HHS Public Access

Author manuscript

J Natl Compr Canc Netw. Author manuscript; available in PMC 2022 March 22.

Published in final edited form as:

J Natl Compr Canc Netw. ; 19(6): 686–692. doi:10.6004/jnccn.2020.7646.

End-of-Life Characteristics Associated With Short Hospice Length of Stay for Patients With Solid Tumors Enrolled in Phase I Clinical Trials

Ramy Sedhom, MD[1], **Amanda L. Blackford, ScM**[2], **Arjun Gupta, MD**[1], **Kelly Griffiths, MHS**[1], **Janet Heussner, MA**[1], **Michael A. Carducci, MD**[1]

[1]Department of Oncology, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland

[2]Division of Biostatistics and Bioinformatics, Department of Oncology, Johns Hopkins University, Baltimore, Maryland

Abstract

Background: Patients participating in phase I trials represent a population with advanced cancer and symptoms, with quality-of-life implications arising from both disease and treatment. Transitions to end-of-life care for these patients have received little attention. Good empirical data are needed to better understand the role of advance care planning and palliative care during phase I trial transitions. We investigated how physician–patient communication at the time of disease progression, patient characteristics, and patterns of care were associated with end-of-life care.

Methods: We conducted a retrospective chart review of all patients with solid tumors enrolled in phase I trials at a comprehensive cancer center from January 2015 to December 2017. We captured physician–patient communication during disease progression. Among patients who died, we assessed palliative care referral, advance care planning, place of death, healthcare use in the final month of life, hospice enrollment, and hospice length of stay (LOS). Factors independently associated with a short hospice LOS (defined as ≤3 days) were estimated from a multivariable model building approach.

Results: Among 207 participants enrolled in phase I intervention studies at Johns Hopkins Hospital, the median age was 61 years (range, 31–91 years), 48% were women, 21% were members of racial minority groups, and 41.5% were referred from an outside institution. At the time of disease progression, 53% had goals of care documented, 47% were previously referred to palliative care, and 41% discussed hospice with their oncologist. A total of 82% of decedents died within 1 year of study enrollment, and 85% enrolled in hospice. Among the 147 participants who

Correspondence: Ramy Sedhom, MD, Department of Oncology, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, 401 North Broadway, Baltimore, MD 21231. rsedhom1@jhmi.edu.

Author contributions: *Study concept and design:* Sedhom, Blackford, Carducci. *Provision of study materials or patients:* Griffiths, Heussner, Carducci. *Data collection and assembly:* Sedhom, Blackford, Gupta, Griffiths. *Data analysis and interpretation:* All authors. *Administrative support:* Carducci. *Manuscript preparation:* All authors.

Disclosures: Dr. Carducci has disclosed that he has a consulting or advisory role with Astellas Pharma, AbbVie, Roche/Genentech, Pfizer, and Foundation Medicine, and has received grant/research support from Bristol-Myers Squibb, Pfizer, AstraZeneca, Gilead Sciences, EMD Serono, and eFFECTOR Therapeutics. The remaining authors have disclosed that they have not received any financial consideration from any person or organization to support the preparation, analysis, results, or discussion of this article.

enrolled in hospice, 22 (15%) had a short LOS (≤3 days). Factors independently associated with an increased risk of short hospice LOS in the multivariable model included age >65 years (odds ratio [OR], 1.12; 95% CI, 1.01–1.24; *P*=.04), whereas remaining at the same institution (OR, 0.72; 95% CI, 0.65–0.80; *P*<.001) and referral to palliative care before progression (OR, 0.83; 95% CI, 0.75–0.92; *P*<.001) were associated with a decreased risk of short hospice LOS.

Conclusions: Reported data support the benefit of palliative care for patients in phase I trials and the risks associated with healthcare transitions for all patients, particularly older adults, regardless of care received. Leaving a clinical trial is a time when clear communication is paramount. Phase I studies will continue to be vital in advancing cancer treatment. It is equally important to advance the support provided to patients who transition off these trials.

Background

The ethical and clinical issues regarding phase I cancer trials have been debated for decades, with concerns of therapeutic misconception[1-8] and misestimation of individual benefit by participants.[4,7,9] Although investigators may note clinical responses, especially in an era of more rational drug design and targeted therapy,[10] the typical aims of a phase I trial are dose-finding and a preliminary assessment of the safety and tolerability of a new agent or drug combination. Patients enrolled in phase I trials typically have symptoms at baseline, which worsen as a result of disease progression, treatment, or both.[11] Patients who are eligible for phase I trials are a highly motivated group who functionally have a better performance status than other patients with advanced cancer. Previous research has suggested that they may differ from similar individuals with advanced cancer in their preference to pursue additional treatment, even when treatments have a low chance of success.[1,12] This combination of toxic drugs, terminal patients, and the low likelihood of direct benefit may expose patients to a risk of adverse effects beyond drug-related toxicity, including limited advance care planning (ACP) and sub-optimal end-of-life (EOL) care.

