New clinical trials :
Integration of new therapies and MRD

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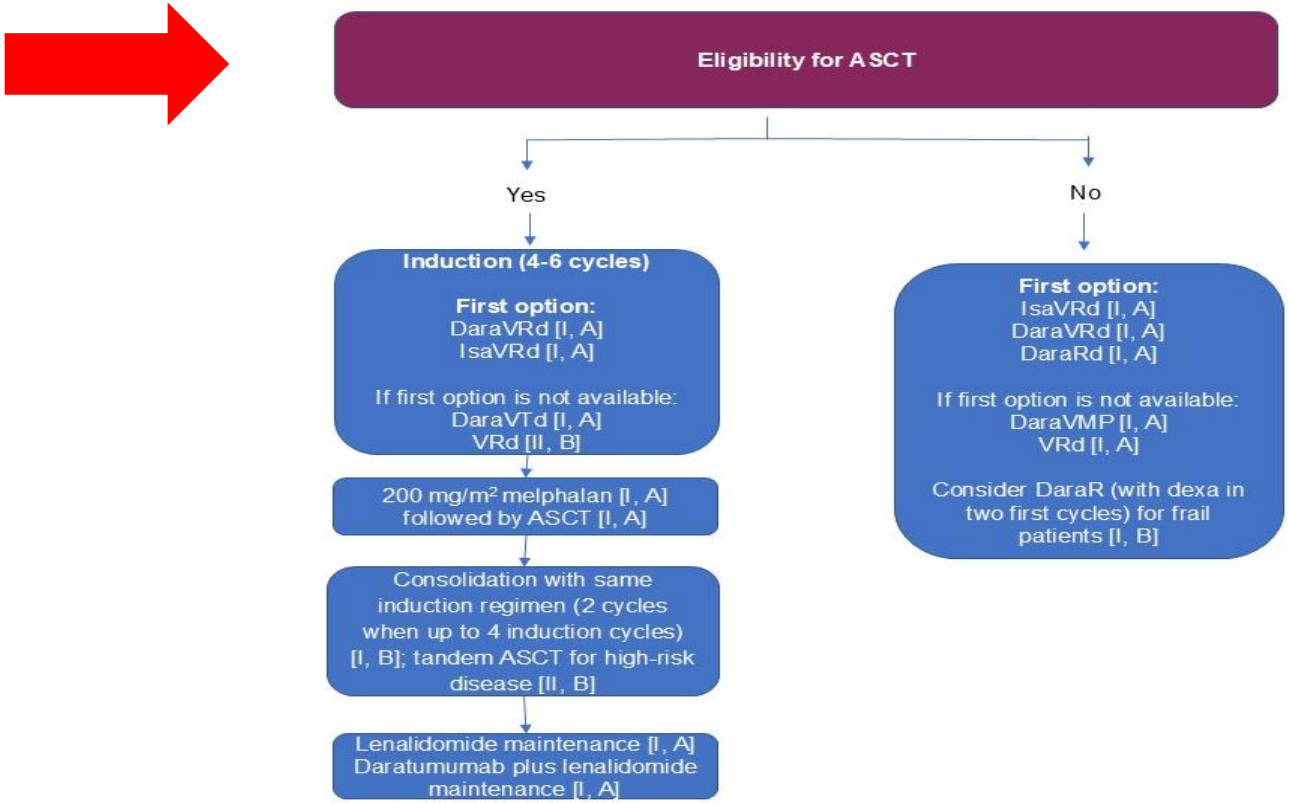
Disclosures

Advisory board and honoraria from :

J&J, Pfizer, Abbvie, Sanofi, Regeneron, Menarini, GSK

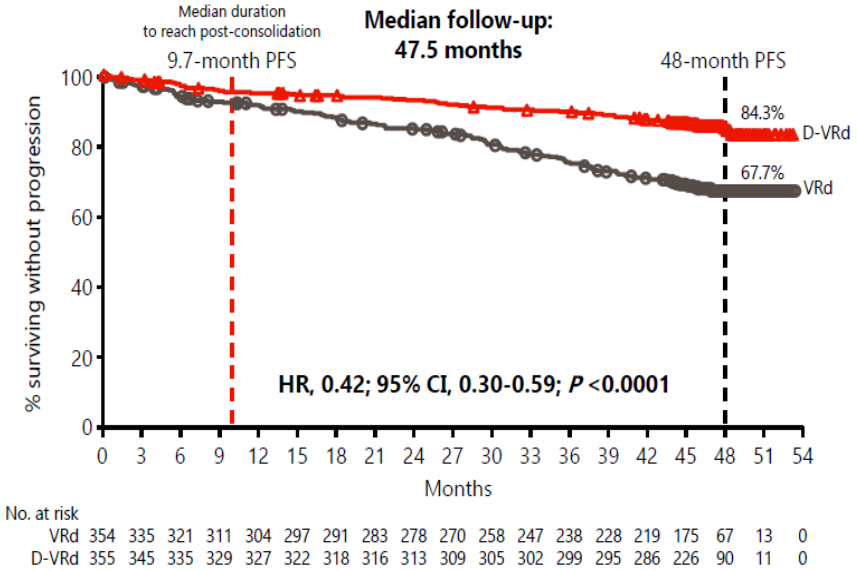
International guidelines



Dimopoulos et al. Nat Rev Clin Oncol 2025

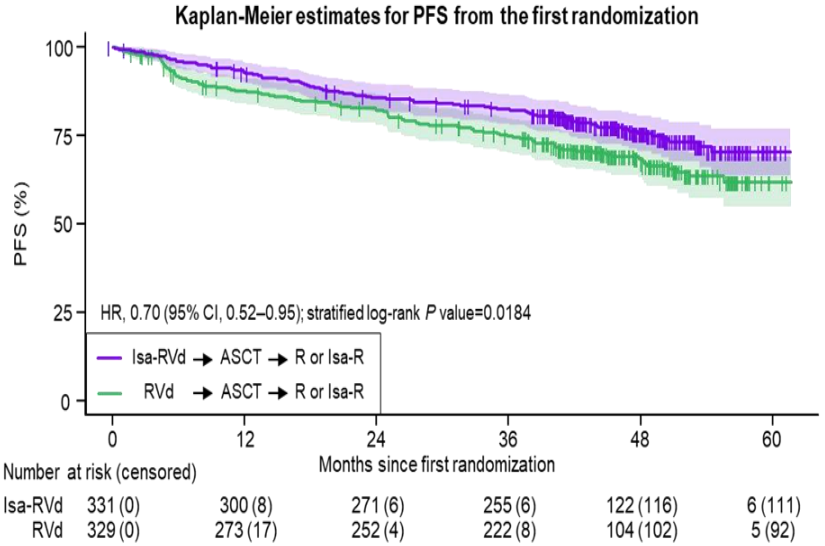
Quad + transplant in transplant eligible myeloma patients

