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Comparison of Subcutaneous versus Intravenous Alemtuzumab for Graft-versus-Host Disease Prophylaxis with Fludarabine/Melphalan–Based Conditioning in Matched Unrelated Donor Allogeneic Stem Cell Transplantation

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The objective of this study was to compare infusion-related reactions and outcomes of using subcutaneous (subQ) alemtuzumab versus intravenous (i.v.) alemtuzumab as graft-versus-host disease (GVHD) prophylaxis for matched unrelated donor stem cell transplantations. Outcomes include incidence of cytomegalovirus (CMV)/Epstein-Barr (EBV) viremia, development of CMV disease or post-transplantation lymphoproliferative disorder, fatal infections, acute and chronic GVHD, time to engraftment, relapse rate, and survival. We conducted a retrospective study of all adult matched unrelated donor stem cell transplantations patients who received fludarabine/melphalan with subQ or i.v. alemtuzumab in combination with tacrolimus as part of their conditioning for unrelated donor transplantation at New York-Presbyterian/Weill Cornell Medical Center from January 1, 2012 to March 21, 2014. Alemtuzumab was administered at a total cumulative dose of 100 mg (divided over days −7 to −3). Forty-six patients received an unrelated donor stem cell transplantation with fludarabine/melphalan and either subQ (n = 26) or i.v. (n = 20) alemtuzumab in combination with tacrolimus. Within the evaluable population, 130 subQ and 100 i.v. alemtuzumab doses were administered. For the primary outcome, ≥grade 2 infusion-related reactions occurred in 11 (8%) versus 25 (25%) infusions in the subQ and i.v. cohorts, respectively ($P = .001$). Overall, 12 injections (9%) in the subQ arm versus 26 infusions (26%) in the i.v. arm experienced an infusion-related reaction of any grade ($P = .001$). There were no significant differences between the subQ and i.v. arms in rates of reactivation of CMV/EBV, development of CMV disease or post-transplantation lymphoproliferative disorder, fatal infections, acute and chronic GVHD, relapse, or survival. Subcutaneous administration of alemtuzumab for GVHD prophylaxis was associated with fewer infusion-related reactions compared with i.v. administration in the SCT setting. Incidences of acute and chronic GVHD were similar between both arms. There was also no difference in reactivation of CMV/EBV viremia, development of CMV disease or post-transplantation lymphoproliferative disorder, fatal infections, relapse, or survival.

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INTRODUCTION

Allogeneic stem cell transplantation is an important treatment option for various malignant and nonmalignant conditions. However, graft-versus-host disease (GVHD) remains a major cause of post-transplantation morbidity and mortality. Alemtuzumab is a humanized monoclonal antibody that targets the CD52 antigen, which is expressed on the surface of T and B lymphocytes, monocytes, eosinophils, macrophages, and some dendritic cells but not on hematopoietic progenitor cells [1]. Based on previously published data, alemtuzumab-containing regimens for allogeneic stem cell transplantation have shown substantial benefit in reducing acute and particularly chronic GVHD [1,2], with survival rates comparable to those after similar regimens with conventional GVHD prophylaxis [3,4].

Many centers, including our own, have adopted alemtuzumab as part of their standard transplantation GVHD prophylaxis [5]. However, intravenous (i.v.) administration of

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alemtuzumab is commonly accompanied by infusion-related side effects, ranging anywhere from local injection site reactions to anaphylaxis [6]. The subcutaneous (subQ) route of administration has been shown to reduce the incidence of infusion-related reactions without a decrease in efficacy when used for chronic lymphocytic leukemia, but its use has not been compared in adult stem cell transplantation [6,7]. In early 2012, we introduced the routine use of subQ alemtuzumab in our unrelated donor transplantation patients. The goal of the current study was to compare the side effect profile and efficacy of subQ versus i.v. alemtuzumab in unrelated donor stem cell transplantation.

Patients and Treatment

This was a institutional review board–approved retrospective cohort study conducted at New York-Presbyterian/Weill Cornell Medical Center and included all adult patients (≥18 years of age) undergoing unrelated donor transplantation using fludarabine-melphalan-alemtuzumab conditioning between January 1, 2012 and March 21, 2014.

