City of Hope

International Society for Cutaneous Lymphomas ISCL

5TH World Congress of Cutaneous Lymphomas

Enhancing the Ability to Diagnose, Interpret and Apply Best Treatment Options for Cutaneous Lymphomas

Therapeutics/Preclinical Studies| #128

Allogenic stem cell transplant for mycosis fungoides and Sezary syndrome: A systematic review and meta-analysis

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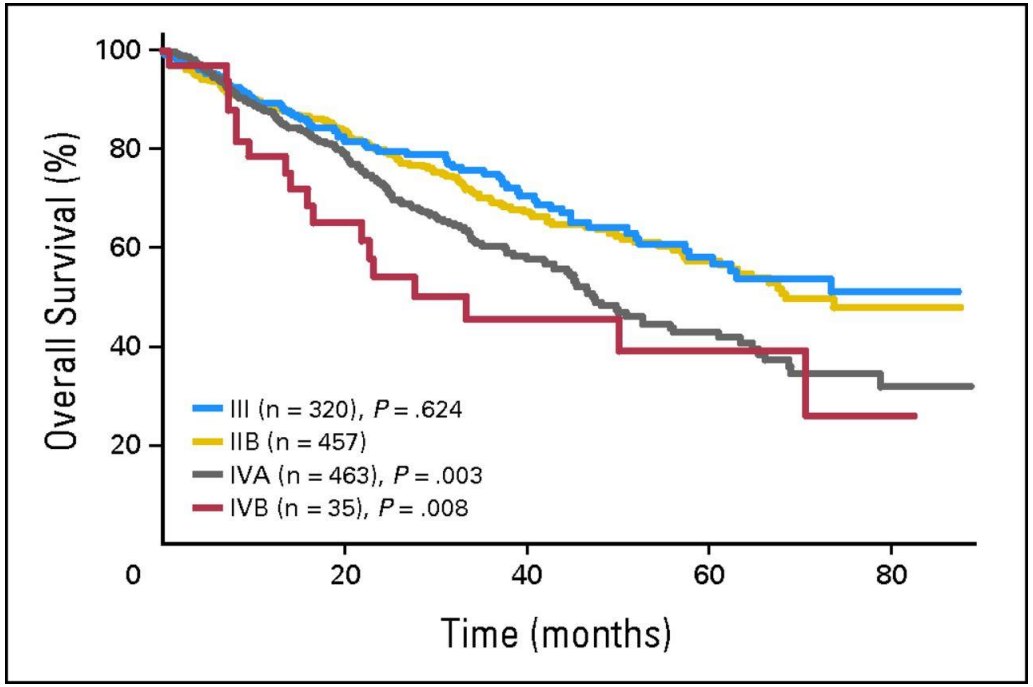
This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Advanced MF/SS is incurable with existing therapies and represents an unmet medical need



Kaplan-Meier plot showing survival by stage (N=1275).

- ProCLIPI was a prospective study of 1,275 patients with advanced MF/SS from 29 international sites

- OS was 63 months, 5-year OS 52%,
  - Median OS IIB 68 mo (5.6 years)
  - Median OS IVA 48 mo (4 years)
  - Median OS IVB 33 mo (2.8 years)

Julia J. Scarisbrick et al. JCO doi:10.1200/JCO.2015.61.7142

We conducted a meta- analysis to determine outcomes after alloBMT for MF/SS

MANUSCRIPT CHARACTERISTICS	Manuscripts N=15
Study type	
Retrospective cohort	12
Prospective cohort	1
Prospective, propensity matched	1
RCT	1
Center vs. Registry	
Single-center	9
Multi-center	2
Registry	4
Diagnosis	
MF vs SS	12
MF/SS or CTCL	3

Author	Institution	Data source	Study type	Number of patients
Duarte et al., 2010	EBMT (Europe)	Registry	Retrospective	60
Duvic et al., 2010	MD Anderson (US)	Single-center	Retrospective	19
Zain et al, 2011	City of Hope (US)	Single-center	Retrospective	13
Delioukina et al., 2012	City of Hope (US)	Single-center	Retrospective	11
Lechowicz et al., 2014	CIBMTR (US)	Registry	Retrospective	129
Hosing et al., 2015	MD Anderson (US)	Single-center	Prospective	47
Mori et al, 2019	Japan Society for HSCT	Registry	Retrospective	48
Isufi et al, 2020	Yale (US)	Single-center	Retrospective	16
Weng et al, 2020	Stanford (US)	Single-center	Prospective, Phase II clinical trial	35
Domingo-Domenech et al., 2020	EBMT (Europe)	Registry	Retrospective	53
Elliott et al., 2021	Peter MacCallum Cancer Center (Australia)	Multi-center	Retrospective	26
Stamouli et al, 2021.	National and Kapodistrian University of Athens (Greece)	Single-center	Retrospective	10
Angelov et al, 2022	St. James Hospital (Ireland)	Single-center	Retrospective	15
Cengiz et al, 2022.	Ankara University School of Medicine (Turkey)	Single-center	Retrospective	20
De Masson et al, 2023	CUTALLO Group (France)	Multi-center	Prospective	55