PERSEUS DVRD vs VRD + transplant



Sonneveld et al. NEJM 2023

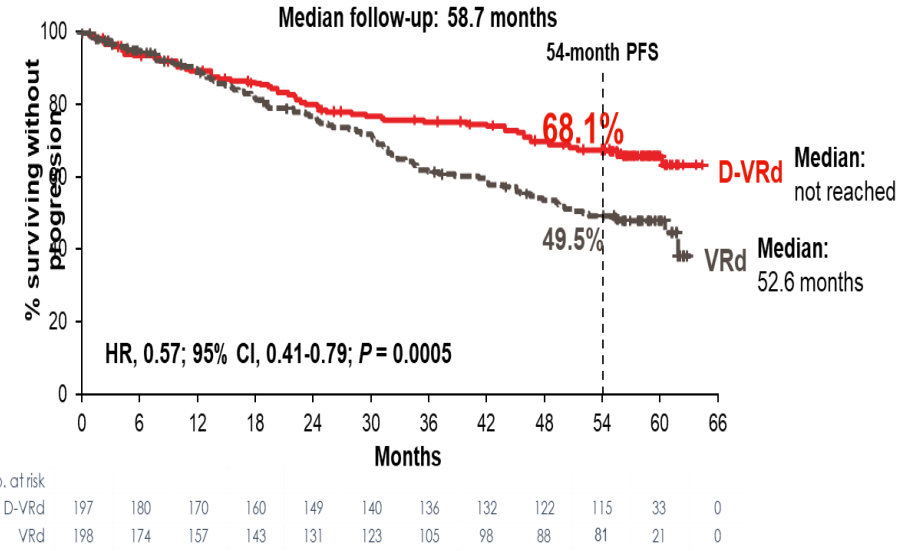
GMMG HD7 IsaVRD vs VRD + transplant



Mai et al. J Clin Oncol 2024

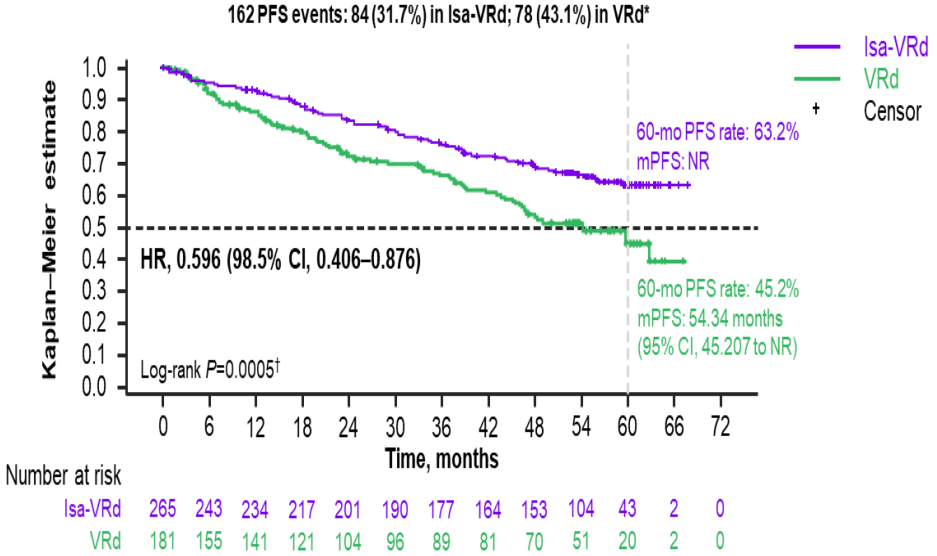
Quad regimen in transplant ineligible myeloma patients

CEPHEUS DVRD vs VRD



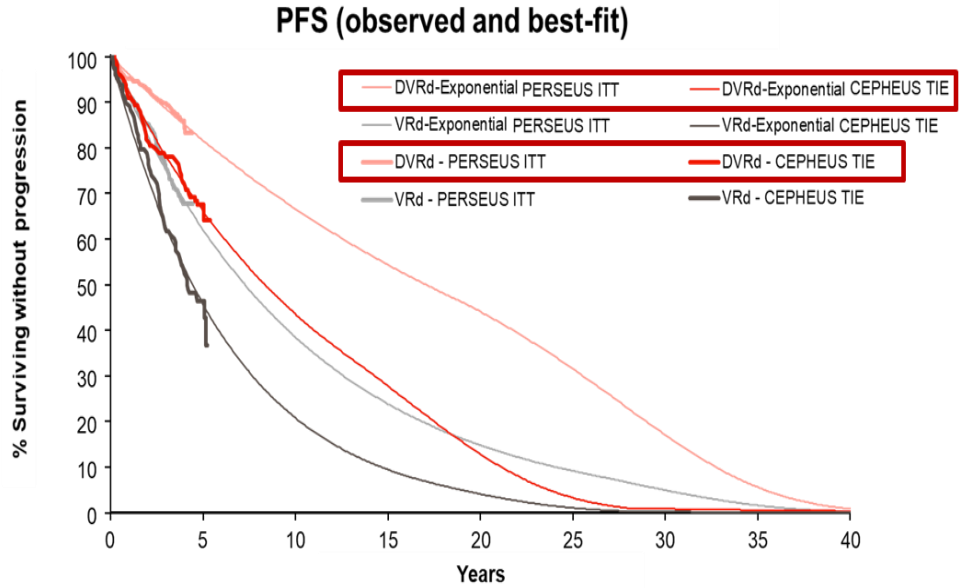
Usmani et al. Nat Med 2025

IMROZ IsaVRD vs VRD



Facon et al. NEJM 2024

Very high projected PFS with Quad +/- ASCT



Estimated PFS, DVRd vs VRd

PERSEUS: **205 months (17.1 years)** vs 87 months (7.3 years)

CEPHEUS: **100 months (8.3 years)** vs 53 months (4.4 years)

