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Comprehensive evaluation of safety and efficacy: TEAM *versus* BEAM as conditioning for autologous transplantation in patients with lymphoma

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Author Contributions

WW was responsible for data retrieval: screening: data analysis: and article writing. DL was mainly responsible for analysis and interpretation of data as well as article writing and review. HCW: HW: PL: JM: QH: LNX: KL: WJZ: and LJX were responsible for project management. ZJL was responsible for the study design and project management.

Competing Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data Availability Statement

The original data contributions presented in the study are included in the article or supplementary material. Further inquiries can be directed to the corresponding author.

Key Words: Autologous Hematopoietic Stem Cell Transplantation; Thiotepa; Carmustine; Lymphoma

Autologous hematopoietic stem cell transplantation (ASCT) is an important treatment for some lymphomas: which can effectively prolong the progression-free survival (PFS) and even overall survival (OS) of chemotherapy-sensitive lymphoma patients.[1] The BEAM regimen: which comprises carmustine: etoposide: cytarabine: and melphalan: is currently the most widely used conditioning regimen for ASCT in patients with lymphoma.[2] However: carmustine is associated with instability of the production: mucositis and pulmonary toxicity: which limits its use in certain conditions.[3]

Thiotepa: is widely used as a pretransplant conditioning regimen for hematologic malignancies: such as multiple myeloma: β-thalassemia: acute leukemia:[4-7] especially for primary central nervous system lymphoma (PCNSL) owing to its superior ability to cross the blood–brain barrier.[8] These suggested that thiotepa-based conditioning regimens were safe: even conducting a favorable long-term survival in certain cohort. Due to carmustine shortage during the COVID-19 pandemic: our center has adopted the TEAM regimen as a pretreatment strategy for patients with lymphoma receiving ASCT. Given the limited data comparing BEAM and TEAM on the efficacy and safety:[9-11] this study sought to address these questions.

We retrospectively analyzed 155 adult lymphoma patients (BEAM: n=101; TEAM: n=54) who underwent ASCT at our center between January 1: 2020 and June 1: 2025. All patients were diagnosed according to the World Health Organization 2016 criteria.

Patients with PCNSL were excluded. The BEAM regimen consisted of carmustine 300 mg/m² day −7; cytarabine 200 mg/m² days −6 to −3; etoposide 200 mg/m² days −6 to −3; melphalan 140 mg/m² day −2.[12] The TEAM regimen replaces carmustine with thiotepa 8 mg/kg on day −7.[11] The TEAM regimen was used from November 2023 as the disruption supply of carmustine. All procedures performed in this study were in compliance with relevant ethical regulations.

OS was defined as the time from ASCT to death or the final follow-up. PFS was defined as the time from ASCT to progressive disease (PD): death: or the final follow-up. Cumulative incidence of relapse (CIR)was defined as the time from ASCT to the first occurrence of relapse. Neutrophil and platelet engraftment were defined as the first day of ANC $\geq 0.5\times10^{9}$/L and PLT $\geq 20\times10^{9}$/L without PLT transfusion for three days.[13] The length of hospital stay was defined as the time from CD34+cells transplanted to hospital discharge. Following the Lugano 2014 criteria: the therapeutic evaluation was divided into complete response (CR): partial response (PR): stable disease: and PD.[14]

The median age of 47 (IQR 36-55) years for the total cohort and including 83 (53.5%) male patients. Among them: 82 (52.9%) patients had DLBCL: 14 (9.0%) had indolent B-cell lymphoma: 41 (26.5%) had T-cell non-Hodgkin lymphoma: 3 (1.9%) had Burkitt lymphoma: and 15 (9.7%) patients had Hodgkin lymphoma. According to the Lugano staging system: 125 (80.6%) patients were at stage III/IV. Prior to transplantation: 139

(89.7%) patients achieved CR: and 16 (10.3%) patients achieved PR. After initial diagnosis: 92 patients (59.4%) received first-line therapy: 46 (29.7%) received second-line therapy: and 17 (11.0%) received more than two lines of therapy before ASCT.

The age: diagnosis: Lugano stage: Eastern Cooperative Oncology Group score: remission status and routine blood test results: were comparable between the BEAM and TEAM groups (**Table 1**). Additionally: we assessed pulmonary function prior to transplantation: as detailed in **Table S1**. Maximum voluntary ventilation was more frequent in TEAM group (25.0% vs 9.6%: P=0.016: **Table S1**): indicating slightly worse baseline pulmonary function. Other lung function parameters and hematopoietic cell transplantation-comorbidity index (HCT-CI) scores were comparable between groups.

