

MRD Testing for Newly Diagnosed Multiple Myeloma (MM)

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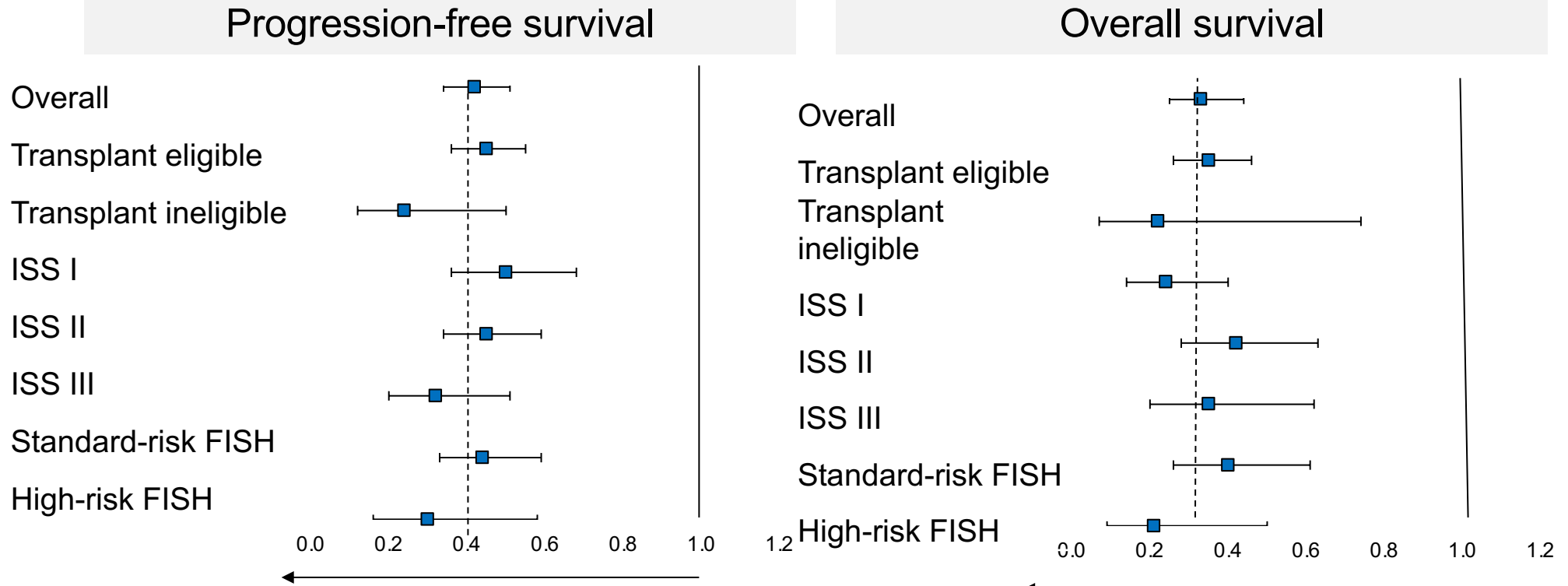


Rochester, Minnesota



Jacksonville, Florida

Pooled Analysis of Three PETHEMA/GEM Trials: Impact of MRD across MM patient subgroups



Reduced risk after MRD-

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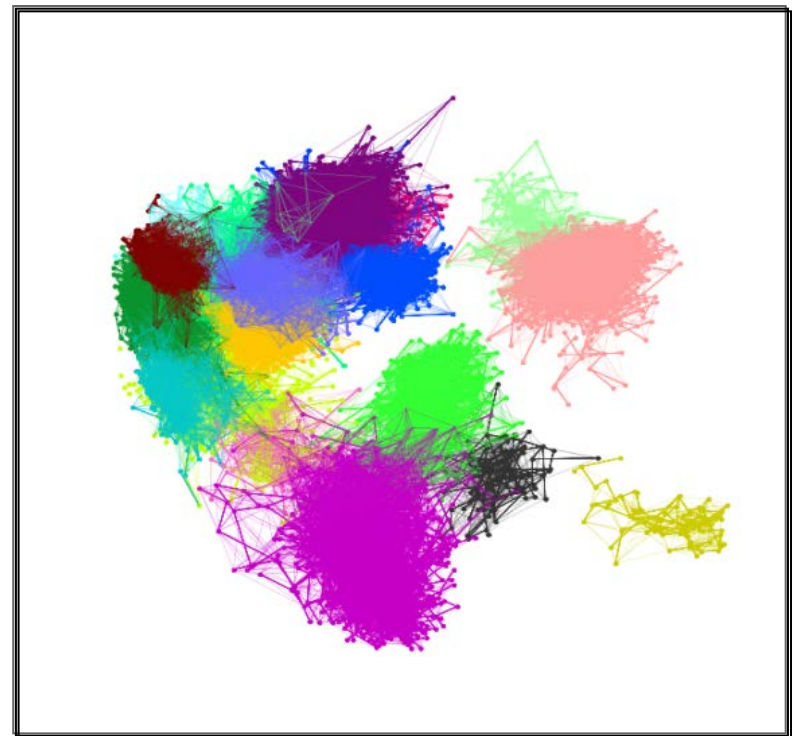
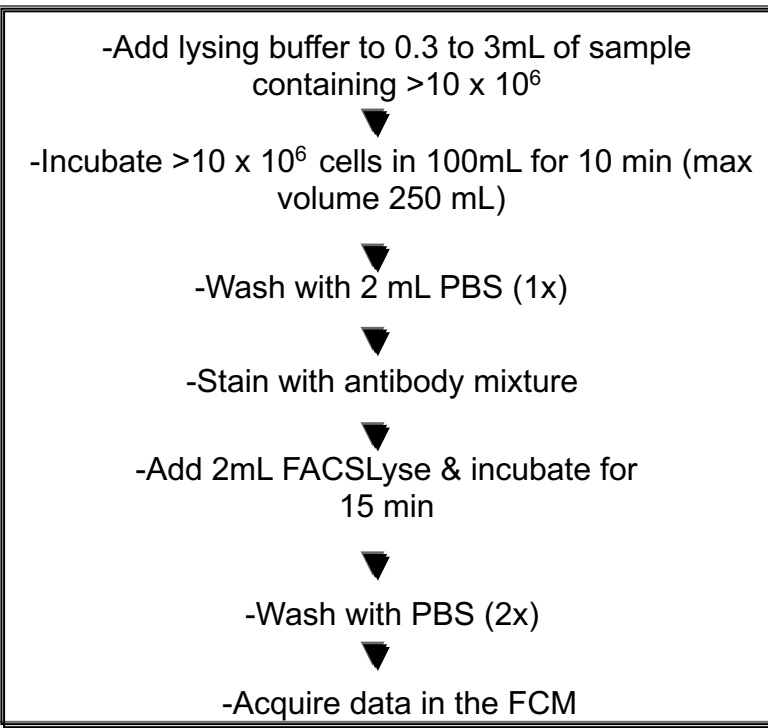
MRD negativity is associated with 60% and 70% reduction in risk of relapse and death respectively.

