

**In-depth look at specific data-sets; which
ones meet requirements?
Individual data 'owners'/cooperative
groups**

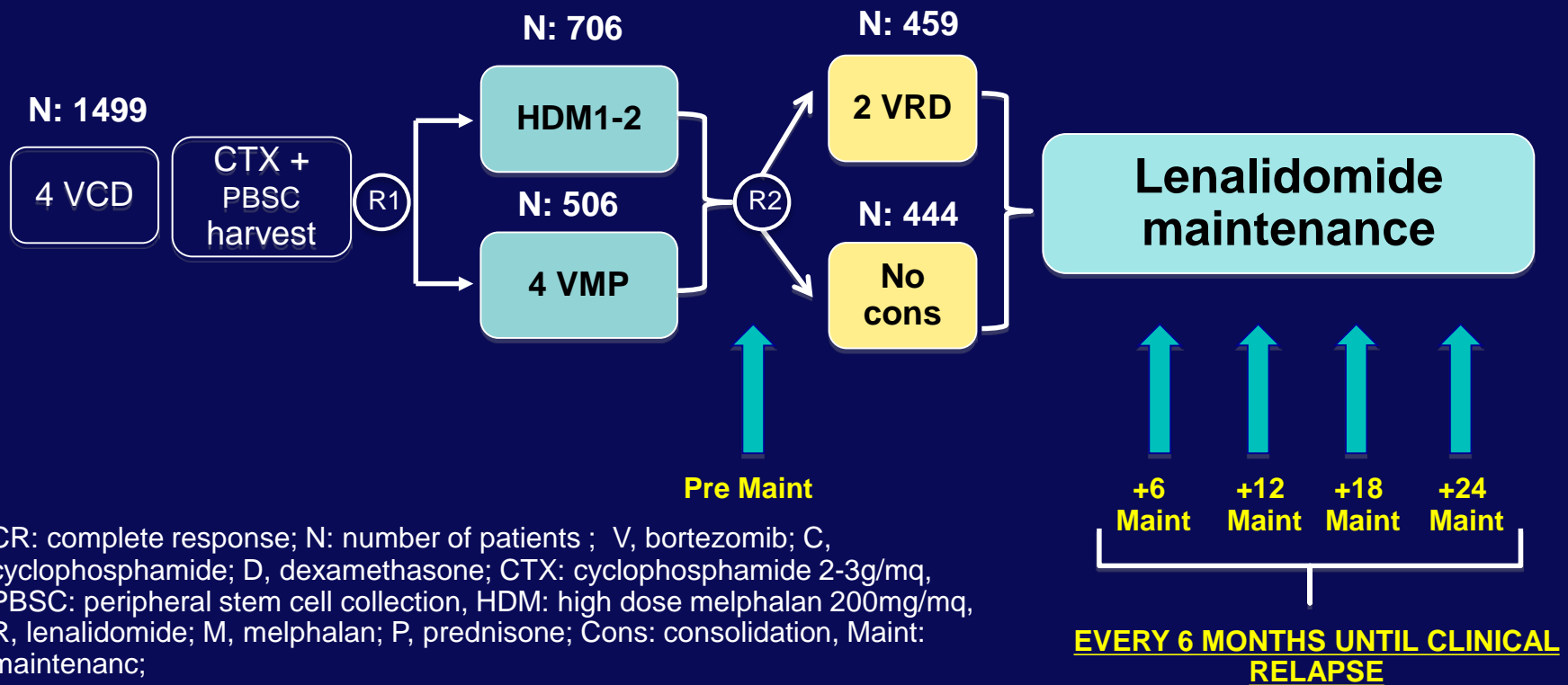
**Minimal Residual Disease (MRD) by
Multiparameter Flow Cytometry (MFC) in
transplant eligible patients with newly
diagnosed multiple myeloma (MM): results from
the EMN02/HO95 phase 3 trial**



Methods

MM patients enrolled in the RV-MM-COOP-0556 (EMN02/HO95 MM; NCT01208766)

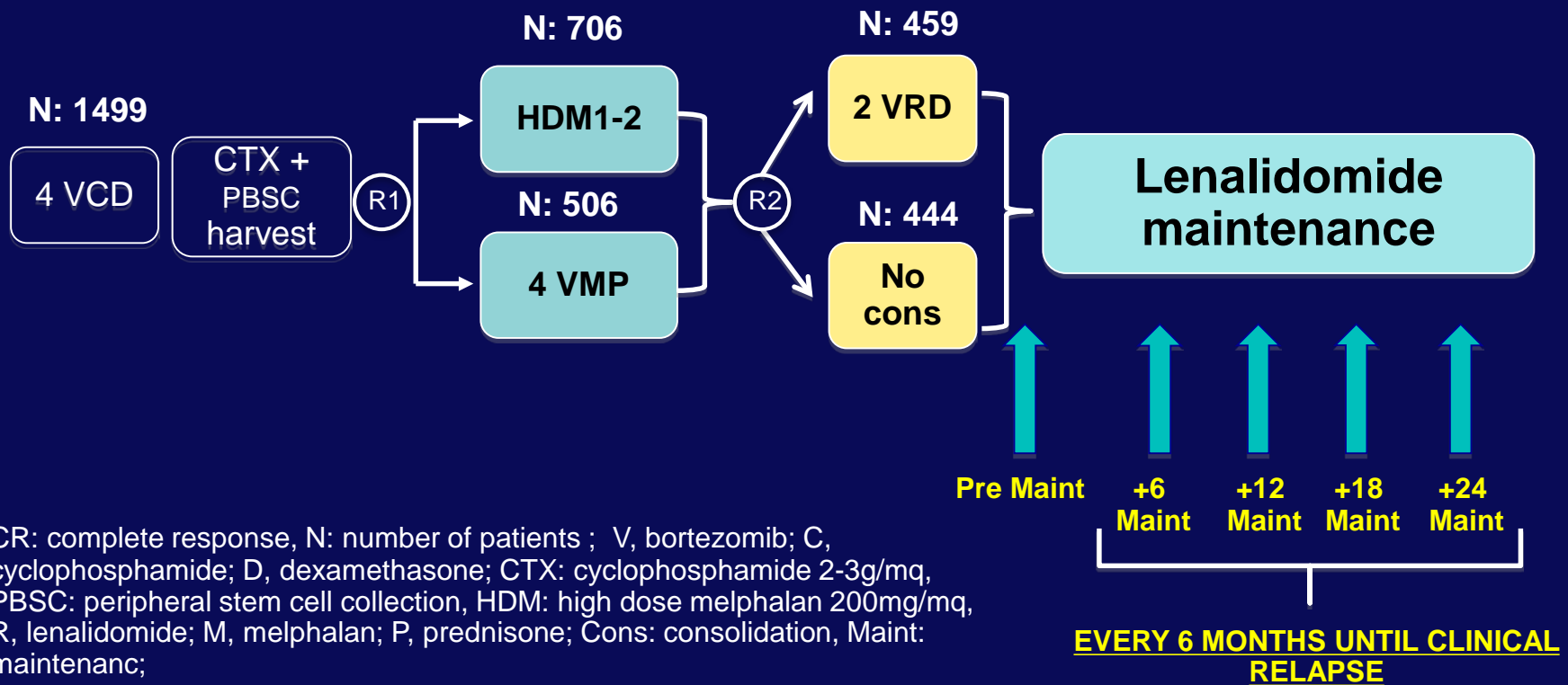
- Newly diagnosed ≤ 65 years
- MRD assesement in patients achieving suspected CR before lenalidomide maintenance



