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Treatment Intensity and Symptom Burden in Hospitalized Adolescent and Young Adult Hematopoietic Cell Transplant Recipients at the End of Life

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Abstract

Adolescent and young adult (AYA) oncology patients experience many physical and psychological symptoms at the end of life (EOL); however, data on these experiences for AYA patients that have undergone hematopoietic cell transplantation (HCT) remains sparse. We sought to investigate the characteristics of AYA patients aged 15 − 25 who received allogeneic HCT and subsequently died while inpatient at our institution between the years 2008 − 2014. A standardized data extraction tool was used to collect information about patient demographics, treatment, and symptoms. We found that during this time frame, 34 AYA patients had received HCT and died while inpatient at our institution, 23 (68%) of which were due to treatment-related complications. Compared to non-HCT AYA oncology patients (n = 35), patients who received HCT (n=34) were more likely to have died in the intensive care unit (71% vs. 23%, $P < .0001$) and to have received mechanical ventilation (68% vs. 17%, $P < .0001$) or hemodialysis (53% vs. 0%, $P < .0001$) in the last 30 days of life. These findings demonstrate that AYA patients who receive allogeneic HCT receive intensive EOL treatment, suggesting that these patients may benefit from early integration of expert interdisciplinary services to prospectively assess and manage distressing symptoms.

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Introduction

Adolescent and young adult (AYA) patients, defined by the National Cancer Institute as patients between the age of 15 and 39,(1) represent a unique population with distinct epidemiological, genetic, and psychosocial characteristics. Cancer remains one of the leading causes of non-accidental death for patients in this age range,(2, 3) and improvements in cancer treatment and survival that have been noted in younger pediatric or older adult patients have not yet been realized in this cohort.(2, 4–6) Additionally, AYA oncology patients often receive intensive medical services at the end of life (EOL)(7–9). Compared to younger children, AYA oncology patients have higher rates of hospitalization, more frequent Intensive Care Unit (ICU) admissions, and receive more chemotherapy treatments during the last 30 days of life.(8, 9) Likely due, in part, to the intensity of treatment received at the EOL, AYA oncology patients also experience a myriad of physical and psychological symptoms, and many of these symptoms are poorly recognized, understood, and treated.(10–13) Control of symptoms in pediatric and AYA patients at the EOL is important as parental perceptions of suffering are associated with distress (14) and may complicate parental bereavement.(15, 16) Additionally, given the age and developmental stage of AYA patients, intensive treatment and poorly controlled symptoms at the EOL may negatively impact grief of those outside the immediate family unit, including peers and partners.

Patients with high-risk or relapsed hematologic malignancies, and certain genetic diseases, may be offered hematopoietic cell transplantation (HCT) as a curative treatment option.(17) Despite significant advances in transplant techniques, including progress in supportive care and greater emphasis placed on symptom management and quality of life, HCT remains a high risk and intensive therapy with an increased burden of suffering and risk of mortality.(18–21) Recent studies, using parent report after patient death, have shown that pediatric patients who undergo HCT are more likely to “suffer highly” from their last therapy and die in the ICU, with less opportunity for EOL care planning.(20, 21) Additionally, pediatric oncology patients who underwent HCT had a shorter time interval between completion of a do not resuscitate (DNR) order and death, were enrolled less often in hospice, and were less likely to die at home as compared to pediatric oncology patients who did not undergo HCT as a part of their treatment.(22)

Based on the authors’ collective clinical experience caring for hospitalized AYA oncology patients at the EOL, we hypothesized that this population often receives intensive medical treatments, requires extensive medical and psychosocial resources, and experiences significant symptoms and distress at the EOL. We therefore conducted a retrospective study to further investigate this vulnerable and understudied population. Almost half of the patients included in this study had received allogeneic HCT and thus warranted additional examination. To further characterize the end-of-life experiences of AYA patients who receive allogeneic HCT as part of their treatment regimen, we conducted a descriptive retrospective study of the psychosocial, demographic, treatment, and EOL characteristics of those patients that died while hospitalized at our institution, a large academic pediatric cancer center. We focused on identifying physical and psychological symptoms documented during the last month of life. We also investigated and compared the differences between EOL characteristics and symptoms of AYA patients who died in the inpatient setting at our

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institution during this same time period, based on whether or not they had received HCT as a part of their therapy. Additionally, we explored differences in EOL features of AYA HCT patients based on their cause of death, regardless of location of death. This descriptive study builds upon very limited literature characterizing the demographic and EOL characteristics of AYA patients who have undergone allogeneic HCT,(20, 22) and to our knowledge it is the first study to assess the physical and psychological symptoms of this uniquely vulnerable patient population during the last month of life.

