

Existe “POD24: no mieloma múltiplo: como manusear?

Prof. Angelo Maiolino MD, PhD

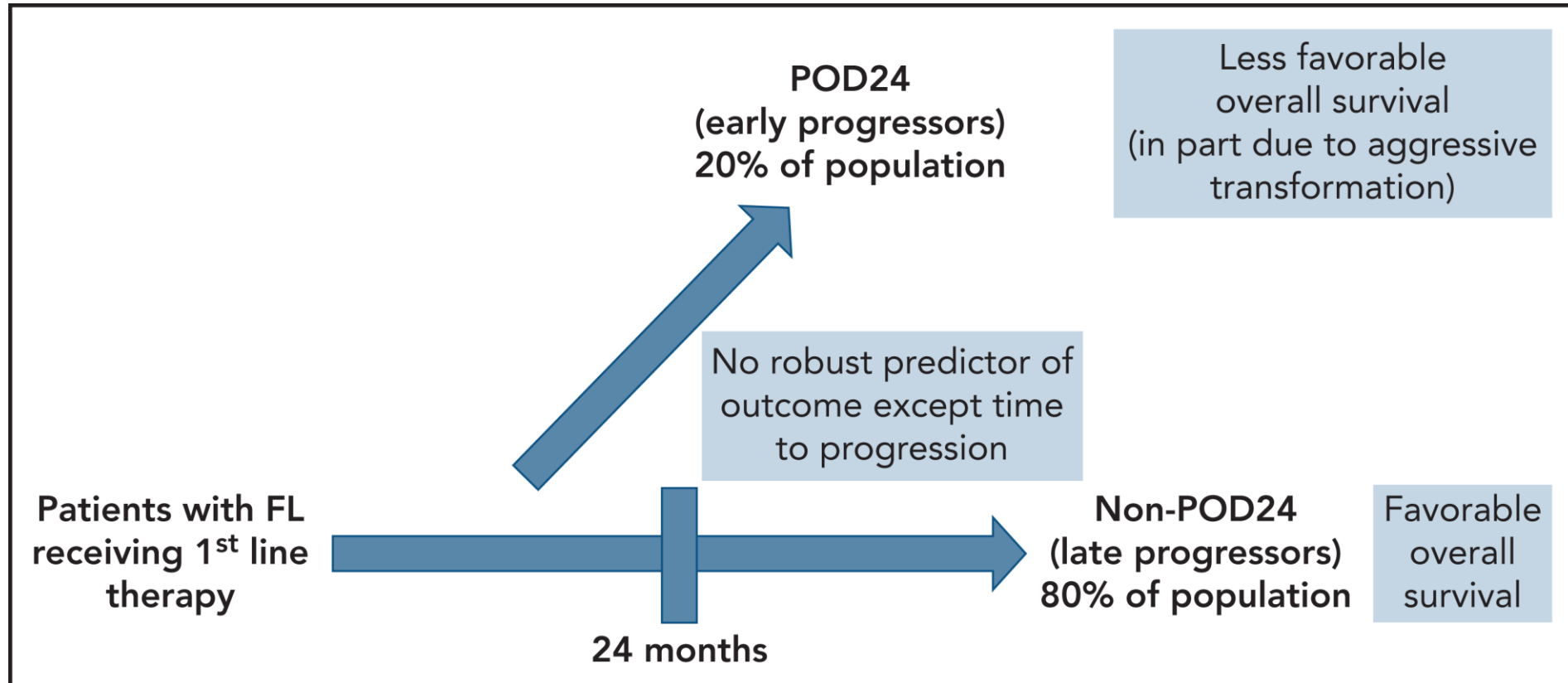
- Professor of Medicine, Universidade Federal do Rio de Janeiro.
- Director, Hematology Service, Oncologia Américas, Rio de Janeiro
- Scientific Coordinator , Instituto Americas
- Vice - President , Grupo Brasileiro de Mieloma Múltiplo – GBRAM
- Member of The International Myeloma Working Group
- President , Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular (ABHH)



Disclosure:

- Consultancy: Janssen, Takeda, Amgen, BMS- Celgene, Sanofi, Novartis, Pfizer, Astra Zeneca
- Research Funding: not applicable
- Honoraria: Janssen, Takeda, Amgen, BMS- Celgene, Sanofi, Novartis, Pfizer, Astra Zeneca
- Patents and Royalties: not applicable
- Membership on an Entity's Board of Directors or Advisory Committees: President Associação Brasileira de Hematologia e Hemoterapia (ABHH) / Member of International Myeloma Working Group
- Discussion of off-label drug use: not applicable

POD24 in follicular lymphoma



Impact of achieving a complete response to initial therapy of multiple myeloma and predictors of subsequent outcome

Marcella Kaddoura¹ | Moritz Binder¹ | David Dingli¹ | Francis K. Buadi¹ |
Martha Q. Lacy¹ | Morie A. Gertz¹ | Angela Dispenzieri¹ | Prashant Kapoor¹ |
Lisa Hwa¹ | Amie Fonder¹ | Miriam Hobbs¹ | Suzanne Hayman¹ |
Nelson Leung² | Ronald S. Go¹ | Yi Lin¹ | Wilson Gonsalves¹ |
Taxiarchis Kourelis¹ | Rahma Warsame¹ | Robert A. Kyle¹ |
Vincent Rajkumar¹ | Shaji Kumar¹

This is a retrospective, pragmatic study investigating the prognostic impact of achievement of CR within 24 months from diagnosis in newly diagnosed MM (NDMM) patients and the impact of known prognostic variables, including FISH and ISS risk in this context. We also describe additional predictors of outcome among this subgroup of patients.

