Palliative and End-of-Life Care for Patients With Hematologic Malignancies

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Hematologic malignancies are a heterogeneous group of diseases with unique illness trajectories, treatment paradigms, and potential for curability, which affect patients' palliative and end-of-life care needs. Patients with hematologic malignancies endure immense physical and psychological symptoms because of both their illness and often intensive treatments that result in significant toxicities and adverse effects. Compared with patients with solid tumors, those with hematologic malignancies also experience high rates of hospitalizations, intensive care unit admissions, and in-hospital deaths and low rates of referral to hospice as well as shorter hospice length of stay. In addition, patients with hematologic malignancies harbor substantial misperceptions about treatment risks and benefits and frequently overestimate their prognosis. Even survivors of hematologic malignancies struggle with late effects, post-treatment complications, and post-traumatic stress symptoms that can significantly diminish their quality of life. Despite these substantial unmet needs, specialty palliative care services are infrequently consulted for the care of patients with hematologic malignancies. Several illness-specific, cultural, and system-based barriers to palliative care integration and optimal end-of-life care exist in this population. However, recent evidence has demonstrated the feasibility, acceptability, and efficacy of integrating palliative care to improve the quality of life and care of patients with hematologic malignancies and their caregivers. More research is needed to develop and test population-specific palliative and supportive care interventions to ensure generalizability and to define a sustainable clinical delivery model. Future work also should focus on identifying moderators and mediators of the effect of integrated palliative care models on patient-reported outcomes and on developing less resource-intensive integrated care models to address the diverse needs of this population.

J Clin Oncol 38:944-953. © 2020 by American Society of Clinical Oncology

INTRODUCTION

Hematologic malignancies are a heterogeneous group of diseases characterized by marked variation in their illness trajectories, treatment paradigms, and potential for curability.^{1,2} Compared with patients with solid tumors, patients with hematologic malignancies experience unique illness trajectories that affect their palliative and end-of-life (EOL) care needs.^{1,2} Specifically, these patients often experience an unpredictable illness course, with the possibility of cure persisting even in relapsed and refractory settings, contrary to most advanced solid tumors.¹⁻³ Many hematologic malignancies require treatment with intensive therapies, including hematopoietic stem-cell transplantation (HCT) and, more recently, chimeric antigen receptor (CAR) T-cell therapy, both of which are associated with significant toxicities and risks of mortality.⁴⁻⁸ Even among patients with more indolent and chronic hematologic malignancies, intermittent or continuous therapies may be required indefinitely, which can contribute to morbidity and long-term quality-of-life (QOL) impairments.

Early integration of specialty palliative care has been shown to improve a wide range of outcomes for patients with advanced solid tumors, including QOL, mood, symptom burden, illness understanding, coping, and quality of EOL care.⁹⁻¹⁴ Although palliative care clinicians are increasingly asked to care for patients with solid tumors, they are rarely consulted for patients with hematologic malignancies.^{1,3,15} Given palliative care clinicians' expertise in managing complex symptoms, facilitating adaptive coping and illness understanding, and addressing the EOL care of patients with cancer, they could play an important role in addressing the palliative and EOL care needs of patients with hematologic malignancies.

In this article, we first describe the unmet palliative care needs of patients with hematologic malignancies and then examine the barriers to palliative care integration and optimal EOL care for this population. We also review the literature on palliative care integration strategies and discuss future directions to enhance the QOL and care of patients with hematologic malignancies through collaborative care.

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on March 6, 2019 and published at ascopubs.org/journal/jco on February 5, 2020; DOI <https://doi.org/10.1200/JCO.18.02386>

UNMET PALLIATIVE CARE NEEDS IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES

Table 1 lists the palliative care needs of patients with hematologic malignancies during key phases of their illness, including during treatment, during survivorship, and at the EOL.

Palliative Care Needs During Treatment

Studies have shown that patients with hematologic malignancies experience a symptom burden that is comparable to or exceeds that of patients with metastatic solid tumors.^{1,16} In a cross-sectional study of 180 patients with hematologic malignancies who received their care at a tertiary hospital, patients experienced a mean of 8.8 symptoms.¹⁷ The most prevalent symptoms were lack of energy, difficulty with sleep, pain, and dry mouth, which affected 40% to 70% of study participants.¹⁷ Of note, the mean number of symptoms and level of distress were comparable to patients with metastatic solid tumors in previously published symptom prevalence studies.¹⁷ In another cross-sectional analysis of patients with cancer who received palliative care across 17 sites within the Global Palliative Care Quality Alliance, rates of pain, dyspnea, nausea, and anorexia were similar among those with hematologic and solid malignancies.¹⁸ However, patients with hematologic malignancies reported higher rates of clinically significant fatigue and drowsiness.¹⁸ Other studies in patients with hematologic malignancies also have demonstrated that the prevalence of fatigue is high, affecting 80% to 90% of patients with acute leukemia, myelodysplastic syndrome, and multiple myeloma.¹⁹⁻²² Thus, patients with hematologic malignancies experience substantial physical symptom burden during their illness that is comparable to patients with metastatic solid tumors.

Many patients with hematologic malignancies receive intensive treatments that require prolonged hospitalization, such as HCT.^{7,23-25} Studies have shown that patients who receive autologous or allogeneic HCT experience a dramatic decline in their QOL, which is associated with an increase in symptoms such as nausea, vomiting, mucositis, fatigue, and diarrhea during their transplantation course.^{23,26-30} Patients with acute leukemia also struggle with toxicities that result from intensive chemotherapy, which often requires a prolonged hospitalization.³¹⁻³⁴ In one study, patients with relapsed acute myeloid leukemia (AML) who received intensive chemotherapy reported a mean of 14.1 moderate to severe symptoms that led to substantial QOL impairment across multiple domains.³⁵ Although the symptoms experienced during intensive treatments are often temporary, they may contribute to long-term psychological distress, including post-traumatic stress symptoms and depression.^{36,37}

Psychological distress, including symptoms of depression and anxiety, are also prevalent in patients with hematologic malignancies and affect 30% to 60% of the population during treatment.^{17,23,38} In a study of 104 patients with hematologic cancers who received chemotherapy, 50% reported clinically significant distress.³⁹ Of note, patients with acute leukemia and those who undergo HCT also struggle with acute stress reactions and post-traumatic stress symptoms as they endure the shock of a life-threatening diagnosis and the need for prolonged and socially isolating hospitalizations.^{31,40-42} A recent population-level analysis suggested that patients with leukemia are among the most distressed of all those with cancer.⁴³ Thus, scalable interventions are critically needed to address the immense emotional and psychological burden that patients with hematologic malignancies experience during their illness course.

