Novel Agents for Initial Therapy of Multiple Myeloma: Comparable Results with Continued Initial Therapy and Delayed Transplantation at Relapse vs. Early Transplantation

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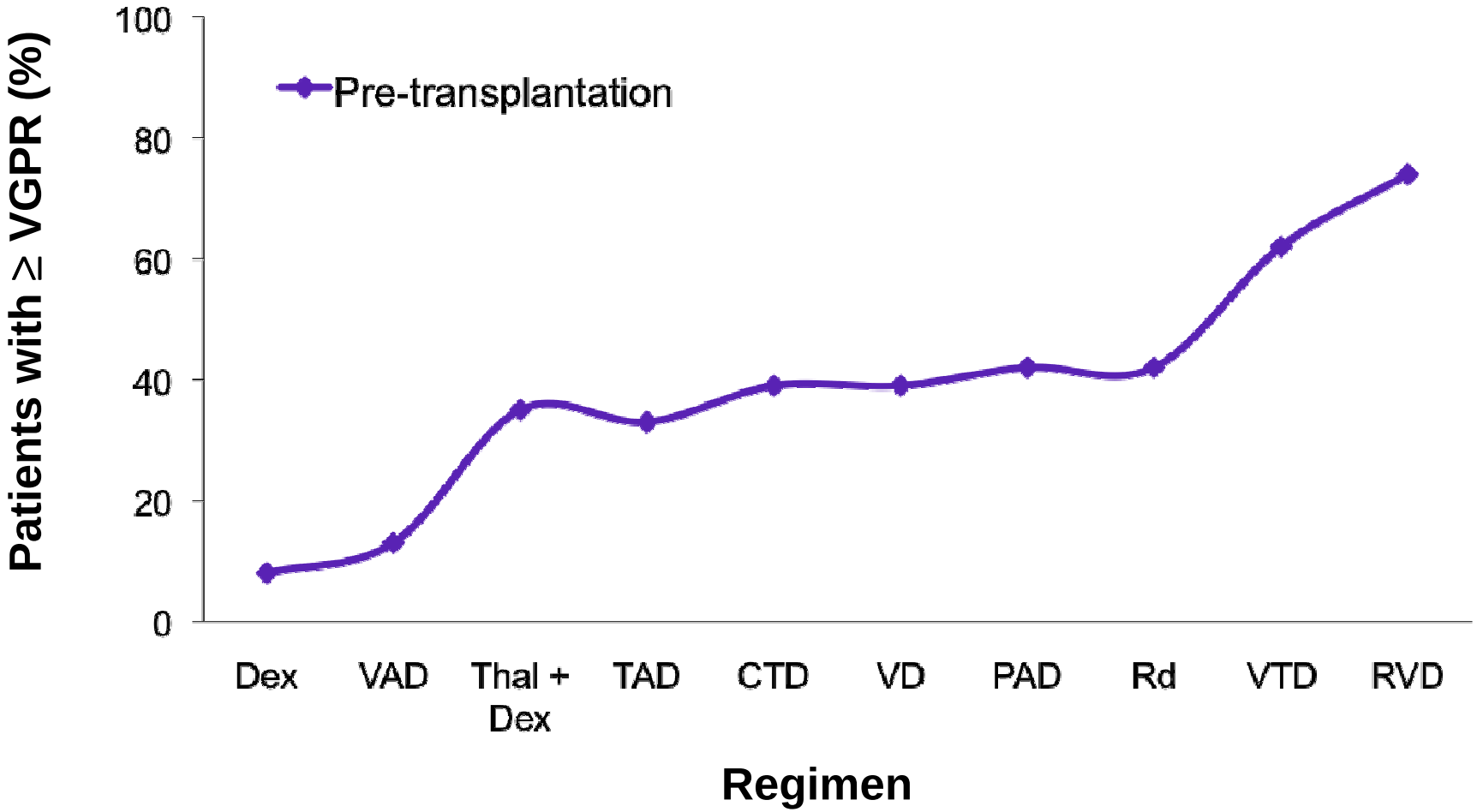
Efficacy improvements with novel induction regimens



Cavo M, et al. Blood. 2008;112:[abstract 158]. Harousseau J-L, et al. ASH/ASCO symposium at ASH, 2008. Lokhorst HM, et al. Haematologica. 2008;93:124-7. Macro M, et al. Blood. 2006;108:[abstract 57]; updated data from ASH 2006. Morgan G, et al. Blood. 2007;110:[abstract 3593]; updated data from ASH 2007. Rajkumar SV, et al. ASH/ASCO symposium at ASH 2008. Richardson P, et al. Blood. 2008;112:[abstract 92]. Sonneveld P, et al. Blood. 2008;112:[abstract 653].

