



CDDF MULTI-STAKEHOLDER WORKSHOP
MINIMAL RESIDUAL DISEASE

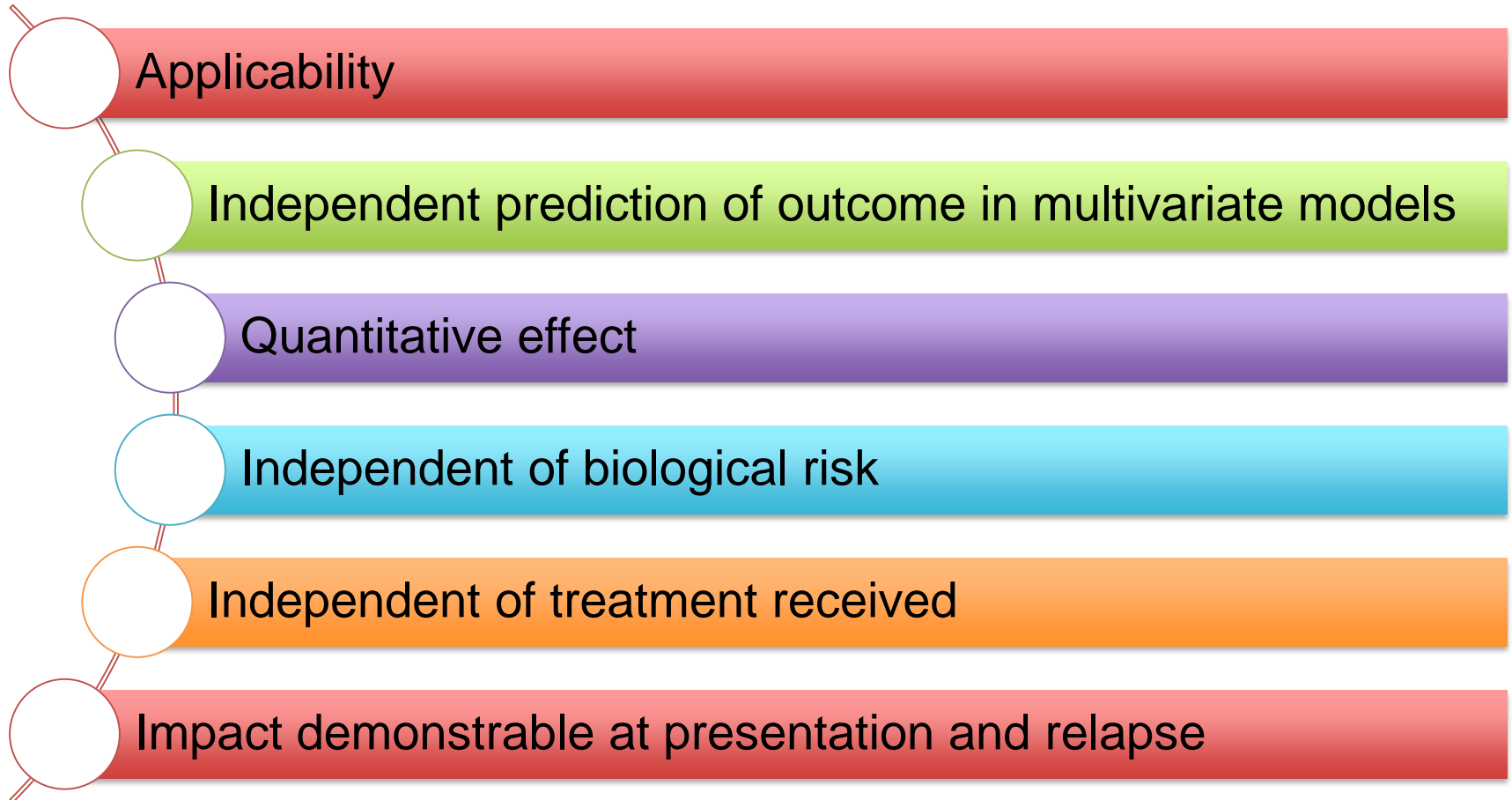
18-19 October 2017
London, UK

Myeloma MRD: UK data

Roger Owen
St James's Institute of Oncology
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What do we need?

