

# Feasibility & efficacy of administration of bortezomib-containing regimens to MM patients over 70 years

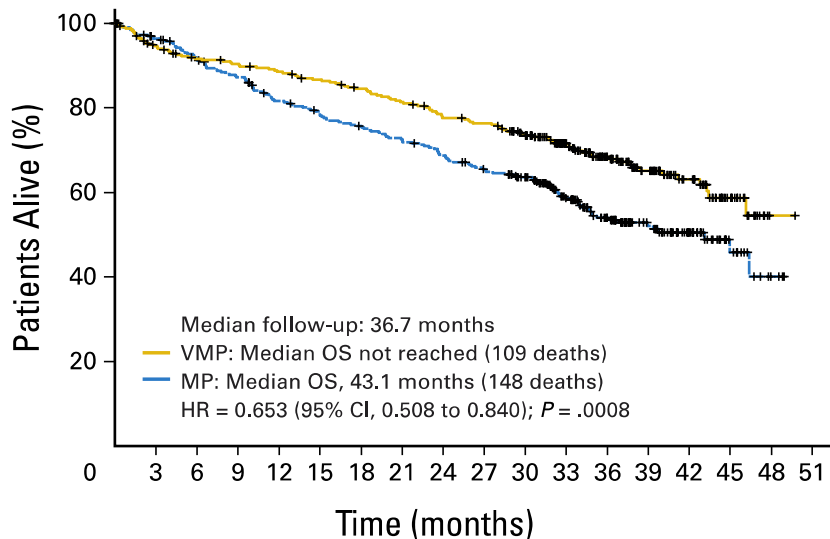
Christopher Parrish

St James's Institute of Oncology, Leeds

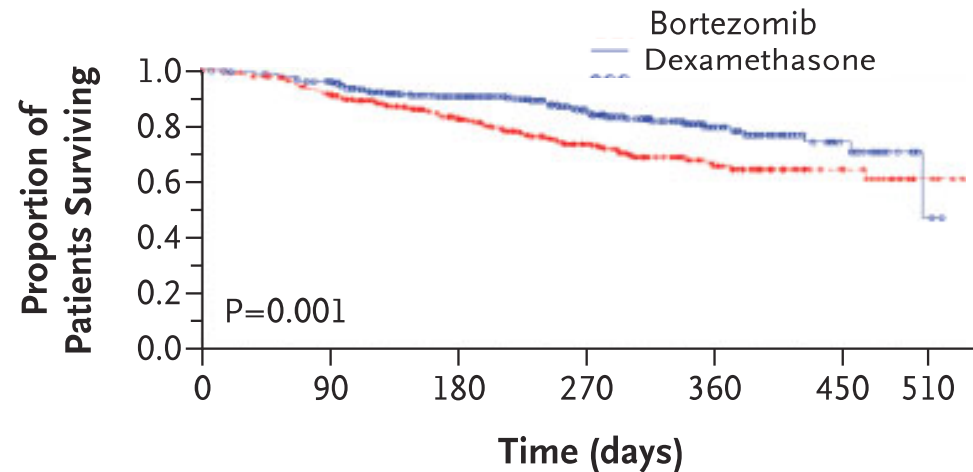


# Bortezomib

- Bortezomib-containing regimens offer response rates and durability of responses superior to standard therapy



