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Transplant for every NDMM transplant eligible?

Immediate Transplant No Longer Required

Morie Gertz MD MACP

18th International Myeloma Workshop
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Disclosures

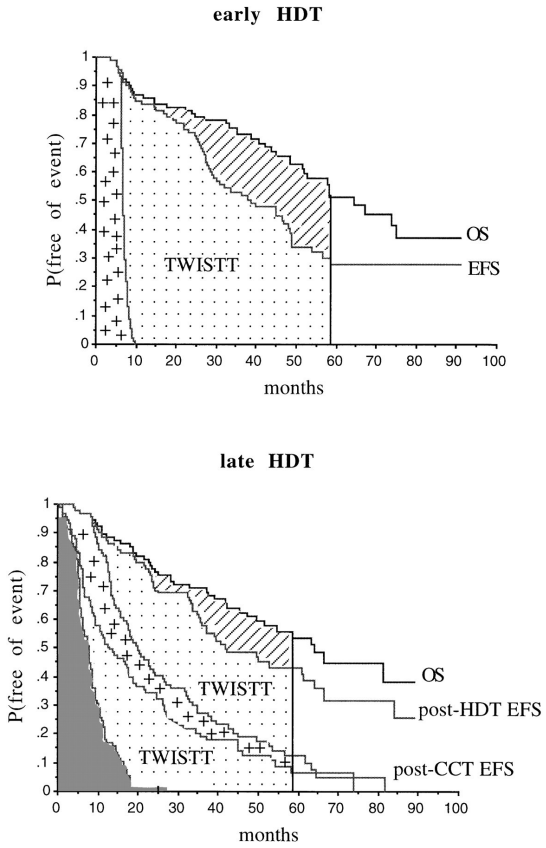
- BMS
- AbbVie
- Prothena
- Janssen
- Takeda
- Ionis

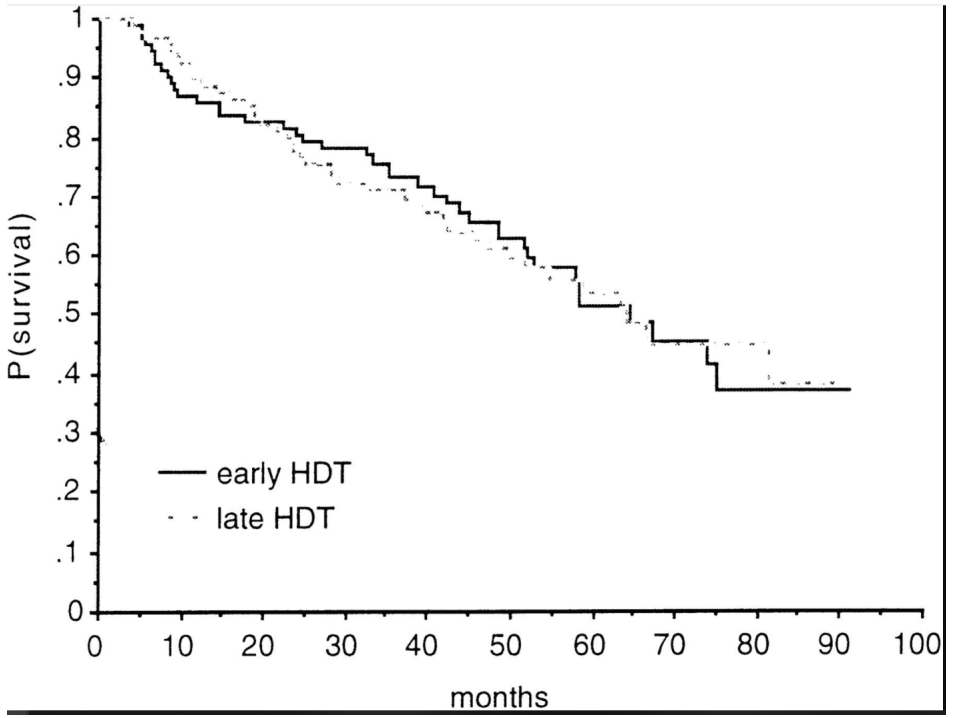
Happy

Uncertain

Confused

OS according to treatment group
At 48 months, OS 66% (range, 56% to 76%) and 61% (range, 51% to 71%), respectively





Even prior to novel agents
Early SCT did not provide OS benefit and time without symptoms and treatment toxicity (TWISTT) inferior with early HDT

https://doi.org/10.1182/blood.V92.9.3131

Early harvest and late transplantation in MM

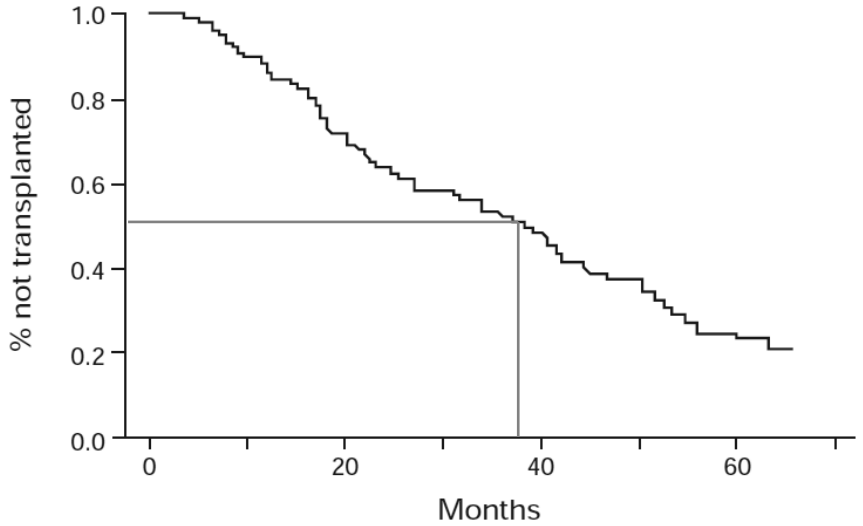


Figure 2 Kaplan–Meier actuarial time from diagnosis to day 0 of bone marrow transplant.

