Highlights from IMW 2021

1-2 febbraio 2022
Bologna
Royal Hotel Carlton

Massimo Offidani
Clinica di Ematologia
AOU Ospedali Riuniti di Ancona

Terapia di prima linea del paziente candidato ad ASCT: induzione e consolidamento

Coordinatore Scientifico
Michele **CAVO**

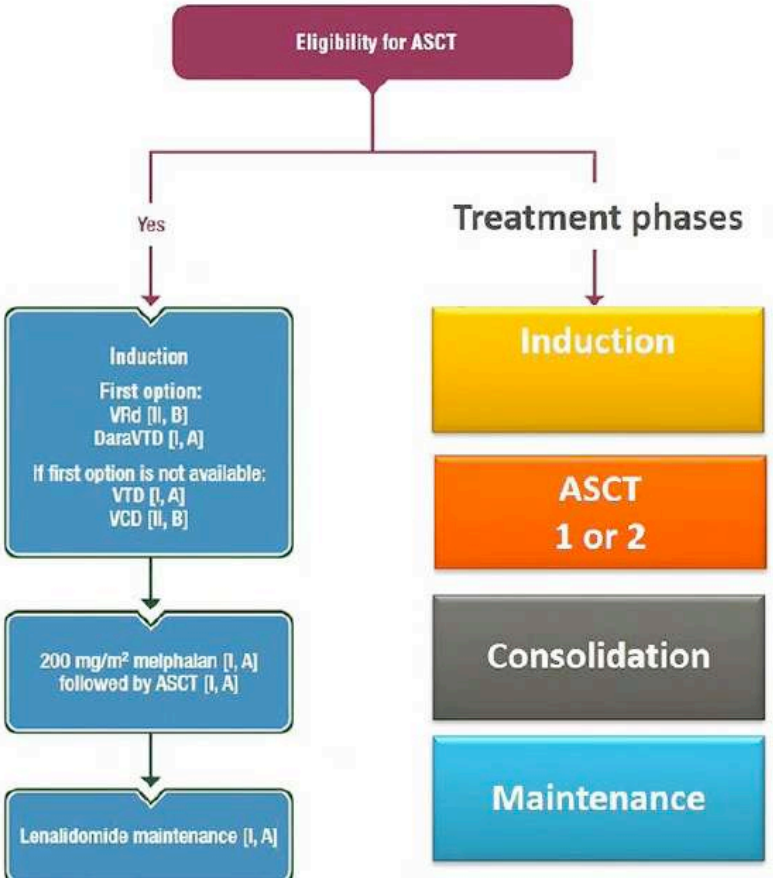
Comitato Scientifico
Michele **CAVO**
Maria Teresa **PETRUCCI**

Onoraria from:
AbbVie, Amgen, BMS, Celgene, Janssen, GSK, Roche, Sanofi, Takeda

Advisory for:
Amgen, BMS, Celgene, Janssen, GSK, Roche, Sanofi, Takeda

Research funds: Sanofi

Evolving treatment paradigm for ASCT-eligible NDMM patients



Endpoints

- To maximize the rate of undetectable MRD
- To sustain MRD negativity
- To prolong PFS/OS, offering a chance of cure (to a fraction of patients)
- To inform clinical decisions and tailor treatment

EARLY *VS.* LATE ASCT

Doctor, what about continuous optimised treatment with novel agents, with the goal of controlling the disease for as long as possible, and to reserve ASCT for relapse?

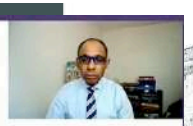
		Early	Late	P
Pooled analysis of two trials (n=529)[1,2]	4-year PFS	**44%**	26%	p<0.001 (HR 0.53)
	4-year OS	**84%**	70%	p<0.001 (HR 0.51)
GIMEMA MM-RV-209… Rd-MPR *vs.* Rd-Mel200 (2nd rand: +/- maintenance) EMN MM-RV-441… Rd-CRD *vs.* Rd-Mel200 (2nd rand: R *vs.* RP Maint.)				
IFM-DFCI 2009 trial[3]	4-year PFS	**47%**	35%	p<0.001 (HR 0.69)
	8-year OS	62%	60%	p=NS
RVD x 8 + ASCT at relapse *vs.* RVD x 3 + ASCT (Mel200) + RVD x 2				
EMN02/HO95[4]	3-year PFS	**65%**	57%	p=0,001 (HR 0.73); High Risk 0.53
	3-year OS	86.3%	84.6%	p=NS
Induction VCD x 3-4 => VMP intensive vs ASCT => VRD conso *vs.* no conso => R maint				
FORTE trial [5]	**3-year PFS**	**78%**	**66%**	p=0,02 (HR 0.64);
	3-year OS	**NA**	**NA**	p=NS
KRDx4 + *ASCT vs KRDx4* + 4 KRD consol + Maintennce (Rvs KR). vs KCD+ASCT (FORTE trial)				

1. Attal M, *et al.* N Engl J Med 2014;371:895–905; 2. Gay F, *et al.* Lancet Oncol 2015;16(16):1617–29; 3. Attal M, *et al.* Blood 2015;126: Abstract 391. Presented at ASH 2015; 4. Cavo M, *et al.* Blood 2016;128: Abstract 673. Presented at ASH 2016, Oliva S ASH 2020 .

Highlights fr

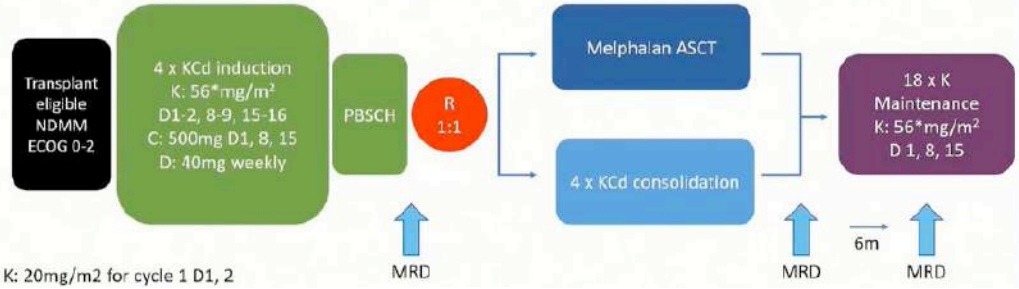
CARDAMON

CARDAMON STUDY DESIGN



18th IMW

Primary Endpoints:
- ≥VGPR pre-randomisation
- PFS at 2 years



* K: 20mg/m2 for cycle 1 D1, 2

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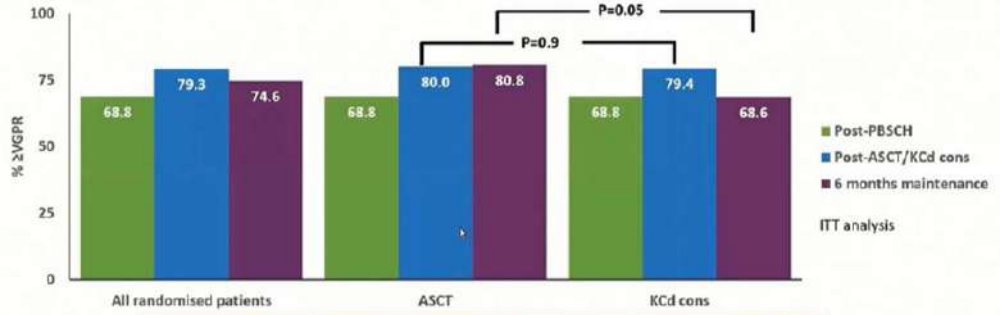
RESPONSES FOLLOWING ASCT/ CONS AND MAINTENANCE



MAINTENANCE VS POST-ASCT/KCD CONS	ASCT N=89	KCD CONS N=91	P VALUE
Response improved	31 (34.8)	11 (12.1)	<0.001
Response remained the same	45 (50.6)	58 (63.7)	0.07
Response worsened	13 (14.6)	22 (24.2)	0.1

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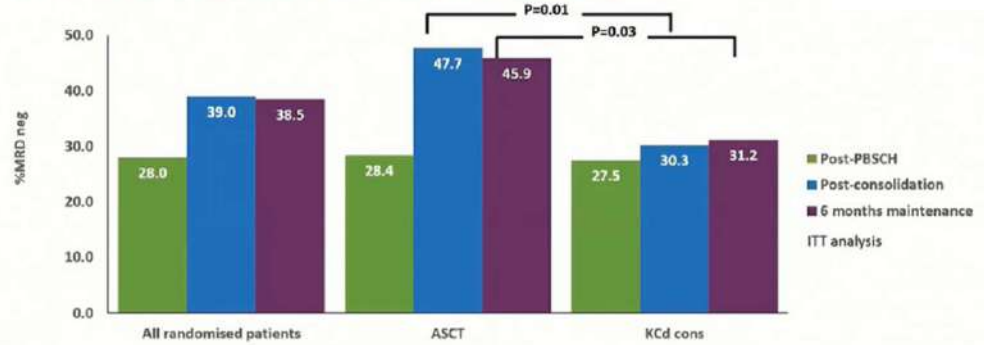
MRD NEGATIVE RATES BY ARM



MAINTENANCE VS POST-ASCT/KCD CONS	ASCT N=75	KCD CONS N=67	P VALUE
MRD neg improved	11 (14.7)	8 (11.9)	0.6
MRD neg remained the same	59 (78.7)	52 (77.6)	0.9
MRD neg worsened	5 (6.7)	7 (10.4)	0.4

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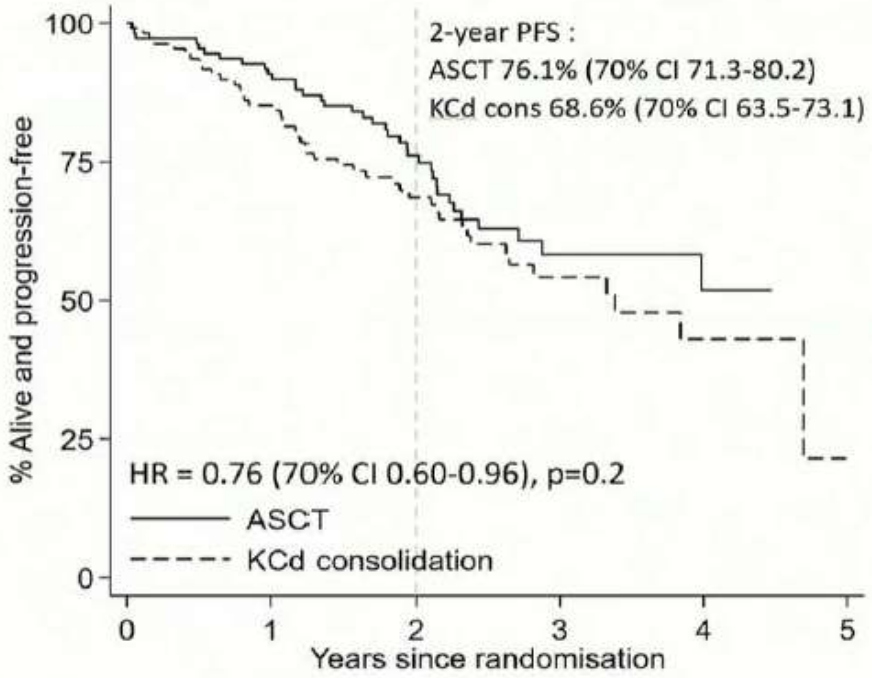
UPDATED PROGRESSION FREE SURVIVAL BY RANDOMISATION ARM

Median follow-up from randomisation
32.1 months

2-year PFS for KCd is not non-inferior to ASCT

The difference in 2-year PFS rate (KCd cons vs ASCT) using the rate in the experimental arm and the HR is

-6.5% (70% CI -11.1% to -1.0%)



In follow-up						
ASCT	109	98	62	23	8	0
KCd consolidation	109	90	54	20	6	0

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JAMA Oncology | Original Investigation

Safety and Effectiveness of Weekly Carfilzomib, Lenalidomide, Dexamethasone, and Daratumumab Combination Therapy for Patients With Newly Diagnosed Multiple Myeloma

The MANHATTAN Nonrandomized Clinical Trial

Ola Landgren, MD, PhD; Malin Hultcrantz, MD, PhD; Benjamin Diamond, MD; Alexander M. Lesokhin, MD; Sham Mailankody, MBBS; Hani Hassoun, MD; Carlyn Tan, MD; Urvi A Shah, MD; Sydney X. Lu, MD, PhD; Meghan Salcedo, RN; Kelly Werner, RN; Jenna Rispoli, RN; Julia Caple, RN; Allison Sams, NP; Dennis Verducci, NP; Katie Jones, NP; Isabel Concepcion, NP; Amanda Ciardello, MS; Aisara Chansakul, BS; Julia Schlossman, BA; Elizabet Tavitian, BS; Tala Shekarkhand, BS; Angela Harrison, MS; Casey Piacentini, BS; Even H. Rustad, MD, PhD; Venkata Yellapantula, PhD; Kylee Maclaughlan, MD, PhD; Francesco Maura, MD; Heather J. Landau, MD; Michael Scordo, MD; David J. Chung, MD, PhD; Gunjan Shah, MD; Oscar B. Lahoud, MD; Katie Thoren, PhD; Kazunori Murata, PhD; Lakshmi Ramanathan, PhD; Maria E. Arcila, MD; Caleb Ho, MD; Mikhail Roshal, MD, PhD; Ahmet Dogan, MD, PhD; Andriy Derkach, PhD; Sergio A. Giralt, MD; Neha Korde, MD

JAMA Oncol. doi:10.1001/jamaoncol.2021.0611
Published online April 15, 2021.

