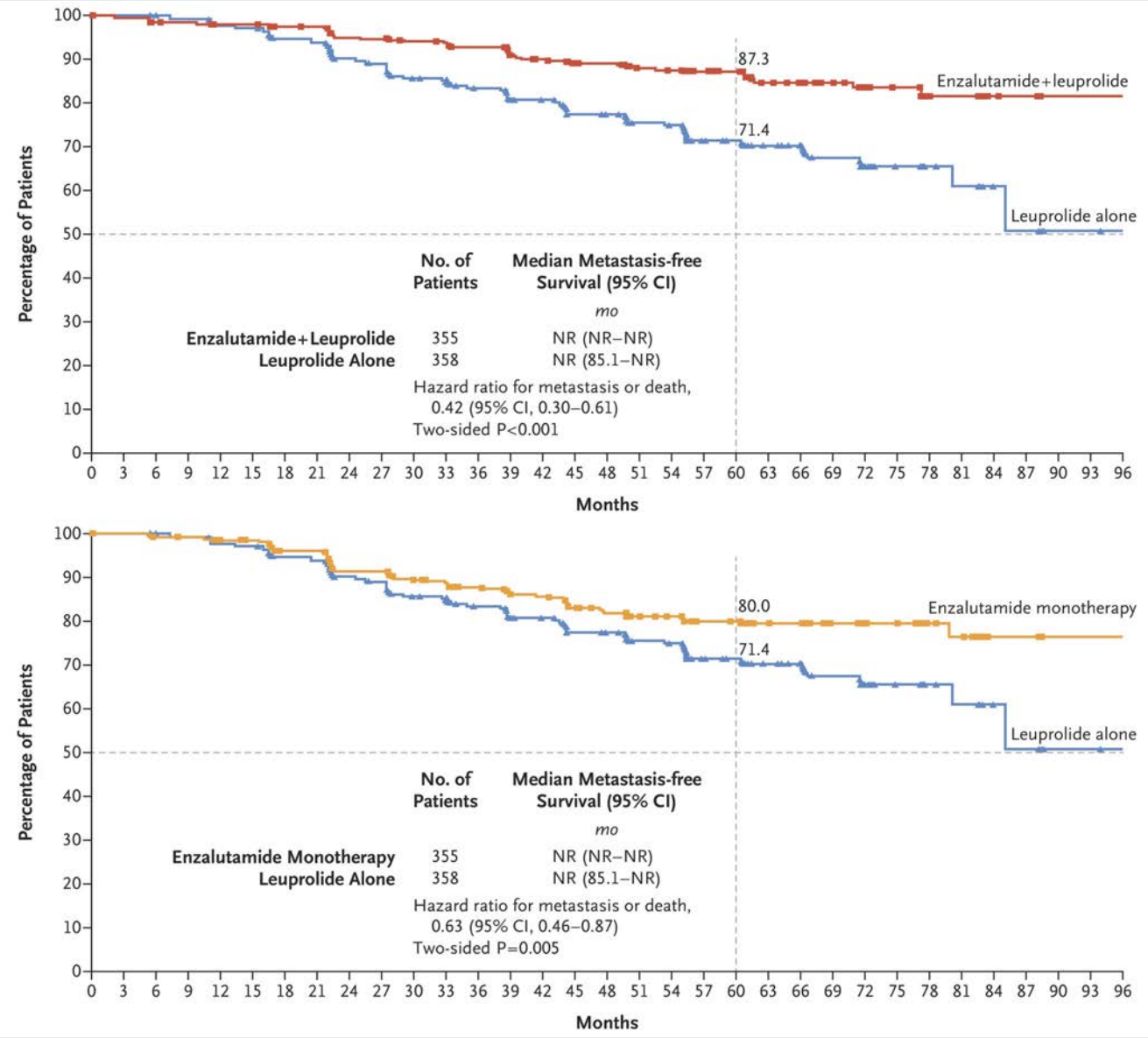
Freedland SJ, et al. *N Engl J Med*. 2023;389:1453–1465.

Shore ND et al. Genitourinary Cancers Symposium 2024;Abstract 15.

# Phase III EMBARK: Metastasis-Free Survival

**Enza + leuprolide**

**Enza monotherapy**

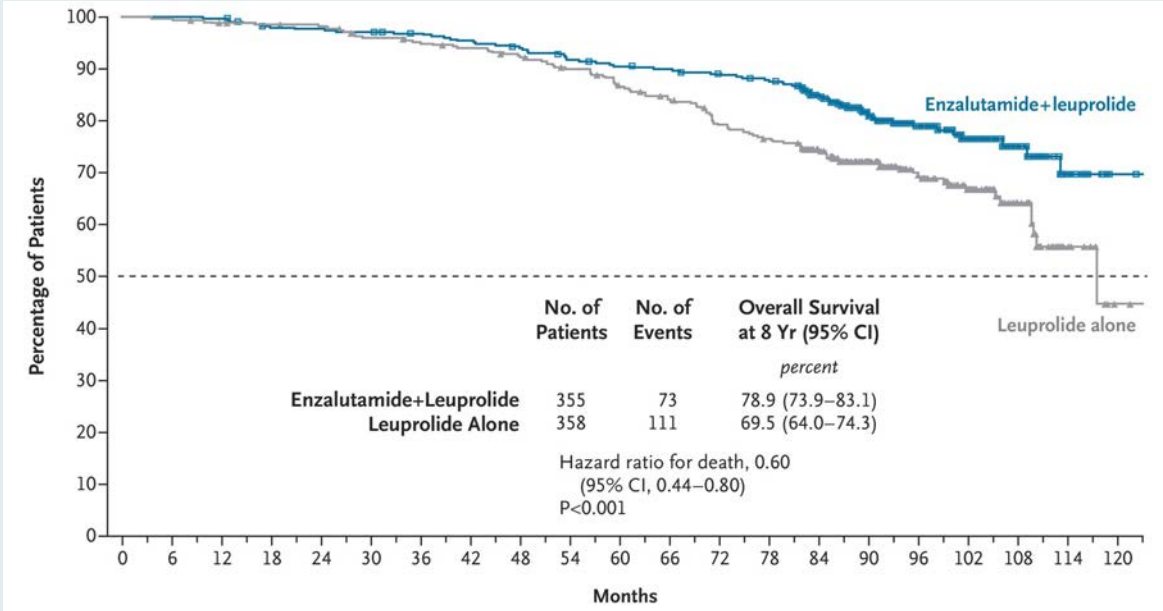



NR = not reached

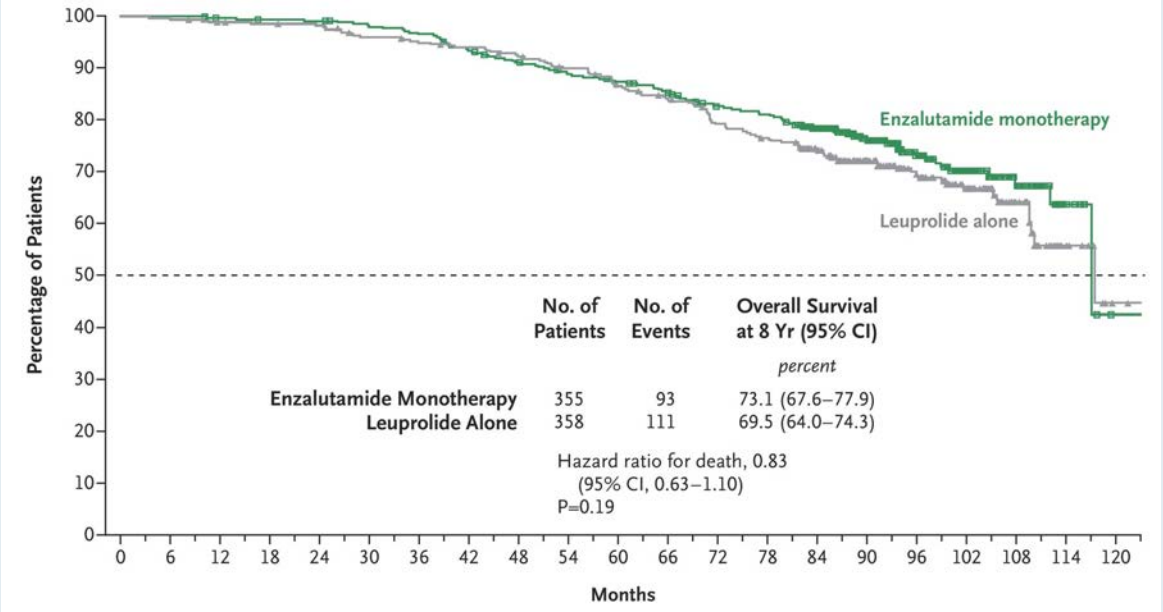
Freedland SJ et al. *N Engl J Med* 2023;389(16):1453-65.

# Phase III EMBARK: 8-Year Overall Survival

**Enza + leuprolide**




**Enza monotherapy**




Shore ND et al. *N Engl J Med* 2026;394(6):563-75.

# First-Line Endocrine Treatment

**Select Datasets**

- Davis ID. Combination therapy in metastatic hormone-sensitive prostate cancer: Is three a crowd? *Ther Adv Med Oncol* 2022 March 29;14:1758359221086827.
- Saad F et al. Efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) in patients with metastatic hormone-sensitive prostate cancer (mHSPC) from the phase III ARANOTE trial. ESMO 2024;Abstract LBA68.
- Saad F et al. Darolutamide in combination with androgen-deprivation therapy in patients with metastatic hormone-sensitive prostate cancer from the phase III ARANOTE trial. *J Clin Oncol* 2024;42(36):4271-81.
- Saad F et al. Darolutamide plus androgen-deprivation therapy in metastatic hormone-sensitive prostate cancer by disease volume and risk subgroups in the phase 3 ARANOTE trial. *Eur Urol* 2026:S0302-2838(26)02313-4.

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# First-Line Endocrine Treatment

**Select Datasets (Continued)**

- Smith MR et al. Darolutamide and survival in metastatic, hormone-sensitive prostate cancer. *N Engl J Med* 2022;386(12):1132-42.
- Smith MR et al. Overall survival with darolutamide versus placebo in combination with androgen-deprivation therapy and docetaxel for metastatic hormone-sensitive prostate cancer in the phase 3 ARASENS trial. Genitourinary Cancers Symposium 2022;Abstract 13.
- Hussain M et al. Darolutamide plus androgen-deprivation therapy and docetaxel in metastatic hormone-sensitive prostate cancer by disease volume and risk subgroups in the phase III ARASENS trial. *J Clin Oncol* 2023;41(20):3595-607.
- Hussain MHA et al. Efficacy and safety of darolutamide (DARO) in combination with androgen-deprivation therapy (ADT) and docetaxel (DOC) by disease volume and disease risk in the phase 3 ARASENS study. Genitourinary Cancers Symposium 2023;Abstract 15.

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# Extended Follow-Up with ADT Combination Therapies

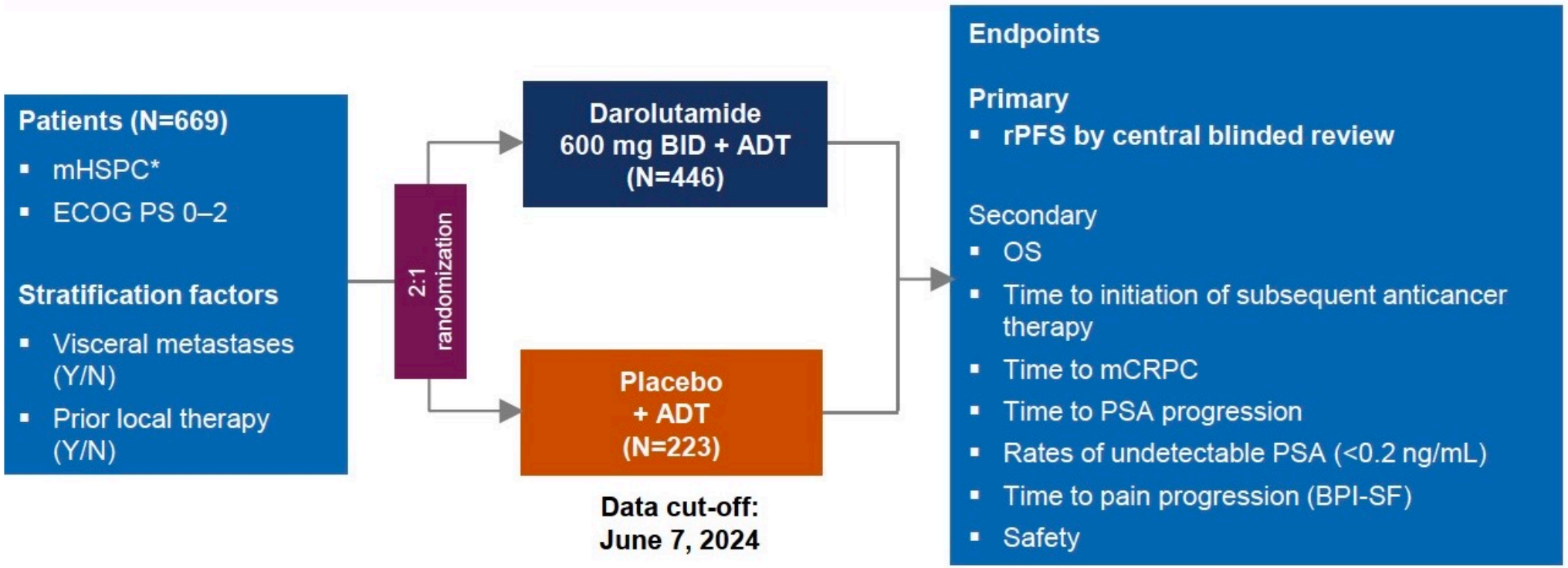
| | Abiraterone | | Darolutamide | Apalutamide | Enzalutamide | | |
|---|---|---|---|---|---|---|---|
| | **LATITUDE (*N*=1199)** | **STAMPEDE (*N*=1917)** | **PEACE-1 (*N*=1173)** | **ARASENS (*N*=1306)** | **TITAN (*N*=1052)** | **ARCHES (*N*=1150)** | **ENZAMET (*N*=1125)** | **STAMPEDE M0 (*N*=1974)** |
| Agent/comparator | ADT + abiraterone + pred/placebo | ADT + abiraterone + pred/placebo | 2×2: SoC/ abiraterone/RT/both, ±docetaxel (RT arms collapsed for analysis) | ADT + docetaxel + darolutamide/placebo | ADT + apalutamide/ placebo | ADT + enzalutamide/ placebo | ADT + enzalutamide/NSAA | SoC\|SoC + abiraterone + pred, ± enzalutamide |
| Primary endpoint: HR (CI) | OS: 0.66 (0.56–0.78) rPFS: 0.47 (0.39–0.55) | OS: 0.63 (0.52–0.76) | rPFS: 0.54 (0.46–0.64) OS: 0.82 (0.69–0.98) | OS: 0.68 (0.57–0.80) | OS: 0.65 (0.53–0.79) rPFS: 0.48 (0.39–0.60) | rPFS: 0.39 (0.30–0.50) (OS (2°): 0.66 (0.53–0.81)) | OS: 0.67 (0.52–0.86) | MFS: 0.53 (0.44–0.64) OS: 0.60 (0.48–0.73) |
| Survival ARI + ADT *vs* ADT | Med OS: 53.3 *vs* 36.5 months Med rPFS: 33.0 *vs* 14.8 months | 3-year OS 83% *vs* 76% | Med rPFS 4.5 *vs* 2.2 year Med OS: 5.7 *vs* 4.7years | Med OS: NE *vs* 48.9 months | Med OS: NR *vs* 52.2 months Med rPFS: NR *vs* 22.1 months | Med rPFS: NR *vs* 19.0 months 3-year OS: 78% *vs* 69% 5-year OS: 71% *vs* 57% | 3-year OS 80% *vs* 72% | 6-year MFS: 82% *vs* 69% 6-year OS: 86% *vs* 77% |
| Relevant "triplet" outcomes | Not applicable | Not applicable | Med rPFS 4.5 *vs* 2.0 years Med OS: NE *vs* 4.4 years | Improved OS Improved secondary endpoints Similar toxicity | Rapid sequencing | Rapid sequencing | No OS benefit at interim analysis. Improved clinical PFS (2°) | Similar efficacy, more toxic |

rPFS = radiographic progression-free survival; ARI = androgen receptor inhibitor

Davis ID. *Ther Adv Med Oncol* 2022 March 29;14:17588359221086827.

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# Phase III ARANOTE Study Design




ClinicalTrials.gov: NCT04736199

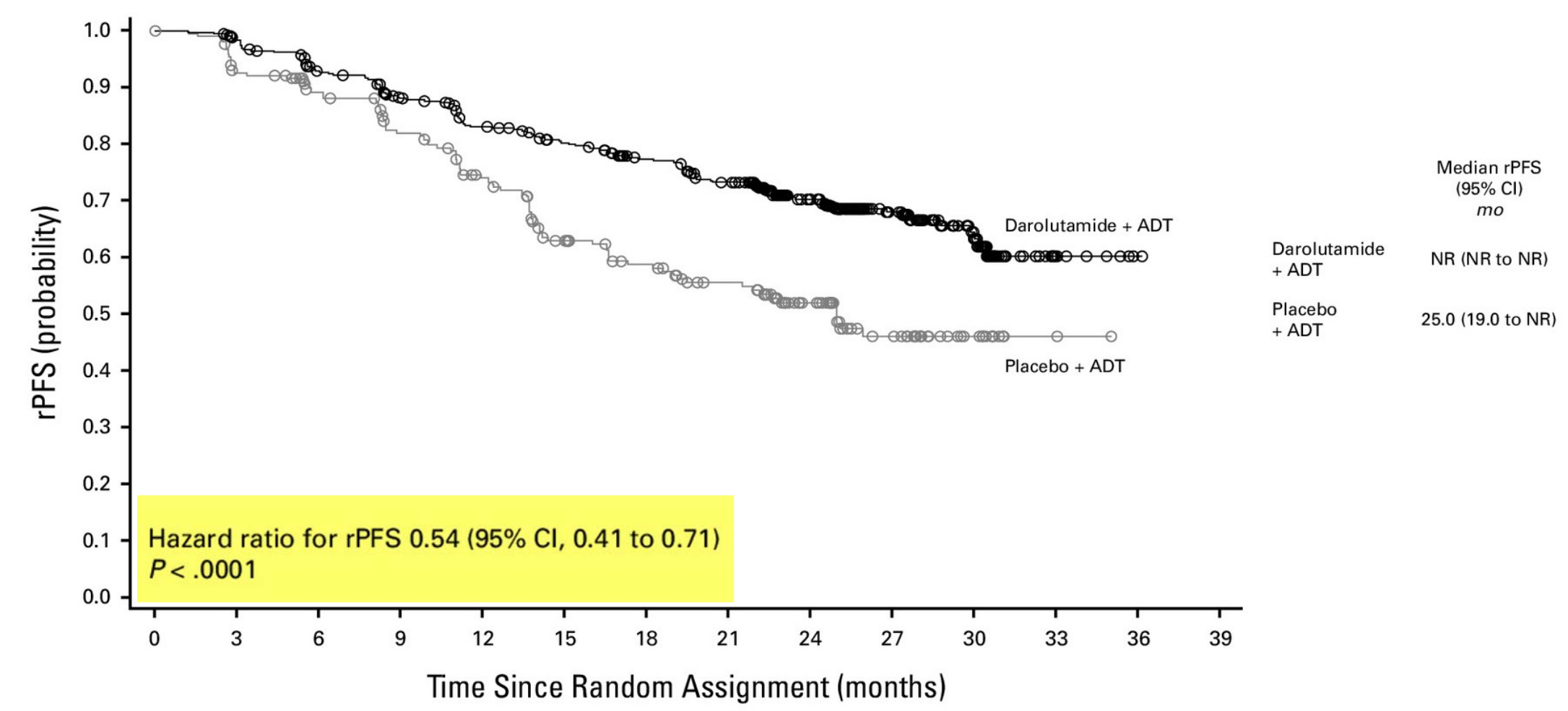
*Metastatic disease confirmed by conventional imaging method as a positive $^{99m}$Tc-phosphonate bone scan or soft tissue/visceral metastases on contrast-enhanced abdominal/pelvic/chest CT or MRI scan, assessed by central review.
BPI-SF, Brief Pain Inventory-Short Form.

BARCELONA 2024 ESMO congress

Saad F et al. ESMO 2024;Abstract LBA68.
Saad F et al. *J Clin Oncol* 2024;42(36):4271-81.

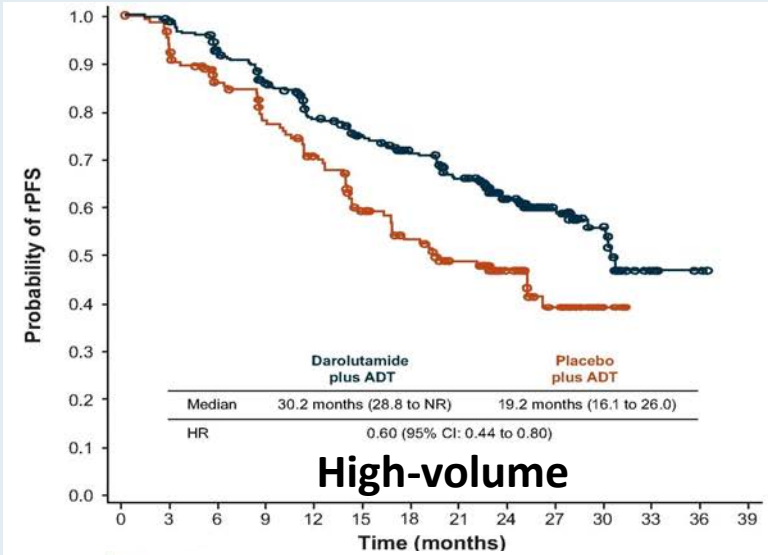
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# Phase III ARANOTE Primary Endpoint: Radiographic Progression-Free Survival (rPFS)

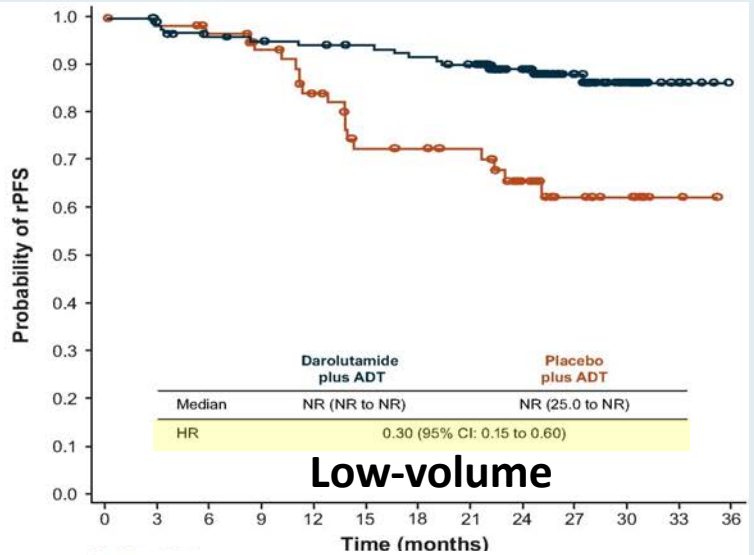



Saad F et al. *J Clin Oncol* 2024;42(36):4271-81.

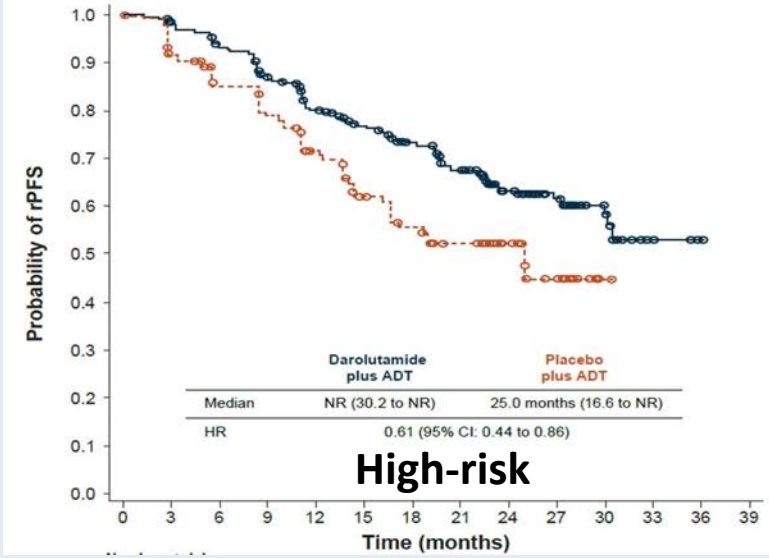
# Phase III ARANOTE: rPFS by Disease Volume and Risk



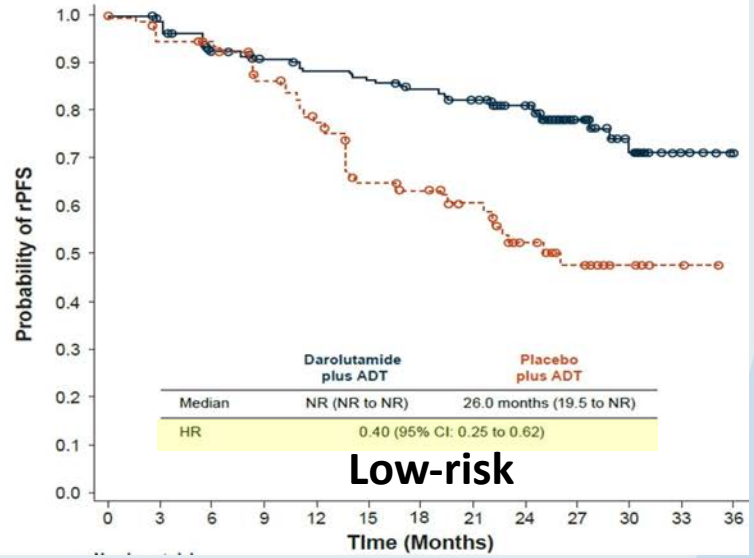

**High-volume**




**Low-volume**



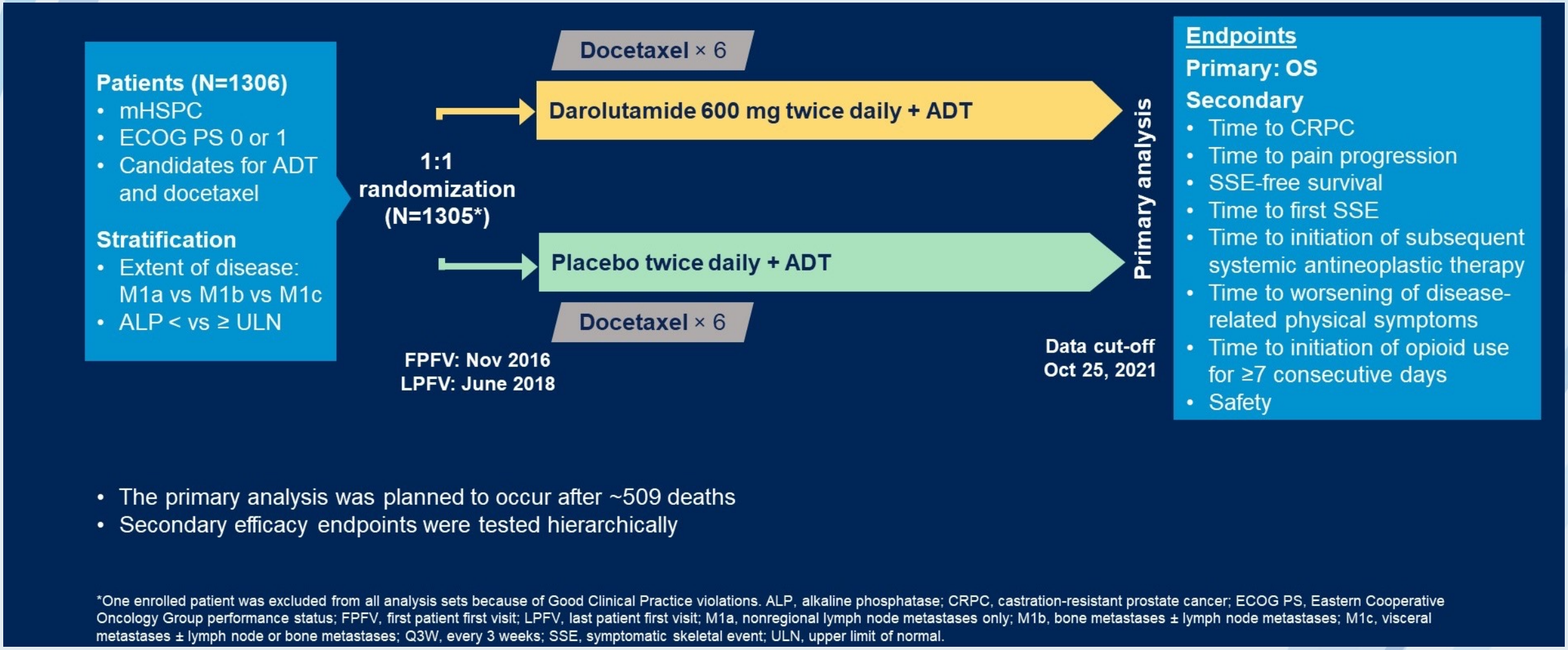

**High-risk**




**Low-risk**

Saad F et al. *Eur Urol* 2026:S0302-2838(26)02313-4.

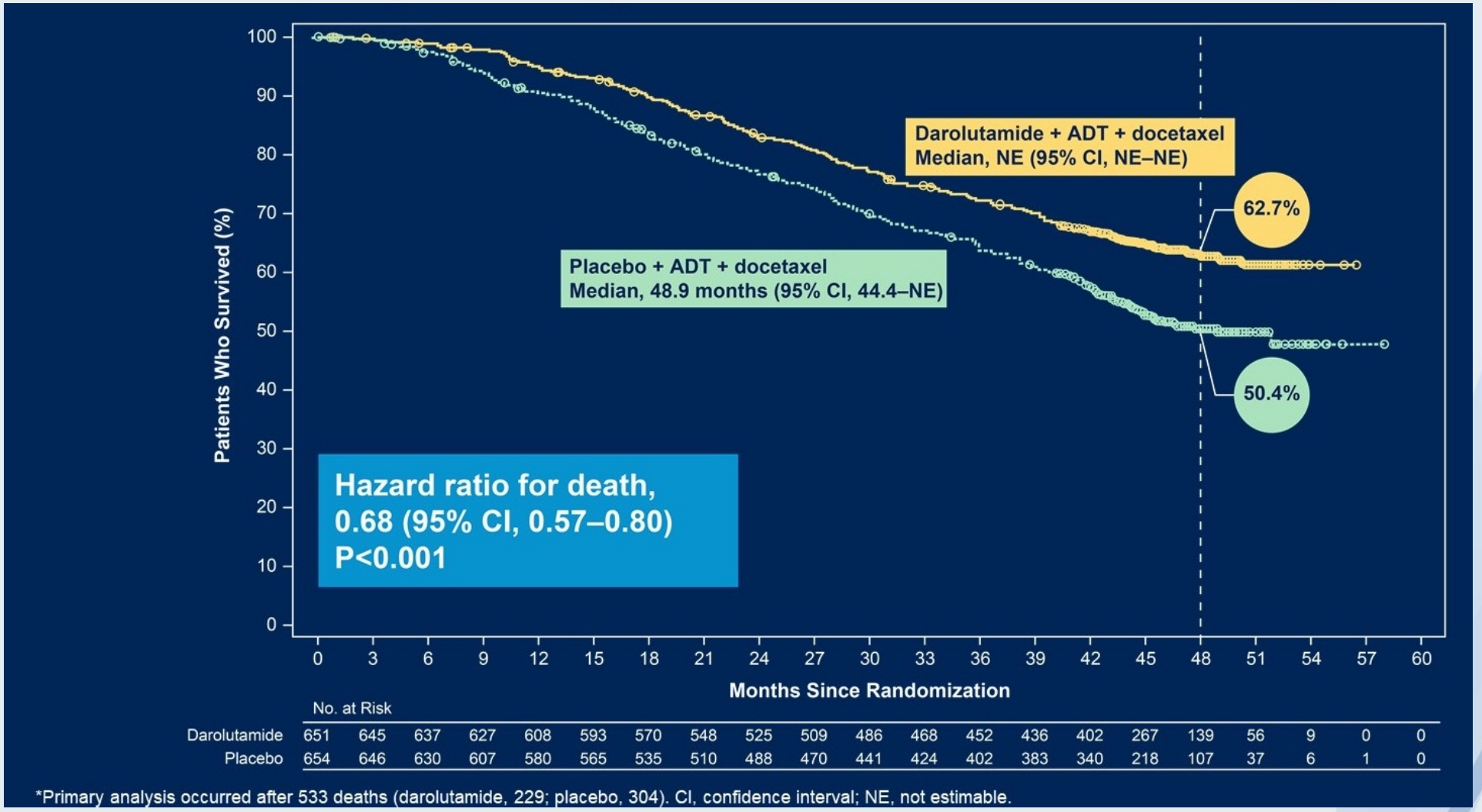
# Phase III ARASENS Study Design




Smith MR et al. *N Engl J Med* 2022;386(12):1132-42.
Smith MR et al. Genitourinary Cancers Symposium 2022;Abstract 13.

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# Phase III ARASENS Primary Endpoint: Overall Survival

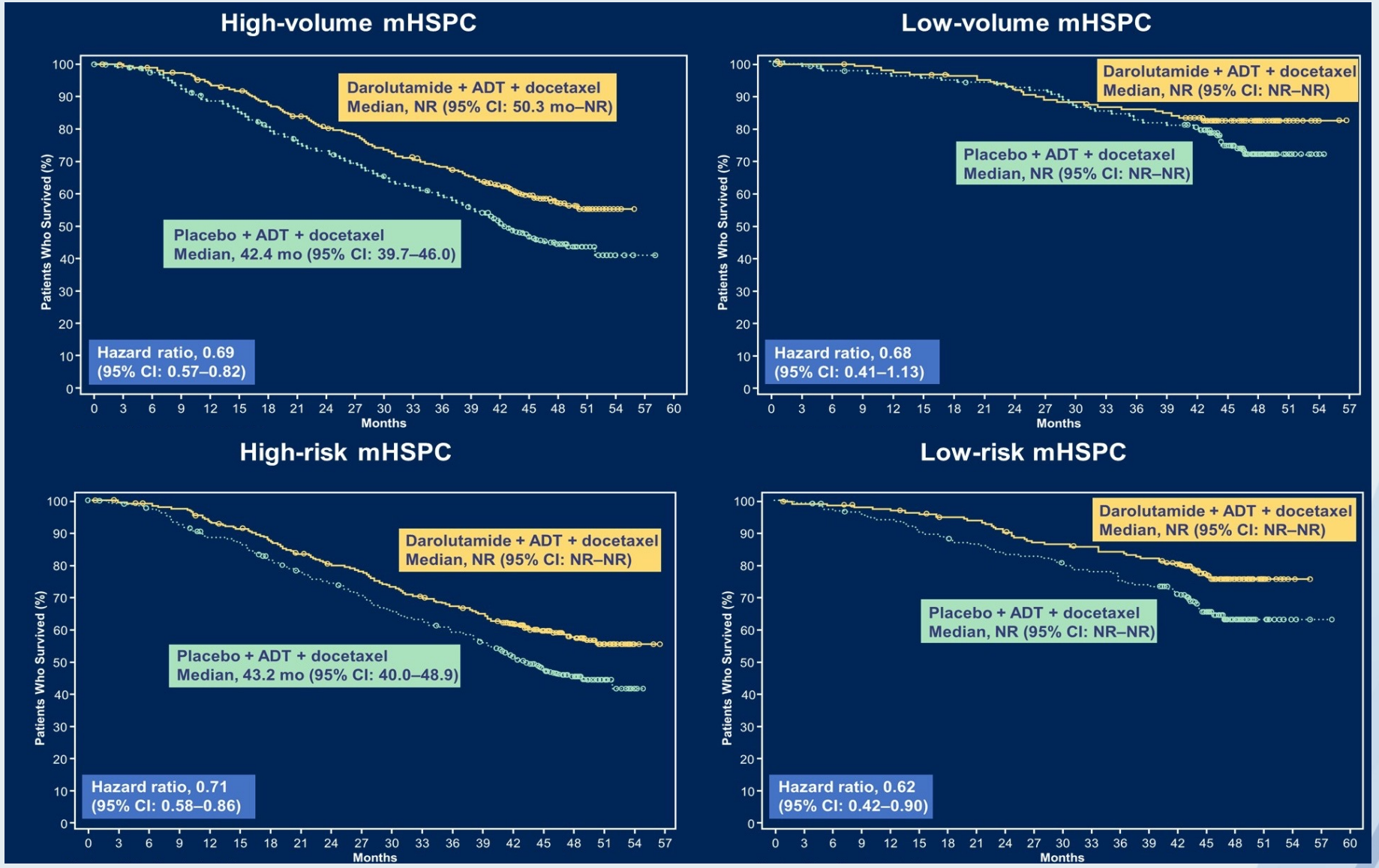



*Primary analysis occurred after 533 deaths (darolutamide, 229; placebo, 304). CI, confidence interval; NE, not estimable.


Smith MR et al. *N Engl J Med* 2022;386(12):1132-42.
Smith MR et al. Genitourinary Cancers Symposium 2022;Abstract 13.


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# Phase III ARASENS: OS by Disease Volume and Risk





Hussain MHA et al. *J Clin Oncol* 2023;41(20):3595-3607.

Hussain MHA et al. Genitourinary Cancers Symposium 2023;Abstract 15.



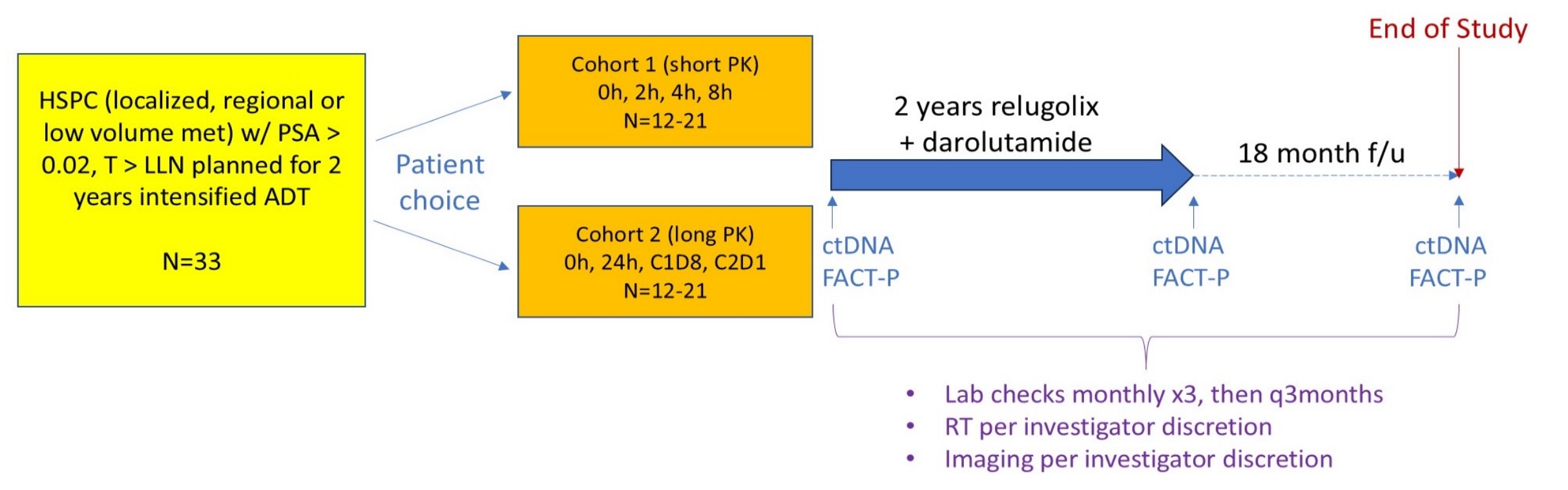
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# First-Line Endocrine Treatment

**Select Datasets**

- Choudhury AD et al. Comeback from long-course ADT with relugolix (rel) and darolutamide (daro) in hormone-sensitive prostate cancer (PC) (CLEARED). ASCO 2026;Abstract 5083.

# Phase II CLEARED Study Design




T = testosterone; LLN = lower limit of normal; PK = pharmacokinetics; ctDNA = circulating tumor DNA

Choudhury AD et al. ASCO 2026;Abstract 5083.

# Phase II CLEARED: Testosterone Decline, PSA Response, Safety

| | Total (N=33) | |
|---|---|---|
| **Testosterone decline** | **N** | **%** |
| Castrate (≤ 50 ng/dL) | 33 | 100.0 |
| "Profound castrate" (≤ 20 ng/dL) | 32[a] | 97.0 |
| **PSA response** | **N** | **%** |
| ≥ 50% decline from baseline | 33 | 100.0 |
| ≥ 90% decline from baseline | 32 | 97.0 |

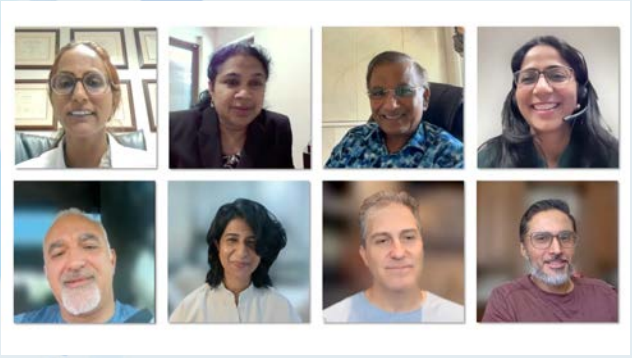
| | Adverse event grade CTCAE v5.0 | | | Total | |
|---|---|---|---|---|---|
| **Grade** | **1** | **2** | **3** | **N** | **%** |
| Hot flashes | 26 | 2 | . | 28 | 84.8% |
| Fatigue | 21 | 1 | . | 22 | 66.7% |
| Anemia | 15 | . | . | 15 | 45.5% |
| Alanine aminotransferase increased | 11 | . | . | 11 | 33.3% |
| Libido decreased | 8 | . | . | 8 | 24.2% |
| Aspartate aminotransferase increased | 7 | . | . | 7 | 21.2% |
| Lymphocyte count decreased | . | 2 | 3 | 5 | 15.2% |
| White blood cell decreased | 2 | 2 | . | 4 | 12.1% |
| Constipation | 3 | 1 | . | 4 | 12.1% |
| Erectile dysfunction | 4 | . | . | 4 | 12.1% |
| Neutrophil count decreased | 1 | 2 | . | 3 | 9.1% |
| Diarrhea | 3 | . | . | 3 | 9.1% |

The combination of relugolix and darolutamide was safe and well-tolerated during the first 6 cycles. Pharmacokinetic parameters were similar to historical monotherapy comparators. Appropriate initial T and PSA reduction were observed, suggesting preliminary clinical efficacy.

Choudhury AD et al. ASCO 2026;Abstract 5083.

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# Faculty Discussion



# Questions for the Faculty

- In what situations are you recommending radical prostatectomy for patients with high/risk localized/locally advanced prostate cancer?
- For which patients would you use the PROTEUS strategy?
- For a patient who received the PROTEUS strategy and attained a pathologic complete response, would you offer the option of forgoing postoperative treatment?
- Do you use intensification of endocrine therapy for patients with high/risk localized/locally advanced disease who are receiving primary radiation therapy?
- For which patients do you use the EMBARK strategy? In which situations, if any, are you recommending enzalutamide monotherapy? In what situations, if any, are you utilizing an intermittent treatment strategy?

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Dr Choksi

# Questions for the Faculty

**66-year-old man presented with PSA of 56 and bone metastases. Very hesitant to receive therapy but agreed to apalutamide/leuprolide. Experienced decreased libido and extreme fatigue. Elected to stop therapy when PSA became undetectable. Disease recurred 9 months later with progressive pain, lymph node involvement, and PSA now more than 100.**

**Questions**

- When and how do you use intermittent hormone therapy?
- What treatment options would you offer this man with a positive PSMA scan who is very hesitant about chemotherapy?

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Dr Ignatius

# Questions for the Faculty

**92-year-old man, ECOG PS 1, somewhat frail, presented with de novo mets to bone, PSA 54. Very supportive family who wished to minimize treatment side effects. Receiving relugolix but hesitant to add darolutamide.**

**Questions**

- Endocrine approach for very elderly, frail patients?
- Choice of ARPI (androgen receptor pathway inhibitor)

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# Agenda

Introduction: ESMO 2026; Recent FDA Approvals

Selection of Endocrine Therapy – Dr Antonarakis

**Utility of PARP Inhibitors – Dr Agarwal**

AKT Inhibition for PTEN-Deficient Disease – Dr Antonarakis

Radiopharmaceuticals – Dr Agarwal

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# Utility of PARP Inhibitors

**Select Datasets**

- Attard G et al. Niraparib and abiraterone acetate plus prednisone for HRR-deficient metastatic castration-sensitive prostate cancer: A randomized phase 3 trial. *Nat Med* 2025;31(12):4109-18.
- Attard G et al. Phase 3 AMPLITUDE trial: Niraparib (NIRA) and abiraterone acetate plus prednisone (AAP) for metastatic castration-sensitive prostate cancer (mCSPC) patients (pts) with alterations in homologous recombination repair (HRR) genes. ASCO 2025;Abstract LBA5006.
- Agarwal N et al. PARP and androgen-signaling inhibition plus ADT in metastatic prostate cancer. *N Engl J Med* 2026;395(5):427-39.

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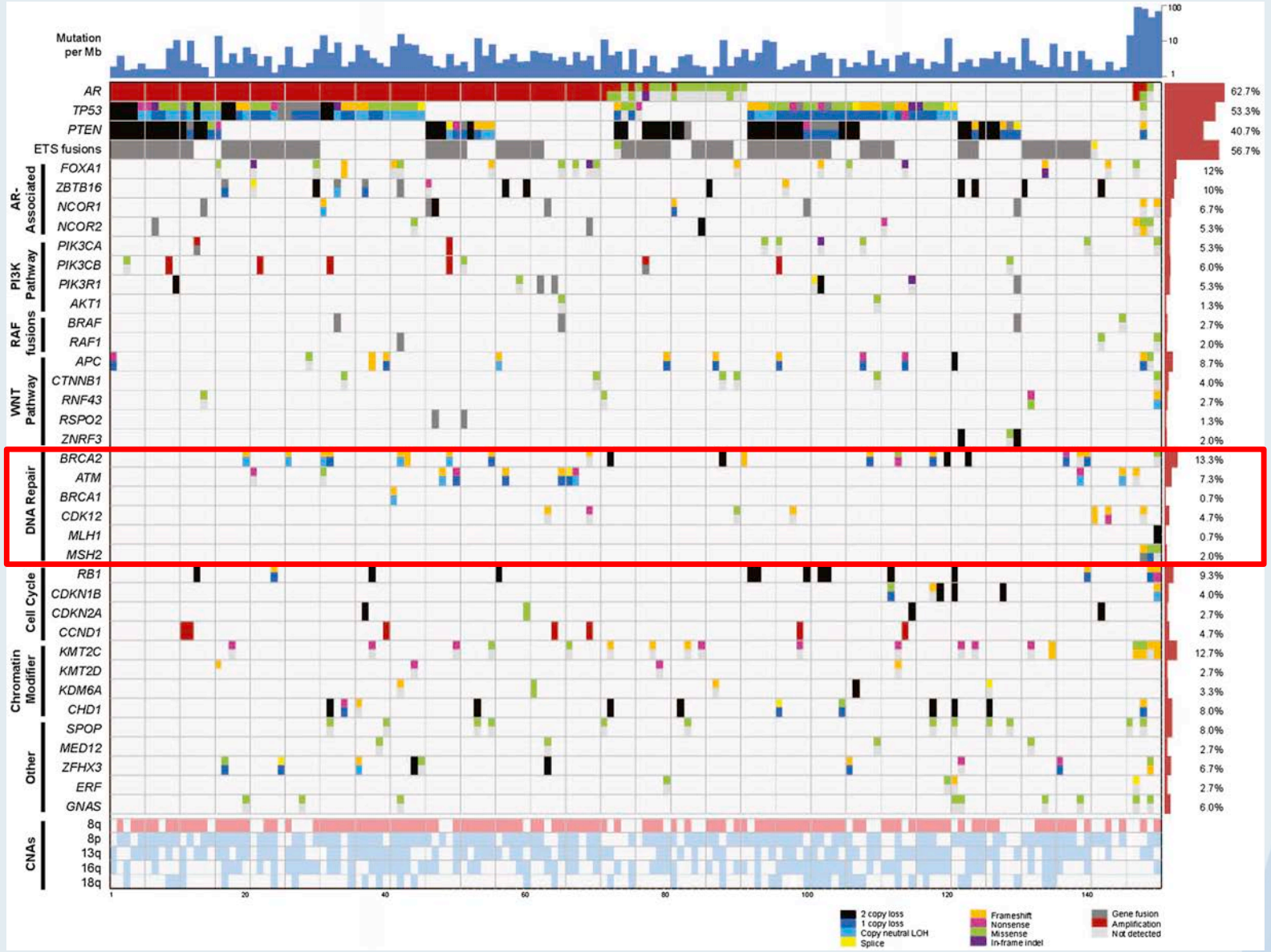
# PARP Inhibition

**Select Datasets (Continued)**

- Agarwal N et al. TALAPRO-3: Talazoparib (TALA) + enzalutamide (ENZA) compared with placebo (PBO) + ENZA for the treatment of patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) harboring homologous recombination repair (HRR) gene alterations. ASCO 2026;Abstract LBA5007.
- Azad A et al. Saruparib + androgen receptor pathway inhibitor (ARPI) + androgen deprivation therapy (ADT) in patients (pts) with metastatic hormone-sensitive prostate cancer (mHSPC): The phase 1/2 PETRANHA trial. Genitourinary Cancers Symposium 2026;Abstract 177.