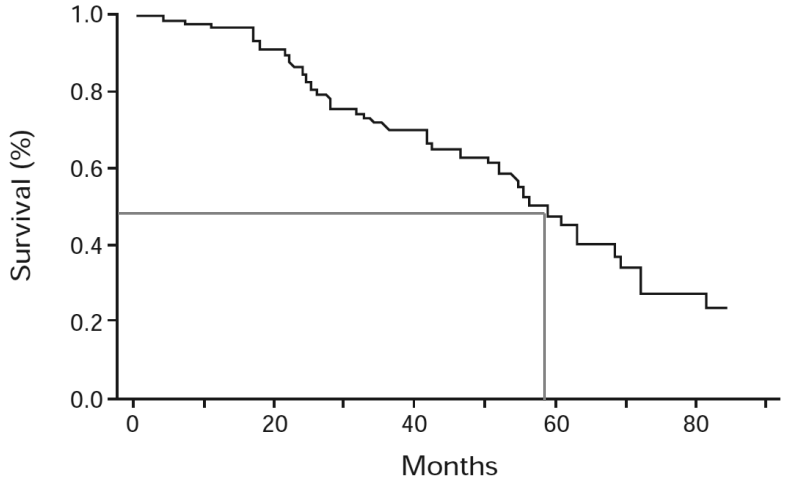
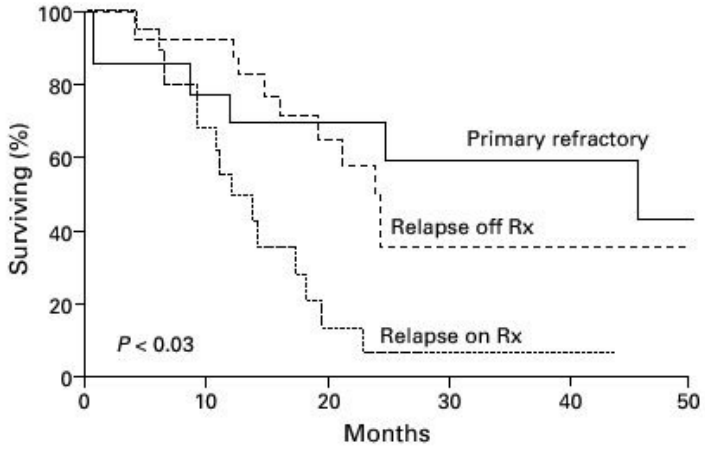


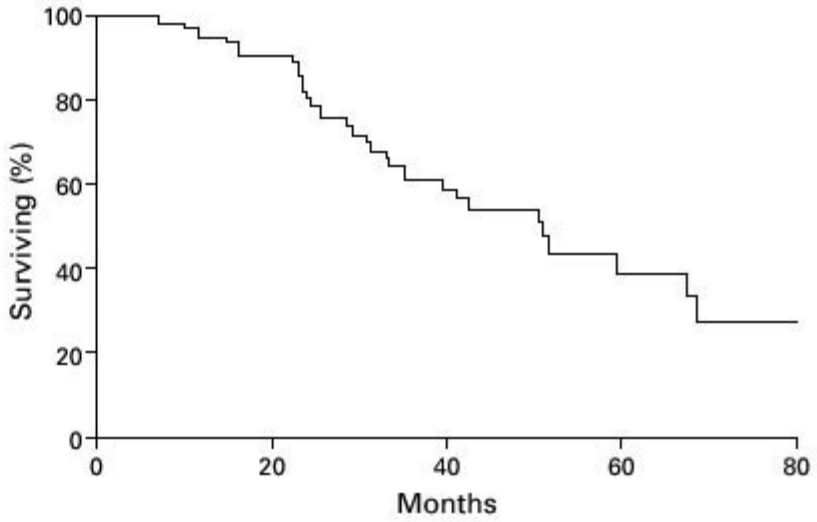
Figure 1 Kaplan–Meier actuarial survival from diagnosis for all 118 patients.

Bone Marrow Transplantation, (1999) 23, 221–226

Delayed stem cell transplantation for the management of relapsed or refractory multiple myeloma



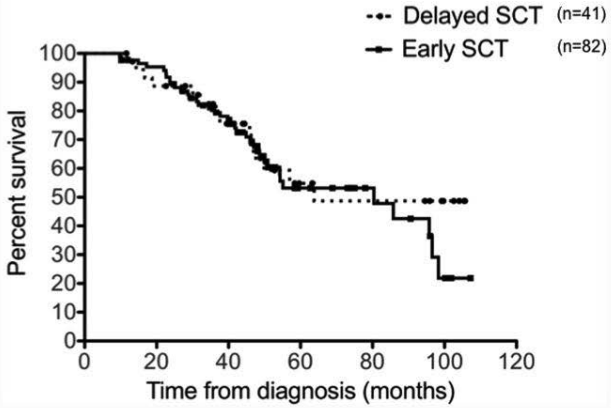
Overall survival after stem cell transplantation based on disease status at the time of transplantation. Rx, treatment.



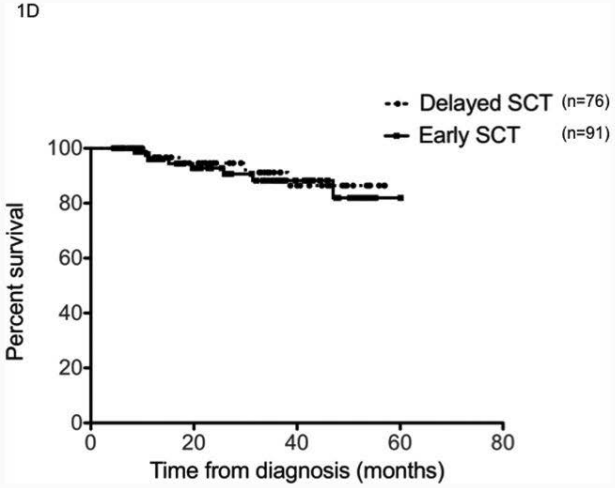
Overall survival from original diagnosis of multiple myeloma.

Bone Marrow Transplantation **volume 26**, pages 45–50 (2000)

Early versus Delayed Autologous Transplantation Following IMiD-based Induction Therapy in Patients with Newly Diagnosed Multiple Myeloma



overall survival from the initiation the first therapy for diagnosis of multiple myeloma for patients receiving initial therapy with thalidomide and dexamethasone n=123



overall survival from the initiation the first therapy for diagnosis if multiple myeloma for patients receiving initial therapy with lenalidomide and dexamethasone (n=167).

