Total therapy is the only approach to achieving long-term disease control

Argument against

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Curing myeloma at last: defining criteria and providing the evidence

Bart Barlogie,[1] Alan Mitchell,[2] Frits van Rhee,[1] Joshua Epstein,[1] Gareth J. Morgan,[1] and John Crowley[2]

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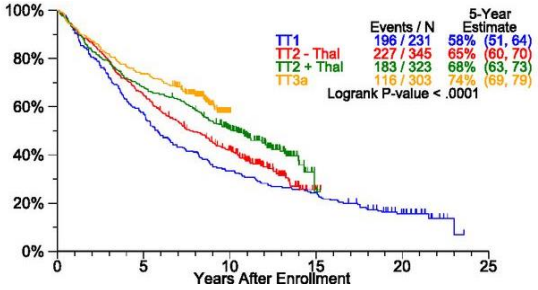
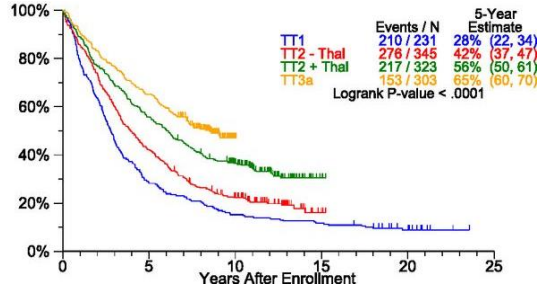
TT1	TT2 (randomization Thal vs No Thal)		TT3A	
INDUCTION	INDUCTION		INDUCTION	
VAD x 3 HD-CTX +HPC Collection EDAP	VAD DCEP 1 CAD +HPC Collection DCEP 2		V-DTPACE +HPC Collection V-DTPACE	
TRANSPLANT	TRANSPLANT		TRANSPLANT	
MEL200 x 2	MEL200 x 2		MEL200 x 2	
CONSOLIDATION	CONSOLIDATION		CONSOLIDATION	
Not Applicable	DPACE x 4 cycles		V-DTPACE x 2	
MAINTENANCE	MAINTENANCE		MAINTENANCE	
	YEAR 1	YEARS 2-3	YEAR 1	YEARS 2-3
IFN TIW	Dex + IFN±Thal	IFN±Thal	Monthly VDT	Thal + Dex

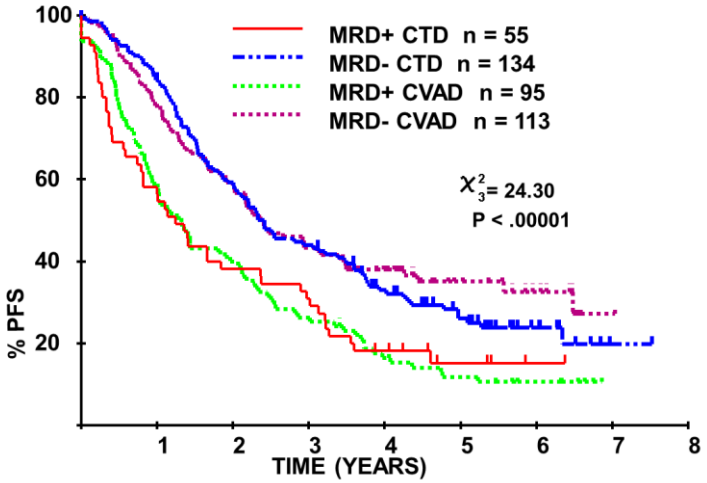
Factor	All Patients
Median Age (Yrs)	56.5 (N=1202) (24.8 - 77.3)
Age >= 65 yr	240/1202 (20%)



