Response, Transplant Access, and Survival Outcomes of Pre-ASCT PD-1 Blockade in R/R Hodgkin Lymphoma

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INTRODUCTION

- **Relapsed/Refractory cHL:** **10–30%** of cHL patients develop relapsed or refractory disease, requiring salvage therapy before ASCT [1].
- **Conventional Salvage:** Standard chemotherapy-based salvage achieves PET-negative CR in **~54–73%** of patients, limiting transplant success [2].
- **PD-1 Inhibitors:** Nivolumab and pembrolizumab have emerged as effective salvage agents, achieving **high response rates**.
- **Evidence Gap:** Existing studies are largely single-arm or retrospective, with **heterogeneous regimens and outcomes**.
- **Objective:** To evaluate **response, transplant access, safety, and post-transplant outcomes** of PD-1 inhibitor-based salvage before ASCT in R/R cHL.

METHODS

- **Study Design:** Systematic review and meta-analysis conducted according to **PRISMA** guidelines and registered with **PROSPERO (CRD420261375713)**.
- **Search Strategy:** Comprehensive searches from inception to **May 2026** were conducted with **6 databases.**
- **Study Selection & Risk of Bias:** Studies were screened, data was extracted, ROB was assessed by two independant reviewers using the **MINORS tool**.
- **Statistical Analysis:** Proportional outcomes were pooled using **random-effects models**, with heterogeneity assessed using **I^2 and Cochran's Q test**; survival outcomes were analyzed using reconstructed individual patient-level data where feasible.
- **Outcomes:** Primary outcomes were **ASCT access rate (TAR) and complete metabolic response (CMR)**, while secondary outcomes included **PFS and OS.**

RESULTS

- **Study Population:** **19 studies** comprising **1,059 patients** were included.
- **Response:** Pooled pre-ASCT **CMR was 73.0%** (95% CI: 65–79%) and **ORR was 94.0%** (95% CI: 90–96%).
- **Transplant Access:** The pooled **TAR was 82.0%** (95% CI: 75–88%).
- **Survival:** Reconstructed IPD analysis (N=421) showed **24-month OS of 94.0%, overall PFS of 83.3%, and post-ASCT PFS of 89.0%.**
- **Meta-regression:** Higher prior **BV exposure was associated with lower pre-ASCT CMR** (p=0.026), while TAR decreased in more recent treatment eras (p=0.045).
- **Safety:** Toxicities were manageable, with **anemia (38.1%) and leukopenia (38.2%)** being the most common; immune-related events were uncommon (**pneumonitis 1.7%, thyroid dysfunction 7.8%**).
- **Robustness:** **Leave-one-out analysis** demonstrated stable estimates, and **Egger's test showed no evidence of publication bias**.

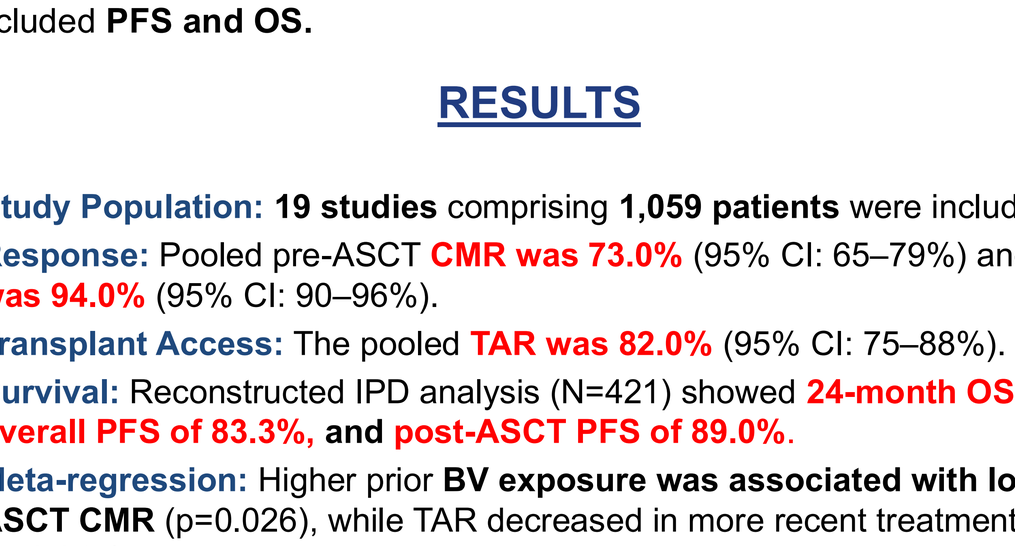

Fig 1. Forest plot of pooled ASCT access rate after PD-1–based salvage in R/R cHL.

