Published in final edited form as:

Clin Cancer Res. 2009 January 1; 15(1): 368–373. doi:10.1158/1078-0432.CCR-08-1302.

ALEMTUZUMAB THERAPY FOR HYPEREOSINOPHILIC SYNDROME AND CHRONIC EOSINOPHILIC LEUKEMIA

Srdan Verstovsek¹, Ayalew Tefferi², Jorge E. Cortes¹, Taghi Manshouri¹, Raja Luthra³, Animesh Pardanani², Alfonso Quintás-Cardama¹, Farhad Ravandi¹, Carlos Bueso-Ramos³, and Hagop Kantarjian¹

¹Department of Leukemia, The University of Texas M.D. Anderson Cancer Center, Houston, TX, U.S.A.

³Hematopathology, The University of Texas M.D. Anderson Cancer Center, Houston, TX, U.S.A.

²Division of Hematology, Department of Internal Medicine, Mayo Clinic College of Medicine, Rochester, MN, U.S.A.

Keywords

alemtuzumab; hypereosinophilic syndrome; chronic eosinophilic leukemia; CD52

Introduction

The hypereosinophilic syndrome (HES) is a heterogeneous group of disorders defined by the presence of non-reactive blood eosinophilia with an absolute eosinophil count of $>1.5 \times 10^9/L$ and evidence of eosinophilia-induced organ damage.¹ The World Health Organization (WHO) classification system for hematopoietic tumors distinguishes HES from clonal eosinophilias, also referred to as chronic eosinophilic leukemia (CEL).² This is a therapeutically relevant distinction since treatment with the tyrosine kinase inhibitor imatinib mesylate is very effective in the subcategory of CEL associated with a rearrangement that fuses the platelet-derived growth factor receptor- α (*PDGFR α*) gene to the uncharacterized human gene FIP1-like-1 (*FIP1L1*), for which this agent is approved first-line therapy.³ Not all patients with HES or *PDGFR α* -negative CEL require therapy in the absence of symptomatic organ damage, such as cardiac, neurological, upper airway, or gastrointestinal disease. Corticosteroids are the first line drug of choice in the management of treatment-requiring patients. Although most patients respond to corticosteroids, many either exhibit resistance or relapse during steroid tapering or withdrawal and develop significant side effects related to long-term steroid use.⁴ HES and *PDGFR α* -negative CEL are potentially fatal diseases with a reported 10-year survival for HES of less than 50%, especially in corticosteroid-resistant cases with cardiac involvement.⁵ Currently, therapy for corticosteroid-refractory patients is inadequate and includes cytoreductive agents such as interferon α and hydroxyurea⁶.

CD52 is a surface glycoprotein expressed at high levels on B and T lymphocytes and at lower levels on monocytes.⁷ Interestingly, CD52 is also expressed on the surface of eosinophils but is absent on neutrophils or bone marrow stem cell precursors.⁸ Alemtuzumab (Campath-1H) is a humanized IgG1k anti-CD52 monoclonal antibody that has been approved for the treatment of fludarabine-refractory B cell chronic lymphocytic leukemia. Two case reports of its use as a therapy for HES has been published so far.^{9,10} We report herein our experience in the therapeutic use of alemtuzumab in eleven patients with advanced HES or CEL.

Methods

The databases of patients with myeloproliferative disorders at the MD Anderson Cancer Center (MDACC; Houston, TX) and the Mayo Clinic (Rochester, MN) were screened for patients with the diagnoses of HES or CEL who had received treatment with alemtuzumab. The aim of the study was to summarize our experience with alemtuzumab in these disorders. The study was approved by the Institutional Review Boards (IRB) at both institutions. HES was defined according to the WHO criteria as an absolute eosinophil count in peripheral blood of at least $1.5 \times 10^9/L$ persistent for longer than 6 months, in the absence of any known cause of eosinophilia (e.g. parasitic infection, neoplastic disorders, atopy/allergic disorders, and collagen vascular diseases), and with evidence of symptoms and/or tissue damage secondary to eosinophil infiltration. In patients with evidence of a clonal eosinophilic disorder (i.e. carrying cytogenetic and/or molecular abnormalities), a diagnosis of CEL was mandated.

Cytogenetic analysis and molecular testing for *PDGFRα* gene activation, *JAK2*^{V617F} gene mutation, and the presence of T-cell receptor gene rearrangements, were done as previously described.^{3,11,12} Because some of these techniques have only become available recently and were not done at the start of alemtuzumab therapy, they were performed on stored tissue samples retrieved from the Hematopathology Tissue Banks of either MDACC or the Mayo Clinic, under IRB-approved laboratory protocols.

