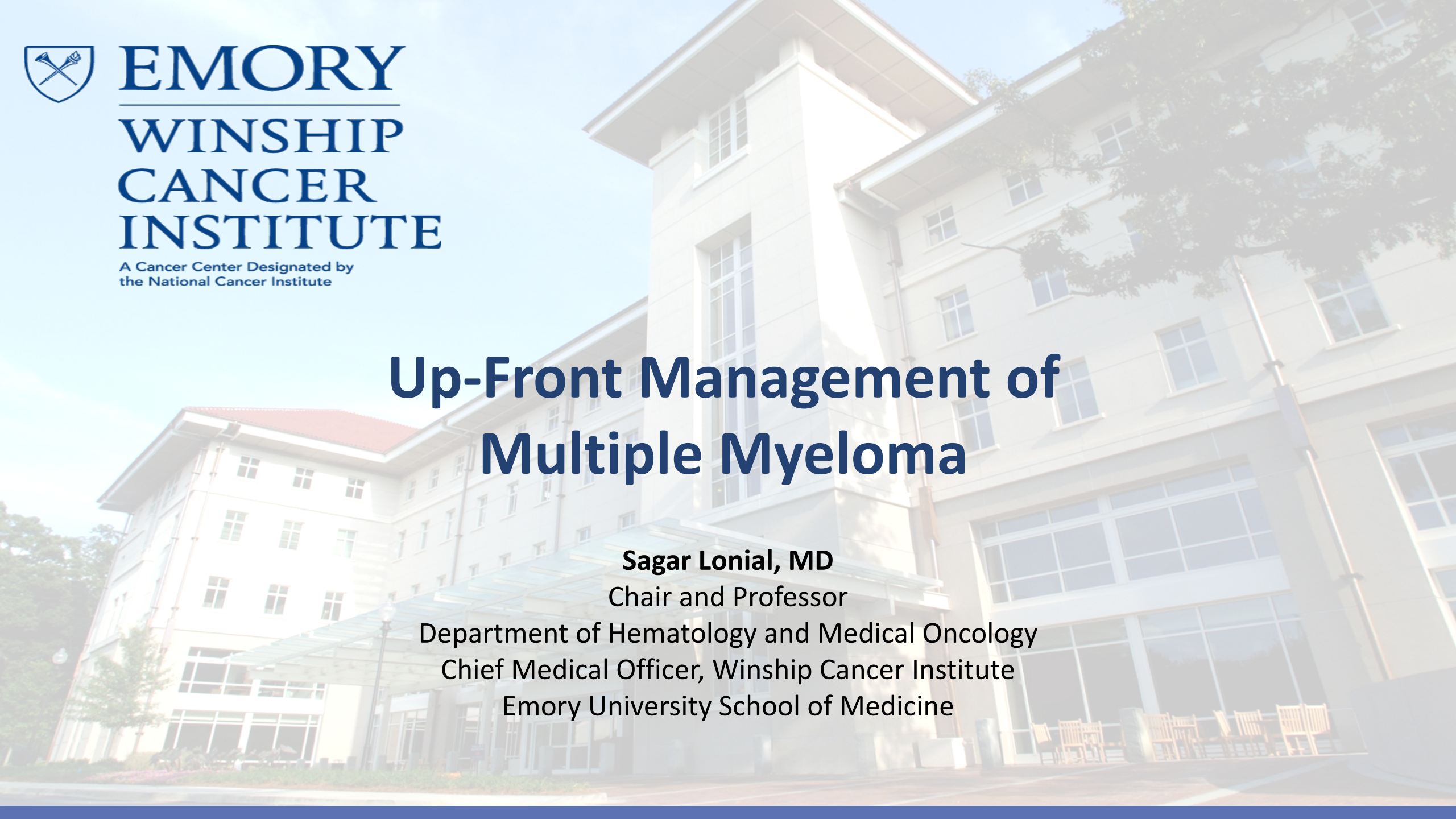
Please note, these are the actual video-recorded proceedings from the live CME event and may include the use of trade names and other raw, unedited content.



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Up-Front Management of Multiple Myeloma

Sagar Lonial, MD
Chair and Professor
Department of Hematology and Medical Oncology
Chief Medical Officer, Winship Cancer Institute
Emory University School of Medicine

Disclosures

Honoraria	Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, GlaxoSmithKline, Janssen Biotech Inc, Merck, Novartis, Onyx Pharmaceuticals, an Amgen subsidiary, Takeda Oncology

Case presentation: Dr Bessnow

61-year-old woman

- Presents with anemia
- Diagnosis: IgG kappa MM
- RVD → transplant → lenalidomide maintenance
- Disease under excellent control but anemia has never fully resolved

