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EHA-GBMTA-AHA Hematology Tutorial

Self-assessment case

MM Session

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EHA-GBMTA-AHA Hematology Tutorial – New Aspects in Diagnostic Choices and Treatment Options of Hematological Malignancies

MM in 2024

Diagnosis and response assessment

Risk stratification

First-line treatment for transplant-eligible patients

First-line treatment for transplant-ineligible patients

Moving BCMA-targeting forward

Diagnostic criteria for MM: beyond «CRAB»

Panel: Revised International Myeloma Working Group diagnostic criteria for multiple myeloma and smouldering multiple myeloma

Definition of multiple myeloma

Clonal bone marrow plasma cells ≥10% or biopsy-proven bony or extramedullary plasmacytoma* and any one or more of the following myeloma defining events:

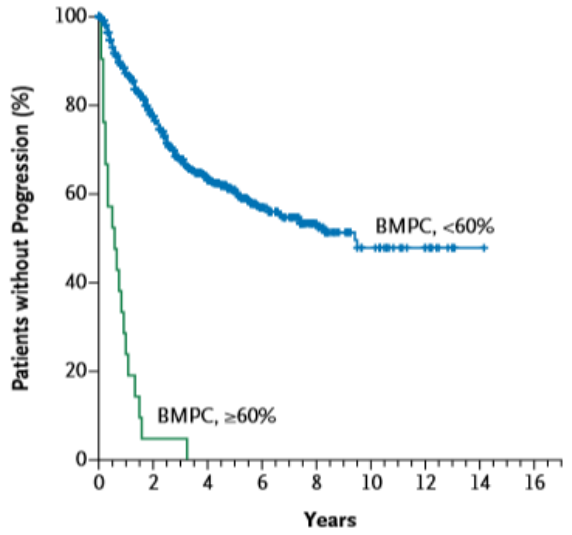
- Myeloma defining events:
  - Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:
    - Hypercalcaemia: serum calcium >0·25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2·75 mmol/L (>11 mg/dL)
    - Renal insufficiency: creatinine clearance <40 mL per min† or serum creatinine >177 μmol/L (>2 mg/dL)
    - Anaemia: haemoglobin value of >20 g/L below the lower limit of normal, or a haemoglobin value <100 g/L
    - Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT‡
  - Any one or more of the following biomarkers of malignancy:
    - Clonal bone marrow plasma cell percentage* ≥60%
    - Involved:uninvolved serum free light chain ratio§ ≥100
    - >1 focal lesions on MRI studies¶

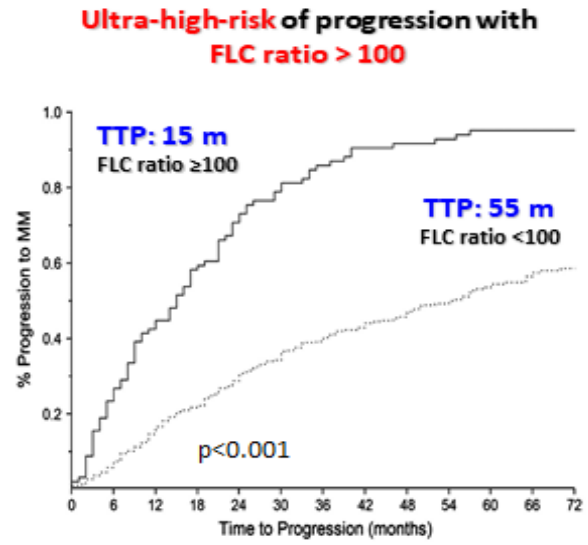
Definition of smouldering multiple myeloma

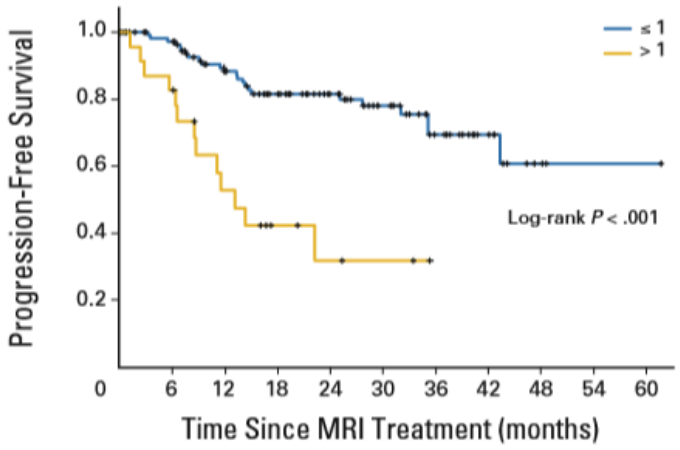
Both criteria must be met:

- Serum monoclonal protein (IgG or IgA) ≥30 g/L or urinary monoclonal protein ≥500 mg per 24 h and/or clonal bone marrow plasma cells 10–60%
- Absence of myeloma defining events or amyloidosis

PET-CT=¹⁸F-fluorodeoxyglucose PET with CT. *Clonality should be established by showing κ/λ-light-chain restriction on flow cytometry, immunohistochemistry, or immunofluorescence. Bone marrow plasma cell percentage should preferably be estimated from a core biopsy specimen; in case of a disparity between the aspirate and core biopsy, the highest value should be used. †Measured or estimated by validated equations. ‡If bone marrow has less than 10% clonal plasma cells, more than one bone lesion is required to distinguish from solitary plasmacytoma with minimal marrow involvement. §These values are based on the serum Freelite assay (The Binding Site Group, Birmingham, UK). The involved free light chain must be ≥100 mg/L. ¶Each focal lesion must be 5 mm or more in size.







Rajkumar, Lancet Oncology 20

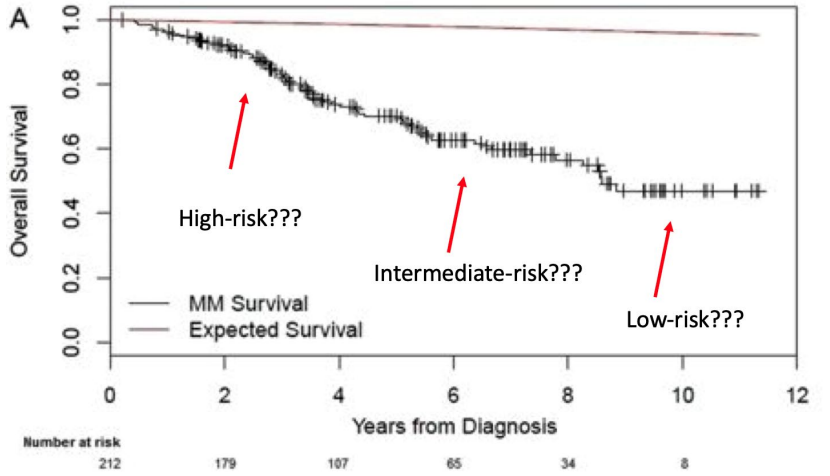
How to define »risk« in MM?

The current risk stratification model does not take into account all the known risk factors

Age

Frailty and performance status

Organ function and comorbidities



R-ISS

Albumin, B2M, LDH and cytogenetics

t(4;14), del17p and t(14;16)

Extramedullary disease

1q gain/amp del1p

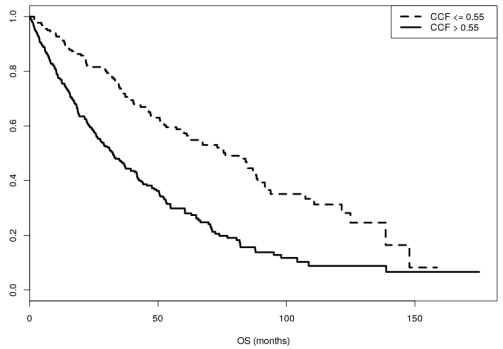
Circulating tumour cells

Plasma cell leukemia

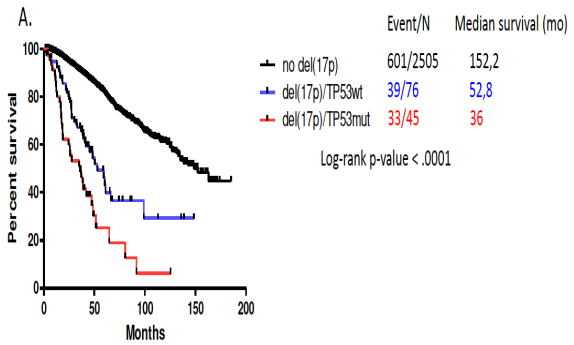
High-risk features: cytogenetics

Del17p / TP53 mutation

Del17p Clonal fraction: 55% cut-off



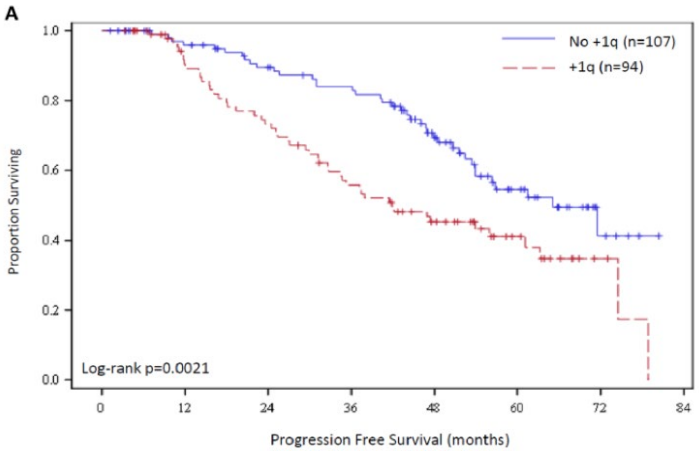
8% at diagnosis
121 patients with del17p: 37% also had TP53 mutation (double hit)



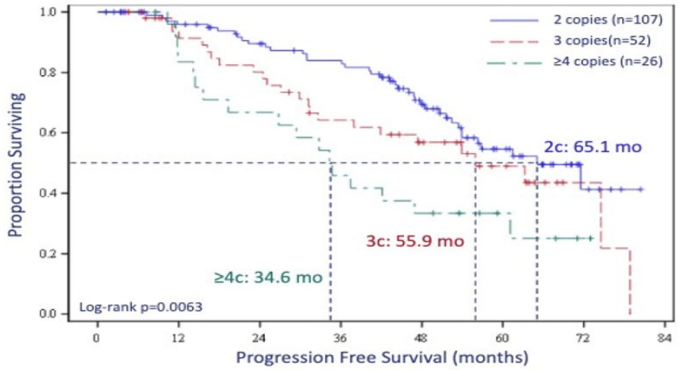
Corre J, et al., Blood 2021; Thakurta et al. Blood 2018

1q gain/amp

30-40% of MM patients carry 1q CNA



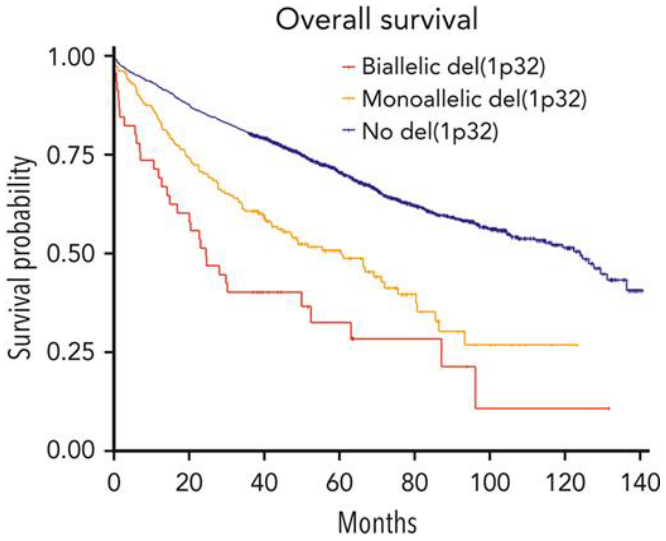
1q copy number predicts patients' outcome



Schmidt et al. Blood Cancer Journal 2019

del1p

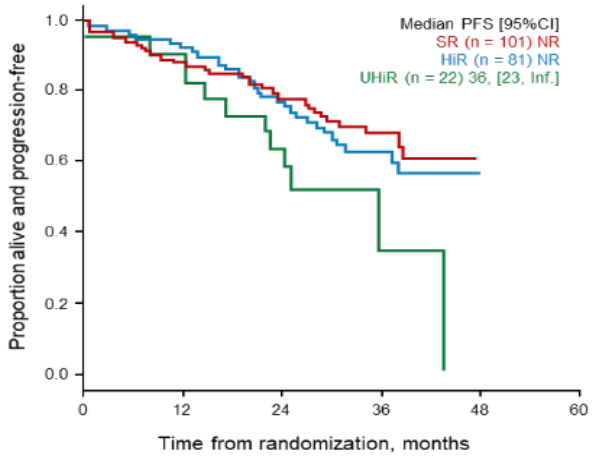
8-10% at diagnosis



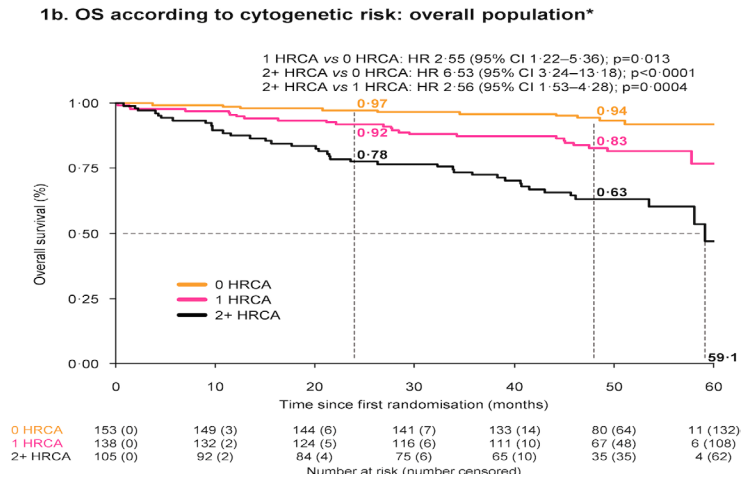
Schavgoulidze A, Blood 2022

The number of genetic lesions matters:
standard risk vs high-risk vs ultra high-risk

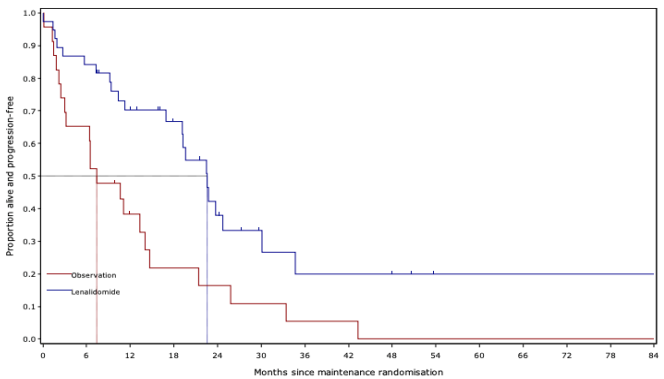
KCRD Myeloma XI



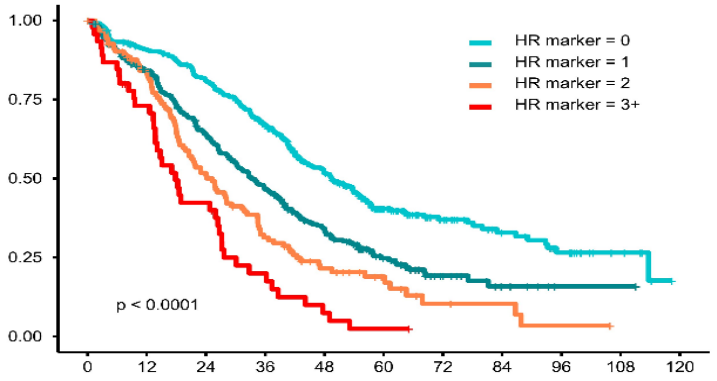
KRd-ASCT vs KRD12 vs KCd-ASCT FORTE



R maintenance Myeloma XI



Bortezomib (GMMG-HD4/MM5)