Adverse events during ASCT are summarized in **Table 2**. During the transplantation process: the incidences of sepsis: fungal infection: and pneumonia in the TEAM group were lower than those in the BEAM group: but with no significant difference. (**Table 2**). The time to neutrophil and thrombocyte engraftment were slightly prolonged in the TEAM group (Table 2); however: this did not lead to adverse outcomes such as increased infection rates or elevated bleeding risks. There was no significant difference in the number of red blood cell transfusions during transplantation between the groups.

The TEAM group required more platelet transfusions (median 3.0 units vs. 2.0 units: P<0.010). A retrospective study evaluated the potential risks and benefits in 47 patients receiving TEAM compared with 75 matched patients receiving BEAM: including those with DLBCL: follicular lymphoma: and Hodgkin lymphoma.[9] The incidences of common infectious and non-infectious complications: including secondary malignancies: were comparable between the TEAM and BEAM cohorts.[9] Collectively: our results suggested that TEAM has a safety profile comparable to that of BEAM.

Follow-up assessment was completed as of August 31: 2025. Four patients (all in the BEAM group) were lost to follow-up after discharge and were excluded from the survival analysis. Among the analyzed patients: the median follow-up time was 25.8 months (range: 3.1–58.6 months). After transplantation: 29 patients (19.2%) experienced relapse: and 4 patients (2.6%) died: with all deaths attributed to disease progression. The overall 1-year OS rate :1-year PFS rate and 1-year CIR rate are shown in **Figure 1A: C and E.**

Cox regression analysis was performed to identify factors potentially influencing prognosis: due to the short follow-up period and the small number of deaths in this study: Cox regression analysis for OS was not performed. In the overall patient cohort: univariate analysis showed that HCT-CI score ≥3: ≥3 treatment lines prior to ASCT: and no CR before ASCT were significantly associated with PFS. (**Table S2**).

Multivariate analysis showed that HCT-CI score ≥3 (HR=3.84: 95% CI: 1.84–8.01: P<0.001) and ≥3 treatment lines prior to ASCT (HR=2.39: 95% CI: 1.00–5.67: P=0.049) were independent risk factors for PFS (**Table S2**).In patients with the DLBCL subtype: the 1-year PFS rates for the CR1 and CR2 groups were 92.2% (95% CI: 84.1%–100.0%) and 80.1% (95% CI: 64.4%–99.7%): respectively (P = 0.1177). In patients with the TCL subtype: the 1-year PFS rates for the CR1 and CR2 groups were 83.4% (95% CI: 69.6%–99.9%) and 75.0% (95% CI: 50.3%–100.0%): respectively (P = 0.7588).

The median follow-up duration was 11.9 months (range: 3.1–21.1 months) in the TEAM group and 36.7 months (range: 5.1–58.6 months) in the BEAM group. The CR rates at 1 month (90.7% vs. 91.8%: P=1.000): 3 months (87.0% vs. 86.6%: P=1.000): and 6 months (83.3% vs. 84.5%: P=0.821) after transplantation were comparable between TEAM and BEAM cohorts. After transplantation: 50% (5/10) of patients in the BEAM group and 66% (4/6) of those in the TEAM group converted from partial response to CR. Following transplantation: disease progression occurred in 9 (16.7%) patients in the TEAM cohort and 20 (20.6%) in the BEAM cohort: while death occurred in 1 (1.9%) and 3 (3.1%) patients: respectively. There were no significant differences between the TEAM and BEAM groups in 1-year OS: 1-year PFS: or the 1-year CIR (Figure 1B: D: F). The PFS in subgroups of patients classified by age: HCT-CI score: KPS score: Lugano stage: treatment lines prior ASCT: lymphoma subtypes (DLBCL and PTCL) and remission status (CR1: CR2 and PR) were non-significant between the

BEAM and TEAM cohorts (**Figure S1**). Post-transplant maintenance therapy was received by 11.1% of TEAM patients (6/54; 3 immunotherapy: 3 targeted) and 28.9% of BEAM patients (28/97; 17 targeted: 6 immunotherapy: 5 combined; P=0.014). The 1-year PFS did not differ between the BEAM and TEAM regimens in the cohort with maintenance(92.4% [95% CI: 82.8%–100.0%] vs. 80.0% [95% CI: 51.6%–100.0%]: P = 0.5128) and without maintenance(83.8% [95% CI: 75.5%–93.0%] vs. 80.7% [95% CI: 69.3%–94.0%]: P = 0.9586).

