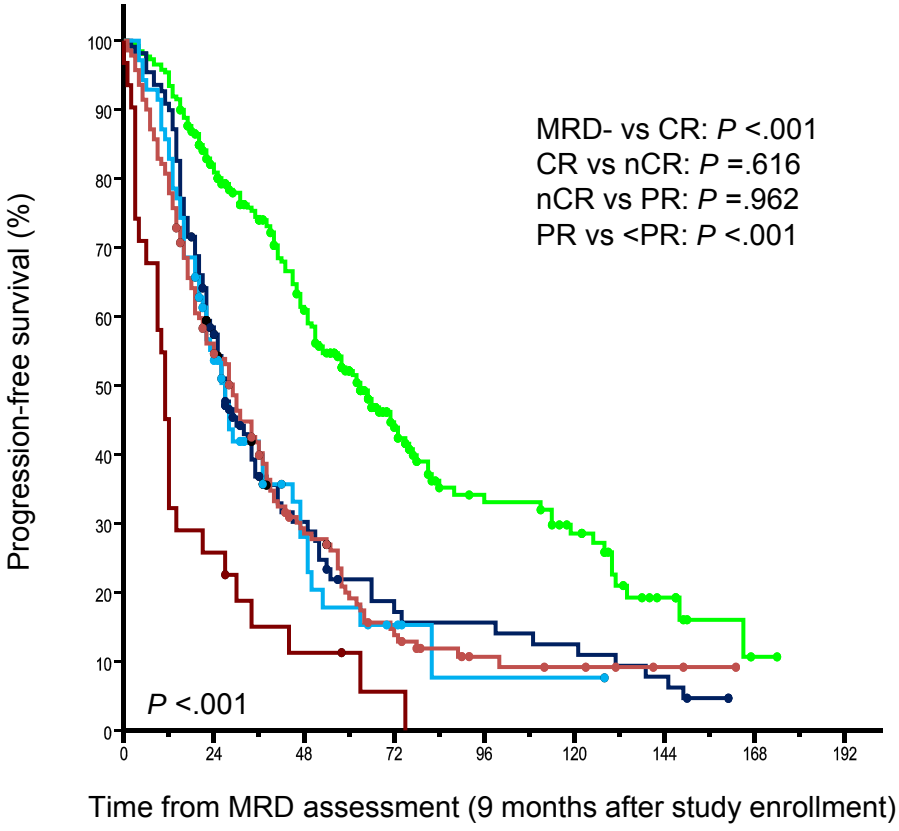
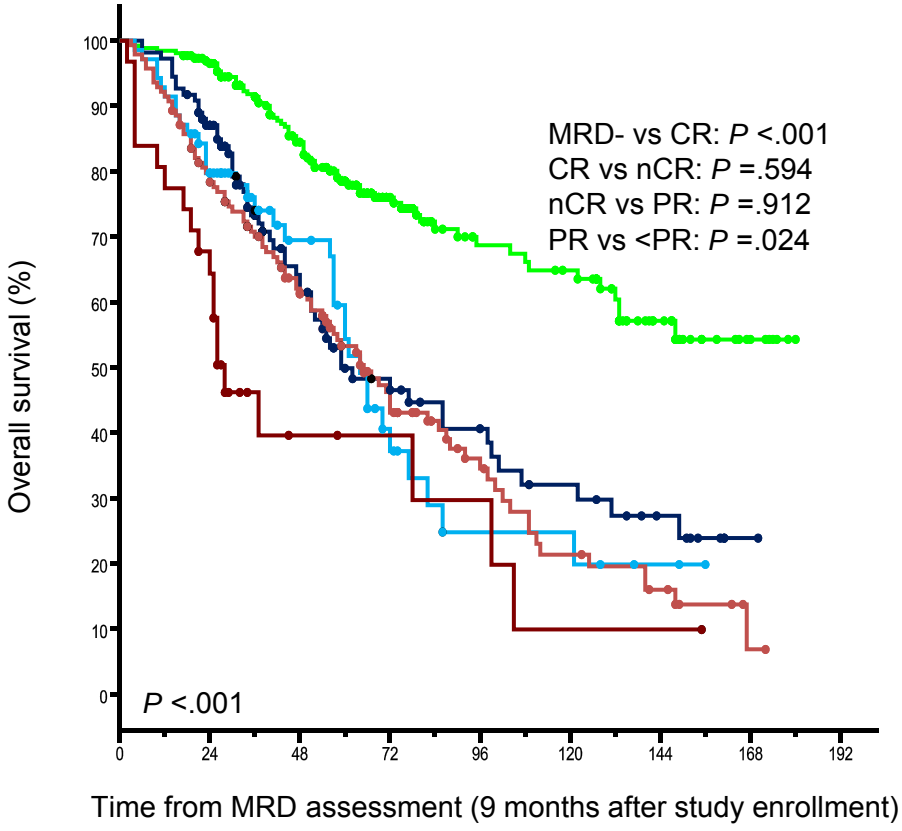
Overview of validated methods and thresholds used to assess MRD in MM

Bruno Paiva

Hematology and Immunology Departments. Clinica Universidad de Navarra
Flow Cytometry Core - CIMA LAB Diagnostics
Universidad de Navarra
EuroFlow Consortium
Spanish Myeloma Group (GEM)

1st generation flow cytometry (4-color; 10^{-4})





