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Liposomal Mitoxantrone- versus Pegylated Liposomal Doxorubicin-Based Conditioning for Allogeneic HSCT in Acute Leukemia: A Propensity Score-Matched Study

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Abstract

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative treatment for acute leukemia, but regimen-related toxicity remains a major barrier to improved outcomes. We conducted a retrospective propensity score-matched study to compare liposomal mitoxantrone (LipMito)-based and pegylated liposomal doxorubicin (PLD)-based conditioning in 132 patients undergoing allo-HSCT. 44 patients received LipMito-based conditioning and 88 received PLD-based conditioning. Baseline characteristics were balanced after matching. Compared with PLD, LipMito was associated with faster hematopoietic recovery($P = 0.001$), lower cumulative incidences of grade II–IV and grade III–IV aGVHD($P = 0.014$;$P = 0.038$), reduced grade III–IV hemorrhagic cystitis($P = 0.011$), and less EBV viremia($P = 0.001$). Oral mucositis and cardiac toxicity were also less frequent($P = 0.008$;$P = 0.033$), although hepatic toxicity was more common and reversible($P = 0.042$). No significant differences were observed in 1-year overall survival, disease-free survival, relapse incidence, or transplant-related mortality.These findings suggest that LipMito-containing conditioning may offer a more favorable peri-transplant safety profile without compromising short-term disease control, but prospective validation is needed.

Keywords: liposomal mitoxantrone, pegylated liposomal doxorubicin, acute leukemia, allogeneic hematopoietic stem cell transplantation, conditioning regimen, efficacy and safety

1. Introduction

Allogeneic hematopoietic stem cell transplantation（allo-HSCT）is a potentially curative treatment for acute myeloid leukemia（AML）and acute lymphoblastic leukemia（ALL）, particularly in patients with high-risk or relapsed disease[1,2]. The conditioning regimen is central to transplant success because it reduces leukemic burden, provides sufficient immunosuppression to prevent graft rejection, and creates marrow space for donor stem-cell engraftment. Conventional myeloablative conditioning（MAC）, including busulfan/cyclophosphamide（BuCy）and fludarabine/busulfan（FluBu）, provides effective cytoreduction and durable engraftment but is limited by regimen-related toxicity（RRT）, especially hepatic, cardiac, and gastrointestinal injury[3]. Modified regimens such as fludarabine/busulfan/cyclophosphamide（FluBuCy）have therefore been developed to preserve antileukemic intensity while improving tolerability. In a Peking University series, a modified Bu/Cy/Flu/ATG protocol achieved successful engraftment, low treatment-related mortality（TRM）, and favorable rates of graft-versus-host disease（GVHD）, relapse, and overall survival（OS）in patients with substantial comorbidities[4]. Nevertheless, toxicity remains a major barrier to intensive conditioning. In the phase III GITMO AML-R2 trial, BuCy was associated with higher 1-year non-relapse mortality（NRM; 17.2% vs 7.9%）and more grade III–IV acute GVHD（10% vs 2%）than BuFlu; among patients aged ≥51 years, 4-year NRM was 27% with BuCy versus 11% with BuFlu[5]. In elderly or comorbid cohorts, BuFlu yielded relatively low 100-day and 1-year NRM rates of 3.8% and 8%, respectively, with a 3-year OS of 80%[6]. However, even FluBu-based conditioning is still constrained by relapse, busulfan-associated sinusoidal obstruction syndrome/veno-occlusive disease（SOS/VOD）, noninfectious pulmonary injury, cardiotoxicity, nephrotoxicity, and mucositis[7]. Safer conditioning regimen that maintain antileukemic efficacy are therefore still needed.

Anthracycline and anthracenedione agents are attractive components of leukemia conditioning because of their potent antitumor activity, but cumulative dose-dependent organ toxicity limits their use. For doxorubicin, the incidence of cardiotoxicity increases from approximately 5% at cumulative doses ≤400 mg/m² to approximately 48% at doses >700 mg/m²[8]. Mitoxantrone, an anthracenedione

structurally related to anthracyclines, has also been associated with cardiac dysfunction, supporting the clinical relevance of dose-related myocardial injury[9]. Liposomal delivery may improve the therapeutic index of these agents by modifying tissue distribution, reducing off-target exposure, and maintaining antileukemic activity. Liposomal mitoxantrone（LipMito）shows reduced generation of reactive oxygen species and distinct pharmacologic handling, which may lessen cardiovascular and renal toxicity while potentially altering hepatic and mucosal exposure. In a prospective single-center open-label study, LipMito was well tolerated and was associated with fewer cardiovascular events and less myelosuppression than conventional mitoxantrone[10]. Similarly, pegylated liposomal doxorubicin（PLD）reduces cardiotoxicity compared with conventional doxorubicin while retaining antileukemic efficacy[11]. However, evidence comparing liposomal anthracycline-related agents in allo-HSCT conditioning remains limited. Most available studies have focused on conditioning intensity rather than direct comparisons between agents used within regimens of similar intensity.

Early post-transplant outcomes are also shaped by infectious and immune-mediated complications, including cytomegalovirus（CMV）and Epstein–Barr virus（EBV）viremia, hemorrhagic cystitis, acute GVHD, and RRT. Because liposomal agents differ in pharmacologic behavior and toxicity profiles, they may also influence immune recovery and peri-transplant complication patterns. We therefore retrospectively compared LipMito-（BuCy/FluBuCy）-rATG and PLD-（BuCy/FluBuCy）-rATG conditioning in patients with acute leukemia undergoing allo-HSCT, with 1 year of follow-up. We assessed hematopoietic engraftment, EBV and CMV viremia, hemorrhagic cystitis, acute GVHD, RRT, relapse, survival, and NRM. By directly comparing two liposomal anthracycline-related agents within an rATG-based conditioning regimen, this study aimed to provide clinical evidence to guide individualized conditioning regimen in allo-HSCT.

2. Materials and Methods

2.1 Study design and patient selection

We retrospectively analyzed patients who underwent (BuCy/FluBuCy)-rATG conditioning at Shenzhen Second People's Hospital between July 2017 and December 2024.Among 220 screened patients, 44 received LipMito-based conditioning and 176 received PLD-based

conditioning.Eligible patients were aged 16 to 65 years, had acute myeloid leukemia or acute lymphoblastic leukemia, had no prior history of hematopoietic stem cell transplantation, and received either LipMito-(BuCy/FluBuCy)-rATG or PLD-(BuCy/FluBuCy)-rATG conditioning. Patients with acute promyelocytic leukemia, incomplete clinical data, loss to follow-up, severe cachexia, significant hepatic or renal dysfunction, poor general condition, or inability to complete the planned conditioning regimen were excluded.

Because treatment allocation was not randomized, propensity score matching（PSM） was performed to minimize baseline imbalance between the two groups. The propensity score model included recipient age, sex, disease type, disease risk stratification, transplant type, donor–recipient blood type, donor source, donor sex, infused CD34+ cell dose, and mononuclear cell count. Patients in the LipMito group were matched with those in the PLD group at a 1:2 ratio using optimal matching with the MatchIt package in R software（version 4.2.2）. Covariate balance was evaluated using standardized mean differences（SMDs）.After matching, 44 patients in the LipMito group and 88 patients in the PLD group were included in the final analysis. The patient selection process, covariate balance, and baseline characteristics before and after matching are shown in Figure 1, the Supplementary Appendix, and Table S1. Clinical outcomes were assessed up to 1 year after transplantation.