The 2015 consensus report *Dying in America* described inefficiencies in cancer care and the lack of ACP and palliative care for patients with cancer.[13] These broad concerns are especially pertinent for patients enrolled in phase I trials,[14] who are vulnerable because of care transitions. Patients may shift from providers or care teams, from a community to an academic center, or even from one state to another. These changes can be anxiety-provoking, burdensome, costly, and confusing. Importantly, these transitions are associated with increases in adverse effects, pain, suffering, and mortality.[15] In addition to these potential risks, participation in phase I trials precludes enrollment in hospice in most settings. As a result, patients and families who enroll in phase I trials could potentially be at risk for a short hospice length of stay (LOS; defined as ≤3 days). Short hospice LOS is associated with poorer outcomes, including higher rates of emotional distress,[16,17] inferior symptom management,[18] greater financial toxicity,[19] and worse patient and caregiver experience.[20] Although many factors are not under the control of the phase I team, research suggests physician decision-making, including poor communication and not recognizing the patient as dying, are the most frequent cause of late hospice referral identified by patients' bereaved family members.[21] Because phase I teams serve as the primary gatekeepers for timely

hospice access, ACP and prognostication at the time of disease progression may influence patient and family decision-making.[22,23]

ACP is a process that involves documenting wishes about values, goals, and preferences.[24] These conversations give patients more control over their cancer care[25] and decrease their risk of receiving unwanted, high-intensity, lower-quality care near EOL.[26] Poor communication regarding patient and family preferences increases the risk for individual harms, including pain and suffering, and family harms, such as psychosocial and financial distress.[27,28] Good normative and empirical data are needed to better understand post-trial communication and ACP for patients with cancer enrolled in phase I studies. We therefore examined the role of ACP among adults with cancer treated in a phase I clinical trial to determine the prevalence and factors associated with short hospice LOS.

Methods

Study Subjects

In this retrospective study, the medical records of 207 patients enrolled in phase I intervention studies at Johns Hopkins Hospital (JHH) between January 1, 2015, and December 31, 2017, were reviewed in December 2019. The study was approved by the Institutional Review Board. Inclusion criteria comprised a diagnosis of a solid cancer and enrollment in a phase I intervention trial. The primary objective of this study was to identify patient and treatment characteristics associated with a short hospice LOS (≤3 days).

Data Collection

Patient demographics and EOL care characteristics were extracted through chart review. Demographic characteristics included age at study entry, sex, race (White, Black/African American, or other), Hispanic ethnicity, cancer type, whether the patient was originally treated at JHH or referred from an outside institution, and number of previous treatments. We also investigated care delivery patterns and abstracted whether patients were referred for palliative care, receipt of additional therapy after disease progression, and healthcare use at EOL. Healthcare use measures included inpatient care in the last 30 days of life, number of hospitalizations in the last 90 days of life, use of skilled nursing facilities, healthcare transitions in the final 3 days of life, intensive care use, and mechanical ventilation during a terminal hospitalization.

We captured physician–patient communication through the electronic health record to extract whether ACP was discussed. All documentation from the time of progression and within the 2 weeks afterward were reviewed. For all patient deaths, documentation of patient goals of care, prognosis, preferred place of death, and EOL planning was captured on a scoring sheet. We also reviewed whether likelihood of response to further treatment or options for alternatives to treatment, such as hospice, were discussed.

For all deaths of patients eligible for study inclusion, we identified a primary diagnosis, a primary oncologist, whether the patient was referred to hospice, an initial referral date to hospice, hospice enrollment date, hospice discharge date, and special circumstances surrounding the referral process (whether the patient declined hospice services or was

deemed inappropriate for hospice [not included in hospice LOS] or died between referral and enrollment to hospice services [recorded as LOS 0]). To ensure data accuracy, case report forms were independently checked by a second reviewer.