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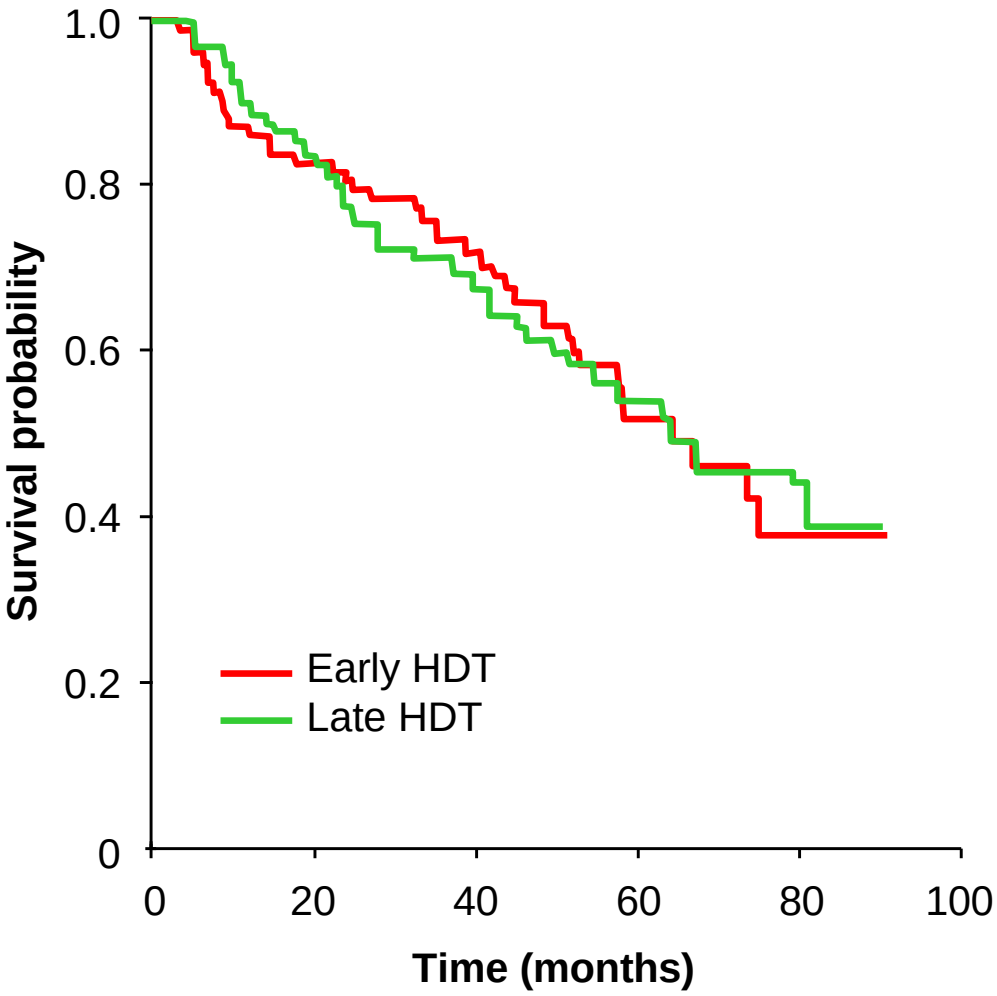
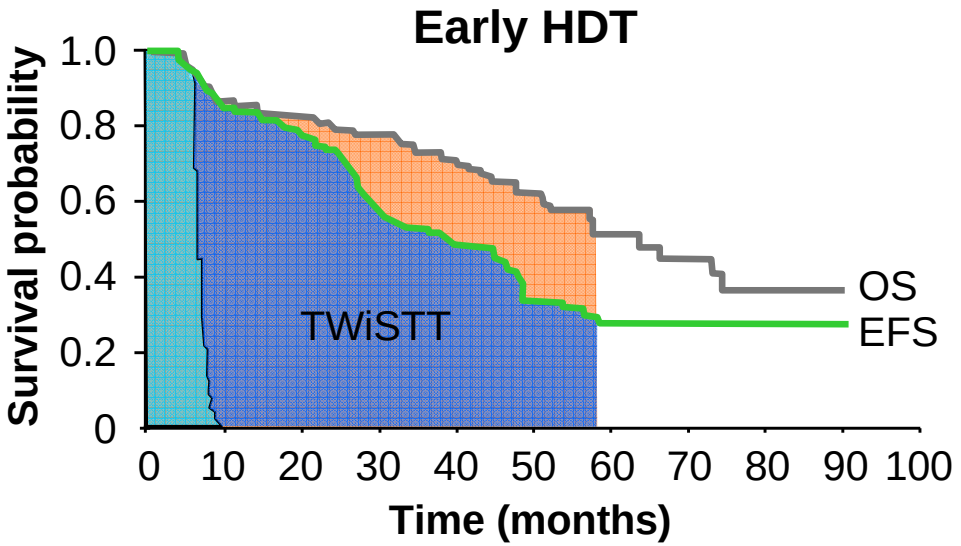
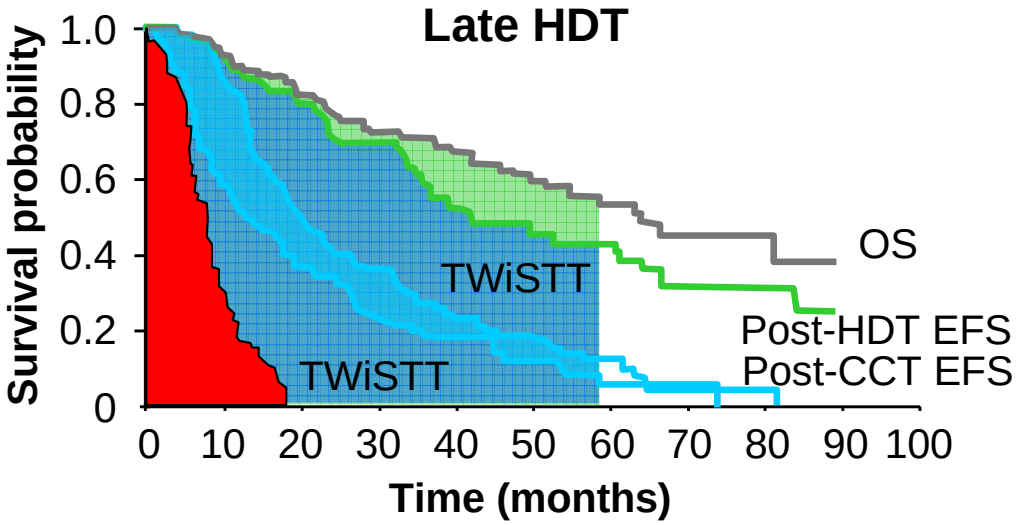
HDT in MM patients < 55 years old: up-front or rescue treatment