Materials and Methods

Study design

This study was conducted at St. Jude Children's Research Hospital (St. Jude). The hospital's institutional review board deemed the study to be exempt in the setting of a retrospective analysis of a deceased cohort. A list of all patients aged 15 years or older who died between 2008 and 2014 was obtained, along with data about each patient's age at death, date of death, and primary medical service. Demographic data and information related to each patient's treatment and EOL experiences were collected by chart review. A data abstraction tool (supplemental material) was created based on a literature review (10, 11, 23–25) in consultation with oncology and palliative care experts. Two researchers (JS, JL) worked together to collect data on a standardized form for the first 20 patients. Thereafter, JL conducted primary data abstraction; data for every third patient was independently collected by both researchers. Concurrent review of the medical record with real-time discussion was used to reach consensus for any discrepancies in data recording. Additionally, if any questions regarding medical records for patients reviewed by a single researcher, the second reviewer independently reviewed the entire record for that patient to answer questions and the two reviewers subsequently met and reviewed the charts together until consensus was reached. No categories of the medical record or data tool demonstrated ongoing difficulty with discrepant results. All medical record components from 30 days prior to the date of death were reviewed including inpatient and outpatient documentation. Other select portions of the medical record were reviewed to obtain information regarding diagnosis, treatment-related sequelae, disease trajectory, and EOL experiences. For patients who died before mid-2012, data were obtained from both electronic medical records and hard-copy charts, as documentation was not fully electronic during that time period. Additional details related to the HCT were obtained from an institutional HCT clinical database. Invasive medical procedures were defined as any potentially painful procedure that required analgesia or anesthesia (e.g., central or arterial line placement, central line removal, chest tube placement, lumbar puncture, or bone marrow aspirate or biopsy).

Symptom burden was assessed using the data abstraction tool described above. The domains captured by this tool have been previously described (7). Each symptom was characterized as present (yes/no) if it was recorded at some point during the last month of life (30 days prior to death), the last week of life (7 days prior to death), or last day of life (24 hours prior to death). We chose not to present the duration of each symptom during the last month of life, given variation in potential documentation of symptoms based on location of care during the last month of life.

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Statistical Analysis

Demographic, treatment, and EOL characteristics of patients were summarized using descriptive statistics. Chi-square and Fisher's exact tests were used to examine differences for categorical variables between patient subgroups. Wilcoxon rank sum tests were used to examine differences for continuous variables between patient subgroups. Patient subgroups were defined by receipt of an allogeneic HCT as part of treatment (yes/no) and cause of death (progressive disease or secondary malignancy vs. treatment complications). Statistical analyses were conducted by using SAS 9.4 (SAS Institute, Cary, NC). A two-sided significance level of $P < .05$ was used for all statistical tests. Raw p-values are reported, but were adjusted for multiple testing using the false discovery rate adjustment to determine statistical significance.

Results

Demographic and Clinical Characteristics

Fifty-three AYA patients received allogeneic HCT as a part of their treatment regimen and subsequently died between the years 2008 and 2014. Of these, 34 died while hospitalized at St. Jude, 8 died while inpatient at a different hospital, 8 died at home, and 3 did not have a location of death documented. In addition to these 34 HCT AYA patients that died while inpatient at St. Jude, there were 35 AYA patients that had not received an allogeneic HCT as part of their treatment, and also died while inpatient St. Jude between 2008 and 2014. The demographic and clinical characteristics of these 69 patients (HCT, n=34; non-HCT, n=35) are summarized in Table 1. The EOL characteristics of this cohort have been previously described.(7)

Demographic and clinical characteristics of the 34 AYA patients that received allogeneic HCT and subsequently died while inpatient at St. Jude are summarized in Table 2. Of the 7 patients (21%) who received cardiopulmonary resuscitation (CPR) during their final admission, none had a DNR order in place at the time of resuscitation. Only two patients survived an initial resuscitation attempt, and both subsequently had a DNR order placed; one patient died later that same day and the second died 18 days following the initial resuscitation. Of the 11 patients that received HCT and subsequently died of progressive disease, 2 (18%) received CPR during their final hospital admission.

