Randomized Trial of a Palliative Care Intervention to Improve End-of-Life Care Discussions in Patients With Metastatic Breast Cancer

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ABSTRACT

Background: Studies show that early, integrated palliative care (PC) improves quality of life (QoL) and end-of-life (EoL) care for patients with poor-prognosis cancers. However, the optimal strategy for delivering PC for those with advanced cancers who have longer disease trajectories, such as metastatic breast cancer (MBC), remains unknown. We tested the effect of a PC intervention on the documentation of EoL care discussions, patient-reported outcomes, and hospice utilization in this population. Patients and Methods: Patients with MBC and clinical indicators of poor prognosis (n=120) were randomly assigned to receive an outpatient PC intervention (n=61) or usual care (n=59) between May 2, 2016, and December 26, 2018, at an academic cancer center. The intervention entailed 5 structured PC visits focusing on symptom management, coping, prognostic awareness, decision-making, and EoL planning. The primary outcome was documentation of EoL care discussions in the electronic health record (EHR). Secondary outcomes included patient-report of discussions with clinicians about EoL care, QoL, and mood symptoms at 6, 12, 18, and 24 weeks after baseline and hospice utilization. Results: The rate of EoL care discussions documented in the EHR was higher among intervention patients versus those receiving usual care (67.2% vs 40.7%; P=.006), including a higher completion rate of a Medical Orders for Life-Sustaining Treatment form (39.3% vs 13.6%; P=.002). Intervention patients were also more likely to report discussing their EoL care wishes with their doctor (odds ratio [OR], 3.10; 95% CI, 1.21–7.94; P=.019) and to receive hospice services (OR, 4.03; 95% CI, 1.10–14.73; P=.035) compared with usual care patients. Study groups did not differ in patient-reported QoL or mood symptoms. Conclusions: This PC intervention significantly improved rates of discussion and documentation regarding EoL care and delivery of hospice services among patients with MBC, demonstrating that PC can be tailored to address the supportive care needs of patients with longer disease trajectories.

ClinicalTrials.gov identifier: NCT02730858

J Natl Compr Canc Netw 2022;20(2):136–143

See related commentary on page 215.
For patients with MBC, many of whom have long disease trajectories, integrating PC from the time of diagnosis may not be feasible. Unlike the disease course of other metastatic solid tumors, MBC has demonstrated substantial improvements in survival in recent years due to treatment advances. Considerable variability in breast cancer prognosis also exists, likely due to heterogeneity in disease subtypes, underscoring the need to identify subgroups among women with MBC with poorer prognosis who may benefit from PC. Yet, defining the subpopulation of patients with MBC who may benefit from outpatient PC is challenging given that published criteria for such referrals use general indicators such as severe symptoms, poor prognosis, and brain metastases. To date, no prospective studies have evaluated a PC intervention specifically for patients with MBC, and trials of early PC with mixed cancer samples have included a minority of patients with breast cancer. Consequently, a gap in clinical research and practice exists with respect to the provision of PC for patients with MBC.

For this study, we identified patients with MBC who had clinical indicators of increased risk of death within 6 months (ClinicalTrials.gov identifier: NCT02730858). The primary study aim was to determine the effect of a structured PC intervention on documentation of EoL care discussions in the electronic health record (EHR). We also assessed the effect of the intervention on patient-reported discussions about EoL care preferences, QoL, and symptoms of anxiety and depression, as well as hospice utilization.

Patients and Methods

Study Design

From May 2, 2016, through December 26, 2018, we enrolled 120 patients with MBC in a single-site, randomized controlled trial of a PC intervention versus usual care. The Dana-Farber/Harvard Cancer Center Institutional Review Board approved this study.

Participants

Eligible participants included patients with MBC who were within 8 weeks of any of the following clinical indicators signifying poor prognosis. We drew on published criteria for referral to outpatient PC in oncology and solicited feedback from the cancer center breast oncology clinicians (physicians: n=9; nurse practitioners: n=4) to identify these indicators: leptomeningeal disease; progressive brain metastasis after initial radiation therapy; brain metastases and starting whole-brain radiation; discharged after an unplanned hospital admission; triple-negative disease and starting second-line chemotherapy; received at least 3 different treatment regimens in a 12-month period; HER2-positive or estrogen receptor-positive disease and starting third-line therapy; and beginning a treatment clinical trial.