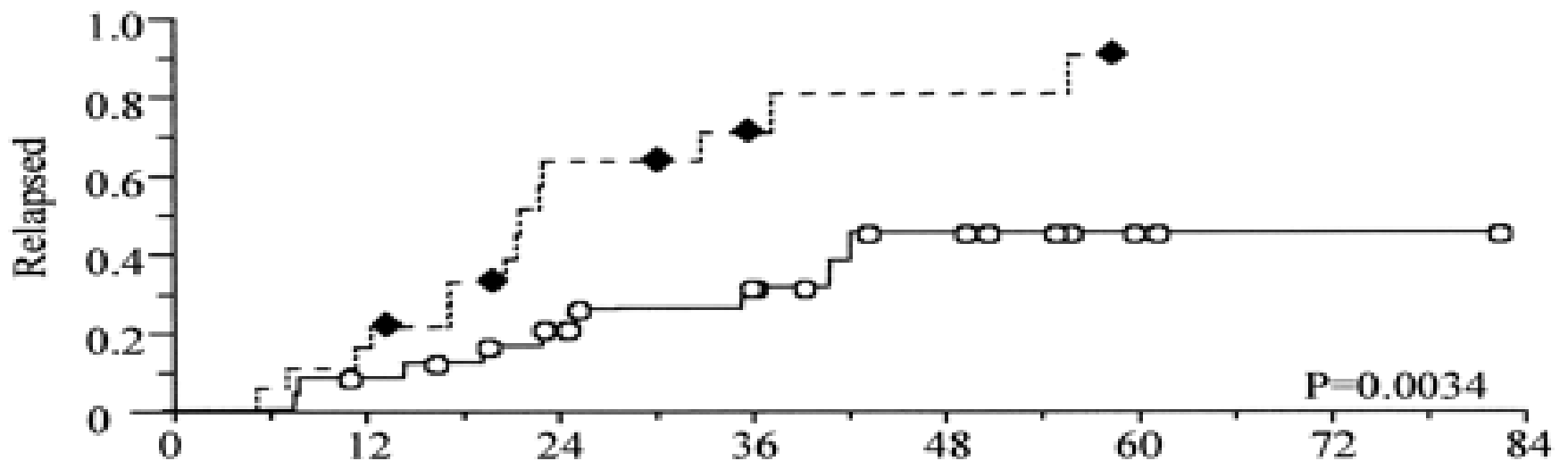


Which trials?

- **Upfront**
 - Myeloma IX
 - Myeloma XI/XI+
 - PADIMAC
 - CARDAMON (ongoing)
 - MUK nine (ongoing)
- **Relapse**
 - Myeloma X
 - MUK five
 - ACCORD / Myeloma XII (ongoing)
- **Planned** – Myeloma XIV and XV

Flow cytometric disease monitoring in multiple myeloma: the relationship between normal and neoplastic plasma cells predicts outcome after transplantation

Andy C. Rawstron, Faith E. Davies, Ranjit DasGupta, A. John Ashcroft, Russell Patmore, Mark T. Drayson, Roger G. Owen, Andrew S. Jack, J. Anthony Child, and Gareth J. Morgan

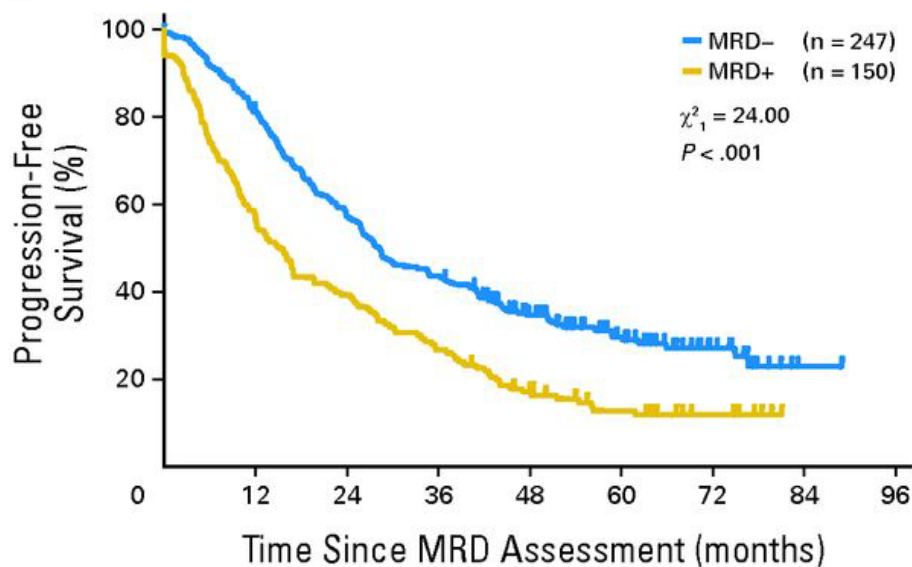


blood

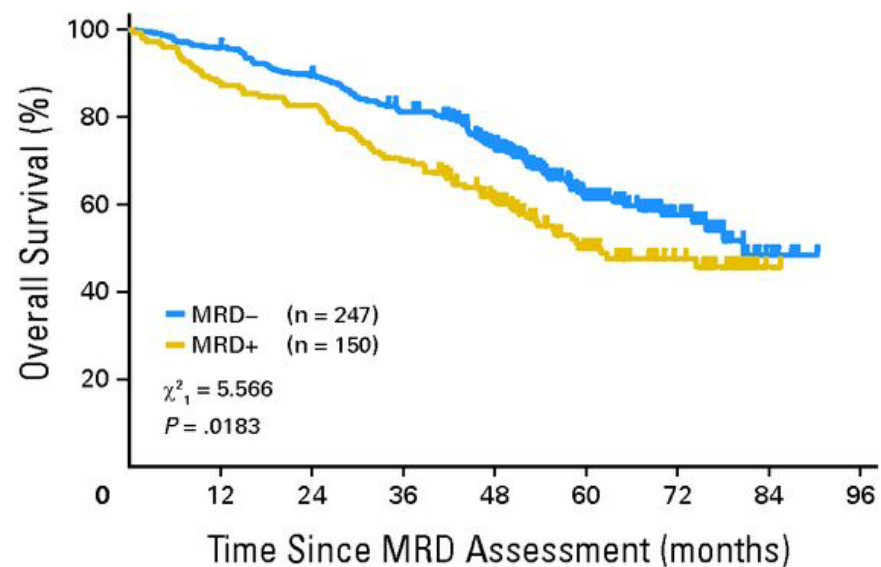
2002!