TABLE 1 Patient characteristics at baseline

Variable	All, N = 1868	CR by 24 months, N = 461	No CR by 24 months, N = 1408	p Value
Baseline characteristics				
Age	63 (27–95)	61 (27–89)	64 (28–95)	
Males	1122 (60%)	251 (54%)	871 (62%)	
HR FISH	291/1317 (22%)	76/315 (24%)	215/1002 (21%)	.35
ISS stage III	362/1213 (30%)	89/305 (29%)	273/908 (30%)	.83
BMPC%	50% (1%–100%)	50% (1%–100%)	50% (1%–100%)	.41
Serum M protein	2.3 (0–10.5)	1.3 (0–10)	2.6 (0–10.5)	<.0001
sFLC ratio	15 (IQR: 0.04–180)	7.4 (IQR: 0.03–112)	17.7 (IQR: 0.04–193)	.21
Non-IgG involved heavy chain	326/1083 (30%)	103/249 (41%)	223/834 (27%)	<.0001
Treatments				
Triplet induction regimen	892/1858 (48%)	267/459 (58%)	625/1399 (45%)	<.0001
PI + IMiD + steroid	377 (20%)	126 (27%)	251 (18%)	<.0001
Alkylator + PI + steroid	399 (21%)	117 (25%)	282 (20%)	.02
Anti-CD38 based therapy	3 (0.2%)			
Quadruplet induction regimen	46 (2.5%)	7 (1.5%)	39 (2.8%)	
Doublet (PI or IMiD + steroid)	714 (38%)	158 (34%)	556 (40%)	.046
ASCT first-line	930 (50%)	308 (67%)	622 (44%)	<.0001
Response				
CR within 24 months	461/1868 (25%)			
CR within 4 months		25/461 (5.4%)		
CR within 12 months		302/461 (66%)		
Time to CR in months		9.9 (0.2–23.8)		
CR after 24 months			136/1141 (12%)	
VGPR			492/1141 (43%)	
PR			358/1141 (31%)	
Less than PR			155/1141 (14%)	

Note: Age, BMPC percentage, serum M spike, sFLC ratios, time to CR from diagnosis, and duration of CR (time from CR to PD) are reported as median (range). Gender, ISS stage III, high-risk FISH, non-IgG involved heavy chain, CR within specified time points, ASCT first-line (transplant within 12 months from first-line therapy initiation), and triplet induction therapy received data are reported as number of patients among the entire cohort with available prognostic data per variable (percentage).

Abbreviations: ASCT, autologous stem cell transplant; BMPC, bone marrow plasma cells; CR, complete response; FISH, fluorescence in situ hybridization; IgG, immunoglobulin G; IMiD, immunomodulatory agent; IQR, interquartile range; ISS, International Staging System; PI, proteasome inhibitor; PR, partial response; sFLC, serum free light chain; VGPR, very good partial response.

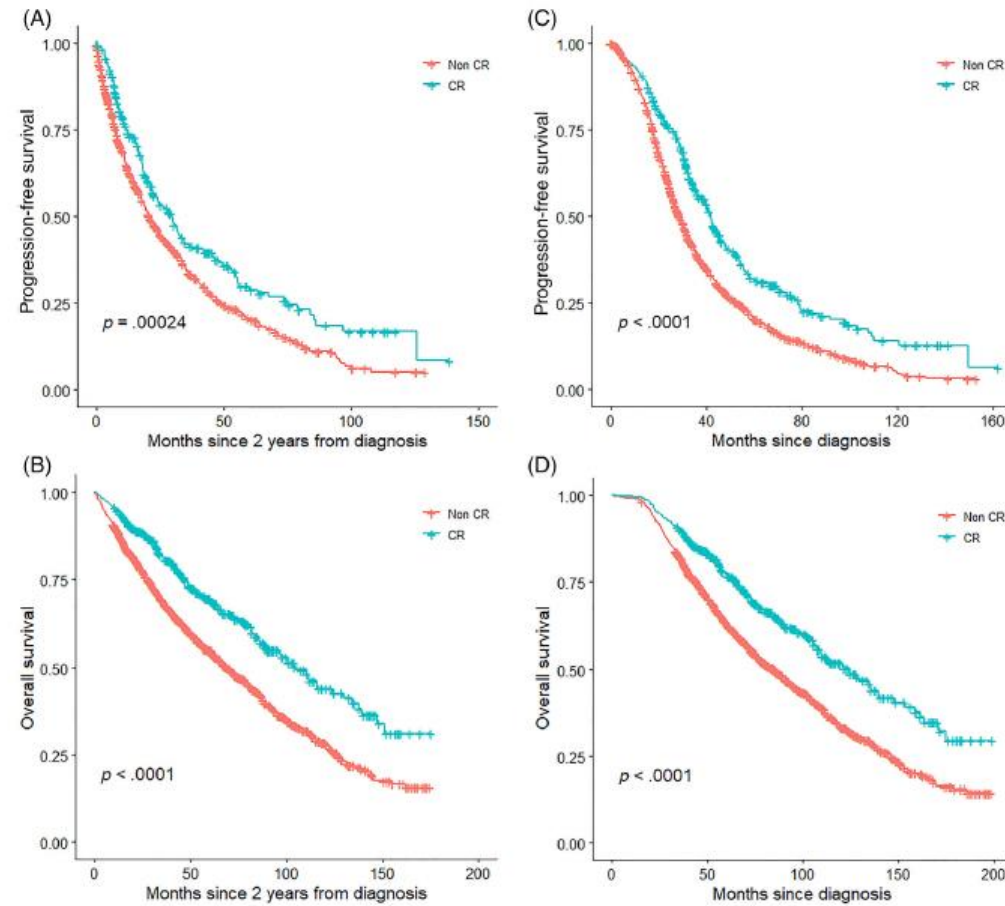


FIGURE 1 Kaplan–Meier plot comparing PFS (A and C) and OS (B and D) based on achievement of CR within 24 months from diagnosis. (A) Landmark analysis at 2 years from diagnosis; CR median PFS 29.8 months; non-CR median PFS 20.9 months. (B) Landmark analysis at 24 months from diagnosis; CR median OS 104 months; non-CR median OS 70 months. (C) CR median PFS 42 months; non-CR median PFS 29.3 months. (D) CR median OS 124 months; non-CR median OS 85.6 months. CR, complete response; [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Multivariable analysis using cox proportional hazards model, adjusting for ISS, FISH, gender, non-IgG involved heavy chain, and ASCT received in the first-line setting