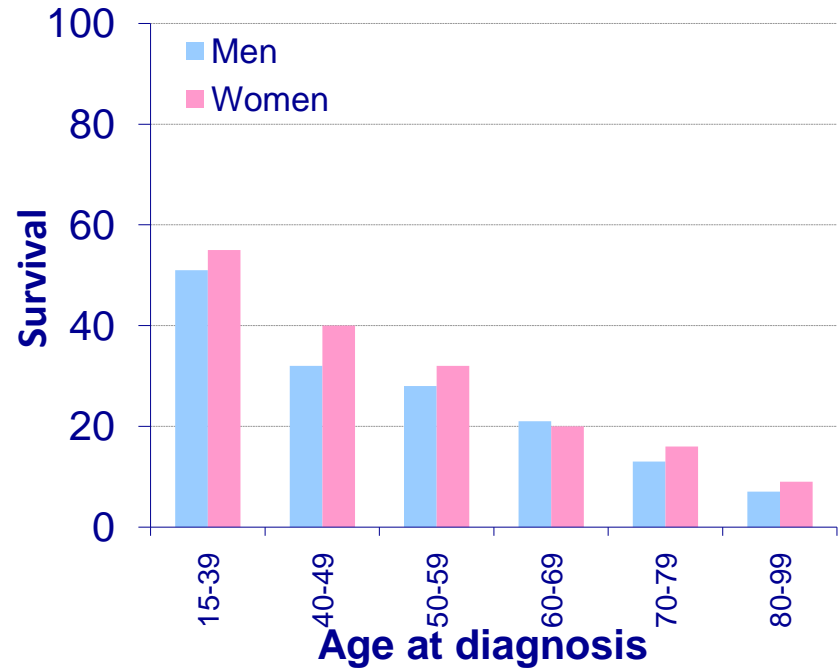
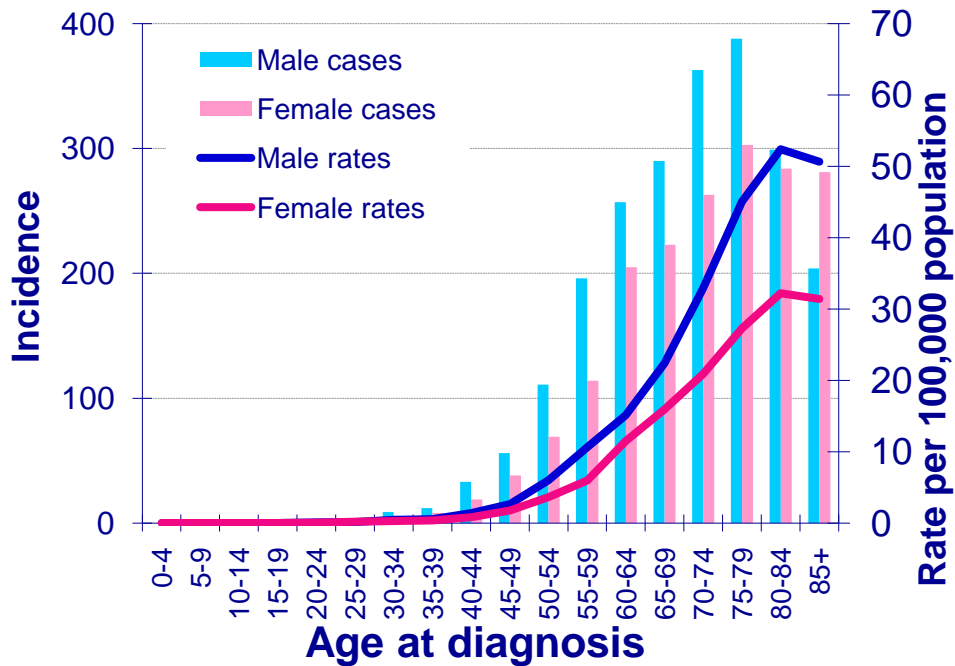
No. of patients at risk																	
MP	338	320	301	284	262	249	240	230	216	203	185	143	103	68	41	15	3
VMP	344	315	300	295	288	280	270	260	246	241	221	173	124	84	54	23	1