Courtesy of Rafael Fonseca, MD

Next generation flow (NGF) cytometry

Tube	BV421	BV510	FITC	PE	PerCP Cy5.5	PECy7	APC	APCC750
1							CD117	CD81
2	CD138	CD27	CD38	CD56	CD45	CD19	cyKappa	cyLambda

} Merged files



Limit of detection (LOD) of 10^{-6} was reached in 88% of samples

* Multi-epitope CD38 (not blocked by anti-CD38 MoAbs)

B cell “fingerprinting”



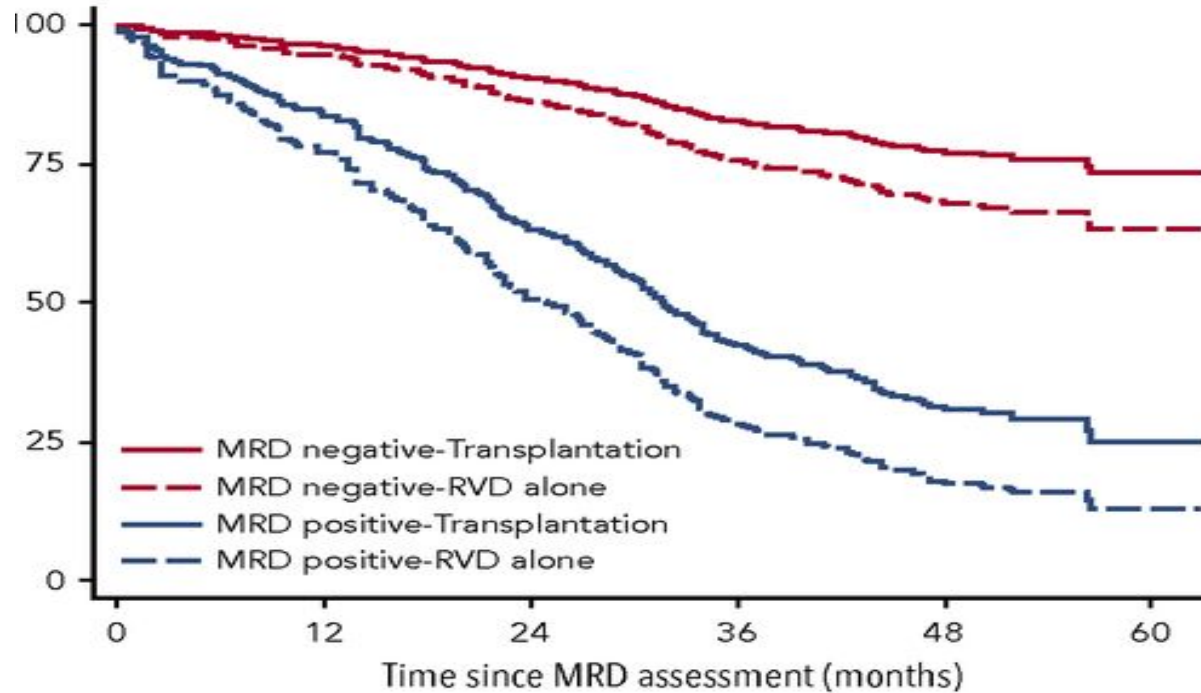
Courtesy of Rafael Fonseca, MD
www.biometrisolutions.com

MRD Controversies

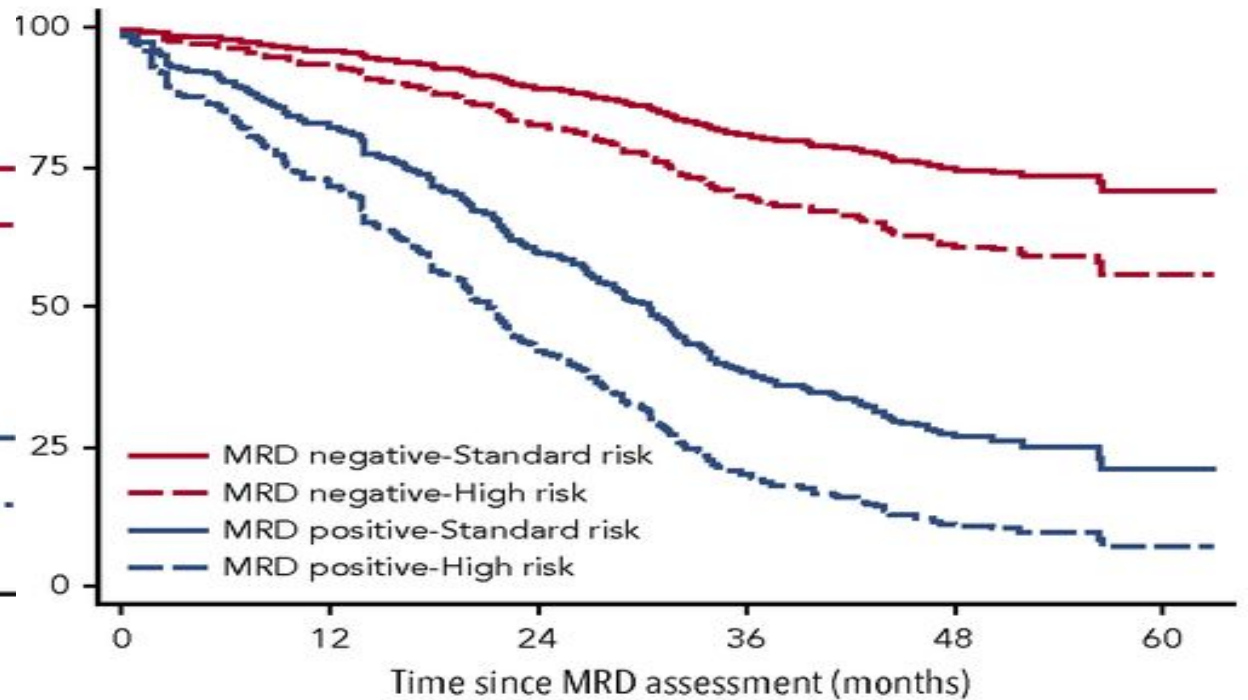
- **Flow versus NGS**
- **Can be used to stop therapy**
 - **Long term CR - maintenance**
 - **Test for it**
 - **If positive – maybe stay on Rx?**
 - **If negative – more confidently stop?**
- **Explore for VGPR**
- **We did not ask for Phase 3 trials to use sFLC**