Additional questions regarding up-front management of multiple myeloma

Dr Sinha

Dr Johl

Case presentation: Dr Cole

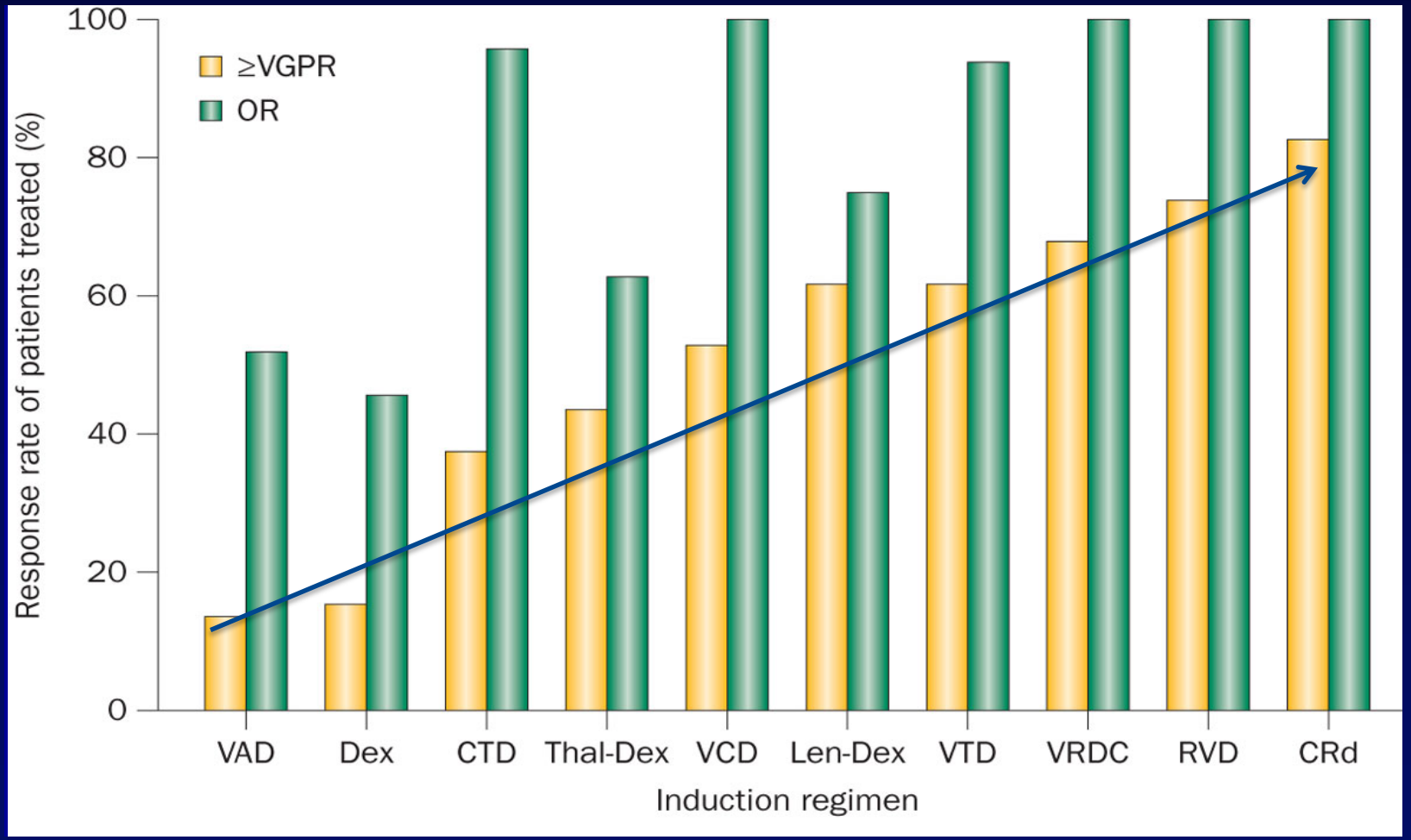
86-year-old woman

- Morbidly obese, ambulating with walker at baseline
- Suffered fall requiring head CT, which revealed lytic lesions on skull
- Workup: Lesions in skull, iliac crest and right humerus
- Bone marrow biopsy: IgG kappa MM
- Radiation therapy to iliac crest lesion; lenalidomide/dexamethasone but unable to tolerate full-dose lenalidomide due to fatigue

Topics

- Choice of Induction regimen
- Transplant vs not: who to consider
- What is new; Role of MRD

Induction RX; Deep remissions will be standard



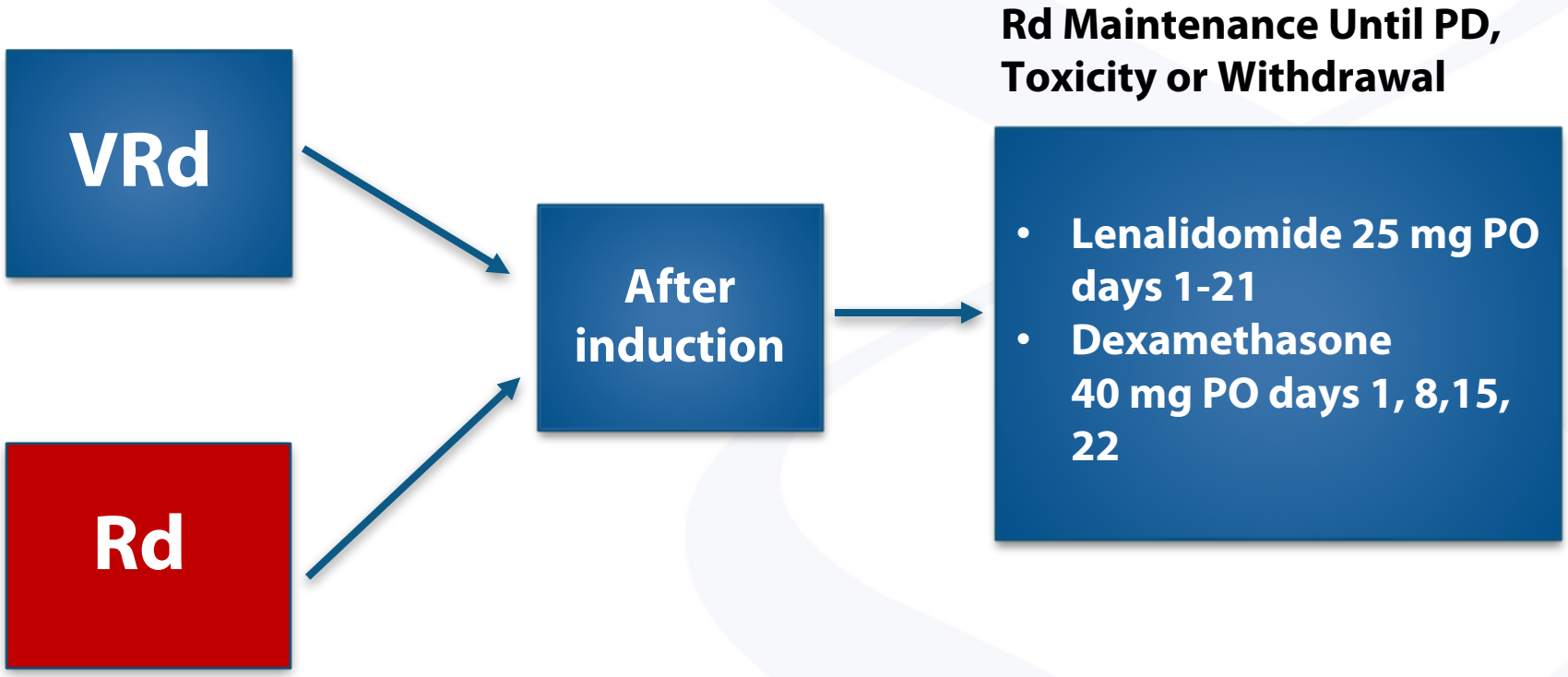
+DARA?

Mailankody S, et al. Nat. Rev. *Clin. Oncol.* 2015; 12:286-95.

What Differentiates Patients at Diagnosis?

- Age (in Europe 65, in US >75-80)
- Frailty (how to define, how to use)
- Comorbidities
- Choice (?)