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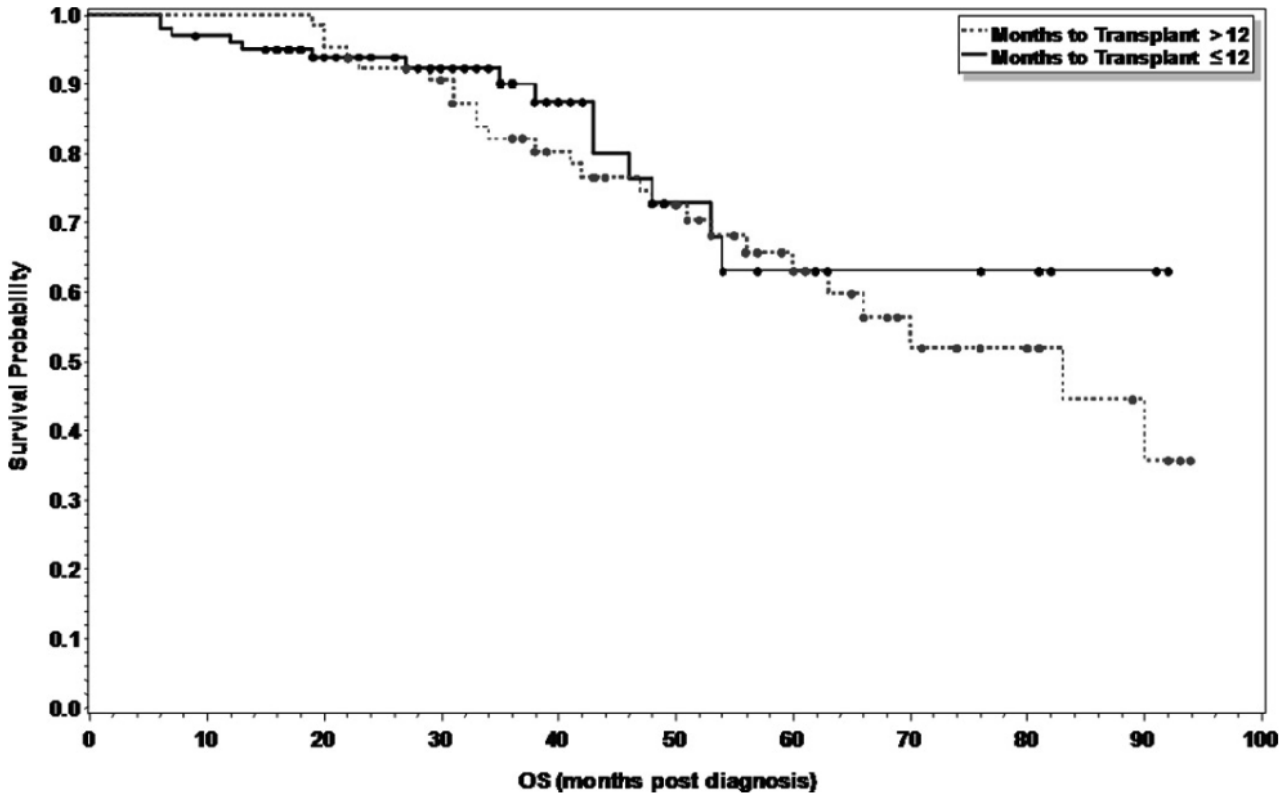
Cancer. 2012 Mar 15; 118(6): 1585–1592.

Early versus delayed autologous stem cell transplantation in patients receiving novel therapies for Multiple Myeloma



Overall Survival comparing early vs. delayed first ASCT in multiple myeloma patients (p=0.45).

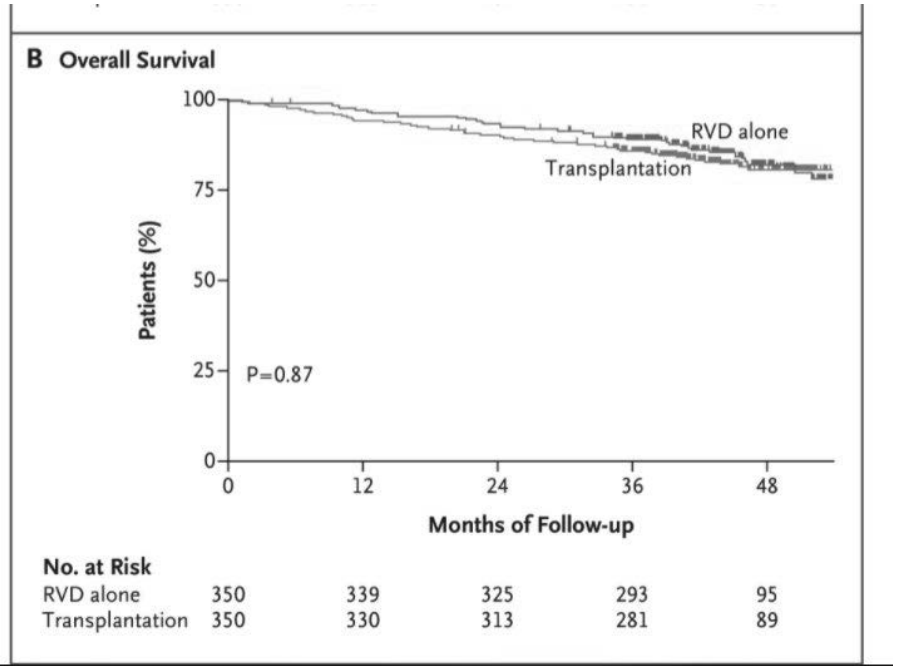
early or late ASCT is a viable option for MM patients receiving induction treatment with novel targeted therapies

	SCT <1 yr	N=102	SCT >1yr	N=65	
	N	%	N	%	
Thalidomide	39	38	43	66	
Bortezomib	64	63	32	49	
lenalidomide	34	33	18	28	

Leuk Lymphoma. 2013 Aug; 54(8): 1658–1664.

Early Versus Late Autologous Stem Cell Transplant in Newly Diagnosed Multiple Myeloma: Long-Term Follow-up Analysis of the IFM 2009 Trial

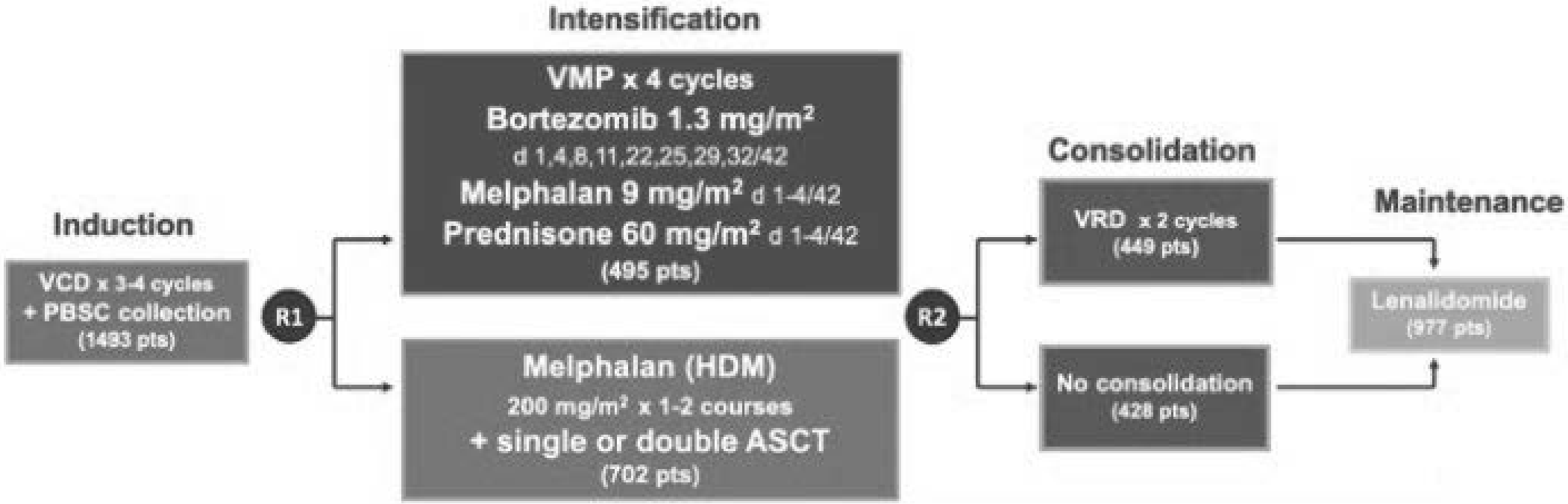
- With a FU of almost 8 years, median OS was NR and there was no difference between the 2 strategies with respect to PFS2 and OS