Outcomes by MRD

MRD Status and SCT vs not



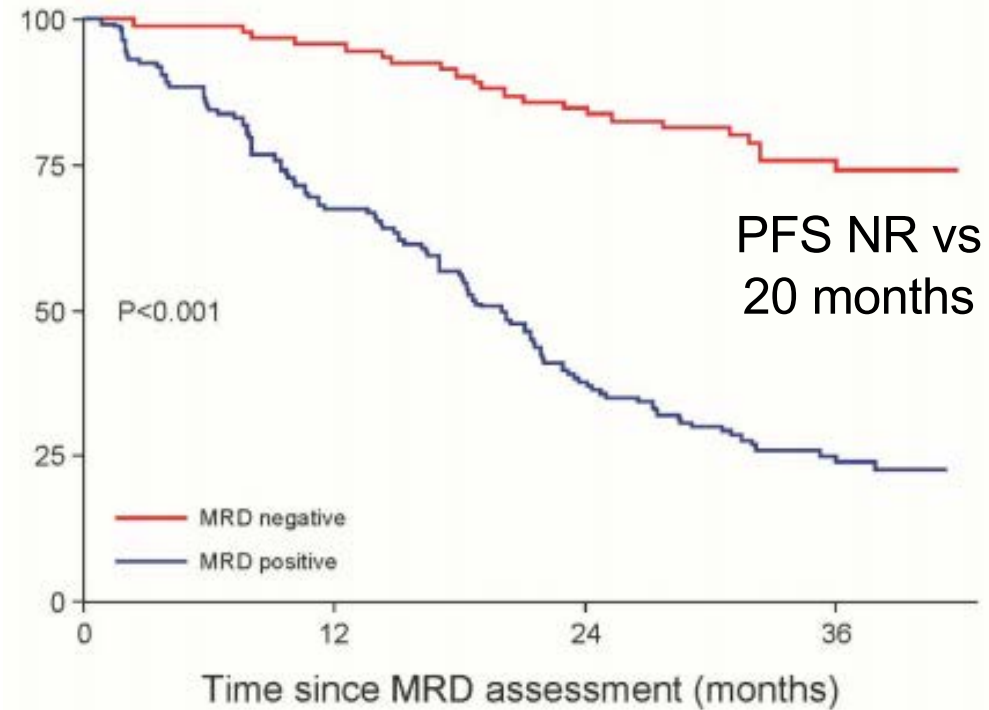
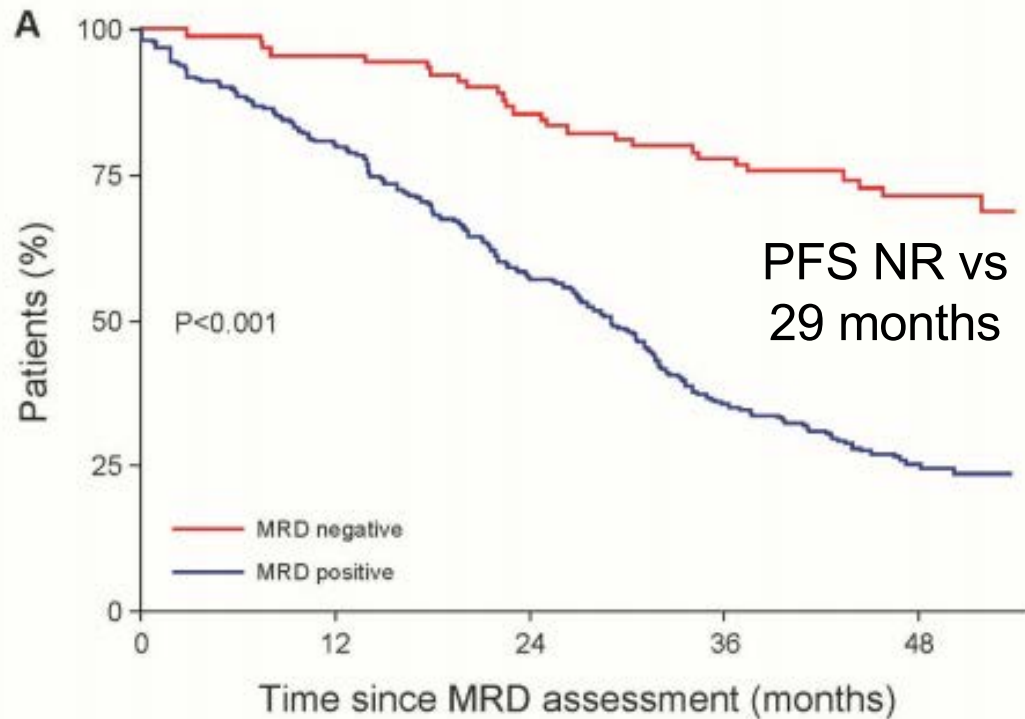
MRD Status and Risk status