TABLE 1. Palliative Care Needs in Patients With Hematologic Malignancies

Illness Phase	Palliative Care Needs
During treatment	Physical symptoms and QOL impairments as a result of the illness Physical symptoms as a result of toxicities from intensive treatment Psychological distress, including anxiety and depression symptoms Traumatic stress and post-traumatic stress symptoms (especially in acute leukemia and HCT) Social isolation (especially in acute leukemia and HCT) Informational needs with regard to treatment decision making and prognosis
During survivorship	Physical symptoms (especially allogeneic HCT survivors living with graft-versus-host disease) Psychological distress, including depression, fear of recurrence, and post-traumatic stress symptoms Financial burden Neurocognitive dysfunction Infertility Late effects as a result of cancer therapy
At the EOL	Physical and psychological symptom burden Frequent hospitalizations and ICU admissions Receipt of chemotherapy near the EOL Lack of advance care planning and EOL discussions Low hospice referrals and short length of stay in hospice

Abbreviations: EOL, end of life; HCT, hematopoietic stem-cell transplantation; ICU, intensive care unit; QOL, quality of life.

Patients with hematologic malignancies also have identified lack of information, difficulty with treatment decision making, and prognostic uncertainty as important challenges in dealing with their illness.^{1,42,44} In addition, studies have shown that these patients have significant misperceptions about their treatment risks and benefits, and they often overestimate their prognosis.^{21,45,46} In one study of older patients with AML, 90% reported that they were somewhat or very likely to be cured of their disease, whereas their oncologists estimated this chance of cure for only 31%.⁴⁶ These gaps in illness and prognostic understanding may have important clinical implications for patients' medical decision making. In fact, patients' understanding of the likelihood of cure is associated with their willingness to accept chemotherapy,⁴⁷⁻⁴⁹ and those who overestimate their survival are more likely to prefer intensive medical care at the EOL.^{50,51} Thus, enhancing patients' illness and prognostic understanding is essential for patients with hematologic malignancies to make informed decisions about their cancer care.

Palliative Care Needs During Survivorship

Survivors of hematologic malignancies often deal with QOL impairments and long-term sequelae of their illness and associated treatments.^{5-7,26-29,52-57} Fatigue, pain, neuropathy, infertility, cardiomyopathy, neurocognitive deficits, psychological distress, fear of recurrence, and post-traumatic stress symptoms may result in diminished QOL compared with the normal population.^{26-29,52-56,58-60} Among allogeneic HCT recipients, chronic graft-versus-host disease (GVHD) is the major cause of morbidity, physical and functional impairments, symptom burden, and poor QOL.^{6,54,61-66} The severity of chronic GVHD is associated with the extent of QOL decline in this population.⁶⁷ In a recent survey of transplantation physicians, 52% perceived GVHD symptoms as an important unmet palliative care need for allogeneic HCT recipients.⁶⁸ Even among patients with highly curable hematologic malignancies, such as Hodgkin's lymphoma, 30% of patients struggle with clinically meaningful distress years after completing their therapy.⁶⁹ Similarly, patients with chronic lymphocytic leukemia, an often indolent disease that patients may live with for more than a decade, have been shown to have worse emotional well-being than patients with more serious solid tumors.⁷⁰ More research is needed to better understand the needs of survivors of hematologic malignancies, especially in the era of new treatments such as CAR T-cell therapy, to inform the development of palliative and supportive care interventions.

Palliative Care Needs at the EOL

In addition to substantial physical and psychological symptom burden at the EOL,^{38,71-73} patients with hematologic malignancies often receive intensive EOL care, including high rates of hospitalizations,^{72,74,75} emergency department visits,⁷⁵ intensive care unit (ICU) admissions,^{72,74,76,77} and chemotherapy administration near the EOL.^{74,75,77,78} One study quantified the amount of contact with the health care

system among older patients with AML from the time of diagnosis until death.⁷⁴ Patients experienced on average 4.2 hospital admissions.⁷⁴ Those who died spent on average 28.3% of their lives postdiagnosis in the hospital and 13.8% of their time in the clinic.⁷⁴ Furthermore, patients with hematologic malignancies have a high likelihood of dying in the hospital, low rates of hospice referral, and a short length of stay in hospice.^{72,75,78-80} In a systematic review and meta-analysis, patients with hematologic malignancies were more than twice as likely to die in the inpatient setting compared with those with other cancers.⁸¹ Although recent studies suggest an increase in hospice use in some patients with hematologic malignancies, hospice length of stay remains very short, with a median time of 6 to 9 days.^{82,83} Despite the intensity of care at the EOL, advance directives and code status documentation are rarely addressed or documented in the medical record.^{1,78,84} These data underscore the need for interventions to optimize the quality of EOL care for patients with hematologic malignancies.

BARRIERS TO PALLIATIVE CARE INTEGRATION

Despite the numerous unmet palliative care needs in patients with hematologic malignancies, specialty palliative care is rarely used in this population.^{2,74,77,78,85,86} Figure 1 summarizes the illness-specific, cultural, and system-based barriers that contribute to low rates of palliative care use.