Minimal Residual Disease Assessed by Multiparameter Flow Cytometry in Multiple Myeloma: Impact on Outcome in the Medical Research Council Myeloma IX Study

Andy C. Rawstron, J. Anthony Child, Ruth M. de Tute, Faith E. Davies, Walter M. Gregory, Sue E. Bell, Alexander J. Szubert, Nuria Navarro-Coy, Mark T. Drayson, Sylvia Feyler, Fiona M. Ross, Gordon Cook, Graham H. Jackson, Gareth J. Morgan, and Roger G. Owen



No. at risk	0	12	24	36	48	60	72	84	96
MRD-	200	145	107	73	41	20	2	0	
MRD+	87	59	42	24	14	7	0	0	

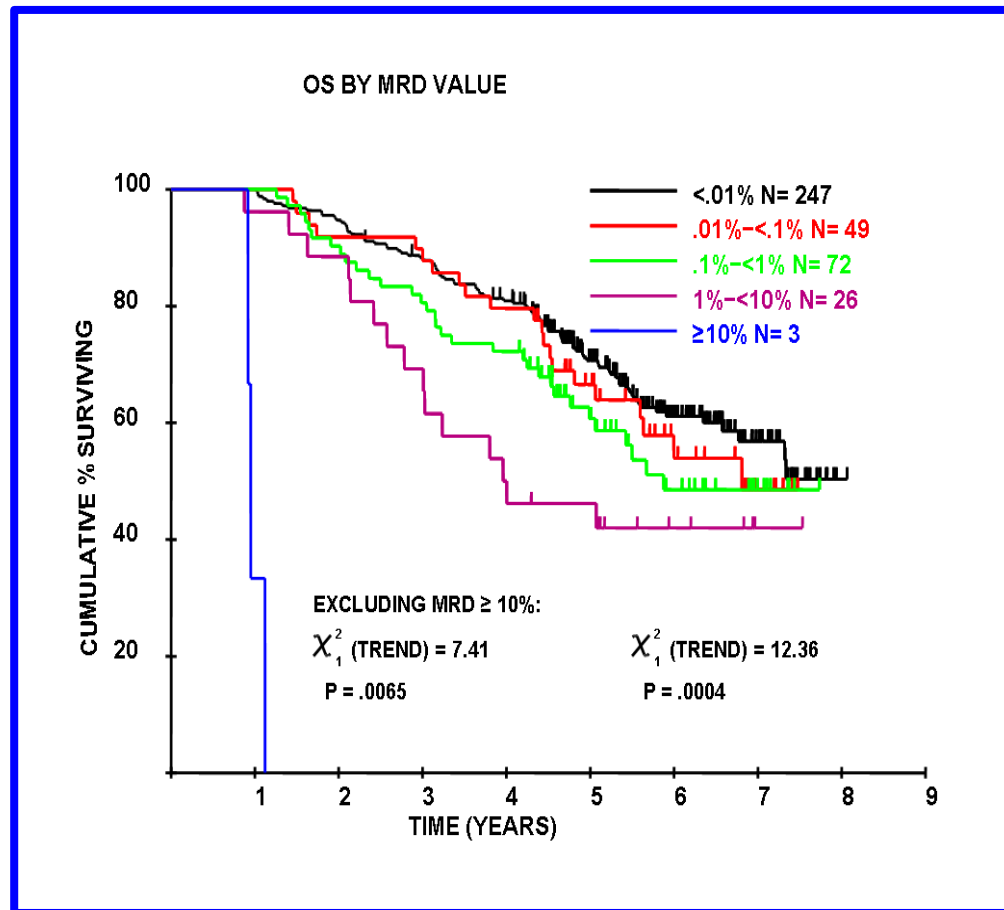


No. at risk	0	12	24	36	48	60	72	84	96
MRD-	237	220	197	157	92	43	9	0	
MRD+	132	124	105	83	46	25	1	0	

LYMPHOID NEOPLASIA

Minimal residual disease in myeloma by flow cytometry: independent prediction of survival benefit per log reduction