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# Alterations to DNA Repair Pathways in Prostate Cancer



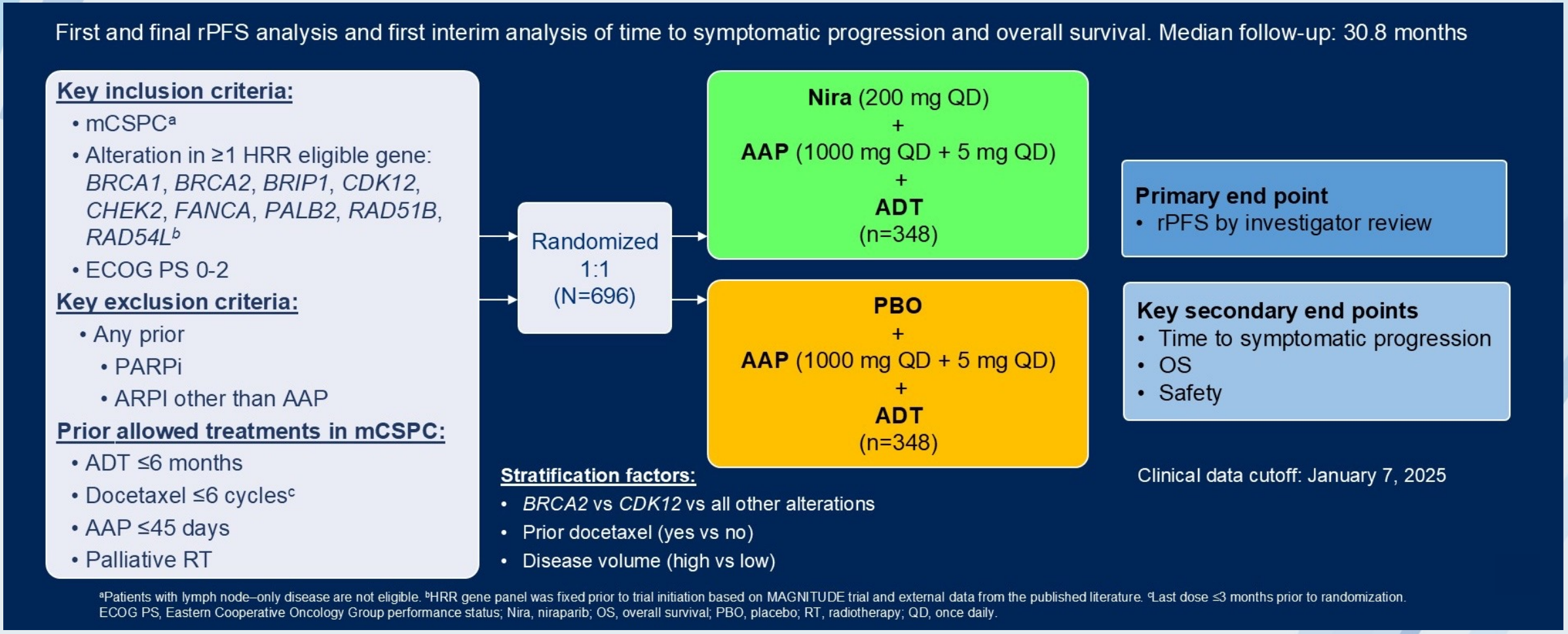

DNA repair gene alterations occur in ~20% of pts with mCRPC

**BRCA2 mutations occur in ~13% of pts**

Robinson D et al. *Cell* 2015;161(5):1215-28.

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# Phase III AMPLITUDE Study Design

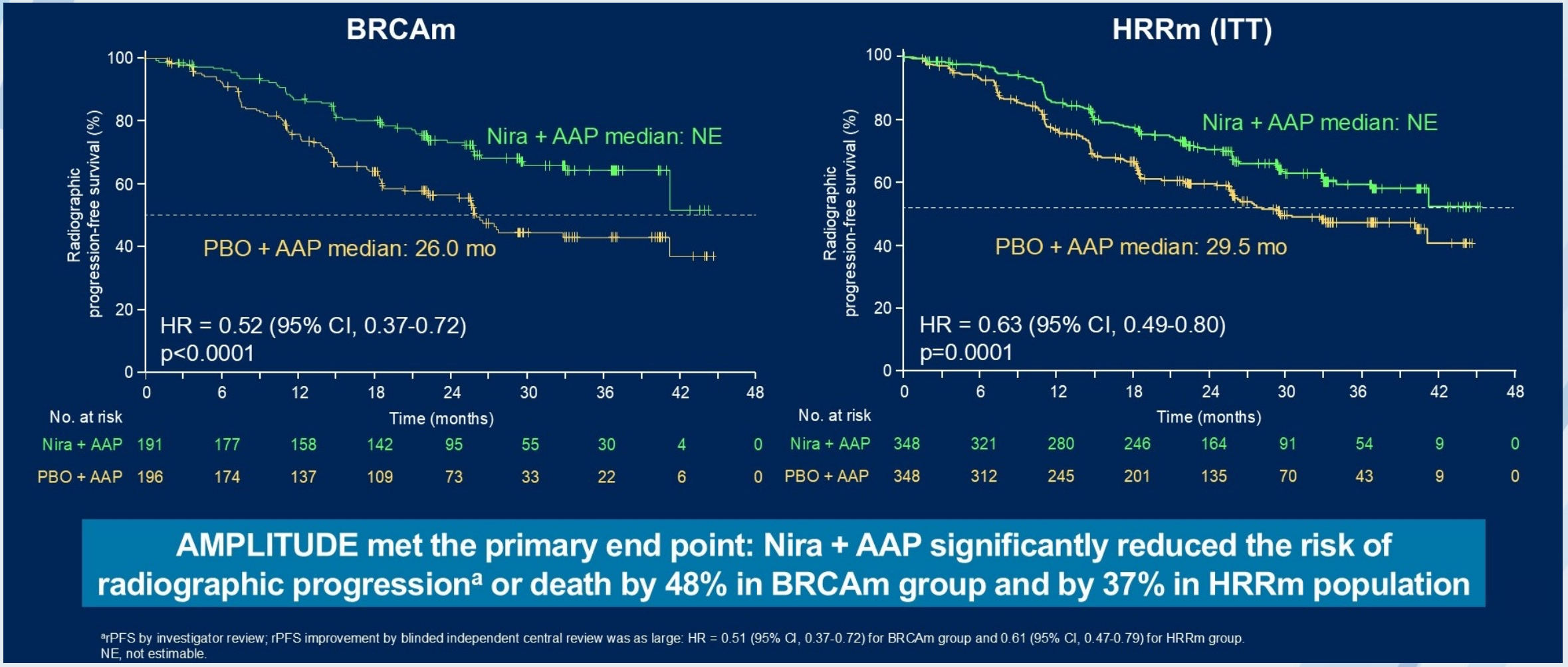



HRR = homologous recombination repair

Attard G et al. *Nat Med* 2025;31(12):4109-4118.
Attard G et al. ASCO 2025;Abstract LBA5006.

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# Phase III AMPLITUDE Primary Endpoint: rPFS



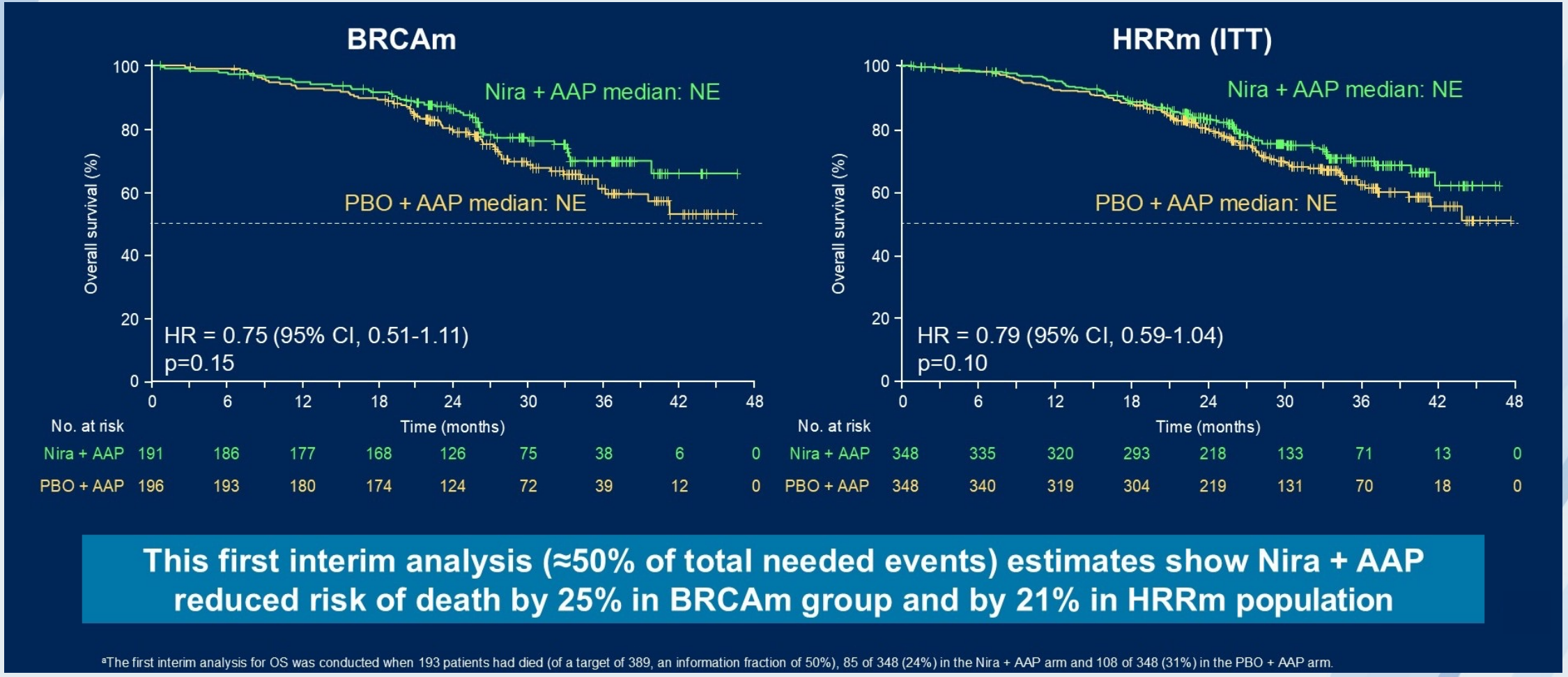

**AMPLITUDE met the primary end point: Nira + AAP significantly reduced the risk of radiographic progression[a] or death by 48% in BRCAm group and by 37% in HRRm population**

[a]rPFS by investigator review; rPFS improvement by blinded independent central review was as large: HR = 0.51 (95% CI, 0.37-0.72) for BRCAm group and 0.61 (95% CI, 0.47-0.79) for HRRm group.
NE, not estimable.


Attard G et al. *Nat Med* 2025;31(12):4109-4118.
Attard G et al. ASCO 2025;Abstract LBA5006.


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# Phase III AMPLITUDE Secondary Endpoint: OS – First Interim Analysis




**This first interim analysis (≈50% of total needed events) estimates show Nira + AAP reduced risk of death by 25% in BRCAm group and by 21% in HRRm population**

[a]The first interim analysis for OS was conducted when 193 patients had died (of a target of 389, an information fraction of 50%), 85 of 348 (24%) in the Nira + AAP arm and 108 of 348 (31%) in the PBO + AAP arm.


Attard G et al. *Nat Med* 2025;31(12):4109-4118.
Attard G et al. ASCO 2025;Abstract LBA5006.


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# Phase III AMPLITUDE: Safety

| Selected categories of TEAEs of interest, n (%) | | Nira + AAP (n=347) | | PBO + AAP (n=348) | |
|---|---|---|---|---|---|
| | | All grades | Grade ≥3 | All grades | Grade ≥3 |
| Patients with ≥1 AE of interest | | 306 (88) | 217 (63) | 261 (75) | 132 (38) |
| Hematologic | **Anemia** | **179 (52)** | **101 (29)** | **83 (24)** | **16 (5)** |
| | Neutropenia | 76 (22) | 33 (10) | 28 (8) | 7 (2) |
| | Thrombocytopenia | 66 (19) | 24 (7) | 20 (6) | 1 (<1) |
| | MDS | 1 (<1) | 1 (<1) | 0 | 0 |
| Cardiovascular | **Hypertension** | **155 (45)** | **93 (27)** | **113 (33)** | **64 (18)** |
| | Arrhythmia | 68 (20) | 19 (5) | 28 (8) | 11 (3) |
| | Cardiac failure | 20 (6) | 9 (3) | 6 (2) | 4 (1) |
| Other | Hypokalemia | 92 (27) | 40 (12) | 70 (20) | 38 (11) |
| | Hepatotoxicity | 46 (13) | 8 (2) | 71 (20) | 19 (5) |

- Other common AEs of any grade: constipation (35% vs 16%), nausea (31% vs 14%), fatigue (26% vs 18%), and arthralgia (21% vs 21%) in the Nira +AAP vs placebo + AAP arms, respectively

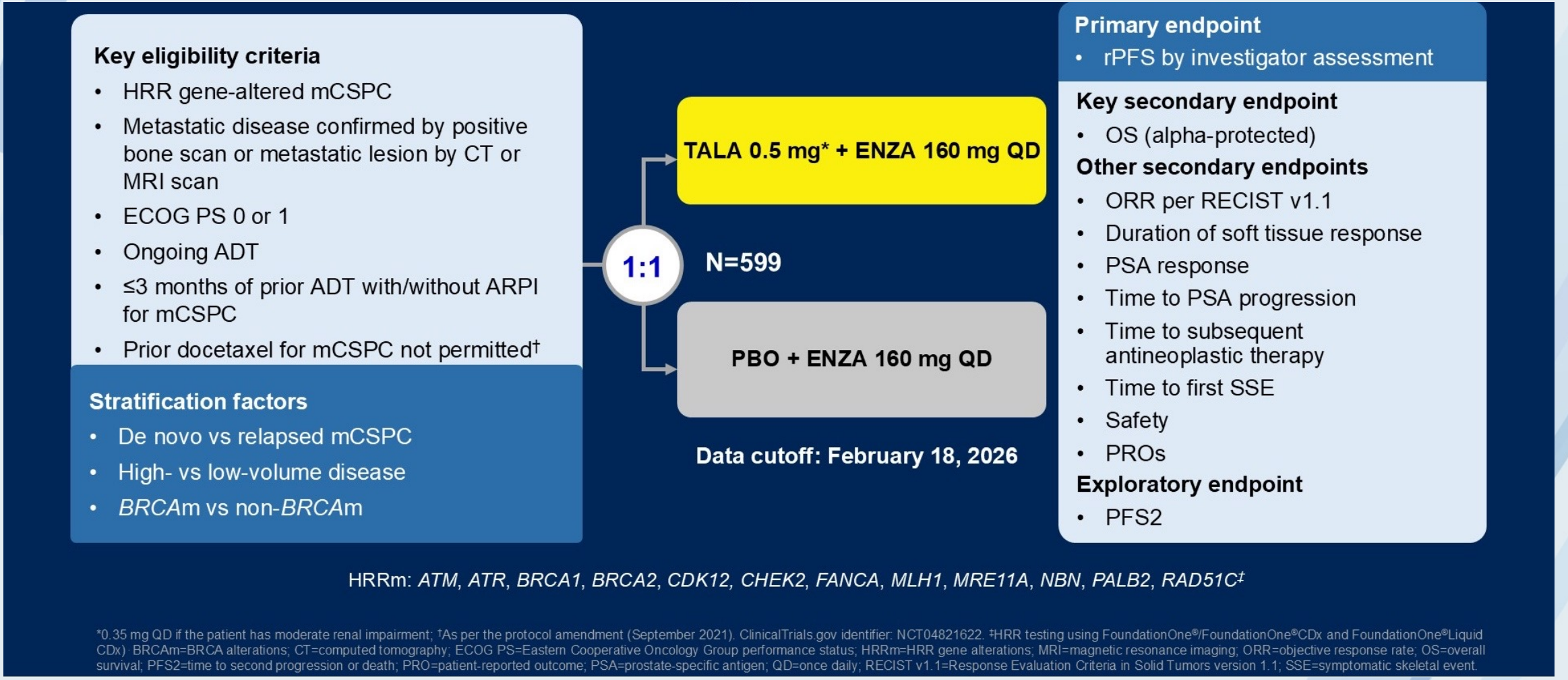
Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. The event experienced by the patient with the worst toxicity is used. If a patient has missing toxicity for a specific AE, the patient is only counted in the total column for that AE.

TEAEs = treatment-emergent adverse events; MDS = myelodysplastic syndromes

Attard G et al. *Nat Med* 2025;31(12):4109-4118.
Attard G et al. ASCO 2025;Abstract LBA5006.

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# Phase III TALAPRO-3 Study Design

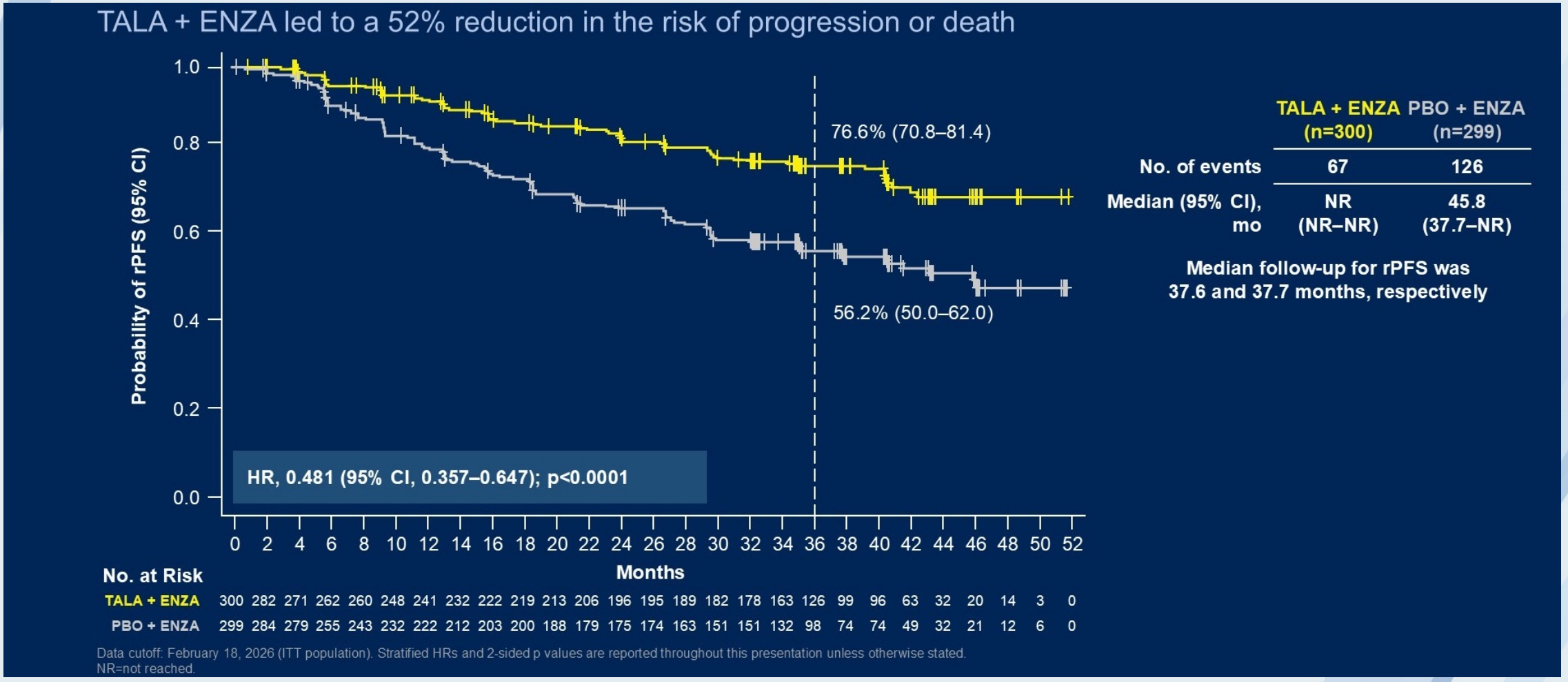



*0.35 mg QD if the patient has moderate renal impairment; †As per the protocol amendment (September 2021). ClinicalTrials.gov identifier: NCT04821622. ‡HRR testing using FoundationOne®/FoundationOne®CDx and FoundationOne®Liquid CDx) · BRCAm=BRCA alterations; CT=computed tomography; ECOG PS=Eastern Cooperative Oncology Group performance status; HRRm=HRR gene alterations; MRI=magnetic resonance imaging; ORR=objective response rate; OS=overall survival; PFS2=time to second progression or death; PRO=patient-reported outcome; PSA=prostate-specific antigen; QD=once daily; RECIST v1.1=Response Evaluation Criteria in Solid Tumors version 1.1; SSE=symptomatic skeletal event.


Agarwal N et al. *N Engl J Med* 2026;395(5):427-439.
Agarwal N et al. ASCO 2026;Abstract LBA5007.


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# Phase III TALAPRO-3 Primary Endpoint: rPFS



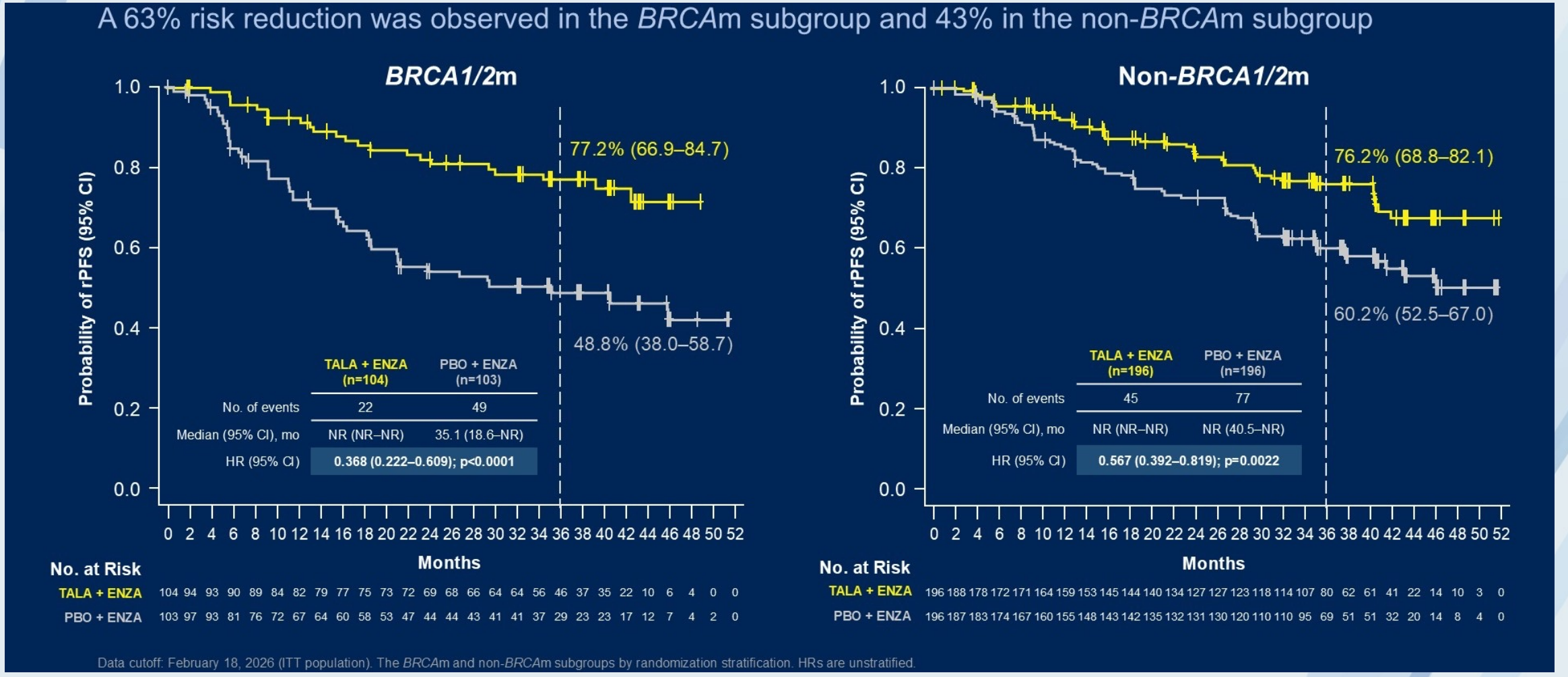


Agarwal N et al. *N Engl J Med* 2026;395(5):427-439.
Agarwal N et al. ASCO 2026;Abstract LBA5007.



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# Phase III TALAPRO-3: rPFS by BRCA Mutation Status

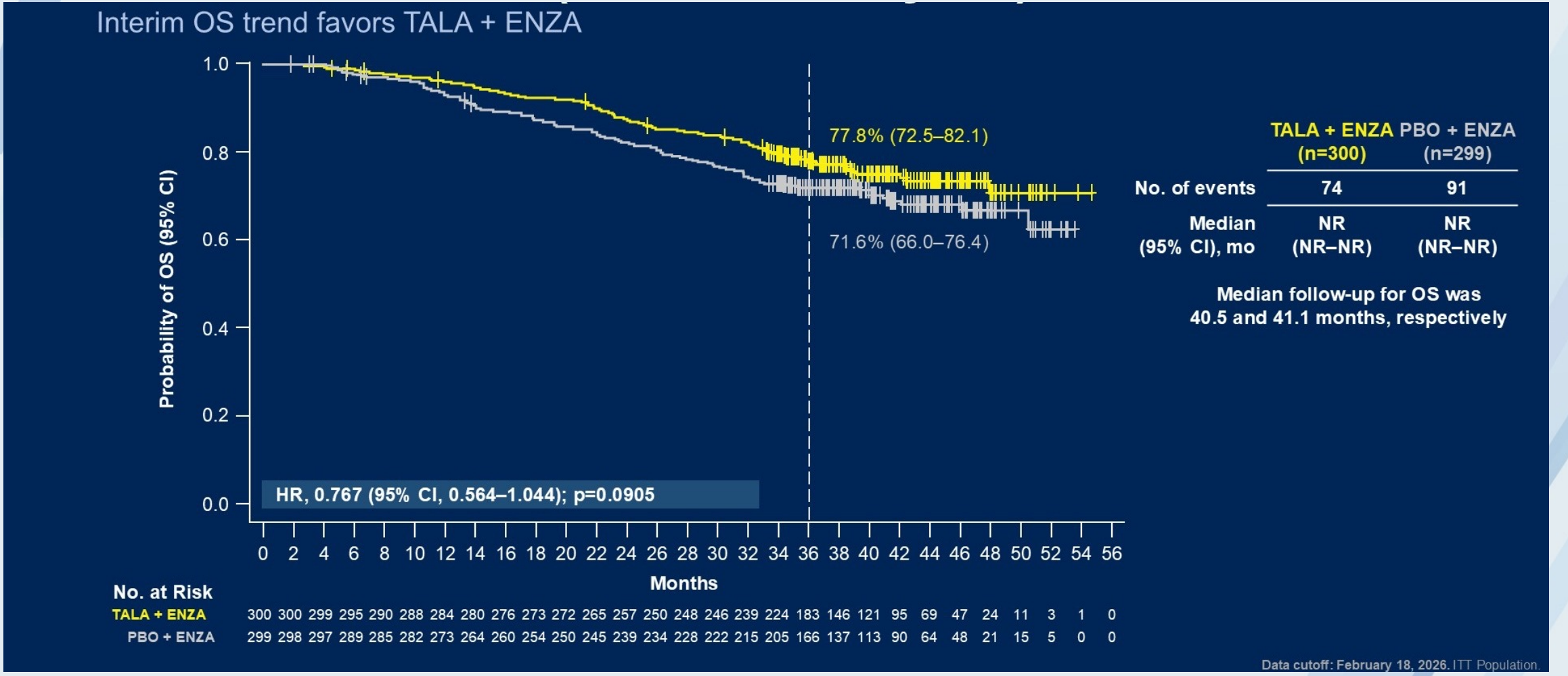




Agarwal N et al. *N Engl J Med* 2026;395(5):427-439.
Agarwal N et al. ASCO 2026;Abstract LBA5007.


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# Phase III TALAPRO-3 Interim Analysis: Overall Survival



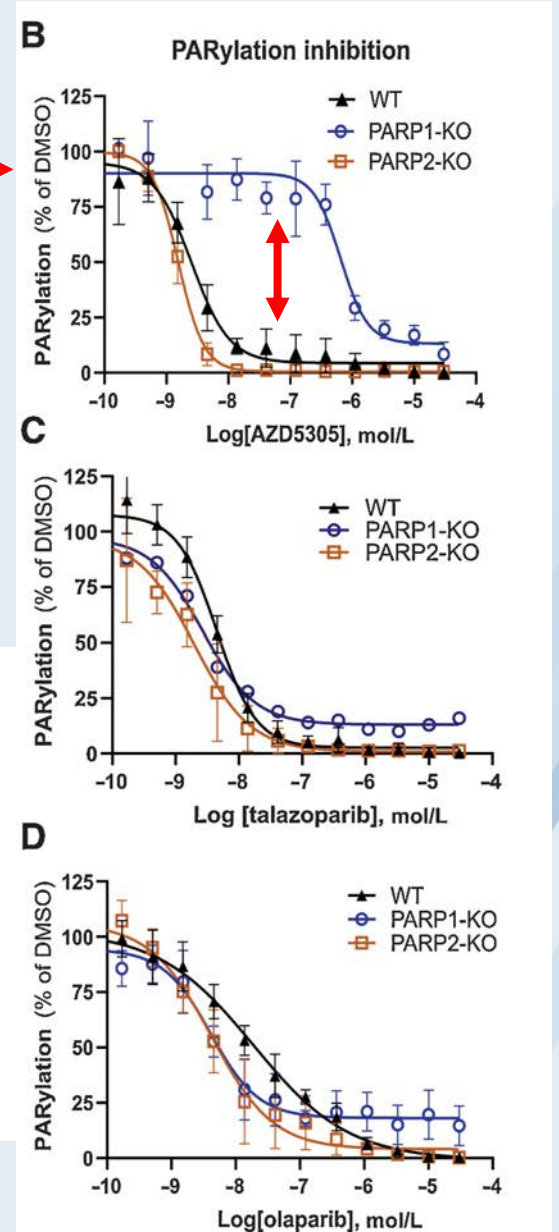


Agarwal N et al. *N Engl J Med* 2026;395(5):427-439.
Agarwal N et al. ASCO 2026;Abstract LBA5007.

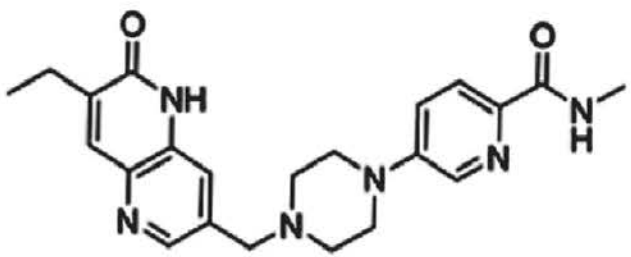
# Saruparib (AZD5305): A PARP1-Specific Inhibitor




**Saruparib selectively inhibits PARP1, reducing hematologic toxicities**




AZD5305



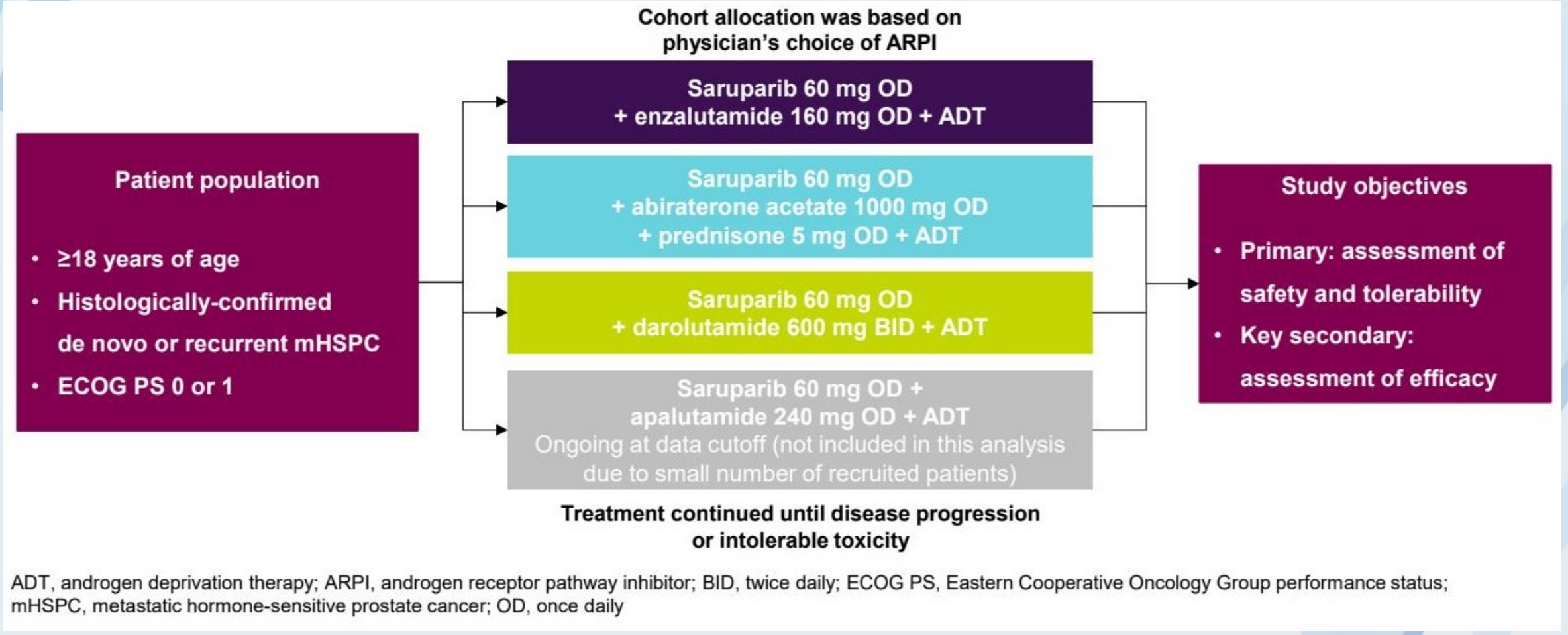
| AZD5305 | Biochemical assay* | Cellular assay |
|---|---|---|
| PARP1 $IC_{50}$ (nmol/L) | 3 | **1.5** |
| PARP2 $IC_{50}$ (nmol/L) | 1,400 | **653** |
| PARP1/2 fold selectivity | 460 | **435** |

**Johannes et al., 2021*

Illuzi G et al. *Clin Cancer Res* 2022;28(21):4724-36.

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# Phase I/II PETRANHA Study Design




ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; mHSPC, metastatic hormone-sensitive prostate cancer; OD, once daily

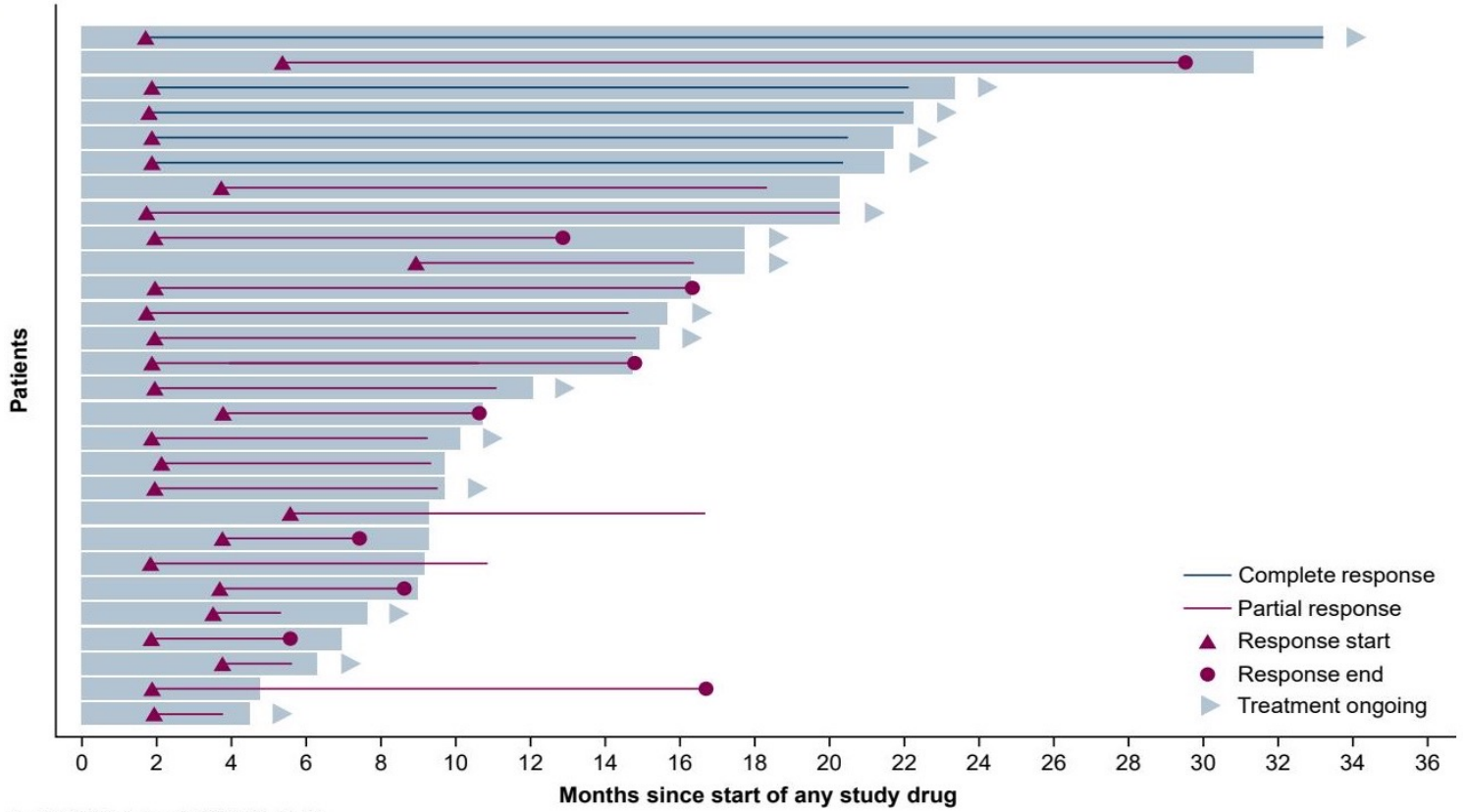
Azad A et al. Genitourinary Cancers Symposium 2026;Abstract 177.

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# Phase I/II PETRANHA: Responses

| | All patients (N=34)* |
|---|---|
| **ORR, % (80% CI)** | 82.4 (71.1–90.5) |
| **Best overall response, n (%)** | |
| Complete response | 5 (14.7) |
| Partial response | 23 (67.6) |
| Stable disease | 4 (11.8) |
| Progressive disease | 1 (2.9) |
| Not evaluable | 1 (2.9) |
| **Median DoR, months (80% CI)** | 24.2 (14.4–NC) |

Per RECIST v1.1 and PCWG3 criteria. Data cutoff 10 June 2025.
*Response evaluable analysis set.
CI, confidence interval; DoR, duration of response; NC, not calculated; ORR, objective response rate; PCWG3, Prostate Cancer Working Group 3; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1



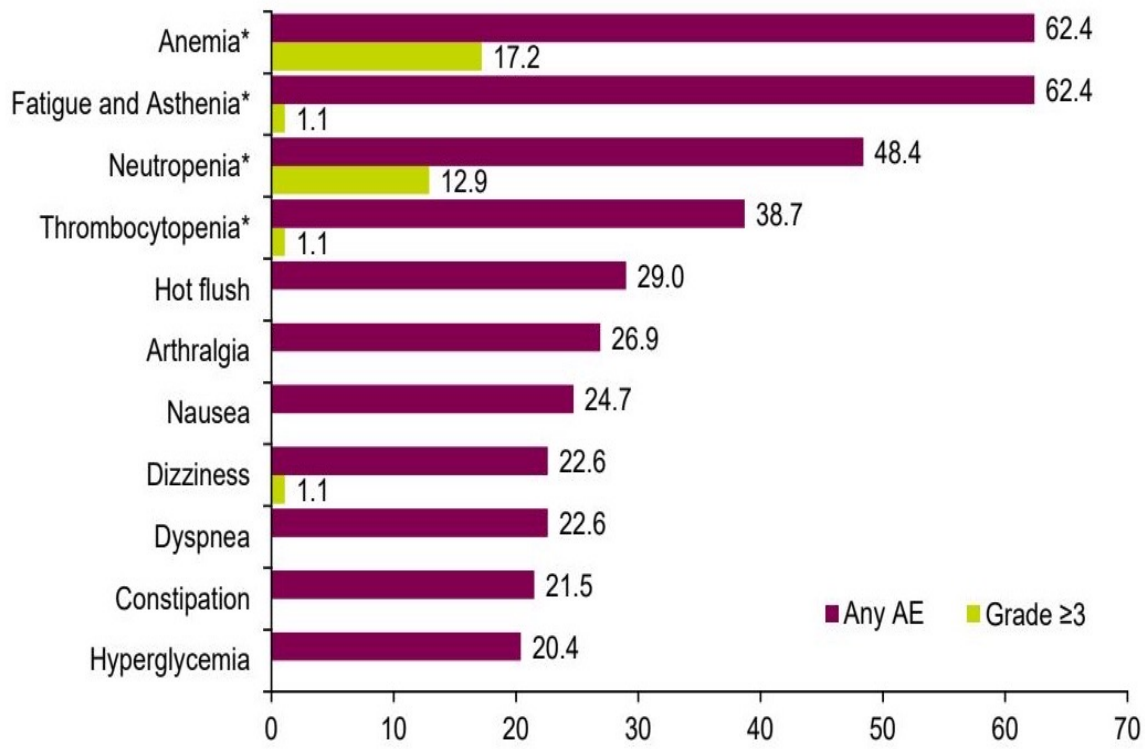

Per RECIST v1.1 and PCWG3 criteria.
Response evaluable analysis set. Data cutoff 10 June 2025.
PCWG3, Prostate Cancer Working Group 3; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Azad A et al. Genitourinary Cancers Symposium 2026;Abstract 177.

# Phase I/II PETRANHA: Safety

| Safety parameter, n (%) | mHSPC (N=93) |
|---|---|
| Any AE | 92 (98.9) |
| Causally related to saruparib* | 83 (89.2) |
| Any Grade ≥3 AE | 45 (48.4) |
| Causally related to saruparib* | 29 (31.2) |
| Any serious AE | 24 (25.8) |
| Causally related to saruparib* | 8 (8.6) |
| Saruparib / ARPI discontinuation due to AE† | 7 (7.5) / 3 (3.2) |
| Saruparib / ARPI dose reduction due to AE† | 24 (25.8) / 3 (3.2) |
| Saruparib / ARPI dose interruption due to AE† | 52 (55.9) / 36 (38.7) |

*Irrespective of relationship to ARPI. †Irrespective of the action taken on other drugs.
AE, adverse event; ARPI, androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer

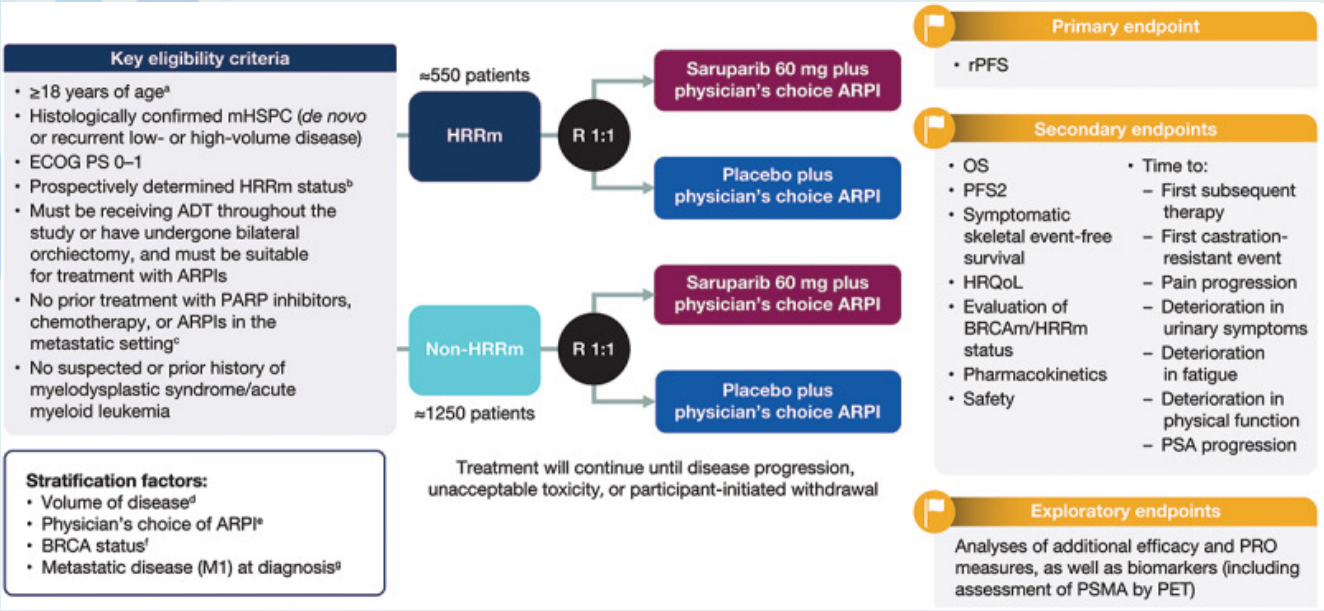



Safety analysis set. Data cutoff 10 June 2025.
*Grouped term.
AE, adverse event

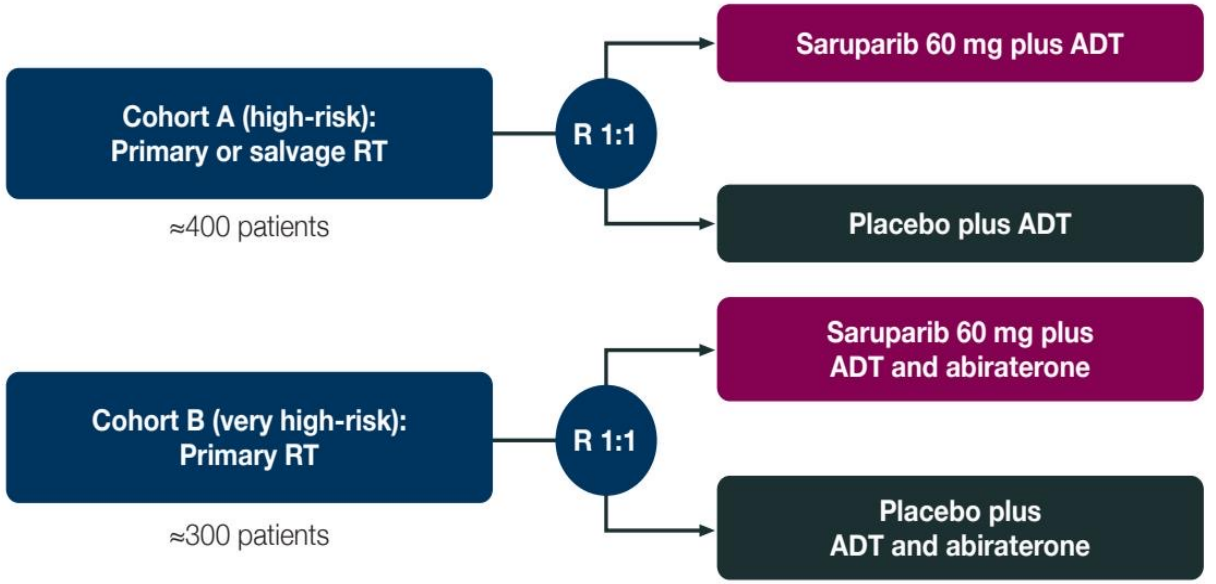
Azad A et al. Genitourinary Cancers Symposium 2026;Abstract 177.