KRd-Dara without ASCT

Figure 1. Response to Therapy, by Number of Cycles and Follow-up

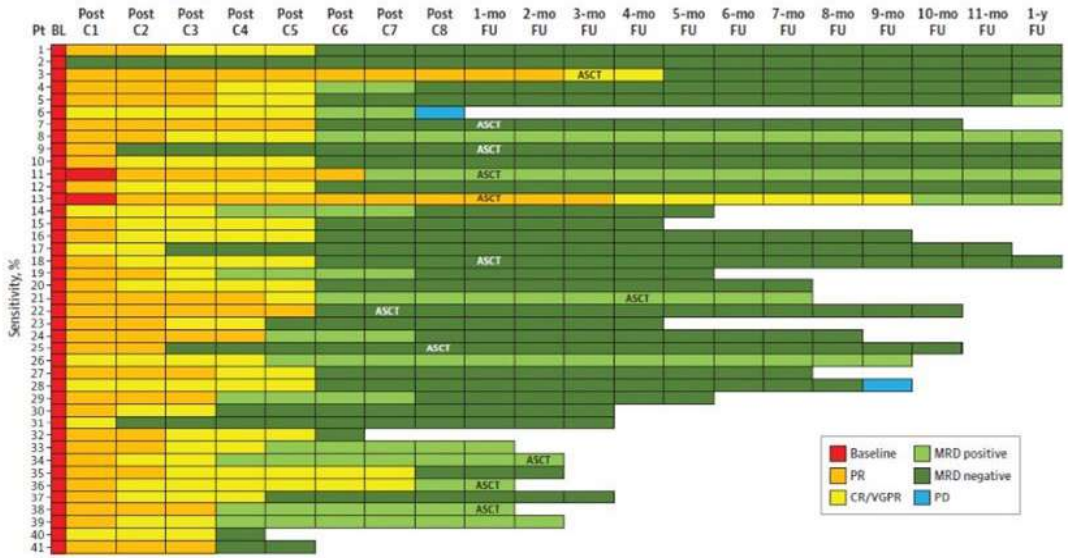
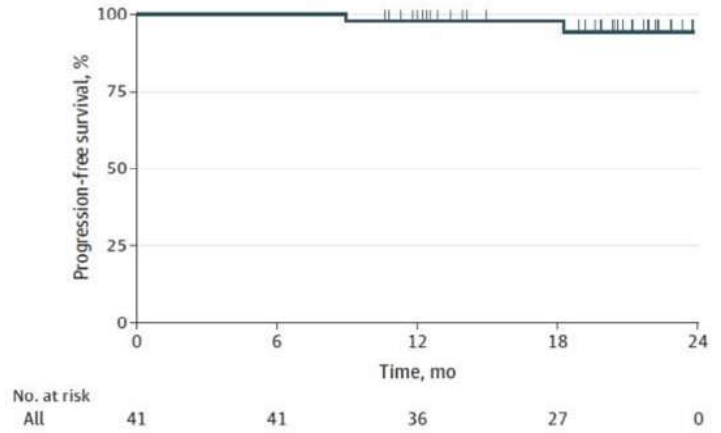
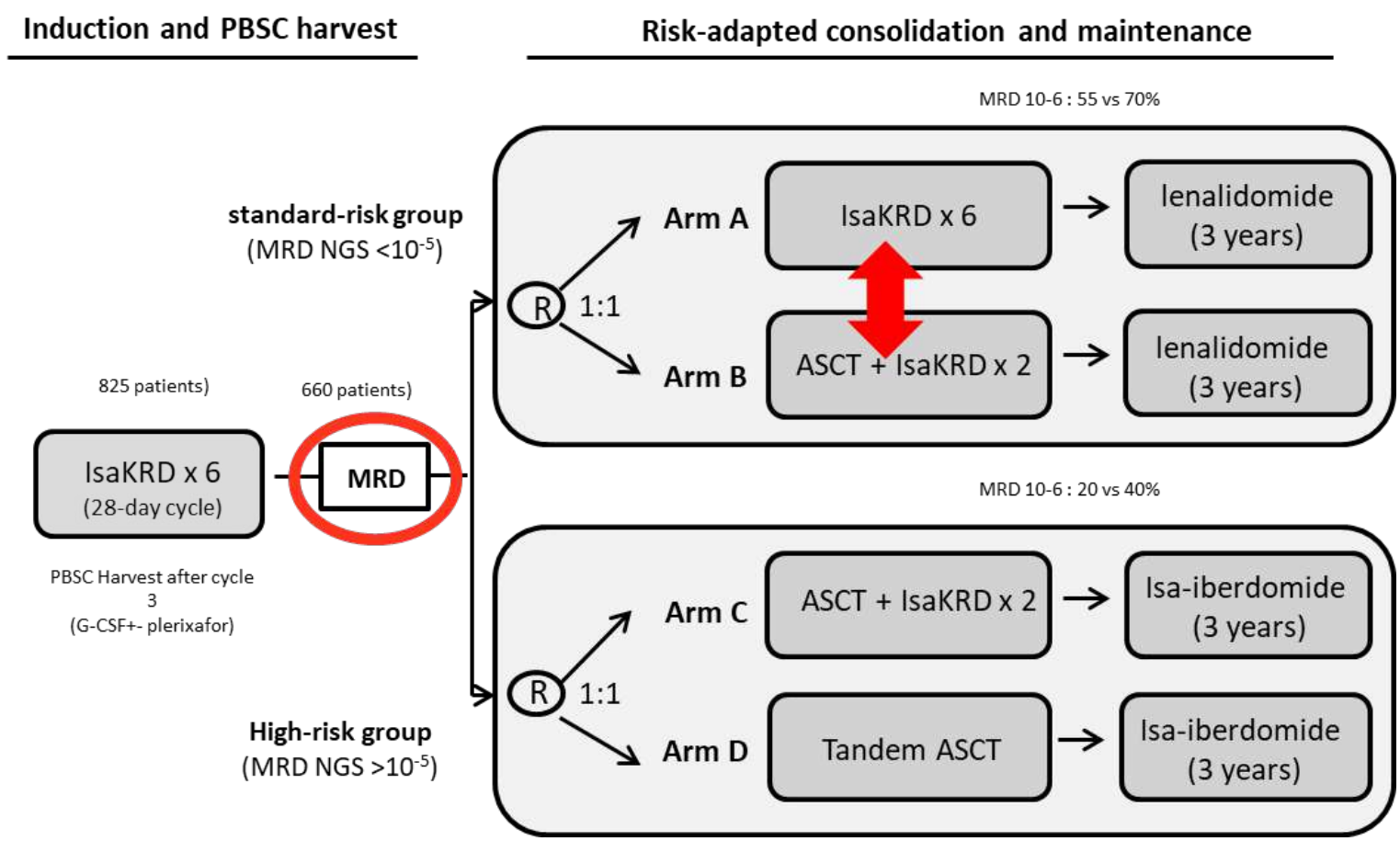


Figure 2. Progression-free Survival



CR: 95%; MRD-: 71%

MIDAS study : MInimal res Disease Adapted Strategy



Which is the best induction therapy? VRd *vs* VTD

Figure 4. ≥ VGPR and MRD-Negative Rates After Induction and ASCT in the GEM Studies[a]

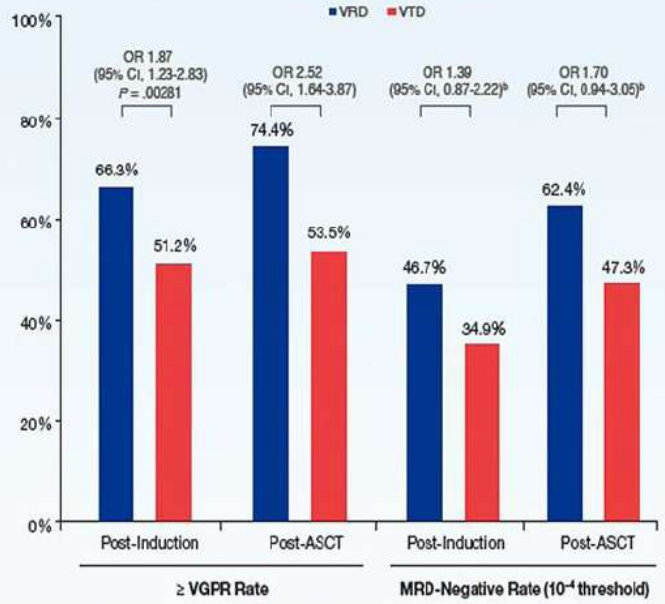
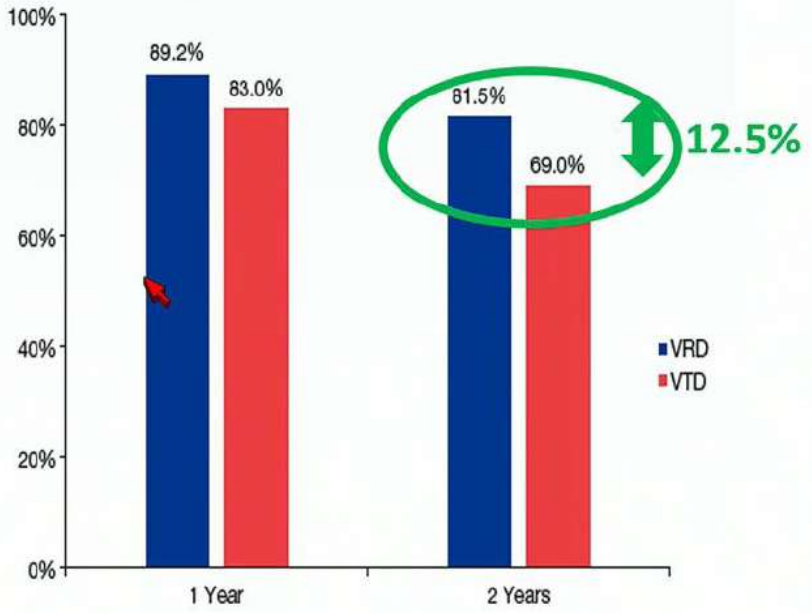


Figure 5. Event-Free PFS in the GEM Studies



Rosinol L et al. Blood. 2019 Oct 17; 134(16): 1337–1345.
Rosinol et al. EHA 2019

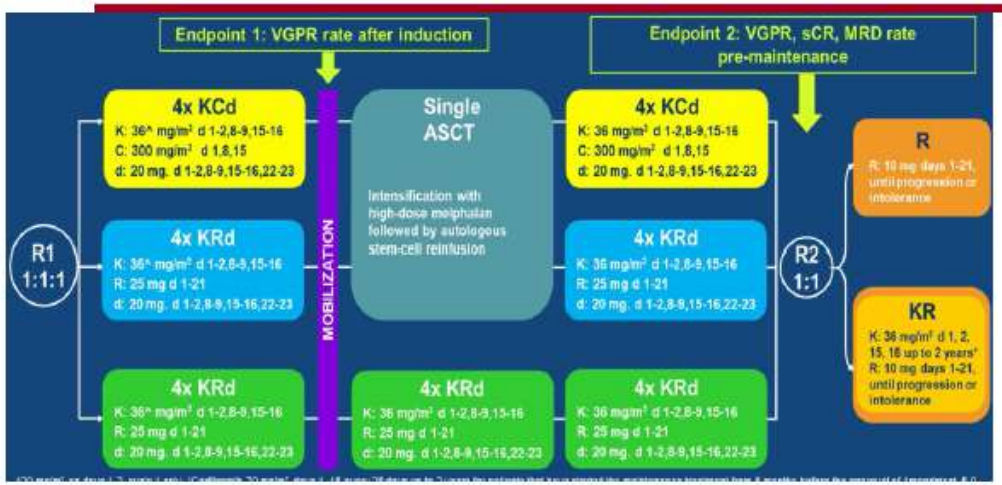
Table 3. Peripheral Neuropathy[a]

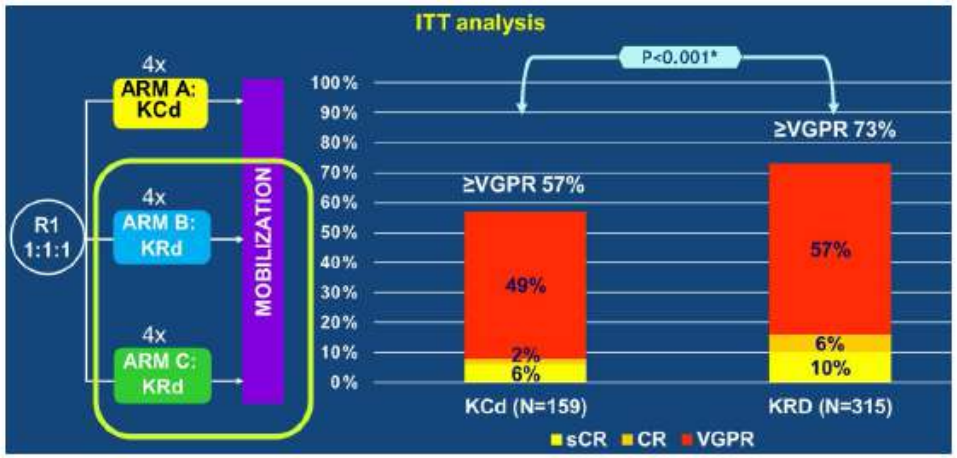
	VRD GEM2012 (n = 458)	VTD GEM2005 (n = 130)
Grade ≥ 2	95 (20.7)	58 (44.6)
Grade 3/4	25 (5.5)	20 (15.4)

INDUCTION phase: how to improve?

2nd generation PIs

FORTE ph.2 trial





Gay F, et al. J Clin Oncol. 2019;37 Suppl:8002. Presented at ASCO 2019.