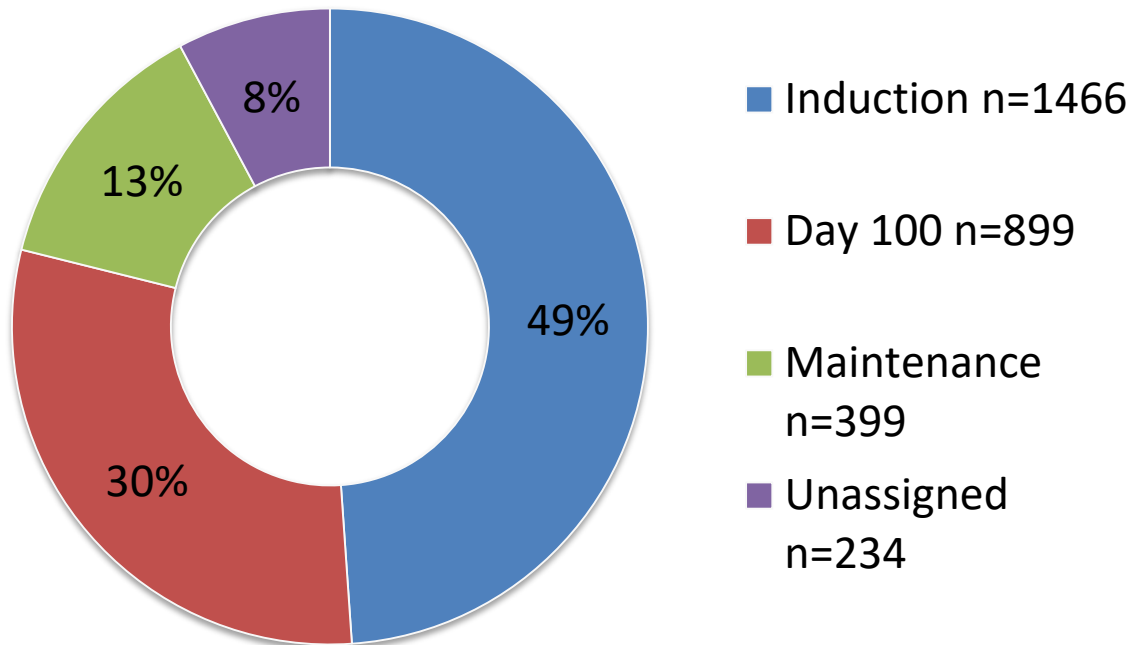
Andy C. Rawstron,¹ Walter M. Gregory,² Ruth M. de Tute,¹ Faith E. Davies,³ Sue E. Bell,² Mark T. Drayson,⁴ Gordon Cook,¹ Graham H. Jackson,⁵ Gareth J. Morgan,³ J. Anthony Child,² and Roger G. Owen¹



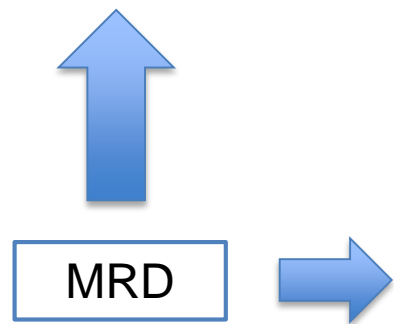
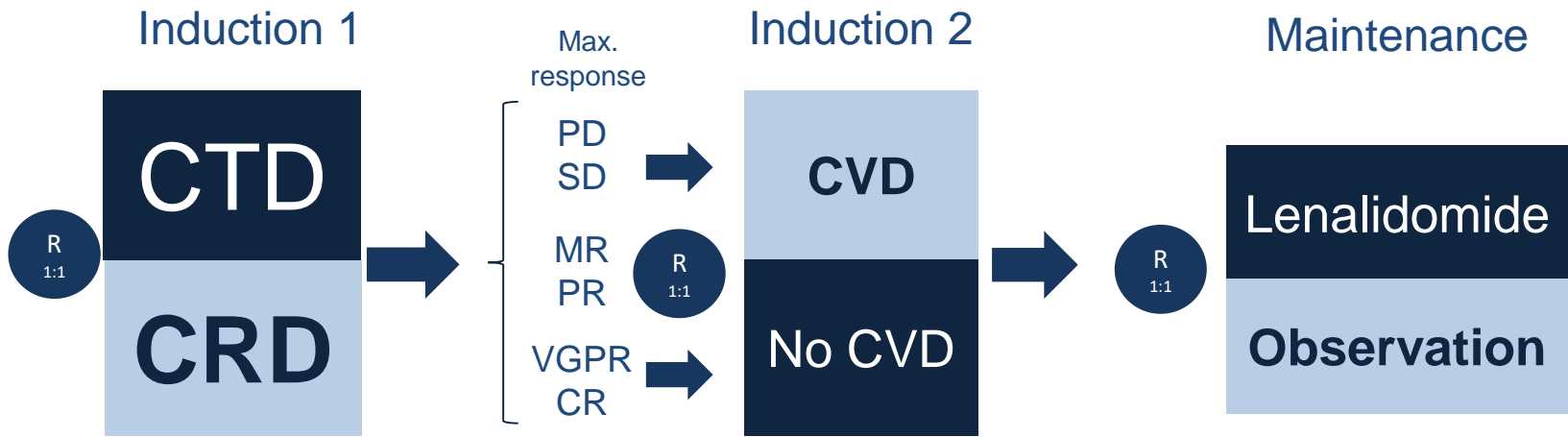
Multivariate analysis.

