Immune Checkpoint Inhibition as a Bridge to Allogeneic Transplant in Relapsed/Refractory Classical Hodgkin Lymphoma: A Meta-Analysis

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Introduction

- PD-1 inhibitors (nivolumab, pembrolizumab) induce high responses in relapsed/refractory classical Hodgkin lymphoma (r/r cHL), but many patients still require allogeneic HCT (allo-HCT) for durable control.
- Bridging with ICIs before allo-HCT may **debulk disease** and **deepen remission**, potentially enhancing graft-versus-lymphoma; however, immune activation may increase **Graft versus host disease (GVHD) risk**.
- Evidence to date is mainly **retrospective**, with **variable timing/washout**, conditioning, and GVHD prophylaxis across centers.
- We performed a meta-analysis to generate **pooled estimates** of survival (OS/PFS), **non relapse mortality (NRM)**, and **GVHD** after ICI→allo-HCT in r/r cHL.

Aim

- To evaluate the **safety** and **effectiveness** of **pre-transplant ICI** as a bridge to **allo-HCT** in **r/r cHL**.

Objectives

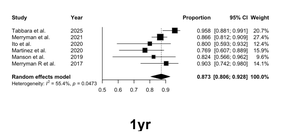
- Estimate pooled **OS** and **PFS** at **1, 2, and 3 years** with **95% CIs**.
- Summarize **NRM** (1/2/3 years) and **GVHD** (**aGVHD G2–4 & G3–4**, **cGVHD 1 & 2 years**).
- Assess **between-study heterogeneity** and explore **ICI agent**, **washout**, and **transplant factors** when reported.

Methods

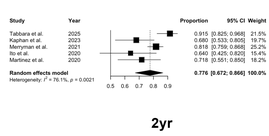
- **Design:** We conducted a systematic review and meta-analysis of observational cohorts.
- **Search:** We searched PubMed and Cochrane from inception to **August 2025** using terms for **PD-1**, **nivolumab**, **pembrolizumab**, **allo-HCT**, and **Hodgkin lymphoma**.
- **Eligibility:** We included adults with **r/r cHL** who received **ICI before allo-HCT** and reported **OS, PFS, NRM, or GVHD**; overlapping cohorts were excluded.
- **Data handling:** Two reviewers screened and extracted data independently and resolved disagreements by consensus.
- **Outcomes/timepoints:** We evaluated **OS** and **PFS** at **1, 2, and 3 years**; **NRM** at **1, 2, and 3 years**; **aGVHD (grades 2-4 and 3 - 4)**; and **cGVHD** at **1 and 2 years**.
- **Statistics:** We pooled event rates using **Mantel Haenszel random effects** in **RevMan 5.4**, reported **95% CIs**, and assessed heterogeneity with I^2 (**$p < 0.05$**).

Results

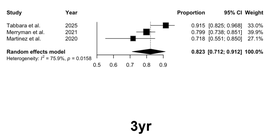
Overall Survival



1yr



2yr

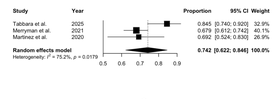


3yr

Progression Free Survival

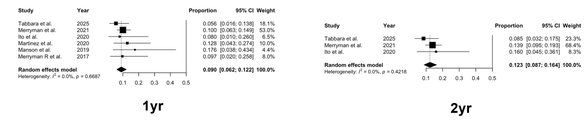


1yr 2yr

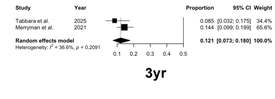


3yr

Non-Relapse Mortality

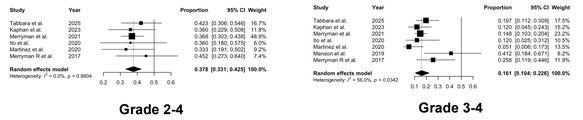


1yr 2yr



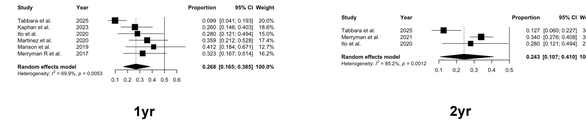
3yr

Acute Graft versus Host Disease (GVHD)



Grade 2-4 Grade 3-4

Chronic Graft versus Host Disease (GVHD)



1yr 2yr

Summary

- **Efficacy:** Pre transplant **ICI** followed by **allo-HCT** showed **high 1–3-year OS and PFS** in pooled analyses.
- **Safety: NRM** remained low, and **GVHD rates** were generally manageable with contemporary prophylaxis.
- **Implication:** The findings support **ICI bridging** as an effective option for selected patients with **r/r cHL**.
- **Context:** Interpretation should consider variation in **timing**, **conditioning**, and **GVHD prophylaxis** across studies.

Discussion

- **Feasibility: ICI → allo-HCT** appears feasible when safeguards are defined and peri-transplant care is standardized.
- **Trade off:** Potential **debulking/graft versus leukemia benefits** must be balanced against **GVHD risk** from immune priming.
- **Implementation:** Programs should select **fit, chemo sensitive** candidates, prespecify a **washout interval**, and favor **post transplant cyclophosphamide based prophylaxis** with early standardized monitoring.
- **Safety practice:** Clinicians should watch for **hepatic/pulmonary immune related adverse events**., **engraftment issues**, and **early GVHD**, using **steroid sparing** approaches when appropriate.
- **Evidence gaps:** The literature is largely **retrospective**, with **center/era heterogeneity** and incomplete reporting of **timing** and **prophylaxis**.
- **Next steps: Prospective multicenter** studies should predefine **washout**, stratify by **agent**, **disease status**, **donor**, and **conditioning**, and include **patient reported outcomes** and **late effects** follow up.

References

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