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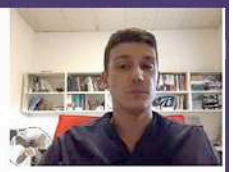
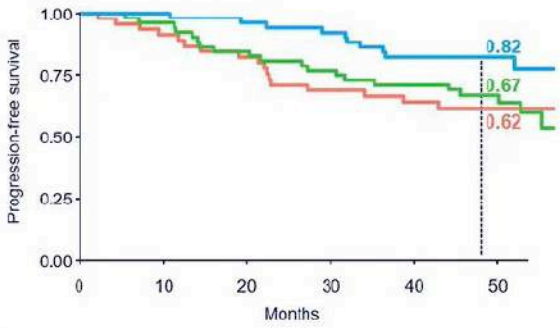
Progression-free survival: Random 1

KCd_ASCT vs. KRd_ASCT vs. KRd12

Median follow-up from Random 1: 51 months (IQR 46-55)



Standard risk (N=153)

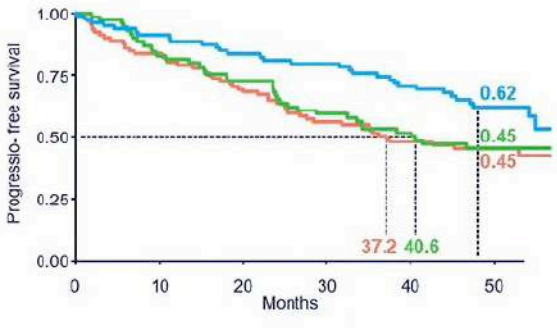


KRd_ASCT vs. KCd_ASCT: HR 0.43, p=0.035

KRd_ASCT vs. KRd12: HR 0.43, p=0.032

KRd12 vs. KCd_ASCT : HR 0.99, p=0.99

High risk (N=243)

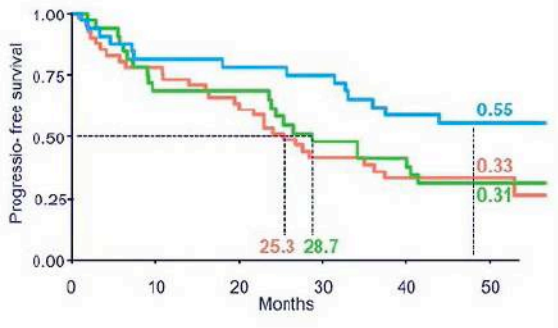


KRd_ASCT vs. KCd_ASCT: HR 0.57, p=0.015

KRd_ASCT vs. KRd12: HR 0.61, p=0.040

KRd12 vs. KCd_ASCT: HR 0.94, p=0.78

Double hit (N=105)



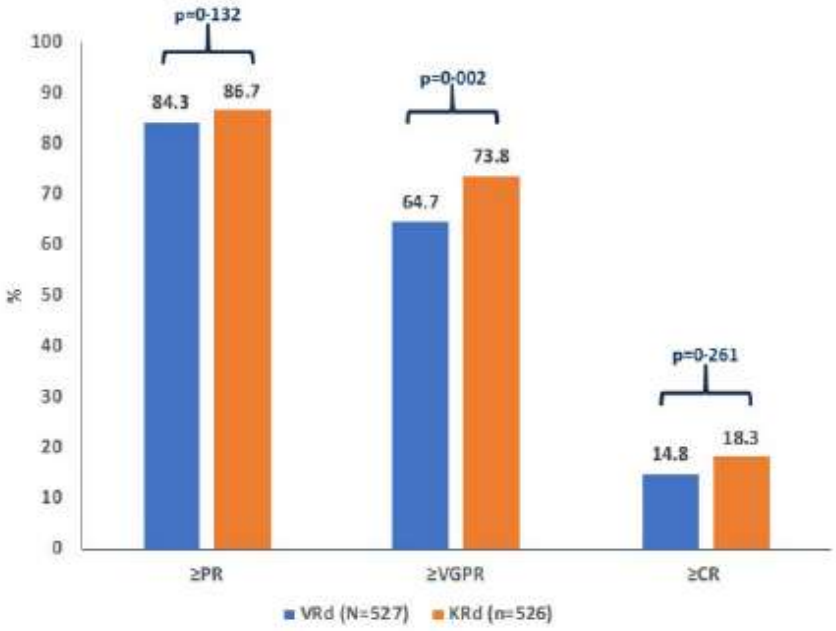
KRd_ASCT vs. KCd_ASCT: HR 0.46, p=0.024

KRd_ASCT vs. KRd12: HR 0.52, p=0.063

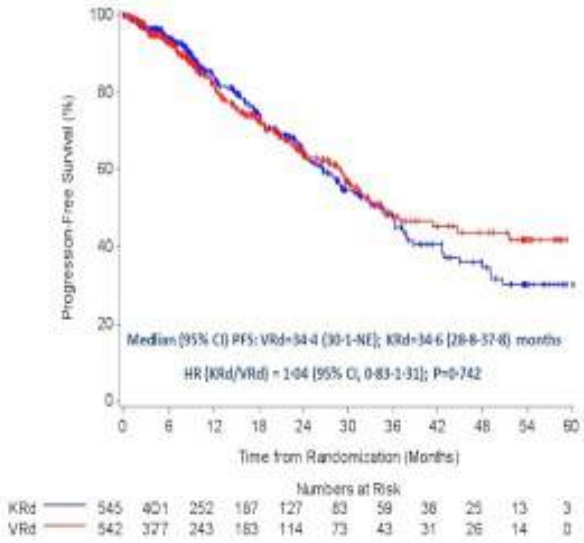
KRd12 vs. KCd_ASCT: HR 0.89, p=0.69

Random 1, first randomization (induction/consolidation treatment); ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; HR, hazard ratio; CI, confidence interval; p, p-value; iQR, interquartile range.

VRD or KRD? The ENDURANCE phase III trial



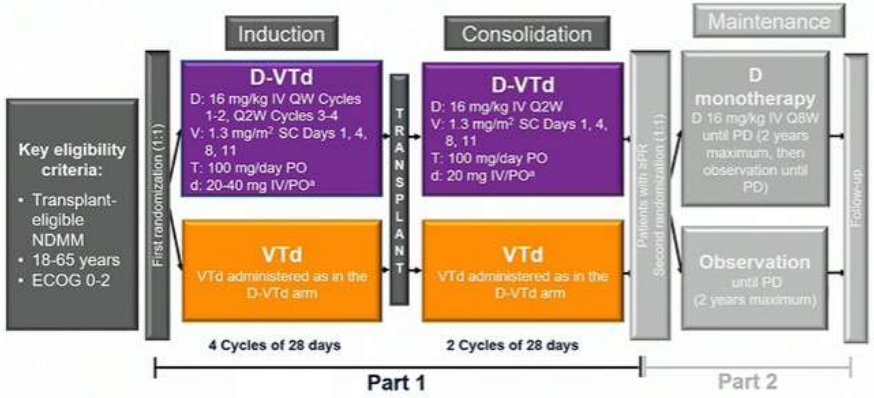
Progression Free Survival from Induction Randomization



- 2nd interim analysis of PFS (Jan 2020): 298 PFS events (75% of 399 planned)
- Median (95% CI) estimated follow up of 15 (13-18) months
- For patients >/= 70 years, median PFS(95% CI) for VRd = 37 (29-NE) and KRd = 28 (24-36) months
- With censoring at SCT or alternative therapy: Median PFS (95% CI) for VRd = 31·7 (28·5-44·6) and KRd = 32·8 (27·2-37·5) months

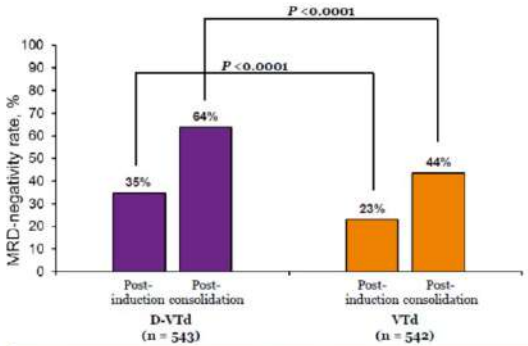
CASSIOPEIA Study Design

- Phase 3 study of D-VTd versus VTd in transplant-eligible NDMM (N = 1,085), 111 sites from 9/2015 to 8/2017

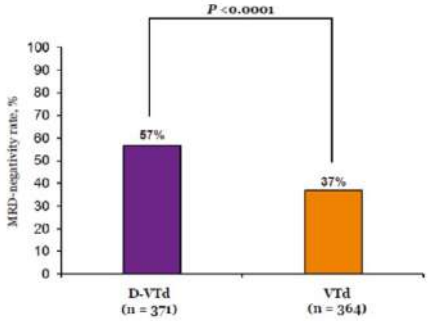


MRD-negativity Rates (10^{-5})

Post-induction and Post-consolidation; Flow Cytometry[a]



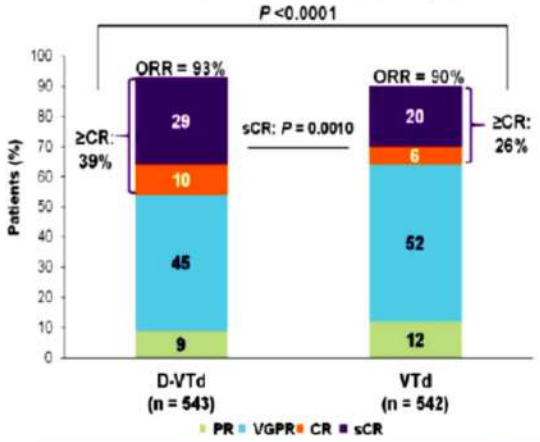
Post-consolidation; NGS[b]



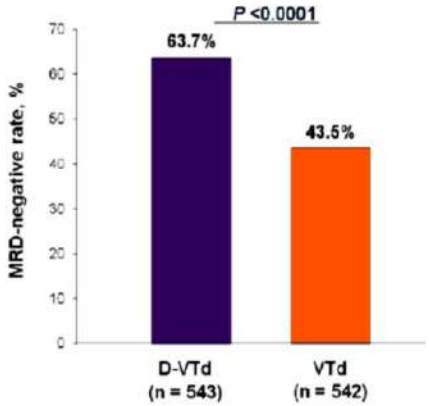
- Early (post-induction) significant difference in MRD-negativity rates for D-VTd versus VTd
- Post-consolidation MRD-negativity rates were significantly higher for D-VTd versus VTd, confirming post-induction MRD-negativity rates

CASSIOPEIA study: depth of response

Post-consolidation rates of response



MRD (Flow Cytometry; 10^{-5})

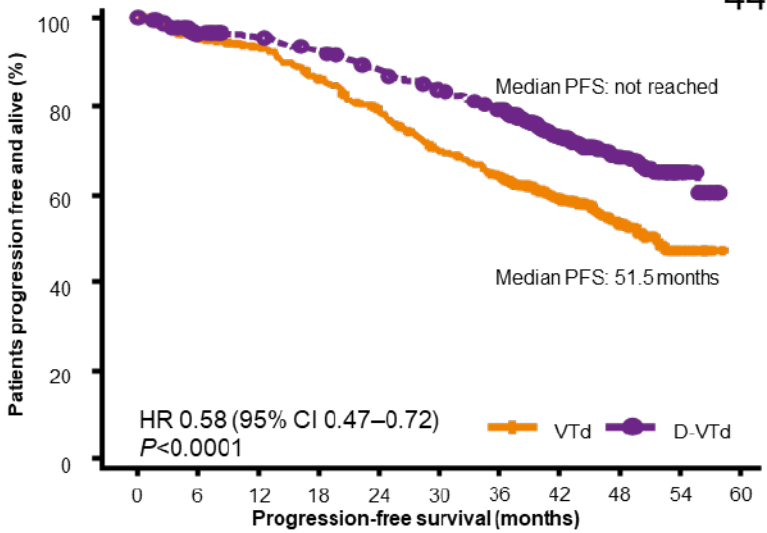


D-VTd improved the rate of sCR (primary study endpoint), ≥CR and MRD negativity

Moreau P et al. Lancet 2019

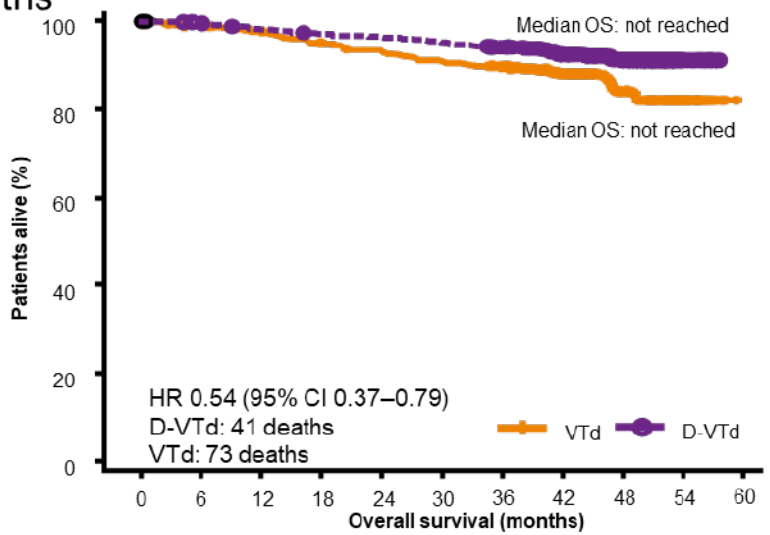
Updated Analyses From First Randomization Confirm Benefits of D-VTd vs VTd Induction/Consolidation

Median follow-up: 44.5 months



Patients at risk

VTd	542	499	472	434	391	345	312	191	90	26	0
D-VTd	543	507	495	478	452	426	395	237	119	29	0

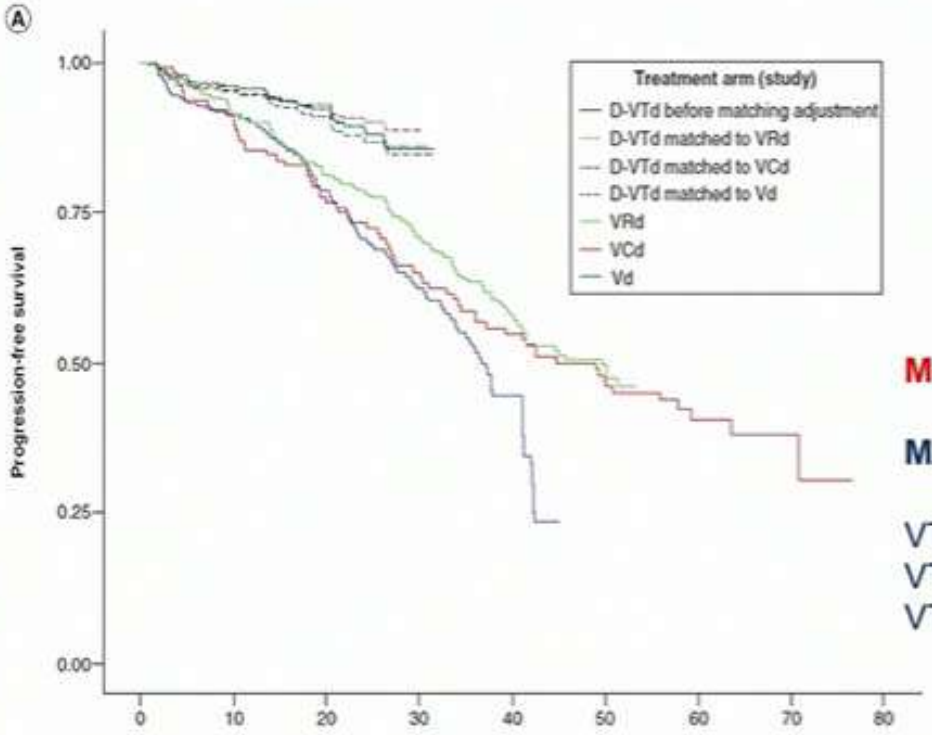


Patients at risk

VTd	542	531	521	505	494	481	468	305	151	42	0
D-VTd	543	536	526	520	517	510	498	327	162	37	0

CI, confidence interval; D-VTd, daratumumab, bortezomib, thalidomide, and dexamethasone; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; VTd, bortezomib, thalidomide, and dexamethasone.

