Comprehensive Cancer Center
Tübingen-Stuttgart

1. Tübinger Symposium für Hämatologische Zelltherapie

Sequenzielle Konditionierung: Was sind die Vorteile?

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Disclosure of conflicts of interest

1. **Employment or Leadership Position**
   None

2. **Advisory Role or Expert Testimony**
   None

3. **Stock Ownership**
   None

4. **Patent, Copyright, Licensing**
   None

5. **Honoraria**
   Speaker's fee abbvie

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   None

7. **Other Financial Relationships**
   None

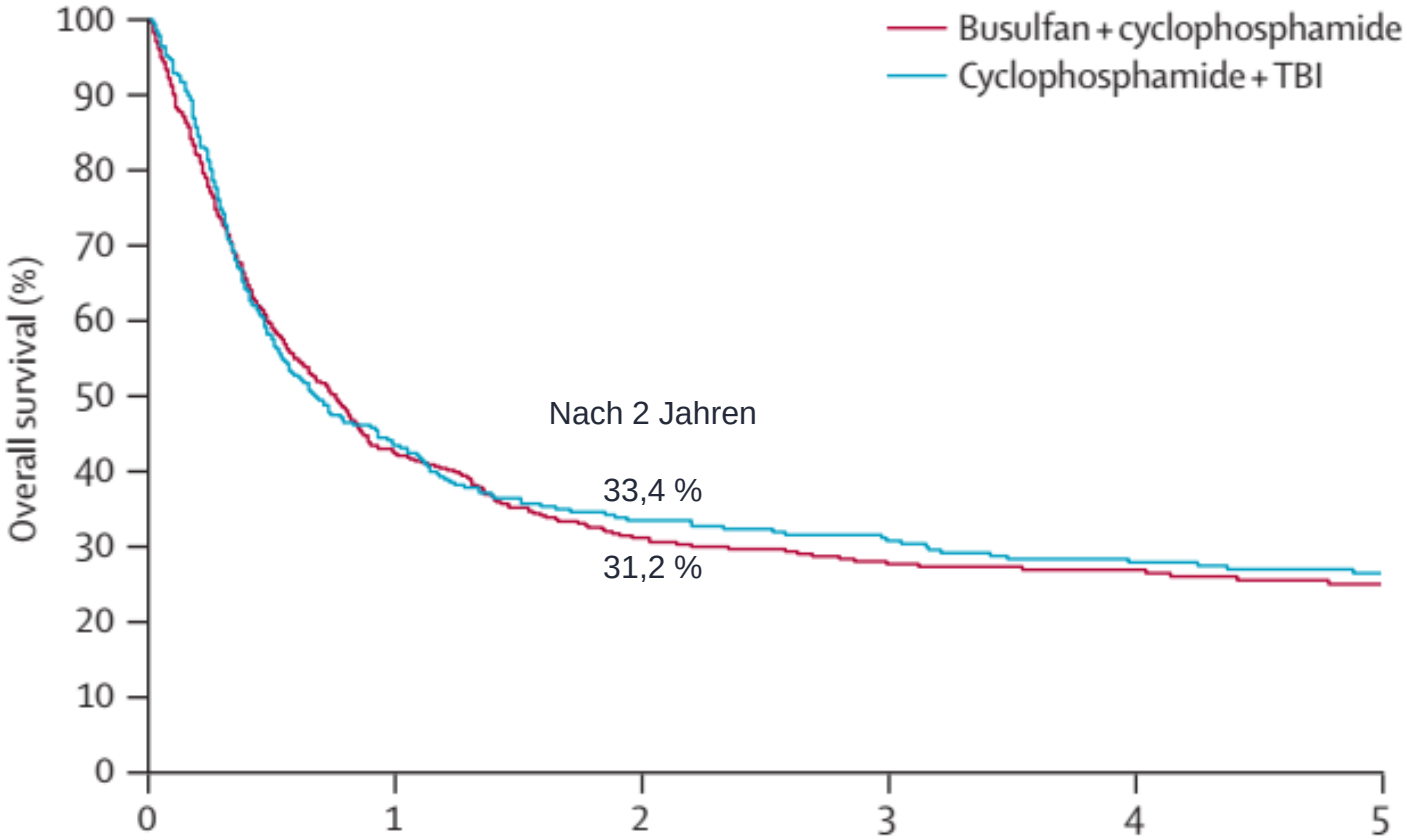
8. **Immaterial Conflicts of Interest**
   None

Sequenzielle Konditionierung: Was sind die Vorteile?

Fokus: Refraktäre/rezidivierte akute myeloische Leukämie (R/R AML)

Outcomes after use of two standard ablative regimens in patients with refractory acute myeloid leukaemia: a retrospective, multicentre, registry analysis

R/R AML, Myeloablative Konditionierung, EBMT-Register, n = 852



Nagle A et al. Lancet Haematol 2015;2: e384–92

München 1999

München

Christoph Schmid

Hans-Jochen Kolb

Long-term survival in refractory acute myeloid leukemia after sequential treatment with chemotherapy and reduced-intensity conditioning for allogeneic stem cell transplantation

Schmid C et al. Blood. 2006;108:1092-1099

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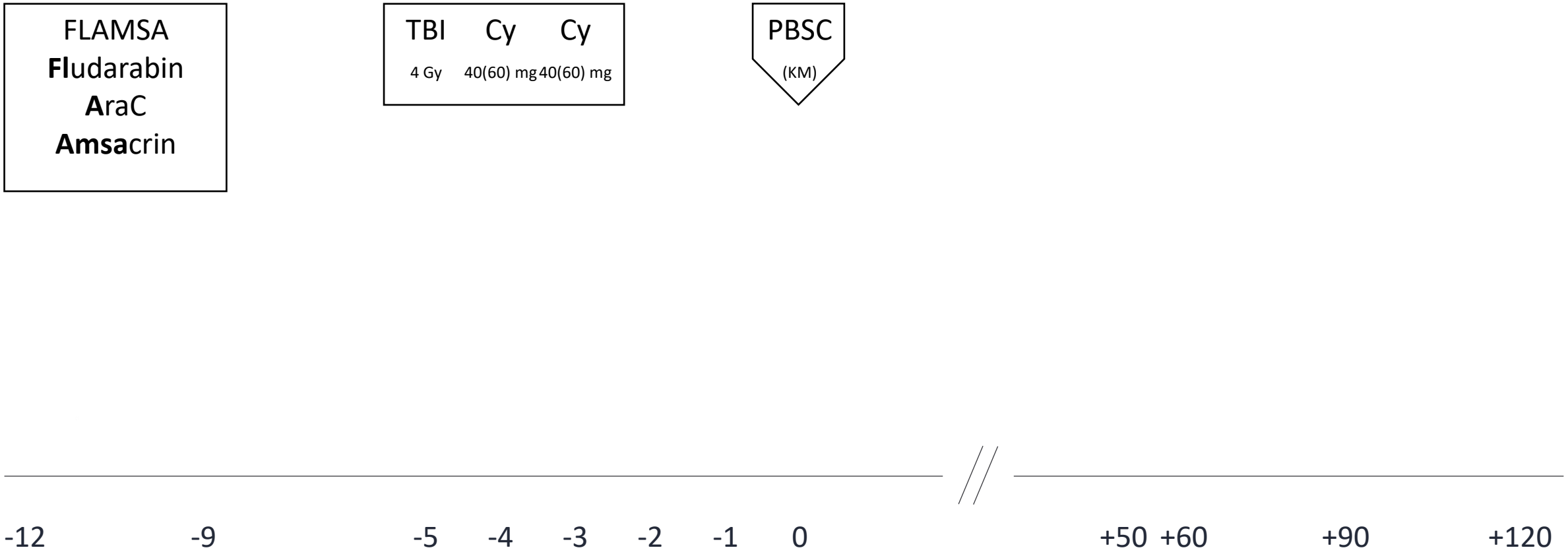

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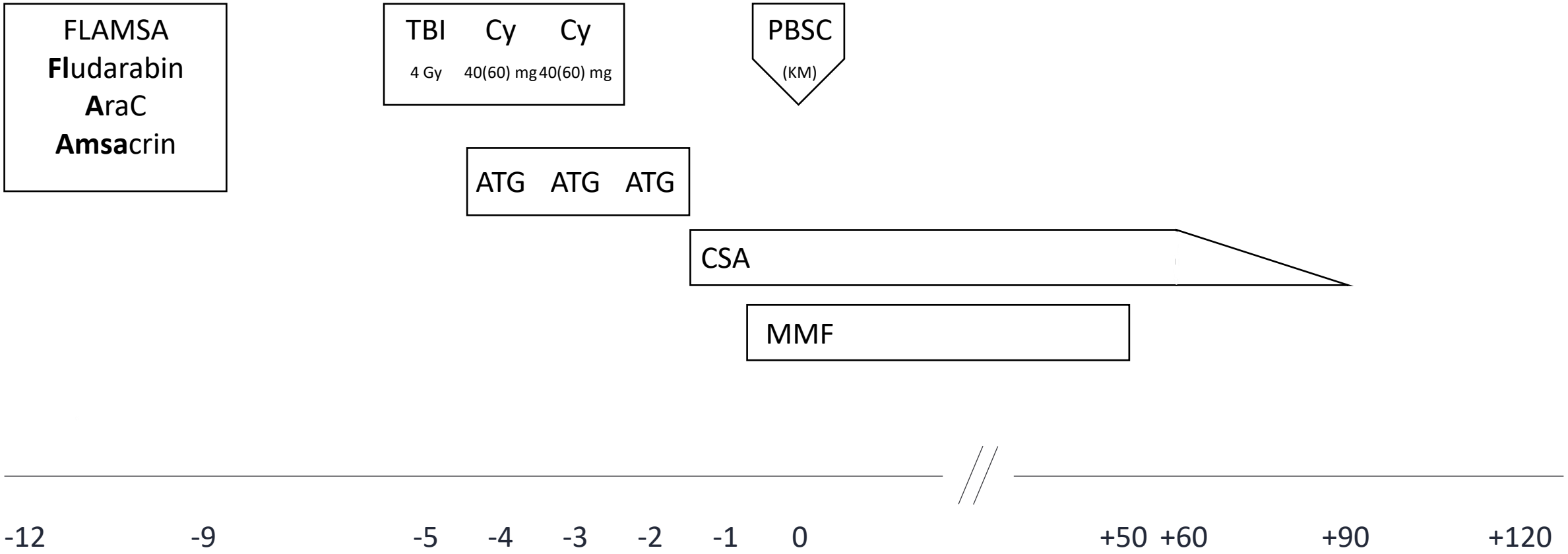