Participants were also required to have an ECOG performance status of 0 to 2, receive their cancer care at the participating institution, and be able to complete questionnaires in English or with minimal assistance. Exclusion criteria included already receiving PC or needed immediate palliative or hospice care, or serious mental illness/cognitive impairment interfering with the ability to participate, per the treating oncologist.

Study Procedures

To identify eligible patients, the research assistant (RA) reviewed the breast oncology clinic schedules. The RA then emailed the oncology clinicians to request permission to approach their patients for study participation. Upon receiving permission, the RA approached potentially eligible patients in the clinic to explain the study procedures, obtain written informed consent, and administer baseline assessments. Patients were then randomly assigned to the intervention or usual care group using a computer-generated randomization schema stratified by the categories of prognostic indicators per the eligibility criteria (ie, central nervous system disease, unplanned hospitalization, or cancer treatment changes). Because patients were randomly assigned, the oncology clinicians could treat patients in both study groups.

Intervention Procedures

Intervention

We adapted the intervention manual from our prior research evaluating an integrated palliative and oncology care model based on feedback from 2 focus groups with breast oncology clinicians (physicians: n=9; nurse practitioners: n=4) and clinical observations of PC clinicians (n=2). The lead study PC clinician conducted 2 half-day trainings with the participating PC physicians and nurse practitioners in administering the study protocol and content of the intervention visits. The study intervention included 5 structured visits addressing the following: rapport building, symptom management, illness understanding, coping, treatment decision-making, and EoL/advance care planning (supplemental eAppendix 1, available with this article at JNCCN.org). The PC clinicians received an email prior to each structured visit reminding them of the intervention content. No clinicians received training in documenting patient EoL care preferences.

Intervention patients participated in their first PC visit within 4 weeks of enrollment. Subsequent intervention visits occurred every 4 weeks until patients completed the 5 structured visits (ie, ~20 weeks). PC visits were scheduled on the same day as oncology visits to minimize trips to the clinic. For the first visit, we...
encouraged the PC and oncology clinicians to meet with the patient together. If a visit was unable to be scheduled within 4 weeks of the prior visit, the PC clinician contacted the patient via telephone. After each study visit, PC clinicians completed an online survey denoting the content addressed during the encounter. Once the 5-visit study intervention ended, patients could request ongoing, unstructured PC visits.

**Usual Care**
Patients assigned to usual care met with a PC clinician only upon request of the patient/caregiver or oncologist. When these patients received PC, they did not follow the intervention protocol.

**Study Measures**

**Documentation of EoL Care Preferences (Primary Outcome)**
To identify clinician documentation of EoL care discussions, we used natural language processing (NLP) methods to query the EHR with a validated algorithm identifying terms for goals of care and EoL discussions. The NLP software, ClinicalRegex, displays clinical notes that contain phrases about EoL discussions. An independent coder (ie, an oncologist blind to group assignment) reviewed the documentation highlighted by NLP to ensure accurate identification of EoL care discussions. We also searched the record for completion of the Massachusetts Medical Orders for Life-Sustaining Treatment (MOLST) form. The timeframe for this EHR query was from patient enrollment until date of death, last follow-up, or data cutoff for analysis among those still alive.

**Participant-Reported Measures (Secondary Outcomes)**
At baseline prior to randomization, participants completed a sociodemographic questionnaire and the following assessments. These measures were repeated at weeks 6, 12, 18, and 24 postbaseline.

**EoL Care Discussions and Prognostic Awareness**
We administered items used in our prior PC studies, including “Have you and your doctor discussed any particular wishes you have about the care you would want to receive if you were dying?” and “My cancer is curable” (yes/no). For these outcomes, we analyzed the 24-week assessment or final assessment prior to patient death, transfer of care, or last follow-up, controlling for baseline values.

**Quality of Life**
We used the 37-item Functional Assessment of Cancer Therapy-Breast (FACT-B) scale, which assesses physical, functional, emotional, and social well-being, as well as breast cancer–specific concerns, over the past week. Higher scores indicate better QoL (range, 0–148; Cronbach $\alpha = 0.90$).

**Anxiety and Depression Symptoms**
Patients completed the 14-item Hospital Anxiety and Depression Scale (HADS), which includes subscales for anxiety and depression symptoms in the past week, each ranging from 0 (no distress) to 21 (maximum distress). Mean internal consistency estimates are 0.83 for the anxiety subscale and 0.82 for the depression subscale.