Statistical Methods

Patient characteristics were summarized with descriptive statistics and frequency distributions. The association between patient characteristics and short hospice LOS were explored with logistic regression analyses and summarized with odds ratios (ORs) and 95% confidence intervals. To identify which patient characteristics were independently associated with short LOS, we conducted a multivariable model building approach using the Fisher exact test and Wilcoxon rank sum test. After examining which variables were associated with short hospice LOS in univariate analyses using a threshold of $P<.05$, we selected the following variables to include in a full model: referral to palliative care before disease progression, whether the patient was originally treated at JHH or referred from an outside institution, whether the patient remained at JHH after disease progression, whether the goals of care were documented, and whether hospice was discussed after progression. Patient age (<65 vs ≥65 years), sex, and race (White vs Black or other race) were also included as covariates. *P* values <.05 were considered statistically significant, and were are 2-sided. Analyses were completed using R version 3.6.0 (R Foundation for Statistical Computing).

Results

Patient demographics are listed in Table 1. Among 207 participants, the median age was 61 years (range, 31–91 years), 48% were women, and 21% were members of racial minority groups. Predominant diagnoses were gastrointestinal (38%), genitourinary (16%), and thoracic/lung cancer (15%). A total of 40.5% of patients enrolled in phase I trials were referred from an outside institution. The median number of treatments before enrollment in a phase I trial was 2 (range, 0–9). At the time of disease progression, 53% had goals of care documented, 47% were previously referred to palliative care, and 41% discussed hospice with their oncologist.

A total of 177 patients (86%) died after enrollment in a phase I trial as of last data collection and, among them, 82% died within 1 year of study enrollment, 85% enrolled in hospice, and 76% died at home. EOL characteristics are reported in Table 2. In the last 30 days of life, 37% were hospitalized, 17% received chemotherapy, and 8% were admitted to the ICU.

Among the 147 patients (71%) who enrolled in hospice, 22 (15%) had a short LOS (≤3 days). Receipt of chemotherapy in the final 30 days of life was associated with a short hospice LOS (OR, 1.35; 95% CI, 1.16–1.56; $P<.001$), as was being hospitalized in the last 30 days of life (OR, 1.43; 95% CI, 1.28–1.60; $P<.001$). Those who died in a hospital or other facility were more likely to have had a short hospice LOS compared with those who died at home (OR, 1.42; 95% CI, 1.21–1.66; $P<.001$), and those with a healthcare transition in the last 3 days of life were more likely to have a short hospice LOS (OR, 2.23; 95% CI, 2.03–2.45; $P<.001$). Data on healthcare use for all patients and those with a hospice LOS >3 days are shown in Table 3.

The multivariable model results describing factors independently associated with a short hospice LOS are shown in Table 4. Variables remaining significantly associated with short hospice LOS at a threshold of $P<.05$ in the full multivariable model included age (<65 vs ≥65 years), remaining at the same institution, and referral to palliative care. Neither sex nor race was associated with short hospice LOS, and there was no evidence of confounding when they were excluded from the model. Factors independently associated with an increased risk of short hospice LOS in the multivariable model included age >65 years (OR, 1.12; 95% CI, 1.01–1.24; $P=.03$), whereas remaining at the same institution (OR, 0.72; 95% CI, 0.65–0.80; $P<.001$) and referral to palliative care before progression (OR, 0.83; 95% CI, 0.75–0.92; $P<.001$) were associated with a decreased risk of short hospice LOS.

Discussion

In this study, we noted that older age, lack of a palliative care referral, and transitioning from one institution to another were associated with an increased risk of short hospice LOS (≤3 days). Changes in phase I oncology trials have been extensive over the past decade and include a better understanding of tumor biology and the development of targeted therapies. Despite these obvious benefits, good communication during disease progression remains paramount for quality EOL care.

ACP protects patient autonomy and allows patients and their loved ones to receive care conforming to their expressed preferences.[25] The high degree of hospice use (85%) in our cohort highlights how far we have come; yet, still 15% of enrolled patients experienced a short hospice LOS, and 17% received chemotherapy in the last month of life. The high rate of hospice use may partially be explained by a simultaneous concurrent care R01 trial (ClinicalTrials.gov identifier: NCT01828775) that promoted integration of palliative care for patients with cancer in phase I trials. Still, 53% of patients were not seen by palliative care specialists before disease progression, despite compelling evidence of benefit and an ASCO endorsement of concurrent care.[29-37] This signals room for improvement. Time constraints in the phase I clinic, lack of connectivity with the palliative care team, and perhaps misunderstanding of what palliative care can offer patients might contribute to these observations.