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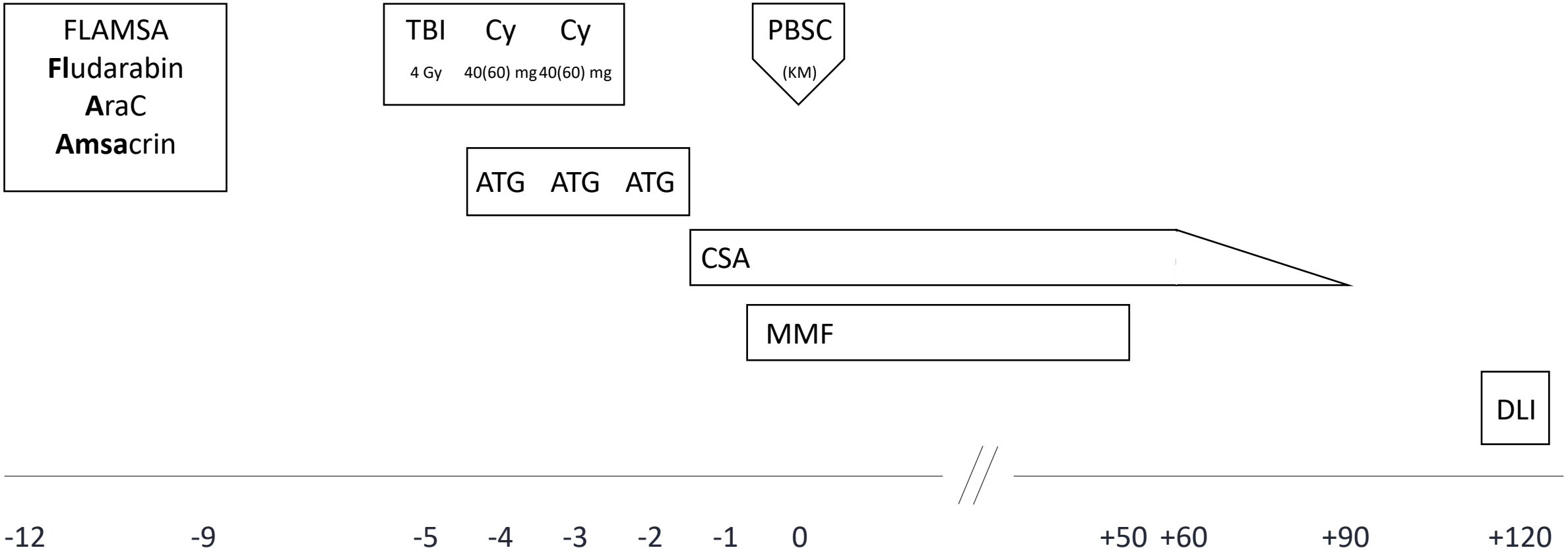

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Long-term survival in refractory acute myeloid leukemia after sequential treatment with chemotherapy and reduced-intensity conditioning for allogeneic stem cell transplantation

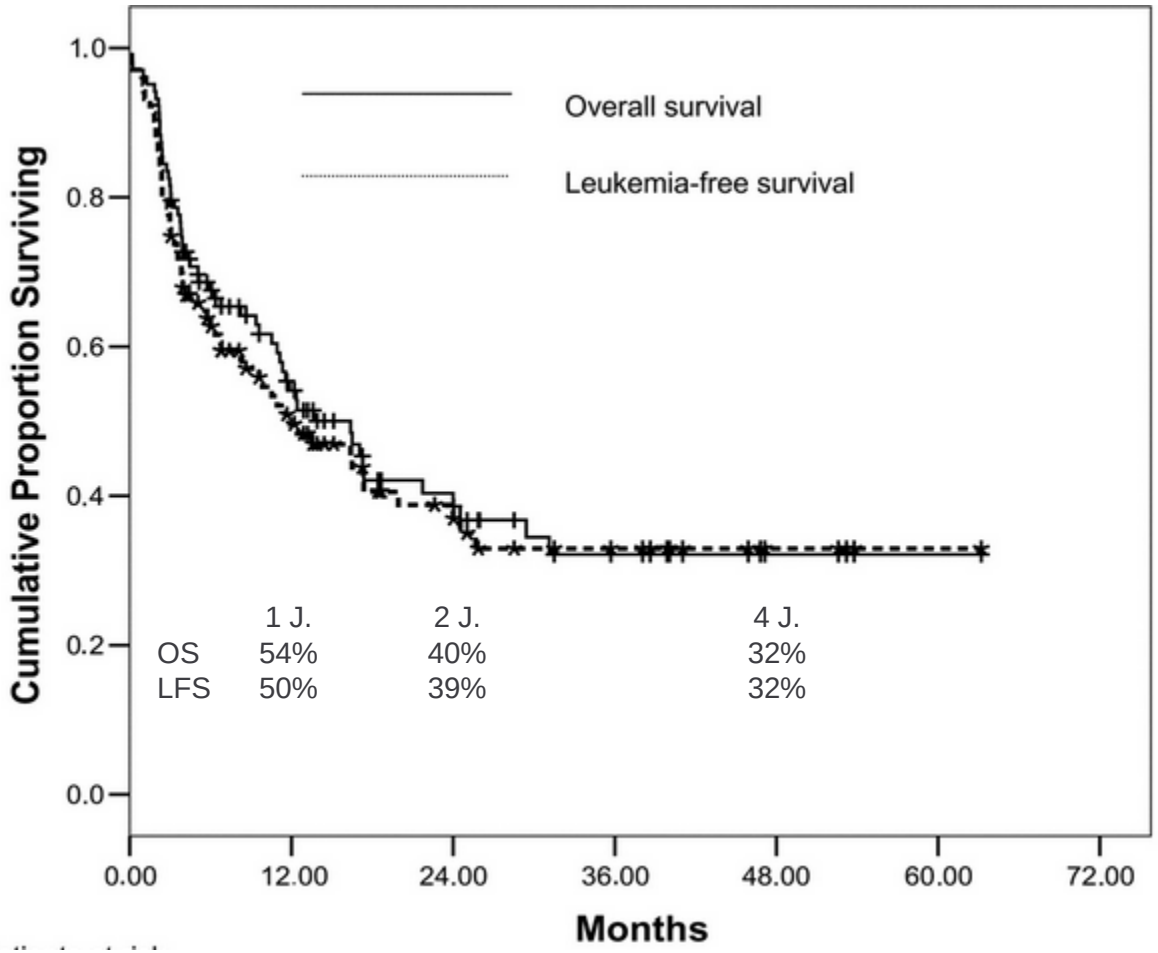
Patient, donor, and transplant characteristics

No. patients	103
Diagnosis, no. (%)	
De novo AML	76 (73.8)
AML secondary to MDS	21 (20.4)
AML secondary to other malignancies	6 (5.8)
Stage at transplantation, no. (%)	
Primary induction failure (PIF)†	37 (35.9)
Relapse after CR1 < 6 mo (ER)	53 (51.5)
Untreated/Ld AraC, no.	29
In aplasia, no.	3
Refractory,‡ no.	20
In CR2, no.	1
Refractory relapse after > 6 mo in CR,‡ no. (%)	8 (7.8)
2nd relapse	5 (4.8)
Untreated, no.	4
Refractory, no.	1

 Schmid C et al. Blood. 2006;108:1092-1099

Long-term survival in refractory acute myeloid leukemia after sequential treatment with chemotherapy and reduced-intensity conditioning for allogeneic stem cell transplantation

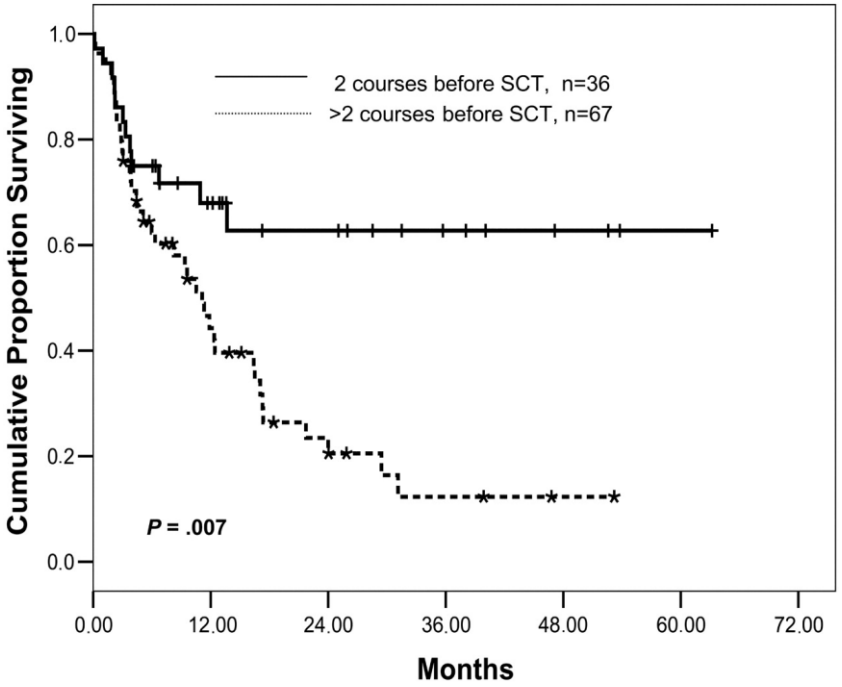
Overall survival and leukemia-free survival



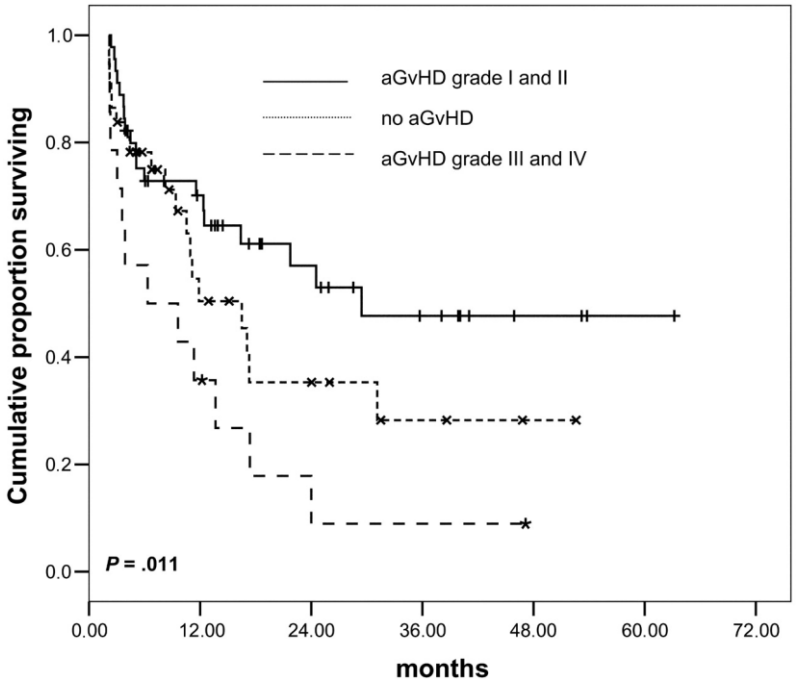
12 Schmid C et al. Blood. 2006;108:1092-1099

