Highlights from
IMS 20th meeting 2023

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Strategie terapeutiche nel paziente "difficile-da-trattare": Con alto/ultra-alto profilo genetico/genomico

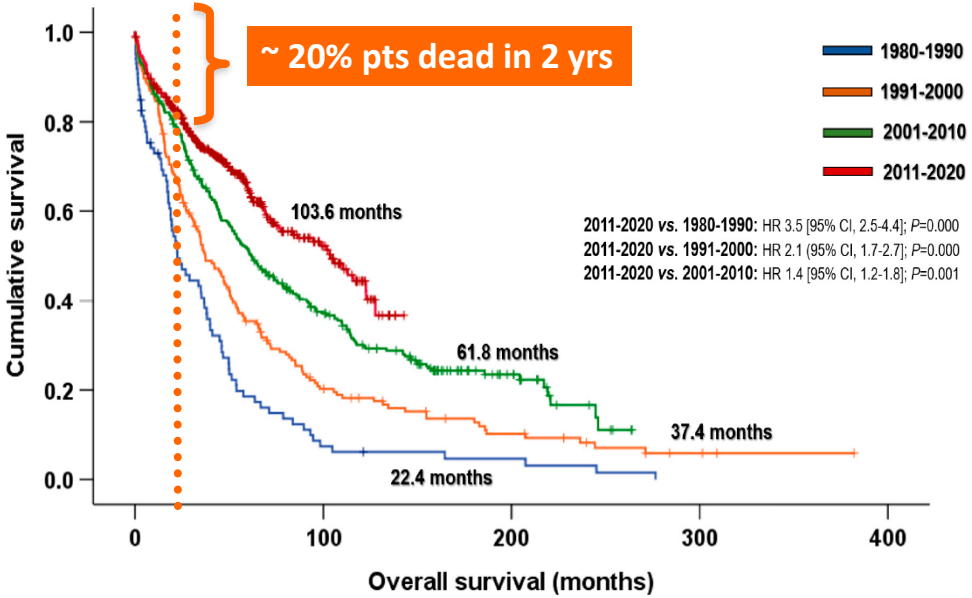
30-31 gennaio 2024
BOLOGNA, Royal Hotel Carlton

Disclosures of Paola Tacchetti

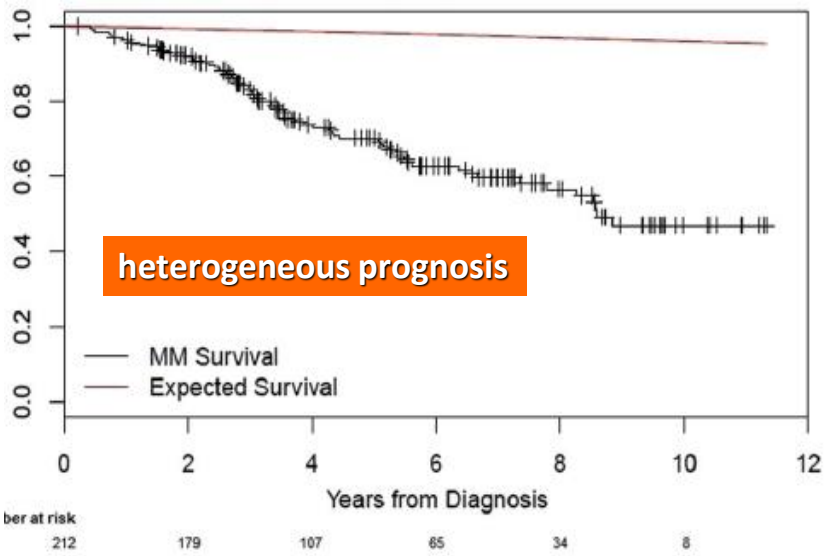
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Janssen						x	Honoraria
BMS/Celgene						x	Honoraria
Amgen						x	Honoraria
Sanofi						x	Honoraria
GSK						x	Honoraria
Abbvie							Honoraria
Takeda							Honoraria
Pfizer							Honoraria

Myeloma is not one disease!!

Continued Improvement in Survival in Multiple Myeloma



OS of pts with MM from diagnosis compared with expected survival of background population



Puertas et al. Cancers 2023; Ravi et al. Blood Cancer Journal 2018

Prognostic factors			
Patient-related	**Disease burden-related**	**Disease biology-related**	**Therapy-related**
Age	High B_2 microglobulin*	Cytogenetic abnormalities	Quality of response
Performance status	Low albumin*	GEP	Early relapse
Comorbidities	Renal impairment	Circulating PCs	
	LDH above ULN	EMD	
		High proliferation rate	

Cytogenetic abnormalities and relationship with outcomes		
Chromosome/region (frequency)	**Gene involved/effect**	**Prognostic implication**
14q32 (locus IGH) (45-50%)		
t(11;14) (20%)	Cyclin D1 hyperexpression	Neutral
t(4;14) (10% to 15%)	FGFR3 and MMSET deregulated	Unfavorable (worsened by chromosome 1 alterations, improved by trisomy 5)
t(14;16) (<5%)	cMAF	Doubt, mainly unfavorable
t(14;20) (<5%)	UK	Doubt, mainly unfavorable
1q21 acquisition (30%)	CKS1B, MCL1	
Gain (2-3 copies)		Partially unfavorable
Amplification (≥4)		Unfavorable
1p32 deletion (10%)	FAF1/ CDKN2C	Unfavorable
17p deletion (8% to 15% according to PC cutoff)	TP53 and UK	
Single-hit	Deletion	Unfavorable
Double-hit	Biallelic inactivation (deletion + mutation)	Very unfavorable

Zamagni E et al. Blood 2022

Why Risk Stratify?

Two important goals

- ***Counsel:*** Need to provide pt with realistic expectations based on the currently available treatments

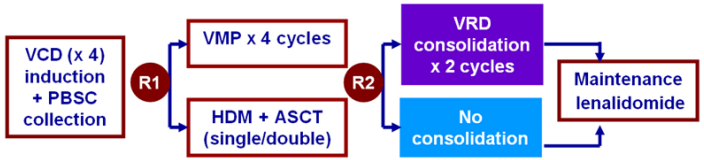
- ***Therapy:*** Decide if particular therapies can be chosen based on their differential effects on the high-risk and standard-risk disease

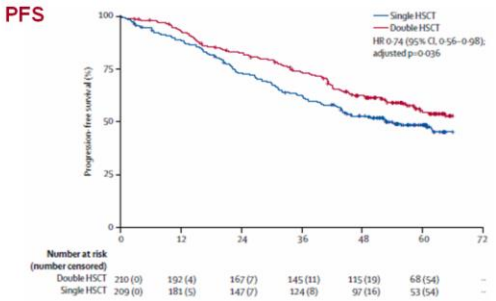
Pitfalls of treatment of HR patients: the black beast of MM

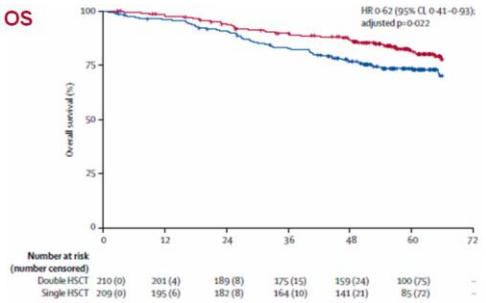
- Inhomogeneity in HR definition in different trials
- Most data coming from retrospective analyses
- Guidelines and recommendations poor on HR
- Lack of specific trials dedicated to HR population