Methods

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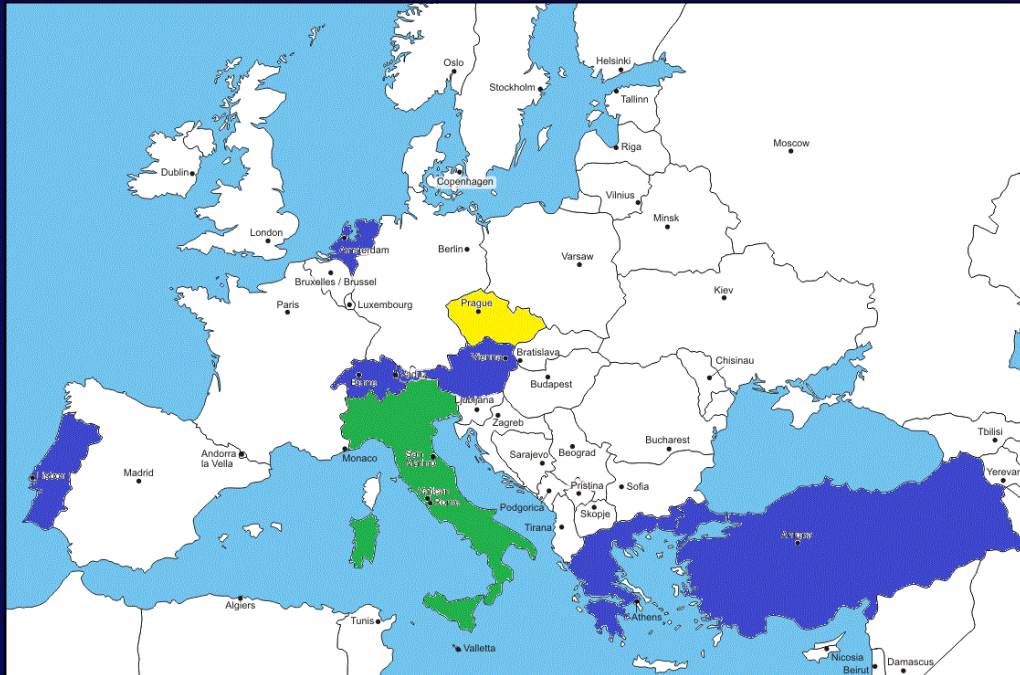
- Newly diagnosed ≤ 65 years
- MRD assesement in patients achieving suspected CR before lenalidomide maintenance



Methods

Sample logistics in the EMNO2 MRD study

Samples were centralized in 3 laboratories from 10 countries



2 workshops:

- 1) Orlando, (ASH) December 2015
- 2) Rotterdam, May 2016

 Brno, Czech republic


 Rotterdam, The Netherlands











 Turin, Italy

Methods




Tube 1:

Tube 2:

CD138		CD138	
CD38		CD38	
CD45		CD45	
CD19		CD19	

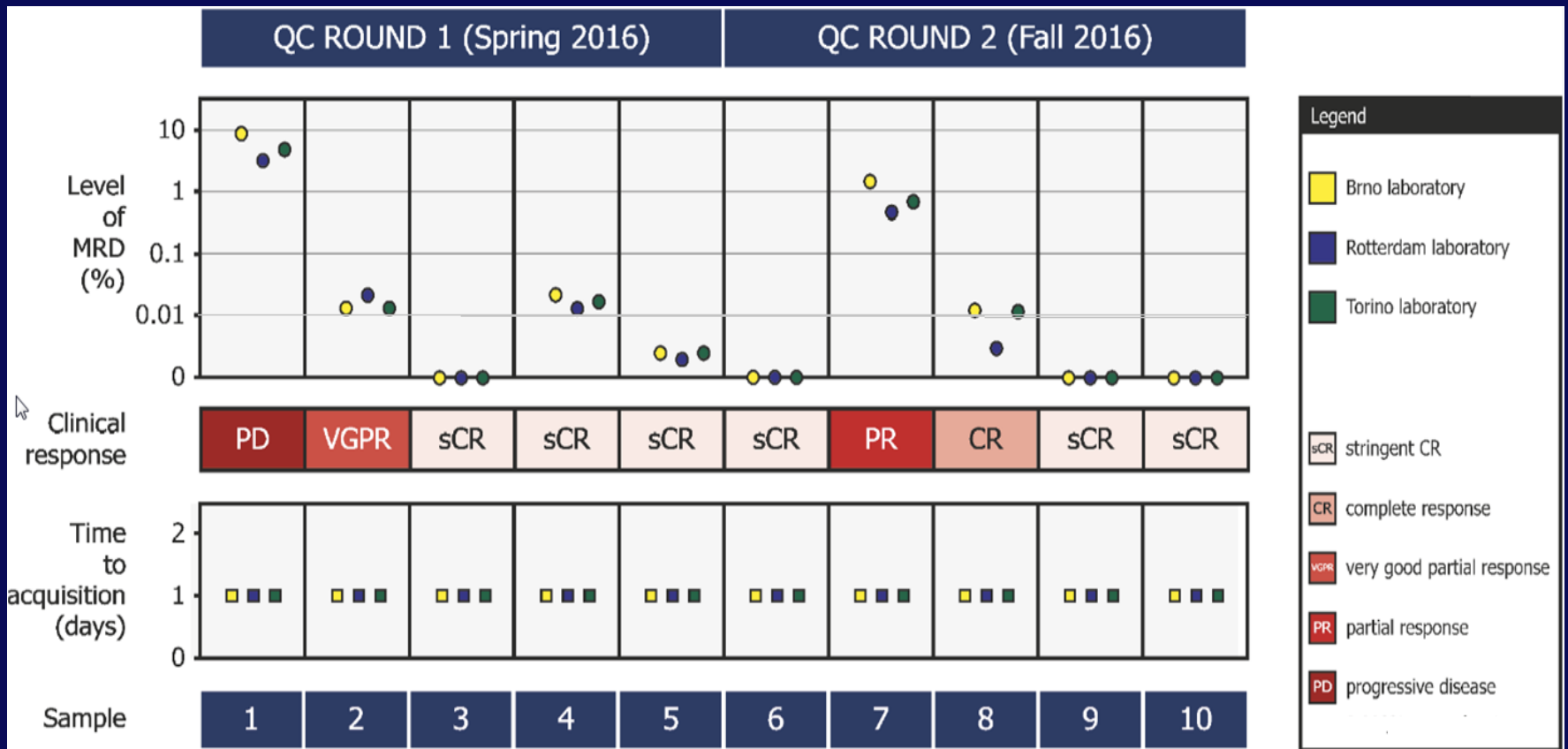
CD81		CD56	
CD27		CyIgk	
CD28		CyIgL	
CD117		CD117	
CD20		β2micro	