Treatment Characteristics at EOL

Table 3 summarizes the treatment characteristics of the 34 AYA patients who received allogeneic HCT as part of their treatment and died while inpatient at St. Jude. During the last month of life, these patients received intensive medical care, with 23 (68%) receiving mechanical ventilation, 32 (94%) receiving supplemental oxygen, 18 (53%) receiving dialysis and 28 (82%) undergoing at least one invasive medical procedure.

Symptom Characteristics at EOL

AYA patients who received allogeneic HCT and died inpatient at St. Jude (n=34) had a median of 11.5 (interquartile range [IQR], 10–14) documented symptoms during the last month of life, with 27 (79%) patients having at least 1 documented refractory symptom.

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Figure 1 summarizes the symptoms present during the last month, week, and day of life for this patient cohort, dichotomized as (yes/no) at any point during the last 30 days of life, the last 7 days or life, or the last day of life. The most common symptoms in the last month of life were pain (97%), fatigue (91%), and edema/lymphedema (82%).

Comparison of Characteristics by Receipt of Transplant

Characteristics of AYA patients who did (n=34) or did not (n=35) receive allogeneic HCT as part of their treatment regimen, and subsequently died while inpatient at St. Jude, are summarized in Table 4. Involvement of the Palliative Care team in the last 30 days of life was similar between both patient cohorts ($P = .377$). Compared to non-HCT AYA oncology patients, those who had received HCT were more likely to die in the ICU ($P < .0001$), to receive hemodialysis in the last month of life ($P < .0001$) and last day of life (<0.001), and to be mechanically ventilated during both the last month of life ($P < .0001$) and the last day of life ($P < .001$). Patients who underwent HCT experienced a greater number of medical procedures in the last 30 days of life ($P < .001$); however, they were less likely to receive chemotherapy during this time period ($P = .001$). The number of both physical and psychosocial symptoms in the last month of life was comparable between the AYA patient cohorts. Compared to those who did not receive HCT, AYA HCT patients were more likely to have diarrhea (26% vs. 74%, $P < .0001$) and were less likely to have constipation (66% vs. 15%, $P < .0001$).

Comparison of Characteristics and Symptoms by Cause of Death

The characteristics of AYA patients (n=53) who received HCT as part of their treatment and subsequently died between 2008 and 2014, at St. Jude or elsewhere, are summarized by cause of death in Table 5. Forty-two (79%) patients died in the hospital, 34 at our institution and 8 at another hospital. Only 8 patients (15%) died at home and the location of death was not found for 3 patients. AYA HCT patients who died of treatment complications (n=24) were more likely to die in the hospital compared to those who died of either progressive disease or second malignancy (n= 29) ($P = .004$). Compared to AYA HCT patients that died of treatment related complications, patients who died of progressive disease or second malignancy had a significantly longer period of time from their last HCT to death ($P < .001$).

Discussion

AYA patients who underwent allogeneic HCT as part of their treatment regimen received intensive medical treatment at the EOL, as evidenced by the large percentage of patients that received mechanical ventilation, hemodialysis, and invasive medical procedures during the last month of life. This patient cohort also received extensive interdisciplinary and psychosocial supportive services (e.g., pain service, psychology, and PC) during their EOL period. Seventy-nine percent of AYA patients that received allogeneic HCT died in the hospital; these data are consistent with literature suggesting that children who receive HCT are more likely to die in a medical setting when compared to pediatric oncology patients that do not receive HCT.(21)

