A PETHEMA study of high-dose therapy/stem cell support (HDT), including tandem transplant, in primary refractory multiple myeloma (MM): identification of two populations with different outcome.

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Background

- It is generally assumed that patients with primary refractory myeloma are the most likely to benefit from early HDT/SCT.
- In four reported series the CR rate was between 8 and 40% and the overall survival ranged from 4 to 6 years.
- However, the outcome of patients with progessive disease versus those with “no change” or “stable disease” was not separately analyzed in published series.

Background (II)
HDT/SCT in Primary Refractory Myeloma

Author, yr	Patients (n)	Age (yrs)	B2M mg/dL	CR (%)	EFS (yrs)	OS (yrs)
Alexanian et al, Blood, 1994	27	45	2.8	8	3.5	6
Vesole et al, Blood 1994	72	50	-	15	1.7	4
Singhal et al, BMT, 2002	43	54	3.3	40	2	-
Kumar et al, BMT, 2004	50	56	2.7	20	2.5	5
Alexanian et al, BMT 2004	89	52	3.7	16	7*	7*

* In patients achiving CR after HDT/SCT

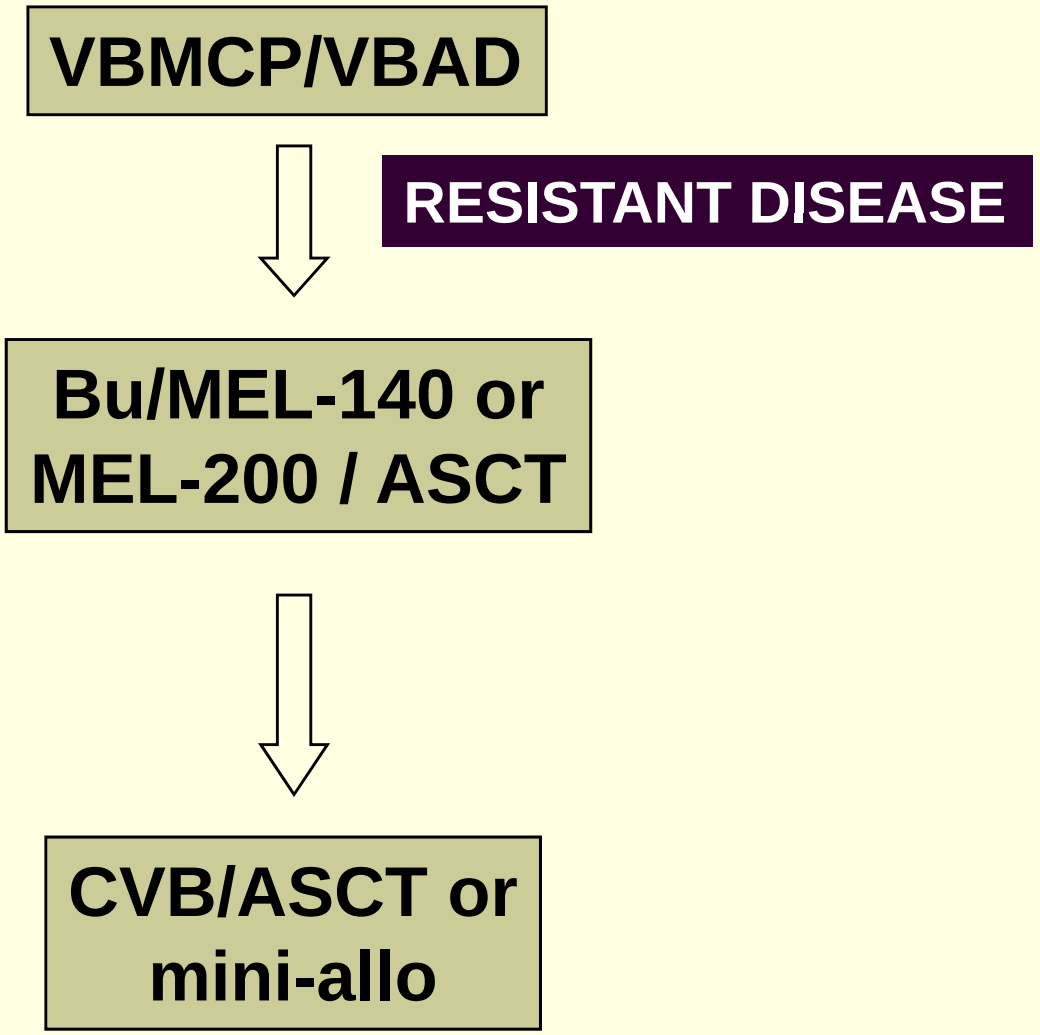
Objective

To investigate the efficacy in terms of response up-grading and survival of early HDT/SCT in patients with primary refractory myeloma.

