

## Allogeneic Hematopoietic Cell Transplantation for Relapsed / Refractory Hodgkin Lymphoma: A Multicenter Real-World Experience

Koyun D. et al.: Allogeneic Hematopoietic Cell Transplantation Hodgkin Lymphoma

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### Abstract

**Objective:** AlloHCT remains a curative option for R/R Hodgkin lymphoma despite advances with BV and CPIs. This study evaluates its role and outcomes in this challenging patient population.

**Materials and Methods:** This retrospective oligocentric analysis involved 70 patients with R/R classical HL who underwent alloHCT.

**Results:** Patients were split into two treatment cohorts: era1 (2004–2010), 16 patients, and era2 (2011–2021), 54 patients. Among the cohort, sixty-three patients had previously received an autologous stem cell transplant. Forty patients were administered only (n=29) BV or BV preceding CPI (n=11) before alloHCT. A median follow-up of 64 months (40.7–87.3) revealed a 100-day non-relapse mortality (NRM) rate of 26%, with the 3-year overall survival (OS) and progression-free survival (PFS) reported as 39% and 28%, respectively. AlloHCT using haplotype-matched donors was linked to better OS and PFS. Post-transplant cyclophosphamide (post-tx CY) as a prophylactic approach for graft versus host disease (GVHD) significantly improved OS and PFS. A complete response (CR) during the post-transplant phase significantly improved OS and PFS. Indeed, better OS, PFS, and a reduced rate of NRM were observed in the pre/post-alloHCT BV and CPI group, although we could not demonstrate statistical significance. The survival (OS, PFS) curves and NRM rates were similar for both eras.

**Conclusion:** AlloHCT is a potentially practical therapeutic approach in responding to R/R HL patients.

**Keywords:** Hodgkin lymphoma, allogeneic stem cell transplantation, brentuximab vedotin, checkpoint inhibitors

### Öz

**Amaç:** Brentuksimab vedotin (BV) ve immün kontrol noktası inhibitörleri (CPI) ile sağlanan önemli ilerlemelere rağmen, nüks/dirençli (R/R) Hodgkin lenfoma (HL) olgularında allojenik hematopoietik kök hücre nakli (AKHN) küratif bir tedavi seçeneği olmaya devam etmektedir.

**Gereç ve Yöntemler:** Çalışmamız, bu zorlu hasta grubunda AKHN'nin rolünü ve klinik sonuçlarını değerlendirmektedir. Retrospektif ve çok merkezli bu çalışmada AKHN yapılmış 70 R/R klasik HL hastası incelenmiştir.

**Bulgular:** Hastalar iki döneme ayrılarak değerlendirilmiştir: dönem 1 (2004–2010, 16 hasta) ve dönem 2 (2011–2021, 54 hasta). Hastaların 63'ü daha önce olog kök hücre nakli olmuştur. Kırk hastaya AKHN öncesinde yalnızca BV (n=29) veya BV sonrası CPI (n=11) uygulanmıştır. Ortanca 64 aylık (40,7–87,3) takip süresinde, 100 günlük nüks dışı mortalite (NDM) oranı %26; 3 yıllık genel sağkalım (GS) ve progresyonsuz sağkalım (PS) sırasıyla %39 ve %28 idi. Haplotip uyumlu donörlerle gerçekleştirilen AKHN daha iyi GS ve PS ile ilişkili bulunmuştur. Graft-versus-host hastalığı (GVHD) profilaksisi amacıyla uygulanan post-transplant siklofosfamid (post-tx CY), GS ve PS'yi anlamlı biçimde iyileştirmiştir. Transplant sonrası tam yanıt (TY) elde edilmesi GS ve PS üzerinde belirgin bir olumlu etki göstermiştir. AKHN öncesi/sonrası BV ve CPI uygulanan grupta daha iyi GS, PS ve daha düşük NDM oranları gözlenmiş olmakla birlikte, bu farklılıklar istatistiksel anlamlılık düzeyine ulaşmamıştır. Sağkalım eğrileri (GS, PS) ve NDM oranları her iki dönemde benzer bulunmuştur.

**Sonuç:** Bulgularımız, AKHN'nin R/R HL hastalarında uygulanabilir ve potansiyel olarak küratif bir tedavi seçeneği olabileceğini göstermektedir.

**Anahtar Kelimeler:** Hodgkin lenfoma, allojenik kök hücre nakli, brentuksimab vedotin, immün kontrol noktası inhibitörleri

## Introduction

Hodgkin lymphoma (HL) generally has a high likelihood of cure, yet up to 20% of patients may face relapse or refractory (R/R) outcomes to initial treatments. High-dose salvage chemotherapy, accompanied by autologous stem cell rescue, has become an established therapeutic approach for patients with chemosensitive disease (1,2). Autologous stem cell transplantation (ASCT) outcomes in R/R HL are generally unfavorable, as approximately 50% of patients experience relapse (2,3). Although emerging therapeutic agents, including immune checkpoint inhibitors (CPIs) (nivolumab, pembrolizumab) and anti-CD30, brentuximab vedotin (BV), have demonstrated substantial therapeutic potential, the risk of pending relapse in this patient population remains high (4,5,6). Even with the advent of novel agents, allogeneic stem cell transplantation (alloHCT) retains its curative potential, albeit with significant morbidity and mortality (3,7). This study aims to assess the benefit of prior exposure to novel therapeutic agents prior to alloHCT outcomes in R/R HL.

## Materials and Methods

This study retrospectively assessed outcomes in 70 patients with R/R classic HL who underwent alloHCT at three transplant centers from 2004 to 2021. Information on age, performance status, disease stage, prior lines of therapy, relapse rate, previous ASCT, duration, and number of doses of BV and/or CPIs, the clinical condition of the disease at transplant, conditioning regimen, donor origin, graft versus host disease (GVHD), and post-transplant outcomes were extracted using medical records. Conditioning intensity was classified as myeloablative (MAC), reduced-intensity (RIC), or non-myeloablative (NMA) according to European Society for Blood and Marrow Transplantation (EBMT) consensus definitions (8). Patients were included from 2010 and earlier (era1) in one center and from 2011 onwards (era2) across all centers. Therapeutic response was in accordance with the Lugano classification (9). Post-transplant BV and CPI were used only for relapsed/refractory disease. Computed tomography (CT) and/or positron emission tomography (PET-CT) were employed to assess the disease condition before transplantation (9). Post-transplant (post-tx) overall response rate (ORR) was the primary endpoint. The secondary endpoints included overall survival (OS), progression-free survival (PFS), non-relapse mortality (NRM), and response rates stratified by transplant years and pre-/post-transplant CPI and/or BV use. Neutrophil and platelet recovery were identified as three consecutive days, with absolute neutrophil counts reaching at least  $0.5 \times 10^9/L$  and platelet counts reaching at least  $20 \times 10^9/L$  without transfusion (10). Acute and chronic GVHD were evaluated based on standard grading criteria (11,12).

## Statistical analysis

Demographic and patient characteristics were summarized and analyzed using descriptive methods. Two era classifications were used in the study. The primary analysis stratified patients into two broad eras based on transplant year (Era 1: 2004–2010; Era 2: 2011–2021). In addition, to highlight the major shift in transplant practice after 2016—including the adoption of post-transplant cyclophosphamide, increased use of haploidentical donors, and wider availability of targeted agents (BV and CPIs)—a secondary two-era comparison was performed (Era 4: 2004–2015; Era 5: 2016–2021). This three-era structure reflects the transition from a pre-novel agent period (2004–2010), to an early targeted-therapy period before widespread PTCy use (2011–2015), and finally to the modern transplant era characterized by routine PTCy use, expansion of haploidentical transplantation, and broad access to BV and CPIs (2016–2021), allowing evaluation of long-term trends across clinically distinct periods.

Categorical variables were compared using Fisher's exact test or the Chi-Square test; continuous variables were analyzed using the T-test. Kaplan-Meier methods were used to estimate survival, and log-rank tests were used to analyze group differences. Statistical significance was defined as a p-value  $<0.05$ . NRM was defined as death occurring prior to lymphoma progression or recurrence and was calculated from the allo-HCT date to the death. The cumulative incidence method was applied to estimate both relapse incidence and NRM. OS, PFS, NRM, and GVHD were analyzed using univariate and multivariate Cox proportional hazards models. To account for competing risks between relapse and non-relapse mortality (NRM), we performed Fine-Gray subdistribution hazard modeling. Variables with  $p < 0.05$  or strong clinical relevance were included in multivariate models. All analyses were performed using IBM SPSS Statistics version 20. The local ethics committee has approved the study (Date: 22.4.2022; Approval No: İ05-247-22). Despite limited statistical power due to sample size constraints, subgroup analyses were conducted to explore potential associations.