Similar to the phase I community, palliative care is also dynamic and evolving.[38] There is an increasing emphasis on palliative care supporting patients' goals and quality of life[39,40] and less focus on achieving a "good" death. The most important implication for phase I trialists is that contemporary palliative care teams may be good partners in early-phase trials for patients with advanced disease.[39,40] Palliative care is relevant for most phase I participants based on their prognosis and symptom burden. On average, patients enrolled in phase I trials have a median survival of approximately 9 months.[41-43] In our cohort, 82% of patients died within 1 year of study enrollment. Furthermore, patients are likely to be symptomatic from their disease and/or treatment. Other studies have documented declines in patient outcomes over the course of a phase I trial, with changes in not only physical but also spiritual, psychosocial, and financial domains.[39,40,44,45] Early integration of palliative care

establishes a relationship before therapeutic intervention and allows palliative care teams to revisit goals, prognosis, and best and worst case scenarios at the time of disease progression.

Patients enrolled in phase I clinical trials typically undergo an extended period of eligibility screening before treatment, which may be the ideal time to meet with the palliative care team. Quality-of-life benefit would then be expected throughout the entirety of the phase I trial and would continue until EOL. Importantly, informed consent requires that all patients should be at least aware of hospice, given the evidence of benefit at EOL.[46] In this study, only 41% of patients had hospice presented as an available option at the time of disease progression. Hospice offers services to improve comfort and quality of life, including symptom assessment and management, care coordination, patient-centered care planning, social work and pastoral care, caregiver support, volunteer services, and bereavement support for families.[47] Recognizing the value of these coordinated services, ASCO asserts that provision of optimal EOL care requires access to hospice,[46] which currently is the best developed model for EOL care in the US healthcare delivery system.[48]

Transitioning from care in phase I clinical trials has received little attention but is a critical time in a patient's life, filled with much uncertainty. In our experience, patients enrolled in early-phase trials who experience unexpected cancer progression are disappointed and often fearful, especially when they have progressed through all standard chemotherapy options. Patients often enter phase I trials with much hope and leave with much despair, knowing that EOL is near. Oncologists generally struggle with initiating discussions about shifting treatment goals, and in particular transitioning to hospice care.[49] Moving forward, we recommend that all patients enrolled in phase I trials with refractory solid tumors meet with palliative care before, during, and after completing treatment. This recommendation is based on clinical studies documenting improvements in prognostic understanding and mood, improved coping, and less-aggressive care at EOL, which are all areas of need for patients considering enrollment in an early-phase trial.

At the time of progression, ACP is a vital measure and should include discussion of benefits and risks of further therapy and whether patients qualify for hospice care. Quality measures focused on this communication may help standardize this practice and allow appropriate benchmarking. As these issues are clarified, it will also be important to develop collaborative relationships between phase I centers and community hospice programs, which could ensure a more seamless transition to hospice or predominant palliation when appropriate. The idea of a "seamless transition" to hospice has been demonstrated by numerous simultaneous care models.[50,51] However, simultaneous hospice care requires changes in reimbursement structures within the Medicare program. Although this was highlighted more than 20 years ago,[52] no such programs currently exist to our knowledge, and the same financial limitations remain a barrier.

The finding of older adults having higher risk of short hospice LOS was significant and surprising. We do not believe that this association is causally related; perhaps it reflects the added vulnerability of older adults to a quick, unexpected decline. This finding should be interpreted in light of study limitations. First, we did not measure disease case severity, and it is possible that older adults had more aggressive disease than younger patients. Second,

patients with hematologic malignancies were excluded from this study. Third, patients with hematologic malignancies are traditionally underrepresented in phase I trials, and prognosis differs from that of patients with advanced solid tumors, given the availability of salvage regimens, stem cell transplant, and more rapid disease progression.[53] Fourth, this study was a singlecenter retrospective review and may not be representative of the experience at other centers conducting phase I trials. In addition, patients who choose not to explore therapy in phase I may have important differences in EOL preferences. Still, this study remains novel in its approach to describing EOL care for patients in modern phase I studies after the increased availability of palliative care teams. The associations noted for short hospice LOS should be seen as hypothesis-generating, and future prospective study is needed to validate these findings. Whether palliative care teams improve survival or quality of life in this population is currently under study (ClinicalTrials.gov identifier: NCT01828775).

Conclusions

Although early-phase drug trials continue to have great promise and are encouraged in order to move the field of cancer therapy forward, clinical trial teams remain responsible for actions that support transitions of care.[54] Progression in a phase I trial is a time when clear communication and prognostication are paramount. Phase I teams should consider partnerships with palliative care teams to initiate ACP discussions focused on helping patients and their families with post-trial needs and in weighing the benefits and burdens of next steps, including hospice care.

Acknowledgments

Ramy Sedhom, MD, is supported by the NIH's National Institute on Aging, grant T32-AG0000247, and by an ASCO Young Investigator Award. Arjun Gupta, MD, is supported by an ASCO Young Investigator Award. Janet Heussner, Amanda Blackford, and Dr. Carducci and this work is supported by UM1 CA 186691.