Variable	PFS		OS	
	Hazard ratio	<i>p</i>	Hazard ratio	<i>p</i>
CR within 24 months	0.56 (0.42–0.74)	<.0001	0.52 (0.37–0.73)	.0001
ISS stage III	1.24 (0.93–1.65)	.14	1.4 (1.0–1.9)	.04
High-risk FISH	1.64 (1.20–2.25)	.002	1.90 (1.37–2.65)	.0001
Male	1.17 (0.91–1.50)	.22	1.32 (1.0–1.8)	.05
Non-IgG MM	1.28 (0.99–1.66)	.06	1.2 (0.9–1.6)	.21
ASCT first line	0.82 (0.64–1.1)	.13	1.21 (0.89–1.6)	.22
IMiD + PI + steroid based induction regimen	0.65 (0.45–0.93)	.018	0.88 (0.62–1.26)	.50

Abbreviations: ASCT, autologous stem cell transplant; CR, complete response; FISH, fluorescence in situ hybridization; IgG, immunoglobulin G; IMiD, immunomodulatory agent; ISS, International Staging System; MM, multiple myeloma; PFS, progression-free survival; PI, proteasome inhibitor; OS, overall survival.

TABLE 3 Univariate analysis using cox proportional hazards model with hazard ratios, comparing best response achieved by 24 months from diagnosis (CR vs. non-CR)

CR status by 24 months	PFS		OS	
	High-risk FISH	ISS 3	High-risk FISH	ISS 3
CR achieved	1.06 (0.71-1.6; $p = .78$)	0.96 (0.68-1.36; $p = .84$)	1.06 (0.70-1.63; $p = .77$)	1.42 (0.97-2.1; $p = .07$)
CR not achieved	1.72 (1.39-2.1; $p < .0001$)	1.54 (1.28-1.84; $p < .0001$)	1.46 (1.19-1.8; $p < .001$)	1.79 (1.48-2.15; $p < .001$)

Abbreviations: CR, complete response; FISH, fluorescence in situ hybridization; ISS, International Staging System; OS, overall survival; PFS, progression-free survival.

Achievement of CR within 2 years from diagnosis is associated with improvement in clinical outcomes.

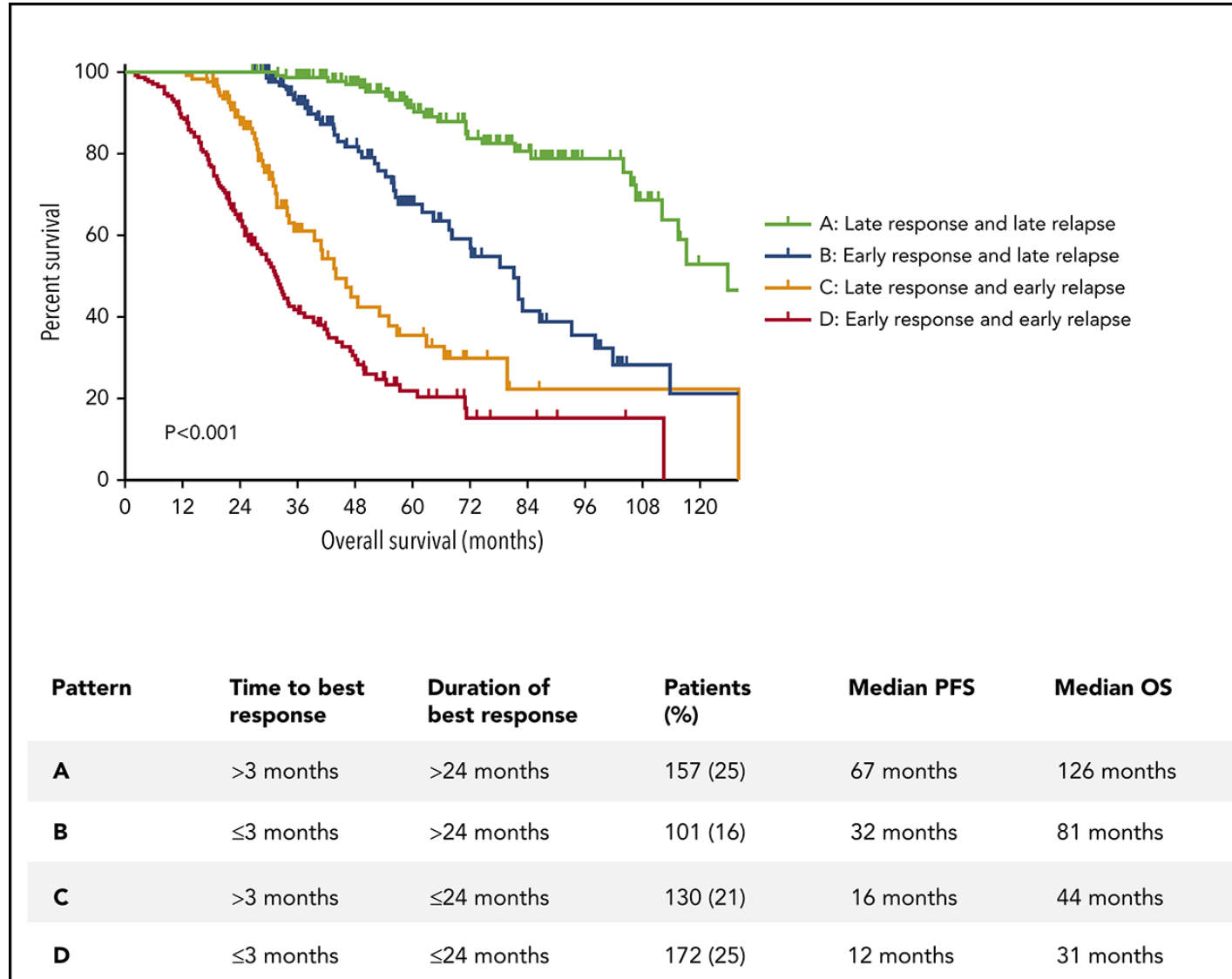
This benefit was irrespective of front-line ASCT status, cytogenetics and FISH risk, and ISS stage.