Patients received fludarabine 30 mg/m^2/day i.v. on day −7 to day −3 and melphalan 140 mg/m^2/day on day −2. For GVHD prophylaxis, patients received alemtuzumab 20 mg/day i.v. over 4 hours or subQ for 5 consecutive days (days −7 to −3) and tacrolimus starting day −2, which was routinely continued until day +180 unless patients developed GVHD (Figure 1). The alemtuzumab subQ formulation was administered as undiluted drug, available as 30 mg/mL vials, for each dose. Tacrolimus target trough levels were maintained between 5 ng/mL and 15 ng/mL. In a few cases, tacrolimus was replaced by either mycophenolate mofetil or sirolimus because of patient intolerance. For patients who developed GVHD, immunosuppressants were adjusted, as clinically required.

Acetaminophen 650 mg and diphenhydramine 50 mg were given to prevent infusion-related reactions from alemtuzumab. Additionally, for the i.v. cohort, methylprednisolone 2 mg/kg was given before alemtuzumab followed by 1 mg/kg halfway through the infusion on each day of infusion. Patients in the subQ cohort received hydrocortisone 100 mg before alemtuzumab. Anti-infective prophylaxis included levofloxacin 500 mg daily until engraftment, fluconazole 400 mg daily or voriconazole 200 mg twice daily until the patient was off all immunosuppressive medications, and sulfamethoxazole/trimethoprim 1 double-strength tablet twice daily from admission through day −2. At day +30 after transplantation, patients resumed pneumocystis pneumonia prophylaxis. For pre-emptive cytomegalovirus (CMV) treatment, all CMV IgG sero-positive donor and/or recipient patients received ganciclovir (5 mg/kg i.v. twice daily from day of admission until day −2), then acyclovir (500 mg/m^2 if <60 years old or 250 mg/m^2 if ≥60 years old every 8 hours i.v. from day −1 until engraftment), followed by high-dose oral valacyclovir (2 g if <60 years old or 1 g if ≥60 years old 4 times daily until day +150) [8]. After day +150, patients received valacyclovir 500 mg orally twice daily, which continued for a minimum of 1 year after stem cell transplantation or longer if patients continued on immunosuppressive medications. All CMV-IgG seronegative (donor and recipient) patients received oral valacyclovir 500 mg twice daily starting on day −1, which continued for a minimum 1 year after stem cell transplantation or longer, if patients remained on immunosuppressive medications. Patients received filgrastim starting day +5 after transplantation or, in some cases, after day +10. Transfusion support was administered if indicated per institutional policy (packed red blood cells for hemoglobin <8 grams/dL and platelets if <10,000/μL).

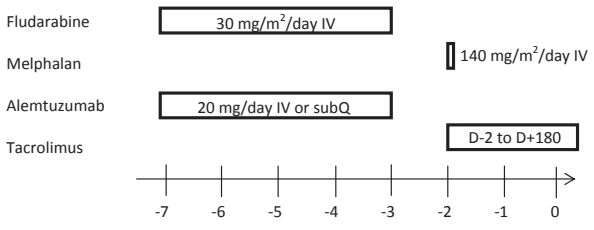

Figure 1. Treatment plan.

Outcomes and Definitions

The primary outcome was the incidence of ≥grade 2 infusion-related reactions within 24 hours of each subQ and i.v. alemtuzumab dose. *Infusion-related reactions* were defined as local injection site reactions (swelling/erythema), fever (defined as ≥38°C), chills/rigors, rash/urticaria, hypotension, bronchospasms/dyspnea, and anaphylaxis. The grade for each infusion-related reaction, as well as for hypotension, was determined using the Common Terminology Criteria for Adverse Events/Cancer Therapy Evaluation program criteria V4.0 (Table 1). Secondary outcomes included incidence of CMV viremia or disease, Epstein-Barr (EBV) viremia and post-transplantation lymphoproliferative disorder, fatal infections, relapse rate, and overall survival in the first year. Times to neutrophil and platelet engraftment and incidences of acute and chronic GVHD were also analyzed.

CMV viremia was defined as the first positive polymerase chain reaction (PCR) ≥200 copies/mL and *CMV disease* was defined as presence of CMV viremia with organ involvement (pneumonia, retinitis, colitis, or marrow involvement) up to 2 weeks after initiation of treatment. *Recurrence* of CMV viremia was defined as CMV viremia occurring after 2 consecutive negative real time PCR assays after treatment of initial episode of infection and requiring empiric treatment. EBV viremia was also recorded at the first positive PCR (≥200 copies/mL) and diagnosis of post-transplantation lymphoproliferative disorder was based on positron emission tomography scan or tissue biopsy. *Neutrophil engraftment* was defined as the first of 3consecutive days with an absolute neutrophil count ≥ .5 × 10^9/L. *Platelet engraftment* was defined as the first of 3 consecutive days with a platelet count ≥ 20 × 10^9/L that was maintained without transfusion support for 7 consecutive days. Acute GVHD assessment and grading were based on the consensus conference on acute GVHD grading [9]. Assessment and grading of chronic GVHD was based on the National Institutes of Health consensus development project on criteria for clinical trials in chronic GVHD [10].

