



AMERICAN SOCIETY OF CLINICAL ONCOLOGY



Myeloma

Outcome Following Early Relapse after Autologous Stem Cell Transplantation for Multiple Myeloma

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Background

- Autologous stem cell transplant (ASCT) improves survival in myeloma
- Patients invariably relapse after ASCT
- Various risk factors have been identified for post ASCT relapse
- Outcome of patient relapsing early after ASCT is not known

Objective of Study

- To study the outcome of patients who relapse / progress early (<12 months) after upfront autologous stem cell transplant (ASCT) for Multiple Myeloma

Materials and Methods

- 432 patients with newly diagnosed Multiple Myeloma transplanted between 1994 and 2005
- All patients underwent ASCT within 12 mos of diagnosis
- Patients were divided into 2 groups:
 1. Early relapse (relapse/progression <12 mos from ASCT)
 2. Late relapse (either relapsed/ progressed >12 months after ASCT or have not at last follow up)

Baseline features: Initial Therapy

- Single agent Dexamethasone: n=166 (38.5%)
- Vincristine, doxorubicin, and dexamethasone (VAD): n = 129 (29.9%)
- Thalidomide-Dexamethasone: n = 117 (24.8%)
- The remaining patients received :
 - Revlimid/Dexamethasone (n=16)
 - Vincristine/BCNU/melphalan/cyclophosphamide/ prednisone (VBMCP) (n=5)
 - Other regimens (n=8)

Baseline features: Stem Cell Collection

- Stem Cells were collected using granulocyte colony-stimulating factor (G-CSF) alone in 172 (39.7%) of patients
- 260 (60.3%) of patients had stem cells collected after receiving cyclophosphamide for 2 days then GM-CSF or G-CSF starting on day 3

Baseline features: Conditioning

- 81.3% of patients underwent conditioning with melphalan alone at 200mg/m²
- 8.5% of patient received dose reduced melphalan at 100-140 mg/m² for advanced age, renal insufficiency or poor performance.
- 10.2% of patients received melphalan 140mg/m² followed by total body radiation (12 Gy) (all prior to June 2000)

Results: *Baseline Features at Transplant*

Characteristics	Early Relapse (N=94)	Late Relapse (N= 338)	P-value
<i>Variable</i>	<i>Median (range)</i>	<i>Median (range)</i>	
Age at diagnosis	56.2 (35.5-72.2)	57.5 (29.4-75.4)	NS
Age at Transplant	56.6 (36.1-72.9)	58.7 (30-75.8)	NS
Time to Transplant	6.3 (1-11.5)	6.0 (2-11.9)	NS
Serum M Protein level	1.3 (0-6.9)	0.9 (0-6.9)	NS
BM Plasma Cell %	14 (0-95)	8.4 (0-91)	NS
LDH	179.5	182	NS
Creatinine	1 (0.6-8.6)	1 (0.6-10.1)	NS