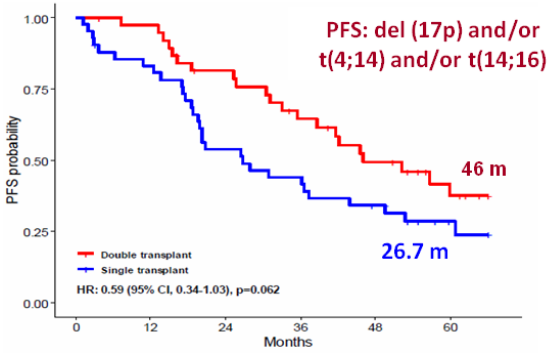
Double ASCT

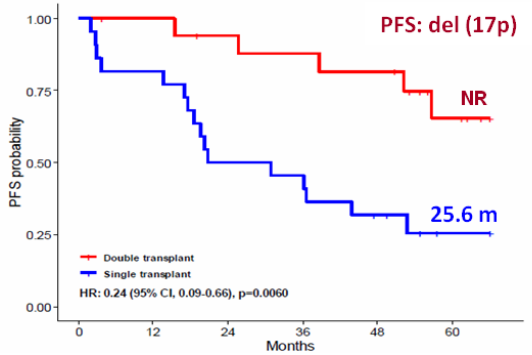
EMN02/HO95 phase 3 study

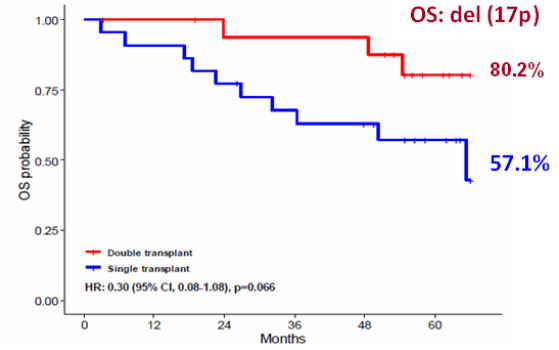












A tandem ASCT is recommended for patients with genetically defined high-risk disease

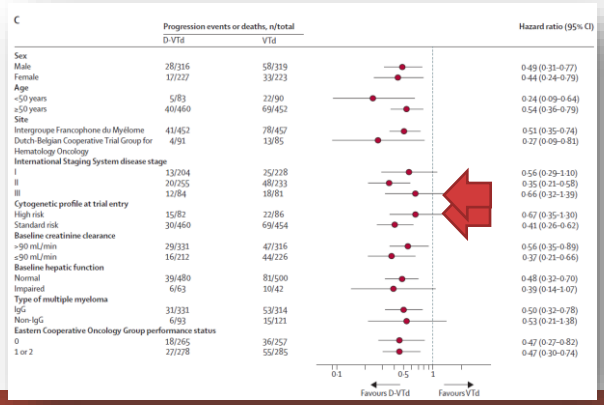
Cavo et al. Lancet Haematol 2020;7:e456–68

Quadruplet induction/consolidation (MoAb-PI-IMiD-dex)

DARA-VTd: CASSIOPEIA phase 3 trial

Subgroup	VTd (minimal residual disease negative, n (%))	D-VTd (minimal residual disease negative, n (%))	Odds Ratio (95% CI)
Sex			
Male	131 (41)	192 (61)	2.22 (1.62–3.05)
Female	105 (47)	154 (68)	2.37 (1.62–3.48)
Age			
<50 years	38 (42)	56 (68)	2.84 (1.53–5.28)
≥50 years	198 (44)	290 (63)	2.19 (1.68–2.85)
Site			
IFM	204 (45)	287 (64)	2.16 (1.65–2.81)
HOVON	32 (38)	59 (65)	3.05 (1.65–5.65)
ISS disease stage			
I	103 (45)	137 (67)	2.48 (1.68–3.67)
II	96 (41)	155 (61)	2.21 (1.54–3.18)
III	37 (46)	54 (64)	2.14 (1.15–4.00)
Cytogenetic profile at trial entry[c]			
High risk	38 (44)	49 (60)	1.88 (1.02–3.46)
Standard risk	197 (43)	296 (64)	2.35 (1.80–3.07)
Baseline creatinine clearance			
>90 ml/min	139 (44)	205 (62)	2.07 (1.51–2.84)
≤90 ml/min	97 (43)	141 (67)	2.64 (1.79–3.89)
Baseline hepatic function			
Normal	216 (43)	310 (65)	2.40 (1.85–3.10)
Impaired	20 (48)	36 (57)	1.47 (0.67–3.21)
Type of multiple myeloma[d]			
IgG	122 (39)	201 (61)	2.43 (1.77–3.34)
Non-IgG	59 (49)	61 (66)	2.00 (1.15–3.50)
ECOG performance status			
0	112 (44)	172 (65)	2.39 (1.68–3.41)
≥1	124 (44)	174 (63)	2.17 (1.55–3.04)

1 5 10
VTd better D-VTd better



DARA-VRd: PERSEUS phase 3 trial

Subgroup	VRd (no. of patients with MRD negativity/total no. (%))	D-VRd (no. of patients with MRD negativity/total no. (%))	Odds ratio (95% CI)
Sex			
Male	94/205 (45.9)	150/211 (71.1)	2.90 (1.94-4.35)
Female	74/149 (49.7)	117/144 (81.3)	4.39 (2.59-7.44)
Age			
<65 y	125/267 (46.8)	204/261 (78.2)	4.07 (2.78-5.94)
≥65 y	43/87 (49.4)	63/94 (67.0)	2.08 (1.14-3.79)
Race			
White	150/323 (46.4)	251/330 (76.1)	3.66 (2.62-5.12)
Other	18/31 (58.1)	16/25 (64.0)	1.28 (0.43-3.80)
ISS stage			
I	88/178 (49.4)	146/186 (78.5)	3.73 (2.36-5.89)
II	58/125 (46.4)	84/114 (73.7)	3.23 (1.87-5.58)
III	21/50 (42.0)	37/55 (67.3)	2.84 (1.28-6.29)
Type of MM			
IgG	89/185 (48.1)	153/204 (75.0)	3.24 (2.11-4.97)
Non-IgG	50/96 (52.1)	63/78 (80.8)	3.86 (1.94-7.71)
Cytogenetic risk			
Standard risk	128/266 (48.1)	204/264 (77.3)	3.67 (2.52-5.33)
High risk	37/78 (47.4)	52/76 (68.4)	2.40 (1.24-4.63)
Indeterminate	3/10 (30.0)	11/15 (73.3)	6.42 (1.09-37.73)
ECOG PS			
0	101/230 (43.9)	168/221 (76.0)	4.05 (2.70-6.06)
≥1	67/124 (54.0)	99/134 (73.9)	2.41 (1.43-4.06)