Outcomes by MRD

MRD Negativity at the start of maintenance

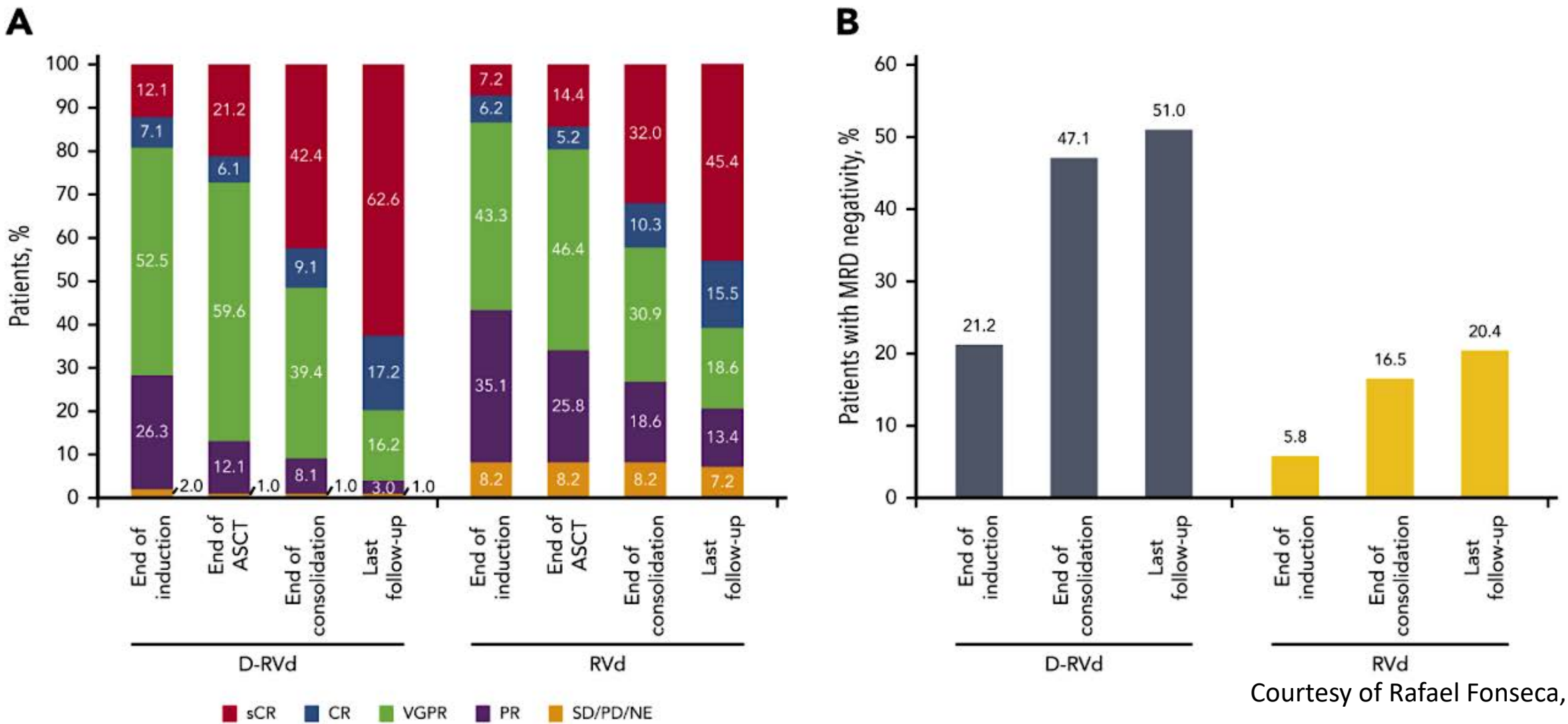
MRD Negativity 12 months later



No. at Risk	0	12	24	36	48
MRD negative	90	86	77	69	40
MRD positive	276	221	157	96	40

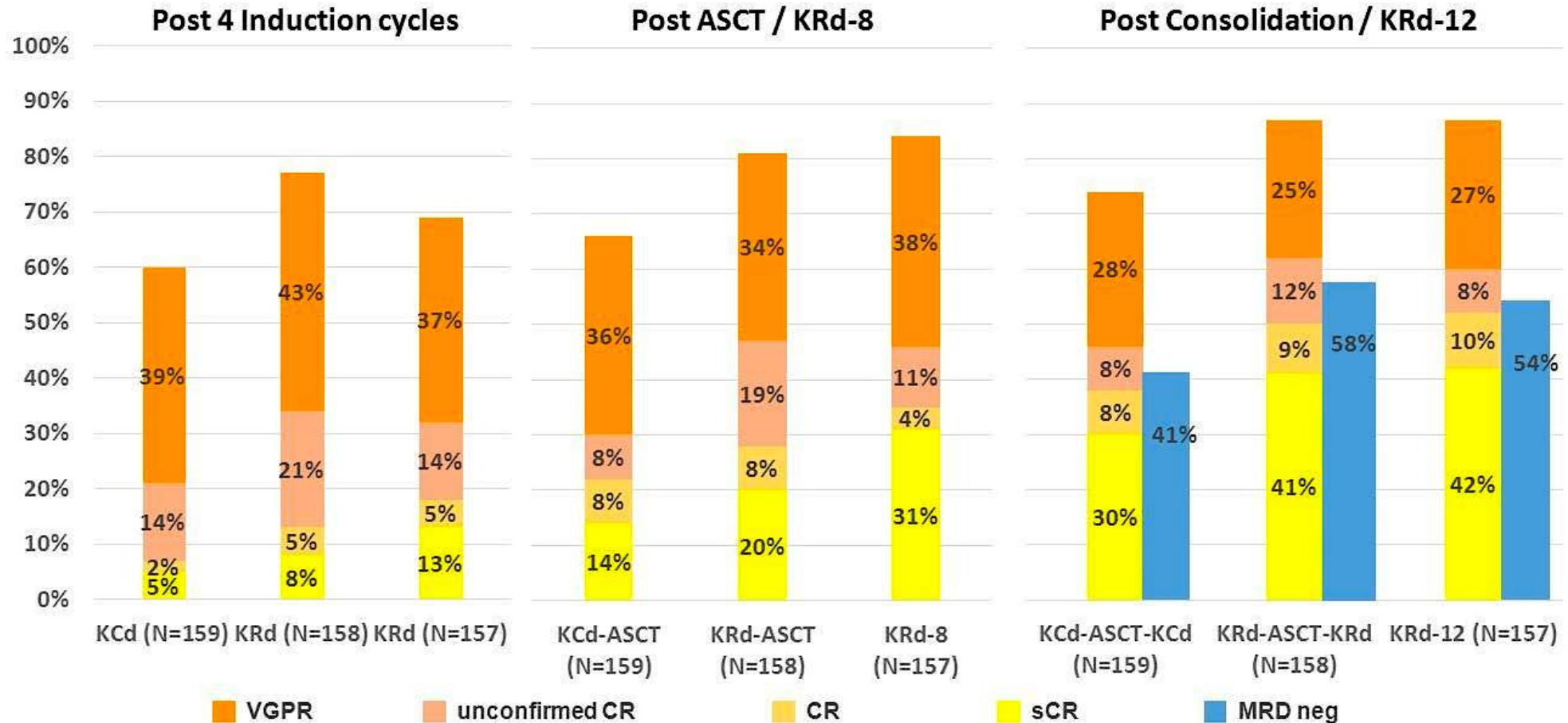
No. at Risk	0	12	24	36
MRD negative	92	88	77	42
MRD positive	147	99	55	23

GRIFFIN Trial of Dara-RVd for Newly Diagnosed MM: ORR and MRD (10^{-5})