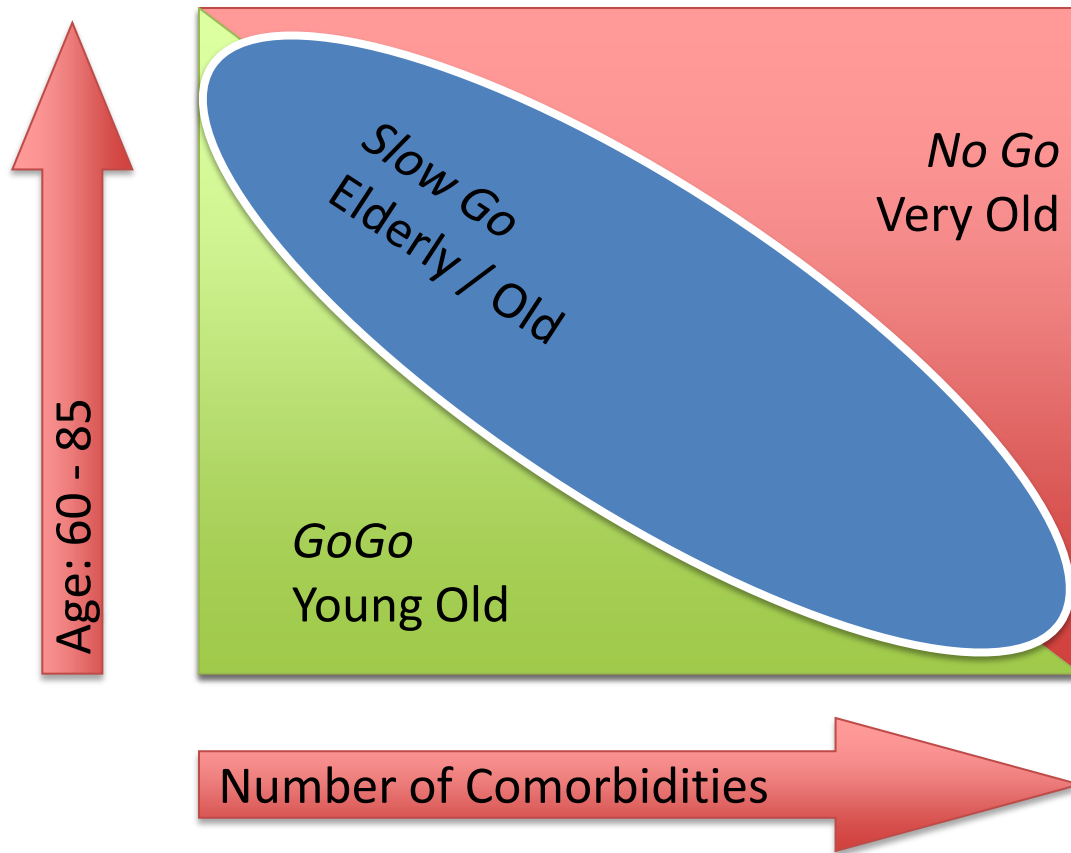
No. at Risk						
Bortezomib	310	219	138	62	21	2
Dexamethasone	292	201	118	59	20	4

Mateos *et al.*, J Clin Oncol **28**:13, 2259-66 (2010)  
 Richardson *et al.*, N Engl J Med **352**:24, 2487-98 (2005)

## Age-specific incidence and survival rates, by sex, multiple myeloma, UK 2007



# Age, Treatment & Myeloma



# Reducing bortezomib toxicity

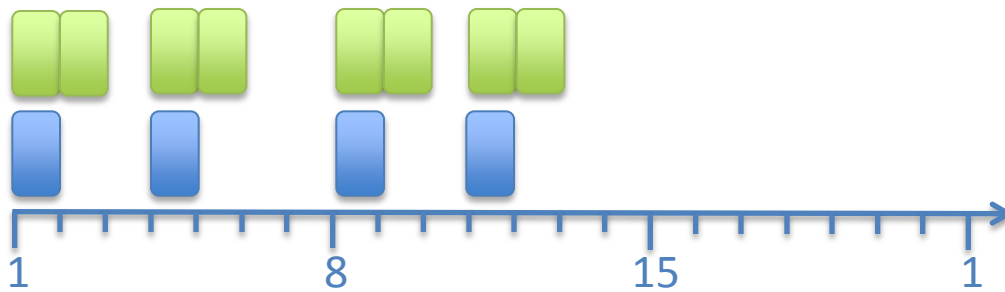
- Phase 3 GIMEMA trial
  - Initially compared bortezomib-melphalan-prednisolone-thalidomide followed by maintenance with bortezomib-thalidomide (VMPT-VT) with VMP.
  - Protocol amended March 2007: bortezomib reduced from twice-weekly to once-weekly.