- Sampling: bone marrow
- Processation: within 24-48 hours
- Preparation: Bulk-lysis protocol (EuroFlow)
- Data acquisition: $\geq 2 \times 10^6$ leucocytes or $\geq 1 \times 10^4$ plasma cells
- Cut-off for MRD positivity: ≥ 20 clonal plasma cells
- Maximal sensitivity: 1×10^{-5}

 Brno, Czech republic
 Rotterdam, The Netherlands
 Turin, Italy

Results

Quality checks were done among the 3 European laboratories to compare sensitivity and to show correlation between protocols



Results

Patient characteristics

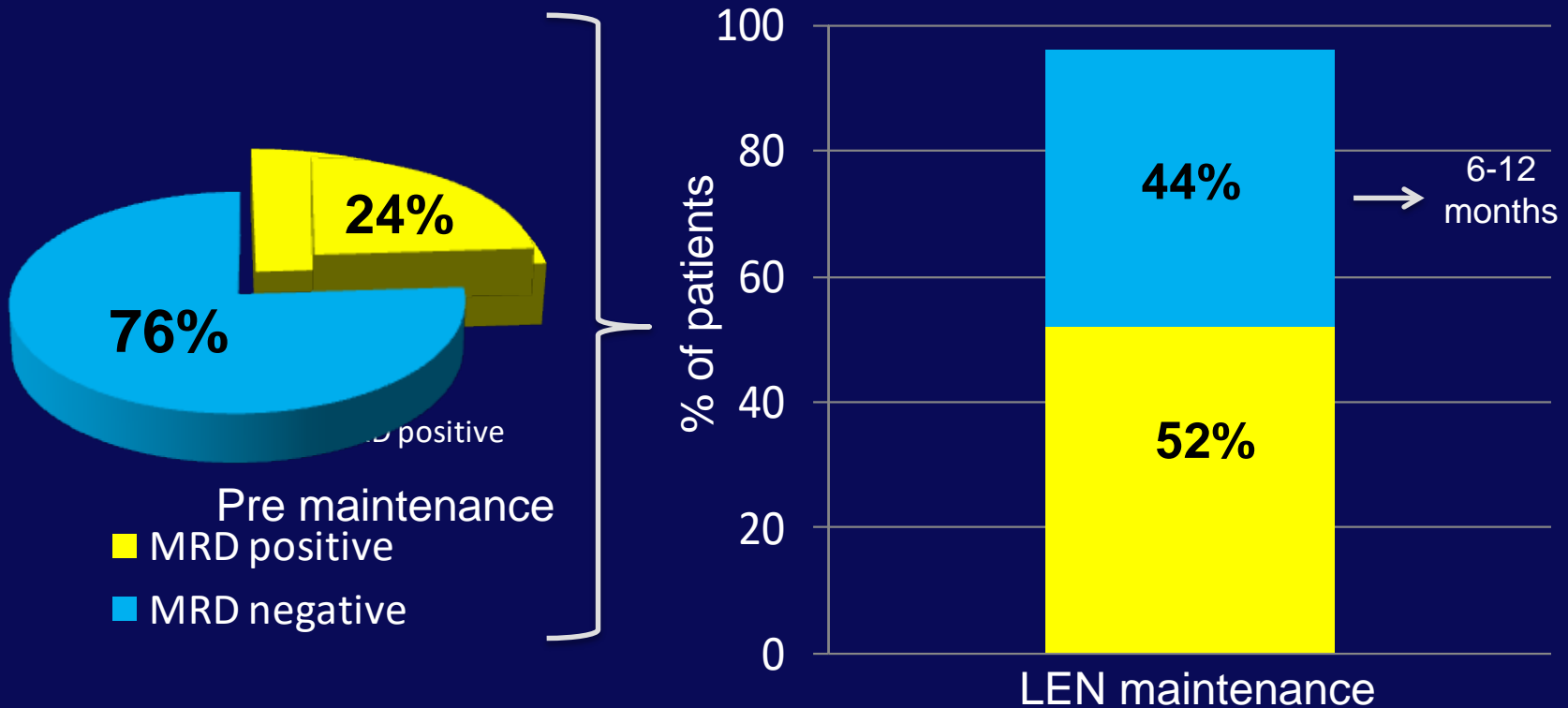
(n = 316)	
Age	
Median, yrs	57
Range (IQR)	52-62
ISS stage at diagnosis, N (%)	
I	139 (44)
II	120 (38)
III	57 (18)
FISH RISK, N (%)	
Standard	186 (52)
High	70 (22)
Missing	60 (19)
Random A, N (%)	
HDM1-2	199 (63)
VMP	117 (37)
Random B, N (%)	
VRD	160 (51)
no consolidation	144 (46)
off	12 (3)

IQR: interquartile range, ISS: International Staging System, FISH : fluorescence in situ hybridization , standard risk : del17 and t(4;14) and t(14; 16) negative, High risk: del17 and/or t(4;14) and/or t(14; 16) positive

