Allogeneic Hematopoietic Cell Transplantation for Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

Qaiser Bashir¹, Denái R. Milton², Uday R. Popat¹, Partow Kebriaei¹, Chitra Hosing¹, Issa F. Khouri¹, Katayoun Rezvani¹, Yago Nieto¹, Betul Oran¹, Samer A. Srour¹, Neeraj Y. Saini¹, Amanda L. Olson¹, Sairah Ahmed¹,³, Gheath Al-Atrash¹, Gabriela Rondon¹, Marina Y. Konopleva⁴, Richard E. Champlin¹, Elizabeth J. Shpall¹, Muzaffar H. Qazilbash¹, Naveen Pemmaraju⁴

¹Department of Stem Cell Transplantation & Cellular Therapy, The University of Texas MD Anderson Cancer Center
²Department of Biostatistics, The University of Texas MD Anderson Cancer Center
³Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center
⁴Department of Leukemia, The University of Texas MD Anderson Cancer Center

Abstract

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is an aggressive hematological malignancy; however, some patients achieve durable remission with allogeneic hematopoietic cell transplantation (allo-HCT). We report on all 17 patients with BPDCN who underwent allo-HCT at our center between 2000 and 2020. The median age was 39 (18-67) years. All (n=16, 94%), except one patient, had systemic disease involving bone marrow and/or other organs. Ten patients (59%) were in first complete remission (CR1) at allo-HCT. The donor source was matched related or unrelated in ten (59%) and alternate donor in seven (41%) patients. Five (31%) patients developed acute graft-versus-host disease (GVHD), all grade I-II. The cumulative incidence (CI) of chronic GVHD at 5-year was 34%. The CI of non-relapse mortality at 1-year was 29%. Progression-free survival (PFS) rates at 2-year and 5-year were 49% (95% CI = 22-71%) and 39% (95% CI = 14-64%), respectively. The 2-year and 5-year overall survival (OS) rates were 65% (95% CI = 38-82%) and 40% (95% CI = 12-68%), respectively. The 5-year rate for both PFS and OS was 80% in CR1 patients versus 0% in patients not in CR1. In conclusion, allo-HCT provides long-lasting remissions in BPDCN patients, particularly when performed in CR1.

Introduction

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare but aggressive hematological malignancy. (1) Previously known as NK cell leukemia/lymphoma, BPDCN...
is currently listed as a separate entity in the World Health Organization 2016 classification of myeloid neoplasms. (2) Cutaneous involvement is one of the clinical hallmarks of this malignancy, present in 85% of patients. (3) Median age is approximately 70 years, and BPDCN is well-known to have a male-predominant incidence. (4) However, the clinical presentation is diverse, with marrow, lymph nodes, and neurological involvement commonly seen. (3) Genomic studies reveal that BPDCN malignant cells originate from plasmacytoid dendritic cells and carry a distinct molecular profile from other acute leukemias. (5, 6) TET2 mutations and variants appear to be the most common molecular aberrations in BPDCN. (7, 8) The immunophenotyping of BPDCN cells generally shows positivity for CD123, CD4, and CD56. (9, 10) Additional markers that are commonly positive include CD36, CD38, CD43, CD45RA, TCL1, TCF4, CD303/BDCA-2, and TdT. (11) BPDCN cells are negative for CD34, CD3, CD13, CD16, CD19, CD20, lysozyme, and MPO. (11, 12)

Until recently, there was a lack of disease-specific agents, and patients with BPDCN have historically been treated with acute leukemia or lymphoma-based regimens, e.g., hyperfractionated cyclophosphamide, vincristine, Adriamycin, dexamethasone, alternating with methotrexate and cytarabine (Hyper-CVAD) or cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP), and other such regimens. (13) The outcomes with these approaches were suboptimal with a median overall survival (OS) ranging from 8.7 to 24 months. (14-16) The treatment landscape changed with the arrival of tagraxofusp, a CD123-directed cytotoxin that showed an overall response rate (ORR) of 90% and two-year OS of 52% in previously untreated patients in an open-label, multicenter clinical trial. (17)