## Results

Patient characteristics are detailed in Table 1. Among the 70 patients, 16 were classified in era 1 (2004–2010), and 54 were classified in era 2 (2011–2021). The median age of the participants was 35 years (18–62 years), and

59% were male. A median of four treatment lines (range, 2–8) was observed before alloHCT. Sixty-three (90%) had undergone a prior ASCT, and four (6%) patients received a second ASCT. Since 2013, 40 patients (57.1%) received only BV (n=29) (median: 3 cycles, range: 1-14) or BV followed by CPIs (nivolumab (n=10), pembrolizumab (n=1)), while one patient received only CPI prior to alloHCT. Among only BV-treated patients, the responses included complete response (CR) (n=8), partial response (PR) (n=8), stable disease (SD) (n=12), and progressive disease (PD) (n=1). One patient receiving nivolumab alone had SD; eleven patients received BV followed by CPI; three achieved complete response (CR), three achieved partial response (PR), three had stable disease (SD), and two had progressive disease (PD). Patients received a median of 6 CPI doses (range, 3-20), with a median interval from the last CPI dose to alloHCT of 4.2 months (range, 1.6-7.9 months). No center-mandated wash-out period was implemented; the CPI-to-alloHCT interval represented routine clinical practice rather than a predefined institutional policy. Nine patients (75%) transitioned directly to alloHCT following CPI therapy, whereas three (25%) received single-line salvage therapy between CPI treatment and alloHCT. The median KPS score was 80 (range: 70–100) among patients. By the time of alloHCT, 11 patients (15.7%) had achieved CR, 18 patients (25.7%) had PR, and 41 patients (58.6%) had SD/PD. Forty-seven patients received reduced-intensity conditioning (RIC) (67.1%), and 46 had fludarabine-based conditioning. A significant proportion of patients in the fludarabine subset were administered the fludarabine/melphalan (Flu/Mel) regimen (n=35) or the Flu/Mel/Total body irradiation (TBI) regimen (n=5) (13,14). In the myeloablative conditioning (MAC) (32.9%) cohort, most patients received the busulfan/cyclophosphamide (Bu4/Cy120) (n=10) or Flu/TBI12 (n=8) regimen (15,16).

Donor origins comprised matched sibling (MRD) (n=39), matched unrelated (MUD) (n=16), haploidentical donors (n=11), and mismatched unrelated donors (MMUD) (n=4). Sixty-two patients received peripheral blood (PB) transplants, seven received bone marrow (BM) transplants, and one received an umbilical cord transplant. T-cell depletion in unrelated and haploidentical donors consisted mainly of antithymocyte globulin (ATG) (n=13) or post-tx CY (n=16). Patients undergoing MRD alloHCT received conventional GVHD prophylaxis with calcineurin inhibitors. Cyclosporin combined with methotrexate was the most frequently administered GVHD prophylactic regimen, with cyclosporin and mycophenolate serving as the primary alternative. The infused CD34+ cell dose had a median value of  $5.6 \times 10^6/\text{kg}$  (range, 0.6– $14.7 \times 10^6/\text{kg}$ ).

Sixty-two patients (88.5%) were fully engrafted. Primary engraftment failure occurred in 8 patients (11.4%). Of these, 2 had MRD donors and 6 had non-MRD donors (haploidentical, MMUD, MUD). Most transplants were performed before 2015. Similar findings have been reported in autologous transplant settings, where low CD34+ or total nucleated cell (TNC) doses were associated with poor hematologic recovery and increased early mortality (17). Engraftment was seen after a median of 16 days (13-28) in neutrophils and 13 days (7-39) in platelets. A chimerism assessment on day +100 was available in 48 patients (68.5%). Complete (95-100% donor cells) donor chimerism (n=44) and mixed chimerism (75.5-94% donor cells) (n=34) were observed in all but one patient (fifteen patients died prior to chimerism assessment, seven patients had no data). Twenty-nine patients (41.4%) experienced acute GVHD, of whom 15 (51.7%) had grade II–IV disease. Chronic GVHD was observed in 17 patients (24.3%), with moderate/severe involvement documented in 7 cases (41.2%). Invasive fungal infections (IFI) were observed in 18 (25.7%) patients, with four cases being fatal. The causes of death were associated with bacterial (n=4), viral (n=3; CMV colitis, CMV pneumonia, tuberculosis), and sepsis-related complications (n=14), including cases with GVHD, relapse, or organ failure. Five cases had no specific pathogen identified.

The median length of follow-up after alloHCT was 64 months (40.7-87.3). Following transplantation, 27 patients (50%) achieved CR; disease relapse or progression was observed in 23 patients (33%), with a median time to relapse of 6.3 months (range, 1–24.5 months). Eleven patients (15.7%) and eight patients (11.4%) who relapsed after alloHCT received chemotherapy with BV and/or CPIs as salvage and/or maintenance therapy post-alloHCT, respectively. Among these, four patients received BV exclusively as maintenance therapy, one patient received nivolumab monotherapy, and seven received BV followed by CPI. After alloHCT, the median courses of BV or CPI therapy were 4 (range, 2-18) and 3 (range, 1-51), respectively. Donor lymphocyte infusion (DLI) was provided to 10 patients to manage relapse or progressive disease following alloHCT: 2 patients received DLI for overt clinical relapse, while eight patients were treated due to loss or decrease of donor chimerism. No patient received DLI prophylactically. Patients underwent a median of two DLIs (1–3), with the first DLI occurring at a median of 8 months (range, 2–57). Six patients (60%) received DLI with salvage chemotherapy. Overall response rates (CR and PR) were 1/4 (25%) among patients receiving DLI alone and 4/6 (66%) for those patients receiving DLI and additional therapy. As of the analysis, twenty-nine patients were alive (41%), comprising 23 in complete response (CR) (79%), four in partial response (PR) (14%), and two in stable disease (SD) (7%). The 3- and 5-year estimated OS were 39% (95% CI 27.2–50.8) and 37% (95% CI 25.2-48.8), respectively; the 3- and 5-year PFS was 28% (95% CI 16.2-39.8); D100 and 1-year non-relapse mortality (NRM) rates were 26% (95% CI 16.2–35.8) and 37% (95% CI 25.2-48.8), respectively (Figure 1).

Regarding donor type, pre-tx CPI ( $p < 0.05$ ), TBI in the conditioning regimen ( $p < 0.001$ ), and post-tx CY ( $p < 0.001$ ) were more frequent in haploidentical tx. ATG was more commonly used for MUD/MMUD than for MRD ( $p < 0.001$ ). A higher incidence of acute GVHD ( $p = 0.09$ , not statistically significant) and a significantly higher rate of chronic GVHD ( $p = 0.02$ ) were observed in patients receiving MRD grafts compared with those receiving MUD/MMUD or haploidentical grafts. Notably, the majority of grade II–IV acute GVHD and moderate/severe chronic GVHD cases occurred in MRD recipients (9 and 6 patients, respectively). The analysis revealed no significant differences between MRD, MUD/MMUD, and haploidentical transplants in terms of transplant centers ( $p = 0.16$ ), year of transplantation ( $p = 0.41$ ), or pre-tx BV use ( $p = 0.19$ ) (Table 2). When OS and PFS were analyzed by donor type, grafts from haploidentical donors were associated with significantly improved OS ( $p = 0.015$ ) and PFS ( $p = 0.03$ ) compared with those from MUD/MMUD and MRD donors. The MUD/MMUD group demonstrated significantly higher NRM in comparison to both haploidentical and MRD donor groups ( $p < 0.05$ ) (Figure 2).

Regarding post-tx CY versus ATG, patients who received post-tx CY had significantly better OS ( $p = 0.04$ ) and PFS ( $p = 0.05$ ), but similar NRM ( $p = 0.19$ ). Patients who received ATG exhibited a significant reduction in OS ( $p = 0.04$ ) and an increase in NRM ( $p = 0.01$ ); however, PFS outcomes remained comparable to those in the other groups ( $p = 0.28$ ). Upon stratifying by conditioning regimen (RIC vs. MAC), no statistically significant differences were observed in OS ( $p = 0.19$ ), PFS ( $p = 0.38$ ), or NRM ( $p = 0.41$ ) (Figure 3).