Results

MRD status at pre-maintenance

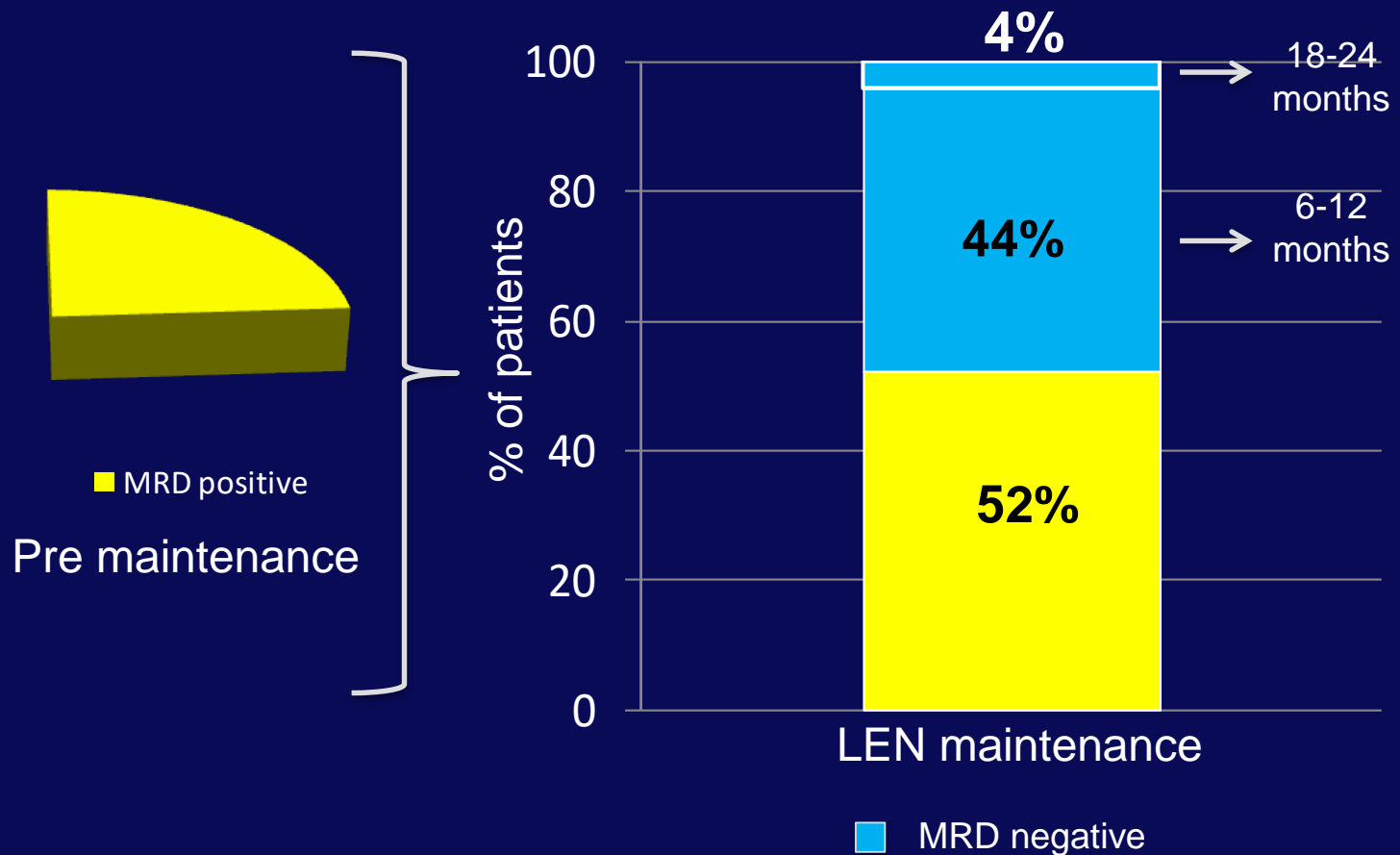
Sub-analysis on MRD positive patients at pre-maintenance who had a second MRD evaluation >1 year of Lenalidomide



Results

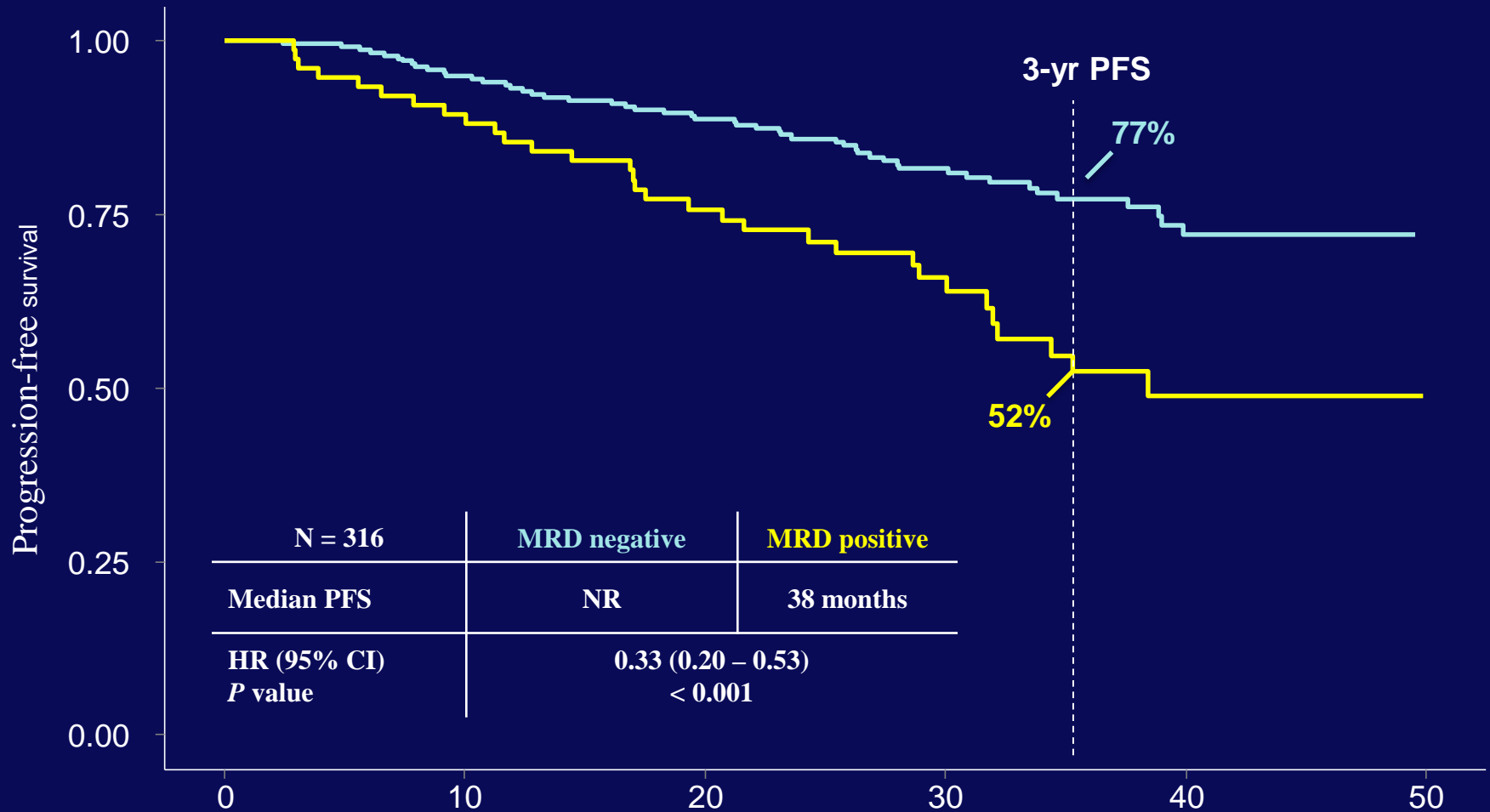
MRD status during maintenance

Sub-analysis on MRD positive patients at pre-maintenance who had a second MRD evaluation >1 year of Lenalidomide