References

1. Agrawal M, Grady C, Fairclough DL, et al. Patients' decision-making process regarding participation in phase I oncology research. J Clin Oncol 2006;24:4479–4484. [PubMed: 16983117]
2. Agrawal M, Emanuel EJ. Ethics of phase 1 oncology studies: reexamining the arguments and data. JAMA 2003;290:1075–1082. [PubMed: 12941681]
3. Godskesen T, Nygren P, Nordin K, et al. Phase 1 clinical trials in end-stage cancer: patient understanding of trial premises and motives for participation. Support Care Cancer 2013;21:3137–3142. [PubMed: 23864288]
4. Horng S, Grady C. Misunderstanding in clinical research: distinguishing therapeutic misconception, therapeutic misestimation, and therapeutic optimism. IRB 2003;25:11–16.
5. Jenkins V, Solis-Trapala I, Langridge C, et al. What oncologists believe they said and what patients believe they heard: an analysis of phase I trial discussions. J Clin Oncol 2011;29:61–68. [PubMed: 21098322]
6. Kass N, Taylor H, Fogarty L, et al. Purpose and benefits of early phase cancer trials: what do oncologists say? What do patients hear? J Empir Res Hum Res Ethics 2008;3:57–68.
7. Pentz RD, White M, Harvey RD, et al. Therapeutic misconception, misestimation, and optimism in participants enrolled in phase 1 trials. Cancer 2012;118:4571–4578. [PubMed: 22294385]
8. Joffe S, Miller FG. Rethinking risk-benefit assessment for phase I cancer trials. J Clin Oncol 2006;24:2987–2990. [PubMed: 16809725]

9. Halpern J, Paolo D, Huang A. Informed consent for early-phase clinical trials: therapeutic misestimation, unrealistic optimism and appreciation. J Med Ethics 2019;45:384–387. [PubMed: 31189726]
10. Arkenau HT, Olmos D, Ang JE, et al. Clinical outcome and prognostic factors for patients treated within the context of a phase I study: the Royal Marsden Hospital experience. Br J Cancer 2008;98:1029–1033. [PubMed: 18349817]
11. Decoster G, Stein G, Holdener EE. Responses and toxic deaths in phase I clinical trials. Ann Oncol 1990;1:175–181. [PubMed: 2148104]
12. Hui D, Parsons H, Nguyen L, et al. Timing of palliative care referral and symptom burden in phase 1 cancer patients: a retrospective cohort study. Cancer 2010;116:4402–4409. [PubMed: 20564164]
13. Institute of Medicine. Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life. Washington, DC: The National Academies Press; 2015.
14. Markman M The ethical dilemma of phase I clinical trials. CA Cancer J Clin 1986;36:367–369. [PubMed: 3096524]
15. World Health Organization. Transitions of Care: Technical Series on Safer Primary Care. Geneva, Switzerland: World Health Organization; 2016.
16. Bradley EH, Prigerson H, Carlson MDA, et al. Depression among surviving caregivers: does length of hospice enrollment matter? Am J Psychiatry 2004;161:2257–2262. [PubMed: 15569897]
17. Kris AE, Cherlin EJ, Prigerson H, et al. Length of hospice enrollment and subsequent depression in family caregivers: 13-month follow-up study. Am J Geriatr Psychiatry 2006;14:264–269. [PubMed: 16505131]
18. Miller SC, Mor V, Teno J. Hospice enrollment and pain assessment and management in nursing homes. J Pain Symptom Manage 2003;26:791–799. [PubMed: 12967728]
19. Schilsky RL, Wehrwein P. Gains against cancer, but enter ‘financial toxicity’. Manag Care 2015;24:46–47, 52–54.
20. Rickerson E, Harrold J, Kapo J, et al. Timing of hospice referral and families’ perceptions of services: are earlier hospice referrals better? J Am Geriatr Soc 2005;53:819–823. [PubMed: 15877557]
21. Teno JM, Casarett D, Spence C, et al. It is “too late” or is it? Bereaved family member perceptions of hospice referral when their family member was on hospice for seven days or less. J Pain Symptom Manage 2012;43:732–738. [PubMed: 22285282]
22. Ahluwalia SC, Tisnado DM, Walling AM, et al. Association of early patient-physician care planning discussions and end-of-life care intensity in advanced cancer. J Palliat Med 2015;18:834–841. [PubMed: 26186553]
23. Sedhom R, Barile D. Discussing goals of care with families using the four steps [published online August 21, 2016]. Gerontol Geriatr Med, doi: 10.1177/2333721416664446
24. Sudore RL, Lum HD, You JJ, et al. Defining advance care planning for adults: a consensus definition from a multidisciplinary Delphi panel. J Pain Symptom Manage 2017;53:821–832.e1. [PubMed: 28062339]
25. Silveira MJ, Kim SYH, Langa KM. Advance directives and outcomes of surrogate decision making before death. N Engl J Med 2010;362:1211–1218. [PubMed: 20357283]
26. Bischoff KE, Sudore R, Miao Y, et al. Advance care planning and the quality of end-of-life care in older adults. J Am Geriatr Soc 2013;61:209–214. [PubMed: 23350921]
27. Khandelwal N, Hough CL, Downey L, et al. Prevalence, risk factors, and outcomes of financial stress in survivors of critical illness. Crit Care Med 2018;46:e530–539. [PubMed: 29505422]
28. Sedhom R, Sedhom D. To grow as a physician, try responding to suffering. J Palliat Care 2019;34:3–4. [PubMed: 29592772]
29. 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 2015;33:1438–1445. [PubMed: 25800768]
30. El-Jawahri A, Greer JA, Pirl WF, et al. Effects of early integrated palliative care on caregivers of patients with lung and gastrointestinal cancer: a randomized clinical trial. Oncologist 2017;22:1528–1534. [PubMed: 28894017]