HDT = high-dose therapy; TWiSTT = time without symptoms, treatment, or treatment toxicity.

Fermand J-P, et al. Blood. 1998;92:3131-6.

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Objective

Is continued therapy with novel agents and high dose therapy with SCT at the time of relapse comparable to early SCT?

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Patients and Methods

- Patients seen at Mayo Clinic between 2001 and 2008
- Received initial therapy with thalidomide-dexamethasone (TD) or lenalidomide-dexamethasone (LD) (n=410)
- 290 (71%) patients in whom a stem cell harvest was attempted (*started on growth factor irrespective of collection success)* were considered transplant eligible for this study

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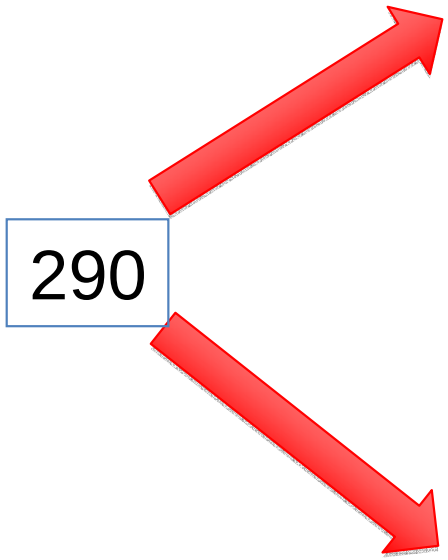
Patients and Methods



Early SCT group (n=173; 60%): SCT within 12 months of diagnosis *and* within 2 months of stem cell harvest

Delayed SCT group (n=117; 40%): Remaining patients; irrespective of whether an SCT was actually done

Majority of patients did not get tandem SCT or maintenance therapy

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Results

- The median estimated follow up for the entire group was 40 months from diagnosis
  - 35 and 42 months respectively for the early and delayed groups.
- 45/117 (39%) patients in the delayed group have been transplanted to date (68 had a second line therapy)
- The median estimated time to SCT was 5.3 months among the early group compared to 39 months in the delayed group.

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Results

- Among the 290 patients initial therapy was:
  - Thalidomide - Dex in 123 (43%)
  - Lenalidomide - Dex in 167 (57%)
- 82 (67%) patients receiving TD had an early SCT compared to 91 (55%) patients in the LD group; P=0.04.
- The median follow up is longer in the TD group compared to LD (58 vs. 24 months)

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Baseline characteristics

Variable	Early SCT (n=174)	Delayed SCT (n=118)	P
Age (Diagnosis)	58	61	NS
Gender (Male)	57%	66%	NS
Serum Creatinine (mg/dL)	0.9	1	NS
Beta 2 microglobulin	2.3	2.4	NS
LDH (U/L)	228	185	< 0.001
Marrow plasma cell %	14%	10%	NS
Plasma cell labeling index	0.4%	1%	NS