Among patients presenting with chemosensitive disease (CR, PR), there was a significant trend for increased use of pre-alloHCT BV ( $p = 0.03$ ), selection of RIC conditioning ( $p = 0.002$ ), and higher Karnofsky Performance Scores (KPS) ( $p = 0.02$ ). In contrast, these patients demonstrated less ATG use ( $p = 0.02$ ). OS, PFS, and NRM were also stratified by response status pre- and post-alloHCT (CR vs. all other outcomes, including PR, SD/PD). Achieving CR before alloHCT showed an association with better OS ( $p = 0.28$ ), PFS ( $p = 0.27$ ), and NRM ( $p = 0.46$ ), though the impact was not statistically significant. Patients in CR at the time of the post-alloHCT showed a significant survival advantage when compared with those who were not in CR (OS,  $p = 0.02$ ; PFS,  $p < 0.001$ ), but no discrepancy was observed in the NRM ( $p = 0.13$ ) (Figure 4).

Patients who received BV at any point pre ( $n = 40$ ) and/or post-alloHCT ( $n = 11$ ) showed a tendency for longer OS (pre-alloHCT,  $p = 0.5$ ; post-alloHCT,  $p = 0.2$ ), PFS (pre-alloHCT,  $p = 0.17$ ; post-alloHCT,  $p = 0.23$ ), and the NRM was low (pre-alloHCT,  $p = 0.95$ ; post-alloHCT,  $p = 0.06$ ). We observed that in patients who received pre ( $n = 12$ ) and post-alloHCT ( $n = 8$ ) CPI at any time point ( $n = 12$ ) improved outcomes (OS (pre-alloHCT,  $p = 0.34$ ; post-alloHCT,  $p = 0.27$ ), PFS (pre-alloHCT,  $p = 0.16$ ; post-alloHCT,  $p = 0.17$ ), NRM (pre-alloHCT,  $p = 0.34$ ; post-alloHCT,  $p = 0.08$ )), but not approaching statistical significance either (Figure 5).

Table 3 presents patient characteristics grouped by transplant era. No statistically significant difference in median age was observed between the two eras ( $p = 0.45$ ). A greater percentage of patients in era1 received  $> 3$  lines of treatment prior to alloHCT (81.3%) than in era2 (57.4%), but this difference was not statistically significant ( $p = 0.08$ ). In era 2, 74.1% received BV at pre-alloHCT and 20.4% post-alloHCT, while 22.2% received CPI pre-alloHCT and 14.8% post-alloHCT. According to the alloHCT response, we did not notice any difference between the two eras ( $p = 0.46$ ), but post-alloHCT CR rates were significantly higher in era 2 ( $p = 0.01$ ). RIC was the predominant conditioning regimen in both era1 (56.3%) and era2 (70.4%) ( $p = 0.29$ ). The median follow-up duration was 53 months (37.3–68.7) for era1 and 139 months (26.6–251.4) for era2. There was a decline in the proportion of ATG administration in era 2 (16.7%) compared with era 1 (25%), but this difference did not reach statistical significance ( $p = 0.45$ ). Analysis of acute GVHD incidence showed a decrease from 50% in era 1 to 38.9% in era 2, though this difference did not reach statistical significance ( $p = 0.11$ ). Chronic GVHD occurred less frequently in era 2 (22.2%) than in era 1 (31.3%) without reaching statistical significance ( $p = 0.12$ ). The analysis of post-alloHCT survival showed comparable OS ( $p = 0.13$ ) and PFS ( $p = 0.14$ ) between the two eras. The prevalence of NRM was similar across the two eras ( $p = 0.73$ ). When stratified by three eras according to transplant years (era1 (2004–2010), era2 (2011–2015), and era3 (2016–2021)), the OS ( $p = 0.2$ ) and PFS ( $p = 0.1$ ) were longer in era3, but the differences were not statistically significant. While the patients were stratified into two different eras (era 4, 2004–2015; era 5, 2016–2021) based on the date of transplant, PFS demonstrated a statistically significant increase ( $p = 0.03$ ) (Figure 6).

Patients undergoing alloHCT during Era 1 (2004–2010) were treated exclusively at a single center, whereas those in Era 2 (2011–2021) received treatment at all centers. The survival outcomes, including OS ( $p = 0.4$ ), PFS ( $p = 0.45$ ), and NRM ( $p = 0.14$ ), did not show statistically significant differences across the two eras.

#### **Univariate and multivariate outcomes**

##### **Graft Versus Host Disease**

Donor type significantly impacted chronic GVHD in univariate analysis (UVA) ( $p = 0.039$ ), with MRD showing a higher incidence of chronic GVHD compared with MUD/MMUD and haploidentical donors. In multivariate analysis, ATG administration was associated with a significantly reduced risk of chronic GVHD (HR 0.13; 95% CI 0–0.8,  $p = 0.039$ ).

## Survival

Univariate analysis showed that haploidentical transplantation compared with MRD was associated with improved OS (HR 3.3; 95% CI 0.96–11.5,  $p=0.005$ ), and post-alloHCT CR/PR disease status correlated with better OS (HR 2.95; 95% CI 1.32–6.61,  $p=0.008$ ). ATG use (HR 2.15; 95% CI 1.04–4.42,  $p=0.037$ ) and poor KPS score ( $\leq 70$ ) (HR 0.18; 95% CI 0.08–0.42,  $p=0.000$ ) were associated with inferior OS.

Multivariate analysis (MVA) confirmed significant associations with OS for KPS score (HR 0.1; 95% CI 0.01–0.66,  $p=0.01$ ) and post-alloHCT disease status (CR/PR vs. SD/PD, HR 4.24; 95% CI 1.32–13.6,  $p=0.01$ ).

## Progression-Free Survival

Univariate analysis revealed that high KPS score (HR 0.26; 95% CI 0.11–0.57,  $p=0.01$ ), haploidentical transplantation (HR 3.9; 95% CI 1.12–13.5,  $p=0.032$ ), and post-alloHCT CR/PR status (HR 3.8; 95% CI 1.86–7.76,  $p=0.000$ ) were significantly associated with improved PFS.

Multivariate analysis showed that high KPS score (HR 0.11; 95% CI 0.01–0.68,  $p=0.01$ ), pre-alloHCT CR/PR status (HR 3.51; 95% CI 1.2–10.2,  $p=0.02$ ), and post-alloHCT CR/PR status (HR 2.76; 95% CI 1.15–6.62,  $p=0.02$ ) were independently associated with better PFS.

## Non-Relapse Mortality

Univariate analysis showed increased NRM in the ATG cohort (HR 2.77; 95% CI 1.24–6.16,  $p=0.01$ ).

Multivariate analysis revealed that high KPS score (HR 0.05; 95% CI 0.04–0.96,  $p=0.047$ ), pre-tx BV (HR 0.11; 95% CI 0.0–0.72,  $p=0.035$ ), and post-tx CPI (HR 0.0; 95% CI 0.0–0.78,  $p=0.039$ ) were significantly associated with reduced NRM. All UVA and MVA results, including non-significant findings, are presented in Tables 4 and 5 for complete transparency.

Fine-Gray analysis revealed that pre-HCT BV significantly reduced NRM (sHR = 0.60, 95% CI: 0.38–0.94,  $p = 0.026$ ), while acute GVHD was associated with increased NRM (sHR = 1.41, 95% CI: 1.01–1.97,  $p = 0.043$ ). Chronic GVHD showed a non-significant trend (Table 6).

## Discussion

This retrospective study analyzed real-life alloHCT outcomes in R/R HL. Despite its role after ASCT, indications and timing remain uncertain. Patients had a median of four prior regimens; 46% received radiation, and 90% underwent ASCT. Despite heavy pretreatment, alloHCT remained feasible and effective. Improved outcomes over time likely reflect advances in supportive care, transplant technologies, patient selection, and integration of novel agents such as BV and CPIs.

Our study showed a rise in alloHCT frequency, BV/CPI use, and post-transplant chemosensitivity. In era 2 (2011–2021), 40 of 54 patients received BV before alloHCT, with 55% chemosensitive at transplant, consistent with prior reports (18). While some studies suggested pre-transplant BV may improve outcomes (19,20), others found no significant effect on OS, PFS, or NRM (21,22), except for improved PFS in chemorefractory patients (21). BV exposure was associated with improved OS/PFS and lower NRM, though only multivariate analysis confirmed a reduced NRM. This protective effect may reflect BV's immunomodulatory activity and lower peri-transplant toxicity (22).