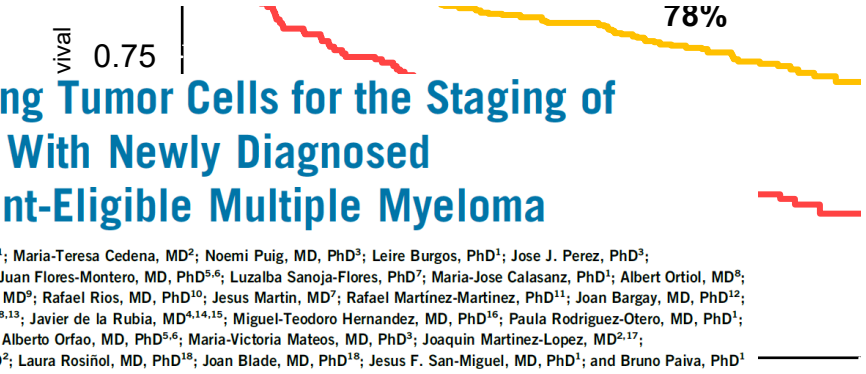
Shah V, et al., Blood 2018, Weinhold et al., Haematologica in print, Mina et al, Lancet Oncol 2023, Croft J, et al., ASH 2019; G. Jackson GH. Et al, Lancet Oncol. 2019 Jan;20(1):57-73;

Circulating plasma cells are an indipendent risk factor

CPC evalubale population: 401/474 subjects - Median CPC 0.02% (IQR 0-0.14) - Cut-off 0.07% (5 cells/ul, 0.005 x10^9/l)

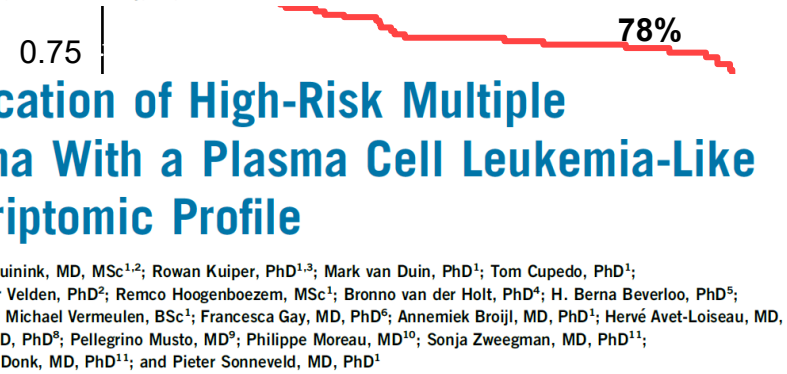
More Than 2% of Circulating Tumor Plasma Cells Defines Plasma Cell Leukemia–Like Multiple Myeloma

Tomas Jelinek, MD, PhD[1]; Renata Bezdekova, PhD[2]; David Zihala, PhD[1]; Tereza Sevcikova, PhD[1,3]; Anjana Anilkumar Sithara, MSc[1,3]; Lenka Pospisilova, MSc[4]; Sabina Sevcikova, PhD[5]; Petra Polackova, MSc[2]; Martin Stork, MD, PhD[6]; Zdenka Knechtova, MCs[6]; Ondrej Venglar, MSc[3]; Veronika Kapustova, MSc[1]; Tereza Popkova, MD[1]; Ludmila Muronova, MD[1]; Zuzana Chyra, PhD[1]; Matous Hrdinka, PhD[1]; Michal Simicek, PhD[1]; Juan-Jose Garcés, PhD[7]; Noemi Puig, MD, PhD[8]; Maria-Teresa Cedena, MD, PhD[9]; Artur Jurczyszyn, MD, PhD[10]; Jorge J. Castillo, MD, PhD[11]; Miroslav Penka, MD[2]; Jakub Radocha, MD, PhD[12]; Maria Victoria Mateos, MD[8]; Jesús F. San-Miguel, MD, PhD[7]; Bruno Paiva, PhD[7]; Ludek Pour, MD, PhD[5]; Lucie Rihova, PhD[2]; and Roman Hajek, MD, PhD[1]



High Levels of Circulating Tumor Plasma Cells as a Key Hallmark of Aggressive Disease in Transplant-Eligible Patients With Newly Diagnosed Multiple Myeloma

Luca Bertamini, MD[1]; Stefania Oliva, MD, PhD[1]; Delia Rota-Scalabrini, MD[2]; Laura Paris, MD[3]; Sonia Morè, MD[4]; Paolo Corradini, MD[5]; Antonio Ledda, MD[6]; Massimo Gentile, MD[7]; Giovanni De Sabbata, MD[8]; Giuseppe Pietrantuono, MD[9]; Anna Pascarella, MD[10]; Patrizia Tosi, MD[11]; Paola Curci, MD[12]; Milena Gilestro, BSc[1]; Andrea Capra, MScEng[1]; Piero Galieni, MD[13]; Francesco Pisani, MD[14]; Ombretta Annibali, MD, PhD[15]; Federico Monaco, MD[16]; Anna Marina Liberati, MD[17]; Salvatore Palmieri, MD[18]; Mario Luppi, MD, PhD[19]; Renato Zambello, MD[20]; Francesca Fazio, MD[21]; Angelo Belotti, MD[22]; Paola Tacchetti, MD, PhD[23]; Pellegrino Musto, MD[12,24]; Mario Boccadoro, MD[1]; and Francesca Gay, MD, PhD[1]

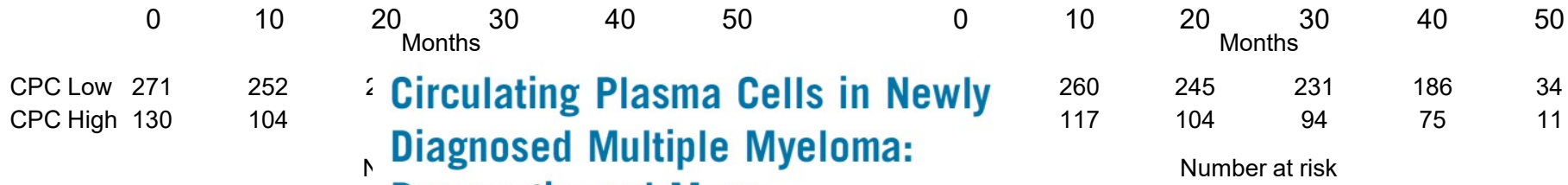


Circulating Tumor Cells for the Staging of Patients With Newly Diagnosed Transplant-Eligible Multiple Myeloma

Juan-Jose Garcés, MSc[1]; Maria-Teresa Cedena, MD[2]; Noemi Puig, MD, PhD[3]; Leire Burgos, PhD[1]; Jose J. Perez, PhD[3]; Lourdes Cordon, PhD[4]; Juan Flores-Montero, MD, PhD[5,6]; Luzalba Sanoja-Flores, PhD[7]; Maria-Jose Calasanz, PhD[1]; Albert Ortiol, MD[8]; María-Jesús Blanchard, MD[9]; Rafael Rios, MD, PhD[10]; Jesus Martin, MD[7]; Rafael Martínez-Martinez, PhD[11]; Joan Bargay, MD, PhD[12]; Anna Sureda, MD, PhD[8,13]; Javier de la Rubia, MD[4,14,15]; Miguel-Teodoro Hernandez, MD, PhD[16]; Paula Rodriguez-Otero, MD, PhD[1]; Javier de la Cruz, MD[2]; Alberto Orfao, MD, PhD[5,6]; Maria-Victoria Mateos, MD, PhD[3]; Joaquin Martinez-Lopez, MD[2,17]; Juan-Jose Lahuerta, MD[2]; Laura Rosiñol, MD, PhD[18]; Joan Blade, MD, PhD[18]; Jesus F. San-Miguel, MD, PhD[1]; and Bruno Paiva, PhD[1]

Identification of High-Risk Multiple Myeloma With a Plasma Cell Leukemia-Like Transcriptomic Profile

Davine Hofste op Bruinink, MD, MSc[1,2]; Rowan Kuiper, PhD[1,3]; Mark van Duin, PhD[1]; Tom Cupedo, PhD[1]; Vincent H.J. van der Velden, PhD[2]; Remco Hoogenboezem, MSc[1]; Bronno van der Holt, PhD[4]; H. Berna Beverloo, PhD[5]; Erik T. Valent, PhD[3]; Michael Vermeulen, BSc[1]; Francesca Gay, MD, PhD[6]; Annemiek Broijl, MD, PhD[1]; Hervé Avet-Loiseau, MD, PhD[7]; Nikhil C. Munshi, MD, PhD[8]; Pellegrino Musto, MD[9]; Philippe Moreau, MD[10]; Sonja Zweegman, MD, PhD[11]; Niels W.C.J. van de Donk, MD, PhD[11]; and Pieter Sonneveld, MD, PhD[1]

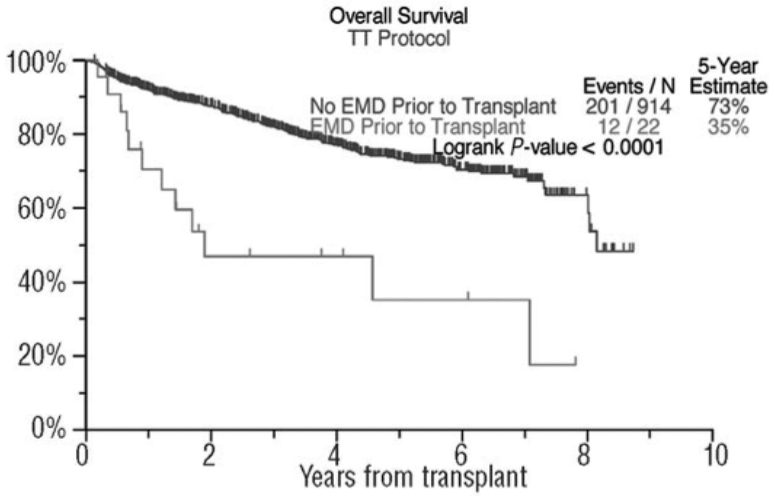


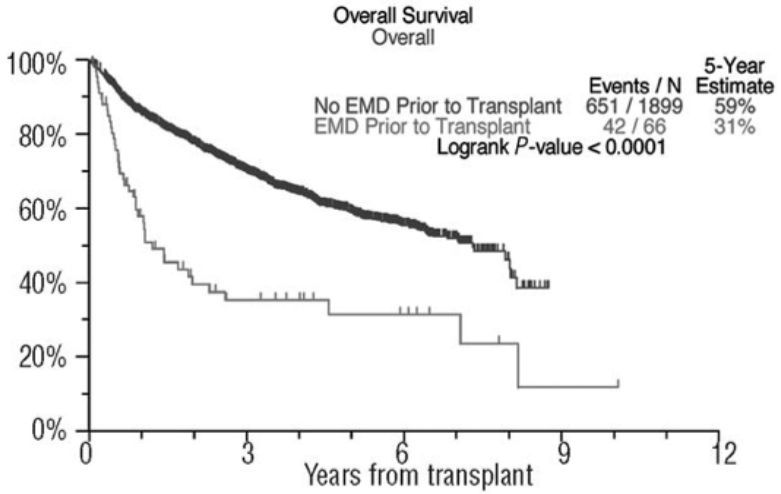
Circulating Plasma Cells in Newly Diagnosed Multiple Myeloma: Prognostic and More

CPC, circulating plasma cells; PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; p, p-value.

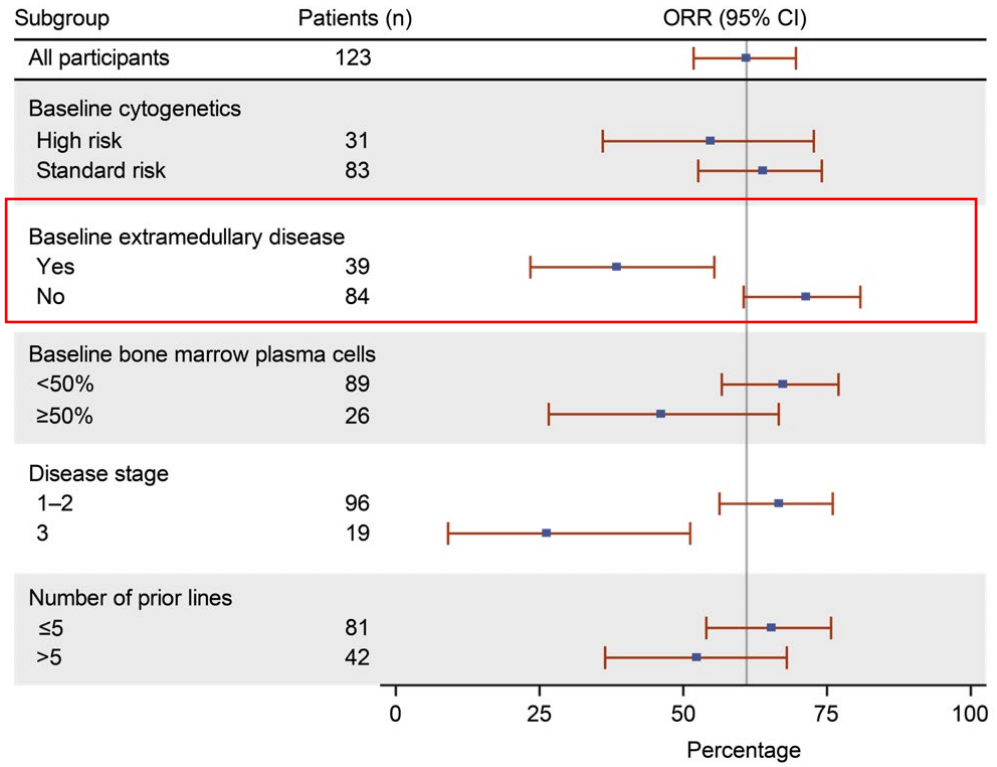
Bertamini L et al. ASH 2020

Extramedullary Myeloma is associated to lower probability of response and worse survival