Lahuerta JJ & Paiva B, et al. J Clin Oncol 2017;35(25):2900-2910

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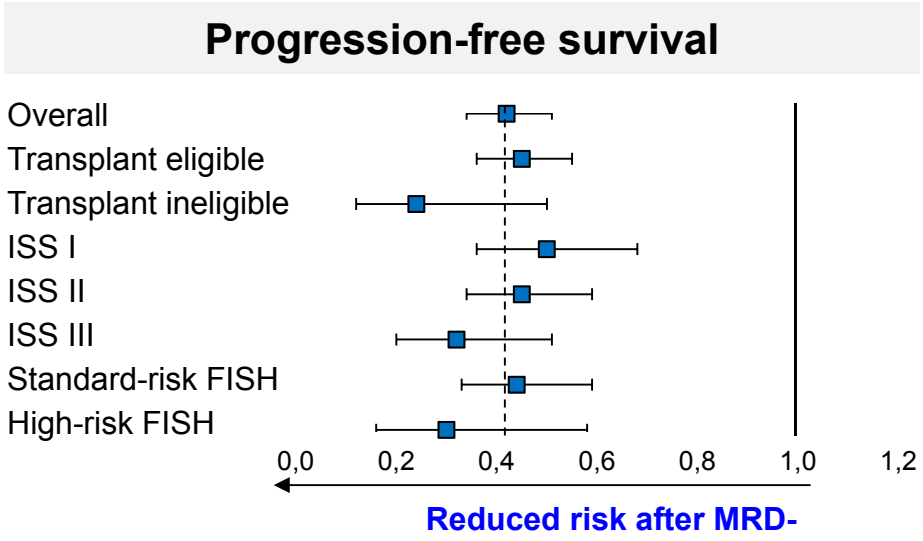