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Favors VRd Favors D-VRd

Subgroup	D-VRd (no. of progression events or deaths/total no.)	VRd (no. of progression events or deaths/total no.)	HR (95% CI)
Sex			
Male	36/211	61/205	0.51 (0.34-0.77)
Female	14/144	42/149	0.29 (0.16-0.53)
Age			
<65 y	30/261	84/267	0.30 (0.20-0.46)
≥65 y	20/94	19/87	0.97 (0.52-1.81)
Race			
White	47/330	95/323	0.42 (0.30-0.60)
Other	3/25	8/31	0.40 (0.11-1.50)
ISS stage			
I	18/186	35/178	0.46 (0.26-0.81)
II	19/114	43/125	0.37 (0.22-0.64)
III	13/55	25/50	0.42 (0.22-0.83)
Type of MM			
IgG	28/204	58/185	0.36 (0.23-0.57)
Non-IgG	13/78	31/96	0.46 (0.24-0.88)
Cytogenetic risk			
Standard risk	25/264	62/266	0.35 (0.22-0.56)
High risk	24/76	38/78	0.59 (0.36-0.99)
Indeterminate	1/15	3/10	0.16 (0.02-1.56)
ECOG PS			
0	28/221	60/230	0.42 (0.27-0.66)
≥1	22/134	43/124	0.41 (0.25-0.69)

0.1 1 10
Favors D-VRd Favors VRd

DARA-VRd: GRIFFIN phase 2 trial

	D-RVd n/N	D-RVd Median PFS (mo)	RVd n/N	RVd Median PFS (mo)	Hazard ratio (95% CI)[a]
ITT (overall)	11/104	NR	18/103	NR	0.45 (0.21-0.95)
Baseline characteristic					
Age ≥65 y	2/28	NR	5/28	NR	0.29 (0.06-1.48)
ISS stage III disease	2/14	NR	6/14	33.1	0.23 (0.05-1.13)
CrCl 30-50 mL/min	2/9	NR	0/9	NR	NE (0.00-NE)
CrCl >50 mL/min	9/95	NR	18/94	NR	0.35 (0.16-0.79)
Cytogenetic risk					
High cytogenetic risk[b]	5/16	NR	5/14	36.1	0.54 (0.15-1.88)
Revised high cytogenetic risk[c]	7/42	NR	10/37	47.9	0.38 (0.14-1.01)
0 HRCA[c]	3/56	NR	7/60	NR	0.39 (0.10-1.51)
1 HRCA[c]	3/32	NR	8/29	47.9	0.19 (0.05-0.75)
≥2 HRCAs[c]	4/10	33.9	2/8	NR	0.55 (0.30-9.18)
Gain/amp(1q21)[d]	6/34	NR	7/28	47.9	0.42 (0.14-1.27)
Gain/amp(1q21) + 1 HRCA[c]	4/9	33.9	2/6	38.7	0.81 (0.15-4.47)
Gain/amp(1q21) isolated[e]	2/25	NR	5/22	47.9	0.21 (0.04-1.09)
Best response to therapy					
<VGPR after induction	3/30	NR	9/44	NR	0.29 (0.08-1.07)
≥VGPR after induction	8/70	NR	9/54	NR	0.58 (0.22-1.51)
<VGPR after 2 y of maintenance	2/4	7.0	3/22	NR	2.21 (0.34-14.49)
≥VGPR after 2 y of maintenance	9/96	NR	15/76	NR	0.40 (0.18-0.92)
MRD status					
MRD[-] after consolidation	9/52	NR	14/82	NR	0.82 (0.35-1.89)
MRD[-] after consolidation	2/52	NR	4/21	NR	0.17 (0.03-0.92)
MRD[-] after 2 y of maintenance	8/37	NR	12/72	NR	1.04 (0.43-2.56)
MRD[-] after 2 y of maintenance	3/67	NR	6/31	NR	0.21 (0.05-0.86)

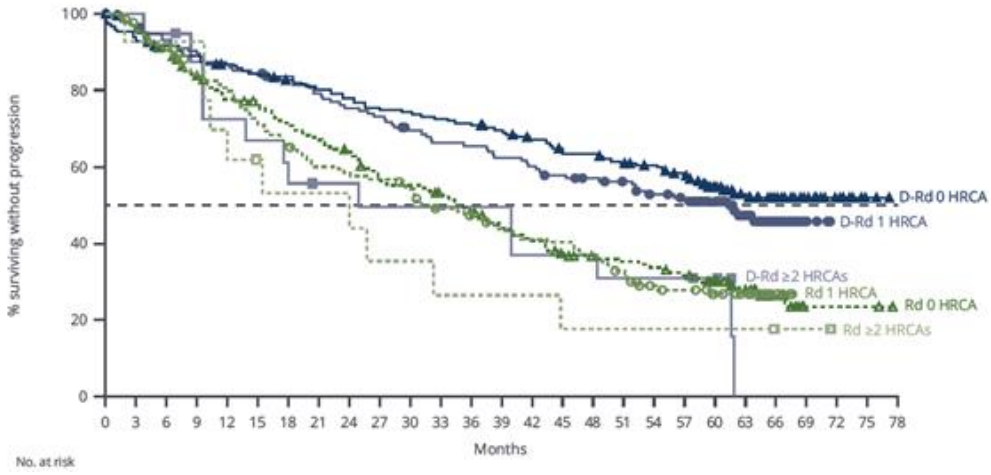
0.1 1 10
D-RVd better RVd better

Moreau P et al, Lancet 2019; Moreau P et al, ASCO 2021; Sonneveld P, et al. ASH 2023; Sonneveld P, et al. N Engl J Med. 2023; Chari A et al. ASH 2022; Voohrees PM et al. Lancet Haematol 2023

In a subgroup analysis of MAIA, patients with TIE NDMM with HRCA had improved outcomes with dara-Rd vs Rd

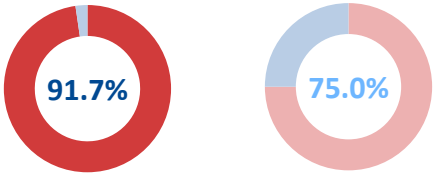
- High cytogenetic risk was defined by the number of HRCAs

PFS among patients with O, 1 or ≥2 HRCAs



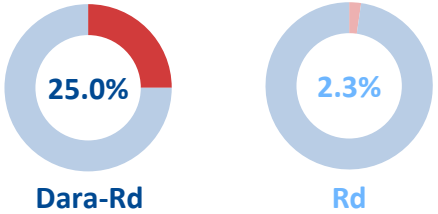
CI, confidence interval; (dara-)Rd, (daratumumab) lenalidomide and dexamethasone; HRCA, high-risk cytogenetic abnormality; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; OR, odds ratio; ORR, objective response rate; PFS, progression-free survival; TIE, transplant-ineligible.