	Twice-weekly bortezomib n=139	Once-weekly bortezomib n=372	p
Complete response rate	35%	30%	.27
3 year progression-free survival	47%	50%	1.00
3 year overall survival	89%	88%	.54
Non-haematological grade 3/4 adverse events	51%	35%	.003
Grade 3/4 peripheral neuropathy	28%	8%	<0.001
Therapy discontinued due to PN	15%	5%	<.001

# Aims & Methods

- Examine feasibility of delivery of bortezomib-containing regimens to an elderly population.
- Retrospective audit/review
- Patients aged over 70
- Relapsed disease
- No previous bortezomib exposure
- Bortezomib + dexamethasone

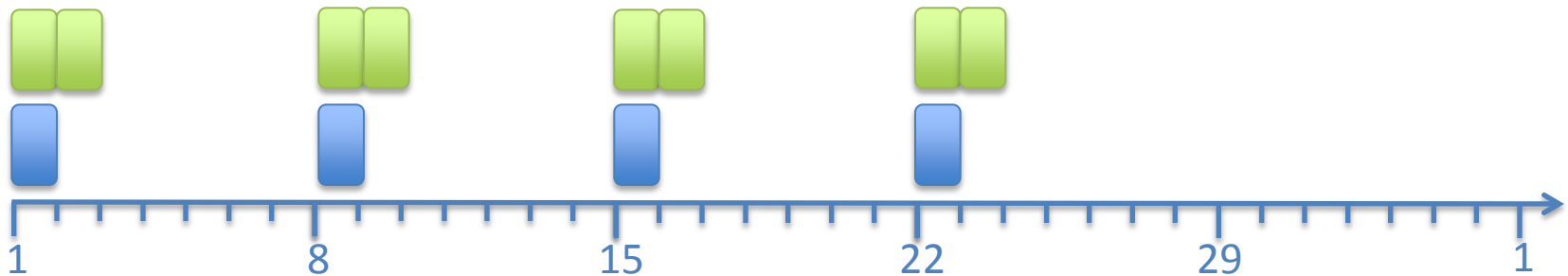
# Regimens



Standard regimen

Dexamethasone 20mg

Bortezomib 1.3mg/kg



Reduced intensity regimen

# Methods

- Response and toxicity assessment once per treatment cycle (IMWG criteria<sup>1</sup> and NIH scores).
- Treatment continued until maximal response or precluded by toxicity.
- Control cohort of patients aged <70 years, matched for number of prior lines of therapy, and treated with the same regimens.