Probabilty of response to Elranatamab in the MagnetisMM-3 study



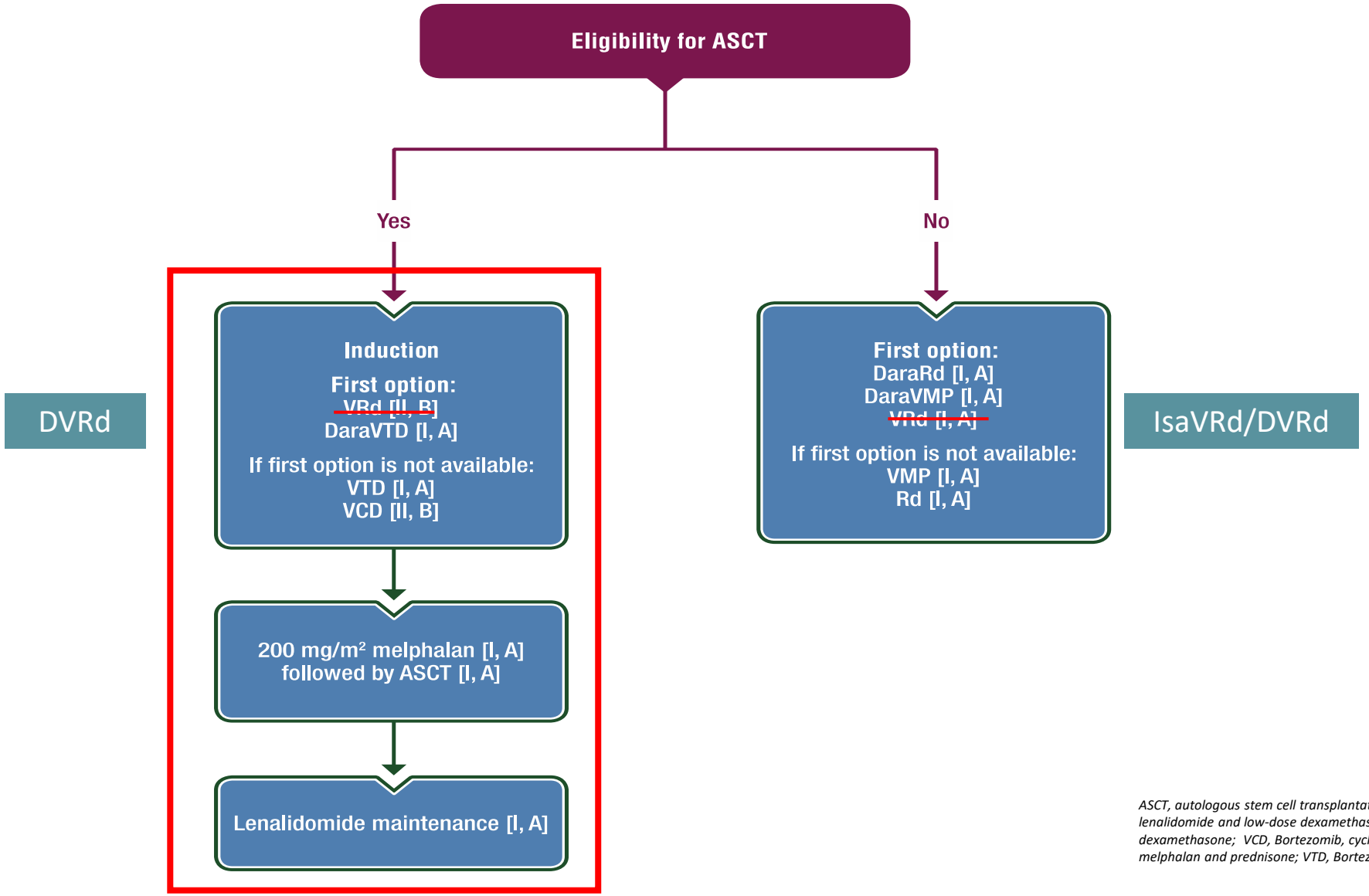
Usmani et al., Haematologica 2012; Bahlis N. et al, ASH22

New IMWG definition of high-risk MM: Barcelona criteria

- Del17p (>20% clonal cells)
- TP53 mutation
- Bi-allelic del1p32
- t(4;14), t(14;16) or t(14;20) + 1q gain/amp or monoallelic del1p
- 1q gain and monoallelic del1p32
- B2M ≥5.5 mg/dl with normal creatinine

How to treat NDMM patients?

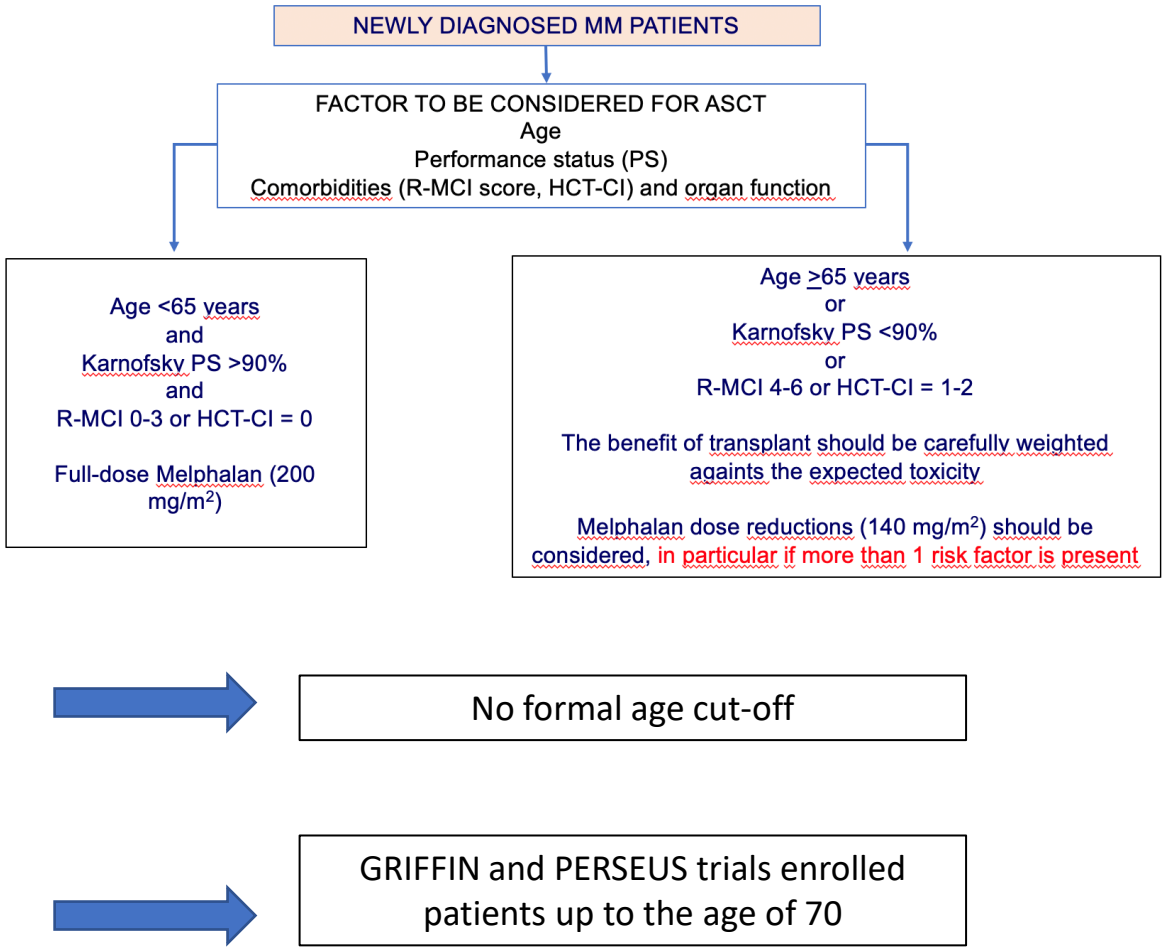
Multiple myeloma: EHA-ESMO Clinical Practice Guidelines
Treatment of Newly diagnosed Multiple Myeloma



ASCT, autologous stem cell transplantation; Dara, daratumumab; PI, proteasome inhibitor; Rd, lenalidomide and low-dose dexamethasone; VRD, bortezomib, lenalidomide, and dexamethasone; VCD, Bortezomib, cyclophosphamide and dexamethasone; VMP, bortezomib, melphalan and prednisone; VTD, Bortezomib, thalidomide and dexamethasone.

Dimopoulos MA, et al. Ann Oncol. 2021;32(3):309-322.

Transplant: defining eligibility and outcomes



Retrospective Studies	Median age, y (range)	Conditioning regimen	TRM (%)	OS
Bashir et al. *Leuk Lymphoma* 2012; 53:118-122.	72 (70-80)	MEL200: 65% of pts MEL140: 25% of pts MEL100: 10% of pts	All pts: 3. <75 y: 2; ≥75 y: 6.	5-year: 67%
Merz et al. *Ann Oncol* 2014; 25:189–195	65	MEL200	60-64 y: 2.4 65-69 y: 1 70-75 y: 0	60-64 y: NR; 65-69 y: NR; 70-75 y: NR.
Ozaki et al. *Acta Haematol* 2014; 132:211–219	65-68	MEL200/140	0	NR
Sanchez et al. *Biol Blood Marrow Transplant* 2017; 23:1203–1207	NA	NA	<65 y: 2.3 ≥65 y: 1.2	NA
Stettler et al. *Leuk Lymphoma* 2017; 58:1076–1083	NA	MEL200: 65-70 y MEL140: >70 y	65-70 y: 0 >70 y: 0	2-year: 65-70 y: 96%; >70 y: 100%.
Belotti et al. *Blood* 2018; 132: Abstract #2151 [ASH 2018 60th Meeting]	NA	MEL200: 68% of pts MEL<200: 32% of pts	0	NA
Ghilardi et al. *Bone Marrow Transplant* 2018; Nov 2 [presented at ASH 2017 59th Meeting]	67.5 (65-77)	MEL200: 75.3% MEL70-180: 24.7%	MEL200: 1.4; MEL70-180: 2.	≤70 y: 82.8 mo; >70 y: 56.2 mo
Marini et al. *Ann Hematol* 2019; 98:369–379	67 (66-70)	MEL200: 38% MEL140: 62%	NA	NA
Mizuno et al. *Blood* 2018; 132: Abstract #3437 [ASH 2018 60th Meeting]	66 (65-76)	MEL200/140/100:	<65 y: 0.4 ≥65 y: 1.2	5-year: <65 y: 63%; ≥65 y: 64%.
Saini et al. 2018 Blood 132:Abstract #4608 [ASH 2018 60th Meeting]	81 (80-83)	MEL140	0	NR; 2-year: 75%

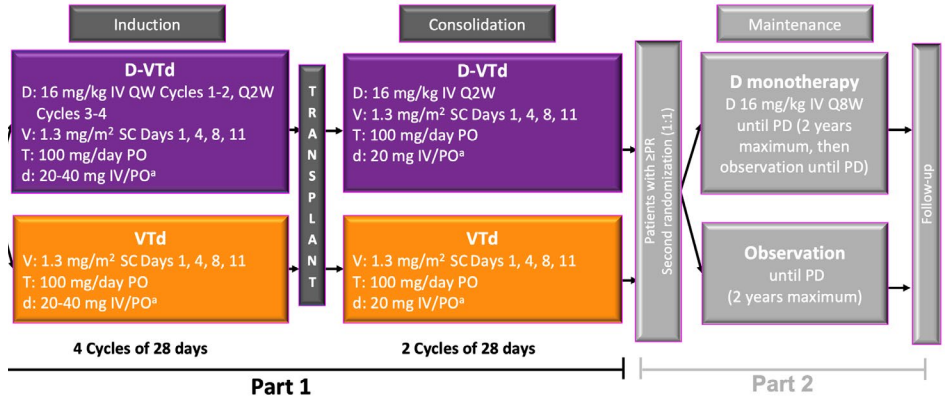
Gay F et al, EMN Guidelines on transplant in MM, Hematologica 2017

Phase III studies challenging triplets as inductiona and consolidation in ASCT-eligible patients

CASSIOPEA

D-VTd versus VTd in transplant-eligible NDMM (N = 1,085)

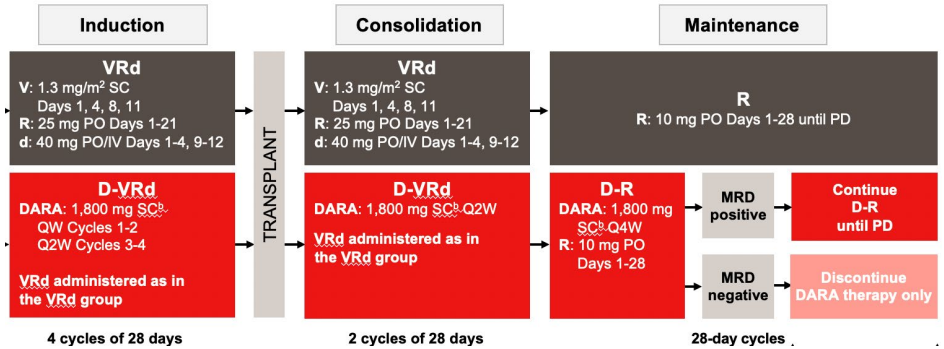
*Primary endpoint: p*ost-consolidation sCR



EMN17 / PERSEUS

D-VRd versus VRd in transplant-eligible NDMM (N = 709)

Primary endpoint: progression-free survival



Phase III studies challenging triplets as inductiona and consolidation in ASCT-eligible patients

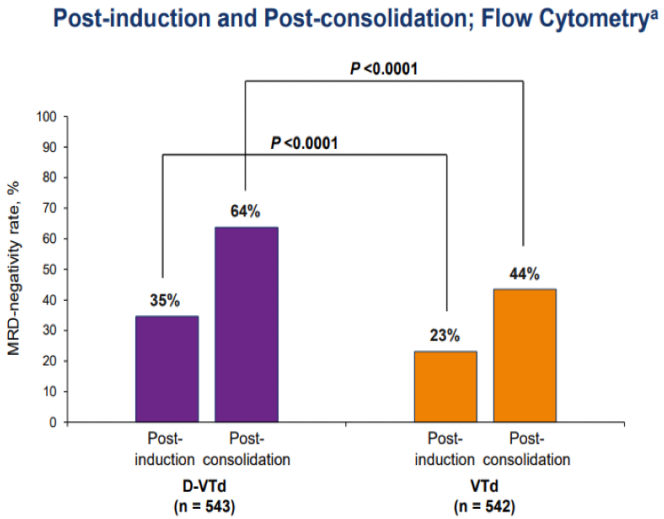
CASSIOPEA

D-VTd versus VTd in transplant-eligible NDMM (N = 1,085)

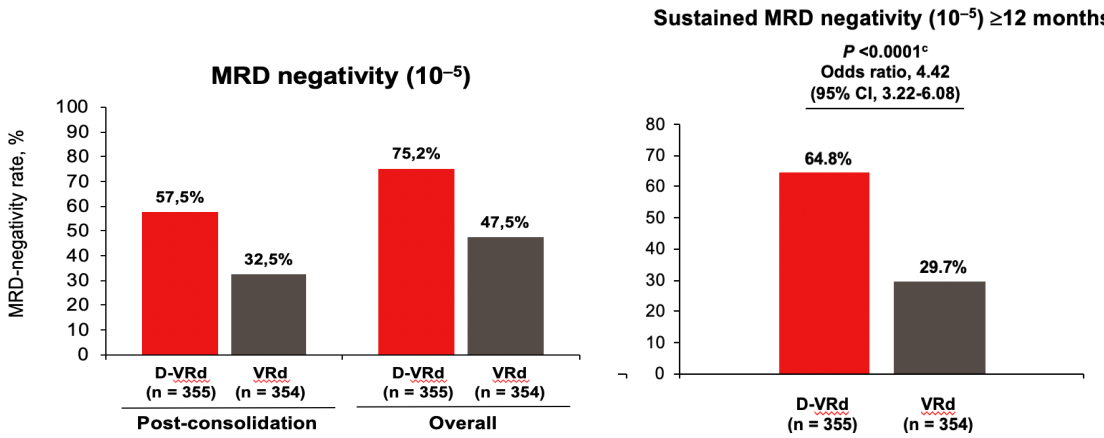
EMN17 / PERSEUS

D-VRd versus VRd in transplant-eligible NDMM (N = 709)