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Of the 34 AYA HCT patients that died while hospitalized at St. Jude, 71% died in the ICU. Additionally, 35% of the patients in this cohort died of treatment-related complications, which may be associated with increased use of intensive life-prolonging and intensive medical interventions, likely related to prognostic uncertainty.(26) These findings are important because pediatric patient death in the ICU is associated with a high level of complicated grief symptoms in parents 6 months after their child's death (27) and severe complicated grief persists up to 18 months following death.(28)

AYA patients who received allogeneic HCT as part of their treatment regimen experienced significant symptom burden during the last month of life, likely as a result of the intensive treatments received. Proper assessment and management of symptoms is essential in AYA patients that undergo HCT throughout their treatment course, but is especially important at the end of life. These findings highlight the importance of an integrative interdisciplinary team approach to address and treat symptoms in this high-risk population. An integrated PC and HCT framework can be used to conduct frequent, prospective, patient-reported symptom and distress assessments in patients undergoing HCT. This information could be applied clinically to address and treat distressing or persistent symptoms, with interdisciplinary team members brought in to augment treatment of refractory symptoms. Management may include a variety of modalities in combination with pharmacotherapy, including psychological support, integrative methods, and interventional or regional anesthetic approaches. Symptom and distress assessments could be used in a research context to provide baseline data with which to study the effect of interventions on improving the care and quality of life of patients and their families during therapy, and at the EOL. We hypothesize that early integration of PC clinicians with expertise in assessing and managing distressing symptoms may help to alleviate patient and family suffering secondary to persistent or refractory symptoms. Recent data from adult patients undergoing HCT for the treatment of hematologic malignancies demonstrates that integration of PC mitigates transplant-related reduction in patient quality of life as early as 2 weeks after transplant, although long-term impact on quality of life remains less well demonstrated.(29)

Although the general principles of PC for both pediatric and adult patients are readily transferrable to AYA HCT patients, there are distinct psychosocial, ethical, developmental, spiritual, and existential issues that characterize this group of patients. AYA patients with cancer may be uniquely positioned to benefit from integration of PC with routine oncology and HCT care that includes appropriate assessment and management of refractory or persistent symptoms, developmentally-appropriate psychological and integrative approaches to symptom management, and inclusion of AYA patients in medical decision making processes. Effective PC requires creation of an individualized care plan,(24) and we advocate for integration of this plan into the care of high-risk AYA patients early in their disease course, allowing for PC principles to guide conversations and decision-making prior to HCT, during the post-HCT period, and at times of relapse or disease progression.(30–32)

Although the majority of patients included in this study received palliative care support during their last month of life, we believe that all patients who undergo allogeneic HCT should have access to expert consultation in symptom management and advanced care planning given evidence of high symptom burden and risk of further disease progression,

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relapse, or treatment-related complications. In the context of these study findings, our institution has invested in a system to integrate PC into the routine care of AYA HCT patients. This model of PC integration is designed to provide varying levels of support for patients and families, based on clinical status and patient and family need, originating prior to transplant and extended into the EOL period and into bereavement. Prospective evaluation of the effectiveness of this model are ongoing and include of patient-reported symptoms, which we hope will build upon the early foundation established by this study's results.

Our study has several limitations. Given the retrospective nature of chart review, the data represent only that information documented in the medical record. To address concerns regarding the potential for incomplete information, we maximized the data collection process by dual abstraction from both electronic and paper records. Data on the EOL characteristics of patients were more completely documented for patients that died while hospitalized but were limited or not present for patients that died elsewhere. In addition, no standardized assessment tool to identify and document patient symptoms was used at our institution during the timeframe of this study; therefore, the medical record primarily reflects what clinicians observed or obtained from patient or parental reports. In the era of patient-reported outcomes and prospective symptom assessment, this is a major limitation. However, the literature describing prospectively collected data on the symptoms experienced by pediatric oncology patients at the end of life is extremely limited and does not include patients that underwent HCT.(33) In the absence of any prospective symptom data for AYA patients that undergo HCT, this retrospective data provides a meaningful step towards filling this knowledge gap. We obtained the number of symptoms at the end of life, but not severity and associated level of distress. The data on the presence of documented symptoms during the last month, last week, and last day of life may also be affected by whether or not the patient was hospitalized during that timeframe and the number of days that a patient was hospitalized. However, even patients that were not hospitalized during the last 30 days of life had regular documentation via outpatient or home-based visits (typically 3–5 times per week). By conducting this study within a tertiary institution that offers experimental and early phase trials, there may be selection bias towards patients with relapsed or refractory oncologic diseases, who wish to pursue aggressive and/or experimental therapy. Despite these limitations, we believe our findings provide meaningful insights into the characteristics, illness, and EOL experiences of AYA patients who undergo HCT and die while hospitalized.