Although there is no randomized controlled trial comparing allogeneic hematopoietic cell transplantation (allo-HCT) to non-transplant therapies in BPDCN, the larger retrospective analyses suggest a potential benefit of transplantation. (14, 15) For instance, in a multicenter study involving 59 patients, the median OS for the entire cohort was 24 months. Only 42% of patients underwent a transplant (autologous or allo-HCT), but the median OS in these patients was 6.6 years. (15) Specifically, for allo-HCT in BPDCN, several retrospective analyses (18-21) and a meta-analysis (22) have shown that a three-year OS of more than 60% for patients transplanted in first complete remission (CR1) and more than 40% for patients beyond CR1 can be expected. For this reason, allo-HCT is offered to eligible patients who achieve remission with the initial therapy.

As newer and more effective treatments emerge for BPDCN, we can expect more patients with BPDCN to become eligible for transplantation. Additional studies are needed to characterize further the patients who can benefit from allo-HCT. To determine this treatment modality’s safety and efficacy, we evaluated the outcome of all patients with BPDCN who underwent allo-HCT at our center.

**Patients and Methods**

**Patients**

We included all consecutive patients diagnosed with BPDCN who underwent allo-HCT between September 1, 2000, and April 1, 2020, at The University of Texas MD Anderson Cancer Center (MDACC). The standard eligibility criteria for allo-HCT were followed,
including adequate organ function (left ventricle ejection fraction >40%, no significant cardiac disease, diffusing lungs capacity for carbon monoxide >50% without any significant pulmonary disease, adequate renal and liver function) and no uncontrolled infection. There were no restrictions for age or remission status at transplantation. The Institutional Review Board at The University of Texas MD Anderson Cancer Center approved this analysis.

**Donor selection, preparative regimens, and engraftment**

Per our institutional policies, a fully matched sibling donor (MRD) or matched unrelated donor (MUD) was used when available. Patients without a matched donor underwent a haploidentical or cord-blood transplant (CBT). The treating physicians selected the conditioning regimens. The graft-versus-host disease (GVHD) prophylaxis consisted of calcineurin inhibitors combined with post-transplant cyclophosphamide, mycophenolate, or methotrexate. Neutrophil engraftment was defined as the first day of absolute neutrophil count >500 μL for three consecutive days. Platelet engraftment was defined as the first day of platelet count >20,000 μL without transfusion.

**Statistical methods**

Patient characteristics as well as acute GVHD (aGVHD) were summarized using descriptive statistics. OS was computed from the date of allo-HCT to the last-known vital sign. Patients alive at the last follow-up date were administratively censored. Progression-free survival (PFS) was computed from the date of allo-HCT to the date of disease progression or death (if the patient died without disease progression), or the last evaluation date. Patients who were alive and did not experience progression of disease at the last follow-up date were administratively censored. The Kaplan-Meier method was used to estimate OS and PFS and differences between groups were assessed using the log-rank test.

Non-relapse mortality (NRM) was computed from date of allo-HCT to last known vital sign. Relapse was computed from date of allo-HCT to date of disease progression. Chronic GVHD (cGVHD) was computed from date of allo-HCT to date of event. The cumulative incidences of NRM, relapse and cGVHD were determined using the competing risks method. The competing risk included for NRM was relapse and patients who were still alive at the last follow-up date were administratively censored, while the competing risk for relapse was death and patients who were still alive at the last follow-up date were administratively censored. For cGVHD, the competing risks included were relapse and death, while those patients who did not experience cGVHD, had not progressed, and were still alive at the last follow-up date were administratively censored. Differences in cumulative incidences were evaluated using Gray’s test.

All statistical analyses were performed using SAS 9.4 for Windows (Copyright © 2002-2012 by SAS Institute Inc., Cary, NC), with a significance level of 5%. No adjustments for multiple testing were made.
Results