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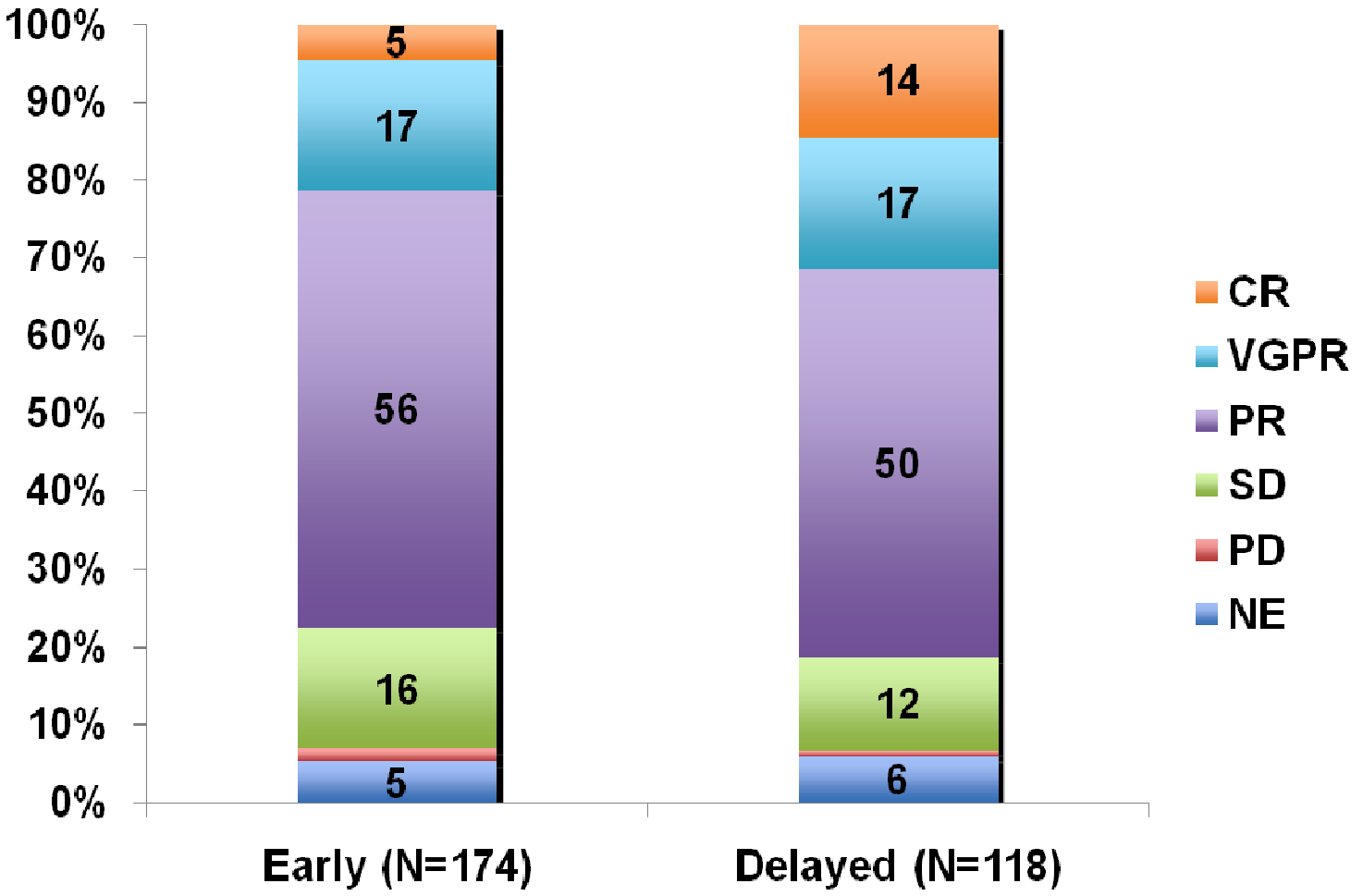
Best response: Initial therapy



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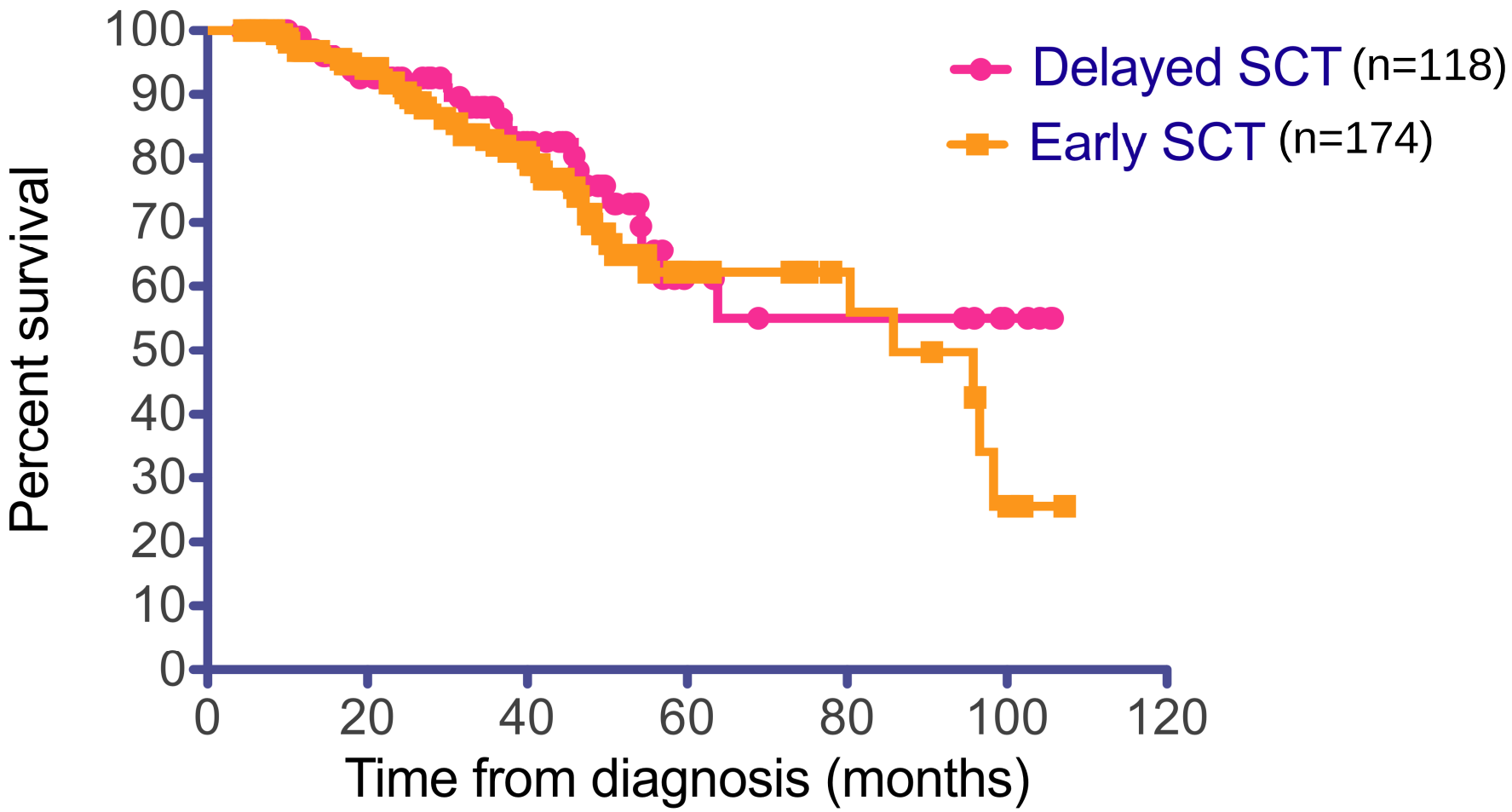
Overall survival from diagnosis