Some studies of BV for R/R HL after alloHCT are limited, though response rates  $\geq 50\%$  have been reported (23–25). In our cohort, BV yielded an ORR of 54.5% and a CR of 18% among 11 relapsed patients; 2 received BV alone, while nine received BV followed by DLI and/or CPIs. Six deaths occurred, mainly due to progression. Post-alloHCT BV did not significantly affect OS/PFS but was associated with reduced NRM, suggesting possible immunomodulatory effects (22). The association of pre-transplant BV and post-transplant CPI use with better disease control and lower systemic toxicity, together with the observed impact of high KPS, which reflects superior baseline fitness, likely contributed to reduced NRM. The 100-day NRM rate of 26% in our cohort was higher than in contemporary series. This likely reflects the combined impact of infectious complications, GVHD-related events, advanced disease at transplant, and variability in supportive care practices.

The success of CPI therapies has called into question the role of alloHCT in HL. In our cohort, CPI-exposed ( $n=12$ ) and non-exposed patients ( $n=58$ ) showed comparable age, prior therapy, KPS, stem cell source, and GVHD rates, with no significant differences. Group distinctions were limited to more prior BV lines and greater TBI use in the CPI group.

This study indicates that CPI use, both pre- and post-alloHCT, was associated with improved survival without increasing immunological toxicities or NRM. In multivariate analysis, post-alloHCT CPI showed a trend toward improved PFS, though this was not statistically significant. Consistent with the multicenter cohort by Perales et al., our pre-alloHCT CPI patients (17.1%) demonstrated no OS or NRM benefit but a favorable PFS trend. Relapse (8%) and GVHD rates (aGVHD 41.7%, cGVHD 16.7%) were lower in our CPI-exposed patients, possibly reflecting differences in prophylaxis and patient selection (26). The updated joint CIBMTR/EBMT analysis by Perales et al. (26), which included more than 2000 alloHCT recipients with HL transplanted between 2008 and 2023, provides an important benchmark for contemporary outcomes. In that study, prior CPI exposure significantly reduced relapse and improved PFS without increasing NRM, while PTCy-based GVHD

prophylaxis led to superior OS and lower rates of acute and chronic GVHD. These findings closely parallel our observations, where BV/CPI exposure and PTCy use were linked to reduced NRM and favorable disease control. The consistency between our real-world cohort and this large modern dataset reinforces the evolving role of targeted agents and PTCy in reshaping alloHCT outcomes in R/R HL. However, these findings should be interpreted as associations rather than independent survival benefits, as neither CPI exposure nor post-transplant cyclophosphamide retained significance in multivariate analyses.

In our series, pre-treatment CPI was associated with an elevated risk of GVHD (27,28). Ijaz et al. reported overall incidences of aGVHD and cGVHD of 59% and 29%, respectively (29). In a larger cohort of 209 patients receiving pre-transplant CPI, rates of aGVHD, cGVHD, and NRM were 54%, 34%, and 14%, respectively, with 2-year PFS and OS of 47% and 69%, respectively (30). Merryman et al. further showed that a CPI-to-alloHCT interval >80 days significantly reduced aGVHD, while  $\geq 10$  CPI doses were significantly associated with lower cGVHD incidence.

Among our patients exposed to pre-transplant CPI, 41.7% developed aGVHD and 16.7% developed cGVHD. Neither the CPI-to-alloHCT interval ( $\leq 80$  vs  $> 80$  days) nor the number of CPI doses ( $< 10$  vs  $\geq 10$ ) influenced GVHD incidence (data not shown). These rates were lower than those reported in earlier studies and consistent with Philippis et al., who observed aGVHD and cGVHD incidences of 41% and 7% in 59 haploidentical donor transplants (31). Several factors may account for the absence of an increased GVHD signal following CPI exposure in our cohort. Patients who underwent alloHCT after CPI exposure likely constituted a more selected group with favorable clinical characteristics. Additionally, the interval between CPI administration and transplantation may have permitted partial immune stabilization. In addition, the predominant use of post-transplant CY in our cohort could have attenuated CPI-related alloreactivity. Other CPI-associated transplant toxicities (e.g., sinusoidal obstruction syndrome/veno-occlusive disease, engraftment syndrome, immune-mediated organ toxicities) could not be evaluated, as these events were not systematically documented across centers in this retrospective dataset.

Although PFS improved within the CPI group, OS, PFS, and NRM did not differ significantly between groups, and GVHD rates remained similar regardless of CPI exposure. These findings may reflect the protective role of post-transplant CY in immune reconstitution. Moreover, RIC regimens with acute GVHD have been linked to reduced relapse risk, supporting a graft-versus-tumor effect (32).

Our analysis included four patients who underwent SCT from haploidentical donors with post-transplant CY prophylaxis, two from MMUDs, three from MUDs, and three from MRDs. Peripheral blood stem cells were used in all but one case. Pre-transplant CPI exposure was associated with a markedly lower post-alloHCT relapse rate (8%) compared with 36.2% in CPI-naïve patients. Similar findings have been reported in other trials, supporting a graft-versus-lymphoma effect. Philippe et al. documented an 8% relapse incidence in CPI-exposed patients (n=59) with 2-year follow-up (31). In comparison, Armand et al. observed a 7% relapse rate within 5.5 months in a phase II study of 44 patients with cHL receiving pre-transplant CPI (6).

In our study, eight patients with R/R disease after alloHCT received CPI (median three cycles; range 1–51), with a median interval of 60 months (range 3.6–63). One patient had prior CPI exposure. Chronic GVHD (liver, eye, oral mucosa) occurred in one patient, and acute hepatic GVHD in another (ORR 50%; 2 CR, 2 PR). Although limited by sample size, multivariate analysis showed that post-alloHCT CPI was significantly associated with reduced NRM. Prior studies similarly support CPI efficacy post-transplant, while shorter alloHCT-to-CPI intervals, higher CPI doses, and prior GVHD have been linked to increased GVHD risk (27,29).

Several recent studies have reported favorable survival outcomes with haploidentical transplantation. Maria et al. observed significantly better PFS and lower relapse rates with haploidentical donors compared with MRD or URD (33). A large-scale analysis found equivalent OS and PFS across MRD, haploidentical, and MUD groups, but noted a lower incidence of chronic GVHD with haploidentical donors (34).

In our study, the haploidentical cohort showed a trend toward longer OS and PFS and lower NRM. Univariate analysis suggested superior survival with haploidentical donors, but multivariate analysis did not confirm these differences. Although haploidentical transplantation appeared to be associated with improved OS and PFS, this observation may be influenced by the higher frequency of post-transplant CY use in this group. Because post-transplant CY was administered predominantly in haploidentical grafts, the observed survival differences cannot be attributed solely to donor type. In multivariable analyses, donor type did not remain significant after adjustment for post-transplant CY, suggesting that these outcomes may reflect the effects of GVHD prophylaxis strategies and temporal changes in transplant practice rather than intrinsic donor characteristics. An international multicenter study demonstrated that GVHD prophylaxis with post-transplant CY improved PFS compared with its absence. However, no OS benefit was observed, while CY combined with ATG was associated with worse survival (30). The apparent survival benefit observed in haploidentical recipients likely reflected post-transplant CY use and era-related advances rather than donor type alone. Although prior studies reported lower NRM with RIC regimens, we observed no survival advantage of RIC over MAC (35). Improved outcomes in post-transplant CY recipients appear attributable to GVHD prophylaxis and era-related factors rather than conditioning intensity.

Earlier studies of alloHCT before novel agents showed much lower survival and higher NRM compared to more recent groups. Our Era 1 results match these earlier findings, which suggests that later improvements are due to better transplant methods and the use of BV, CPI, and post-transplant CY. Era-based findings should be interpreted cautiously, as multiple concurrent shifts in transplant practice—rather than novel agents alone—contribute to differences between eras; therefore, outcome interpretation primarily relies on direct BV/CPI-stratified analyses. When comparing outcomes across transplant eras, several factors may explain the absence of statistically significant survival differences despite increased BV and CPI use. Although exposure to BV and/or CPI was higher in era 2, survival did not differ significantly between eras. This likely reflects shorter follow-up and limited sample size, which may have attenuated any measurable survival advantage despite increased BV/CPI use. Notably, patients who received these agents post-allo demonstrated improved OS, reduced NRM, and a significantly higher CR rate. The shorter median follow-up in Era 1 reflects higher early mortality, as follow-up information for earlier-era patients was complete.