Statistical Analysis

Fisher's exact or the chi-square test were used to compare categorical variables between groups. Mann-Whitney test was used to compare continuous variables. Group comparisons were 2-sided with a type 1 error of <.05. Estimates for each group are reported along with 95% confidence intervals. Breslow-Gehan-Wilcoxon tests were used to compare the time-related measures between groups.

Table 1
Grading Criteria

Event	1	2	3	4	5
Infusion-related reaction	Mild reaction, infusion interruption not indicated, intervention not indicated	Therapy or infusion interruption indicated but responds promptly to symptomatic treatment	Prolonged (eg, not rapidly responsive to symptomatic medication and/or brief interruption of infusion), recurrence of symptoms after initial improvement	Life-threatening consequences, pressor or ventilatory support indicated, urgent intervention indicated	Death
Hypotension	Asymptomatic, intervention not indicated	Nonurgent medical intervention indicated	Medical intervention	Life-threatening and urgent intervention indicated	Death

Grading according to the Common Terminology Criteria for Adverse Events/Cancer Therapy Evaluation Program, version 4.0.

RESULTS

Forty-six consecutive patients received an unrelated donor stem cell transplant with fludarabine/melphalan-based conditioning and either subQ or i.v. alemtuzumab in combination with tacrolimus as GVHD prophylaxis.

Twenty-six patients received subQ alemtuzumab and 20 received i.v. alemtuzumab. Overall, 130 subQ doses and 100 i.v. alemtuzumab doses were administered. Treatment groups were balanced with respect to age, gender, and disease state (Table 2). Disease status at transplantation and graft source were different between the 2 groups, most notably the subQ group had more patients with stable disease and all the patients in the subQ group received peripheral blood stem cell transplants whereas in the i.v. group, 50% had stem cells derived from bone marrow. Karnofsky performance status at the time of transplantation was similar between the treatment groups. There was no difference in Sorror comorbidity score and American Society for Blood and Marrow Transplantation risk category between the 2 groups ($P = .434$) [11].

Infusion-related Reactions

Infusion-related reactions of grade 2 or higher occurred in 11 (8%) versus 25 (25%) infusions in the subQ and i.v. cohorts ($P = .001$). Overall, 12 injections (9%) in the subQ arm versus 26 infusions (26%) in the i.v. arm resulted in any grade infusion-related reactions ($P = .001$). Hypotension of any grade was seen in 1.5% of injections in the subQ arm and in 1% of infusions in the i.v. arm ($P = .229$) (Table 3).

If a reaction occurred, the infusion was stopped, rescue medication was given, if required, and the infusion was resumed at a slower rate. No patients had delayed or missed doses. Minor local site reactions were common after subQ injection, but no grade 3 or 4 reactions occurred.

Infectious Complications

There was no significant difference between subQ and i.v. alemtuzumab for infectious complications outcomes. CMV viremia occurred in 10 patients in the subQ arm and 8 patients in the i.v. arm ($P = .916$); however, CMV disease only occurred in 1 patient in the i.v. arm. Median time to CMV viremia was also similar in the subQ arm versus i.v. arm (45 versus 55 days, $P = .091$). EBV viremia occurred in 6 patients in the subQ arm and 5 patients in the i.v. arm ($P = .88$). Median time to EBV viremia was significantly shorter in the subQ arm than in the i.v. arm (166 versus 350 days, $P = .044$; respectively). There was only 1 patient in the subQ group who developed post-transplantation lymphoproliferative disorder. Death due to a fatal infection occurred in 1 patient in the subQ arm and 2 patients in the i.v. arm. Fatal infections included *E. coli* bacteremia with concomitant Coronavirus in the subQ arm and viridans group *Streptococcus* bacteremia and vancomycin-resistant *Enterococcus* bacteremia in the i.v. arm.