Median OS for early group was 86 mos (95% CI; 80,98) vs. NR (95% CI; 54, NR) for delayed group (P = 0.3)

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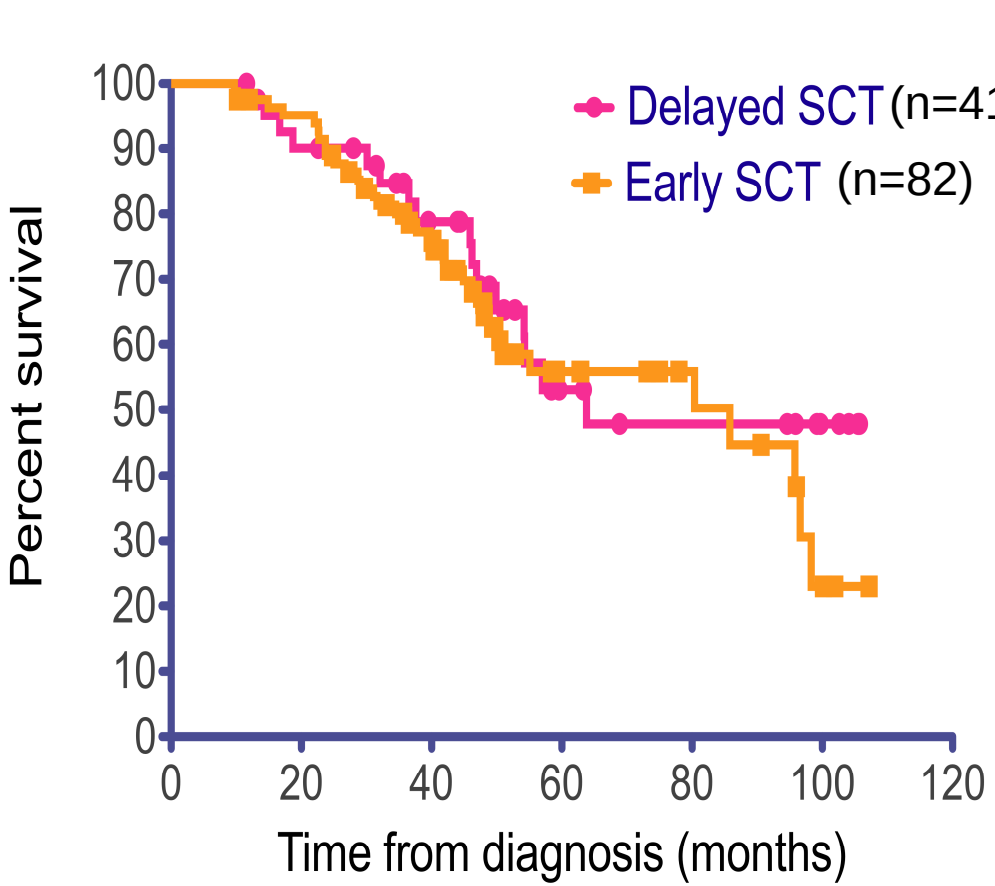
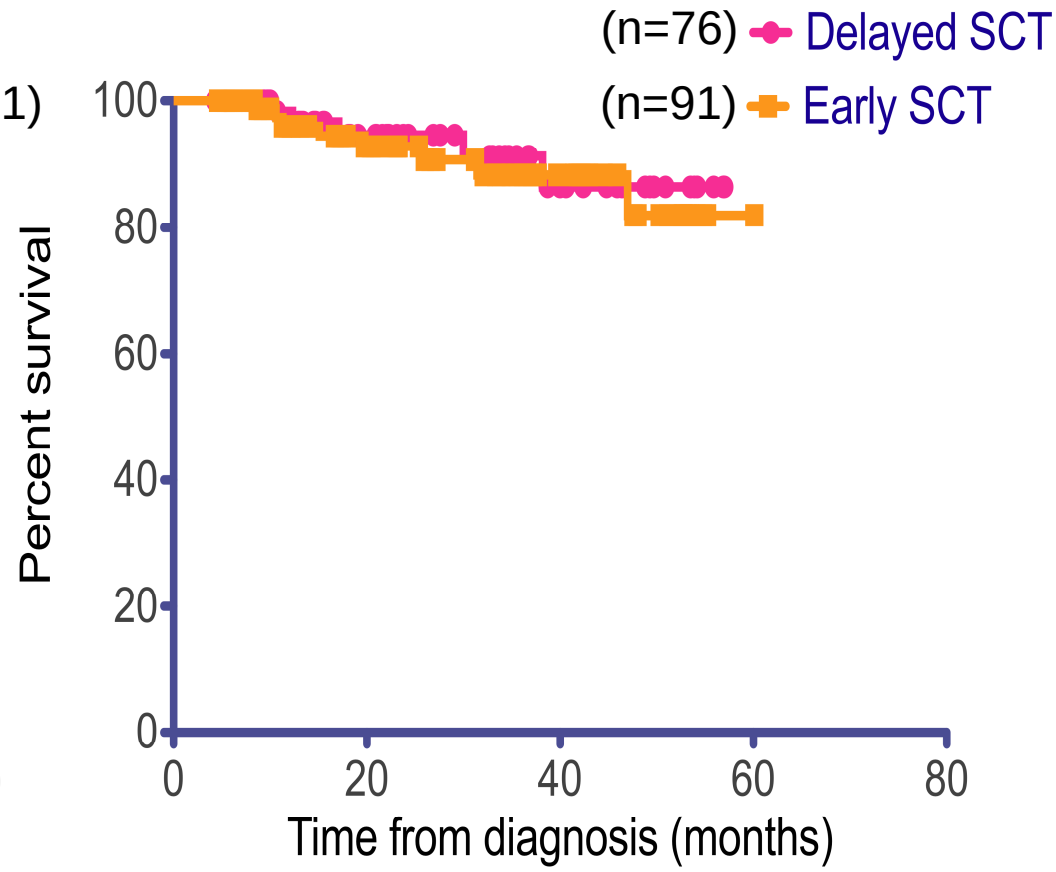
Overall survival: By initial therapy