Patients and outcomes

PATIENT CHARACTERISTICS	
	N=557
Diagnosis	
MF	254
SS	150
MF/SS	153
Gender	
Male	321
Female	225
Follow-up (median, range)	32 months (10.5-86.4 months)
Time from diagnosis to transplant (median, range)	28.8 months (12-47.3 months)

Survival		
		% (95% CI)
OS	1 year	51% (39-64)
	3+ year	40% (32-49)
PFS	1 year	42% (31-53)
	3+ year	33% (25-42)

Meta-analysis: relapse

Relapse	
	% (95% CI)
Non-relapse mortality	18% (13-23)
Incidence of relapse	47% (40-53)
Time to relapse	7.9 months (range 1.6-24 months)

Cause of death	N=213	% deaths
Progression/relapse	106	52.2%
GVHD	23	11.3%
Infection	45	22.1%
Organ failure	19	9.4%
Second malignancy	6	2.9%
Unspecified	14	6.9%

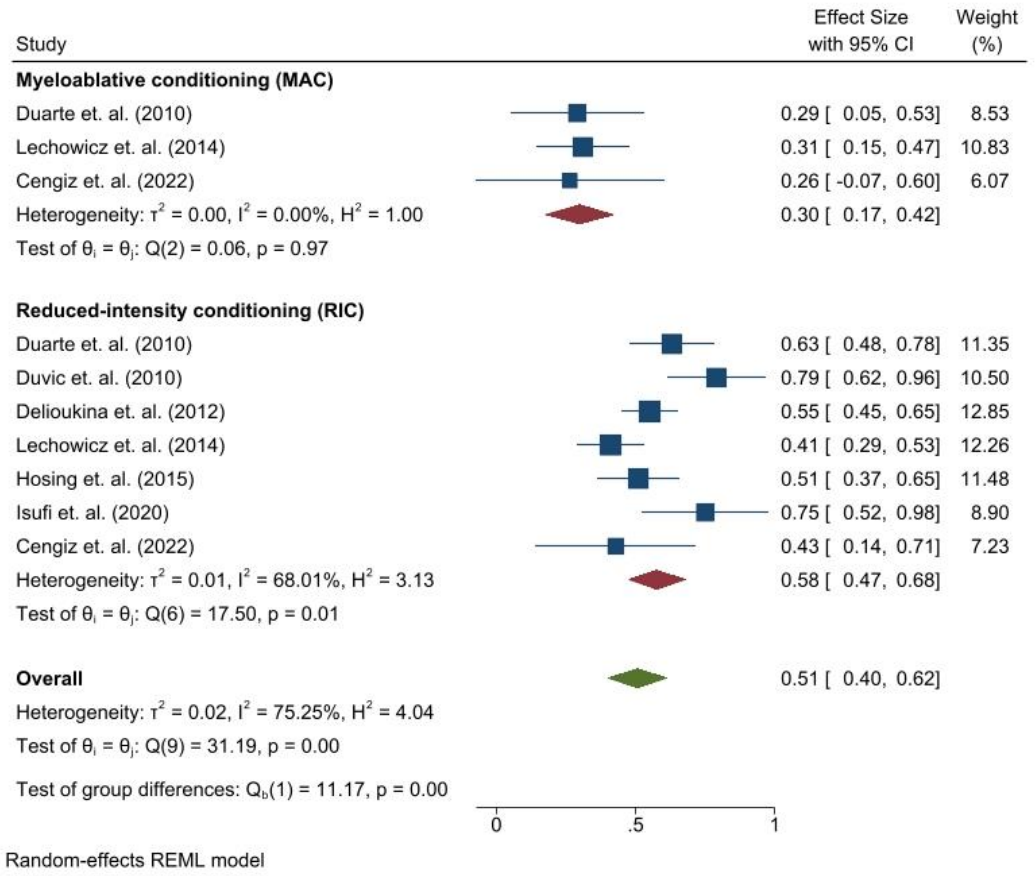
Weng et al.
-Majority of relapses involved the skin
-Majority of patients with residual disease after transplant had isolated cutaneous disease

Relapse common, but approximately half of patients had durable remissions

Meta-analysis- conditioning and GVHD

CONDITIONING			
		% (95% CI)	
Conditioning regimen (cumulative OS)	RIC	58% (47-68)	P<0.001
	MAC	30% (17-24)	

GVHD		
		% (95% CI)
aGVHD	All	44% (33-55)
	Grade III-IV	14% (8-20)
cGVHD	All	40% (33-48)
	Extensive	17% (10-24)



RIC for MF/SS shows with better OS than MAC, and generally associated with lower morbidity/mortality

Meta-analysis: DLI for relapse

DONOR LYMPHOCYTE INFUSION		
		% (95% CI)
Donor lymphocyte infusion for relapse (n=51)	CR	24/51 (47%)
	PR	7/51 (14%)
	PD	16/51 (31%)

DLI may be an effective treatment option for MF/SS patients with relapse or residual disease after allo-HSCT

Role of TSEB, TBI, and TLI

- Domingo-Domenech et al. Use of TBI decreased incidence of relapse (HR 0.48, 95% CI 0.24-0.96). There was no difference in NRM, PFS, or OS
- Weng et al. Regimen of TSEBT-TLI-ATG was highly effective in cytoreduction; TSEBT critical for skin-specific debulking
- Isufi et al. Trend to better early post-transplant disease control with TBI/TSEBT
- Duvic et al. Use of 36 Gy in 8 fractions to debulk the skin may reduce severity of post-transplant cutaneous GVHD
- Mori et al. No difference in OS or PFS based on 2-4 Gy vs. 12 Gy

Data suggest that debulking of skin lesions with TSEBT may result in better outcomes and lower rates of cutaneous GVHD.