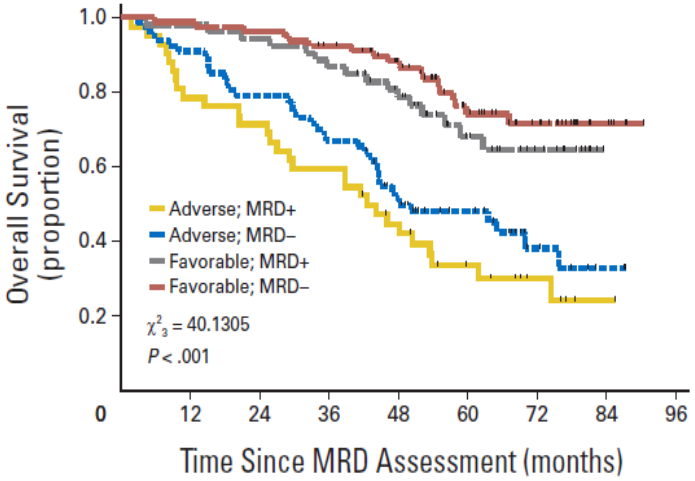


MRD negativity: the key to survival

Outcomes irrespective of treatment

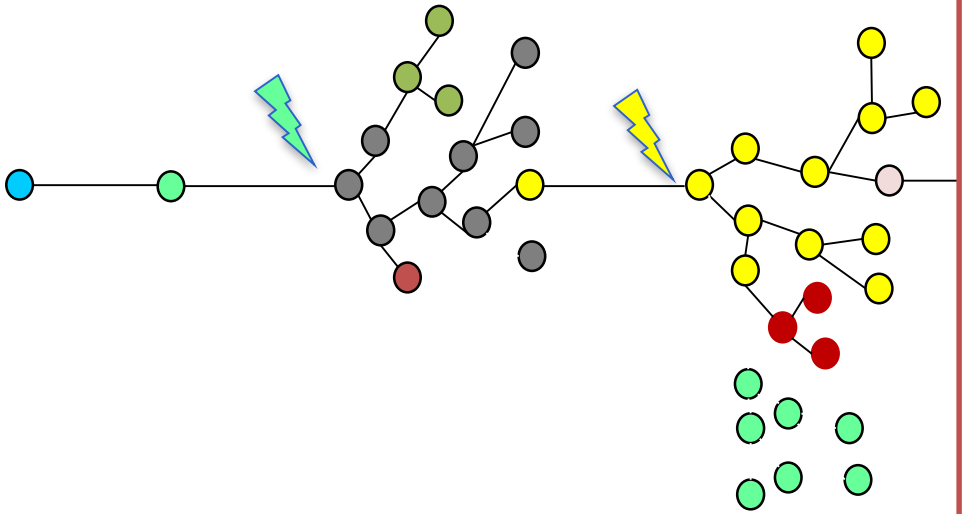


Cytogenetic risk remains predictive



De Tute et al (2013) *Clin Lymphoma Myeloma Leuk*
Rawstrom et al (2013) *JCO*

Intraclonal heterogeneity and clonal evolution



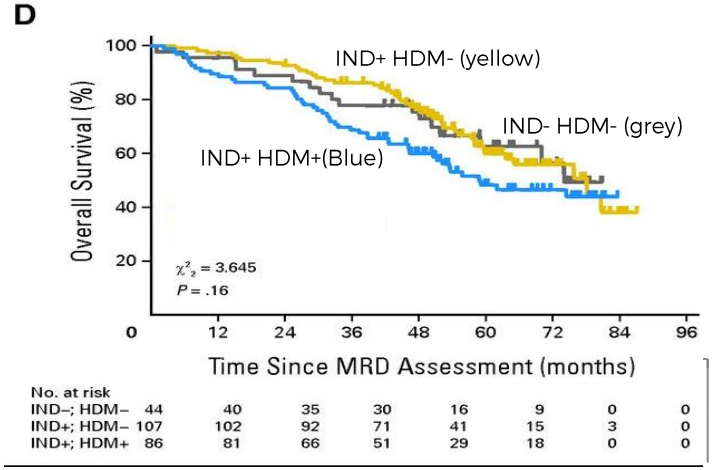
Can all clones be stopped with TT?