TD



LD

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Characteristics at SCT

Variable	Early SCT (n=174)	Delayed SCT (n=45)	P
Age	58	62	0.06
Serum Creatinine (mg/dL)	0.9	1	NS
Beta 2 microglobulin	2.2	2.6	NS
LDH (U/L)	180	177	NS
Serum M-Spike (gm/dL)	0.7	0.8	NS
Marrow plasma cell %	7%	10%	NS
Plasma cell labeling index	0.2%	0.5%	0.06

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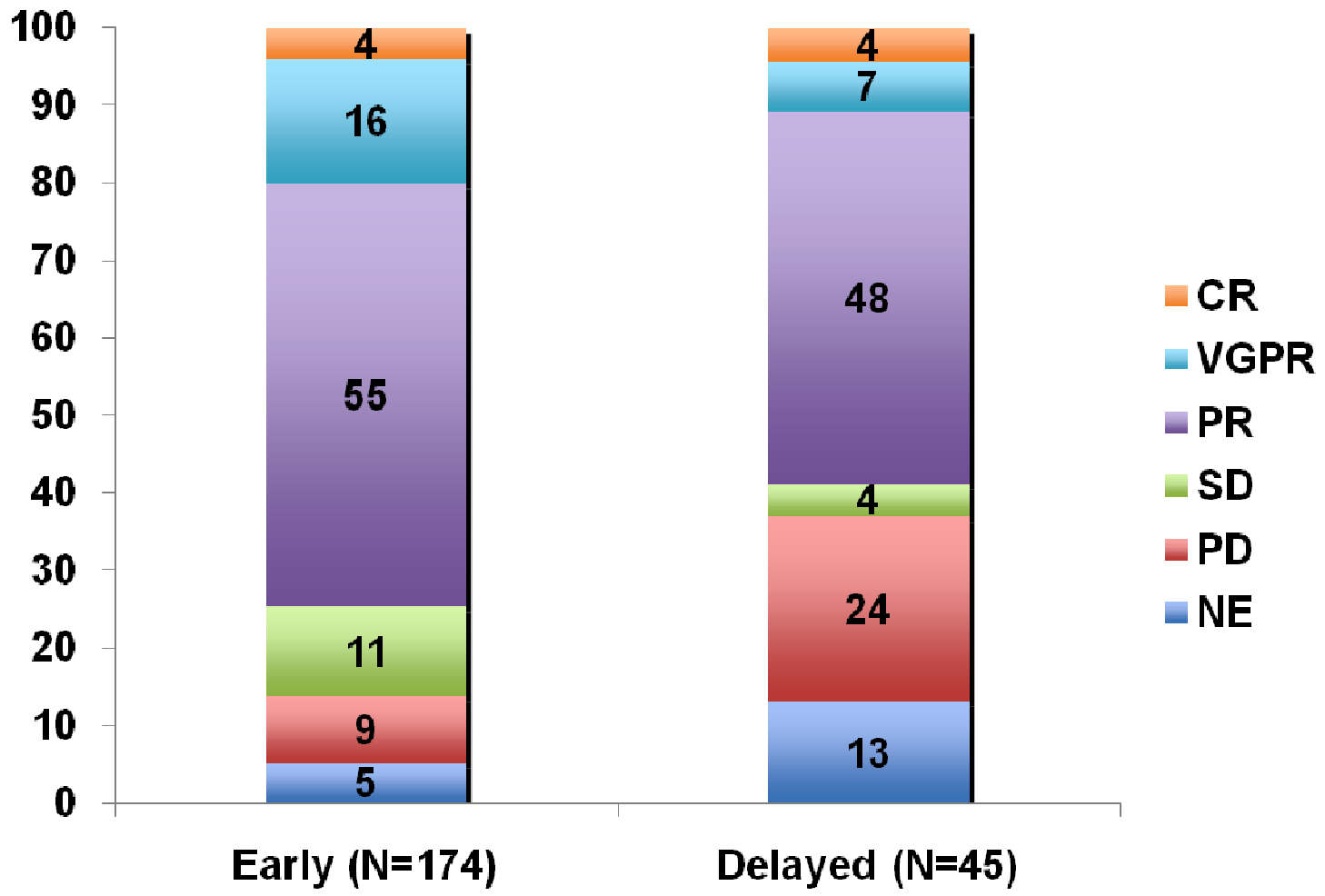
Response at time of SCT