This study was approved by the Institutional Ethics Committee of Shenzhen Second People’s Hospital (approval No. 2025-069-01PJ). The study was conducted in accordance with the Declaration of Helsinki and its later amendments. The requirement for informed consent was waived because of the retrospective design and the use of de-identified data.

2.2 Conditioning regimen and supportive care

Conditioning was donor-adapted and differed between groups mainly in the liposomal agent given on day −11. In the LipMito-(BuCy/FluBuCy)-rATG regimen, patients with HLA-matched donors received liposomal mitoxantrone 35 mg/m² on day −11, busulfan 0.8 mg/kg every 6 hours on days −10 to −7, cyclophosphamide 60 mg/kg on days −6 and −5, and rATG 2.5 mg/kg on days −3 and −2. For haploidentical donors, fludarabine 50 mg（~30 mg/m²）daily on days −11 to −7 was added, and

rATG was administered on days −4 to −2; the doses and schedules of liposomal mitoxantrone, busulfan, and cyclophosphamide were unchanged.

The PLD-(BuCy/FluBuCy)-rATG regimen followed the same donor-adapted backbone, with pegylated liposomal doxorubicin replacing liposomal mitoxantrone on day −11. PLD was given at 40 mg/m² on day −11. Patients with HLA-matched donors then received busulfan, cyclophosphamide, and rATG as described above, whereas those with haploidentical donors received the same fludarabine-containing regimen and rATG schedule used in the LipMito haploidentical setting.

aGVHD prophylaxis consisted of cyclosporine A（CsA）, mycophenolate mofetil（MMF）, and short-course methotrexate（MTX）. Anti-infective prophylaxis before transplantation included piperacillin‐tazobactam, levofloxacin, trimethoprim‐sulfamethoxazole, ganciclovir, and oral posaconazole for gastrointestinal decontamination. After entry into protective isolation, posaconazole was continued for fungal prophylaxis, and oral vancomycin was used for intestinal coccal prophylaxis.

Cyclophosphamide-associated hemorrhagic cystitis was prevented with urinary catheterization before cyclophosphamide, mesna at 0, 4, and 8 hours after cyclophosphamide, sodium bicarbonate alkalinization, and hydration at 2000 mL/m²/day with furosemide-induced diuresis. Transfusion support, nutritional support, infection surveillance, viral monitoring schedules, GVHD prophylaxis, donor-selection practice, and ICU/anti-infective management followed institutional standards and remained unchanged during the study period.

2.3 Definitions and outcome evaluation

High-risk ALL was defined by any of the following: age >35 years; a white blood cell count >30 × 10^9/L in B-ALL or >100 × 10^9/L in T-ALL; early/precursor/mature B-cell immunophenotype; or adverse cytogenetics, including Philadelphia chromosome positivity, BCR::ABL positivity, t(4;11), MLL-AF4 positivity, or a complex karyotype[11‐13]. High-risk AML was defined as a white blood cell count >100 × 10^9/L, extramedullary or central nervous system involvement, AML secondary to myelodysplastic syndrome, chromosome 5 or 7 deletion, wild-type NPM1 with FLT3-ITD^high, or TP53, ASXL1, or RUNX1 mutation[14].

Neutrophil engraftment was defined as an absolute neutrophil count >0.5 × 10^9/L for three consecutive days, and platelet engraftment as a platelet count >20 × 10^9/L for five consecutive days without transfusion. Acute graft-versus-host disease (aGVHD) was diagnosed and graded according to the Seattle criteria[15]. Hemorrhagic cystitis (HC) was graded according to the Droller criteria[16], and only grade II–IV HC was included in the analysis. Regimen-related toxicities (RRTs) were assessed according to the Bearman criteria[17].

After transplantation, CMV and EBV DNA levels were monitored twice weekly until day +100 and subsequently as clinically indicated. CMV viremia was defined as the first of two consecutive measurements with a viral DNA level ≥1000 copies/mL. Preemptive anti-CMV therapy was initiated according to institutional practice once this threshold was exceeded on serial testing. EBV viremia was defined as the first of two consecutive measurements with a viral DNA level ≥500 copies/mL. As no universally accepted threshold for EBV-directed intervention has been established in allo-HSCT, management of EBV DNAemia was guided by center-specific cutoff values, viral kinetics, and the patient's overall immunologic risk. In patients with significant or rising EBV DNAemia, immunosuppressive therapy was reduced whenever clinically feasible, and rituximab-based preemptive therapy was administered according to institutional practice.

Overall survival (OS) was defined as the time from transplantation to death from any cause or last follow-up. Disease-free survival (DFS) was defined as the time from transplantation to relapse or death from any cause. Cumulative incidence of relapse (CIR) was defined as relapse with >5% blasts in peripheral blood or bone marrow, or extramedullary leukemic infiltration. Transplant-related mortality (TRM) was defined as death without relapse or disease progression. Study outcomes included 1-year OS, DFS, CIR, and TRM; time to engraftment; grade II–IV and grade III–IV aGVHD within 100 days; grade II–IV HC within 100 days; CMV and EBV viremia within 100 days; and RRTs.

2.4 Statistical analysis

Patients were analyzed according to assignment to the LipMito-(BuCy/FluBuCy)-rATG or PLD-(BuCy/FluBuCy)-rATG group. Analyses were performed using SPSS 26.0, GraphPad Prism 10.1.2, and EZR[18].Continuous variables were tested for normality using the Kolmogorov–Smirnov

and Shapiro–Wilk tests and are reported as mean ± SD or median（interquartile range [IQR], Q1–Q3）, as appropriate. Categorical variables are summarized as counts and percentages. Between-group comparisons used the chi-square test or Fisher’s exact test for categorical variables and the Mann–Whitney U test for non-normally distributed continuous variables.OS and DFS were estimated by the Kaplan–Meier method and compared using the log-rank test. Cox proportional hazards regression was used to evaluate factors associated with OS and DFS; variables with $P < 0.10$ in univariable analysis or considered clinically relevant were entered into multivariable models. Grade II–IV aGVHD, grade II–IV HC, CIR, and TRM were analyzed using competing-risk methods, with Gray’s test for group comparisons and Fine–Gray models for multivariable analysis. Covariates included age, sex, graft type, disease risk stratification, donor–recipient blood type, graft source, CD34 cell group, mononuclear cell group, and conditioning regimen. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

3. Results

3.1 Patient characteristics

After matching, 132 patients were included: 44 in the LipMito-based conditioning group and 88 in the PLD-based conditioning group. The median recipient age was 33.5 years (IQR, 28.75–47.00) in the LipMito group and 37.0 years (IQR, 29.75–45.00) in the PLD group. In the LipMito group, 25 patients had AML, 19 had ALL, and 36 (81.82%) underwent haploidentical hematopoietic stem cell transplantation. In the PLD group, 48 patients had AML, 40 had ALL, and 69 (78.41%) underwent haploidentical transplantation. Haploidentical transplantation was the predominant transplant modality in both groups ($P = 0.647$). Baseline characteristics, including recipient age, sex, disease type, risk stratification, donor source, ABO compatibility, donor age, donor sex, infused MNC dose, and CD34+ cell dose, were well balanced between groups (Table 1).

3.2 Hematopoietic engraftment and recovery

Neutrophil engraftment was achieved in 43 of 44 patients (97.7%) in the LipMito group and 87 of 88 patients (98.9%) in the PLD group. The median time to neutrophil engraftment was shorter in the

LipMito group than in the PLD group (14 days [range, 7 – 23] vs 16 days [range, 10 – 26]; P = 0.001; Figure 2a). One patient in each group failed to achieve neutrophil engraftment because of early death from severe infection.Platelet engraftment occurred in 40 patients (90.9%) in the LipMito group and 83 patients (94.3%) in the PLD group. Median platelet engraftment was also earlier in the LipMito group (16 vs 19 days; P = 0.001; Figure 2b). Failure to achieve platelet engraftment was mainly related to early post-transplant death, grade IV aGVHD, or platelet refractoriness.