SWOG-S0777 Study Design



- **All patients received Aspirin 325 mg/day**
- **VRd patients received HSV prophylaxis**

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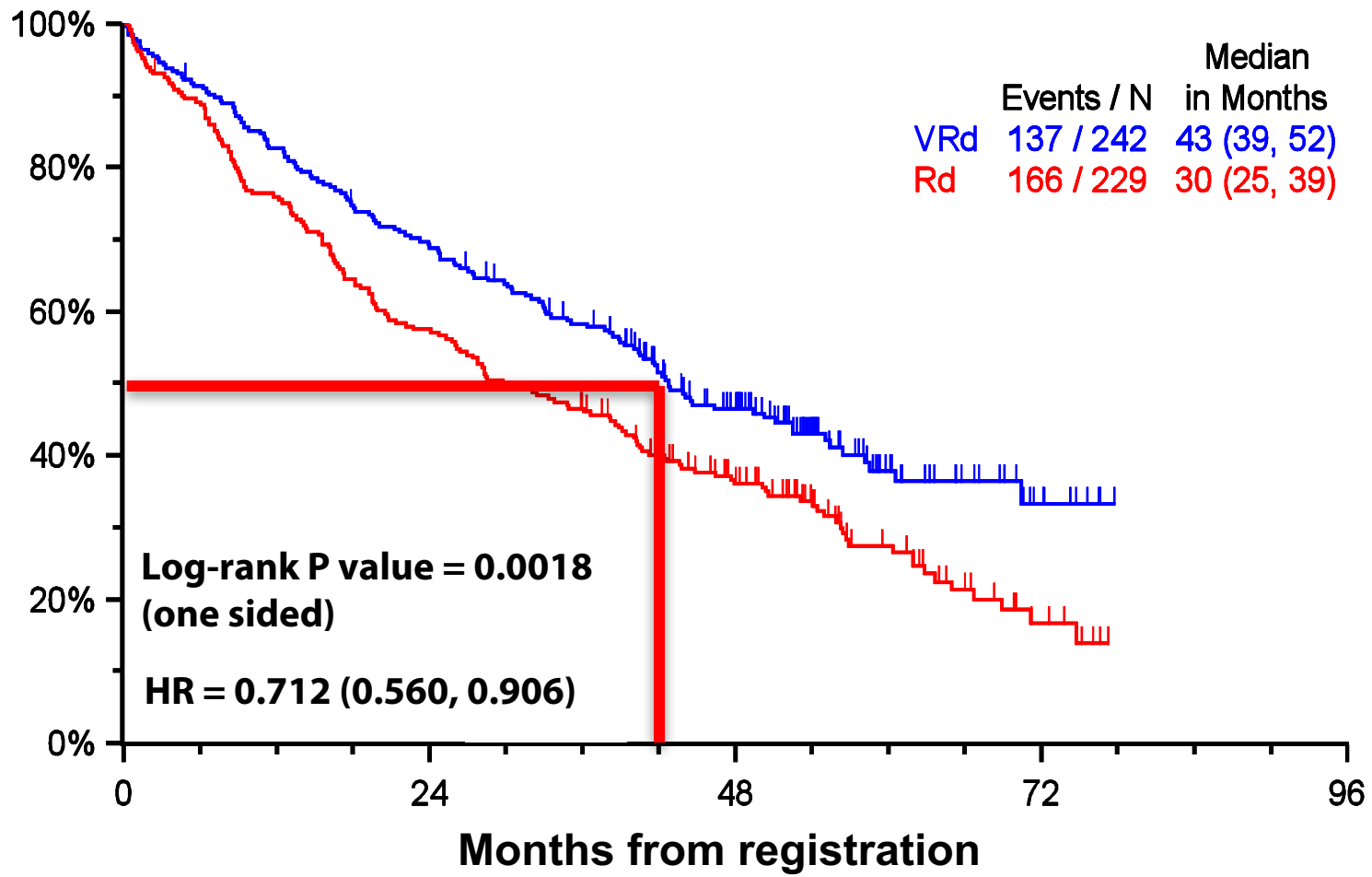
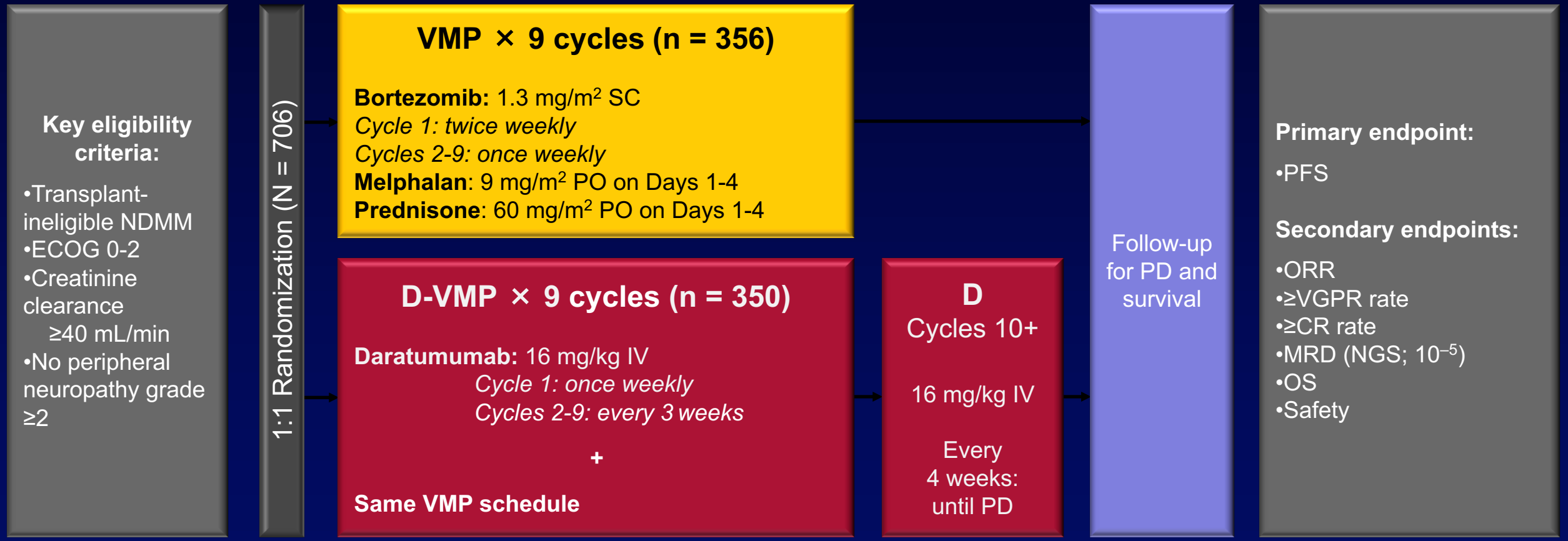
Durie et al, Lancet 2017

Progression-Free Survival By Assigned Treatment Arm



Durie et al, Lancet 2017

ALCYONE Study Design



Stratification factors
- ISS (I vs II vs III)
- Region (EU vs other)
- Age (<75 vs ≥75 years)