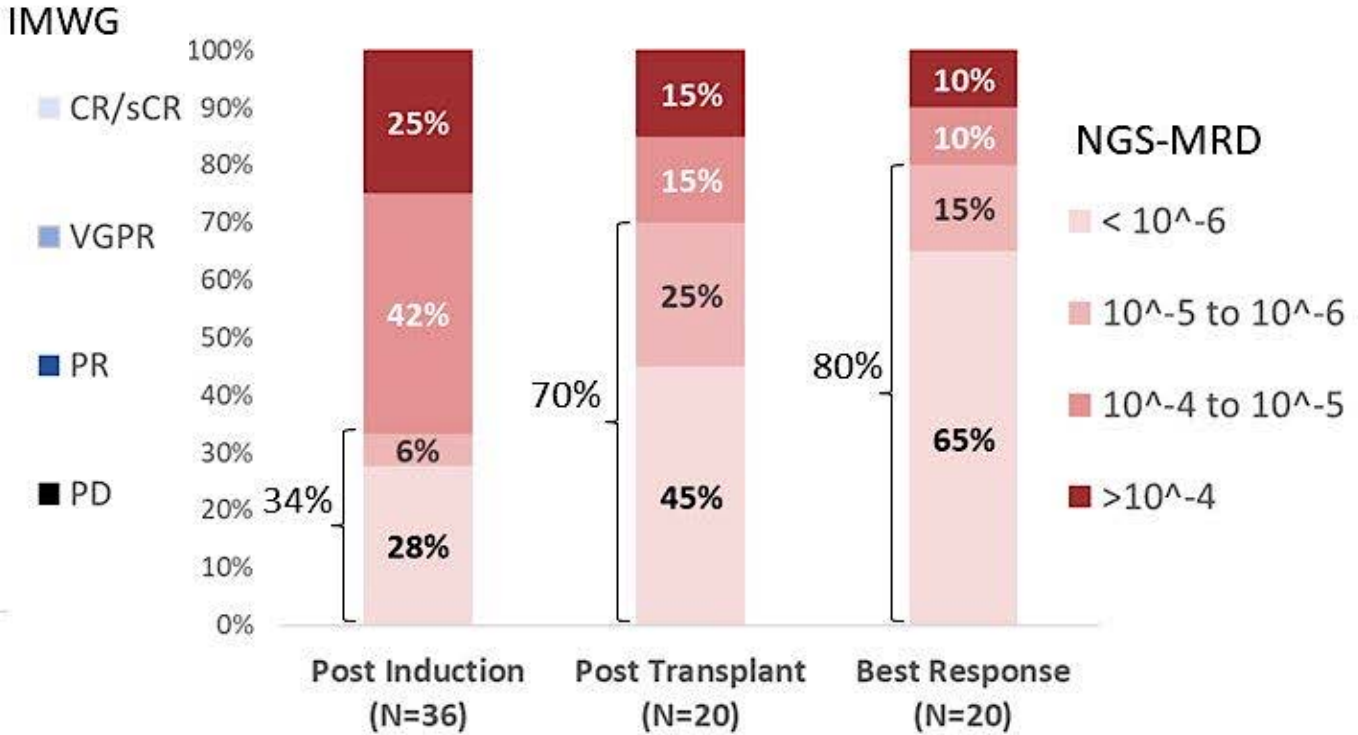
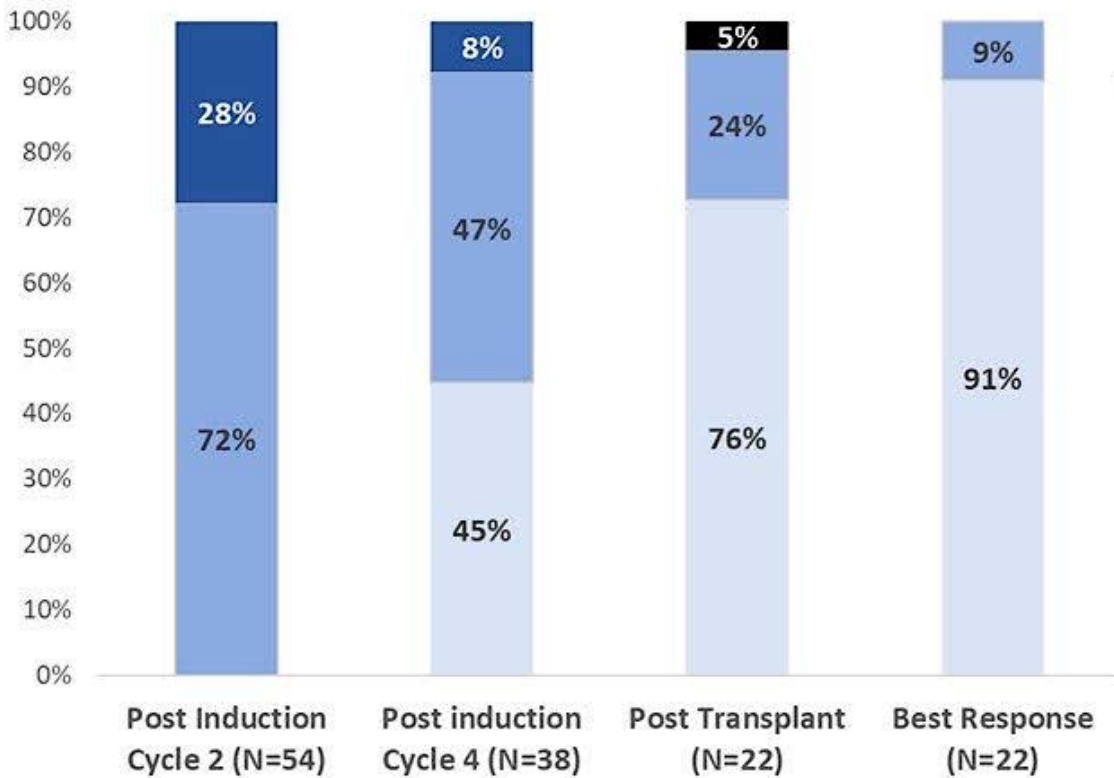