In the BEAM group: HCT-CI score ≥3 and treatment lines ≥3 before ASCT were significantly associated with PFS. Multivariate analysis showed that HCT-CI score ≥3 (HR=8.81: 95% CI: 3.47–22.34: P<0.001) and ≥3 treatment lines before ASCT (HR=3.31: 95% CI: 1.14–9.58: P=0.027) were independent risk factors for poorer PFS (**Table S2**). In the TEAM group: univariate analysis showed that ≥3 treatment lines prior to ASCT and no CR before ASCT were significantly associated with PFS. Multivariate analysis showed that ≥3 treatment lines prior to ASCT (HR=9.07: 95% CI: 2.26–36.41: P=0.002) and no CR before ASCT (HR=7.10: 95% CI: 1.50–33.65: P=0.014) were significantly associated with PFS (**Table S2**). Previous studies have also recognized disease remission status at the time of transplantation as a powerful prognostic indicator[15]. Gherman et al. retrospectively analyzed clinical factors impacting outcomes in patients undergoing ASCT after TEAM (n=63) and BEAM (n=333).[11] In the BEAM cohort: decreased OS was associated with pre-transplant

DLCOcSB (diffusing capacity of the lung for carbon monoxide: single-breath) ≤60%: PD: KPS ≤80%: HCT-CI ≥4: and cardiac disease.[11] Their results indicated that the use of BEAM conditioning in patients with impaired pulmonary function was associated with worse outcomes. In the TEAM cohort: only pre-transplant PD predicted inferior OS.[11]

In summary: this retrospective analysis demonstrates that the TEAM regimen is a feasible alternative to BEAM as a conditioning therapy prior to ASCT in patients with lymphoma. The two regimens showed comparable CR rates: 1-year PFS: OS: and CIR rates: and this efficacy appeared to be applicable across different lymphoma subtypes. The inherent bias of a historical cohort design limits our findings to a historical comparison; longer follow-up is needed to confirm long-term equivalence.

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Table 1. Basic clinical characteristics comparing patients conditioned with the BEAM and TEAM regimens.

	TEAM (n=54)	BEAM (n=101)	*P VALUE*
Age at diagnosis: median (IQR)	47 (37-55)	45 (33-53)	0.196
Age at ASCT: median (IQR)	48 (38-56)	47 (35-55)	0.275
Male: n (%)	29 (53.7%)	54 (53.5%)	1.000
Diagnosis: n (%)			0.353
DLBCL	31 (57.4%)	51 (50.5%)	
Indolent B-NHL	2 (3.7%)	12 (11.9%)	
T-NHL	15 (27.8%)	26 (25.7%)	
Burkitt's lymphoma	0 (0.0%)	3 (3.0%)	
Hodgkin's lymphoma	6 (11.1%)	9 (8.9%)	
Lugano stage at diagnosis: n (%)			0.671
I-II	9 (16.7%)	21 (20.8%)	
III-IV	45 (83.3%)	80 (79.2%)	
The number of extranodal organs at diagnosis: median (IQR)	2 (0-3)	2 (0-3)	0.642
B symptoms at diagnosis: n (%)	13 (24.1%)	39 (38.6%)	0.076
Fever: n (%)	10 (18.5%)	27 (26.7%)	0.324
Night sweats: n (%)	5 (9.3%)	17 (16.8%)	0.235
Unexplained weight loss: n (%)	2 (3.7%)	13 (12.9%)	0.088
KPS≤80 at ASCT: n (%)	14 (25.9%)	32 (31.7%)	0.580
ECOG score at ASCT: n (%)			1.000
0-2	52 (95.3%)	96 (95.0%)	
≥3	2 (3.7%)	5 (5.0%)	
Treatment lines prior HSC collection: n (%)			0.545
1-2	51 (94.4%)	91 (90.1%)	
≥3	3 (5.6%)	10 (9.9%)	
Treatment lines prior ASCT: n (%)			1.000
1-2	48 (88.9%)	90 (89.1%)	
≥3	6 (11.1%)	11 (10.9%)	
Remission status at ASCT: n (%)			0.895
CR1	28 (51.9%)	55 (54.5%)	
CR2	14 (25.9%)	28 (27.7%)	
CR3/4	6 (11.1%)	8 (7.9%)	
PR1	4 (7.4%)	5 (5.0%)	
PR2/3	2 (3.7%)	5 (5.0%)	