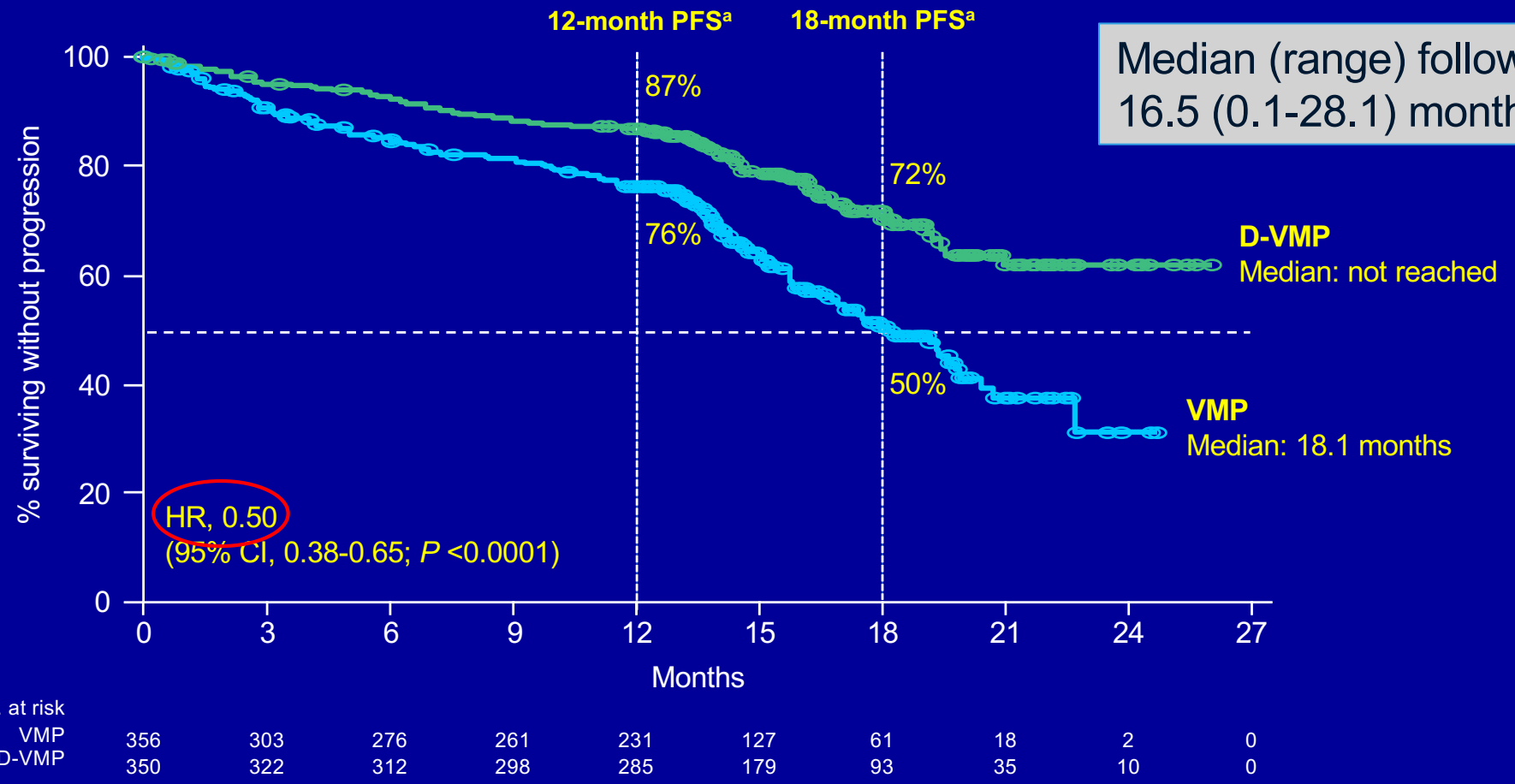
- Cycles 1-9: 6-week cycles
- Cycles 10+: 4-week cycles

Statistical analyses
- 360 PFS events: 85% power for 8-month PFS improvement[a]
- Interim analysis: ~216 PFS events

ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System; EU, European Union; SC, subcutaneously; PO, orally; D, daratumumab; IV, intravenously; PD, progressive disease; PFS, progression-free survival; ORR, overall response rate; VGPR, very good partial response; CR, complete response; MRD, minimal residual disease; NGS, next-generation sequencing; OS, overall survival.

[a]8-month PFS improvement over 21-month median PFS of VMP.

Efficacy: PFS

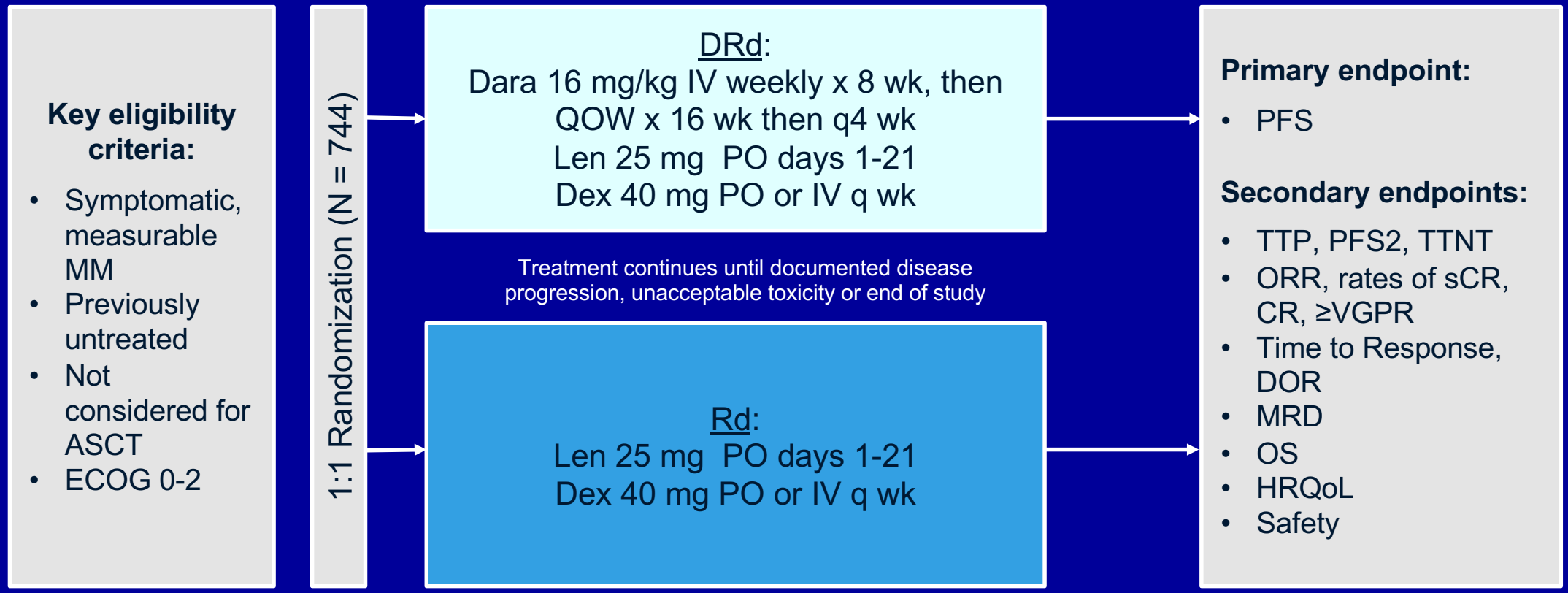


Median (range) follow-up:
16.5 (0.1-28.1) months

50% reduction in the risk of progression or death in patients receiving D-VMP

HR, hazard ratio; CI, confidence interval.
[a] Kaplan-Meier estimate.