3.3 aGVHD, HC, and infection

Within 100 days after transplantation, aGVHD developed in 4 patients in the LipMito group and 24 patients in the PLD group. Competing-risk analysis showed a lower day-100 cumulative incidence of grade II – IV aGVHD in the LipMito group than in the PLD group (9.1% [95% CI, 2.85% – 19.86%] vs 27.3% [95% CI, 18.41% – 36.88%]; P = 0.014; Figure 3a). Grade III – IV aGVHD was also less frequent in the LipMito group (6.8% [95% CI, 1.74% – 16.88%] vs 20.5% [95% CI, 12.73% – 29.46%]; P = 0.038; Figure 3b). Two patients with grade III gastrointestinal aGVHD died in the LipMito group, and two deaths from grade IV aGVHD occurred in the PLD group. By day 100, grade II – IV HC occurred in 14 of 44 patients in the LipMito group and 37 of 88 patients in the PLD group. The cumulative incidence of grade II – IV HC did not differ significantly between groups (31.8% [95% CI, 18.65% – 45.80%] vs 42.07% [95% CI, 31.60% – 52.16%]; P = 0.281; Figure 4a). However, grade III – IV HC was significantly lower in the LipMito group (6.8% [95% CI, 1.74% – 16.88%] vs 25.0% [95% CI, 16.48% – 34.44%]; P = 0.011; Figure 4b). One HC-related death occurred in the PLD group. CMV viremia occurred in 33 patients in the LipMito group and 73 patients in the PLD group, with a median onset of 32 days in both groups. The day-100 cumulative incidence was 75.0% (95% CI, 58.90% – 85.53%) and 81.8% (95% CI, 71.84% – 88.54%), respectively, without a significant difference (P = 0.363; Figure 5a). By contrast, EBV viremia was significantly less frequent in the LipMito group. It occurred in 23 patients at a median of 32 days (range, 5 – 67), compared with 73 patients at a median of 26 days (range, 14 – 98) in the PLD group. The day-100 cumulative incidence was 52.2% (95% CI, 36.41% – 65.94%) versus 82.8% (95% CI, 72.81% – 89.33%) (P = 0.001; Figure 5b). No PTLD was observed in either group within 100 days after transplantation.

3.4 Regimen-related toxicity (RRT)

After excluding common gastrointestinal reactions, RRTs occurred in 28 patients (63.6%) in the LipMito group and 78 patients (88.6%) in the PLD group. Single-organ toxicity was observed in 21 and 57 patients, respectively; multi-organ toxicity occurred in 7 and 21 patients.Oral mucositis was less common in the LipMito group than in the PLD group (45.5% vs 69.3%; P = 0.008), as was grade II oral mucositis (11.4% vs 29.5%; P = 0.020). All cases improved with routine oral care and supportive treatment. Cardiac toxicity was also less frequent in the LipMito group (2.3% vs 13.6%; P = 0.033). The two LipMito patients with cardiac toxicity had grade I events and recovered after monitoring. In the PLD group, cardiac events included ventricular premature beats, palpitations, pericardial effusion, and cardiac insufficiency.Hepatic toxicity was more frequent in the LipMito group (34.1% vs 18.2%; P = 0.042). All cases were grade II, reversible, and improved after hepatoprotective and symptomatic treatment. Renal toxicity did not differ significantly (2.3% vs 5.7%; P = 0.663), and no conditioning-related pulmonary or central nervous system toxicity was observed (Table 2).

3.5 Clinical outcomes

The 1-year OS rate was similar between the LipMito and PLD groups (79.5% vs 81.8%; HR, 1.093; 95% CI, 0.478 – 2.502; P = 0.830; Figure 6a). Median survival was not reached in either group. The 1-year DFS rate was also comparable (75.0% vs 73.9%; HR, 0.947; 95% CI, 0.465 – 1.929; P = 0.881; Figure 6b).In univariable analysis for OS, recipient age, donor source, ABO compatibility, time to neutrophil engraftment, time to platelet engraftment, and grade II – IV aGVHD were significant, but none remained significant in multivariable analysis (Table 3). For DFS, recipient age, ABO compatibility, time to neutrophil engraftment, time to platelet engraftment, and grade II – IV aGVHD were significant in univariable analysis. In the multivariable model, delayed neutrophil engraftment was the only independent adverse factor for DFS; neutrophil engraftment at $\geqslant$15 days was associated with a higher risk of relapse or death than engraftment before 15 days (HR, 3.55; 95% CI, 1.13 – 11.11; P = 0.029; Table 3).

Relapse and TRM were evaluated using competing-risk methods. In the LipMito group, 3 patients relapsed, all from the high-risk AML subgroup, with a 1-year CIR of 6.8% (95% CI, 1.73% – 16.90%). In the PLD group, 12 patients relapsed, including 8 with ALL and 4 with AML; the 1-year CIR was 8.0% (95% CI, 3.48% – 18.84%). There was no significant difference in CIR between groups (P = 0.840;

Figure 7a). The 1-year TRM was 18.18% (95% CI, 8.42% – 30.89%) in the LipMito group and 17.05% (95% CI, 10.03% – 25.63%) in the PLD group (P = 0.939; Figure 7b).Fine – Gray competing-risk regression showed that transplant type was independently associated with CIR (sHR, 0.24; 95% CI, 0.07 – 0.82; P = 0.023; Table 4). For TRM, delayed platelet engraftment remained an independent risk factor in multivariable analysis (sHR, 3.70; 95% CI, 1.07 – 12.76; P = 0.038; Table 4).

4. Discussion

In this retrospective study of patients with acute leukemia undergoing allo-HSCT, we compared LipMito-containing conditioning with PLD-containing conditioning within a BuCy/FluBuCy-rATG platform. The main findings were consistent across several peri-transplant endpoints. Patients in the LipMito group had faster hematopoietic recovery and lower incidences of grade II – IV and grade III – IV aGVHD, grade III – IV HC, EBV viremia, oral mucositis, and cardiac toxicity. Hepatic toxicity was more frequent with LipMito, but all events were grade II, reversible, and clinically manageable. At 1 year, OS, DFS, CIR, and TRM were comparable between the two groups. The above results suggest that the potential advantages of the LipMito regimen are primarily reflected in improved safety and tolerability during the peri-transplant period, while its impact on long-term recurrence and survival outcomes still requires further validation through longer-term follow-up.Similar observations have been reported in recent studies of liposomal mitoxantrone in intensive therapy and transplantation-related settings, where its potential value appeared to lie mainly in toxicity-profile optimization rather than early separation of survival curves [19,20].