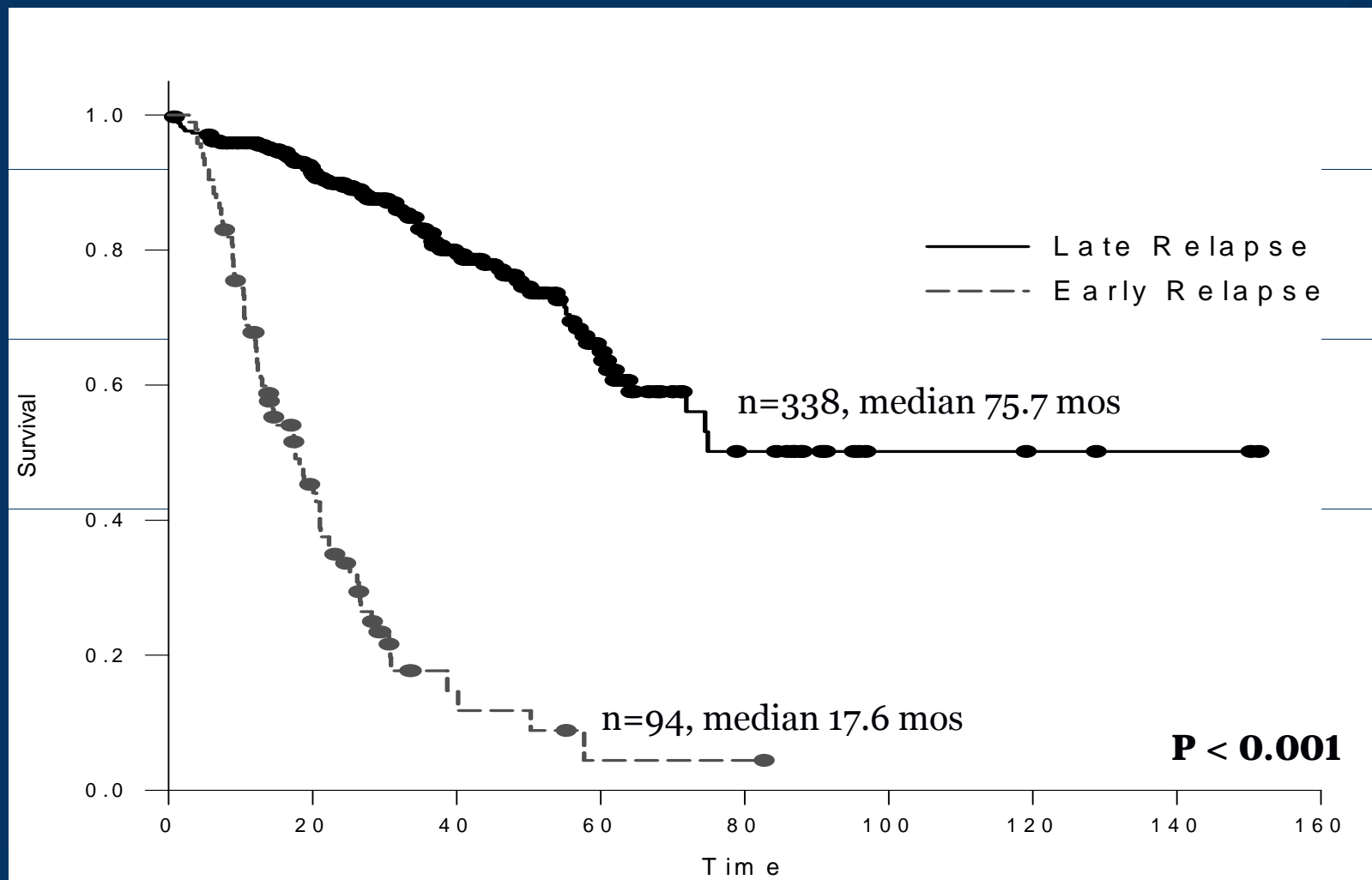
Results: *Baseline Features at Transplant*

Characteristics	Early Relapse (N=94)	Late Relapse (N= 338)	P-value
<i>Variable</i>	%	%	
Gender: male	61.7	57.7	NS
PCLI >/= 1%	41.9	15.5	< 0.001
β2 Microglobulin >3.5 mg/dL	28.7	23.1	NS
Bone disease	12.8	15.4	NS
Refractory at transplant	41.5	29.3	0.03
Durie Salmon: Stage: 2	27.6	36.2	NS
Stage: 3	72.4	63.8	NS
> 1 Induction regimen	18	8	0.007
Abnormal Karyotype	34	14.8	< 0.0001
Circulating PC at Collection	51.1	36.4	0.01