Sonneveld et al. EMN 2025

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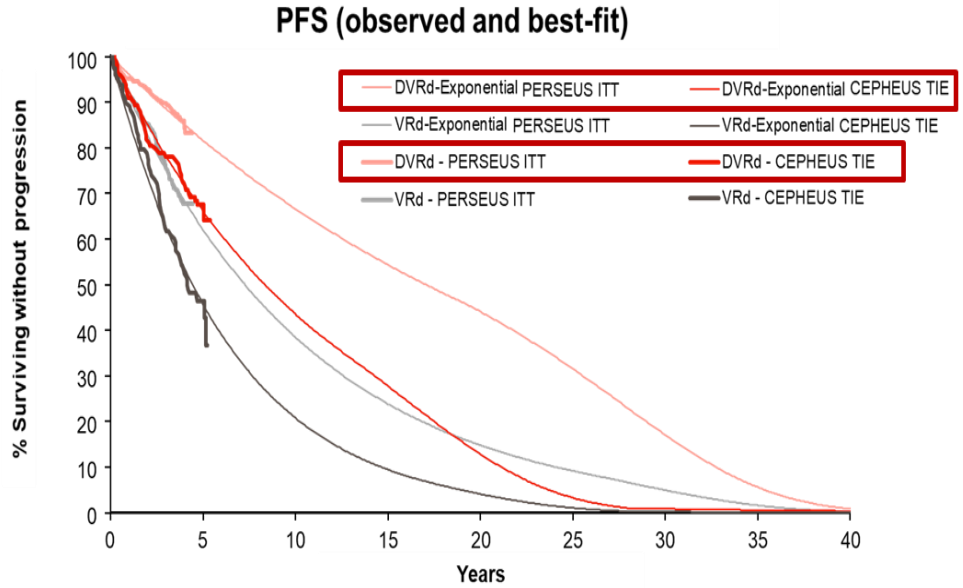

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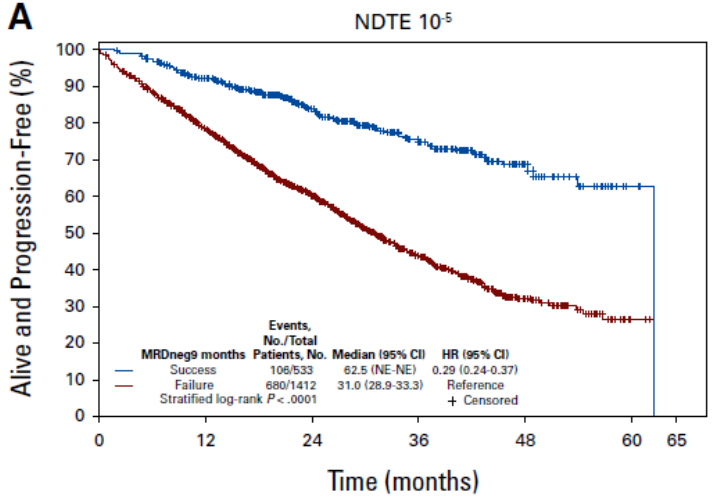
Sonneveld et al. EMN 2025

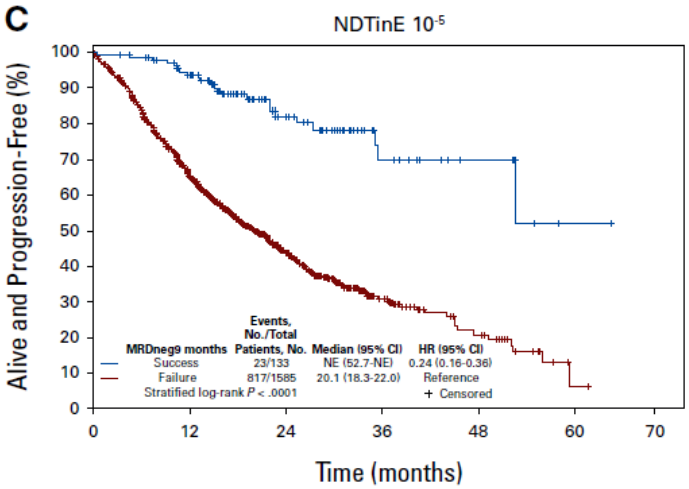
PFS remains the gold standard Primary endpoint for registration ph3 trials.

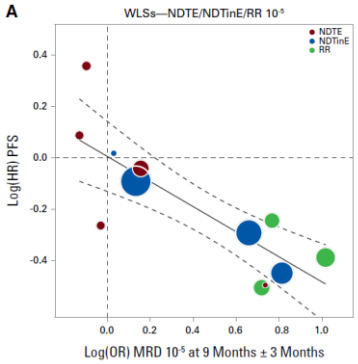
However, future trials will need long follow up to detect significant PFS difference

New endpoints are therefore needed to accelerate access to therapeutic innovation

MRD endpoint for accelerated assessment of clinical trials in myeloma







i2TEAMM initiative :

- Individual patient data from 11 randomized studies (n=4773)
- MRD-CR (at 9 or 12 months) strongly correlates with PFS at patient level
- Strong trial-level correlations (MRD-CR/PFS) observed in NDMM