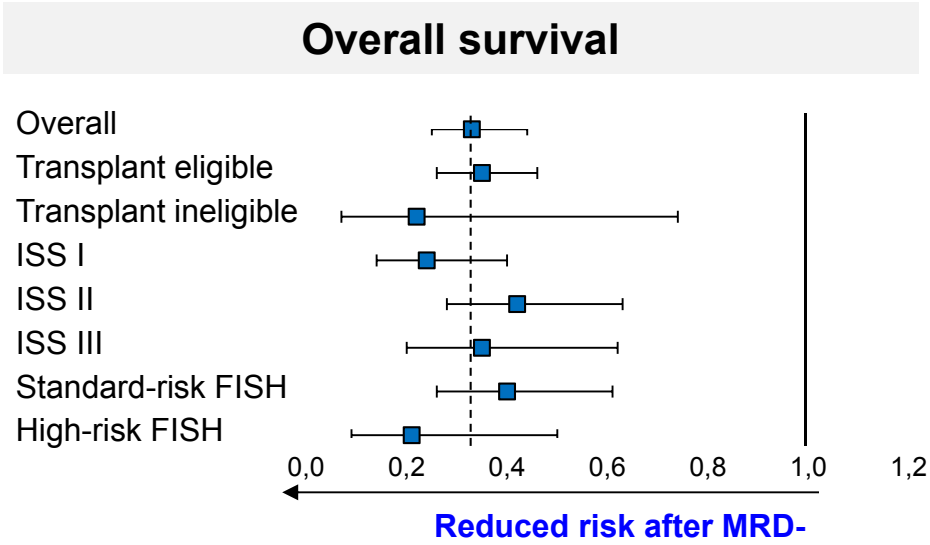
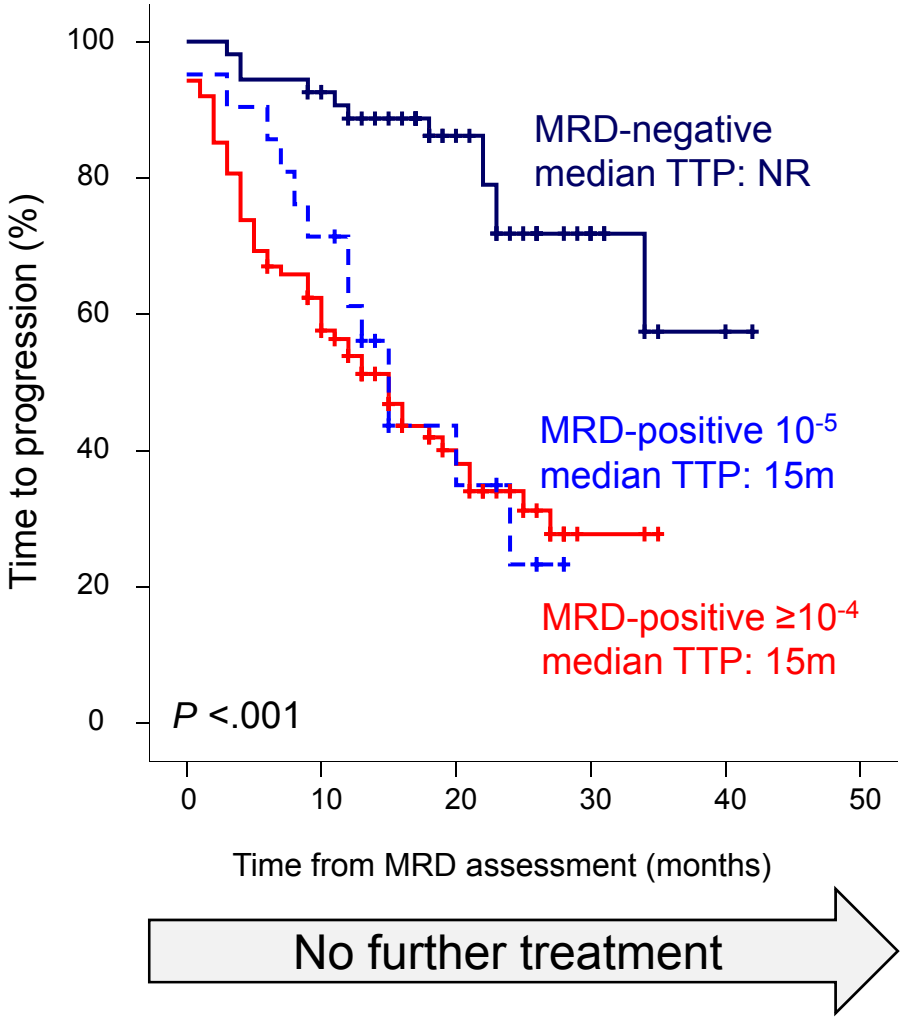
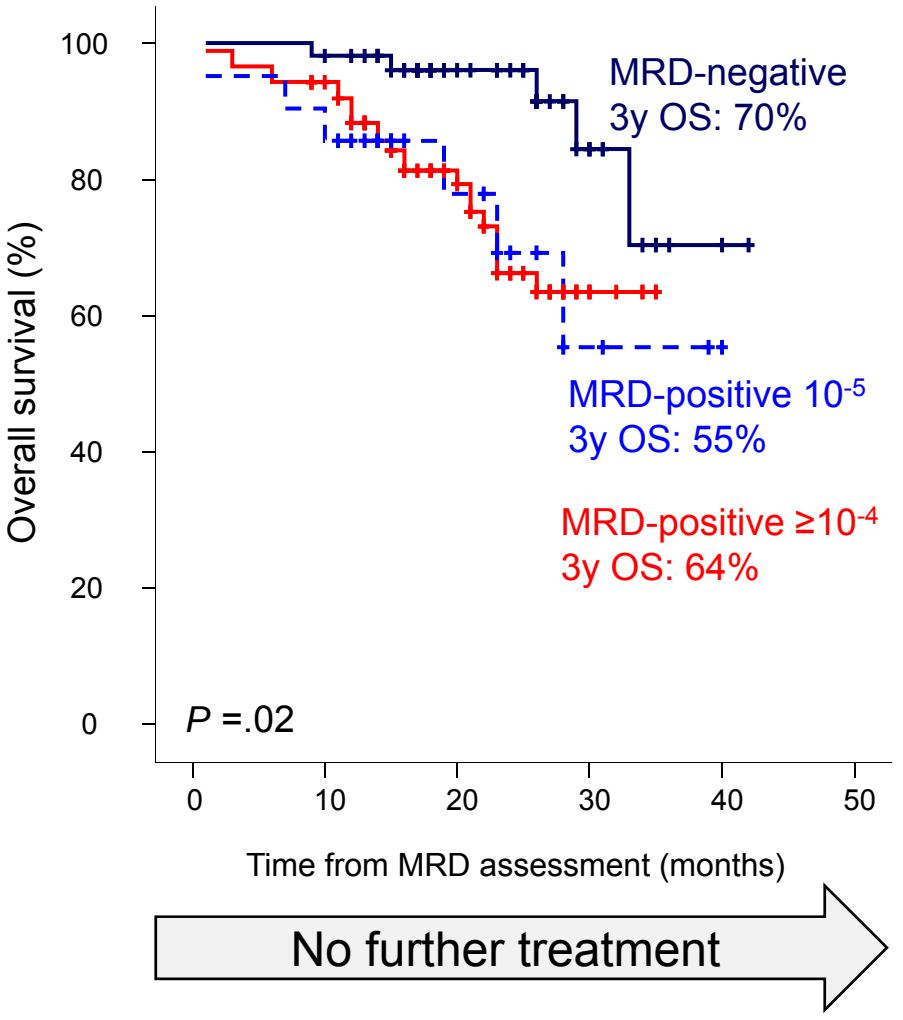