Results

Patient characteristics

Eleven patients (7 male, 4 female) received treatment with alemtuzumab (Table 1). Nine patients were treated at MDACC and two at the Mayo Clinic. All patients underwent a baseline bone marrow biopsy and aspiration with cytogenetic studies. Nine of the eleven study patients fulfilled the WHO criteria for HES. In two patients, the presence of cytogenetic abnormalities mandated a diagnosis of CEL. All but patient 3 (test not done) were negative for the *FIPIL1-PDGFRα* rearrangement. All patients tested negative for the presence of the *JAK2*^{V617F} mutation. All but patient 1 (test not done) were negative for T-cell receptor gene rearrangements.

The median age was 62 years (range, 24 to 82). The median time from diagnosis to alemtuzumab therapy was 20 months (range, 0.5 to 191). In two patients, alemtuzumab represented the initial therapy while other 9 patients had failed a median of 4 prior therapies,

including steroids in all and interferon-alpha in three patients, respectively. The latter nine patients were receiving therapy with poor symptomatic control prior to alemtuzumab start (Table 1). Eight of these nine patients had also failed tyrosine kinase inhibitor therapy, including imatinib (n=7), dasatinib (n=3), and nilotinib (n=2). Patient 3 was not tested for the *PDGFRα* transcripts but the lack of response to imatinib suggests *FIP1L1-PDGFRα* negativity given the exquisite sensitivity of PDGFR kinase to this agent.³

Response criteria

A complete hematologic response (CHR) was defined as the reduction of the absolute eosinophil count and the percentage of eosinophils in peripheral blood to normal values ($0.4 \times 10^9/L$ and 4%, respectively) with disappearance of all signs and symptoms of disease (e.g. organomegaly, skin rash, pruritus). Patients with CHR who also normalized the percentage of eosinophils in the bone marrow were considered to have achieved a true complete response (true CR). A partial response (PR) was defined as the reduction of peripheral blood eosinophilia and/or extent of organomegaly by at least 50% from the baseline values. Recovery of the organ function (e.g. depressed cardiac function) was not required for CHR, true CR, or PR achievement.

Treatment schedule and patient evaluation during therapy

Informed consent was obtained prior to alemtuzumab start in all instances in accordance with the Declaration of Helsinki. The schedule for patients treated at MDACC was generally as follows: alemtuzumab was administered at 3mg intravenously (IV) on day 1; if this dose was tolerated (i.e. grade 2 toxicity), it was increased to 10mg IV on day 2 and to 30mg IV on day 3. Then, alemtuzumab was administered at 30mg (or 10mg if 30mg was not tolerated) three times per week, either IV or subcutaneously (SC). After a total of 12 doses, patients with complete hematologic response (CHR) continued alemtuzumab at 30mg IV or SC once weekly as maintenance. Those without CHR were continued on alemtuzumab 30mg three times a week for 4 more weeks and then weekly, as the maintenance of the response. The duration of maintenance therapy differed based on patients' and physicians' preference (Table 1). The treatment schedule at the Mayo Clinic was SC in all instances and flexible in its dosing, depending on a response.

Patients were examined every 2-4 weeks for the first 3 months and every 8-12 weeks thereafter. Complete blood counts with differential and serum chemistries were obtained every 1-2 weeks during the first 8 weeks, then every 4-8 weeks. Bone marrow biopsies were performed during therapy at the discretion of a treating physician, as indicated. Prophylaxis against *Pneumocystis jiroveci* with trimethoprim/sulfamethoxazole 160mg/800mg twice daily 3 times weekly and against cytomegalovirus (CMV) with valganciclovir 500mg orally daily was administered during alemtuzumab treatment and at least for 2 months after discontinuation. CMV antigenemia was routinely assessed, as previously reported,¹³ in all patients treated at MDACC before entering the study and every 12 weeks thereafter or up to 2 months upon alemtuzumab discontinuation. At the Mayo Clinic, CMV antigenemia was assessed only if clinically indicated.