Results

Progression free Survival: Median Follow-Up from MRD enrollement of 33 Months



Numbers at risk

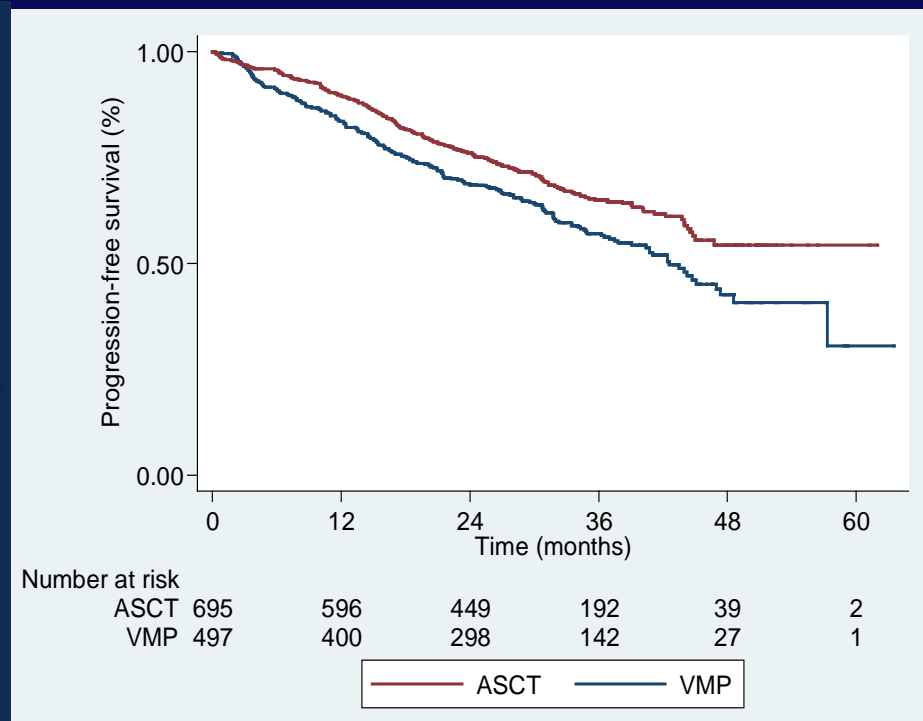
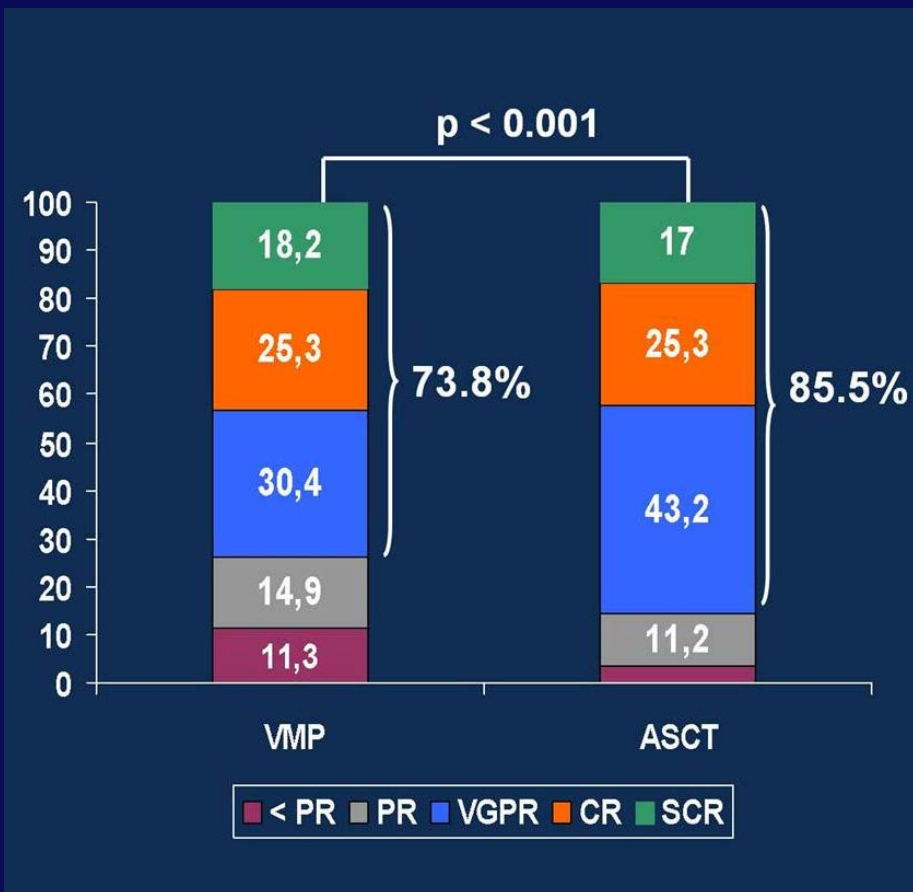
	0	10	20	30	40	50
MRD Negative	239	222	192	131	53	13
MRD Positive	77	68	52	33	14	4