Lahuerta JJ & Paiva B, et al. J Clin Oncol 2017;35(25):2900-2910

2nd generation flow cytometry (8-color; 10^{-5})





GEM2010MAS65

Paiva B et al. Blood 2016;127(25):3165-74

Leukemia (2017) 31, 2094–2103
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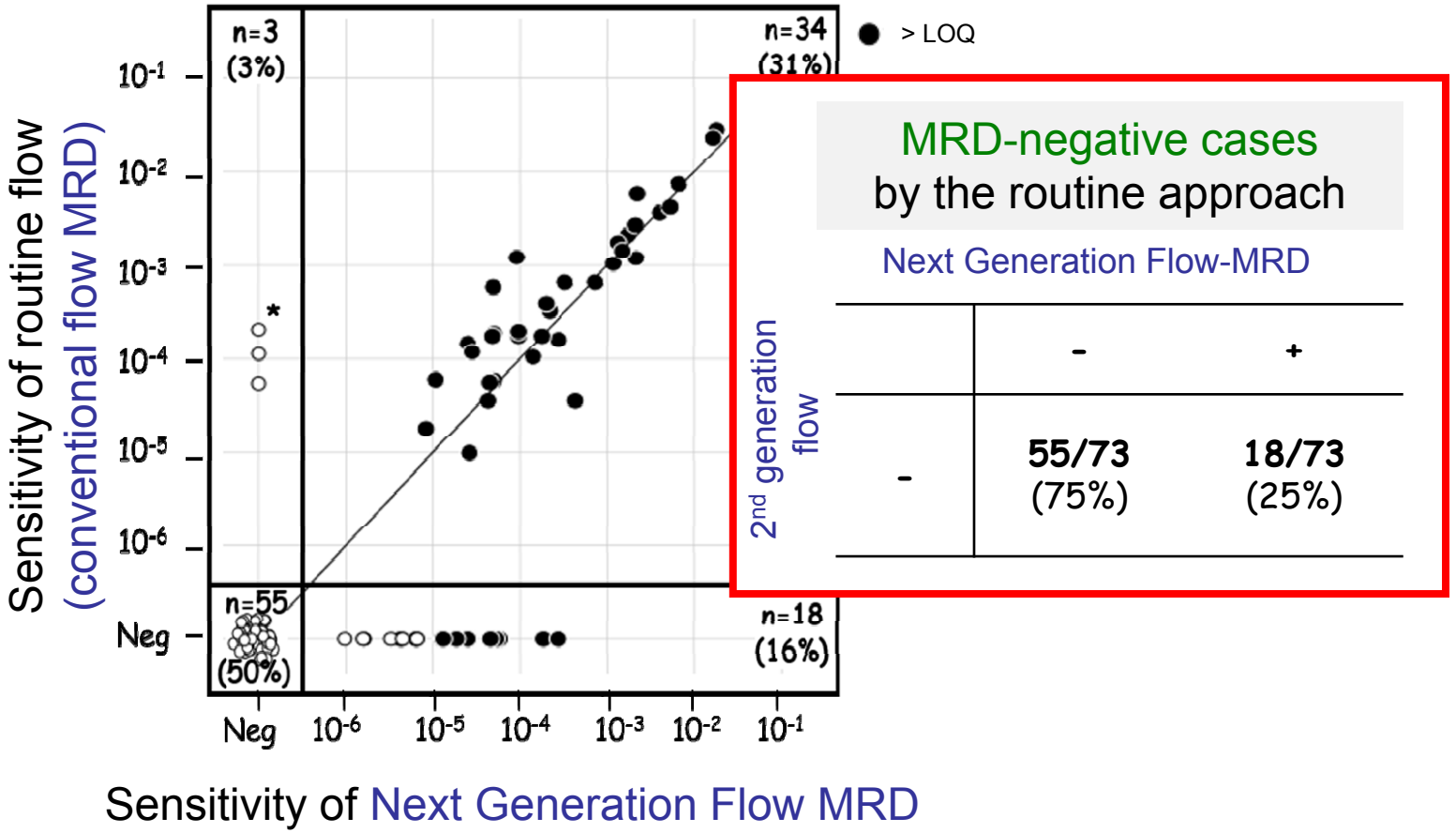
ORIGINAL ARTICLE

Next Generation Flow for highly sensitive and standardized detection of minimal residual disease in multiple myeloma

J Flores-Montero[1,19], L Sanoja-Flores[1,19], B Paiva[2,19], N Puig[3], O García-Sánchez[3], S Böttcher[4], VHJ van der Velden[5], J-J Pérez-Morán[3], M-B Vidriales[3], R García-Sanz[3], C Jimenez[3], M González[3], J Martínez-López[6], A Corral-Mateos[1], G-E Grigore[7], R Fluxá[7], R Pontes[8], J Caetano[9], L Sedek[10], M-C del Cañizo[3], J Bladé[11], J-J Lahuerta[6], C Aguilar[12], A Bárez[13], A García-Mateo[14], J Labrador[15], P Leoz[1], C Aguilera-Sanz[16], J San-Miguel[2,20], M-V Mateos[3,20], B Durie[17,21], JJM van Dongen[5,18,21] and A Orfao[1,21]

Next generation flow cytometry (10-color; 10^{-6})