Extramedullary disease
Plasma cell leukemia

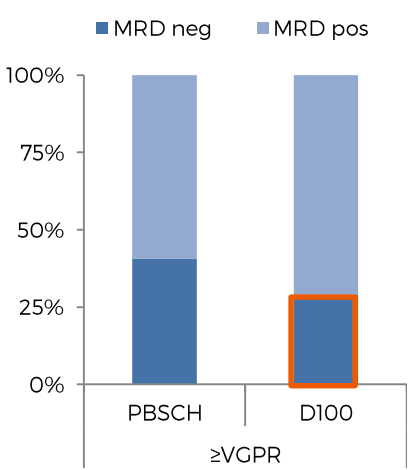
Morgan et al (2012) *Nat Reviews Cancer*

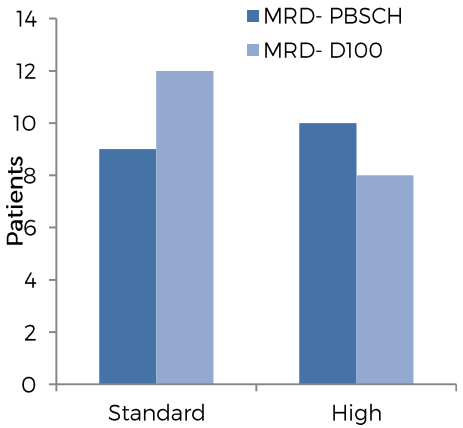
MRD negativity and genetic risk to guide therapy

Myeloma IX Overall Survival by MRD status



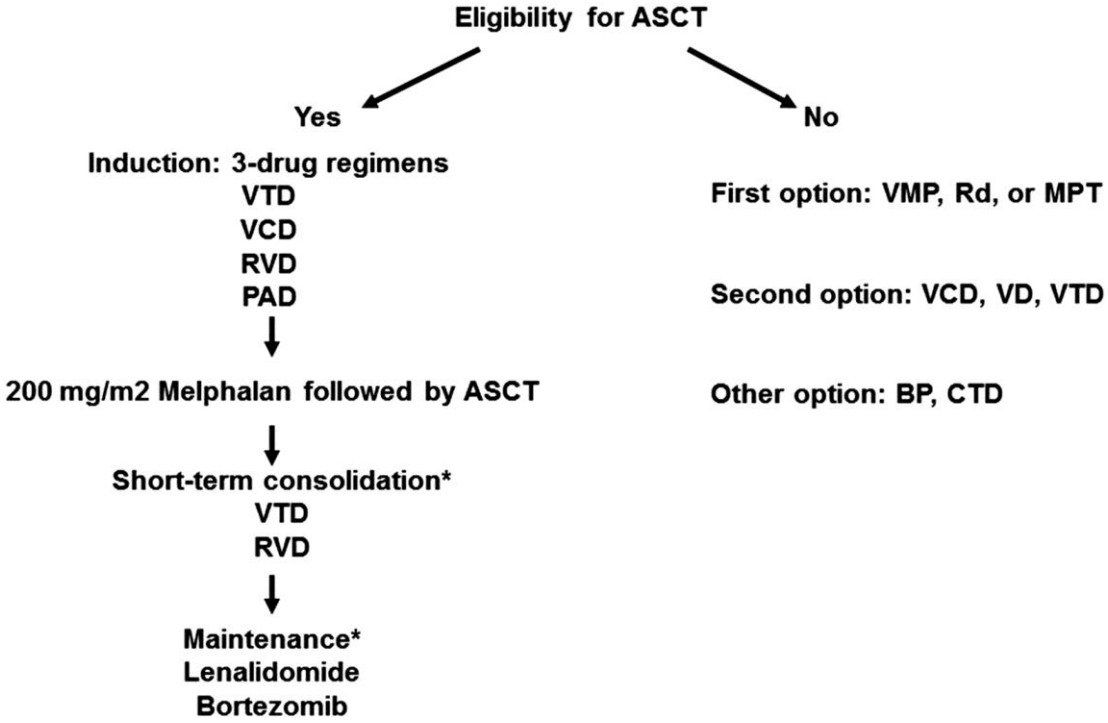
PADIMAC Trial: MRD following PAD induction only