Response to alemtuzumab therapy

Therapy with alemtuzumab resulted in a brisk decline in absolute eosinophil count and the percentage of eosinophils in the peripheral blood in all patients, with negligible effect on the absolute leukocyte or neutrophil counts. Ten patients (91%) achieved CHR in a median of 2 weeks (range, 0.5-5 weeks), that lasted for a median of 18 weeks or 4.5 months (range, 6 to 56 weeks; or 1.5 to 14 months). Of them, four had CHR that lasted for 6+ months, including five who remained in CHR off-alemtuzumab for at least one month (maximum 8 months). Seven patients relapsed; 2 patients relapsed while receiving alemtuzumab therapy. Patient 7 achieved an ongoing PR on weekly alemtuzumab, with only 50% decrease in the percentage of peripheral blood eosinophils (70 to 33%) but a remarkable decrease in the absolute eosinophil count from 14.2 to $1.0 \times 10^9/L$.

Five of the 8 patients in CHR that had bone marrow biopsy done, had also a true CR, with normalization of the bone marrow differential (Figures 1A and 1B show bone marrow findings from patient 3). Two patients with chromosomal abnormalities prior to alemtuzumab had follow-up cytogenetic studies showing no change. Patients 8 and 10 lost their response but achieved a second response upon alemtuzumab rechallenge. Notably, patient 10 presented with severe eosinophilic dermatitis consisting of widespread urticaria and eczematous lesions, as well as severe edema and tenseness in all four limbs. Upon the initiation of therapy his WBC count and eosinophils rapidly decreased (Figure 1C) and he achieved a CHR with the elimination of all cutaneous lesions and resolution of the edema (15lbs weight loss in 2 weeks), shortly upon alemtuzumab administration (Figure 1D), that lasted for 10 months. Flow cytometry studies demonstrated the elimination of CD52-positive eosinophils in bone marrow in this patient (Figures 1E and 1F). After remaining in CHR for 7 months off alemtuzumab this patient relapsed with eosinophilic dermatitis and eosinophilia but achieved a second CHR soon after resuming alemtuzumab.

Five patients died during the follow up, 2 while still in CHR off alemtuzumab therapy (Patient 3 due to unrelated medical reasons, and Patient 11 due to concomitant metastatic thyroid cancer) and 3 that relapsed while off alemtuzumab therapy and then had a grave development (Patient 1 due to fungal pneumonia after a matched unrelated SCT; Patient 4 died in hospice; Patient 5 failed both nilotinib and intensive chemotherapy).

Toxicity

Therapy with alemtuzumab was generally well tolerated. Two (18%) of 11 patients (Patients 1 and 7) developed CMV reactivation: Patient 1 while in CHR off-alemtuzumab and Patient 7 after 3 weeks on therapy. Both cases presented with positive CMV antigenemia and fever of unknown origin with no associated organ disease. Both episodes resolved after the administration of short courses of gancyclovir or valgancyclovir, respectively. In Patient 7, alemtuzumab was also interrupted for 4 weeks. Patient 3 developed preorbital cellulitis while in CHR and off-alemtuzumab, requiring a course of intravenous antibiotics. Three patients experienced grade 3 fever and rigors during alemtuzumab infusion. Two of these patients also experienced infusion-related shortness of breath and hypotension, requiring transient (~2 weeks) dose reductions and supportive care with low-dose hydrocortisone, acetaminophen, and diphenhydramine. In all instances, infusion-related reactions were first

noted during the loading doses of alemtuzumab on days 1 to 3 and subsided over the course of subsequent doses. However, in Patient 4 alemtuzumab had to be terminated due to persistent infusion-related fever, even after dose reductions to 10mg and 5mg, respectively. All patients developed lymphopenia during treatment as a direct effect of the pharmacologic action of alemtuzumab. Patient 8 developed Epstein Barr virus (EBV)-positive orbital/maxillary sinus diffuse large B-cell lymphoma (DLBCL) while being rechallenged with alemtuzumab for relapsed HES. Alemtuzumab therapy was stopped (patient is currently in CHR for 5 months) and the patients underwent surgical debulking and local radiotherapy of the involved site, achieving complete remission from lymphoma.

Discussion

The present study demonstrates the value of alemtuzumab as salvage therapy for advanced HES or CEL. The rationale for the use of alemtuzumab for the treatment of patients with diseases characterized by blood and tissue eosinophilia has been provided by the fact that anti-CD52 monoclonal antibodies bind homogeneously to CD52 on the surface of human eosinophils, which unlike neutrophils, constitutively express this surface marker.⁸ The majority of our 11 patients had failed multiple prior therapies including small-molecule tyrosine kinase inhibitors (e.g. imatinib, nilotinib, dasatinib) and cytotoxics. Responses were documented in all patients, including CHR in 10 (91%) patients. Seven patients relapsed but only 2 while on alemtuzumab therapy, suggesting that maintenance of a response (e.g. alemtuzumab given every 2-4 weeks) might be necessary to provide optimal therapy to the patients. Notably, two patients who lost their CHR after cessation of alemtuzumab therapy achieved a second CHR after alemtuzumab was resumed.