Shi et al. JCO 2025

MRD endpoint for accelerated assessment of clinical trials in myeloma

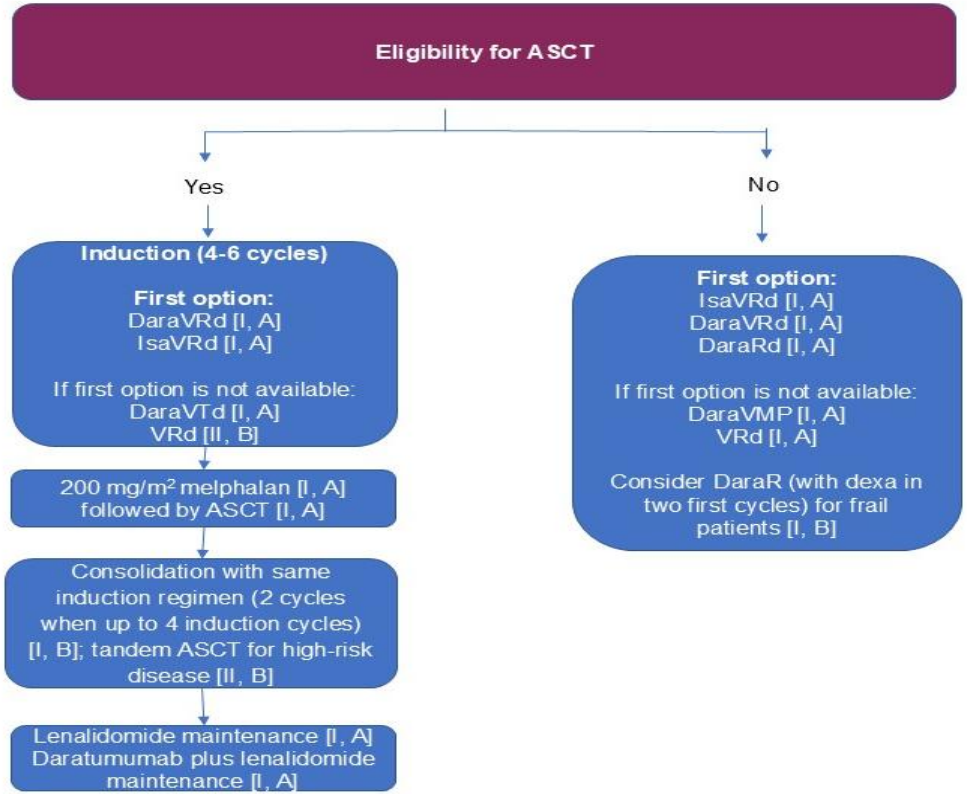
April 12, 2024 , the FDA's ODAC voted 12 to 0 that available data supports the use of minimal residual disease (MRD) as an end point for accelerated approval of new treatments for patients with multiple myeloma.

Ongoing /future trials in NDMM

- **Incorporation of MRD in trial design**
    - (co) primary endpoint
    - MRD driven strategies
- **Incorporation of novel immunotherapies (ADC, CART, Bispab) in frontline**