MRD appears to predict outcome and might be used after induction to identify those pts who probably do not require a transplant.

As MRD- rates rise with novel agents need for SCT will continue to decline

EMN02/HO95 MM study design



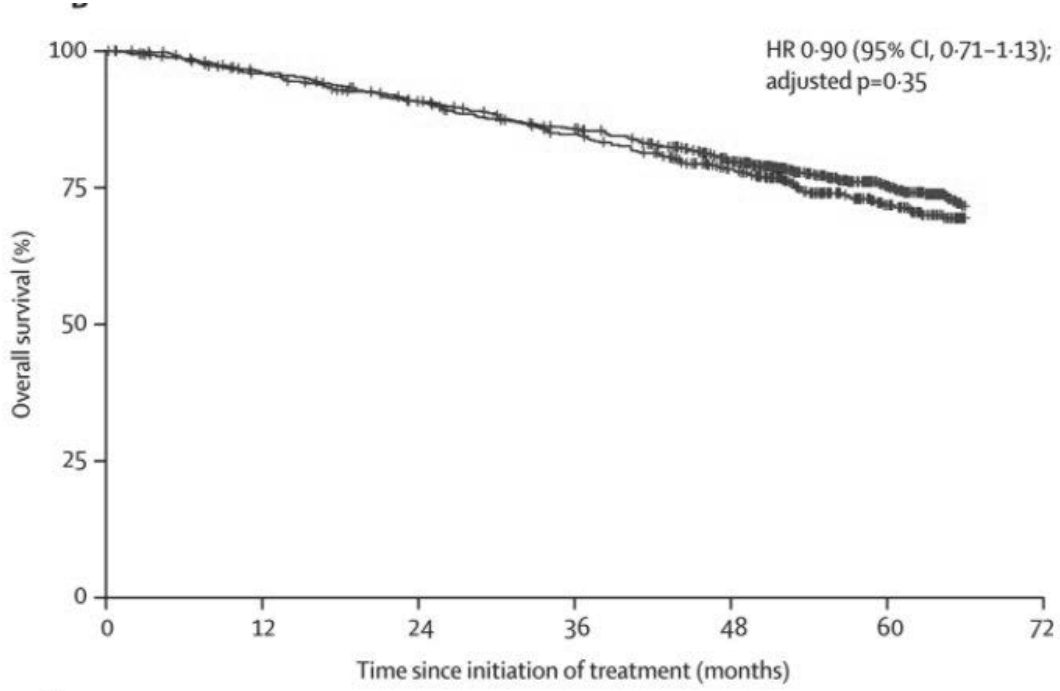
Primary endpoints:

- PFS from R1: ASCT *vs* VMP
- PFS from R2: VRD consolidation *vs* no consolidation

Secondary endpoints:

- PFS from R1: HDM-1 *vs* HDM-2
- Rates of response to ASCT or VMP
- OS from R1: ASCT *vs* VMP
- Toxicities with ASCT and VMP

