Decitabine-Containing Conditioning Regimen for Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Intermediate- and High-Risk Myelodysplastic Syndrome/Acute Myeloid Leukemia: Potential Decrease in the Incidence of Acute Graft versus Host Disease

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Purpose: To evaluate the role of Decitabine in the allo-HSCT conditioning regimen for intermediate- and high-risk patients with MDS or AML.

Patients and methods: Retrospective analysis of data pertaining to 76 intermediate- and high-risk patients with MDS or AML who underwent allo-HSCT between December 2005 and June 2018 at the Peking University First Hospital. Forty patients received Decitabine-containing conditioning regimen before transplantation, while thirty-six patients received regimen without Decitabine.

Results: Over a median follow-up of 40 months (range, 1 to 155), the cumulative incidence of grade II to IV acute graft versus host disease was 12.4% [95% confidence interval (CI) 4.9–30.9%] in the Decitabine group and 41.5% (95% CI 28.1–61.2%) in the non-Decitabine group (P=0.005). On multivariate analysis, Decitabine-containing conditioning regimen was found to protect against grade II to IV aGVHD (HR=0.279, 95% CI 0.102–0.765, P=0.013). Incidence of respiratory infection in the Decitabine and non-Decitabine groups was 22.5% and 52.78%, respectively (P=0.012). No significant between-group difference was observed with respect to 3-year OS, DFS, or RR (P=0.980, 0.959, and 0.573, respectively), while the median relapse time was longer in the Decitabine group [7 months (range, 2–12) versus 3 months (range, 2–4), P=0.171]. Decitabine-containing conditioning showed a tendency for lower relapse rate among higher risk patients, as assessed by IPSS R; however, the between-group difference was not statistically significant (P=0.085).

Conclusion: Inclusion of Decitabine in the conditioning regimen for allo-HSCT in intermediate- and high-risk patients may lower the incidence of aGVHD and respiratory infections, and contribute to longer median relapse time.

Keywords: myelodysplastic syndrome, acute myeloid leukemia, Decitabine, transplantation conditioning, graft versus host disease, allogeneic hematopoietic stem cell transplantation

Introduction

Myelodysplastic Syndrome (MDS) is a clonal hematopoietic disorder characterized by ineffective hematopoiesis, refractory cytopenia, and hyperproliferative bone marrow. Patients categorized as international prognostic scoring system (IPSS)
intermediate-2 and high-risk groups [currently considered as higher risk MDS (HR-MDS)] have aggressive malignancies with a median survival of 1.1 years and 0.4 years, respectively, if treated only with supportive care.\textsuperscript{1}

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only curative treatment for intermediate/high-risk MDS and acute myeloid leukemia (AML). For low- and intermediate-1-risk MDS, delayed hematopoietic stem cell transplantation was shown to achieve maximal life expectancy; however, immediate transplantation conferred the highest survival benefit in patients with intermediate-2- and high-risk disease.\textsuperscript{2,3} The National Comprehensive Cancer Network (NCCN) guidelines recommend allo-HSCT for MDS of intermediate-2- and high-risk as soon as possible. However, relapse and graft versus host disease (GvHD) are two main causes of treatment failure. Recent studies have implicated epigenetic changes such as abnormal DNA methylation, histone modification, and non-coding RNA in the pathogenesis of MDS.\textsuperscript{4} Decitabine (Dec, 5-aza deoxycytidine), a pyrimidine analogue with significant antileukemic activity, acts as an inhibitor of cytosine methylation, which results in activation of silent genes.\textsuperscript{5} Some clinical studies have demonstrated the efficacy of Dec in the treatment of refractory leukemia and MDS before or after allo-HSCT. Dec therapy was shown to be associated with reduced incidence of GvHD, lower relapse rate, and increased overall survival with acceptable tolerance.\textsuperscript{6–9} Thus, Dec may be an ideal candidate for use in combination with standard preparative regimen for patients scheduled to undergo allo-HSCT. In this study, we retrospectively evaluated the efficacy and safety of Dec-containing conditioning regimen in 76 patients with intermediate- or high-risk MDS/AML.

