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ORIGINAL ARTICLE

Azacitidine for the treatment of patients with relapsed acute myeloid leukemia after allogeneic stem cell transplantation

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ABSTRACT

We retrospectively analyzed 38 patients with AML who received azacitidine (AZA) to treat disease relapse after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Patients with objective response (OR) ($n = 20$) after AZA had significantly higher 2-year overall survival (OS) (45.0% vs 5.6%; $p = 0.004$) than progressive disease. The 2-year OS was significantly higher in the retransplant group ($n = 23$) than in the nonretransplant group ($n = 15$) (34.8% vs 13.3%; $p = 0.034$). We analyzed 167 patients who underwent the second allo-HSCT to clarify the impact of pretransplant AZA after the second allo-HSCT. Patients in the AZA group ($n = 21$) had significantly higher 2-year disease-free survival (DFS) (32.7% vs 14.5%; $p = 0.012$) and OS (38.1% vs 17.5%; $p = 0.044$) than those in the SOC group ($n = 146$). Our data demonstrate that AZA is an effective and well-tolerated bridging therapy to the second allo-HSCT.

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Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an important curative option in patients with acute myeloid leukemia (AML) [1,2]. Relapse after allo-HSCT, which eventually occurs in 40%–70% of patients, remains the major obstacle of treatment failure and is associated with a dismal prognosis [3,4]. The commonly used treatment options for those patients are mainly restricted to reductions of immunosuppressive therapy, chemotherapy with or without donor lymphocyte infusion (DLI), followed by the second allo-HSCT [3,4]. However, many patients either cannot tolerate intensive treatments or are refractory to those conventional interventions. Consequently, there is a need for potent antileukemic activity, acceptable toxicity, and mechanisms to direct the donor immune system toward an enhanced graft-versus-leukemia (GVL) effect without exacerbating graft-versus-host disease (GVHD) in this situation.

Azacitidine (AZA) is a DNA methyltransferase inhibitor that demonstrates significant clinical activity with relatively low toxicity profiles in AML and MDS who are not eligible for intensive chemotherapy [5,6]. In addition to its antileukemic activity, recent data have shown that AZA upregulates the expression of epigenetically silenced putative tumor antigens and induces a CD8+ T cell response [7]. Furthermore, the administration of AZA after transplantation results in the expansion of Tregs [8–11], suggesting a potential mechanism for suppressing GVHD. Thus, AZA would be one of the optimal treatment options for patients with AML who relapsed after allo-HSCT for avoiding severe toxicities induced by the conventional salvage chemotherapy while evoking the GVL effects *via* post-HSCT status. Recent studies have also confirmed significant antileukemic activity in patients with AML who have relapsed after allo-HSCT [12–15]. Therefore, we retrospectively examined the tolerability and efficacy of AZA therapy in patients who relapsed after allo-HSCT for AML.

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Supplemental data for this article can be accessed here.