**EHR Review**
Data were manually extracted from the EHR regarding tumor biomarkers, presence of brain metastasis, smoking status, ECOG performance status, cancer treatment, and hospice referral.

**Statistical Analysis**
Statistical analyses were performed on data obtained through July 1, 2019, using SPSS Statistics, version 25 (IBM Corp); STATA, version 14.2 (StataCorp LP); and R version 3.6.2 (R Foundation for Statistical Computing). To summarize participant characteristics, we first calculated descriptive statistics. Following the intent-to-treat principle, we used the Fisher exact test and logistic and linear regression modeling to examine group differences in rates of documentation of EoL care discussions and time to documentation from enrollment, respectively. These analyses controlled for patient age given the
baseline imbalance in this variable. We also conducted logistic regression to examine patient-reported discussions with clinicians about EoL care and perceptions of cure, controlling for age and baseline ratings of these outcomes. All \( P \) values were 2-sided, with \( P < .05 \) considered statistically significant.

To examine group differences in QoL and symptoms of anxiety and depression across all assessment time points, we used the terminal-decline joint modeling approach, which accounts for missing data and models the trend in outcomes backward from death (or from date of last follow-up or data cutoff for analysis among those alive) rather than prospectively from enrollment.36 Terminal-decline joint modeling is an advantageous approach to account for deterioration in patient-reported outcomes closer to death while using a mixed-effects model for longitudinal outcomes to provide valid estimates for missing data.36 All models controlled for age and baseline scores of the outcomes. We did not adjust for multiple testing, because the secondary outcomes were exploratory and hypothesis-generating.

To evaluate differences in hospice utilization rates, we conducted the Fisher exact test followed by logistic regression, controlling for patient age. We also used the Mann-Whitney \( U \) test to examine days on hospice between groups.

Enrolling at least 50 patients per group provided 80% power to detect an increase from 20% to 48% in documentation of EoL care discussions. To account for missing data due to patient withdrawal and death, we increased the sample size from 100 to 120 patients.

Results

Participant Characteristics

Of 177 patients eligible for participation (Figure 1), we approached 92.7% (\( n = 164 \)) and enrolled 73.2% (\( n = 120 \)). Table 1 and supplemental eAppendix 2 detail the sample characteristics. Of the enrolled patients, 85.8% (\( n = 103 \)) had previous early-stage breast cancer, and 14.2%...
(n=17) presented with advanced disease. At the data cut-off date, 58.7% (64/109) of patients had died and 11 had unknown survival status (ie, lost to follow-up, withdrew, or transferred care).

**Intervention Delivery**

Of the 61 patients assigned to the intervention, 55.7% (n=34) completed all 5 structured PC visits, with an additional 27.9% (n=17) completing as many visits as possible before death or transfer of care (Figure 1). The 10 remaining patients either did not initiate (n=5; 8.2%) or complete the intervention (n=5; 8.2%). Among the 59 patients assigned to usual care, 22% (n=13) had at least 1 PC visit (range, 1–4) by 24 weeks.

PC clinicians completed 216 surveys detailing the content of their intervention visits. During these visits, 44.3% (n=27) of the 61 patients had at least 1 joint visit with their PC clinician and oncologist. Figure 2 shows the proportion of intervention patients whose PC clinicians discussed the prespecified topics across the 5 structured visits. Most PC visits occurred in the clinic, with 4.9% (n=3) of intervention patients having at least 1 telephone visit (range, 1–2). Finally, 34.4% (n=21) of intervention patients had a median of 5 additional unstructured PC visits (range, 1–15).

**Documentation and Discussion About EoL Care**

Per the NLP query (see Table 2 for key terms), intervention patients had higher rates of documented EoL care discussions (67.2% [41/61] vs 40.7% [24/59]; P=.006) and completion of MOLST forms (39.3% [24/61] vs 13.6% [8/59]; P=.002) compared with usual care patients. Controlling for age, differences in documented EoL care discussions (odds ratio [OR], 2.92; 95% CI, 1.38–6.18; P=.005) and MOLST form completion (OR, 4.09; 95% CI, 1.65–10.14; P=.002) remained significant. The time from enrollment to documentation of EoL care discussions was shorter for intervention patients versus usual care patients (mean [SD] days, 165.63 [22.75] vs 316.75 [45.55]; adjusted B = −152.38; 95% CI, −244.53 to −60.23; P=.002).