### **Study Limitations**

Limitations include non-uniform era stratification, which reduces the clarity of temporal comparisons. Advances in care likely explain the improved PFS observed in 2016-2021. Retrospective design, varied patient populations, and small CPI cohorts limit the interpretation of GVHD. Different donor types and treatment regimens reduce generalisability. Response assessments relied on Lugano criteria, as PET/Deauville was not routinely available at the time. Outcomes with BV/PD-1 inhibitors around alloHCT should be interpreted cautiously, given the small sample size and lack of statistical significance. In addition, the limited sample size—particularly within the BV and CPI subgroups—substantially reduces statistical power. Therefore, these subgroup findings should be interpreted as exploratory and hypothesis-generating rather than definitive, and non-significant trends should not be overinterpreted. Additionally, some hazard ratio estimates showed wide confidence intervals, reflecting the limited number of events and reduced model stability.

### **Conclusion**

AlloHCT remains a viable option for R/R HL. Donor type, GVHD prophylaxis, and integration of BV and CPIs influenced survival. Haploidentical transplantation with post-transplant CY showed promising outcomes. Disease control and NRM improved with novel agents, yet survival benefit was minimal. Larger prospective studies are needed to confirm these outcomes and clarify alloHCT's role in targeted therapy.

### **Declarations**

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**Table 1.** Patients' characteristics

<b>Center</b>	Center1	28	40.0%
	Center2	27	38.6%
	Center3	15	21.4%
<b>Tx-year</b>	Era 1	16	22.9%
	Era 2	54	77.1%
<b>Age</b>		35 (18-62)	
<b>Follow-up time, month</b>		64.0 (40.7-87.3)	
<b>Age</b>	≤40	49	70.0%
	>40	21	30.0%
<b>Sex</b>	Male	41	58.6%
	Female	29	41.4%
<b>PrealloHCT KPS Score</b>	≤70	25	35.7%
	>70	45	64.3%
<b>Stage</b>	Early	24	34.3%
	Advanced	46	65.7%
<b>PrealloHCT treatment</b>	≤3 line	26	37.1%
	>3 line	44	62.9%
<b>PrealloHCT RT use</b>	Yes	32	45.7%
	No	38	54.3%
<b>PrealloHCT BV use</b>	Yes	40	57.1%
	No	30	42.9%
<b>PrealloHCT CPI use</b>	Yes	12	17.1%
	No	58	82.9%
<b>PrealloHCT disease status</b>	CR	11	15.7%
	PR	18	25.7%
	SD/PD	41	58.6%

<b>Conditioning regimen</b>	RIC	47	67.1%
	MAC	23	32.9%
<b>Stem cell source</b>	PB	62	88.6%
	BM	7	10.0%
	Umbilical cord	1	1.4%
<b>ATG use</b>	Yes	13	18.6%
	No	57	81.4%
<b>Acute GVHD</b>	Yes	29	41.4%
	No	40	57.1%
	N/A	1	1.4%
<b>Chronic GVHD</b>	Yes	17	24.3%
	No	52	74.3%
	N/A (Exitus at D100)	1	1.4%
<b>PostalloHCT BV use</b>	Yes	11	15.7%
	No	59	84.3%
<b>PostalloHCT CPI use</b>	Yes	8	11.4%
	No	62	88.6%
<b>PostalloHCT status at D100</b>	CR	27	50.0%
	PR	13	24.1%
	SD/PD	14	25.9%
	N/A (Exitus at D100)	16	
<b>NRM</b>	Yes	29	41.4%
	No	41	58.6%
<b>PostalloHCT D100 mortality</b>	Yes	18	25.7%
	No	52	74.3%

AlloHCT: Allogeneic stem cell transplant, ATG: Anti Thymocyte Globulin, BM: Bone marrow, BV: Brentuximab vedotin, CPI: Checkpoint inhibitors, CR: Complete Response, D100: post HCT day 100, Era 1: 2004–2010, Era 2: 2011–2021, GVHD: Graft versus host disease, *KPS*: *Karnofsky Performance Status*, MAC: Myeloablative Conditioning, N/A: Not applicable, NRM: Non-relapse Mortality, PB: Peripheral Blood, PR: Partial response, RIC: Reduced-intensity conditioning, RT: Radiotherapy, SD/PD: Stable disease/Progressive disease, Tx: Transplant.

**Table 2.** Patients characteristics' regarding to donor type

		MRD		MUD/MMUD		Haploidentical		P
Center	Center1	16	41.0%	6	30.0%	6	54.6%	0.16
	Center2	15	38.5%	11	55.0%	1	9.1%	
	Center3	8	20.5%	3	15.0%	4	36.4%	
Tx-year	Era 1	9	23.1%	6	30.0%	1	9.1%	0.41
	Era 2	11	28.2%	5	25.0%	3	27.3%	
	Era 3	19	48.7%	9	45.0%	7	63.6%	
Age	≤40	28	71.8%	11	55.0%	10	90.9%	0.11
	>40	11	28.2%	9	45.0%	1	9.1%	
Sex	Male	21	53.8%	13	65%	7	63.6%	0.67
	Female	18	46.2%	7	35%	4	36.4%	
Pre-alloHCT KPS Score	≤70	13	33.3%	9	45.0%	3	27.3%	0.55
	>70	26	66.7%	11	55.0%	8	72.7%	
Disease Stage	Early	16	41.0%	5	25.0%	3	27.3%	0.41
	Advanced	23	59.0%	15	75.0%	8	72.7%	
Pre-alloHCT treatment	≤3 line	17	43.6%	6	30.0%	3	27.3%	0.45
	>3 line	22	56.4%	14	70.0%	8	72.7%	
RT	No	23	59.0%	8	40.0%	7	63.6%	0.31
	Yes	16	41.0%	12	60.0%	4	36.4%	
Pre-alloHCT BV	No	18	46.2%	10	50.0%	2	18.2%	0.19
	Yes	21	53.8%	10	50.0%	9	81.8%	
Pre-alloHCT CPI	No	36	92.3%	15	75.0%	7	63.6%	<b>&lt;0.05</b>
	Yes	3	7.7%	5	25.0%	4	36.4%	
TBI	No	34	89.5%	13	68.4%	2	18.2%	<b>&lt;0.001</b>
	Yes	4	10.5%	6	31.6%	9	81.8%	
Conditioning regimen	MAC	11	28.2%	5	25.0%	7	63.6%	0.06
	RIC	28	71.8%	15	75.0%	4	36.4%	
Post-Tx Cy use	No	35	89.7%	17	85.0%	2	18.2%	<b>&lt;0.001</b>
	Yes	4	10.3%	3	15.0%	9	81.8%	
ATG use	No	38	97.4%	8	40.0%	11	100 %	<b>&lt;0.001</b>
	Yes	1	2.6%	12	60.0%	0	0.0%	
Acute (a)GVHD	No	20	51.3%	12	60.0%	8	80.0%	0.09
	Yes	19	48.7%	8	40.0%	2	20.0%	
II-IV aGVHD	No	30	76.9%	14	70.0%	10	100 %	
	Yes	9	23.1%	6	30.0%	0	0%	
Chronic(c)GVHD	No	25	64.1%	18	90.0%	9	90.0%	<b>0.02</b>
	Yes	14	35.9%	2	10.0%	1	10.0%	
Severe cGVHD	No	33	84.6%	17	85.0%	10	100 %	
	Yes	6	15.4%	3	15.0%	0	0%	

AlloHCT: Allogeneic stem cell transplantation, ATG: Anti Thymocyte Globulin, BV: Brentuximab vedotin, CPI: Checkpoint inhibitors, Era 1: 2004–2010, Era 2: 2011-2015, Era 3: 2016-2021, GVHD: Graft versus host disease, *KPS*: *Karnofsky Performance Status*, MAC: Myeloablative conditioning, MRD: matched sibling donor, MUD: matched unrelated donor, MMUD: Mismatched unrelated donor, Cy: Cyclophosphamide, RIC: Reduced-intensity conditioning, RT: Radiotherapy, TBI: Total body irradiation, Tx: Transplantation.