# Ongoing Phase III Trials with Saruparib

## EvoPAR-Prostate01

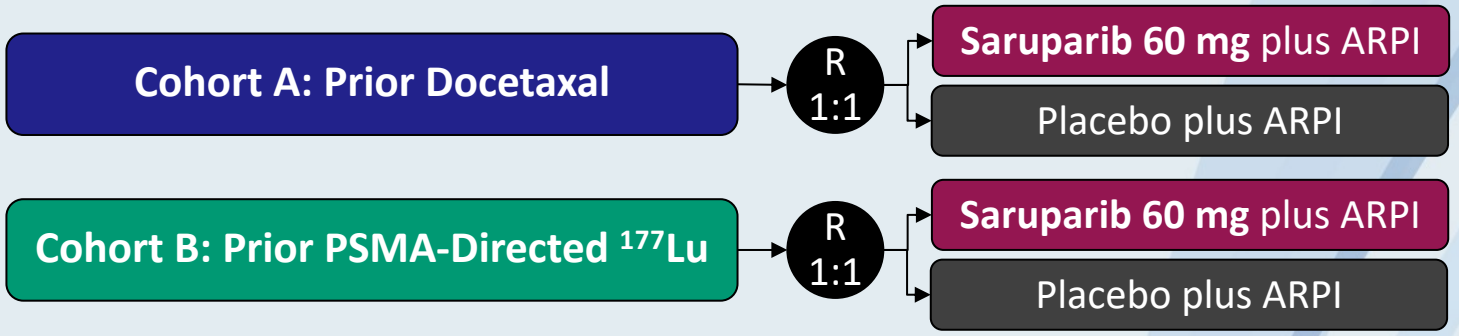



## EvoPAR-Prostate02




## EvoPAR-Prostate05

**Primary Endpoint:** rPFS
**Secondary Endpoints:** OS, PFS2





Azad A et al. Genitourinary Cancers Symposium 2025;Abstract TPS279.
McKay R et al. Genitourinary Cancers Symposium 2026;Abstract TPS412.
www.clinicaltrials.gov. NCT07711002. Accessed October 2026.


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# Faculty Discussion



Dr Apuri

# Questions for the Faculty

**A man in his early 80s with mCRPC with BRCA2 somatic prostate cancer has been on olaparib for 8 months. The patient has fatigue, which is likely multifactorial but in general he is doing well.**

**Questions**

- How do you select a PARP inhibitor for mCRPC, and if paired with endocrine therapy, which one?
- When are you opting for PARP inhibitor-based therapy for your patients with mHSPC?
- For which mutations would you use a PARPi?
- Somatic versus germline testing?
- Liquid biopsy, tissue or both, and when?
- How do you prevent and manage cytopenias, including anemia, and GI and other quality-of-life adverse effects?

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# Agenda

Introduction: ESMO 2026; Recent FDA Approvals

Selection of Endocrine Therapy – Dr Antonarakis

Utility of PARP Inhibitors – Dr Agarwal

**AKT Inhibition for PTEN-Deficient Disease – Dr Antonarakis**

Radiopharmaceuticals – Dr Agarwal

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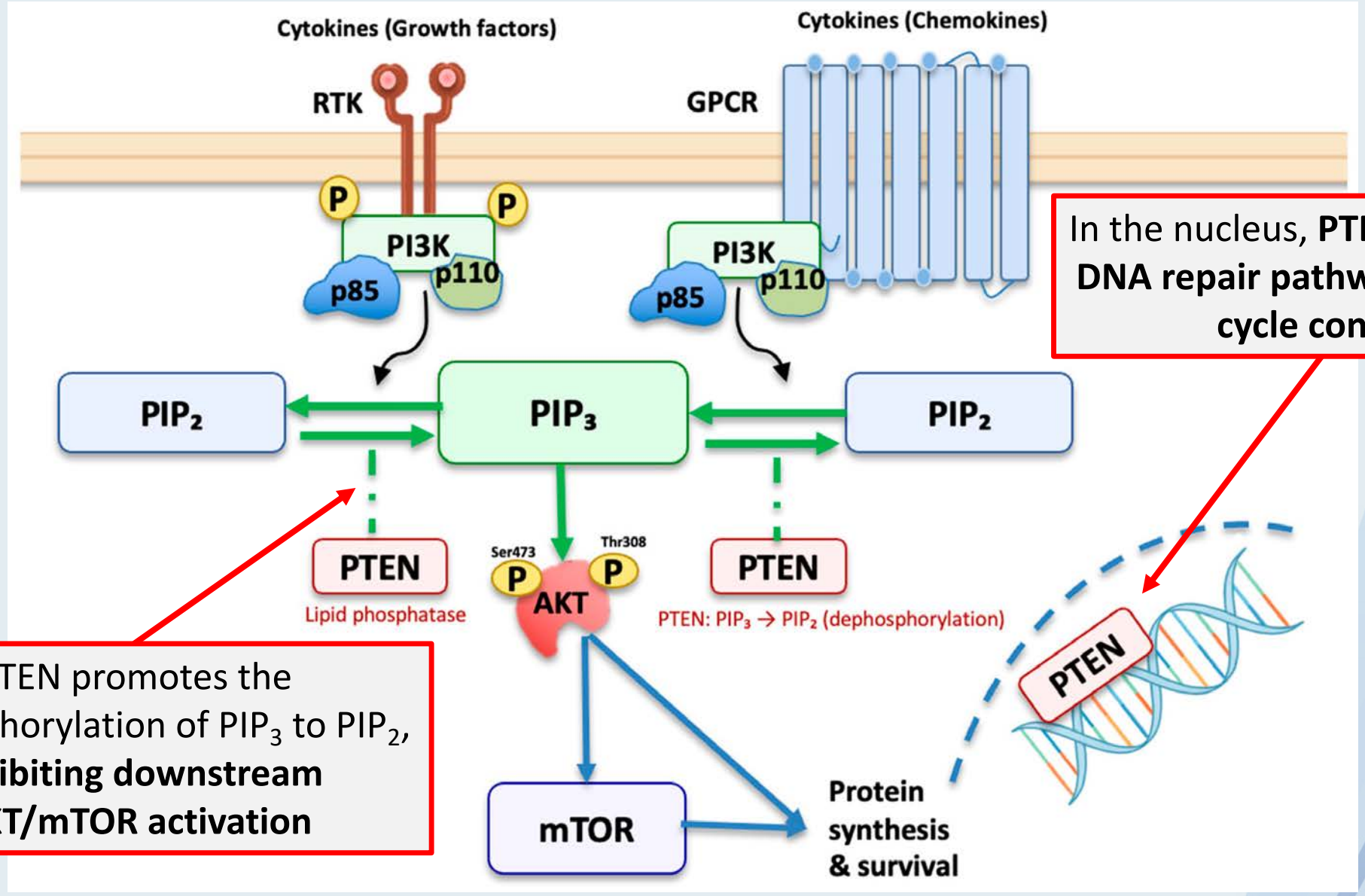
# AKT Inhibition for PTEN-Deficient Disease

**Select Datasets**

- Kisiel F et al. Prognostic significance of PTEN loss in prostate cancer: A meta-analysis of Gleason grade and clinical outcomes. *Cancers (Basel)* 2025 August 30;17(17):2862.
- George DJ et al. Patient reported outcomes (PRO) and tolerability of capivasertib (capi) plus abiraterone (abi) versus placebo (pbo) plus abi in patients (pts) with PTEN-deficient metastatic hormone-sensitive prostate cancer (mHSPC): CAPItello-281. Genitourinary Cancers Symposium 2026;Abstract 14.
- Fizazi K et al. Capivasertib plus abiraterone in PTEN-deficient metastatic hormone-sensitive prostate cancer: CAPItello-281 phase III study. *Ann Oncol* 2026;37(1):53-68.

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# Wild-Type PTEN Signaling and the AKT/mTOR Pathway




In the nucleus, **PTEN promotes DNA repair pathways and cell cycle control**

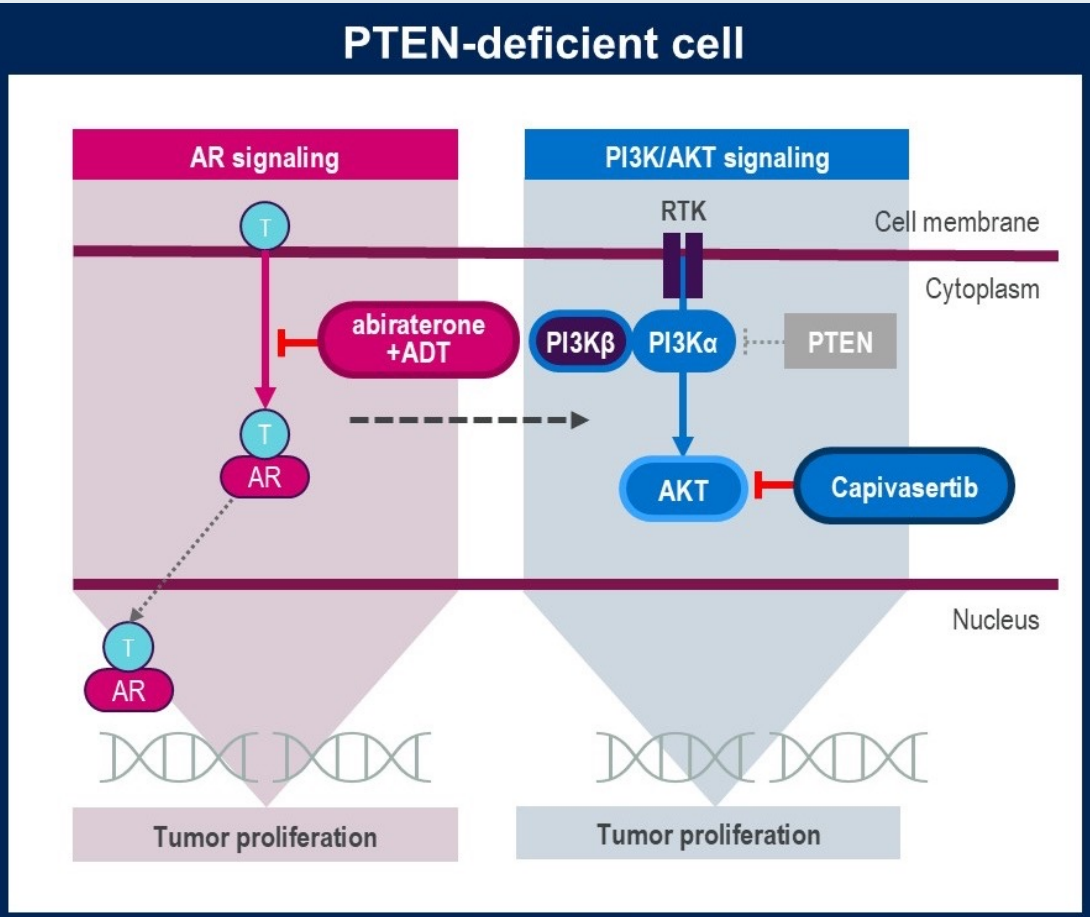
PTEN promotes the dephosphorylation of $PIP_3$ to $PIP_2$, **inhibiting downstream AKT/mTOR activation**

Kisiel F et al. *Cancers (Basel)* 2025 August 30;17(17):2862.

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# PTEN Deficiency in Prostate Cancer

- In **PTEN-proficient** hormone-sensitive tumor cells, **AR signaling** is the key driver of proliferation[1]
- In PTEN-deficient tumor cells, there is an **additional proliferative drive** from upregulation of the PI3K/AKT pathway that complements and provides an alternative survival mechanism to AR signaling[2]
- **PTEN deficiency** is associated with poor prognosis[2–4]
- **Capivasertib** is a potent, selective inhibitor of all three AKT isoforms (AKT1/2/3)
- **Phase II/III evidence** showed benefits with ipatasertib (AKTi) plus abiraterone in **PTEN-deficient mCRPC (mAPMR)**[2,3]



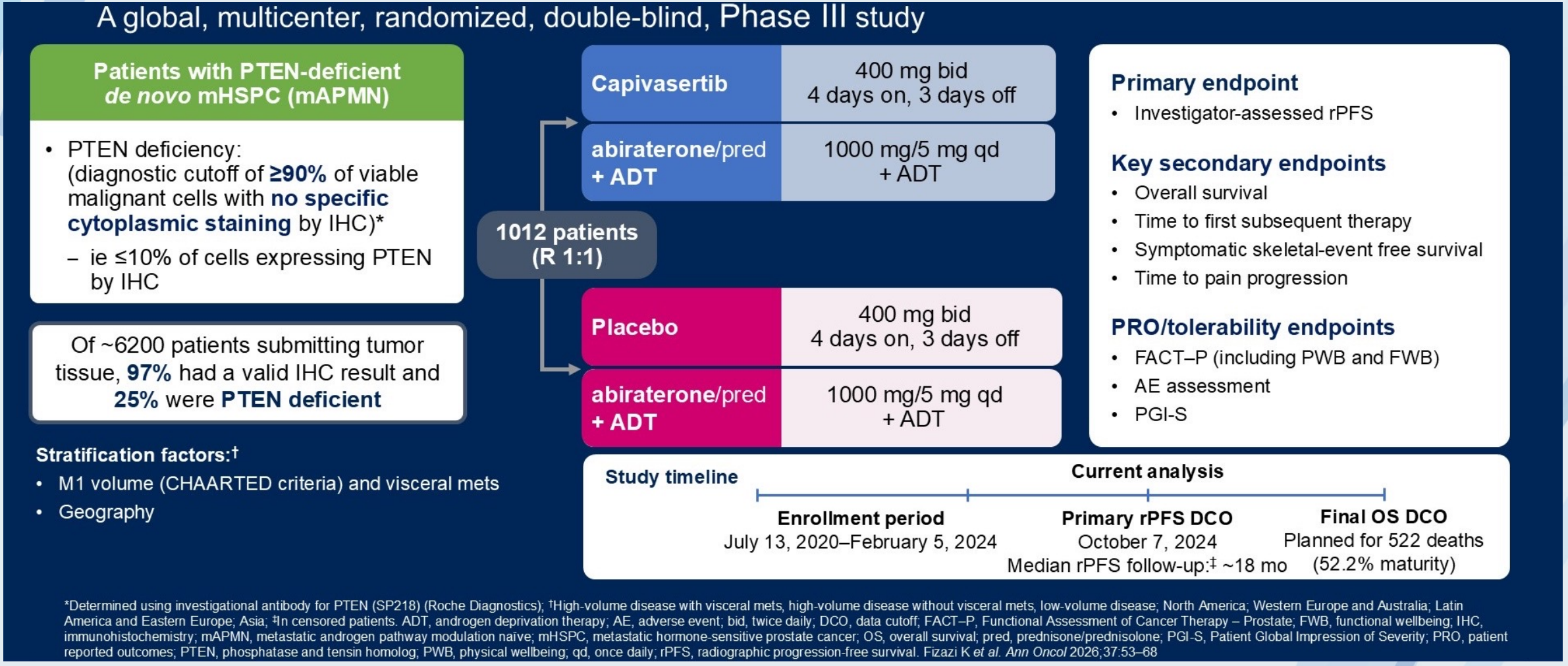

AR, androgen receptor; mAPMR, metastatic androgen pathway modulation resistant; mCRPC, metastatic castration resistant prostate cancer; PTEN, phosphatase and tensin homolog; RTK, receptor tyrosine kinase; T, testosterone

1. Quistini A *et al. Res Rep Urol.* 2025;17:211-23; 2. De Bono JS *et al. Clin Cancer Res* 2019;25:928–36; 3. Sweeney C *et al. Lancet* 2021;398:131–42; 4. Rathkopf D *et al. J Clin Oncol* 2025;43:abst 5096

George DJ et al. Genitourinary Cancers Symposium 2026;Abstract 14.

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# Phase III CAPItello-281 Study Design

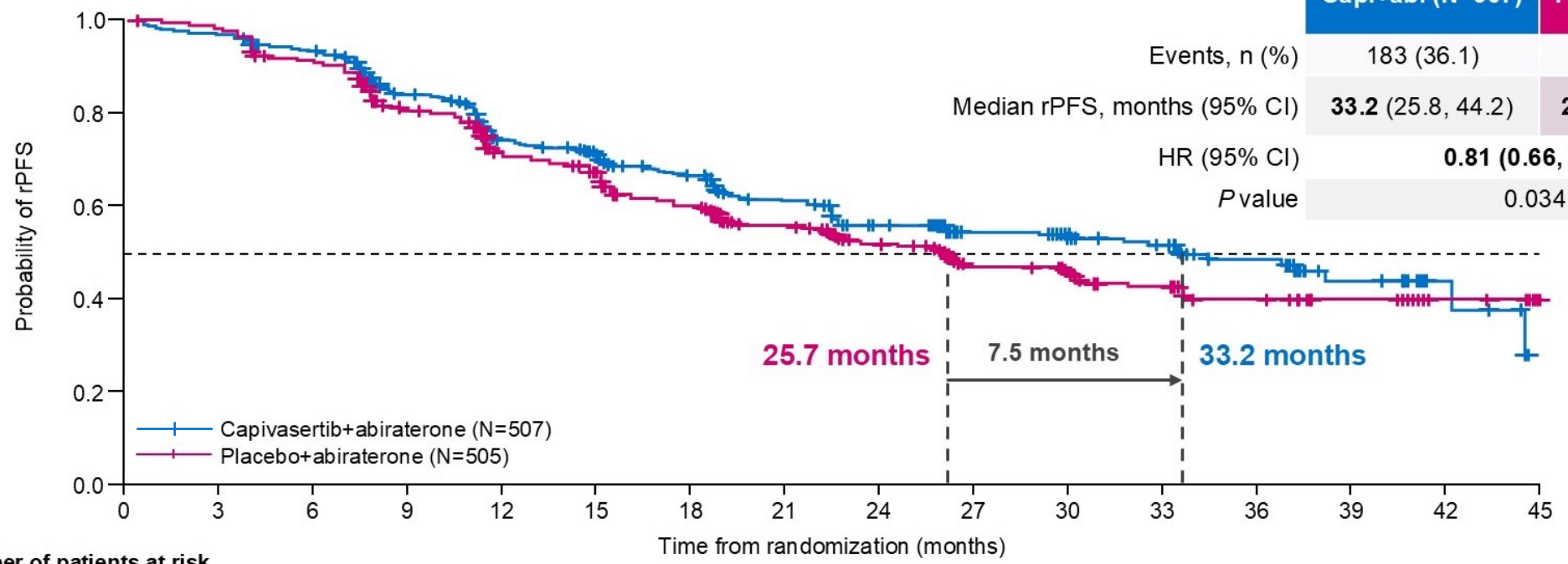



*Determined using investigational antibody for PTEN (SP218) (Roche Diagnostics); †High-volume disease with visceral mets, high-volume disease without visceral mets, low-volume disease; North America; Western Europe and Australia; Latin America and Eastern Europe; Asia; ‡In censored patients. ADT, androgen deprivation therapy; AE, adverse event; bid, twice daily; DCO, data cutoff; FACT–P, Functional Assessment of Cancer Therapy – Prostate; FWB, functional wellbeing; IHC, immunohistochemistry; mAPMN, metastatic androgen pathway modulation naïve; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; pred, prednisone/prednisolone; PGI-S, Patient Global Impression of Severity; PRO, patient reported outcomes; PTEN, phosphatase and tensin homolog; PWB, physical wellbeing; qd, once daily; rPFS, radiographic progression-free survival. Fizazi K *et al. Ann Oncol* 2026;37:53–68


Fizazi K et al. *Ann Oncol* 2026;37(1):53-68.
George DJ et al. Genitourinary Cancers Symposium 2026;Abstract 14.


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# Phase III CAPItello-281 Primary Endpoint: rPFS




| | Capi+abi (N=507) | Pbo+abi (N=505) |
|---|---|---|
| Events, n (%) | 183 (36.1) | 215 (42.6) |
| Median rPFS, months (95% CI) | **33.2** (25.8, 44.2) | **25.7** (22.0, 29.9) |
| HR (95% CI) | **0.81 (0.66, 0.98)** | |
| *P* value | 0.034 | |

**Number of patients at risk**

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Capi+abi | 507 | 460 | 435 | 353 | 282 | 233 | 217 | 165 | 123 | 93 | 69 | 62 | 41 | 21 | 6 | 0 |
| Pbo+abi | 505 | 479 | 440 | 359 | 276 | 215 | 198 | 154 | 113 | 83 | 59 | 51 | 37 | 23 | 8 | 0 |

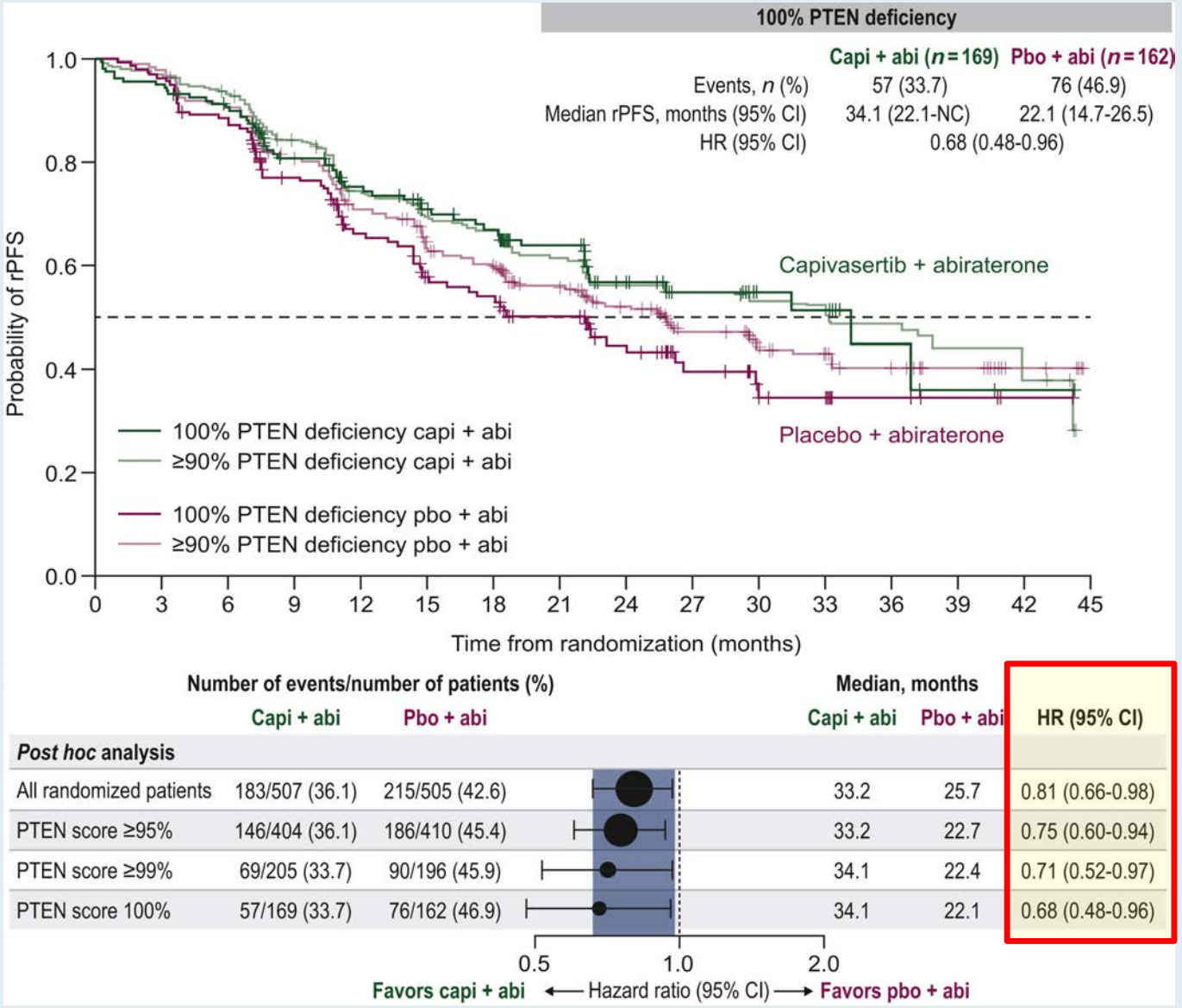
A stratified log-rank test was used to calculate two-sided *P* values. HRs and 95% CIs were calculated using a stratified Cox proportional-hazards model. Median follow-up: 18.4 months (capi+abi), 18.5 months (pbo+abi)
abi, abiraterone; capi, capivasertib; CI, confidence interval; HR, hazard ratio; pbo, placebo; rPFS, radiographic progression-free survival
Fizazi K *et al. Ann Oncol* 2026;37:53–68

rPFS = radiographic progression-free survival


Fizazi K et al. *Ann Oncol* 2026;37(1):53-68.
George DJ et al. Genitourinary Cancers Symposium 2026;Abstract 14.


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# Phase III CAPItello-281 PTEN Subgroup Analysis: rPFS

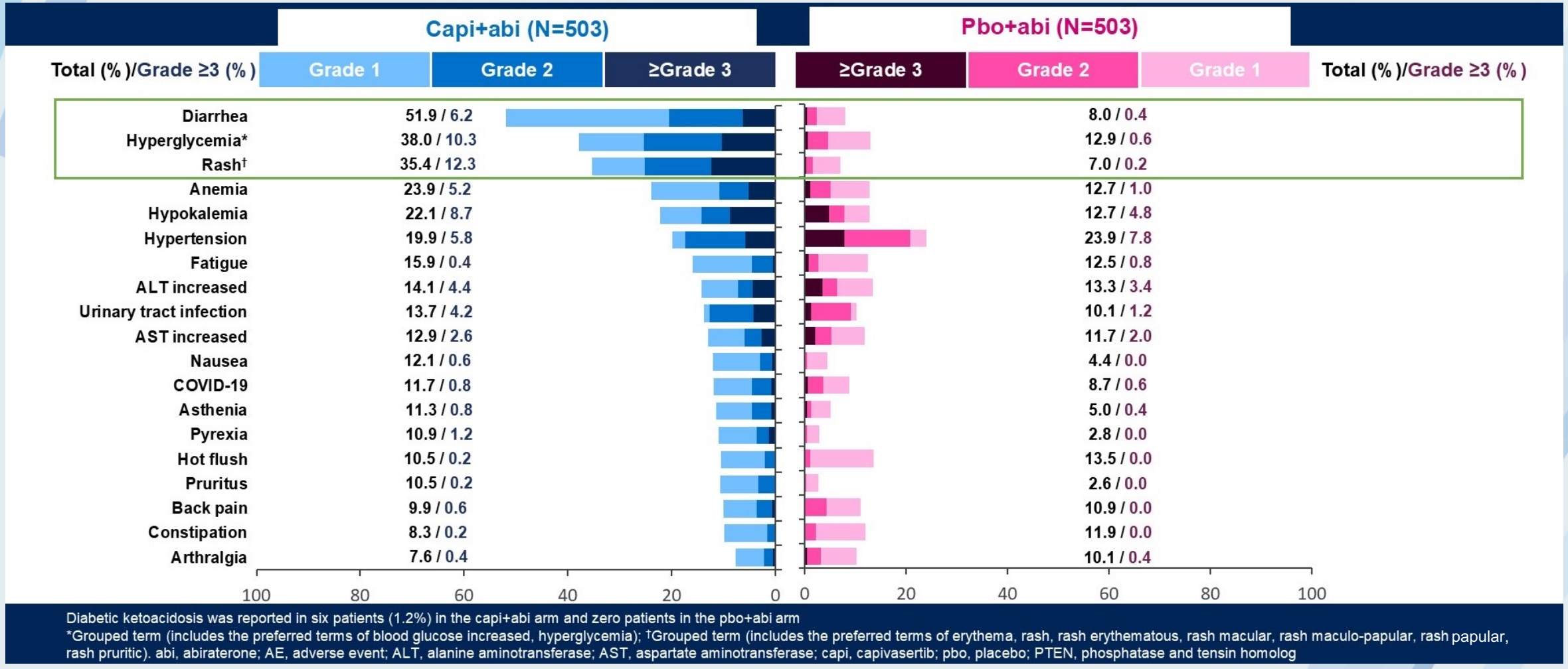



| | Number of events/number of patients (%) | | Median, months | | |
|---|---|---|---|---|---|
| | Capi + abi | Pbo + abi | Capi + abi | Pbo + abi | HR (95% CI) |
| ***Post hoc* analysis** | | | | | |
| All randomized patients | 183/507 (36.1) | 215/505 (42.6) | 33.2 | 25.7 | 0.81 (0.66-0.98) |
| PTEN score ≥95% | 146/404 (36.1) | 186/410 (45.4) | 33.2 | 22.7 | 0.75 (0.60-0.94) |
| PTEN score ≥99% | 69/205 (33.7) | 90/196 (45.9) | 34.1 | 22.4 | 0.71 (0.52-0.97) |
| PTEN score 100% | 57/169 (33.7) | 76/162 (46.9) | 34.1 | 22.1 | 0.68 (0.48-0.96) |



Fizazi K et al. *Ann Oncol* 2026;37(1):53-68.

# Phase III CAPItello-281: Safety




Diabetic ketoacidosis was reported in six patients (1.2%) in the capi+abi arm and zero patients in the pbo+abi arm

*Grouped term (includes the preferred terms of blood glucose increased, hyperglycemia); †Grouped term (includes the preferred terms of erythema, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic). abi, abiraterone; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; capi, capivasertib; pbo, placebo; PTEN, phosphatase and tensin homolog


Fizazi K et al. *Ann Oncol* 2026;37(1):53-68.

George DJ et al. Genitourinary Cancers Symposium 2026;Abstract 14.



RTP RESEARCH TO PRACTICE

# Phase III CAPItello-281: AEs Associated with AKT Inhibition

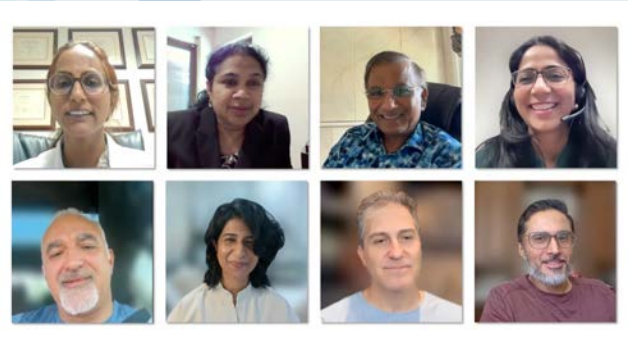
| | Rash* | | Diarrhea | | Hyperglycemia† | |
|---|---|---|---|---|---|---|
| | Capi+abi (N=503) | Pbo+abi (N=503) | Capi+abi (N=503) | Pbo+abi (N=503) | Capi+abi (N=503) | Pbo+abi (N=503) |
| Any grade AE, n (%) | 178 (35.4) | 35 (7.0) | 261 (51.9) | 40 (8.0) | 191 (38.0) | 65 (12.9) |
| Grade ≥3 AE,‡ n (%) | 62 (12.3) | 1 (0.2) | 31 (6.2) | 2 (0.4) | 52 (10.3) | 3 (0.6) |
| Median (IQR) time to onset, days | 13 (11–43) | 78 (37–195) | 12 (3–43) | 142 (28–339) | 54 (15–114) | 114 (71–326) |
| **AE leading to, n (%)** | | | | | | |
| Interruption of capi/pbo | 85 (16.9) | 3 (0.6) | 63 (12.5) | 1 (0.2) | 55 (10.9) | 4 (0.8) |
| Reduction of capi/pbo | 43 (8.5) | 2 (0.4) | 22 (4.4) | 0 | 33 (6.6) | 1 (0.2) |
| Discontinuation of capi/pbo | 24 (4.8) | 0 | 5 (1.0) | 0 | 5 (1.0) | 0 |
| Supportive treatment given, n (%) | 146 (29.0) | 20 (4.0) | 167 (33.2) | 19 (3.8) | 127 (25.2) | 23 (4.6) |
| Outcome at time of DCO, n (%) | | | | | | |
| Recovered/recovering | 164 (32.6) | 28 (5.6) | 238 (47.3) | 36 (7.2) | 140 (27.8) | 43 (8.5) |
| Not recovered | 24 (4.8) | 8 (1.6) | 45 (8.9) | 4 (0.8) | 65 (12.9) | 25 (5.0) |

*Grouped term including the preferred terms of erythema, rash, rash erythematous, rash macular, rash maculopapular, rash papular, rash pruritic. †Grouped term including the preferred terms of blood glucose increased, hyperglycemia. ‡A diarrhea AE of Grade 4 was reported for one patient (0.2%) in the capi+abi arm only, hyperglycemia AEs of Grade 4 and Grade 5 were reported for one patient (0.2%) each in the capi+abi arm only, no Grade 4–5 AEs of rash were reported. No primary prophylaxis interventions were used during the CAPItello-281 trial for prospective AE management. Additional data on supportive treatment received are available via QR code.
abi, abiraterone; AE, adverse event; capi, capivasertib; DCO, data cutoff; IQR, interquartile range; pbo, placebo

AE = adverse event

Fizazi K et al. *Ann Oncol* 2026;37(1):53-68.
George DJ et al. Genitourinary Cancers Symposium 2026;Abstract 14.

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# Questions for the Faculty

- Optimal method to test for PTEN deficiency — IHC vs NGS? Is % positivity important?
- What are the clinical implications of PTEN phenotype? (Poor prognosis, clinical/imaging progression without PSA progression)
- Use of capivasertib in patients with suboptimal response to initial therapy
- Contraindications to capivasertib? HbA1c; indications for metformin
- Tolerability in men

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# Agenda

Introduction: ESMO 2026; Recent FDA Approvals

Selection of Endocrine Therapy – Dr Antonarakis

Utility of PARP Inhibitors – Dr Agarwal

AKT Inhibition for PTEN-Deficient Disease – Dr Antonarakis

**Radiopharmaceuticals – Dr Agarwal**

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# Radiopharmaceuticals

**Select Datasets**

- Gillessen S et al. Final overall survival results from EORTC 1333/PEACE-3 trial of enzalutamide plus radium-223 in metastatic castration-resistant prostate cancer. *Ann Oncol* 2026;37(5):736-42.
- Gallardo E et al. Final overall survival results from the EORTC 1333/PEACE-3 trial: Enzalutamide with or without radium-223 in metastatic castration-resistant prostate cancer. Genitourinary Cancers Symposium 2026;Abstract 15.
- Fizazi K et al. Final overall survival and safety analyses of the phase III PSMAfore trial of [$^{177}$Lu]Lu-PSMA-617 versus change of androgen receptor pathway inhibitor in taxane-naive patients with metastatic castration-resistant prostate cancer. *Ann Oncol* 2025;36(11):1319-30.
- Sartor O et al. Phase III trial of [177Lu]Lu-PSMA-617 in taxane-naive patients with metastatic castration-resistant prostate cancer (PSMAfore). ESMO 2023;Abstract LBA13.
- Tagawa ST et al. [$^{177}$Lu]Lu-PSMA-617 in patients with PSMA-positive metastatic androgen pathway modulator-naive/sensitive prostate cancer (PSMAddition): A phase 3 randomised, controlled trial. *Lancet* 2026;408(10557):793-807.

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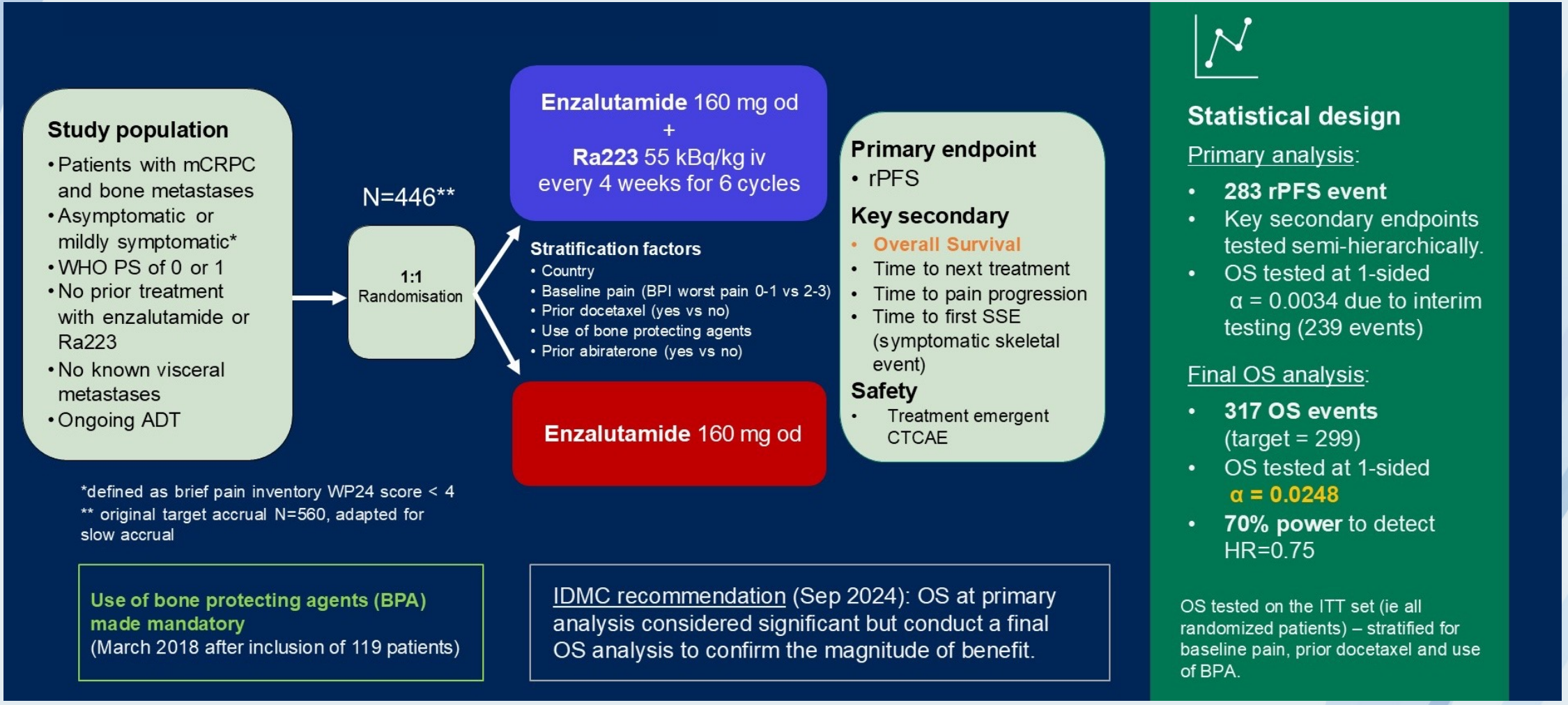
# Radiopharmaceuticals

**Select Datasets (Continued)**

- Saad F et al. Subgroup analyses by disease volume and *de novo*/recurrent mHSPC in the PSMAddition study of [$^{177}$Lu]Lu-PSMA-617. ASCO 2026;Abstract 5020.
- Tagawa ST et al. Phase 3 trial of [177Lu]Lu-PSMA-617 combined with ADT + ARPI in patients with PSMA-positive metastatic hormone-sensitive prostate cancer (PSMAddition). ESMO 2025;Abstract LBA6.
- Saad F et al. First-in-human assessment of actinium-225-prostate-specific membrane antigen ($^{225}$Ac-PSMA)-Trillium (BAY 3563254) in mCRPC: Dose-escalation results of the phase 1 PAnTHa study. Genitourinary Cancers Symposium 2026;Abstract 19.
- Delpassand E et al. Preliminary efficacy and safety results from the (TATCIST) trial: A PSMA-directed targeted alpha therapy with FPI-2265 (225Ac-PSMA-I&T) for the treatment of metastatic castration-resistant prostate cancer (mCRPC). AACR 2024;84(7_Supplement):CT224.
- Emmett L et al. AcTION: Phase 1 study of [$^{225}$Ac]AC-PSMA-617 ($^{225}$Ac-PSMA-617) in men with metastatic castration-resistant prostate cancer (mCRPC) with or without prior [$^{177}$Lu]Lu-PSMA ($^{177}$Lu-PSMA) radioligand therapy (RLT). ASCO 2026;Abstract 5010.

RTP RESEARCH TO PRACTICE

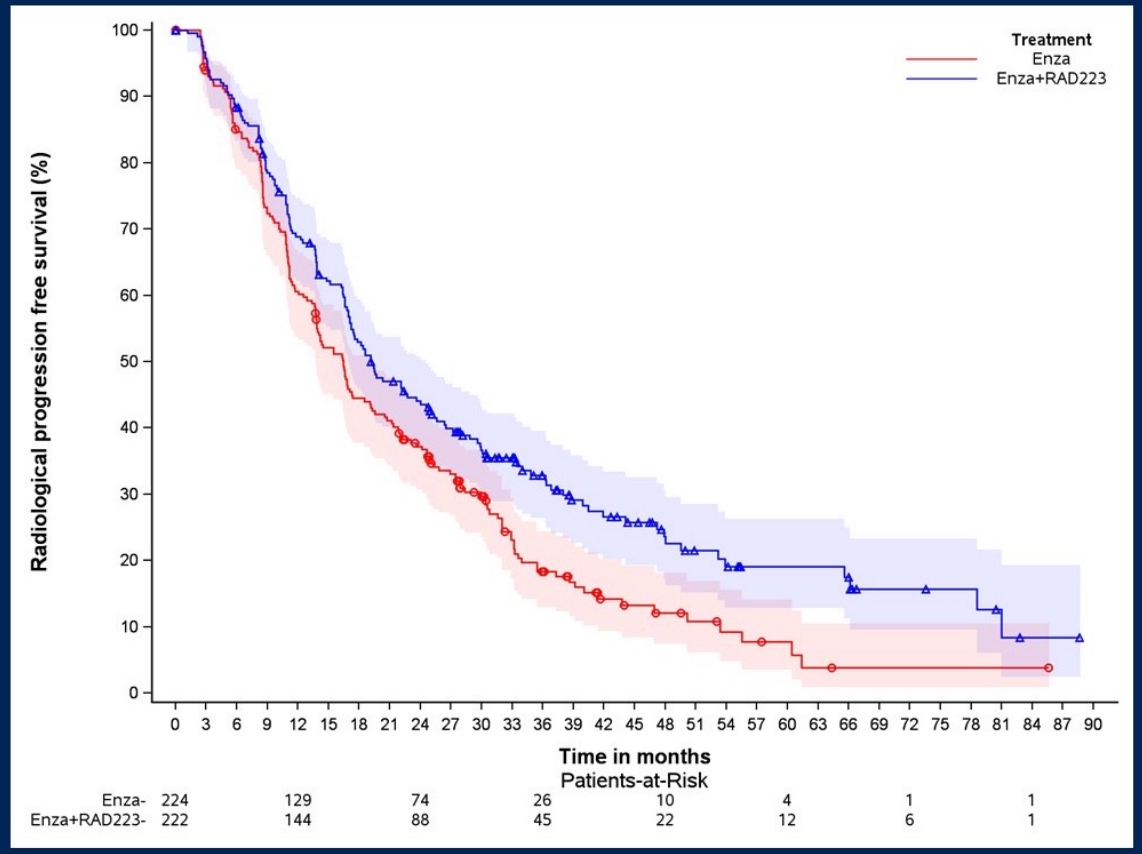
# Phase III PEACE-3 Study Design





Gillessen S et al. *Ann Oncol* 2026;37(5):736-742.
Gallardo E et al. Genitourinary Cancers Symposium 2026;Abstract 15.

# Phase III PEACE-3: Final rPFS




Database locked on 12 January 2026 (cut off date: 01 May 2025)

| | Event/ Total | Median (95% CI) (months)[1] | Hazard Ratio (95% CI)[2] |
|---|---|---|---|
| **Treatment** | | | |
| **Enza** | 176/224 | **16.43** (13.77-19.15) | Reference |
| **Enza+Ra223** | 156/222 | **19.19** (16.92-24.57) | **0.71 (0.57-0.89)** |

[1]Kaplan-Meier method; [2]Cox model

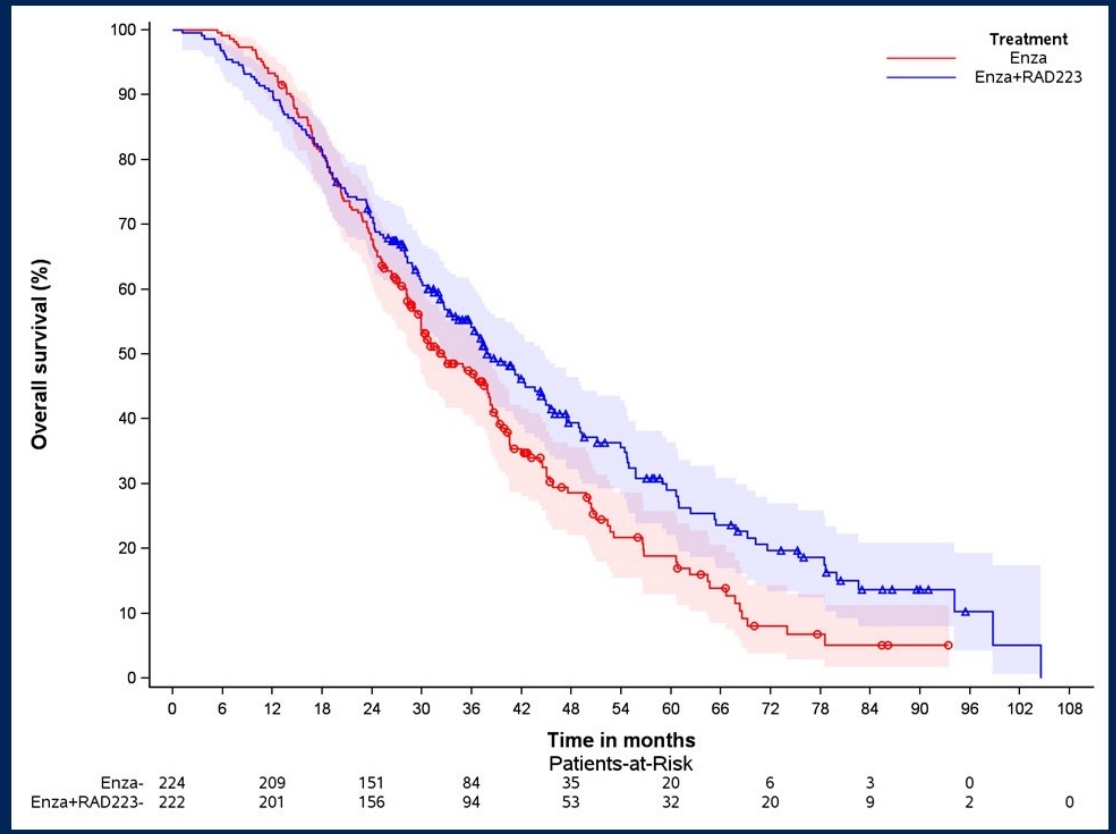
| | Enza+RAD223 (N=222) (95% CI) | Enza (N=224) (95% CI) |
|---|---|---|
| **6 months** | 88.4 (83.3-92.0%) | 84.6 (79.1-88.8%) |
| **12 months** | 68.9 (62.2-74.7%) | 60.6 (53.8-66.8%) |
| **18 months** | 52.9 (45.9-59.4%) | 44.5 (37.7-51.0%) |
| **24 months** | 44.1 (37.2-50.7%) | 37.2 (30.7-43.7%) |

**rPFS results confirmed with longer follow-up and appear little changed from primary analysis.**


Gillessen S et al. *Ann Oncol* 2026;37(5):736-742.
Gallardo E et al. Genitourinary Cancers Symposium 2026;Abstract 15.


