Relapse–Mortality Trade-off Between Autologous and Allogeneic Stem Cell Transplantation in Relapsed Follicular Lymphoma and Marginal Zone Lymphoma: A Registry-Based Proportional Meta-Analysis

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Background

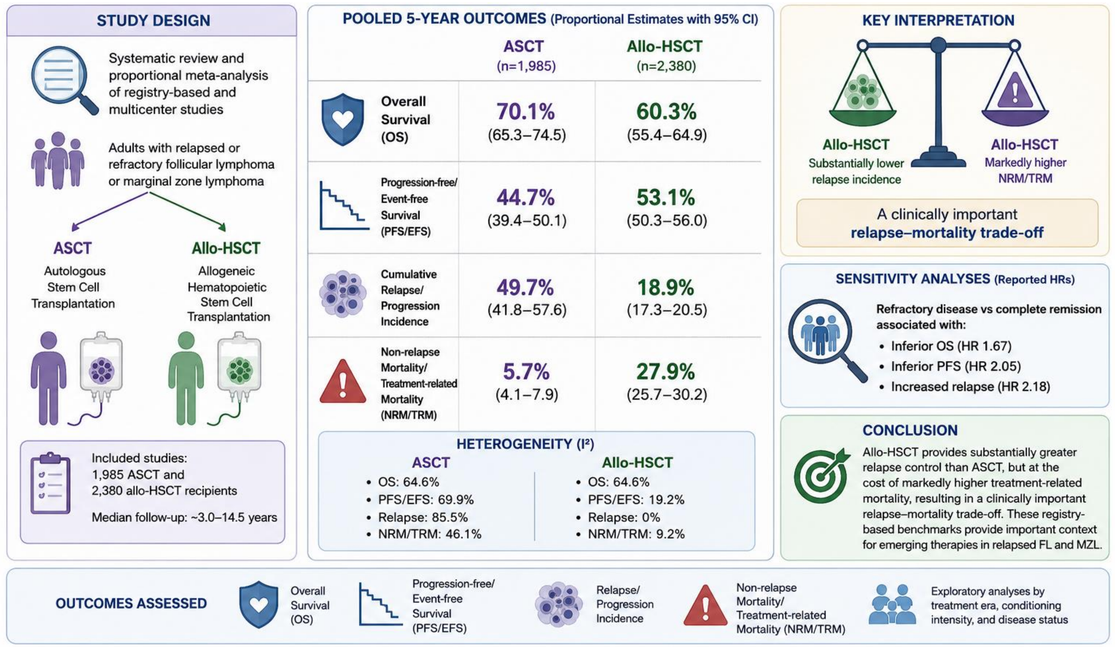
The role of autologous stem cell transplantation (ASCT) and allogeneic hematopoietic stem cell transplantation (allo-HSCT) in relapsed follicular lymphoma (FL) and marginal zone lymphoma (MZL) continues to evolve in the rituximab and targeted therapy era. Pooled contemporary outcome data examining the balance between relapse control and treatment-related mortality across transplant modalities remain limited.

Methods

We performed a systematic review and exploratory proportional meta-analysis of registry-based and multicenter studies evaluating ASCT and allo-HSCT in adults with relapsed FL and MZL, identifying five aggregate transplant cohorts comprising 3,336 patients (1,600 ASCT; 1,736 allo-HSCT recipients) with median follow-up of 3.0–14.5 years.

Primary outcomes were overall survival (OS) and progression-free/event-free survival (PFS/EFS); secondary outcomes were relapse incidence (RI) and non-relapse/treatment-related mortality (NRM/TRM). ASCT and allo-HSCT cohorts were pooled separately using random-effects models given expected clinical and methodological heterogeneity, with subgroup analyses by histology, conditioning intensity, and treatment era.

Figure 1. ASCT vs. allo-HSCT in relapsed FL/MZL: design, pooled outcomes, and interpretation



Results

↓32%
Relative reduction in relapse incidence with allo-HSCT

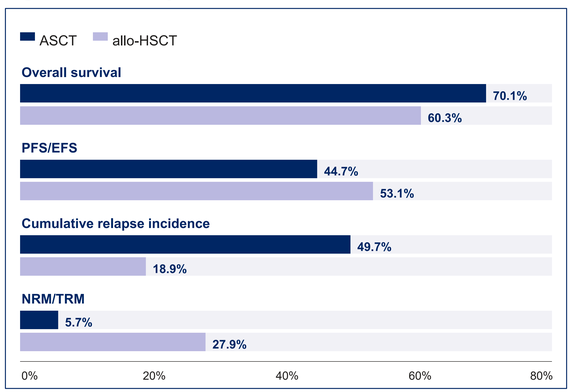
3.6×
Higher non-relapse/treatment-related mortality with allo-HSCT

Five aggregate transplant cohorts comprising 3,336 patients were included. Pooled ASCT outcomes demonstrated OS of 73.6% and NRM/TRM of 5.8%, while allo-HSCT demonstrated OS of 60.3% and NRM/TRM of 20.7%. Allo-HSCT showed lower relapse incidence than ASCT (28.4% vs. 41.6%) but substantially higher NRM/TRM, reflecting a clinically important relapse–mortality trade-off. In sensitivity analyses, refractory disease versus complete remission was associated with inferior OS (HR 1.67), inferior PFS (HR 2.05), and higher relapse incidence (HR 2.18).

Table 1. Included transplant cohorts

Study	Histology	Strategy	N	Follow-up
Jiménez-Ubieto 2017	FL	ASCT	655	12 y
Jiménez-Ubieto 2019	FL (ETF)	ASCT	134	NR
Robinson 2013	FL	ASCT	726	69 mo
Avivi 2018	MZL	ASCT	199	5 y
Klyuchnikov 2015	Grade 1–2 FL	ASCT	164	5 y
Klyuchnikov 2016	Grade 3 FL	ASCT	107	53 mo
Sureda 2018	FL	allo-HSCT	1,567	55 mo
Robinson 2013	FL	allo-HSCT	149	65 mo
Piñana 2010	FL	allo-HSCT	37	52 mo
Robinson 2016	FL post-ASCT relapse	allo-HSCT	183	73 mo
Klyuchnikov 2015	Grade 1–2 FL	allo-HSCT	354	5 y
Klyuchnikov 2016	Grade 3 FL	allo-HSCT	90	53 mo

Figure 2. Pooled 5-year outcomes: ASCT vs. allo-HSCT



Bars show pooled 5-year outcomes by transplant strategy (Table 2). Scale is 0–80%.

Table 2. Pooled outcomes and heterogeneity

5-year outcome	ASCT	allo-HSCT
Overall survival	70.1%	**60.3%**
PFS/EFS	44.7%	**53.1%**
Cumulative relapse incidence	49.7%	**18.9%**
NRM/TRM	5.7%	**27.9%**
Heterogeneity (I²)		
Overall survival	64.6%	64.6%
PFS/EFS	69.9%	19.2%
Relapse incidence	85.5%	0%
NRM/TRM	46.1%	9.2%

Conclusions

ASCT and allo-HSCT provide durable disease control in selected patients with relapsed FL and MZL, although allo-HSCT is associated with substantially greater NRM/TRM despite lower relapse incidence.

The role of transplantation in FL and MZL must increasingly be interpreted within an evolving therapeutic landscape that includes CAR-T therapy, bispecific antibodies, and other targeted immune-based approaches.

References

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