Higher ORR was observed with dara-Rd vs Rd in patients with high-risk cytogenetics



(OR, 3.67; 95% CI, 1.07–12.55)

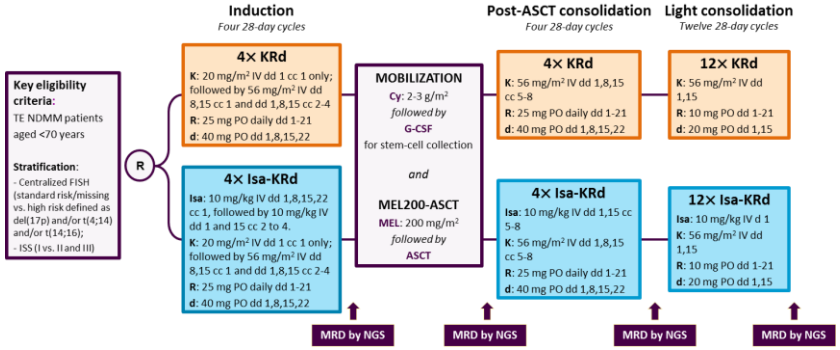
Higher rates of MRD-negativity (10^{-5}) were observed with dara-Rd vs Rd in patients with high-risk cytogenetics



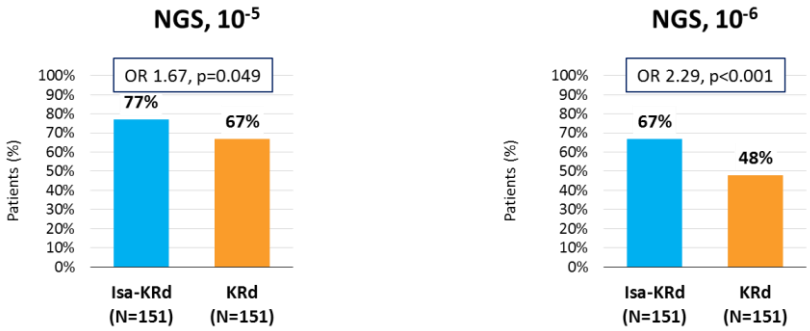
(OR, 14.33; 95% CI, 1.78–115.59)

Moreau P, et al. ASH 2022

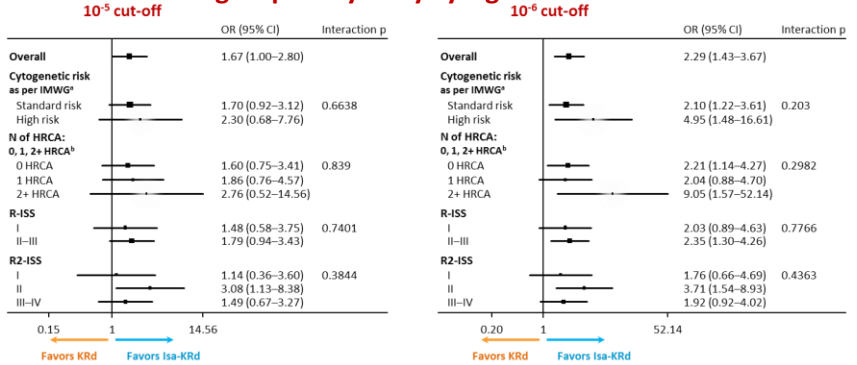
Isa-KRd Vs KRd Pre-Transplant Induction and Post-Transplant Consolidation in NDMM: IsKia trial

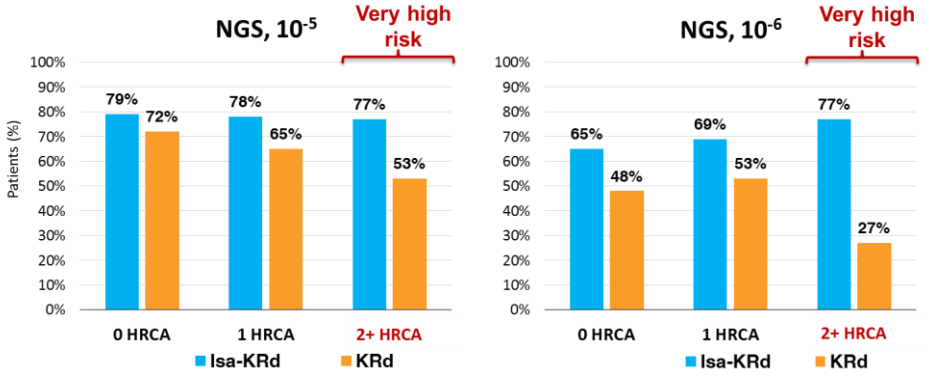


Primary Endpoint: Post-consolidation MRD negativity (ITT analysis)



Post-consolidation MRD negativity by NGS
Subgroup analysis by cytogenetic risk





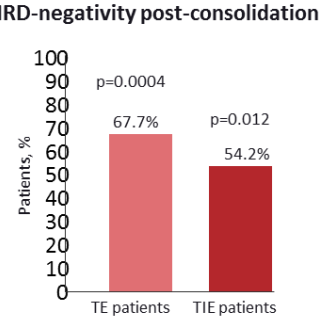
1 HRCA was defined as the presence of one of the following high-risk cytogenetic abnormalities: del(17p13.1), t(4;14) (p16.3;q32.3), t(14;16) (q32.3;q23), gain(1q21), or amp(1q21); 2+ HRCA was defined as the presence of at least two high-risk cytogenetic abnormalities.

Gay F, et al. ASH 2023

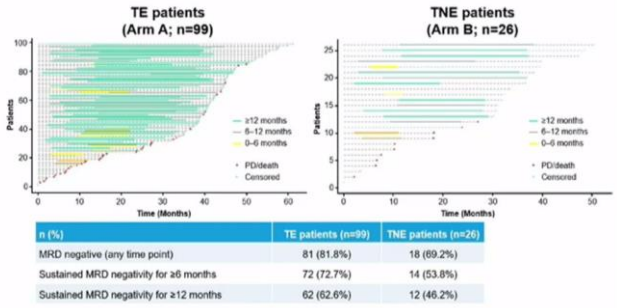
In GMMG-CONCEPT, high-risk patients with NDMM had durable responses with isa-KRd with and without subsequent ASCT

Patients with NDMM at high cytogenetic risk, defined as ISS stage II or III plus ≥1 of the following: t(14;16), t(4;14), del(17p), >3 copies of 1q21 (N=153)[2]

Primary endpoint:
MRD-negativity
Secondary endpoint:
PFS

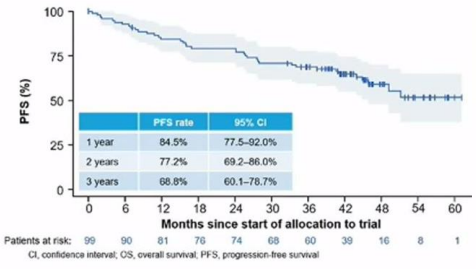


- 81.8% of TE and 69.2% of TNE patients achieved MRD negativity at any timepoint
- ≥1-year sustained MRD negativity was achieved in 62.6% of TE and 46.2% of TNE patients

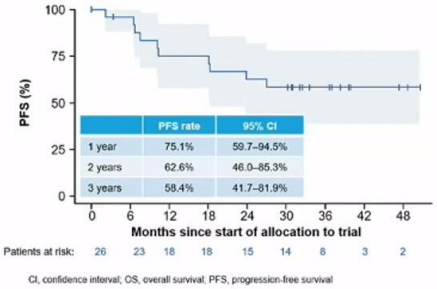


n (%)	TE patients (n=99)	TNE patients (n=26)
MRD negative (any time point)	81 (81.8%)	18 (69.2%)
Sustained MRD negativity for ≥6 months	72 (72.7%)	14 (53.8%)
Sustained MRD negativity for ≥12 months	62 (62.6%)	12 (46.2%)