**Table 3.** Patients characteristics' regarding to tx year

		Era 1 (2004-2010)		Era 2 (2011-2021)		P
<b>Center</b>	Center1	0	0.0%	28	51.9%	<b>&lt;0.001</b>
	Center2	16	100.0%	11	20.4%	
	Center3	0	0.0%	15	27.8%	
<b>Age</b>		34 (18-16)		36 (21-62)		0.45
<b>Follow-up time, month</b>		53.0 (37.3 – 68.7)		139.0 (26.6-251.4)		<b>0.03</b>
<b>Age (years)</b>	≤40	12	75.0%	37	68.5%	0.62
	>40	4	25.0%	17	31.5%	
<b>Sex</b>	Male	6	37.5%	35	64.8%	0.05
	Female	10	62.5%	19	35.2%	
<b>Pre-alloHCT KPS Score</b>	≤70	7	43.8%	18	33.3%	0.45
	>70	9	56.3%	36	66.7%	
<b>Stage</b>	Early	6	37.5%	18	33.3%	0.76
	Advanced	10	62.5%	36	66.7%	
<b>Pre-alloHCT treatment</b>	≤3 line	3	18.8%	23	42.6%	0.08
	>3 line	13	81.3%	31	57.4%	
<b>RT</b>	No	6	37.5%	32	59.3%	0.13
	Yes	10	62.5%	22	40.7%	
<b>Pre-alloHCT BV</b>	No	16	100.0%	14	25.9%	<b>&lt;0.001</b>
	Yes	0	0.0%	40	74.1%	
<b>Pre-alloHCT CPI</b>	No	16	100.0%	42	77.8%	<b>0.04</b>
	Yes	0	0.0%	12	22.2%	
<b>Pre-allo disease</b>	CR	1	6.3%	10	18.5%	0.46
	PR	4	25.0%	14	25.9%	
	SD/PD	11	68.8%	30	55.6%	
<b>Conditioning regimen</b>	MAC	7	43.8%	16	29.6%	0.29
	RIC	9	56.3%	38	70.4%	
<b>Stem cell source</b>	PB	12	75.0%	50	92.6%	0.07
	BM	3	18.8%	4	7.4%	
	Cord	1	6.3%	0	0.0%	
<b>ATG use</b>	No	12	75.0%	45	83.3%	0.45
	Yes	4	25.0%	9	16.7%	
<b>TBI</b>	No	10	71.4%	39	72.2%	0.95
	Yes	4	27.6%	15	26.8%	

<b>Acute GVHD</b>	N/A	1	6.3%	0	0.0%	0.11
	Yes	8	50.0%	21	38.9%	
	No	7	43.8%	33	61.1%	
<b>Chronic GVHD</b>	N/A	1	6.3%	0	0.0%	0.12
	Yes	5	31.3%	12	22.2%	
	No	10	62.5%	42	77.8%	
<b>Post-alloHCT BV</b>	Yes	0	0.0%	11	20.4%	<0.05
	No	16	100.0%	43	79.6%	
<b>Post-alloHCT CPI</b>	Yes	0	0.0%	8	14.8%	0.10
	No	16	100.0%	46	85.2%	
<b>Disease status at Tx</b>	CR	2	15.4%	25	61.0%	0.01
	PR	6	46.2%	7	17.1%	
	SD/PD	5	38.5%	9	22.0%	
<b>NRM</b>	Yes	7	43.8%	22	40.7%	0.83
	No	9	56.3%	32	59.3%	
<b>Post-alloHCT Day 100 transplant mortality</b>	Yes	5	31.3%	13	24.1%	0.56
	No	11	68.8%	41	75.9%	

AlloHCT: Allogeneic stem cell transplantation, ATG: Anti Thymocyte Globulin, BM: Bone marrow, BV: Brentuximab vedotin, CPI: Checkpoint inhibitors, CR: Complete response, GVHD: Graft versus host disease, *KPS*: *Karnofsky Performance Status*, MAC: Myeloablative conditioning, NRM: Non-relapse mortality, PB: Peripheral blood, PR: Partial response, RIC: Reduced-intensity conditioning, RT: Radiotherapy, SD/PD: Stable disease/Progressive disease, TBI: Total body irradiation.

**Table 4.** Univariate Analysis of GVHD, Overall Survival (OS), Progression-Free Survival (PFS), and Non-Relapse Mortality (NRM)

Variable	Outcome	HR (95% CI)	p-value
Age ( $\leq 40$ vs $>40$ )	OS	1.27 (0.65–2.46)	0.47
Treatment lines ( $\leq 3$ vs $>3$ )	OS	1.38 (0.72–2.65)	0.32
Pre-tx BV	OS	1.23 (0.66–2.28)	0.51
Pre-tx CPI	OS	0.41 (0.12–1.35)	0.14
CPI cycles (1–9 vs 10+)	OS	0.71 (0.31–1.64)	0.43

Variable	Outcome	HR (95% CI)	p-value
CPI to alloHCT (days)	OS	0.85 (0.65–1.12)	0.26
Pre-alloHCT disease status	OS	1.19 (0.62–2.26)	0.59
Conditioning (RIC vs MAC)	OS	1.6 (0.78–3.27)	0.19
Post-tx BV	OS	1.76 (0.73–4.24)	0.20
Post-tx CPI	OS	1.8 (0.64–5.1)	0.26
Post-tx CY	OS	0.36 (0.12–1.01)	0.053
Haplo vs MRD	OS	3.3 (0.96–11.5)	<b>0.005</b>
Post-alloHCT CR/PR vs SD/PD	OS	2.95 (1.32–6.61)	<b>0.008</b>
ATG use	OS	2.15 (1.04–4.42)	<b>0.037</b>
KPS ≤70	OS	0.18 (0.08–0.42)	<b>0.000</b>
Pre-tx CPI	PFS	0.39 (0.14–1.09)	0.073
Post-tx CY	PFS	0.44 (0.18–1.04)	0.061
KPS ≤70	PFS	0.26 (0.11–0.57)	<b>0.01</b>
Haplo vs MRD	PFS	3.9 (1.12–13.5)	<b>0.032</b>
Post-alloHCT CRPR vs SDPD	PFS	3.8 (1.86–7.76)	<b>0.000</b>
Post-tx BV	PFS	0.68 (0.34–1.35)	0.27
Post-tx CPI	PFS	0.61 (0.28–1.32)	0.20
Donor type	cGVHD	—	<b>0.039</b>
All variables above	aGVHD	—	>0.05
ATG use	NRM	2.77 (1.24–6.16)	<b>0.01</b>

**Abbreviations:** OS, overall survival; PFS, progression-free survival; NRM, non-relapse mortality; GVHD, graft-versus-host disease; aGVHD, acute GVHD; cGVHD, chronic GVHD; CRPR, complete response or partial response; SDPD, stable disease or progressive disease; KPS, Karnofsky performance status; RIC, reduced-

intensity conditioning; MAC, myeloablative conditioning; MRD, matched related donor; Haplo, haploidentical donor; ATG, anti-thymocyte globulin; BV, brentuximab vedotin; CPI, checkpoint inhibitor; CY, cyclophosphamide; alloHCT, allogeneic hematopoietic cell transplantation; HR, hazard ratio; CI, confidence interval.

**Table 5.** Multivariate Analysis of OS, PFS, NRM, and cGVHD

Variable	Outcome	HR (95% CI)	p-value
KPS ≤70	OS	0.1 (0.01–0.66)	<b>0.01</b>
Post-alloHCT CRPR vs SDPD	OS	4.24 (1.32–13.6)	<b>0.01</b>
KPS ≤70	PFS	0.11 (0.01–0.68)	<b>0.01</b>
Pre-alloHCT CRPR vs SDPD	PFS	3.51 (1.2–10.2)	<b>0.02</b>
Post-alloHCT CRPR vs SDPD	PFS	2.76 (1.15–6.62)	<b>0.02</b>
Post-tx CPI	PFS	0.28 (0.07–1.14)	0.07
KPS >70	NRM	0.05 (0.04–0.96)	<b>0.047</b>
Pre-tx BV	NRM	0.11 (0.0–0.72)	<b>0.035</b>
Post-tx CPI	NRM	0.0 (0.0–0.78)	<b>0.039</b>
ATG use	cGVHD	0.13 (0–0.8)	<b>0.039</b>

**Abbreviations:** ATG, anti-thymocyte globulin; alloHCT, allogeneic hematopoietic cell transplantation; BV, brentuximab vedotin; CPI, checkpoint inhibitor; CR/PR, complete response/partial response; cGVHD, chronic graft-versus-host disease; KPS, Karnofsky Performance Status; NRM, non-relapse mortality; OS, overall survival; PFS, progression-free survival; Post-tx, post-transplant; Pre-tx, pre-transplant; SD/PD, stable disease/progressive disease.