Long-term survival in refractory acute myeloid leukemia after sequential treatment with chemotherapy and reduced-intensity conditioning for allogeneic stem cell transplantation

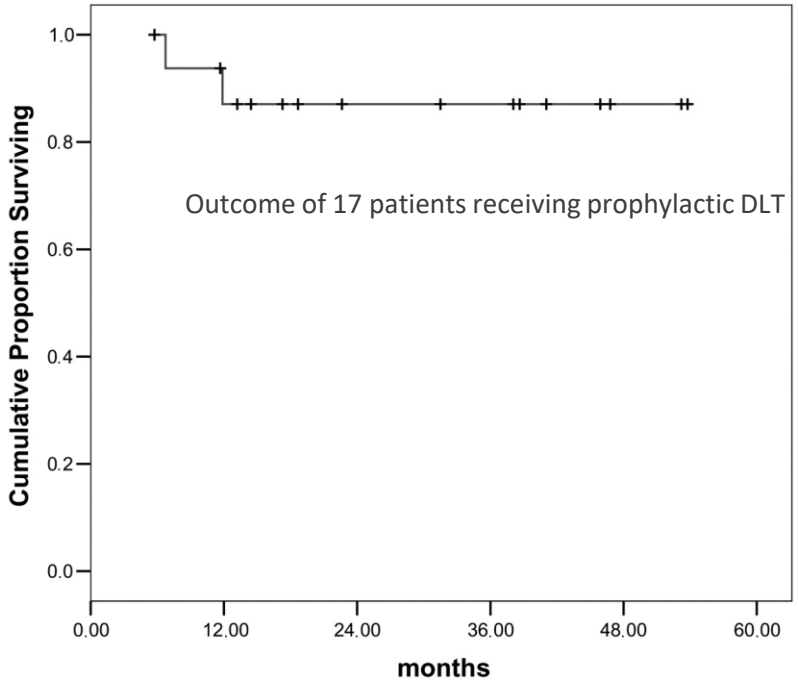
Number of chemotherapy cycles prior to SCT



Influence of acute GvHD



Prophylactic DLT



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High-dose melphalan-based sequential conditioning chemotherapy followed by allogeneic haematopoietic stem cell transplantation in adult patients with relapsed or refractory acute myeloid leukaemia

AML, n = 292, primär refraktär = 144, secondary refractory = 97 patients, relapsed AML = 51

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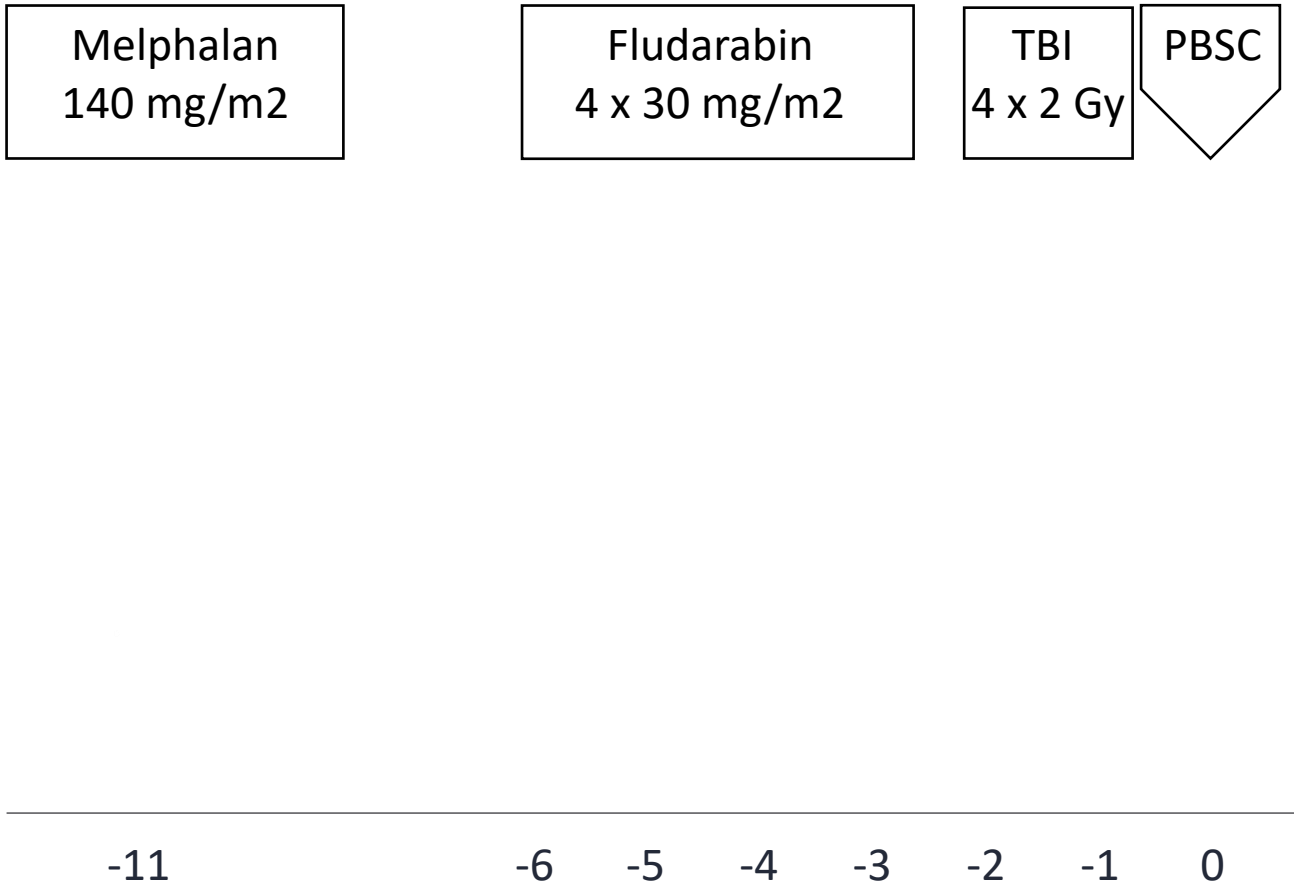

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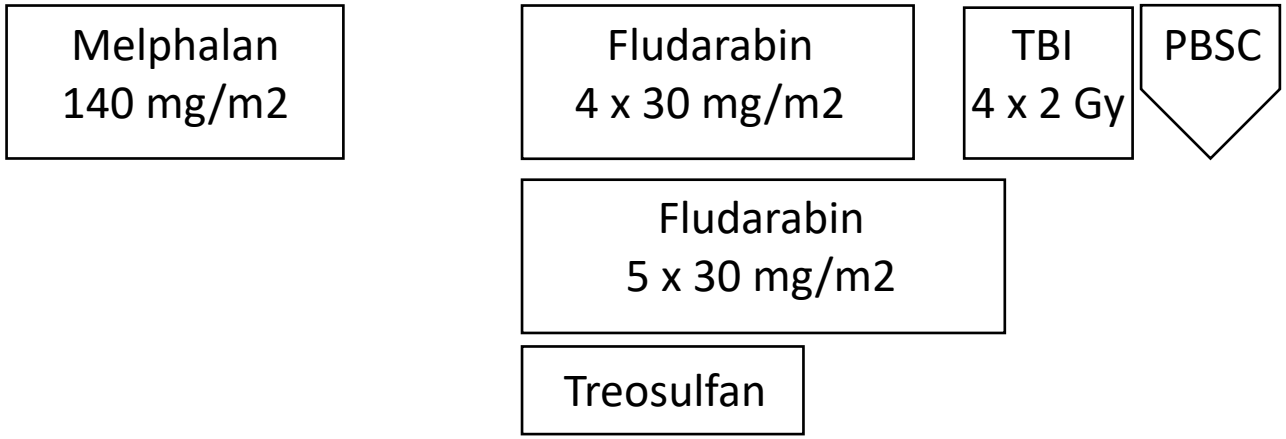

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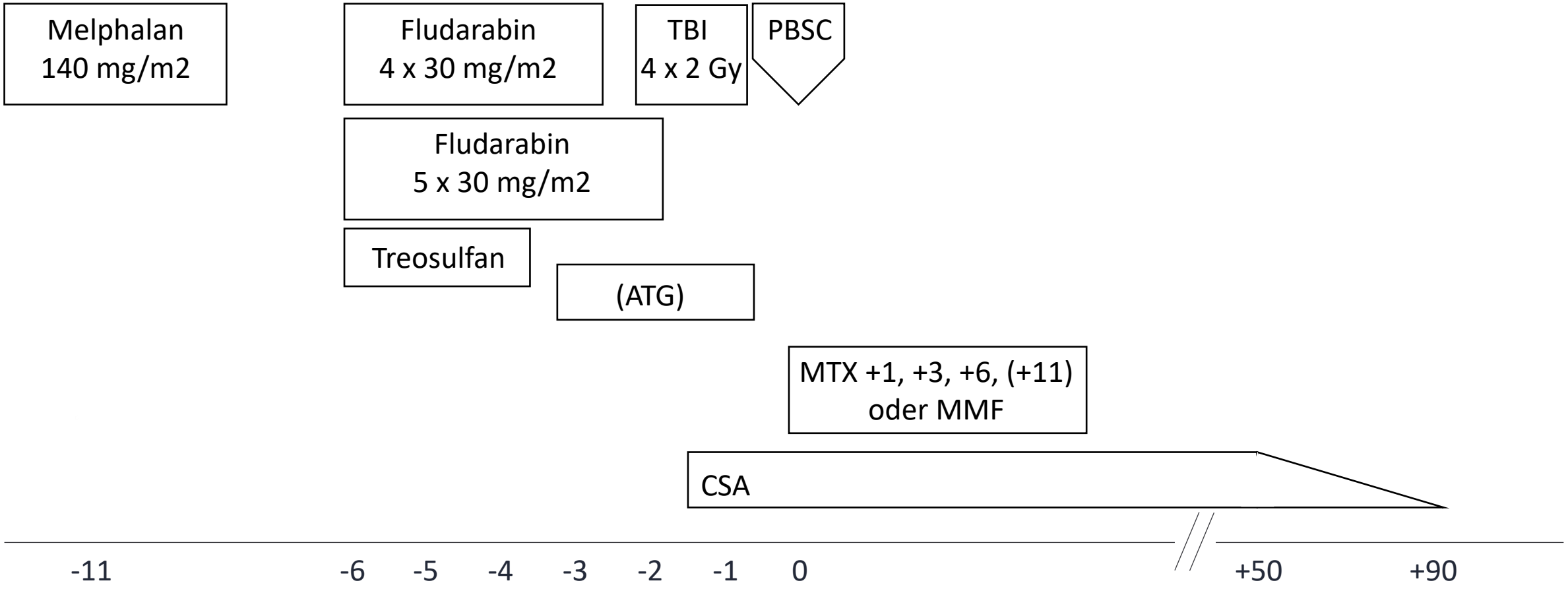