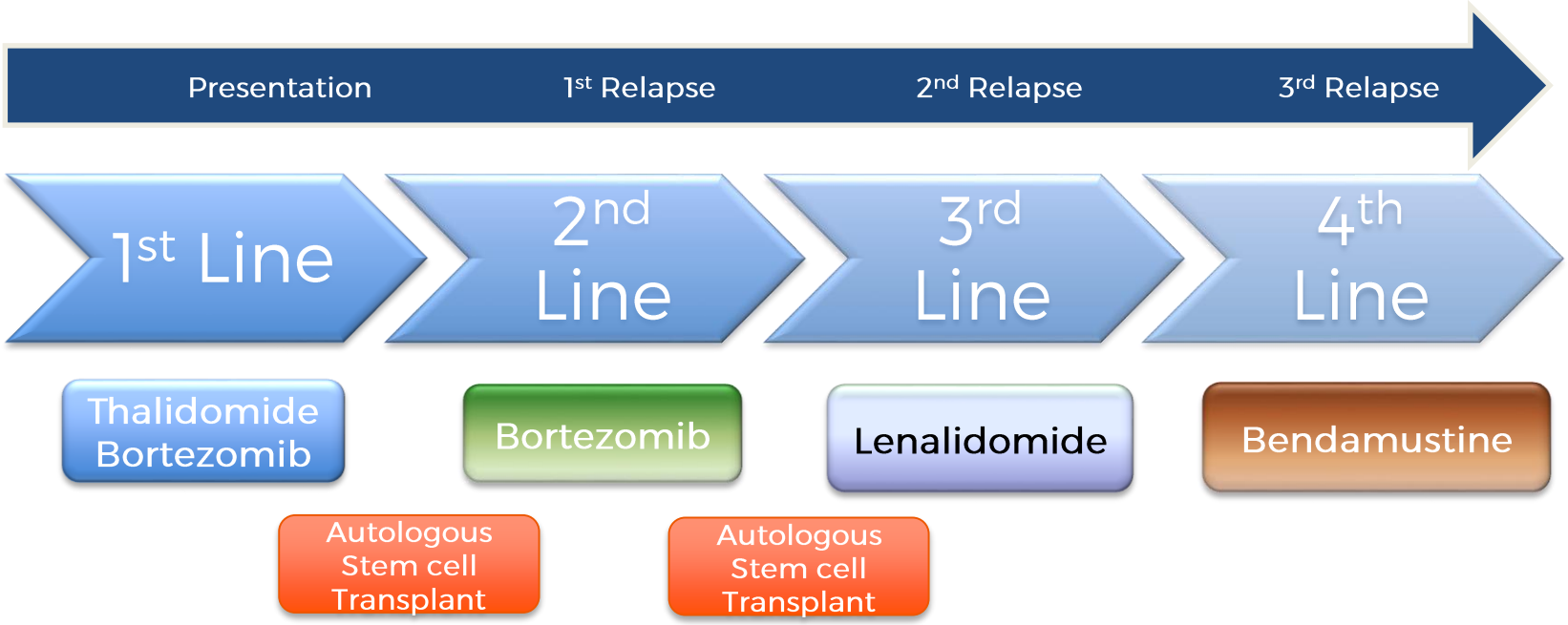
Rawstron et al (2013) *JCO*
Popat et al (2014) *ASH Abstract*