EMN02/HO95

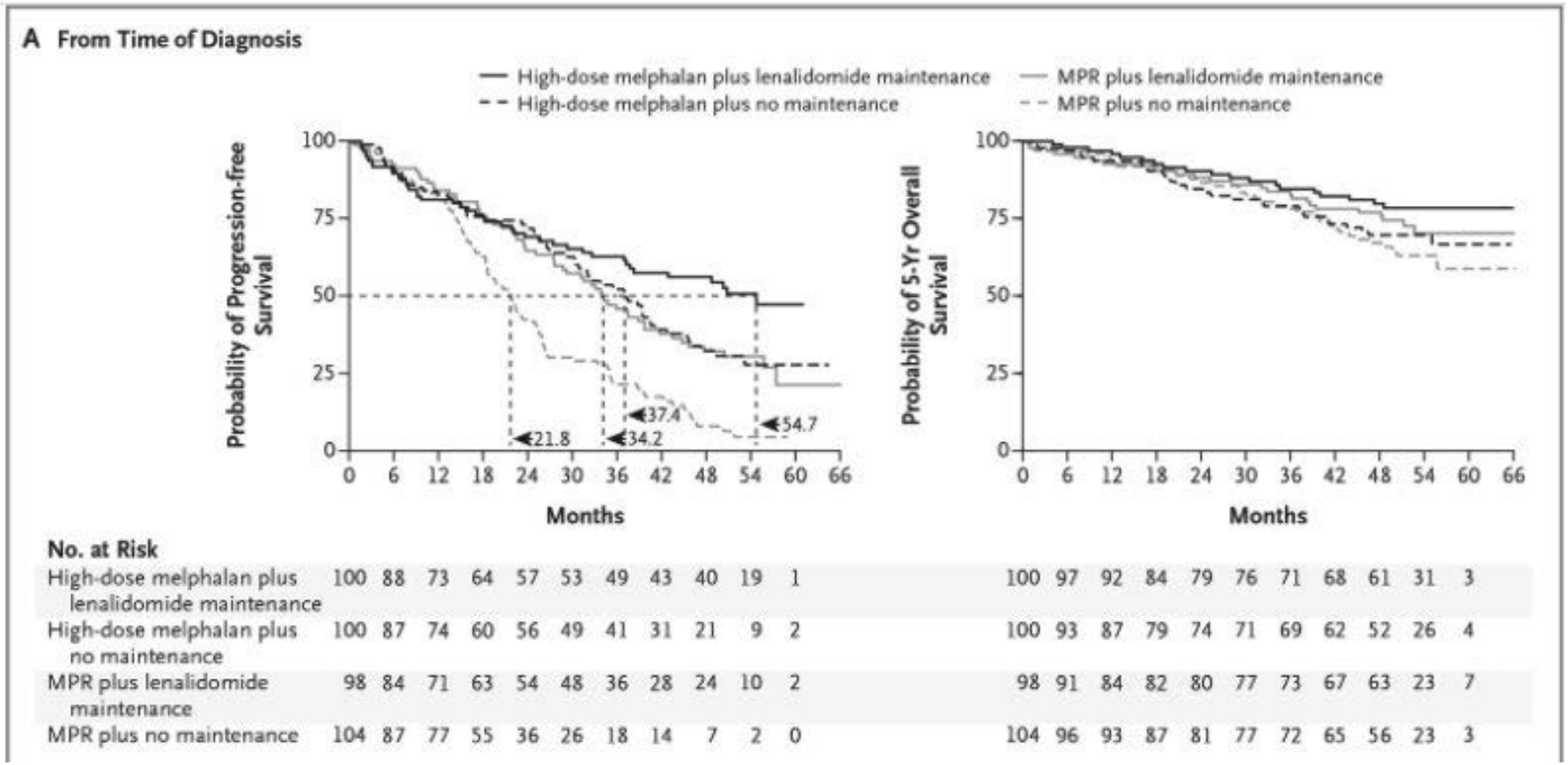


Number at risk (number censored)							
Autologous HSCT	702 (0)	658 (16)	614 (24)	569 (36)	487 (78)	276 (268)	..
VMP	495 (0)	463 (12)	430 (20)	391 (31)	331 (62)	174 (198)	..

Figure 2

Lancet Haematology, The, 2020-06-01, Volume 7, Issue 6, Pages e456-e468

ASCT + R maintenance vs MPR-R



3-year overall survival was not significantly prolonged (88.0% vs. 79.2%; hazard ratio for death, 0.64; 95% CI, 0.36 to 1.15; P=0.14).

N Engl J Med 2014; 371:895-905
DOI: 10.1056/NEJMoa1402888

Interpretation

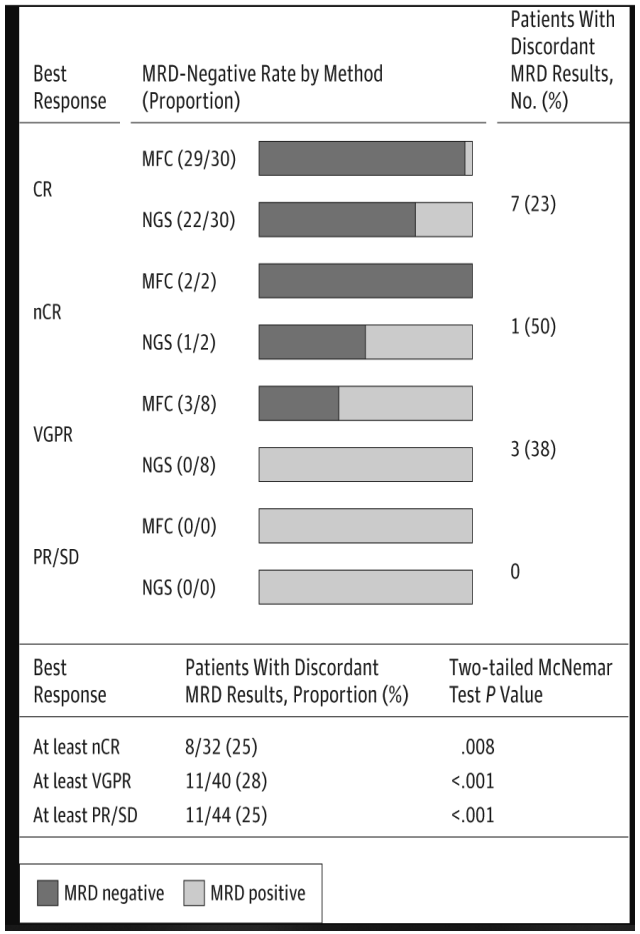
- the lack of overall survival benefit suggests that deferred stem cell transplant until relapse is feasible without compromising outcome

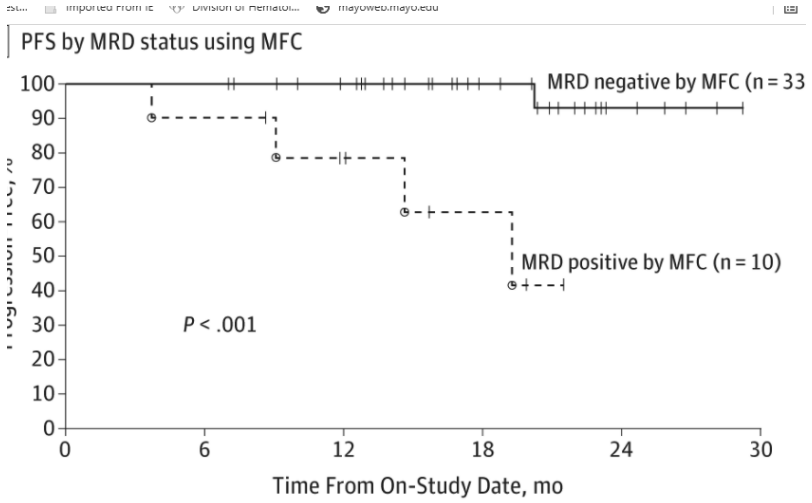
Conclusions

- The goal of therapy is MRD-
  - No matter how this goal is achieved outcomes are identical
  - As combinations of non cross resistant agents are used in induction, consolidation and maintenance the need/role for SCT will continue to decline
  - In Castor Pollux Alcyone and Maia median MRD- 28%