Patient and disease characteristics

Seventeen patients were identified. The median age was 39 (range: 18-67) years. As expected, the majority of the patients were male (n=14, 82%). Eleven patients (65%) had cutaneous involvement, thirteen (76%) patients had bone marrow involvement, and ten (59%) patients had both cutaneous and bone marrow involvement. Eight patients (47%) had diploid cytogenetics, while nine patients (53%) had one or more chromosomal abnormalities on conventional karyotyping. The data on next-generation sequencing was available on 15 (88%) patients. Eight (53%) of these patients did not have any detectable mutation. Of the seven (47%) patients who had a detectable mutation, TET2 mutation was the most frequent, detected in 5 (33%) patients. The majority of patients (n=11, 65%) received induction therapy with hyper-CVAD, with (n=3, 27%) or without (n=8, 73%) tagraxofusp. Three patients (18%) received tagraxofusp alone before allo-HCT. Only ten patients (59%) were in CR1 at allo-HCT. The majority of patients (n=13, 76%) received myeloablative conditioning. Ten (59%) patients received MRD or MUD grafts, while seven patients (41%) received alternate donor grafts. Table 1 summarizes the patient and treatment characteristics.

Engraftment, GVHD, non-relapse mortality, and relapse

The median time to neutrophil and platelet engraftment was 18 (range: 11-30) days and 24 (range: 11-45) days. Five of 16 (31%) evaluable patients experienced acute GVHD (aGVHD), where 3 (19%) had grade II aGVHD. We did not observe grade III-IV aGVHD. The 1-year and 5-year cumulative incidences of cGVHD were 13% and 34%, respectively. The cumulative incidence of NRM was 6% at 100-day and 29% at 1-year. The 1-year NRM rate was higher in patients with a history of prior hematologic malignancy (75% vs. 15% in others, p <0.001), and in those receiving alternate donor transplant (100% in CBT; 25% in haploidentical; 20%, in MUD, and 0% in MRD, p = 0.027). Overall, eight patients died during the study period. The causes of death were infection in seven (88%) and disease relapse in one (13%) patient. No patient developed veno-occlusive disease.

The 1-year and 5-year cumulative incidence of relapse were 6% and 22%, respectively.

Survival

The median follow up in surviving patients was 21.5 (range: 11.5-76.1) months. The median PFS was 19.9 months with 2-year and 5-year PFS rates of 49% (95% CI = 22-71%) and 39% (95% CI = 14-64%), respectively (Figure 1A). The median OS was 32.9 months with 2-year and 5-year OS rates of 65% (95% CI = 38-82%) and 40% (95% CI = 12-68%), respectively (Figure 1B).

Median PFS was not reached for patients in CR1 at the time of transplant, while the median PFS for patients not in CR1 was 4.1 months (p = 0.002, Figure 2A). Similarly, the median OS was not reached in patients transplanted in CR1 and was 9.1 months in patients not in CR1 (p=0.011. Figure 2B). The 5-year rate for both PFS and OS was 80% in CR1 patients compared to 0% in patients not in CR1. Absence of a prior hematologic malignancy was also associated with significantly longer PFS and OS (Table 2).
Discussion

A better understanding of disease biology and potential molecular targets has made it possible to design effective therapies for BPDCN. In addition to these targeted approaches, an increasing body of data suggests that allo-HCT, particularly when performed earlier in the disease course, provides long-term remission in most patients.\(^{(22)}\) The bulk of the published reports consist of registry analyses due to the rarity of this disease. We report the largest single-center study of BPDCN patients who underwent allo-HCT. Our results show a 5-year PFS rate of ~40% in all patients, with significantly longer median OS in CR1 patients. These data highlight the importance of early referral for transplant in these patients. Since no randomized trial of allo-HCT in BPDCN exists, all data has been extrapolated from retrospective studies. An exhaustive investigation of different variables affecting the transplant outcomes has not been possible for this reason. One consistent theme, though, which is also true for transplantation in most hematological malignancies, is the positive impact of remission status on outcomes. In a registry analysis from the European Society for Blood and Marrow Transplantation (EBMT), Roos-Weil and colleagues analyzed 34 patients with BPDCN who underwent allo-HCT.\(^{(18)}\) The 3-year OS rate was 52% in patients allografted in CR1 compared to 29% in patients allografted in more advanced disease. Similarly, a US multicenter study showed a 3-year OS rate of 74% when allo-HCT was performed in CR1 patients compared to 0% in patients not in CR1.\(^{(20)}\) Consistent with the published data, we noticed a significantly higher 5-year OS rate of 80% in CR1 patients than 0% in those not in CR1.