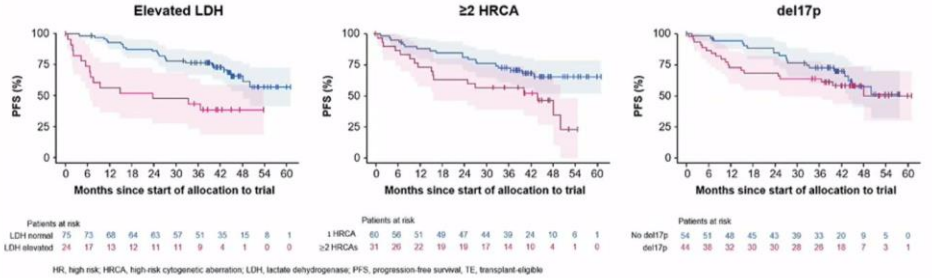
TE



TIE



HR markers associated with impaired survival were elevated LDH, ≥2 HRCA, and del17p



Weisel KC, et al. ASH 2022 (Abstract No. 759 – Presentation); Leypoldt LB, et al. IMW 2023

DaraKRd induction and consolidation with double ASCT in HR NDTEMM: phase 2 study IFM 2018-04

2018-04 study design

Key inclusion criteria:

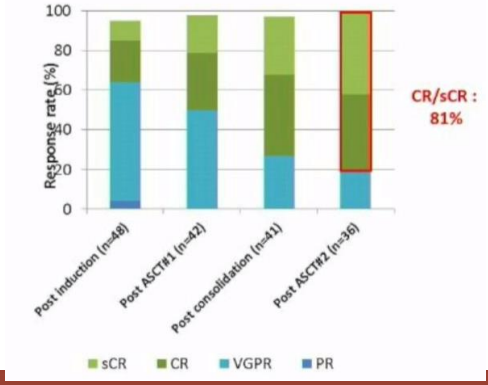
- Age < 66
- **Newly diagnosed multiple myeloma**
- **Transplant-eligible**
- **High-risk FISH :** t(4;14), 17p Del, t(14;16)
- ECOG 0-2

Objectives:

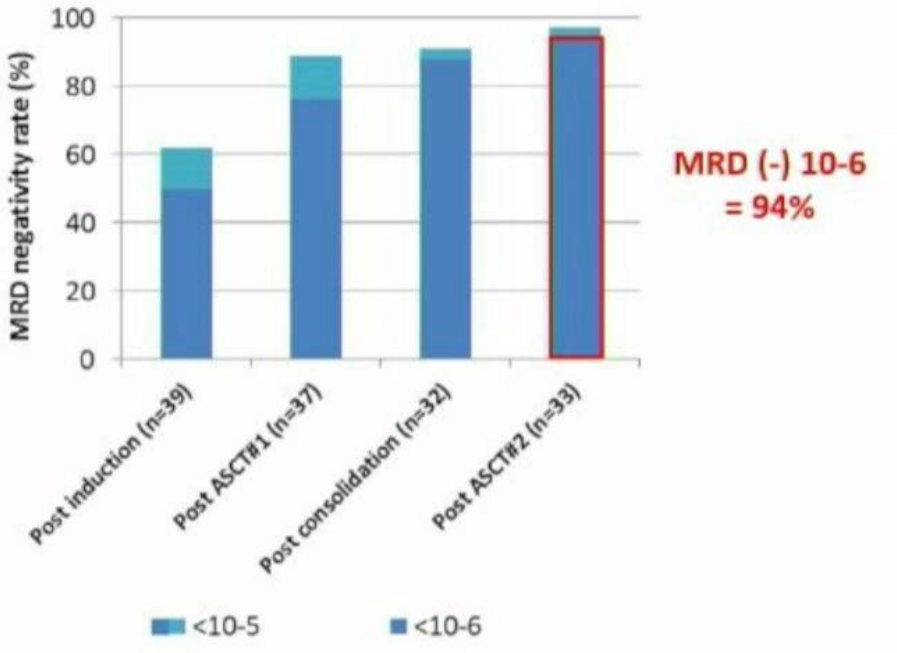
- **Primary Objective :** Feasability
  primary endpoint : >70% patients receiving 2nd transplant
- **Secondary Objectives:** Safety, ORR, PFS, OS, stem-cell collection

Induction Dara-KRd x 6	Stem cell collection	ASCT#1	Consolidation Dara KRd x 4	ASCT#2	Maintenance Dara Len 2 years
Dara : 16 mg/kg IV D1,8,15,22 (cycle 1 and 2) D1 D15 (Cycle 3 to 6) **K :** (20)36 mg/m2 IV D1-2, 8-9, 15-16 **Len :** 25 mg D1-21 **Dex :** 20 mg D1-2, 8-9, 15-16, 22-23 28-day cycle	Cyclo GCSF +/- Plerix	Mel 200	**Dara :** 16 mg/kg IV D1 D15 **K :** 56 mg/m2 IV D1, 8, 15 **Len :** 15 mg D1-21 **Dex :** 40 mg D1, 8, 15, 22 28-day cycle	Mel 200	**Dara :** 16 mg/kg IV every 8 weeks **Len :** 10 mg 21/28

Response Rates *



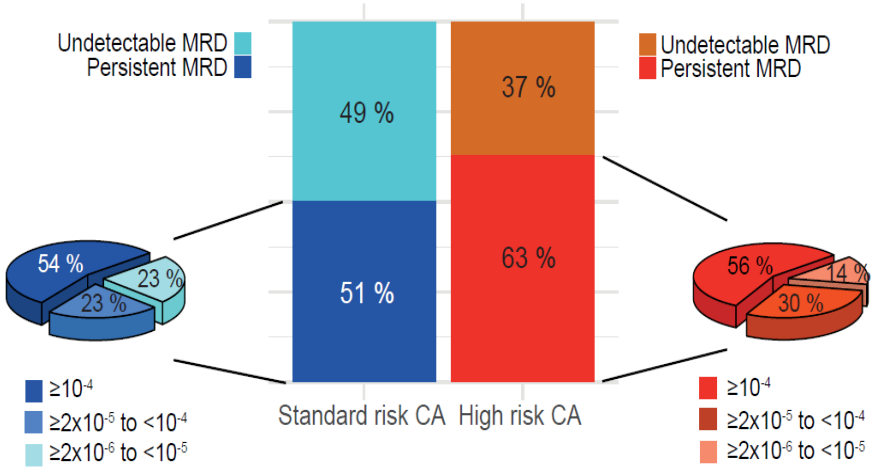
MRD negativity rates (NGS) *

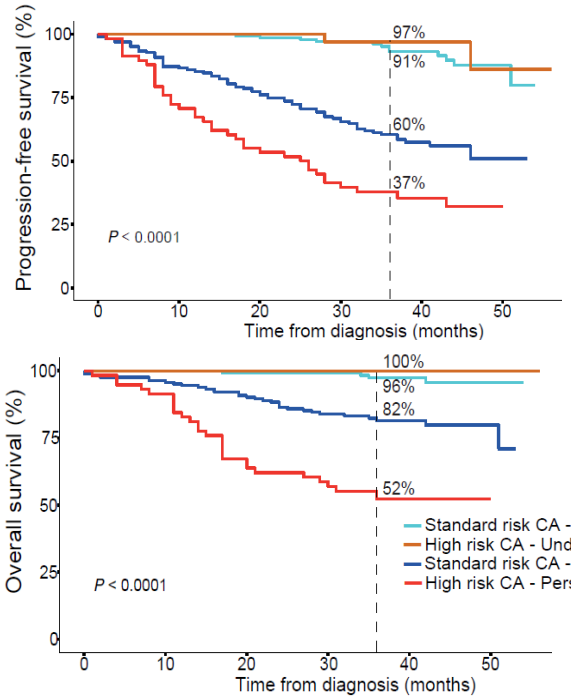


Touzeau C, et al. IMWG 2023

MRD and genetically high-risk patients

MRD status according to cytogenetic risk in the PETHEMA/GEM2012MENOS65 clinical trial