Patients achieving a CR were more likely to receive triplet induction therapy and ASCT in the first-line setting, and had lower serum monoclonal protein levels at diagnosis.

Moreover, the achievement of a CR neutralizes the prognostic impact of baseline FISH and ISS stage risk stratification.


Predictors for inferior survival among the CR cohort include age > 75 years, male gender, hypoalbuminemia at the time of CR, and non-IgG involved heavy chain.

The impact of response kinetics for multiple myeloma in the era of novel agents



Yuting Yan, Xuehan Mao, Jiahui Liu, Huishou Fan, Chenxing Du, Zengjun Li, Shuhua et.al., The impact of response kinetics for multiple myeloma in the era of novel agents, Blood Adv, 2019,

Original Study

 Check for updates

Predictors and Impact of Timing of Disease Progression Following Primary Therapy in Multiple Myeloma

Sarah Goldman-Mazur,¹ Alissa Visram,^{1,2} S. Vincent Rajkumar,¹ Prashant Kapoor,¹ Angela Dispenzieri,¹ Martha Q. Lacy,¹ Morie A. Gertz,¹ Francis K. Buadi,¹ Suzanne R. Hayman,¹ David Dingli,¹ Taxiarchis Kourelis,¹ Wilson Gonsalves,¹ Rahma Warsame,¹ Eli Muchtar,¹ Nelson Leung,³ Robert A. Kyle,¹ Shaji K. Kumar¹

Our primary objective was to contrast baseline characteristic, management and outcome of short and long PFS patients. We also aimed to describe whether the influence of relapse-free period on survival is independent from cytogenetic risk. We focused on patients treated in real-world settings.

Figure 1 Survival estimates in 1557 treated patients with multiple myeloma stratified by duration of PFS from diagnosis into short (PFS <2 years), PFS between 2 and 5 years and long (PFS >5 years). Panel A presents overall survival (OS) from the time of diagnosis for 3 main subgroups. Panel B presents additional stratification of the above groups into standard cytogenetic risk (SR, continuous lines) and high cytogenetic risk (HR, dashed lines) according to fluorescent in situ hybridization (FISH) results. HR FISH was defined as presence of deletion 17p and/or translocation t(4;14) and/or t(14;16) and/or t(14;20). CI = confidence interval.

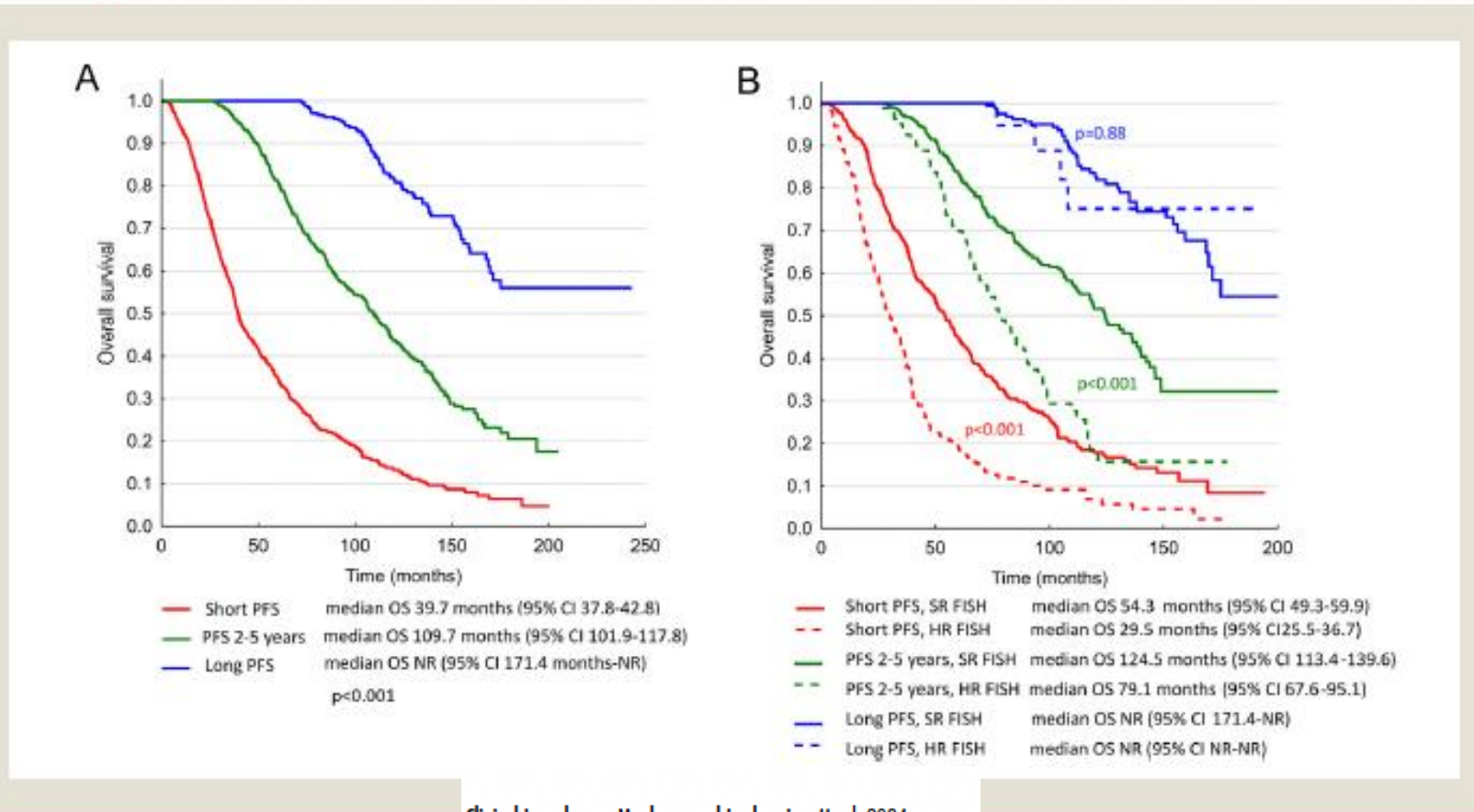


Table 3 Multivariable Logistic Regression Model for Short (<2 Years) and Long (>5 Years) PFS