**Materials and Methods**

**Patients and Methods**

Seventy-six patients who were diagnosed with intermediate- or high-risk MDS or transformed acute myeloid leukemia (t-AML) at the Peking University First Hospital between December 2005 and June 2017 were analyzed in this study. Of these, 40 patients had received Dec-containing conditioning before allo-HSCT (Dec group). Another 36 patients received non-Decitabine conditioning before allo-HSCT (non-Dec group). All patients were classified according to the 2008 WHO MDS Classification and were evaluated by revised international prognostic scoring system (IPSS-R) risk category. We performed allo-HSCT immediately after the diagnosis of MDS of high- and higher-risk categories. As for t-AML patients, standard-dose “3+7” induction chemotherapy (Cytarabine 100–200 mg continuous infusion for 7 days with Idarubicin 12 mg/m\(^2\) or Daunorubicin 60–90 mg/m\(^2\) for 3 days) or priming chemotherapy was administered before allo-HSCT. In China, CAG priming chemotherapy is widely used in patients with AML. It consists of a small dose of cytarabine (10 mg/m\(^2\), every 12 h, subcutaneous injection, \(\times 14\) days), plus G-CSF and administered in combination with aclacinomycin.\textsuperscript{10} CR was defined as bone marrow with \(\leq 5\%\) myeloblasts with normal maturation of all cell lines, hemoglobin \(\geq 11\) g/dL, platelets \(\geq 10^9/L\), neutrophils \(\geq 10^3/L\), and no circulating blasts. This study was conducted in accordance with the declaration of Helsinki and was approved by the institutional review board at the Peking University First Hospital in June 2018. The requirement for written informed consent was waived off due to the retrospective nature of the study. All data used in this manuscript were anonymized.

**Treatment Plan**

**Conditioning Regimen**

The conditioning regimens were modified Bu/Cy and Bu/Flu, which were recommended in China.\textsuperscript{11} Conditioning protocols were as follows: cytarabine 2 g/m\(^2\)/d for 3 days; busulfan 3.2 mg/kg/d intravenously for 3 days, combined with cyclophosphamide 1.8g/m\(^2\)/d for 2 days or fludarabine 50 mg for 3–6 days (total dose: 200 mg/m\(^2\)).\textsuperscript{12} Dec was administered at a dose of 15 mg/m\(^2\) intravenously from day −16 to −12. Rabbit anti-thymocyte globulin (ATG) was used for 3 days before transplantation; patients with haploidentical or unrelated donors were administered 7.5–10 mg/kg ATG as part of conditioning, and patients with HLA identical sibling donors were administered 0 to 5mg/kg ATG.

**GvHD Prophylaxis and Treatment**

GvHD prophylaxis consisted of cyclosporin A (CsA), mycophenolate mofetil (MMF), and methotrexate (MTX). MMF 50 mg every 12 hrs was administered orally from the start of conditioning up to 30 days after transplantation. Intravenous (i.v.) CsA 5 mg/kg daily was administered from day −6 to the time of bowel function recovery, and then switched to oral CsA. Serum CsA concentration was monitored, and the dosage was adjusted to achieve serum concentrations in the range of 150 to 250 ng/mL. MTX was administered at a dose
of 10–15 mg/m² i.v. on days +1, +3, +5, +11 after transplantation. Grade I aGvHD was controlled by topical treatment and optimization of treatment (e.g., adjustment of CsA dosage). Firstline therapy of grade II–IV aGvHD was methylprednisolone 1 to 2 mg/kg daily. Patients refractory to steroid therapy received secondary therapy, such as basiliximab i.v. 1 mg/kg.

Stem Cell Mobilization, Collection, and Transplantation

Donors received G-CSF 5 µg/kg subcutaneously every 12 hrs starting from 3 days prior to the collection of bone marrow stem cells. Peripheral blood harvesting was carried out on the fourth day after G-CSF treatment.

Supportive Care

Antibiotics were used to prevent microbial infections as appropriate. Co-trimoxazole (SMZ/TMP) was used to prevent pneumocystis carinii pneumonitis (PCP) until 6 months after allo-HSCT. Ganciclovir was used between days −9 to −1 in order to prevent cytomegalovirus (CMV) infection. Acyclovir was used as herpes virus prophylaxis therapy from +1d to 6 months after transplantation. After hematopoietic reconstitution, CMV and Epstein-Barr virus (EBV) polymerase chain reaction (PCR) were monitored every week.