Illness-Specific Barriers

Many patients with hematologic malignancies require treatment with intensive therapies such as HCT, CAR T-cell therapy, or high-dose chemotherapy regimens given in hospital settings. Although these treatments carry a significant risk of morbidity and mortality, they are also potentially curative.^{4,8} Given that specialty palliative care has been traditionally offered to patients with advanced cancer who receive noncurative therapy, patients who pursue curative treatments generally have been excluded from referral to palliative care.^{9-11,14,87,88} Furthermore, a clear transition is absent between the curative and palliative phase of treatment because many patients with relapsed and refractory hematologic malignancies can still achieve a cure, which also contributes to the lack of early palliative care use.^{1,2} The extent of prognostic uncertainty in patients with hematologic malignancies makes the identification of triggers for palliative care use rather challenging if only patients with incurable disease are referred for these services.

Cultural Barriers

Oncologists who care for patients with hematologic malignancies have significant misperceptions that equate palliative care with just EOL care.^{68,84,89} In a recent survey of transplantation physicians, 52% reported that palliative care is synonymous with EOL care, and 66% stated that the service name can decrease hope in patients and families.⁶⁸ Studies show that oncologists who care for patients with hematologic malignancies also have a strong sense of

FIG 1. Barriers to palliative care use in patients with hematologic malignancies. EOL, end of life.

ownership over addressing the palliative care needs of their patients, which may also result in low palliative care referral rates.^{68,84} In fact, 84% of transplantation physicians in a recent survey stated that the oncologist should coordinate the care of patients across all stages of disease, including the EOL.⁶⁸ Finally, oncologists' limited knowledge about the potential benefits of palliative care for improving the experience of patients and families also represents an important cultural barrier to palliative care use.^{68,90}

System-Based Barriers

Most studies that have evaluated the efficacy of early integrated palliative and oncology care focused on patients with advanced solid tumors and excluded those with hematologic malignancies, which reflects these early biases.^{9,10,14} Thus, the lack of data that support the role of palliative care for patients with hematologic malignancies, rather than evidence to the contrary, has served as an important barrier to palliative care integration in the past decade. Recent studies that demonstrated the potential benefit of integrated palliative care for patients with hematologic malignancies may overcome this barrier in the coming years.^{91,92} Increasing demand for integrated palliative care may exacerbate the shortage of palliative care clinicians and an adequate outpatient specialty palliative care infrastructure, which will limit access to palliative care for many patients with hematologic malignancies, especially those treated in community centers and rural areas.^{93,94}

BARRIERS TO OPTIMAL EOL CARE

Figure 2 summarizes the illness, cultural, and system-based barriers to optimal EOL care for patients with hematologic malignancies

Illness-Specific Barriers

Patients with hematologic malignancies often experience a rapid and unpredictable trajectory of decline at the EOL.^{95,96} The rapid decline and absence of a clear transition between the curative and palliative phases of treatment of many patients with hematologic malignancies often result in the receipt of intensive medical care at the EOL, including hospitalization and ICU admission. Even in patients with hematologic malignancies admitted to the ICU, there is substantial prognostic uncertainty because 50% of these patients may survive and recover after an ICU admission.⁹⁷ Moreover, patients with hematologic malignancies have unique needs at the EOL, including the need for blood product support and intravenous antibiotics, which additionally complicates the delivery of EOL care.¹⁻³ Of note, the routine assumption that most patients wish to die at home may not apply as uniformly to those with hematologic malignancies and their caregivers.⁹⁸ After spending months receiving intensive treatments in the hospital setting, some patients and their caregivers feel more comfortable in the inpatient setting and less equipped to address their EOL care needs at home.⁹⁸ Studies are needed to enhance our understanding of the EOL care needs of patients with hematologic malignancies and the optimal EOL care delivery models for this population.

Cultural Barriers

Oncologists who care for patients with hematologic malignancies have identified unrealistic expectations from both patients and oncologists as important barriers to optimizing EOL care.⁹⁹ In a survey of 182 oncology clinicians who care for patients with solid tumors and hematologic malignancies, hematologic specialists also reported

FIG 2. Barriers to optimal end-of-life (EOL) care for patients with hematologic malignancies.

feeling less comfortable with discussing death and dying (72% v 88%) and hospice referral (81% v 93%) and were more likely to feel a sense of failure with disease progression (46% v 31%).¹⁰⁰ In a qualitative study of 10 oncologists who care for patients with hematologic malignancies, the oncologists expressed concerns that EOL discussions may undermine their relationship with their patients.¹⁰¹ Consequently, EOL care discussions occur late in the illness course for patients with hematologic malignancies, which results in poor-quality EOL care.^{95,102} In addition, oncologists who care for patients with hematologic malignancies are more likely to prescribe cancer therapy at the EOL than solid tumor oncologists, which also contributes to the intensity of EOL care in this population.¹⁰⁰

System-Based Barriers

Our current EOL care delivery models are inadequate for addressing the needs of patients with hematologic malignancies. Many of these patients require transfusion support to palliate symptoms, reduce the risk of serious complications like bleeding, or promote longevity. Unfortunately, many hospice agencies do not allow any transfusion support because of the logistics and costs involved. Several analyses point to transfusions as a barrier to hospice referral and high-quality EOL care in the United States.^{76,82,83} In a recent large SEER Medicare analysis of US adults age 65 years and older with myelodysplastic syndrome, transfusion dependence was associated with a lower rate of hospice enrollment.⁷⁶ Similarly, in another SEER Medicare analysis of patients with leukemia, those who were transfusion dependent had a markedly shorter hospice length of stay, which suggests that transfusion dependence precludes timely hospice referral.⁸² In one study, 46% of

oncologists who care for patients with hematologic malignancies reported that home hospice care is inadequate to address their patients' EOL needs, and more than half of respondents stated that they would refer more patients to hospice care if blood transfusions were permitted.¹⁰³

PALLIATIVE CARE INTEGRATION STRATEGIES

Despite the significant barriers to palliative care integration for patients with hematologic malignancies, recent studies have demonstrated the feasibility, acceptability, and benefits of integrating palliative care with oncologic care in this population (Table 2). Several studies have reported on the feasibility of integrating palliative care as a consultative or embedded service in the care of patients with multiple myeloma and those undergoing HCT.^{104,105,108,109} In a recent study, Loggers et al¹⁰⁶ reported that early palliative care consultation before transplantation is feasible and acceptable for patients with high-risk hematologic malignancies who undergo allogeneic HCT. The overall participation rate was 63%, and 82% of participants reported feeling very comfortable with the intervention.