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# Phase III PEACE-3: Final Overall Survival




| | Event/ Total | Median (95%CI) (months)[1] | Hazard Ratio (95% CI)[2] | 1-sided P-value |
|---|---|---|---|---|
| **Treatment** | | | | **Logrank: 0.0096[3]** **Permutation:0 .0105** |
| **Enza** | 165/224 | **32.62** (29.31-38.24) | **0.76** (0.60-0.96) | |
| **Enza+Ra223** | 152/222 | **38.21** (33.08-44.75) | | |

[1]Kaplan-Meier method; [2]Cox model; [3] Stratified Logrank test

| | Enza+Ra223 (N=222) | Enza (N=224) |
|---|---|---|
| | (95% CI) | (95% CI) |
| **6 mths** | 96.8 (93.5-98.5%) | 99.1 (96.5-99.8%) |
| **12 mths** | 90.5 (85.9-93.7%) | 92.9 (88.6-95.6%) |
| **18 mths** | 81.1 (75.3-85.6%) | 80.8 (74.9-85.3%) |
| **24 mths** | 71.1 (64.7-76.6%) | 67.7 (61.2-73.4%) |
| **36 mths** | 54.2 (47.1-60.6%) | 47.4 (40.6-54.0%) |

**Preset level of significance at final analysis: <0.0248**
**Crossing of the curves (still) present at month 18**
**Only 3 patients censored < 24 months**

Database locked on 12 January 2026 (cut off date: 01 May 2025)


Gillessen S et al. *Ann Oncol* 2026;37(5):736-742.
Gallardo E et al. Genitourinary Cancers Symposium 2026;Abstract 15.


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# Phase III PEACE-3: Grade ≥3 TEAEs

| *Number of patients (%) with grade 3-5 TEAE* | Enza+RAD223 (N=218) | Enza (N=224) |
|---|---|---|
| | N (%) | N (%) |
| **All** | **151 (69.3%)** | **129 (57.6%)** |
| **Hypertension** | 78 (35.8) | 80 (35.7) |
| **Fatigue** | 12 (5.5) | 4 (1.8) |
| **Fracture** | 12 (5.5) | 3 (1.3) |
| **Anemia** | 13 (6) | 5 (2.2) |
| **Neutropenia** | 10 (4.6) | 0 |
| **Bone pain** | 13 (6) | 12 (5.4) |
| **Weight decreased** | 10 (4.6) | 2 (0.9) |
| **Spinal cord compression** | 7 (3.2) | 8 (3.6) |
| **Drug-related** | **63 (28.9%)** | **42 (18.8%)** |
| **Hypertension** | 26 (11.9) | 27 (12.1) |
| **Fatigue** | 9 (4.1) | 3 (1.3) |
| **Anemia** | 6 (2.8) | 0 |
| **Neutropenia** | 7 (3.2) | 0 |

**Side effects of special interest:**

- 1 MDS
- 1 AML
- 1 CML (drug-related)

All 3 in the combination arm

- 17 osteonecrosis of the jaw:
  - 14 in the combo (5 grade 3)
  - 3 in the enza arm

**No individual TEAE ≥ grade 3 has increased by more than 5% in the combination compared to the enzalutamide alone arm.**

Treatment-emergent AEs are all AEs arising from start of treatment until 28 days after last dose of any study drug

MDS = myelodysplastic syndromes; AML = acute myeloid leukemia; CML = chronic myeloid leukemia

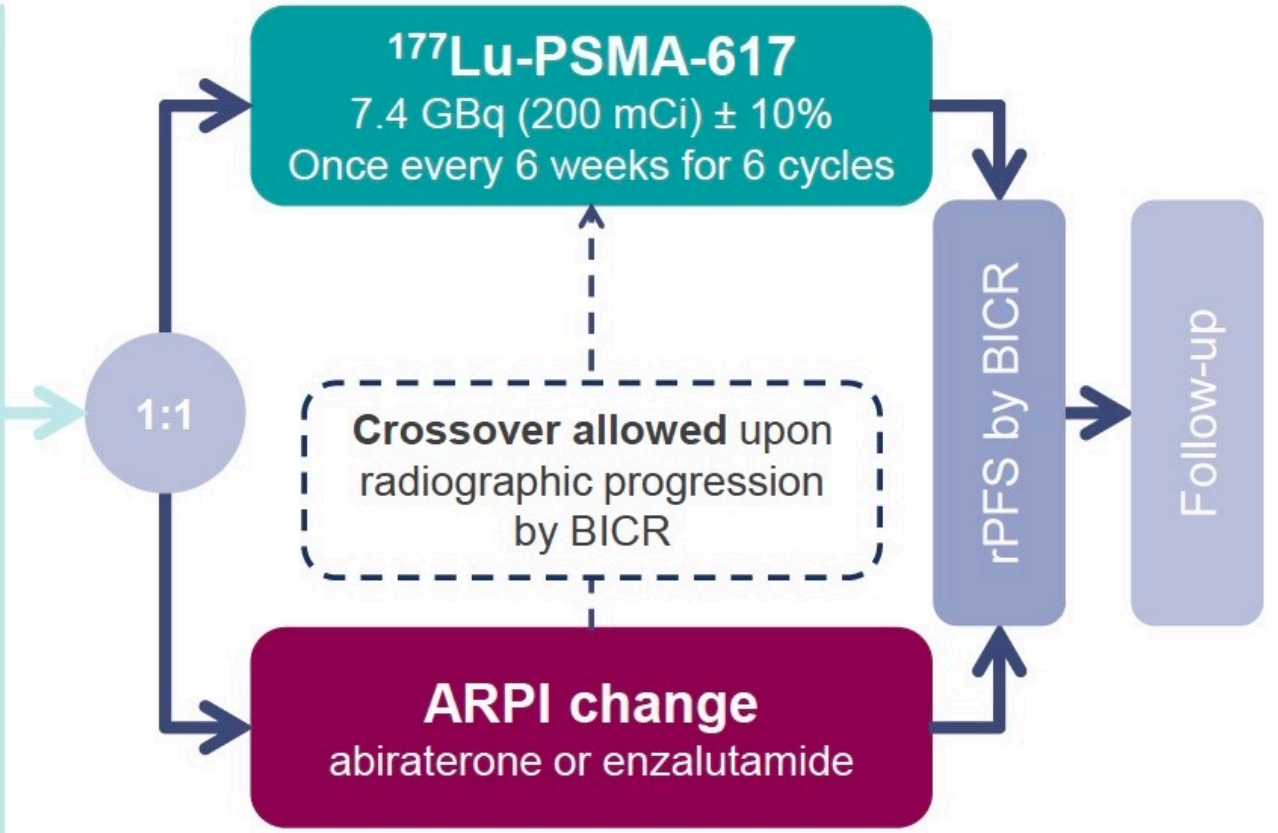
Gillessen S et al. *Ann Oncol* 2026;37(5):736-742.
Gallardo E et al. Genitourinary Cancers Symposium 2026;Abstract 15.

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# Phase III PSMAFore Study Design

**Eligible adults**

- Confirmed progressive mCRPC
- ≥ 1 PSMA-positive metastatic lesion on [$^{68}$Ga]Ga-PSMA-11 PET/CT and no exclusionary PSMA-negative lesions
- Progressed once on prior second-generation ARPI
  - Candidates for change in ARPI
- Taxane-naive (except [neo]adjuvant > 12 months ago)
  - Not candidates for PARPi
- ECOG performance status 0–1




**Stratification factors**

- Prior ARPI setting (castration-resistant vs hormone-sensitive)
- BPI-SF worst pain intensity score (0–3 vs > 3)

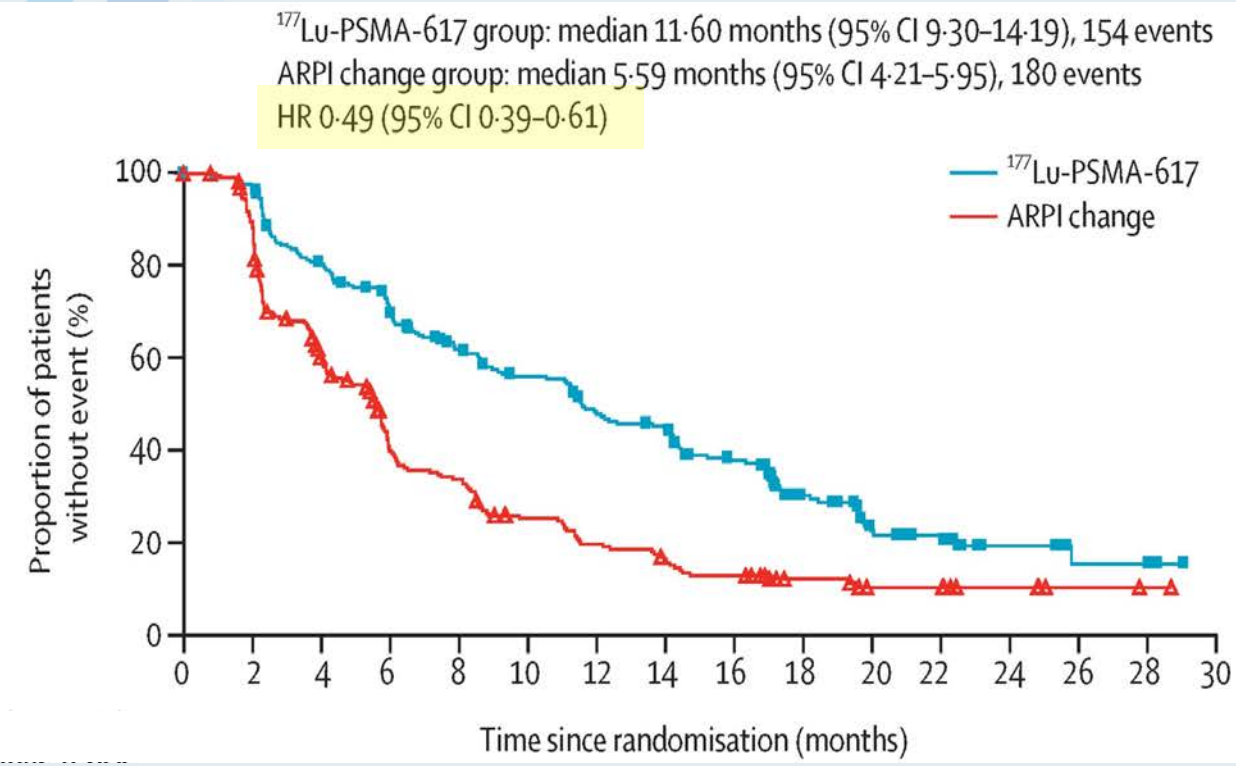
MADRID 2023 ESMO congress


Fizazi K et al. *Ann Oncol* 2025;36(11):1319-1330.
Sartor O et al. ESMO 2023;Abstract LBA13.

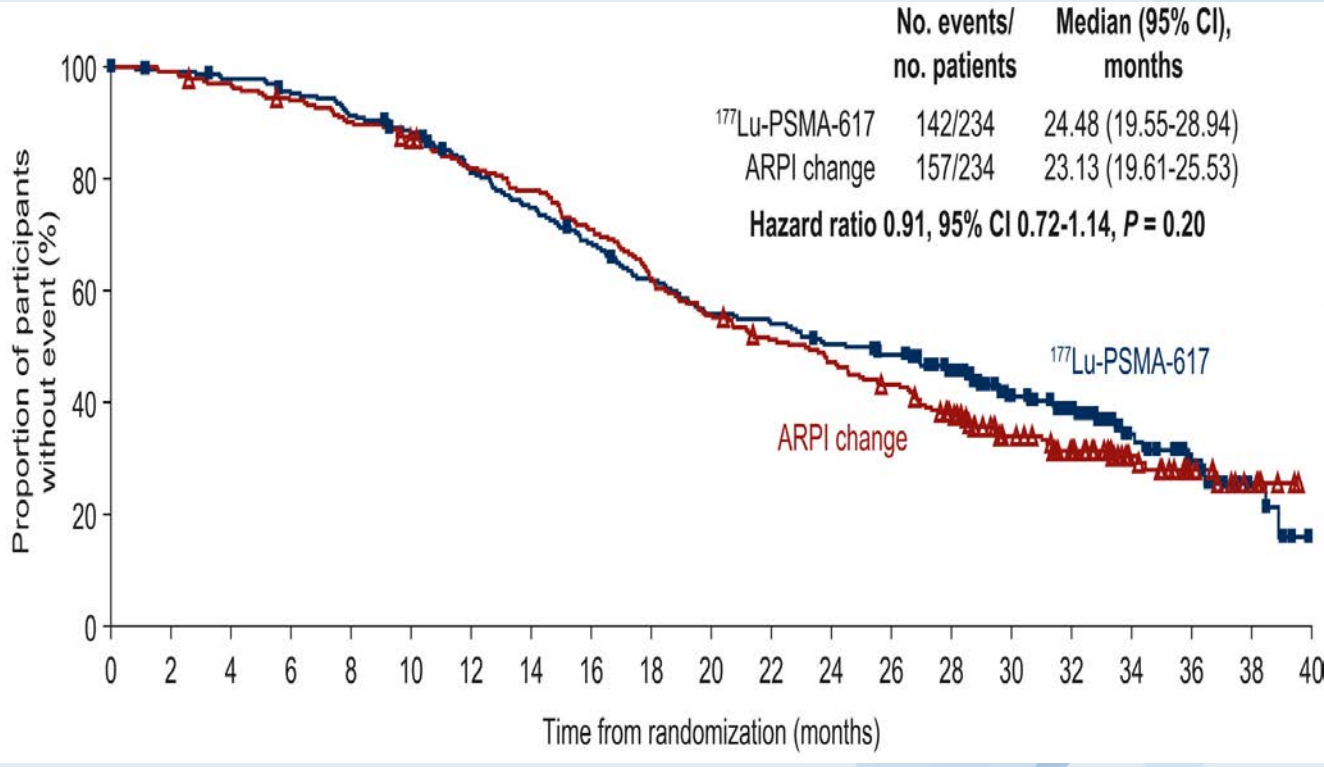

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# Phase III PSMAFore: Survival

## rPFS (Primary endpoint)



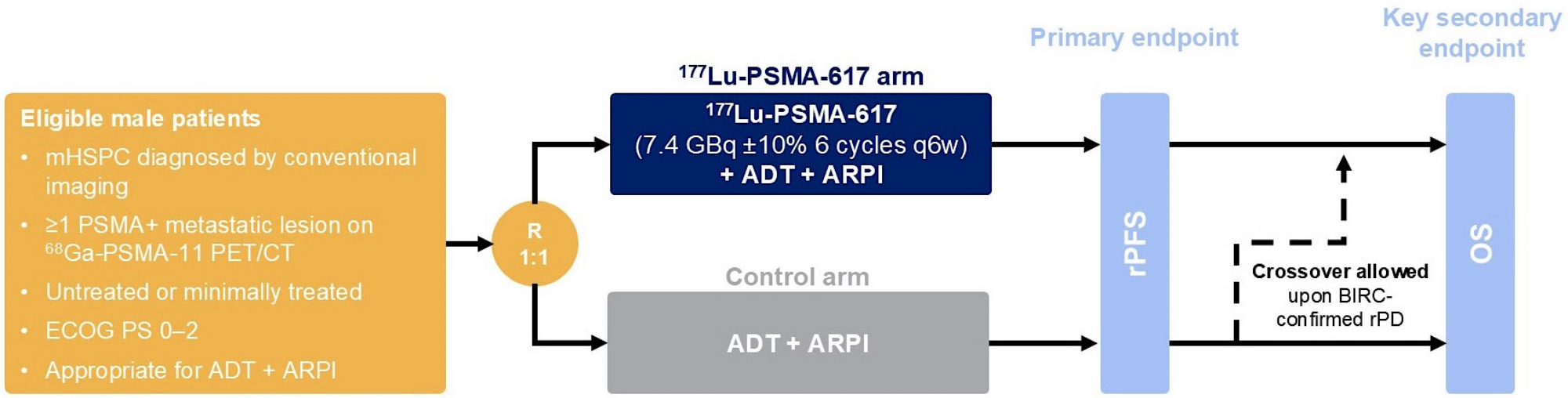

## Final OS (ITT analysis)




ITT = intention to treat


Fizazi K et al. *Ann Oncol* 2025;36(11):1319-1330.
Sartor O et al. ESMO 2023;Abstract LBA13.

# Phase III PSMAddition Study Design




**We now report data by subgroups of patients by:**

**Disease volume per CHAARTED criteria using conventional imaging**
- **High:** presence of visceral metastases and/or ≥4 bone lesions with ≥1 lesions beyond the vertebral bodies and pelvis
- **Low:** absence of high disease volume

**mHSPC status**
- ***De novo*:** stage IVB at initial diagnosis[2]
- **Recurrent:** stage below IVB at initial diagnosis[2]

ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; BIRC, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; IA2, second interim analysis; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PET/CT, positron emission therapy/computed tomography; PSMA, prostate-specific membrane antigen; rPD, radiographic progression of disease; rPFS, radiographic progression-free survival. 1. Tagawa ST *et al. Ann Oncol* 2025;36:S1627–8 (ESMO 2025); 2. *AJCC Cancer Staging Manual* 8th edition

Tagawa ST et al. *Lancet* 2026;408(10557):793-807.
Saad F et al. ASCO 2026;Abstract 5020.

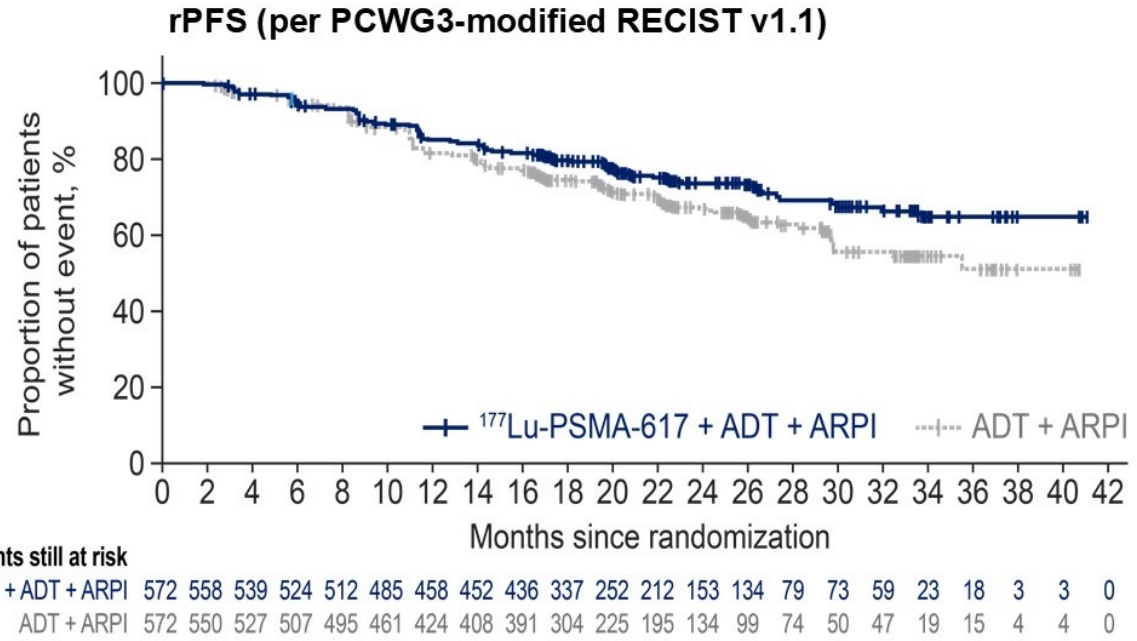
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# Phase III PSMAddition: Key Results from Second Interim Analysis

**rPFS primary endpoint (met)[1]**

- Significantly improved rPFS with $^{177}$Lu-PSMA-617 + ADT + ARPI versus ADT + ARPI at IA2

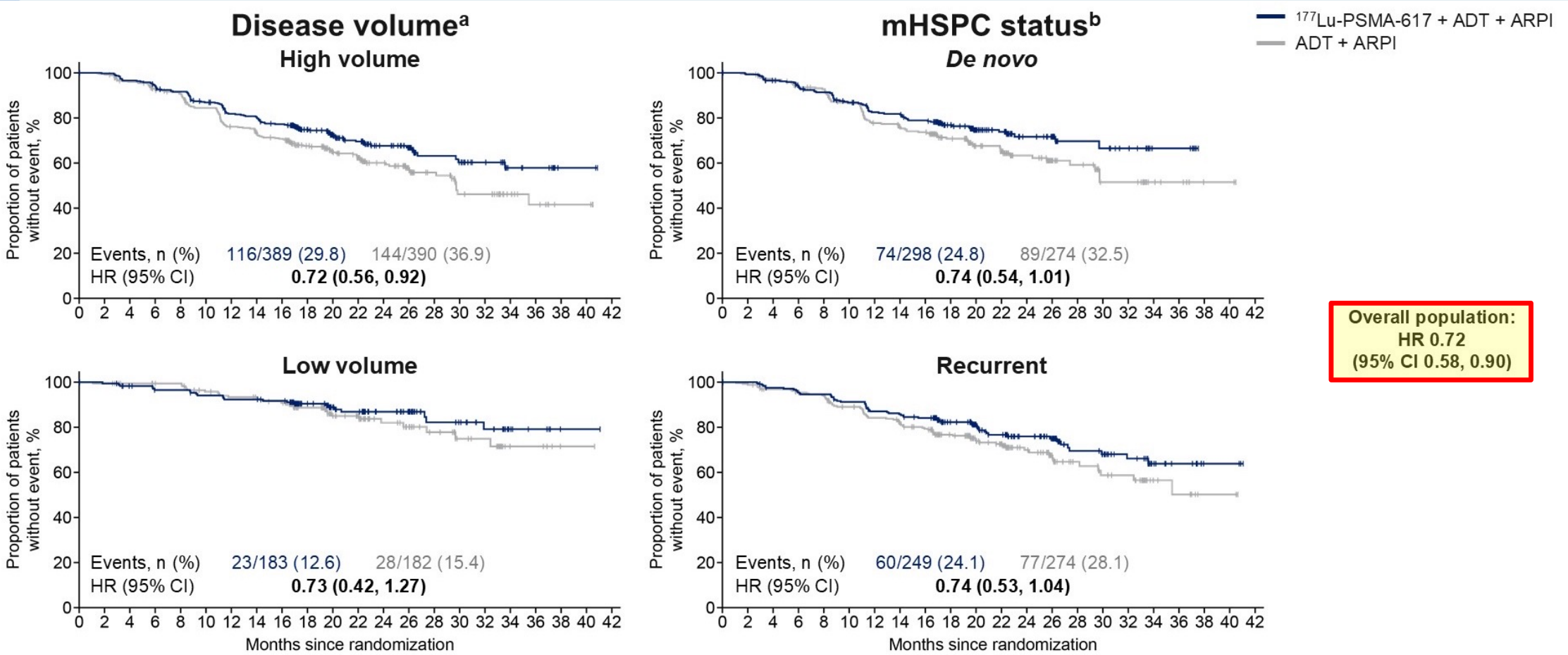
| | $^{177}$Lu-PSMA-617 + ADT + ARPI n = 572 | ADT + ARPI n = 572 |
|---|---|---|
| Median rPFS (95% CI) – months | NR (NE–NE) | NR (29.7–NE) |
| **HR (95% CI)[a]** | **0.72 (0.58, 0.90)** ***p* = 0.002** | |




[a]Significance threshold at rPFS IA2: 0.009 (one-sided; stratified log-rank test); information fraction, 74.4%
ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; CI, confidence interval; HR, hazard ratio; IA2, second interim analysis; NE, not evaluable; NR, not reached; rPFS, radiographic progression-free survival. 1. Tagawa ST *et al. Ann Oncol* 2025;36:S1627–8 (ESMO 2025)


Tagawa ST et al. *Lancet* 2026;408(10557):793-807.
Tagawa ST et al. ESMO 2025;Abstract LBA6.
Saad F et al. ASCO 2026;Abstract 5020.

# Phase III PSMAddition: rPFS by Subgroup




rPFS per PCWG3-modified RECIST v1.1 (primary endpoint). [a]Per CHAARTED criteria using conventional imaging. [b]Subgroup not prespecified; *de novo:* stage IVB at initial diagnosis *(AJCC Cancer Staging Manual* 8th edition). ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; rPFS, radiographic progression-free survival

Tagawa ST et al. *Lancet* 2026;408(10557):793-807.
Saad F et al. ASCO 2026;Abstract 5020.

# Phase III PSMAddition: Safety

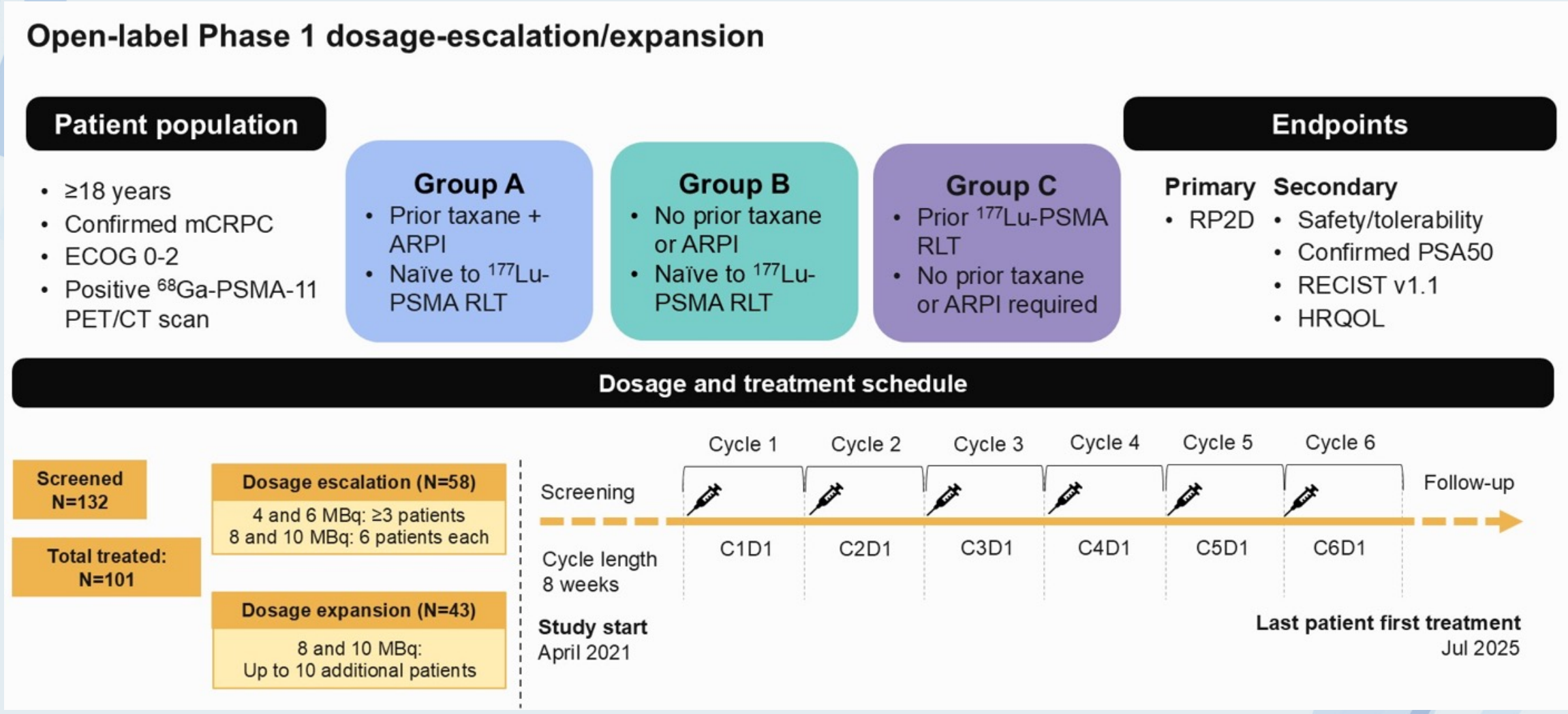
| | Disease volume[a] | | | | mHSPC status[b,c] | | | |
|---|---|---|---|---|---|---|---|---|
| | $^{177}$Lu-PSMA-617 + ADT + ARPI | | ADT + ARPI | | $^{177}$Lu-PSMA-617 + ADT + ARPI | | ADT + ARPI | |
| | High (n = 387) | Low (n = 177) | High (n = 385) | Low (n = 180) | *De novo* (n = 296) | Recurrent (n = 244) | *De novo* (n = 271) | Recurrent (n = 270) |
| **Patients with AE** – n (%) | | | | | | | | |
| Any | 381 (98.4) | 174 (98.3) | 373 (96.9) | 173 (96.1) | 291 (98.3) | 240 (98.4) | 263 (97.0) | 259 (95.9) |
| Grade ≥3 | 202 (52.2) | 84 (47.5) | 173 (44.9) | 70 (38.9) | 145 (49.0) | 129 (52.9) | 125 (46.1) | 108 (40.0) |
| Serious | 129 (33.3) | 51 (28.8) | 117 (30.4) | 45 (25.0) | 94 (31.8) | 80 (32.8) | 80 (29.5) | 72 (26.7) |
| Leading to $^{177}$Lu-PSMA-617 discontinuation | 34 (8.8) | 11 (6.2) | NA | NA | 20 (6.8) | 23 (9.4) | NA | NA |
| Safety topics of interest (patients with AE in grouping)[d] | | | | | | | | |
| Cytopenias | 170 (43.9) | 78 (44.1) | 82 (21.3) | 33 (18.3) | 121 (40.9) | 114 (46.7) | 59 (21.8) | 52 (19.3) |
| Dry mouth | 170 (43.9) | 92 (52.0) | 16 (4.2) | 6 (3.3) | 127 (42.9) | 124 (50.8) | 9 (3.3) | 13 (4.8) |
| Renal events | 27 (7.0) | 13 (7.3) | 20 (5.2) | 6 (3.3) | 19 (6.4) | 19 (7.8) | 10 (3.7) | 15 (5.6) |
| Second primary malignancies | 25 (6.5) | 12 (6.8) | 20 (5.2) | 11 (6.1) | 16 (5.4) | 20 (8.2) | 13 (4.8) | 15 (5.6) |

Safety set
[a]Per CHAARTED criteria using conventional imaging. [b]Subgroup not prespecified; *de novo:* stage IVB at initial diagnosis *(AJCC Cancer Staging Manual* 8th edition). [c]49 patients had missing mHSPC stage at initial diagnosis (25 in the $^{177}$Lu-PSMA-617 arm; 24 in the control arm). [d]Not all safety topics of interest reported here
ADT, androgen deprivation therapy; AE, adverse event; ARPI, androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; NA, not applicable

Tagawa ST et al. *Lancet* 2026;408(10557):793-807.
Saad F et al. ASCO 2026;Abstract 5020.

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# Phase I AcTION Study Design




Emmett L et al. ASCO 2026;Abstract 5010.

# Phase I AcTION: Safety Profile and Antitumor Activity

| **Overall pts** | **A: Prior ChT + ARPI; N=34** | **B: ChT/ARPI-naive; N=27** | **C: Prior $^{177}$Lu-PSMA RLT; N=40** |
|---|---|---|---|
| **Selected AEs regardless of study dose, n (%): All Gs / G ≥3** | | | |
| Dry mouth | 33 (97.1) / 0 | 26 (96.3) / 0 | 36 (90.0) / 0 |
| Fatigue | 18 (52.9) / 0 | 4 (14.8) / 0 | 27 (67.5) / 0 |
| Anemia | 9 (26.5) / 6 (17.6) | 4 (14.8) / 4 (14.8) | 16 (40.0) / 6 (15.0) |
| Thrombocytopenia | 2 (5.9) / 0 | 2 (7.4) / 1 (3.7) | 5 (12.5) / 0 |
| Renal impairment | 1 (2.9) / 1 (2.9) | 0 / 0 | 3 (7.5) / 1 (2.5) |
| **Anti-tumor activity, n (%) [95% CI]** | | | |
| PSA50 | 20 (**58.8%**) [40.7, 75.4] | 23 (**85.2%**) [66.3, 95.8] | 21 (**52.5%**) [36.1, 68.5] |
| PSA90 | 15 (**44.1%**) [27.2, 62.1] | 22 (**81.5%**) [61.9, 93.7] | 7 (**17.5%**) [7.3, 32.8] |

ChT = chemotherapy; RLT = radioligand therapy

Emmett L et al. ASCO 2026;Abstract 5010.

RTP RESEARCH TO PRACTICE

$^{255}$Ac-PSMA-I&T - zadavotide guraxetan

# Phase II TATCIST Study Design

**Participant population:** Progressive mCRPC based on serum PSA, soft tissue, and/or bone progression; positive PSMA PET/CT[a] scans to confirm PSMA expression; ECOG PS 0–2/0–1[b]

Enrolling in the US

**Key Inclusion Criteria**
- Progressive mCRPC
- Positive PSMA PET/CT
- Must have received ≥1 ARPI
- Prior Lu-PSMA RLT permitted
- Prior taxanes were allowed

**Key Exclusion Criteria**
- <6 weeks from prior myelosuppressive therapy
- Skeletal metastases presenting as superscan[b,d]
- Known CNS or liver metastases[b]
- >4 prior therapies[b]

**FPI-2265**
**100 kBq/kg (± 10%) IV**
every 8 weeks
for up to 4 cycles[c]

**Dose could be de-escalated based on PSA response:**
- PSA ≥50% decline: dose should be de-escalated to 87 kBq/kg
- PSA >85% decline: additional de-escalation to 75 kBq/kg, then 50 kBq/kg

**Primary endpoint:**
- PSA50 (≥50% decline in PSA by 12 weeks after first treatment)

**Secondary endpoints include:**
- Safety and tolerability
- Maximum % PSA decline
- Response based on RECIST v1.1 criteria
- Non-progression by PCWG3

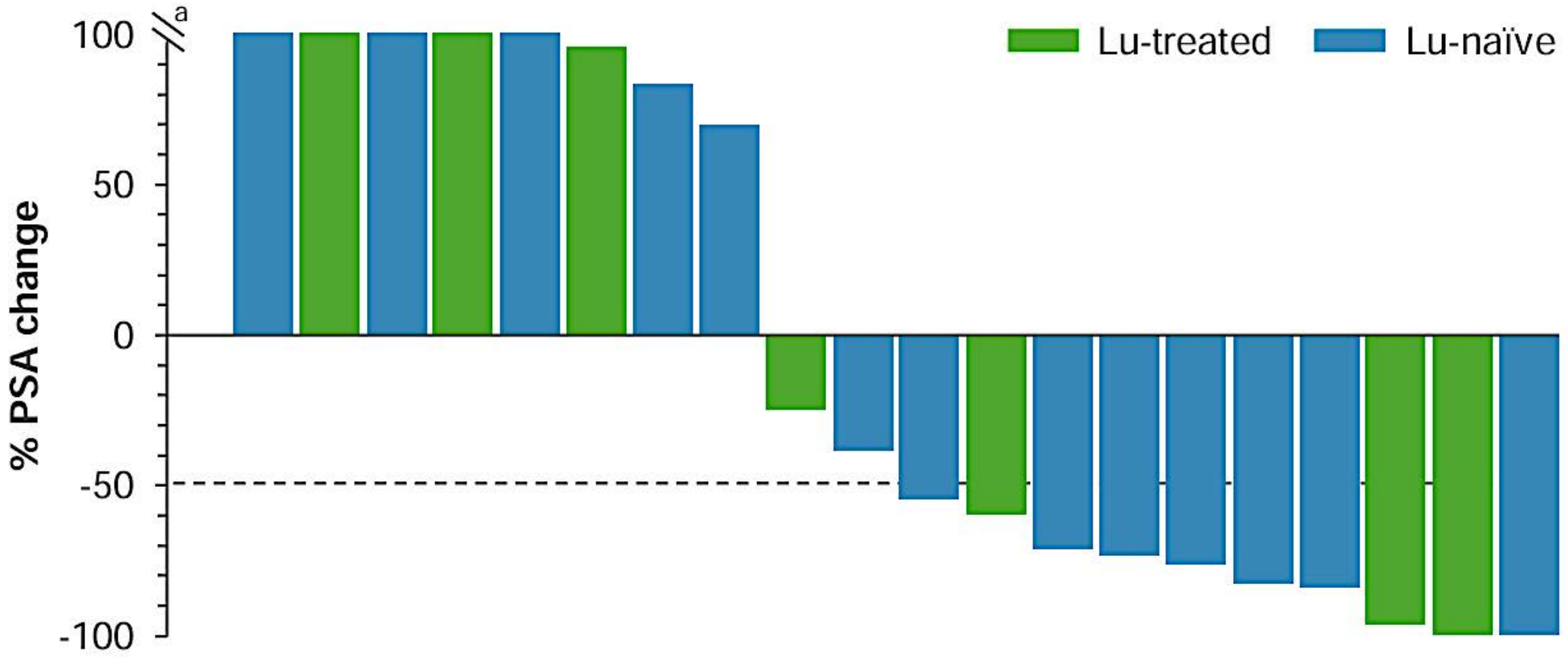
Delpassand et al. AACR 2024;Abstract CT224.

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$^{255}$Ac-PSMA-I&T - zadavotide guraxetan

# Phase II TATCIST: PSA50 Response

**Figure 4. Maximum percent PSA change from baseline during the treatment period (weeks 0–28) by prior Lu treatment**




[a]% maximum PSA increase shown to 100%.

PSA50 = drop in blood PSA level by at least 50% from baseline

Delpassand et al. AACR 2024;Abstract CT224.

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# Phase I PAnTHa Study Design

## Dose Escalation Phase

### Patient population

- ≥18 years of age
- ECOG PS 0 or 1
- Confirmed mCRPC
- ≥1 PSMA-positive metastases[a]
- Prior ARPI treatment
- 1 or 2 prior taxanes[b]
- No prior radionuclide therapy

### Objectives

**Primary objectives:**

- Safety
- Efficacy
- Establish recommended dose for expansion (RDE)
- **Exploratory analyses:**
- Baseline PSMA PET SUVmean
- Longitudinal ctDNA

1 or 2 prior taxanes[b] in the castration-resistant setting

No prior radionuclide therapy

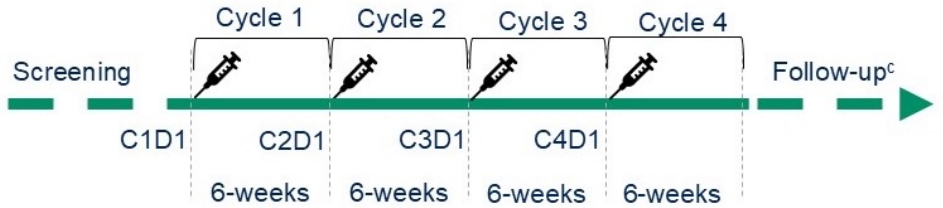
Dose expansion

| Group A | Group B | Group C |
|---|---|---|
| 1 or 2 prior taxanes in the castration-resistant setting<br>No prior radionuclides | No prior taxane chemotherapy since castration-resistance<br>No prior radionuclides | 1 or 2 prior taxanes<br>Prior treatment with $^{177}$Lu-PSMA |

### Dosing

- $^{225}$Ac-PSMA-Trillium administered on Day 1 of a 6-week cycle for max 4 cycles over 18 weeks
  - Dose range 75–150 kBq/kg
  - 3–4 patients were treated per dose level
- Based on safety and preliminary efficacy data, select dose cohorts were backfilled with up to 9 additional patients for determination of the RDE

### Treatment schedule




[a]No significant PSMA-negative lesions. [b]Unless refused or ineligible. [c]Data cut off 29 December 2025

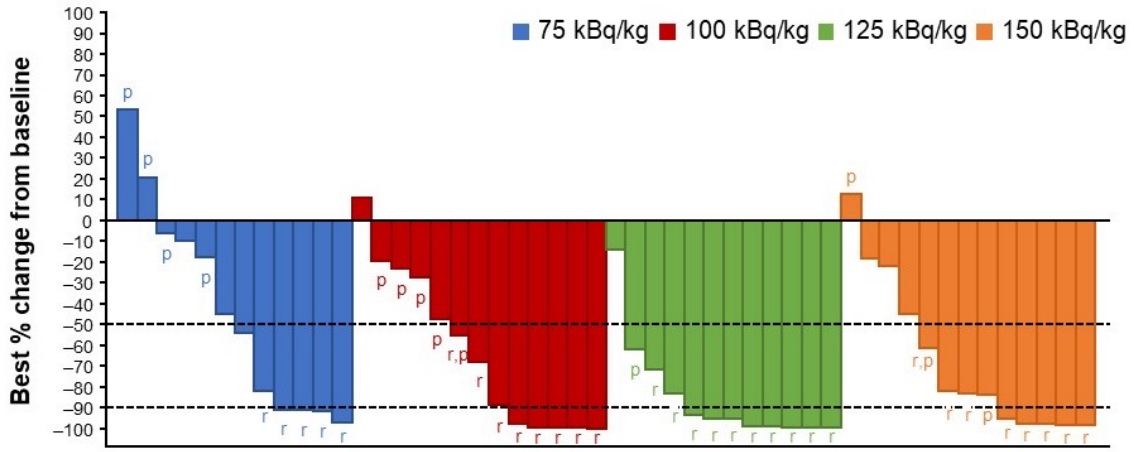
$^{177}$Lu, lutetium-177; $^{225}$Ac, Actinium-225; ARPI, androgen receptor pathway inhibitor; ctDNA, circulating tumor DNA; ECOG PS, Eastern Cooperative Oncology Group performance status; mCRPC, metastatic castration-resistant prostate cancer; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; RDE, recommended dose for expansion; SUV, standardized uptake value.

Saad F et al. Genitourinary Cancers Symposium 2026;Abstract 19.

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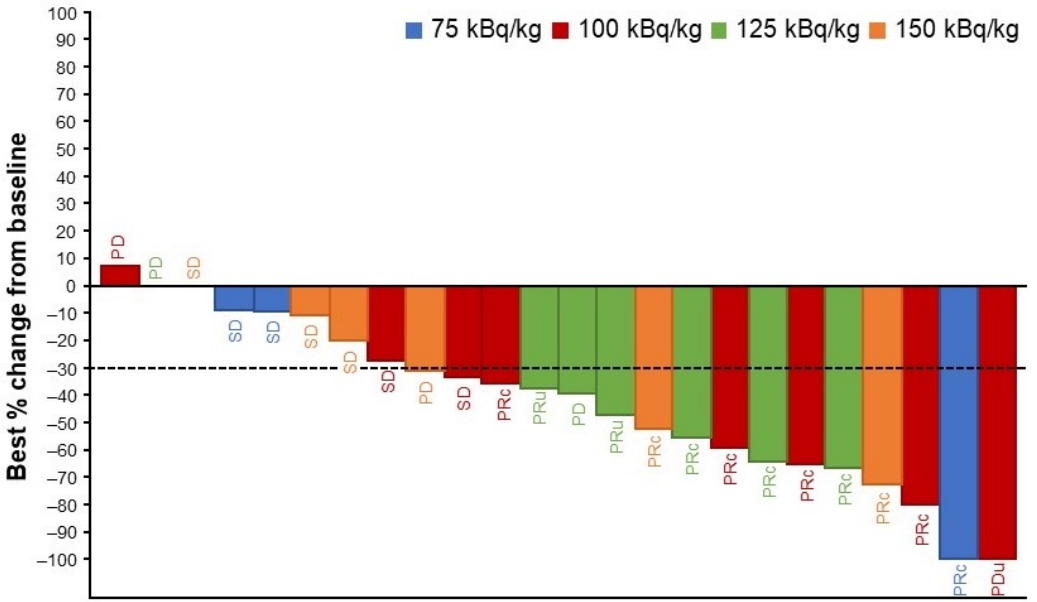
# Phase I PAnTHa: Responses

## PSA response (N=50)




| | All patients (N=50) | 125 kBq/kg dose (N=12) |
|---|---|---|
| **PSA50 response rate, %** | 62 | 83 |
| **PSA90 response rate, %** | 40 | 67 |
| **Overall response rate[a,c], %** | | |
| Confirmed responses only | 42 | 43 |
| Confirmed and unconfirmed | 50 | 71 |
| **Disease control rate[a,c], %** | 79 | 71 |

## Radiographic response (N=24)[a,b]




**Based on the observed efficacy and safety data, the recommended dose for expansion was established as 125 kBq/kg**

[a]Only patients with measurable disease at baseline. [b]Sum of diameters of all target lesions. Longest diameter for non-nodal target lesions and short-axis for nodal target lesions. [c]Per PCWG3 criteria; for all patients N=24; for 125kBq/kg dose n=7. $^{225}$Ac, Actinium-225; mCRPC, metastatic castration-resistant prostate cancer; p, confirmed PSA progression; PCWG3, Prostate Cancer Working Group 3; PD, progressive disease; PDu, unconfirmed progressive disease; PRc, confirmed partial response; PRu, unconfirmed partial response; PSA, prostate-specific antigen; PSAx response, decline of x% from baseline in PSA; r, confirmed PSA response; r,p, confirmed PSA response and subsequent progression; SD, stable disease.

Saad F et al. Genitourinary Cancers Symposium 2026;Abstract 19.

# Select Ongoing Phase III Trials for PSMA-Positive mCRPC

| Trial name | ClinicalTrials.gov ID | Investigational agent | Comparator arm |
|---|---|---|---|
| VECTRA-01 | NCT07611110 | $^{225}$Ac-PSMA-I&T (zadavotide guraxetan) | Investigator's choice of SOC |
| AcTFirst | NCT06855277 | $^{255}$Ac-PSMA-Trillium | Investigator's choice of SOC |
| PSMAcTION | NCT06780670 | $^{225}$Ac-PSMA-617 | Investigator's choice of SOC |

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# Faculty Discussion



Dr Zafar

# Questions for the Faculty

**A man in his mid 50s presented with de novo metastatic, high-volume, mostly bone disease. Very healthy otherwise. Very educated. He meets the CHAARTED criteria with multiple bone lesions but also the recent first-line lutetium approval, but I told him we don't have any overall survival data**

**The patient did his own research. We went back and forth about doublet versus triplet. But he decided to do the lutetium and he just started, and he's also receiving relugolix and darolutamide.**

**Questions**

- When are you opting for lutetium-based therapy for your patients with mHSPC? What about mCRPC?
- Do you see cytopenias with lutetium? What management strategies do you employ to treat dry mouth?
- Do you think it's necessary to give patients all 6 doses of lutetium?

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Dr Gandhi

# Questions for the Faculty

**88-year-old Vietnamese man with de novo metastatic disease to the bone did well for 3 years on hormone management but then had disease progression**

**Now doing very well on lutetium with relief of bone pain and reduced PSA levels — no tolerability issues at all**

**Questions**

- If he has disease progression and a return of his bone pain, what do I do?
- Like almost all patients this age, he does not want chemotherapy. Any new agents in clinical trials that might be helpful? Other radioligands (actinium)? PROTACs? Bispecific antibodies? Novel agents that would be safe in very elderly patients?