Main Outcome Measures

To assess the treatment response, bone marrow aspiration was performed every month within 6 months after transplantation. Relapse was defined as the presence of >5% blasts in patients with previously normal BM or evidence of extramedullary leukemia. Data pertaining to engraftment, transplantation-related complications, relapse rate (RR), 3-year disease-free survival (DFS), 3-year overall survival (OS), and no relapse mortality (NRM) were retrospectively analyzed. Grading of acute and chronic GvHD (aGvHD, cGvHD) was performed according to the standard criteria. Successful engraftment was defined according to the European Society for Blood and Marrow Transplantation criteria for hematopoietic repopulation; the criteria include 3 consecutive days with leucocytes ≥1.0×10⁹/L, neutrophils ≥0.5×10⁹/L, and thrombocytes ≥50×10⁹/L without any transfusion in the immediately preceding 7 days. Transplantation-related complications include CMV viremia, EBV viremia, de novo pneumonia, hemorrhagic cystitis, aGvHD and cGvHD. DFS was defined as the period from diagnosis to relapse or death. OS was defined as the time from diagnosis to death or the most recent follow-up. NRM was defined as death caused by any reasons before day 28, or death caused by reasons other than relapse after day 28.

Statistical Analysis

Between-group differences were assessed using the Pearson Chi-squared test for categorical variables and Students t-test for continuous variables. The cumulative incidence of acute GVHD, relapse, and NRM was estimated considering the competing risks. Univariate analysis for acute GVHD was performed using Gray’s method. Fine and Gray semiparametric proportional hazards regression model was used for multivariate analysis. OS and DFS were calculated by Kaplan-Meier method and compared using the Log-rank test. P<0.05 was considered indicative of statistical significance. All statistical analyses were performed with SPSS 24.0 (SPSS Inc./IBM, Amonk, NY, USA), R statistical software and the cmprsk package (Comprehensive R Archive Network, TUNA, Tsinghua University, China).

Results

Baseline Characteristics

Baseline characteristics are summarized in Table 1 (Baseline Characteristics). Pre-transplantation therapy, WHO classification, and IPSS-R category were comparable between the two groups. However, there were some differences between the two groups. Compared to the non-Dec group, Dec recipients were older (41 vs 33 years, P=0.028), received smaller amount of MNCs (9.76×10⁸/kg vs 12.48×10⁸/kg, P=0.007) but larger amount of CD34 positive cells (5.77×10⁶/kg vs 3.65×10⁶/kg, P=0.004). Thirteen patients in the Dec group and 7 patients in the non-Dec group were in complete remission (CR) prior to allo-HSCT. As significant between-group difference was also observed with respect to the conditioning regimen; Bu/Cy was used in 5 non-Dec recipients and 0 Dec recipients (P=0.015).

Engraftment

Neutrophil engraftment was successful in all 76 patients. Thirty-nine patients in the Dec group and 35 patients in the non-Dec group had platelet (PLT) repopulated successfully. Median neutrophil engraftment in the Dec group was 13 days, which was similar to that in the non-Dec group (P=0.935). The median PLT engraftment in the Dec and non-Dec groups was 21 (8–86) days and 18 (8–80) days, respectively (P=0.321).
Transplantation-Related Complications

The incidence of CMV viremia, EBV viremia, and hemorrhagic cystitis was comparable in the two groups. However, the de novo incidence of respiratory infection was 22.5% in Dec group as against 53% in the non-Dec group (P=0.006) (shown in Table 2 – Incidence of transplantation-related complications).