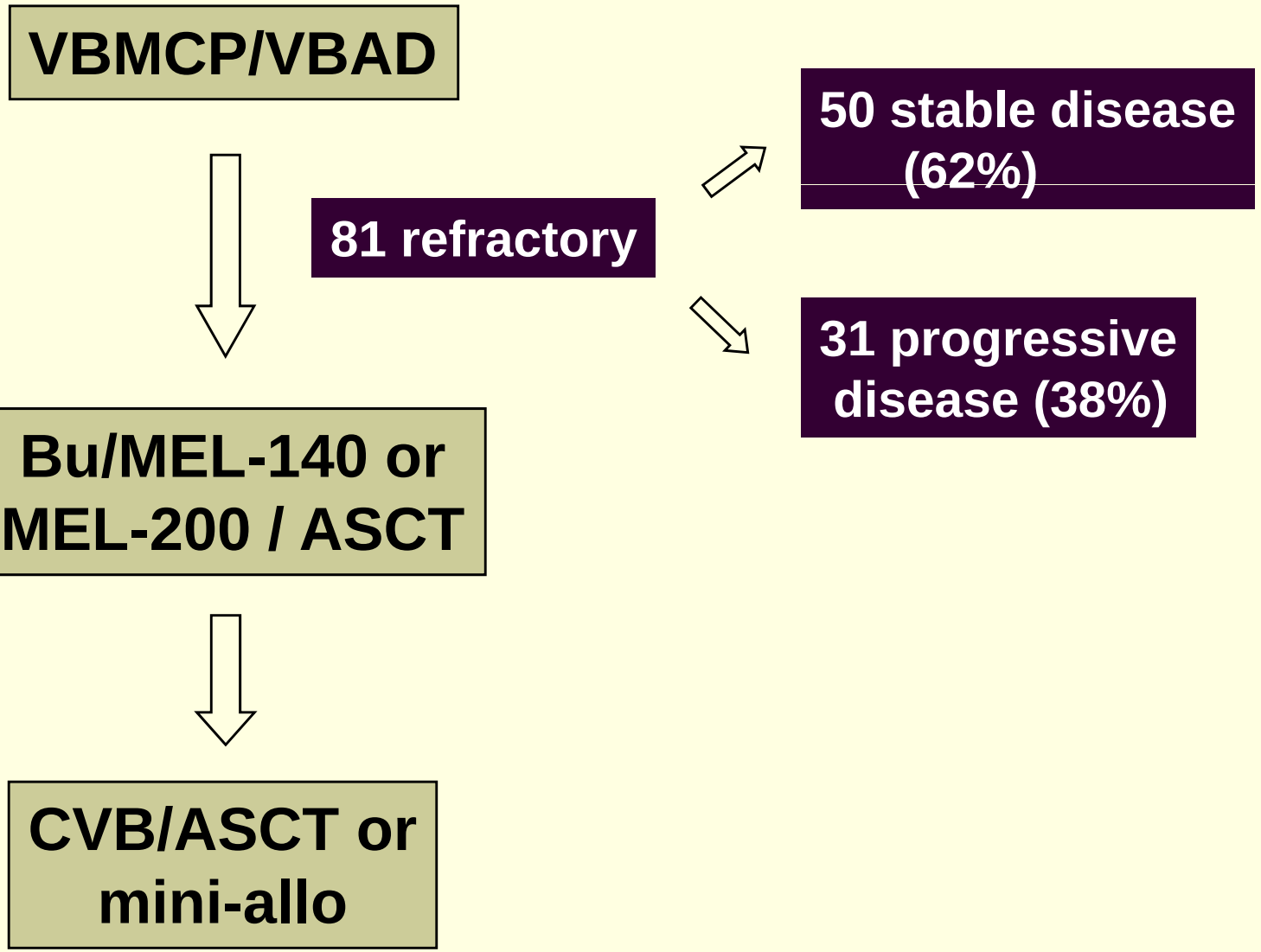
Patients and Methods

- 81 refractory patients (49 M, 32F, median age 56.5 yrs) identified.
- Response and progression defined according to the EBMT criteria.
- Statistical methods: Kaplan & Meier, log-rank test