The faster neutrophil and platelet engraftment observed in the LipMito group is clinically relevant. Differences in carrier retention and toxicity to the bone marrow microenvironment are the primary factors contributing to variations in the rate of hematopoietic recovery. PLDs typically encapsulate small-molecule drugs; their carriers remain relatively stable in the bloodstream but leak into tumor tissues or sites of inflammation via the EPR effect (enhanced permeation and retention)[21]. This leakage characteristic may lead to drug accumulation in non-target tissues, such as the bone marrow stroma, causing prolonged damage to the bone marrow stroma and delaying hematopoietic recovery. In contrast, according to pharmacodynamic studies, LipMito’s multivalent counterion precipitation technology is designed to ensure high stability in the bloodstream, with rapid drug release occurring

only in specific microenvironments (such as tumors or damaged tissues). This characteristic reduces long-term exposure toxicity to normal bone marrow stromal cells, protects the hematopoietic niche, and thereby accelerates hematopoietic recovery.Further multivariate analysis revealed that delayed neutrophil engraftment is an independent risk factor for poor DFS, while delayed platelet engraftment is an independent risk factor for increased TRM. This indicates that engraftment rate is not merely a procedural indicator, but a key variable influencing prognosis. Studies in the field of transplantation have also shown that delayed engraftment is often associated with an increased risk of infection, deterioration of organ function, and non-relapse mortality [22]. Therefore, the clinical significance of the LipMito regimen in promoting early hematopoietic recovery may lie not only in shortening recovery time but also in reducing the burden of subsequent complications by optimizing the peri-transplant microenvironment.

Within 100 days post-transplant, the cumulative incidence of Grade II–IV and Grade III–IV aGVHD in the LipMito group was significantly lower than that in the PLD group, and there was also a relative reduction in deaths associated with severe aGVHD. Multiple studies have shown that mitoxantrone exhibits significantly stronger cytotoxic activity against donor T cells in vitro than doxorubicin [23]. During the conditioning phase, LipMito more thoroughly eliminates mature T cells from the infused hematopoietic stem cell suspension. Furthermore, due to its liposomal targeting and long circulation half-life, LipMito accumulates more readily in lymphoid organs, thereby suppressing early immune responses more effectively than PLD. Furthermore, whereas the prolonged retention time of PLD in vivo causes immunosuppression that disrupts the balance of early immune reconstitution, LipMito’s release kinetics maintain high concentrations of immunosuppressive activity prior to transplantation and are subsequently rapidly metabolized and cleared, creating a low-inflammatory environment conducive to hematopoietic stem cell engraftment [24]. In contrast, PLD remains in the body for an extremely long time, which may lead to excessive prolongation of immunosuppression, thereby disrupting the balance of early immune reconstitution, or cause delayed inflammation due to drug accumulation in the later stages. At the same time, the combination of rATG in this regimen is also key to controlling GVHD. The co-administration of LipMito and rATG may produce a double-hit effect, further reducing the activity of residual T cells. Combined with the protective effects of the LipMito pretreatment regimen on the bone marrow microenvironment (as evidenced by the rapid hematopoietic

recovery mentioned earlier), may enhance tolerance to the cytokine release or intensity of immunosuppression induced by rATG. Consequently, while ensuring effective prevention of GVHD, this approach reduces the risk of infections or relapses caused by excessive immunosuppression.

Another important finding regarding post-transplant complications was that the incidence of Grade III – IV HC was significantly lower in the LipMito group than in the PLD group, while the overall difference in Grade II – IV HC was not statistically significant. This result reveals that LipMito provides stronger protection for the bladder microvascular endothelial system, thereby preventing the occurrence of severe hemorrhagic complications. Compared to the significant mitochondrial toxicity of PLD, the structure of mitoxantrone results in extremely low mitochondrial toxicity, preventing mitochondrial-mediated production of large amounts of reactive oxygen species (ROS) that lead to apoptosis, as well as blocking the release of inflammatory factors (such as TNF-α and IL-6) and chemokines at the nuclear transcriptional level. This also prevents the overexpression of vascular endothelial growth factor[25], thereby preventing plasma extravasation and red blood cell leakage (i.e., gross hematuria) caused by increased vascular permeability, and protecting the integrity of the bladder microvascular endothelium through multiple mechanisms. The reason for the lack of a significant difference in the overall incidence of Grade II – IV HC between the LipMito group and the PLD group may be that Flu and Cy in the pretreatment regimen are themselves associated with mucositis and bladder toxicity; regardless of which anthracycline drug is combined with them, the bladder will sustain a certain degree of damage (i.e., Grade II injury). The primary advantage of LipMito lies in preventing the occurrence of severe HC, rather than completely avoiding injury. Therefore, mild to moderate bladder mucosal inflammation may still occur, resulting in no statistically significant difference in the overall incidence compared to the PLD group; however, it demonstrated a clear safety advantage in the most high-risk severe category. Recent systematic reviews and cohort studies have consistently shown that severe HC significantly increases the need for blood transfusions, bladder irrigation, and analgesic support, and prolongs hospital stays, thereby markedly affecting the quality of peri-transplant recovery [32]. Therefore, from a clinical practicality perspective, the significance of the LipMito regimen in reducing severe HC may outweigh the significance of merely lowering the overall incidence of HC.

Regarding viral reactivation, the cumulative incidence of CMV viremia was similar between the two patient groups, but the incidence of EBV viremia was significantly lower in the LipMito group than in the PLD group. The key mechanism underlying this phenomenon lies in the difference in the drugs' ability to kill EBV-specific memory T-cell subsets. The occurrence of CMV viremia is often related to the rate of recovery of innate immunity and early-stage T cells. Since the BuCy/FluBuCy components of the pre-treatment regimens were identical in both patient groups, and rATG had a consistent effect on early-stage cell lines, the incidence rates of CMV were similar. In contrast, EBV control relies more heavily on specific CD8+ subsets within the adaptive immune system. To maintain high-intensity cytotoxic activity, CD8+ TEM cells are highly dependent on mitochondria for energy via oxidative phosphorylation. The mitochondrial toxicity of PLD can integrate into mitochondrial DNA, blocking ATP production and leading to rapid cell apoptosis [26]. Furthermore, PLD has a plasma half-life of 55–79 hours and tends to accumulate in the reticuloendothelial system [27], causing newly generated T cells to be suppressed by the drug immediately upon their emergence. This weakens the body's surveillance of EBV, leading to viral reactivation. In contrast, LipMito causes relatively minor disruption to mitochondrial function and induces a milder systemic release of inflammatory cytokines compared to the PLD group. CD8+ TEM cells do not need to remain in a constant state of high stress, thereby reducing abnormal cell death. Furthermore, LipMito has a short and concentrated non-specific retention time; after completing its tumor cell killing and pretreatment tasks, the drug concentration declines rapidly, providing a relatively flexible time window for early T-cell reconstitution and allowing the immune surveillance function against EBV to recover first. This misalignment between the drug's characteristics and the physiological characteristics of immune cells during the window period enables critical antiviral T cells to survive. No cases of PTLD occurred in either group, indicating that existing monitoring and intervention strategies are generally effective. The significant reduction in EBV viremia observed in the LipMito group suggests its potential value in reducing the infection-related burden during the peri-transplant period.

Regarding pre-treatment-related toxicities, the incidence of oral mucositis in the LipMito group was significantly lower than that in the PLD group, with a particularly marked reduction in Grade II mucositis. Oral mucositis is one of the most common early toxicities encountered during allogeneic transplant pre-treatment. Its mechanism is similar to that of bladder protection mentioned above; the

key lies in reducing the leakage and accumulation of drugs in the microvasculature of the oral mucosa and maintaining the metabolic activity of the mucosal basal layer cells. The oral mucosa renews extremely rapidly (7–14 days) and is highly sensitive to chemotherapeutic agents. Although PLD has a high molecular weight, leakage still occurs at highly permeable blood vessels, and the lack of lymphatic drainage in mucosal tissue leads to prolonged drug retention [28]. In contrast, LipMito's carrier design results in a lower leakage rate in normal or mildly damaged tissue. Consequently, less of the drug leaks into and remains in the capillaries of the oral mucosa, reducing the concentration of the drug in contact with the basal cells of the mucosal epithelium and thereby mitigating direct toxicity [29]. Recent systematic reviews and meta-analyses have further confirmed that patients who develop oral mucositis after HSCT have a significantly increased risk of infectious complications. This suggests that this condition is not merely a manifestation of localized epithelial damage but also an important indicator of the overall inflammatory burden and risk of infection during the peri-transplant period [30]. Therefore, the reduction in mucositis observed in the LipMito group in this study not only reflects the relatively good tolerability of this regimen but may also be one of the upstream factors contributing to the group's concurrent benefits in endpoints such as hematopoietic recovery, aGVHD, and EB viremia.