Therapy with alemtuzumab was generally well tolerated. Severe infusion reactions during the administration of the first alemtuzumab doses were reported in three patients and were managed with supportive treatment and dose reductions. In all but one patient with recurrent infusion-related fever, these side effects subsided with subsequent infusions, allowing for escalation to the baseline standard dose of the study drug. No significant shifts in the relative proportions of neutrophils in blood were observed during alemtuzumab therapy and only one episode of bacterial infection (orbital cellulitis) was observed in a patient after 6 months off-alemtuzumab. In keeping with prior reports,¹³ two (18%) patients experienced CMV reactivation with no evidence of invasive disease and were successfully managed with short courses of antiviral therapy. Importantly, one patient developed EBV-positive DLBCL during alemtuzumab therapy. Although the contribution of the study drug to this occurrence is uncertain, the development of lymphoid malignancies during alemtuzumab therapy has been previously reported and may relate to strong impairment of immunosurveillance due to T-cell depletion.⁷

In summary, our data indicate that patients with HES or CEL benefit from treatment with alemtuzumab. Given the lack of effective therapies for these disorders when in advanced or aggressive phase, our results may change the therapeutic paradigm for this subset of patients. However, it must be emphasized that indiscriminate alemtuzumab use is discouraged because of the possibility of significant complications associated with long-term drug use, such as the development of opportunistic infections (e.g. CMV reactivation) or

cardiac toxicity.⁷ Based on our limited dataset we cannot advocate the widespread use of alemtuzumab, but our encouraging results support the clinical evaluation of alemtuzumab in a larger controlled trial for patients with advanced HES or CEL resistant to standard therapy.

References

1. Chusid MJ, Dale DC, West BC, Wolff SM. The hypereosinophilic syndrome: analysis of fourteen cases with review of the literature. *Medicine (Baltimore)*. 1975; 54:1–27. [PubMed: 1090795]
2. Bain, B.; Pierre, R.; Imbert, M.; Vardiman, JW.; Brunning, RD.; Flandrin, G. Chronic eosinophilic leukemia and the hypereosinophilic syndrome. In: Jaffe, ES.; Harris, NL.; Stein, H.; Vardiman, JW., editors. *World Health Organization Classification of Tumors: Tumours of the Haematopoietic and Lymphoid Tissues*. International Agency for Research on Cancer (IARC) Press; Lyon, France: 2001. p. 29–31.
3. Cools J, DeAngelo DJ, Gotlib J, et al. A tyrosine kinase created by fusion of the PDGFRA and FIP1L1 genes as a therapeutic target of imatinib in idiopathic hypereosinophilic syndrome. *N Engl J Med*. 2003; 348:1201–14. [PubMed: 12660384]
4. Tefferi A, Patnaik M, Pardanani A. Eosinophilia: secondary, clonal and idiopathic; *BJH*. 133:468–492. Review. [PubMed: 16681635]
5. Lefebvre C, Blety O, Degoulet P, et al. Prognostic factors of hypereosinophilic syndrome. Study of 40 cases. *Ann Med Interne (Paris)*. 1989; 140:253–7. [PubMed: 2675714]
6. Kalac M, Quintas-Cardama A, Vrhovac R, Kantarjina H, Verstovsek S. A critical appraisal of conventional and investigational drug therapy in patients with hypereosinophilic syndrome and clonal eosinophilia. *Cancer*. Sep 1; 2007 110(5):955–64. Review. [PubMed: 17654661]
7. Alinari L, Lapalombella R, Andritsos L, Baiocchi RA, Lin TS, Byrd JC. Alemtuzumab (Campath-1H) in the treatment of chronic lymphocytic leukemia. *Oncogene*. 2007:3644–3653. Review. [PubMed: 17530018]
8. Elsner J, Hochstetter R, Spiekermann K, Kapp A. Surface and mRNA expression of the CD52 antigen by human eosinophils but not by neutrophils. *Blood*. 1996; 88:4684–93. [PubMed: 8977262]
9. Pitini V, Teti D, Arrigo C, Righi M. Alemtuzumab therapy for refractory idiopathic hypereosinophilic syndrome with abnormal T cells: a case report. *Br J Haematol*. Dec.2004 127(5): 477. [PubMed: 15566349]
10. Sefcick A, Sowter D, DasGupta E, Russell NH, Byrne JL. Alemtuzumab therapy for refractory idiopathic hypereosinophilic syndrome. *Br J Haematol*. Feb; 2004 124(4):558–9. [PubMed: 14984510]
11. Nussenzweig RH, Swierczek SI, Jelinek J, et al. Polycythemia vera is not initiated by JAK2V617F mutation. *Exp Hematol*. 2007; 35:32–8. [PubMed: 17198871]
12. Vega F, Medeiros LJ, Jones D, Abruzzo LV, Lai R, Manning J, Dunmire V, Luthra R. A novel four-color PCR assay to assess T-cell receptor gamma gene rearrangements in lymphoproliferative lesions. *Am J Clin Pathol*. Jul; 2001 116(1):17–24. [PubMed: 11447747]
13. Nguyen DD, Cao TM, Dugan K, Starcher SA, Fechter RL, Coutre SE. Cytomegalovirus viremia during Campath-1H therapy for relapsed and refractory chronic lymphocytic leukemia and prolymphocytic leukemia. *Clin Lymphoma*. 2002; 3:105–10. [PubMed: 12435283]