MRD negativity rates, 10^{-5}



Primary endpoint: Post-consolidation sCR:
29% D-VTd vs 20% VTd
Odds ratio, 1.60; *P* = 0.0010



CR or sCR rates:
88% D-VRd vs 70% VRd
Odds ratio, 3.13; *P* < 0.0001

Moreau P. et al; Lancet Oncol 2019; Sonneveld P. et al; NEJM2023

Phase III studies challenging triplets as inductiona and consolidation in ASCT-eligible patients

CASSIOPEA

D-VTd versus VTd in transplant-eligible NDMM (N = 1,085)

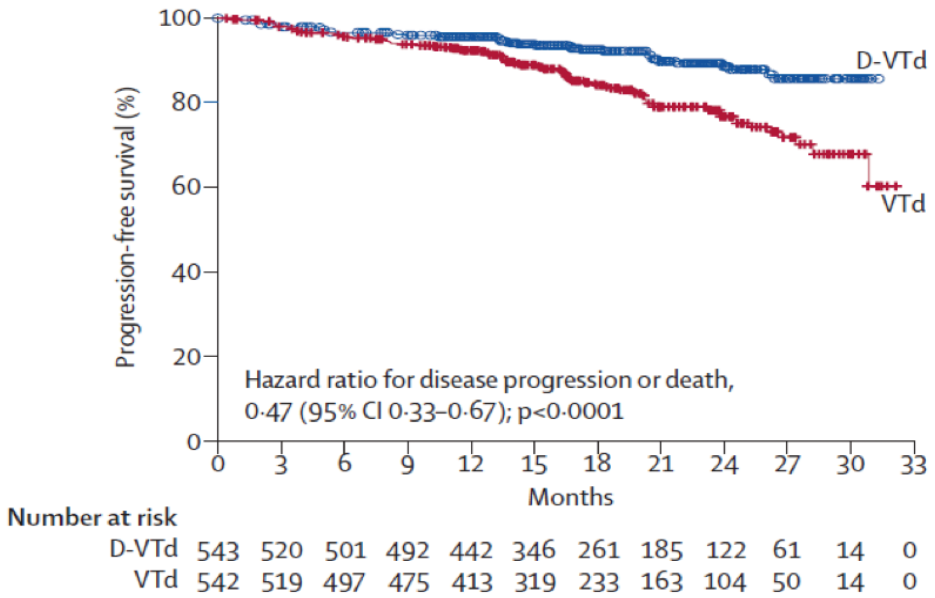
Median follow-up: 18.8 months

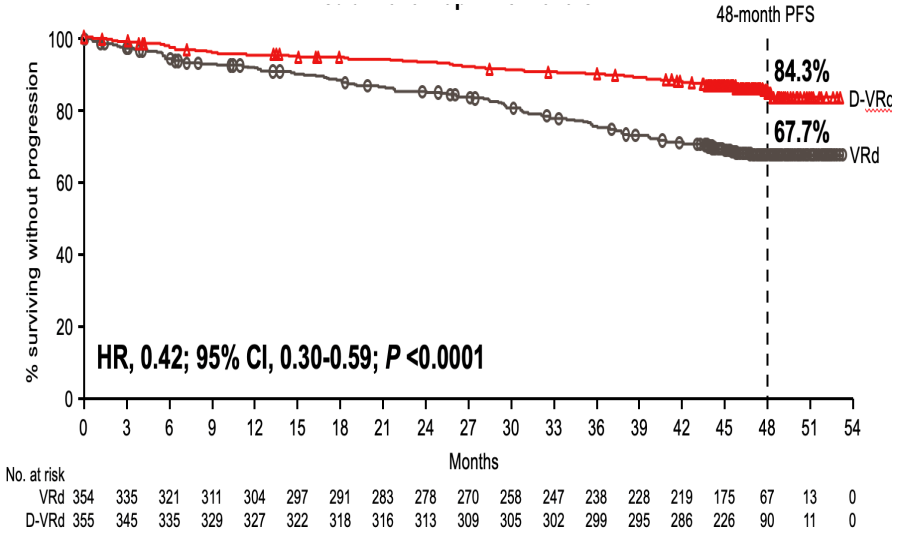
EMN17 / PERSEUS

D-VRd versus VRd in transplant-eligible NDMM (N = 709)

Median follow-up: 47.5 months

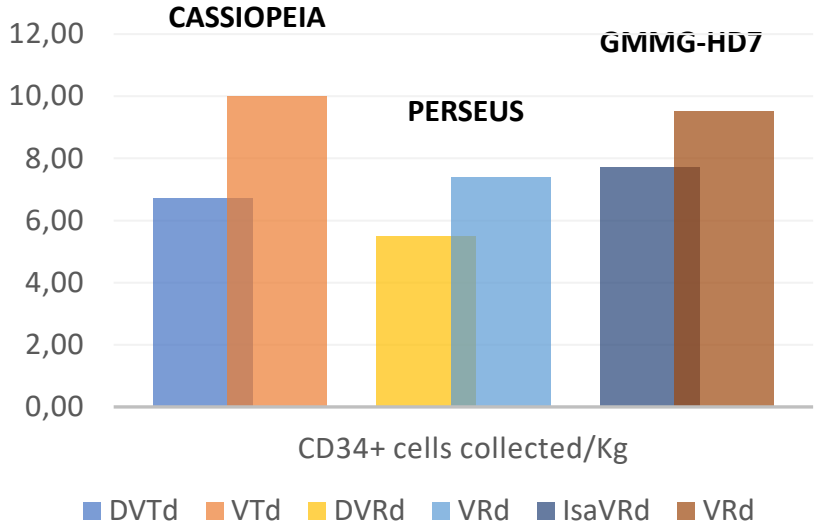
Progression-free survival



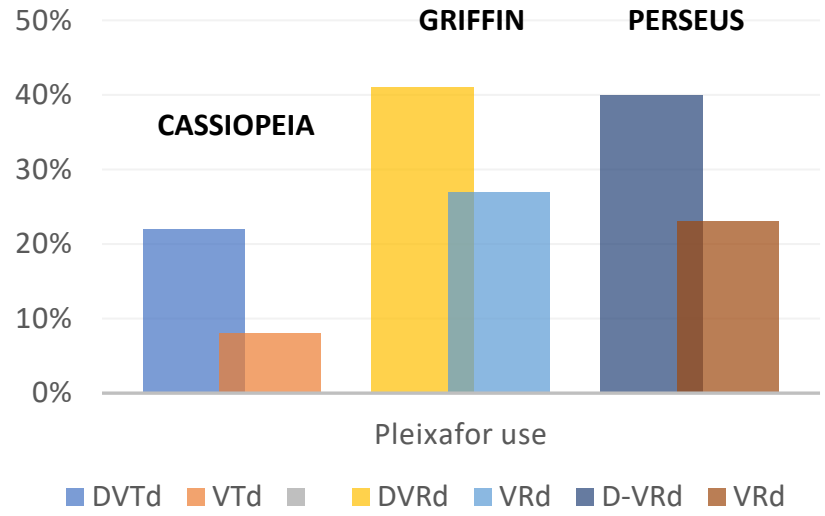


Moreau P. et al; Lancet Oncol 2019; Sonneveld P. et al; NEJM2023

What is the impact of anti-CD38 MoAb on hematopoietic stem cell mobilization?



Hematopoietic stem cell yield



Use of plerixafor as rescue

- Anti-CD38 Moab regimens seem to impact on hematopoietic stem cell yield **(↓)** and the use of plerixafor **(↑)**
- No significantly impact on mobilization successfulness or hematopoeitic engraftment

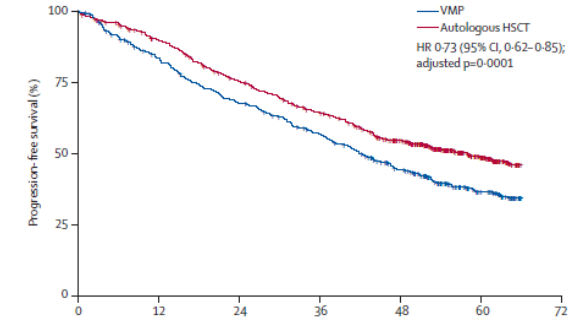
D: daratumumab; V: bortezomib; d: dexamethasone; T: thalidomide; C: cyclophosphamide; R: lenalidomide; K, carfilzomib; HDC: high-dose chemotherapy; ASCT: autologous stem cell transplantation; y: years;TE, transplant eligible; VGPR, very good partial response; HSC, hematopoietic stem cell; GCSF, granulocyte-colony stimulating factor; PLX, plerixafor; CTX, cyclophosphamide

Hulin C et al., CASSIOPEIA study. Haematologica. 2021
S. Chhabra et al., MASTER & GRIFFIN Transplantation and Cellular Therapy 29 (2023)

The role of ASCT: PFS benefits

EMN-02/HO95

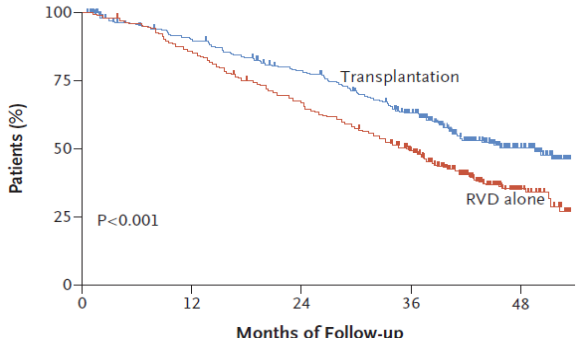
Median follow-up: 60 months



mPFS: **56.7 months** in the ASCT group vs. **41.9 months** in the VMP group

IFM-2009

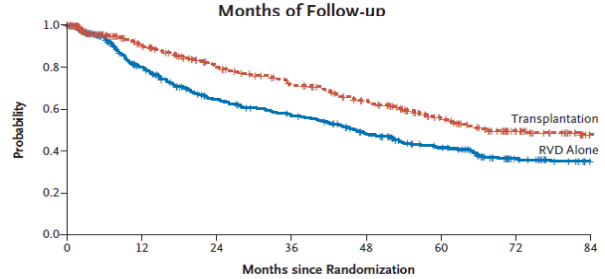
Median follow-up: 43-44 months



mPFS: **50 months** in the ASCT group vs. **36 months** in the RVD-alone group

DETERMINATION

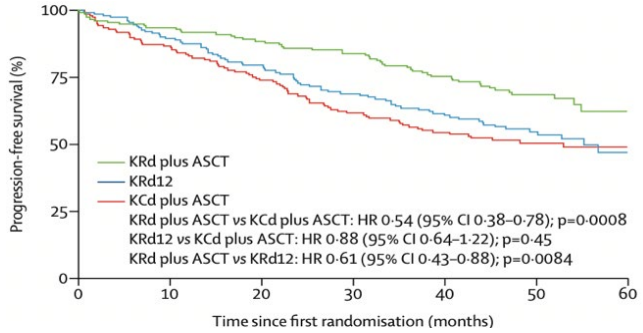
Median follow-up: 76 months



mPFS: 67.5 months in the ASCT group and **46.2 months** in the RVD-alone group

FORTE

Median follow-up: 51 months



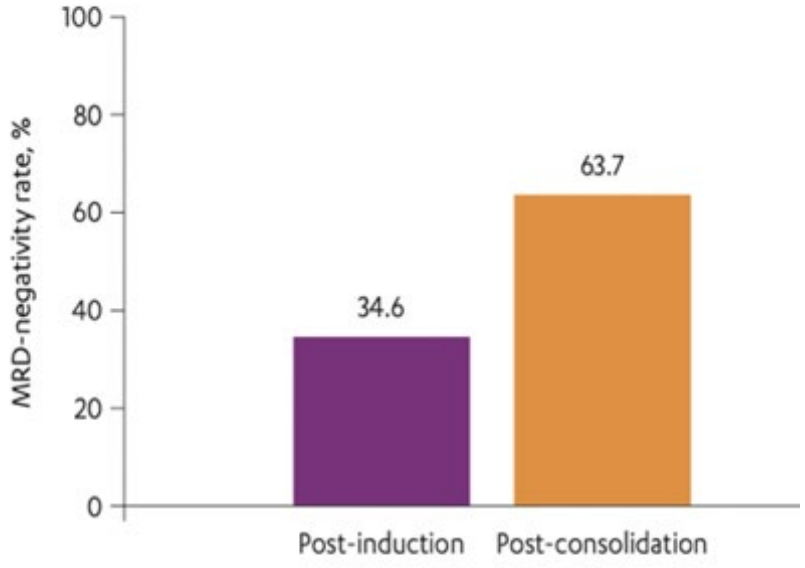
4-y PFS: **69%** in the ASCT group and **56%** in the KRD12 group
mPFS: **NR** vs 55 months

HDM, high-dose melphalan; ASCT, autologous stem-cell transplantation; K, carfilzomib; R, lenalidomide; d, dexamethasone; C, cyclophosphamide; R, lenalidomide, V, bortezomib, KRd plus ASCT, 4 KRD induction cycles, MEL200-ASCT, 4 KRd consolidation cycles; ; KRd12, 12 KRd cycles; HR, hazard ratio; CI, confidence interval; p, p-value; Nr, not reached; PFS, progression free survival

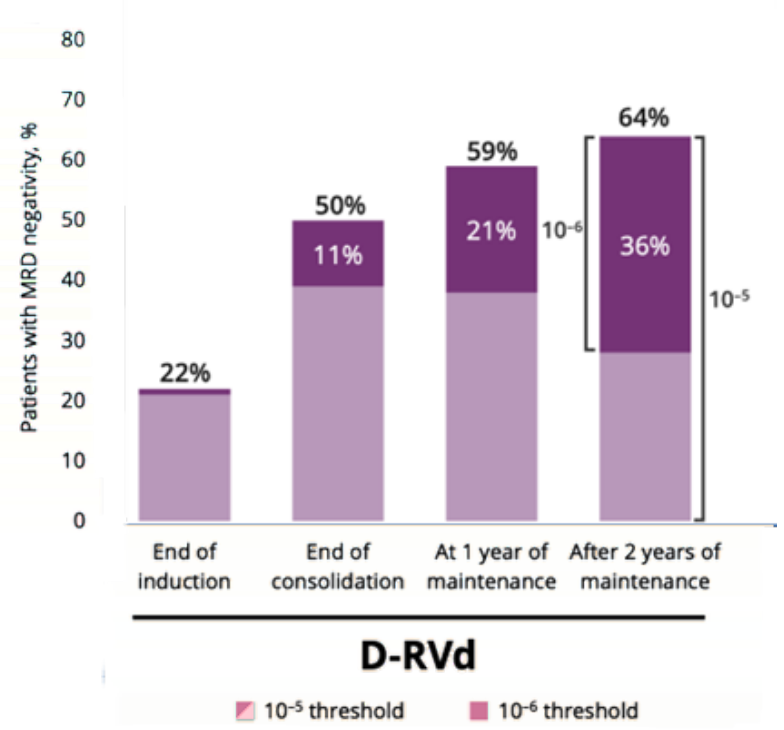
Cavo et al., EMN02, Lancet 2020; Gay F et al., FORTE trial, Lancet Oncol 2021; Attal M et al., IFM-2009, N Engl J Med 2017; Richardson P et al., DETERMINATION study, N Engl J Med 2022

ASCT remains a standard of care in the era of anti-CD38 monoclonal antibodies-based quadruplets