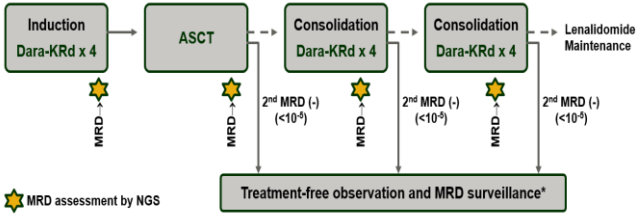


Undetectable MRD may overcome the dismal survival of patients with MM with high risk CA

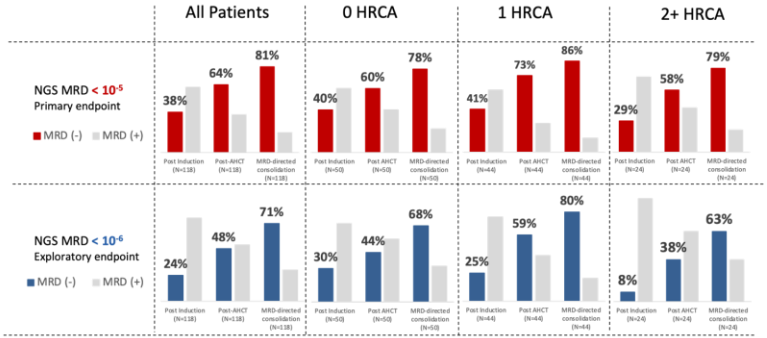
CA, cancer; MM, multiple myeloma; MRD, minimal residual disease

Goicoechea et al. Blood 2021;137(1):49–60

MRD-MODULATED CONSOLIDATION AND TREATMENT CESSATION: MASTER study



- N=123, Median age 60 years, 57% MM high-risk cytogenetics (gain/amp 1q, t(4;14), t(14;16), t(14;20) or del(17p))



	All Patients	0 HRCA	1 HRCA	2+ HRCA
CR + MRD<10^{-5}	72%	76%	75%	58%
Transition to MRD-SURE	71%	66%	82%	63%
Sustained (12 mo.) MRD <10^{-5}	65%	66%	73%	46%

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

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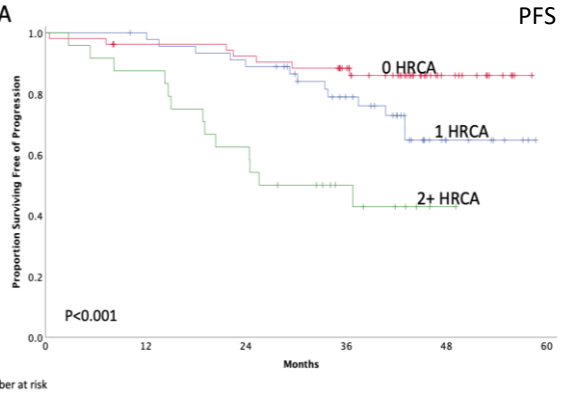
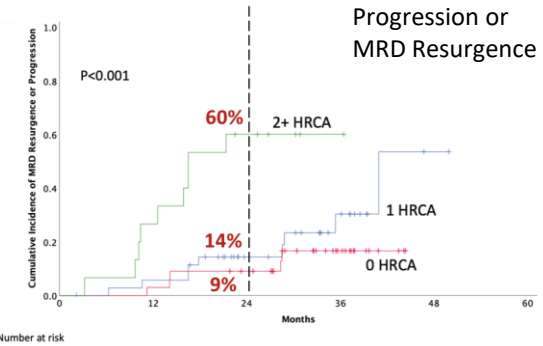
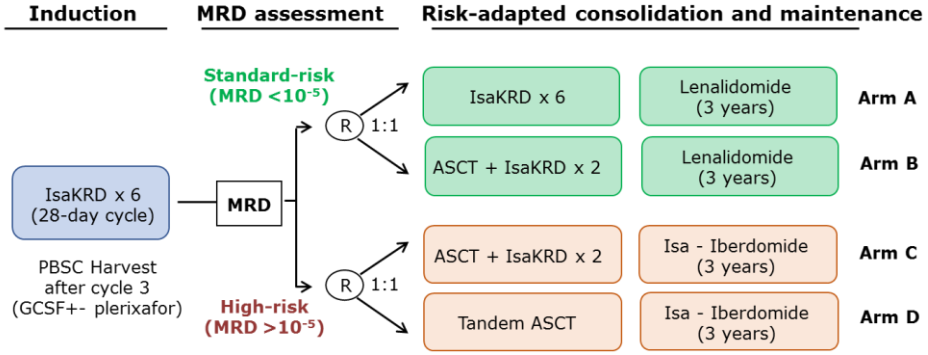


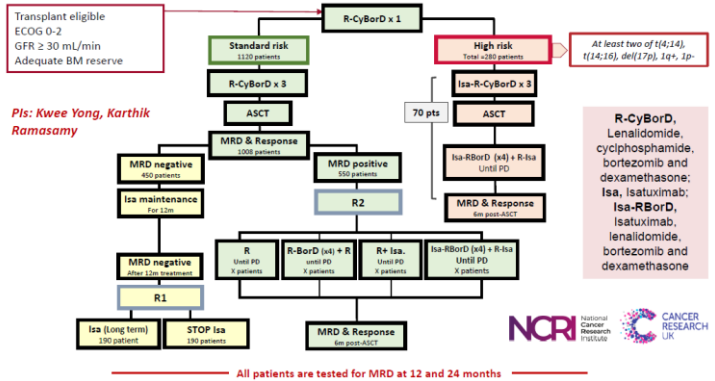


Costa LJ et al, JCO 2022, EHA 2023

IFM 2020-02: Minimal Residual Disease Adapted Strategy (MIDAS)