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# Integrating New Advances into Community Oncology Practice

*CME/MOC, NCPD and ACPE Accredited*

**Saturday, October 17, 2026**
**7:15 AM – 12:00 PM ET**

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# Agenda

**Module 1 — Breast Cancer:** *Drs Geyer, Lustberg, Nanda and Wander*

**Module 2 — Prostate Cancer:** *Drs Agarwal and Antonarakis*

**Module 3 — Multiple Myeloma:** *Drs Lonial and Richardson*

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# Multiple Myeloma Faculty



**Sagar Lonial, MD, FACP, FASCO**
Chair and Professor
Department of Hematology and Medical Oncology
Anne and Bernard Gray Family Chair in Cancer
Chief Medical Officer
Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia



**Paul G Richardson, MD**
Clinical Program Leader and Director of Clinical Research
Jerome Lipper Multiple Myeloma Center
Dana-Farber Cancer Institute
RJ Corman Professor of Medicine
Harvard Medical School
Boston, Massachusetts

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# Consulting General Medical Oncologists



**Susmitha Apuri, MD**
Florida Cancer Specialists & Research Institute
Inverness and Lecanto, Florida



**Mamta Choksi, MD**
Florida Cancer Specialists & Research Institute
Trinity, Florida



**Sunil Gandhi, MD**
Florida Cancer Specialists & Research Institute
Lecanto, Florida



**Shaachi Gupta, MD, MPH**
Florida Cancer Specialists & Research Institute
West Palm Beach, Florida



**Maen Hussein, MD**
Florida Cancer Specialists & Research Institute
The Villages, Florida



**Renjitha Ignatius, MD**
Florida Cancer Specialists & Research Institute
Sun City Center, Florida



**Shachar Peles, MD**
Florida Cancer Specialists & Research Institute
Lake Worth, Florida



**Syed F Zafar, MD**
Florida Cancer Specialists & Research Institute
Fort Myers, Florida

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# Agenda

**Introduction: ESMO 2026; Recent FDA Approvals**

**Chimeric Antigen Receptor T-Cell Therapy – Dr Lonial**

**Bispecific Antibodies – Dr Lonial**

**Antibody-Drug Conjugates – Dr Richardson**

**Up-Front Treatment; CELMoDs – Dr Richardson**

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# Agenda

**Introduction: ESMO 2026; Recent FDA Approvals**

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**Up-Front Treatment; CELMoDs – Dr Richardson**

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# Select ESMO 2026 Abstracts

## Multiple Myeloma

**Abstract 1454O**

High MRD Negativity Rates and Prolonged PFS with Belantamab Mafodotin plus Daratumumab, Lenalidomide, and Dexamethasone in Transplant Ineligible Newly-Diagnosed Myeloma: Results of the Bela-DRd Study
Meletios A Dimopoulos et al.

**Abstract 1455O**

Belantamab Mafodotin with Lenalidomide/Dexamethasone in Newly Diagnosed Not Transplant Eligible Multiple Myeloma: Long-Term Results from the Phase 1/2 BelaRd Clinical Trial
Ioannis Ntanasis-Stathopoulos et al.

**Abstract 1456O**

A First-in-Human Phase I Study of LBL-034, a GPRC5D/CD3 Bispecific Antibody, in Relapsed/Refractory Multiple Myeloma (RRMM)
Xuelin Dou et al.

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# Recent FDA Approvals

| | |
|---|---|
| **FDA APPROVAL**<br>**August 13, 2026** | **Accelerated Approval to Iberdomide with Daratumumab and Hyaluronidase-fihj and Dexamethasone for Multiple Myeloma** |
| **FDA APPROVAL**<br>**March 5, 2026** | **Teclistamab in Combination with Daratumumab and Hyaluronidase-fihj for Relapsed or Refractory Multiple Myeloma** |
| **FDA APPROVAL**<br>**January 27, 2026** | **Daratumumab and Hyaluronidase-fihj with Bortezomib, Lenalidomide, and Dexamethasone for Newly Diagnosed Multiple Myeloma** |

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# Recent FDA Approvals (Continued)

| | |
|---|---|
| **FDA APPROVAL**<br>**November 6, 2025** | **Daratumumab and Hyaluronidase-fihj for High-Risk Smoldering Multiple Myeloma** |
| **FDA APPROVAL**<br>**October 23, 2025** | **Belantamab Mafodotin-blmf for Relapsed or Refractory Multiple Myeloma** |

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# Agenda

**Introduction: ESMO 2026; Recent FDA Approvals**

**Chimeric Antigen Receptor T-Cell Therapy – Dr Lonial**

- Idecabtagene Vicleucel and Ciltacabtagene Autoleucel
- Anitocabtagene Autoleucel and Arlocabtagene Autoleucel

**Bispecific Antibodies – Dr Lonial**

**Antibody-Drug Conjugates – Dr Richardson**

**Up-Front Treatment; CELMoDs – Dr Richardson**

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# Chimeric Antigen Receptor T-Cell Therapy: Idecabtagene Vicleucel and Ciltacabtagene Autoleucel

**Select Datasets**

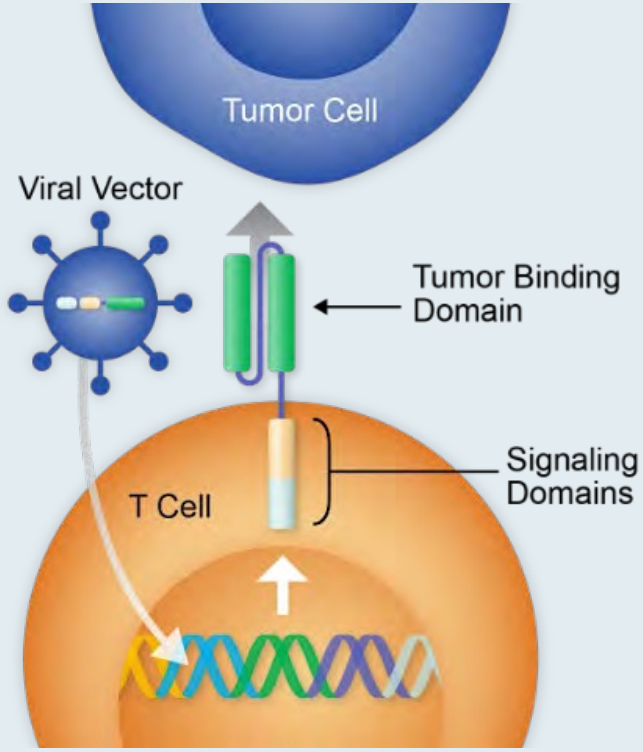
- Einsele H et al. Cilta-cel in Lenalidomide-Refractory Multiple Myeloma (CARTITUDE-4): An Updated Analysis Including Overall Survival from an Open-Label, Multicentre, Randomised, Phase 3 Trial. *Lancet Oncol* 2026;27(2):254-68.

- Cohen AD et al. Long-Term (≥5-Year) Remission and Survival with Ciltacabtagene Autoleucel in Relapsed/Refractory Multiple Myeloma with 1-3 Prior Lines of Therapy: CARTITUDE-2 Cohort A. IMS 2026;Abstract PA-288.

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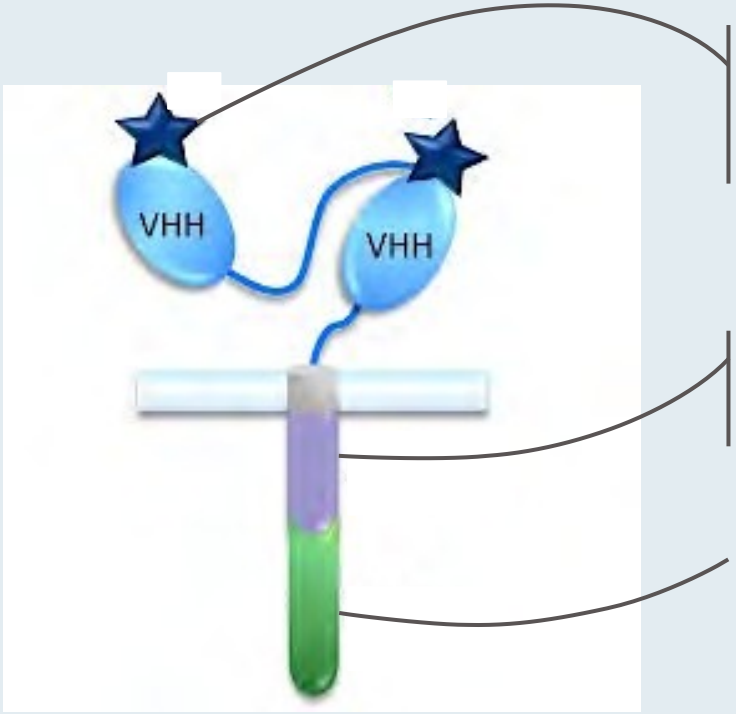
# Ide-cel and Cilta-cel Constructs

## Idecabtagene vicleucel (ide-cel) CAR T




Second-generation CAR construct[1]

## Ciltacabtagene autoleucel (cilta-cel) CAR T




**Two BCMA-targeting domains[3]**

The two BCMA-targeting single-domain antibodies were designed to confer high avidity binding

**4-1BB[4]**

**CD3-ζ[5]**

Dual epitope-binding CAR construct[1,2]

Content courtesy of Noopur Raje, MD

CAR = chimeric antigen receptor; BCMA = B-cell maturation antigen; CD = cluster of differentiation

1. Raje N et al. *N Engl J Med* 2019;380(18):1726-37. 2. Friedman KM et al. *Hum Gene Ther* 2018;29(5):585-601. 3. Song DG et al. *Cancer Res* 2011;71(13):4617-27.
Zhao WH et al. *J Hematol Oncol* 2018;11(1):141. Berdeja JG et al. ASCO 2020;Abstract 8505.

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# Ide-cel and Cilta-cel for Heavily Pretreated Multiple Myeloma

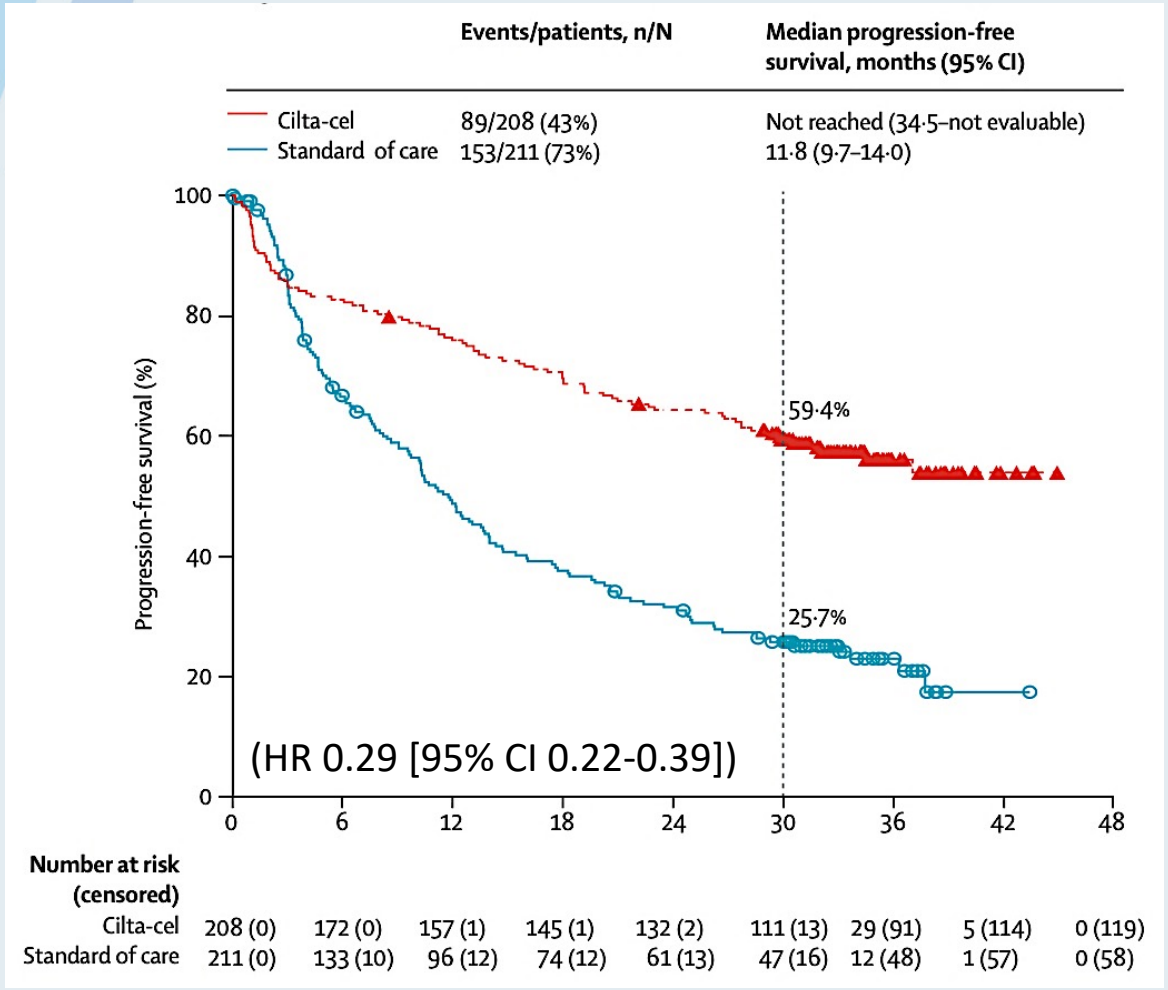
| Parameter | KarMMa[1]<br>Ide-cel<br>N = 128 | CARTITUDE-1[2,3]<br>Cilta-cel<br>N = 97 |
|---|---|---|
| Inclusion criteria | • ≥3 prior regimens<br>• Prior PI, IMiD and anti-CD38 mAb exposure | • ≥3 prior regimens or double refractory to a PI and an IMiD<br>• Prior PI, IMiD and anti-CD38 mAb exposure |
| Overall response | 73% | 97.9% |
| PFS | Median 8.6 mo | 33% of patients were progression-free at ≥5 years |
| Median OS | 24.8 mo | 60.7 mo |

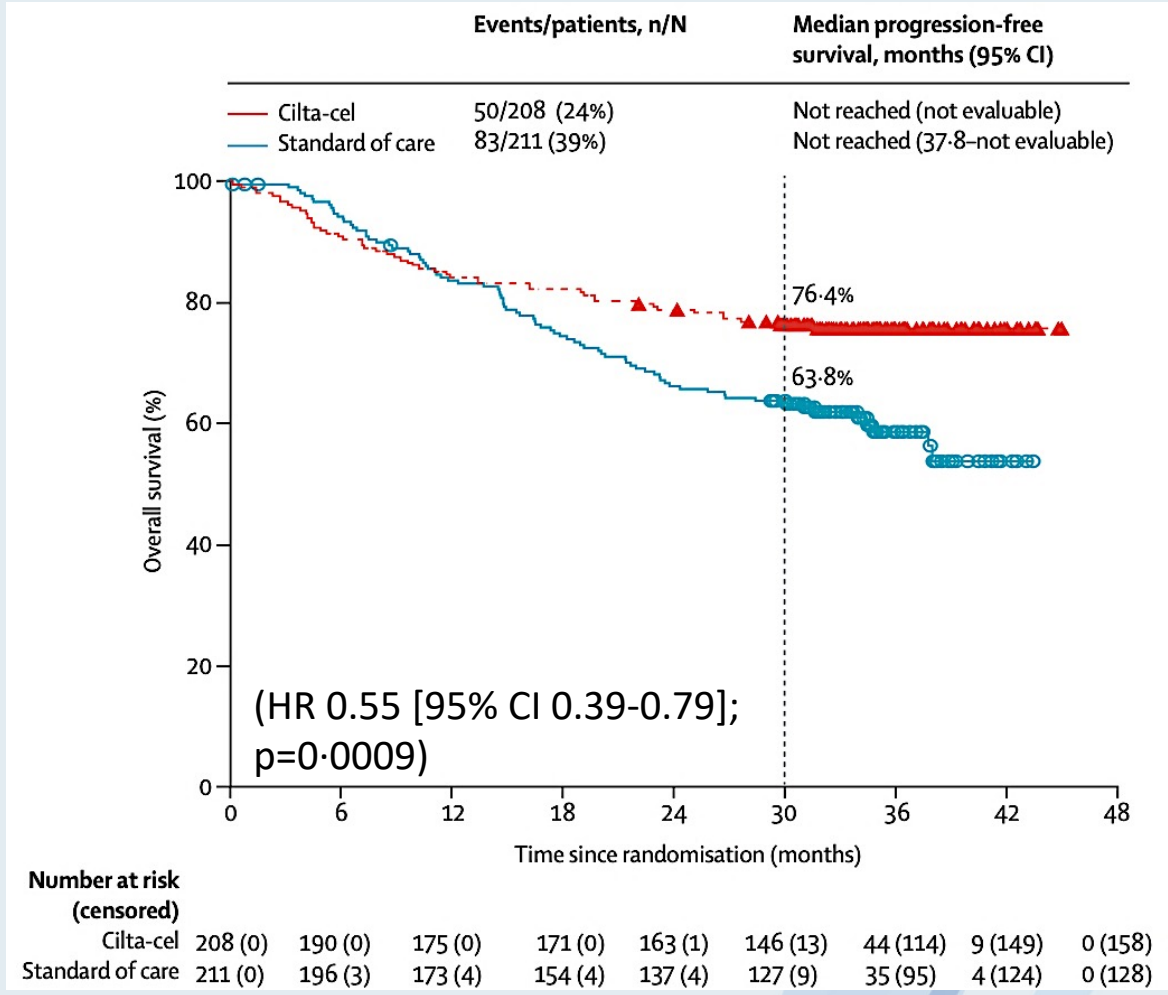
PI = proteasome inhibitor; IMiD = immunomodulatory drug; mAb = monoclonal antibody; PFS = progression-free survival; OS = overall survival

[1] Anderson LD et al. IMW 2021;Abstract OAB27; [2] Voorhees PM et al. ASCO 2025;Abstract 7507; [3] Jagannath S et al. *J Clin Oncol* 2025;43(25):2766-71.

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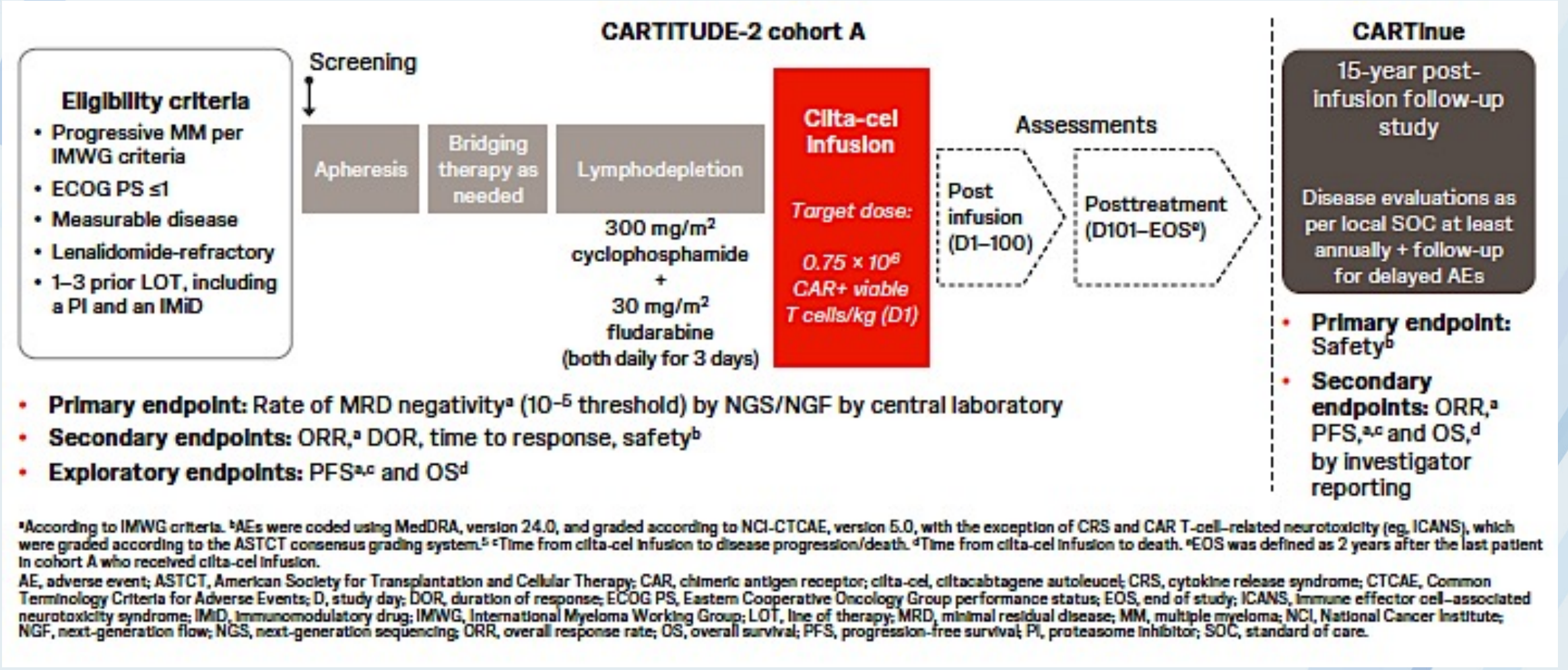
# CARTITUDE-4 Study: PFS and OS with Cilta-cel versus Standard Therapy After 1 to 3 Prior Lines of Treatment




Einsele H et al. *Lancet Oncol* 2026;27(2):254-68.

# Phase II CARTITUDE-2 Study of Cilta-cel for Relapsed/Refractory MM: Cohort A



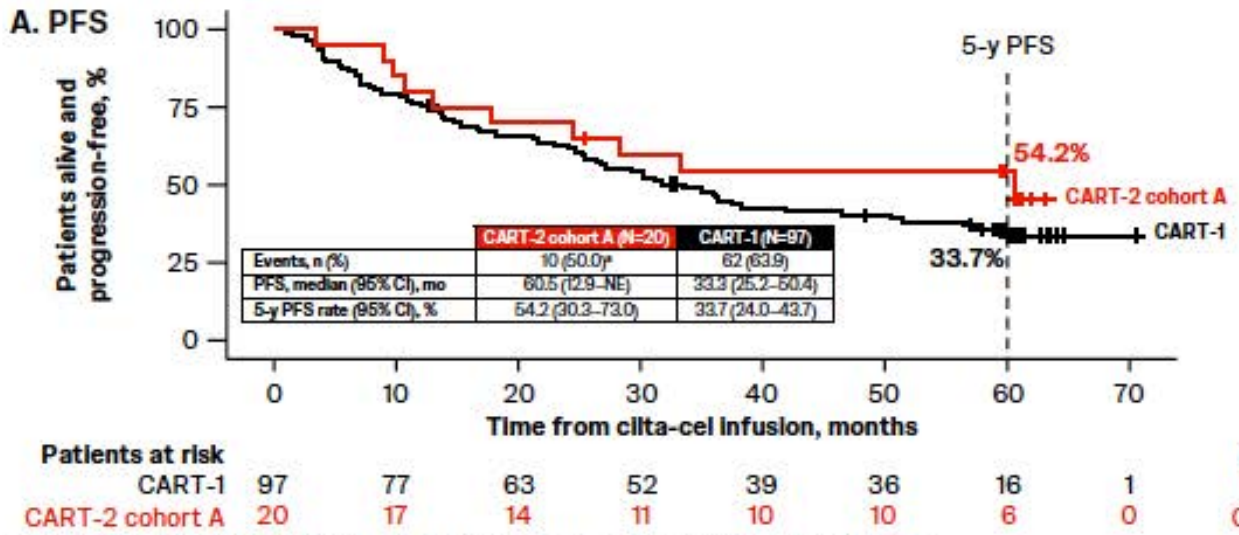

[a]According to IMWG criteria. [b]AEs were coded using MedDRA, version 24.0, and graded according to NCI-CTCAE, version 5.0, with the exception of CRS and CAR T-cell–related neurotoxicity (eg, ICANS), which were graded according to the ASTCT consensus grading system.[5] [c]Time from cilta-cel infusion to disease progression/death. [d]Time from cilta-cel infusion to death. [e]EOS was defined as 2 years after the last patient in cohort A who received cilta-cel infusion.

AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; D, study day; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOS, end of study; ICANS, immune effector cell–associated neurotoxicity syndrome; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; LOT, line of therapy; MRD, minimal residual disease; MM, multiple myeloma; NCI, National Cancer Institute; NGF, next-generation flow; NGS, next-generation sequencing; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; SOC, standard of care.

Cohen AD et al. IMS 2026;Abstract PA-288.

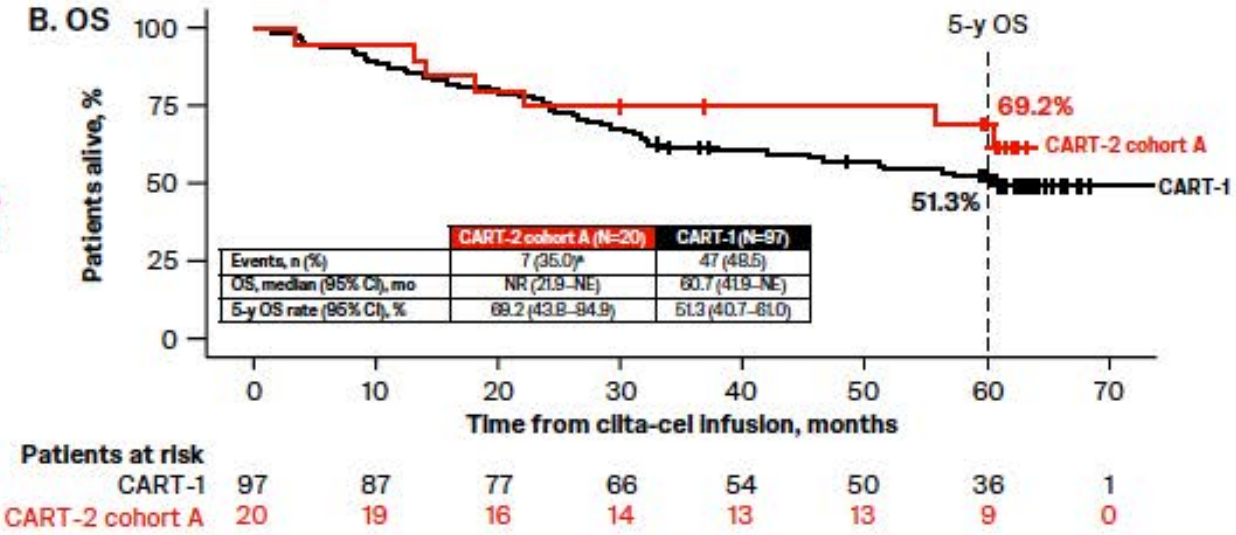
# CARTITUDE-2 Cohort A: Long-Term Remissions and Survival with Cilta-cel for Relapsed/Refractory MM

**Figure 3: Earlier use of cilta-cel was associated with numerically higher PFS and OS than observed in CARTITUDE-1 which enrolled patients with ≥3 prior LOT**




| | CART-2 cohort A (N=20) | CART-1 (N=97) |
|---|---|---|
| Events, n (%) | 10 (50.0)* | 62 (63.9) |
| PFS, median (95% CI), mo | 60.5 (12.9–NE) | 33.3 (25.2–50.4) |
| 5-y PFS rate (95% CI), % | 54.2 (30.3–73.0) | 33.7 (24.0–43.7) |

| Patients at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| CART-1 | 97 | 77 | 63 | 52 | 39 | 36 | 16 | 1 |
| CART-2 cohort A | 20 | 17 | 14 | 11 | 10 | 10 | 6 | 0 |




| | CART-2 cohort A (N=20) | CART-1 (N=97) |
|---|---|---|
| Events, n (%) | 7 (35.0)* | 47 (48.5) |
| OS, median (95% CI), mo | NR (21.9–NE) | 60.7 (41.9–NE) |
| 5-y OS rate (95% CI), % | 69.2 (43.8–84.9) | 51.3 (40.7–61.0) |

| Patients at risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| CART-1 | 97 | 87 | 77 | 66 | 54 | 50 | 36 | 1 |
| CART-2 cohort A | 20 | 19 | 16 | 14 | 13 | 13 | 9 | 0 |

*In C-2 cohort A, 1 PFS/OS event after 5 years was a death due to unrelated breast cancer without progression of myeloma.
CART-1, CARTITUDE-1; CART-2, CARTITUDE-2; cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

- 95% (19/20) of patients achieved CR/stringent CR as their best response. One patient had minimal response and died due to COVID-19 pneumonia
- Three patients among those alive and progression-free at ≥5 years underwent assessment by bone marrow at ≥5 years (not required per protocol) and all were MRD-negative (at the $10^{-6}$ threshold)

CR, complete response; MRD, minimal residual disease.

Cohen AD et al. IMS 2026;Abstract PA-288.

# CAR T-Cell Therapy: Anitocabtagene Autoleucel and Arlocabtagene Autoleucel

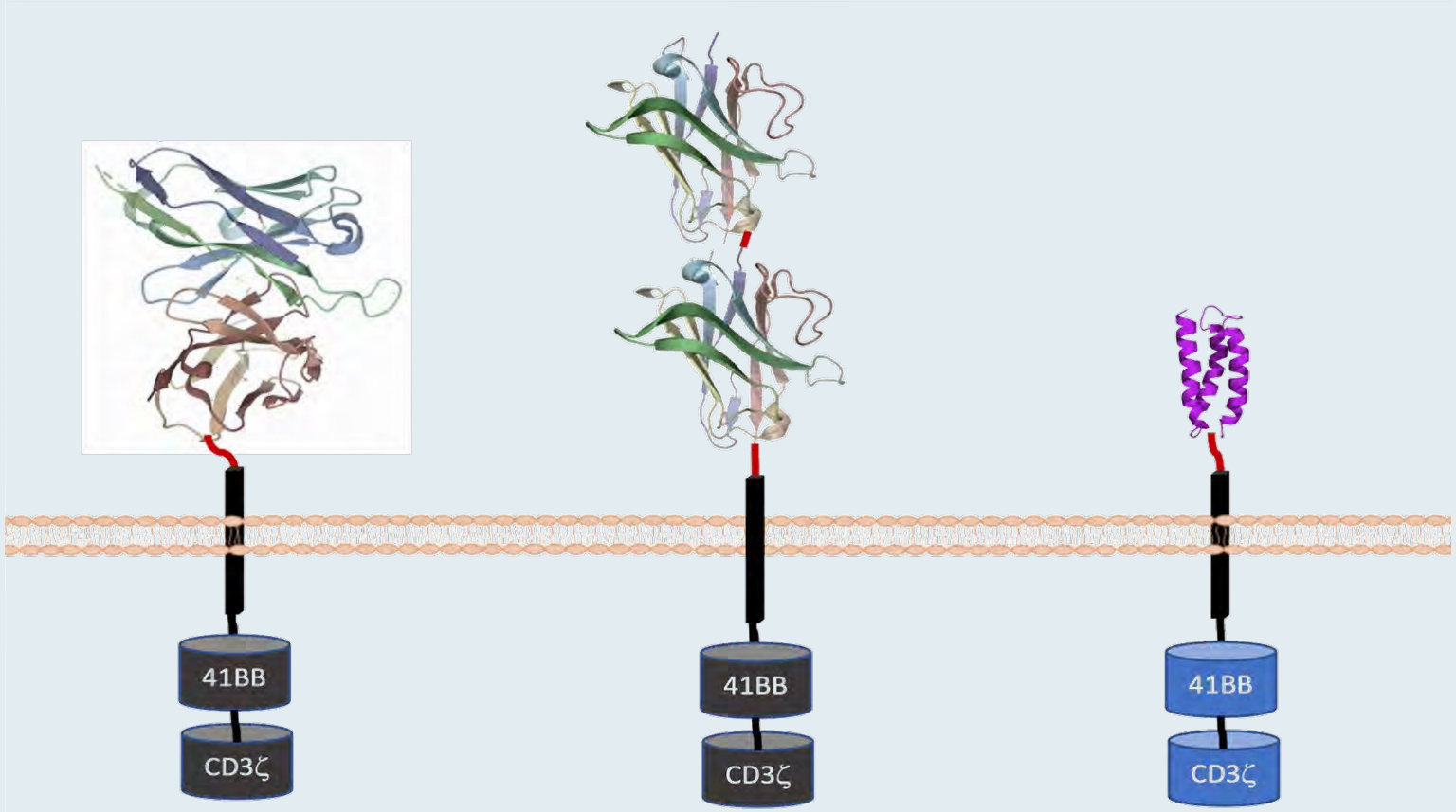
## Select Datasets

- Patel K et al. Phase 2 Registrational Study of Anitocabtagene Autoleucel for the Treatment of Patients with Relapsed and/or Refractory Multiple Myeloma: Updated Results from iMMagine-1. ASH 2025;Abstract 256.
- Martin T et al. IMMAGINE-3: A Phase 3, Randomized Study to Compare the Efficacy and Safety of Anitocabtagene Autoleucel (Anito-cel) with Standard of Care in Patients with Relapsed/Refractory Multiple Myeloma (RRMM). EHA 2024;Abstract PB2724.
- Bal S et al. Arlocabtagene Autoleucel: A GPRC5D-targeted CAR T-Cell Therapy for Heavily Pretreated Relapsed/Refractory Multiple Myeloma. *Blood* 2026;148(10):1240-50.
- Bal S et al. Efficacy and Safety with Extended Follow-Up in a Phase 1 Study of BMS-986393, a G Protein-Coupled Receptor Class C Group 5 Member D (GPRC5D)-Targeted CAR T Cell Therapy, in Patients (Pts) with Heavily Pretreated Relapsed/Refractory (RR) Multiple Myeloma (MM). ASH 2024;Abstract 922.
- Lebel E et al. QUINTESSENTIAL-2: A Phase 3 Study of Arlocabtagene Autoleucel versus Standard of Care in Adult Patients with Relapsed and Refractory Multiple Myeloma (RRMM) Exposed to Lenalidomide. ASCO 2026;Abstract TPS7577.

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# Anitocabtagene Autoleucel (Anito-cel, CART-ddBCMA)

## Autologous BCMA-directed CAR T-cell therapy using a novel D-Domain binder[1]




scFv
(~25 kDa)

Bivalent camelid VHh
(~25 kDa)

**D-Domain**
**(~8 kDa)**

### D-Domain attributes: nonantibody-derived synthetic protein[1,2]

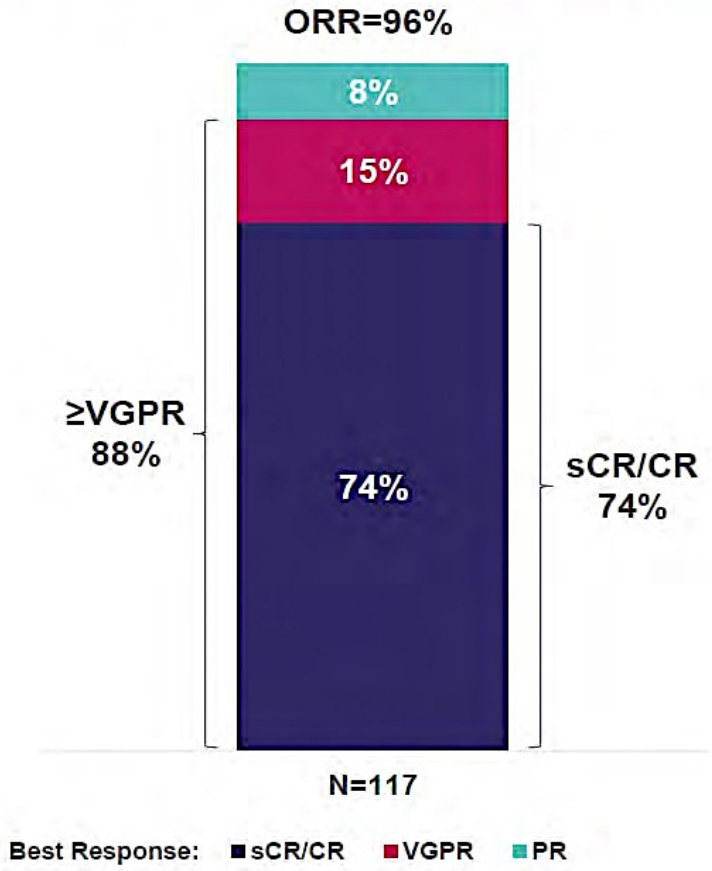
| | |
|---|---|
| **Size** | **Small D-Domain construct facilitates high transduction efficiency, CAR positivity, and CAR density on the T-cell surface[2-4]** |
| **Stability** | **Rapid D-Domain folding, lack of disulfide bonds, and a hydrophobic core enables stability at and beyond physiologic conditions[5,6]** |
| **Structure** | **Due to small size and compact structure, D-Domain CARs have a low risk of tonic signaling[6]** |

[1] Rotte A et al. *Immuno-oncol Insights* 2022;3(1):13-24; [2] Frigault MJ et al. *Blood Adv* 2023;7(5):768-77; [3] Canté-Barrett K et al. *BMC Res Notes* 2016;9:312; [4] Buonato JM et al. *Mol Cancer The* 2022;21(7):1171-83; [5] Zhu Y et al. *Proc Nat Acad Sci* 2003;100(26):15486-91; [6] Qin H et al. *Mol Ther* 2019;27(7):1262-74.

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# Phase II iMMagine-1 Trial: Overall Response Rate (ORR) and Depth of Response with Anito-cel for Relapsed/Refractory MM

## Efficacy Evaluable Patients, N=117




- Responses continue to deepen over time
- At a median follow-up of 15.9 months, IRC-assessed ORR was 96% and sCR/CR rate was 74%

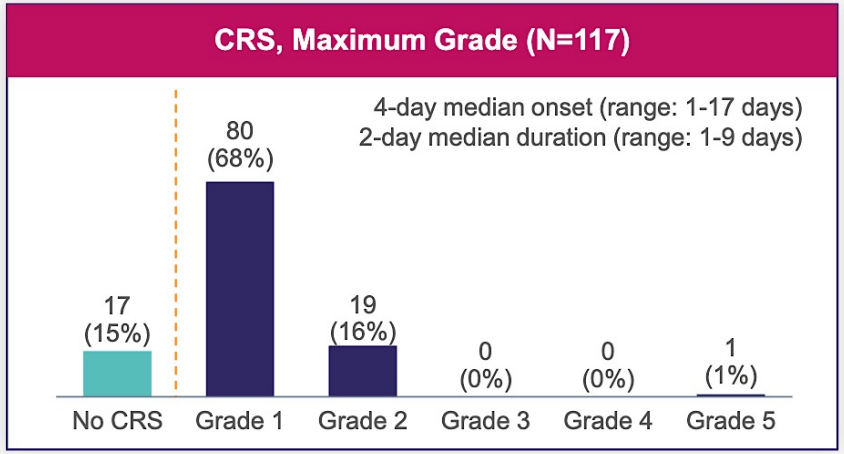
| | Median (months) | Interquartile Range | Min, Max |
|---|---|---|---|
| Time to first response | 1.0 | 1.0, 1.9 | 0.9, 13.8 |
| Time to best response | 4.8 | 2.1, 9.0 | 0.9, 23.8 |
| Time to sCR/CR | 3.2 | 2.0, 9.2 | 0.9, 23.8 |

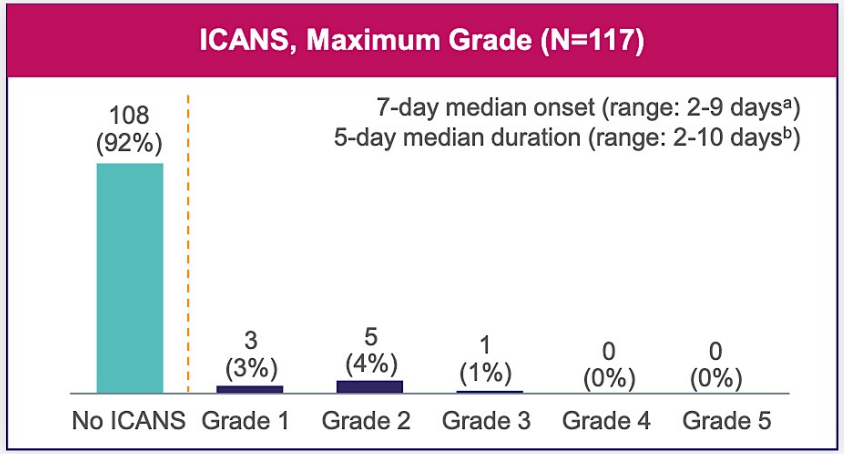
IRC = independent review committee; sCR = stringent complete response; CR = complete response; VGPR = very good partial response; PR = partial response

Patel K et al. ASH 2025;Abstract 256.

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# iMMagine-1: Safety Update




- 95% (111/117) of patients had either no CRS or CRS that resolved by ≤10 days of anito-cel infusion
- No new treatment-related or treatment-emergent deaths have occurred since the previous May 1, 2025 datacut
- No secondary primary malignancies of T-cell origin have occurred
- No replication competent lentivirus detected

**No delayed or non-ICANS neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome, and no immune effector cell-associated enterocolitis have been observed to date at ≥10 months since anito-cel infusion**

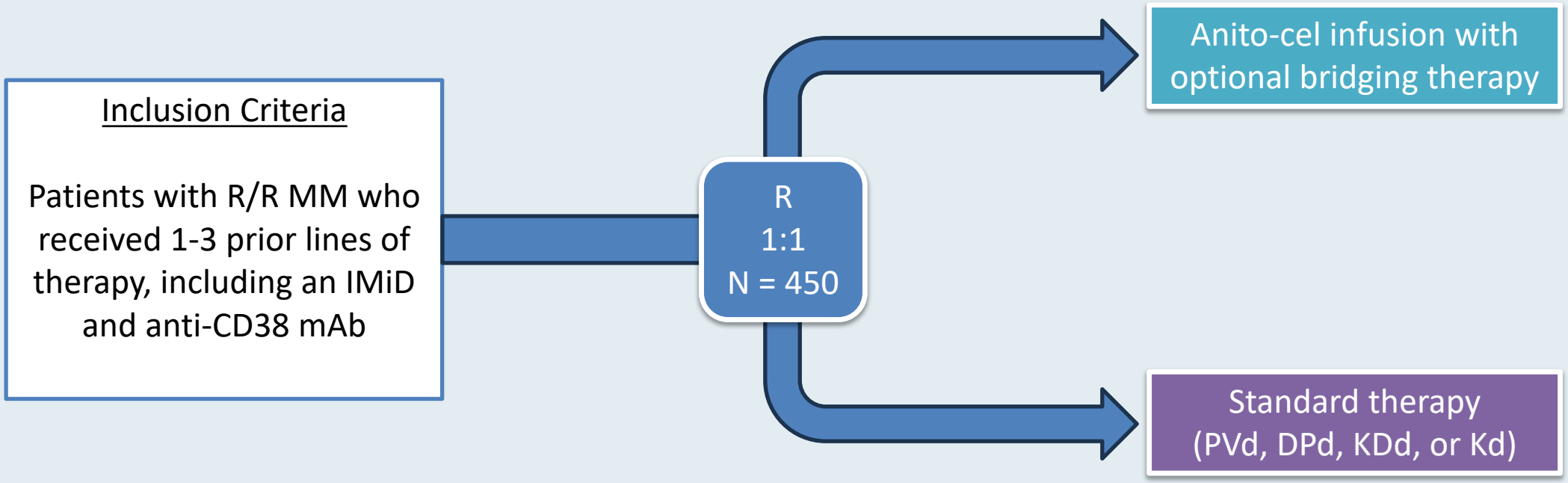
*[a]With the exception of n=1 Grade 1 ICANS (confusion) on day 31 post infusion that rapidly resolved. [b]With the exception of n=1 max Grade 2 ICANS with 29-day duration to resolution*
*Note: Updates to data resulting from ongoing data review; CRS and ICANS assessed per American Society for Transplantation and Cellular Therapy criteria*
*CRS, cytokine release syndrome; ICANS, immune-effector cell-associated neurotoxicity syndrome*

*February 23, 2026: Biologics license application for anito-cel as a fourth-line treatment for patients with relapsed or refractory multiple myeloma is supported by results from the Phase 1 study (NCT04155749) and the pivotal Phase 2 iMMagine-1 study (NCT05396885) and has been accepted by the FDA with an anticipated Prescription Drug User Fee Act (PDUFA) action date of December 23, 2026.*

Patel K et al. ASH 2025;Abstract 256; https://www.gilead.com/news/news-details/2026/gilead-sciences-to-acquire-arcellx-to-maximize-long-term-potential-of-anito-cel. Accessed October 2026.

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# iMMagine-3: A Phase III Study of Anito-cel




Primary endpoint: PFS per independent review

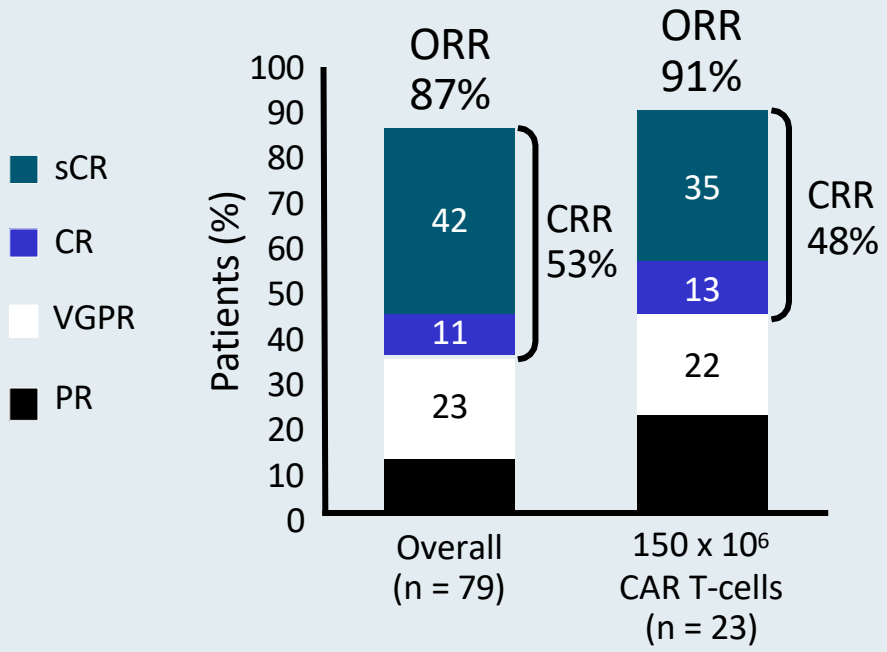
Key secondary endpoints: CR rate (CR/sCR), MRD negativity, OS, safety

R/R = relapsed/refractory; MRD = minimal residual disease

Martin T et al. EHA 2024;Abstract PB2724.

RTP RESEARCH TO PRACTICE

# Phase I Study of Arlocabtagene Autoleucel for R/R MM: Extended Follow-Up




| Response | Evaluable patients (n = 79) |
|---|---|
| Median DoR, mo (95% CI) | 18.0 (13.3-23.0) |
| Median TTR, mo (range) | 1 .0 (0.9-6.0) |
| Median follow-up, mo (range) | 16.1 (2.8-25.2) |

| Median PFS | mo (95% CI) |
|---|---|
| All evaluable patients (n = 79) | 18.3 (11.8 -21.9) |
| Prior anti-BCMA therapy (n = 38) | 19.0 (8.9-NA) |
| No prior anti-BCMA therapy (n = 41) | 18.3 (11.8-23.9) |

| OS | All patients (n = 84) |
|---|---|
| Median OS, mo | NR |
| 12-mo OS rate, % (95% CI) | 90 (81-95) |
| 18-mo OS rate, % (95% CI) | 87 (76-93) |
| 21-mo OS rate, % (95% CI) | 84 (72-91) |

DoR = duration of response; TTR = time to response

Bal S et al. *Blood* 2026;148(10):1240-50; Bal S et al. ASH 2024;Abstract 922.

RTP RESEARCH TO PRACTICE

# Phase I Study of Arlocabtagene Autoleucel for R/R MM: Select Treatment-Related Adverse Events (TRAEs)

| TRAE, n (%) | All patients (n = 84) | |
|---|---|---|
| | Any grade | Grade 3/4 |
| CRS | 69 (82) | 3 (4) |
| ICANS | 8 (10) | 2 (2) |
| Other neurotoxicity events | 10 (12) | 6 (7) |
| MAS/HLH | 0 | 3 (4) |

- CRS was primarily Grade 1 and 2. Grade 5 CRS occurred in 1 patient, who received the 450 x $10^6$ dose
- Select Grade ≤4 neurotoxicity events occurred at the 150-450 x $10^6$ dose level: dizziness, ataxia, neurotoxicity dysarthria, and/or nystagmus
  - Median time to onset: 30.5 days
- Weight loss (n = 5), palsy and Guillain-Barré syndrome were also reported
- No reports of parkinsonism, cranial nerve

| On-target/off-tumor event | All patients (N = 84) |
|---|---|
| Skin* | |
| ▪ Patients with an event, n (%) | 25 (30) |
| ▪ Patients with event resolution, n (%) | 22 (88) |
| ▪ Median time to resolution, days | 26 |
| Nail* | |
| ▪ Patients with an event, n (%) | 16 (19) |
| ▪ Patients with event resolution, n (%) | 12 (75) |
| ▪ Median time to resolution, days | 98 |
| Oral*† | |
| ▪ Patients with an event, n (%) | 27 (32) |
| ▪ Patients with event resolution, n (%) | 19 (70) |
| ▪ Median time to resolution, days | 66 |

* No Grade 3 or 4; intervention was not required for 79% of patients
† Including dysgeusia and dysphagia

CRS = cytokine release syndrome; MAS = macrophage activation syndrome; HLH = hemophagocytic lymphohistiocytosis

Bal S et al. *Blood* 2026;148(10):1240-50; Bal S et al. ASH 2024;Abstract 922.