In terms of cardiac toxicity, the LipMito group exhibited lower levels than the PLD group. This result validates the dual protective role of drug delivery system engineering and molecular structure optimization in peri-transplant therapy. Although doxorubicin encapsulated in liposomes exhibits reduced cardiotoxicity compared to conventional free anthracycline drugs, allogeneic transplant patients typically undergo high-intensity, multi-drug combination therapy in a highly inflammatory environment, which may amplify subclinical myocardial injury. Normal cardiac tissue, particularly cardiomyocytes, lacks mechanisms to uptake macromolecular liposomes, and the microvascular endothelium of normal myocardium is tightly sealed, lacking the leaky pore effect observed in tumor tissue. In contrast to free doxorubicin, which can freely penetrate the vascular wall and enter myocardial tissue, LipMito's PEGylated liposome structure allows it to circulate for an extended period in the bloodstream, where it is primarily distributed within the vascular lumen. This physical barrier significantly reduces the drug's volume of distribution in myocardial tissue, thereby preventing drug accumulation in the heart [31]. Even if a small amount of the drug enters cardiomyocytes, the side-chain structure of mitoxantrone results in low affinity for cardiolipin, thereby reducing direct

damage to myocardial mitochondrial membranes and lowering the risk of calcium overload and the opening of mitochondrial permeabilization pores. In this study, only mild, reversible cardiotoxicity was observed in the LipMito group, suggesting that it may offer a better margin of cardiac safety during the peri-transplant period. For patients who have previously received cumulative treatment with anthracyclines, have underlying cardiac weakness, or require intensive supportive care during the peri-transplant period, this characteristic holds significant clinical relevance.

It should be noted that the incidence of hepatotoxicity in the LipMito group was higher than that in the PLD group, which in fact reveals the fundamental pharmacokinetic differences between the drug-metabolizing organ (the liver) and the target organs (the heart and mucous membranes). This is a reverse manifestation of LipMito’s targeted accumulation properties, and the fact that it is a Grade II, reversible adverse event indicates that this risk is within a clinically manageable range. Unlike cardiac muscle, the heart lacks endocytic receptors and thus rejects liposomes, thereby avoiding toxicity; in contrast, the liver is rich in the reticuloendothelial system. As a nanoliposome, LipMito is easily enveloped by opsonins in the bloodstream after entering the body and is subsequently recognized and phagocytosed by Kupffer cells in the liver [32]. This results in drug concentrations in liver tissue that are significantly higher than those in plasma. Although this aids in the elimination of liver metastases, high concentrations of mitoxantrone directly interfere with mitochondrial function in hepatocytes, leading to elevated ALT/AST levels. Although PLD also accumulates in the liver, mitoxantrone itself—as a potent topoisomerase II inhibitor—may exhibit greater direct toxicity to hepatocytes at the single-molecule level than doxorubicin, thereby offsetting some of the protection provided by the carrier. On the other hand, the /BuCy-FluBuCy regimen used in this study includes fludarabine and cyclophosphamide, both of which have well-established hepatotoxicity. Although the incidence of hepatotoxicity with LipMito is relatively high, all cases were Grade II and reversible; as long as liver function is closely monitored and hepatoprotective agents are administered promptly, this toxicity typically does not lead to treatment interruption or serious consequences. Regarding the increased incidence of hepatotoxicity in the LipMito group, the toxicity data in this study were derived from retrospective medical record reviews; mild toxicity is particularly susceptible to the influence of documentation completeness and subjective judgment. Furthermore, factors such as cumulative prior anthracycline doses, exposure to pre-transplant bridging therapy, prophylactic azole antifungal therapy,

concomitant use of other hepatotoxic drugs, blood transfusion burden, and underlying liver disease may all confound the occurrence of hepatotoxicity.

Although the LipMito regimen performed better in terms of engraftment, aGVHD, EBV viremia, and several pre-treatment-related toxicity endpoints, there were no significant differences between the two groups in 1-year OS, DFS, CIR, and TRM. These results should be interpreted objectively and with caution. First, the intensity of the pre-transplant conditioning regimen directly affects the ability of T cells to eliminate residual leukemic cells. Although LipMito reduces tissue damage, if the inflammatory environment it generates is insufficient to induce a strong GVL effect, or if it leaves patients in a state of excessive immunosuppression, patients may face a relapse risk similar to that in the PLD group. Second, at current transplant centers, advances in supportive care have generally reduced 1-year TRM to low levels. When the incidence of endpoint events is very low, a very large sample size is required to detect differences between groups. Although there was no difference in 1-year survival outcomes, the LipMito group demonstrated advantages in engraftment rate and aGVHD control.The LipMito regimen stabilizes survival outcomes by reducing the risk of TRM, while optimizing the patient’s recovery pathway by improving engraftment and GVHD control. This provides a more patient-centered option for the clinical selection of pre-transplant regimens. However, its impact on long-term relapse risk and long-term survival still requires further validation through longer follow-up and higher-level evidence.

This study is a single-center retrospective analysis with a follow-up period of only 1 year, which is currently insufficient to evaluate chronic GVHD, long-term immune reconstitution, late-onset organ toxicity, and long-term survival benefits. Furthermore, due to the small sample size in the LipMito group, it is currently difficult to conduct subgroup analyses for AML/ALL with sufficient statistical power. This implies that the overall effect observed may be influenced to some extent by differences in disease composition and intradisease heterogeneity. Therefore, the conclusions of this study should be interpreted primarily as preliminary clinical signals in the acute leukemia population. Future studies should conduct further stratified analyses by disease type, risk stratification to identify the patient subgroups that truly benefit from the LipMito regimen.

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7. Author Contributions

(I) Conception and design: YXZ; (II) Administrative support: XD, SYC; (III) Provision of study materials or patients: SYC, XHZ; (IV) Collection and assembly of data: YXZ, MYD; (V) Data analysis and interpretation: YXZ, MYD; (VI) Manuscript writing: YXZ; (VII) Funding acquisition: XD; (VIII) Final approval of manuscript: All authors.

8. Competing Interests

The authors declare that they have no competing interests.

9. Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request. Individual participant data will not be shared.