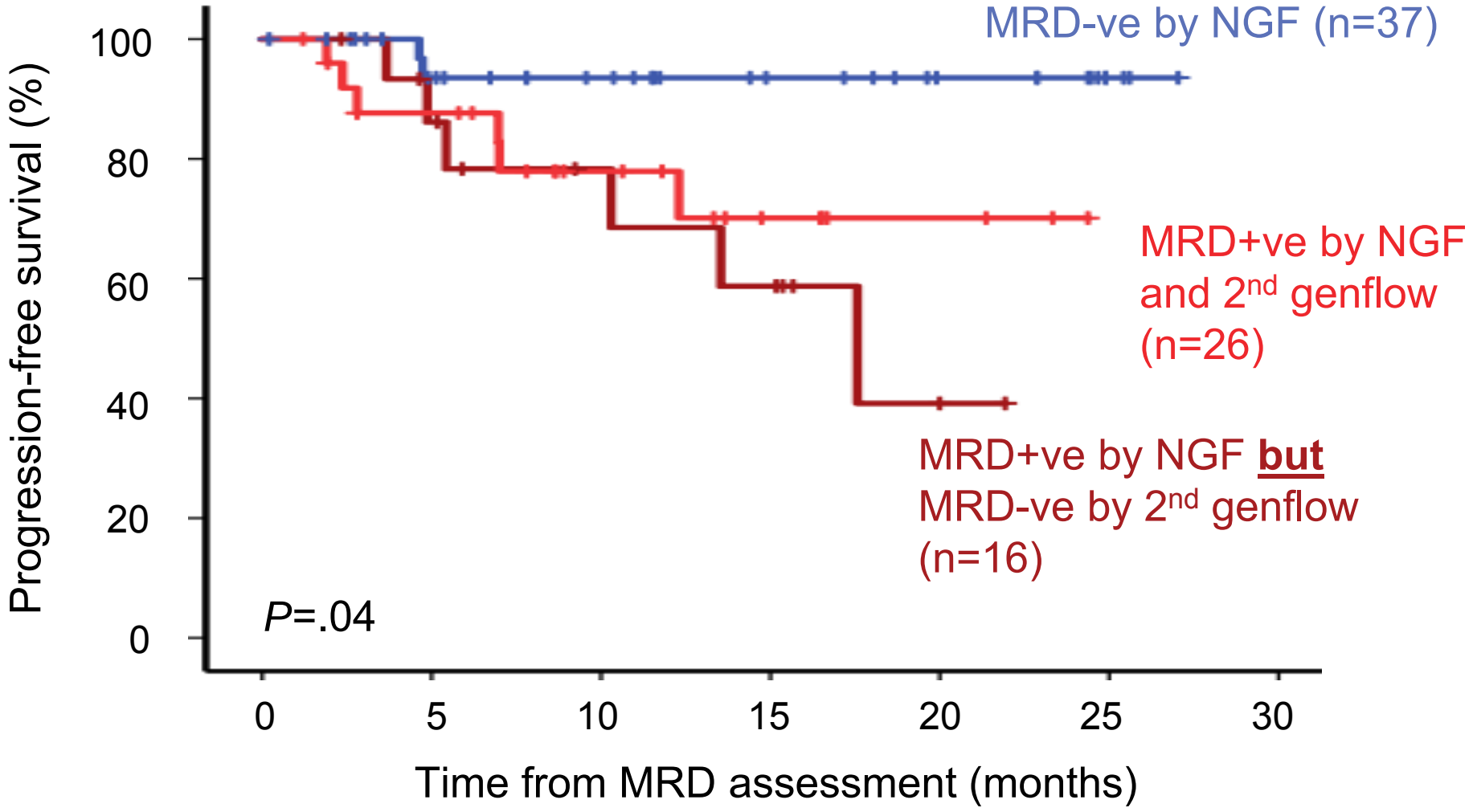
MRD-negative cases
by the routine approach

2nd generation flow	Next Generation Flow-MRD -	Next Generation Flow-MRD +
-	**55/73** (75%)	**18/73** (25%)

* 2 samples proven polyclonal by CyIg staining

Flores-Montero J, et al. Leukemia. 2017.;31(10):2094-2103.

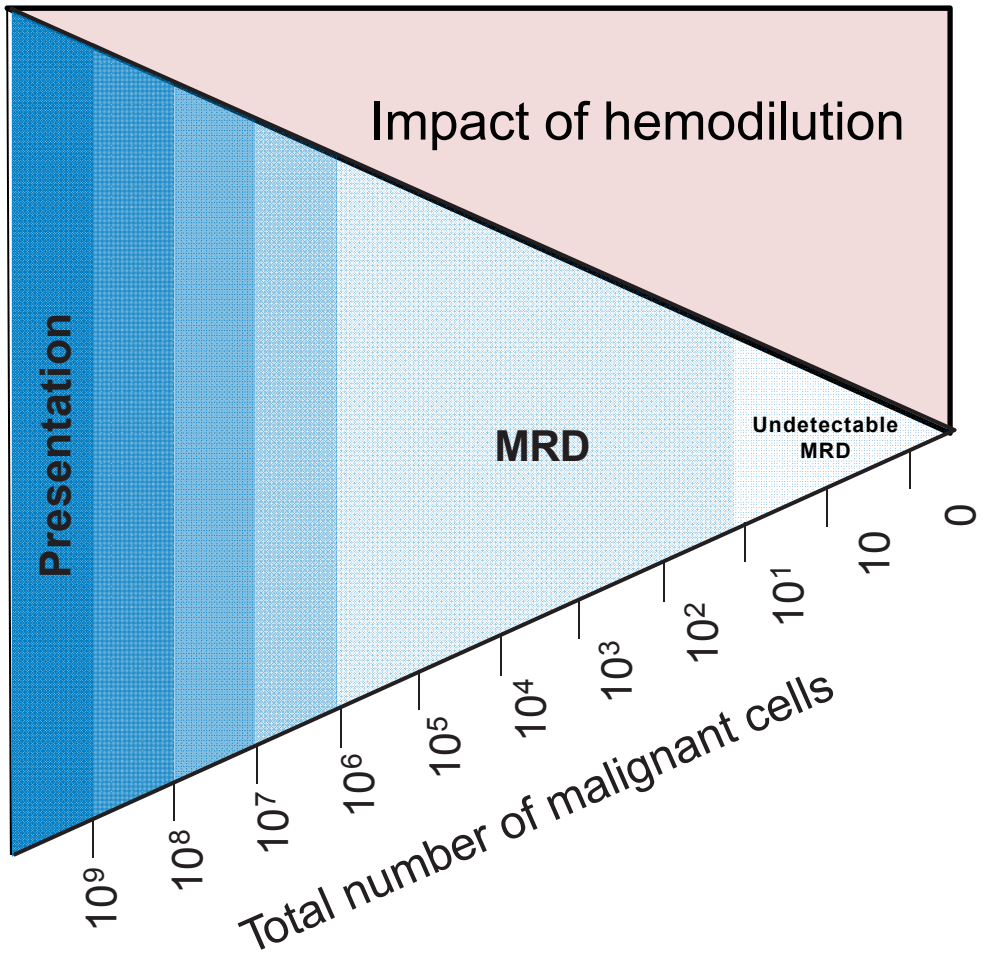
Next generation flow cytometry (10-color; 10^{-6})