SPANISH PETHEMA / GEM-2000 TRIAL



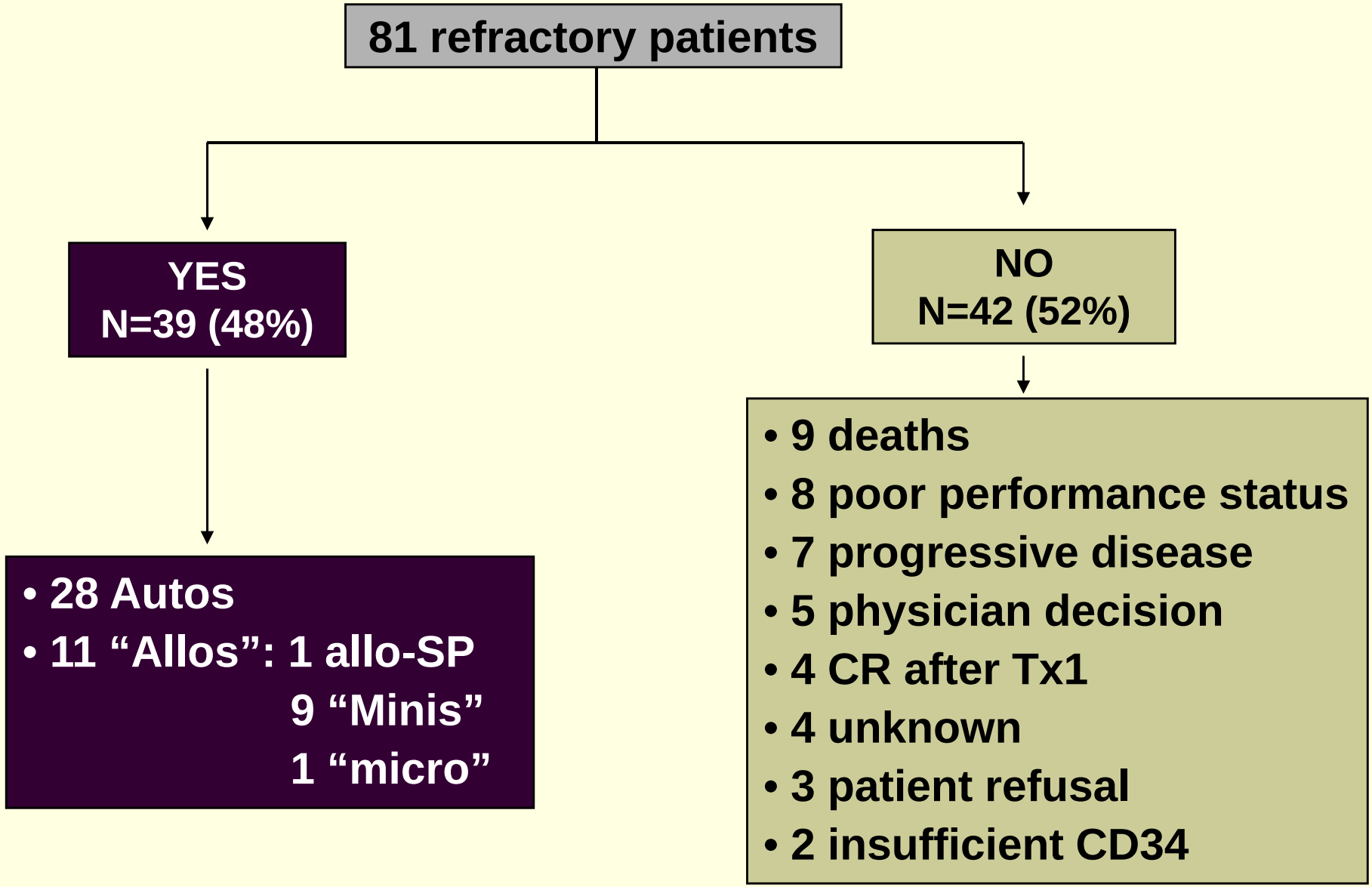
SPANISH TRIAL PETHEMA / GEM-2000
Primary Refractory patients