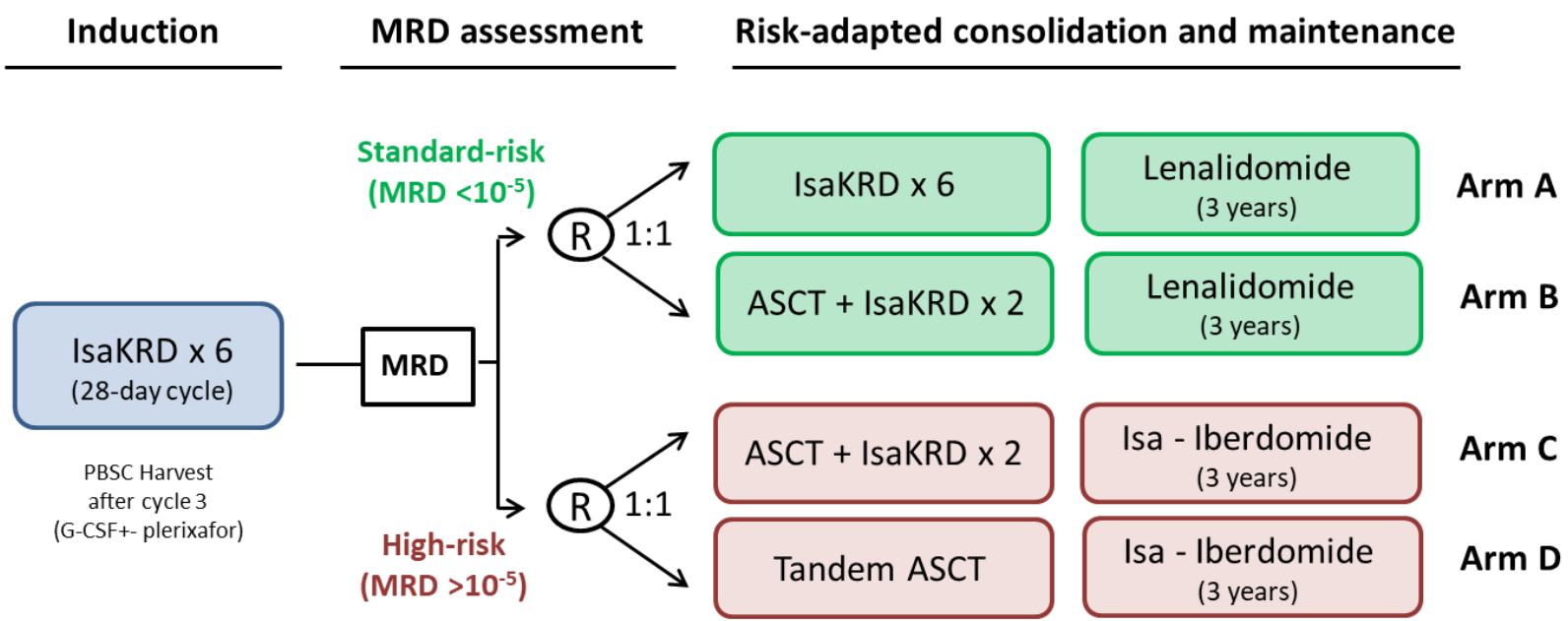
International guidelines

New trials
In TE NDMM

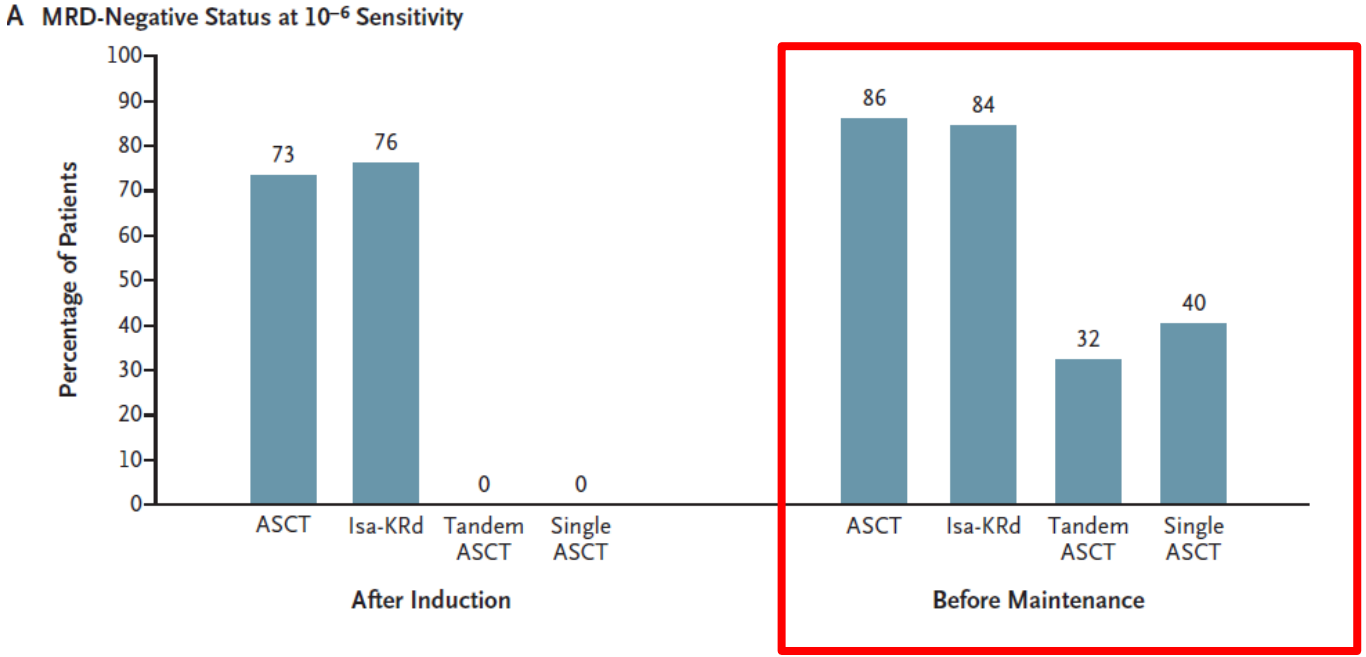


Dimopoulos et al. Nat Rev Clin Oncol 2025

MRD driven strategies



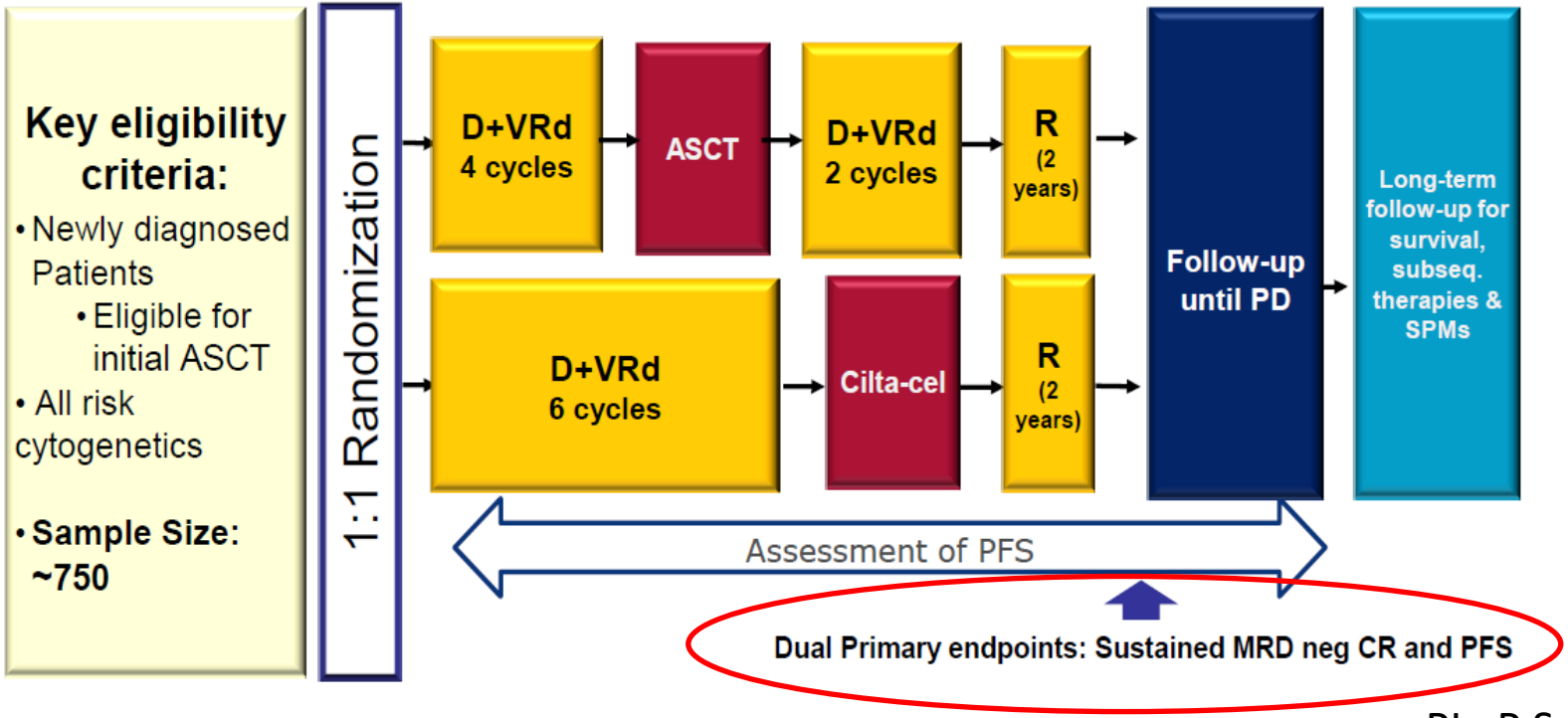
MRD driven strategies



Perrot et al. NEJM 2025

To challenge ASCT with CART

CARTITUDE-6



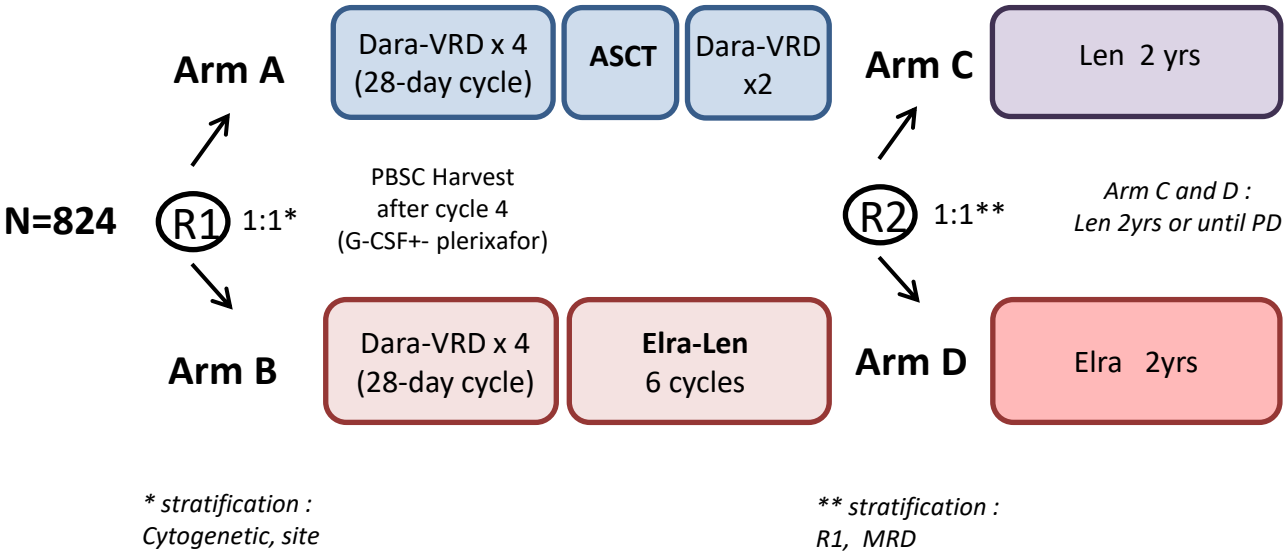
PI : P Sonneveld

To challenge ASCT with Bispabs

Population

- **NDMM**
- **Transplant eligible**

Study design



Objectives

- Primary :
- R1 : MRD (10-5) pré R2
- R2 : PFS

- Secondary:
Sustained MRD
OS
Safety
QoL
Rework

- Exploratory:
genomic, immuno, PET, Mass spec, CTCs)

200 patients randomized (march 2026)

PI : C Touzeau , A Perrot

To challenge ASCT with Bispabs