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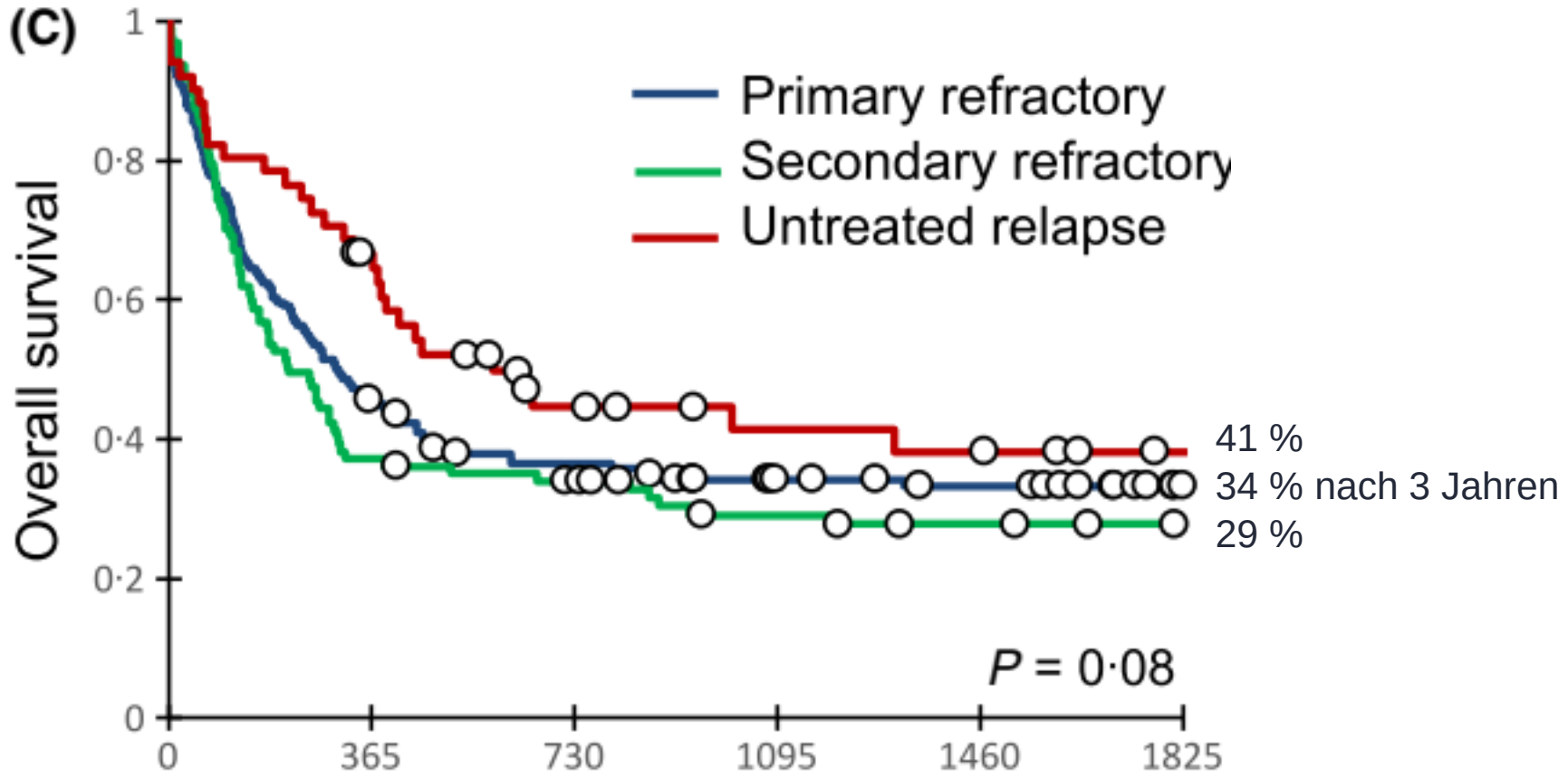

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Evaluation of six different types of sequential conditioning regimens for allogeneic stem cell transplantation in relapsed/refractory acute myelogenous leukemia – a study of the Acute Leukemia Working Party of the EBMT

Table 1. Sequential regimens groups.

Regimen group	TCI score	Regimens	*N* (%)	*N* total (2132)	Number of centers
FLAMSA-TBI4	3–3.5	FLAMSA-TBI4Gy-Cy	751 (96.04)	783	80
		FLAMSA-TBI4Gy	31 (3.96)		
FLAMSA-Chemo	3–3.5	FLAMSA-Mel	89 (12.23)	728	78
		FLAMSA-Treo-Cy	64 (8.79)		
		FLAMSA-Bu-Flu	234 (32.14)		
		FLAMSA-Bu-Cy	341 (46.84)		
Mel-Flu-TBI8	4.5	Mel-Flu-TBI8Gy	253 (100)	253	15
Mel-Treo-Flu	5.5	Mel-Treo-Flu	153 (100)	153	16
Thio-ETO-Cy-Bu2-Flu	4	Thio-ETO-Cy-Bu2-Flu	65 (100)	65	27
Clo-ARAC-(Bu2/TBI4)-Cy	3.5	Clo-ARAC-TBI4Gy-Cy	31 (20.67)	150	15
		Clo-ARAC-Bu2-Cy	119 (79.33)		

TCI: transplant conditioning intensity score of the prototype of the regimen group [26]; FLAMSA: fludarabine/cytarabine/amsacrine; TBI: total body irradiation; Gy: gray; Cy: cyclophosphamide; Flu: fludarabine; ETO: etoposide; Clo: clofarabine; Mel: melphalan; Treo: treosulfan; Thio: thiotepa; ARAC: cytarabine.

 Heinicke T et al. DOI: 10.1080/10428194.2020.1827248

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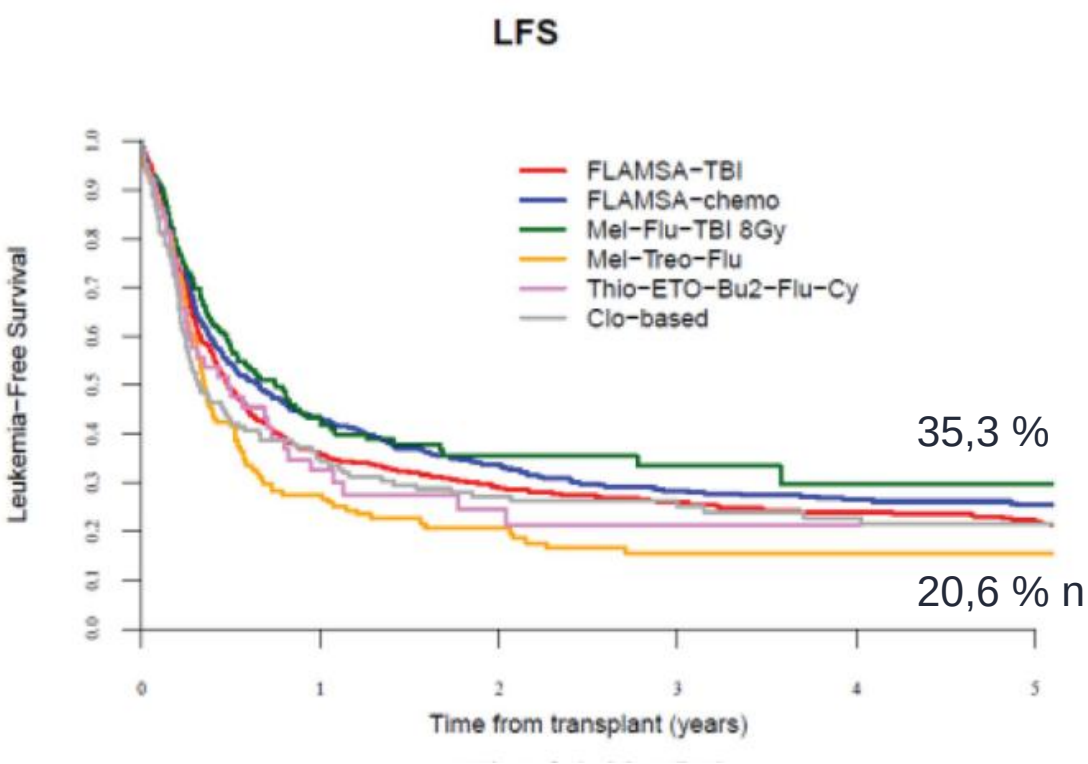