Philippe Moreau et al., Lancet Oncol 2021, https://doi.org/10.1016/ S1470-2045(21)00428-9



No. at risk

Treatment arm									
D-VTd before matching adjustment	543	486	206	14	0	0	0	0	0
D-VTd matched to VRd	529	472	199	14	0	0	0	0	0
D-VTd matched to VCd	206	185	69	5	0	0	0	0	0
D-VTd matched to Vd	416	370	150	10	0	0	0	0	0
VRd	350	314	275	229	151	47	0	0	0
VCd	126	111	88	70	57	46	22	6	0
Vd	240	195	144	91	43	0	0	0	0

Moreau et al. Immunotherapy 2021

MAIC for PFS

VTD-dara vs VRD, HR 0.47
VTD-dara vs VCD, HR 0.35
VTD-dara vs VD, HR 0.42

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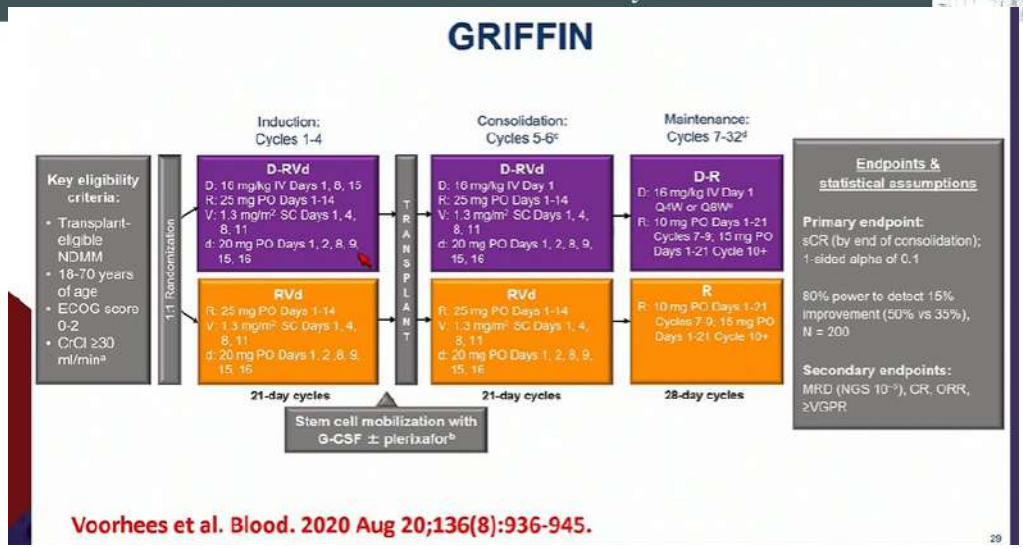
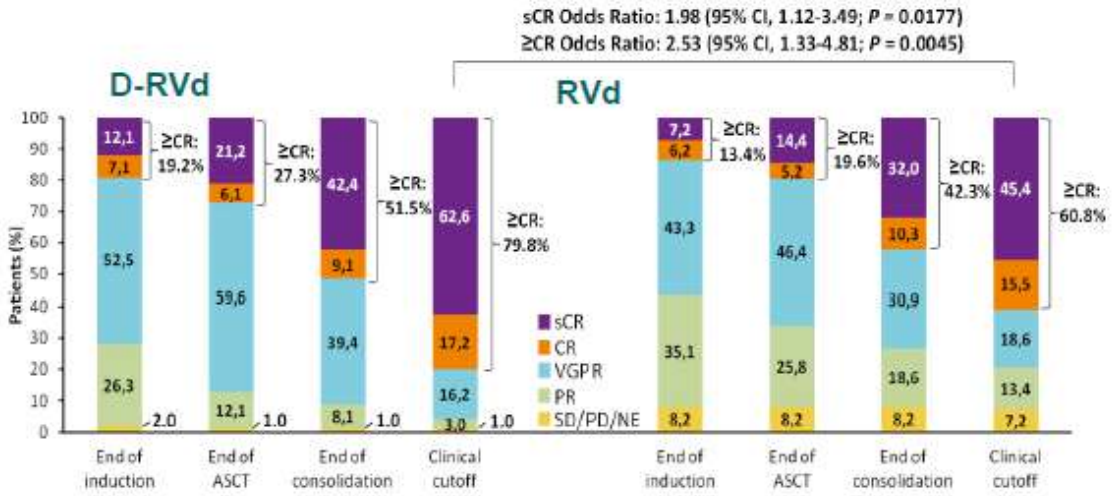


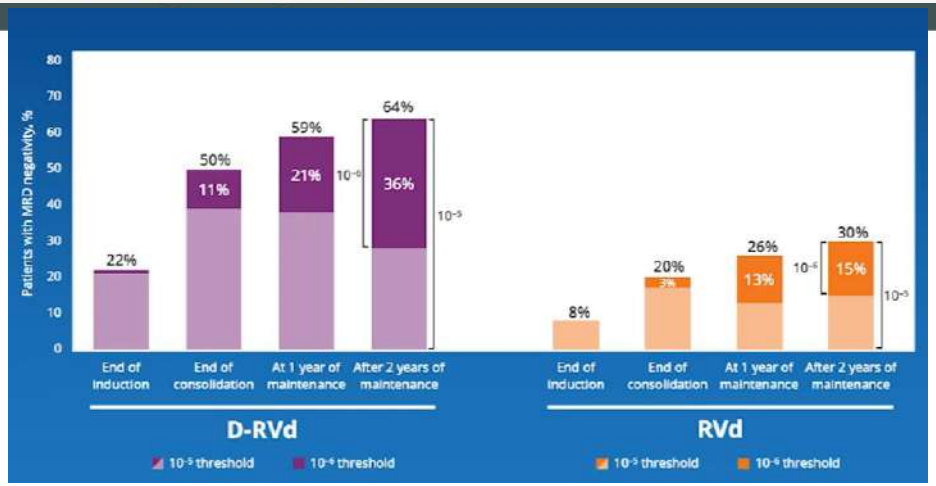
Voorhees et al. Blood. 2020 Aug 20;136(8):936-945.



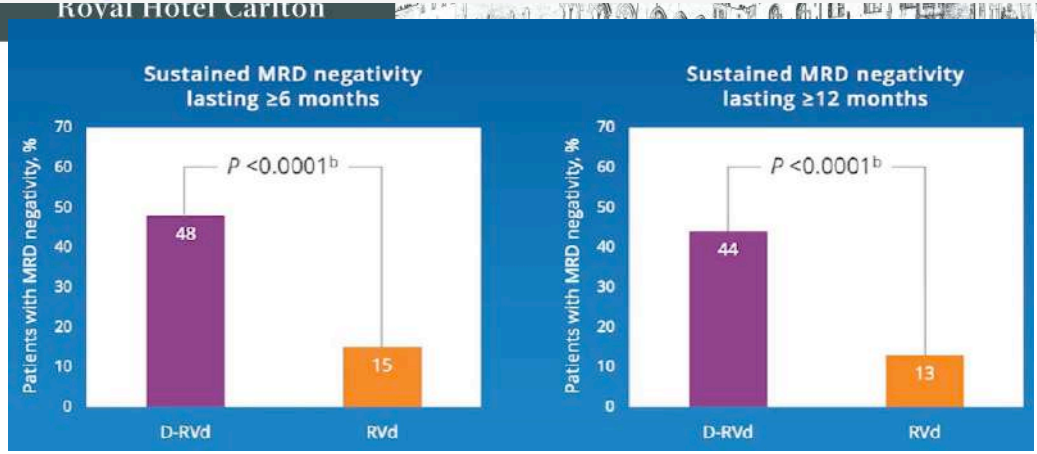
MRD-negativity (10^{-5}) post-induction:

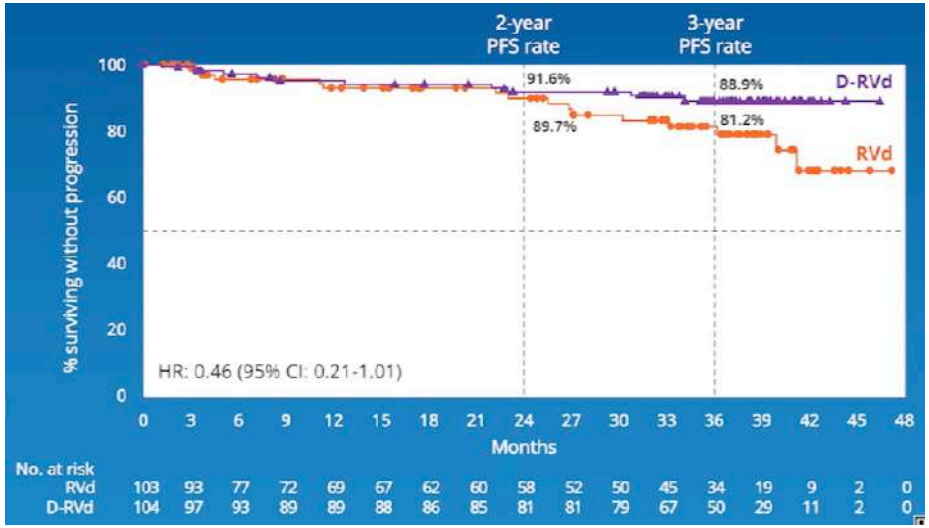
21.2% vs 5.8%

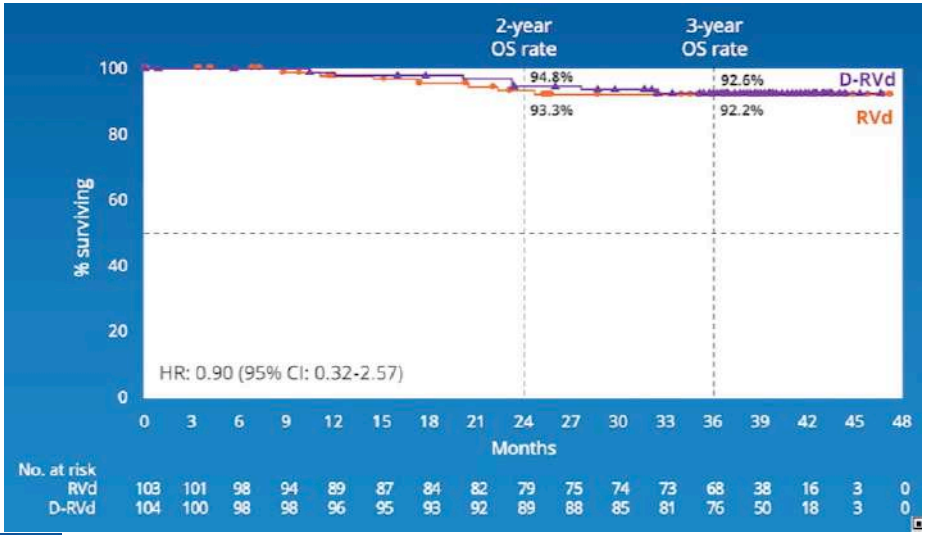
GRIFFIN: MRD-negativity[a] Rates Improved Throughout the DR Maintenance Period



GRIFFIN: D-RVd Improved Rates of Durable MRD Negativity[a] (10^{-5}) Lasting ≥6 Months or ≥12 Months Versus RVd





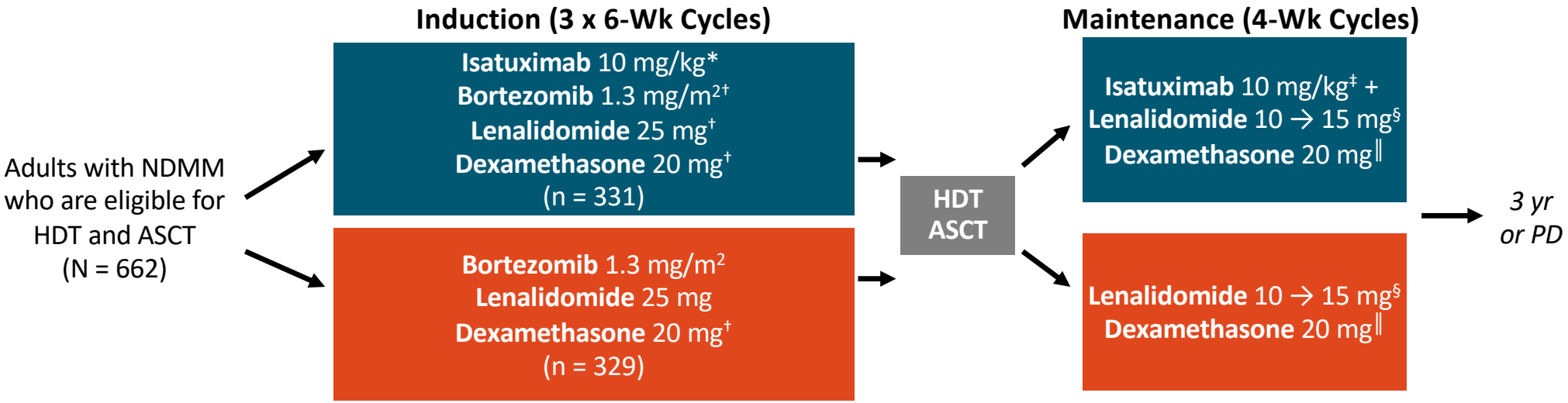


Median follow-up: 38.6 months

Laubach J et al, ASH 2021

GMMG-HD7: Study Design

- Open-label, randomized, multicenter phase III trial



*Cycle 1: D1, 8, 15, 22, 29; cycles 2-3: D1, 15, 29.
†Bortezomib D1, 4, 8, 11, 22, 25, 29, 32; lenalidomide Days 1-14 and 22-35; dexamethasone D1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32, 33.
Data cutoff: April 2021.