MAIA Trial Design



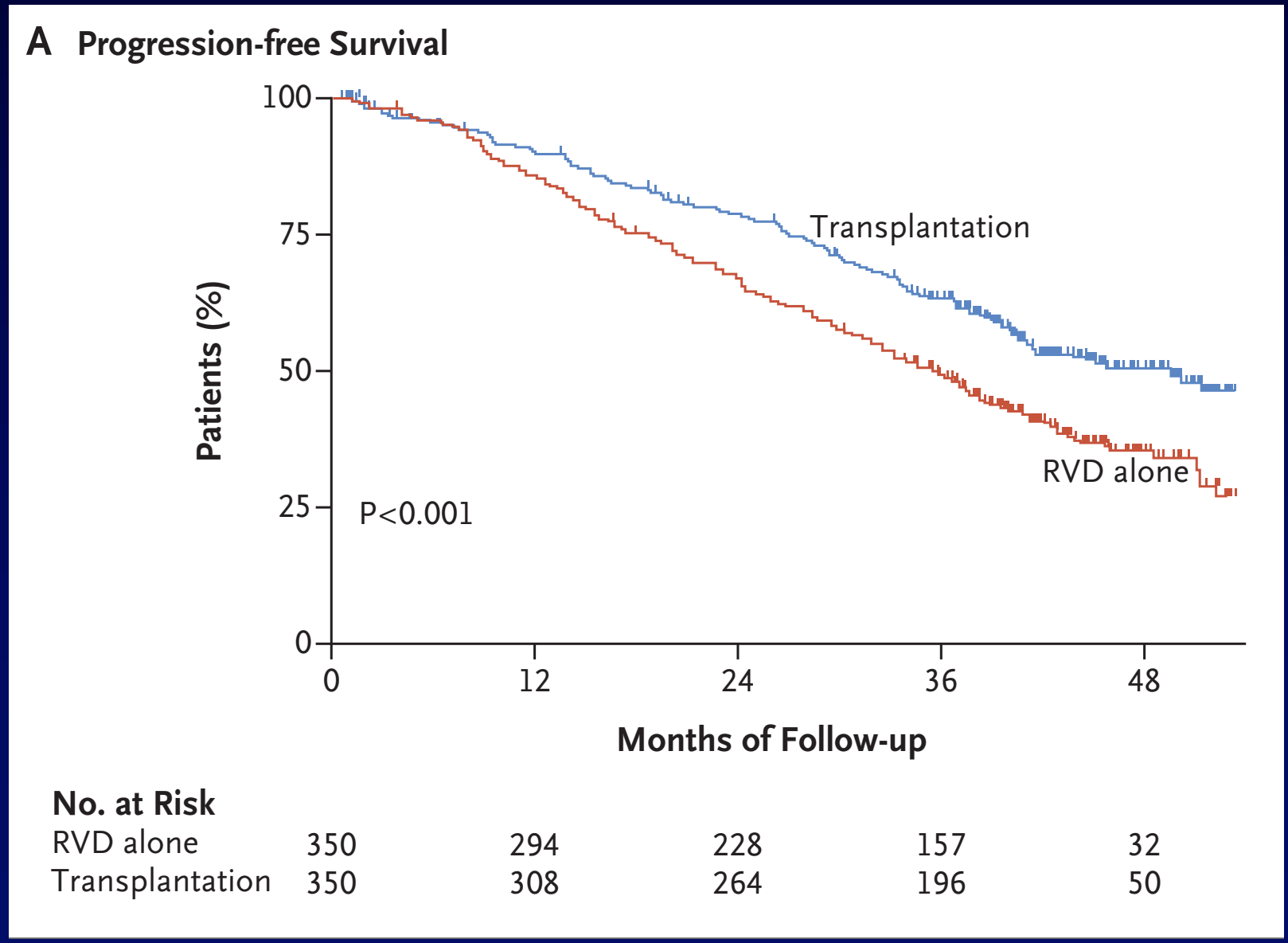
MAIA Topline Interim Results

Positive Topline Results Announced in Phase III MAIA Study of Daratumumab in Front Line Multiple Myeloma

- The study met the primary endpoint of improving PFS at a pre-planned interim analysis (HR = 0.55 (95% CI 0.43 – 0.72), $p < 0.0001$) resulting in a 45% reduction in the risk of progression or death in patients treated with DRd.
- The median PFS for patients treated with daratumumab in combination with Rd has **not been reached**, compared to an estimated median PFS of 31.9 months for patients who received Rd alone.