| Table 1 Between-Group Differences of Baseline Characteristics | Dec | Non-Dec | P Value |
|---------------------------------------------------------------|-----|---------|---------|
| Total                                                         | 40  | 36      |         |
| Age at HSCT (years)                                           | 41±12| 33±14   | 0.028   |
| Gender                                                       |     |         |         |
| Male                                                         | 20(50%)| 17(47%) | 0.809   |
| Female                                                      | 20(50%)| 19(53%) |         |
| Therapy before transplantation                                |     |         |         |
| Chemotherapy                                                | 24(60%)| 16(44.5%)| 0.093   |
| Cyclosporin A                                               | 5(12.5%)| 12(33.3%)|         |
| No                                                          | 11(27.5%)| 8(22.2%)|         |
| WHO classification                                           |     |         |         |
| RA                                                          | 0(0%)| 1(2.8%) | 0.299   |
| RCMD                                                       | 8(20%)| 13(36.1%)|         |
| RAEB-1                                                     | 8(20%)| 3(8.3%) |         |
| RAEB-2                                                     | 7(17.5%)| 5(13.9%)|         |
| t-AML                                                      | 17(42.5%)| 14(38.9%)|         |
| IPSS-R                                                     |     |         |         |
| Intermediate                                               | 8(20%)| 15(41.7%)| 0.092   |
| High                                                       | 14(35%)| 7(19.4%) |         |
| Higher                                                     | 18(45%)| 14(38.9%)|         |
| HCT-CI                                                     |     |         |         |
| 0–2                                                       | 25(62.5%)| 19(52.8%)| 0.391   |
| ≥3                                                        | 15(37.5%)| 17(47.2%)|         |
| Disease course before transplantation (months)              |     |         |         |
| ≤12 months                                                | 27(67.5%)| 28(77.8%)| 0.317   |
| >12 months                                               | 13(32.5%)| 8(22.2%) |         |
| Bone marrow blasts before transplantation                   |     |         |         |
| ≤5%                                                      | 30(75%)| 25(69.4%)| 0.589   |
| >5%                                                       | 10(25%)| 11(30.6%)|         |
| Type of donor                                              |     |         |         |
| MSD-HSCT                                                   | 11(27.5%)| 9(25%) | 0.956   |
| Haplo-HSCT                                                 | 22(55%)| 21(58.3%)|         |
| MUD-HSCT                                                   | 7(17.5%)| 6(16.7%) |         |
| Graft source                                               |     |         |         |
| BM+PB                                                      | 30(75%)| 29(80.6%)| 0.562   |
| PB                                                        | 10(25%)| 7(19.4%) |         |
| MNC(×10^6/kg)                                              | 9.76±3.37| 12.48±5.07| 0.007   |
| CD34+(×10^6/kg)                                            | 5.77±2.73| 3.65±3.10| 0.004   |
| Donor age (years)                                          | 32±13| 35±10   | 0.357   |
| Donor/recipient gender                                      |     |         |         |
| Female to male                                             | 10(25%)| 4(11.1%) | 0.147   |
| Others                                                   | 30(75%)| 32(88.9%)|         |

Table 1 (Continued).

| Table 1 (Continued). | Dec | Non-Dec | P Value |
|-----------------------|-----|---------|---------|
| ABO compatibility     |     |         |         |
| Matched               | 23(57.5%)| 29(80.6%)| 0.055   |
| Major mismatched      | 8(20%)| 4(11.0%) |         |
| Minor mismatched      | 8(20%)| 1(2.8%) |         |
| Major and minor mismatched | 1(2.5%)| 2(5.6%) |         |
| Conditioning regimen  |     |         |         |
| Bu/Flu                | 40(100%)| 31(86.1%)| 0.015   |
| Bu/Cy                 | 0(0%)| 5(13.9%) |         |
| ATG (g/kg)            |     |         |         |
| Yes                   | 39(97.5%)| 31(86.1%)| 0.066   |
| No                    | 1(2.5%)| 5(13.9%) |         |

Table 2 Between-Group Differences of Transplantation-Related Complications Incidence

| Table 2 | Dec | Non-Dec | P Value |
|---------|-----|---------|---------|
| CMV viremia              | 30% (12/40) | 53% (19/36) | 0.044   |
| EBV viremia               | 13% (5/40) | 17% (6/36) | 0.606   |
| Respiratory infection     | 22.5% (9/40) | 53% (19/30) | 0.006   |
| Hemorrhagic cystitis      | 20% (8/40) | 17% (6/36) | 0.708   |

Abbreviations: CMV, cytomegalovirus; EBV, Epstein-Barr virus.

Transplantation-Related Complications

The incidence of CMV viremia, EBV viremia, and hemorrhagic cystitis was comparable in the two groups. However, the de novo incidence of respiratory infection was 22.5% in Dec group as against 53% in the non-Dec group (P=0.006) (shown in Table 2 – Incidence of transplantation-related complications).

Graft versus Host Disease

Grading of aGVHD was performed according to the International Bone Marrow Transplant Registry (IBMTR), while cGVHD was graded according to the National Institutes of Health (NIH) global severity of cGVHD. Cumulative incidence of grade II to IV aGVHD in the Dec group (12.4%, 95% CI 4.9–30.9%) was significantly lower than that [41.5%, 95% confidence interval (CI) 28.1–61.2%] in the non-Dec group (P=0.005). The

(Continued)
incidence rate of cGvHD in the Dec and non-Dec groups was 17.5% and 25%, respectively (P=0.436). Results are shown in Figure 1 [Incidence of (a) aGvHD and (b) cGvHD in the Dec group and the non-Dec group].