Courtesy of Rafael Fonseca, MD

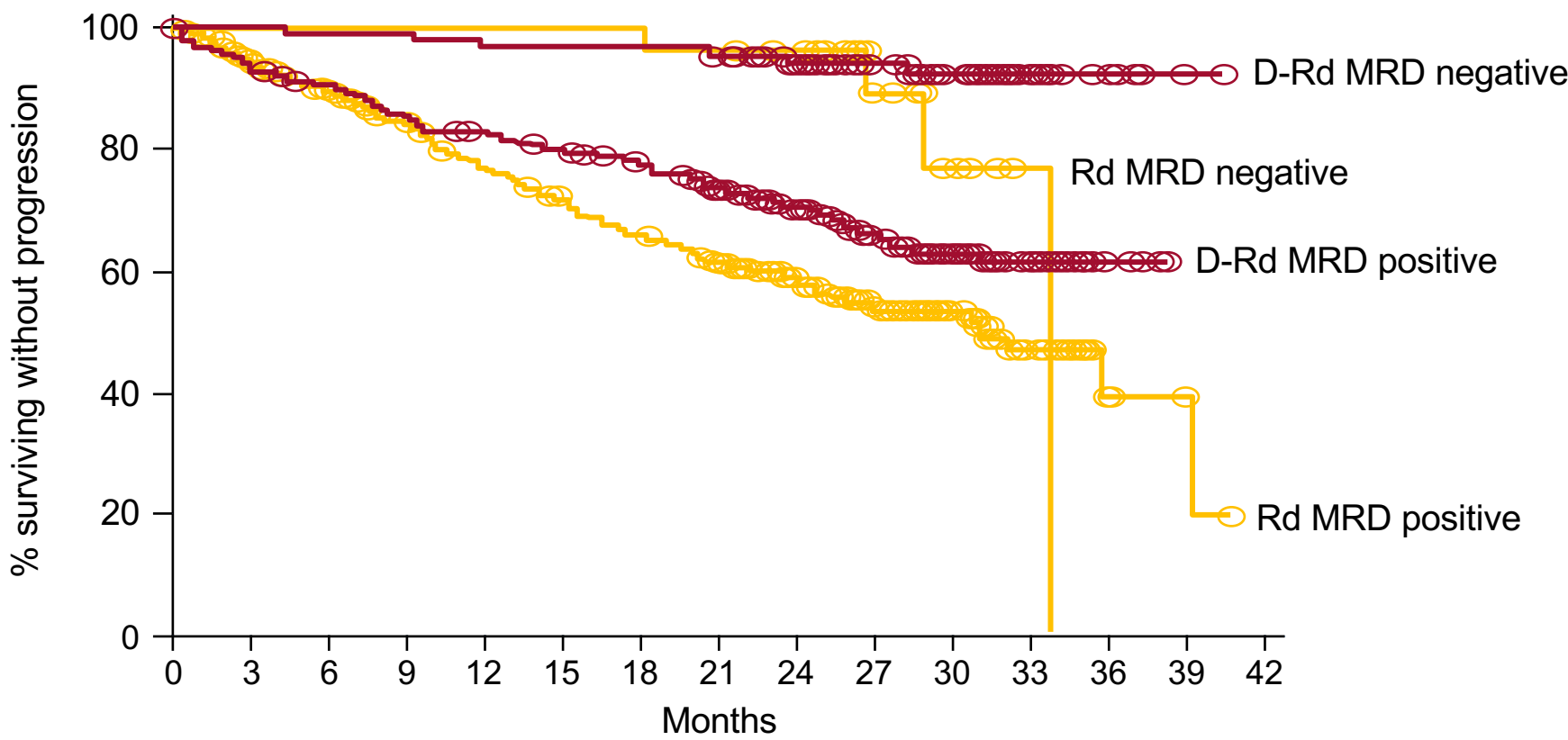
KRd in Newly Dx MM: Summary (Forte Trial)



MASTER Trial: Dara-KRD in Newly Diagnosed MM



MAIA: PFS by MRD Status

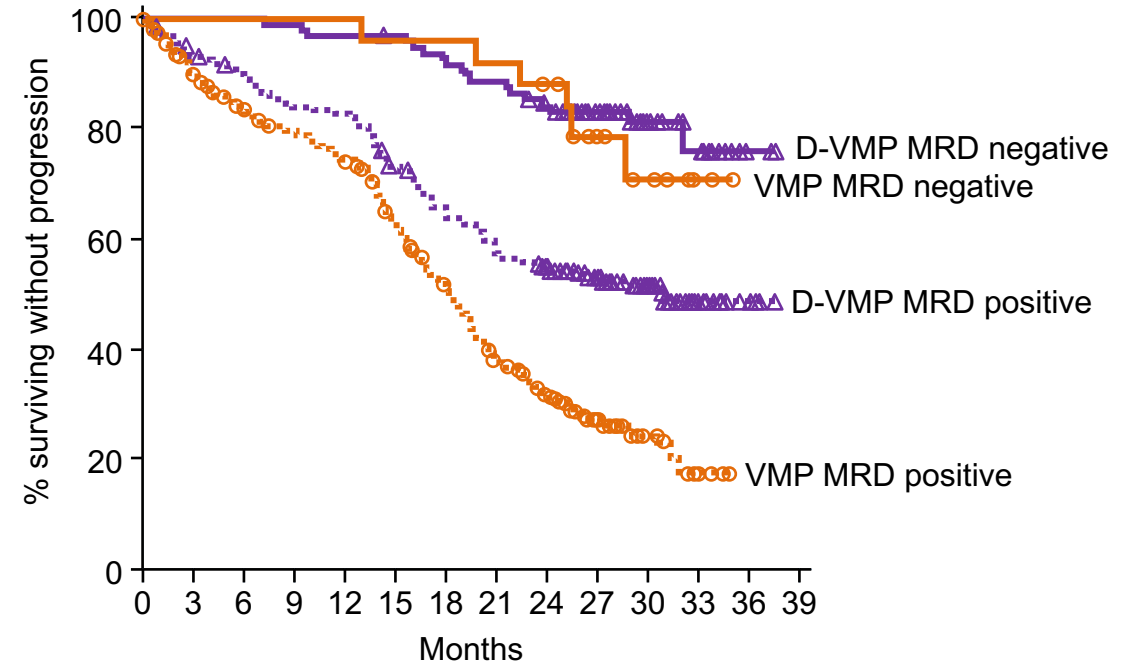
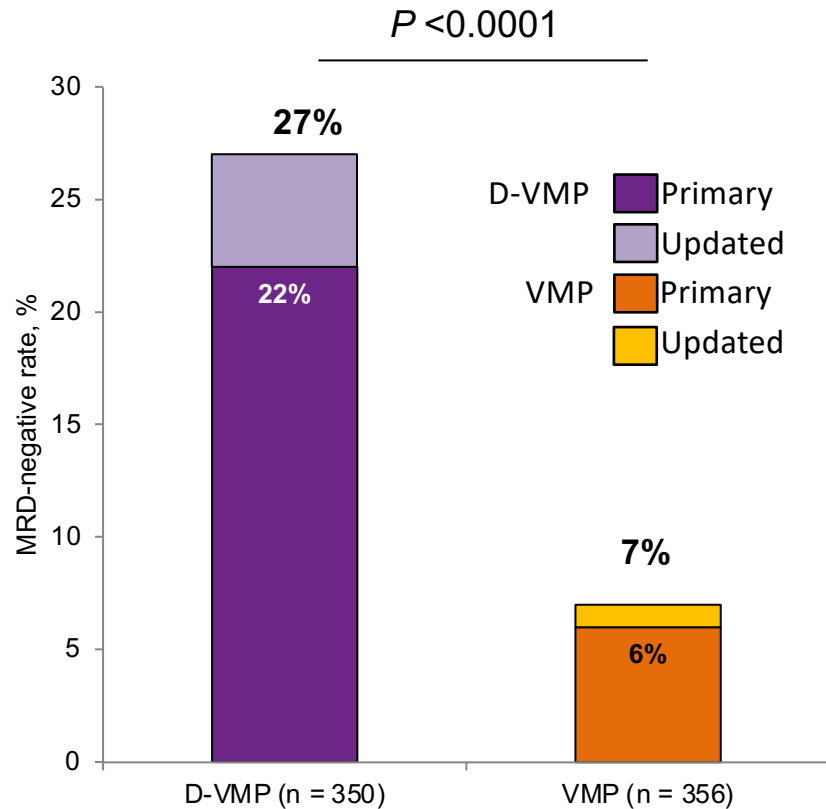