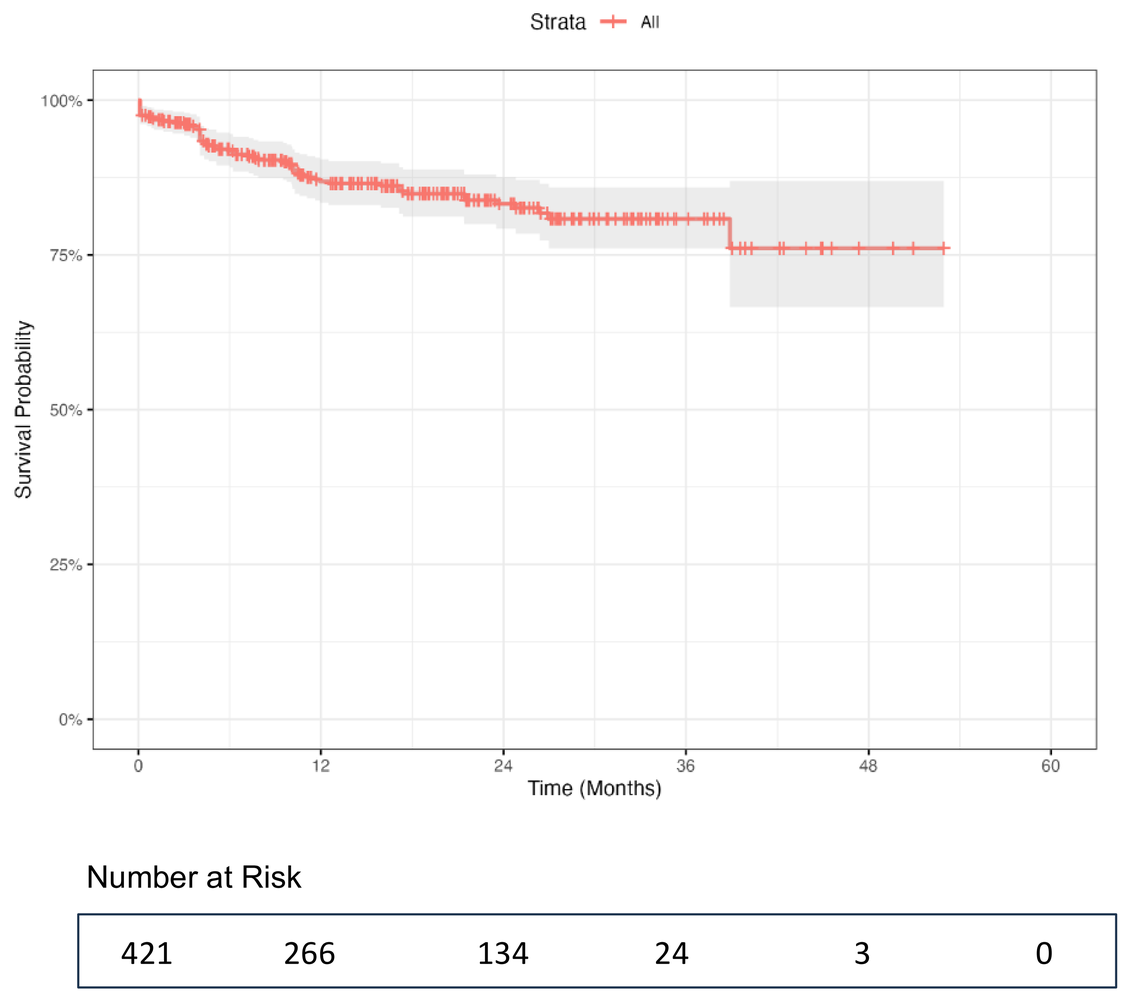

Fig 2. Reconstructed pooled KM curve for PFS after PD-1–based salvage in R/R cHL.

DISCUSSION

- **Key Findings:** PD-1 inhibitor-based salvage demonstrated **high efficacy**, with 82% ASCT access, 73% CMR, and 94% ORR, supporting its role as an **effective bridge to ASCT in R/R cHL.**
- **Limitations:** Significant heterogeneity across **regimens, patient populations, treatment eras, and study designs**, along with predominantly non-randomized evidence, limits direct comparisons and causal inference.
- **Future Directions:** Prospective comparative studies are needed to **identify optimal PD-1–based regimens**, clarify the impact of prior BV exposure, and define the best sequencing of PD-1 blockade and ASCT.
- **Conclusion:** **PD-1 inhibitor-based salvage is an effective and feasible transplant-bridging strategy**, achieving high response rates and favorable survival outcomes in patients with R/R cHL.

REFERENCES

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