Engraftment and Immune Reconstitution

There was no difference in time to engraftment for neutrophils between the 2 arms; however, median time to platelet engraftment was shorter for the subQ cohort than the i.v. cohort (15 days versus 19 days, $P = .037$). In the i.v. cohort, 1 patient did not engraft both neutrophils and platelets and 4 patients who did not recover platelets. Causes

Table 2
Baseline Characteristics

Characteristic	Subcutaneous (n = 26)	Intravenous (n = 20)	*P* Value
Age at transplantation, median (range), yr	62 (40-73)	60 (39-71)	.673
Gender			.855
Male	15 (58)	11 (55)	
Female	11 (42)	9 (45)	
Disease state			.494
AML	15 (58)	11 (55)	
MDS	9 (35)	5 (25)	
Other*	2 (8)	4 (20)	
Disease status at transplantation			.029
CR	8 (31)	7 (35)	
PR	1 (4)	4 (20)	
SD	11 (42)	1 (5)	
PD	3 (12)	4 (20)	
Other†	3 (12)	4 (20)	
Prior stem cell transplantation‡	0	3 (15)	.075
Sorror comorbidity score, median	3	4	.434
Karnofsky performance score, median	80	75	.062
ASBMT risk category			.537
Low	10 (38)	7 (35)	
Intermediate	3 (12)	5 (25)	
High	13 (50)	8 (40)	
CMV IgG seropositive			
Donor	14 (54)	8 (40)	.351
Recipient	17 (65)	14 (70)	.741
Graft source			<.001
Peripheral blood	26 (100)	10 (50)	
Bone marrow	0	10 (50)	
Days to start of GCSF, median (range)	10 (1-12)	10 (5-14)	.311

AML indicates acute myeloid leukemia; MDS, myelodysplastic syndrome; CR, complete remission; PR, partial response; SD, stable disease; PD, progressive disease; ASBMT, American Society for Blood and Marrow Transplantation; GCSF, granulocyte colony–stimulating factor.
Data presented are n (%), unless otherwise indicated.

* Others include follicular lymphoma, systemic mastocytosis, histiocytic sarcoma, non-Hodgkin lymphoma, myelofibrosis, and chronic neutrophilic leukemia.

† Others include CR2, PR2.

‡ All patients previously had an autologous stem cell transplantation.

Table 3
Primary Outcomes

	Subcutaneous	Intravenous	*P* Value
Doses administered, n	130	100	
Any reaction*	12 (9)	26 (26)	.001
≥Grade 2 infusion-related reactions	11 (8)	25 (25)	.001
Grade 2	9 (7)	21 (21)	
Grade 3	2 (2)	4 (4)	
Grade 4	0	0	
Hypotension of any grade	2 (1.5)	1 (1)	.229
Grade 1	0	1 (1)	
Grade 2	1 (.7)	0	
Grade 3	1 (.7)	0	
Grade 4	0	0	
Rescue medication/IVF administered	12 (9)	26 (26)	.01

IVF indicates intravenous fluids.
Data presented are n (%), unless otherwise indicated.
* Fever (≥38°C), chills/rigors, anaphylaxis, rash/urticaria, hypotension, bronchospasms/dyspnea, local injection site reaction (swelling/erythema).

of death in these patients included relapse (n = 1), multiorgan failure (n = 1), bacteremia (n = 1), and complications of engraftment failure (n = 2). In the subQ arm, 1 patient did not engraft both neutrophils and platelets. The cause of death for this patient was sepsis.

All evaluable patients were assessed for lymphocyte reconstitution at days +28, +100, and +180. The median lymphocyte counts on these days were identical for both the subQ and i.v. cohorts (.1, .4, and .7 cells/μL). *Mixed chimerism*, defined as less than 90% donor chimerism, is common after alemtuzumab-based conditioning, but we found no difference between the 2 groups. For the i.v. group, 35%, 40%, and 40% of patients had <90% CD3 donor cells and 5%, 10%, and 20% had <90% CD33 donor cells at day +28, +100, and +180, respectively. For the subQ group, 38%, 58%, and 54% of patients had <90% CD3 donor cells and 0%, 12%, and 35% had <90% of CD33 donor cells at day +28, +100, and +180, respectively.

GVHD

Acute GVHD ≥ grade 2 was seen in 6 patients in the subQ arm and 3 patients in the i.v. arm ($P = .711$). Organs affected by acute GVHD included the gastrointestinal tract, skin, or both. Median time to onset of acute GVHD seemed shorter in the subQ arm than in the i.v. arm (64 days versus 220 days), but this difference was not statistically significant ($P = .302$). Chronic GVHD occurred in a small number of patients in each group and no patients in either group developed severe chronic GVHD. Median time to chronic GVHD was also similar between the 2 groups (341 versus 221 days, $P = .221$) (Table 4).