Recommended approach to front line therapy



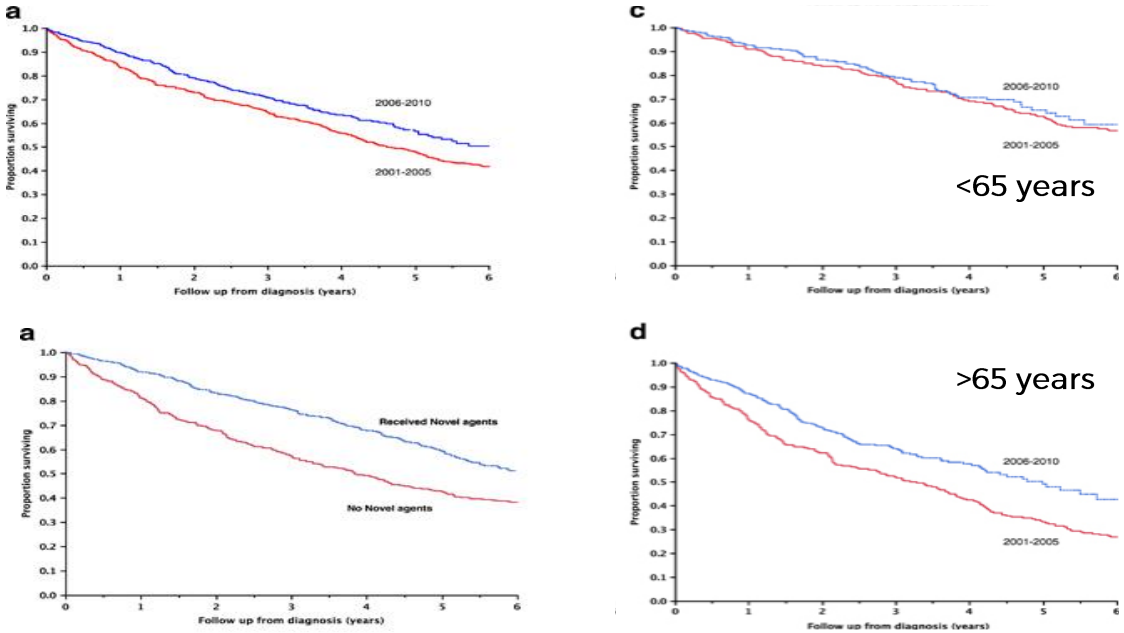
Moreau et al (2015) *Blood*

UK Myeloma Funded Treatment Pathway



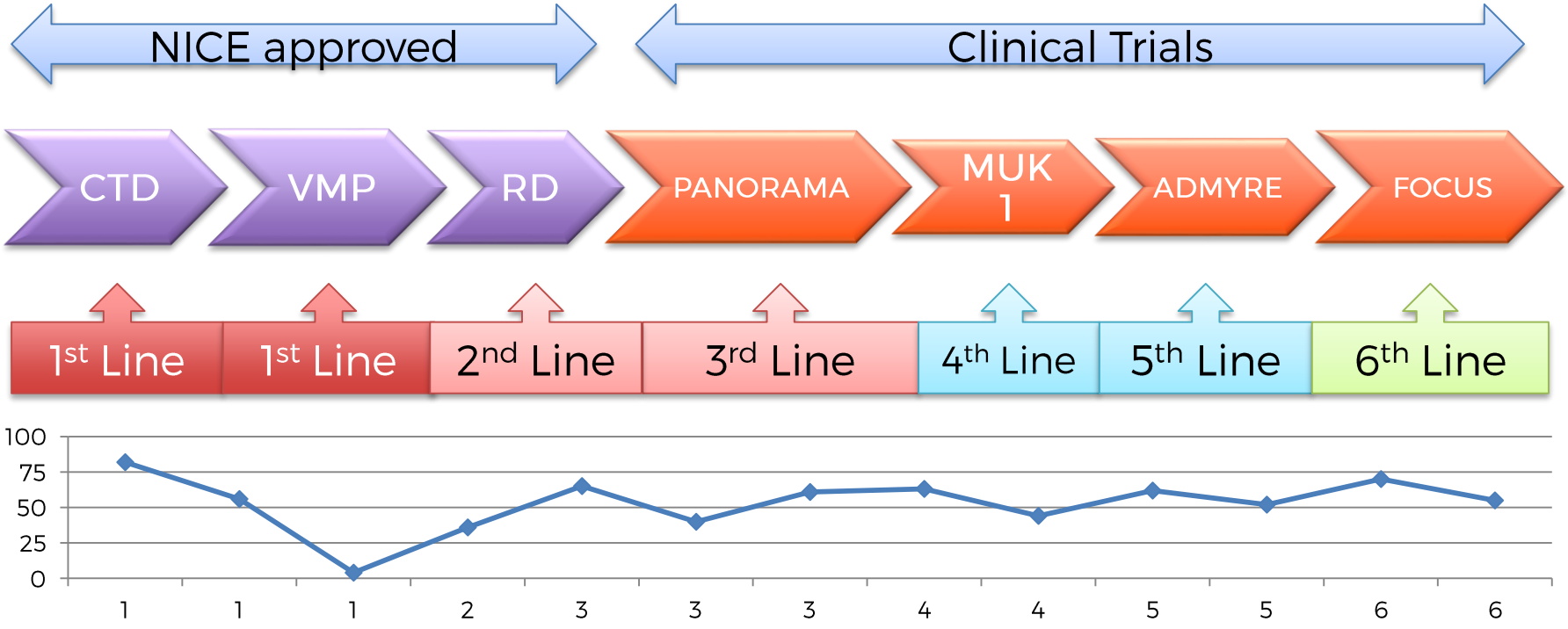
Reflects November 2015 CDF changes

Continued Improvement in Survival: Impact of novel therapies and age



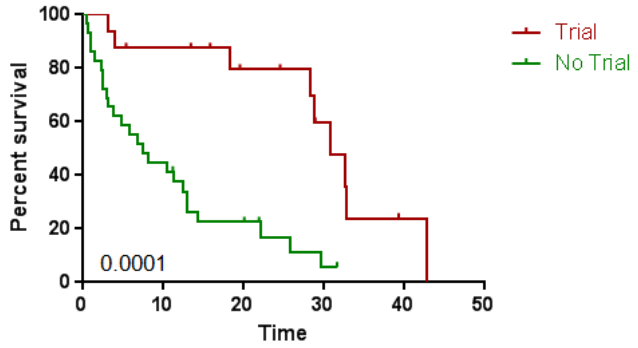
Kumar et al (2014) *Leukemia*

Sequential therapy an example: Case t(4;14) 2008-2013

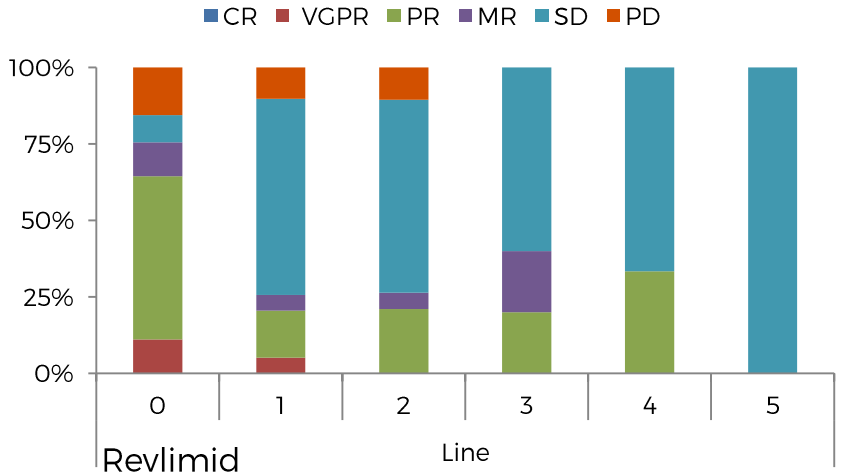


Sequential therapy to control relapsed disease