Study Objective: To demonstrate the efficacy and safety of Tec+DR induction therapy and fixed duration BsAb-Dara maint. post ASCT in TE NDMM patients

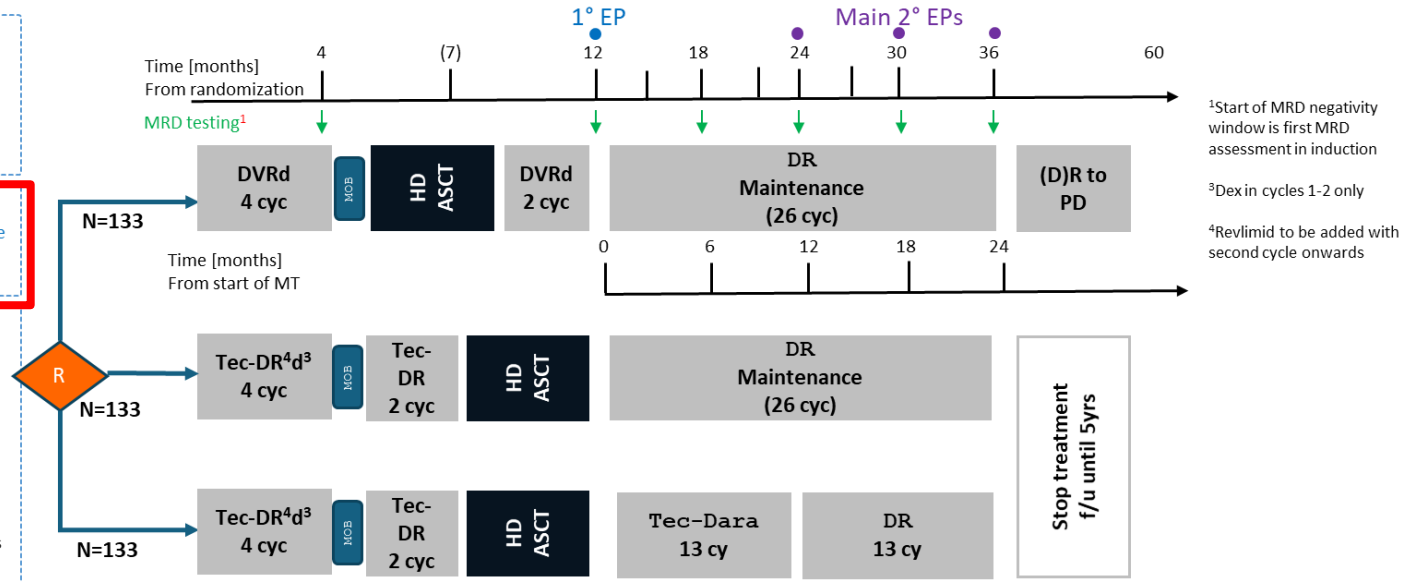
Inclusion Criteria:
- Newly diagnosed TE MM
- Age ≤ 70
- Eligible for ASCT
- ECOG 0 or 1

Primary Endpoints:
- VGPR/MRD neg. (10^{-6}) pre maintenance (NGS)
  (Arm A vs Arm B+Arm C)

Key Secondary Endpoints:
- Cumulative 12 months sustained CR/MRD negativity up to 24 months of maintenance (10^{-6})(Arm A vs Arm C)
- Event rate (descriptive only).

Event defined as
  a. Progression
  b. Death
  c. G3/4 infection
  d. Discontinuation of all study drugs
- Best overall MRD neg.
- PFS *(5 years)*

Stratification :
- Age (<65/≥65)
- HR/no HR (IMWG 2024 definition)