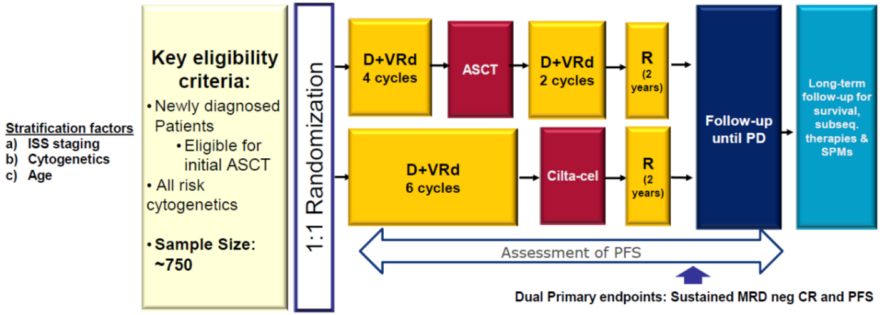


Risk-Adapted therapy Directed According to Response (RADAR)



Will novel immunotherapies replace single/double ASCT? EMN 28- CARTITUDE 6 trial

Dual primary endpoints:
Sustained MRD-neg CR and PFS



CARTITUDE-5: A Randomized, Phase 3, Multicenter Study

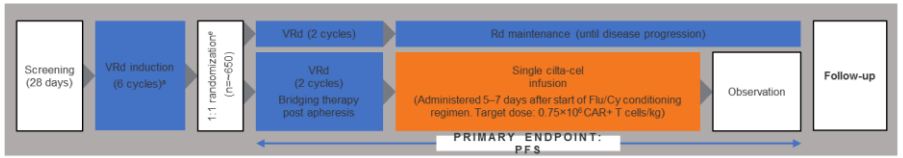
All patients will complete 6[a] cy (21 d each) of VRd induction therapy[b] prior to randomization (1:1)

VRd + cilta-cel arm

- Apheresis and 2 more cycles of VRd as bridging therapy
- Lymphodepletion daily for 3 days[c]
- Cilta-cel as a single infusion

VRd + Rd arm (SOC)

- Two more cycles of VRd
- Rd maintenance therapy[d] continues until progressive disease or unacceptable toxicity



RRMM: How to make the right choice

1. TYPE OF RELAPSE

2. STANDARD OR HIGH RISK

HIGH RISK

3. TYPE & EFFICACY OF PREVIOUS TREATMENTS

4. TOXICITIES OF TREATMENTS AND COMORBIDITIES

Cut-off values for affected cell ratios in MM trials

Trial	Arms	del(17p)	t(4;14)	t(14;16)	amp1q21
Pomalidomide-based regimens					
ICARIA-MM	Isa-Pd vs Pd	≥50%	≥30%	≥30%	≥30%
APOLLO	DPd vs Pd	NR	NR	NR	-
ELOQUENT-3	EPd vs Pd	NR	NR	NR	-
PI-based regimens					
IKEMA	Isa-Kd vs Kd	≥50%	≥30%	≥30%	≥30%
CANDOR	DKd vs Kd	NR	NR	NR	-
CASTOR	DVd vs Vd	NR	NR	NR	-
OPTIMISMM	PVd vs Vd	NR	NR	NR	-
BOSTON	XVd vs Vd	≥10%	≥10%	≥10%	≥10%
Lenalidomide-based regimens					
POLLUX	DRd vs Rd	NR	NR	NR	-
TOURMALINE-MM1	IRd vs Rd	≥5%	≥3%	≥3%	-
Anti-BCMA therapies					
KarMMA	Idecabtagene vicleucel	NR	NR	NR	
CARTITUDE-1	Ciltacabtagene vicleucel	≥20%	≥3%	≥2%	-
Majes-TEC1	Teclistamab	NR	NR	NR	-

Lenalidomide-based regimens applicable from 2nd line

	ASPIRE		POLLUX		TOURMALINE-1		ELOQUENT-2	
Median, months	KRd	Rd	DRd	Rd	IRd	Rd	ERd	Rd
Standard	29.6	19.5	52.0	19.9	20.6	15.6	19.7	16.6
High	23.1	13.9	26.8	8.8	21.4	9.7	15.2	7.4

Stewart AK et al. N Engl J Med 2015;372:142-52; Dimopoulos MA et al. Haemeatologica 2018,103(12):2088-2096; Dimopoulos MA et al, EHA 2019; Avet-Loiseau H et al. Blood 2017.130(24):2610-2618; Dimopoulos MA et al. Cancer 2018,124(20):4032-4043

Lenalidomide sparing regimens applicable from 2nd line

	ENDEAVOR		CASTOR		OPTIMISMM		CANDOR		IKEMA		APOLLO	
Median, months	Kd	Vd	DVd	Vd	PVd	Pd	DKd	Kd	Isa-Kd	Kd	DPd	Pd
Standard	NR	10.2	18.4	6.8	NR	NR	NR	16.6	NR, HR in favour	19.4	21.0	7.4
High	8.8	6.0	13.4	7.2	8.4	5.3	15.6	5.6	NR,HR in favour	18.2	5.8	4.0

Chng WJ et al. Leukemia 2017; Weisel K et al, EHA 2019; Kaufman JL et al ASH 2019; Richardson P et al. Lancet Oncol 2019; Dimopoulos M et al, ASH 2020, Dimopoulos M et al, Lancet 2021; Spicka I, ASCO 2021; Dimopoulos M al. Lancet. 2020; Moreau P. et al. Lancet 2021; Dimopoulos et al. Lancet 2021; Spicka I et al. Eur J Haematol 2022; Martin T. et al. Blood Cancer Journal 2023.

Pomalidomide-based regimens applicable from 2nd or 3rd line

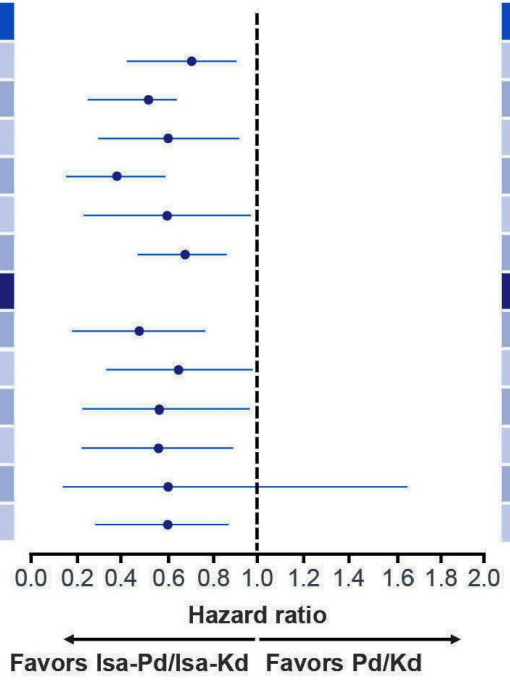
Trial	Arm	Len-refractory (%)	ITT population		Cytogenetics group PFS (months)		
			PFS (months)	Hazard ratio (95% CI)	HR	SR	Hazard ratio (95% CI)
ICARIA*[1,2]	**Isa-Pd**	94	11.1	0.60 (0.46-0.78)	**7.5**	11.6	**HR: 0.66** (0.33-1.28)
	Pd	92	5.9		3.7	7.4	SR: 0.62 (0.42-0.93)
APOLLO*[3]	**DPd**	79	12.4	0.63 (0.47-0.85)	**5.8**	21.0	**HR: 0.85** (0.49-1.44)
	Pd	80	6.9		4.0	7.4	SR: 0.51 (0.32-0.81)
OPTIMISMM‡[4,5]	**PVd**	71	11.2	0.61 (0.49-0.77)	**14.7** (1 prior LoT)	--	**HR: 0.39** (0.13-1.17)
	Vd	69	7.1		9.9 (1 prior LoT)	--	
ELOQUENT-3#[6]	**Elo-Pd**	90	10.3	0.54 (0.34-0.86)	**6.5**	NE	**HR: 0.52** (0.22-1.25)
	Pd	84	4.7		2.5	4.9	SR: 0.56 (0.27-1.14)

1. Harrison Sj et al, Br J Haematol. 2021; 2. Richardson PG, et al, The Lancet Oncology. 2022;
3. Dimopoulos MA, et al, The Lancet Oncology. 2021;
4. Richardson PG, et al, European Journal of Haematology. 2021; 5. Richardson PG, et, The Lancet Oncology, 2019
6. Dimopoulos MA et al, N Engl J Med 2018.