Response after first autologous transplant

Response	Overall (n=81)	No change (n=50)	Progressive disease (n=31)
CR1 (IF-)	4 (5%)	1 (2%)	3 (10%)
Near-CR (EP-)	2 (2.5%)	1 (2%)	3 (10%)
PR	39 (48%)	24 (48%)	14 (45%)
MR	11 (13%)	9 (18%)	2 (6%)
No change	10 (12%)	10 (20%)	-
Progressive disease	8 (10%)	1 (2%)	7 (22.5%)
Early death (< 2 mos)	7 (8.6%)	3 (6%)	4 (13%)

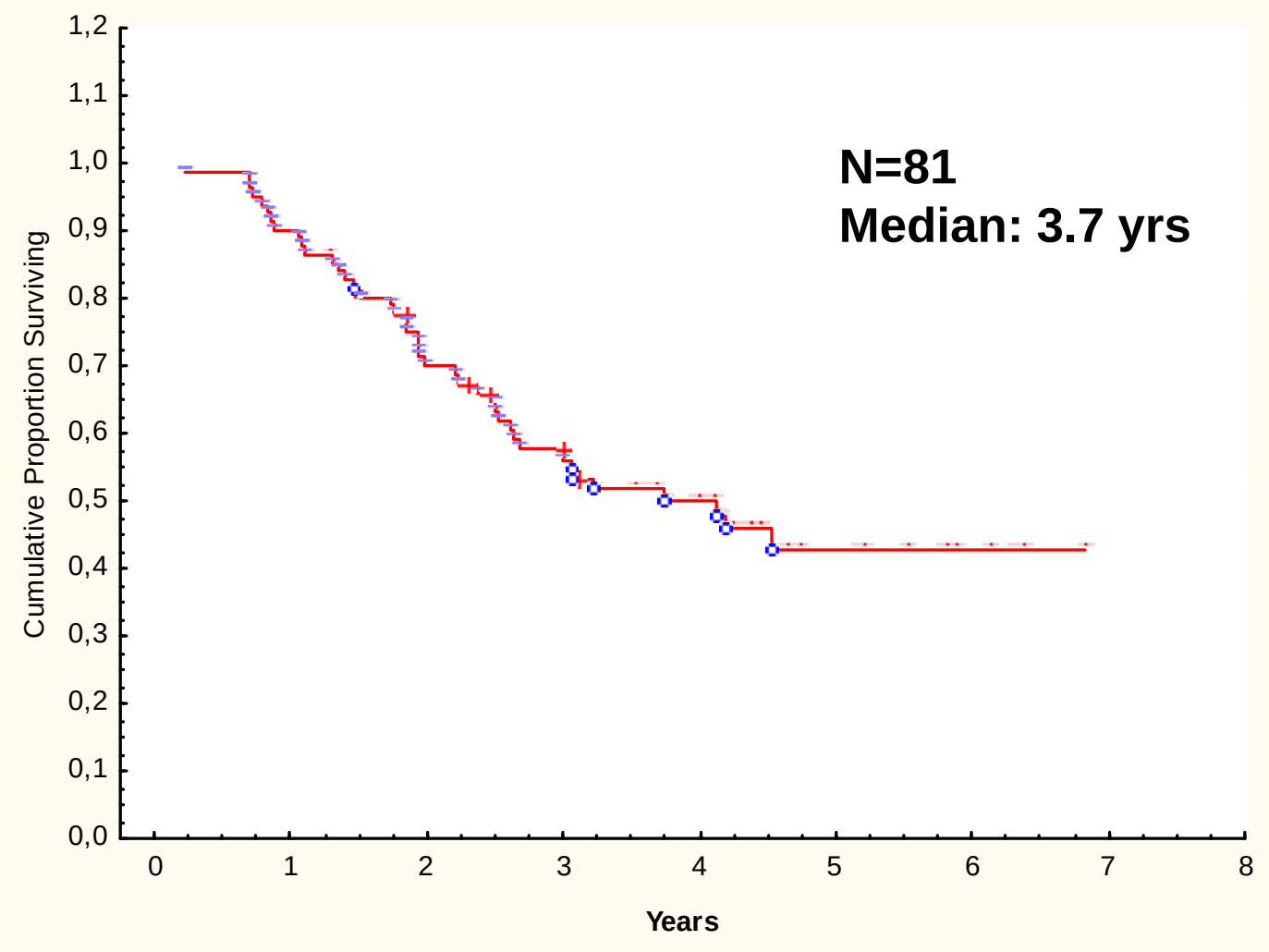
Second High-dose Procedure



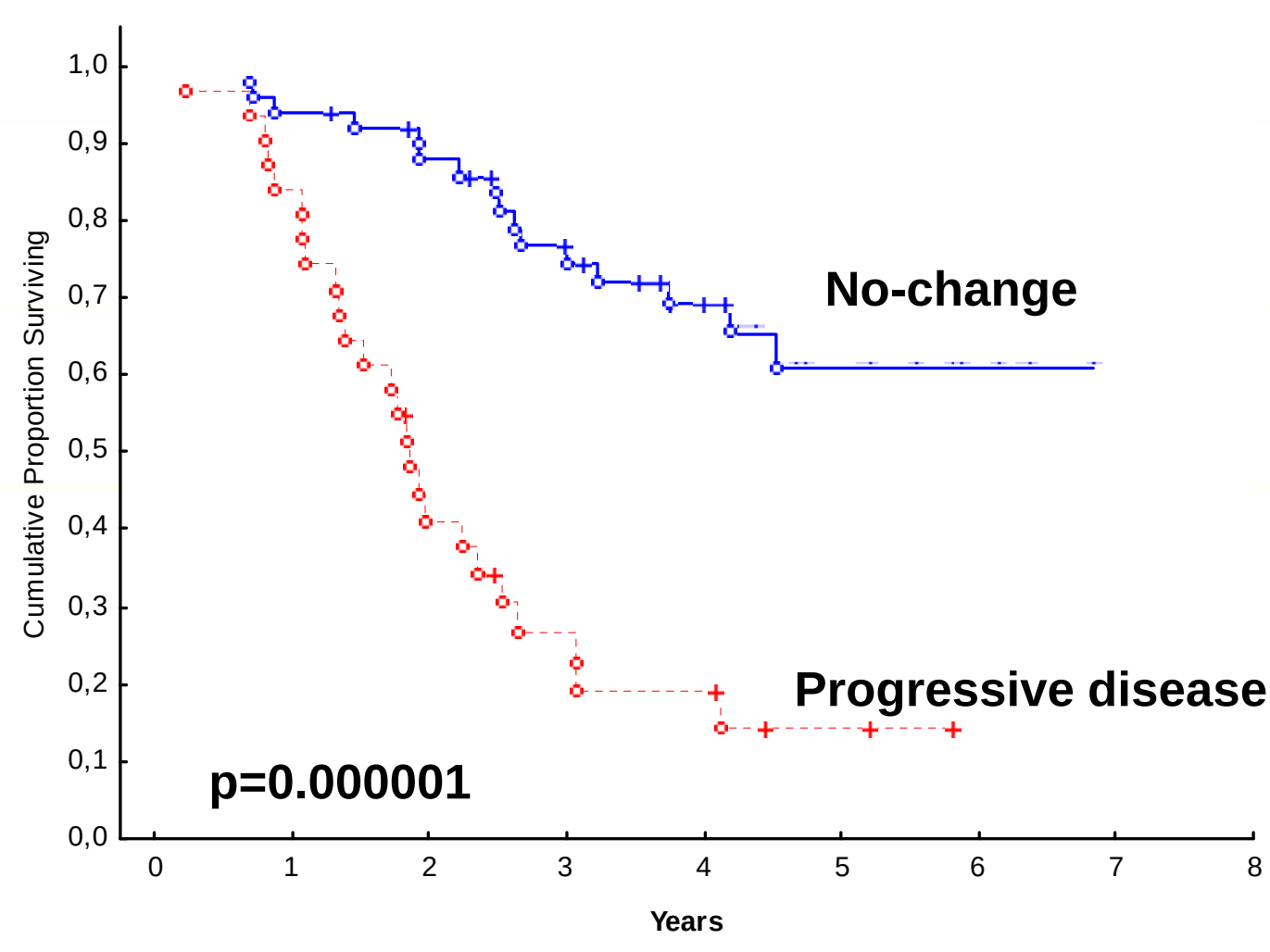
Response Up-grading with Second HDT
"Auto" vs "Allo"