Variable	Short PFS				Long PFS			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Sex, male	1.16 (0.95-1.42)	.15	0.84 (0.52-1.35)	.47	0.78 (0.59-1.04)	.09	0.981 (0.53-1.79)	.94
Age > 65 years	1.20 (0.98-1.47)	.08	0.75 (0.46-1.22)	.24	0.85 (0.64-1.13)	.26	0.59 (0.32-1.10)	.10
Bone marrow infiltration	1.011 (1.007-1.015)	<.001	0.99 (0.98-1.00)	.18	0.987 (0.982-0.992)	<.001	1.010 (0.997-1.014)	.14
Plasma cells in S-phase ≥2%	2.54 (1.78-3.62)	<.001	1.97 (1.10-3.56)	.02	0.41 (0.23-0.74)	.003	0.88 (0.38-2.02)	.77
Abnormal cytogenetics	2.15 (1.66-2.79)	<.001	1.66 (0.97-2.83)	.06	0.43 (0.28-0.66)	<.001	0.87 (0.43-1.76)	.71
High risk FISH at diagnosis	1.96 (1.48-2.59)	<.001	3.28 (1.79-6.00)	<.001	0.37 (0.22-0.61)	<.001	0.15 (0.04-0.54)	.003
Extramedullary plasmacytoma at diagnosis	1.62 (1.20-2.20)	.002	3.80 (1.79-8.09)	.001	0.74 (0.47-1.16)	.19	-	
IgG isotype at diagnosis	0.74 (0.60-0.90)	.003	0.45 (0.27-0.75)	.002	1.63 (1.22-2.18)	<.001	2.86 (1.51-5.42)	.001
Anemia at diagnosis	1.35 (1.09-1.69)	.007	0.90 (0.51-1.60)	.73	0.54 (0.38-0.76)	<.001	0.80 (0.38-1.70)	.56
Hypercalcemia at diagnosis	1.98 (1.41-2.79)	<.001	0.94 (0.35-2.56)	.91	0.54 (0.31-0.96)	.03	0.71 (0.17-2.98)	.64
Renal insufficiency at diagnosis	1.69 (1.26-2.26)	<.001	1.38 (0.56-3.42)	.49	0.43 (0.25-0.73)	.002	1.77 (0.44-7.12)	.42
Serum beta-2-microglobulin	1.039 (1.018-1.061)	<.001	1.03 (0.96-1.12)	.40	0.93 (0.89-0.97)	.001	0.92 (0.80-1.06)	.26
Elevated lactate dehydrogenase	2.19 (1.57-3.04)	<.001	1.30 (0.64-2.64)	.47	0.46 (0.26-0.80)	.006	0.99 (0.39-2.51)	.98
Stage 3 ISS	1.81 (1.43-2.28)	<.001	0.90 (0.48-1.80)	.76	0.56 (0.39-0.80)	.002	1.40 (0.50-3.94)	.52
PI-based first line therapy	1.58 (1.26-1.99)	<.001	1.46 (0.75-2.85)	.26	0.36 (0.24-0.54)	<.001	0.44 (0.17-1.11)	.08
IMiD-based first line therapy	0.61 (0.50-0.75)	<.001	0.61 (0.34-1.12)	.11	2.19 (1.66-2.90)	<.001	1.17 (0.58-2.37)	.67
Lenalidomide maintenance	0.57 (0.43-0.77)	<.001	0.60 (0.32-1.15)	.12	1.36 (0.94-1.96)	.11	-	
Upfront ASCT	0.32 (0.26-0.39)	<.001	0.29 (0.17-0.50)	<.001	1.68 (1.27-2.23)	<.001	1.49 (0.79-2.80)	.22
≥VGPR after first line therapy	0.29 (0.23-0.36)	<.001	0.25 (0.15-0.42)	<.001	3.02 (2.16-4.23)	<.001	2.99 (1.54-5.79)	.001

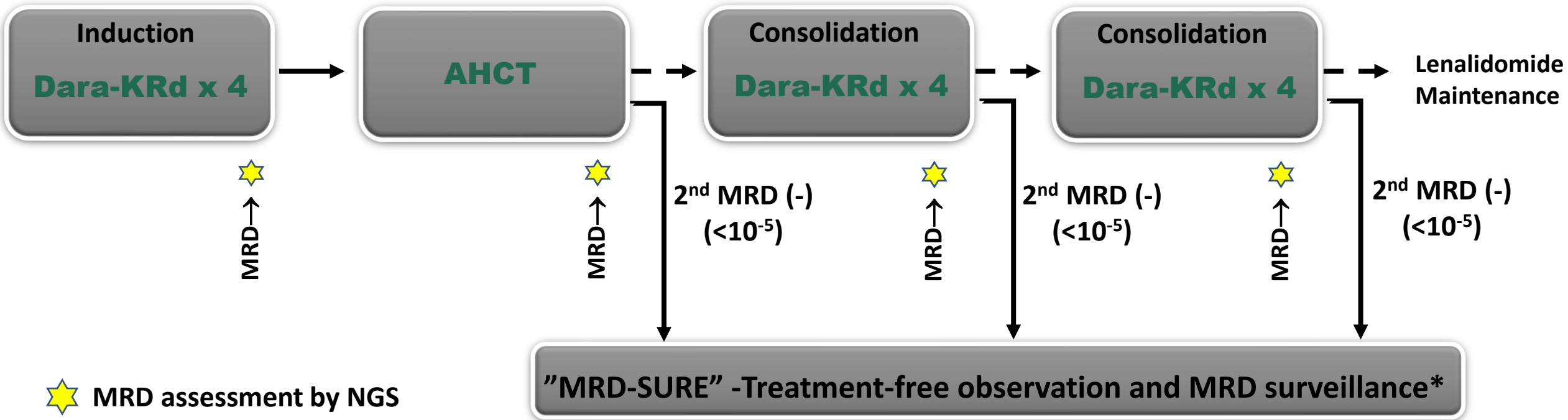
Abbreviations: ASCT = autologous stem cell transplantation; CI = confidence interval; FISH = fluorescence in situ hybridization; IgG = immunoglobulin G; IMiD = immunomodulatory drugs; ISS = International Staging System; OR = odds ratio; PI = proteasome inhibitors; VGPR = very good partial remission.