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11. Generative AI Use

During the preparation of this work, the authors used ChatGPT (OpenAI) to assist with English-language editing, improving clarity and conciseness of scientific writing, and organizing the manuscript structure. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

Table 1. Baseline characteristics of patients undergoing allo-HSCT according to conditioning regimen

Variable	Total (n = 132)	LipMito group (n = 44)	PLD group (n = 88)	P value
Age, median (IQR), years	36.50 (29.00–46.00)	33.50 (28.75–47.00)	37.00 (29.75–45.00)	0.998
Sex, n (%)				0.801
Female	52 (39.39)	18 (40.91)	34 (38.64)	
Male	80 (60.61)	26 (59.09)	54 (61.36)	
Diagnosis, n (%)				0.804
AML	73 (55.30)	25 (56.82)	48 (54.55)	
ALL	59 (44.70)	19 (43.18)	40 (45.45)	
Risk stratification, n (%)				0.166
Favorable risk	17 (12.88)	9 (20.45)	8 (9.09)	
Intermediate risk	17 (12.88)	6 (13.64)	11 (12.50)	
Poor risk	98 (74.24)	29 (65.91)	69 (78.41)	
Transplant type, n (%)				0.647
HRD	105 (79.55)	36 (81.82)	69 (78.41)	
MRD	27 (20.45)	8 (18.18)	19 (21.59)	
ABO compatibility, n (%)				0.896
BTI	43 (32.58)	14 (31.82)	29 (32.95)	
BTC	89 (67.42)	30 (68.18)	59 (67.05)	
Donor source, n (%)				0.902
Offspring	62 (46.97)	21 (47.73)	41 (46.59)	
Parent	70 (53.03)	23 (52.27)	47 (53.41)	
Donor age, median (IQR), years	31.00 (21.00–44.00)	31.50 (22.75–42.50)	30.50 (20.00–44.25)	0.910
Donor sex, n (%)				0.898
Female	47 (35.61)	16 (36.36)	31 (35.23)	

Male	85 (64.39)	28 (63.64)	57 (64.77)	
Infused CD34+ cells, median (IQR), ×10^6/kg	5.13 (4.04–7.65)	5.34 (4.35–7.35)	5.07 (3.96–7.92)	0.673
Infused MNCs, median (IQR), ×10^8/kg	7.32 (6.04–8.93)	7.36 (6.07–8.89)	7.31 (6.04–9.05)	0.960

Abbreviations: *allo-HSCT, allogeneic hematopoietic stem cell transplantation; LipMito, liposomal mitoxantrone; PLD, pegylated liposomal doxorubicin; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; HRD, haploidentical related donor; MRD, matched related donor; BTI, blood type identical; BTC, blood type compatible; MNC, mononuclear cell. Note: Continuous variables were compared using the Wilcoxon rank-sum test; categorical variables were compared using the chi-square test.*

Table 2. Regimen-related toxicities assessed according to the Bearman grading system

Variable	LipMito group (n = 44)	PLD group (n = 88)	OR (95% CI)	P value
Number of organs involved, n (%)			—	—
0	16 (36.4)	10 (11.4)		
1	21 (47.7)	57 (64.8)		
2	6 (13.6)	17 (19.3)		
3	1 (2.3)	4 (4.5)		
Incidence of organ toxicity, n (%)				
Oral mucositis	20 (45.5)	61 (69.3)	2.711 (1.285–5.720)	0.008
Grade I	15 (34.1)	35 (39.8)		
Grade II	5 (11.4)	26 (29.5)	3.271 (1.159–9.232)	0.020
Cardiac toxicity	2 (4.5)	16 (18.2)	4.660 (1.022–21.304)	0.033
Grade I	1 (2.3)	12 (13.6)		
Grade II	1 (2.3)	3 (3.4)		
Grade III	0	1 (1.1)		

Hepatic toxicity	15 (34.1)	16 (18.2)	0.430 (0.188–0.981)	0.042
Grade I	0	3 (3.4)		
Grade II	15 (34.1)	13 (14.8)		
Renal toxicity	1 (2.3)	5 (5.7)	2.590 (0.293–22.878)	0.663
Grade I	1 (2.3)	1 (1.1)		
Grade II	0	4 (4.5)		

Abbreviations: OR, odds ratio; CI, confidence interval. Odds ratios are reported as provided in the source table. Please verify the original dataset for the "number of organs involved" and cardiac-toxicity rows before final submission, as the uploaded table and the narrative text were not fully identical.

Table 3. Univariable and multivariable Cox regression analyses for overall survival and disease-free survival

Characteristic	Comparison	OS: Univariable P value	OS: Multivariable P value (HR, 95% CI)	DFS: Univariable P value	DFS: Multivariable P value (HR, 95% CI)
Age	≥40 vs <40	0.008	0.087 (2.11, 0.90–4.98)	0.026	0.096 (1.83, 0.90–3.71)
Sex	Male vs Female	0.429	—	0.189	—
Disease type	AML vs ALL	>0.999	—	0.983	—
Transplant type	Matched related vs Haploidentical	0.546	—	0.391	—
Risk stratification	Intermediate vs Favorable	0.122	—	0.212	—
	Poor vs Favorable	0.585	—	0.502	—
Donor source	Offspring vs Parent	0.040	0.131 (0.50, 0.20–1.23)	0.098	—

ABO compatibility	Mismatched vs Matched	0.005	0.093 (2.16, 0.88–5.28)	0.042	0.374 (1.38, 0.68–2.78)
MNC (×10^8/kg)	≥8.1 vs <8.1	0.221	—	0.092	—
CD34+ cell count (×10^6/kg)	≥5.69 vs <5.69	0.234	—	0.463	—
Time to neutrophil engraftment	≥15 vs <15 days	0.009	0.139 (3.26, 0.68–15.55)	0.004	0.029 (3.55, 1.13–11.11)
Time to platelet engraftment	≥19 vs <19 days	0.002	0.079 (2.85, 0.89–9.19)	0.028	0.724 (1.16, 0.52–2.59)
Grade II–IV aGVHD	Yes vs No	0.020	0.455 (1.38, 0.59–3.22)	0.023	0.164 (1.69, 0.81–3.53)
Grade II–IV HC	Yes vs No	0.240	—	0.198	—
EBV viremia	Yes vs No	0.733	—	0.928	—
CMV viremia	Yes vs No	0.473	—	0.454	—
Conditioning regimen	LipMito group vs PLD group	0.834	—	0.879	—

Abbreviations: OS, overall survival; DFS, disease-free survival; HR, hazard ratio; CI, confidence interval; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MNC, mononuclear cell; aGVHD, acute graft-versus-host disease; HC, hemorrhagic cystitis; EBV, Epstein–Barr virus; CMV, cytomegalovirus. Blank cells indicate variables not retained in the final multivariable model.

Table 4. Univariable and multivariable Fine–Gray regression analyses for cumulative incidence of relapse and transplant-related mortality

Characteristic	Comparison	CIR: Univariable P value	CIR: Multivariable P value (sHR, 95% CI)	TRM: Univariable P value	TRM: Multivariable P value (sHR, 95% CI)
Age	≥40 vs <40	0.880	—	0.008	0.096 (2.16, 0.87–5.35)

Sex	Male vs Female	0.220	—	0.360	—
Disease type	AML vs ALL	0.780	—	0.950	—
Transplant type	Matched related vs Haploidentical	0.023	0.023 (0.24, 0.07–0.82)	0.360	—
Risk stratification	Intermediate vs Favorable	0.120	—	0.120	—
	Poor vs Favorable	0.630	—	0.710	—
Donor source	Offspring vs Parent	0.840	—	0.032	0.130 (0.48, 0.19–1.24)
ABO compatibility	Mismatched vs Matched	0.360	—	0.005	0.065 (2.36, 0.95–5.86)
MNC (×10^8/kg)	≥8.1 vs <8.1	0.220	—	0.170	—
CD34+ cell count (×10^6/kg)	≥5.69 vs <5.69	0.660	—	0.390	—
Time to neutrophil engraftment	≥15 vs <15 days	0.300	—	0.015	0.240 (2.54, 0.54–11.89)
Time to platelet engraftment	≥19 vs <19 days	0.051	—	0.001	0.038 (3.70, 1.07–12.76)
Grade II–IV aGVHD	Yes vs No	0.930	—	0.009	0.350 (1.50, 0.64–3.53)
Grade II–IV HC	Yes vs No	0.540	—	0.370	—
EBV viremia	Yes vs No	0.350	—	0.580	—
CMV viremia	Yes vs No	0.980	—	0.700	—
Conditioning regimen	LipMito group vs PLD group	0.840	—	0.940	—

Abbreviations: CIR, cumulative incidence of relapse; TRM, transplant-related mortality; sHR, subdistribution hazard ratio; CI, confidence interval; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MNC, mononuclear cell; aGVHD, acute graft-versus-host disease; HC, hemorrhagic cystitis; EBV, Epstein–Barr virus; CMV, cytomegalovirus. Blank cells indicate variables not retained in the final multivariable model.