In addition to descriptive reports, published literature now includes a prospective randomized clinical trial that demonstrated the efficacy of palliative care for improving patient and caregiver QOL and psychosocial outcomes. In a single-center randomized trial of 160 patients with hematologic malignancies who underwent autologous or allogeneic HCT, patients were randomly assigned to receive integrated palliative and transplantation care versus standard transplantation care.⁹¹ Patients randomly assigned to the intervention were seen by palliative care clinicians twice per week throughout their HCT hospitalization. Patients

TABLE 2. Summary of Studies of Palliative Care Integration for Patients With Hematologic Malignancies

First Author	Study Design/ Population	Intervention	Findings
Selvaggi ¹⁰⁴	Quality improvement project on HCT unit	Consultative specialty palliative care model for patients admitted to the HCT unit	392 palliative consultations provided to 256 unique patients Palliative care clinicians documented the first goals of care conversation in 67% of participants Rate of hospice referral increased from a preimplementation of 5% to 41% postimplementation Oncologists reported high level of satisfaction with the program
Roeland ¹⁰⁵	Implementation project on HCT unit	Embedded specialty palliative care clinicians on the HCT unit	The embedded care model was feasible and acceptable to palliative care and transplantation clinicians Palliative care clinicians addressed physical and psychological symptoms during HCT
Loggers ¹⁰⁶	Feasibility study in patients who received allogeneic HCT	Early palliative care consultation before HCT admission with at least monthly visits (n = 20)	63% participation rate 82% of patients reported feeling very comfortable with the intervention Participants reported stable or improved mood and sense of hope without apparent negative effects
Foxwell ¹⁰⁷	Program development for inpatient hematologic malignancy service	Palliative care nurse practitioners offered office hours during weekdays for hematologic malignancy clinicians	Mean of 11 patients discussed per week 14.7% of patients discussed required a full palliative care consult Reduction in palliative care consultation rate from 19.5% to 10.2% with an increase in consults to address goals of care
Porta-Sales ¹⁰⁸	Retrospective study of patients with multiple myeloma	Outpatient early integrated palliative care for patients with multiple myeloma (n = 67)	Moderate to severe pain decreased from 57% to 18% in patients attending the clinic Physical and emotional symptoms improved after attending clinic visits
El-Jawahri ^{91,92}	Randomized clinical trial in patients who received autologous or allogeneic HCT	Inpatient palliative care integrated with transplantation care during HCT hospitalization (n = 160)	Patients who received the intervention reported improvement in their QOL, symptom burden, and symptoms of depression and anxiety during HCT hospitalization Caregivers reported improvement in their depression symptoms and coping Patients experienced sustained improvement in their depression symptoms and post-traumatic stress symptoms up to 6 months after HCT

Abbreviations: HCT, hematopoietic stem-cell transplantation; QOL, quality of life.

who received the intervention reported clinically significant improvements in their QOL, symptom burden, depression, and anxiety symptoms. In addition, caregivers of patients randomly assigned to the intervention also reported significant improvement in their coping and depression symptoms compared with caregivers of those who received transplantation care alone.⁹¹ Of note, the effects of the intervention were sustained at 3 and 6 months after HCT, with patients randomly assigned to the intervention reporting improvement in their depression and post-traumatic stress symptoms compared with those who received transplantation care alone.⁹² These findings highlight the potential benefits of integrated palliative care for improving the QOL and care of patients with hematologic malignancies and their caregivers. However, it is important to note that palliative care integration research in hematologic malignancies remains in its early stages, with a lot of the literature focused on feasibility and acceptability testing and the needs of the HCT population. A critical need exists

to expand the evidence base to demonstrate the benefits of palliative care in patients with various hematologic malignancies and across care settings. Several promising randomized clinical trials are currently under way to test the efficacy of palliative care additionally for addressing the palliative and EOL care needs of this population (ClinicalTrials.gov identifiers: [NCT02975869](#), [NCT03310918](#), and [NCT03641378](#)).

In recognition of the challenges posed by the palliative care workforce shortage, Foxwell et al¹⁰⁷ developed a novel program that consisted of palliative care nurse practitioner office hours to provide support for clinicians who care for patients with hematologic malignancies in the inpatient setting. The program entailed having a palliative care nurse practitioner visit the inpatient hematology-oncology advanced practice offices daily at a consistent time to discuss patients and answer questions. Discussions typically included medication recommendation, resources for patients with hematologic malignancies and their families, and

FIG 3. Potential strategies for palliative care (PC) integration in patients with hematologic malignancies. Note that the diseases included here are only examples and do not represent a comprehensive list of hematologic malignancies.

informal education. A mean of 11 patients were discussed per week during office hours. Of the 299 patients discussed, 14.7% subsequently required a full palliative care consultation. Overall, the program resulted in a decrease in palliative care consultation rate from 19.6% to 10.2% with an increase in consults focused on addressing goals of care.¹⁰⁷ Although these data are encouraging, future studies that investigate the impact of such programs on patient outcomes are needed.

FUTURE DIRECTIONS

In summary, patients with hematologic malignancies have substantial unmet palliative care needs that span their illness course from diagnosis to the EOL as well as during the survivorship period. Significant illness, cultural, and system-based barriers to integrating palliative care and optimizing EOL care for this population exist. However, recent evidence has demonstrated that integrated palliative and oncology care models are feasible and acceptable and have promising potential to improve the QOL and care of patients with hematologic malignancies and their caregivers.