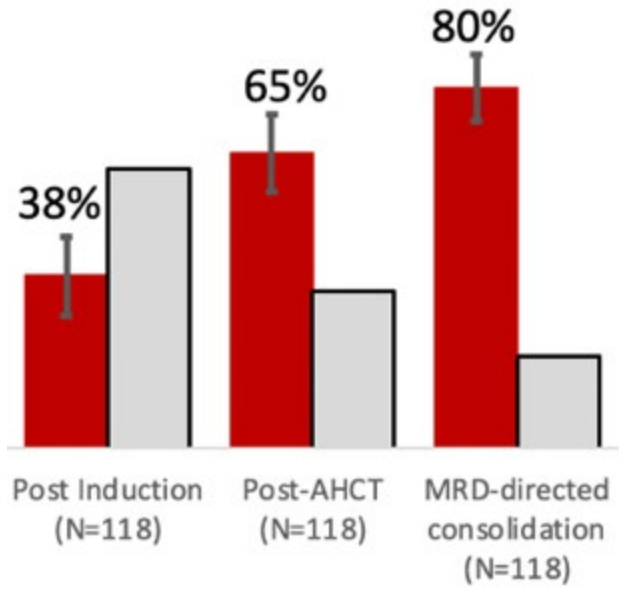
CASSIOPEA
Dara-VTd



GRIFFIN
Dara-VRd



MASTER
Dara-KRd



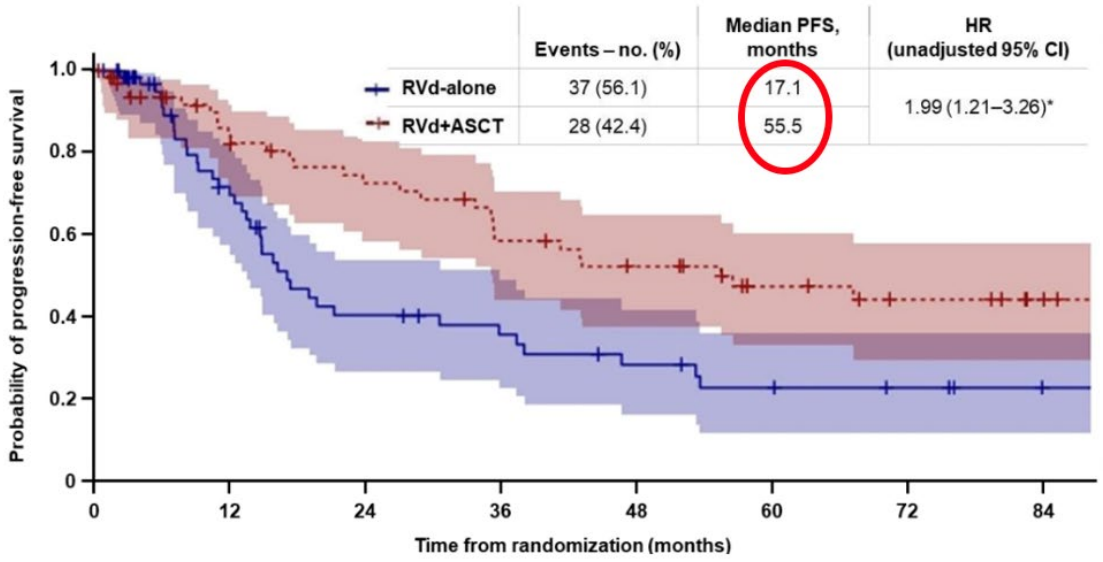
HDM, high-dose melphalan; MRD, minimal residual disease; Dara, D, daratumumab; V, bortezomib; T, thalidomide; d, dexamethasone; R, lenalidomide; K, carfilzomib

Avet-Loiseau H et al. ASH 2021;abstract 82 (oral presentation); Laubach JP et al. ASH 2021;abstract 79 (oral presentation); Costa LJ et al. ASH 2021;abstract 481 (oral presentation)

What is the role of autologous stem cell transplant in high-risk patients?

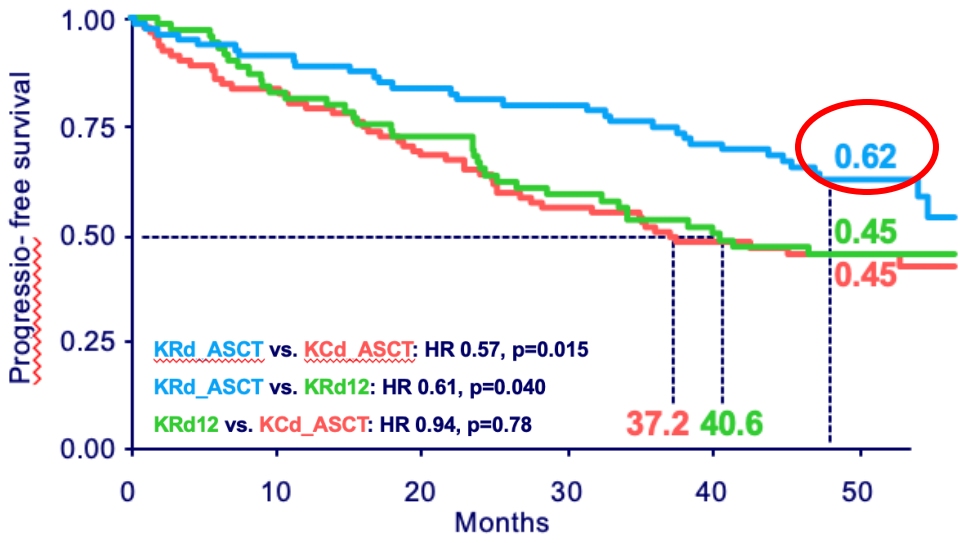
DETERMINATION study:
VRd + ASCT vs VRd alone

Progression-free survival



FORTE study:
KRd/KCyd + ASCT vs KRd alone

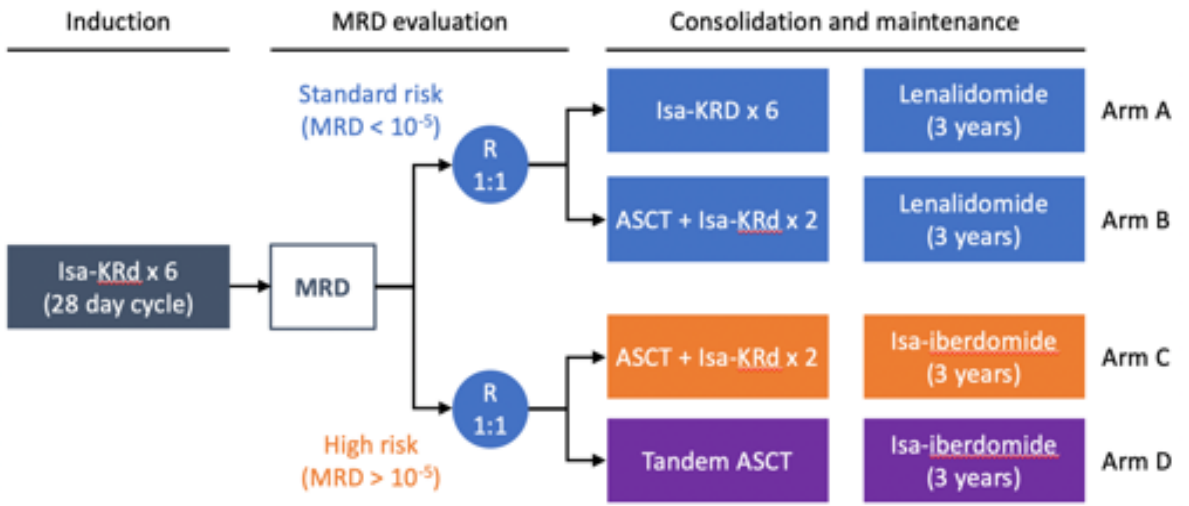
Progression-free survival



Richardson PG. Et al NEJM 2022. Mina R. et al, Lancet Oncol 2023

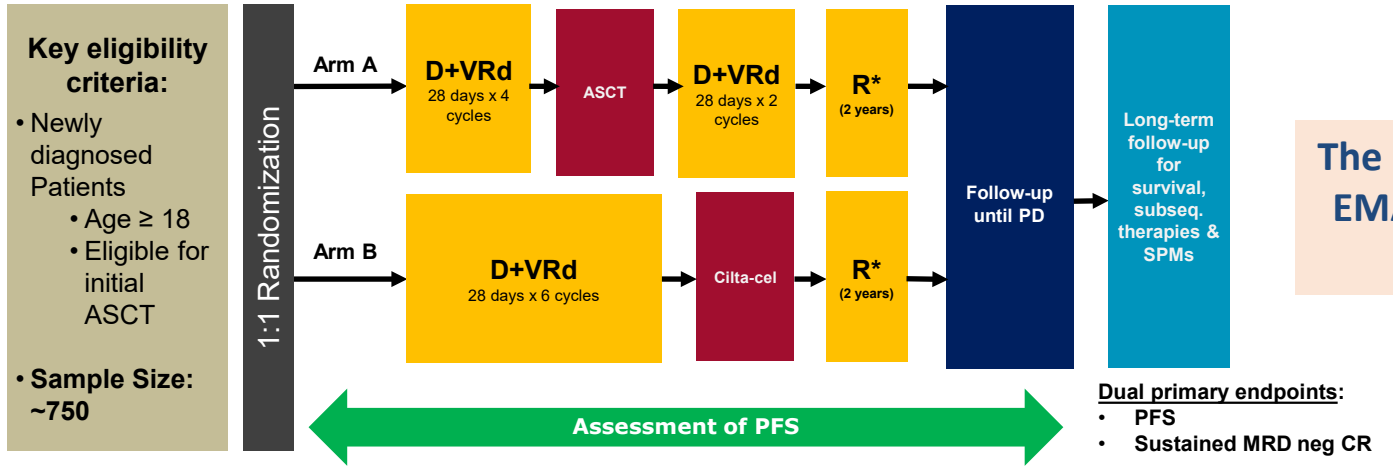
Is there still a role for ASCT?

Will ASCT be necessary in all NDMM patients?



The randomized, phase III IFM 2020-02 Minimal Residual Disease Adapted Strategy (MIDAS) study

Will CAR T-cell therapy replace HDM-ASCT as upfront treatment in NDMM patients?



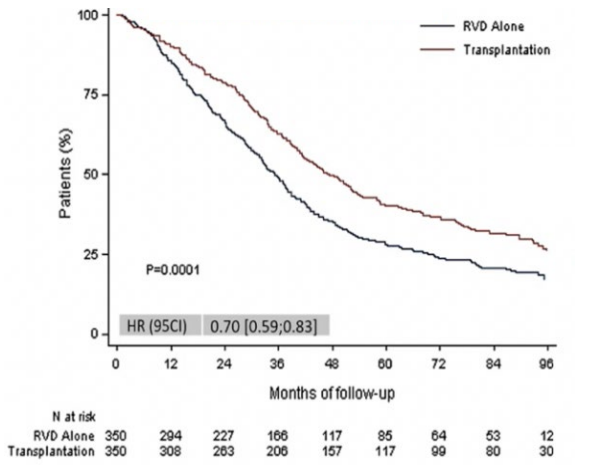
The randomized, phase III EMAGINE/CARTITUDE-6 (EMN28) study

CAR, chimeric antigen receptor; HDM, high-dose melphalan; ASCT, autologous stem-cell transplantation; NDMM, newly diagnosed multiple myeloma; D, daratumumab; V, bortezomib; R, lenalidomide; d, dexamethasone; Cilta-cel, ciltacabtagene autoleucel; PFS, progression-free survival; PD, progressive disease; SPMs, second primary malignancies; subseq., subsequent; ISS, International Staging System; MRD, minimal residual disease; neg, negativity; CR, complete response; Isa, isatuximab; K, carfilzomib

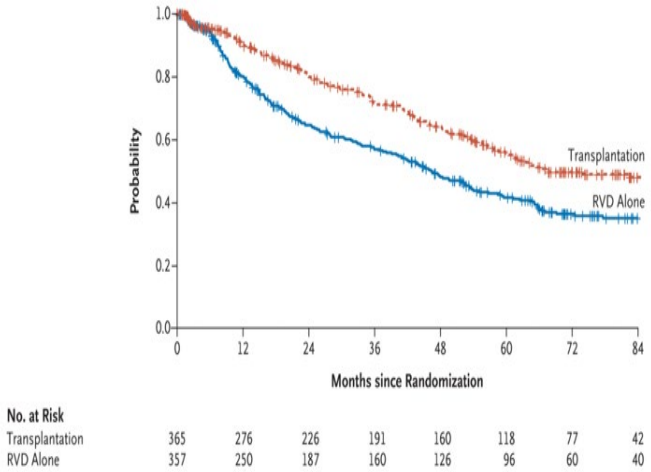
ClinicalTrials.gov Identifier: NCT05257083
ClinicalTrials.gov Identifier: NCT04934475

Results supporting post-transplant maintenance in MM

Lenalidomide maintenance

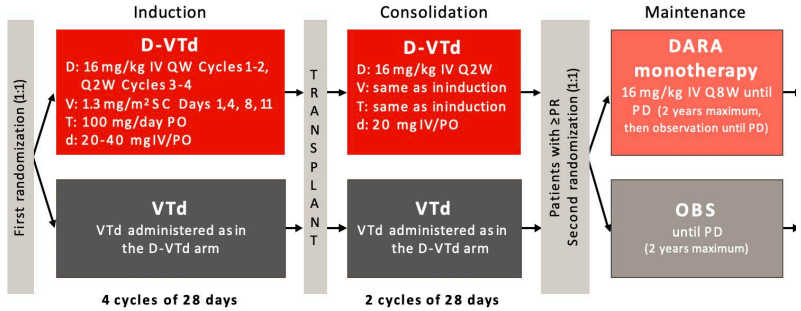


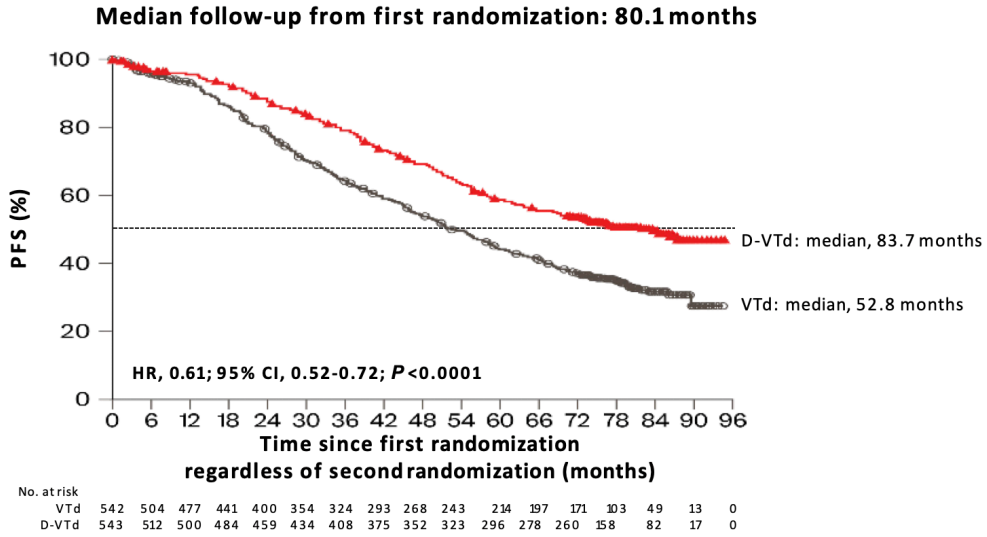
IFM 2009: len 1 year
PFS: Median, 47 vs. 35 months
(N=700)