CD34+ cells transplanted: (10^6/kg): median (IQR)	4.7(3.0-7.0)	4.0 (2.9-5.5)	0.203
WBC at ASCT: (10^9/L): median (IQR)	4.0 (2.7-5.7)	3.6 (2.8-4.9)	0.410
RBC at ASCT: (10^{12}/L): median (IQR)	3.9 (3.4-4.3)	4.0 (3.3-4.3)	0.931
PLT at ASCT: (10^9/L): median (IQR)	190.5 (149-228)	197 (151-246)	0.640
HB at ASCT: (g/L): median (IQR)	120 (109-129)	119 (105-130)	0.700
ANC at ASCT: (10^9/L): median (IQR)	2.4 (1.6-3.6)	2.1 (1.5-3.5)	0.386
Lymphocyte at ASCT: (10^9/L): median (IQR)	0.8 (0.5-1.1)	0.8 (0.6-1.1)	0.724
LVEF at ASCT: (%): median (IQR)	64.5 (62-66)	64 (61.3-65.8)	0.498

Abbreviations: DLBCL: diffuse large B-cell lymphoma; B-NHL: B-cell non-Hodgkin lymphoma; T-NHL: T-cell non-Hodgkin lymphoma; KPS: Karnofsky performance status; ECOG: Eastern Cooperative Oncology Group; HSC: hematopoietic stem cell; ASCT: autologous hematopoietic stem cell transplantation; CR: complete response; PR: partial response; WBC: white blood cells; RBC: red blood cells; PLT: platelet count; HB: hemoglobin; ANC: absolute neutrophil count; LVEF: left ventricular ejection fraction; IQR: interquartile range.

Table 2. Adverse events and engraftment times during ASCT with the BEAM and TEAM conditioning regimens.

	TEAM (n=54)	BEAM (n=101)	*P* VALUE
Adverse events during ASCT			
Diarrhea: n (%)	31 (57.4%)	57 (56.4%)	1.000
Fever: n (%)	45 (83.3%)	69 (68.3%)	0.056
Nausea and vomiting: n (%)	39 (72.2%)	75 (74.3%)	0.849
Septicemia: n (%)	1 (1.9%)	7 (6.9%)	0.263
Fungal infection: n (%)	1 (1.9%)	6 (5.9%)	0.423
Pneumonia: n (%)	5 (9.3%)	19 (18.8%)	0.162
Aphthous ulcer: n (%)	11 (20.4%)	17 (16.8%)	0.662
cardiotoxicity: n (%)	1 (1.9%)	7 (6.9%)	0.263
Gastrointestinal hemorrhage: n (%)	13 (24.1%)	19 (18.8%)	0.533
Hospital stays from transplanted to discharge (day): median (IQR)	16 (14-19)	14 (13-17)	0.092
The lowest WBC: median (IQR)	0.03 (0.02-0.04)	0.03 (0.02-0.05)	0.031
The lowest ANC: median (IQR)	0.00 (0.00-0.03)	0.00 (0.00-0.01)	0.176
The lowest HB: median (IQR)	82 (68-93)	78 (64-87)	0.234
The lowest PLT: median (IQR)	7 (5-10)	7 (4-12)	0.953
Transfusion and engraftment time			
RBC transfusion(U): median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.412
Patients received RBC transfusion: n (%)	9 (16.7%)	21 (20.8%)	0.536
PLT transfusion(U): median (IQR)	3.0 (2.9-5.0)	2.0 (2.0-3.0)	<0.010
NET (day): median (IQR)	10 (10-11)	10 (9-11)	0.024
TET (day): median (IQR)	14 (12-18)	12 (11-14)	<0.010

Abbreviations: ASCT: autologous hematopoietic stem cell transplantation; WBC: white blood cells; RBC: red blood cells; HB: hemoglobin; ANC: absolute neutrophil count; PLT: platelet count; NET: neutrophil engraftment time; TET: thrombocyte engraftment time; IQR: interquartile range.