Given the heterogeneous nature of hematologic malignancies, the emerging models of palliative care integration must appropriately fit patients' needs and their disease trajectories. Figure 3 depicts a potential approach for identifying the appropriate palliative care integration strategy in patients with various illness

trajectories. For example, patients who live with a more indolent disease and low symptom burden, such as indolent lymphomas, may benefit from a palliative care consultation when their prognosis becomes poor. In contrast, patients with high symptom burden and risk of mortality, such as those with acute leukemias, may benefit from early integrated longitudinal palliative care involvement. Population-specific palliative care interventions can more effectively address the unique needs of patients with various hematologic malignancies while appropriately allocating palliative care resources. Of note, models of palliative care integration must be tested rigorously in randomized clinical trials and implementation and dissemination studies to ensure their efficacy, generalizability, and effectiveness for improving the care of patients with hematologic malignancies. Future work also should focus on identifying mediators and moderators of the effect of palliative care interventions on patient-reported outcomes because this information can help us to develop a sophisticated understanding of how these interventions work and for whom they are most effective. The development of less resource-intensive integrated care models, such as stepped care models, and primary palliative care interventions to address the growing needs of patients with hematologic malignancies amid growing workforce challenges is also an important priority for the field.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI <https://doi.org/10.1200/JCO.18.02386>.

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REFERENCES

1. Epstein AS, Goldberg GR, Meier DE: Palliative care and hematologic oncology: The promise of collaboration. *Blood Rev* 26:233-239, 2012
2. LeBlanc TW, El-Jawahri A: When and why should patients with hematologic malignancies see a palliative care specialist? *Hematology (Am Soc Hematol Educ Program)* 2015:471-478, 2015
3. Manitta VJ, Philip JA, Cole-Sinclair MF: Palliative care and the hemato-oncological patient: Can we live together? A review of the literature. *J Palliat Med* 13: 1021-1025, 2010
4. Braamse AM, Gerrits MM, van Meijel B, et al: Predictors of health-related quality of life in patients treated with auto- and allo-SCT for hematological malignancies. *Bone Marrow Transplant* 47:757-769, 2012
5. Curtis RE, Rowlings PA, Deeg HJ, et al: Solid cancers after bone marrow transplantation. *N Engl J Med* 336:897-904, 1997
6. Duell T, van Lint MT, Ljungman P, et al: Health and functional status of long-term survivors of bone marrow transplantation. *Ann Intern Med* 126:184-192, 1997
7. Gratwohl A, Baldomero H, Frauendorfer K, et al: EBMT activity survey 2004 and changes in disease indication over the past 15 years. *Bone Marrow Transplant* 37:1069-1085, 2006
8. Wilkins O, Keeler AM, Flotte TR: CAR T-cell therapy: Progress and prospects. *Hum Gene Ther Methods* 28:61-66, 2017
9. Temel JS, Greer JA, Muzikansky A, et al: Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 363:733-742, 2010
10. Temel JS, Greer JA, El-Jawahri A, et al: Effects of early integrated palliative care in patients with lung and GI cancer: A randomized clinical trial. *J Clin Oncol* 35: 834-841, 2017
11. Bakitas M, Lyons KD, Hegel MT, et al: Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: The Project ENABLE II randomized controlled trial. *JAMA* 302:741-749, 2009
12. Bakitas MA, Tosteson TD, Li Z, et al: Early versus delayed initiation of concurrent palliative oncology care: Patient outcomes in the ENABLE III randomized controlled trial. *J Clin Oncol* 33:1438-1445, 2015
13. Greer JA, Jacobs JM, El-Jawahri A, et al: Role of patient coping strategies in understanding the effects of early palliative care on quality of life and mood. *J Clin Oncol* 36:53-60, 2018
14. Zimmermann C, Swami N, Krzyzanowska M, et al: Early palliative care for patients with advanced cancer: A cluster-randomised controlled trial. *Lancet* 383: 1721-1730, 2014
15. Howell DA, Shellens R, Roman E, et al: Haematological malignancy: Are patients appropriately referred for specialist palliative and hospice care? A systematic review and meta-analysis of published data. *Palliat Med* 25:630-641, 2011
16. LeBlanc TW, Roeland EJ, El-Jawahri A: Early palliative care for patients with hematologic malignancies: Is it really so difficult to achieve? *Curr Hematol Malig Rep* 12:300-308, 2017
17. Manitta V, Zordan R, Cole-Sinclair M, et al: The symptom burden of patients with hematological malignancy: A cross-sectional observational study. *J Pain Symptom Manage* 42:432-442, 2011
18. Hochman MJ, Yu Y, Wolf SP, et al: Comparing the palliative care needs of patients with hematologic and solid malignancies. *J Pain Symptom Manage* 55:82-88.e1, 2018
19. Efficace F, Gaidano G, Breccia M, et al: Prevalence, severity and correlates of fatigue in newly diagnosed patients with myelodysplastic syndromes. *Br J Haematol* 168:361-370, 2015
20. Steensma DP, Heptinstall KV, Johnson VM, et al: Common troublesome symptoms and their impact on quality of life in patients with myelodysplastic syndromes (MDS): Results of a large Internet-based survey. *Leuk Res* 32:691-698, 2008
21. Sekeres MA, Stone RM, Zahrieh D, et al: Decision-making and quality of life in older adults with acute myeloid leukemia or advanced myelodysplastic syndrome. *Leukemia* 18:809-816, 2004
22. Ramsenthaler C, Osborne TR, Gao W, et al: The impact of disease-related symptoms and palliative care concerns on health-related quality of life in multiple myeloma: A multi-centre study. *BMC Cancer* 16:427, 2016
23. El-Jawahri AR, Traeger LN, Kuzmuk K, et al: Quality of life and mood of patients and family caregivers during hospitalization for hematopoietic stem cell transplantation. *Cancer* 121:951-959, 2015
24. Majhail NS, Mau LW, Chitphakdithai P, et al: National Survey of Hematopoietic Cell Transplantation Center personnel, infrastructure, and models of care delivery. *Biol Blood Marrow Transplant* 21:1308-1314, 2015
25. Gratwohl A, Baldomero H, Aljurf M, et al: Hematopoietic stem cell transplantation: A global perspective. *JAMA* 303:1617-1624, 2010
26. Pidala J, Anasetti C, Jim H: Health-related quality of life following haematopoietic cell transplantation: Patient education, evaluation and intervention. *Br J Haematol* 148:373-385, 2010
27. Pidala J, Anasetti C, Jim H: Quality of life after allogeneic hematopoietic cell transplantation. *Blood* 114:7-19, 2009
28. McQuellon RP, Russell GB, Rambo TD, et al: Quality of life and psychological distress of bone marrow transplant recipients: The 'time trajectory' to recovery over the first year. *Bone Marrow Transplant* 21:477-486, 1998
29. Bevans MF, Marden S, Leidy NK, et al: Health-related quality of life in patients receiving reduced-intensity conditioning allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplant* 38:101-109, 2006
30. Fife BL, Huster GA, Cornetta KG, et al: Longitudinal study of adaptation to the stress of bone marrow transplantation. *J Clin Oncol* 18:1539-1549, 2000
31. LeBlanc TW, Fish LJ, Bloom CT, et al: Patient experiences of acute myeloid leukemia: A qualitative study about diagnosis, illness understanding, and treatment decision-making. *Psychooncology* 26:2063-2068, 2017
32. Alibhai SM, Leach M, Kermalli H, et al: The impact of acute myeloid leukemia and its treatment on quality of life and functional status in older adults. *Crit Rev Oncol Hematol* 64:19-30, 2007
33. Alibhai SM, Breunis H, Timilshina N, et al: Quality of life and physical function in adults treated with intensive chemotherapy for acute myeloid leukemia improve over time independent of age. *J Geriatr Oncol* 6:262-271, 2015
34. Burnett AK, Hills RK, Milligan DW, et al: Attempts to optimize induction and consolidation treatment in acute myeloid leukemia: Results of the MRC AML12 trial. *J Clin Oncol* 28:586-595, 2010
35. Kayastha N, Wolf SP, Locke SC, et al: The impact of remission status on patients' experiences with acute myeloid leukemia (AML): An exploratory analysis of longitudinal patient-reported outcomes data. *Support Care Cancer* 26:1437-1445, 2018
36. Ghodraty-Jabloo V, Alibhai SM, Breunis H, et al: Keep your mind off negative things: Coping with long-term effects of acute myeloid leukemia (AML). *Support Care Cancer* 24:2035-2045, 2016
37. Ghodraty-Jabloo V, Alibhai SM, Breunis H, et al: One day at a time: Improving the patient experience during and after intensive chemotherapy for younger and older AML patients. *Leuk Res* 39:192-197, 2015