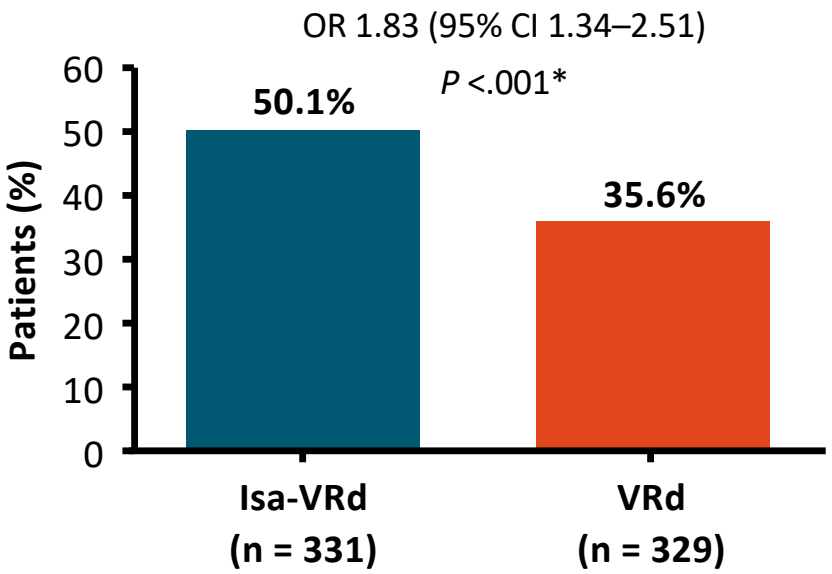
‡Cycle 1: D1, 8, 15, 22;
Cycles 2-3: D1, 15; Cycle 4+: D1.
§Days 1-28. Increase dose to 15 mg after 3 mos
‖Dexamethasone D1, 8, 15, 22 in C1.

- Primary endpoint: MRD negativity at end of induction (NGF, sensitivity 10^{-5}) stratified according to R-ISS
- Secondary endpoints: CR after induction, safety
- MRD negativity assessed after cycle 3, HDT, 12 mos, and 24 mos as well as at end of study

Goldschmidt. ASH 2021. Abstr 463.

GMMG-HD7: MRD Negativity (Primary Endpoint) and Response Rates at End of Induction

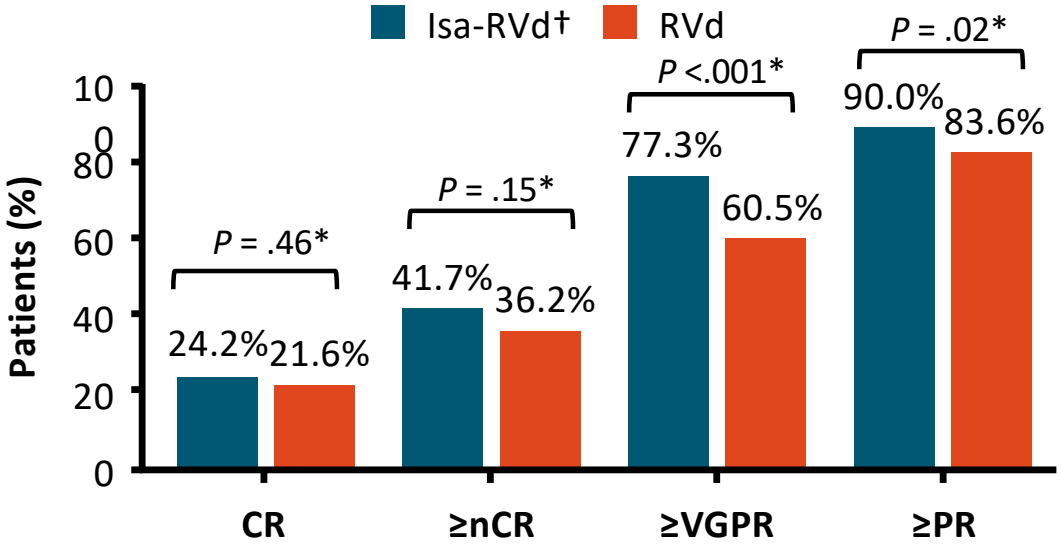
Patients with MRD Negativity at End of Induction



- Not assessable/missing* MRD status low: Isa-VRd, 10.6%; VRd, 15.2%

*Due either to loss to follow-up, missing bone marrow samples, or technical failures in measurement counted as nonresponders.

Response Rates at End of Induction

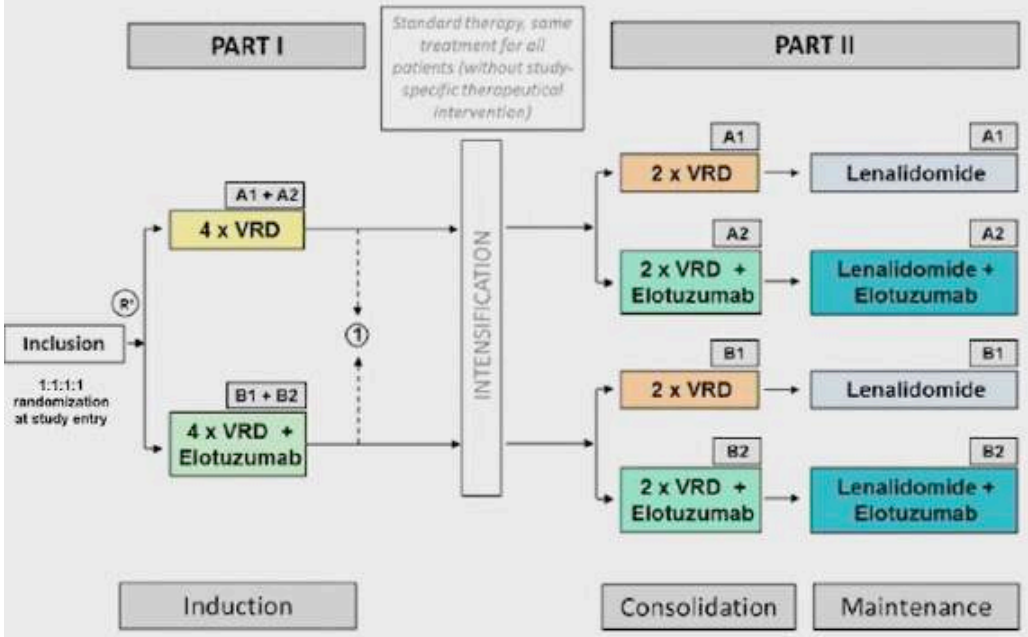


- Significant increase in ≥VGPR with Isa-VRd
- Significant increase in ORR

Goldschmidt. ASH 2021. Abstr 463.

Elotuzumab in Combination with Lenalidomide, Bortezomib, Dexamethasone and Autologous Transplantation for Newly-diagnosed Multiple Myeloma: Results from the Randomized Phase III GMMG-HD6 Trial

GMMG-HD6: flow chart, eligibility criteria and endpoints



Key eligibility criteria

- TE NDMM 18 – 70 years
- WHO performance status 0-2 or 3 if MM-related

Primary efficacy endpoint

- PFS from randomization

Secondary endpoints (selection)

- OS from randomization
- CR rates after induction / consolidation
- best response on treatment

Response rates on study

(n / %)	RVD (N=278)	RVD + Elotuzumab (N=278)	p
≥ PR	237 / 85.2	230 / 82.7	0.54
≥ VGPR	147 / 52.9	163 / 58.6	0.14
CR	9 / 3.3	9 / 3.2	1.00
PD	8 / 2.9	6 / 2.2	0.79

post induction therapy

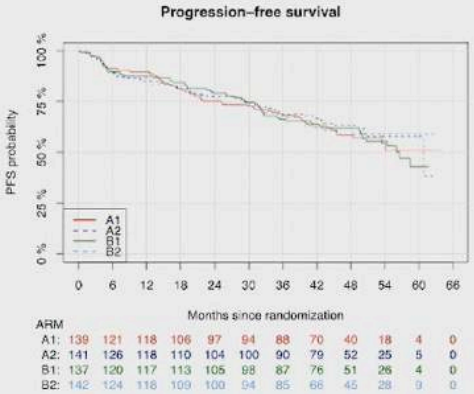
(n / %)	A1 (RVD+R) (n=123)	A2 (RVD+EloR) (n=124)	B1 (Elo-RVD+R) (n=119)	B2 (Elo-RVD+EloR) (n=124)	p
≥ VGPR	97 / 78.9	97 / 78.2	97 / 81.5	100 / 80.7	0.95
≥ PR	116 / 94.3	114 / 91.9	113 / 95.0	113 / 91.1	0.48

prior to consolidation therapy

Addition of elotuzumab to RVd did not increase high-quality responses (≥VGPR) after induction or consolidation compared to RVd alone

RVd, lenalidomide, bortezomib, dexamethasone; Elo, elotuzumab; R, lenalidomide; WHO, World Health Organization; PR, partial response; VGPR, very good partial response; CR, complete response; PD, progressive disease.

Progression-free survival



3-year PFS rates

Overall: 67.7% (95% CI: 63.7-71.7%)

A1: 68.8% (95% CI: 60.9-76.8%)

A2: 68.5% (95% CI: 60.7-76.4%)

B1: 66.2% (95% CI: 58.2-74.3%)

B2: 67.2% (95% CI: 59.2-75.2%)

Primary endpoint „to detect a difference between the four treatment arms" (adjusted logrank p value stratified by ISS at randomization, p=0.86)

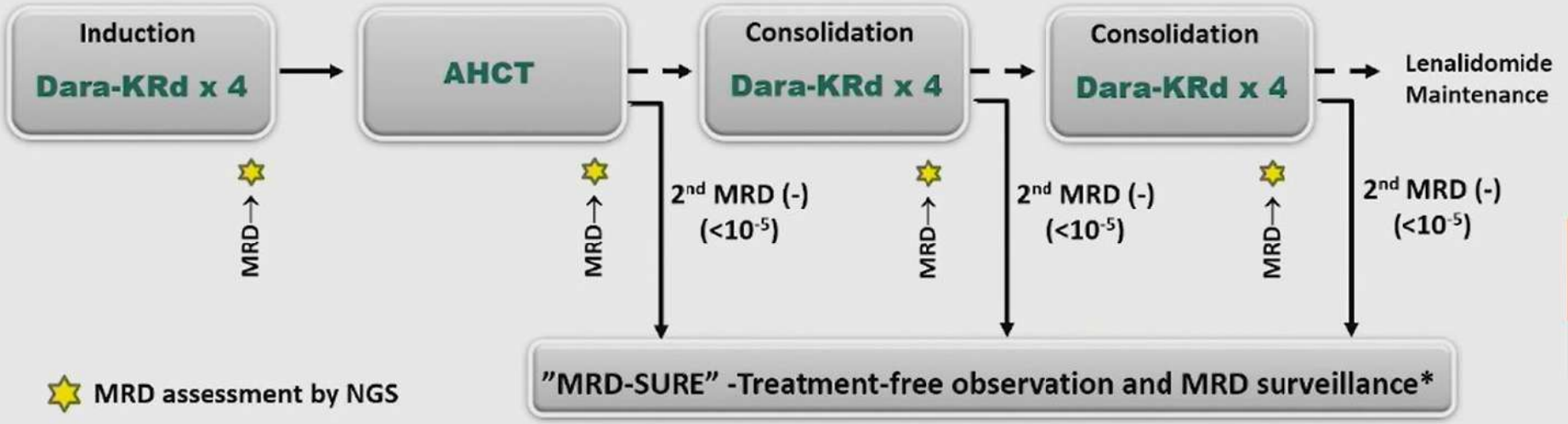
A1: RVd+R; A2: RVd+EloR; B1: Elo-RVd+R; B2: Elo-RVd+EloR; RVd, lenalidomide, bortezomib, dexamethasone; elo, elotuzumab; PFS, progression-free survival; ISS, International Staging System; 95 % CI: 95% confidence interval.