Figure Legends

Figure 1. Kaplan－Meier survival curves of patients in BEAM and TEAM groups post ASCT. The OS (A)，PFS (C) and 1-year CIR (E) of the total 151 patients with lymphoma post ASCT. The OS (B), PFS (D) and 1-year CIR (F) compared in the BEAM and TEAM groups post ASCT. ASCT: autologous hematopoietic stem cell transplantation; OS: overall survival; PFS: progress free survival; CIR: cumulative incidence of relapse.

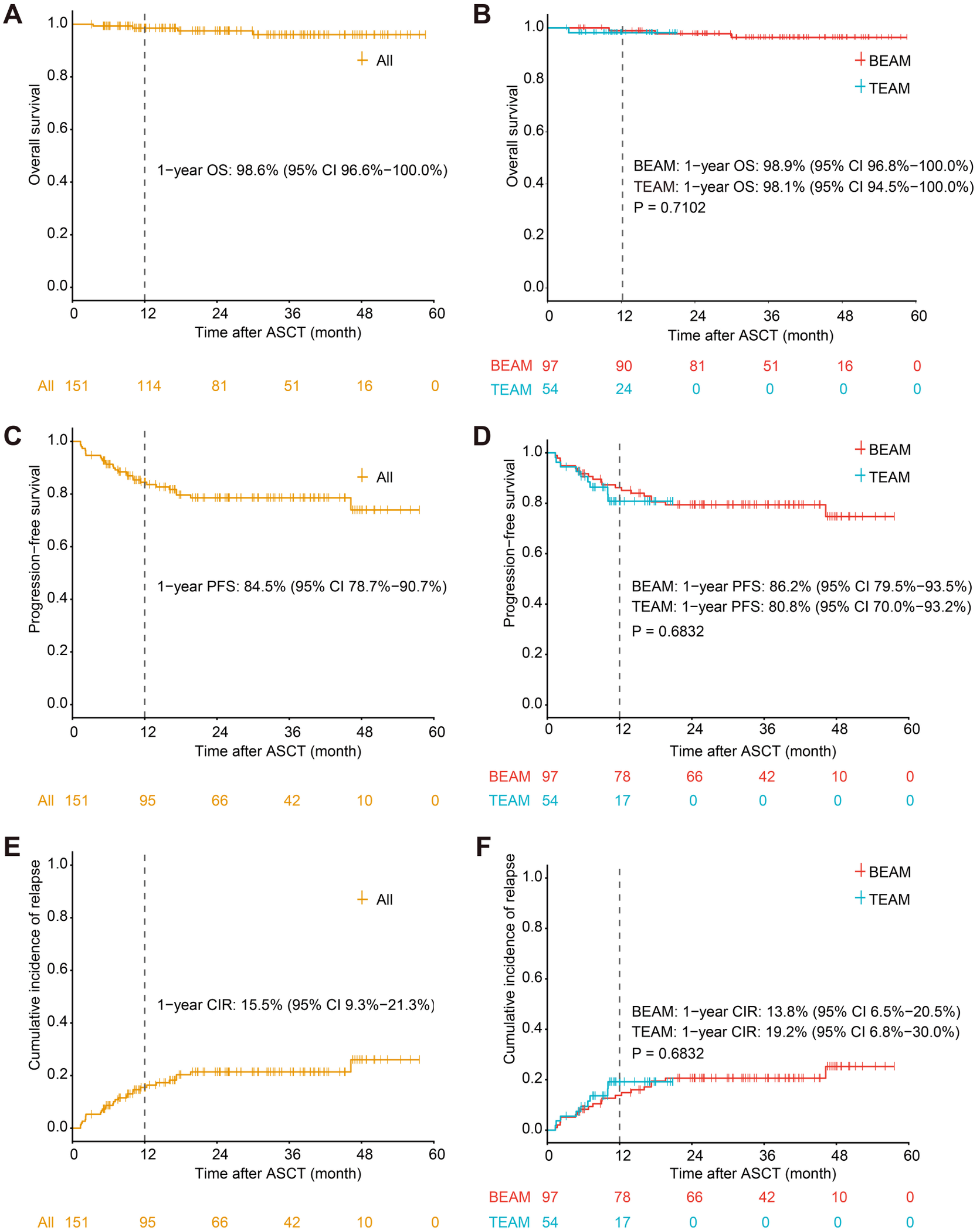

A
Overall survival
All
1−year OS: 98.6% (95% CI 96.6%−100.0%)
Time after ASCT (month)
All 151 114 81 51 16 0
B
Overall survival
BEAM
TEAM
BEAM: 1−year OS: 98.9% (95% CI 96.8%−100.0%)
TEAM: 1−year OS: 98.1% (95% CI 94.5%−100.0%)
P = 0.7102
Time after ASCT (month)
BEAM 97 90 81 51 16 0
TEAM 54 24 0 0 0 0
C
Progression−free survival
All
1−year PFS: 84.5% (95% CI 78.7%−90.7%)
Time after ASCT (month)
All 151 95 66 42 10 0
D
Progression−free survival
BEAM
TEAM
BEAM: 1−year PFS: 86.2% (95% CI 79.5%−93.5%)
TEAM: 1−year PFS: 80.8% (95% CI 70.0%−93.2%)
P = 0.6832
Time after ASCT (month)
BEAM 97 78 66 42 10 0
TEAM 54 17 0 0 0 0
E
Cumulative incidence of relapse
All
1−year CIR: 15.5% (95% CI 9.3%−21.3%)
Time after ASCT (month)
All 151 95 66 42 10 0
F