Relapse and Survival

There was no difference in the number of patients who relapsed or the time to relapse between the 2 cohorts (Table 4). Of the 10 patients who relapsed in the i.v. group, 6 patients died of progressive disease. In the subQ group, 6 of the 11 relapsed patients died from progressive disease. There was no difference in 30-day mortality or 1-year overall survival between the subQ and the i.v. group (0 versus 5%, P = not significant and 50% versus 50%, P = not significant). Causes of death in the i.v. arm included relapse (n = 5), fatal infection (n = 2), multiorgan failure (n = 1), and complications of graft failure (n = 2). Causes of death in the subQ arm included relapse (n = 6), pneumonia (n = 1), post-transplantation lymphoproliferative disorder (n = 1), acute respiratory distress syndrome (n = 1), and fatal infection (n = 1).

Table 4
Secondary Outcomes

Outcome	Subcutaneous (n = 26)	Intravenous (n = 20)	*P* Value
CMV viremia (≥200 copies/mL)	10 (38)	8 (40)	.916
Median time to CMV viremia, days (range)	45 (23-93)	55 (42-170)	.091
CMV disease	0	1 (5)	.435
Recurrence of CMV viremia	4 (15)	3 (15)	.971
EBV viremia (≥200 copies/mL)	6 (23)	5 (25)	.880
Median time to EBV viremia, days (range)	166 (47-321)	350 (153-357)	.044
PTLD	1 (4)	0	.375
Fatal infection	1 (3)	2 (10)	
Relapse	11 (42)	10 (50)	.604
Time to relapse, median (range), d	140 (98-349)	158 (34-358)	.412
Time to engraftment, median (range), d			
Neutrophil	12 (10-16)	14 (6-18)	.07
Platelet	15 (10-41)	19 (11-32)	.036
≥Grade 2 acute GVHD	6 (23)	3 (15)	.711
Grade 2	4 (15)	2 (10)	
Grade 3	1 (4)	1 (5)	
Grade 4	1 (4)	0	
Organ affected by acute GVHD*			
Gut	3 (12)	2 (10)	
Skin	1 (4)	0	
Gut and skin	1 (4)	0	
Time to acute GVHD, median (range), d	64 (30-499)	220 (43-268)	.302
Any stage chronic GVHD	1 (4)	2 (10)	.572
Mild	1 (4)	1 (5)	
Moderate	0	1 (5)	
Severe	0	0	
Time to chronic GVHD, median (range), d	341	221 (169-273)	.221
30-Day mortality	0	1 (5)	.537
1-Year overall survival	16 (62)	10 (50)	.433

PTLD indicates post-transplantation lymphoproliferative disorder.
Data presented are n (%), unless otherwise indicated.
* One patient in the subcutaneous arm and 1 patient in the intravenous arm were not defined.

DISCUSSION

Each year, thousands of patients with hematologic malignancies undergo allogeneic stem cell transplantation, which offers a chance at cure. Acute and chronic GVHD are often severe, sometimes debilitating, and potentially deadly complications of transplantation. Alemtuzumab has been used successfully to prevent GVHD in allogeneic stem cell transplantations with positive long-term outcomes [5]. With the exception of recent data in pediatric patients who underwent transplantation for nonmalignant disease states, only the i.v. route of administration for alemtuzumab has been used in stem cell transplantation [12]. However, i.v. alemtuzumab has been associated with serious infusion-related reactions that include fever, chills, rigors, rash, hypotension, shortness of breath, bronchospasm, and anaphylaxis. Prevention of these reactions requires pretreatment with antihistamines, corticosteroids, and antipyretics. Here, we report our institutional experience with 46 patients in approximately a 2-year period, 20 of whom

received i.v. and 26 who received subQ alemtuzumab. We found a significantly lower rate of ≥grade 2 infusion-related reactions with subQ administration compared with the i.v. route (8% versus 25%, $P = .001$).