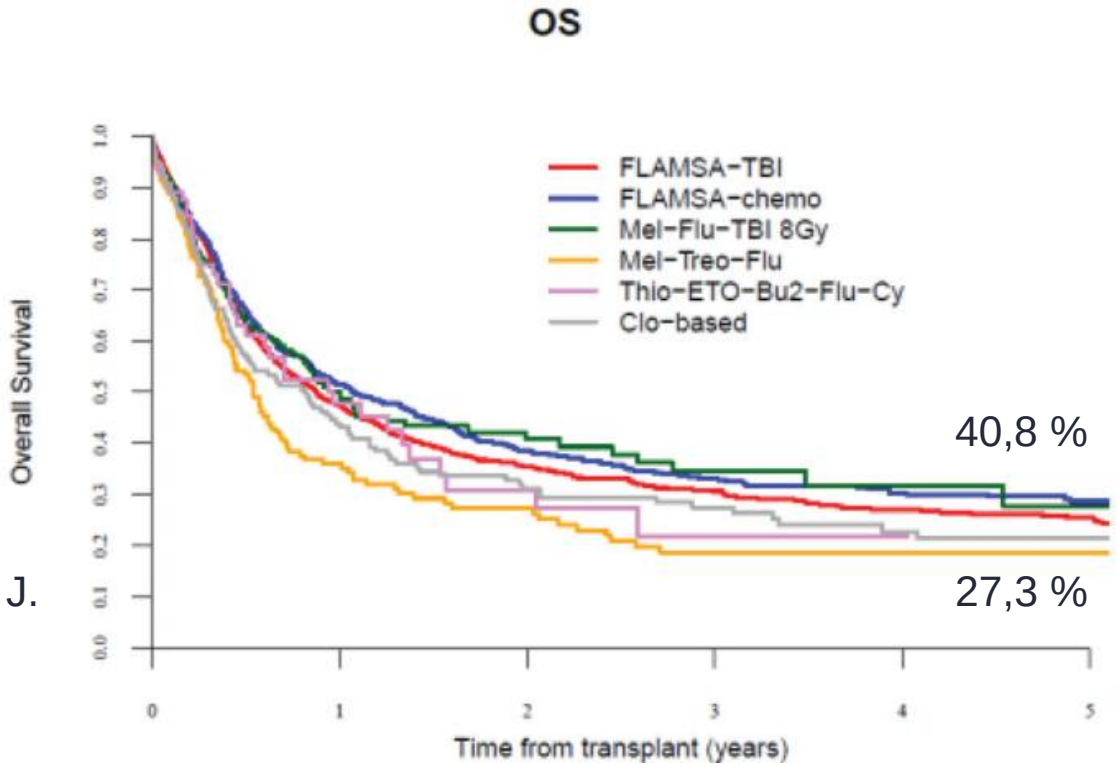

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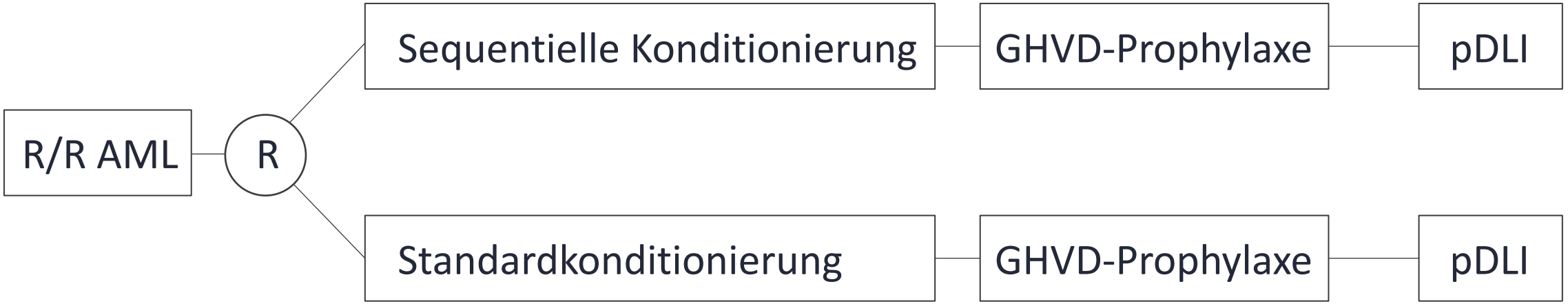
Prospektive kontrollierte Studien?

Studiendesign



Prospektive kontrollierte Studien?

FLAMSA-Based Reduced-Intensity Conditioning versus Myeloablative Conditioning in Younger Patients with Relapsed/Refractory Acute Myeloid Leukemia with Active Disease at the Time of Allogeneic Stem Cell Transplantation: An Analysis from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation

R/R AML, n = 1018, 18 – 50 J., 258 BuCy, 314 CyTBI, 318 FLAMSA-TBI, 128 FLAMSA-CT

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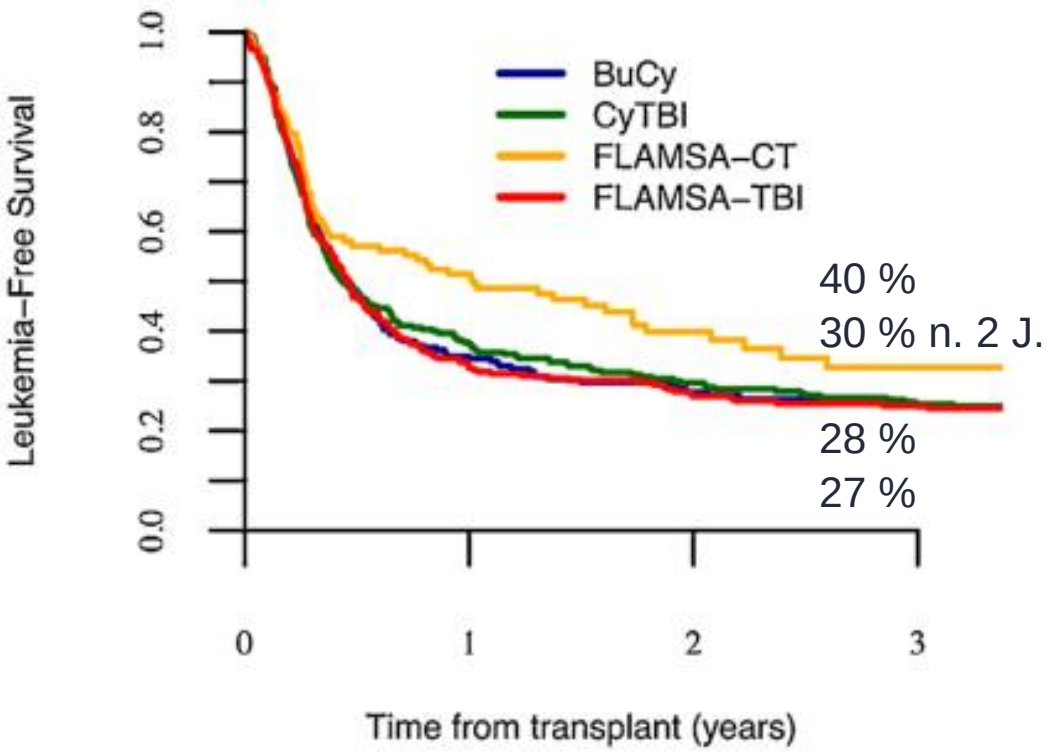

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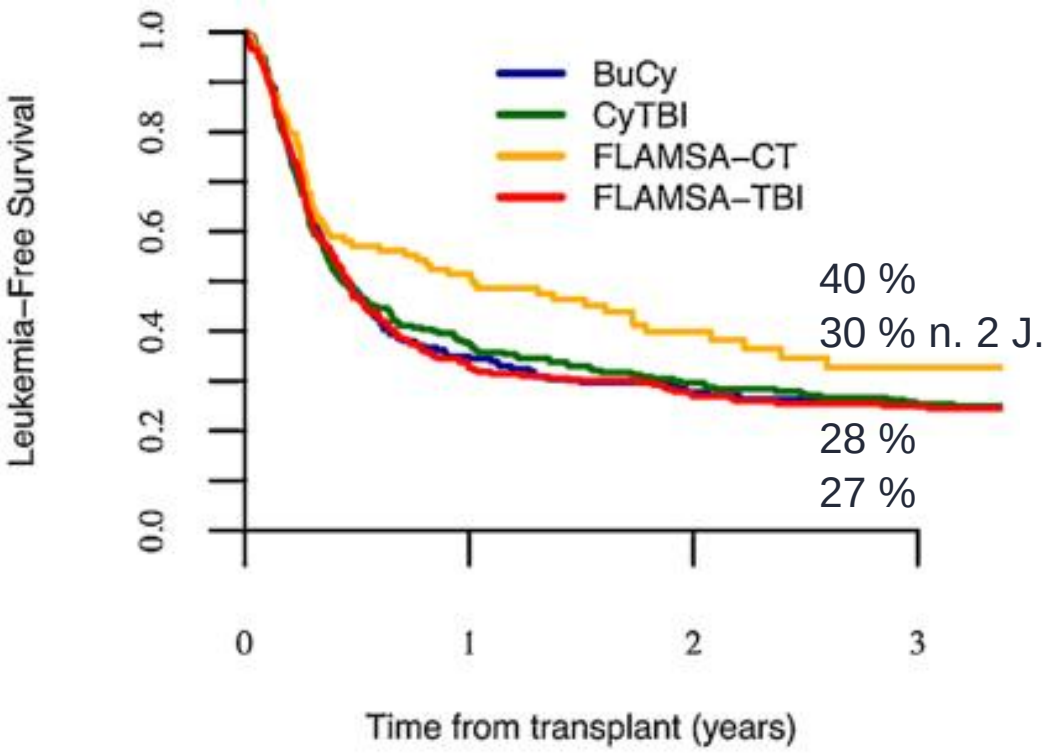