Flores-Montero J, et al. Leukemia. 2017.;31(10):2094-2103.

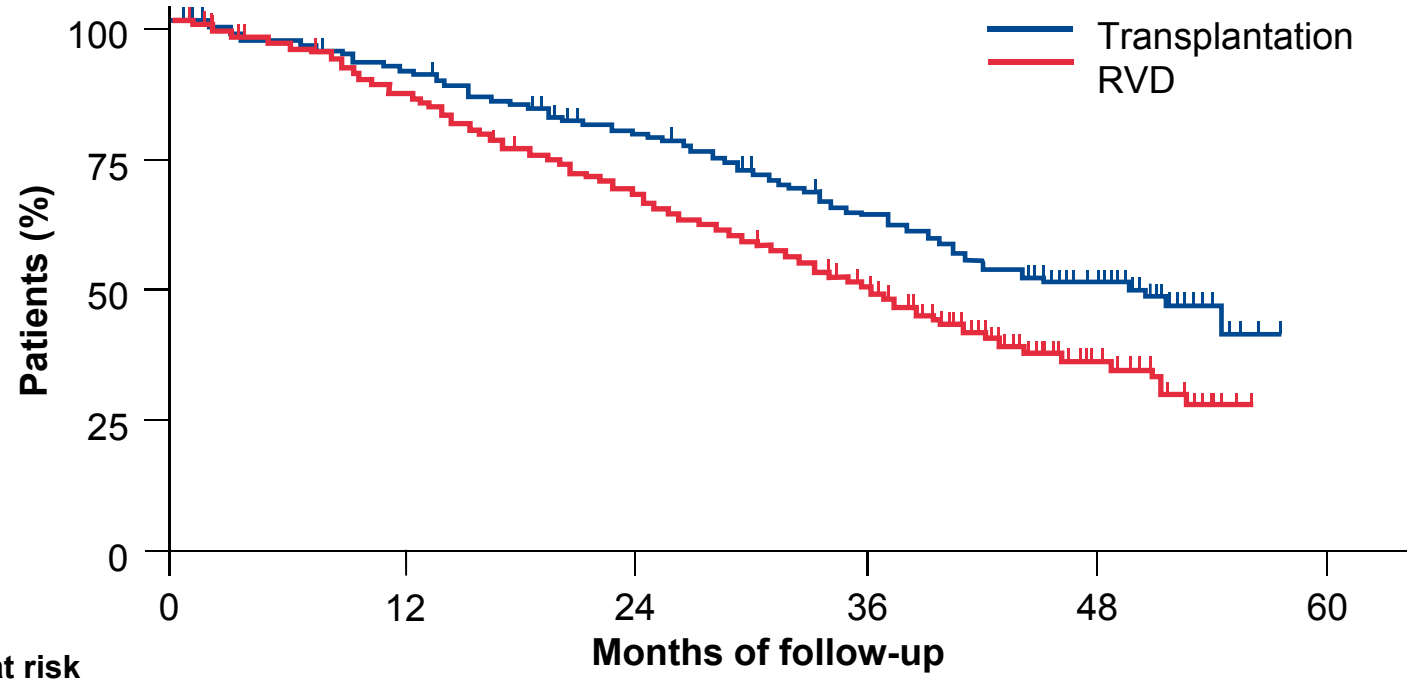
10^{-6} is the most informative threshold for patient prognostication, but should 10^{-6} be used as threshold for surrogacy in clinical trials?