Months

Results

PFS by Random 1

VCD-ASCT vs VCD-VMP

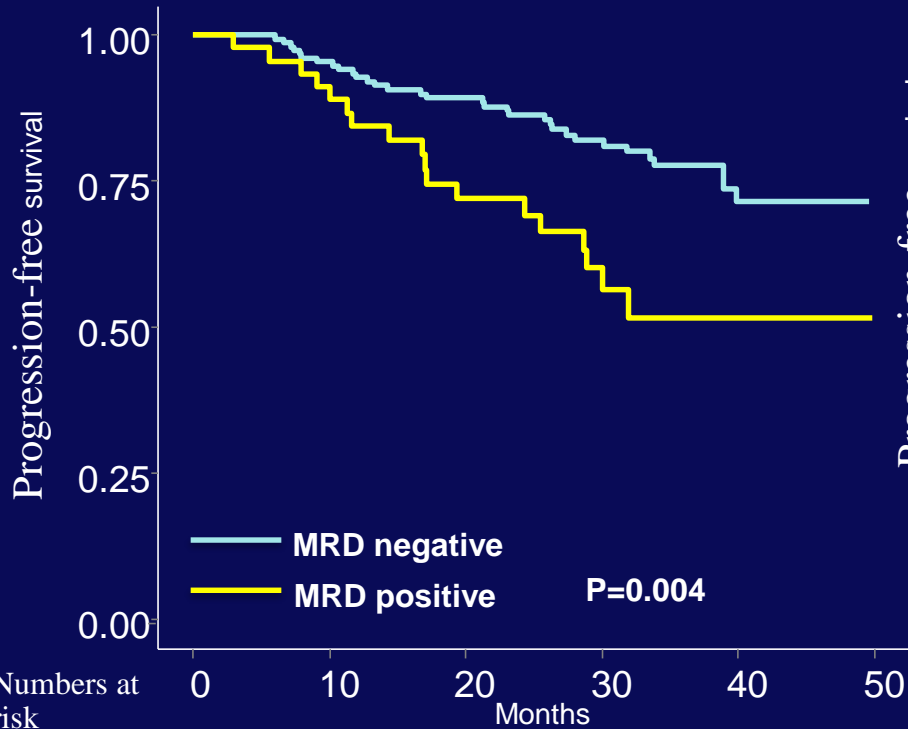


	ASCT	VMP
PFS median, mos	NR	42.5
PFS at 3 yrs, %	65.0	57.1

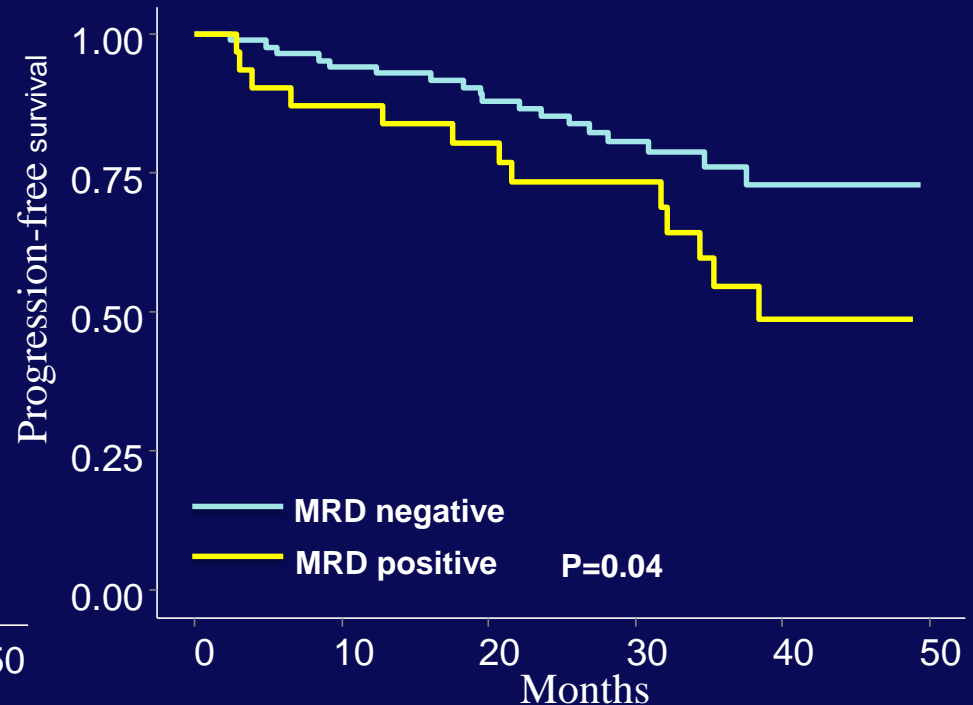
Results

Independence from treatment

MRD for ARM A



MRD for ARM B



Numbers at risk	0	10	20	30	40	50
MRD Negative	153	143	125	87	34	8
MRD Positive	46	41	29	16	6	2

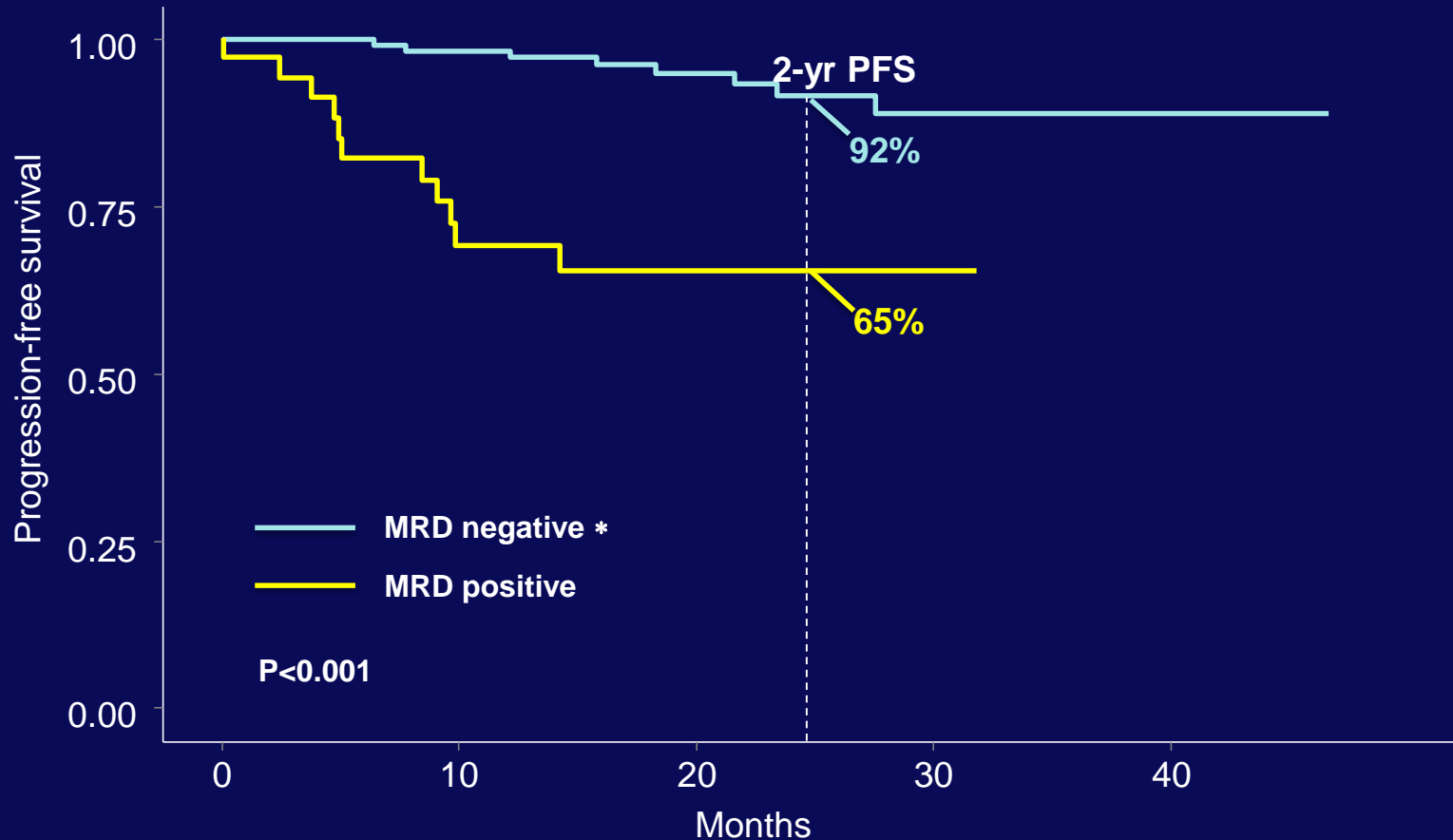
Numbers at risk	0	10	20	30	40	50
MRD Negative	86	79	67	44	19	5
MRD Positive	31	27	23	17	8	2