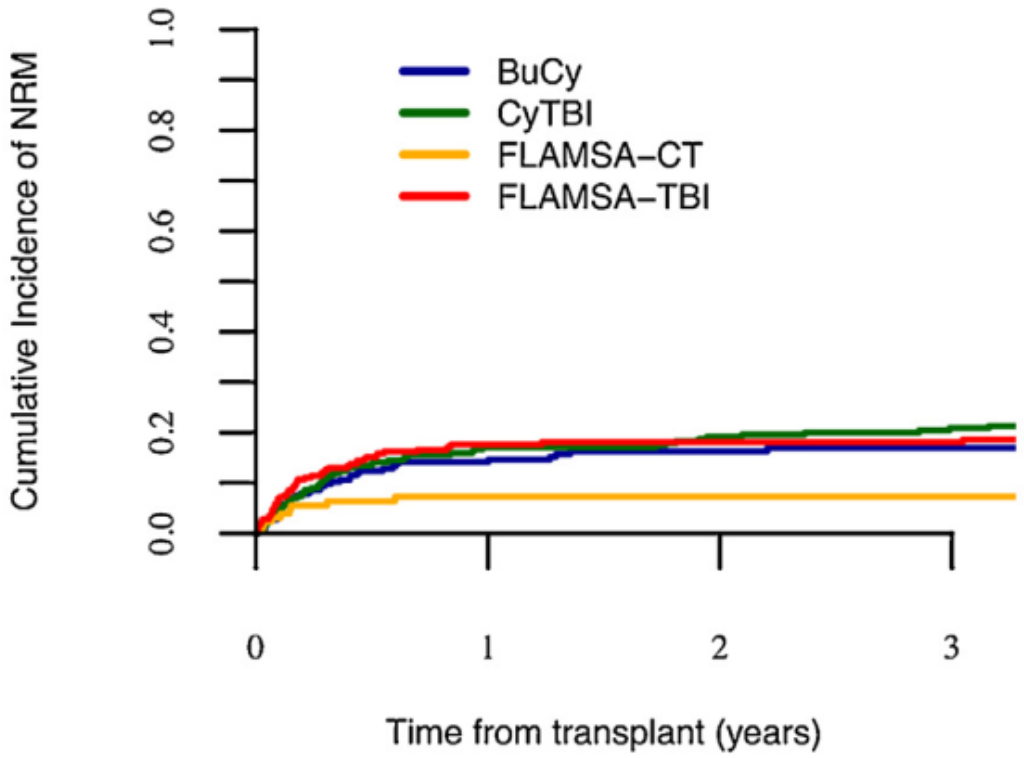

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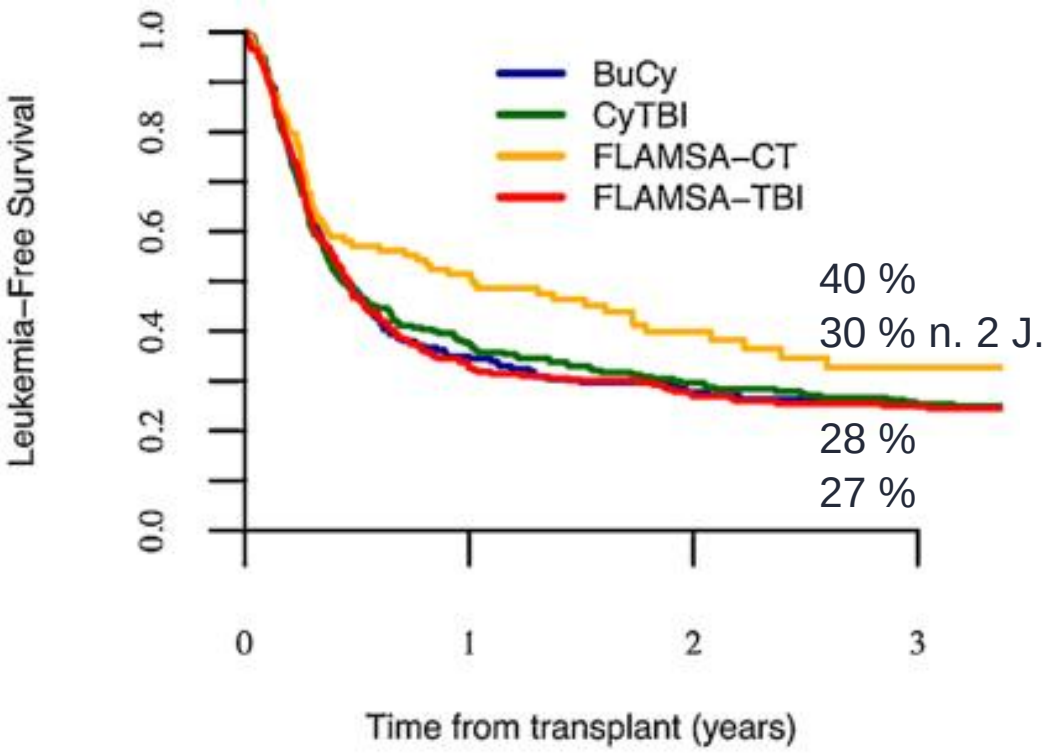

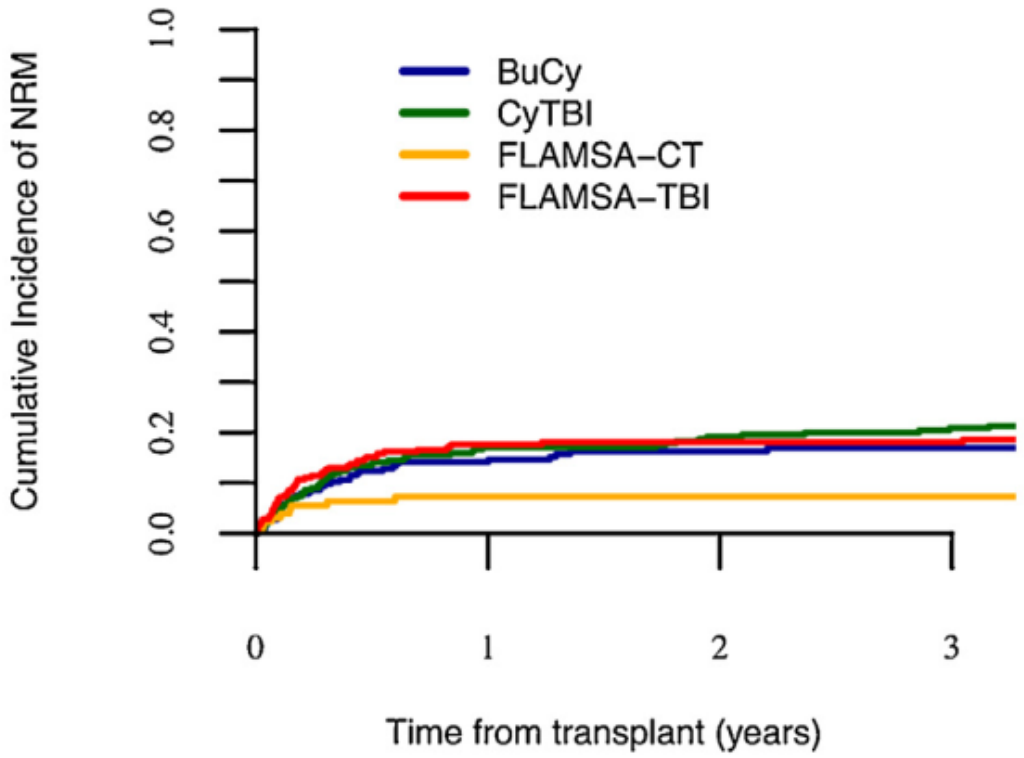

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R/R AML, n = 856, 18 – 50 J., FLAMSA versus RIC

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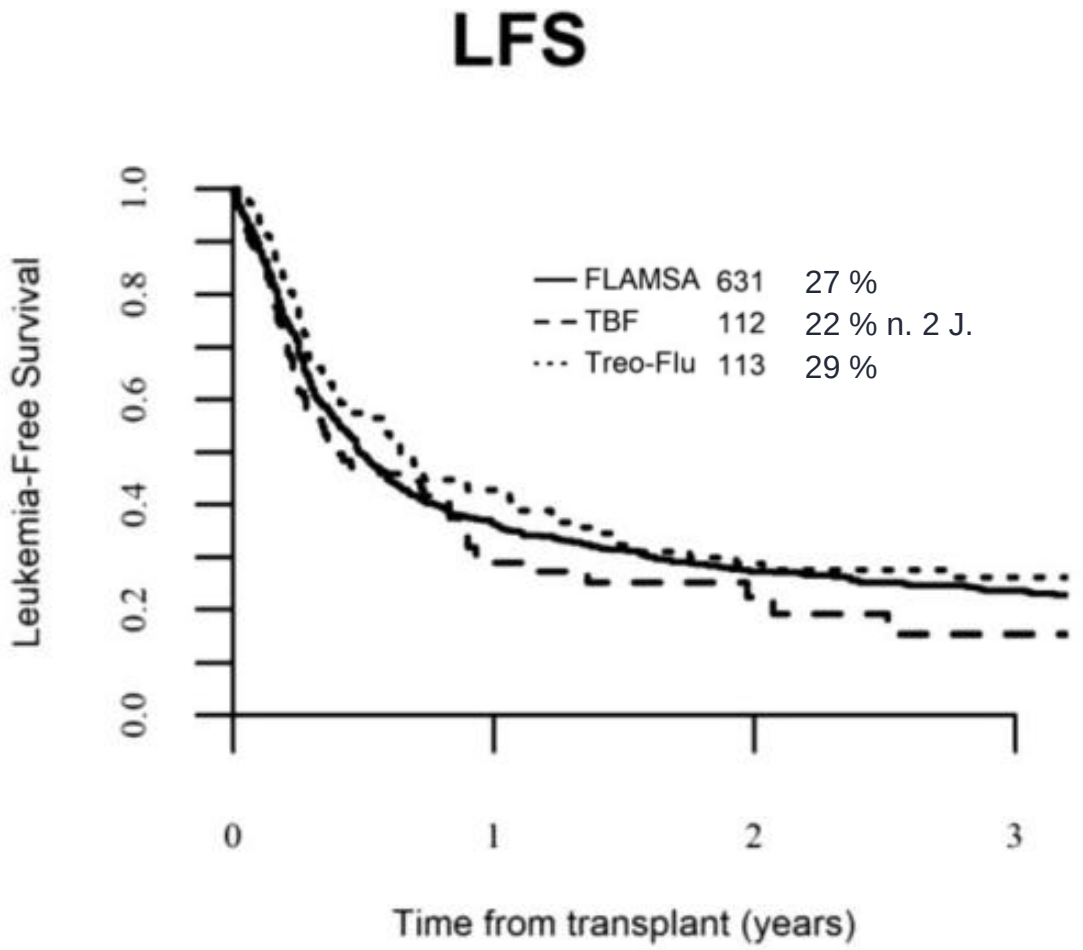

