Donor Lymphocyte Infusion After Allogeneic Hematopoietic Cell Transplantation for Indolent and Mantle Cell Lymphomas: A Systematic Review and Meta-Analysis

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Background

Donor lymphocyte infusion (DLI) is used after allogeneic hematopoietic cell transplantation (allo-HCT) to augment graft-versus-lymphoma activity in relapsed or persistent disease. Although indolent non-Hodgkin lymphomas (iNHL) and mantle cell lymphoma (MCL) are considered highly immune-sensitive malignancies, evidence supporting DLI in this setting remains limited to retrospective cohorts and registry analyses.

We performed a systematic review and exploratory Bayesian pooled analysis evaluating outcomes of DLI after allo-HCT in iNHL/MCL.

Methods

We systematically reviewed studies reporting outcomes of DLI in patients with iNHL/MCL after allo-HCT, including follicular lymphoma (FL), mantle cell lymphoma (MCL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), marginal zone lymphoma, and other low-grade B-cell lymphomas. Four principal cohorts comprising 68 extractable patients treated with DLI after allo-HCT were included.

Extracted outcomes included overall response rate (ORR), complete response (CR), graft-versus-host disease (GVHD), and durability of remission.

Given sparse cohorts, heterogeneous transplant and DLI practices, and limited patient-level data, pooled proportional synthesis was performed as an exploratory analysis. Bayesian hierarchical random-effects modeling was used to account for between-study variability and sparse-study effects.

Results

83.9%
Crude pooled ORR (47/56)

73.2%
Crude pooled CR (41/56)

Among 56 evaluable patients included in pooled response analyses, DLI produced a crude pooled ORR of 83.9% (47/56) and CR rate of 73.2% (41/56). Frequentist random-effects proportional analysis demonstrated no measurable statistical heterogeneity for ORR (I^2=0%, τ^2=0.00) or CR (I^2=0%, τ^2=0.00), although clinically meaningful heterogeneity remained present across cohorts with respect to histology, DLI indication, transplant platform, and dosing strategies.

Bayesian pooled analysis demonstrated a posterior mean ORR of 83.1% (95% credible interval [CrI], 69.1%–93.5%) and CR rate of 72.4% (95% CrI, 56.2%–85.8%).

Durable remissions extending beyond 5 years were observed across cohorts, including several patients maintaining ongoing complete remission without additional therapy. Acute GVHD ranged from 15%–45% across studies, while chronic GVHD remained a clinically significant complication.

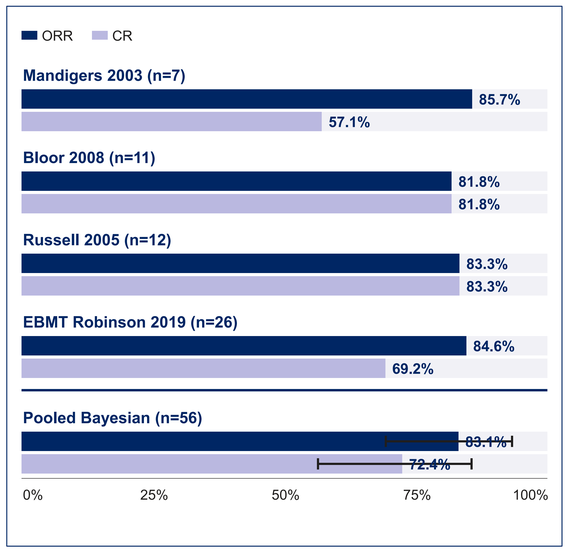
Included studies

Table 1. Included studies and extracted outcomes

Study	Histology	n	ORR	CR
Mandigers 2003	FL/SLL	7	6/7	4/7
Bloor 2008	Indolent lymphoid	11	9/11	9/11
Russell 2005	FL/CLL/MCL	12	10/12	10/12
EBMT Robinson 2019	FL/MCL	26	22/26	18/26

Key findings by cohort: durable molecular remissions (Mandigers); high CR rate after relapse or progression (Bloor); sustained remissions with only one relapse (Russell); largest multicenter DLI-only lymphoma cohort (EBMT).

Figure 1. Response to DLI by cohort and pooled Bayesian estimate



Bars show observed ORR and CR proportions in each cohort. The pooled row shows the Bayesian posterior mean with its 95% credible interval (whisker). Scale is 0–100%.

Table 2. Pooled outcomes

Crude pooled ORR	**83.9% (47/56)**
Crude pooled CR	**73.2% (41/56)**
Bayesian posterior mean ORR	**83.1% (95% CrI, 69.1%–93.5%)**
Bayesian posterior mean CR	**72.4% (95% CrI, 56.2%–85.8%)**
Acute GVHD range	**15%–45%**
Heterogeneity (ORR)	**I^2=0%, τ^2=0.00**
Heterogeneity (CR)	**I^2=0%, τ^2=0.00**

Conclusions

Despite substantial clinical heterogeneity and limitations inherent to retrospective cohort data, exploratory pooled analyses suggest that DLI after allo-HCT is associated with meaningful and durable antitumor activity in relapsed or persistent iNHL/MCL, supporting clinically relevant graft-versus-lymphoma effects in indolent B-cell malignancies.

The high posterior probability of response and prolonged remissions observed across cohorts suggest that DLI may remain a potentially effective immune-based salvage strategy in carefully selected patients with post-transplant relapse.

Limitations and next steps

Evidence is limited to four small retrospective cohorts with heterogeneous transplant platforms, DLI indications and dosing, and sparse patient-level data; pooled estimates are therefore exploratory rather than confirmatory. Prospective registry collection with harmonized DLI dosing and response definitions is needed to define which patients benefit and to weigh response against the risk of chronic GVHD.

References

1. Mandigers CM, et al. Bone Marrow Transplant. 2003;32(12):1159-63.
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3. Russell NH, et al. Bone Marrow Transplant. 2005;36(5):437-41.
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