In all other respects, the outcomes of both groups of patients were remarkably similar. Incidences of acute and chronic GVHD were similar between the subQ and i.v. arms, indicating that subQ alemtuzumab may have similar efficacy to i.v. alemtuzumab in preventing GVHD. Only 1 patient in the subQ arm experienced grade 4 acute GVHD and no patients experienced severe chronic GVHD. This is consistent with most studies of i.v. alemtuzumab-containing regimens, which have observed an incidence of 10% to 20% acute GVHD and a low incidence of severe chronic GVHD [2,3]. We also did not observe a difference in risk of disease recurrence, nor did we notice an increase in the incidence of CMV or EBV reactivation. The number of infection-related deaths, most of them due to bacterial infections, was not significantly different between the patients given subQ versus i.v. alemtuzumab. Lastly, there was no differences in 30-day mortality and 1-year overall survival after transplantation between the 2 treatment groups.

Consistent with our results, subQ administration of alemtuzumab has been shown to reduce the incidence of infusion-related reactions while maintaining the same efficacy when used for treatment of chronic lymphocytic leukemia. Lundin et al. conducted a phase II open-label study that determined the efficacy and safety of alemtuzumab delivered subQ as first-line therapy, over a prolonged treatment period of 18 weeks in patients with symptomatic B cell chronic lymphocytic leukemia (n = 41). On day 1, 3 mg alemtuzumab was administered by subQ injection. If well tolerated, the dose was raised to 10 mg on day 3 and then raised to the target dose of 30 mg, split into 2 injection sites (1.5 mL at each site) on day 5. The 30 mg dose was then given 3 times weekly for a maximum of 18 weeks. Prophylactic medications against first-dose reactions included an antipyretic and antihistamine, given 30 minutes before the injections. Most first dose reactions, which are frequently seen after i.v. administration of alemtuzumab, were rare or absent in this study. Transient rigor was seen in 17% of patients, fever was observed in 70% of patients, and injection site reaction was seen in 90% of patients, but there were no episodes of rash/urticaria, bronchospasm, or hypotension [13]. It appears that subQ administration induced more local injection site reactions, instead of "flu-like" symptoms, than i.v. administration did. Given the relative urgency and the compressed time frame of transplantation conditioning regimens, we successfully omitted the initial dosing ramp-up of subQ or i.v. alemtuzumab without excessive incidence of reactions.

By contrast, when subQ alemtuzumab was used for treatment of T cell prolymphocytic leukemia, efficacy appeared diminished [14]. This cautionary observation underscores the need to study the pharmacokinetics and biodistribution of alemtuzumab, which may differ according to disease, remission status, and route of administration. From pharmacokinetic studies undertaken in patients with chronic lymphocytic leukemia, it is clear that the same peak levels of antibody are obtained with both i.v. and subQ administration of alemtuzumab [15,16]. However, further pharmacokinetic studies need to be conducted to fully understand the utility of obtaining the meaning of serum levels after subQ administration of alemtuzumab in other settings, including bone marrow transplantation.

Our analysis has limitations, despite the study being designed to minimize confounding variables. The data were collected retrospectively and, therefore, are subject to the usual restriction and bias of this type of analysis. However, microbiological and laboratory data were collected using electronic medical records, minimizing absent data and under-reporting. The relatively small sample size also makes it difficult to obtain statistical significance for the secondary endpoints. However, our primary aim was to report the difference in infusion-related reactions between subQ and i.v. administration of alemtuzumab, which was shown to be statistically significant and consistent with the current literature published for chronic lymphocytic leukemia. Our analysis was also limited to patients receiving a matched unrelated allogeneic stem cell transplantation. Larger studies are needed to assess the role of subQ alemtuzumab in all transplantation types, as well as the pharmacokinetic differences of i.v. and subQ administration, if any, as this was not the primary focus of this study. There was a difference in graft source between the i.v. and subQ cohorts, with all patients in the subQ arm receiving peripheral blood stem cells and 50% of the patients in the i.v. cohort receiving bone marrow stem cells; however, this did not result in a statistically significant increased incidence of GVHD in the subQ cohort. Our analysis on engraftment is limited because of the differences in graft source. We continue to use subQ alemtuzumab and monitor data, as a long-term follow-up period is needed to assess outcomes such as overall survival and chronic GVHD.

In conclusion, this study, albeit retrospective, represents the first direct comparative analysis of subQ versus i.v. alemtuzumab in adult stem cell transplantation patients with hematological malignancies. No significant differences in infectious complications, relapse, GVHD, and survival were found between the 2 groups with the exception of a shorter median time to EBV viremia and platelet engraftment in the subQ arm. Transplantation centers utilizing i.v. alemtuzumab for GVHD prophylaxis may consider transitioning to subQ alemtuzumab. SubQ administration may lower infusion-related reactions compared with i.v. administration without jeopardizing efficacy of reducing GVHD.

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