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Delayed SCT

- Mel 200 was the conditioning regimen for nearly all patients
- Post SCT hospitalization days were higher among delayed SCT group (median 4 vs. 0; $P < 0.01$)
- The response rate to SCT was higher among the early group: 93% vs. 83% ($P = 0.049$)

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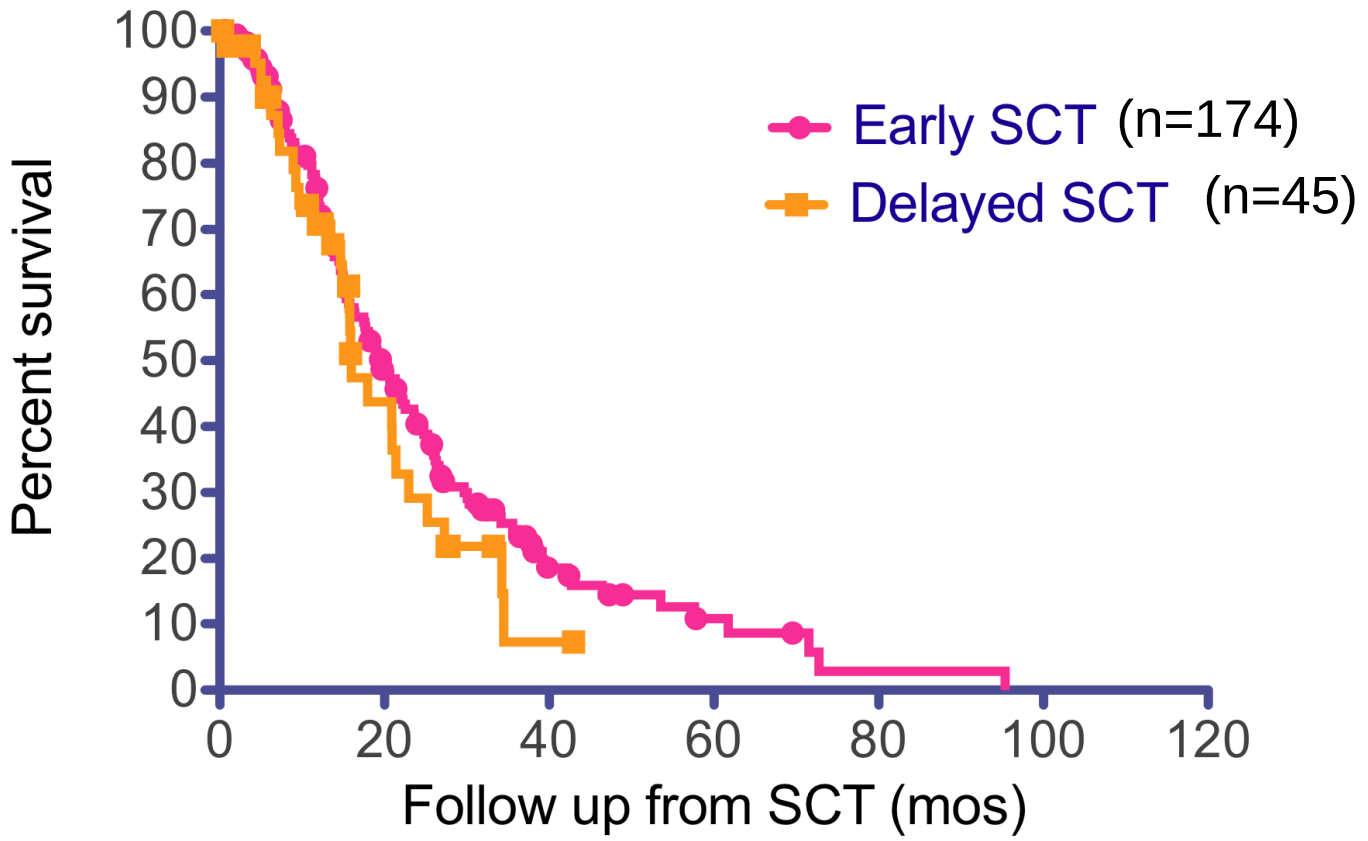
Post SCT-TTP