	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42
No. at risk															
Rd MRD negative	27	27	27	27	27	27	27	25	21	12	5	1	0	0	0
D-Rd MRD negative	89	89	88	88	86	86	86	84	70	55	33	12	5	1	0
Rd MRD positive	342	305	280	253	227	209	192	175	128	82	45	17	3	2	0
D-Rd MRD positive	279	258	247	232	223	214	204	187	133	91	53	23	6	0	0

- >3-fold higher MRD negativity achieved with D-Rd

ALCYONE: MRD status (10^{-5})

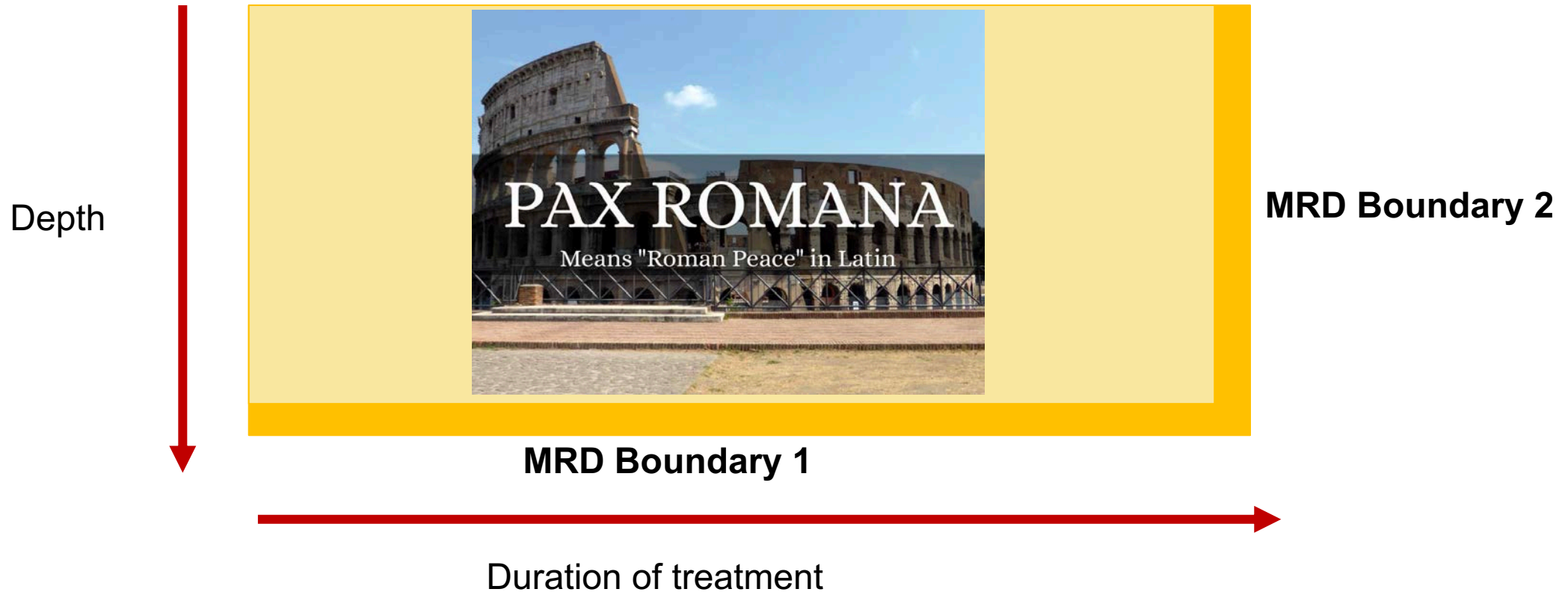
- Median (range) follow-up: 27.8 (0-39.2) months



	No. at risk														
	0	3	6	9	12	15	18	21	24	27	30	33	36	39	
VMP MRD negative	25	25	25	25	25	24	24	23	20	12	6	2	0	0	
DVMP MRD negative	96	96	96	95	93	92	89	84	77	57	28	14	2	0	
VMP MRD positive	331	279	252	237	220	182	145	104	82	47	21	3	0	0	
D-VMP MRD positive	254	226	216	203	199	173	154	136	126	81	45	17	7	0	

- Deepening MRD-negative rate with longer follow-up for D-VMP
- Lower risk of progression or death in all MRD-negative patients
 - ~4-fold higher MRD negativity achieved with D-VMP

MRD is not everything, it's the only thing!



High risk MM Like ALL?

Test Results

Minimal Residual Disease (MRD) Status	Estimated Myeloma Molecules per Million Cells
NEGATIVE	0.0

Interpretation

The sample is **NEGATIVE** for the presence of myeloma gene rearrangements. Myeloma gene rearrangements were previously identified in an ID sample (December 24, 2015, Accession No. 205825). The previously identified myeloma gene rearrangements are **NOT** present in the current MRD sample, which is consistent with the sample being **NEGATIVE** for myeloma cells. The results of this test should be interpreted in the complete clinical context, including the patient's clinical presentation and current treatment regimen.

MRD Monitoring (Cellular Compartment)



Hyperdiploid Like FL?

Test Results

Minimal Residual Disease (MRD) Status	Estimated Myeloma Molecules per Million Cells
POSITIVE	174

Interpretation

The sample is **POSITIVE** for the presence of myeloma gene rearrangements. Myeloma gene rearrangements were previously identified in an ID sample (November 11, 2016, Accession No. 210889). The presence of myeloma gene rearrangements is consistent with the sample being **POSITIVE** for myeloma cells. The results of this test should be interpreted in the complete clinical context, including the patient's clinical presentation and current treatment regimen.