31. Ferrell BR, Temel JS, Temin S, et al. Integration of palliative care into standard oncology care: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 2017;35:96–112. [PubMed: 28034065]
32. Greer JA, Jackson VA, Meier DE, et al. Early integration of palliative care services with standard oncology care for patients with advanced cancer. CA Cancer J Clin 2013;63:349–363. [PubMed: 23856954]
33. Greer JA, Pirl WF, Jackson VA, et al. Effect of early palliative care on chemotherapy use and end-of-life care in patients with metastatic nonsmall-cell lung cancer. J Clin Oncol 2012;30:394–400. [PubMed: 22203758]
34. Hui D, Kim SH, Roquemore J, et al. Impact of timing and setting of palliative care referral on quality of end-of-life care in cancer patients. Cancer 2014;120:1743–1749. [PubMed: 24967463]
35. 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 2012;30:880–887. [PubMed: 22312101]
36. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 2010;363:733–742. [PubMed: 20818875]
37. Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. Lancet 2014;383:1721–1730. [PubMed: 24559581]
38. Sedhom R, Gupta A, MacNabb L, et al. The impact of palliative care dose intensity on outcomes for patients with cancer. Oncologist 2020;25:913–915. [PubMed: 32813308]
39. Ferrell BR, Chung V, Koczywas M, et al. Palliative care and phase 1 trials: intervention to improve quality of life and provide education. Clin J Oncol Nurs 2017;21:473–479. [PubMed: 28738035]
40. Ferrell BR, Chung VM, Koczywas M,et al. Integration of palliative care for patients with solid tumors on phase I clinical trials [abstract]. J Clin Oncol 2016;34(Suppl):Abstract 138.
41. Zafar SF, Heilbrun LK, Vishnu P,et al. Participation and survival of geriatric patients in phase I clinical trials: the Karmanos Cancer Institute (KCI) experience. J Geriatr Oncol 2011;2:18–24. [PubMed: 21503272]
42. Wheler J, Tsimberidou AM, Hong D, et al. Survival of 1,181 patients in a phase I clinic: the MD Anderson Clinical Center for targeted therapy experience. Clin Cancer Res 2012;18:2922–2929. [PubMed: 22452943]
43. Stephen B, Wheler JJ, Tsimberidou AM, et al. Survival of 1,181 patients in a phase I clinic: the University of Texas M. D. Anderson Cancer Center experience [abstract]. J Clin Oncol 2011;29(Suppl):Abstract 2528. [PubMed: 21606430]
44. Sun V, Cooke L, Chung V, et al. Feasibility of a palliative care intervention for cancer patients in phase I clinical trials. J Palliat Med 2014;17: 1365–1368. [PubMed: 25014572]
45. Ferrell BR, Paterson CL, Hughes MT, et al. Characteristics of participants enrolled onto a randomized controlled trial of palliative care for patients on phase I studies. J Palliat Med 2017;20:1338–1344. [PubMed: 28609257]
46. Smith TJ, Schnipper LJ. The American Society of Clinical Oncology program to improve end-of-life care. J Palliat Med 1998;1:221–230. [PubMed: 15859832]
47. Byock I Completing the continuum of cancer care: integrating life-prolongation and palliation. CA Cancer J Clin 2000;50:123–132. [PubMed: 10870488]
48. Cancer care during the last phase of life. J Clin Oncol 1998;16:1986–1996. [PubMed: 9586919]
49. Sedhom R, Gupta A, Von Roenn J, et al. The case for focused palliative care education in oncology training. J Clin Oncol 2020;38:2366–2368. [PubMed: 32271674]
50. Esper P, Hampton JN, Finn J, et al. A new concept in cancer care: the supportive care program. Am J Hosp Palliat Care 1999;16:713–722. [PubMed: 11094908]
51. Meyers FJ, Carducci M, Loscalzo MJ, et al. Effects of a problem-solving intervention (COPE) on quality of life for patients with advanced cancer on clinical trials and their caregivers: simultaneous care educational intervention (SCEI): linking palliation and clinical trials. J Palliat Med 2011;14:465–473. [PubMed: 21413846]
52. Byock I, Miles SH. Hospice benefits and phase I cancer trials. Ann Intern Med 2003;138:335–337. [PubMed: 12585832]