Lower MRD levels are more susceptible to variability in case of hemodilution



Predicting treatment effect according to MRD rates: IFM2009 study

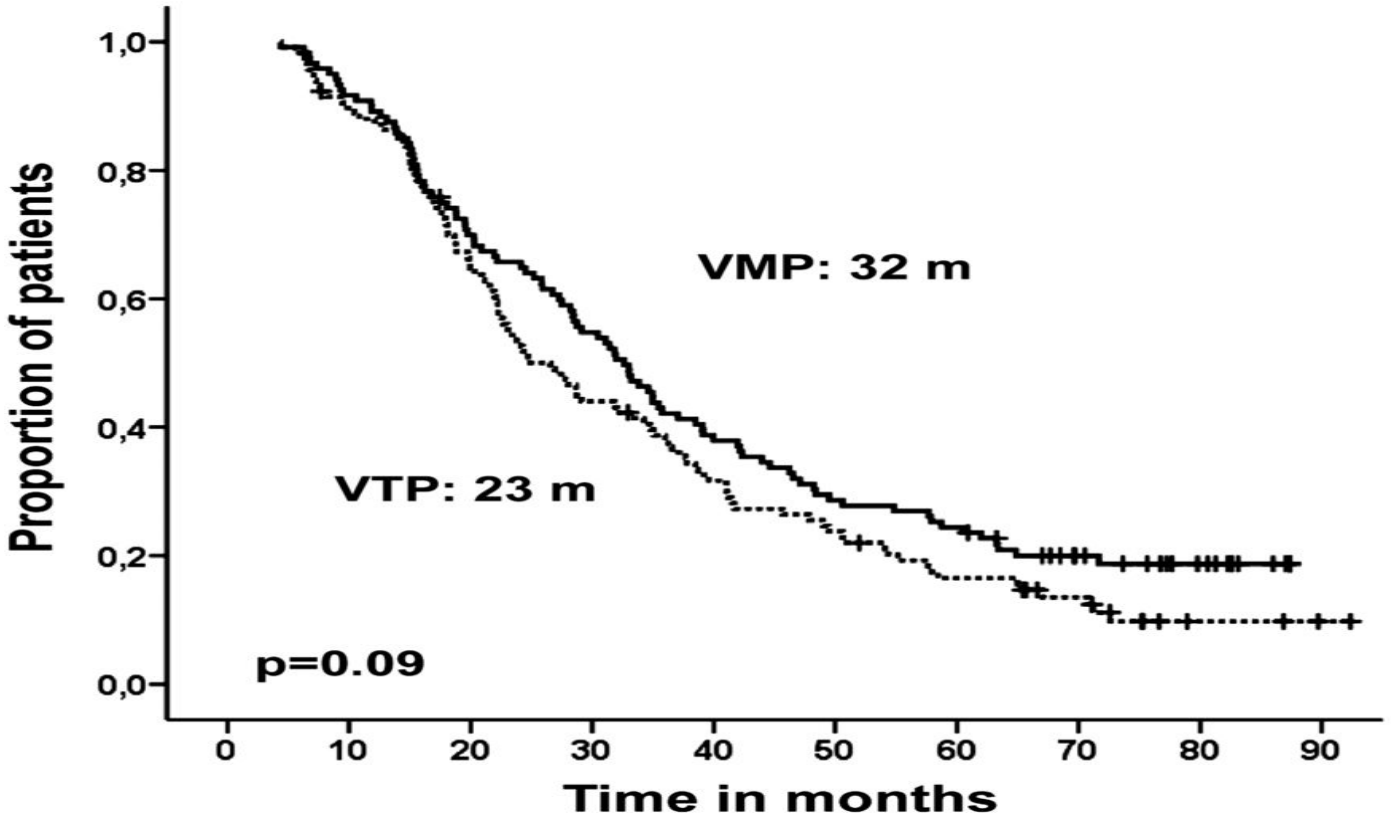
	RVD	ASCT	Δ	P-value
MRD-ve (%)	65	79	14	<.001
PFS	36	50	14	<.001



Attal M, et al. N Engl J Med 2017;376:1311-20

Predicting treatment effect according to MRD rates: GEM2005MAS65 study

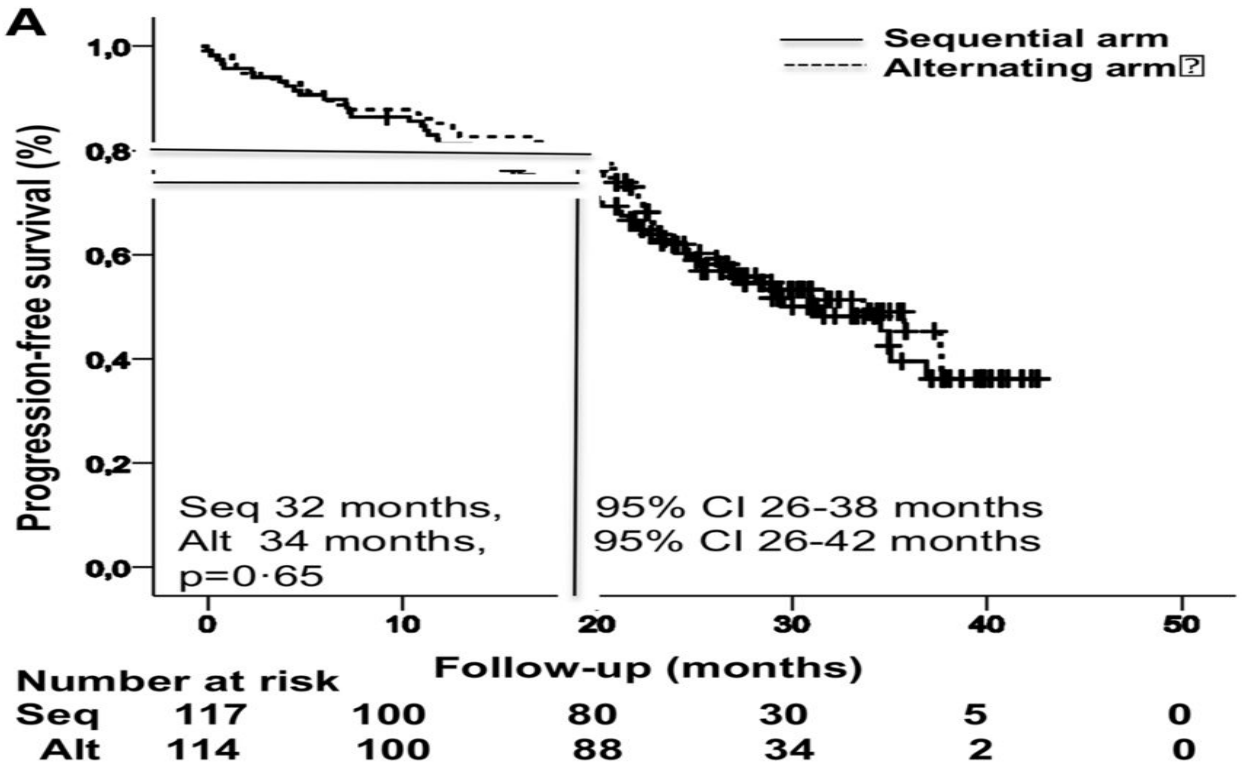
	VTP	VMP	Δ	P-value
MRD-ve (%)	20	24	4	.86
PFS (months)	23	32	9	.09