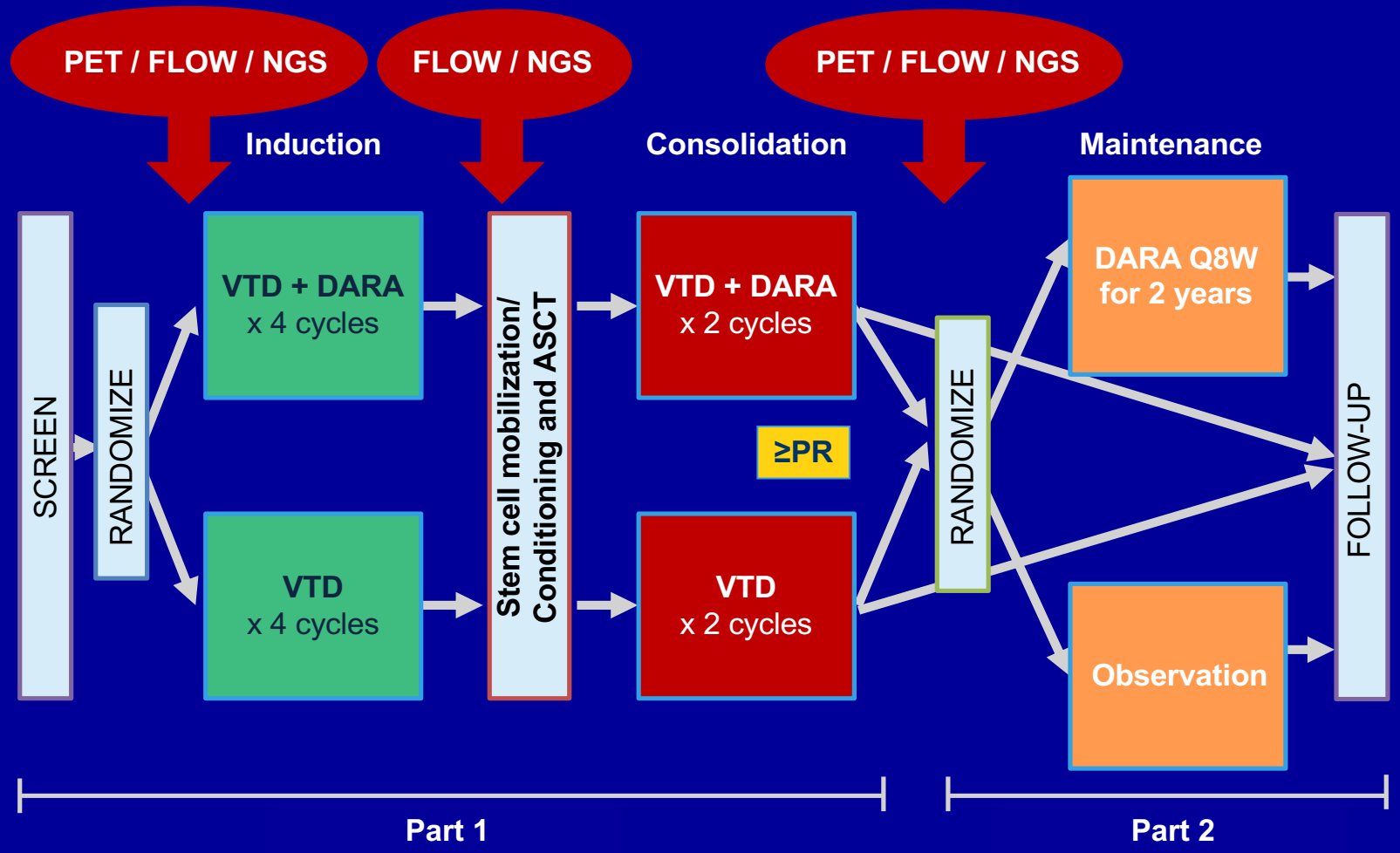
IFM RVD with and without HDT

PFS
50 months (HDT)
vs
36 months (no HDT)



Attal et al, NEJM 2017

CASSIOPEIA trial



https://www.clinicaltrials.gov/ct2/show/NCT02541383

CASSIOPEIA trial

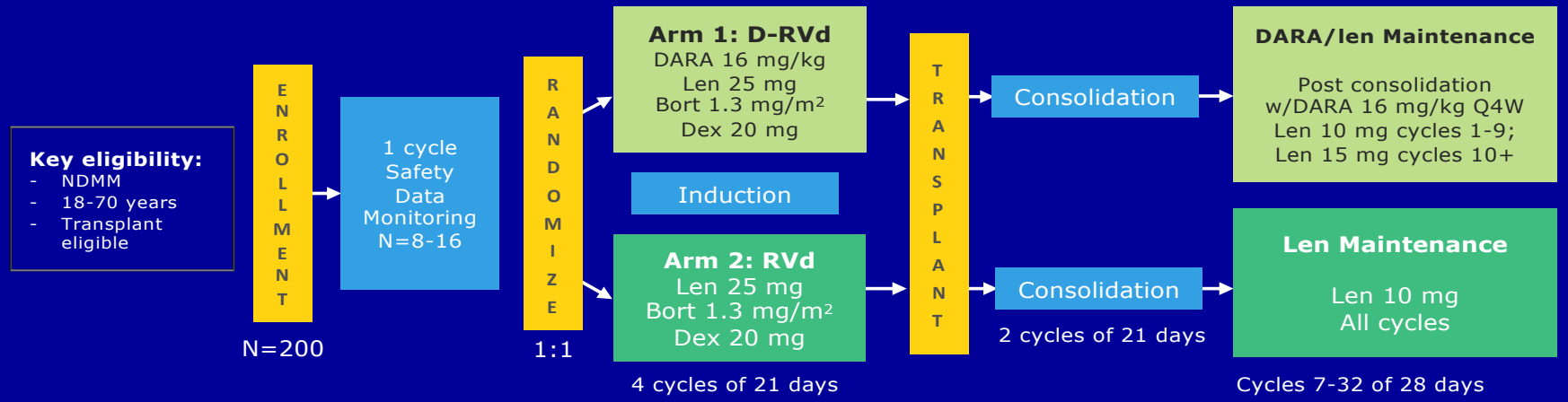
Positive Topline Results Announced in Phase III CASSIOPEIA Study of Daratumumab in Front Line Multiple Myeloma

- The first part of the study met the primary endpoint of number of patients that achieved **a sCR, which was reported in 28.9%** of patients treated with D-VTD, compared to 20.3% of patients who received VTD alone with an odds ratio of 1.60 (95% CI: 1.21 – 2.12, $p \leq 0.001$).
- In the second part of the study, all responders have been re-randomized to receive either maintenance treatment with daratumumab monotherapy or observation (no treatment).

https://www.clinicaltrials.gov/ct2/show/NCT02541383

GRIFFIN (MMY2004) Study Design

- Phase 2, randomized, open-label study of D-RVd vs RVd in transplant-eligible, newly diagnosed MM



Patient Characteristics	D-VRd n=16
Completed ≥9 cycles of D-VRD, %	100
Median age, years	62.5
Male sex, %	50
ISS stage	
I, n (%)	12 (75)
II or III, n (%)	4 (25)
ECOG PS = 1, %	63