**Table 6.** Fine-Gray Subdistribution Hazard Ratios for Non-Relapse Mortality

Variable	sHR (95% CI)	p-value
Pre-alloHCT BV	0.60 (0.38–0.94)	<b>0.026</b>
Post-alloHCT BV	0.75 (0.47–1.20)	0.230
Pre-alloHCT CPI	1.21 (0.74–1.98)	0.440
Post-alloHCT CPI	0.92 (0.58–1.46)	0.670
aGVHD	1.41 (1.01–1.97)	<b>0.043</b>
cGVHD	1.32 (0.91–1.91)	0.130

Variable	sHR (95% CI)	p-value
Haploidentical	0.84 (0.53–1.33)	0.460
KPS $\leq$ 70	1.36 (0.92–2.01)	0.120
Disease: SDPD	1.19 (0.78–1.82)	0.410

Abbreviations: alloHCT, allogeneic hematopoietic cell transplantation; aGVHD, acute graft-versus-host disease; BV, brentuximab vedotin; CI, confidence interval; CPI, checkpoint inhibitor; cGVHD, chronic graft-versus-host disease; KPS, Karnofsky Performance Status; NRM, non-relapse mortality; SDPD, stable disease/progressive disease; sHR, subdistribution hazard ratio.

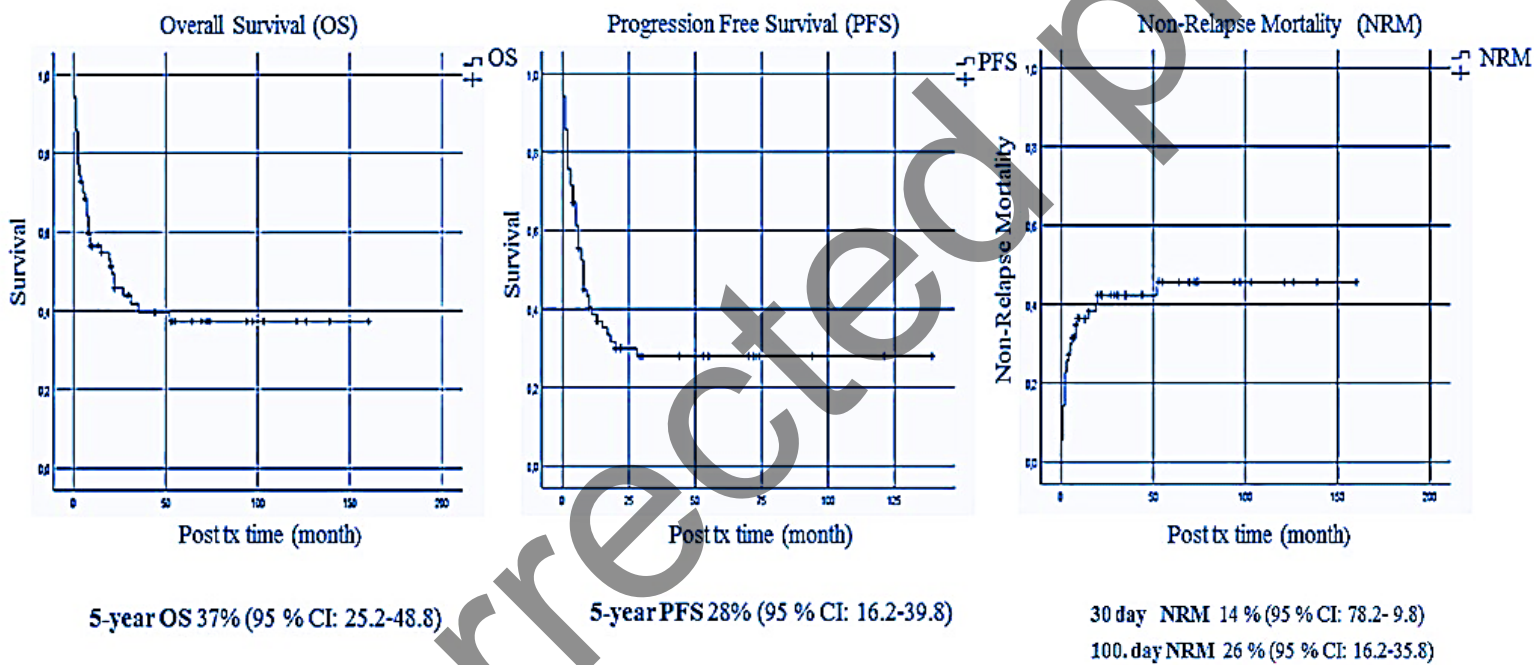
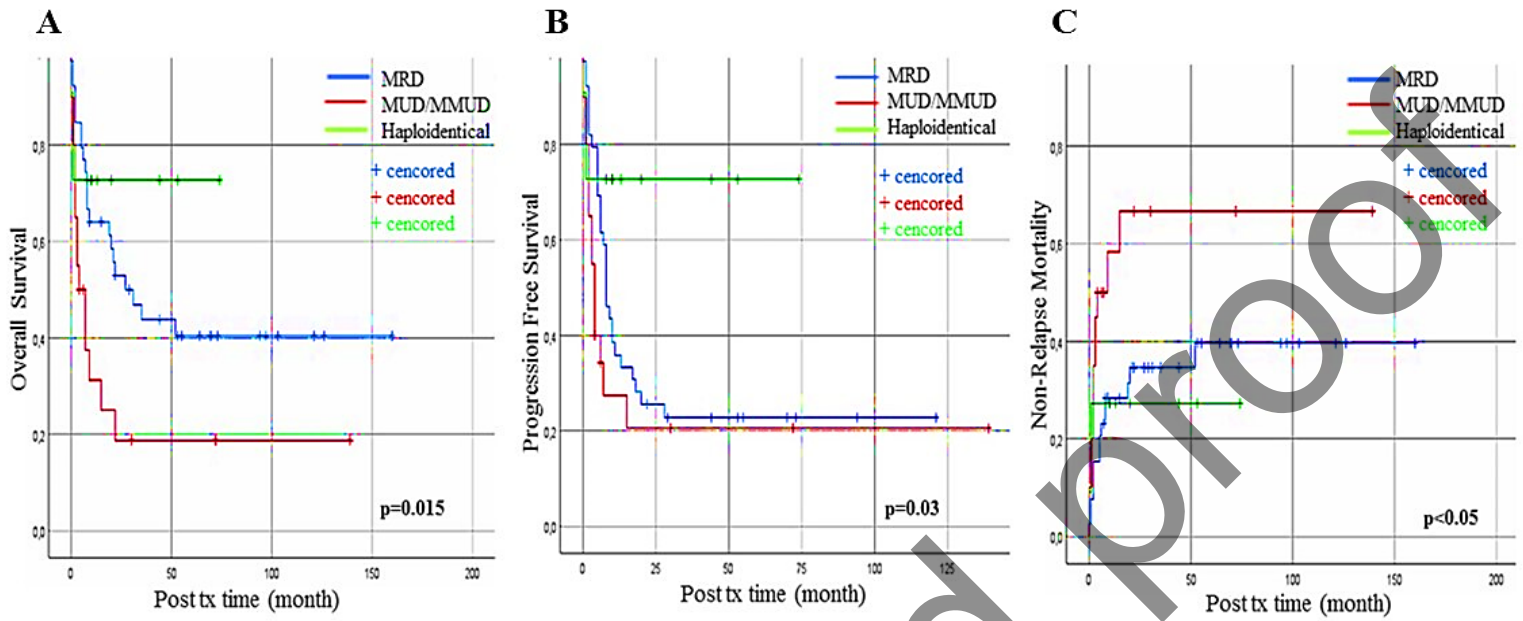
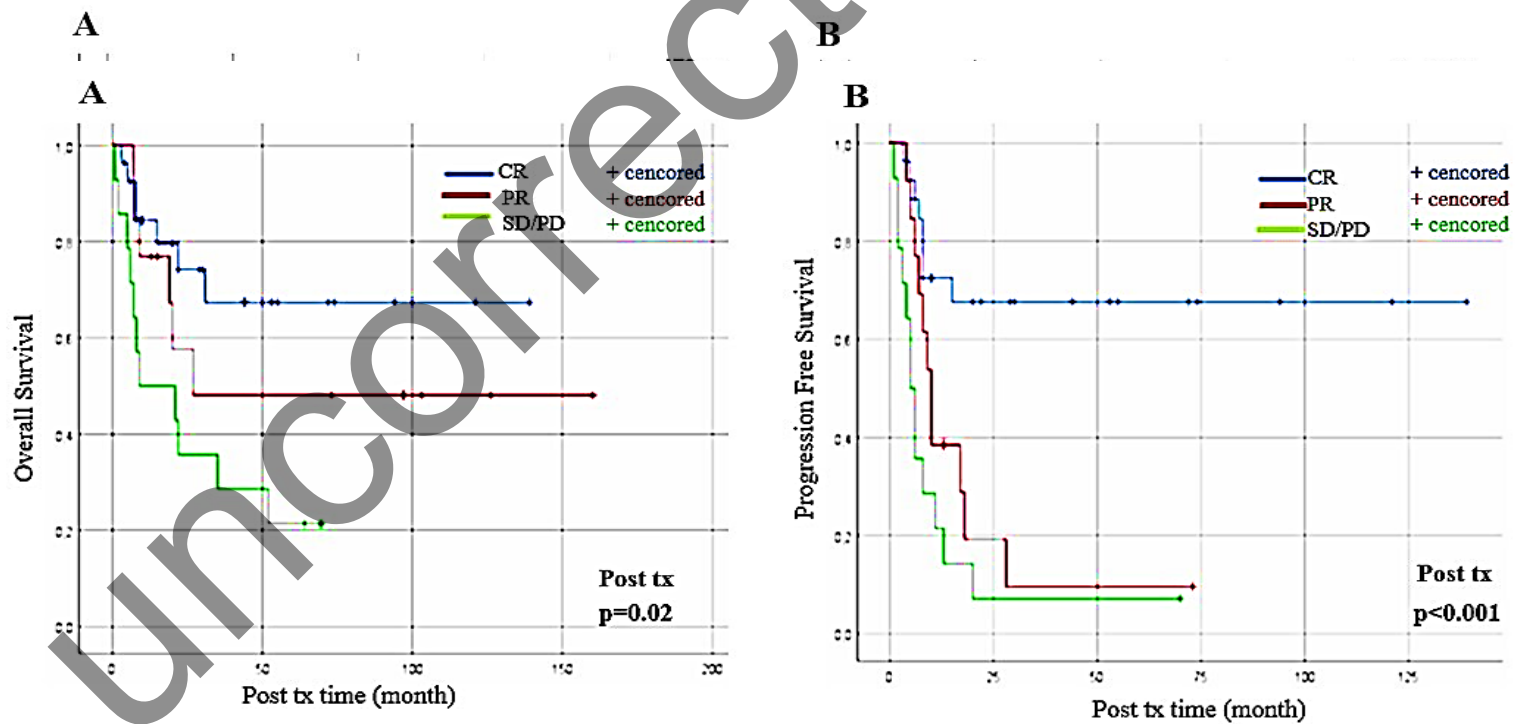