Variable	PFS				OS			
	Univariate		Multivariate		Univariate		Multivariate	
	χ^2	p-value	χ^2	p-value	χ^2	p-value	χ^2	p-value
Log(MRD)	33.0	<.0001	19.4	<.0001	12.4	.0004	11.8	.0006
Response post ASCT [^]	20.5	<.0001	1.3	.25	6.60	.01	.00	.99
International Staging System (1-3)	4.5	.03	.72	.40	12.9	.0003	1.9	.16
Cytogenetics [‡]	39.8	<.0001	41.3	<.0001	36.9	<.0001	35.5	<.0001
Log(β 2 microglobulin)	8.3	.004	1.8	.18	11.9	.0006	.34	.56
Platelets*	10.6	.001	3.8	.05	2.1	.14	.00	.98
Haemoglobin**	15.0	.0001	7.5	.006	8.5	.003	1.7	.19
Age (continuous)	.1	.75	.01	.92	1.7	.20	1.9	.17
Gender	.3	.58	.23	.63	.01	.93	.04	.85

Myeloma XI/XI+ (n=2998).



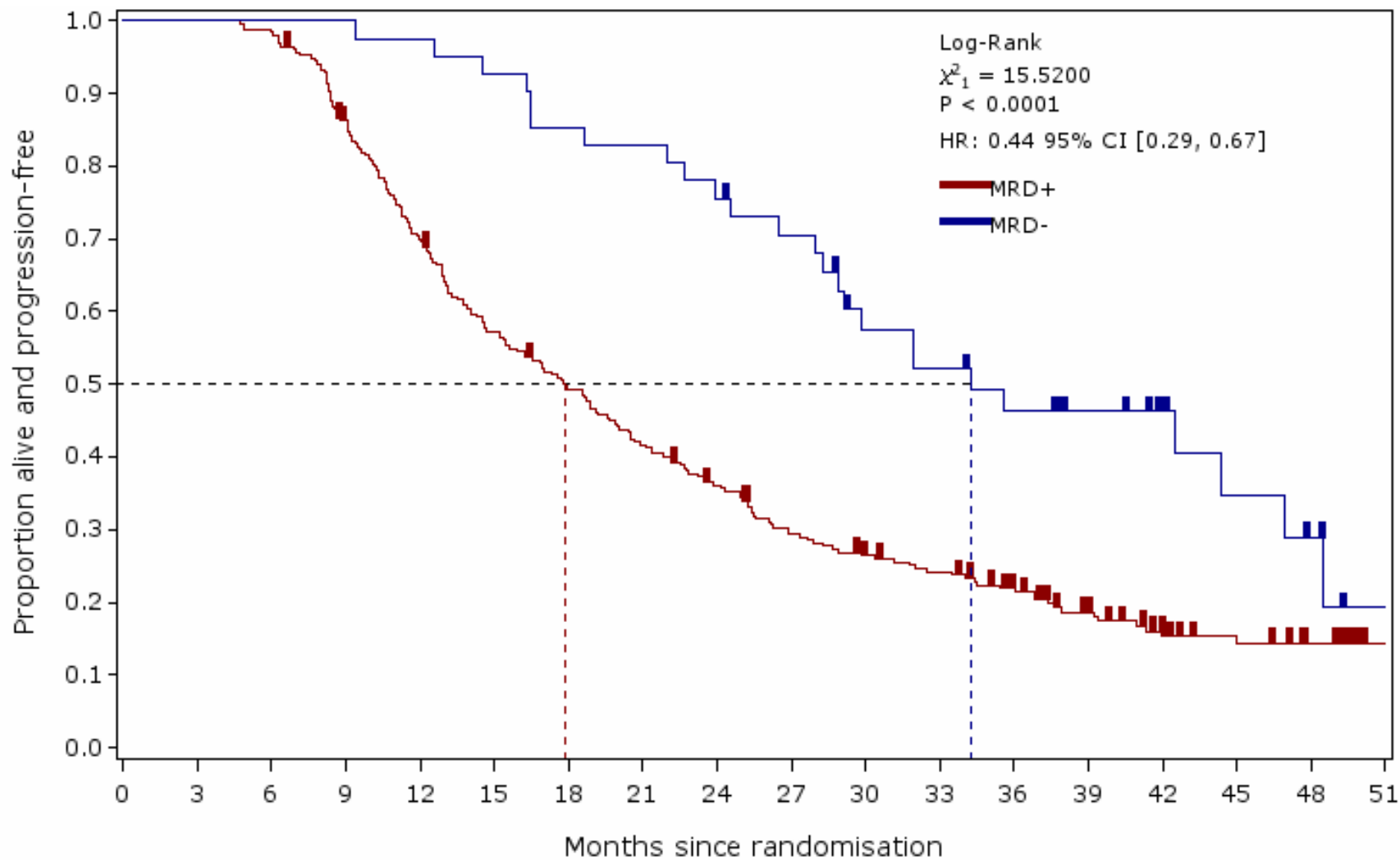
Myeloma XI – transplant ineligible schema