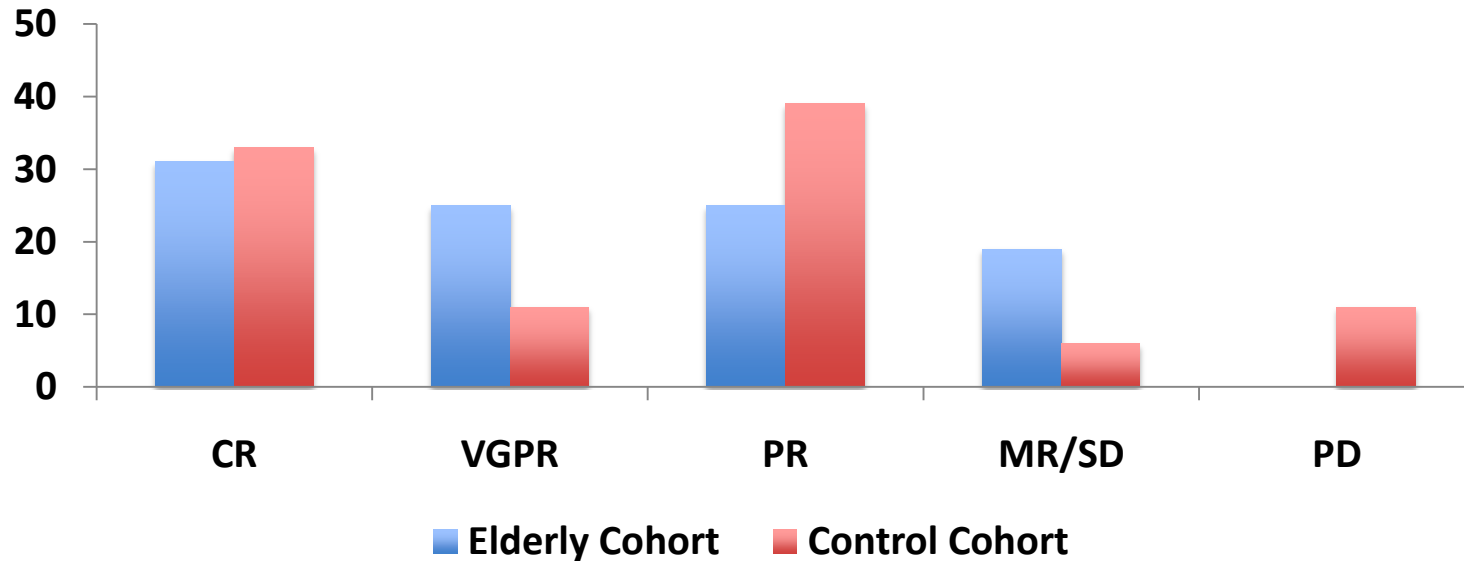
# Patient Characteristics

	Elderly, n=19	Control, n=19
Age: median (range)	80 (74, 94)	61 (39, 70)
Prior lines: median (range)	1 (1,4)	1 (1,4)
Paraprotein		
IgG	14	11
IgA	2	3
Light chain	3	5
ISS score: median (range)	2 (1, 3)	2 (1,3)
Beta-2-microglobulin (mg/l): median (range)	3.2 (1.8, 13)	3.1 (2, 11.2)
GFR (ml/min/1.72sq.m): median (range)	49 (12, 69)	71 (14, 90)
Bone marrow plasmacytosis (%): median (range)	13 (0.9, 51)	17.2 (2.3, 36)
Serum paraprotein (g/l): median (range)	22.5 (0, 46)	22.5 (0, 53)

