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LETTER TO THE EDITOR

HLA-haploidentical hematopoietic stem cell transplantation with low-dose thymoglobulin GVHD prophylaxis for an adult T cell leukemia/lymphoma patient treated with pretransplant mogamulizumab

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Dear Editor,

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) has been considered as standard therapy for aggressive adult T cell leukemia/lymphoma (ATLL) patients to achieve a long-term survival [1, 2]. Anti-CCR4 monoclonal antibody mogamulizumab (Mog) is the first immunotherapeutic agent targeting ATLL. Since CCR4 is expressed on regulatory T cells (Treg), there is growing concern regarding increased risk of severe and refractory acute graft-versus-host disease (aGVHD) in ATLL patients treated with Mog before allo-HSCT (pretransplant Mog) [3–6].

We describe a case of an acute-type ATLL patient who underwent HLA-haploidentical peripheral blood stem cell transplantation (haplo-PBSCT) following pretransplant Mog. The interval between the last Mog administration and haplo-PBSCT was 49 days. A 65-year-old Japanese male presented with a 2-week history of fatigue, anorexia, and nausea. He was diagnosed as acute-type ATLL with hypercalcemia. His ATLL including abnormal bone lesions was chemorefractory. Therefore, he was further treated with two doses of Mog (1 mg/kg weekly for 2 weeks). The disease status significantly improved after Mog administration. Unmanipulated haplo-PBSCT was performed from his son (Table 1). The conditioning consisted of fludarabine (25 mg/m^2/day, days −8 to −4), melphalan (80 mg/m^2, day −3), rabbit anti-thymocyte globulin (thymoglobulin; 2.5 mg/kg, day −2), and TBI (4 Gy). Tacrolimus and mycophenolate mofetil were further used for GVHD prophylaxis. Stable and complete donor chimerism was obtained. On day 30, he only developed grade I aGVHD (stage 1 skin rash). One year later, the number of CD4 + CD25 + CD127-/low Treg cells and CD4 + T cells in his PB remained below the normal range (15/μL and 183/μL, respectively), showing delayed T cell reconstitution. He has been in complete remission (CR) without chronic GVHD for 2 years.

Low-dose thymoglobulin, in addition to its T cell depleting properties, stimulates the recovery of Treg cells [7, 8]. In this regard, Motohashi et al. reported an acute-type ATLL patient who achieved CR following Mog treatment and subsequently received unrelated bone marrow transplantation (uBMT) [9]. Two months after the last Mog administration, uBMT was performed from a serologically two antigen (HLA-C and -DR) mismatched donor by using conditioning with 1.25 mg/kg of thymoglobulin. As a result, they only observed grade I aGVHD.

In ATLL, allo-HSCT at disease regression induced by initial treatment has been shown to improve the clinical outcome [10]. Pretransplant Mog significantly improved the disease status before haplo-PBSCT. Moreover, a recent nationwide study of ATLL patients with pretransplant Mog in Japan showed that pretransplant Mog with intervals of <50 days to allo-HSCT was associated with increased risk of GVHD-related mortality [6]. In our case, the interval between pretransplant Mog and haplo-PBSCT was 49 days. The nationwide study also pointed out the possibility that in vivo effector T cell depletion with anti-thymocyte globulin contributes to the reduction of severe aGVHD in ATLL patients with

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Table 1 HLA status of the patient and donor

	Sex	Relation	Blood type	HLA-A	HLA-B	HLA-C	HLA-DR
Recipient	Male		A+	0201/2402	3901/5502	0702/0102	1201/0901
Donor	Male	Son	A+	0201/0206	3901/5101	0702/1402	1201/0803

pretransplant Mog [6]. To our knowledge, our case is the first report of successful prevention of aGVHD with low-dose thymoglobulin in haplo-PBSCT following pretransplant Mog. Low-dose thymoglobulin is an effective option for aGVHD prophylaxis in ATLL patients with pretransplant Mog.

Compliance with ethical standards Written informed consent was obtained from the patient for publication.

Conflict of interest The authors declare that they have no conflict of interest.

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