Clinical Practice Points

- Short (<2 years) and long (>5 years) PFSs in MM patients are strong predictors of better and worse post-progression outcomes.
- Short PFS has a strong negative influence on survival, irrespective of cytogenetic risk.
- The information on relapse-free period should be an important parameter in stratifying patients at relapse and should be included in the randomization and analysis process in clinical trials, especially those on relapsed MM patients.
- The achievement of at least VGPR should be a primary goal for every patient.

MRD-Guided Treatment Augmentation and Cessation- MASTER Trial

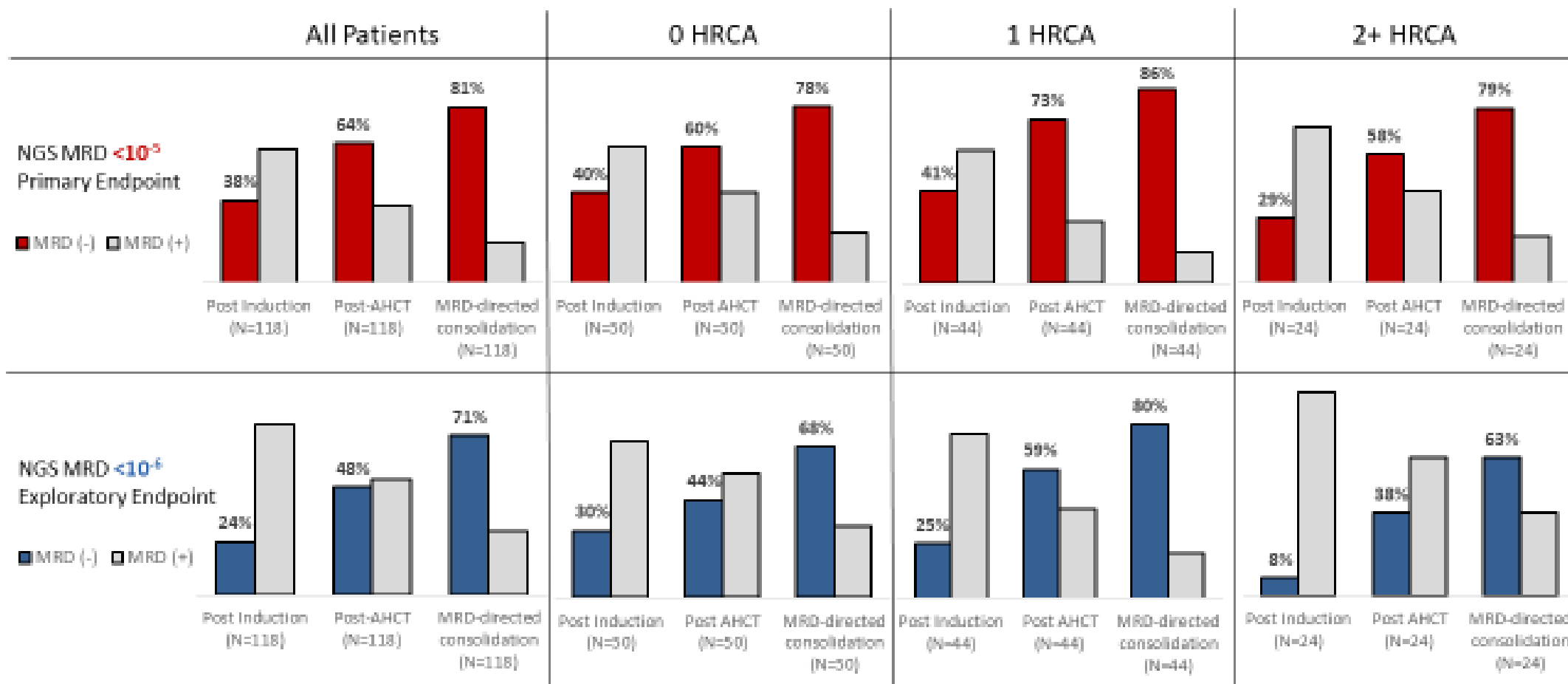
Phase 2: D-KRd + AHCT with MRD-guided cessation in patients with NDMM