Mateos et al. Blood 2014;124:1887-1893

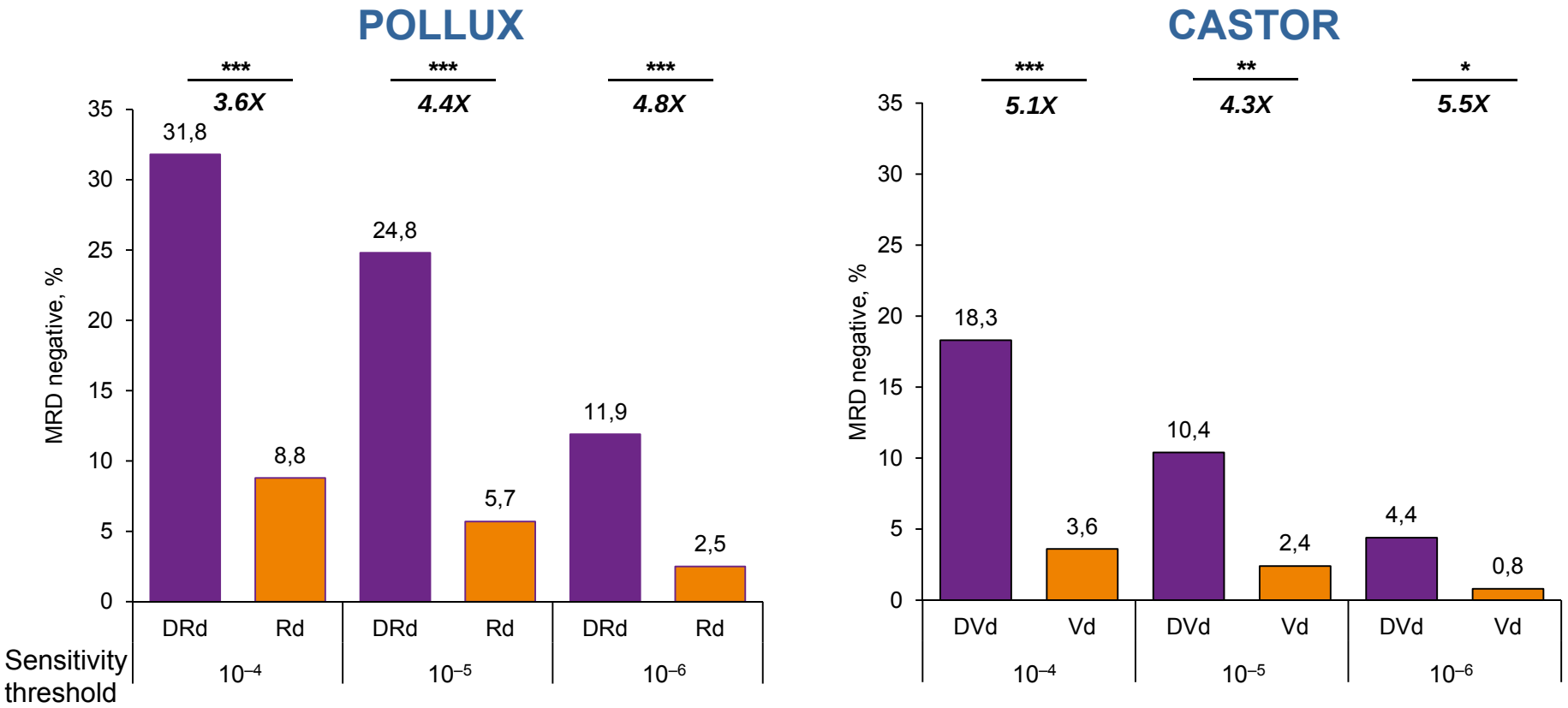
Predicting treatment effect according to MRD rates: GEM2010MAS65 study

	SEQ	ALT	Δ	P-value
MRD-ve (%)	36	30	-6	.48
PFS (months)	32	34	2	.65



Mateos et al. Blood 2016;127:420-425

Proportion of MRD-negative Patients at 10^{-4}, 10^{-5}, and 10^{-6} Thresholds



- **Investigational as compared to control arm significantly improved MRD-negative rates at all thresholds**

*** *P* <0.0001
** *P* <0.005
* *P* <0.05

P values calculated using likelihood-ratio chi-square test.

Avet-Loiseau H, et al. Blood 2016;128:246