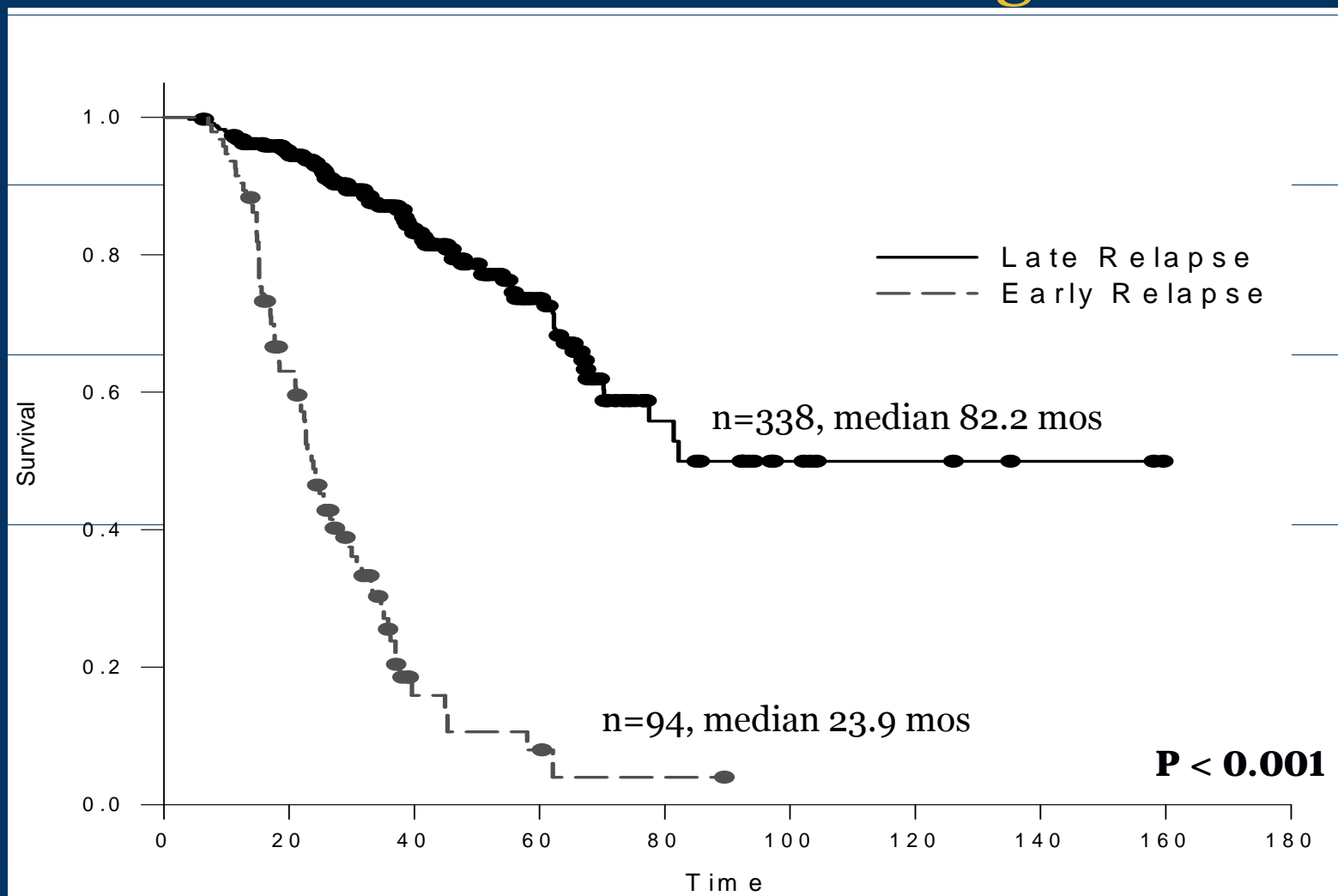
Results: Response rates

	Early Relapse (N=94)	Late Relapse (N= 338)
Overall Response	96%	96%
Complete Response	18%	43%