Whether autologous (auto)-HCT is of value in BPDCN patients remains to be seen. In a report from the Japan Society for Hematopoietic Cell Transplantation in 2015, Aoki and colleagues showed equivalent survival with auto and allo-HCT in patients transplanted in CR1.\(^{(19)}\) In the pivotal study of tagraxofusp in BPDCN patients, 13 out 29, previously untreated patients were bridged to transplantation (allo-HCT, n=10; auto-HCT, n=3). At the time of reporting, 8 of 10 patients who received allo-HCT and 2 of 3 patients who received auto-HCT had not experienced disease progression.\(^{(17)}\) On the other hand, in a multicenter US study, three of eight patients who received auto-HCT relapsed at a median of four months. All three patients were transplanted in remission with two in CR1. The 1-year OS rate was only 11%.\(^{(20)}\) The high relapse rate with autografting was also highlighted in another study conducted by Reimer et al., where three of four patients with BPDCN (CR1, n=3), who underwent auto-HCT, died of relapse within two years.\(^{(23)}\) In comparison, a meta-analysis of published studies of allo-HCT showed pooled PFS and OS rates of 53% and 67%, respectively, in BPDCN patients transplanted in CR1.\(^{(22)}\) More recently, Laribi et al. reported a large retrospective analysis involving 398 patients from 75 centers. In this study, sixty-one (15.5%) patients underwent allo-HCT, and 16 (4.1%) patients received auto-HCT following chemotherapy. The patients who received a non-Hodgkin lymphoma type regimen followed by allo-HCT had the best results. The median OS was not reached, compared to 65 months in patients who received chemotherapy followed by auto-HCT.\(^{(24)}\) While there is no prospective head-to-head comparison between the two approaches, the current data favor the use of allo-HCT in eligible patients.
The higher intensity of conditioning appears to impart a beneficial effect by reducing the relapse rate, although, the reports are conflicting. In the EBMT analysis, no RIC patient experienced long-term disease control. In contrast, the probability of disease-free survival appeared to reach a plateau in the MAC group. The cumulative incidence of relapse in the report by the French Society of Bone Marrow Transplantation and Cell Therapy was 7% with MAC and 36% with RIC/NMA conditioning, but this difference was not statistically significant. The NRM, PFS, and OS were also comparable. Last but not least, a meta-analysis involving 128 patients showed a higher relapse rate with RIC, 40% vs. MAC, 18%. We did not notice a difference in survival or NRM between MAC and RIC/NMA. However, most patients (74%) received MAC thereby making an adequate comparison almost impossible. Taken together, it appears reasonable to offer MAC to younger and fit patients while reserving RIC/NMA for the frail or elderly.

Like most of the published data for BPDCN, our study’s primary constraint is low patient numbers. Moreover, ours is a retrospective analysis with expected limitations, including heterogeneity of patients and treatments. The study included patients transplanted over the course of 20 years when diagnostic and response criteria evolved, thus creating an inevitable lack of standardization of treatments and disease status.

In summary, we report the results of a large single-center study of allo-HCT in this rare malignancy. As BPDCN becomes more recognized, the number of cases undergoing transplant is expected to increase. This assumption is corroborated because the number of allografts reported to the Center for International Blood & Marrow Transplant Research (CIBMTR) for BPDCN has risen from 10 in 2013 to 20 in 2019 (personal communication). Our results add to the growing body of literature showing the efficacy of allo-HCT in this rare but aggressive malignancy. Since the disease relapse remains a concern, we have initiated a post-transplant maintenance therapy study with tagraxofusp after transplantation in BPDCN patients (NCT04317781). In the future, with the arrival of more effective agents and improvements in peri-transplant care, one can expect better disease control and more durable remissions.

Acknowledgements

QB, MHQ, and NP designed the study, interpreted the data, and wrote the manuscript; DRM analyzed the data and created figures; all authors contributed to data collection, writing and revision of the manuscript and approved the final version.