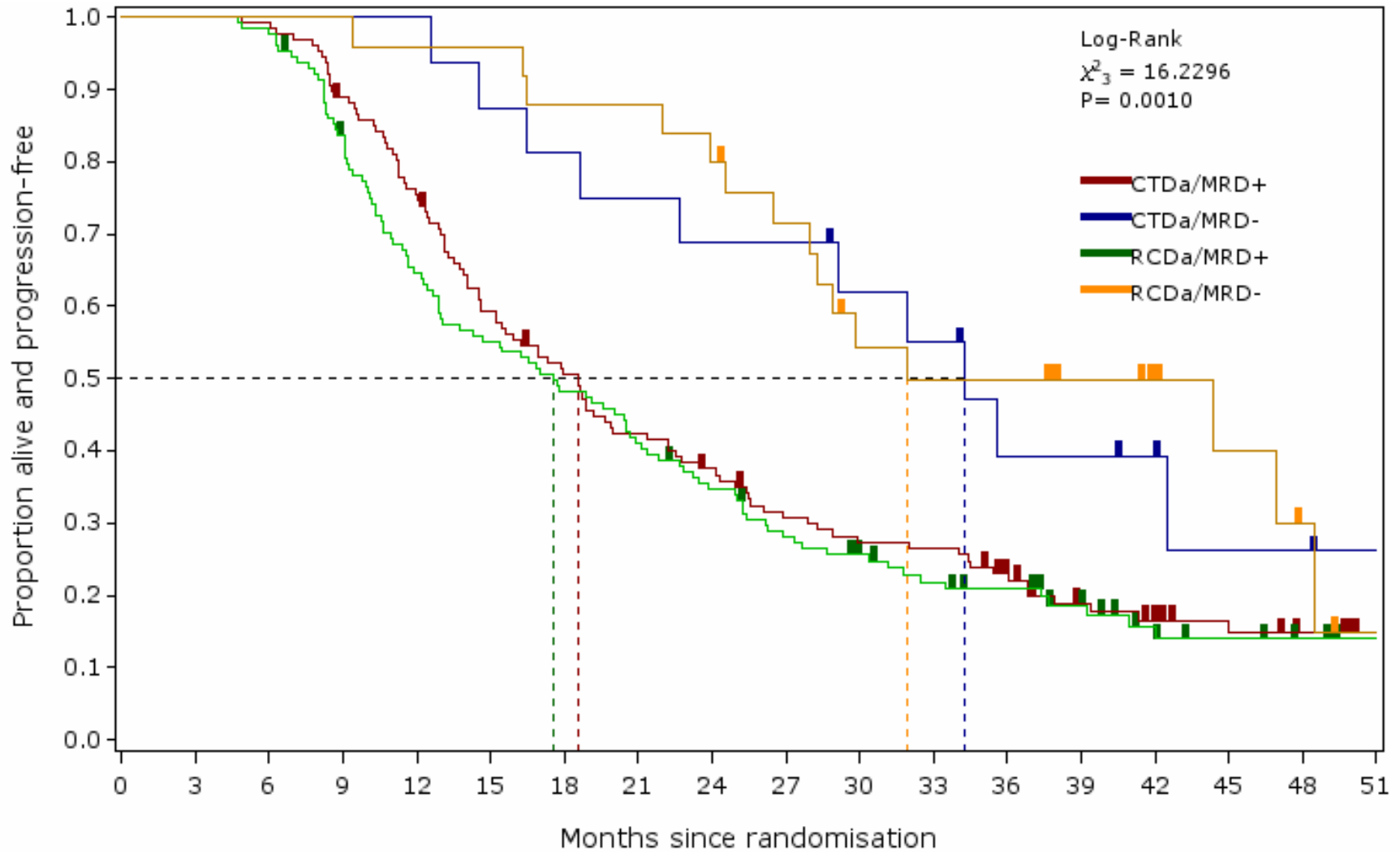
N=297/1852

- Median age 74.0 yrs (56-87)
- 62.8% male
- IgG 60.5%
- ISS III 34.2%

PFS according to MRD (qualitative)