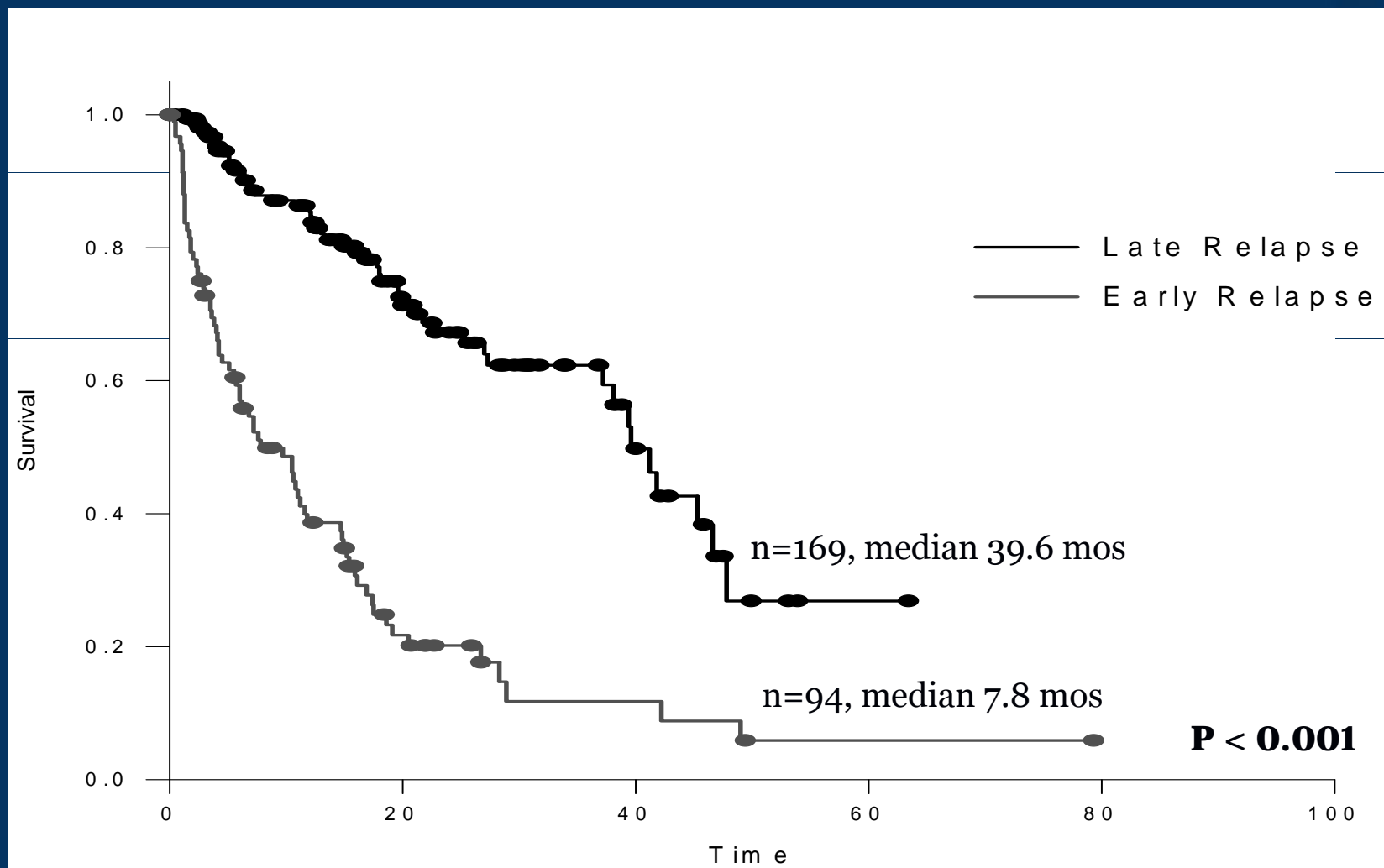
Post-ASCT overall survival



Overall survival from diagnosis



Overall survival from relapse



Results: Risk Factors for Relapse < 12 mos (univariate)

Variable	HR (95% CI)	P-Value
>1 Induction Regimen	2.5 (1.3, 4.9)	0.005
Refractory @ Tx	1.7 (1.1, 2.8)	0.03
BMPC > 30%	2.4 (1.4-4.1)	0.002
PCLI > 1%	3.9 (2.4, 6.5)	< 0.0001
Abnormal karyotype	3.0 (1.8, 5.1)	< 0.0001
No CR	3.1 (1.7, 5.4)	0.002
Circulating PC at harvest	1.8 (1.2, 2.9)	0.01