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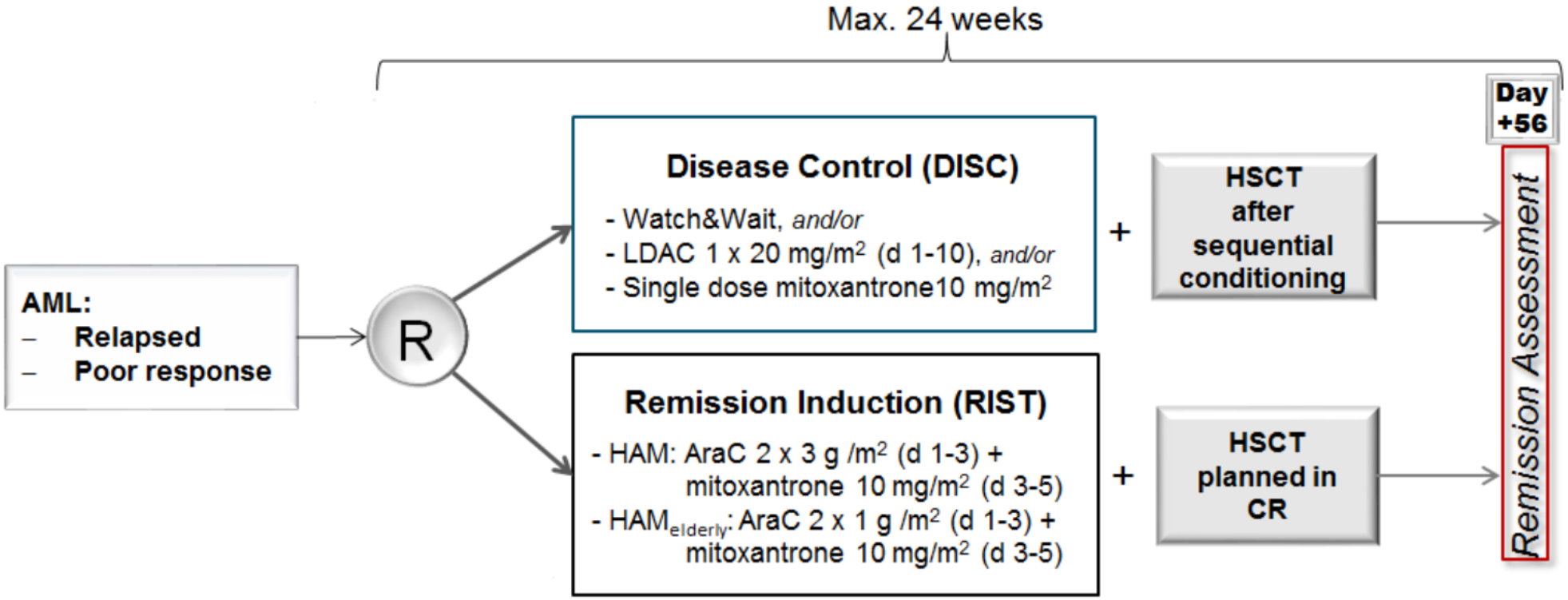
Remission induction versus immediate allogeneic haematopoietic stem cell transplantation for patients with relapsed or poor responsive acute myeloid leukaemia (ASAP): a randomised, open-label, phase 3, non-inferiority trial



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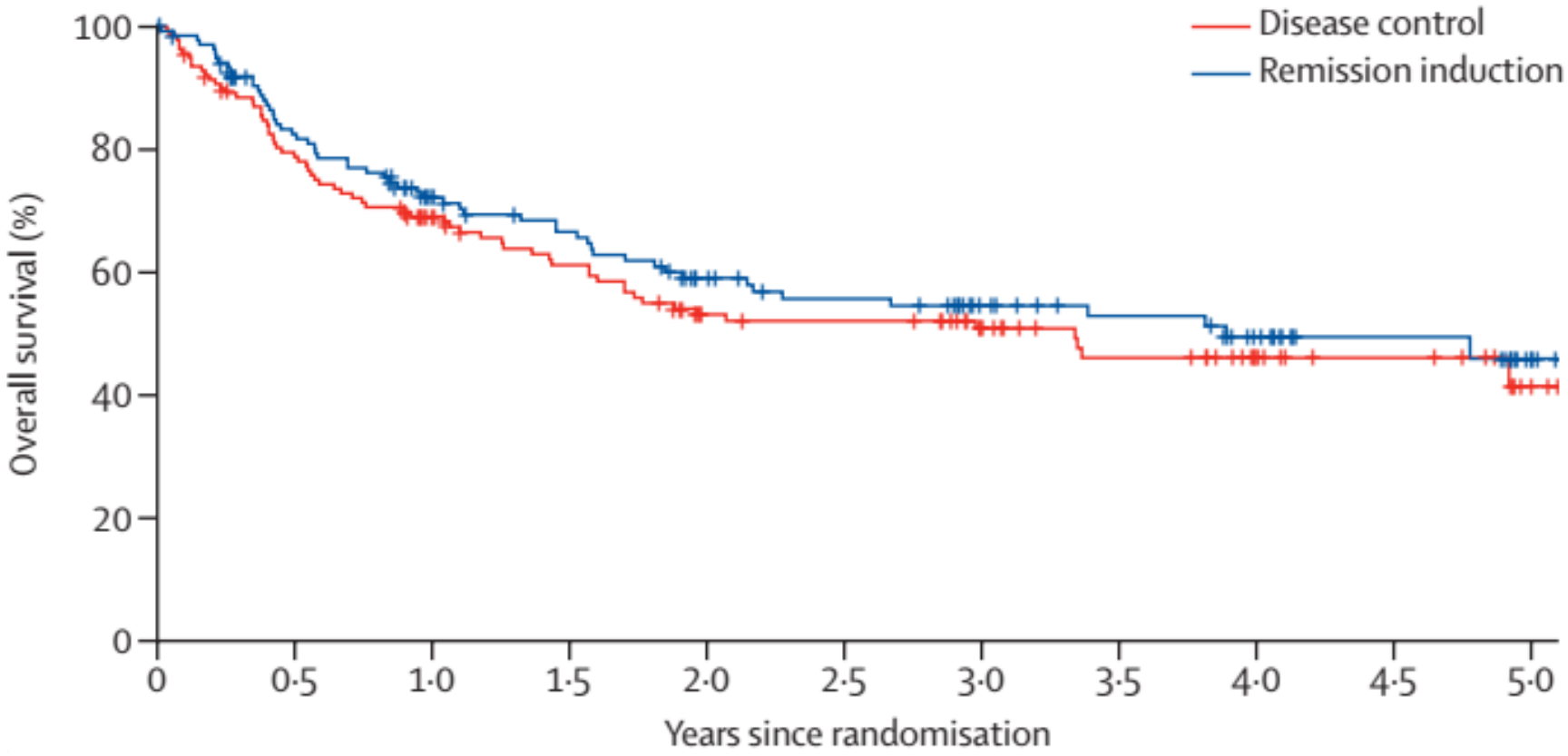

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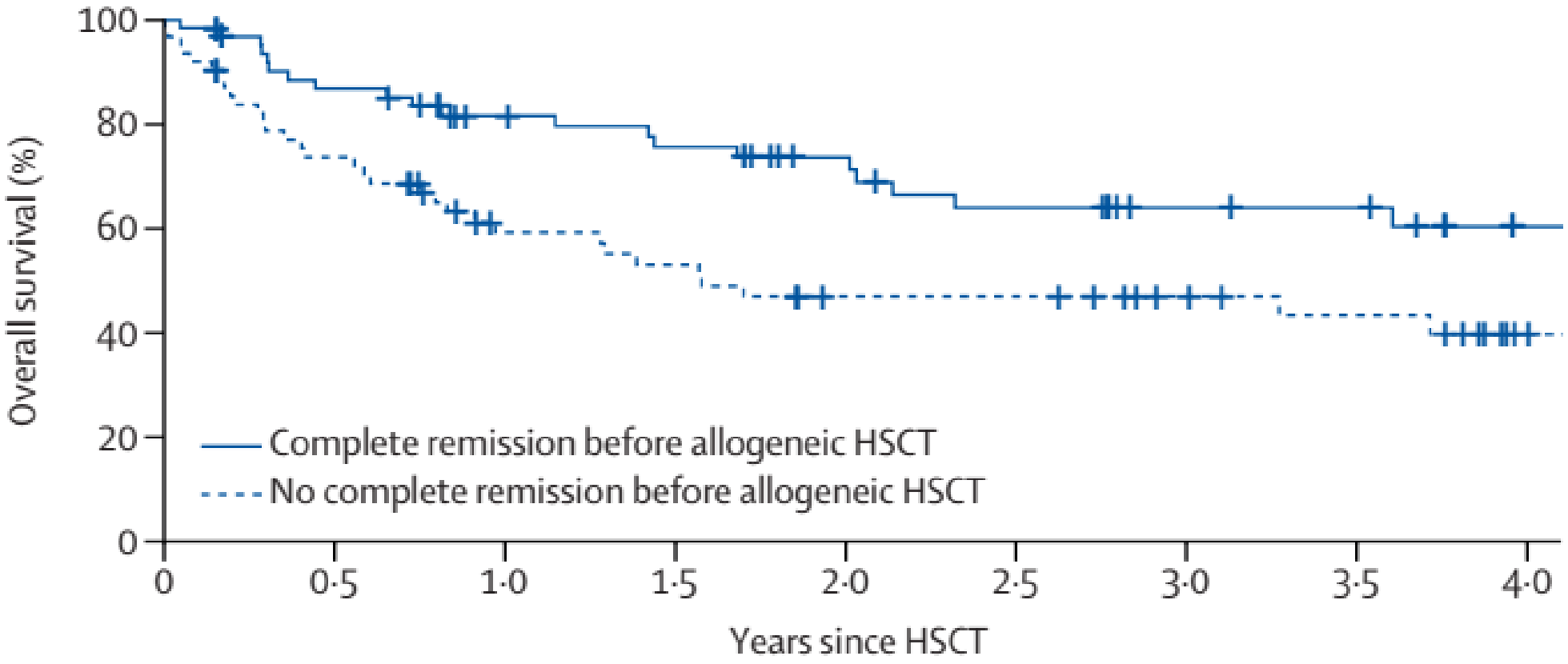

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Variablen mit Einfluss auf den Erfolg

Variablen mit Einfluss auf den Erfolg

Konditionierung

Sequentiell
Myeloablativ
Reduzierte Intensität
Minimal

Variablen mit Einfluss auf den Erfolg

Konditionierung	**Transplantat**
Sequentiell	MRD
Myeloablativ	MUD
Reduzierte Intensität	Haploid.
Minimal	Non-HLA

Variablen mit Einfluss auf den Erfolg

Konditionierung	**Transplantat**	**GVHD-Prophylaxe**
Sequentiell	MRD	ATG
Myeloablativ	MUD	PTCy
Reduzierte Intensität	Haploid.	…
Minimal	Non-HLA	

Variablen mit Einfluss auf den Erfolg

Konditionierung	**Transplantat**	**GVHD-Prophylaxe**	**Erhaltung**
Sequentiell	MRD	ATG	DLI
Myeloablativ	MUD	PTCy	TKI
Reduzierte Intensität	Haploid.	…	AZA
Minimal	Non-HLA		VEN
			IDH 1/2