In summary, AYA patients who undergo allogeneic HCT and die in the hospital receive intensive therapy and require significant medical care and support at the EOL. As a result, these patients experience a large number of symptoms during their last month of life. Early integration of PC into the care of patients undergoing allogeneic HCT may result in improved symptom management and may lead to fewer intensive interventions at the EOL. Further prospective investigation is needed to determine the effect of early PC integrative services on the illness and EOL experiences of AYA HCT patients and their families.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Data abstraction tool used to collect information from the medical record on adolescent and young adult patients that died in the hospital.

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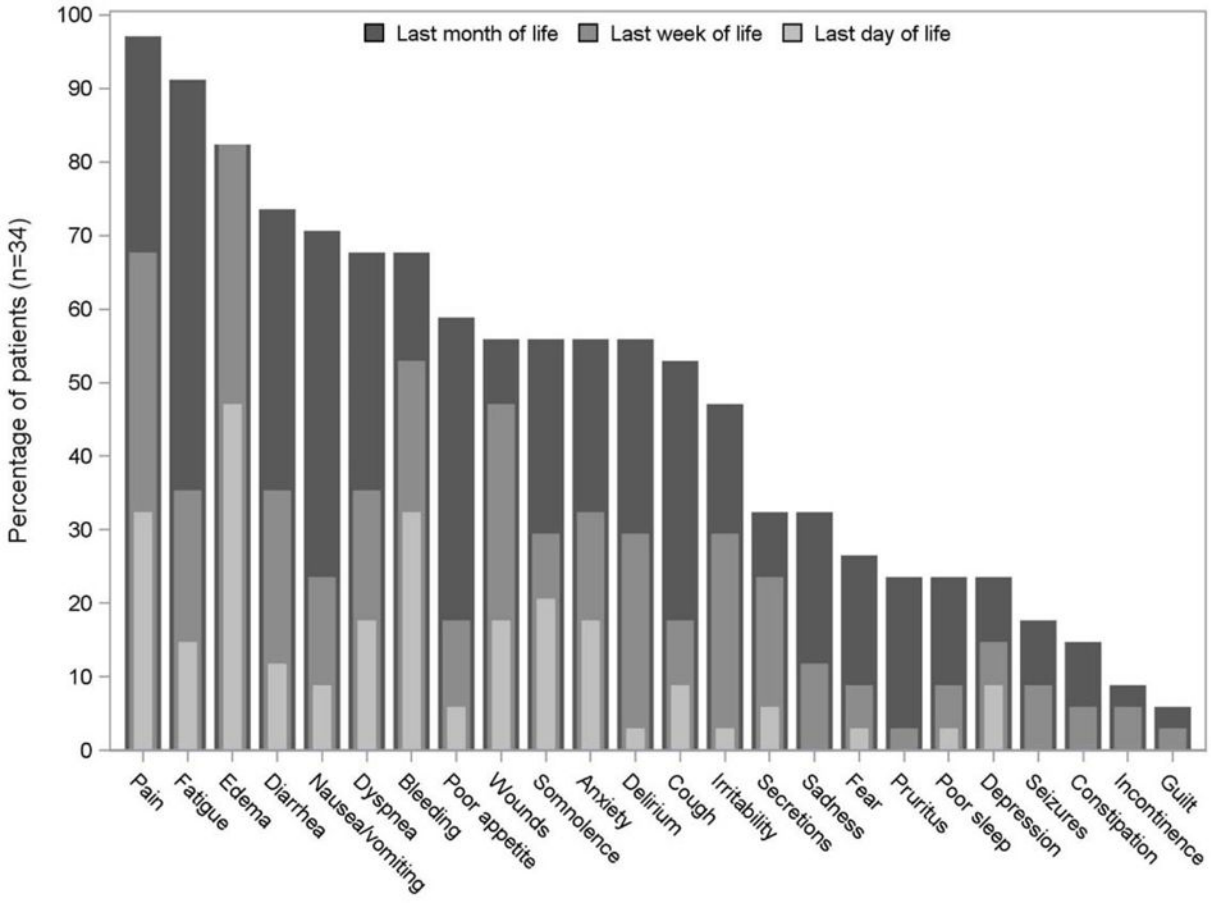