Univariate analyses on influencing factors of II to IV grade aGvHD were carried out by Log-rank test of Kaplan-Meier. Results of univariate analyses showed that recipients older than 40 years may be more susceptible to grade II to IV aGvHD (P=0.018) (Table 3 Univariate analysis).

Factors associated with a significance level of P<0.1 on univariate analysis (including age at transplantation and donor type) were further evaluated on multivariate analysis. Risk factor analysis showed that Dec-containing conditioning regimen was a protective factor against grade II–IV aGvHD [hazard ratio (HR): 0.279, 95% CI: 0.102–0.765, P=0.013] (Table 4 – Multivariate analysis).

Outcomes
The median follow-up duration in the entire study cohort was 40 (1 to 155) months. The median follow-up in the Dec and non-Dec groups was 27.5 (range, 1 to 57) months and 70 (range, 1 to 155) months, respectively. No significant between-group difference was observed with respect to the 3-year OS, DFS, or relapse rate (P=0.980, 0.959, and 0.573, respectively).

### Table 3 Univariate Analysis for II to IV Acute Graft versus Host Disease

| Factor                                      | P Value | OR (95% CI) |
|---------------------------------------------|---------|-------------|
| Age at transplantation (≤40 years/>40 years) | 0.018   | 0.487 (0.185–1.285) |
| Gender (male/female)                        | 0.918   | 1.430 (0.846–2.417) |

### Table 4 Multivariate Analysis for Acute Graft versus Host Disease

| Factor                                      | P Value | OR (95% CI) |
|---------------------------------------------|---------|-------------|
| Donor type (MSD/other types)                | 0.180   | 1.430 (0.846–2.417) |

Abbreviations: RA, refractory anemia; RCMD, refractory cytopenia with multilineage dysplasia; RAEB, refractory anemia with excess.

**Figure 1** Incidence of (A) aGvHD and (B) cGvHD in the Dec group and the non-Dec group.

**Abbreviations:** HSCT, hematopoietic stem cell transplantation; aGvHD, acute graft versus host disease; cGvHD, chronic graft versus host disease.
Some researchers

Finally, Dec alleviates tissue damage by inhibiting which leads to loss of DNA methylation, thus exerting a therapeutic epigenetic modulation effect. Some researchers have suggested that the effects of Decitabine are mediated by mechanisms other than DNA hypomethylation. Though some clinical studies have recommended addition of 15 or 20 mg/m² before or after stem cell transplantation, the dose of Decitabine is still not standardized. Therefore, we are currently seeking answers to this question. Based on the previous study, we supposed that adding Decitabine to conditioning regimen may be a rational treatment plan.

Subgroup Analysis

Subgroup analyses were performed according to the IPSS-R risk category. The results suggested that, in the higher risk subgroup, Dec-containing conditioning may potentially decrease the relapse rate (10.6% vs 21.6%, P=0.370), increase disease-free survival (72.2% vs 57.1%, P=0.314), and enhance overall survival (72.2% vs 64.3%, P=0.628). NRM was 10.8% in the Dec group vs 0% in the non-Dec group (P<0.001). However, there were only 2 patients in the Dec group and none of the patients in the non-Dec group developed no relapse death in the competing risk model; therefore, we cannot draw the conclusion that Dec increases NRM in higher-risk patients. The results are summarized in Figure 2 (differences of (a) overall survival, (b) disease-free survival, (c) relapse rate, and (d) no relapse survival between the Dec group and the non-Dec group of IPSS-R higher-risk patients).

Discussion

Decitabine, a hypomethylation agent, can incorporate into deoxyribonucleic acid (DNA) and subsequently bind to DNA methyltransferase (DNMT) covalently. At high concentrations, the predominant effect appears to be cytotoxic effect; however, lower concentrations result in DNMT inhibition which leads to loss of DNA methylation, thus exerting therapeutic epigenetic modulation effect. Some researchers have suggested that the effects of Decitabine are mediated by mechanisms other than DNA hypomethylation. Though some clinical studies have recommended addition of 15 or 20 mg/m² before or after stem cell transplantation, the dose of Decitabine is still not standardized. Therefore, we are currently seeking answers to this question. Based on the previous study, we supposed that adding Decitabine to conditioning regimen may be a rational treatment plan.