[1]Start of MRD negativity window is first MRD assessment in induction

[3]Dex in cycles 1-2 only

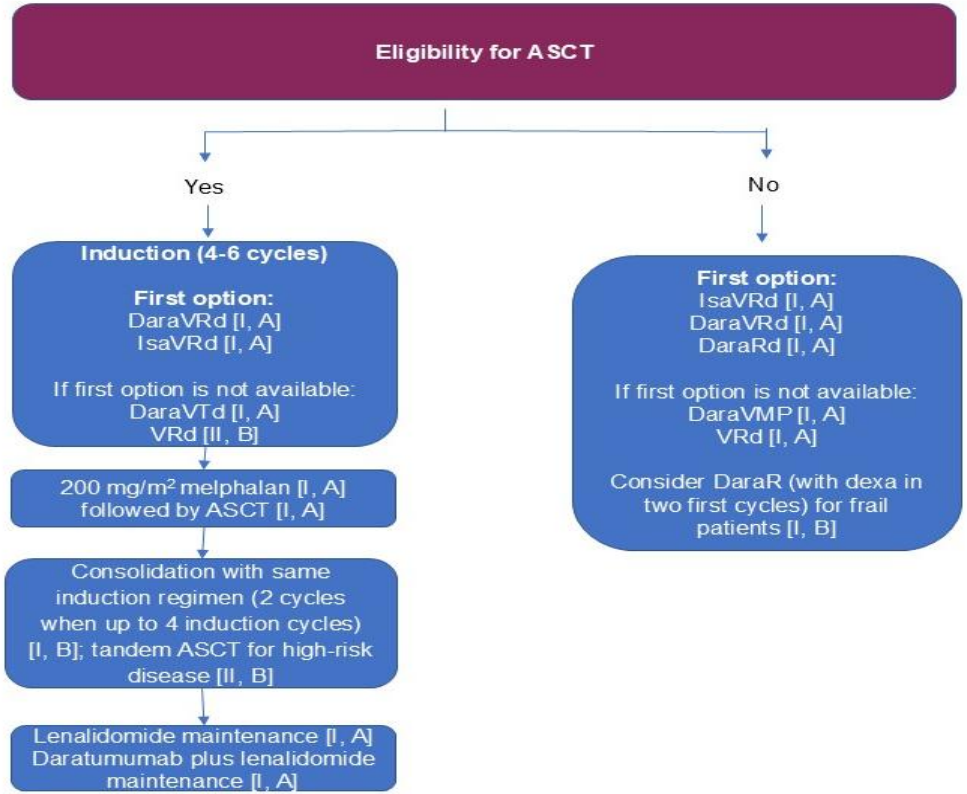
[4]Revlimid to be added with second cycle onwards

deutsche studiengruppe multiples myelom
dsmm
doing studies on multiple myeloma

GM MG GERMAN-SPEAKING MYELOMA MULTICENTER GROUP

PI : Marc Raab, Leo Rasche

International guidelines

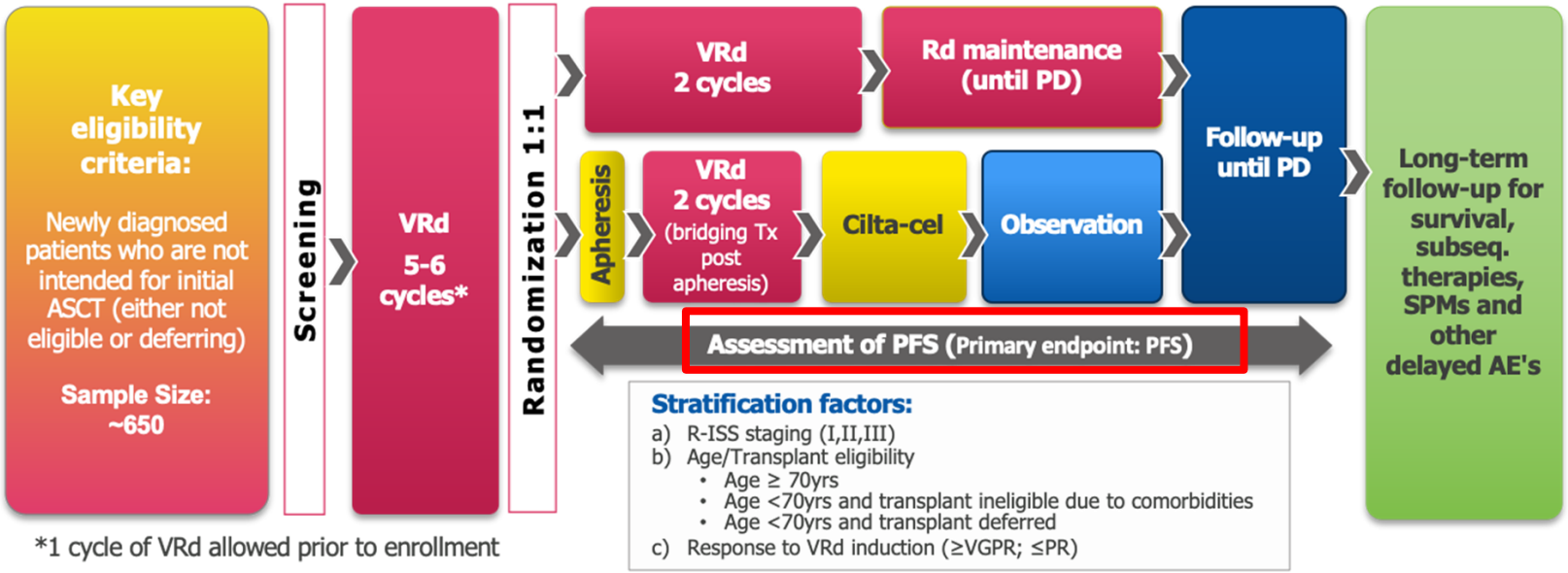


New trials In TI NDMM

Dimopoulos et al. Nat Rev Clin Oncol 2025

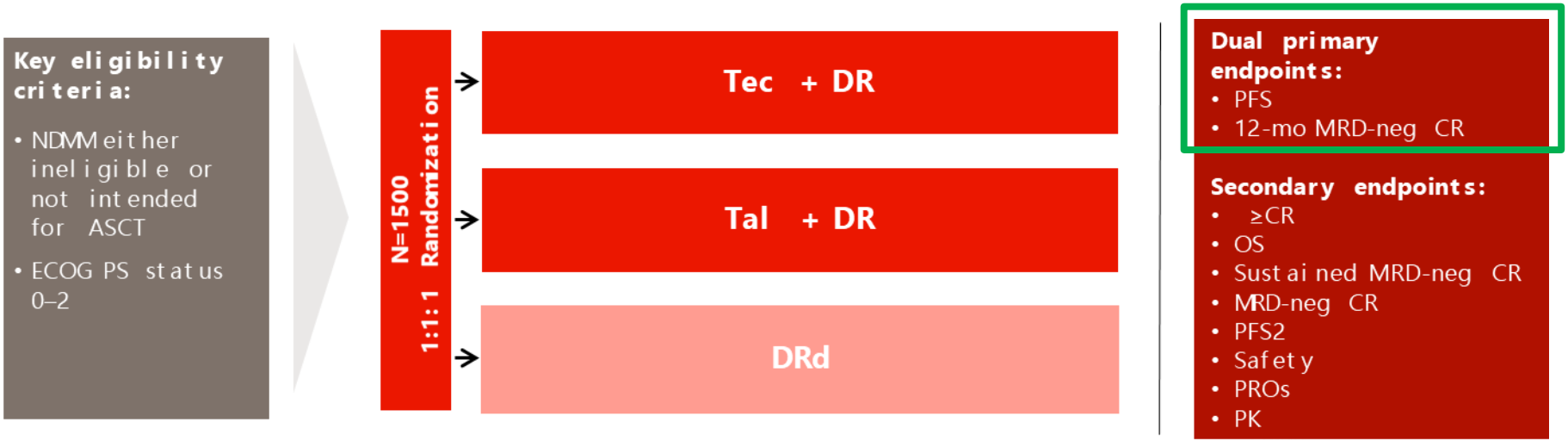
New trials in TI NDMM : incorporation of TCR