https://doi.org/10.1182/blood.2021011101

MRD negativity with non transplant regimens

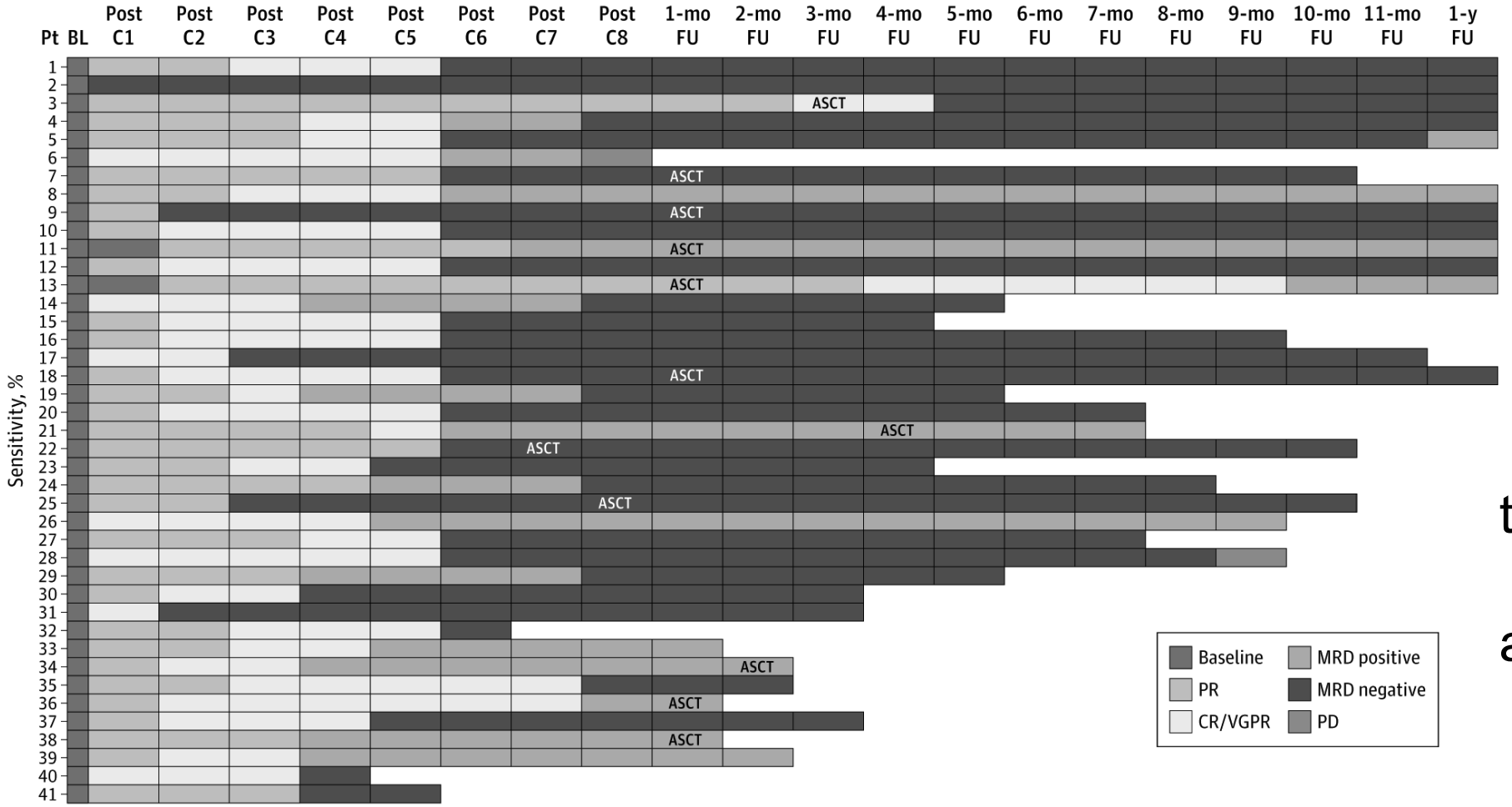




- carfilzomib with lenalidomide and dexamethasone followed by lenalidomide to patients with NDMM N=45
- near-complete response or better (n = 28), minimal residual disease negativity was 100% by multiparametric flow cytometry and 67% by next-generation sequencing.

JAMA Oncol. 2015;1(6):746-754. doi:10.1001/jamaoncol.2015.2010

carfilzomib-lenalidomide-dexamethasone-daratumumab combination therapy-**MANHATTAN Nonrandomized Clinical Trial**

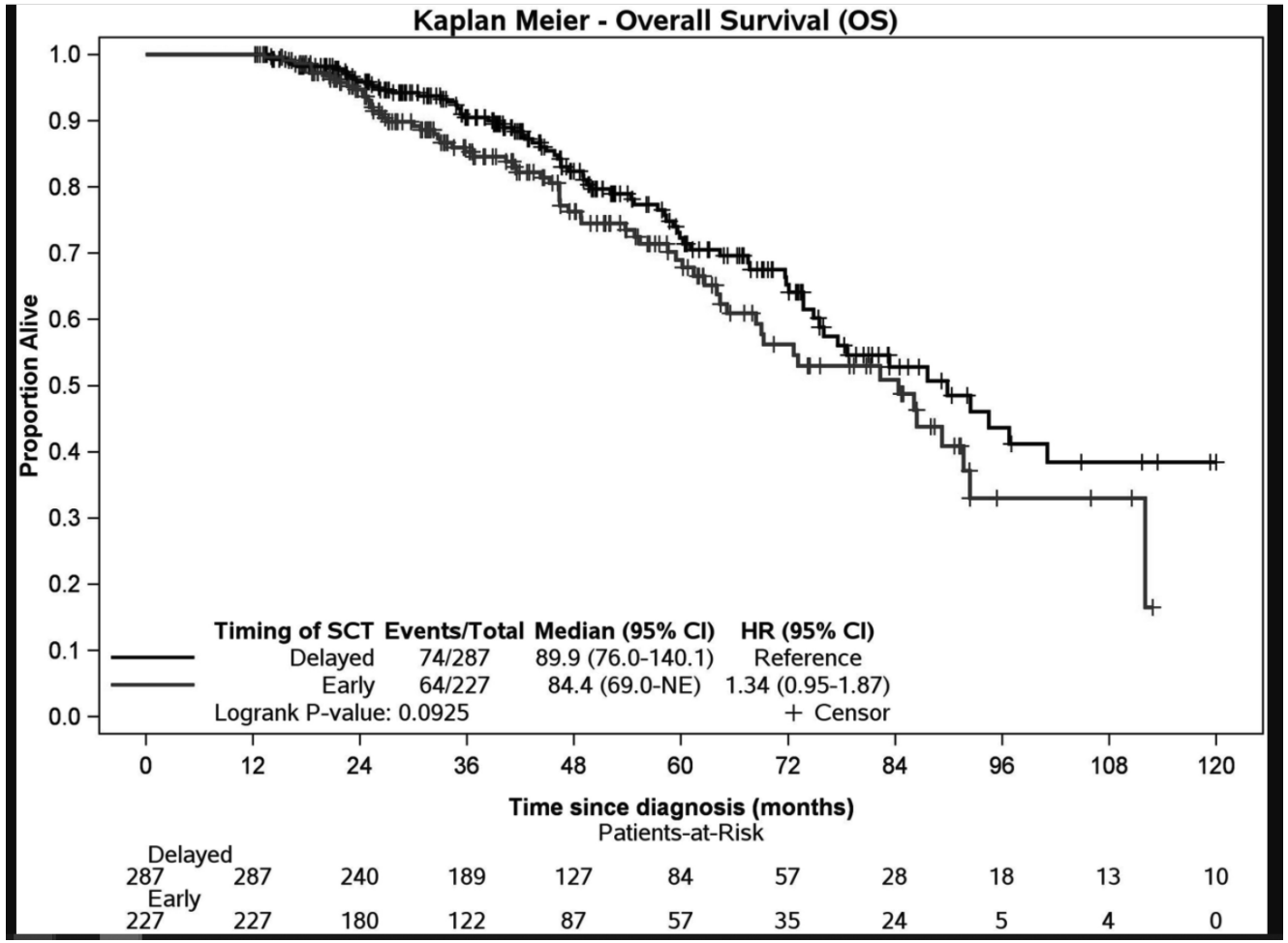


MRD negativity in the bone marrow; 10^{-5} sensitivity) was achieved in 29 of 41 patients (71%;

the 1-year PFS rate and the OS rate were 98% and 100%, respectively

JAMA Oncol. 2021 Jun 1;7(6):862-868. doi: 10.1001/jamaoncol.2021.0611. PMID: 33856405; PMCID: PMC8050789.