Figure 1.

Symptoms present during the last month, last week, and last day of life for adolescent and young adult patients who received allogeneic hematopoietic cell transplant and died while inpatient at St. Jude (n=34).

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Table 1

Demographic and clinical characteristics of all adolescent and young adult oncology patients that died while inpatient at St. Jude from 2008 to 2014 (N=69)

Characteristics	Value
Age at death (years)	
Median (range)	17.3 (14.7–25.2)
Gender	
Female	24 (35%)
Male	45 (65%)
Cancer diagnosis	
Brain tumor	8 (12%)
Hematology	2 (3%)
Leukemia/lymphoma	41 (59%)
Solid tumor	18 (26%)
Number of phase I/II trial enrollments	
0	34 (49%)
1	29 (42%)
2	5 (7%)
Unknown	1 (1%)
Received allotransplant as part of treatment	**34 (49%)** *
Days from diagnosis to death	
Median (IQR) [range]	577 (306–1,012) [13–5,666]
Days from last hospitalization to death	
Median (IQR) [range]	18 (6–46) [1–168]
Number of patients hospitalized for the entire last month of life	24 (35%)
Cause of death	
Progressive disease	45 (65%)
Treatment complications	24 (35%)
Location of death	
Treatment floor	37 (54%)
ICU	32 (46%)
Number of days in ICU during last month of life	
Median (IQR) [range]	11.5 (4–23.5) [0–51]
POST/DNR order in place	60 (87%)
Days to death from POST/DNR order,	
Median (IQR) [range]	4.5 (2–15) [0–368]
Received CPR prior to death	8 (12%)
Diagnosis: leukemia/lymphoma	8 (100%)
Received an allotransplant	7(88%)

* These patients that received allogeneic transplant were included for further analysis

Abbreviations: IQR, interquartile range; LMOL, last month of life; ICU, intensive care unit; POST, physician scope of treatment; DNR, do not resuscitate; CPR, cardiopulmonary resuscitation.

[a]Only applicable for those patients that were not hospitalized the entire last month of life, n=45.

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Table 2

Demographic and clinical characteristics of adolescent and young adult patients who received allogeneic hematopoietic cell transplant and died while inpatient at St. Jude (n=34).

Characteristics	Value
Age at death (years)	
Median [Range]	17.3 [14.8–24]
Sex, n (%)	
Female	12 (35%)
Male	22 (65%)
Race, n (%)	
White	26 (76%)
Black	4 (12%)
Other	4 (12%)
Cancer diagnosis, n (%)	
ALL	13 (38%)
AML	12 (35%)
Other Leukemia	2 (6%)
Lymphoma	4 (12%)
MDS	1 (3%)
Aplastic anemia	2 (6%)
Experienced remission prior to HCT, n (%)	25 (74%)
Donor type, n (%)	
Haploidentical	16 (47%)
Matched Sibling	3 (9%)
Matched Unrelated	15 (44%)
Product type, n (%)	
Apheresis	20 (59%)
Umbilical cord	1 (3%)
Bone marrow	13 (38%)
No. of allogeneic transplants received	
Median (IQR) [Range]	1 (1–1) [1–3]
ANC engraftment[a], n (%)	33 (97%)
Platelet engraftment >20K[b], n (%)	20 (59%)
Days from last HCT to death	
Median (IQR) [Range]	154 (69–309) [26–1428]
Cause of death, n (%)	
Progressive disease	11 (32%)
Treatment complications	23 (68%)
Location of death, n (%)	
Inpatient unit	10 (29%)
ICU	24 (71%)
Days from last hospital admission to death	

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Characteristics	Value
Median (IQR) [Range]	39 (13–75) [1–168]
POST/DNR order in place, n (%)	28 (82%)
Received CPR prior to death, n (%)	7 (21%)

Abbreviations: IQR, interquartile range; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; ANC, absolute neutrophil count; HCT, hematopoietic cell transplant; ICU, intensive care unit; POST, physician scope of treatment; DNR, do not resuscitate; CPR, cardiopulmonary resuscitation.