# Results – treatment delivered

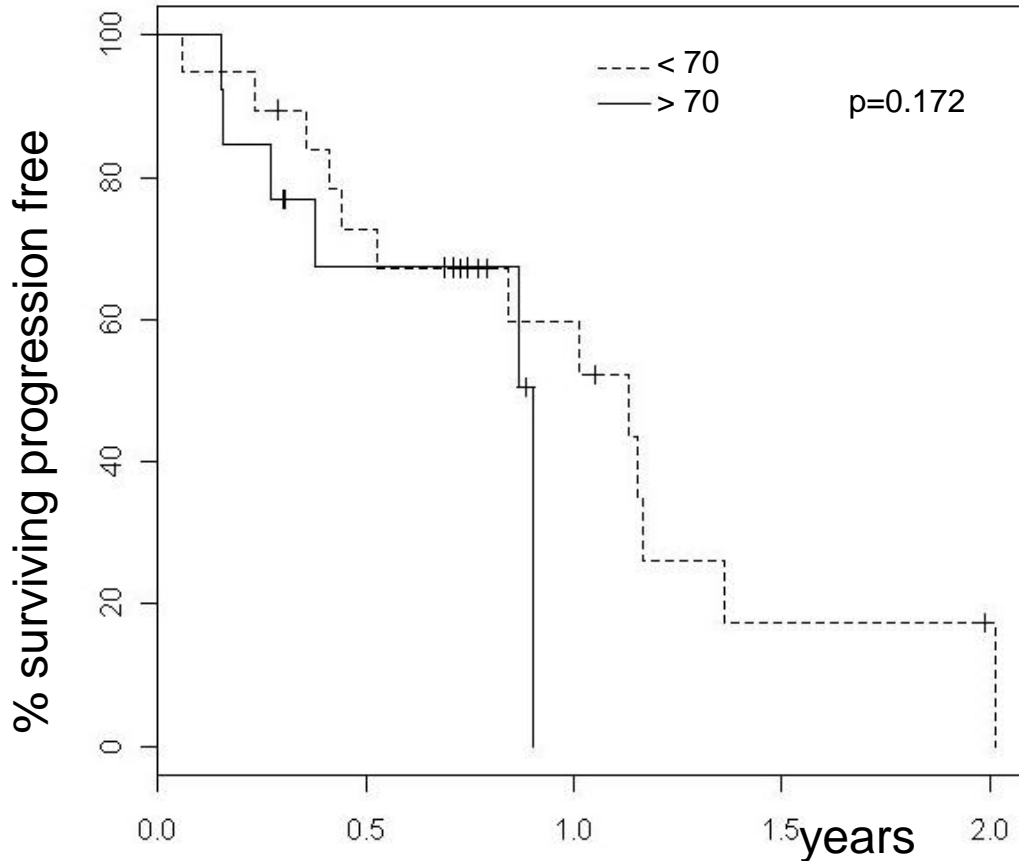
		Elderly cohort	Control cohort
Initial regimen:	standard	12	19
	reduced	7	0
Reductions from initial regimen			
	transfer from standard to reduced	2	0
	reduction in bortezomib dose	0	5
	reduction in dexamethasone dose	4	1
Cycles received:	median	3	4
	mean	3.53	4.32
	range	1, 6	1, 6

# Response rates



	Elderly cohort	Control cohort
Complete response	5 (31%)	6 (33%)
Very good partial response	4 (25%)	2 (11%)
Partial response	4 (25%)	7 (39%)
Minimal response or stable disease	3 (19%)	1 (6%)
Progressive disease	0	2 (11%)

# Results - Durability



Median follow-up:  
 elderly: 5.1 months  
 control: 12.1 months

		Elderly cohort	Control cohort
Time to progression (months):	median	11.0	7.3
	range	3.3, 16.8	0, 21.3



# Results – Toxicity

	Elderly cohort	Control cohort
Grade 3-4 haematological toxicity	2 (11%)	4 (21%)
Grade 3-4 non-haematological toxicity	6 (32%)	5 (26%)
sensory neuropathy	2	5
motor neuropathy	1	0
fatigue	2	0
infection	2	0
Patients requiring hospital admission	2	1

# Conclusions

- Response rates are comparable.
- Combined response rate (i.e. CR + PR) = 81%
- Overall rate of grade 3-4 adverse events in the elderly cohort = 37%.
  - Equivalent figure in APEX trial for subgroup analysis of patients aged over 65: 75%<sup>1</sup>
  - Suggests reduction of bortezomib dose delivery with addition of dexamethasone improves response rates without an increase in toxicity.
- Further delivery modifications e.g. subcutaneous, may offer further improvements in tolerability whilst maintaining efficacy

1. Richardson *et al.*, Br J Haematol **137**:5, 429-35 (2007)

# Acknowledgements

UKMF – Travel bursary to ASH 2010

Leeds Myeloma Team

*Julian Cromack*

*Sylvia Feyler*

*John Ashcroft*

*Roger Owen*

*Gordon Cook*

All patients and carers

Rachel Pearce

Thank you