38. Fadul NA, El Osta B, Dalal S, et al: Comparison of symptom burden among patients referred to palliative care with hematologic malignancies versus those with solid tumors. *J Palliat Med* 11:422-427, 2008
39. Bergerot CD, Clark KL, Nonino A, et al: Course of distress, anxiety, and depression in hematological cancer patients: Association between gender and grade of neoplasm. *Palliat Support Care* 13:115-123, 2015
40. El-Jawahri AR, Vandusen HB, Traeger LN, et al: Quality of life and mood predict posttraumatic stress disorder after hematopoietic stem cell transplantation. *Cancer* 122:806-812, 2016
41. Rodin G, Yuen D, Mischitelle A, et al: Traumatic stress in acute leukemia. *Psychooncology* 22:299-307, 2013
42. Nissim R, Zimmermann C, Minden M, et al: Abducted by the illness: A qualitative study of traumatic stress in individuals with acute leukemia. *Leuk Res* 37: 496-502, 2013
43. Batty GD, Russ TC, Stamatakis E, et al: Psychological distress in relation to site specific cancer mortality: Pooling of unpublished data from 16 prospective cohort studies. *BMJ* 356:j108, 2017
44. Boucher NA, Johnson KS, LeBlanc TW: Acute leukemia patients' needs: Qualitative findings and opportunities for early palliative care. *J Pain Symptom Manage* 55:433-439, 2018
45. El-Jawahri A, Traeger L, Kuzmuk K, et al: Prognostic understanding, quality of life and mood in patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplant* 50:1119-1124, 2015
46. El-Jawahri A, Nelson-Lowe M, VanDusen H, et al: Patient-clinician discordance in perceptions of treatment risks and benefits in older patients with acute myeloid leukemia. *Oncologist* 24:247-254, 2019
47. Brundage MD, Davidson JR, Mackillop WJ: Trading treatment toxicity for survival in locally advanced non-small cell lung cancer. *J Clin Oncol* 15:330-340, 1997
48. Hirose T, Yamaoka T, Ohnishi T, et al: Patient willingness to undergo chemotherapy and thoracic radiotherapy for locally advanced non-small cell lung cancer. *Psychooncology* 18:483-489, 2009
49. Silvestri G, Pritchard R, Welch HG: Preferences for chemotherapy in patients with advanced non-small cell lung cancer: Descriptive study based on scripted interviews. *BMJ* 317:771-775, 1998
50. Weeks JC, Cook EF, O'Day SJ, et al: Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA* 279:1709-1714, 1998
51. Mack JW, Weeks JC, Wright AA, et al: End-of-life discussions, goal attainment, and distress at the end of life: Predictors and outcomes of receipt of care consistent with preferences. *J Clin Oncol* 28:1203-1208, 2010
52. Syrjala KL, Langer SL, Abrams JR, et al: Recovery and long-term function after hematopoietic cell transplantation for leukemia or lymphoma. *JAMA* 291: 2335-2343, 2004
53. Altmaier EM, Ewell M, McQuellon R, et al: The effect of unrelated donor marrow transplantation on health-related quality of life: A report of the unrelated donor marrow transplantation trial (T-cell depletion trial). *Biol Blood Marrow Transplant* 12:648-655, 2006
54. Syrjala KL, Chapko MK, Vitaliano PP, et al: Recovery after allogeneic marrow transplantation: Prospective study of predictors of long-term physical and psychosocial functioning. *Bone Marrow Transplant* 11:319-327, 1993
55. Schulz-Kindermann F, Mehnert A, Scherwath A, et al: Cognitive function in the acute course of allogeneic hematopoietic stem cell transplantation for hematological malignancies. *Bone Marrow Transplant* 39:789-799, 2007
56. Tzelepis F, Paul CL, Sanson-Fisher RW, et al: Unmet supportive care needs of haematological cancer survivors: Rural versus urban residents. *Ann Hematol* 97:1283-1292, 2018
57. Lee SJ, Joffe S, Kim HT, et al: Physicians' attitudes about quality-of-life issues in hematopoietic stem cell transplantation. *Blood* 104:2194-2200, 2004
58. Damlaj M, El Fakih R, Hashmi SK: Evolution of survivorship in lymphoma, myeloma and leukemia: Metamorphosis of the field into long term follow-up care. *Blood Rev* 33:63-73, 2019
59. Lee SJ, Fairclough D, Parsons SK, et al: Recovery after stem-cell transplantation for hematologic diseases. *J Clin Oncol* 19:242-252, 2001
60. Lee SJ, Loberiza FR, Antin JH, et al: Routine screening for psychosocial distress following hematopoietic stem cell transplantation. *Bone Marrow Transplant* 35:77-83, 2005
61. Socié G, Stone JV, Wingard JR, et al: Long-term survival and late deaths after allogeneic bone marrow transplantation. *N Engl J Med* 341:14-21, 1999
62. Sullivan KM, Witherspoon RP, Storb R, et al: Prednisone and azathioprine compared with prednisone and placebo for treatment of chronic graft-v-host disease: Prognostic influence of prolonged thrombocytopenia after allogeneic marrow transplantation. *Blood* 72:546-554, 1988
63. Wingard JR, Piantadosi S, Vogelsang GB, et al: Predictors of death from chronic graft-versus-host disease after bone marrow transplantation. *Blood* 74: 1428-1435, 1989
64. Loughran TP Jr, Sullivan K, Morton T, et al: Value of day 100 screening studies for predicting the development of chronic graft-versus-host disease after allogeneic bone marrow transplantation. *Blood* 76:228-234, 1990
65. Sutherland HJ, Fyles GM, Adams G, et al: Quality of life following bone marrow transplantation: A comparison of patient reports with population norms. *Bone Marrow Transplant* 19:1129-1136, 1997
66. Lee SJ, Flowers ME: Recognizing and managing chronic graft-versus-host disease. *Hematology (Am Soc Hematol Educ Program)* 2008:134-141, 2008
67. Pidala J, Kurland B, Chai X, et al: Patient-reported quality of life is associated with severity of chronic graft-versus-host disease as measured by NIH criteria: Report on baseline data from the chronic GVHD consortium. *Blood* 117:4651-4657, 2011
68. El-Jawahri A, LeBlanc TW, Burns LJ, et al: What do transplant physicians think about palliative care? A national survey study. *Cancer* 124:4556-4566, 2018
69. Troy JD, Locke SC, Samsa GP, et al: Patient-reported distress in Hodgkin lymphoma across the survivorship continuum. *Support Care Cancer* 10.1007/s00520-018-4523-4 [epub ahead of print on October 30, 2018]
70. Shanafelt TD, Bowen D, Venkat C, et al: Quality of life in chronic lymphocytic leukemia: An international survey of 1482 patients. *Br J Haematol* 139:255-264, 2007
71. Kaiser F, Rudloff LV, Vehling-Kaiser U, et al: Palliative home care for patients with advanced haematological malignancies-a multicenter survey. *Ann Hematol* 96:1557-1562, 2017
72. Lowe JR, Yu Y, Wolf S, et al: A cohort study of patient-reported outcomes and healthcare utilization in acute myeloid leukemia patients receiving active cancer therapy in the last six months of life. *J Palliat Med* 21:592-597, 2018
73. LeBlanc TW, Smith JM, Currow DC: Symptom burden of haematological malignancies as death approaches in a community palliative care service: A retrospective cohort study of a consecutive case series. *Lancet Haematol* 2:e334-e338, 2015
74. El-Jawahri AR, Abel GA, Steensma DP, et al: Health care utilization and end-of-life care for older patients with acute myeloid leukemia. *Cancer* 121: 2840-2848, 2015
75. Hui D, Didwania N, Vidal M, et al: Quality of end-of-life care in patients with hematologic malignancies: A retrospective cohort study. *Cancer* 120:1572-1578, 2014