DETERMINATION:
len until progression
PFS: Median, 68 vs. 46 months
(N=722)

Daratumumab maintenance





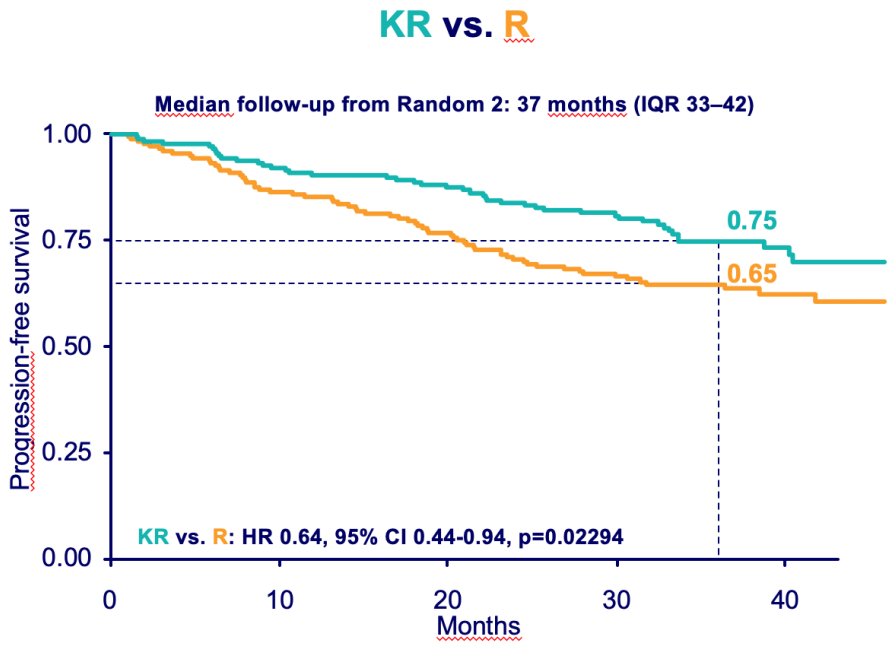
PFS, HR DVTd-dara vs DVTd-no dara: HR, 0.76; 95% CI, 0.58-1.00; $P = 0.0480$

*McCarthy et al. J Clin Oncol 2017; * Sonneveld P. et al JCO21, Richardson P. et al, NEJM22*

Moreau P. et al EHA24

Building upon lenalidomide maintenance

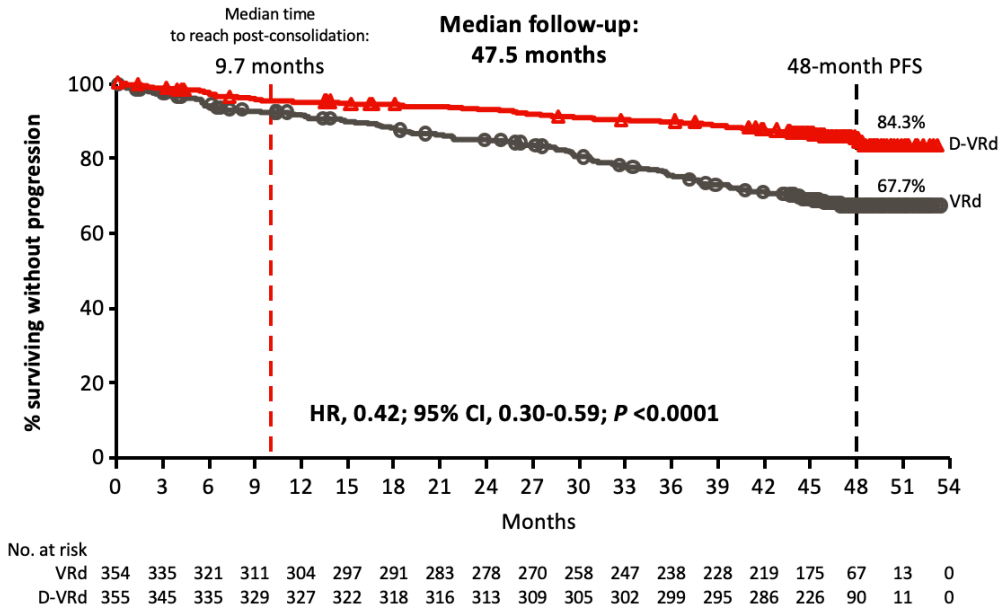
Phase II, FORTE study
Carfilzomib-Lenalidomide vs lenalidomide maintenance



Patients converting from MRD pos to neg during maintenance @10^{-5}: 46 vs 30%

Gay F. Lancet Oncol 2021

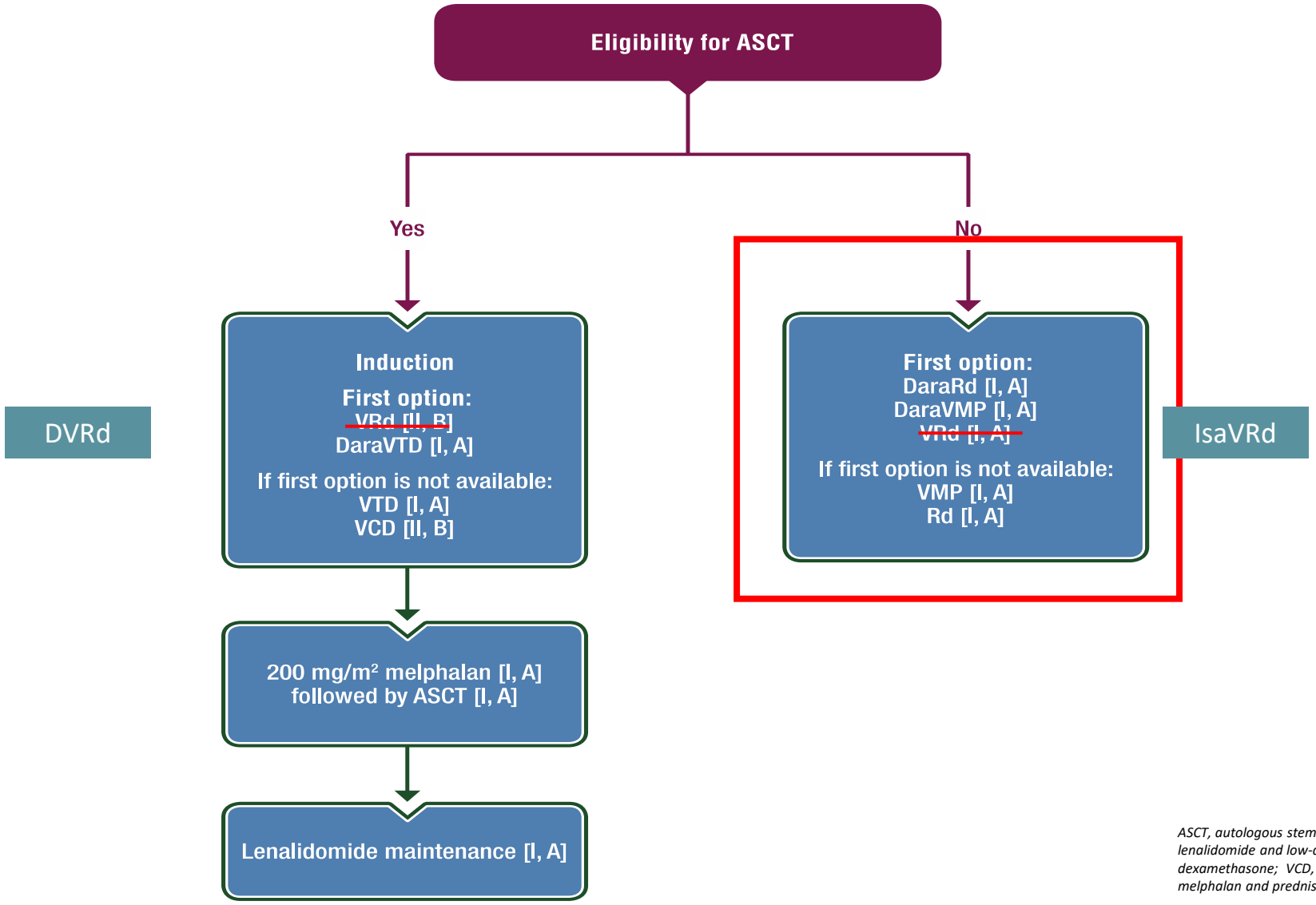
Phase III, PERSEUS
Daratumumab-lenalidomide vs lenalidomide maintenance



Patients converting from MRD pos to neg during maintenance @10^{-5}: 60 vs 40%

Otero PR EHA 2024

Multiple myeloma: EHA-ESMO Clinical Practice Guidelines
Treatment of Newly diagnosed Multiple Myeloma

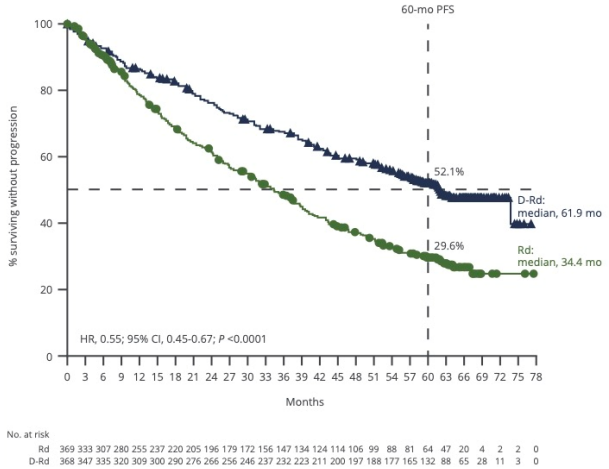


ASCT, autologous stem cell transplantation; Dara, daratumumab; PI, proteasome inhibitor; Rd, lenalidomide and low-dose dexamethasone; VRD, bortezomib, lenalidomide, and dexamethasone; VCD, Bortezomib, cyclophosphamide and dexamethasone; VMP, bortezomib, melphalan and prednisone; VTD, Bortezomib, thalidomide and dexamethasone.

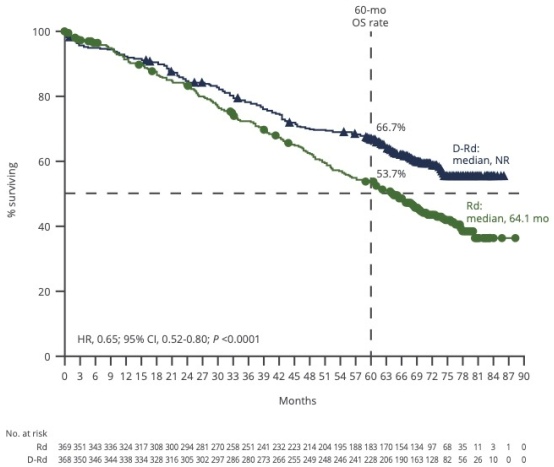
Dimopoulos MA, et al. Ann Oncol. 2021;32(3):309-322.

First-line treatment approach to ASCT-ineligible patients

Dara-Rd vs Rd: phase III MAIA study

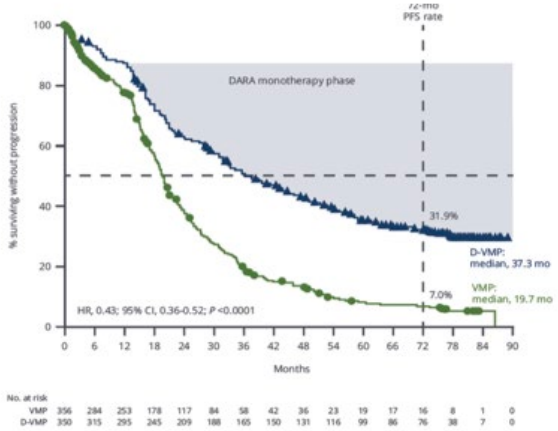


PFS
DRd vs Rd
61.9 vs 34.3 months
(median)

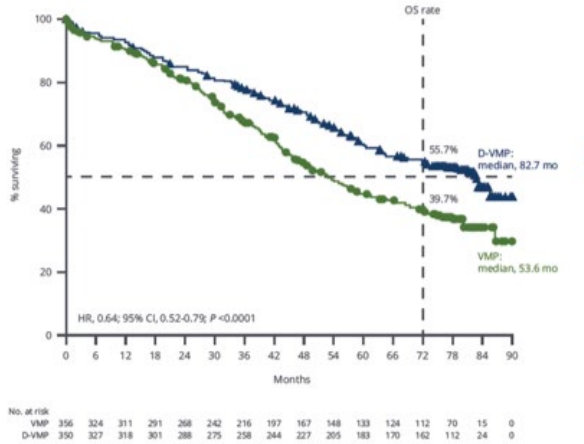


OS
DRd vs Rd
NR vs 64.1 months
(median)

Dara-VMP vs VMP: phase III ALCYONE study



PFS
DRd vs Rd
37.3 vs 19.7 months
(median)



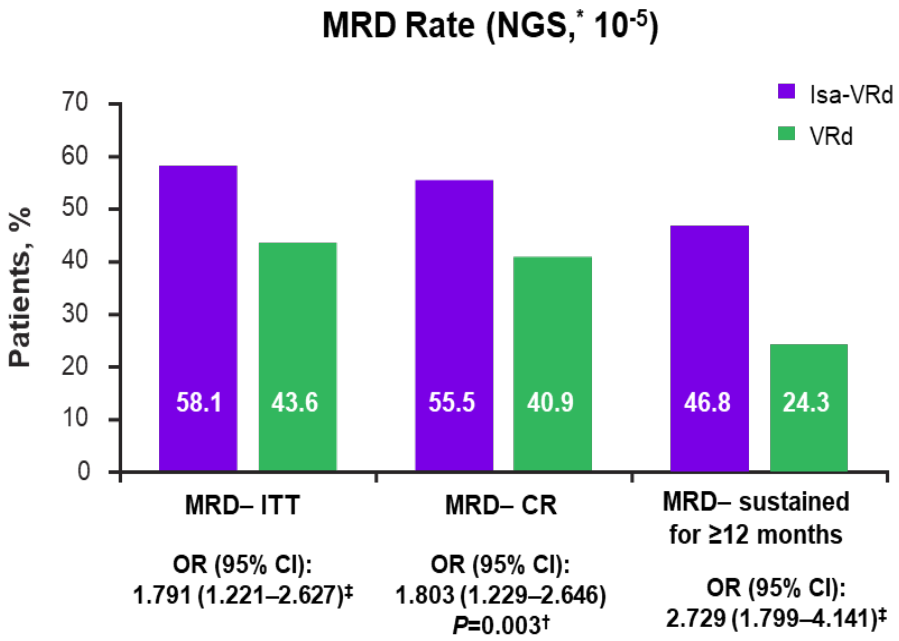
OS
DRd vs Rd
82.7 vs 53.6 months
(median)