RTP RESEARCH TO PRACTICE

# Positive Topline Results Announced from the Registrational Phase II QUINTESSENTIAL Trial of Arlocabtagene Autoleucel

## Press Release: September 8, 2026

"[The manufacturer] announced positive Phase 2 results from the registrational QUINTESSENTIAL trial (NCT06297226) of arlocabtagene autoleucel (arlo-cel; BMS-986393) in adult patients with quadruple-class exposed relapsed and refractory multiple myeloma (RRMM).

Results show the study met its primary endpoint with arlo-cel demonstrating a statistically significant and clinically meaningful overall response rate (ORR) in patients with quadruple-class exposed RRMM who had received four or more prior lines of therapy. Quadruple-class exposed consists of those who had been treated with an immunomodulatory inhibitor (IMiD), a proteasome inhibitor (PI), an anti-CD38 therapy and a BCMA-targeted therapy.

The study also met the key secondary endpoint of complete response rate (CRR) in patients with RRMM who had been quadruple-class exposed after four or more prior lines of therapy, and the key secondary endpoints of ORR and CRR after three or more prior lines of therapy. The safety profile of arlo-cel was consistent with that of other CAR T cell therapies and other GPRC5D-targeting therapies in multiple myeloma."

https://news.bms.com/news/corporate-financial/2026/Bristol-Myers-Squibb-Announces-Positive-Topline-Results-from-Registrational-Phase-2-QUINTESSENTIAL-Trial-of-the-Potential-First-in-Class-GPRC5D-Directed-CAR-T-Cell-Therapy-Arlocabtagene-Autoleucel----/default.aspx

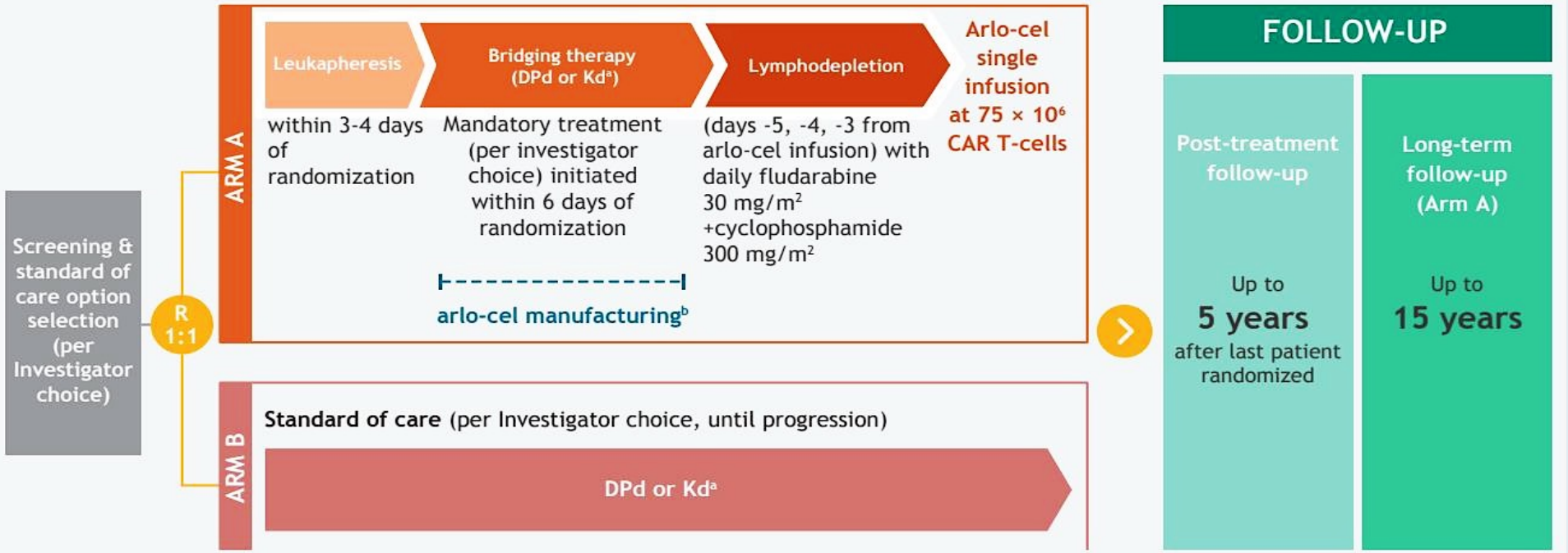
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# QUINTESSENTIAL-2: A Phase III Study of Arlo-cel

**INCLUSION CRITERIA**

- Men and women ≥ 18 years of age
- Documented diagnosis of MM per IMWG criteria
- Received 1-3 prior LOTa including prior exposure to lenalidomide with ≥ 2 consecutive cycles, unless PD was the best response to lenalidomide-containing treatment or if there was lenalidomide intolerance or unacceptable toxicity
- Measurable disease
- ECOG performance status 0 or 1
- Documented disease progression during or after their last anti-myeloma regimen

**QUINTESSENTIAL-2 is a randomized, open-label, multicenter, phase 3 confirmatory study comparing the efficacy and safety of arlo-cel versus standard of care in adults with RRMM and prior lenalidomide exposure**




[a]DPd or Kd dosed per labeling; [b]Once arlo-cel is manufactured and available to the treatment center, the patient will undergo pretreatment evaluation to ensure they remain eligible to receive lymphodepletion and arlo-cel infusion.
arlo-cel, arlocabtagene autoleucel; DPd, daratumumab, pomalidomide, and dexamethasone; Kd, carfilzomib and dexamethasone; R, randomization; RRMM, relapsed and refractory multiple myeloma.

Lebel E et al. ASCO 2026;Abstract TPS7577.

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# Faculty Discussion



Dr Gandhi

# Questions for the Faculty

**82-year-old man with MM who received ide-cel CAR-T therapy 18 months ago for relapsed standard-risk disease. Responded with minimal toxicity, currently under observation**

**Questions**

- Choice of CAR T-cell therapy
- Age, performance status and eligibility for CAR-T
- Current requirements for social support and remaining closer to tertiary centers
- Post-CAR-T management: vaccines, IVIG, prophylactic antimicrobials

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Dr Hussein

# Questions for the Faculty

**70-year-old man with relapsed MM who received ida-cel CAR T-cell therapy: Responded but disease progressed after 1 year, received second GPRC5 directed CAR T-cell therapy and responded again.**

**Questions**

- Are there any situations in which you would consider repeating CAR T-cell therapy a second time in the same patient? Would you use the same or different constructs?
- Have you used the novel CAR T-cell therapies anito-cel and arlo-cel? What is your experience with these constructs?

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# Agenda

Introduction: ESMO 2026; Recent FDA Approvals

Chimeric Antigen Receptor T-Cell Therapy – Dr Lonial

**Bispecific Antibodies – Dr Lonial**

Antibody-Drug Conjugates – Dr Richardson

Up-Front Treatment; CELMoDs – Dr Richardson

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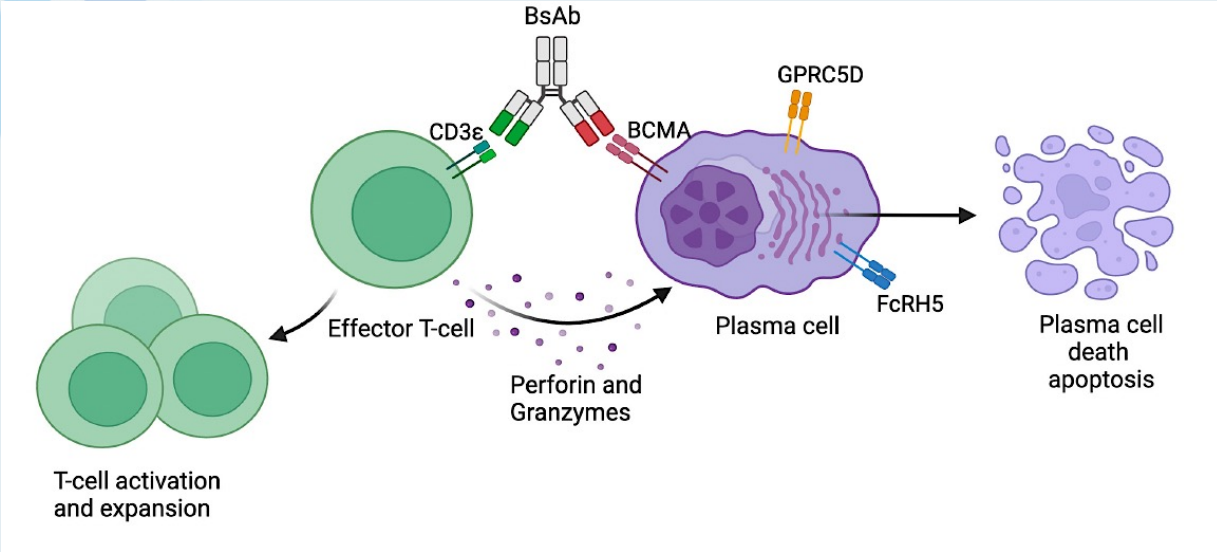
# Bispecific Antibodies

**Select Datasets**

- Mateos M-V et al. Phase 3 Randomized Study of Teclistamab plus Daratumumab versus Investigator's Choice of Daratumumab and Dexamethasone with Either Pomalidomide or Bortezomib in Patients with Relapsed Refractory Multiple Myeloma: Results of Majestec-3. ASH 2025;Abstract LBA-6.
- Costa LJ et al. Teclistamab plus Daratumumab in Relapsed or Refractory Multiple Myeloma. *N Engl J Med* 2026;394:739-52.
- Mina R et al. MajesTEC-9: A Phase 3 Randomized Study of Teclistamab Monotherapy vs Investigator's Choice of Pomalidomide, Bortezomib, and Dexamethasone or Carfilzomib and Dexamethasone (PVd/Kd) in Patients (Pts) with Relapsed Refractory Multiple Myeloma (RRMM). ASCO 2026;Abstract 7507.
- Touzeau C et al. Teclistamab in Multiple Myeloma with One to Three Previous Lines of Therapy. *N Engl J Med* 2026;395:440-53.
- Voorhees P et al. Phase 3, Randomized Study of Talquetamab (TAL) plus Daratumumab (Dara) ± Pomalidomide (Pom) vs Dara plus Pom and Dexamethasone (DPD) in Relapsed/Refractory Multiple Myeloma (RRMM): MonumenTAL-3. EHA 2026;Abstract S100 and IMS 2026;Abstract PA-350.
- Mina R et al. Talquetamab-Daratumumab in Relapsed or Refractory Myeloma. *N Engl J Med* 2026;395:671-83.

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# Bispecific Antibody Targets and Mechanism of Action




| | BCMA | GPRC5D | FcRH5 |
|---|---|---|---|
| **Expression** | Plasma cells, plasmablasts | Plasma cells, hair follicles, eccrine glands, filiform papillae of tongue | B-cell lineage cells, including plasma cells |
| **Biological significance** | Survival/growth of plasma cells | Unclear | Unclear |
| **Location** | 16p13 | 12p13 | 1q21 |
| **Extracellular shedding?** | Yes | No | Yes |
| **Select agents** | Elranatamab, teclistamab, linvoseltamab | Talquetamab | Cevostamab |

Rees M et al. *Front Immunol* 2024;15:1424925; Yu B et al. *J Hematol Oncol* 2020;13:125; Rodrigueze-Otero P et al. *Blood Cancer J* 2024;14:24; Li J et al. *Cancer Cell* 2017;31:383-95; Ise T et al. *Leukemia* 2007;21:169-74.

Adapted from content provided courtesy of Hans Lee, MD

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# Approved Bispecific T-Cell Antibodies as Monotherapy: Clinical Data

| Drug | N | Pivotal trial | Response | PFS/DOR | CRS |
|---|---|---|---|---|---|
| **Teclistamab**[1] **FDA approved, 2022** | 165 | MajesTEC-1 | ORR 63%<br>≥VGPR 59% | Median PFS 11.4 mo<br>Median DOR 24 mo | All grade (72%)<br>Grade 3/4 (0.6%) |
| **Elranatamab**[2] **FDA approved, 2023** | 123 | MagnetisMM-3 | ORR 61%<br>≥VGPR 56% | Median PFS: 17.2 months<br>18-month DOR: 68.8% | All grade (56%),<br>Grade 2 (14%);<br>Grade 3-4 (0%) |
| **Linvoseltamab**[3] **FDA approved, 2025** | 117 | LINKER-MM1 | ORR 71%<br>≥VGPR (200 mg cohort) 63% | 12-month median PFS: 70%<br>Median DOR: 29.4 months | 200 mg cohort:<br>All grade (46%),<br>Grade 2 (10%),<br>Grade 3 (1%), |
| **Talquetamab**[4] **FDA approved, 2023** | 232 | MonumenTAL-1 | ORR 70% (405 μg/kg weekly)<br>ORR 64% (800 μg/kg biweekly) | Median DOR 10.2 mo (405 μg/kg weekly)<br>Median DOR 7.8 mo (800 μg/kg biweekly) | All grade 405 μg/kg weekly (77%)<br>All grade 800 μg/kg biweekly (80%) |

[1] Garfall A et al. ASCO 2024;Abstract 7540; [2] Lesokhin A et al. *Nat Med* 2023;29:2259-67; [3] Bumma N et al. *J Clin Oncol* 2024;42:2702-12;
[4] Chari A et al. *N Engl J Med* 2022;387:2232-44.

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# MajesTEC-3 Phase III Study of Teclistamab with Daratumumab for MM After 1 to 3 Prior Lines of Therapy

**Key inclusion criteria**

- RRMM
- 1–3 prior LOTs including a PI and lenalidomide
  - Patients with only 1 prior LOT must have been lenalidomide refractory per IMWG criteria
- ECOG PS score of 0–2

**Key exclusion criteria**

- Prior BCMA-directed therapy
- Refractory to anti-CD38 mAbs[a]

**1:1 randomization N=587**

22 Oct 2021 to 29 Sept 2023[b]

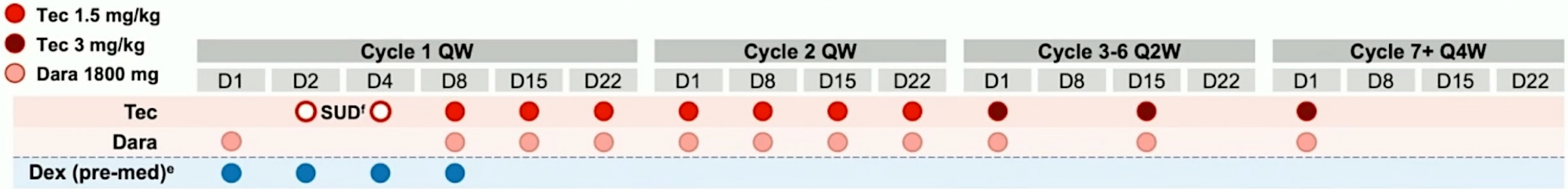
**Tec-Dara**
N=291
SC dosing following Dara schedule

**DPd/DVd**
N=296
by investigator's choice[c]

**Primary endpoint**
- PFS per IRC

**Key secondary endpoints**
- ≥CR[d] and ORR[d]
- MRD negativity ($10^{-5}$)
- OS
- MySIm-Q Total Symptom score

**Other secondary endpoints**
- Safety
- PK and immunogenicity



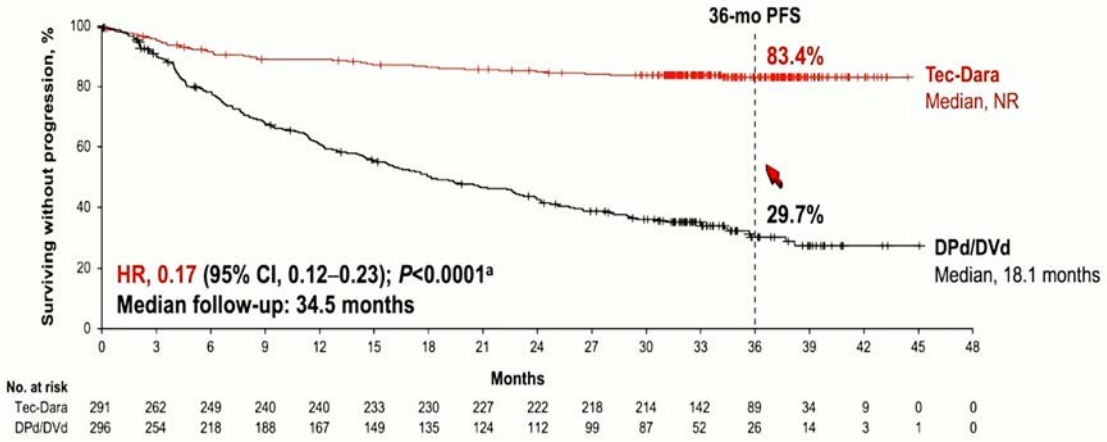

**SC dosing aligned with Dara schedule, with monthly dosing after 6 cycles; steroid sparing after Cycle 1 Day 8**

Mateos M-V et al. ASH 2025;Abstract LBA-6.

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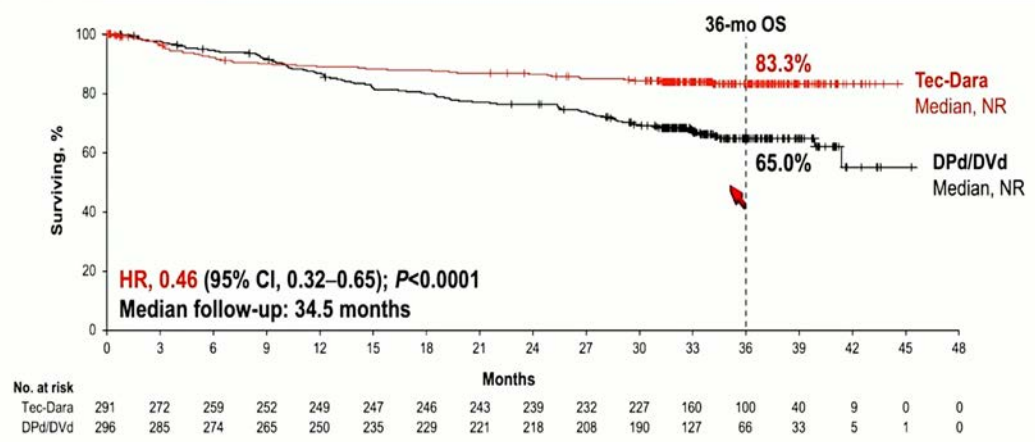
# MajesTEC-3: Survival

## MajesTEC-3: PFS (Primary Endpoint)




Tec-Dara significantly improved PFS, with a plateauing curve after ~6 months and >90% of patients progression-free at 6 months sustaining such a benefit at 3 years

## MajesTEC-3: OS




Tec-Dara significantly improved OS versus DPd/DVd, with 83% of patients alive at 3 years

Mateos M-V et al. ASH 2025;Abstract LBA-6; Costa LJ et al. *N Engl J Med* 2026;394:739-52.

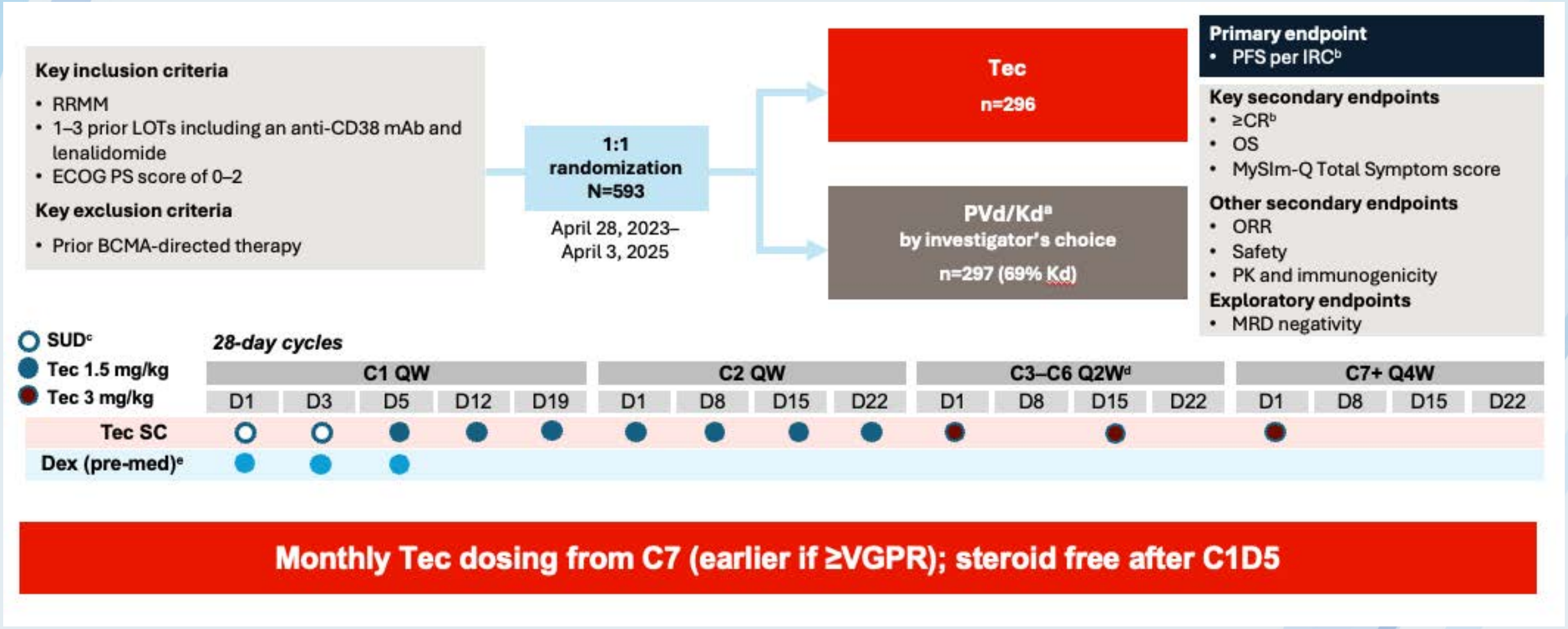
# MajesTEC-3: Most Common Adverse Events — Safety Population

| Adverse Event | Teclistamab–Daratumumab (N=283) | | DPd or DVd (N=290) | |
|---|---|---|---|---|
| | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 |
| | *number of patients (percent)* | | | |
| **Any adverse event** | 283 (100) | 269 (95.1) | 290 (100) | 280 (96.6) |
| Hematologic | | | | |
| Neutropenia | 222 (78.4) | 214 (75.6) | 240 (82.8) | 228 (78.6) |
| Anemia | 111 (39.2) | 58 (20.5) | 103 (35.5) | 50 (17.2) |
| Thrombocytopenia | 103 (36.4) | 55 (19.4) | 126 (43.4) | 68 (23.4) |
| Lymphopenia | 63 (22.3) | 59 (20.8) | 50 (17.2) | 32 (11.0) |
| Leukopenia | 51 (18.0) | 30 (10.6) | 61 (21.0) | 46 (15.9) |
| Nonhematologic | | | | |
| Hypogammaglobulinemia | 194 (68.6) | 16 (5.7) | 104 (35.9) | 4 (1.4) |
| Cytokine release syndrome | 170 (60.1) | 0 | 0 | 0 |
| Diarrhea | 147 (51.9) | 10 (3.5) | 89 (30.7) | 7 (2.4) |
| Cough | 136 (48.1) | 1 (0.4) | 66 (22.8) | 0 |
| Covid-19 | 124 (43.8) | 17 (6.0) | 97 (33.4) | 6 (2.1) |
| Upper respiratory tract infection | 115 (40.6) | 12 (4.2) | 88 (30.3) | 7 (2.4) |
| Pyrexia | 104 (36.7) | 4 (1.4) | 55 (19.0) | 1 (0.3) |
| Pneumonia | 65 (23.0) | 47 (16.6) | 53 (18.3) | 43 (14.8) |
| Covid-19 pneumonia | 34 (12.0) | 32 (11.3) | 12 (4.1) | 7 (2.4) |

Mateos M-V et al. ASH 2025;Abstract LBA-6; Costa LJ et al. *N Engl J Med* 2026;394:739-52.

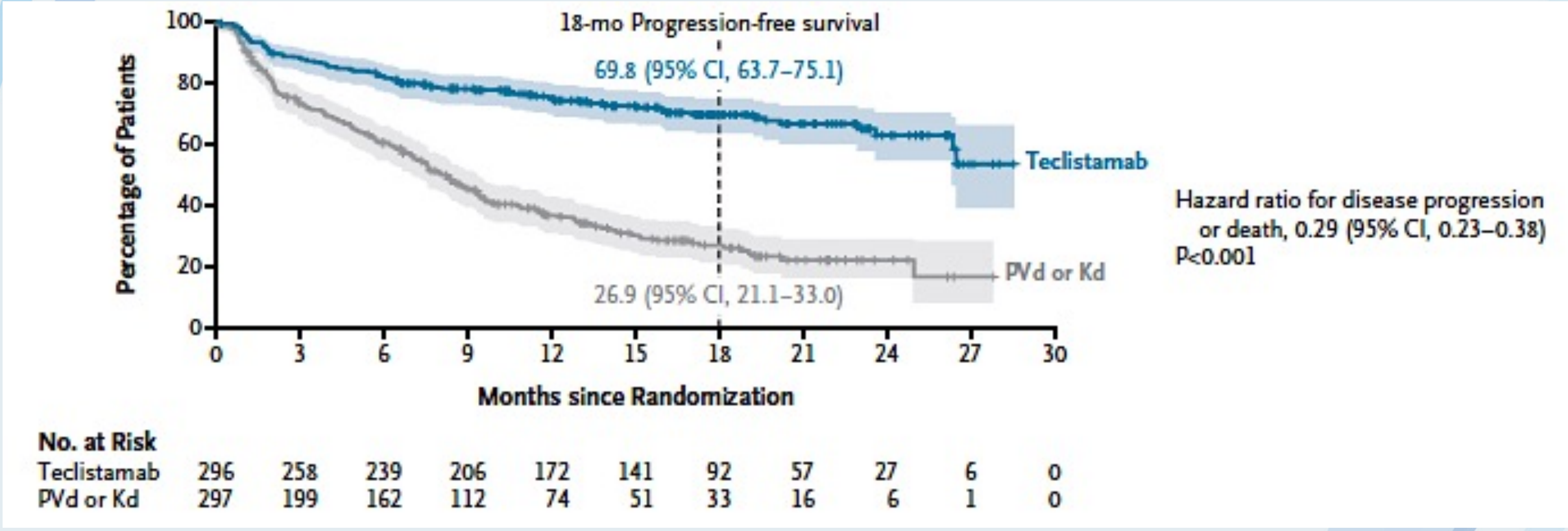
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# MajesTEC-9: A Phase III Study of Teclistamab for MM After 1 to 3 Prior Lines of Therapy



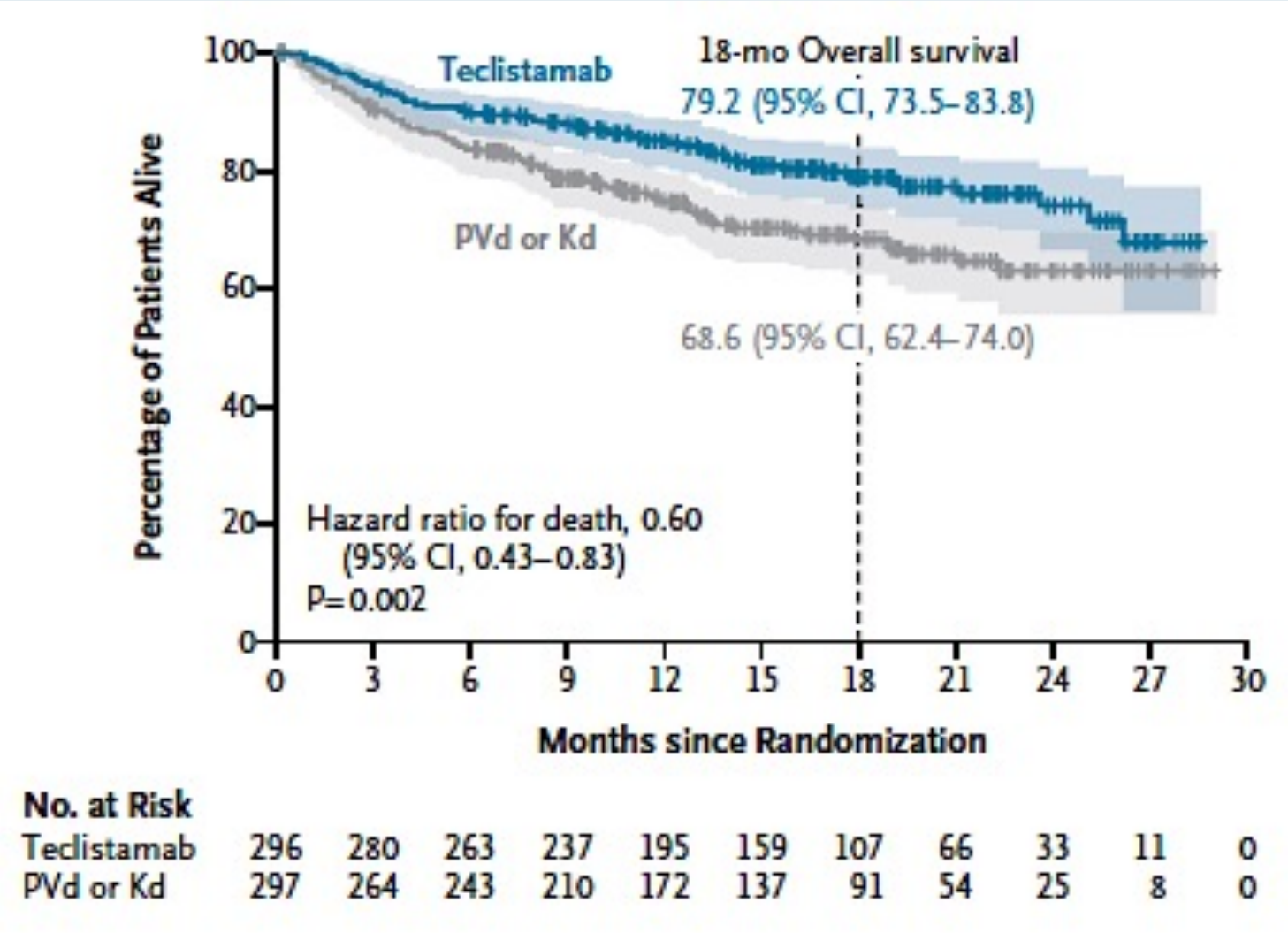

Mina R et al. ASCO 2026;Abstract 7507.

# MajesTEC-9 Primary Endpoint: PFS




Mina R et al. ASCO 2026;Abstract 7507; Touzeau C et al. *N Engl J Med* 2026;395:440-53.

# MajesTEC-9: OS




Mina R et al. ASCO 2026;Abstract 7507; Touzeau C et al. *N Engl J Med* 2026;395:440-53.

# Elranatamab Significantly Improves Progression-Free Survival for Double Class-Exposed Patients with R/R MM

## Press Release: April 29, 2026

"[The manufacturer] announced positive topline results from the Phase 3 MagnetisMM-5 study evaluating elranatamab as monotherapy in adults with relapsed or refractory multiple myeloma (RRMM) who received at least one prior line of treatment.

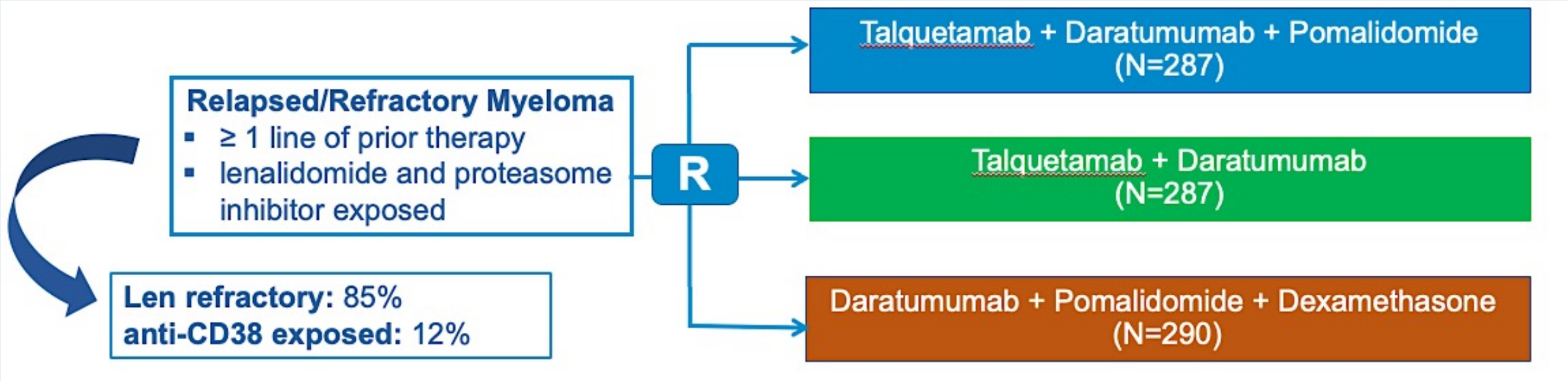
The study demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of progression-free survival (PFS), as assessed by blinded independent central review (BICR), versus standard-of-care daratumumab plus pomalidomide and dexamethasone (DPd). The safety and tolerability of elranatamab was consistent with its known safety profile.

The PFS results exceeded the pre-specified interim analysis target hazard ratio for efficacy, with most elranatamab-treated patients remaining progression-free. The trial remains ongoing to assess overall survival, a key secondary endpoint, which was not yet mature at the time of this interim analysis. These data will be discussed with global health authorities, and detailed results from MagnetisMM-5 will be submitted for presentation at a future medical congress."

https://www.pfizer.com/news/press-release/press-release-detail/pfizers-elrexfio-significantly-improves-progression-free

RTP RESEARCH TO PRACTICE

# MonumenTAL-3: A Phase III Study of Talquetamab with Daratumumab with or without Pomalidomide for MM After 1 or More Prior Lines of Therapy

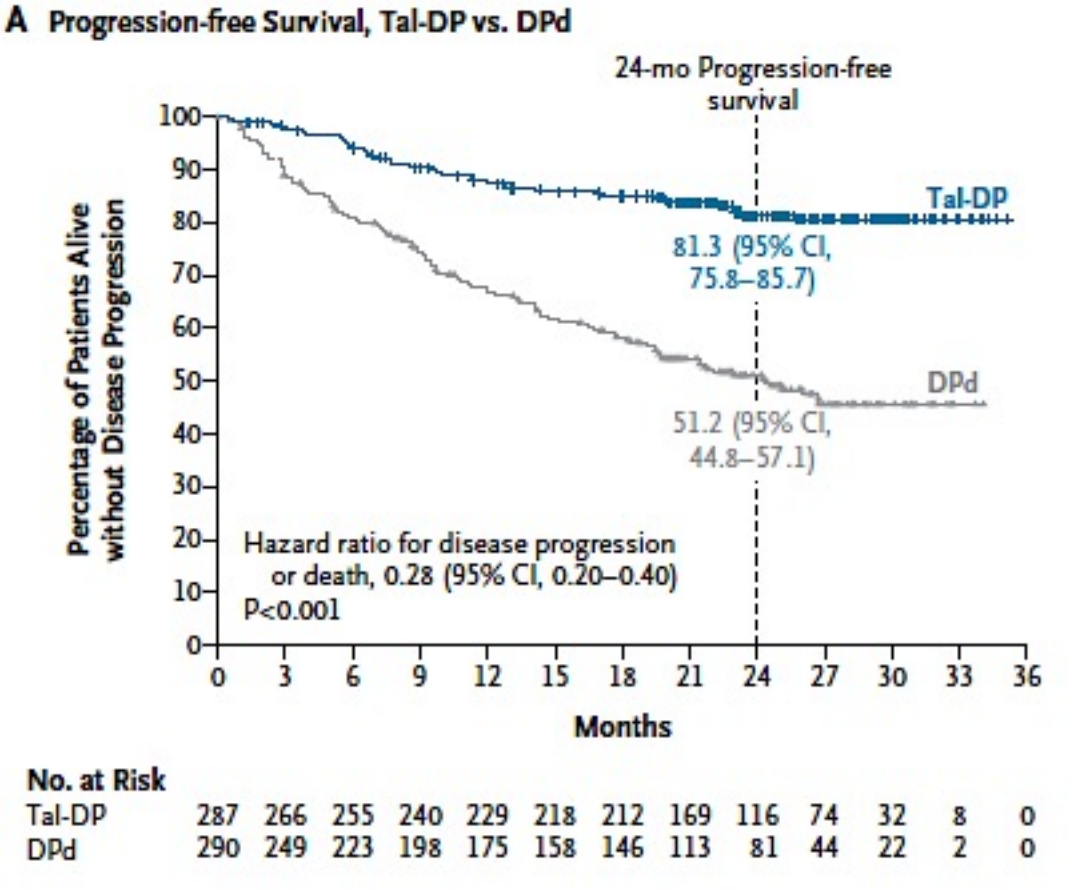


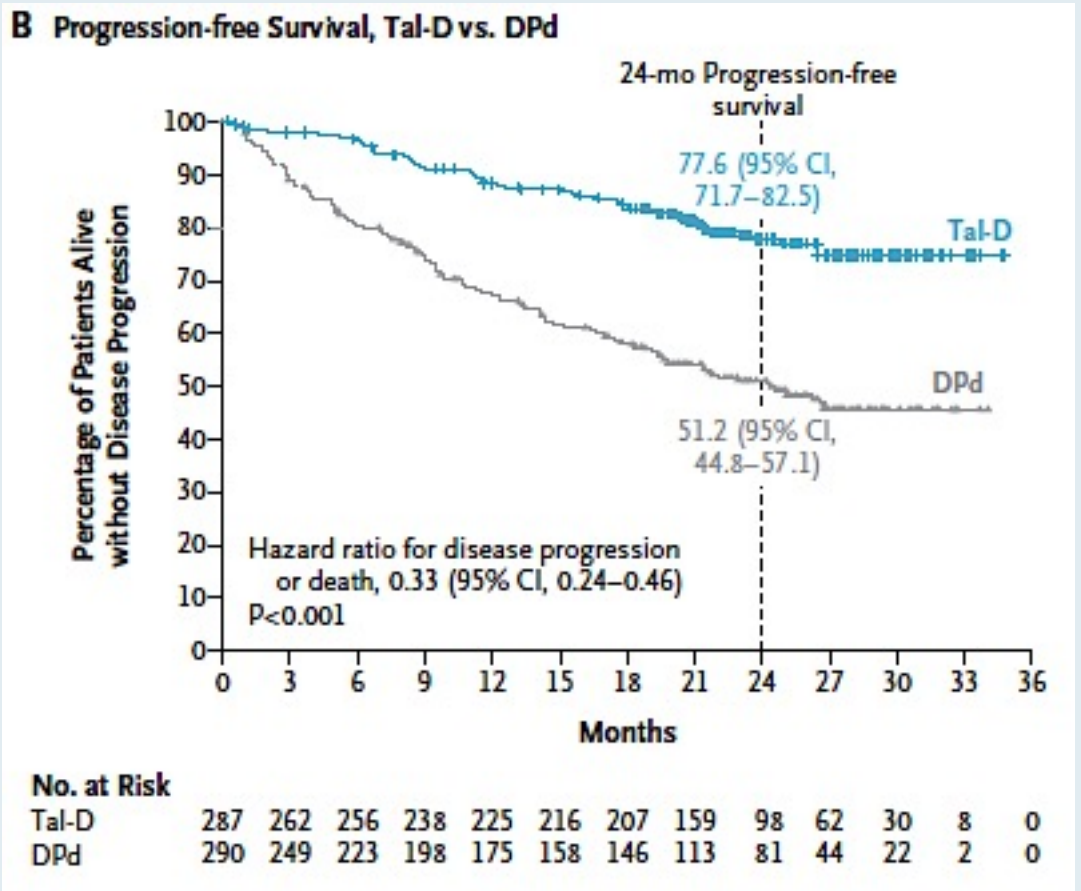

Voorhees P et al. EHA 2026;Abstract S100.

Content courtesy of Hans Lee, MD

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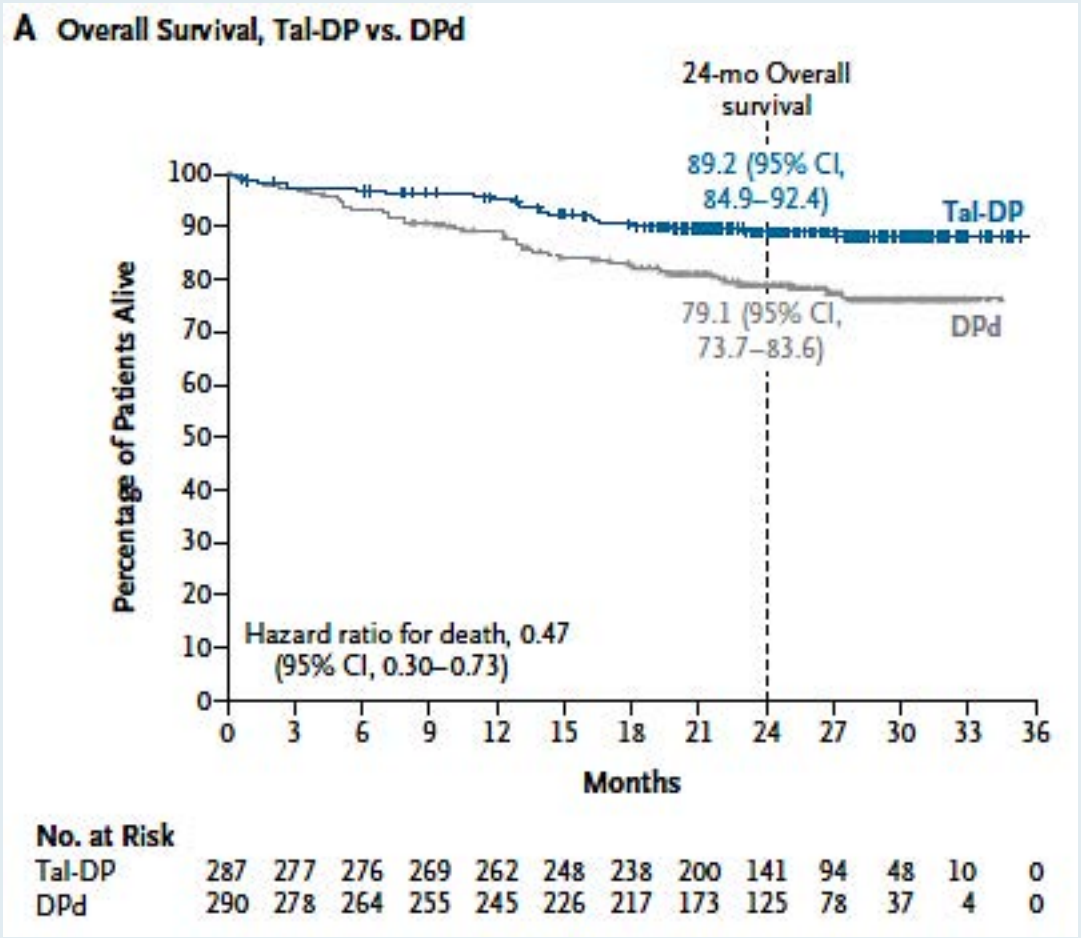
# MonumenTAL-3 Primary Endpoint: PFS

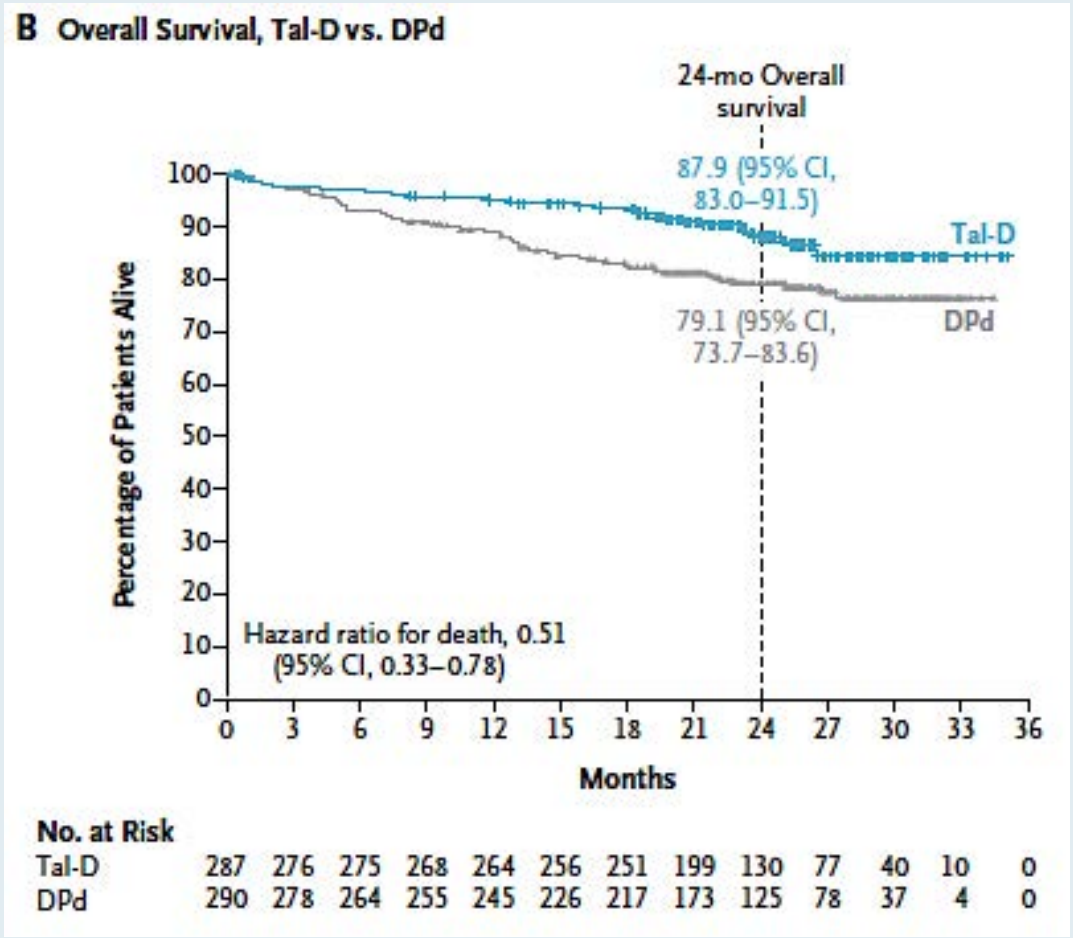



Voorhees P et al. EHA 2026;Abstract S100; Mina R et al. *N Engl J Med* 2026;395:671-83; Voorhees PM et al. IMS 2026;Abstract PA-350.

# MonumenTAL-3: OS




Voorhees P et al. EHA 2026;Abstract S100; Mina R et al. *N Engl J Med* 2026;395:671-83; Voorhees PM et al. IMS 2026;Abstract PA-350.

# Positive Topline Results from the MonumenTAL-6 Phase III Trial of Teclistamab with Talquetamab in Earlier Lines of Therapy for R/R MM

## Press Release: July 23, 2026

"[The manufacturer] announced positive topline results from the three-arm investigational Phase III MonumenTAL-6 study evaluating teclistamab-cqyv + talquetamab-tgvs, a BCMA and GPRC5D dual antigen targeting regimen, and talquetamab-tgvs + pomalidomide in adult patients with relapsed or refractory multiple myeloma (RRMM) who received 1 to 4 prior lines of therapy, including an anti-CD38 antibody and lenalidomide.