Conflict of Interest Statement

QB has research funding from Acrotech and Stemline. QB served on advisory board of Purdue and Spectrum. MQ has research funding from Janssen, Bioline, Angiococrine, Amgen and Neximmune. SA has served on an advisory board and received research funding from Tessa Therapeutics and SeaGen. PK has research support from Amgen and Ziopharm; has served on advisory boards for Pfizer, Kite and Novartis; consulting fees from Jazz. MK has received grants and other from AbbVie, Genentech, F. Hoffman La-Roche, Stemline Therapeutics, and Forty-Seven. MK has received grants from Eli Lilly, Cellectis, Calithera, Ablynx, Agios, Ascentage, Astra Zeneca, Rafael Pharmaceutical and Sanofi. MK has received other from Amgen, Kisyoji and Reata Pharmaceutical. MK holds US patent 7,795,305 B2, “CDDO-compounds and combination therapies thereof” with royalties paid to Reata Pharmaceutical, a patent Combination Therapy with a mutant IDH1 Inhibitor and a BCL-2 licensed to Eli Lilly, and patent 62/993,166 Combination of a MCL-1 Inhibitor And Midostaurin, Uses And Pharmaceutical Composition Thereof pending to Novartis. ES has received consultant fees and honoraria from Bayer HealthCare
Pharmaceuticals, Novartis, Magenta and Adaptimmune. ES has received honoraria from Partner Therapeutics, Mesoblast and Axio. ES is the co-inventor on a provisional patent application owned by MD Anderson and licensed to TaKeda. All other authors report no COI.

This research was supported in part by the National Institutes of Health through the University of Texas MD Anderson Cancer Center’s Support Grant (CA016672).

References

1. Guru Murthy GS, Pemmaraju N, Atallah E. Epidemiology and survival of blastic plasmacytoid dendritic cell neoplasm. Leuk Res. 2018;73:21–3. [PubMed: 30189324]
2. Arber DA, Orazi A, Hasserman R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391–405. [PubMed: 27069254]
3. Deconinck E, Petrella T, Garnache Ottou F. Blastic Plasmacytoid Dendritic Cell Neoplasm: Clinical Presentation and Diagnosis. Hematol Oncol Clin North Am. 2020;34(3):491–500. [PubMed: 32336414]
4. Togami K, Chung SS, Madan V, Kenyon CM, Cabal-Hierro L, Taylor J, et al. Sex-biased ZRSR2 mutations in myeloid malignancies impair plasmacytoid dendritic cell activation and apoptosis. bioRxiv. 2020:2020.10.29.360503.
5. Sapienza MR, Fuligni F, Agostinelli C, Tripodo C, Righi S, Laginestra MA, et al. Molecular profiling of blastic plasmacytoid dendritic cell neoplasm reveals a unique pattern and suggests selective sensitivity to NF-kB pathway inhibition. Leukemia. 2014;28(8):1606–16. [PubMed: 24504027]
6. Villani AC, Satija R, Reynolds G, Sarkizova S, Shekhar K, Fletcher J, et al. Single-cell RNA-seq reveals new types of human blood dendritic cells, monocytes, and progenitors. Science. 2017;356(6335).
7. Beird HC, Khan M, Wang F, Alfayez M, Cai T, Zhao L, et al. Features of non-activation dendritic state and immune deficiency in blastic plasmacytoid dendritic cell neoplasm (BPDCN). Blood Cancer J. 2019;9(12):99. [PubMed: 31811114]
8. Alayed K, Patel KP, Konoplev S, Singh RR, Routbort MJ, Reddy N, et al. TET2 mutations, myelodysplastic features, and a distinct immunoprofile characterize blastic plasmacytoid dendritic cell neoplasm in the bone marrow. Am J Hematol. 2013;88(12):1055–61. [PubMed: 23940084]
9. Pemmaraju N, Konopleva M. Approval of tagraxofusp-erzs for blastic plasmacytoid dendritic cell neoplasm. Blood Adv. 2020;4(16):4020–7. [PubMed: 32841341]
10. Wang W, Khoury JD, Miranda RN, Jorgensen JL, Xu J, Loghavi S, et al. Immunophenotypic characterization of reactive and neoplastic plasmacytoid dendritic cells permits establishment of a 10-color flow cytometric panel for initial workup and residual disease evaluation of plasmacytoid dendritic cell neoplasm. Haematologica. 2020.
11. Yun S, Chan O, Kerr D, Vincelette ND, Idrees A, Mo Q, et al. Survival outcomes in blastic plasmacytoid dendritic cell neoplasm by first-line treatment and stem cell transplant. Blood Adv. 2020;4(14):3435–42. [PubMed: 32722779]
12. Sukswai N, Aung PP, Yin CC, Li S, Wang W, Wang SA, et al. Dual Expression of TCF4 and CD123 Is Highly Sensitive and Specific For Blastic Plasmacytoid Dendritic Cell Neoplasm. Am J Surg Pathol. 2019;43(10):1429–37. [PubMed: 31261288]
13. Pemmaraju N, Konopleva M, Lane AA. More on Blastic Plasmacytoid Dendritic-Cell Neoplasms. N Engl J Med. 2019;380(7):695–6.
14. Pagano L, Valentinii CG, Pulsoni A, Fisogni S, Carluccio P, Mannelli F, et al. Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation: an Italian multicenter study. Haematologica. 2013;98(2):239–46. [PubMed: 23065521]
15. Taylor J, Haddadin M, Upadhyay VA, Grussie E, Mehta-Shah N, Brunner AM, et al. Multicenter analysis of outcomes in blastic plasmacytoid dendritic cell neoplasm offers a pretargeted therapy benchmark. Blood. 2019;134(8):678–87. [PubMed: 31243042]
16. Martin-Martin L, Lopez A, Vidriales B, Caballero MD, Rodrigues AS, Ferreira SI, et al. Classification and clinical behavior of blastic plasmacytoid dendritic cell neoplasms according
to their maturation-associated immunophenotypic profile. Oncotarget. 2015;6(22):19204–16. [PubMed: 26056082]