In our study, Decitabine was added to conditioning regimen since 2008; after that, our organization started using Decitabine in most high-risk patients, and 20 patients of the non-Dec patients were acquired between 2005 and 2008. Other therapies before or after hematopoietic stem cell transplantation, including prevention and treatment for GVHD, have not been changed. Patients in the Dec group were older and were at a higher risk (as indicated by the IPSS-R risk category) than those in the non-Dec group; however, they achieved similar OS, DFS, RR, and showed longer median time to relapse. These results suggest that Dec may ameliorate the unfavorable prognosis of high-risk patients. Besides, on subgroup analysis, the relapse rate in the Dec group was lower than that in the non-Dec group (10.6% vs 21.6%); however, considering the very small sample, a larger study is required to draw more definitive evidence. In line with our results, previous studies have also demonstrated lower relapse rates with hypomethylation therapy in combination with allo-HSCT. In a study by Field et al, bridge therapy with 5-Aza prior to allo-HSCT achieved a lower relapse rate as compared to that with traditional chemotherapy (20% vs 32%). Moreover, Decitabine bridging therapy has been shown to be a safe regimen before allo-HSCT. In other studies, post-HSCT maintenance therapy with hypomethylation agents was found to strengthen graft versus tumor effects and decrease the incidence of GVHD at the same time. Decitabine combined with donor lymphocytes infusion was deemed as an effective therapy for relapsed AML and MDS after allo-HSCT.

In our study, Dec-containing conditioning regimen was found to protect against grade II to IV aGvHD and relapse. Previous studies have demonstrated that the addition of Decitabine may contribute to better aGvHD control post transplantation; however, in our study, the incidence rate of grade II to IV aGvHD was 17.5%, which is lower than that achieved with hypomethylation agents bridge therapy and maintenance therapy. The differences may be attributable to the timing of Decitabine therapy. As suggested by previous studies, we believe that the underlying mechanism is related to the immune modulatory effects of Dec. Firstly, Dec induces immunosuppressive effects by increasing the number of regulatory T cells (Treg) with upregulation of the expressions of Foxp3 and HLA-G. Secondly, Dec was shown to exert a protective role after HSCT by modulating the proliferation and differentiation of T cells in a TET2-dependent way. Finally, Dec alleviates tissue damage by inhibiting the production of proinflammatory cytokines, such as interferon γ and tumor necrosis factor β. Moreover, Dec may be a promising epi-immunotherapeutic agent against solid tumors and hematologic cancers.

Studies have also demonstrated a critical role of Dec in promoting the graft versus tumor (GvT) effect. The underlying mechanisms may be as follows: firstly, it may upregulate the expressions of antigenic genes that are silenced because of hypermethylation. Secondly, Dec remodels specific immune responses by inducing the expression of tumor-associated antigen, restoring the expression of HLA class I antigen, upregulating the expressions of...
costimulatory molecules expression, inducing heterogeneous expression of killer immunoglobulin-like receptor (KIR) genes, and promoting enrichment or differentiation of tumor-derived APCs. In summary, Dec exerts its antitumor effects via direct cytotoxicity and strengthened tumor immunity, without sacrificing its GvHD protective effects.

There are some obvious limitations of our research, as this was a small-sample retrospective study; therefore, the treatment allocation algorithm is not clear. Moreover, there were significant between-group differences with respect to some variables; however, these variables were found to have no significant influence on the incidence of aGvHD.

Our study indicates that Dec-containing conditioning regimen probably prevents GvHD whilst maintaining the GvT effect, and may potentially increase the overall survival and disease-free survival with relatively few side effects. However, some limitations of our study should be considered while interpreting our results. These include the small sample size and the retrospective study design, which may have introduced an element of bias.

In conclusion, Dec-containing conditioning regimen in combination with allo-HSCT may have the effect of
reducing the incidence of aGvHD and relapse; certainly, a larger prospective study with a longer follow-up period is required to provide more definitive evidence.

**Conclusion**

In conclusion, Dec-containing conditioning regimen in combination with allo-HSCT may help reduce the incidence of aGvHD and potentially decrease the incidence of relapse. A larger prospective study with a longer follow-up period is required to provide more definitive evidence.

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**Disclosure**

The authors report no conflicts of interest in this work.

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