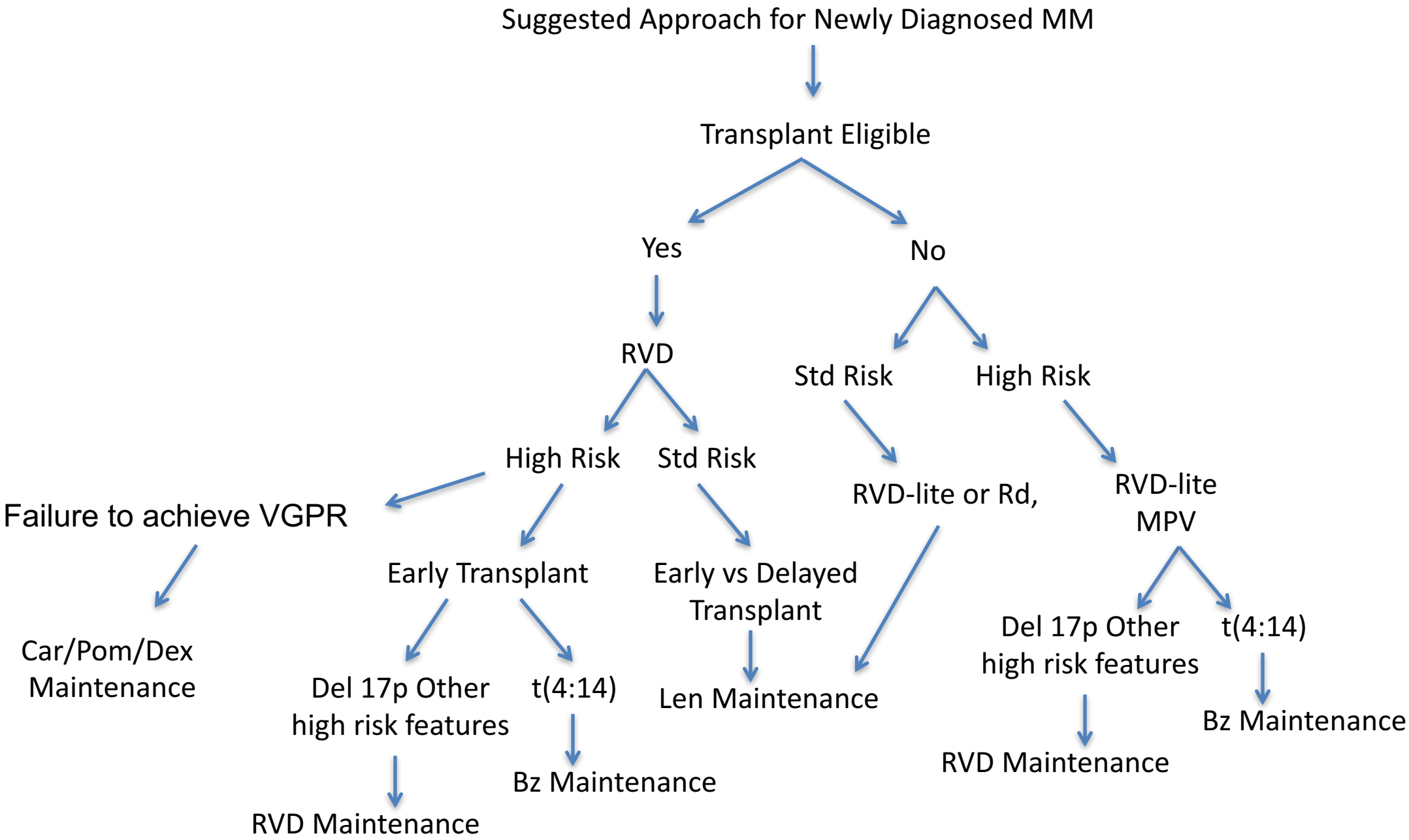
Primary Endpoint: sCR rate

Secondary Endpoints

- CR and sCR rate following induction, ASCT, post-ASCT consolidation, and maintenance treatment
- ORR, ≥VGPR, MRD
- Duration of and time to sCR and time to CR, ≥VGPR, or ≥PR
- TTP, PFS, OS
- Duration of response
- Safety and tolerability of D-RVd
- PK and immunogenicity
- PROs
- Evaluate stem cell yield after mobilization

D-RVd, daratumumab-lenalidomide/bortezomib/dexamethasone; PRO, patient-reported outcome.
https://clinicaltrials.gov/ct2/show/NCT02874742

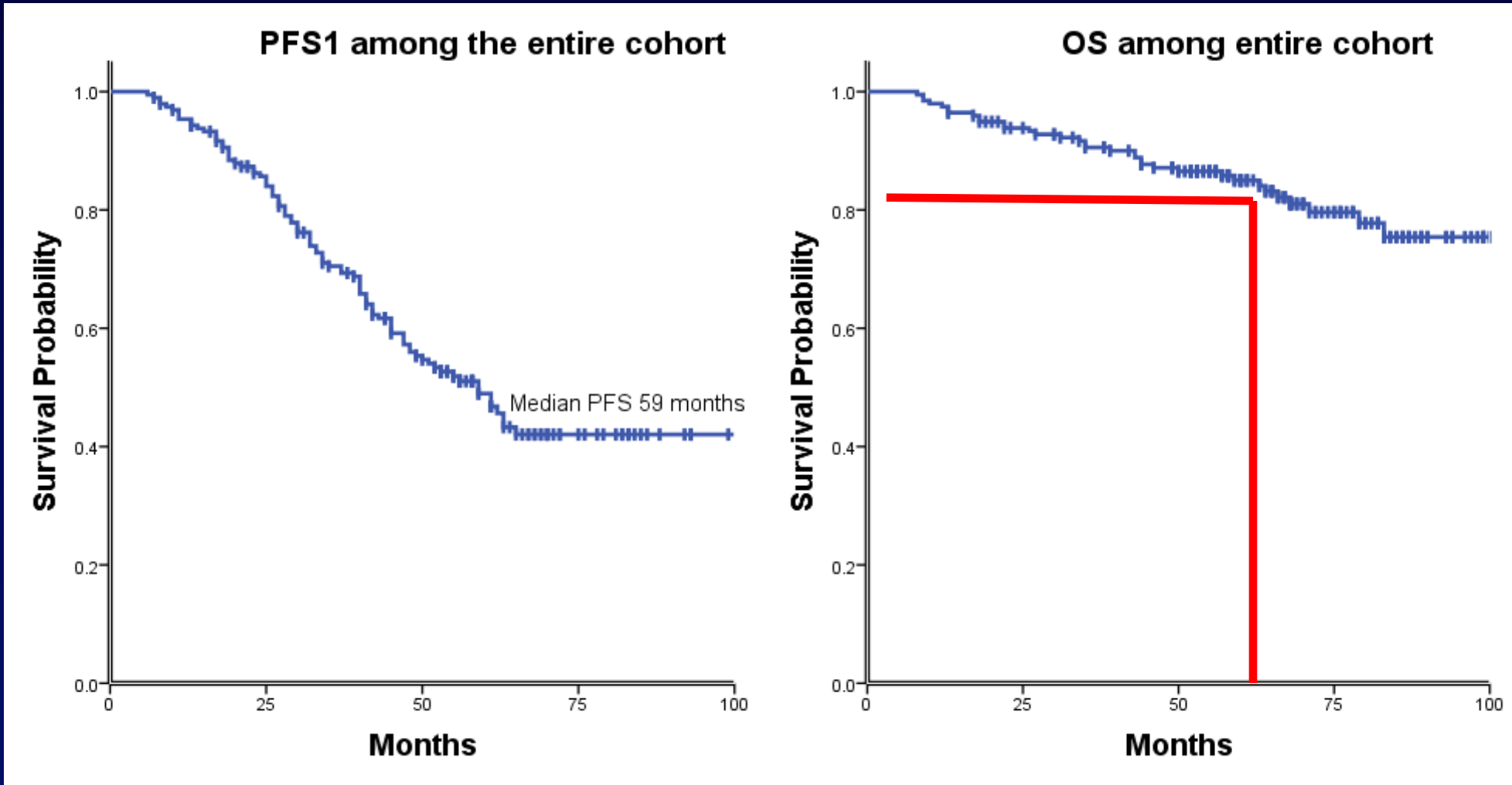
https://ash.confex.com/ash/2018/webprogram/Paper113122.html



Nooka et al, *JOP* 2016

Survival outcomes in newly diagnosed myeloma with RVD induction among all patients

(with a median follow-up of 66 months)