17. Pemmaraju N, Lane AA, Sweet KL, Stein AS, Vasu S, Blum W, et al. Tagraxofusp in Blastic Plasmacytoid Dendritic-Cell Neoplasm. N Engl J Med. 2019;380(17):1628–37. [PubMed: 31018069]

18. Roos-Weil D, Dietrich S, Boumendil A, Polge E, Bron D, Carreras E, et al. Stem cell transplantation can provide durable disease control in blastic plasmacytoid dendritic cell neoplasm: a retrospective study from the European Group for Blood and Marrow Transplantation. Blood. 2013;121(3):440–6. [PubMed: 23203822]

19. Aoki T, Suzuki R, Kuwatsuka Y, Kako S, Fujimoto K, Taguchi J, et al. Long-term survival following autologous and allogeneic stem cell transplantation for blastic plasmacytoid dendritic cell neoplasm. Blood. 2015;125(23):3559–62. [PubMed: 25918345]

20. Kharfan-Dabaja MA, Al Malki MM, Deotare U, Raj RV, El-Jurdi N, Majhail N, et al. Haematopoietic cell transplantation for blastic plasmacytoid dendritic cell neoplasm: a North American multicentre collaborative study. Br J Haematol. 2017;179(5):781–9. [PubMed: 28980314]

21. Leclerc M, Peffault de Latour R, Michallet M, Blaise D, Chevallier P, Rohrlich PS, et al. Can a reduced-intensity conditioning regimen cure blastic plasmacytoid dendritic cell neoplasm? Blood. 2017;129(9):1227–30. [PubMed: 27986653]

22. Kharfan-Dabaja MA, Reljic T, Murthy HS, Ayala E, Kumar A. Allogeneic Hematopoietic Cell Transplantation Is an Effective Treatment for Blastic Plasmacytoid Dendritic Cell Neoplasm in First Complete Remission: Systematic Review and Meta-analysis. Clin Lymphoma Myeloma Leuk. 2018;18(11):703–9 e1. [PubMed: 30145196]

23. Reimer P, Rudiger T, Kraemer D, Kunzmann V, Weissinger F, Zettl A, et al. What is CD4+CD56+ malignancy and how should it be treated? Bone Marrow Transplant. 2003;32(7):637–46. [PubMed: 13130309]

24. Laribi K, Baugier de Materre A, Sobh M, Cerroni L, Valentini CG, Aoki T, et al. Blastic plasmacytoid dendritic cell neoplasms: results of an international survey on 398 adult patients. Blood Adv. 2020;4(19):4838–48. [PubMed: 33027528]
Figure 1A.
Probability of progression-free survival in all patients
**Figure 1B.**
Probability of overall survival in all patients
Figure 2A.
Probability of progression-free survival in patients in first complete remission (CR1) versus others

$p = 0.002$
Figure 2B.
Probability of overall survival in patients in first complete remission (CR1) versus others.
## Table 1.