Results

Landmark analysis at 1 year of len maintenance

VCD-int-
± cons

Lenalidomide Continuous Therapy



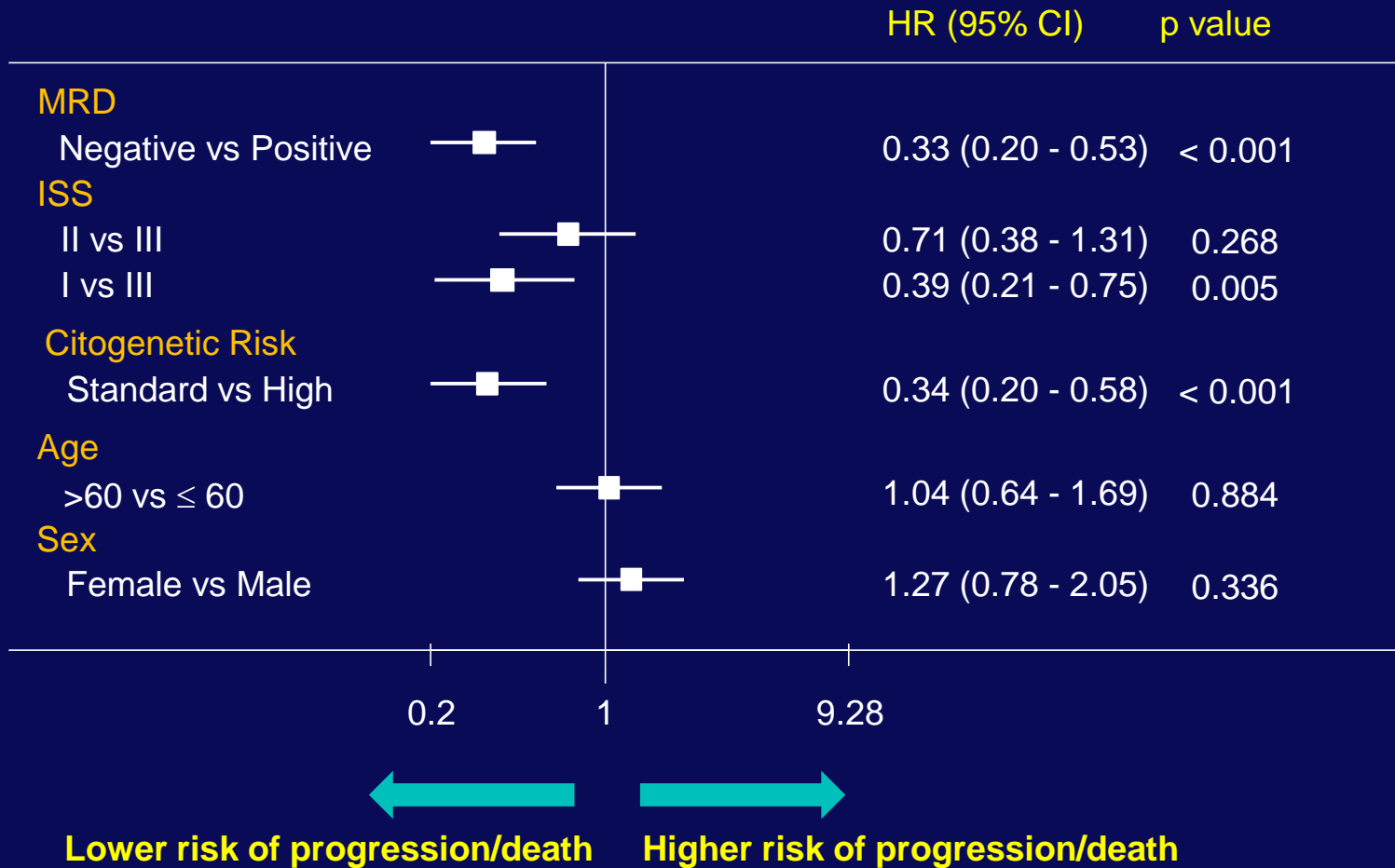
Preliminary results: Longer follow-up needed

Int: intensification; Cons: consolidation

* 85% were persistent MRD negative (first negativity pre-maintenance)