Figure 1. Effect of alemtuzumab therapy

(A) Bone marrow (BM) specimen from Patient 3 showing extensive dense interstitial infiltration by eosinophils prior to alemtuzumab therapy. (B) A hematoxylin-and-eosin-stained BM specimen obtained from the same patient within 3 months from alemtuzumab therapy shows remarkable reduction in the percentage of eosinophils with respect to the total BM cellularity. (C) Alemtuzumab therapy normalized white blood cell (WBC) and eosinophil counts in peripheral blood of Patient 10. Note the “rebound” in the eosinophil levels after alemtuzumab dose reduction (5 mg) secondary to infusion-related side effects

prior to achieving a durable complete hematologic response (CHR) on 10 mg twice weekly that was maintained for several months even after alemtuzumab discontinuation. (D) Upper panels show extensive erythematous dermatitis in Patient 10 prior to alemtuzumab therapy characterized by significant interstitial eosinophilic infiltration of the dermis and subcutis (inset) with remarkable blistering and hemorrhage of the hands. Lower panels show complete resolution of all the cutaneous changes during alemtuzumab therapy. Original magnification, $\times 100$ (A) and $\times 200$ (B and inset D). (E and F) Bone marrow cells obtained from Patient 10 were labeled with fluorescent anti-CD52 and anti-CD123 monoclonal antibodies (to highlight eosinophils) and subjected to flow immunophenotypic analysis. Left panel (E) shows strong positivity (82%, right upper quadrant) in pre-therapy sample, while right panel (F) shows absence of eosinophils in post-therapy sample.

Table 1
Clinical characteristics and response to alemtuzumab in 11 patients with HES or CEL