### Patient Characteristics

| Variable                                      | All patients (N=17) |
|-----------------------------------------------|---------------------|
| Age at allo-HCT (years)                       |                     |
| Median (Range)                                | 39 (18 - 67)        |
| Age at allo-HCT, n (%)                        |                     |
| < 60 years                                    | 13 (76)             |
| ≥60 years                                     | 4 (24)              |
| Gender, n (%)                                 |                     |
| Female                                        | 3 (18)              |
| Male                                          | 14 (82)             |
| Year of allo-HCT, n (%)                       |                     |
| ≤2010                                         | 1 (6)               |
| 2011-2015                                     | 5 (29)              |
| > 2015                                        | 11 (65)             |
| History of prior auto-HCT                     |                     |
| Yes *                                         | 2 (12)              |
| No                                            | 15 (88)             |
| Prior hematologic malignancy, n (%)           |                     |
| No                                            | 13 (76)             |
| Yes                                           | 4 (24)              |
| Lymphoblastic lymphoma                        | 1 (6)               |
| Multiple myeloma                              | 1 (6)               |
| Mycoses fungoides                             | 1 (6)               |
| Myelofibrosis                                 | 1 (6)               |
| Organs involved, n (%)                        |                     |
| Skin                                          | 11 (65)             |
| Bone marrow                                   | 13 (76)             |
| Skin + Bone marrow                            | 10 (59)             |
| Other Organs involved                         | 10 (59)             |
| Cytogenetic abnormalities, n (%)              |                     |
| Absent                                        | 8 (47)              |
| Present                                       | 9 (53)              |
| Complex karyotype‡, n (%)                     |                     |
| Absent                                        | 14 (82)             |
| Present                                       | 3 (18)              |
| TET2 mutation, n (%)                          |                     |
| Absent                                        | 10 (67)             |
| Present                                       | 5 (33)              |
| Unknown                                       | 2                   |
| ASXL1 mutation, n (%)                         |                     |
| Variable                                      | All patients (N=17) |
|----------------------------------------------|---------------------|
| Absent                                       | 14 (93)             |
| Present                                      | 1 (7)               |
| Induction therapy, n (%)                     |                     |
| Tagraxofusp only                             | 3 (18)              |
| HYPER-CVAD                                   | 8 (47)              |
| HYPER-CVAD+Tagraxofusp                       | 3 (18)              |
| Other                                        | 3 (18)              |
| Months from diagnosis to allo-HCT            |                     |
| Median                                       | 6.7                 |
| Range                                        | (3.9 - 42.4)        |
| Disease status at allo-HCT, n (%)            |                     |
| CR1                                          | 10 (59)             |
| CR2                                          | 4 (24)              |
| PR                                           | 2 (12)              |
| SD                                           | 1 (6)               |
| Conditioning regimen, n (%)                  |                     |
| Fludarabine + Busulfan                       | 9 (53)              |
| Fludarabine + Melphalan                      | 6 (35)              |
| Other                                        | 2 (12)              |
| Myeloablative                                | 13 (76)             |
| Non-myeloablative                            | 4 (24)              |
| Donor type, n (%)                            |                     |
| Matched-related                              | 5 (29)              |
| Matched unrelated                            | 5 (29)              |
| Haploidentical                               | 4 (24)              |
| Cord blood                                   | 3 (18)              |
| GVHD prophylaxis, n (%)                      |                     |
| Tacrolimus + PTCy                            | 4 (24)              |
| Tacrolimus + MMF + PTCy                      | 6 (35)              |
| Tacrolimus + MMF                             | 1 (6)               |
| Tacrolimus + Methotrexate                    | 6 (35)              |

Allo-HCT, allogeneic hematopoietic cell transplantation; auto-HCT, autologous hematopoietic cell transplantation; Hyper-CVAD, hyperfractionated cyclophosphamide, vincristine, Adriamycin, dexamethasone, alternating with methotrexate and cytarabine; CR1, first complete remission; CR2, second complete remission; PTCy, post-transplant cyclophosphamide; MMF, mycophenolate mofetil