18th IMW

Treatment

Dara-KRd

- Daratumumab 16 mg/m^2 days 1,8,15,22 (days 1,15 C 3-6; day 1 C >6)
- Carfilzomib (20) 56 mg/m^2 Days 1,8,15
- Lenalidomide 25 mg Days 1-21
- Dexamethasone 40mg PO Days 1,8,15,22



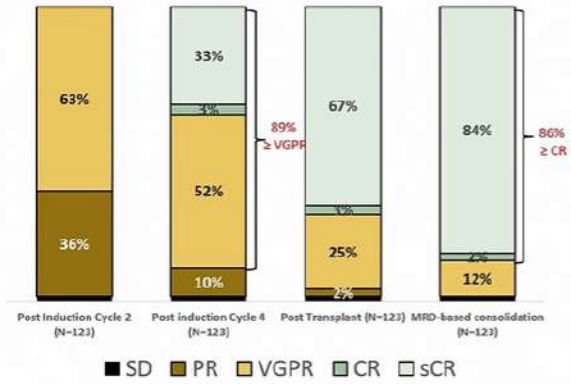
*24 and 72 weeks after completion of therapy

MASTER trial

Highlights from IMW 2021

1-2 Febbraio 2022
Bologna
Royal Hotel Carlton

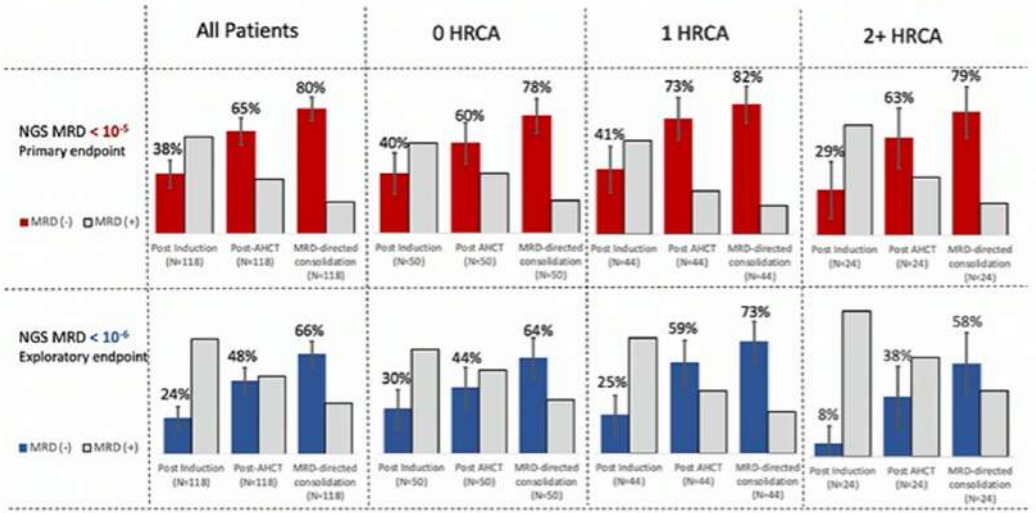
Best IMWG response by phase of therapy



- 6 progressions during therapy
  - 1 during induction,
  - 1 after AHCT
  - 4 on consolidation
- All with gain/amp of 1q
- 5/6 had 2+ HRCA

MASTER trial

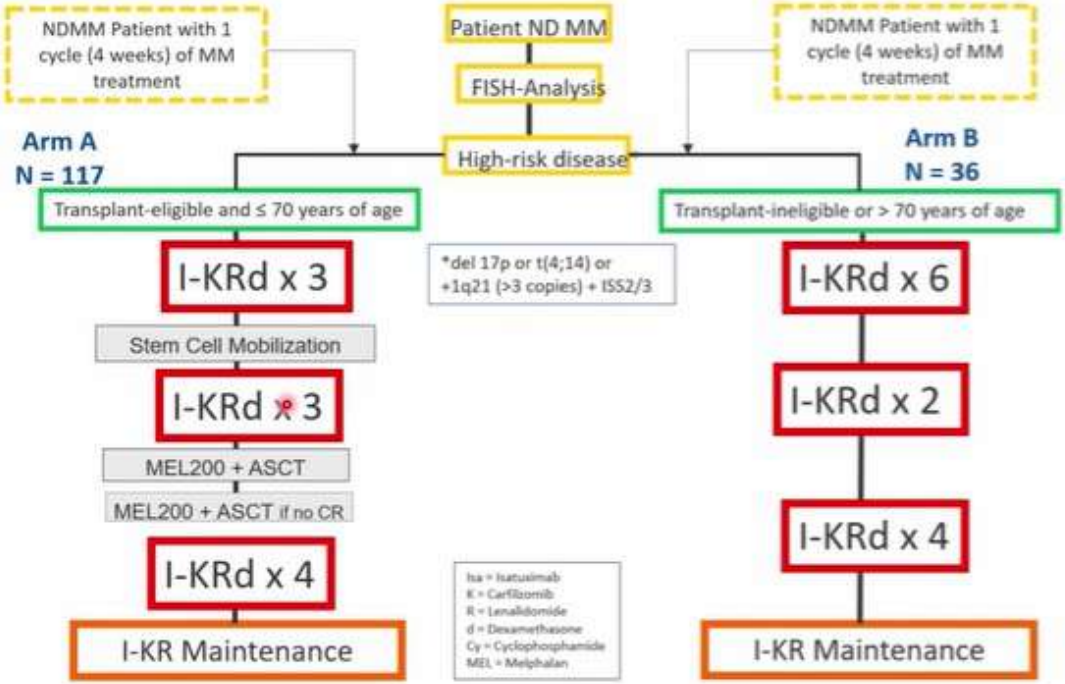
Best MRD response by phase of therapy



HRCA = gain/amp 1q, t(4;14), t(14;16), t(14;20) or del(17p)

MASTER trial

Study Design – GMMG CONCEPT (NCT03104842)



Isa-KRd Induction

Cycle 1

Isatuximab	10 mg/kg	day 1, 8, 15, 22
Carfilzomib	20 mg/m²	day 1, 2
Carfilzomib	36 mg/m²	day 8, 9, 15, 16
Lenalidomide *	25 mg	day 1-21
Dexamethasone**	40 mg*	day 1, 8, 15, 22

28-day-cycle

Isa-KRd Induction

Cycle 2-6

Isatuximab	10 mg/kg	day 1, 15
Carfilzomib	36 mg/m²	day 1, 2, 8, 9, 15, 16
Lenalidomide **	25 mg	day 1-21
Dexamethasone***	40 mg*	day 1, 8, 15, 22

28-day-cycle

* Cy-based mobilisation was moved in an amendment to time point after 3 induction cycles
**Dose adaption of lenalidomide according to renal function
***20 mg in patients ≥75 years

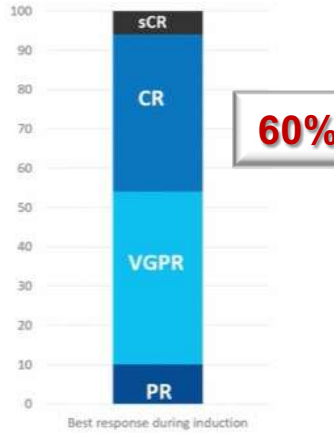
Highlights from IMW 2021

1-2 Febbraio 2022
Bologna
Royal Hotel Carlton

Results: Best response to therapy, 6 induction cycles

All evaluable patients: n = 50

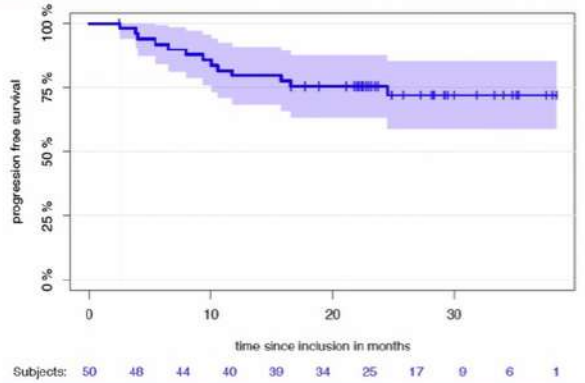
- Overall response rate (ORR, ≥ PR): 100%
- ≥ VGPR : 90%; CR/sCR: 46%
  - Arm A: 41/46 ≥ VGPR
  - Arm B: all (n = 4) VGPR
- Arm A: MRD-assessment in 33 patients during induction
  - 20 patients MRD negative
  - 11 patients MRD positive
  - 2 not assessable



Results of MRD assessments after induction treatment are not reported and available yet

60% MRD neg

Progression-free Survival



Median follow-up: 24.9 months

- 12-month PFS: 79.6% (68.3%; 90.9%)
- 24-month PFS: 75.5% (63.5%; 87.6%)

Data cut-off: Jan. 26, 2021
(95%-confidence level)

40/50 patients were relapse-free after 1 year

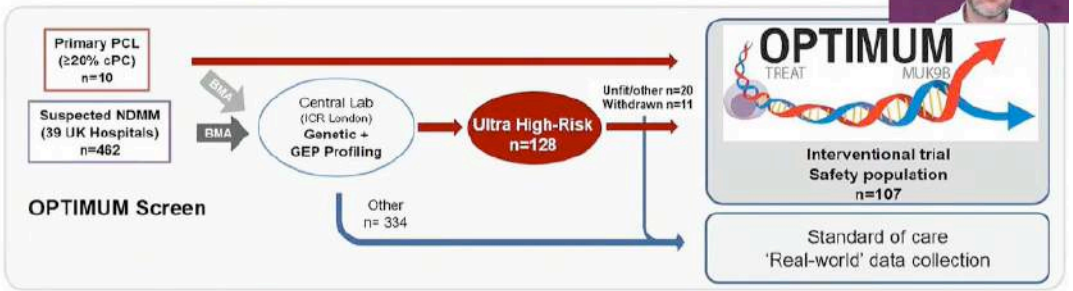
Leipoldt LB et al, EHA 2021

Highlights from IMW 2021

1-2 Febbraio 2022
Bologna
Royal Hotel Carlton

18th IMW

OPTIMUM design



Patient population (Screen)

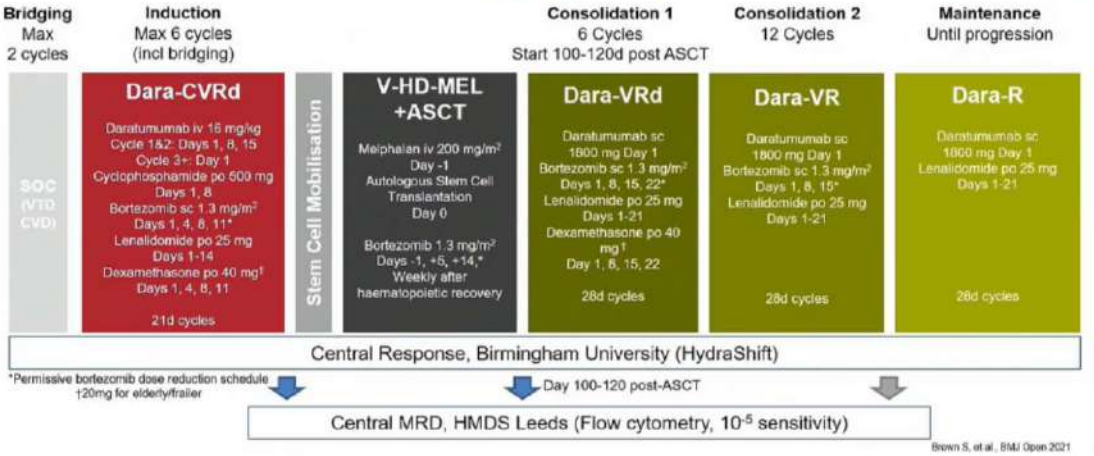
- Patients with (suspected) newly diagnosed myeloma (NDMM) or pPCL fit for intensive therapy

Trial objectives (Treat)

- Evaluate efficacy of Dara-CVRd combination therapy + ASCT in Ultra High-Risk MM and pPCL
  - Response and MRD after induction and ASCT
  - Progression free survival – compared to matched Ultra High-Risk control group from Myeloma XI
- Determine safety and toxicity of Dara-CVRd in Ultra High-Risk MM and pPCL

Brown S, et al., BMJ Open 20

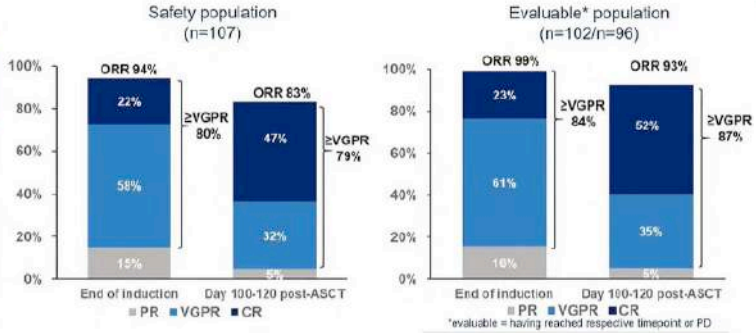
Trial therapy



Brown S, et al., BMJ Open 2021

Central response results

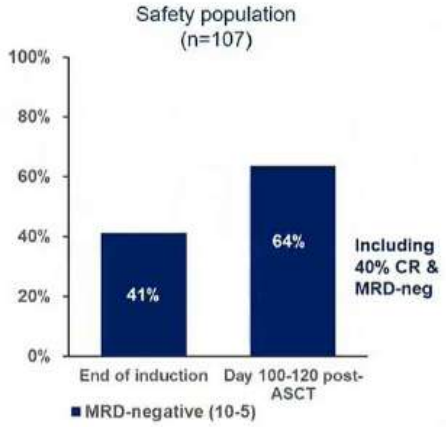
Response Safety Population (n=107)	End of induction	100-120 days post-ASCT
CR	23 (21.5%)	50 (46.7%)
VGPR	62 (57.9%)	34 (31.8%)
PR	16 (15.0%)	5 (4.7%)
PD	1 (0.9%)	7 (6.5%)
Timepoint not reached	5 (4.7%)	11 (10.3%)

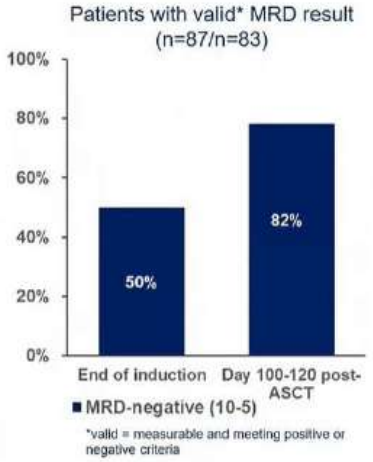


pPCL (evaluable D100-120; n=8)
- CR: 2 (25%)
- VGPR: 2 (25%)
- PR: 2 (25%)
- PD: 2 (25%)