Response	Auto (n=28)	Allo (n=9)
CR1 (IF-)	3 (10%)	3 (33%)
PR	3 (11%)	
MR	5 (18%)	1 (11%)
No change	3 (10%)	1 (11%)
Progressive disease	4 (14%)	3 (33%)
Early deaths (< 2mos)	2 (7%)	1 (11%)

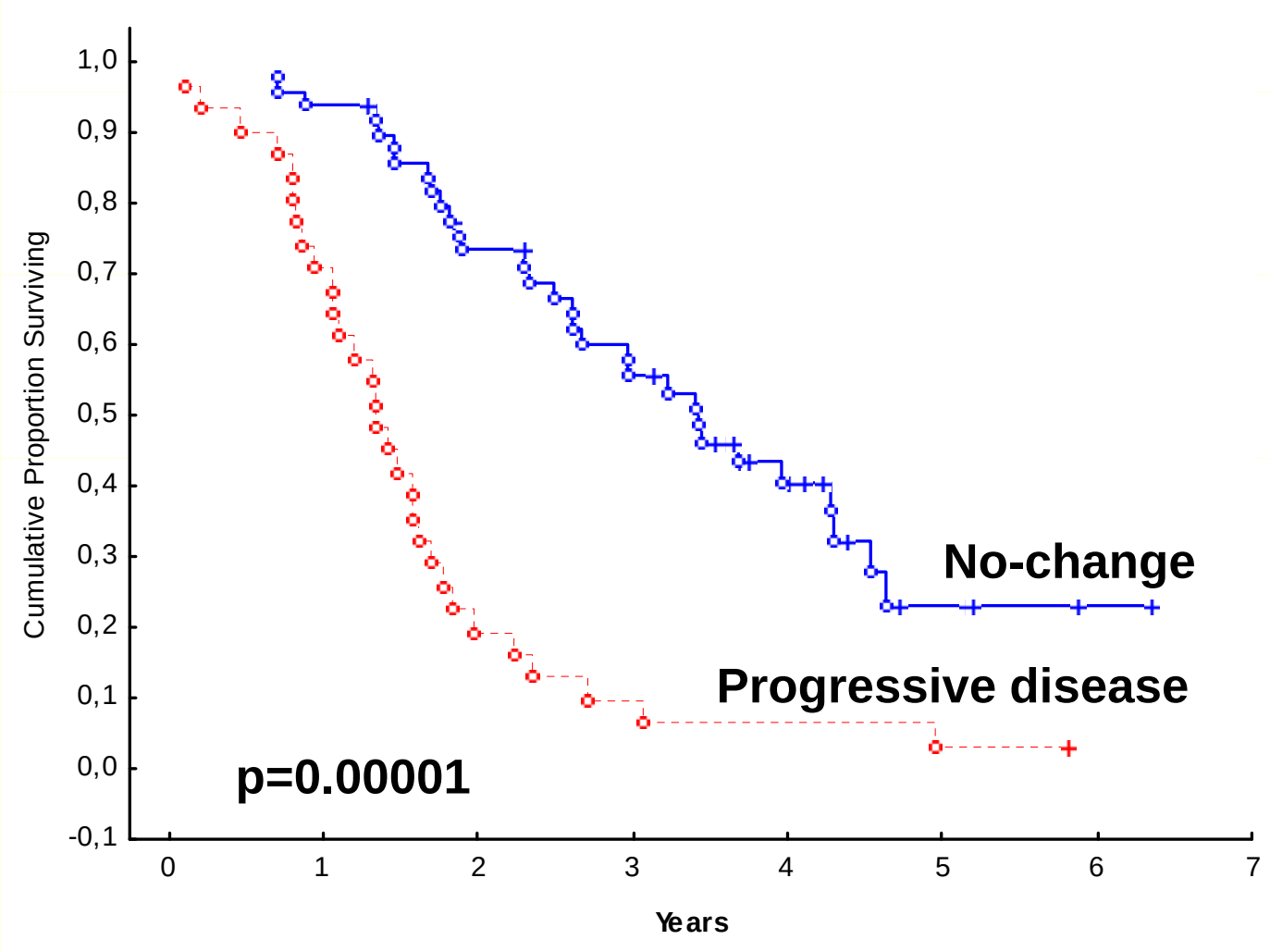
Primary Refractory Myeloma
Overall Survival