[a] ANC engraftment was defined as ANC of at least 500/mm3 for 3 consecutive days

[b] Platelet engraftment was defined as the first day on which the platelet count was at least 20 × 103/mm3, without transfusion in the preceding 7 days.

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Table 3

Treatment characteristics at the end of life of adolescent and young adult patients who received allogeneic hematopoietic cell transplant and died while inpatient at St. Jude (n=34).

Characteristics	Value
Interdisciplinary and Psychosocial Support during the last month of life, n (%)	
Palliative care team involvement	23 (68%)
Pain service involvement	8 (24%)
Psychology involvement	28 (82%)
Medical Support	
Received chemotherapy during LMOL, n (%)	10 (29%)
Received chemotherapy during LWOL, n (%)	3 (9%)
Received medical procedure during LMOL, n (%)	28 (82%)
No. of procedures, Median (IQR)	3 (2–5)
Received PRBC transfusion during LMOL, n (%)	32 (94%)
No. in LMOL, Median (IQR)	10 (5.5–16)
Received platelet transfusion during LMOL, n (%)	33 (97%)
No. in LMOL, Median (IQR)	40 (16–51)
Received IVFs during LMOL, n (%)	27 (79%)
Duration in days, Median (IQR) [Range]	12 (7–28) [1–31]
Received TPN during LMOL, n (%)	28 (82%)
Duration in days, Median (IQR) [Range]	22 (9.5–31) [2–31]
Received mechanical ventilation during LMOL, n (%)	23 (68%)
Duration in days, Median (IQR) [Range]	9 (5–23) [1–31]
Received mechanical ventilation during LDOL, n (%)	18 (53%)
Received dialysis during LMOL, n (%)	18 (53%)
Duration in days, Median (IQR) [Range]	16.5 (4–24) [2–31]
Received oxygen during LMOL, n (%)	32 (94%)
Duration in days, Median (IQR) [Range]	25 (11.5–31) [3–31]
Received opioids during LMOL, n (%)	33 (97%)
Duration in days, Median (IQR) [Range]	28 (9–31) [1–31]

Abbreviations: LMOL, last month of life; LWOL, last week of life; IQR, interquartile range; PRBC, packed red blood cell; IVFs, intravenous fluids; TPN, total parenteral nutrition.

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Table 4

End-of-life characteristics of adolescent and young adult patients who died while inpatient at St. Jude by receipt of allogeneic hematopoietic stem cell transplant.

	Received allogeneic HCT?		
Characteristics	**No (n=35)**	**Yes (n=34)**	**P**
Age at death			
Median [Range]	17.6 [14.7–25.2]	17.3 [14.8–24]	0.986
Location of death, n (%)			
Inpatient unit	27 (77%)	10 (29%)	<0.0001 *
ICU	8 (23%)	24 (71%)	
POST/DNR order in place at time of death, n (%)	32 (91%)	28 (82%)	0.306
Days to death after POST/DNR order, Median (IQR) [Range]	5.5 (2.5–17) [0–368]	2.5 (1–12) [0–154]	0.059
Received CPR prior to death, n (%)	1 (3%)	7 (21%)	0.028
Received chemotherapy during the LMOL, n (%)	24 (69%)	10 (29%)	0.001 *
Received chemotherapy during the LWOL, n (%)	9 (26%)	3 (9%)	0.064
Palliative care team involvement during the LMOL, n (%)	27 (77%)	23 (68%)	0.377
Received mechanical ventilation during the LMOL, n (%)	6 (17%)	23 (68%)	<0.0001 *
Received mechanical ventilation during the LDOL, n (%)	4 (11%)	18 (53%)	<0.001 *
Received dialysis during the LMOL, n (%)	0 (0%)	18 (53%)	<0.0001 *
Received dialysis during the LDOL, n (%)	0 (0%)	10 (29%)	<0.001 *
Received medical procedure during the LMOL, n (%)	21 (60%)	28 (82%)	0.041
No. of medical procedures during the LMOL, Median (IQR)	1 (0–2)	3 (1–5)	<0.001 *
No. of documented symptoms in the LMOL[a]			
Median (IQR)	11 (10–14)	11.5 (10–14)	0.591
No. of documented physical symptoms in the LMOL[b]			
Median (IQR)	9 (8–11)	8.5 (7–11)	0.463
No. of documented psychological symptoms in the LMOL[c]			
Median (IQR)	3 (1–3)	3 (1–4)	0.908