*One patient had a prior auto-HCT for a previous diagnosis of multiple myeloma

‡Three or more unrelated chromosomal abnormalities
Table 2.
Univariate analysis for progression-free survival and overall survival

| Variable                                                                 | PFS                     | OS                      |
|--------------------------------------------------------------------------|-------------------------|-------------------------|
|                                                                          | Median (95% CI) months  | p-value                 |
|                                                                          |                         |                         |
| Age at allo-HCT                                                          |                         |                         |
| < 60 years                                                               | 19.9 (4.1, NE)          | 0.99                    |
| ≥ 60 years                                                               | 29.5 (1.2, 29.5)        |                         |
| Gender                                                                   |                         |                         |
| Male                                                                     | 13.3 (4.1, NE)          | 0.39                    |
| Female                                                                   | NE (19.9, NE)           |                         |
| Prior hematologic malignancy                                             |                         |                         |
| No                                                                       | NE (5.9, NE)            | 0.015                   |
| Yes                                                                      | 4.1 (1.2, 29.5)         |                         |
| Cytogenetic abnormalities present                                       |                         |                         |
| No                                                                       | NE (4.1, NE)            | 0.08                    |
| Yes                                                                      | 13.3 (1.2, 29.5)        |                         |
| Complex karyotype                                                        |                         |                         |
| No                                                                       | 29.5 (4.1, NE)          | 0.63                    |
| Yes                                                                      | 13.3 (1.1, NE)          |                         |
| TET2                                                                     |                         |                         |
| No                                                                       | 13.3 (1.1, NE)          | 0.49                    |
| Yes                                                                      | 29.5 (19.9, NE)         |                         |
| ASXL1                                                                    |                         |                         |
| No                                                                       | 29.5 (4.1, NE)          | 0.51                    |
| Yes                                                                      | NE (NE, NE)             |                         |
| Induction therapy                                                        |                         |                         |
| Tagraxofusp only                                                         | NE (19.9, NE)           | 0.34                    |
| Hyper-CVAD                                                               | NE (4.1, NE)            |                         |
| Hyper-CVAD+Tagraxofusp                                                   | 29.5 (1.2, 29.5)        |                         |
| Other                                                                    | 8.7 (3.3, NE)           |                         |
| Disease status at allo-HCT                                               |                         |                         |
| CR1                                                                      | NE (4.3, NE)            | 0.002                   |
| Other                                                                    | 4.1 (1.2, 19.9)         |                         |
| CR1/CR2                                                                  | NE (4.3, NE)            | 0.014                   |
| Other                                                                    | 3.3 (1.2, 19.9)         |                         |
| Conditioning regimen                                                     |                         |                         |
| Myeloablative                                                            | 19.9 (4.1, NE)          | 0.16                    |
| Non-myeloablative                                                        | NE (4.1, NE)            |                         |
| Donor type                                                               |                         |                         |
| MRD/MUD                                                                  | 19.9 (1.2, NE)          | 0.44                    |
| Haploidentical/CBT                                                        | 5.9 (4.1, NE)           | 0.12                    |

Bone Marrow Transplant. Author manuscript; available in PMC 2022 May 23.
| Variable                  | PFS Median (95% CI) months | p-value | OS Median (95% CI) months | p-value |
|--------------------------|-----------------------------|---------|---------------------------|---------|
| Donor type               |                             |         |                           |         |
| MRD                      | NE (3.3, NE)                | 0.50    | NE (9.1, NE)              | 0.15    |
| MUD/Haploidential/CBT    | 19.9 (4.1, NE)              |         | 29.5 (4.1, NE)            |         |

Allo-HCT, allogeneic hematopoietic cell transplantation; NE, not estimated/not reached; Hyper-CVAD, hyperfractionated cyclophosphamide, vincristine, Adriamycin, dexamethasone, alternating with methotrexate and cytarabine CR1, first complete remission; CR2, second complete remission; MRD, matched-related donor; MUD, matched-unrelated donor; CBT, cord blood transplant.