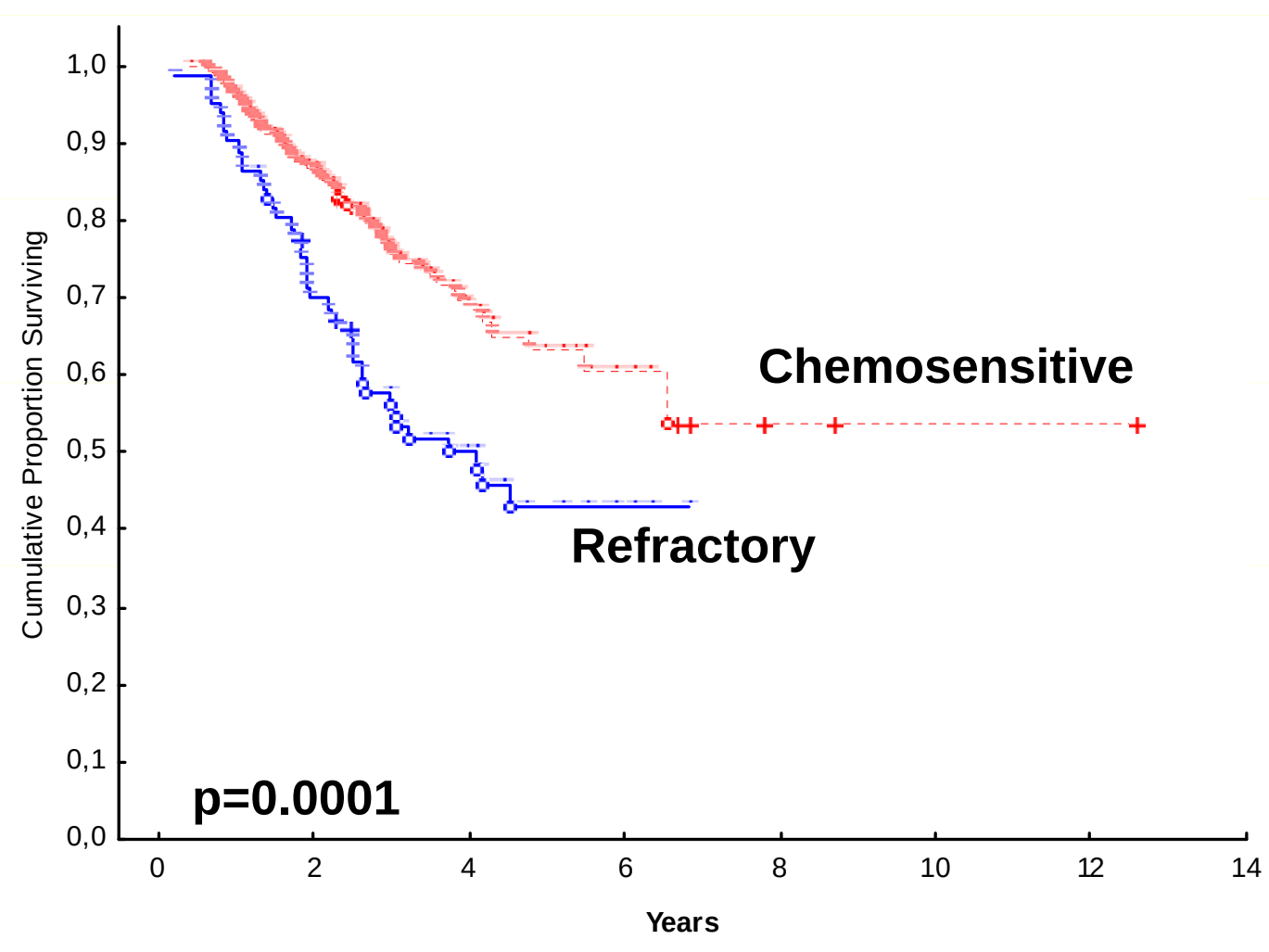
Overall Survival
No-change vs Progressive Disease