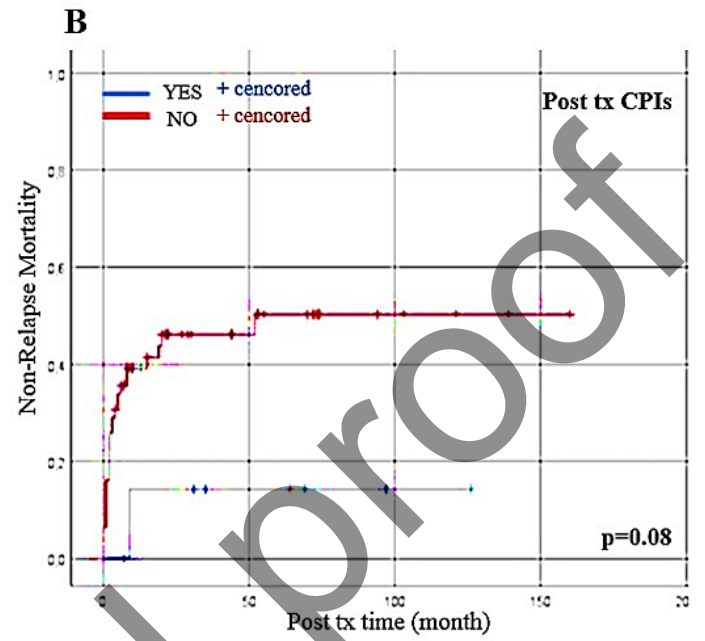
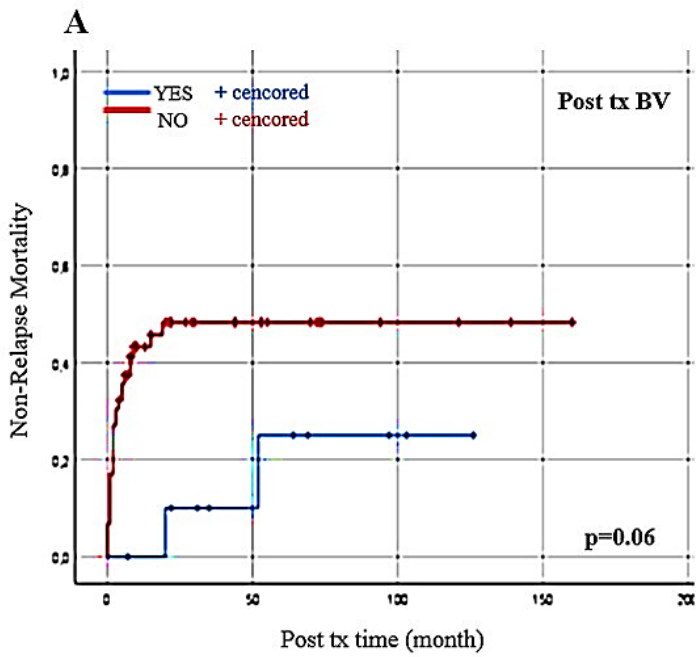
Figure 1. Overall survival, progression-free survival, non-relapse mortality after alloHCT



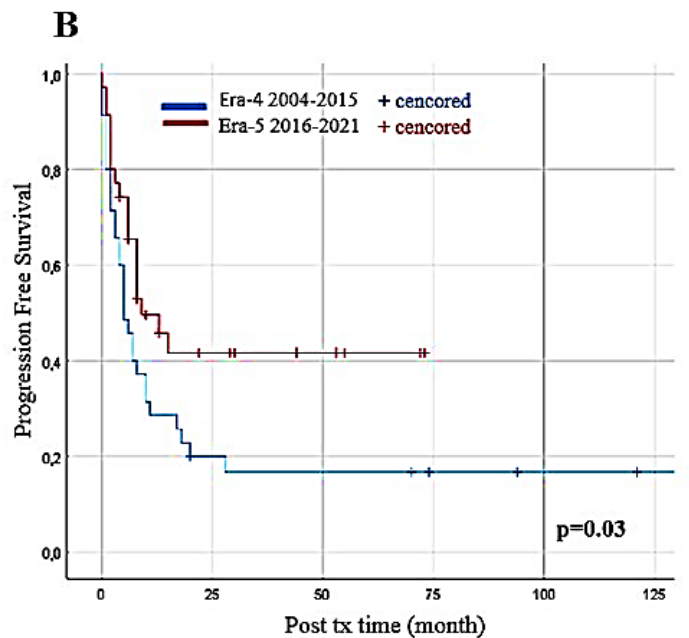
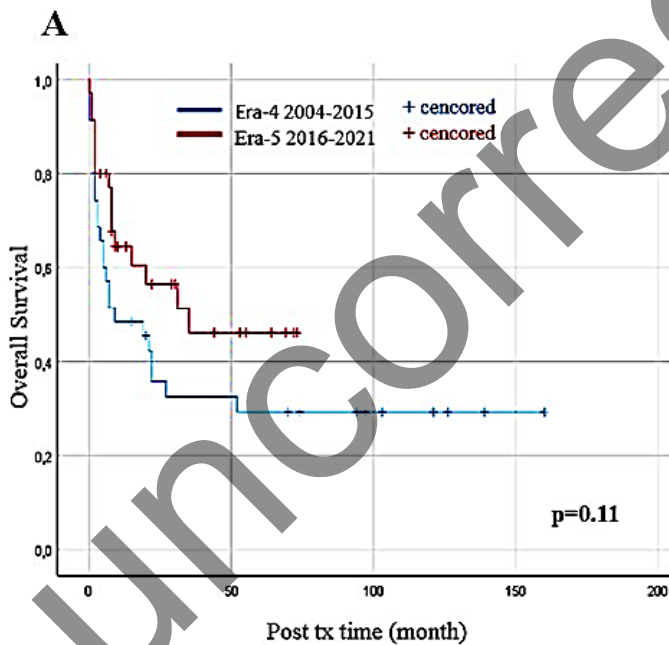
**Figure 2.** (A) Overall survival, (B) progression-free survival, and (C) non-relapse mortality K-M curves based on donor type.



**Figure 4.** (A) Overall survival, (B) progression-free survival according to the response status post alloHCT



**Figure 5.** Non-relapse mortality according to the use of post alloHCT (A) BV, (B) CPI.



**Figure 6.** (A) Overall survival, (B) progression-free survival according to era of Tx.