Additionally, a greater proportion of intervention than usual care patients reported discussing with their clinicians any particular wishes about the care they would want if dying (38.5% [20/52] vs 21.4% [12/56]; adjusted OR, 3.10; 95% CI, 1.21–7.94; P=.019). Yet, we observed no significant differences between study groups regarding the proportion of patients who reported that their cancer is curable (intervention: 16.0% [8/50] vs usual care: 17.9% [10/56]; adjusted OR, 0.37; 95% CI, 0.04–3.78; P=.400).

**QoL and Mood Symptoms**

Analyses of patient-reported outcomes using the terminal-decline joint modeling showed no significant differences in ratings of patient-reported QoL or symptoms of anxiety and depression over time (Table 3). Table 4 details the descriptive statistics for these outcomes at each assessment time point.

**Hospice Utilization**

Among the patients who died by the data cutoff date, a greater proportion of those in the intervention group used hospice services (88.6% [31/35] vs 65.5% [19/29]; P=.035). Controlling for age, this difference remained significant (adjusted OR, 4.03; 95% CI, 1.10–14.73; P=.035). Median days from hospice referral to death was 16.5 (range, 1–243) for intervention patients versus 15.0 (range, 1–228) for usual care patients (P=.511).

**Discussion**

Patients with MBC remain at risk for worse EoL outcomes despite advances in cancer therapies prolonging survival in this population.\(^2,9,10,20\) To address this concern, we conducted a randomized trial of a population-specific PC intervention, which led to higher rates of discussions regarding EoL care preferences between patients and their clinicians. Compared with the control group, a greater proportion of patients with MBC assigned to the intervention reported discussing with clinicians any wishes about the care they would want if dying, had these discussions documented in the EHR, and completed a MOLST form. The intervention also resulted in documentation of EoL care discussions closer to the time of enrollment and higher rates of hospice use compared with the usual care group. The study findings show that providing a PC intervention later in the illness course is beneficial for supporting women with MBC.
by not only improving patient-clinician discussions but also enhancing the quality of EoL care.

Only one prior study evaluated a PC model specifically for patients with MBC in which PC clinicians were embedded in a breast oncology clinic. This embedded model of care was feasible and acceptable to patients and oncologists and was associated with increased referrals to PC and fewer ICU stays in the last month of life, compared with an earlier 24-month period of standalone PC. To our knowledge, our study advances the field as the first randomized trial to demonstrate improved discussion and documentation of EoL care as well as hospice utilization with a PC intervention integrated within a breast oncology clinic for patients with MBC.

Interestingly, the mean time to documentation of discussions about EoL care was longer than 5 months in the intervention group, underscoring the need to build patient-clinician trust over time to facilitate effective discussions with patients regarding these concerns. Moreover, although the number of intervention visits was fewer than those of prior studies of early integrated PC, questions regarding the scalability of implementing 5 structured visits remain, especially given that approximately one-third of intervention patients received additional unstructured PC visits, which may have affected outcomes.

Patients with advanced cancer who have EoL discussions with their clinicians are more likely to receive EoL care that is consistent with their wishes and less intensive, which is associated with better patient QoL and caregiver bereavement. Still, clinicians are often hesitant to discuss such topics because of concerns that patients will become distressed. In our study, we did not observe worse QoL or mood symptoms with the higher rates of EoL care discussions in the intervention versus the usual care group. Yet, the timing of the patient-reported assessments was anchored to enrollment, with predefined intervals that did not necessarily correspond to when EoL care discussions occurred. We also did not find that intervention patients reported improvements in QoL or mood symptoms relative to usual care patients. These results are inconsistent with prior trials of early, integrated PC for patients with advanced lung cancer who have reported

Table 2. Key Terms Used in NLP Method to Query the Electronic Health Record

<table>
<thead>
<tr>
<th>Domain</th>
<th>Key Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospice</td>
<td>Hospice</td>
</tr>
<tr>
<td>Advance care planning/EoL care</td>
<td>End of life, end-of-life, EoL, end-of-life care, dying, death, comfort care, comfort approach, comfort directed care, comfort measures, CMO, advance care plans/goals, advance care planning, ACP, advanced care planning</td>
</tr>
<tr>
<td>Limitation of life-sustaining treatment</td>
<td>DNR, DNRTN, DNR/DNI, DNI, DNR/DNI, do not resuscitate, do-not-resuscitate, do not intubate, do-not-intubate, no intubation, no mechanical ventilation, no ventilation, no CPR, declines CPR, no cardiopulmonary resuscitation, chest compressions, no defibrillation, no dialysis, no NIPPV, no bipap, no endotracheal intubation, no mechanical intubation</td>
</tr>
</tbody>
</table>

Abbreviations: ACP, advance care planning; CMO, comfort measures only; CPR, cardiopulmonary resuscitation; DNI, do not intubate; DNR, do not resuscitate; EoL, end of life; NIPPV, noninvasive positive pressure ventilation; NLP, natural language processing.