Cumulative incidence of relapse
BEAM
TEAM
BEAM: 1−year CIR: 13.8% (95% CI 6.5%−20.5%)
TEAM: 1−year CIR: 19.2% (95% CI 6.8%−30.0%)
P = 0.6832
Time after ASCT (month)
BEAM 97 78 66 42 10 0
TEAM 54 17 0 0 0 0

Table S1. HCT-CI and lung function parameters in patients conditioned with BEAM and TEAM prior to ASCT.

	TEAM (n=54)	BEAM (n=101)	*P* VALUE
HCT-CI score ≥3, n (%)	11 (20.4%)	21 (20.8%)	1.000
VC downgrade, n/N (%)	5/52 (9.6%)	8/88 (9.1%)	1.000
FVC downgrade, n/N (%)	5/52 (9.6%)	6/94 (6.4%)	0.522
FEV_1 downgrade, n/N (%)	8/52 (15.4%)	11/94 (11.7%)	0.609
FEV_1/FVC downgrade, n/N (%)	5/52 (9.6%)	13/94 (13.8%)	0.602
NEF50 downgrade, n/N (%)	10/52 (19.2%)	15/94 (16.0%)	0.650
NEF25 downgrade, n/N (%)	32/52 (61.5%)	50/94 (53.2%)	0.385
MMEF downgrade, n/N (%)	16/52 (30.8%)	29/94 (30.9%)	1.000
MVV downgrade, n/N (%)	13/52 (25.0%)	9/94 (9.6%)	0.016
TLC downgrade, n/N (%)	4/52 (7.7%)	7/42 (16.7%)	0.210
RV, n/N (%)			0.506
downgrade	1/52 (1.9%)	1/42 (2.4%)	
upgrade	30/52 (57.7%)	19/42 (45.2%)	
RV/TLC, n/N (%)			0.452
downgrade	0/52 (0.0%)	1/42 (2.4%)	
upgrade	34/52 (65.4%)	24/42 (57.1%)	
DLCO downgrade, n/N (%)	32/52 (61.5%)	26/59 (61.9%)	1.000
DLCO/VA downgrade, n/N (%)	25/52 (48.1%)	22/59 (52.4%)	0.836