Outcomes of patients post thalidomide, velcade and revlimid



Trial 30.5 months
No trial 7.5 months

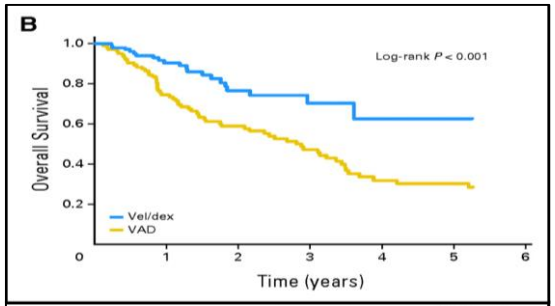


Unpublished UCLH data

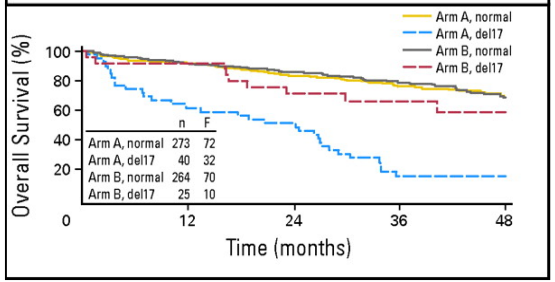
Risk adapted therapy in routine practice

Bortezomib for high risk myeloma

Imids for trisomy & t(11;14)



t(4;14)



17p-

Characteristics of patients with PFS >72 months with revlimid and dexamethasone

Table 2. Distribution of primary cytogenetic categories