Impact of disease status at transplant

- Zain et al: CR/PR has trend to better OS than non-CR/PR (72.9% vs 43.2%, p=0.07)
- Mori et al: CR/PR has better OS than non-CR/PR (55.0% vs 20.1%, p<0.05)
- Isufi et al: no difference in OS for CR vs. PR on multivariate analysis (p=0.884)

Better disease control at the time of transplant may be associated with improved outcomes

Response : MF vs Sezary

- Elliott et al: SS had a higher OS than MF (100% vs 52.4%, p=0.04), higher 5-yr TFS (88.9% vs 15.6%, p=0.005), and longer TTNT (not reached vs. 24.0 months, p=0.02)
- Weng et al: 73% of SS patients achieved CR vs 31% of MF (p<0.05)
- Hosing et al: SS has higher PFS than MF (72% vs 11.5%, p=0.04), but no difference in OS (p=0.33)
- Cengiz et al: No significant difference in PFS for SS vs. MF (p=0.4)

In general, patients with SS had better response to allo-HSCT than those with MF

Conclusions and future directions

- Allo-HSCT results in durable remission for some patients with MF/SS
- Relapse after allo-HSCT for MF/SS is common; DLI may be effective for relapse
- Rates of aGVHD and cGVHD are similar to other malignancies
- Disease burden at time of transplant may impact outcome, and TBI/TSEBT may be important for debulking of skin compartment

Graft-versus-lymphoma (GVL) critical to success of allo-HSCT

- High efficacy of DLI in relapse
- GVL may be more effective in clearing extracutaneous disease
- Better efficacy of allo HSCT for SS than MF
- Some evidence that MF relapse/residual disease most commonly in skin

Future questions

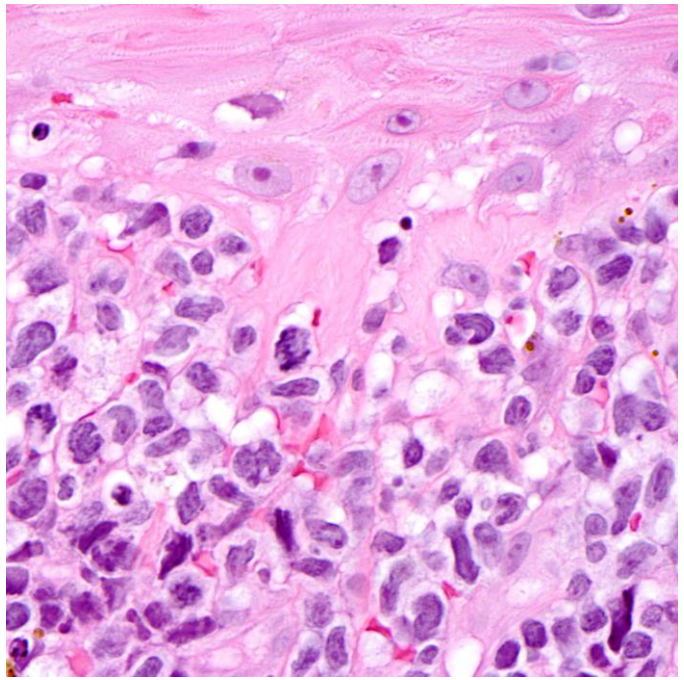


Image: Histology of MF with LCT

- Assess outcomes of allo-HSCT for MF/SS in the context of recent improvements in regimens, donor availability, and supportive care

- Define parameters for optimization of allo-HSCT for MF/SS
  - Conditioning regimen (MAC vs. RIC ± TBI)
  - Post-transplant cyclophosphamide for GVHD prophylaxis
  - Time from diagnosis to transplant
  - Disease control at time of transplant
  - DLI for relapse or minimal residual disease

Clinical Practice Recommendations for Allogeneic Stem Cell Transplant for Mycosis Fungoides and Sezary Syndrome: Delphi-Based Consensus Guidelines from the NCCN, ASTCT, and USCLC

Thank you!

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MANUSCRIPT SELECTION CRITERIA

2993 references

- Search of Pubmed, EMBASE, and Cochrane
- Manual search of reference lists
- Deletion of duplicates

118 references

- Inclusion: MF/SS, English-language, peer-reviewed, 10 or more patients
- Exclusion: Analysis including other CTCL histologies, abstract-only

14 references

- 14 manuscripts included in meta-analysis