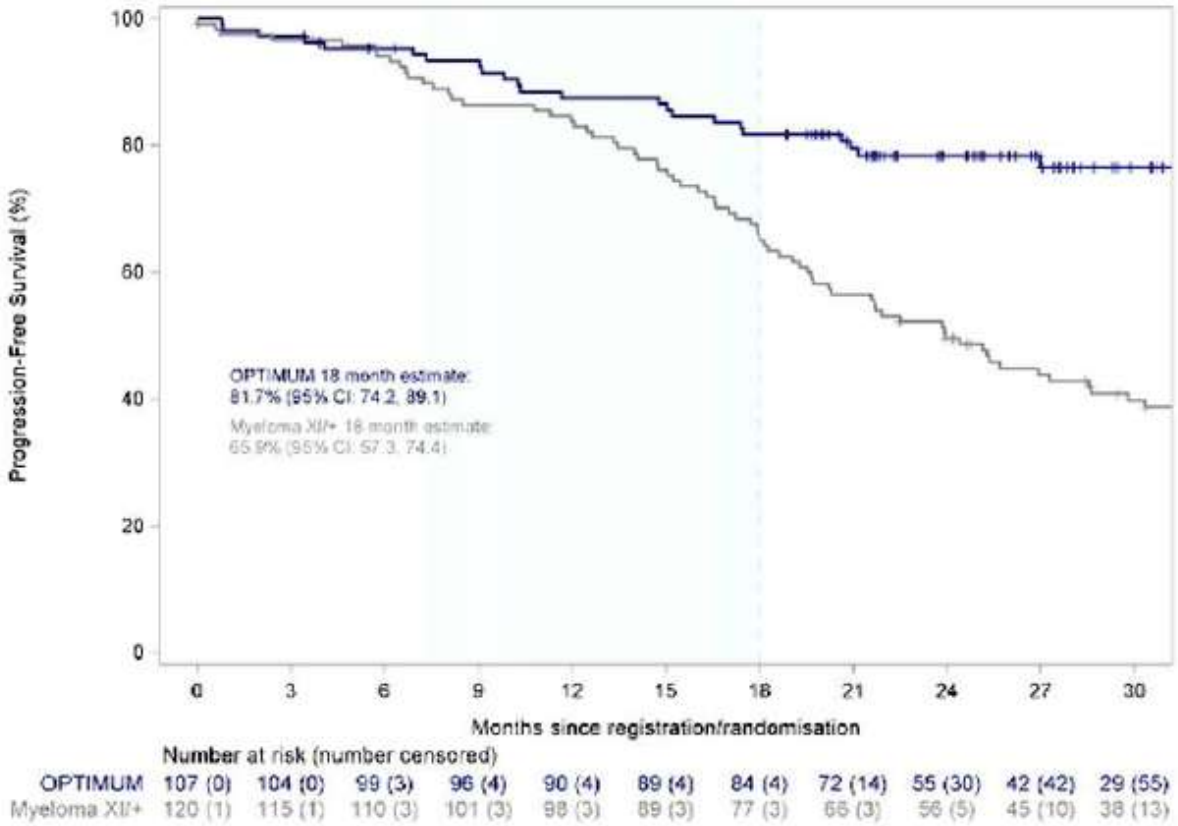
Central response results - MRD

MRD Safety Population (n=107)	End of induction	100-120 days post-ASCT
MRD-neg	44 (41.1%)	68 (63.6%)
MRD-pos	43 (40.2%)	15 (14.0%)
Inadequate or no sample	15 (14.0%)	13 (12.1%)
Timepoint not reached	5 (4.7%)	11 (10.3%)





OPTIMUM vs. Myeloma XI



Daratumumab Plus Ixazomib, Lenalidomide and Dexamethasone as Extended Induction and Consolidation Followed by Lenalidomide maintenance in Standard-Risk Transplant-Eligible Newly Diagnosed Multiple Myeloma Patients (IFM 2018-01): a phase II study of the IFM group

IFM 2018-01 study design

NDMM < 66y
FISH screening
No t(4;14)
No t(14;16)
No del17p

Induction IRd-Dara_21d-cycles 1-6

Ixazomib 3mg	Lenalidomide 25mg	Dexamethasone 40mg	Daratumumab 16mg/kg (IV)
D1, D4, D8, D11	D1-D14	D1, D8, D15	C1-4: D1, D8, D15 ; C5-6: D1, D15

Mobilization & HSC collection

Cyclophosphamide 3g/m² IV	G-CSF 10 µg/kg/d	HSC collection

Intensification & ASCT

Melphalan 200 mg/m² IV D-2	HSC infusion D0	PegG-CSF D+2

Consolidation IRd-Dara_28d-cycles 7-10

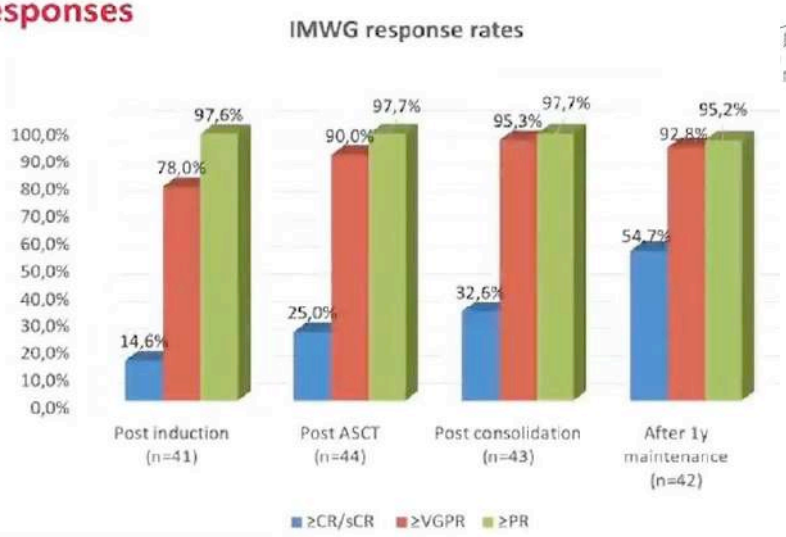
Ixazomib 4mg	Lenalidomide 25mg	Dexamethasone 20mg	Daratumumab 16mg/kg (IV)
D1, D8, D15	D1-D21	C7-8: D1, D8, D15, D22; C9-10: D1, D15	D1, D15

Maintenance 28d-cycles x 26 (2y) or until progression

Lenalidomide 10 mg D1-D21

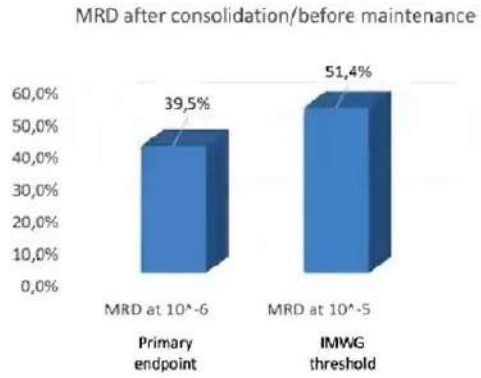
Highlights fro

IMWG Responses

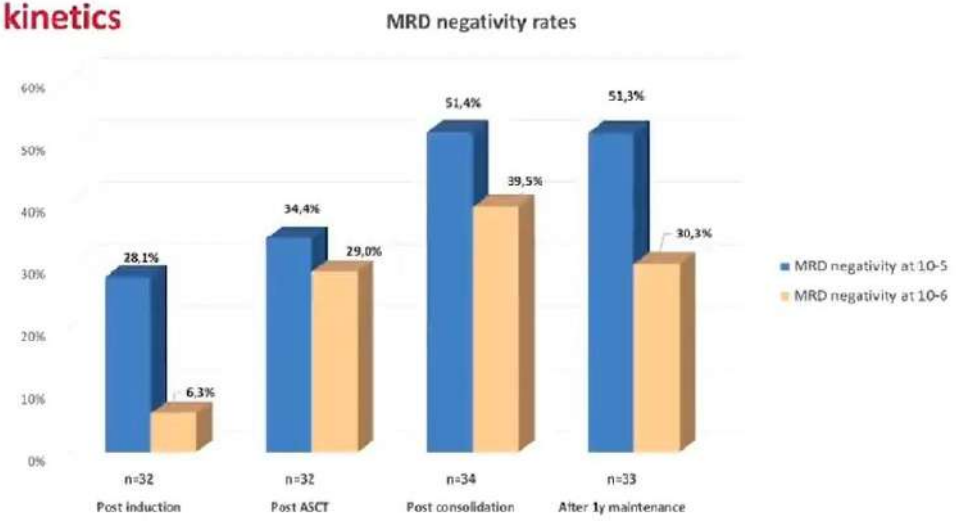


Primary endpoint: MRD-negativity rate before maintenance

- MRD negativity was assessed using **NGS method** (sensitivity threshold up to 10^{-6})
- **38 patients were evaluable** for the primary endpoint at 10^{-6}
- **MRD negativity rate**
  39.5% [CI 26.1-54.1] at 10^{-6}
  51.4% [CI 36.8-65.7] at 10^{-5}

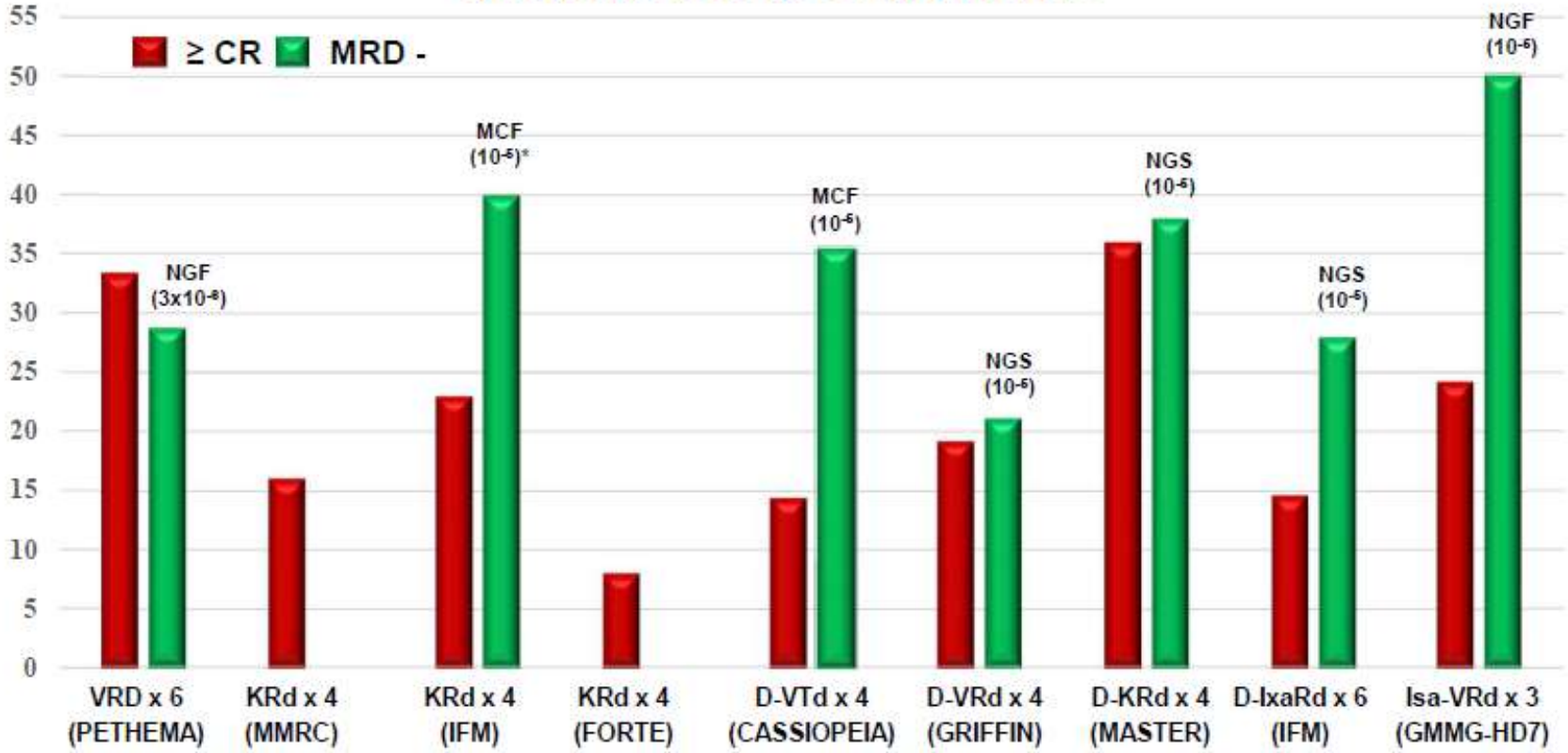


MRD kinetics



Perrot A et al, ASH 2021

Response rates after induction of the main triplet and quadruplet drug combinations