*24 and 72 weeks after completion of therapy

MRD-Guided Treatment Augmentation and Cessation- MASTER Trial

Phase 2: D-KRd + AHCT with MRD-guided cessation in patients with NDMM

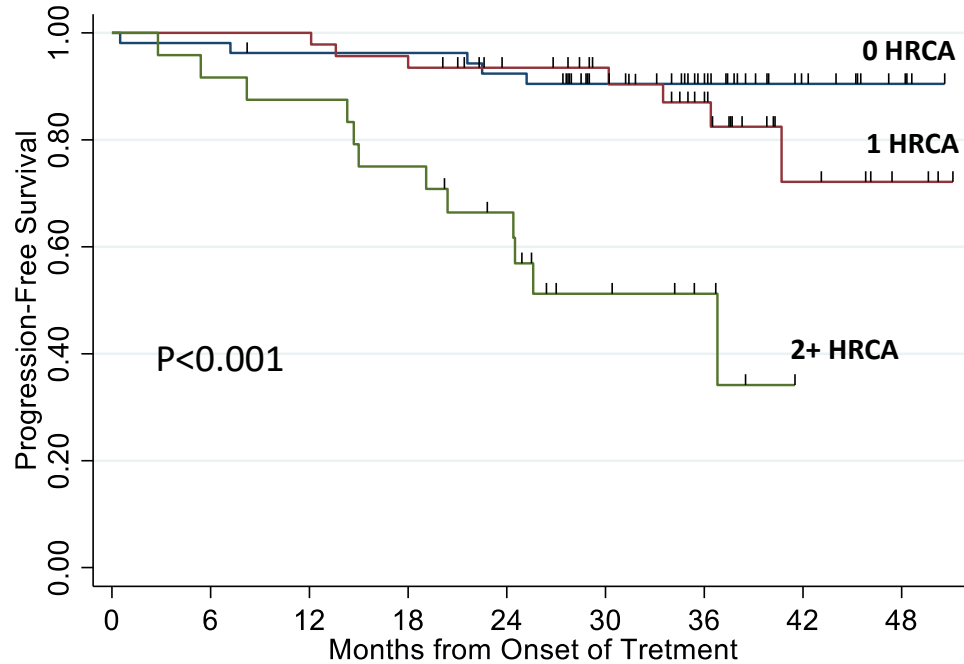


HRCA = gain/amp 1q, t(4;14), t(14;16), t(14;20) or del(17p)

MRD-Guided Treatment Augmentation and Cessation- MASTER Trial

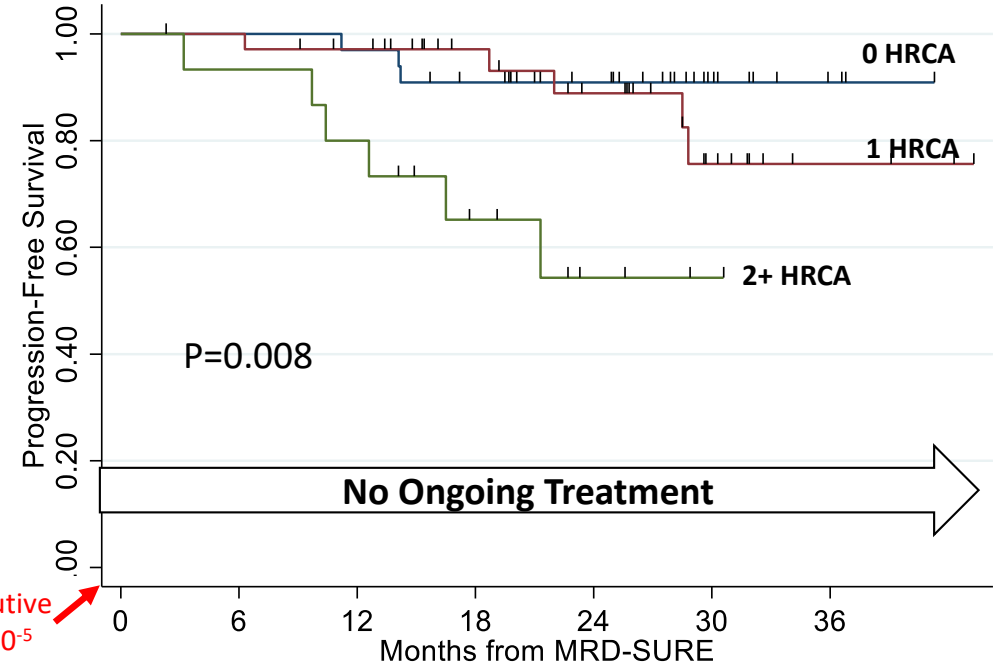
Phase 2: D-KRd + AHCT with MRD-guided cessation in patients with NDMM

PFS – All Patients (N=123)



Number at risk	0	6	12	18	24	30	36	42	48
0 HRCA	53	52	50	50	48	35	25	10	4
1 HRCA	46	46	46	44	35	30	20	7	3
2+ HRCA	24	22	21	18	14	7	4	0	0

PFS – Patients in MRD-SURE (N=84)



2 consecutive MRD 10^{-5}

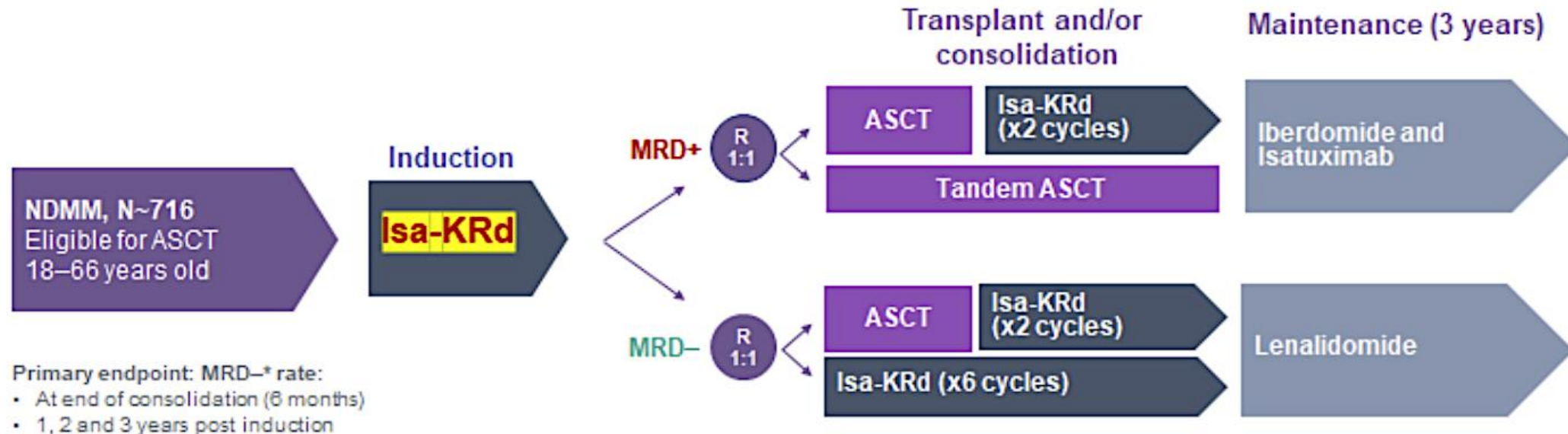
Number at risk	0	6	12	18	24	30	36
0 HRCA	33	33	32	28	20	9	3
1 HRCA	36	35	32	24	19	9	3
2+ HRCA	15	14	12	7	3	1	0

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

Median follow up 34.1 mo.