Molecular cytogenetic classification	*All patients in whom cytogenetic studies were done (n = 28) No. of patients (%)*
Trisomies[a]	19 (68)
t(11;14)(q13;q32)	2 (7)
t(4;14)(p16;q32)	0 (0)
MAF translocations [t(14;16)(q32;q23) and t(14;20)(q32;q11)]	0 (0)
Other/unknown IgH translocation partner	0 (0)
Both IgH translocation and trisomies[b]	1(4)
Monosomy13/del(13q) in the absence of IgH translocation or trisomies[c]	3 (11)
Normal or insufficient plasma cells	4 (14)

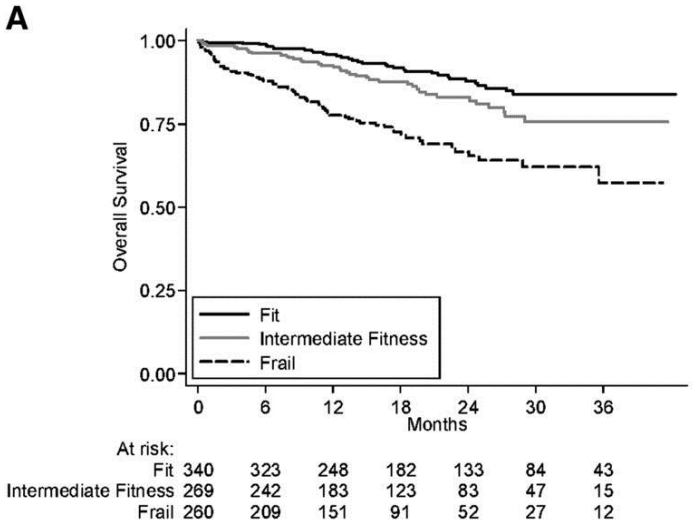
Molecular profiling will ultimately define risk