76. Fletcher SA, Cronin AM, Zeidan AM, et al: Intensity of end-of-life care for patients with myelodysplastic syndromes: Findings from a large national database. *Cancer* 122:1209-1215, 2016
77. Beaussant Y, Daguindau E, Chauchet A, et al: Hospital end-of-life care in haematological malignancies. *BMJ Support Palliat Care* 8:314-324, 2018
78. Wang R, Zeidan AM, Halene S, et al: Health care use by older adults with acute myeloid leukemia at the end of life. *J Clin Oncol* 35:3417-3424, 2017
79. LeBlanc TW, Abernethy AP, Casarett DJ: What is different about patients with hematologic malignancies? A retrospective cohort study of cancer patients referred to a hospice research network. *J Pain Symptom Manage* 49:505-512, 2015
80. Howell DA, Wang HI, Smith AG, et al: Place of death in haematological malignancy: Variations by disease sub-type and time from diagnosis to death. *BMC Palliat Care* 12:42, 2013
81. Howell DA, Roman E, Cox H, et al: Destined to die in hospital? Systematic review and meta-analysis of place of death in haematological malignancy. *BMC Palliat Care* 9:9, 2010
82. LeBlanc TW, Egan PC, Olszewski AJ: Transfusion dependence, use of hospice services, and quality of end-of-life care in leukemia. *Blood* 132:717-726, 2018
83. Odejide OO, Li L, Cronin AM, et al: Meaningful changes in end-of-life care among patients with myeloma. *Haematologica* 103:1380-1389, 2018
84. LeBlanc TW: Advance care planning and palliative care specialists in malignant hematology and stem-cell transplantation: On why it takes a village. *J Oncol Pract* 14:3-5, 2018
85. Hui D, Kim SH, Roquembourg J, et al: Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. *Cancer* 120:1743-1749, 2014
86. Fadul N, Elsayem A, Palmer JL, et al: Predictors of access to palliative care services among patients who died at a comprehensive cancer center. *J Palliat Med* 10:1146-1152, 2007
87. Zimmermann C, Riechelmann R, Krzyzanowska M, et al: Effectiveness of specialized palliative care: A systematic review. *JAMA* 299:1698-1709, 2008
88. Smith TJ, Temin S, Alesi ER, et al: American Society of Clinical Oncology provisional clinical opinion: The integration of palliative care into standard oncology care. *J Clin Oncol* 30:880-887, 2012
89. LeBlanc TW, O'Donnell JD, Crowley-Matoka M, et al: Perceptions of palliative care among hematologic malignancy specialists: A mixed-methods study. *J Oncol Pract* 11:e230-e238, 2015
90. Hui D, Park M, Liu D, et al: Attitudes and beliefs toward supportive and palliative care referral among hematologic and solid tumor oncology specialists. *Oncologist* 20:1326-1332, 2015
91. El-Jawahri A, LeBlanc T, VanDusen H, et al: Effect of inpatient palliative care on quality of life 2 weeks after hematopoietic stem cell transplantation: A randomized clinical trial. *JAMA* 316:2094-2103, 2016
92. El-Jawahri A, Traeger L, Greer JA, et al: Effect of inpatient palliative care during hematopoietic stem-cell transplant on psychological distress 6 months after transplant: Results of a randomized clinical trial. *J Clin Oncol* 35:3714-3721, 2017
93. Lupu D: Estimate of current hospice and palliative medicine physician workforce shortage. *J Pain Symptom Manage* 40:899-911, 2010
94. Kamal AH, Bull JH, Swetz KM, et al: Future of the palliative care workforce: Preview to an impending crisis. *Am J Med* 130:113-114, 2017
95. McCaughan D, Roman E, Smith AG, et al: Palliative care specialists' perceptions concerning referral of haematology patients to their services: Findings from a qualitative study. *BMC Palliat Care* 17:33, 2018
96. Odejide OO, Salas Coronado DY, Watts CD, et al: End-of-life care for blood cancers: A series of focus groups with hematologic oncologists. *J Oncol Pract* 10:e396-e403, 2014
97. Azoulay E, Mokart D, Pène F, et al: Outcomes of critically ill patients with hematologic malignancies: Prospective multicenter data from France and Belgium—a Groupe de Recherche Respiratoire en Réanimation Onco-Hématologique study. *J Clin Oncol* 31:2810-2818, 2013
98. Howell DA, Wang HI, Roman E, et al: Preferred and actual place of death in haematological malignancy. *BMJ Support Palliat Care* 7:150-157, 2017
99. Odejide OO, Cronin AM, Condrón NB, et al: Barriers to quality end-of-life care for patients with blood cancers. *J Clin Oncol* 34:3126-3132, 2016
100. Hui D, Bansal S, Park M, et al: Differences in attitudes and beliefs toward end-of-life care between hematologic and solid tumor oncology specialists. *Ann Oncol* 26:1440-1446, 2015
101. Prod'homme C, Jacquemin D, Touzet L, et al: Barriers to end-of-life discussions among hematologists: A qualitative study. *Palliat Med* 32:1021-1029, 2018
102. Odejide OO, Cronin AM, Condrón N, et al: Timeliness of end-of-life discussions for blood cancers: A national survey of hematologic oncologists. *JAMA Intern Med* 176:263-265, 2016
103. Odejide OO, Cronin AM, Earle CC, et al: Why are patients with blood cancers more likely to die without hospice? *Cancer* 123:3377-3384, 2017
104. Selvaggi KJ, Vick JB, Jessell SA, et al: Bridging the gap: A palliative care consultation service in a hematological malignancy-bone marrow transplant unit. *J Community Support Oncol* 12:50-55, 2014
105. Roeland E, Mitchell W, Elia G, et al: Symptom control in stem cell transplantation: A multidisciplinary palliative care team approach. Part 2: Psychosocial concerns. *J Support Oncol* 8:179-183, 2010
106. Loggers ET, LeBlanc TW, El-Jawahri A, et al: Pretransplantation supportive and palliative care consultation for high-risk hematopoietic cell transplantation patients. *Biol Blood Marrow Transplant* 22:1299-1305, 2016
107. Foxwell AM, Moyer ME, Casarett DJ, et al: Palliative care office hours for patients with hematologic malignancies: An innovative model for symptom management and education. *J Palliat Med* 20:1148-1151, 2017
108. Porta-Sales J, Guerrero-Torrelles M, Moreno-Alonso D, et al: Is early palliative care feasible in patients with multiple myeloma? *J Pain Symptom Manage* 54:692-700, 2017
109. Roeland E, Mitchell W, Elia G, et al: Symptom control in stem cell transplantation: A multidisciplinary palliative care team approach. Part 1: Physical symptoms. *J Support Oncol* 8:100-116, 2010