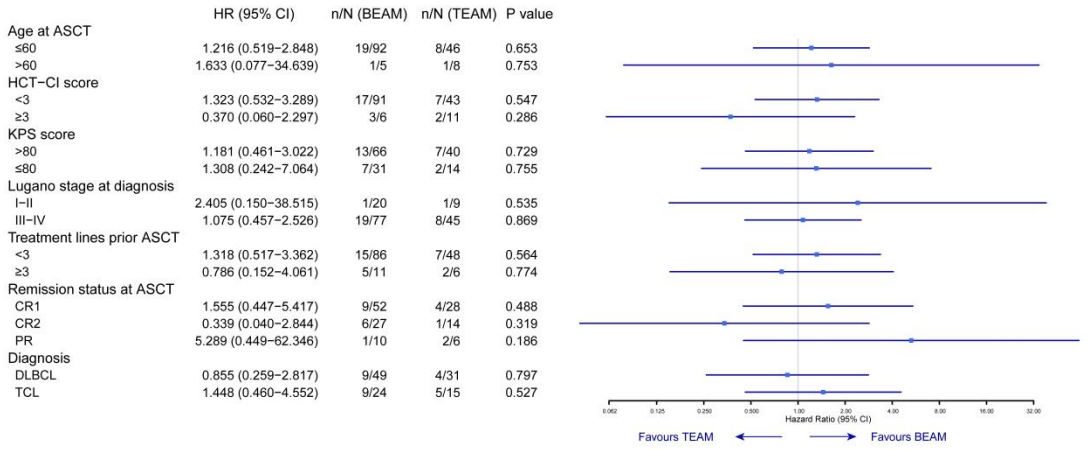
Abbreviations: HCT-CI: hematopoietic cell transplantation-comorbidity index; VC: vital capacity; FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s; NEF50: normalized expiratory flow at 50% of FVC; NEF25: normalized expiratory flow at 25% of FVC; MMEF: maximal mid-expiratory flow; MVV: maximum voluntary ventilation; TLC: total lung capacity; RV: residual volume; DLCO: diffusing capacity of the lung for carbon monoxide; VA: alveolar volume.

Table S2. Univariate and multivariable analyses of risk factors associated with PFS in the BEAM, TEAM, and overall patient cohorts

variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Overall				
Age ≥ 60 years	2.09 (0.72-6.03)	0.174	-	-
Lugano stages III/IV	29.72 (0.69-1284.96)	0.078	-	-
HCT-CI score ≥3	4.79 (2.31-9.94)	<0.001	3.84 (1.84-8.01)	<0.001
KPS ≤ 80%	1.26 (0.59-2.71)	0.554	-	-
≥3 treatment lines before ASCT	2.95 (1.25-6.96)	0.013	2.39 (1.00-5.67)	0.049
Non-CR before ASCT	2.60 (1.06-6.39)	0.037	1.604 (0.649-3.963)	0.306
BEAM (n=97)				
Age ≥ 60 years	1.04 (0.14-7.82)	0.967	-	-
Lugano stages Ⅲ/Ⅳ	31.14 (0.40-2429.77)	0.122	-	-
HCT-CI score ≥3	8.68 (3.45-21.82)	<0.001	8.81 (3.47-22.34)	<0.001
KPS ≤ 80%	1.18 (0.47-2.96)	0.730	-	-
≥3 treatment lines before ASCT	3.24 (1.16-9.01)	0.025	3.31(1.14-9.58)	0.027
Non-CR before ASCT	1.58 (0.46-5.41)	0.463	-	-
TEAM (n=54)				
Age ≥ 60 years	3.04 (0.76-12.20)	0.116	-	-
Lugano stages Ⅲ/Ⅳ	26.74 (0.01-52542.08)	0.396	-	-
HCT-CI score ≥3	1.13 (0.23-5.43)	0.883	-	-
KPS ≤ 80%	1.45 (0.36-5.78)	0.603	-	-
≥3 treatment lines before ASCT	9.17 (2.44-34.47)	0.001	9.07 (2.26-36.41)	0.002
Non-CR before ASCT	7.13 (1.72-29.58)	0.007	7.10 (1.50-33.65)	0.014

Abbreviations: PFS: progression-free survival; HR: hazard ratio; CI: confidence interval; HCT-CI: hematopoietic cell transplantation-comorbidity index; KPS: Karnofsky performance status; ASCT: autologous hematopoietic stem cell transplantation; CR: complete response.

Figure S1. Subgroup analysis of progression-free survival (PFS) comparing TEAM versus BEAM regimens. Forest plot displaying hazard ratios (HRs) and 95% confidence intervals (CIs) for PFS in predefined subgroups based on clinical characteristics.



Abbreviations: ASCT: autologous hematopoietic stem cell transplantation; HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index; KPS: Karnofsky Performance Status; CR: complete response; PR: partial response; DLBCL: diffuse large B-cell lymphoma; B-NHL: B-cell non-Hodgkin lymphoma; T-NHL: T-cell non-Hodgkin lymphoma; n/N: number of events/total number of patients.