Supplementary Table S1. Baseline covariates before and after propensity score matching

Values are presented as mean (SD) for continuous variables and n (%) for categorical variables. Covariate balance was assessed using standardized mean differences (SMDs).

Variable	Level	Before matching			After matching		
		PLD group	LipMito group	SMD	PLD group	LipMito group	SMD
n		175	44		88	44	
Age, years		35.44 (10.37)	37.34 (12.30)	0.155	36.70 (10.70)	37.34 (12.30)	0.052
Sex, n (%)	Female	74 (42.3)	18 (40.9)	-0.028	34 (38.6)	18 (40.9)	0.046
	Male	101 (57.7)	26 (59.1)	0.028	54 (61.4)	26 (59.1)	-0.046
Diagnosis, n (%)	AML	109 (62.3)	25 (56.8)	-0.110	48 (54.5)	25 (56.8)	0.046
	ALL	66 (37.7)	19 (43.2)	0.110	40 (45.5)	19 (43.2)	-0.046
Transplant type, n (%)	HRD	116 (66.3)	36 (81.8)	0.403	69 (78.4)	36 (81.8)	0.088
	MRD	49 (28.0)	8 (18.2)	-0.255	19 (21.6)	8 (18.2)	-0.088
	URD	10 (5.7)	0 (0.0)	-0.275	0 (0.0)	0 (0.0)	0.000
ABO compatibility, n (%)	BTC	58 (33.1)	14 (31.8)	-0.028	29 (33.0)	14 (31.8)	-0.024
	BTI	117 (66.9)	30 (68.2)	0.028	59 (67.0)	30 (68.2)	0.024
Donor source, n (%)	Offspring	89 (50.9)	21 (47.7)	-0.063	41 (46.6)	21 (47.7)	0.023
	Parent	76 (43.4)	23 (52.3)	0.177	47 (53.4)	23 (52.3)	-0.023
	Unrelated donor	10 (5.7)	0 (0.0)	-0.275	0 (0.0)	0 (0.0)	0.000
Donor age, years		35.41 (14.47)	32.23 (13.35)	-0.238	32.30 (14.57)	32.23 (13.35)	-0.005
Donor sex, n (%)	Female	62 (35.4)	16 (36.4)	0.019	31 (35.2)	16 (36.4)	0.024

Variable	Level	Before matching			After matching		
		PLD group	LipMito group	SMD	PLD group	LipMito group	SMD
	Male	113 (64.6)	28 (63.6)	-0.019	57 (64.8)	28 (63.6)	-0.024
Infused CD34+ cell dose, ×10^6/kg		6.41 (3.50)	5.88 (2.55)	-0.209	5.79 (2.57)	5.88 (2.55)	0.036
Mononuclear cell count, ×10^8/kg		8.64 (2.51)	7.68 (2.05)	-0.468	7.77 (2.15)	7.68 (2.05)	-0.042

Abbreviations: AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; HRD, haploidentical related donor; MRD, matched related donor; URD, unrelated donor; BTC, blood type compatible; BTI, blood type identical; SMD, standardized mean difference.

Figure legends

Figure 1. Flow chart of the study. The final analysis included 44 subjects in the LipMito group and 88 subjects in the PLD control group.

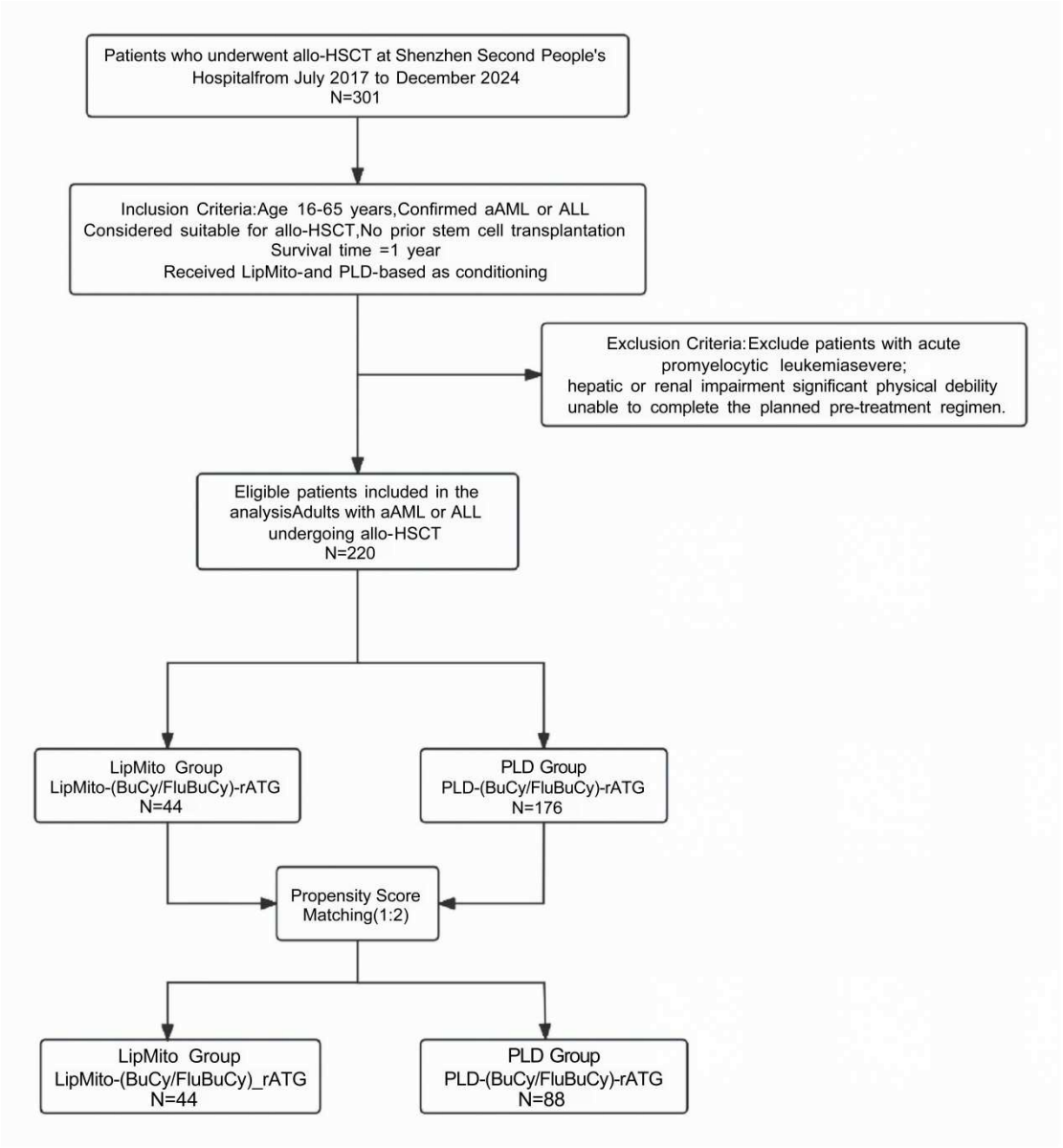


Figure 2. Outcomes From Transplantation according to the Conditioning Regimen. Cumulative Granulocyte of Lineage Reconstitution and PLT（P = 0.001）.