Abbreviations: HCT, hematopoietic cell transplant; IQR, interquartile range; ICU, intensive care unit; POST, physician scope of treatment; DNR, do not resuscitate; CPR, cardiopulmonary resuscitation; LMOL, last month of life; LDOL, last day of life.

[a] Refers to all physical and psychological symptoms (total=24).

[b] Physical symptoms (total=17): pain, dyspnea, cough, increased secretions, edema/lymphedema, skin breakdown/wounds, pruritus, constipation, diarrhea, changes in bowel or bladder function/incontinence, nausea/vomiting, seizures, poor appetite, poor sleep, somnolence, bleeding, and fatigue.

[c] Psychological symptoms (total=7): depression, sadness, anxiety, irritability/personality changes, fear, confusion/delirium, and guilt.

* Remains statistically significant after adjustment for false discovery rate (P<.05).

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Table 5

Characteristics of deceased adolescent and young adult patients who received allogeneic hematopoietic cell transplant by cause of death

Characteristics	Cause of death		*P*
	Progressive disease or second malignancy (n=29)	Treatment complications (n=24)	
Age at death (years)			
Median [Range]	17.9 [8.9–24]	17.2 [15.1–23.6]	0.416
Sex, n (%)			
Female	11 (38%)	8 (33%)	0.728
Male	18 (62%)	16 (67%)	
Race[a], n (%)			
White	21 (72%)	17 (74%)	1.000
Black	4 (14%)	3 (13%)	
Other	4 (14%)	3 (13%)	
Specific cancer diagnosis, n (%)			
ALL	7 (24%)	9 (38%)	
AML	14 (48%)	9 (38%)	
Aplastic anemia	0 (0%)	2 (8%)	
Ewing's sarcoma	1 (3%)	0 (0%)	
Hurler's Syndrome	1 (3%)	0 (0%)	
Lymphoma	6 (21%)	1 (4%)	
MDS	0 (0%)	1 (4%)	
Other Leukemia	0 (0%)	2 (8%)	
Location of death[b], n (%)			
Home	8 (31%)	0 (0%)	0.004 *
Hospital	18 (69%)	24 (100%)	
Donor type, n (%)			
Haploidentical	16 (55%)	10 (42%)	0.238
Matched sibling	4 (14%)	2 (8%)	
Matched unrelated	9 (31%)	12 (51%)	
Product type, n (%)			
Apheresis	17 (59%)	15 (63%)	0.888
Umbilical cord	1 (3%)	1 (4%)	
Bone marrow	11 (38%)	8 (33%)	
No. allogeneic transplants			
Median (IQR) [Range]	1 (1–2) [1–3]	1 (1–1) [1–3]	0.011 *
Days from last HCT to death			
Median (IQR) [Range]	527 (250–758) [35–5510]	107.5 (67.5–227.5) [26–943]	<0.001 *

Abbreviations: IQR, interquartile range; ALL, acute lymphoblastic leukemia;

AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; HCT, hematopoietic cell transplant.

[a]The total sample size does not sum to 53 because one patient has unknown race.

[b] The total sample size does not sum to 53 because three patients have unknown location of death.

[*] Remains statistically significant after adjustment for false discovery rate (P<.05).

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