Treatment Augmentation and De-escalation – MIDAS TRIAL

Sponsor: Intergroupe Francophone du Myelome (IFM)
Estimated primary completion: September 2024

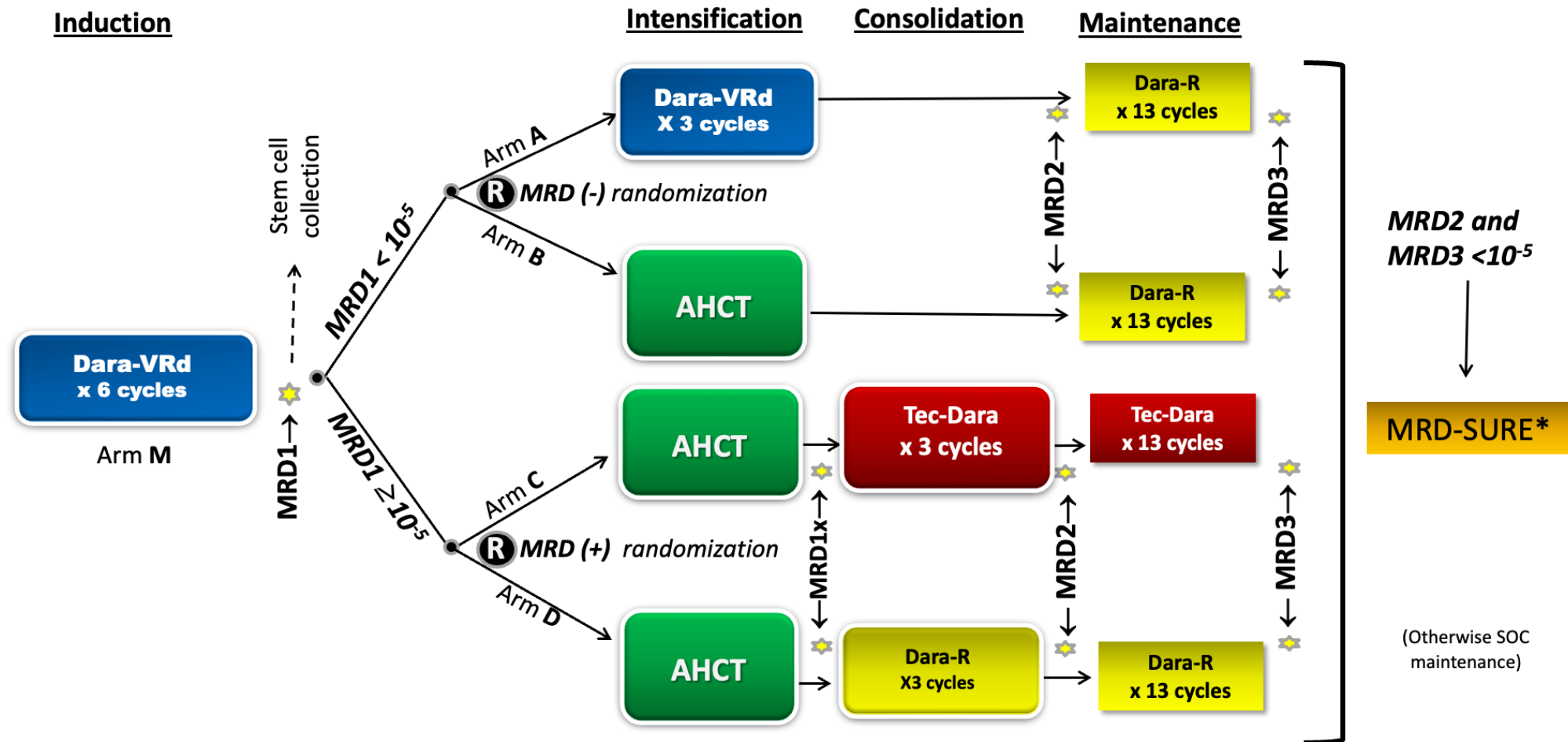


**Primary analysis will evaluate MRD (NGS, 10⁻⁴ threshold)*

Isa-KRd is an investigational combination that has not been approved by any regulatory authority. Sanofi does not recommend the use of their products outside the approved indication. Please consult your local label before prescribing

Courtesy and personal communication Prof Mohty

Treatment Augmentation and De-escalation– MASTER 2 Trial



★ MRD assessment by ClonoSEQ®

*MRD-SURE – Treatment-free observation and MRD surveillance

Personal communication Dr Costa

Conclusions:

Depth of response to therapy continues to serve as a valuable prognostic indicator on clinical outcomes

The availability of novel therapies and combinations in myeloma in the upfront setting has allowed for increasing CR rates, approaching 50% or more.

With CR rates on the rise, assessment of response kinetics in myeloma has gained attention and remains an area of debate,

The benefit of achieving a complete response (CR), including minimal residual disease (MRD) negativity in myeloma has been demonstrated to confer improvement in clinical outcomes, irrespective of the treatment used to achieve this desired state

Conclusions:

Is there “POD24: in multiple myeloma??

Not Exactly!

However, a dynamic better response can be correlated with patient treatment outcomes.



 **International
Myeloma Society**

**21ST ANNUAL
Meeting
& Exposition**

September 25-28, 2024 • Rio Centro
Rio De Janeiro, Brazil





OBRIGADO!

- angelomaiolino@americasoncologia.com.br
- [linkedin.com/in/angelo-maiolino-9748a7a0](https://www.linkedin.com/in/angelo-maiolino-9748a7a0)