IMROZ phase 3 Study
Isa-VRd vs VRd in TNE NDMM: PFS

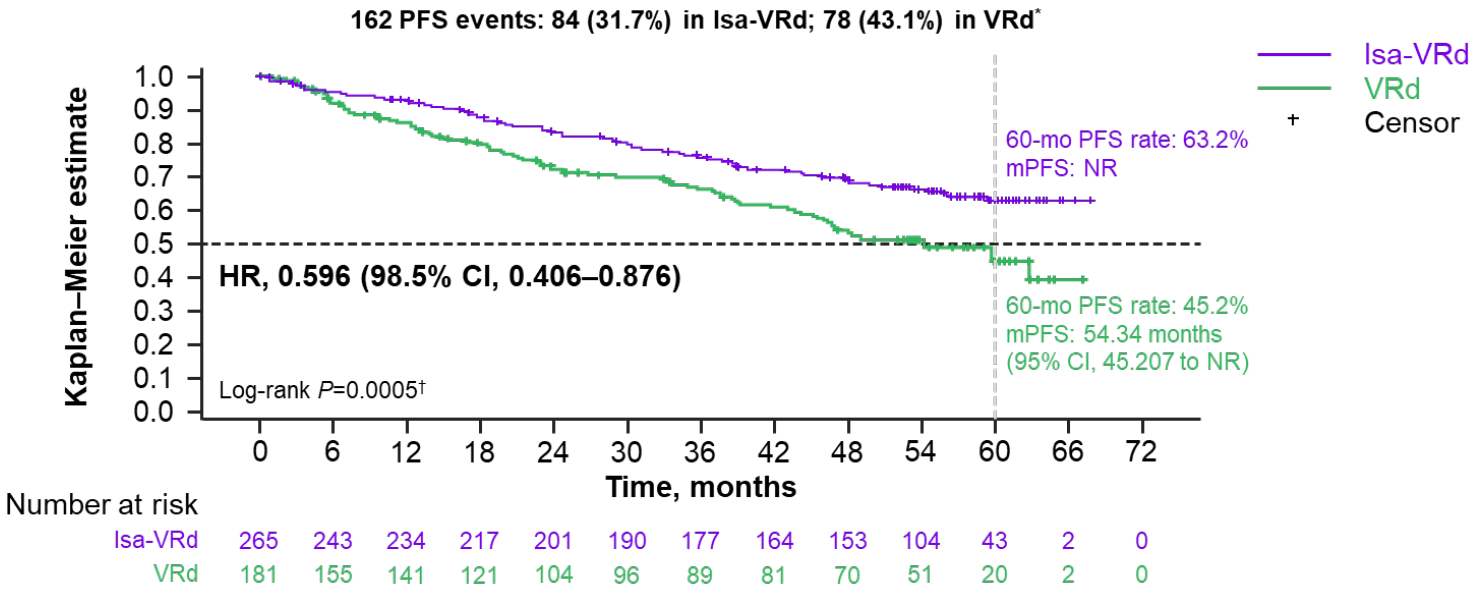
Median follow-up of 59.7 months

Response rates

≥CR: 74.7% vs 64.1%, P=0.01



Progression-free survival



*Cutoff date for PFS analysis: September 26, 2023 (median follow-up, ~5 years). †Nominal one-sided *P* value.NR, not reached.

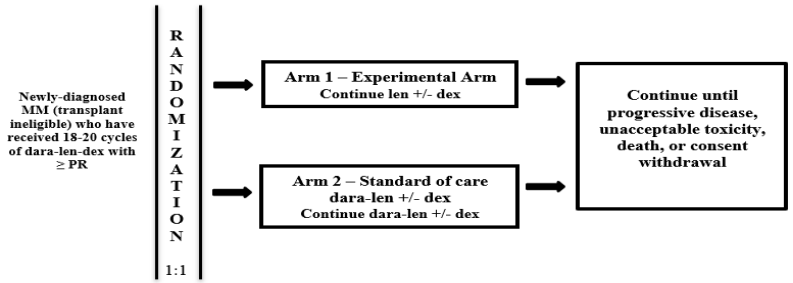
Facon T. et al.. June 3, 2024, NEJM.. Oral presentation presented at the American Society of Clinical Oncology (ASCO 2024), Chicago, IL, USA, May 31–June 4, 2024

Future directions in the first-line treatment of older patients

Treatment de-escalation

DRd vs DRd→Rd

MY 13 STUDY – CANADIAN CANCER TRIAL GROUPS[1]



n = 559

Cycle = 28 days

Abbreviations

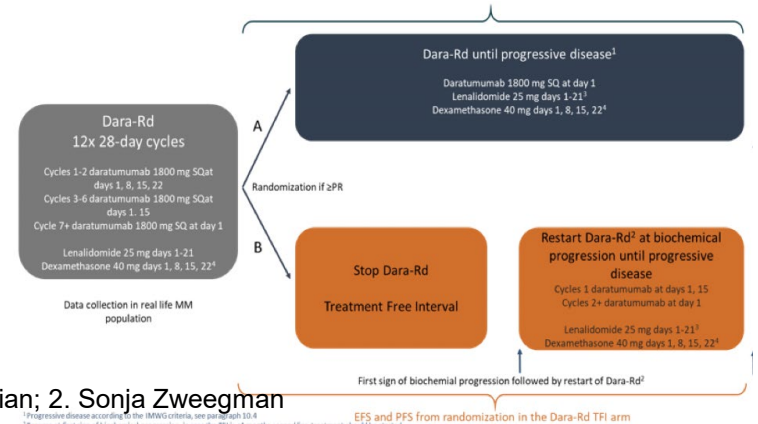
Dara-len-dex = Daratumumab-lenalidomide-dexamethasone

MM = Multiple myeloma

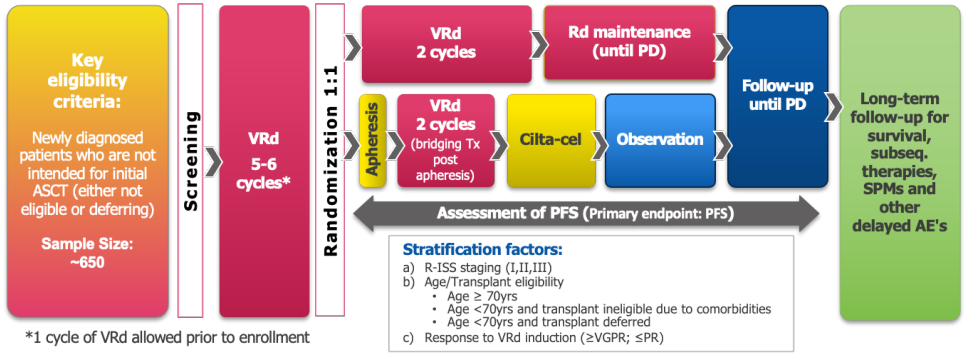
PR = Partial Response

DRd continuous vs DRd12+ th at progression

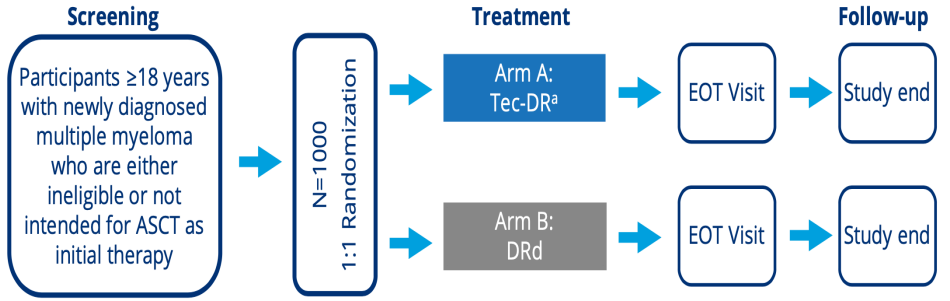
HOVON FABULOUS STUDY[2]

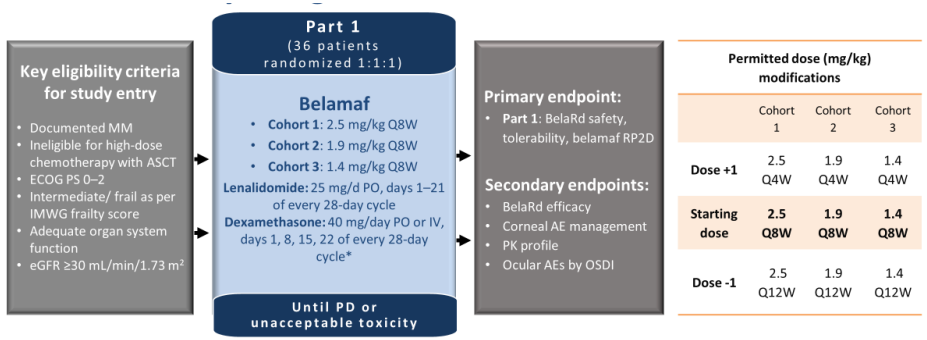


Early use of BCMA



*1 cycle of VRd allowed prior to enrollment





Permitted dose (mg/kg) modifications

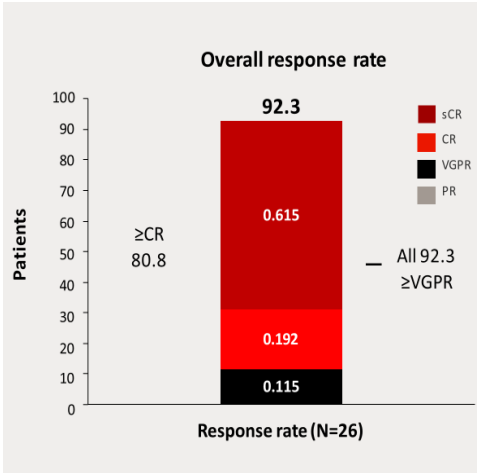
	Cohort 1	Cohort 2	Cohort 3
Dose +1	2.5 Q4W	1.9 Q4W	1.4 Q4W
Starting dose	**2.5 Q8W**	**1.9 Q8W**	**1.4 Q8W**
Dose -1	2.5 Q12W	1.9 Q12W	1.4 Q12W

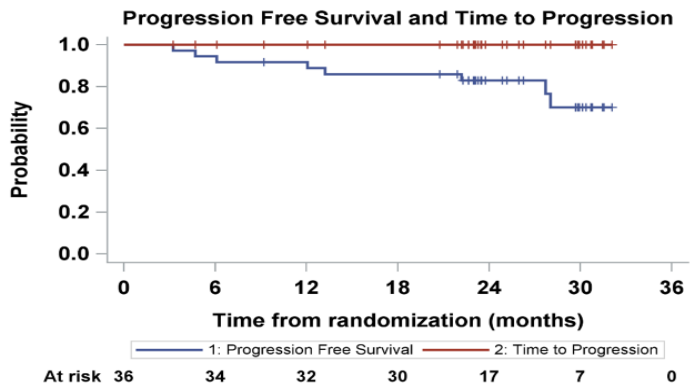
1. PIs: Hira Mian; 2. Sonja Zweegman

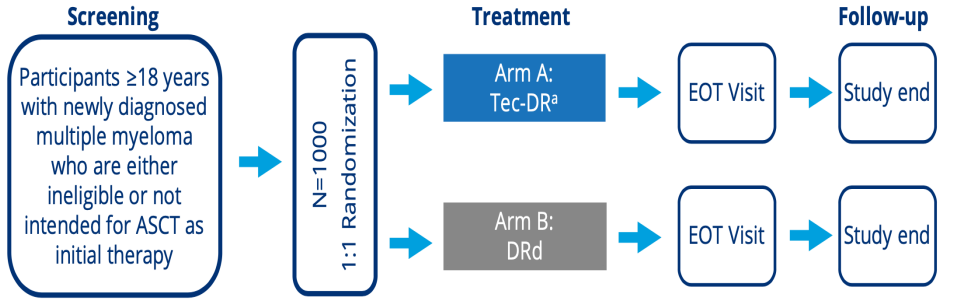
Future directions in the first-line treatment of older patients

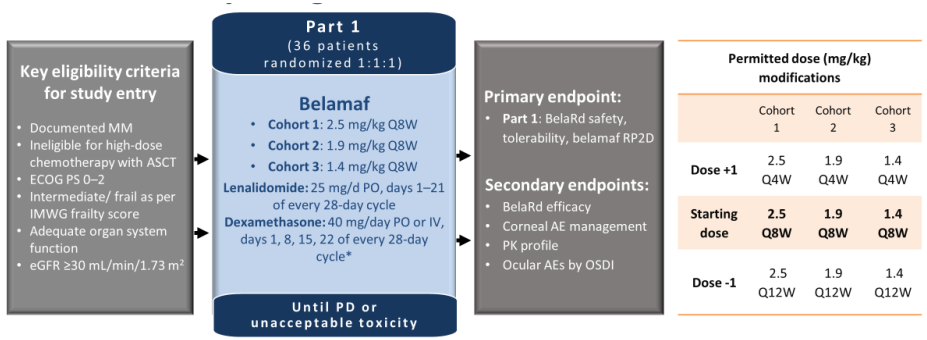
Early use of BCMA

Majestec-7 SRI Cohort 1
Dara-Tec-Len





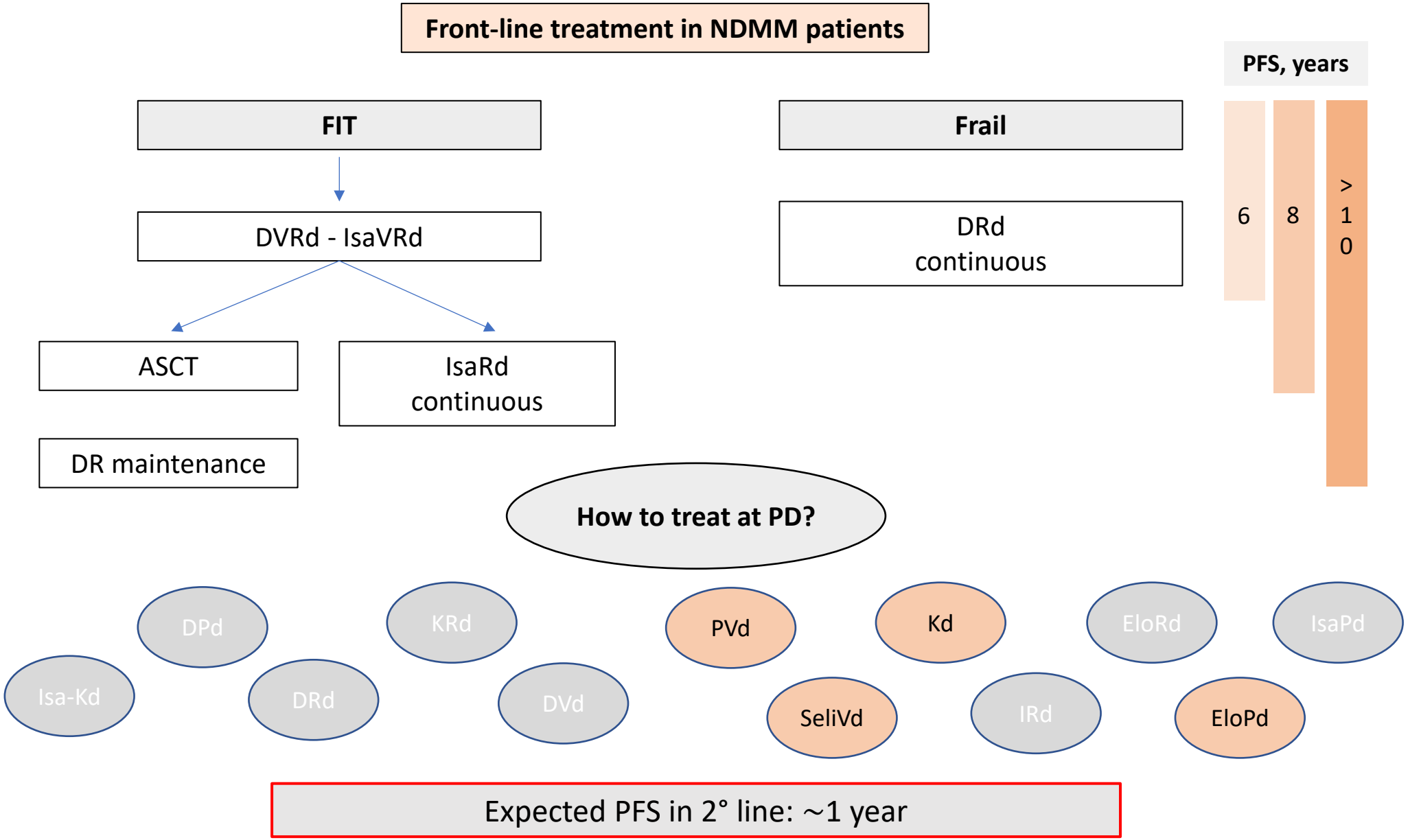




Cyrille Touzeau et al. American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Terpos E. et al. EMN 2024