The study demonstrated statistically significant and clinically meaningful improvements in progression-free survival and overall survival for both investigational arms compared with investigator's choice standard of care. Teclistamab-cqyv + talquetamab-tgvs delivered the greatest benefit, reducing the risk of disease progression or death by 89% (HR, 0.11) and the risk of death by 62% (HR, 0.38).

Based on the strength of the data, the Independent Data Monitoring Committee recommended unblinding the study at the first interim analysis. The full results of the Phase 3 MonumenTAL-6 study will be presented at a future major medical meeting and shared with global health authorities."

https://www.jnj.com/media-center/press-releases/tecvayli-talvey-reduced-the-risk-of-disease-progression-or-death-by-89-and-the-risk-of-death-by-62-in-earlier-line-relapsed-refractory-multiple-myeloma.

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# Faculty Discussion



Dr Peles

# Questions for the Faculty

**61-year-old woman with standard-risk MM who received RVd induction and autologous transplant followed by maintenance lenalidomide for 10 years. Now with disease progression. Clinically well: PS 0**

**Questions**

- For a 61-year-old patient, do you generally recommend CAR T before bispecific antibodies or vice versa?
- Do you normally use bispecific antibodies as monotherapy or in combination?
- How concerned are you about the risk of infections for your patients receiving teclistamab/daratumumab? Are there any other complications or recommendations about that? Do you use IVIG?

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Dr Zafar

# Questions for the Faculty

**A man in his early 60s with del(17p) IgA kappa MM and rapid progression with extramedullary disease through quadruplet induction. His disease progressed through salvage treatment. Couldn't get to CAR T. Treated with teclistamab with progression in the liver.**

**Questions**

- What other options? CAR T? Talquetamab alone or with daratumumab or teclistamab? Belantamab? Can we get a BCMA assay?
- New agents? What about trispecific antibodies?

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# Agenda

Introduction: ESMO 2026; Recent FDA Approvals

Chimeric Antigen Receptor T-Cell Therapy – Dr Lonial

Bispecific Antibodies – Dr Lonial

**Antibody-Drug Conjugates – Dr Richardson**

Up-Front Treatment; CELMoDs – Dr Richardson

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# Antibody-Drug Conjugates

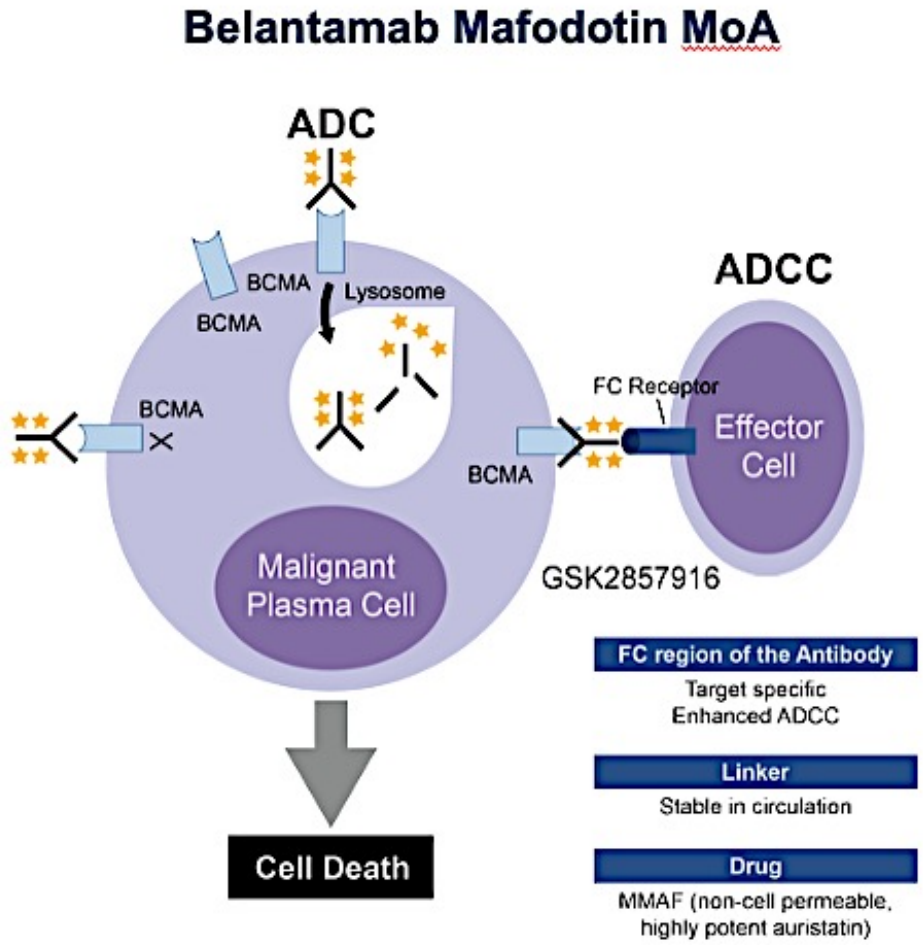
**Select Datasets**

- Hungria V et al. Belantamab Mafodotin, Bortezomib, and Dexamethasone vs Daratumumab, Bortezomib, and Dexamethasone in Relapsed/Refractory Multiple Myeloma: Updated 4-Year Results of the Phase 3 DREAMM-7 Trial. IMS 2026;Abstract PA-049.
- Trudel S et al. Deep Responses and Durable Outcomes in Patients Treated with Belantamab Mafodotin plus Pomalidomide and Dexamethasone from Long-Term Follow-Up of the Phase 3 DREAMM-8 Study. ASH 2025; Abstract 2264.
- Trudel S et al. Long-Term Outcomes with Sustained Minimal Residual Disease Negativity in Belantamab Mafodotin–Treated Patients with Relapsed/Refractory Multiple Myeloma: An Update from DREAMM-8. IMS 2026;Abstract OA-38.
- Mateos MV et al. Modification of Belantamab Mafodotin Dosing to Balance Efficacy and Tolerability in the DREAMM-7 and DREAMM-8 Trials. *Blood Adv* 2025;9(22):5708-19.
- Usmani SZ et al. DREAMM-9 Patient-Reported Vision-Related Function with Extended Belantamab Mafodotin Dosing Intervals with Bortezomib, Lenalidomide, Dexamethasone (BRVD) in Transplant Ineligible Multiple Myeloma. IMS 2026;Abstract OA-20.

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# Belantamab Mafodotin Mechanism of Action

- **B-cell maturation antigen (BCMA)**
  - Selectively expressed on plasmablasts and PCs
  - Requisite for long-lived plasma cell survival
- **Belantamab mafodotin**
  - Humanized afucosylated IgG1 ADC that targets BCMA
  - Multimodal MoA
  - Developed as an off the shelf, outpatient, steroid-sparing BCMA-directed approach
  - Convenient IV 0.5 – 1 h outpatient infusion

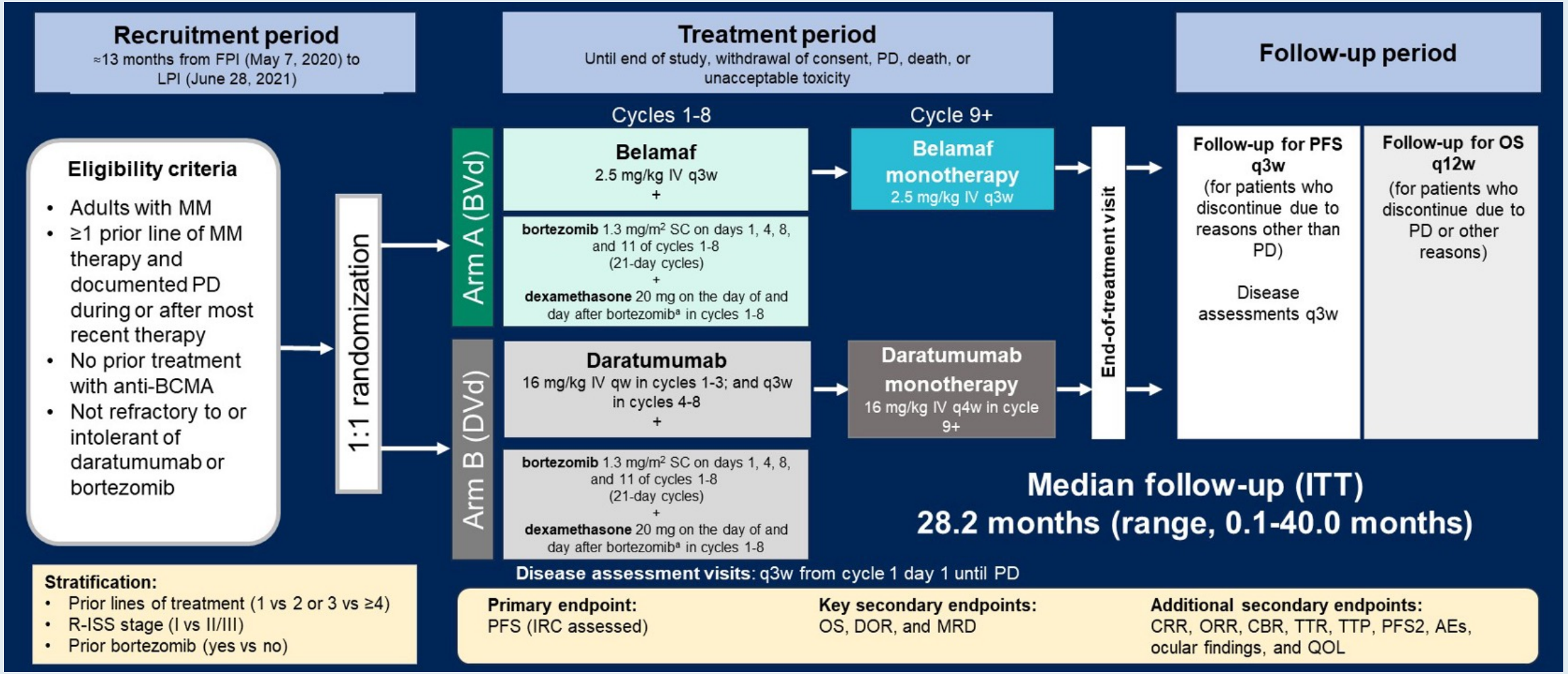



Cho, Front Immunol 2018; Sheikh, Future Oncol 2020

Content courtesy of Douglas W Sborov, MD, MS

RTP RESEARCH TO PRACTICE

# DREAMM-7: A Phase III Trial of Belantamab Mafodotin (Belamaf) with Bortezomib/Dexamethasone (BVd) versus Daratumumab with Vd (DVd) for R/R MM




Mateos M-V et al. ASCO 2024;Abstract 7503.

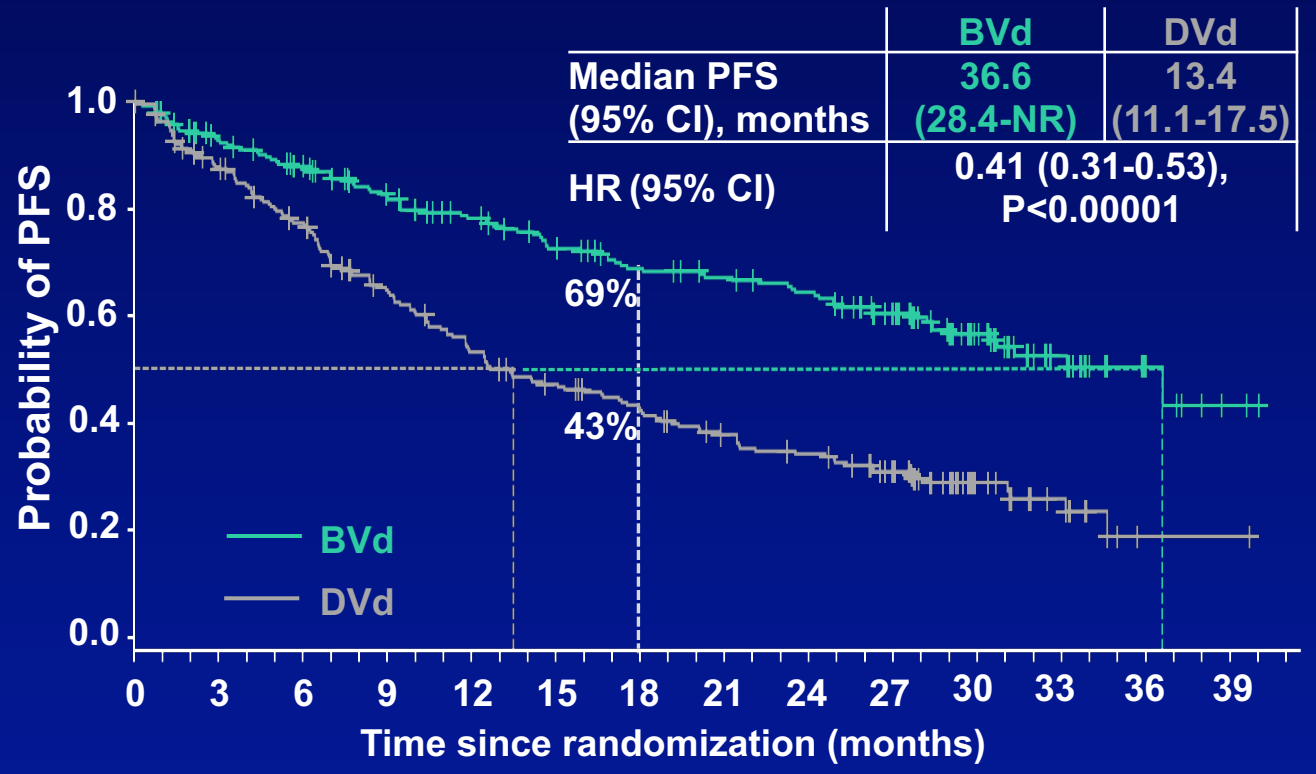
# Belantamab mafodotin for early-relapse RRMM

# DREAMM-7: Belantamab mafodotin + Vd vs Dara-Vd as ≥2nd-line therapy

**Phase 3 DREAMM-7 study**

- Belamaf+Vd x 8 cycles, then belamaf Q3W, N=243
- Dara-Vd x 8 cycles, then Dara Q4W, N=251

| Patients | Belamaf-Vd, N=243 | Dara-Vd, N=251 |
|---|---|---|
| Median age, years | 65 | 64 |
| Age ≥75 years | 15% | 12% |
| High-risk cytogenetics | 28% | 27% |
| EMD | 5% | 10% |
| 1 / 2-3 / ≥4 prior lines | 51 / 36 / 12% | 50 / 39 / 11% |
| Prior PI | 90% | 86% |
| Prior IMiD | 81% | 86% |
| R-refractory | 33% | 35% |
| Prior Dara | 1% | 2% |
| Prior ASCT | 67% | 69% |




**Outcomes**

- Significant PFS benefit seen across prespecified subgroups, including R-refractory patients (HR 0.37), patients with high-risk cytogenetics (HR 0.36), and patients with prior V (HR 0.45)
- Early OS trend favoring belamaf-Vd – 18-month OS 84% vs 73% (HR 0.57)

Hungria V, et al. N Engl J Med 2024;391(5):393–407.

# Belantamab mafodotin for early-relapse RRMM

# DREAMM-7: Belantamab mafodotin + Vd vs Dara-Vd as ≥2nd-line therapy

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## Sustained MRD status: Bela-Vd vs Dara-Vd

- Patients achieving MRD-neg status
  - Patients with CR: 70% vs 59% ($10^{-5}$) / 45% vs 23% ($10^{-6}$)
  - ITT: 25% vs 10% ($10^{-5}$) / 16% vs 4% ($10^{-6}$)
  - Median time to first MRD-neg status: 11.1 vs 17.0 months
- Patients achieving sustained MRD-neg status ($10^{-5}$)
  - Patients with CR: 57% vs 42%
  - ITT: 14% vs 4%

Mateos M-V, et al. Blood 2025;146(Supplement 1):2265.

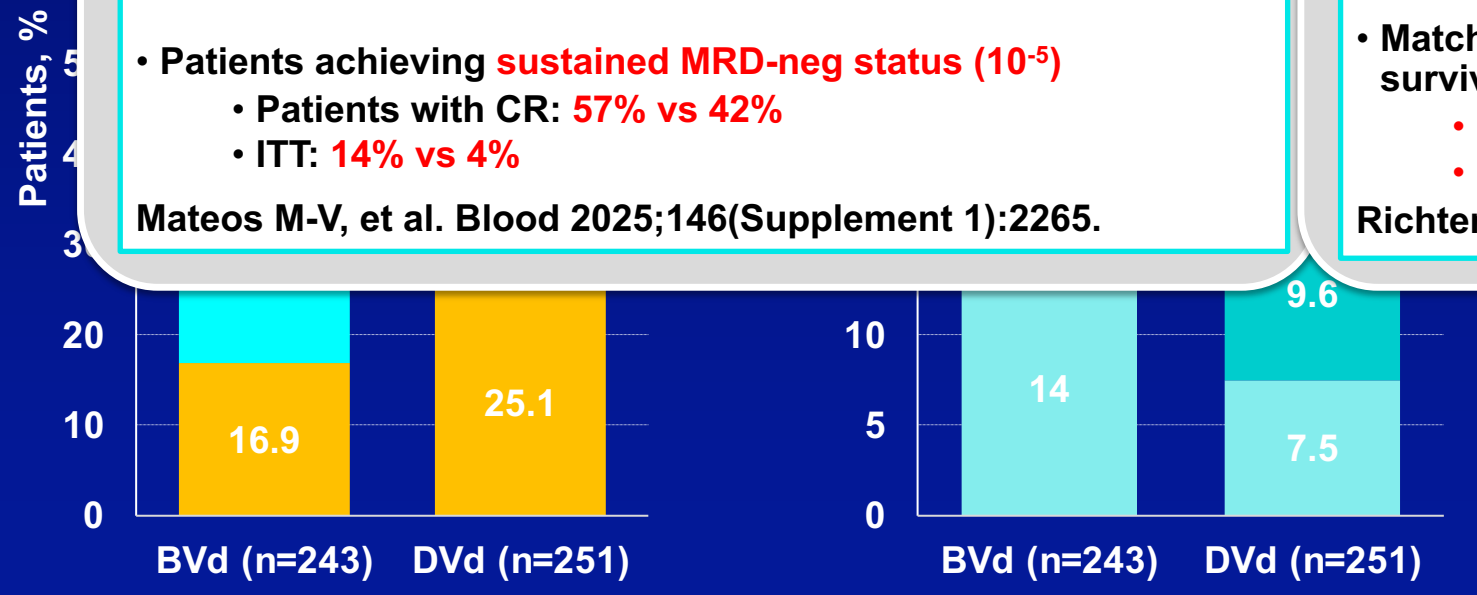
## Indirect comparisons: Bela-Vd vs SoC / Dara-Tec

- Indirect treatment comparisons of PFS and OS: Bela-Vd vs Pom-Vd / Elo-Pom-dex / Isa-Pom-dex / ide-cel
  - PFS HRs 0.52 / 0.34 / 0.54 / 0.47
  - OS HRs 0.60 / 0.41 / 0.35 / 0.51

Richter JR, et al. J Clin Oncol 2026;44(16_Suppl):7568.

- Matching adjusted indirect comparison of OS restricted mean survival time (RMST) and infections: Bela-Vd vs Dara-Tec
  - OS RMST ratio 1.01–1.04 at 1–3 years
  - Odds ratio for infections 0.24

Richter J, et al. HemaSphere 2026;10(S1):PS1933.




Median DOR 40.8 vs 17.8 months

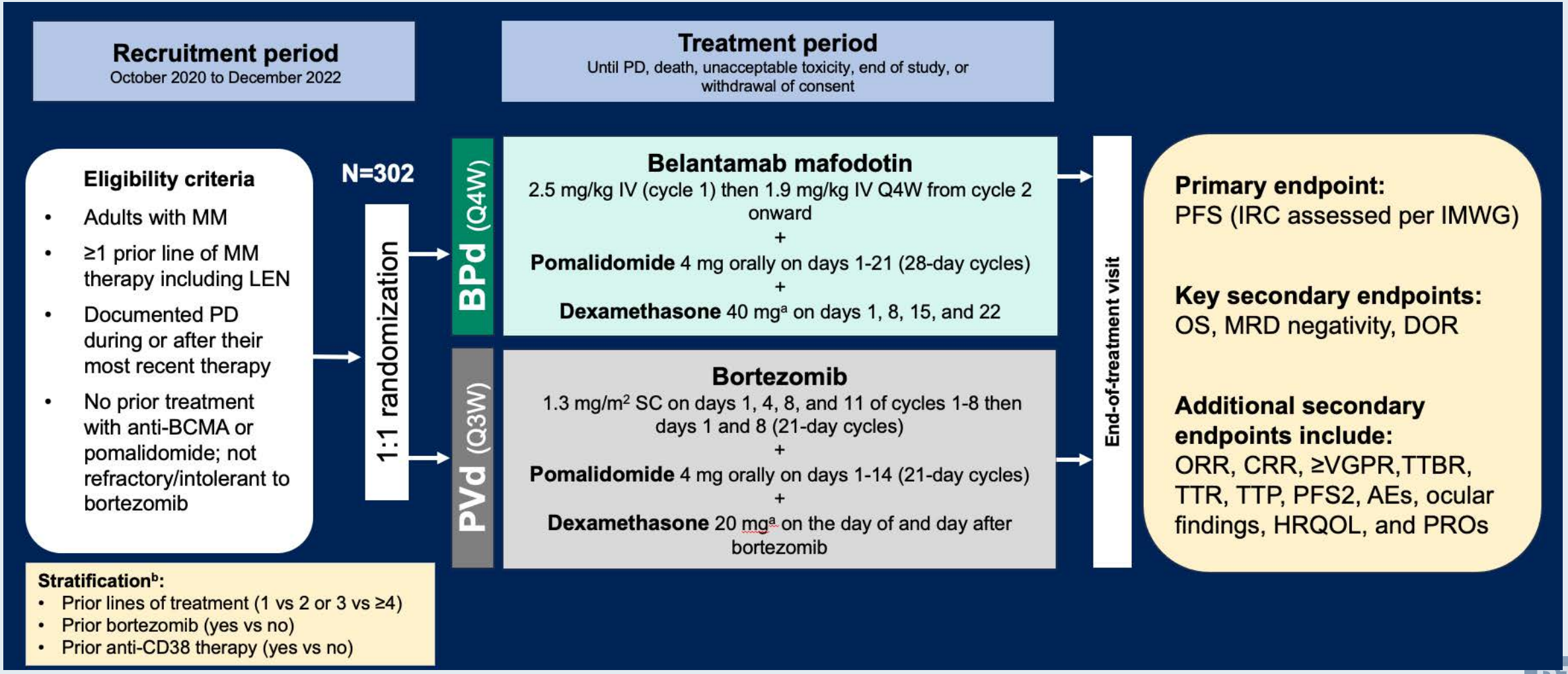



Median PFS2 NR vs 33.4 months (HR 0.59)

| | | |
|---|---|---|
| Grade ≥3 | 33% | 20% |
| Pneumonia | 12% | 4% |
| Ocular AEs (Grade ≥3) | 79% (34%) | 29% (3%) |
| Vision blurred | 68% (24%) | 11% (<1%) |
| Dry eye | 51% (7%) | 7% (0) |
| Photophobia | 47% (2%) | 2% (0) |
| Eye irritation | 43% (5%) | 5% (0) |

Hungria V, et al. N Engl J Med 2024;391(5):393–407. Hungria V, et al. Blood 2024;144(supplement 1):772.

# DREAMM-8: A Phase III Trial of Belamaf with Pomalidomide/ Dexamethasone (BPd) versus Pomalidomide with Vd (PVd) for R/R MM




Trudel S et al. ASCO 2024;Abstract LBA105.

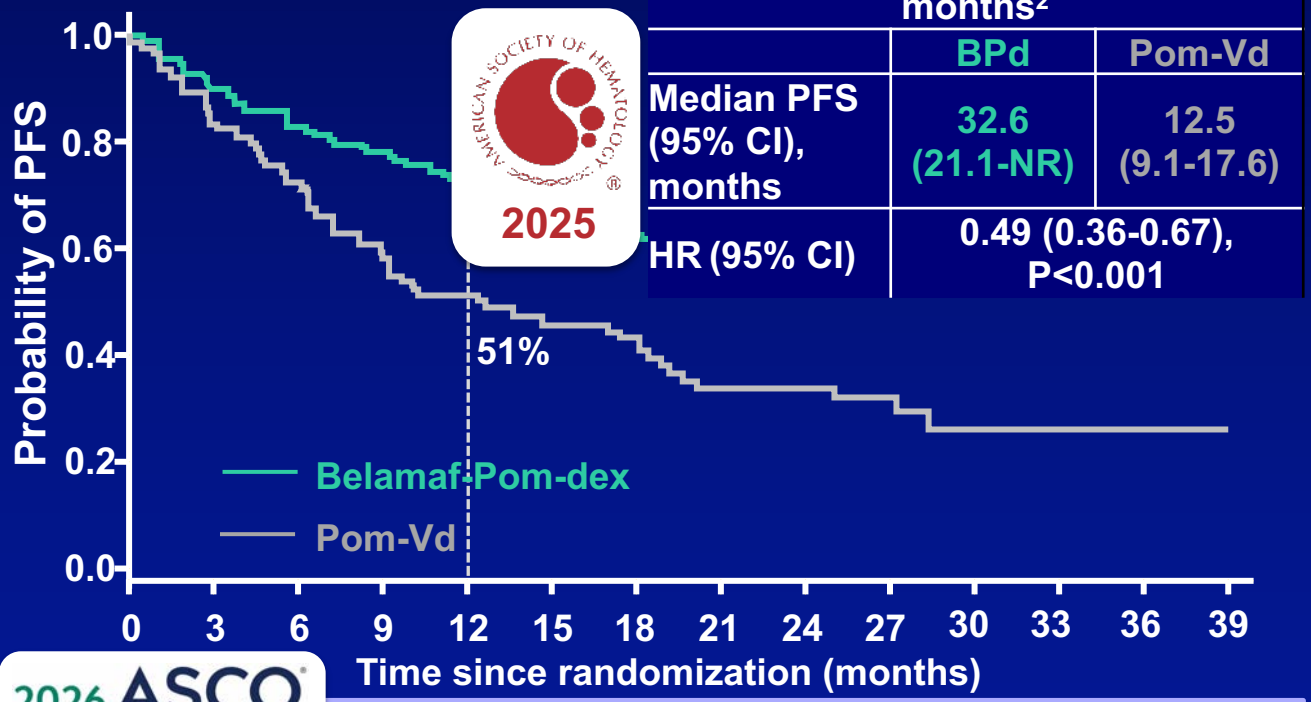
# Belantamab mafodotin for early-relapse RRMM

# DREAMM-8: Belantamab mafodotin + Pom-dex vs Pom-Vd as ≥2nd-line therapy

**Phase 3 DREAMM-8 study[1]**

- Patients with ≥1 prior line, including lenalidomide
- Belamaf-Pom-dex until PD/death, N=155
- Pom-Vd until PD/death, N=147

| Patients | Belamaf-Pom-dex, N=155 | Pom-Vd, N=147 |
|---|---|---|
| Median age, years | 67 | 68 |
| Age ≥75 years | 12% | 24% |
| High-risk cytogenetics | 34% | 32% |
| EMD | 13% | 7% |
| 1 / 2 or 3 / ≥4 prior lines | 53 / 35 / 12% | 52 / 33 / 15% |
| Prior PI | 90% | 93% |
| Prior IMiD | 100% | 100% |
| IMiD-refractory | 82% | 76% |
| Prior CD38 mAb | 25% | 29% |
| CD38 mAb-refractory | 23% | 24% |
| Prior ASCT | 64% | 56% |




**UPDATE: median follow-up 35.8 months[2]**

| | BPd | Pom-Vd |
|---|---|---|
| Median PFS (95% CI), months | 32.6 (21.1-NR) | 12.5 (9.1-17.6) |
| HR (95% CI) | 0.49 (0.36-0.67), P<0.001 | |

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**Outcomes**

- Significant PFS benefit – seen across prespecified subgroups, including R-refractory patients (HR 0.45), CD38 mAb-refractory patients (HR 0.65), and patients with high-risk cytogenetics (HR 0.57)[1]
- PFS2 benefit (median 47.1 vs 21.7 months, HR 0.52) seen across patient subgroups including R-refractory and CD38-exposed/refractory patients[3]
- Early OS trend favoring belamaf-Pom-dex – 12-month OS 83% vs 76% (HR 0.77)[1]

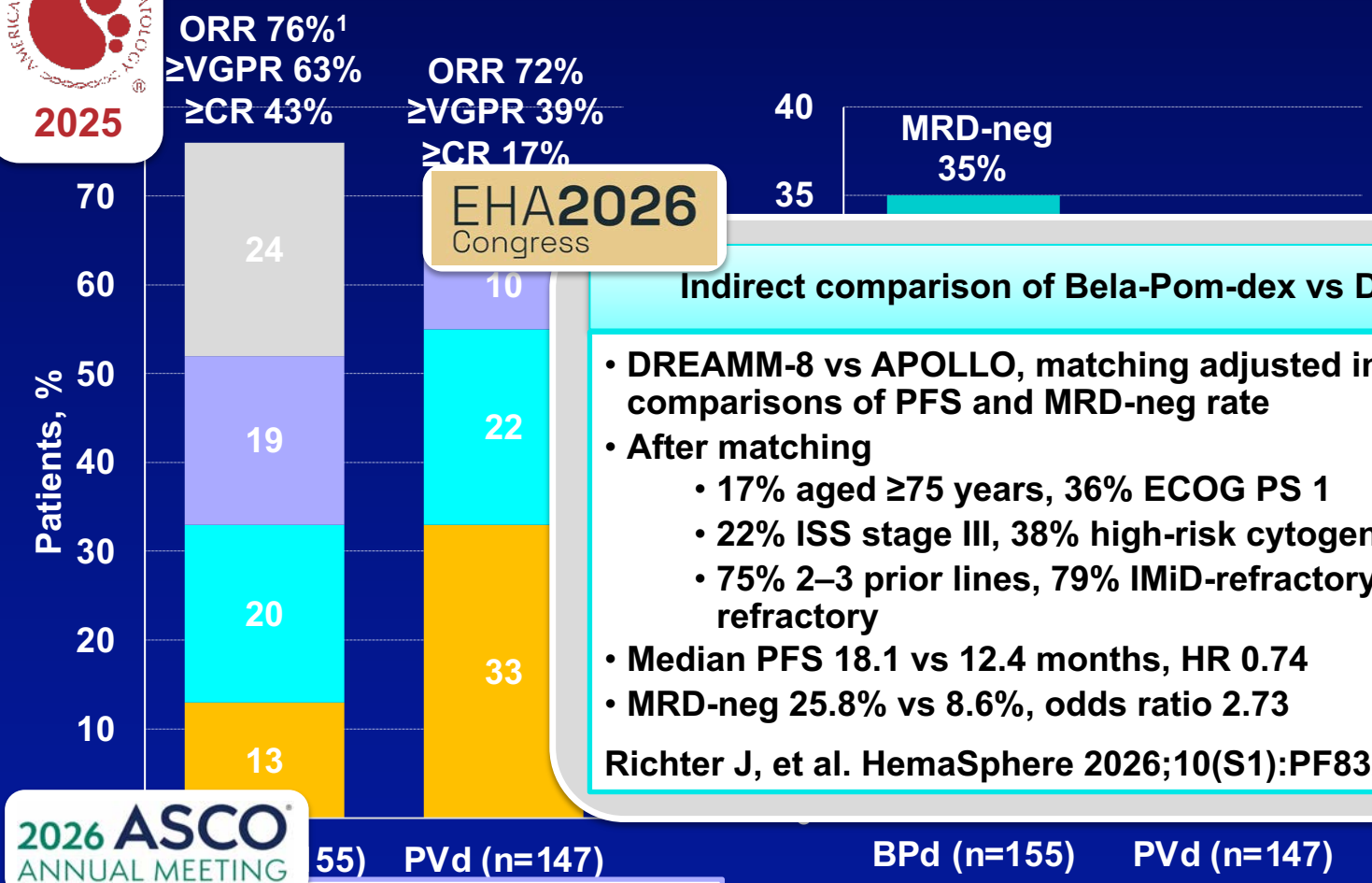

1. Dimopoulos MA, et al. N Engl J Med 2024;391(5):408–421. 2. Trudel S, et al. Blood 2025;146(Supplement 1):2264.
3. Cengiz Seval G, et al. J Clin Oncol 2026;44(16_suppl):7566.

# Belantamab mafodotin for early-relapse RRMM

## DREAMM-8: Belantamab mafodotin + Pom-dex vs Pom-Vd as ≥2nd-line therapy

2025

EHA2026 Congress




**Indirect comparison of Bela-Pom-dex vs Dara-Pom-dex**

- DREAMM-8 vs APOLLO, matching adjusted indirect comparisons of PFS and MRD-neg rate
- After matching
  - 17% aged ≥75 years, 36% ECOG PS 1
  - 22% ISS stage III, 38% high-risk cytogenetics
  - 75% 2–3 prior lines, 79% IMiD-refractory, 47% PI-refractory
- Median PFS 18.1 vs 12.4 months, HR 0.74
- MRD-neg 25.8% vs 8.6%, odds ratio 2.73

Richter J, et al. HemaSphere 2026;10(S1):PF832.

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55) PVd (n=147)

24-month DOR 65% vs 40%[1]
Long-term responders (PFS ≥30 months): 38% vs 15%[3]

Sustained 12-month MRD-neg ≥CR 15% vs 3%[1]

| Safety[2] | Belamaf-Pom-dex, N=155 | Pom-Vd, N=147 |
|---|---|---|
| Grade ≥3 AE | 94% | 76% |
| Related | 80% | 59% |
| to AEs | 15% | 12% |
| | 63% | 45% |
| | 11% | 11% |
| AEs | | |
| | 24% | 20% |
| | 42% | 28% |
| | 10% | 13% |
| | 82% | 68% |
| | 49% | 26% |
| ade ≥3 AEs, ≥10%) | | |
| | 79% (17%) | 15% (0) |
| | 61% (8%) | 10% (0) |
| tion in eye | 61% (6%) | 6% (0) |
| | 50% (4%) | 9% (0) |
| Photophobia | 44% (3%) | 4% (0) |
| Eye pain | 33% (2%) | 5% (0) |
| Cataract | 27% (6%) | 10% (4%) |
| Reduced visual acuity | 23% (13%) | 6% (1%) |


1. Trudel S, et al. Blood 2025;146(Supplement 1):2264. 2. Dimopoulos MA, et al. N Engl J Med 2024;391(5):408–421.
3. Dimopoulos MA, et al. J Clin Oncol 2026;44(16_suppl):7565.

# Real-world practical guidance for the clinical management of belantamab mafodotin-associated ocular events

## Expert Experience Program

- Independent expert panel of hematologists and ophthalmologists
- Risk factors for ocular events
- Modifications of dose and/or treatment schedule
- Best practices for referral to and collaboration with an eye specialist
- Communication of benefits and risks

### Illustrative images of changes in visual acuity included in KVA scale

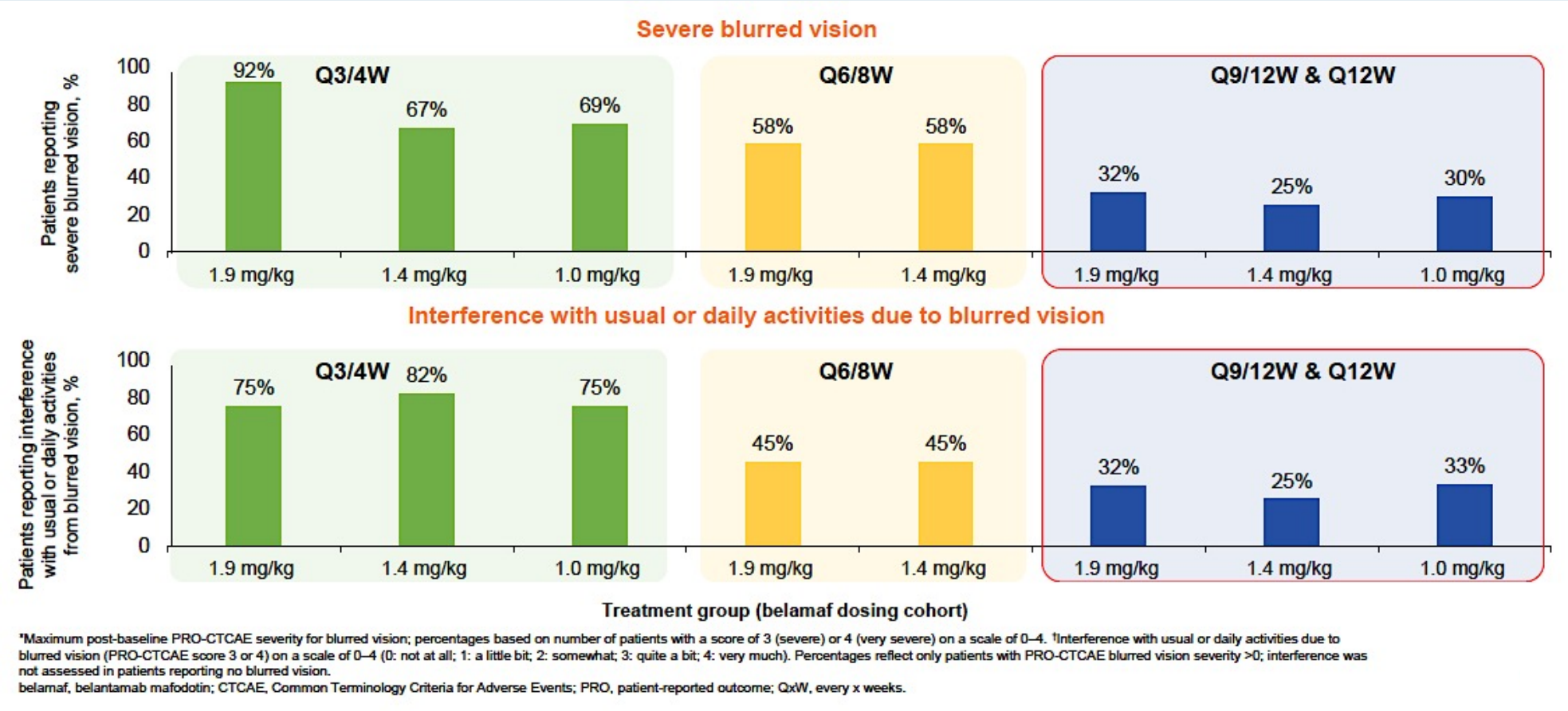



| | Grade per KVA scale | | | |
|---|---|---|---|---|
| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
| Corneal examination finding(s) | *Mild superficial keratopathy*<br>Mild superficial punctate keratopathy (documented worsening from baseline), with or without symptoms | *Moderate superficial keratopathy*<br>Any/or a combination of:<br>• *Moderate* superficial | *Severe superficial keratopathy*<br>Any/or a combination of:<br>• *Severe* superficial | *Corneal epithelial defect*<br>Such as corneal erosion(s) or …eal ulcer(s)[b] |
| Grade 3 | Corneal examination finding(s)<br>• Severe superficial punctate keratopathy[d]<br>Change in BCVA[b]<br>• Decline from baseline by more than three lines (and Snellen Visual Acuity not worse than 20/200) | | | • Reduce belamaf dose[e] AND extend dose interval to at least 12 weeks and maintain at new dose interval, provided recovery to Grade 1<br>• If dose interval exceeds 16 weeks, further reduce belamaf dose[e] |
| Grade 4 | Corneal examination finding(s)<br>• Corneal epithelial defect<br>Change in BCVA[b]<br>• Snellen Visual Acuity worse than 20/200 | | | • Consider treatment hold until Grade 1<br>• If continuing treatment with belamaf is being considered, reduce belamaf dose[e] AND extend dose interval to at least 12 weeks and maintain at new dose interval |

Terpos E, Richardson PG, et al. Am J Hematol 2025;100(10):1839–50.

# DREAMM-9 Trial: Patient-Reported Vision-Related Functioning (VRF) and Blurred Vision with Extended Belamaf Dosing Intervals

- DREAMM-9 explored the safety and efficacy of multiple doses and schedules of belamaf in the BVRd combination for transplant-ineligible newly diagnosed MM
- Extended dosing schedules were associated with maintained VRF




*Maximum post-baseline PRO-CTCAE severity for blurred vision; percentages based on number of patients with a score of 3 (severe) or 4 (very severe) on a scale of 0–4. †Interference with usual or daily activities due to blurred vision (PRO-CTCAE score 3 or 4) on a scale of 0–4 (0: not at all; 1: a little bit; 2: somewhat; 3: quite a bit; 4: very much). Percentages reflect only patients with PRO-CTCAE blurred vision severity >0; interference was not assessed in patients reporting no blurred vision.
belamaf, belantamab mafodotin; CTCAE, Common Terminology Criteria for Adverse Events; PRO, patient-reported outcome; QxW, every x weeks.

Usmani SZ et al. IMS 2026;Abstract OA-20.

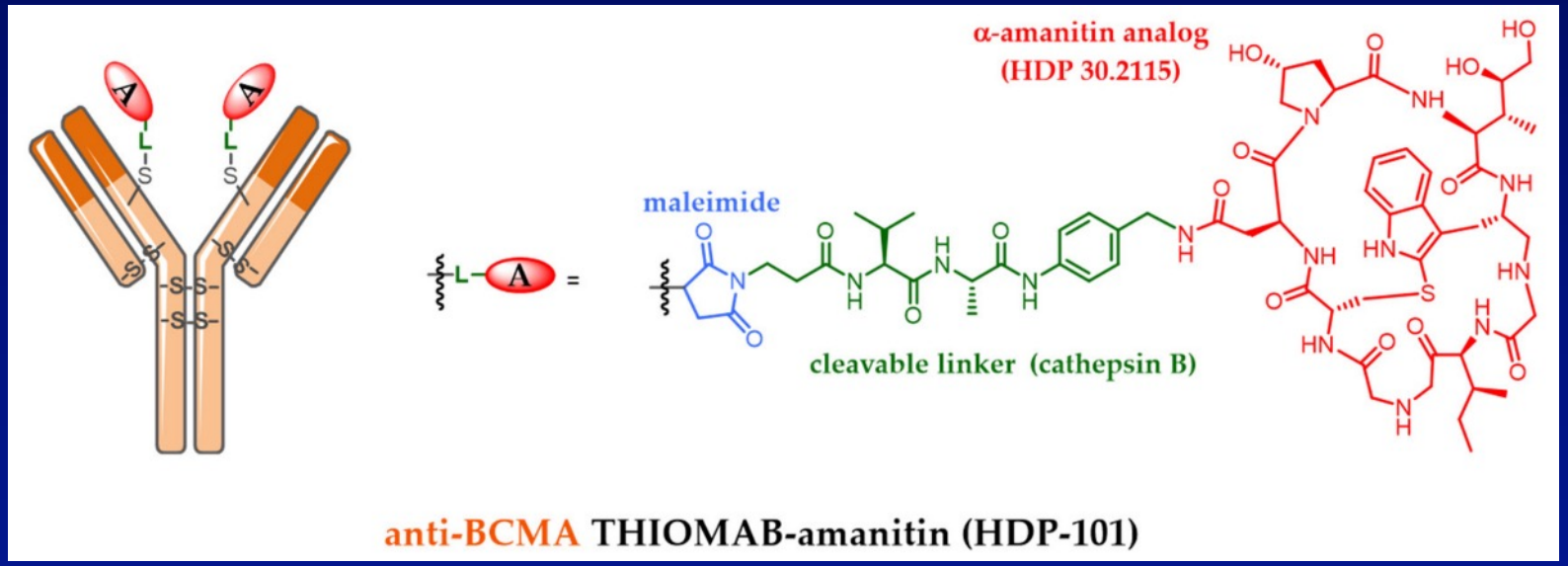
# Steps Prior to First Infusion of Belamaf

- Due to the risk of ocular toxicity, Belantamab mafodotin is only available through a Risk Evaluation and Mitigation Strategy (REMS)
- Ophthalmic exams must be completed at baseline, prior to each dose, with new or worsening symptoms, and as clinically indicated.
  - Ophthalmologist or optometrist
- Establish line of communication with the eye care professional for baseline and ongoing ocular assessments
- Understand ophthalmic exam findings interpretation and potential dose modifications

Content courtesy of Douglas W Sborov, MD, MS

RTP RESEARCH TO PRACTICE

# Novel BCMA-targeted ADC: HDP-101




- Antibody-targeted amanitin conjugate (ATAC; RNA polymerase II inhibitor)[1]
- ATAC mechanism based on internalization and lysosomal degradation in BCMA-positive tumor cells
- HDP-101 resulted in complete tumor remissions in mice in vivo[2]
- Favorable therapeutic window in mice and monkeys[2]
- Potent anti-myeloma activity against cell lines[3]
- Potential activity (↑ belantamab mafodotin) in del17p MM models[3]

## First-in-human phase 1/2a study[4]

### 34 RRMM patients

- Median age 69 years
- Median 6 prior regimens

### Safety

- Grade 2–4 transient, asymptomatic thrombocytopenia in most patients at 100 µg/kg Q3W
- Reduced thrombocytopenia with 90 µg/kg Q3W + premedication, 30 µg/kg, days 1, 8, and 15, and 45 µg/kg, days 1 and 8
- No ocular toxicity to date

### Efficacy

- 100 µg/kg Q3W: 1 sCR after 15 months on treatment (patient had prior BCMA CAR T and GPRC5D BsAb); 2 PRs; 1 SD (17 cycles)
- 90 µg/kg Q3W: 2 PRs, 2 SDs (n=10)

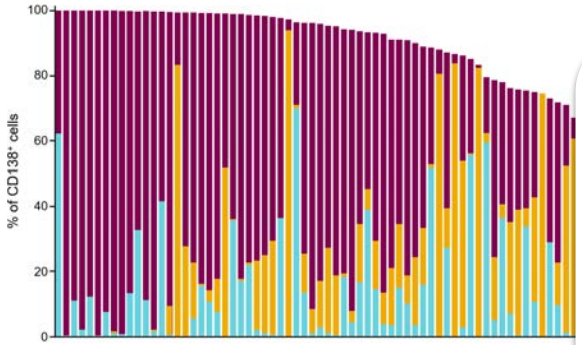
1. Joubert N, et al. Pharmaceuticals 2020;13(9):245. 2. Figueroa-Vazquez V, et al. Mol Cancer Ther 2021;20(2):367–78.
3. Kumar Singh R, et al. Res Sq [preprint] 2024;rs.3.rs-3843028. 4. Richards S, et al. HemaSphere 2025;9(S1):885–6, abstract PF749.

# Novel ADCs for RRMM

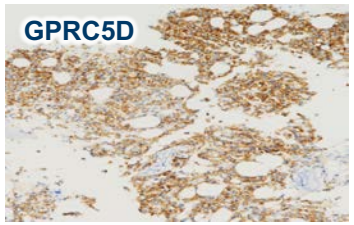
# GPRC5D ADC for targeting RRMM

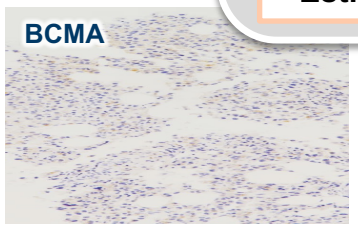
## GPRC5D is a validated target in MM, expressed at all stages of disease[1,2]

GPRC5D expressed in MM patient samples…




…including post-BCM




## AZD0305 is a GPRC5D-targeting ADC[2,3]

### Ongoing phase 1/2 study of AZD0305 in RRMM

- NCT06106945
- Patients with RRMM enrolled to three modules:
  - AZD0305 alone (≥3 prior lines)
  - AZD0305 + elranatamab (1–3 prior lines)
  - AZD0305 + Pom-dex (1–3 prior lines)
- Estimated enrolment: 226 patients
- Primary endpoints: DLTs, safety, tolerability
- Estimated primary completion date: August 2027

## Rationale for GPRC5D-targeting ADC[2]

- Activity may not rely on immune fitness in late-line patients
- Potential for rapid administration
- May be for use in orthogonal combination


1. Smith EL, et al. Sci Transl Med 2019;11(485):eaau7746.
2. In-house data, AstraZeneca Pharmaceuticals LP.
3. Huang W, et al. Cancer Res 2022;82(12_Supplement):abstract 6020, poster presentation at AACR 2022.


ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; GPRC5D, G protein-coupled receptor, class C, group 5, member D; mAB, monoclonal antibody; (RR)MM, (relapsed/refractory) multiple myeloma; vc-MMAE, valine-citrulline monomethyl auristatin E.

# Faculty Discussion



Dr Ignatius

# Questions for the Faculty

**91-year-old woman with IgG kappa MM and complex karyotype initially treated with daratumumab/lenalidomide/dexamethasone. Lenalidomide was discontinued due to poor tolerance. This 91-year-old is extremely focused on quality of life, as she should be.**

**Subsequently received ixazomib, and more recently she was started on belantamab single-agent therapy, which she is tolerating well with close ophthalmologic evaluation. Goals of care we discuss every time, and she has great support.**

**Questions**

- Dose was reduced from the get-go just to ensure her tolerance. Would you do that for a patient to avoid toxicity and maintain quality of life?
- How long would you wait to assess a response to belantamab therapy? She really doesn’t get symptomatic with treatment, even with biochemical progression.

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Dr Ignatius

# Questions for the Faculty (Continued)

**Questions**

- Would you, for such a patient, focus on the development of CRAB features, concerning symptoms or biochemical progression alone before you consider stopping or switching treatment?
- What other treatment options would you consider for this woman just to maintain quality of life? And given the improved tolerance of bispecific and CAR-T therapy, would you even look at such therapies?
- Belantamab mafodotin has been very a manageable drug, and I have been able to establish a good connection with an ophthalmologist nearby. Anything else I should be aware of other than the ophthalmic toxicity, especially for the older population we cater to?

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Dr Gandhi

# Questions for the Faculty

**80-year-old man with MM who received belamaf (years ago) and was stable for 9 months and died due to an unrelated cardiac event. No issues with eye toxicities**

**Questions**

- We participated the DREAMM-7 and 8 trials in FCS that led to the reapproval of belamaf. Now we are participating in the Phase III DREAMM-10 trial evaluating belamaf, lenalidomide and dexamethasone up front versus daratumumab/len/dex for transplant-ineligible patients. What other up-front trials of belamaf are ongoing, and is it likely this will become part of first-line treatment?
- What's the ideal time between belamaf treatments? Can you give it every 3 months?

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# Agenda

**Introduction: ESMO 2026; Recent FDA Approvals**

**Chimeric Antigen Receptor T-Cell Therapy – Dr Lonial**

**Bispecific Antibodies – Dr Lonial**

**Antibody-Drug Conjugates – Dr Richardson**

**Up-Front Treatment; CELMoDs – Dr Richardson**

- Up-Front Treatment; Ongoing Trials
- CELMoDs

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# Up-Front Treatment; Ongoing Trials

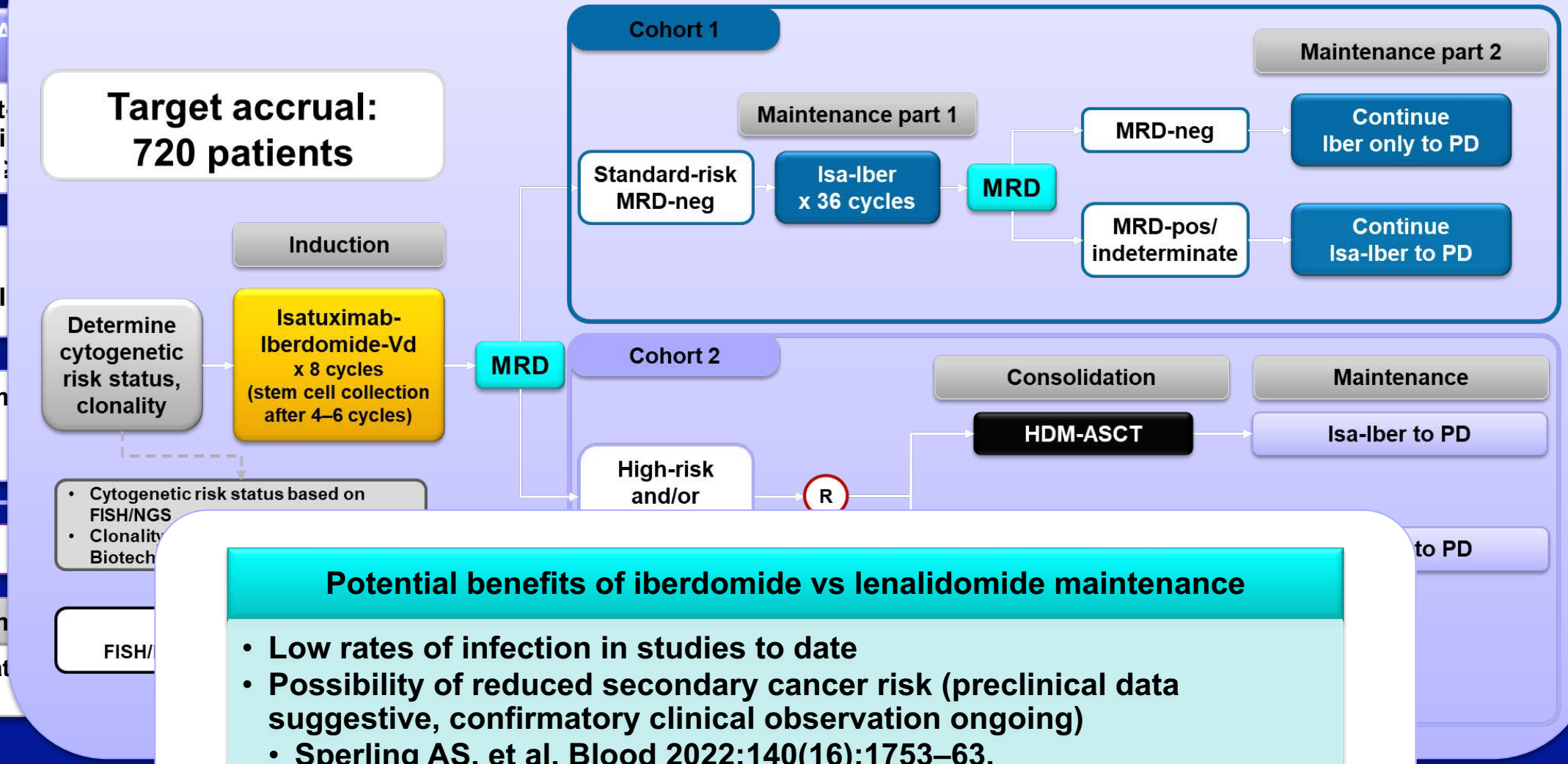
**Select Dataset**

- NCT07624513: DETERMINATION 2 - Isatuximab, Iberdomide, Bortezomib and Dexamethasone Induction, Followed by Risk- and Response-Adapted Consolidation and Maintenance Therapy, in Transplant-Eligible Patients with Newly Diagnosed Multiple Myeloma (NDMM)

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# Iberdomide in NDMM: a replacement for lenalidomide?

## DETERMINATION 2 study design




### Potential benefits of iberdomide vs lenalidomide maintenance

- Low rates of infection in studies to date
- Possibility of reduced secondary cancer risk (preclinical data suggestive, confirmatory clinical observation ongoing)
  - Sperling AS, et al. Blood 2022;140(16):1753–63.

# Faculty Discussion



Dr Hussein

# Questions for the Faculty

**35-year-old man with recently diagnosed del(17p) MM who is receiving daratumumab/RVd induction with a plan for transplant**

**Questions**

- Myeloma in young patients?
- How, if at all, does your treatment approach to relapsed myeloma change if the patient still has del(17p) disease?
- Current role of transplant for high- and standard-risk disease?
- Current or future role of CAR T, bispecifics for high- and standard-risk disease?
- MRD and duration of maintenance therapy?
- Interesting ongoing trials in the up-front setting? DETERMINATION-2?

RTP RESEARCH TO PRACTICE

# CELMoDs (Cereblon E3 Ligase Modulators)

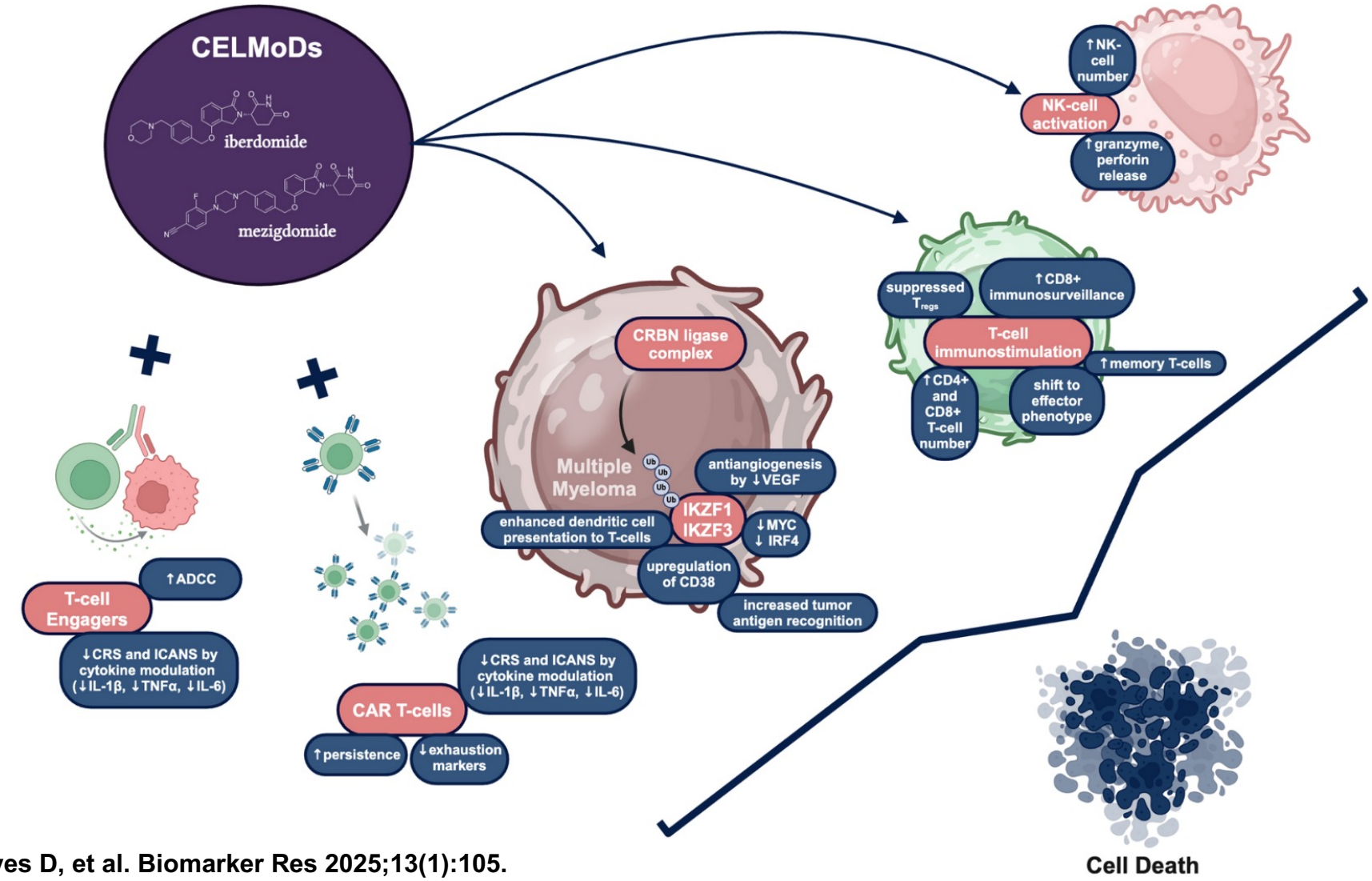
**Select Datasets**

- Lonial S et al. Iberdomide plus Daratumumab and Dexamethasone versus Daratumumab, Bortezomib, and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma (EXCALIBERRRMM): An Open-label, Randomised, Controlled, Phase 3 Trial. *Lancet Oncol* 2026 September 25;[Online ahead of print].
- Lonial S et al. Iberdomide, Daratumumab, Dexamethasone (IberDd) vs Daratumumab, Bortezomib, Dexamethasone (DVd) in Patients With Relapsed/Refractory Multiple Myeloma (RRMM): Results from EXCALIBER-RRMM Phase 3 Study. IMS 2026;Abstract LBA-12.
- Richardson PG et al. Mezigdomide, Carfilzomib, and Dexamethasone (MeziKd) vs Carfilzomib and Dexamethasone (Kd) in Relapsed/Refractory Multiple Myeloma (RRMM): Results from the Phase 3 SUCCESSOR-2 Trial. ASCO 2026;Abstract LBA7506.
- Dimopoulos MA et al. Mezigdomide, Carfilzomib, and Dexamethasone versus Carfilzomib and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma (SUCCESSOR-2): A Phase 3, Open-Label, Randomized Controlled Trial. *Lancet* 2026;408(10551):219-33.
- Dimopoulos MA et al. Mezigdomide, Carfilzomib, and Dexamethasone (MeziKd) vs Carfilzomib and Dexamethasone (Kd) in Relapsed/Refractory Multiple Myeloma (RRMM): Results from the Phase 3 SUCCESSOR-2 trial. IMS 2026;Abstract PA-305.

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# CELMoDs: summary of pharmacodynamics

## CELMoDs: overview of immunologic effects

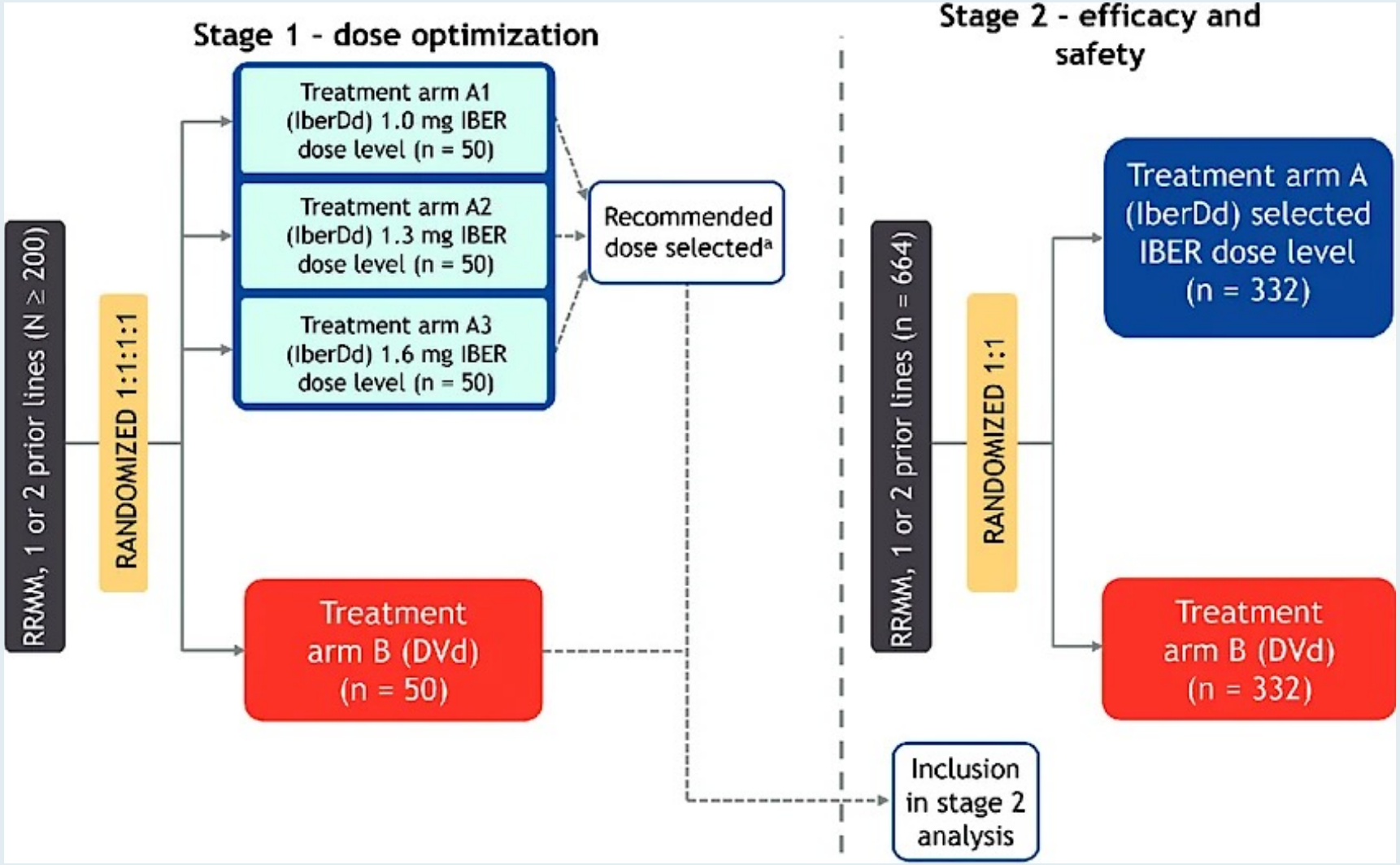



Kegyes D, et al. Biomarker Res 2025;13(1):105.

Mo CC, et al. Expert Opin Emerg Drugs 2025;30(3):209–19.

•High baseline EZH2 expression → poorer PFS

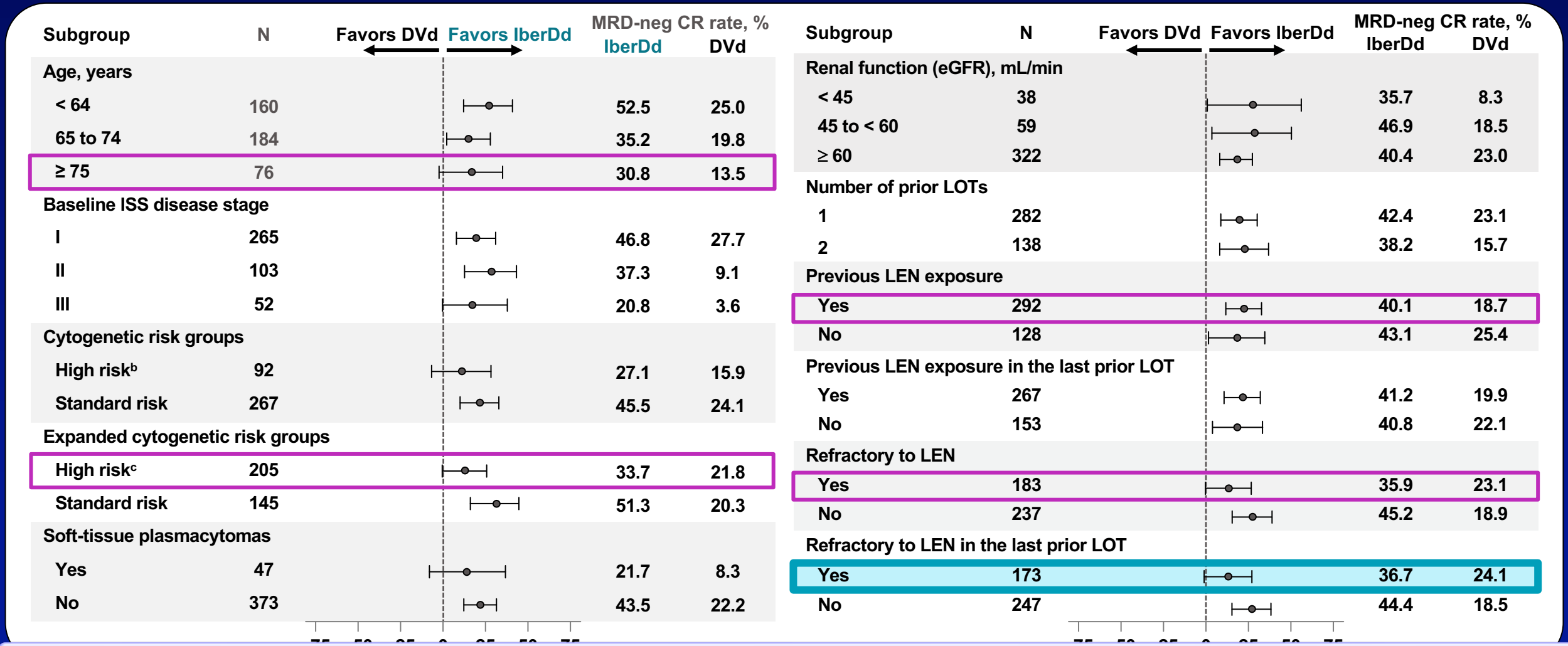
# EXCALIBER-RRMM: A Phase III Trial of Iberdomide in Combination with Daratumumab and Dexamethasone for R/R MM




Lonial S et al. *Future Oncol* 2025;21(14):1761-69.

International Myeloma Society 23rd Annual MEETING & EXPOSITION
September 23-26, 2026 • Glasgow, Scotland

# EXCALIBER-RRMM: Dual primary endpoint
# MRD-negative CR at any time – subgroup analysis




| Subgroup | N | MRD-neg CR rate, % IberDd | MRD-neg CR rate, % DVd |
|---|---|---|---|
| **Age, years** | | | |
| < 64 | 160 | 52.5 | 25.0 |
| 65 to 74 | 184 | 35.2 | 19.8 |
| ≥ 75 | 76 | 30.8 | 13.5 |
| **Baseline ISS disease stage** | | | |
| I | 265 | 46.8 | 27.7 |
| II | 103 | 37.3 | 9.1 |
| III | 52 | 20.8 | 3.6 |
| **Cytogenetic risk groups** | | | |
| High risk[b] | 92 | 27.1 | 15.9 |
| Standard risk | 267 | 45.5 | 24.1 |
| **Expanded cytogenetic risk groups** | | | |
| High risk[c] | 205 | 33.7 | 21.8 |
| Standard risk | 145 | 51.3 | 20.3 |
| **Soft-tissue plasmacytomas** | | | |
| Yes | 47 | 21.7 | 8.3 |
| No | 373 | 43.5 | 22.2 |
| **Renal function (eGFR), mL/min** | | | |
| < 45 | 38 | 35.7 | 8.3 |
| 45 to < 60 | 59 | 46.9 | 18.5 |
| ≥ 60 | 322 | 40.4 | 23.0 |
| **Number of prior LOTs** | | | |
| 1 | 282 | 42.4 | 23.1 |
| 2 | 138 | 38.2 | 15.7 |
| **Previous LEN exposure** | | | |
| Yes | 292 | 40.1 | 18.7 |
| No | 128 | 43.1 | 25.4 |
| **Previous LEN exposure in the last prior LOT** | | | |
| Yes | 267 | 41.2 | 19.9 |
| No | 153 | 40.8 | 22.1 |
| **Refractory to LEN** | | | |
| Yes | 183 | 35.9 | 23.1 |
| No | 237 | 45.2 | 18.9 |
| **Refractory to LEN in the last prior LOT** | | | |
| Yes | 173 | 36.7 | 24.1 |
| No | 247 | 44.4 | 18.5 |

**Treatment benefit with IberDd was consistent across prespecified subgroups, including LEN-exposed/-refractory patients**

Lonial S, et al. Clin Lymphoma Myeloma Leuk 2026;26(Suppl 2):S378–9, abstract LBA-12. Lonial S, et al. Lancet Oncol 2026;doi:10.1016/S1470-2045(26)00450-X

# Superior PFS with Iberdomide, Daratumumab and Dexamethasone versus Standard Therapy for R/R MM in the Phase III EXCALIBER-RRMM Trial

## Press Release: October 8, 2026

Positive topline results were announced from the Phase 3 EXCALIBER-RRMM study, evaluating iberdomide in combination with daratumumab and dexamethasone (ZDd) in 800 patients with multiple myeloma (MM), as early as first relapse.

“Results showed ZDd demonstrated a statistically significant improvement in the dual-primary endpoint of progression-free survival (PFS), with median PFS of 42 months for ZDd vs. 20 months for daratumumab, bortezomib and dexamethasone (DVd) [HR:0.49, p<0.000001], representing a 51% reduction in the risk of disease progression or death. Median follow-up was 23 months. The safety profile of iberdomide in combination with standard therapies remained consistent with previously reported safety findings from the study.

These results build on the previously reported improvement in minimal residual disease (MRD)-negative complete response vs. DVd, the other dual-primary endpoint, which supported the U.S Food and Drug Administration approval of iberdomide for RRMM. Detailed MRD results were presented at the International Myeloma Society 23rd annual meeting and simultaneously published in *Lancet Oncology*.”

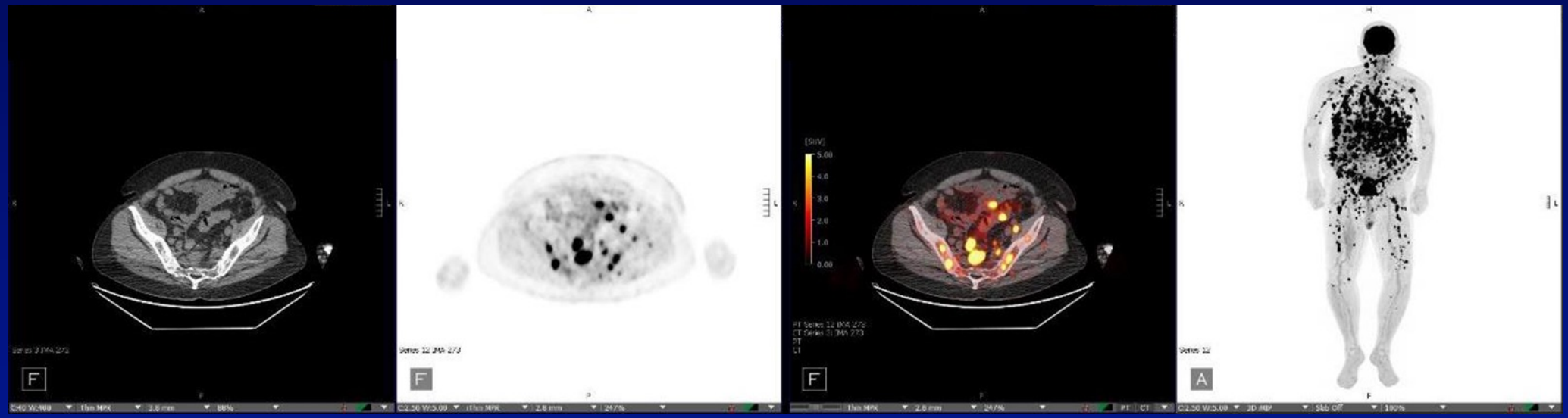
https://news.bms.com/news/corporate-financial/2026/Bristol-Myers-Squibb-Announces-ZENBEXUSTM-iberdomide-in-Combination-with-Daratumumab-and-Dexamethasone-ZDd-Demonstrates-Superior-Progression-Free-Survival-vs--Standard-of-Care-in-Relapsed-and-Refractory-Multiple-Myeloma-in-Phase-3---/default.aspx

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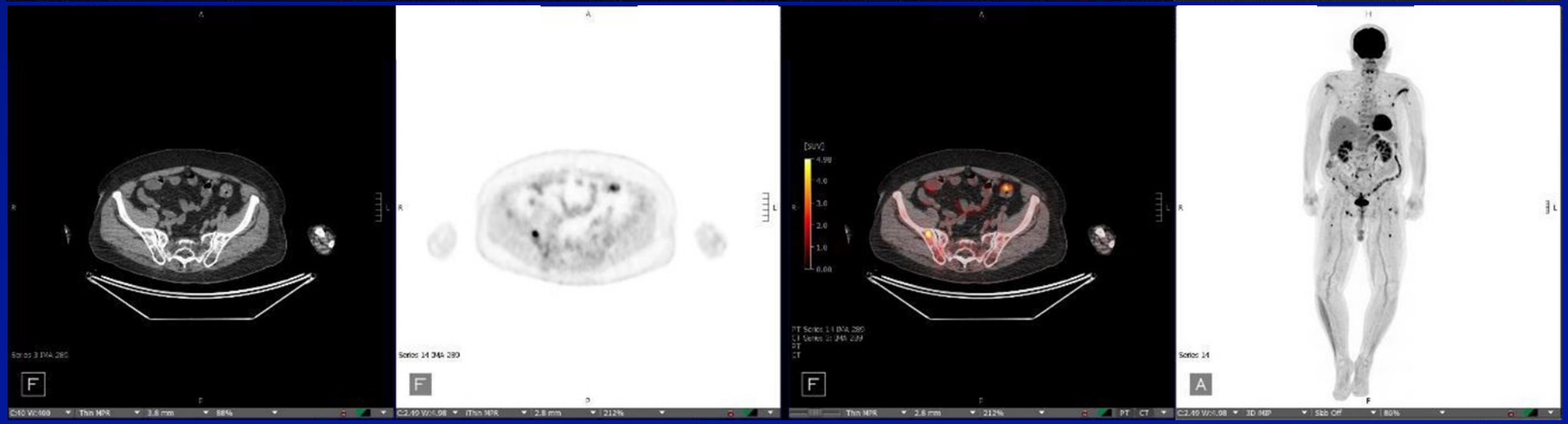
## CELMoD doublet for later-relapse RRMM

# Mezigdomide + dex induces responses in patients with EMD

**At start of treatment (study entry)**

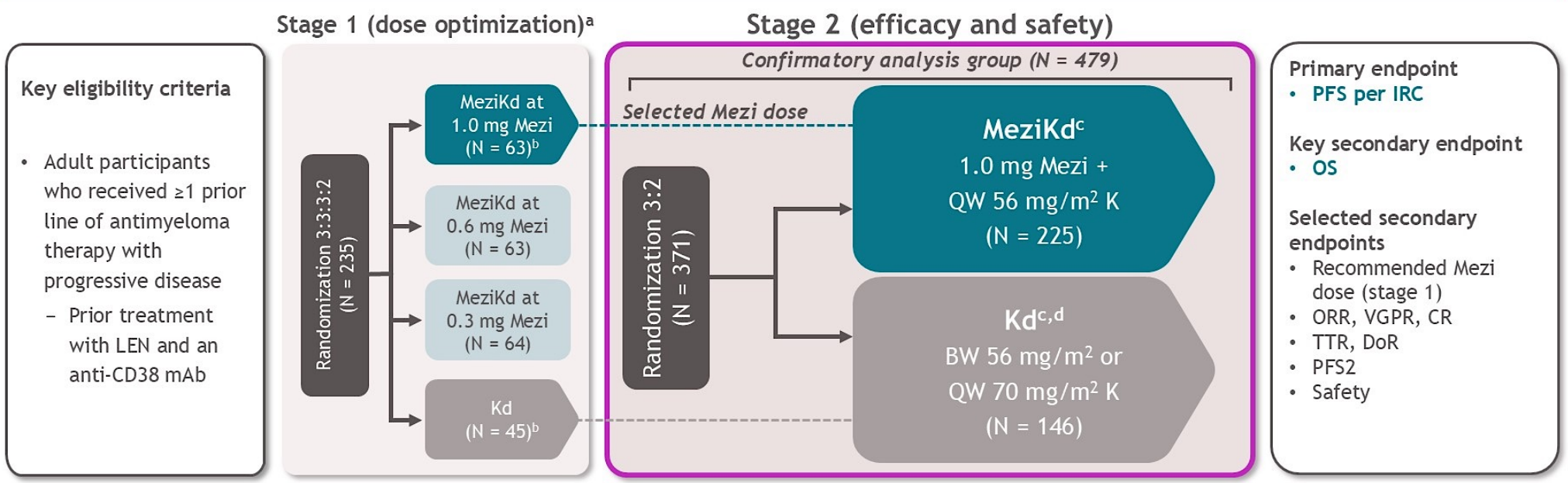


**After 4 months of treatment with Mezi 1.0 mg, D1–21 every 28 days, + Dex**



Richardson PG, et al. Blood 2022;140(Supplement 1):1366–8. Richardson PG, et al. N Engl J Med 2023;389(11):1009–22.

# SUCCESSOR-2: A Phase III Trial of Mezigdomide, Carfilzomib and Dexamethasone versus Carfilzomib and Dexamethasone for R/R MM




NCT05552976. [a]Patients enrolled in stage 1 on a dose of Mezi not chosen for stage 2 had the option to move to the selected dose if some criteria were met; [b]Patients from these stage 1 arms were included in the confirmatory analysis groups; [c]DEX dosing - MeziKd arm: 40 mg, option of 20 mg if > 75 years of age, BMI < 18.5 kg/m², poorly controlled diabetes, or prior intolerance to steroid therapy; Kd arm: 20 mg, 10 mg option for stated criteria (BW regimen) or 40 mg, 20 mg option for stated criteria (QW regimen); [d]QW regimen made available July 2023; [e]K dose on C1D1 was 20 mg/m². BMI, body mass index; BW, twice weekly; C, cycle; D, day; DEX, dexamethasone; DoR, duration of response; IRC, independent review committee; K, carfilzomib; OS, overall survival; PFS2, second progression-free survival; QW, weekly; TTR, time to response.

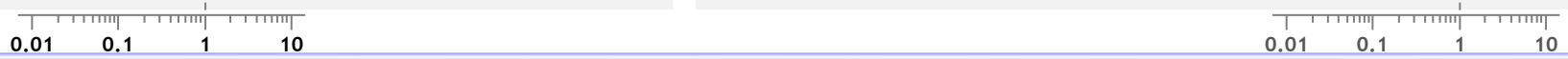
Richardson PG, et al. ASCO 2026, Presentation LBA7506

Richardson PG et al. ASCO 2026;Abstract LBA7506.

# SUCCESSOR-2: Subgroup analysis of PFS

## Subgroup analysis of PFS in confirmatory analysis group by ITT, n = 479

| Subgroup | N | HR (95% CI) |
|---|---|---|
| **Age, years** | | |
| < 65 | 181 | 0.52 (0.34–0.80) |
| 65 to < 75 | 178 | 0.43 (0.27–0.67) |
| ≥ 75 | 120 | 0.52 (0.29–0.94) |
| **Baseline ISS disease stage** | | |
| I | 245 | 0.42 (0.28–0.64) |
| II | 146 | 0.51 (0.31–0.84) |
| III | 88 | 0.60 (0.34–1.05) |
| **Cytogenetic risk groups** | | |
| High risk | 136 | 0.49 (0.30–0.80) |
| Standard risk | 280 | 0.51 (0.35–0.74) |
| **Soft-tissue plasmacytomas** | | |
| Yes | 118 | 0.34 (0.21–0.54) |
| No | 361 | 0.58 (0.42–0.82) |
| **Extra-medullary plasmacytomas** | | |
| Yes | 45 | 0.33 (0.16–0.67) |
| No | 434 | 0.51 (0.38–0.69) |
| **Prior LOTs** | | |
| ≤ 2 | 253 | 0.54 (0.37–0.80) |
| > 2 | 226 | 0.44 (0.30–0.64) |
| **Refractory to anti-CD38 mAbs** | | |
| Yes | 411 | 0.48 (0.36–0.64) |
| No | 68 | 0.50 (0.23–1.08) |
| **Refractory to LEN** | | |
| Yes | 363 | 0.50 (0.36–0.67) |
| No | 116 | 0.40 (0.21–0.76) |
| **Refractory to anti-CD38 mAbs and LEN** | | |
| Yes | 326 | 0.47 (0.34–0.65) |
| No | 153 | 0.48 (0.28–0.82) |
| **Refractory to POM** | | |
| Yes | 155 | 0.51 (0.33–0.78) |
| No | 324 | 0.44 (0.31–0.64) |

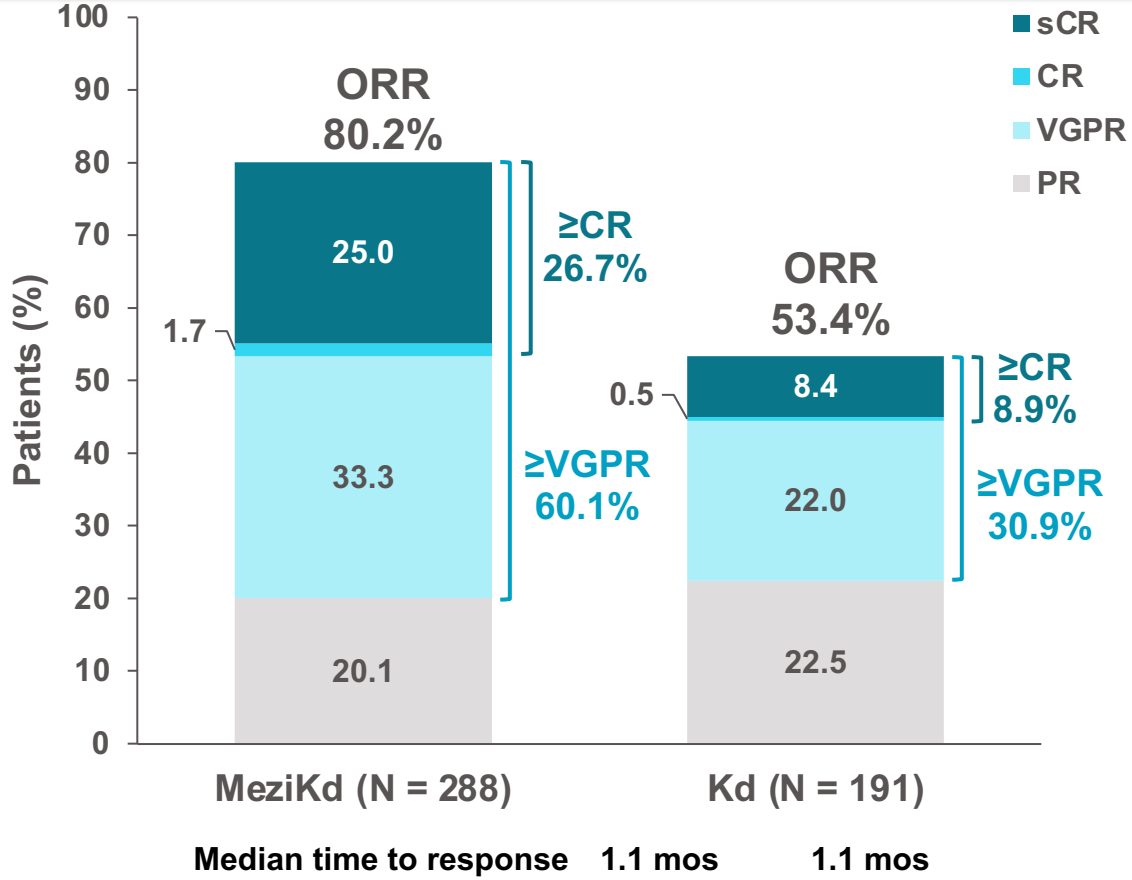



**PFS survival benefit with MeziKd superior across all prespecified subgroups**

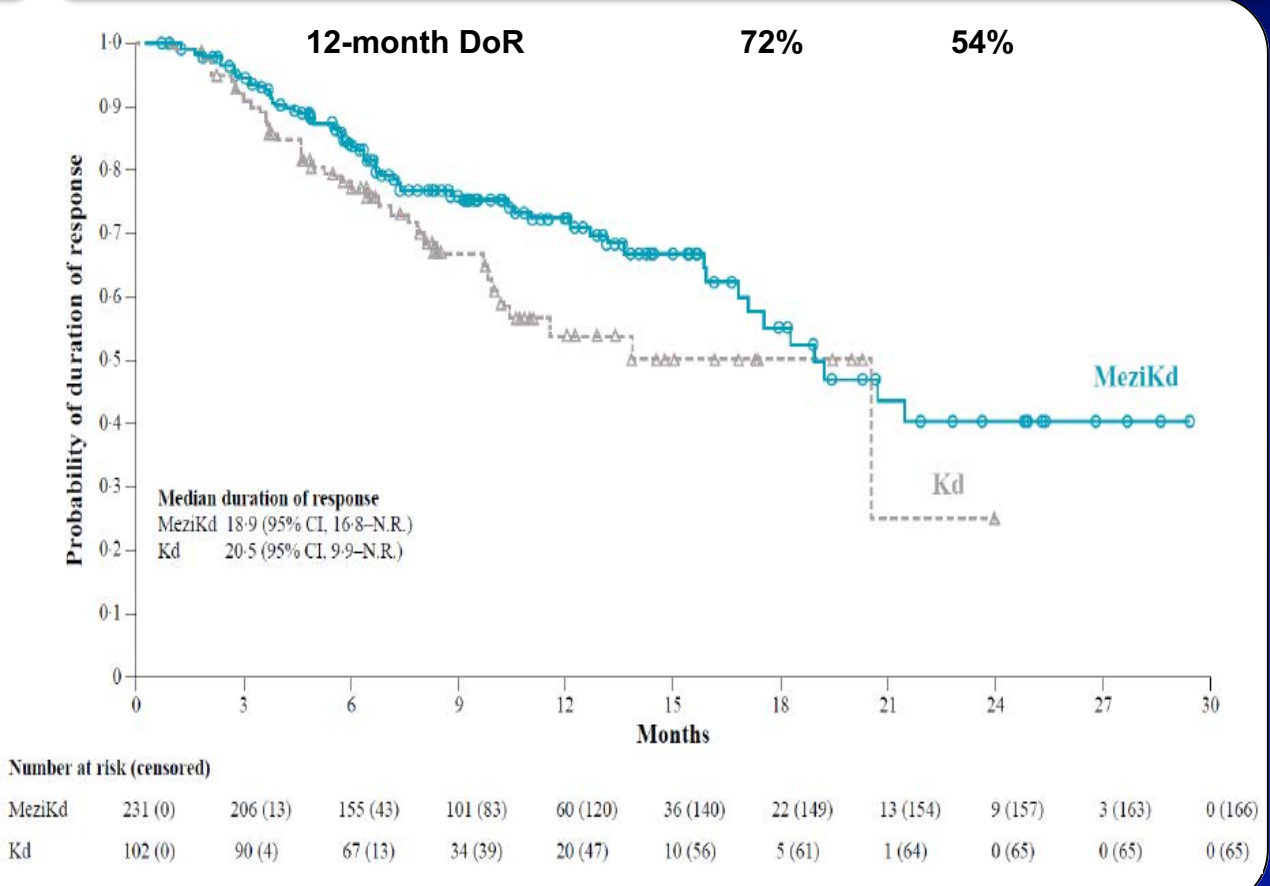
Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506. Dimopoulos MA, et al. HemaSphere 2026;10(S1):LB5004. Dimopoulos MA, et al. Lancet 2026;408(10551):219–33.

# SUCCESSOR-2: Response and DOR

## Treatment response, n = 479




## DOR, n = 333

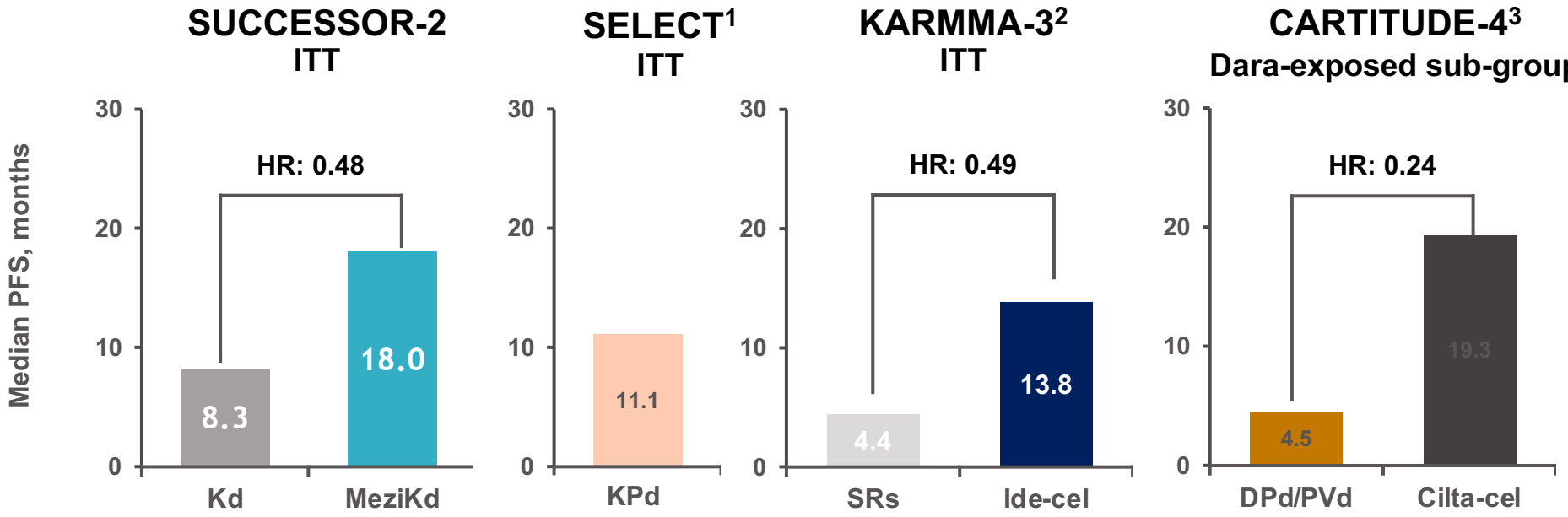



**Addition of Mezi to Kd deepened response, doubling the rate of ≥VGPR and tripling the rate of ≥CR**

Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506. Dimopoulos MA, et al. HemaSphere 2026;10(S1):LB5004. Dimopoulos MA, et al. Lancet 2026;408(10551):219–33.

# SUCCESSOR-2: How does it compare?

## Contextualization of clinical benefit seen in SUCCESSOR-2 for anti-CD38 mAb- and R-exposed RRMM patients across multiple settings and implications for real-world practice[1]



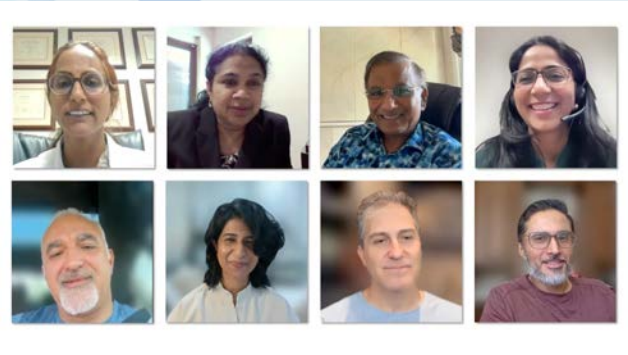

All patients[a] were anti-CD38 mAb- and R-exposed

| | SUCCESSOR-2 | | SELECT[1] | KARMMA-3[2] | | CARTITUDE-4[3] | |
|---|---|---|---|---|---|---|---|
| | Kd | MeziKd | KPd | SRs | Ide-cel | DPd/PVd | Cilta-cel |
| | N= 191 | N = 288 | N = 52 | N = 132 | N = 254 | N = 54 | N = 51 |
| Median prior LoT, n (range) | 2 (1–9) | 2 (1–9) | 2 (1–2) | 3 (2-4) | 3 (2-4) | NR | NR |
| R refractory, % | 76.9 | 74.4 | 100 | 73 | 79 | 100 | 100 |
| Anti-CD38 refractory, % | 85.3 | 86.1 | 75 | 95 | 94 | 83.3 | 90.5 |

Trials are not intended for direct comparison. Side-by-side data are presented solely to summarize information.
[a]77% of patients received prior anti-CD38 mAb in the SELECT trial.

Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506. Dimopoulos MA, et al. HemaSphere 2026;10(S1):LB5004. Dimopoulos MA, et al. Lancet 2026;408(10551):219–33.
1. Richardson PG, et al. Blood Cancer J 2018;8(11):109. 2. Perrot A, et al. Leuk Lymphoma 2024;65(6):833-842; 3. Ailawadhi S, et al. Blood 2024;144(23):2389-2401;
4. Einsele H, et al. Lancet Oncol 2026;27(2):254-268.

# Faculty Discussion



# Questions for the Faculty

- How are you planning to use IberDd relative to other options in the R/R setting?
- If mezigdomide is approved, how will you decide between iberdomide- and mezigdomide-containing regimens? Are there specific patients for which you would prefer one over the other? Would you use them in sequence?
- How do CELMoDs compare to standard IMiDs in terms of gastrointestinal toxicities and rates of second cancer?

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Susmitha Apuri, MD



Mamta Choksi, MD



Sunil Gandhi, MD



Shaachi Gupta, MD, MPH



Maen Hussein, MD



Renjitha Ignatius, MD



Shachar Peles, MD



Syed F Zafar, MD

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