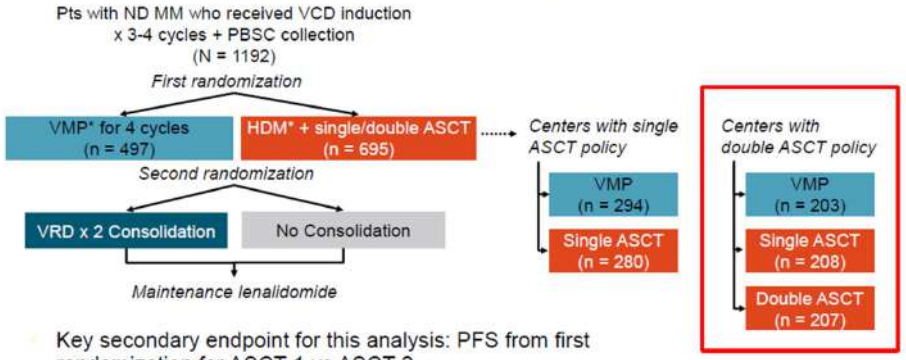


* Only patients with ≥ CR

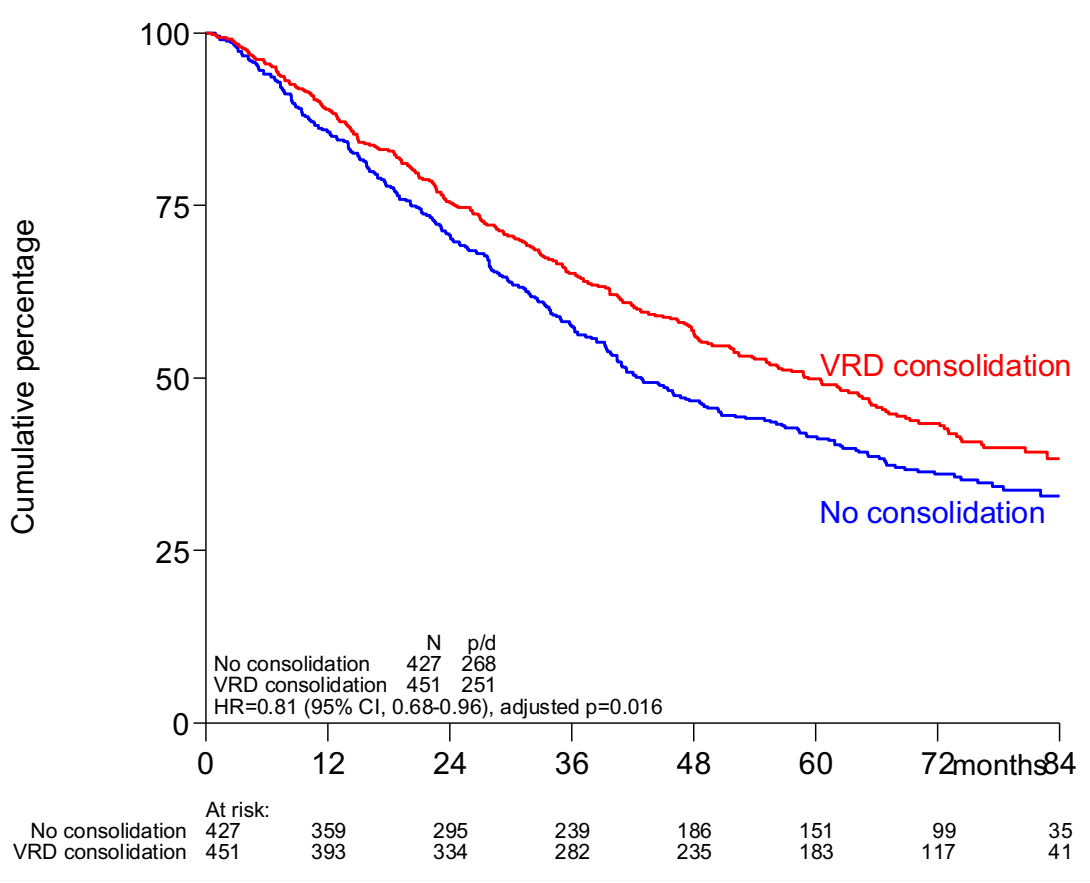
Consolidation

18th IMW

EMN02/HO95: Phase III Study Design



Key secondary endpoint for this analysis: PFS from first randomization for ASCT-1 vs ASCT-2

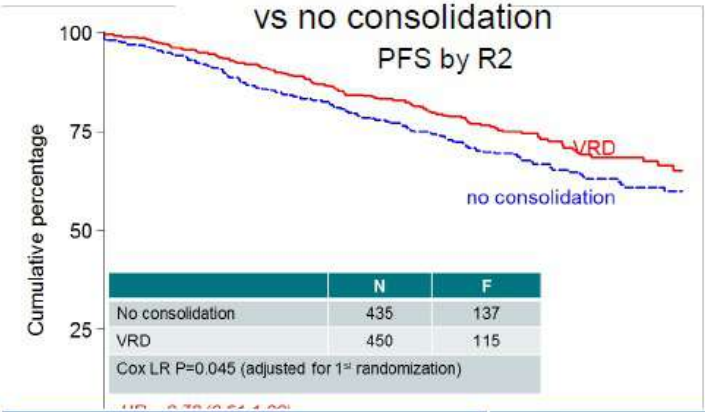


Sonneveld P, et al. JCO 2021

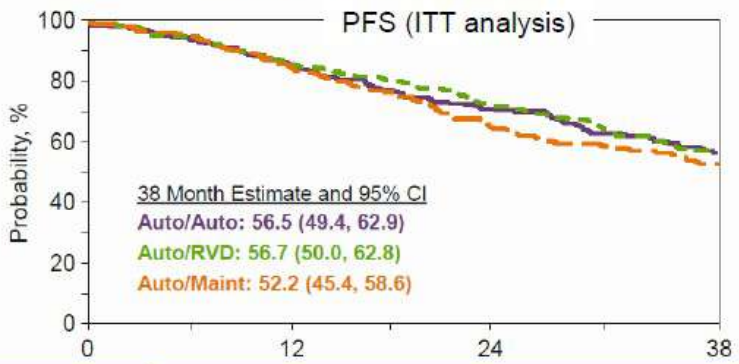
Consolidation

VTD: upgrade to CR by 30%
VRD: upgrade CR 38% vs 26%

EMN02 phase 3 study of VRD consolidation vs no consolidation

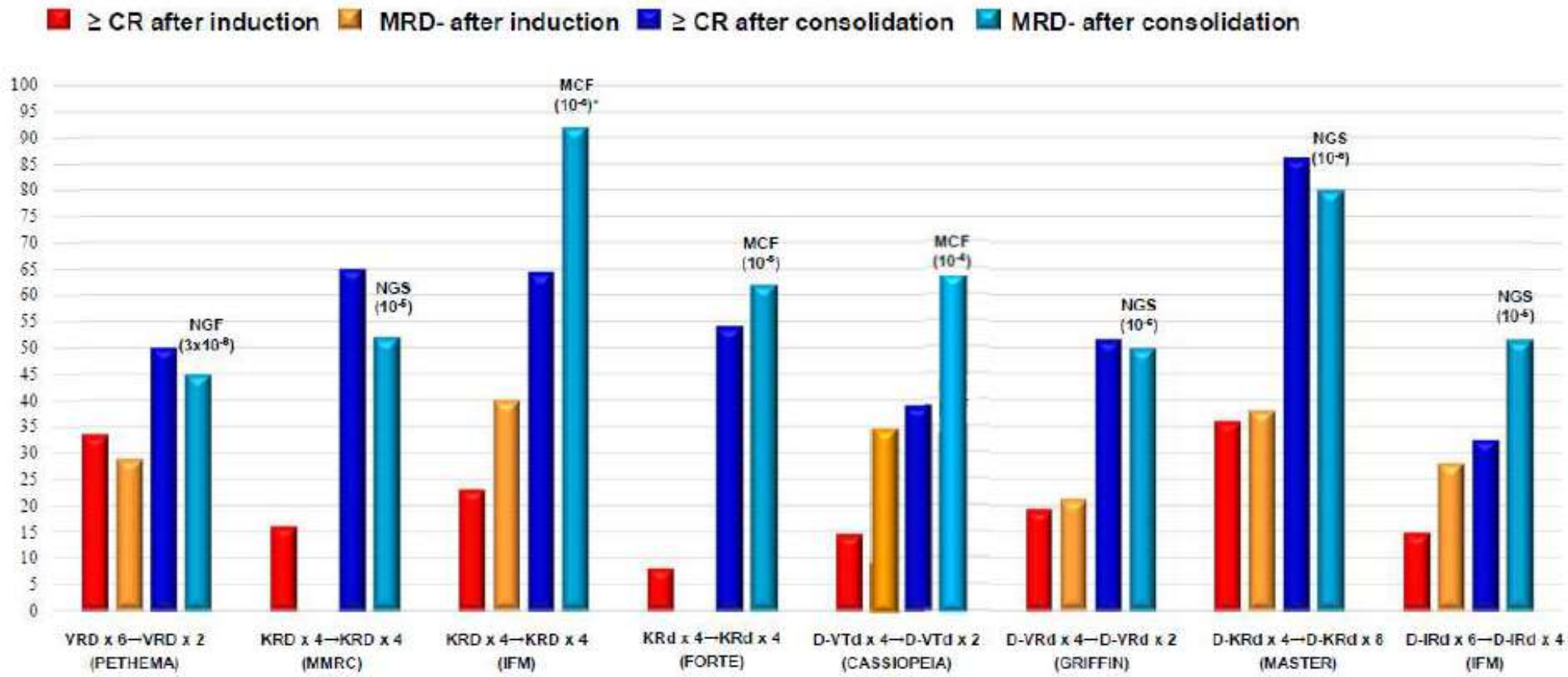


STaMINA phase 3 study of VRD consolidation vs no consolidation



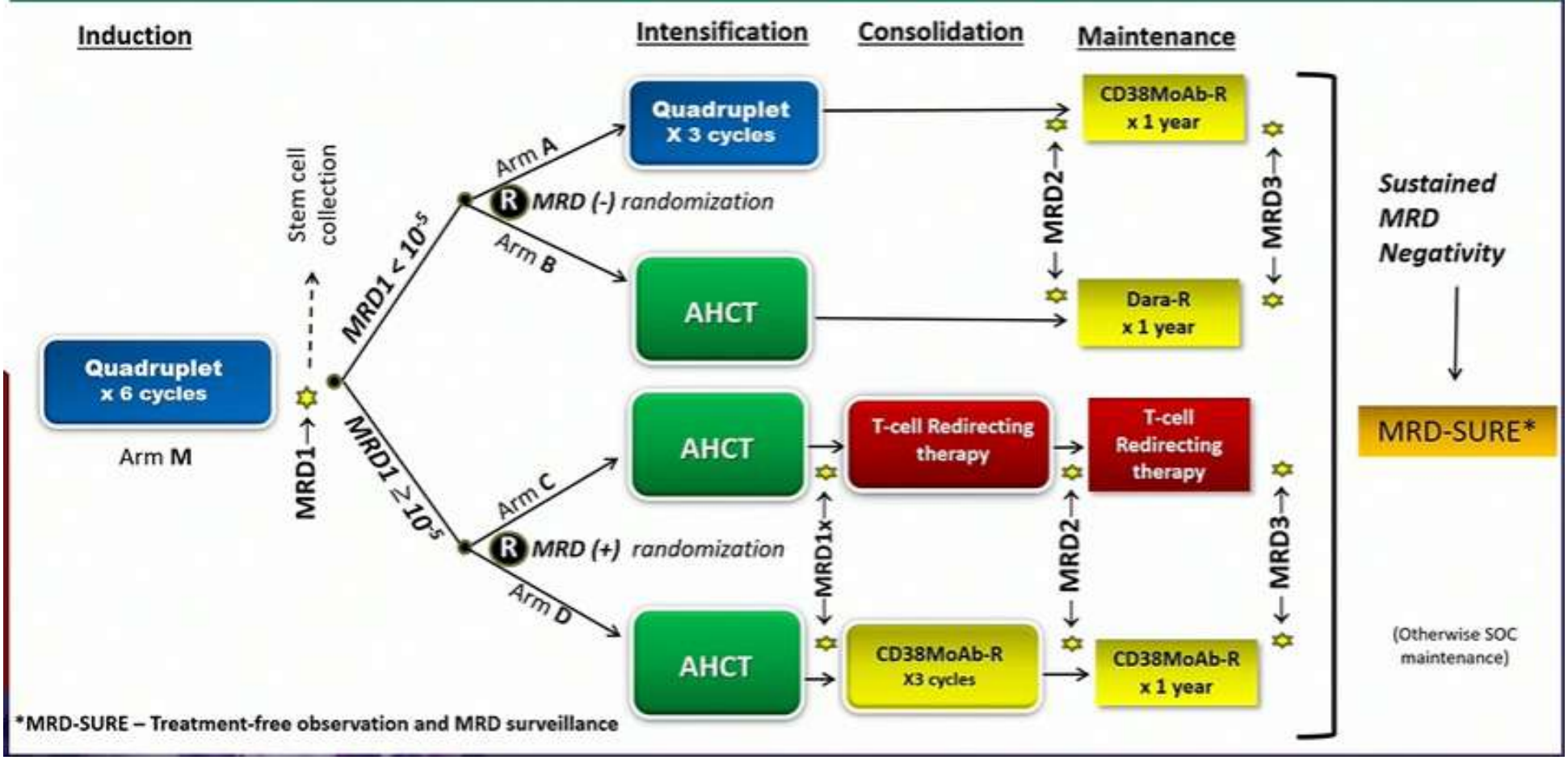
	EMN02	STAMINA
Induction regimen (%)	VCD (100)	VCD (13.4); VRD (57)
Pre-planned induction thp (mths)	2–3	2–12
Failure to receive double ASCT (%)	19.8	32
Double ASCT plus Consolidation (%)	50	0
Maintenance therapy	Len (10 mg)	Len (10–15 mg)

Response rates after induction and consolidation of the main triplet and quadruplet drug combinations



* Only patients with ≥ CR

Future


Induction
Intensification
Consolidation
Maintenance
Quadruplet x 6 cycles
Arm M
Stem cell collection
MRD1→
MRD1 < 10-5
MRD1 ≥ 10-5
Arm A
Arm B
Arm C
Arm D
R MRD (-) randomization
R MRD (+) randomization
Quadruplet X 3 cycles
AHCT
AHCT
AHCT
T-cell Redirecting therapy
CD38MoAb-R X3 cycles
MRD1x→
MRD2→
MRD3→
CD38MoAb-R x 1 year
Dara-R x 1 year
T-cell Redirecting therapy
CD38MoAb-R x 1 year
Sustained MRD Negativity
MRD-SURE*
(Otherwise SOC maintenance)
*MRD-SURE – Treatment-free observation and MRD surveillance