Variablen mit Einfluss auf den Erfolg

Konditionierung	Transplantat	GVHD-Prophylaxe	Erhaltung	Ergebnis
Sequentiell	MRD	ATG	DLI	OS
Myeloablativ	MUD	PTCy	TKI	DFS
Reduzierte Intensität	Haploid.	…	AZA	Rezidiv
Minimal	Non-HLA		VEN	NRM
			IDH 1/2	GVHD
				GRFS

Variablen mit Einfluss auf den Erfolg

Diagnose	Patient	Konditionierung	Transplantat	GVHD-Prophylaxe	Erhaltung	Ergebnis
R/R AML	HCT-CI	Sequentiell	MRD	ATG	DLI	OS
HR-MDS	…	Myeloablativ	MUD	PTCy	TKI	DFS
		Reduzierte Intensität	Haploid.	…	AZA	Rezidiv
		Minimal	Non-HLA		VEN	NRM
					IDH 1/2	GVHD
						GRFS

Fazit

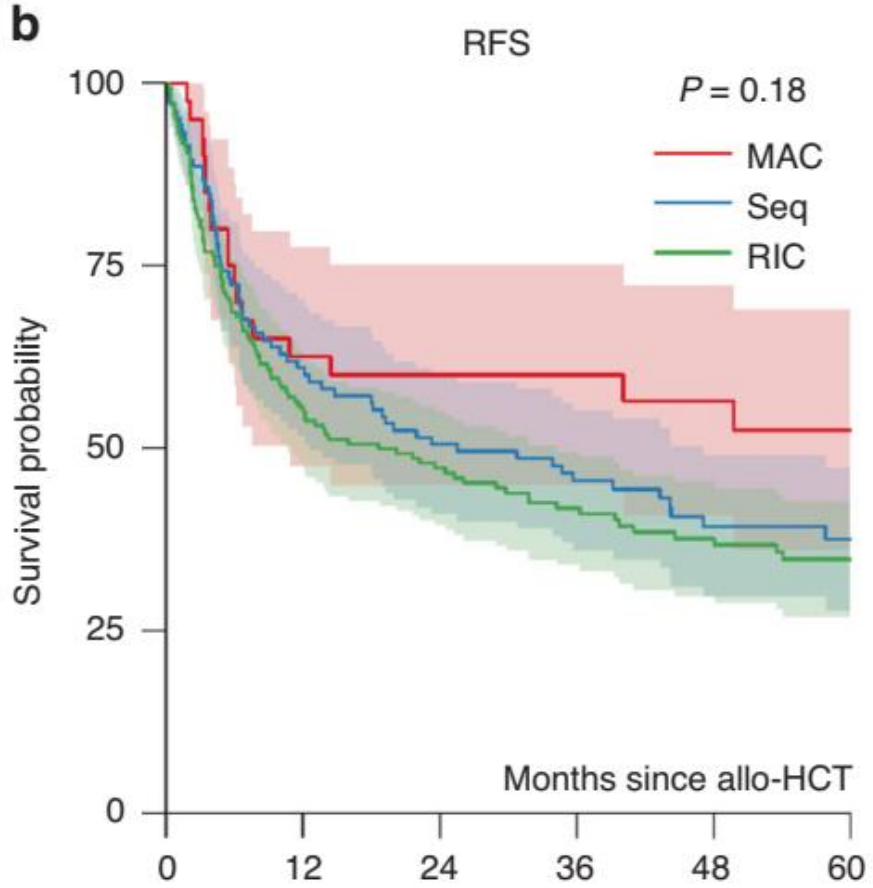
- Überlegenheit von SqC nicht bewiesen
- Dennoch etablierte Praxis bei R/R AML
- Toxizität akzeptabel
- Aplasie verlängert
- Krankheitscharakteristik bleibt ausschlaggebend
- Schnelle Reduktion der Immunsuppression ± pDLI evtl. relevanter als Konditionierung
- Allo HCT eher früher als später im Krankheitsverlauf
- Keine Empfehlung zur SqC bei MDS
- Ergebnisse bei R/R AML unbefriedigend, Verbesserungen notwendig

Vielen Dank für Ihre Aufmerksamkeit

Universitätsklinikum Tübingen

Sequential vs myeloablative vs reduced intensity conditioning for patients with **myelodysplastic syndromes with an excess of blasts** at time of allogeneic haematopoietic cell transplantation: a retrospective study by the chronic malignancies working party of the EBMT

MDS <20 % Blasten, n = 303, 20 % EB 1, 47 % EB2, 33 % AML, 158 RIC, 105 Seq, 40 MAC



 Potter V et al. Bone Marrow Transplantation (2024) 59:224–231

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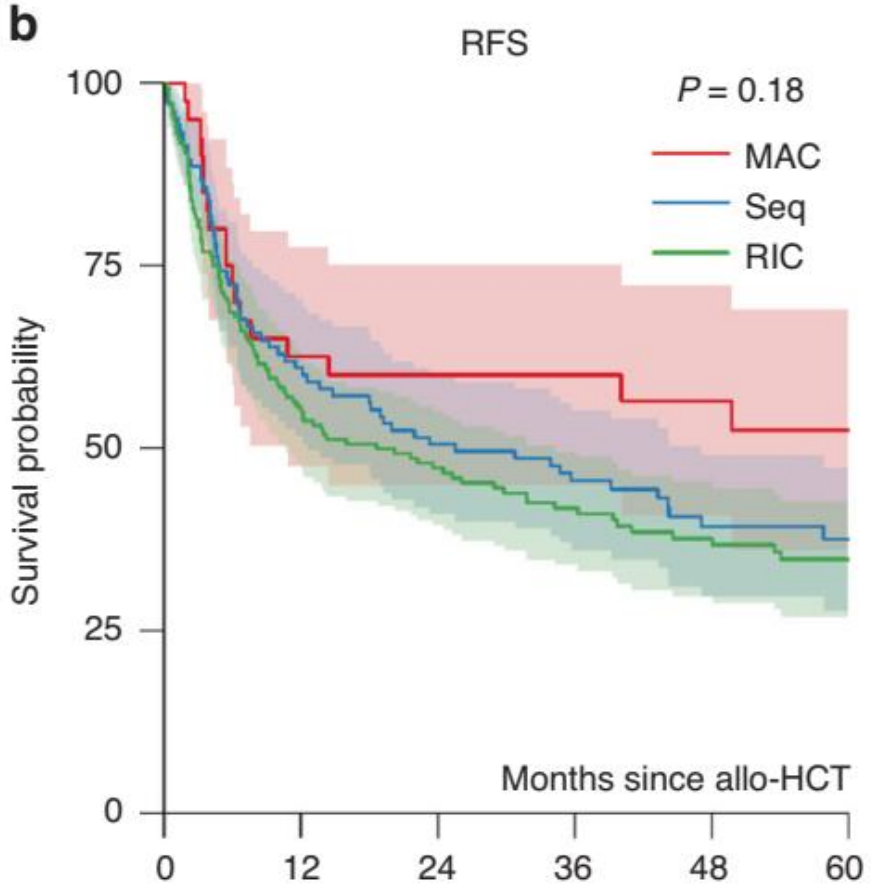

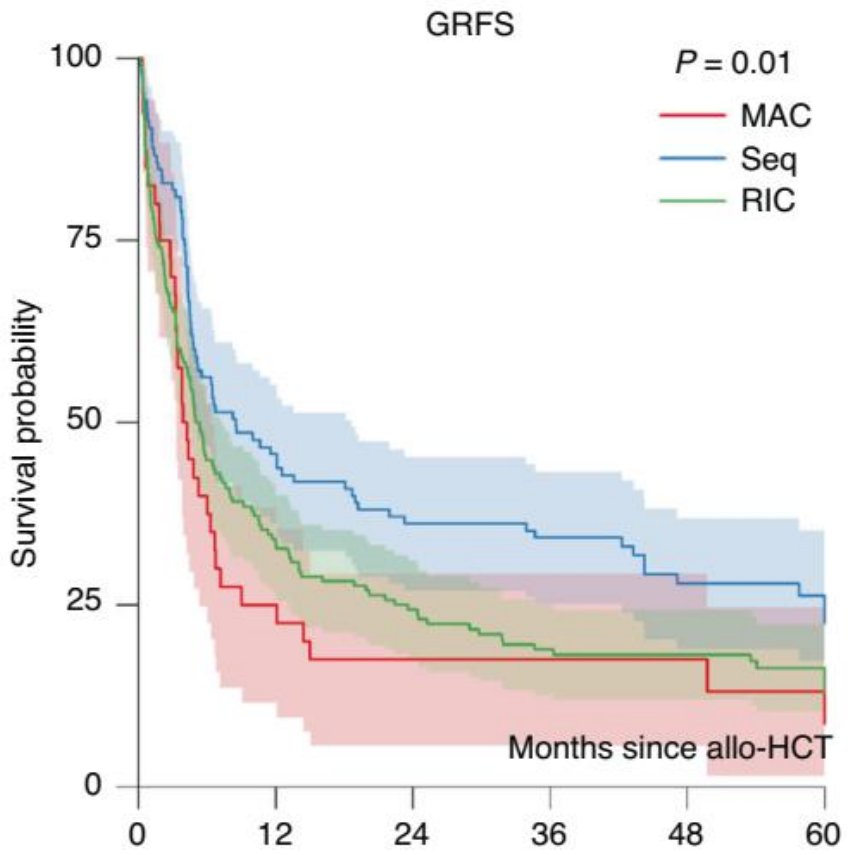

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Multivariate analysis	RFS	
	HR (95% CI)	*p*-value
Conditioning regimen		
RIC	1.00	(0.28[a])
MAC	0.65 (0.38–1.10)	0.11
Seq	0.92 (0.66–1.28)	0.63
Age at allo-HCT (per 10 years older)	1.01 (0.86–1.19)	0.93
Karnofsky score at allo-HCT		
≥90	1.00	
<90	1.54 (1.12–2.11)	0.008
IPSS-R cytogenetic score		
Intermediate/good/very good	1.00	
Poor/very poor	1.96 (1.42–2.71)	<0.0001
Donor type		
HLA-Identical sibling	1.00	
Matched (8/8) unrelated	0.69 (0.51–0.95)	0.02
Interval diagnosis - allo-HCT (per year longer)	1.10 (1.01–1.20)	0.02
BM blast % at allo-HCT		
<20%	1.00	
≥20%	1.39 (0.99–1.95)	0.06

 Potter V et al. Bone Marrow Transplantation (2024) 59:224–231