Frontline CAR-T cells in transplant ineligible patients
CARTITUDE-5



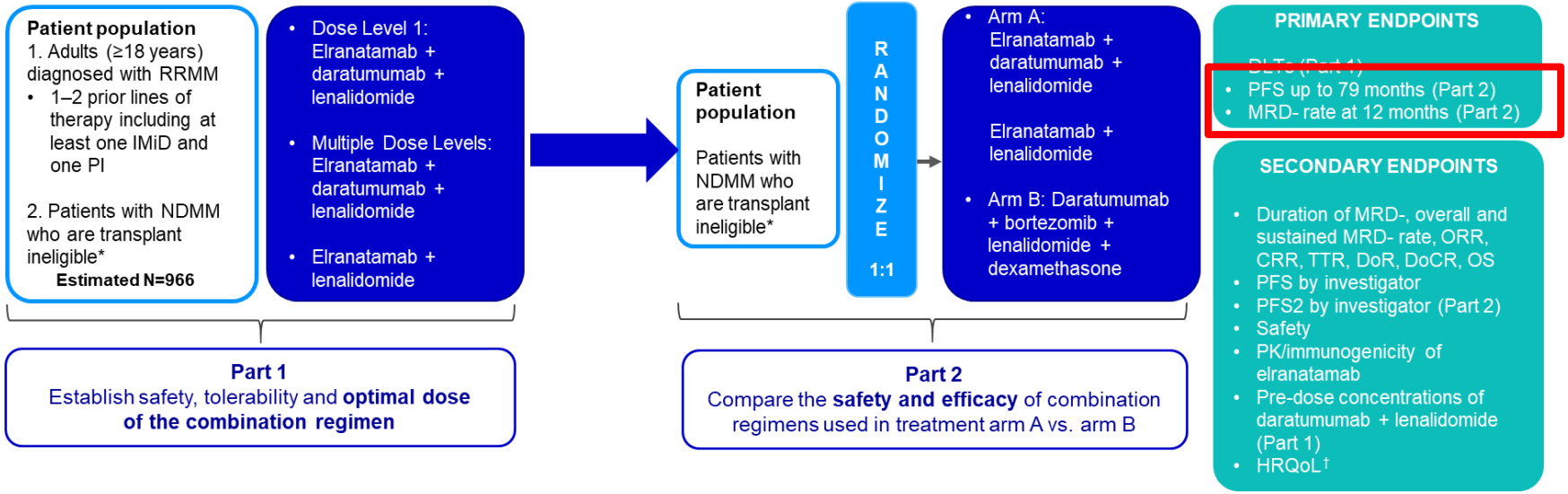
*1 cycle of VRd allowed prior to enrollment

MajesTEC-7: Phase 3 Design



New trials in TI NDMM : incorporation of TCR

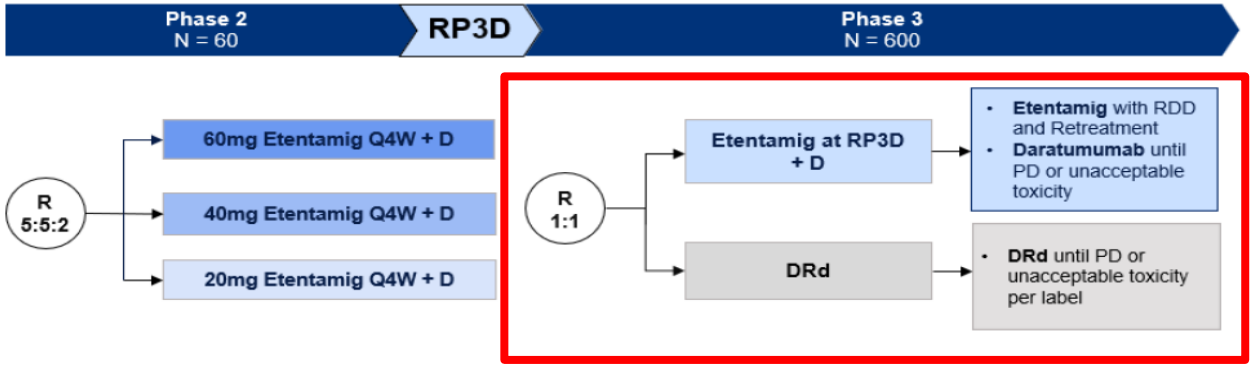
MagnetisMM-6



IFM/PETHEMA Philae trial (M25-586): elderly unfit patients

Sponsor Abbvie - Collaboration IFM/PETHEMA
Phase 3 randomized trial
Response-adapted strategy

Newly dg MM
Age ≥ 18 yo
Transplant Ineligible
ECOG 0-2
Unfit



Study Endpoints :
- **Dual Primary: PFS & MRDneg CR rate**
- **Key Secondary:** OS, 12m sustained MRDneg CR, Response rates ≥CR and ≥ VGPR
- Other Secondary: ORR, EFS, PFS2, Safety and Tolerability, PROs

Ph2 start feb 2026

Response-directed discontinuation of etenta

- At least 24 cycles of etenta
- MRD neg CR, sustained MRD ≥12 months
- Continuation of dara

CONCLUSION

Current standard of care allows median PFS > 10 years in TE NDMM and > 7 years in TI NDMM

New endpoints are therefore needed to accelerate access to therapeutic innovation

MRD- CR (at 9 or 12 months) has been endorsed by FDA as a valid endpoint for accelerated approval in MM.

Most ongoing ph3 trials in NDMM have MRD as co-primary endpoint

Key ongoing trials in NDMM are incorporating T-cell redirecting immunotherapies to improve efficacy, and potentially replace transplant in young patients

Thank you!

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