Patient No.	Age/ Sex	Prior Therapy	Rx (symptoms at study entry)	Absolute baseline PB eosinophils ($\times 10^9/L$)/ percent	Baseline BM eosinophil percent	Cytogenetic findings	Alemtuzumab therapy	Best hematologic response/Time to response	Overall duration of response/ Response off therapy	True CR while in CHR (BM with normal %Eo)	Current Status
1	54/m	Steroids, imatinib, 2CdA, PEG-IFN- α	None/Bone pain, profound fatigue	1.7/24%	14%	46,XY	10 mg tiw $\times$ 12 doses	CHR/0.5 wk	6 wk/3 wk	Yes	Relapsed and died after allo- SCT
2	24/m	Steroids, imatinib, cromolyn, PEG-IFN- α , nilotinib, dasatinib	PRD 30 mg daily/ diarrhea, nausea, vomiting	1.8/21%	38%	46,XY	[^] 30 mg SC tiw $\times$ 12 doses, then 30 mg tiw $\times$ 3 doses every 1-2 months for 10 months	CHR/3 wk	56+ wk/16+ wk	No (BM Eo 7%)	CHR off alemtuzumab
3	45/f	Steroids, MTX, imatinib	PRD 15 mg daily/ Renal insufficiency, diarrhea	1.2/10%	35%	46,XX	[^] 30 mg SC tiw $\times$ 12 doses, then weekly $\times$ 2 doses	CHR/0.5 wk	32 wk/31 wk	Yes	Died of unrelated medical reasons
4	69/m	Steroids, dasatinib	PRD 30 mg daily/ nausea, vomiting, diarrhea	10.1/23%	14%	Monosomy Y, trisomy 8	[^] 30 mg SC tiw $\times$ 12 doses	CHR/0.5 wk	7 wk/4 wk	No	Relapsed off therapy and died in hospice
5	53/m	CsA, steroids, ATG, cytarabine, imatinib	HU 3 g daily/Rash, progressive splenomegaly	25.2/49%	10%	46,XY	[^] 30 mg IV tiw $\times$ 24 doses	CHR/1.5 wk	9 wk/2 wk	Yes	Relapsed off therapy. Died after not responding to nilotinib, and 2CdA+cytarabine
6	31/f	Imatinib, splenectomy , HU, steroids	HU 2 g daily/Pleural effusion, chest pain, dyspnea, fever	29.7/9%	32%	t(5;6)(q22;q21)	[^] 30 mg IV tiw $\times$ 3 doses, then SC tiw	CHR/1 wk	6 wk/0 wk	No (BM Eo 6%)	Relapsed on therapy; in CR post allo-SCT
7	62/m	Steroids, imatinib, dasatinib	PRD 80 mg daily+Furosemide 120 mg twice daily/Extensive edema	14.3/70%	68%	46X,Y	[^] 30 mg SC tiw $\times$ 9 doses. Therapy stopped 4 wks due to CMV reactivation; then resumed at 30 mg SC tiw $\times$ 15 doses, then weekly	PR/12 wk	2+ wk/0 wk	No (BM Eo 28%)	PR on weekly alemtuzumab

Patient No.	Age/ Sex	Prior Therapy	Rx /symptoms at study entry	Absolute baseline PB eosinophils ($\times 10^9/L$)/ percent	Baseline BM eosinophil percent	Cytogenetic findings	Alentuzumab therapy	Best hematologic response/Time to response	Overall duration of response/ Response off therapy	True CR while in CHR (BM with normal %Eo)	Current Status
8	70/f	PEG-IFN- α + Steroids, HU	PRD 40 mg daily/ Heart failure (EF 33%), fever, bone pain	0.7/14%*	10%	46,XX	30 mg SC/wk $\times 8$ des	CHR/4 wk	12 wk/8 wk	ND	Relapsed off therapy. Rechallenged with 30 mg SC every week $\times 8$ then other week $\times 4$, then every 3 weeks $\times 4$. Currently in CHR off therapy for 5 months
9	50/f	Steroids +MTX, imatinib,	High-dose steroids /Cerebritis, thalamic infarcts, panniculitis	15.0/50%	60%	46,XX	30 mg SC once or twice a week	CHR/5 wk	24 wks/0 wk	ND	Relapsed on therapy; receiving dasatinib
10	82/m	None	None/Severe peripheral edema with skin blistering, severe fatigue	28.7/82%	68%	46,XY	[^] 30 mg IV $\times 1$ caused hypotension. Reduction to 10 mg $\times 1$, then 5 mg tiw $\times 6$, followed by 10 mg tiw $\times 6$. Then 10 mg SC twice weekly $\times 28$	CHR/5 wk	40 wk/28 wk	Yes	Relapsed off therapy. Rechallenged with 30 mg SC every week $\times 8$ then every other week $\times 2$. Currently in CHR off therapy for 2 months
11	61/m	None	None/Dyspnea, fatigue	36.3/49%	28%	46,XY	[^] 30 mg IV tiw $\times 12$ doses	CHR/1 wk	6 wk/2 wk	Yes	Died of unrelated medical reasons

Abbreviations: m: male; f: female; PEG-IFN- α : pegylated interferon- α ; HU: hydroxyurea; 2CdA: cladribine; ATG: antithymocyte globulin; MTX: methotrexate; CsA: cyclosporine A; iv: intravenous; sc: subcutaneous; ND: not done; SC: subcutaneous; wk: weeks; tiw: three times a week; MUD: matched unrelated donor; allo-SCT: allogeneic stem cell transplantation; CHR: complete response; PR: partial response; PRD: prednisone;

* After a bolus of high dose methylprednisolone at 1 mg/kg/d $\times 1$.

[^] Patients were given alemtuzumab initially at the dose of 5mg IV on day 1, then 10mg IV on day 2 and 30mg IV on day 3.