Table 3. Group Differences in Patient-Reported Outcomes Using Terminal Decline Modeling

<table>
<thead>
<tr>
<th>Outcome</th>
<th>4 Months Prior to Death*</th>
<th>6 Months Prior to Death*</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Mean (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>FACT-B</td>
<td>97.44 (93.65–101.23)</td>
<td>.386</td>
</tr>
<tr>
<td>Intervention</td>
<td>95.11 (91.54–98.68)</td>
<td>96.48 (93.15–99.81)</td>
</tr>
<tr>
<td>Usual care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS-Anxiety</td>
<td>5.87 (4.93–6.82)</td>
<td>.587</td>
</tr>
<tr>
<td>Intervention</td>
<td>6.23 (5.35–7.12)</td>
<td>6.23 (5.41–7.04)</td>
</tr>
<tr>
<td>Usual care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS-Depression</td>
<td>5.79 (5.08–6.50)</td>
<td>.913</td>
</tr>
<tr>
<td>Intervention</td>
<td>5.74 (5.06–6.42)</td>
<td>5.51 (4.88–6.13)</td>
</tr>
<tr>
<td>Usual care</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: FACT-B, Functional Assessment of Cancer Therapy-Breast; HADS, Hospital Anxiety and Depression Scale; QoL, quality of life.

*We estimated terminal decline and survival distributions with semiparametric models to analyze patient-reported outcomes across all study time points, comparing QoL and symptoms of anxiety and depression between study groups at 4 and 6 months prior to death (or prior to date of last follow-up or data cutoff for analysis among those alive). All terminal decline modeling analyses include the patient-reported assessments through week 24 and control for patient age and baseline scores of the outcome variables of interest.
improved QoL and depression symptoms. The null findings may be related to when the intervention was delivered in the course of disease or because the sample did not report expected decrements in QoL and mood over time often seen in patients with poor-prognosis cancers.

Identifying subgroups of patients with advanced cancer who have unmet PC needs remains a challenge. For those with longer disease trajectories, such as patients with MBC, early engagement with PC from the time of diagnosis may be neither clinically indicated nor an efficient use of limited resources. Despite drawing on expert recommendations from breast oncology clinicians to identify patients who have clinical indicators of poor prognosis, >40% of our sample was still alive approximately 7 months after closing study enrollment, suggesting wide variability in survival. Because EHR documentation data are often limited in quality and comprehensiveness, future work ought to consider ways to enhance computer-assisted tools, such as deep NLP, not only to assist in identifying patients at risk for unmet PC needs but also to specify EoL care process measures and patient-centered outcomes.

Several limitations of the study warrant consideration. First, as a single-site trial at a comprehensive cancer center, study findings may not apply to other care settings with more diverse patient populations. Moreover, 22% of the usual care group had at least 1 PC consultation by 24 weeks, potentially diminishing intervention effects. We did not assess caregiver outcomes, which should be included in future research. Finally, excluding patients already receiving or needing immediate PC at the time of enrollment may have biased the sample to include healthier individuals and limited the capacity of the intervention to improve QoL and mood symptoms.

Conclusions
This study demonstrates the beneficial role of ambulatory PC when targeted to the needs of a specific population, such as patients with MBC. Tailored PC interventions will become increasingly necessary given clinician workforce shortages and progress in novel cancer therapeutics prolonging survival in many subgroups of patients diagnosed with metastatic disease. Thus, this study represents an important step forward in enhancing access to essential supportive care services in a timely manner and for improving the quality of EoL care.