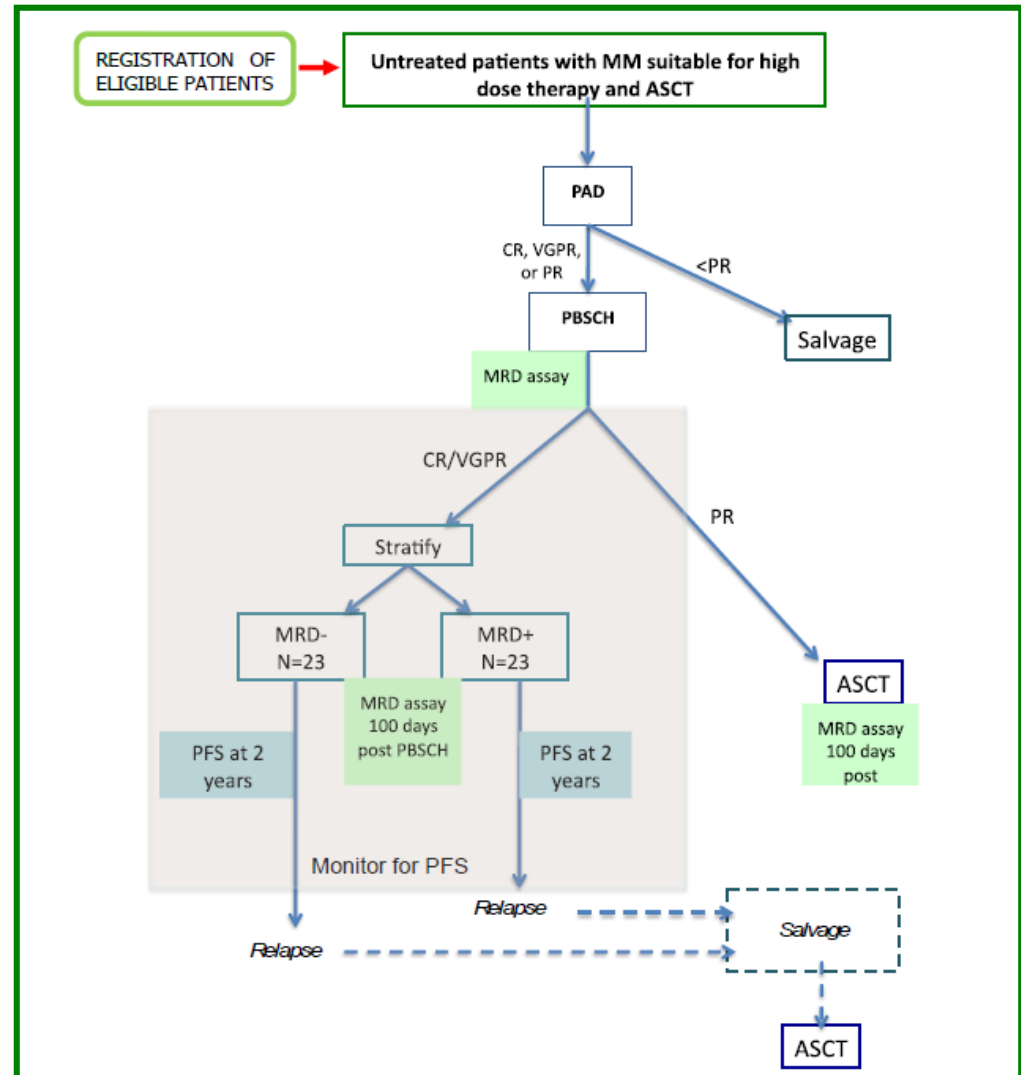
Impact of therapy.