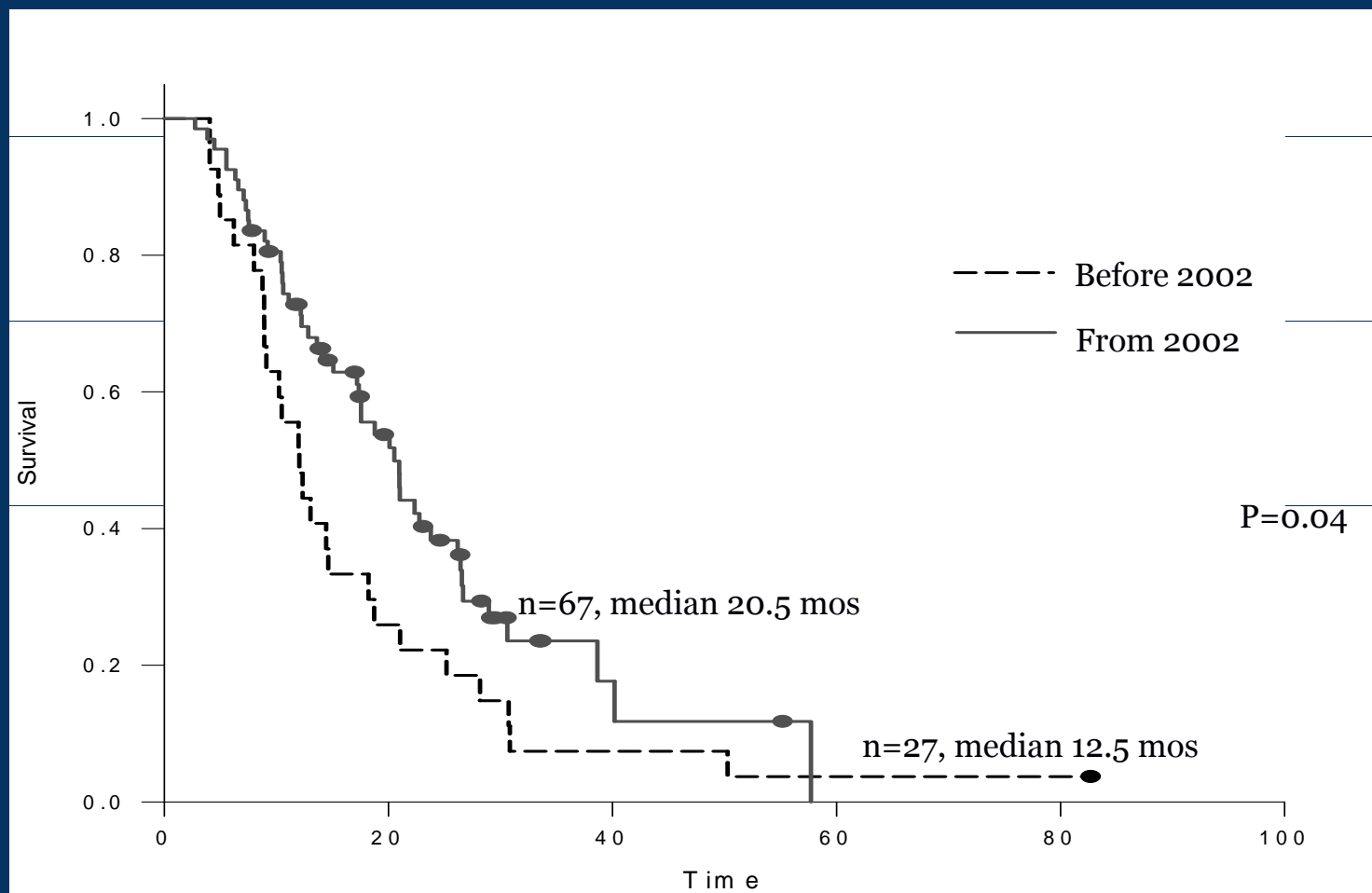
Results: Risk Factors for Relapse < 12 m (multivariate)

Variable	HR (95% CI)	P-Value
>1 Induction Regimen	2.3 (1.1, 5.0)	0.03
PCLI ≥ 1%	2.9 (1.6, 5.4)	0.0005
No CR	3.2 (1.8, 5.9)	0.0002

Results: Prognostic Factors for OS from ASCT

Variable	HR (95% CI)	P-Value
PCLI > 1%	1.5 (1.02, 2.18)	0.037
β 2M > 5.5 mg/dL	2.2 (1.3, 3.5)	0.002
Relapse < 12 mos from ASCT	7.3 (5.1, 10.6)	< 0.0001

Results: Effect of time of relapse



Conclusions

- Early relapse after ASCT represents a novel predictor for poor outcome
- These patients have high risk disease that may not be obvious from conventional risk factors
- These patients should be enrolled in clinical trials examining novel drugs and combinations
- These numbers provide a reference baseline for these trials