53. Levine DR, Johnson LM, Mandrell BN, et al. Does phase 1 trial enrollment preclude quality end-of-life care? Phase 1 trial enrollment and end-of-life care characteristics in children with cancer. Cancer 2015;121:1508–1512. [PubMed: 25557437]

54. Cho HL, Danis M, Grady C. Post-trial responsibilities beyond post-trial access. Lancet 2018;391:1478–1479. [PubMed: 29676274]

Table 1.

Patient Characteristics

Characteristic	n (%)
Total, N	207
Study type	
Externally peer-reviewed	27 (13.0)
Industrial	122 (58.9)
Institutional	58 (28.0)
Age, median (range), y	61 (31–91)
Sex	
Female	99 (47.8)
Male	108 (52.2)
Race	
Black/African American	29 (14.0)
Other	15 (7.2)
White	163 (78.7)
Ethnicity	
Hispanic	7 (3.4)
Non-Hispanic	200 (96.6)
Cancer type	
Breast/Gynecologic	23 (11.1)
Central nervous system	14 (6.8)
Gastrointestinal	78 (37.7)
Genitourinary	33 (15.9)
Melanoma/Sarcoma	28 (13.5)
Thoracic/Lung	31 (15.0)
Referred from outside institution	
No	121 (58.5)
Yes	86 (41.5)
Treatments before study, median (range), n	2 (0–9)
Referred to palliative care before progression (n=207)	98 (47.3)
Goals of care documented (n=207)	109 (52.7)
Hospice discussed after progression (n=207)	84 (40.6)
Received other treatment after progression (n=206)	109 (52.9)
Died (n=207)	177 (85.5)
Died within 1 y of study enrollment (n=177)	145 (81.9)

Table 2.

End-of-Life Characteristics of Decedents

Characteristic	n (%)
Total, N	177
Place of death	
Home	135 (76.3)
Hospital	21 (11.9)
Facility	17 (9.6)
Referred to hospice before death (n=173)	148 (85.5)
Enrolled in hospice (n=173)	147 (85.0)
Hospice LOS ≤3 d (n=147)	22 (15.0)
Inpatient care in last 30 d of life (n=147)	25 (17.0)
Mechanical ventilation during terminal hospitalization (n=172)	5 (2.9)
Hospitalized in last 30 d of life (n=171)	64 (37.4)
Hospitalizations in last 90 d of life, median (range), n	1 (0–5)
Nursing home care in last 90 d of life (n=173)	8 (4.6)
Healthcare transition in last 3 d of life (n=173)	39 (22.5)
>3 Hospitalizations in last 90 d of life (n=173)	17 (9.8)

Abbreviation: LOS, length of stay.

Table 3.