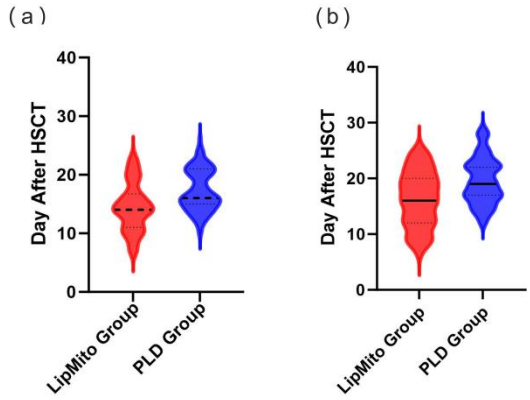


Figure 3. (a) Cumulative incidence of II~IV AGVHD within 100 days. (b) Cumulative incidence of III~IV AGVHD within 100 days.

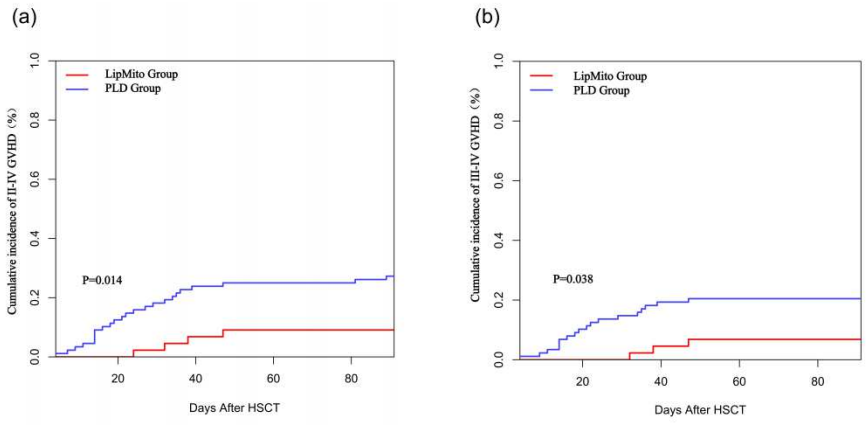


Figure 4. (a) Cumulative incidence of II~IV HC within 100 days. (b) Cumulative incidence of III ~IV HC within 100 days.

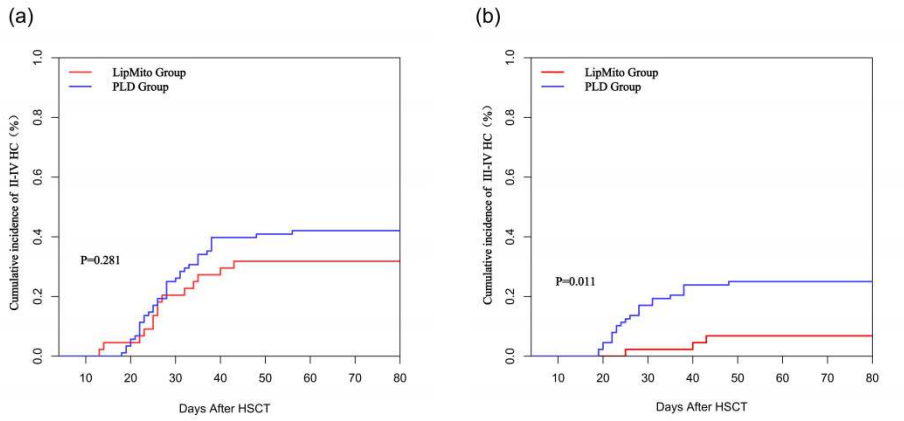


Figure 5. (a) Cumulative incidence of CMV within 100 days. (b) Cumulative incidence of EBV within 100 days.

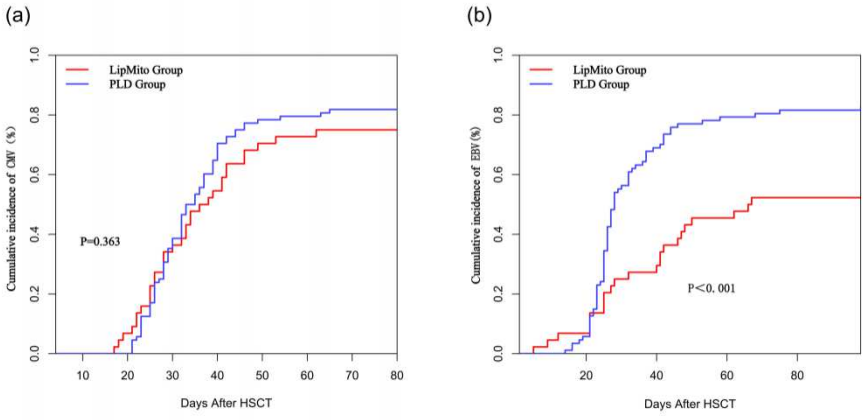


Figure 6. (a) Kaplan-Meier Estimate of Overall Survival. (b) Kaplan-Meier Estimate of Disease-free Survival.

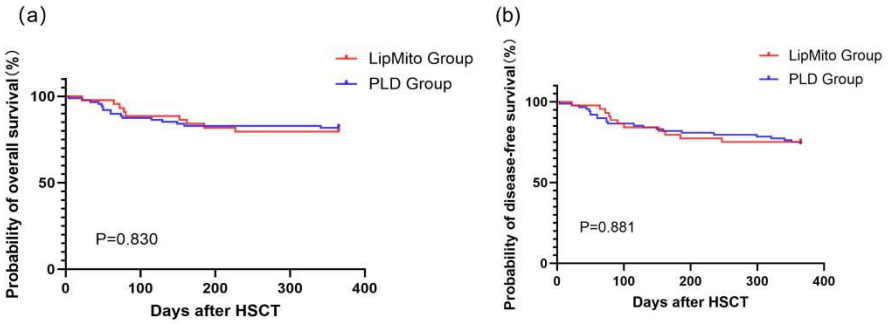
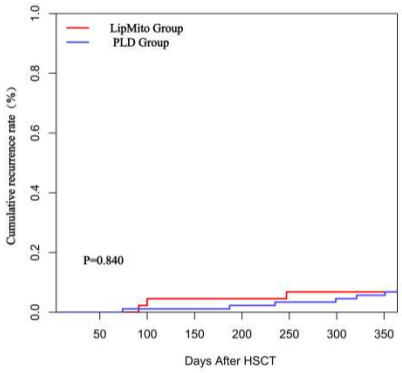
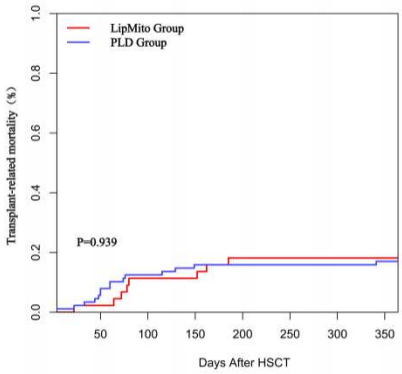


Figure 7. (a) Cumulative Incidence of Relapse. (b) Cumulative Incidence of Transplant-related mortality.

(a)


LipMito Group
PLD Group
Cumulative recurrence rate (%)
0.0
0.2
0.4
0.6
0.8
1.0
P=0.840
50
100
150
200
250
300
350
Days After HSCT

(b)


LipMito Group
PLD Group
Transplant-related mortality (%)
0.0
0.2
0.4
0.6
0.8
1.0
P=0.939
50
100
150
200
250
300
350
Days After HSCT