Progression-free Survival
No-change vs Progressive Disease

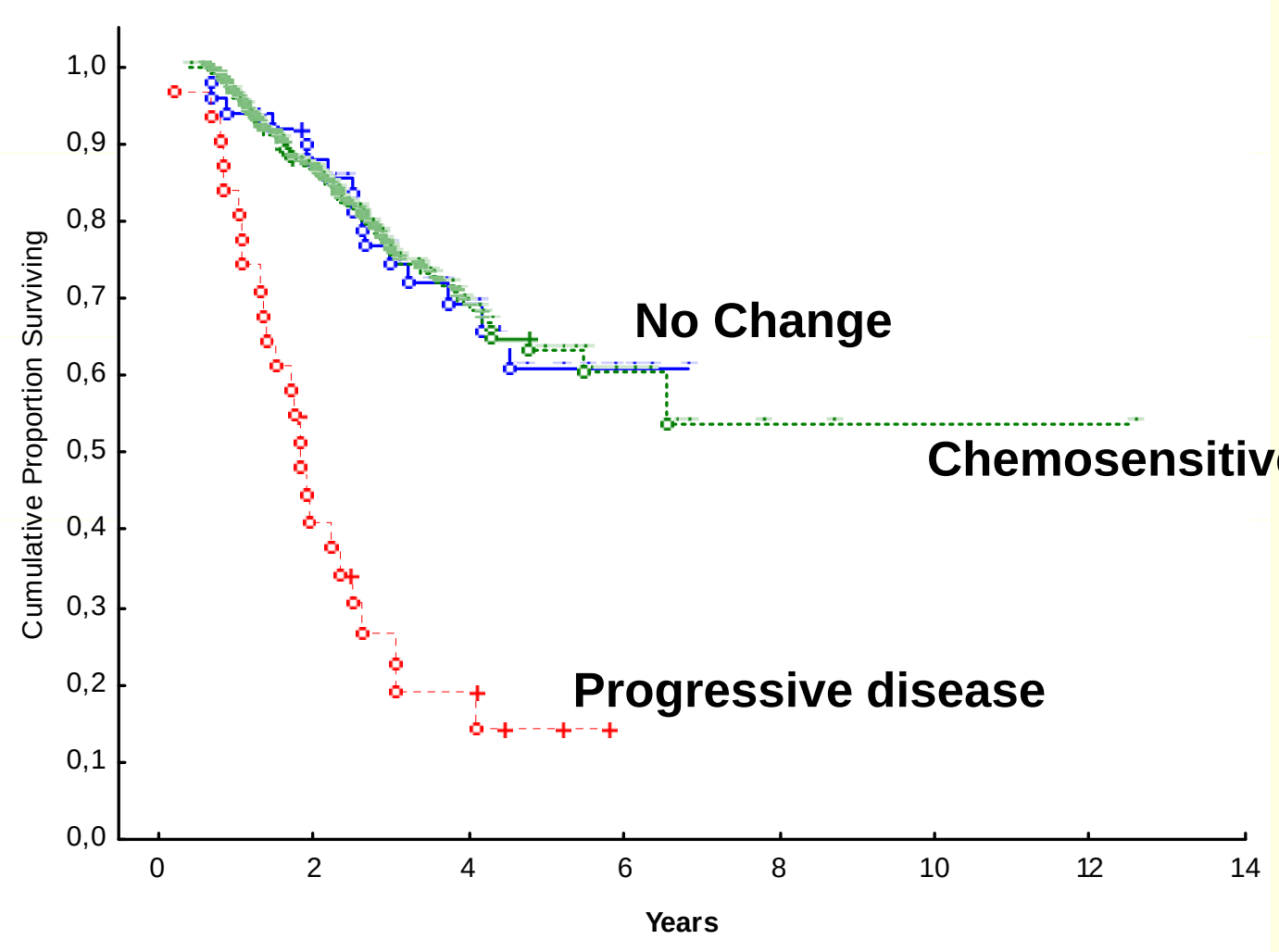


Overall Survival
Primary Refractory vs Chemosensitive Myeloma



Overall Survival

Progressive disease vs No-change vs Chemosensitive



Conclusions

- Althought a high-dose therapy approach in patients with primary refractory myeloma results in a high overall response the CR rate is low.
- Patients with progressive disease to the initial chemotherapy have a short survival despite the intensive approach.
- Patients with “non-responding, non-progressive disease” have a similar survival than chemosensitive patients. Whether the good outcome of this population is mainly due to the effect of HDT or to the natural history of a more indolent disease remains to be determined.