Avet-Loiseau H et al (2010) *JCO*; Sonneveld et al (2012) *JCO*

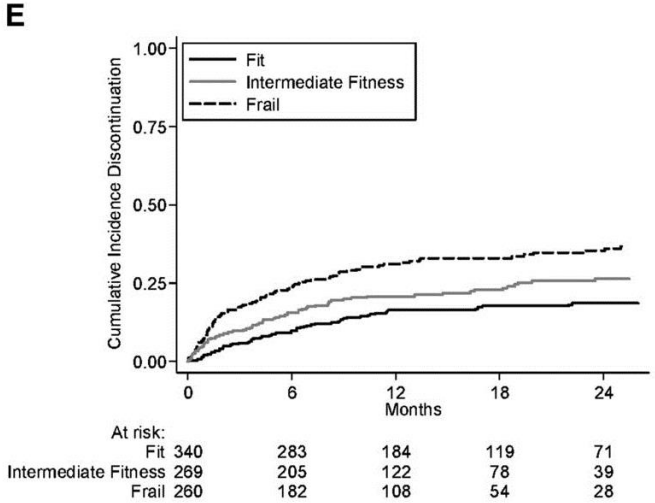
Vu et al Blood (2015) *Cancer Journal*

Performance adapted therapy

Overall Survival



Discontinuations



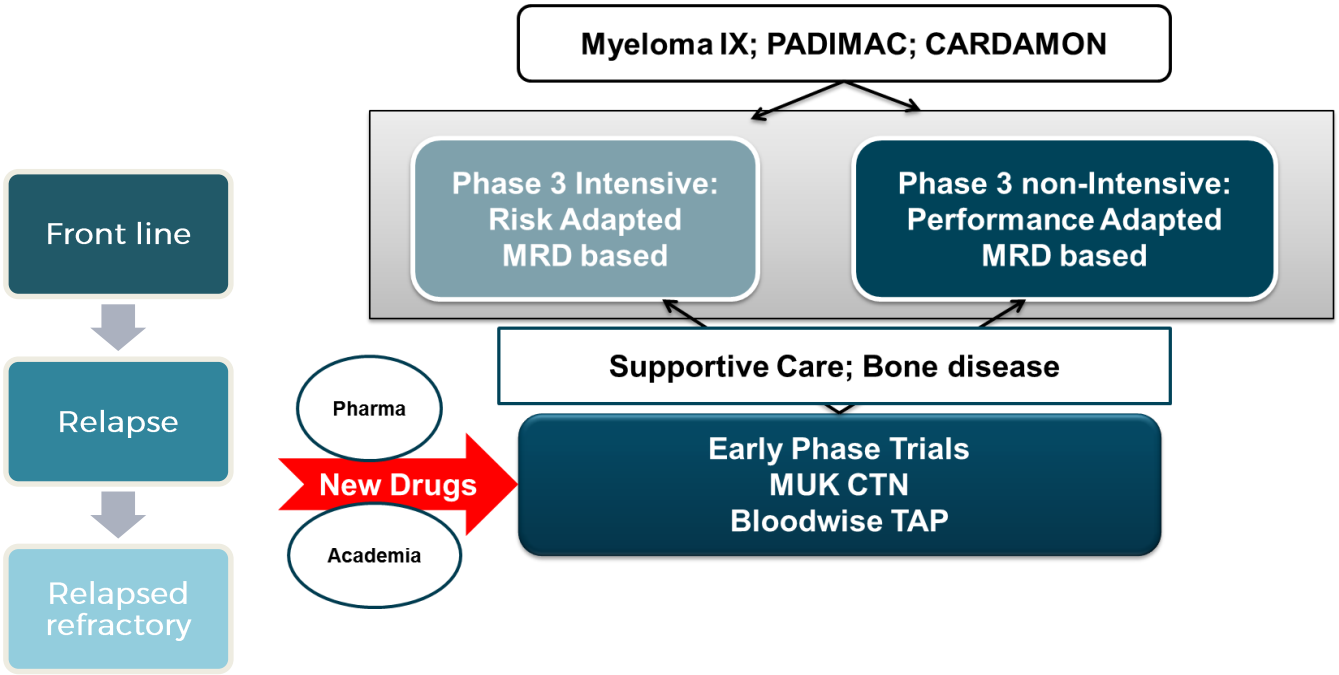
Elderly patients have more frequent discontinuations, toxicities and poorer survival

Palumbo et al (2015) *Blood*

Total therapy for long term disease control

- Performance adapted therapy
- Risk Adapted therapy
- Sequential exposure of drugs
- Initial aim to achieve and maintain CR
- At late relapses disease control may be sufficient
- Avoid provoking explosive relapses
- Immunotherapies may provide long term control

Developing a UK Total Therapy



NICE

Which Total therapy? You decide...

NHS
The Freeman Hospital

ucl NHS