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**Palliative and End-of-Life Care for Patients With Hematologic Malignancies**

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/journal/jco/site/ifc.

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Honoraria: Mallinckrodt

Consulting or Advisory Role: Incyte, Pfizer, EMD Serono (I), Pfizer (I), Kadmon, MSD Oncology (I), Sanofi (I), Genzyme (I), Regeneron Pharmaceuticals (I)

Research Funding: Kadmon, Takeda Pharmaceuticals, Amgen, Bristol-Myers Squibb (I), EMD Serono (I), Merck Sharp & Dohme (I)

Patents, Royalties, Other Intellectual Property: Patent pending for high-affinity T-cell receptors that target the Merkel polyomavirus (I)

Travel, Accommodations, Expenses: Mallinckrodt, Incyte

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Honoraria: Celgene, Helsinn Therapeutics, Quintiles

Consulting or Advisory Role: Flatiron Health, Helsinn Therapeutics, Otsuka, Heron, Amgen, Seattle Genetics, Pfizer, Agios, AbbVie, Genentech, Medtronic, AstraZeneca

Research Funding: Seattle Genetics (Inst), AstraZeneca (Inst)

Travel, Accommodations, Expenses: Celgene, Otsuka, Heron, Amgen, Agios, AbbVie, Genentech

No other potential conflicts of interest were reported.