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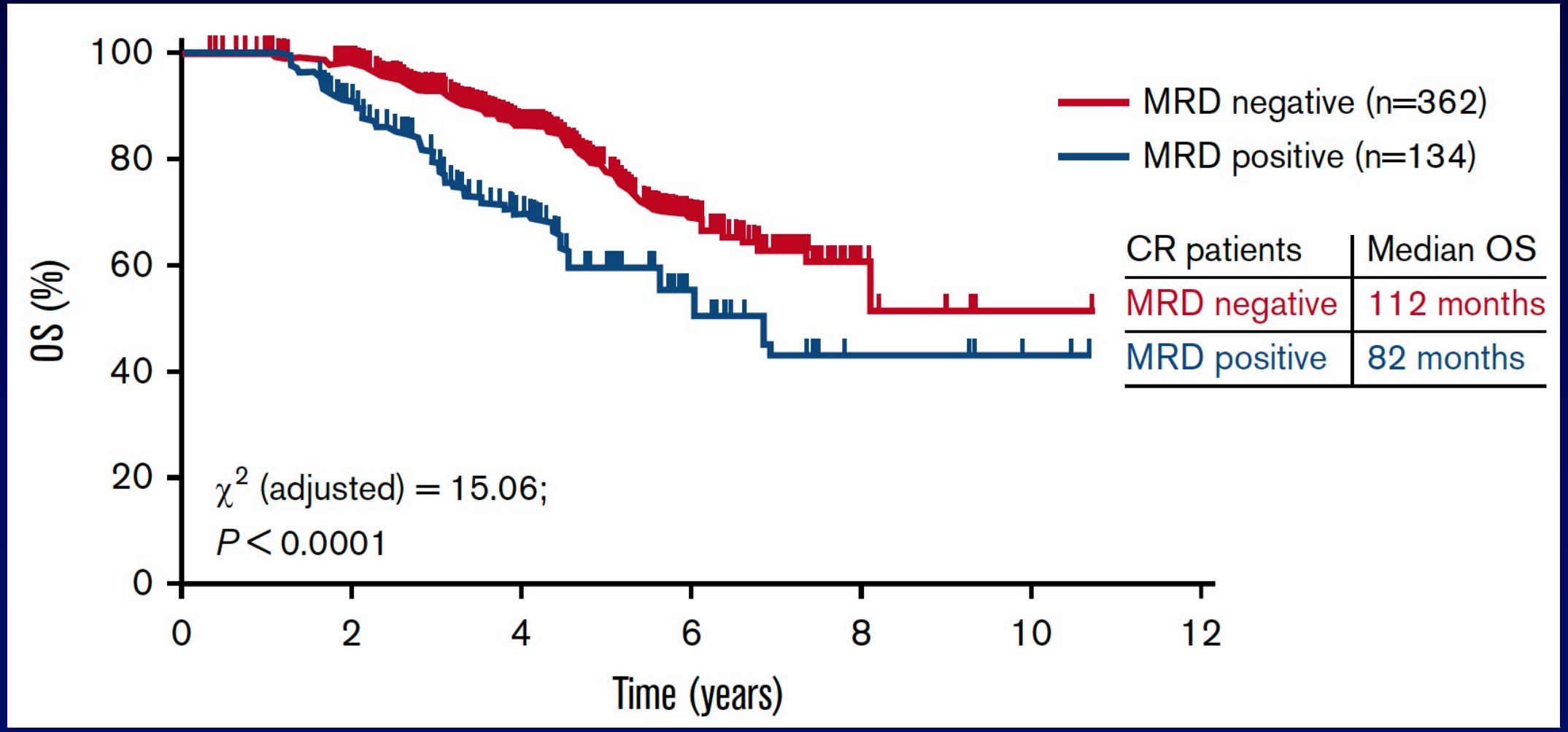
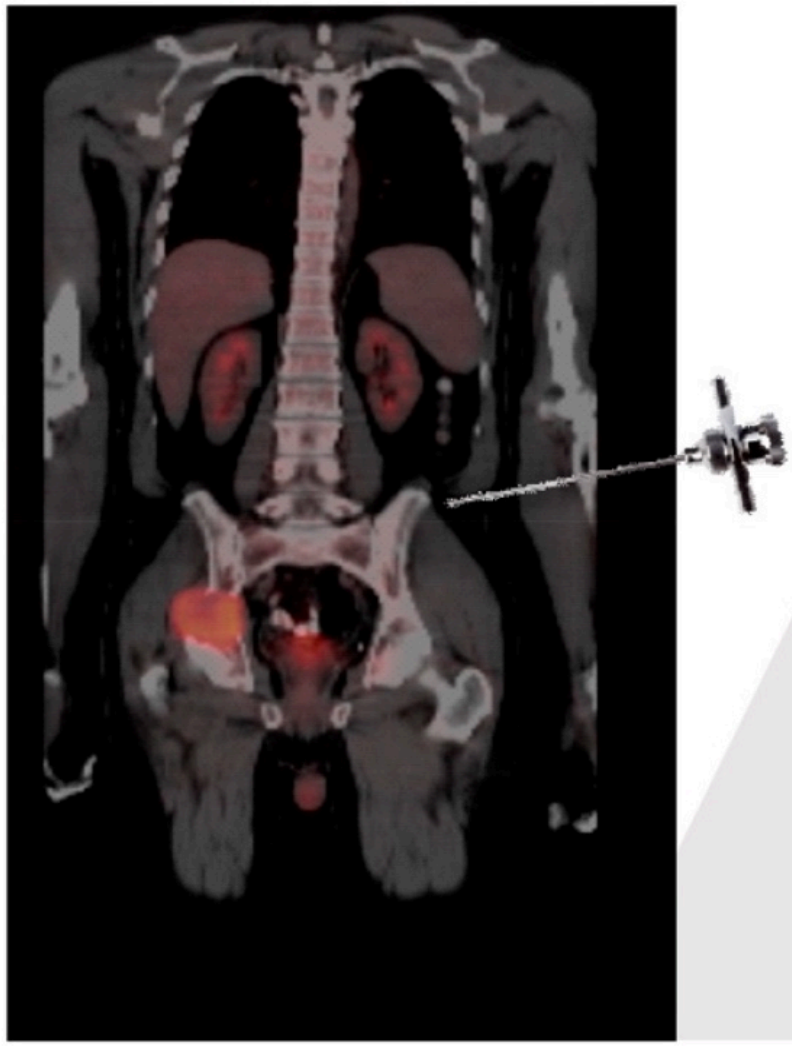
Joseph et al, ASH 2017

Impact of MRD on Survival in Patients Who Achieved Conventional CR: A Meta-Analysis



Anderson KC. Blood Adv 2017;1(8):517-521 (Modified from Munshi NC et al. JAMA Oncol 2017)

Sensitivity of Different Techniques in Assessing Myeloma Disease Burden



sFLC & immunofixation

out of 10^2 – 10^3 cells

4- to 6-color cytometry

out of 10^4 - 10^5 cells

8- to 10-color cytometry

out of 10^5 - 10^6 cells

Next-generation sequencing

out of 10^5 - 10^6 cells

Functional imaging

Lesion size 0.5 – 1 ccm; raised or abnormal background signal

Davies FE. Hematol Am Soc Hematol Educ Program 2017;7(1):205-211.

New directions

- IMID/PI is the standard of care for newly diagnosed MM; question of optimal PI remains the subject of trials (K vs V vs I)
- Defining transplant ineligible can have an impact on outcomes and choice of treatment
- If we consider 4-drug induction, we need to be clear on endpoints that translate to benefit, and duration of therapy
- Other new agents are competing for the same space