Median TTP post SCT 20 mos for early vs. 16 mos for delayed (P=0.2)

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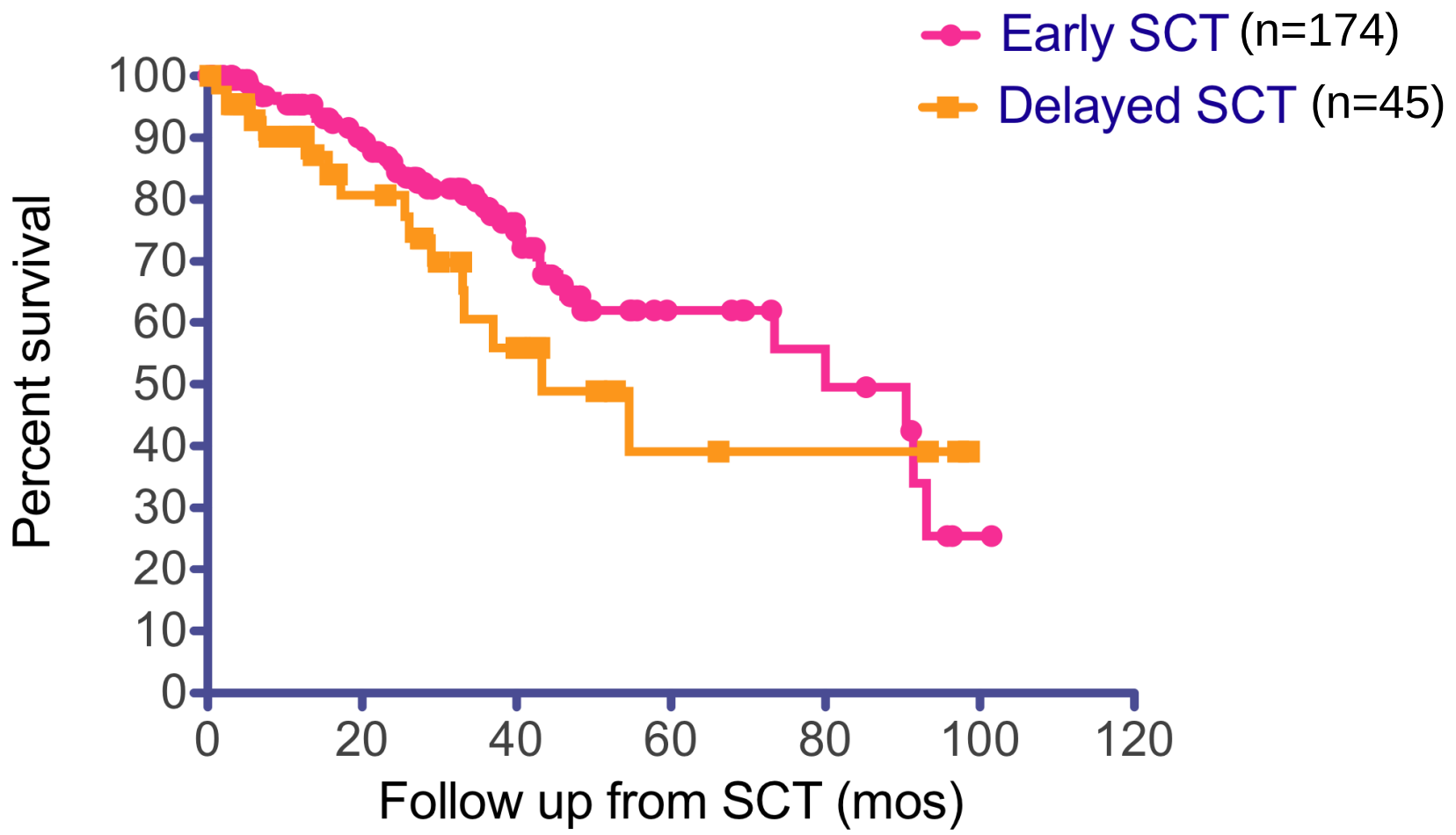
Post-SCT Overall survival



Trend to better OS post SCT for early SCT group, 80 mos vs. 43 mos, P = 0.04 (Breslow Gehan); P = 0.16 (logrank)

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Conclusions

- In a group of patients receiving initial therapy with IMiDs, the overall survival appears to be comparable, whether an upfront approach or SCT at relapse is used.
- The time to progression appears comparable following SCT, likely reflecting lack of alkylator exposure pre-SCT
- However, OS post SCT appear to be lower for the delayed SCT group reflecting less options for salvage therapy (already used up)

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Conclusions

- SCT should be considered a "regimen" for myeloma therapy not a platform to base all therapy on
- No QOL measurements in this study, but clearly plays an important role in the decision making process of “early” vs. “delayed”
- Retrospective nature precludes understanding reason for early vs. delayed decision and prospective studies are needed

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Acknowledgements

Patients who make research possible

Mayo Clinic Dysproteinemia Group

Clinical