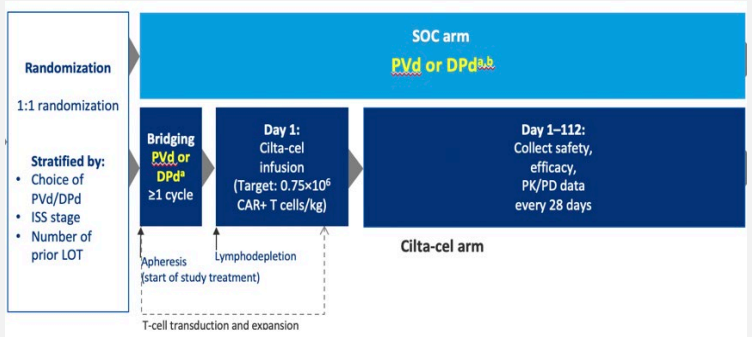
Moving BCMA-targeting forward

Treatment of triple-class exposed patients in early lines before BCMA

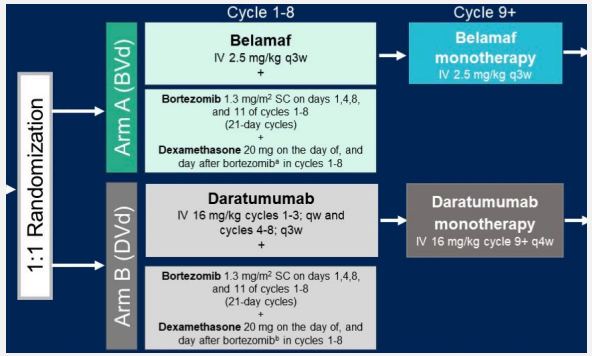


Treatment of triple-class exposed patients in early lines in the BCMA era

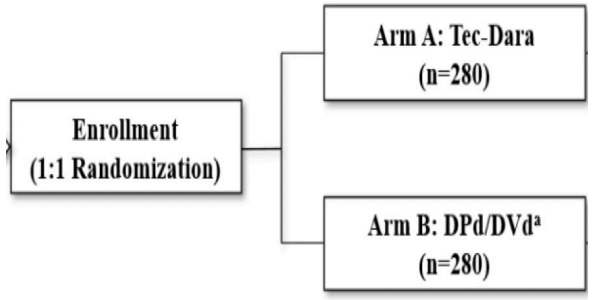
CARTITUDE-4



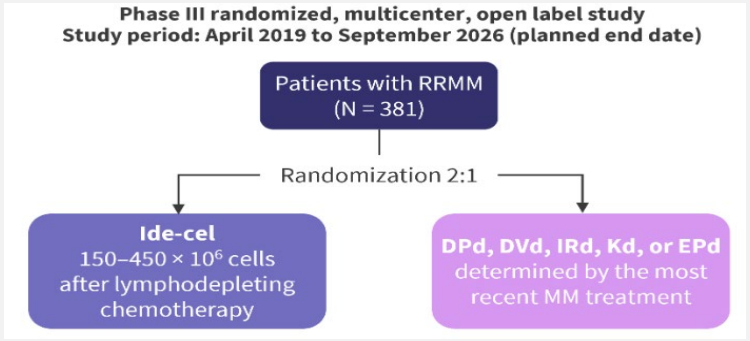
DREAMM-7



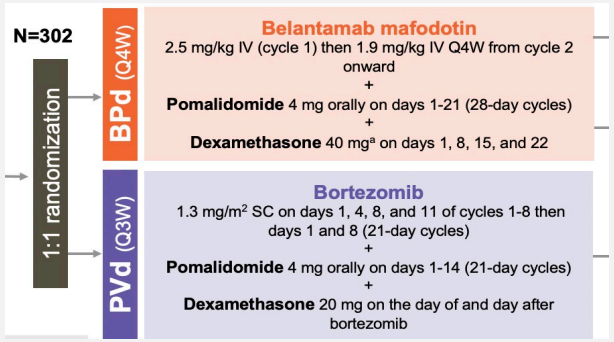
MAJESTEC-3



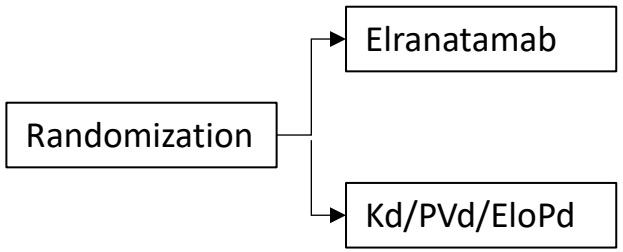
KarMMa-3



DREAMM-8



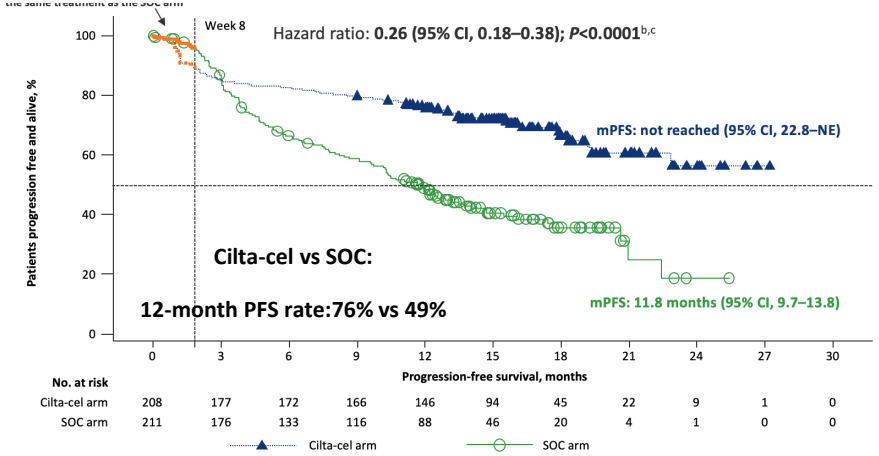
MAGNETISMM-32

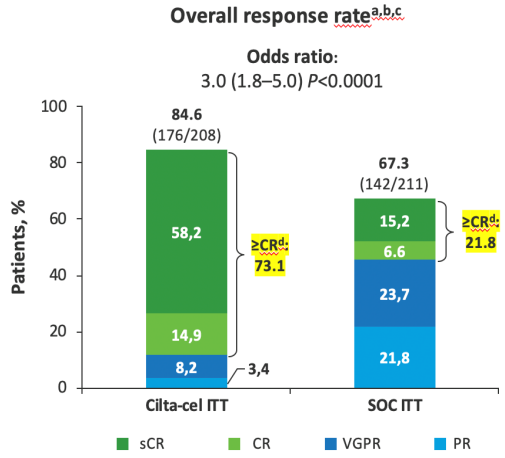


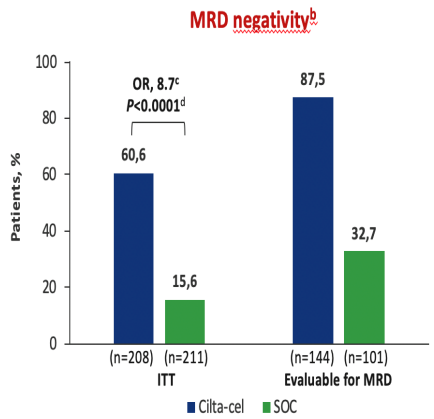
CAR-T cell versus standard of care in early lines for RRMM patients

CARTITUDE-4

Median prior lines of therapy: 1 (1-3)
100% lenalidomide refractory

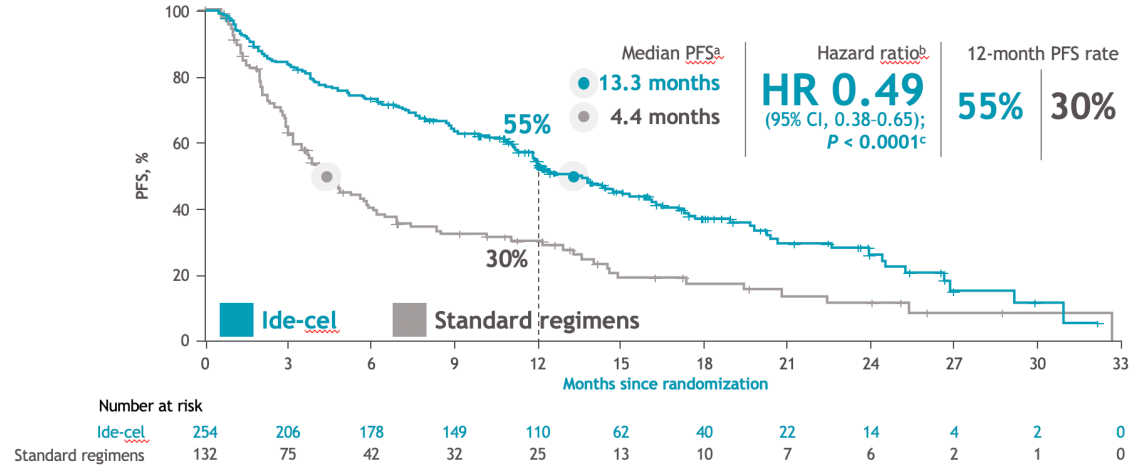


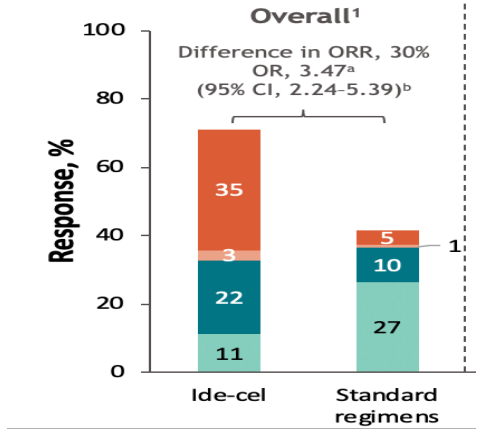




KarMMa-3

Median prior lines of therapy: 3 (2-4)
65-67% triple-class refractory





MRD negativity (10^{-5}) in CR patients:
20% vs 1%

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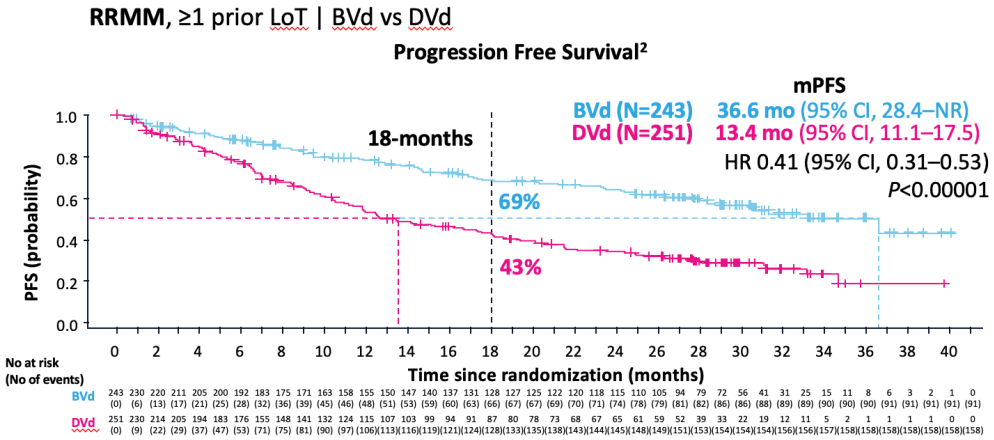
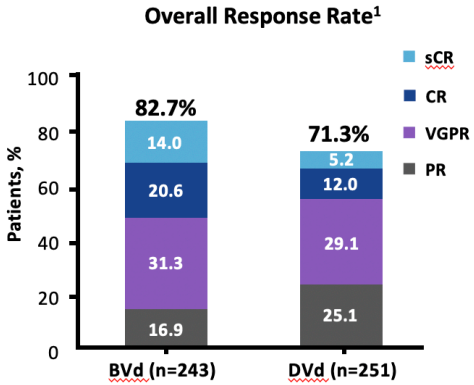
ADC versus standard of care in early lines for RRMM patients

DREAMM-7

Median prior lines of therapy: 1
33-35% lenalidomide refractory



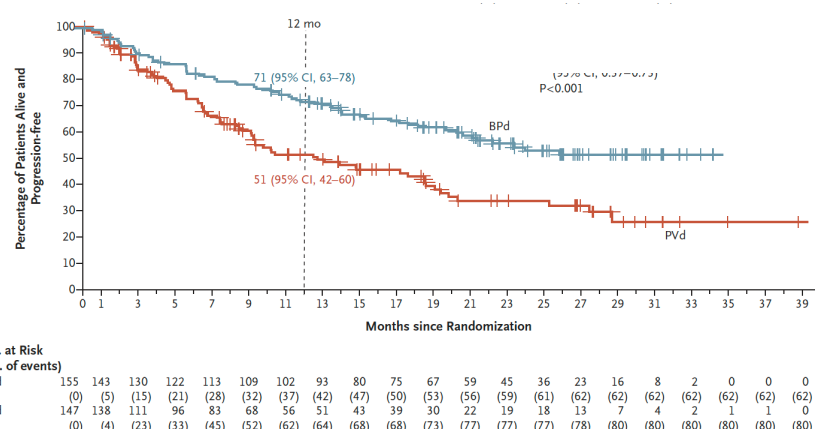


MRD negativity (10^{-5}):
39% vs 17%

Key Safety: Ocular toxicity in 79% vs 29% of patients

DREAMM-8

Median prior lines of therapy: 1
76-81% lenalidomide refractory – 23-24% antiCD38 MoAb refractory



Efficacy outcomes	BPd (n=155)	PVd (n=147)
ORR / ≥CR, %	77 / 40	72 / 16
mDOR, mo (95% CI)	NR (24.9–NR)	17.5 (12.1–26.4)
MRD– (10^{-5}) with ≥CR, %	24	5

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Conclusions

- Risk stratification in MM is becoming increasingly important in MM and should rely on a comprehensive list of risk factors, including ISS, FISH and clinical factors (EMD, CTCs)
- Quadruplets (PI + IMiDs + anti-CD38 mAb) induction and consolidation followed by ASCT and lenalidomide maintenance until progression is the current SoC for TE MM patients
- Upfront ASCT was a SoC in the era of triplets (↑ MRD rates and longer PFS as compared to a non transplant approach) and still is a backbone in studies with quadruplets (CASSIOPEIA, GRIFFIN, PERSEUS, ISKIA).
- DRd is a SoC for older, transplant ineligible patients; quadruplets (IsaVRd) may replace triplets in older fit patients.
- The early use of anti-BCMA agents (CAR T-cells, TCE and ADC) will revolutionize the treatment of MM patients

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EMN