Results

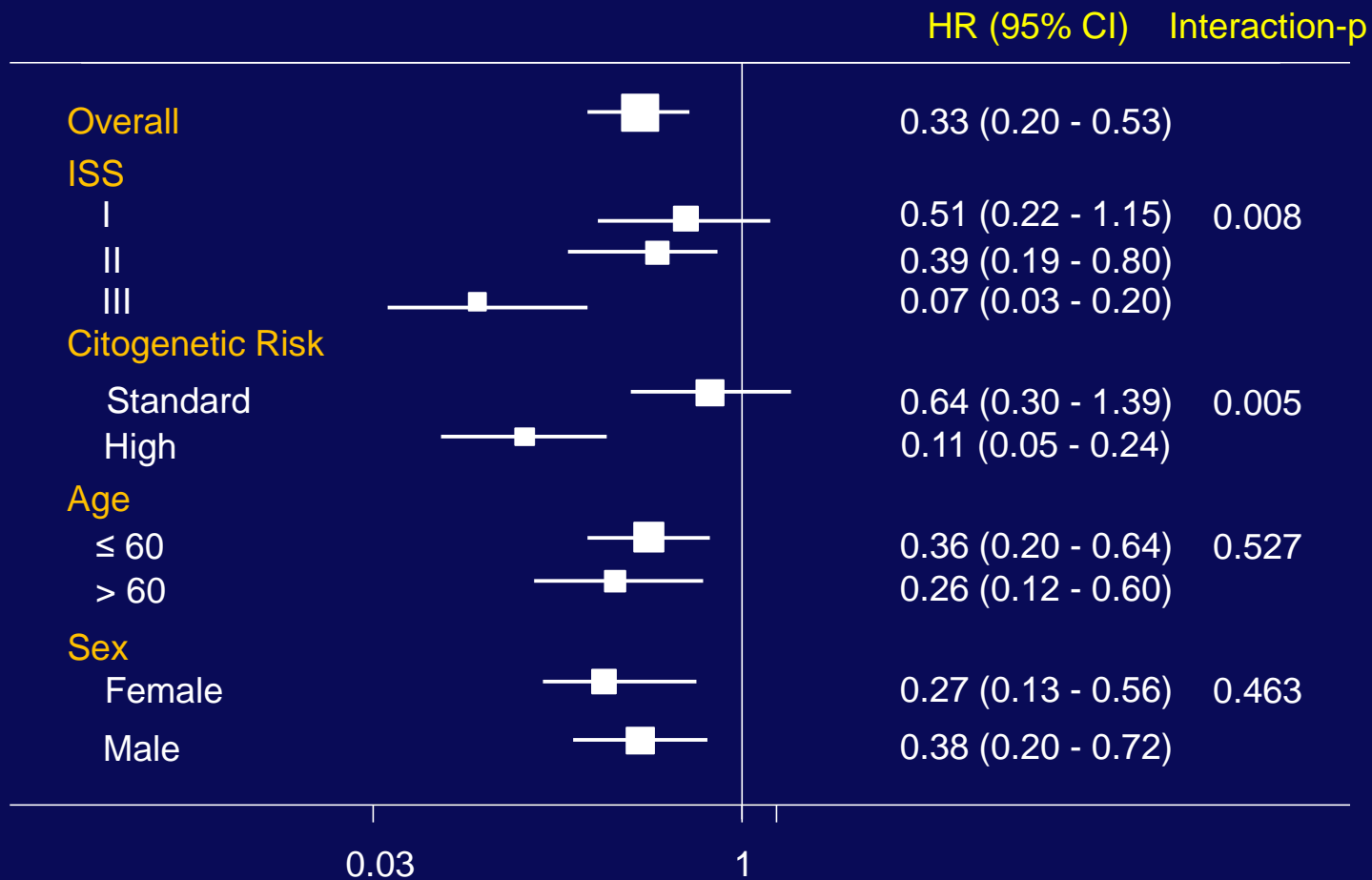
Multivariable Cox analysis for PFS



* Adjusted for random therapies

Results

Subgroup analyses for PFS



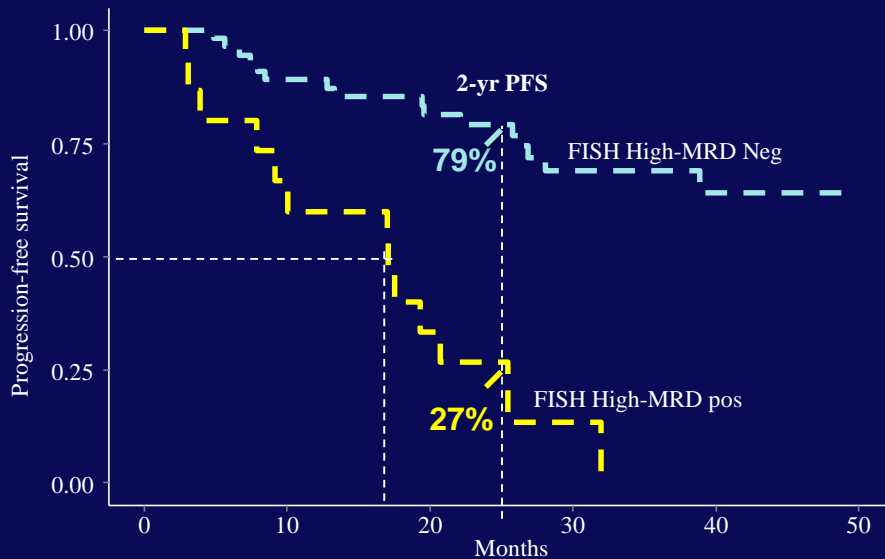
Lower risk for MRD -

* Adjusted for random therapies

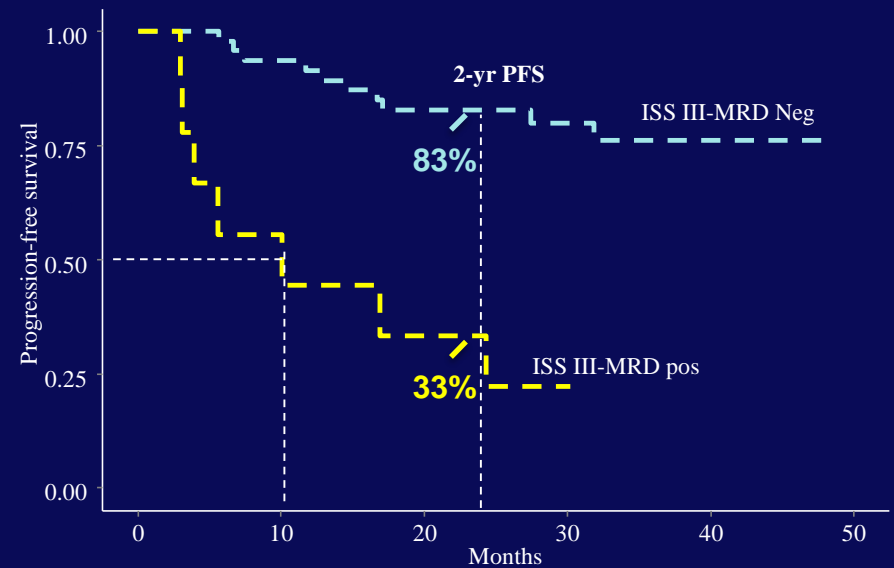
Results

Subgroup analyses for PFS: High Risk patients and MRD

FISH – HIGH RISK



ISS III



Del17p : 25 patients; 8/9 MRD + relapsed, 5/16 (31%) MRD- relapsed
t (4; 14): 41 patients; 5/6 MRD + relapsed, 10/35 (28%) MRD - relapsed
t (14; 16): 10 patients, all MRD - at pre-maintenance

Conclusions

- MRD by MFC is a strong prognostic factor in MM patients receiving intensification with novel agents or transplant
- During Lenalidomide maintenance 48% of MRD positive patients with at least one evaluation after 1 year of therapy became MRD-negative
- The achievement of MRD negativity suggest the importance of deep response in high-risk MM patients defined by FISH abnormalities and ISS stage

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Thank you!