Characteristics of Patients Enrolled in Hospice

Characteristic	All Enrolled in Hospice n (%)	Hospice LOS >3 d n (%)	Hospice LOS ≤3 d n (%)	*P* Value[a]
Total, N	147	125	22	
Age, median (range), y	61 (31–91)	61 (31–91)	66 (34–81)	.105
Sex				>.99
Female	71 (48.3)	60 (48.0)	11 (50.0)	
Male	76 (51.7)	65 (52.0)	11 (50.0)	
Race				.113
Black/African American	18 (12.2)	18 (14.4)	0 (0)	
Other	11 (7.5)	10 (8.0)	1 (4.5)	
White	118 (80.3)	97 (77.6)	21 (95.5)	
Ethnicity				.387
Hispanic	3 (2.0)	2 (1.6)	1 (4.5)	
Non-Hispanic	144 (98.0)	123 (98.4)	21 (95.5)	
Cancer type				.694
Breast/Gynecologic	18 (12.2)	16 (12.8)	2 (9.1)	
Central nervous system	12 (8.2)	12 (9.6)	0 (0)	
Gastrointestinal	59 (40.1)	48 (38.4)	11 (50.0)	
Genitourinary	20 (13.6)	16 (12.8)	4 (18.2)	
Melanoma/Sarcoma	16 (10.9)	14 (11.2)	2 (9.1)	
Thoracic/Lung	22 (15.0)	19 (15.2)	3 (13.6)	
Originally treated at JHH				<.001
Yes	89 (60.5)	86 (68.8)	3 (13.6)	
No (referred)	58 (39.5)	39 (31.2)	19 (86.4)	
Remained at JHH after disease progression	94/147 (63.9)	91/125 (72.8)	3/22 (13.6)	<.001
Treatments before study, median (range), n	2 (0–9)	2 (0–9)	2 (1–7)	.753
Referred to palliative care before progression	84/147 (57.1)	78/125 (62.4)	6/22 (27.3)	.004
Goals of care documented	94/147 (63.9)	87/125 (69.6)	7/22 (31.8)	.001

Characteristic	All Enrolled in Hospice n (%)	Hospice LOS >3 d n (%)	Hospice LOS ≤3 d n (%)	*P* Value[a]
Hospice discussed after progression	79/147 (53.7)	73/125 (58.4)	6/22 (27.3)	.01
Received other treatment after progression	65/147 (44.2)	55/125 (44.0)	10/22 (45.5)	>.99
Referred by JHH outpatient team	86/147 (58.5)	83/125 (66.4)	3/22 (13.6)	<.001
Received chemotherapy in last 30 d of life	25/145 (17.2)	15/123 (12.2)	10/22 (45.5)	<.001
Hospice LOS, median (range), d	20 (0–184)	24 (4–184)	2 (0–3)	<.001
Place of death				<.001
Home	127 (86.4)	114 (91.2)	13 (59.1)	
Hospital	3 (2.0)	0 (0)	3 (13.6)	
Facility	17 (11.6)	11 (8.8)	6 (27.3)	
Inpatient care in last 30 d of life	25/147 (17.0)	14/125 (11.2)	11/22 (50.0)	<.001
Hospice provided in home or nursing home	122/145 (84.1)	111/124 (89.5)	11/21 (52.4)	<.001
ICU admission in last 30 d of life	2/147 (1.4)	0/125 (0)	2/22 (9.1)	.022
Hospitalized in last 30 d of life	45/146 (30.8)	27/124 (21.8)	18/22 (81.8)	<.001
Nursing home care in last 90 d of life	7/147 (4.8)	4/125 (3.2)	3/22 (13.6)	.069
Healthcare transition in last 3 d of life	23/147 (15.6)	4/125 (3.2)	19/22 (86.4)	<.001
>3 Hospitalizations in last 90 d of life	12/147 (8.2)	9/125 (7.2)	3/22 (13.6)	.39

Abbreviations: JHH, Johns Hopkins Hospital; LOS, length of stay.

[a] *P* values for Fisher exact test for categorical variables or Wilcoxon rank sum test for continuous variables for differences between groups of patients according to hospice LOS (≤3 vs >3 days).

J Natl Compr Canc Netw. Author manuscript; available in PMC 2022 March 22.

Table 4.

Multivariable Models for Describing Factors Associated With a Short Hospice Stay (≤3 Days)

	Full Model		Trimmed Model		Slim Model	
	OR (95% CI)	***P* Value**	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Age at consent: <65 vs ≥65 y	1.12 (1.01–1.24)	.04	1.13 (1.01–1.25)	.03	1.12 (1.01–1.24)	.03
Sex: female vs male	0.98 (0.88–1.08)	.68	0.97 (0.87–1.07)	.50		
Race: White vs Black or other race	1.07 (0.94–1.22)	.29	1.07 (0.94–1.22)	.30		
Facility: referred to vs originally treated at JHH	1.13 (0.96–1.32)	.14				
Referred to palliative care before disease progression: yes vs no	0.84 (0.73–0.97)	.02	0.84 (0.76–0.93)	<.001	0.83 (0.75–0.92)	<.001
Goals of care: documented vs not documented	0.98 (0.84–1.14)	.80				
Remained at JHH after progression: yes vs no	0.80 (0.68–0.94)	.008	0.73 (0.66–0.81)	<.001	0.72 (0.65–0.80)	<.001
Hospice care: discussed after progression vs not discussed	1.01 (0.90–1.14)	.85				

All variables were included in a single logistic regression model, shown as one model per column of results.

Abbreviations: JHH, Johns Hopkins Hospital; OR, odds ratio.