MRD Monitoring (Cellular Compartment)



Case 1

- 53 yo male
- New diagnosis MM
- Induction with KRd
- Completed SCT
- Recovered and comes for day 100

SPECIMEN TYPE / SPECIMEN SOURCE Fresh Bone Marrow	COLLECTION DATE 09/11/2020	DATE RECEIVED 09/15/2020	SAMPLE ID SP-825063
ICD CODE C90.00 Multiple myeloma not having achieved remission			
ORDERING PHYSICIAN Rafael Fonseca		INSTITUTION Mayo Clinic Arizona Division of Hematology and Medical Oncology	

SAMPLE-LEVEL MRD RESULT

No Residual Sequences Detected

ESTIMATED MRD VALUE:

0 residual clonal cells (Range: 0 - 1) **

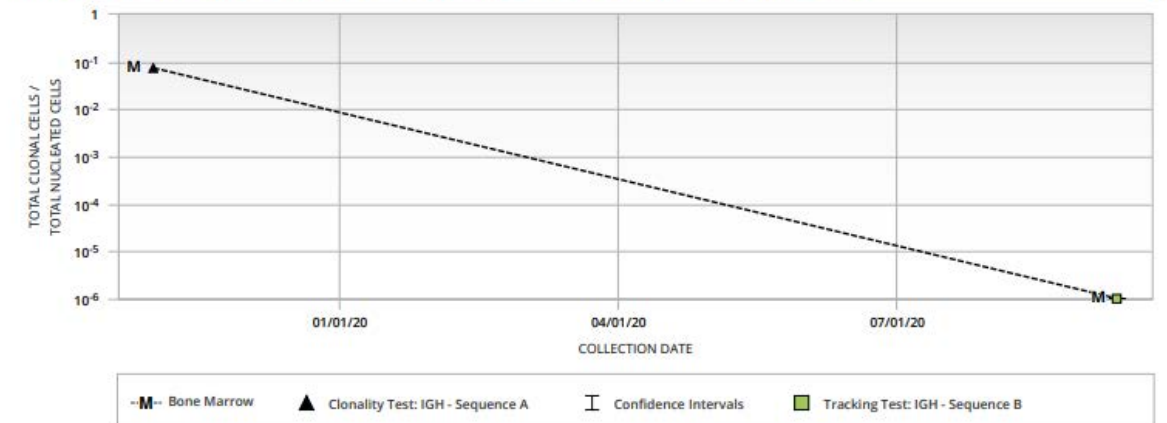
Total nucleated cells evaluated from this sample: 4,311,991

The MRD range presented above represents the 95% confidence interval for the measured number of residual clonal sequences per million nucleated cells. Details for each identified dominant sequence from this sample are provided on subsequent pages of this report.

RESULTS SUMMARY

- Genomic DNA was extracted from a fresh bone marrow sample.
- The 3 dominant sequences identified in a diagnostic sample from this patient were not detected in this current sample.
- ** The sensitivity of this assay is directly related to the total number of cells (or cellular equivalents of genomic DNA) analyzed. There were 4,311,991 total nucleated cells evaluated from this sample.
- ▶ **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

SAMPLE-LEVEL MRD TRACKING (shows only the sequence determining the MRD result for each time point)



The number of clonal cells may vary by sample type. As such, changes in clonal cell values over time are best compared using the same sample type, indicated by connecting lines.



Case 2

- 58 yo male
- New diagnosis MM
- Induction with KRd
- Completed SCT
- 11/2018 MRD+
 - Dara-Rd
- Aug 2019 MRD+
 - More Dara-Rd
- Feb 2020 MRD-
 - R maintenance

ICD CODE
C90.00 Multiple myeloma not having achieved remission

ORDERING PHYSICIAN
Rafael Fonseca

INSTITUTION
Mayo Clinic Arizona Division of Hematology and Medical Oncology

SAMPLE-LEVEL MRD RESULT

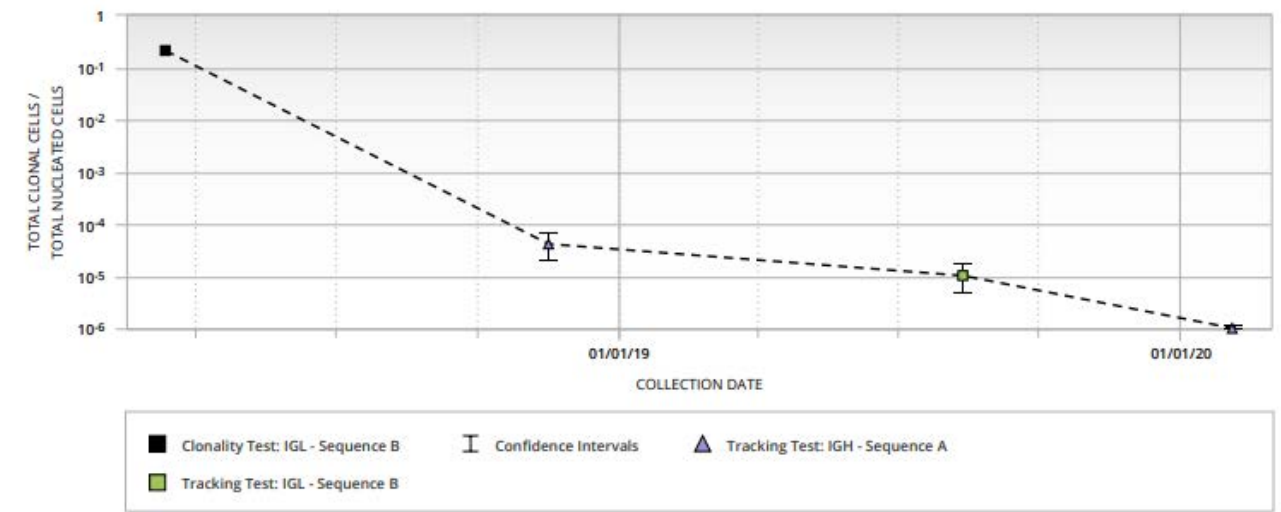
No Residual Sequences Detected
 ESTIMATED MRD VALUE:
0 residual clonal cells (Range: 0 - 1) **
Sequence determining MRD result: IGH Sequence A

The MRD range presented above represents the 95% confidence interval for the measured number of residual clonal sequences per million nucleated cells. Details for each identified dominant sequence from this sample are provided on subsequent pages of this report.

RESULTS SUMMARY

- Genomic DNA was extracted from a fresh bone marrow sample.
- The 2 dominant sequences identified in a diagnostic sample from this patient were not detected in this current sample.
- ** The sensitivity of this assay is directly related to the total number of cells (or cellular equivalents of genomic DNA) analyzed. There were 1,678,265 total nucleated cells evaluated from this sample.
- ▶ **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

SAMPLE-LEVEL MRD TRACKING (shows only the sequence determining the MRD result for each time point)



Thank you!