*Prepecified subgroup analysis
‡Post-hoc subgroup analysis
#Exploratory subgroup analysis
--Not reported

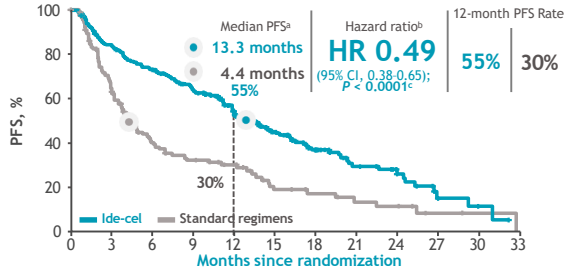
1q+ subgroups

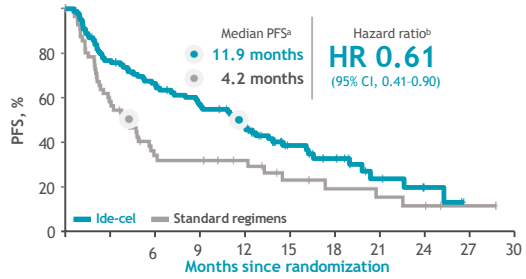
1q21+ subgroup	Event rate (n/N)		Median (mo)		Hazard ratio (95% CI)
ICARIA-MM	Isa-Pd	Pd	Isa-Pd	Pd	ICARIA-MM
Standard risk	50/103	48/78	11.6	7.4	0.62 (0.42–0.93)
1q21+	41/76	37/52	9.5	3.8	0.40 (0.25–0.63)
Isolated 1q21+	32/56	20/29	11.2	4.6	0.50 (0.28–0.88)
Gain(1q21)	22/49	23/31	13.3	4.3	0.32 (0.17–0.59)
Amp(1q21)	19/27	14/21	8.9	2.3	0.49 (0.24–0.99)
All patients	73/154	89/153	11.5	6.5	0.60 (0.44–0.81)
IKEMA	Isa-Kd	Kd	Isa-Kd	Kd	IKEMA
Standard risk	14/65	20/43	NC	20.3	0.40 (0.20–0.79)
1q21+	26/75	26/52	NR	16.2	0.57 (0.33–0.98)
Isolated 1q21+	13/47	15/31	NC	16.2	0.46 (0.22–0.97)
Gain(1q21)	12/43	19/37	NC	18.2	0.46 (0.22–0.94)
Amp(1q21)	14/32	7/15	18.8	13.2	0.69 (0.28–1.71)
All patients	48/179	55/123	NC	19.2	0.53 (0.32–0.89)*

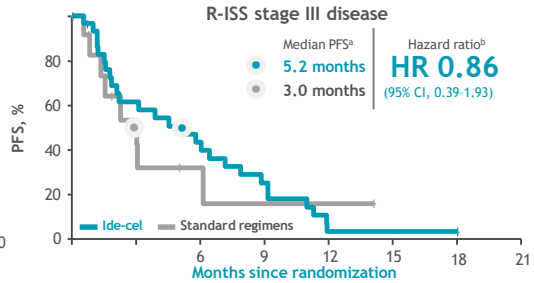


Martin T et al, Haematologica 2022

Ide-cel versus standard regimens in patients with TCE RRMM: a KarMMa-3 analysis in high-risk subgroups

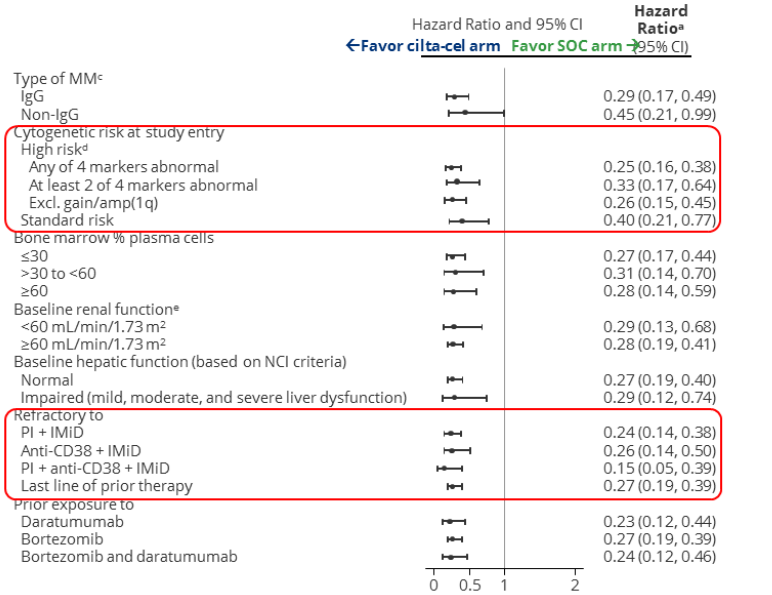






Cilta-cel Versus Standard of Care (PVd or DPd) in Lenalidomide-Refractory MM: CARTITUDE-4 Subgroup Analysis (ITT)

median follow-up was 15.9 months (range, 0.1–27)



Rodríguez-Otero P, et al. N Engl J Med 2023;388:1002–1014; Patel K et al. EHA 2023

Dhakal, B, et al. ASCO 2023. LBA106

COCLUSION AND OPEN ISSUES

- Treatment regimens that consistently overcome the poor prognosis of HR MM remain to be found
  - There is a need to harmonise the definition of HR patients in future clinical trials, need for a consensus, maybe different MM entities
- The goal of treatment should be to achieve and sustain MRD negativity
- Double ASCT improves outcomes in patients with HR cytogenetic abnormalities vs single ASCT.
  - Role of double ASCT vs newer quadruplets + single ASCT or vs alternative strategies (i.e. T-cell redirecting therapies)? Maybe tailored upon MRD status?
- The addition of anti-CD38 antibodies has improved treatment outcomes for HR TE or TI NDMM
  - PFS is still shorter particularly in ultra HR disease
- Triplets combinations of PIs, IMiDs, and MoAbs versus doublets showed positive results in HR RRMM patients, albeit less pronounced than standard risk
  - Improvement and not an abrogation of the unfavorable impact of genetic alterations
- Quadruplet regimens and emerging treatments, including CAR-T cell therapies and BsAbs, may provide a benefit

Thanks!

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