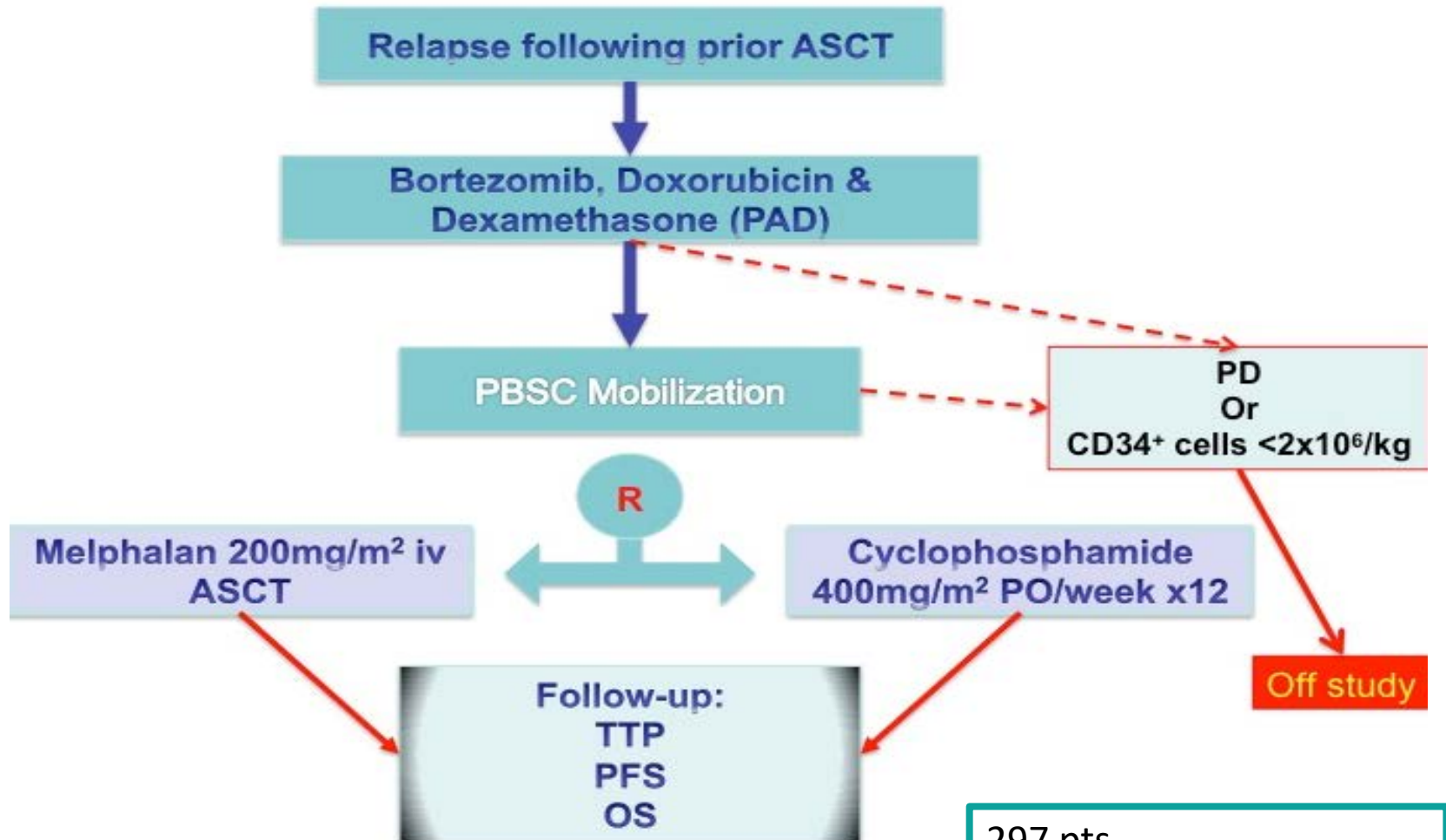
Padimac

Phase II study of Bortezomib, Adriamycin and Dexamethasone (**PAD**) therapy for previously untreated patients with multiple myeloma: **I**mpact of minimal residual disease (**MRD**) in patients with deferred **ASCT** (**PADIMAC**).

MRD samples = 196

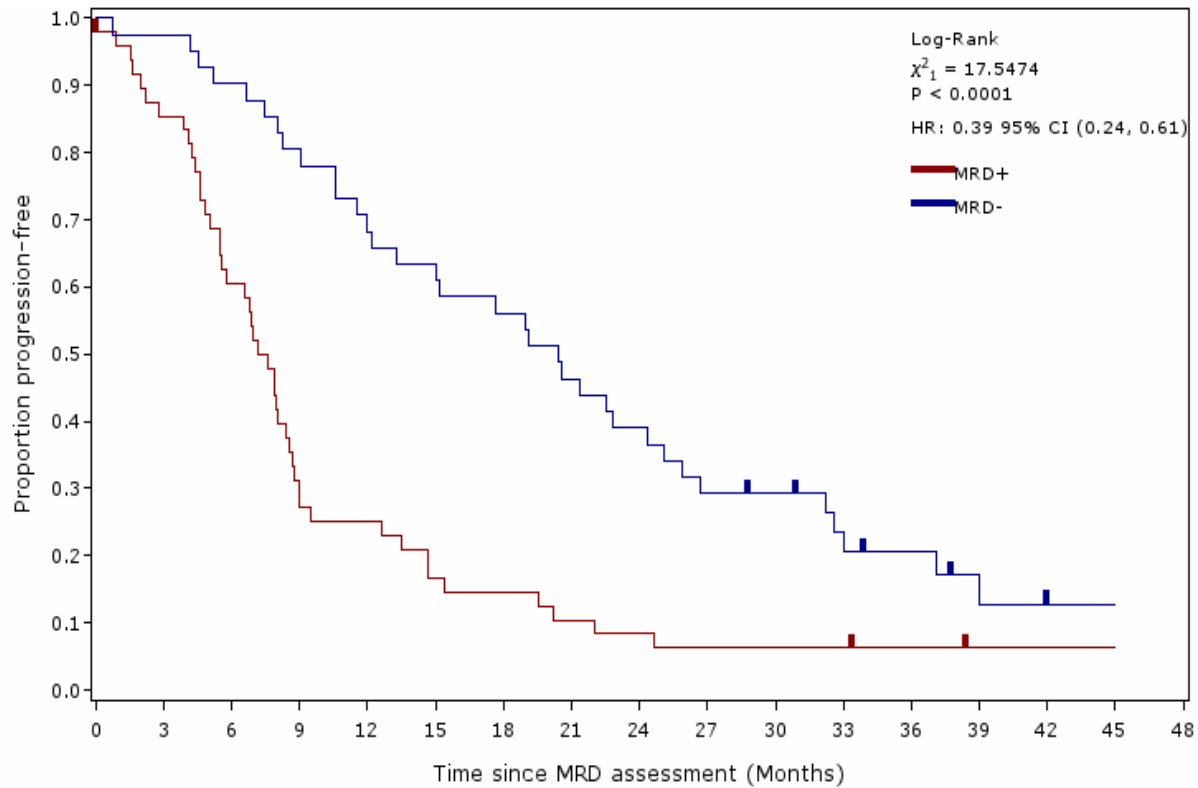


Myeloma X Study Schema



297 pts
184 pts randomised
Day 100 MRD 90 pts

Myeloma X: TTP according to MRD



The Future.....

- Regulatory endpoint
- MRD directed academic studies
- Routine care