Timing of Autologous Stem Cell Transplantation for Multiple Myeloma in the Era of Current Therapies

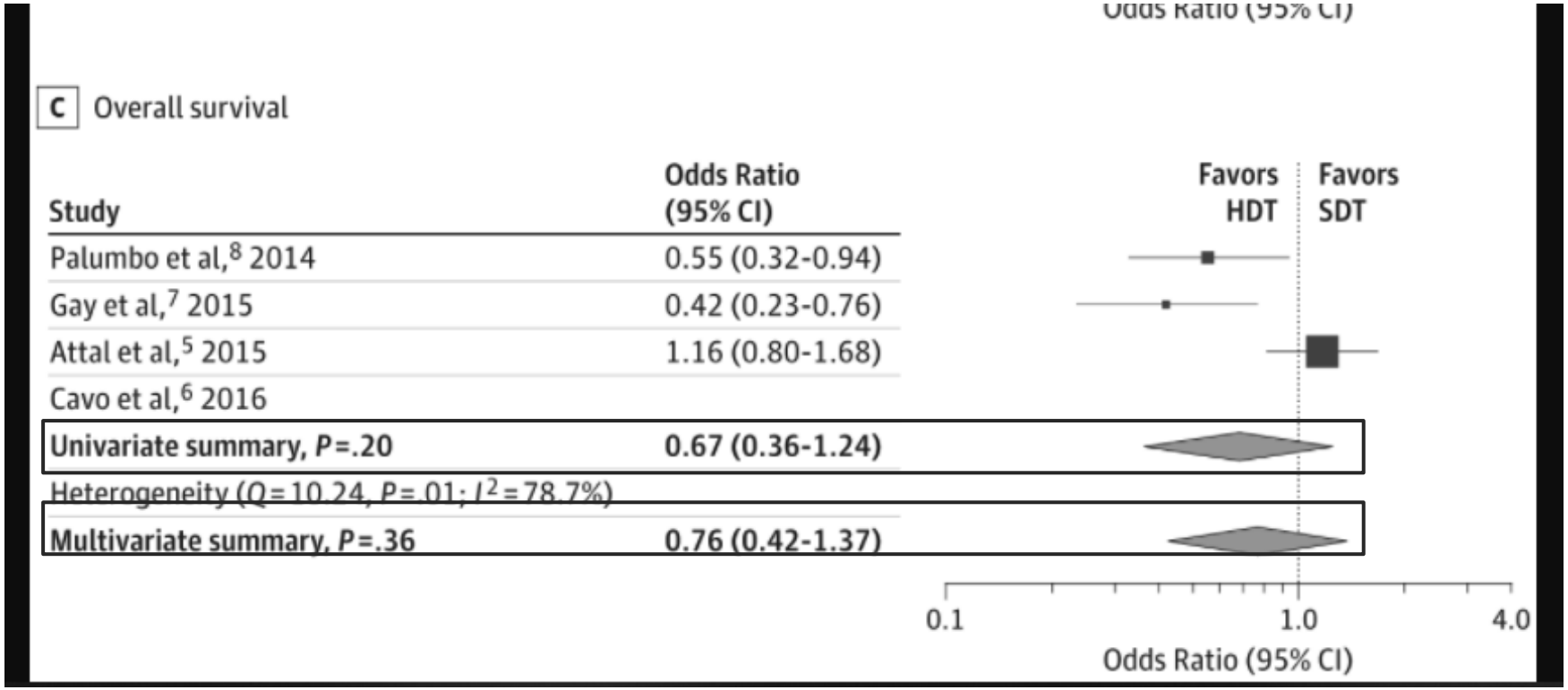


consecutive patients with newly diagnosed myeloma who had undergone stem cell harvest (SCH) from 2005 to 2014 and separated them into early (SCT within 12 months of diagnosis) and delayed.

Delaying SCT did not affect OS or even PFS to second relapse

Clin Lymphoma Myeloma Leuk. 2020 Oct;20(10):e734-e751. doi: 10.1016/j.clml.2020.05.027. Epub 2020 Jun 7. PMID: 32660906.