Table 4. Descriptive Statistics for Patient-Reported Outcome Measures Across Time Points

<table>
<thead>
<tr>
<th>Variable</th>
<th>Usual Care Mean [SD]</th>
<th>Intervention Mean [SD]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (n=120)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-B</td>
<td>96.45 [19.57]</td>
<td>101.36 [16.64]</td>
</tr>
<tr>
<td>HADS-Anxiety subscale</td>
<td>7.38 [3.93]</td>
<td>5.95 [3.37]</td>
</tr>
<tr>
<td>HADS-Depression subscale</td>
<td>5.47 [3.57]</td>
<td>5.16 [3.59]</td>
</tr>
<tr>
<td>6 weeks (n=107)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-B</td>
<td>98.94 [19.27]</td>
<td>102.01 [17.90]</td>
</tr>
<tr>
<td>HADS-Anxiety subscale</td>
<td>6.40 [4.33]</td>
<td>5.79 [3.89]</td>
</tr>
<tr>
<td>HADS-Depression subscale</td>
<td>5.13 [3.21]</td>
<td>5.37 [3.70]</td>
</tr>
<tr>
<td>12 weeks (n=95)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-B</td>
<td>99.32 [20.90]</td>
<td>101.03 [18.58]</td>
</tr>
<tr>
<td>HADS-Anxiety subscale</td>
<td>6.26 [4.46]</td>
<td>5.82 [3.42]</td>
</tr>
<tr>
<td>HADS-Depression subscale</td>
<td>5.04 [3.49]</td>
<td>5.67 [4.12]</td>
</tr>
<tr>
<td>18 weeks (n=85)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-B</td>
<td>97.95 [19.94]</td>
<td>99.77 [20.72]</td>
</tr>
<tr>
<td>HADS-Anxiety subscale</td>
<td>7.07 [4.13]</td>
<td>5.49 [3.42]</td>
</tr>
<tr>
<td>HADS-Depression subscale</td>
<td>5.91 [3.60]</td>
<td>5.75 [4.43]</td>
</tr>
<tr>
<td>24 weeks (n=79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-B</td>
<td>96.33 [20.76]</td>
<td>101.15 [19.35]</td>
</tr>
<tr>
<td>HADS-Anxiety subscale</td>
<td>7.08 [4.88]</td>
<td>5.87 [4.42]</td>
</tr>
<tr>
<td>HADS-Depression subscale</td>
<td>5.31 [3.83]</td>
<td>4.83 [3.71]</td>
</tr>
</tbody>
</table>

Abbreviations: FACT-B, Functional Assessment of Cancer Therapy-Breast; HADS, Hospital Anxiety and Depression Scale.

References


41. Norals TE, Smith TJ. Advance care planning discussions: why they should happen, why we don’t, and how we can facilitate the process. Oncology (Williston Park) 2015;29:567–571.


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*J Natl Compr Canc Netw* 2022;20(2):136–143

eAppendix 1: Intervention Topics for the 5 Structured Palliative Care Visits
eAppendix 2: Proportion of Patients by Eligibility Criteria Indicating Poor Prognosis
eAppendix 1. Intervention Topics for the 5 Structured Palliative Care Visits

- Visit 1
  ➢ Rapport building: introducing palliative care, understanding the patient and caregiver experience, and building trust with the patient and caregiver

- Visits 2–3
  ➢ Symptom management: preparing patients for symptoms, assessing and treating symptoms, including referrals to other clinicians, and coordinating management with oncology
  ➢ Illness understanding: exploring goals and values, assessing and informing patient expectations of prognosis and illness process, and communicating with caregivers about illness understanding
  ➢ Coping: reviewing and validating prior coping efforts, discussing and advocating for different methods of coping, and supporting caregiver coping

- Visits 4–5
  ➢ Treatment decision-making: assessing patient goals and values in treatment decision making, discussing treatment considerations, and supporting treatment decisions
  ➢ End of life (EoL) and advance care planning: discuss EoL care options, advance care planning, and supporting caregivers

eAppendix 2. Proportion of Patients by Eligibility Criteria Indicating Poor Prognosis

- Leptomeningeal disease, n=3 (2.5%)
- Progressive brain metastasis after initial radiation therapy, n=7 (5.8%)
- Brain metastases and starting whole-brain radiation, n=3 (2.5%)
- Discharged after an unplanned hospital admission, n=38 (31.7%)
- Triple-negative disease and starting second-line chemotherapy, n=8 (6.7%)
- Received at least 3 different treatment regimens in a 12-month period, n=32 (26.7%)
- HER2-positive or estrogen receptor-positive disease and starting third-line therapy, n=4 (3.3%)
- Beginning a treatment clinical trial, n=25 (20.8%)