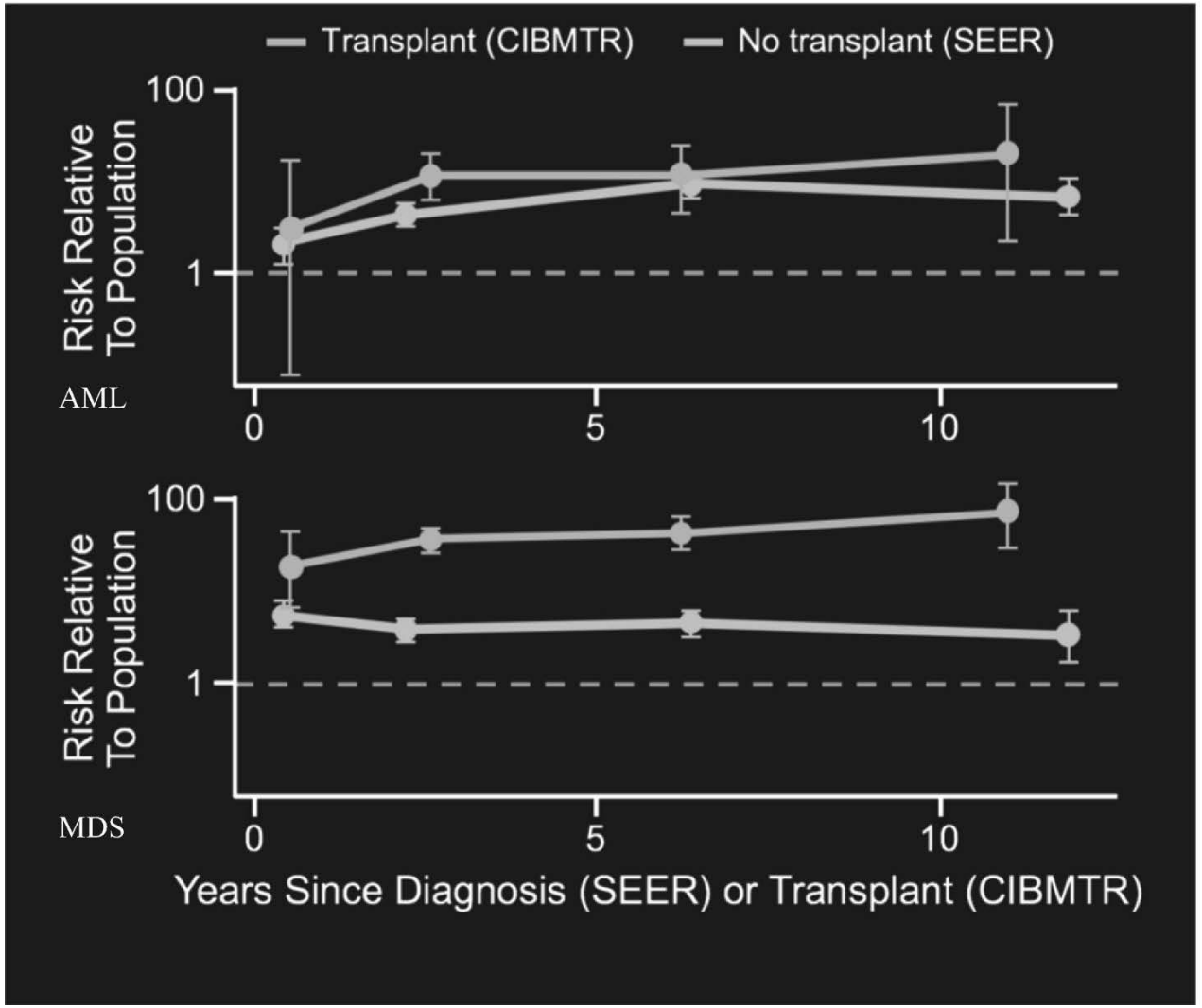
Autologous Transplantation for Newly Diagnosed Multiple Myeloma in the Era of Novel Agent Induction



3171 patients in these trials

JAMA Oncol. 2018;4(3):343-350. doi:10.1001/jamaoncol.2017.4600

The role of high-dose melphalan with autologous stem-cell transplant in multiple myeloma: is it time for a paradigm shift?

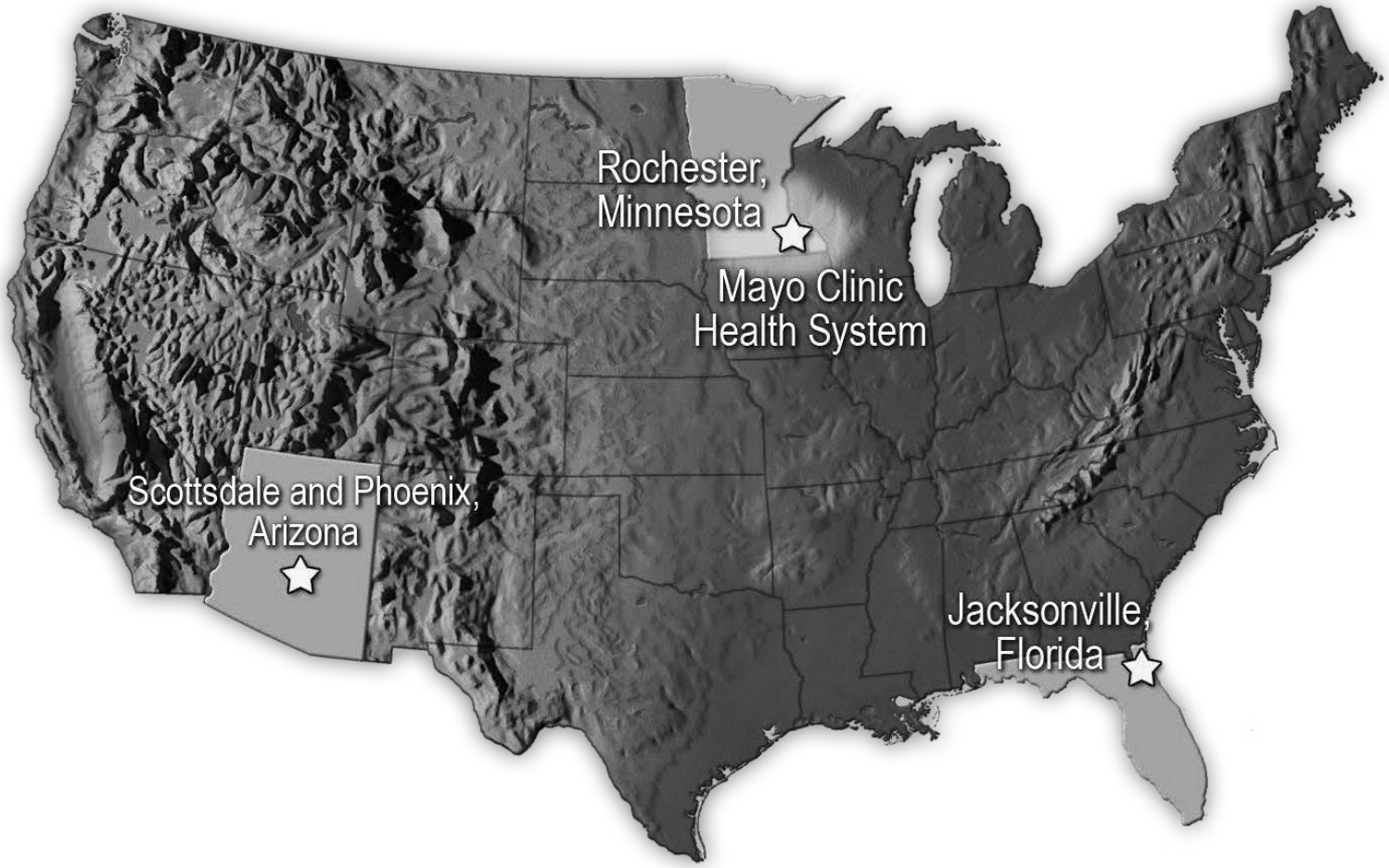


British Journal of Haematology, Volume: 191, Issue: 5, Pages: 692-703, First published: 05 June 2020, DOI: (10.1111/bjh.16764)

Summary

- We need to stop thinking of SCT as the platform on which all myeloma therapy is built (transplant eligible is no longer question 1)
- Sct **is a regimen** and selection, and sequencing depends on availability of other regimens, reimbursement, trial access and availability of novel agents

Mayo Clinic
Locations



Questions & Discussion

@moriegertz
gertm@mayo.edu

