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Evaluation of an Innovative Outpatient Palliative Care Model for Patients with Advanced Cancer: A Multicenter Randomized Clinical Trial

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Abstract

Background. As European healthcare increasingly relies on outpatient services, including palliative care, additional ambulatory options are needed to meet demand. The rising complexity and scope of patients' palliative care needs call for new outpatient tools. Our study evaluates the impact of an innovative palliative care clinic on health status in adults with advanced cancer.

Methods. A superiority multicenter randomized clinical trial comparing an innovative palliative care day hospital (intervention arm) with traditional outpatient palliative care clinics (standard arm) over a six month-period. Adults with solid tumors newly referred to outpatient palliative care at six centers were enrolled, with the option to nominate a primary caregiver for caregiver needs assessment. The primary outcome was health-related quality-of-life deterioration–free survival, assessed using the EORTC Core Quality of Life questionnaire (QLQ-C30). Secondary outcomes included anxiety and depression symptoms, satisfaction with care, indicators of aggressive end-of-life care, overall survival, and caregivers' supportive care needs among those with an identified primary caregiver. Exploratory outcomes included advance care planning discussions and patients' perceptions of prognosis and treatment goals.

Results. Among 139 participants (mean age 67 years; 70% female; 31% breast cancer) randomized to the intervention (n=70) or standard arm (n=69), 34 (48.7%) and 33 (47.1%), respectively, designated a caregiver. The primary outcome was negative (p>0.05). Over time, secondary endpoints showed a significant decrease in depression scores in the interventional arm (mean difference: -2.30; 95% CI: -4.57 to -0.04; p = 0.046), while the standard arm had significantly lower psychological/emotional needs (mean difference: 0.50; 95% CI: 0.15–0.99; p = 0.044) and communication/family support needs (mean difference: 0.27; 95% CI: 0.01–0.52; p = 0.043). No significant differences were found in satisfaction with care, supportive care needs, aggressive end-of-life care, advance care planning, prognosis perception, or overall survival.

Conclusions. Although our intervention did not improve the quality of life, it contributed to alleviating depression symptoms, potentially by strengthening reassurance and may benefit complex cancer patients. An ancillary medico-economic analysis is ongoing.

Trial registration: NCT04604873 in the registry IDRCB 2019-A03116–51. Date of registration: October 27, 2020.

Introduction

As evidence accumulated that early palliative care improves quality of life, and reduces symptom burden, the 2016 ASCO guidelines explicitly endorsed early palliative care for patients with advanced cancer (1), accelerating the move toward systematic outpatient services. Several models now coexist – standalone, embedded, telehealth interventions, hybrid models – which differ in setting, staffing, referral pathways,

and visit structure, but all aim at earlier access and longitudinal support (2). However, the most efficient model for delivering palliative care in the outpatient setting remains uncertain (3, 4).

Patients with advanced cancer are presenting with increasingly complex needs. With the 5-year relative survival rate for all cancers rising from 49% in the mid-1970s to 69% in 2014–2020, more patients are living longer with advanced and chronic disease (5). Coupled with high rates of multimorbidity – present in 47.9% of all cancer-related hospitalizations and increasing steeply with age – this means a growing number of patients are living for years with treatment-related toxicities, disability, and dependence on health and social care systems (6). In this context, traditional outpatient palliative care models may no longer be sufficient, underscoring the need to develop and test innovative outpatient clinic structures.

To better respond to the growing intensity and breadth of patients' palliative care needs, an innovative comprehensive outpatient clinic model – the palliative care day hospital (PCDH) – was developed, designed to offer patients and caregivers extended time and to deliver intensive, interdisciplinary palliative care within an ambulatory stay (7). Prior work has suggested that PCDH is a promising approach to reduce aggressive end-of-life care, particularly by lowering hospital admission rates compared with traditional outpatient clinics in patients with advanced soft tissue sarcomas (HR 0.19, 95% CI 0.07–0.31; p = 0.02 and HR 0.58, 95% CI 0.38–0.81; p = 0.004, respectively) (8). Additionally, a multicentric qualitative study highlighted the advantages of longer visits in PCDH and the strong collaboration between palliative care and oncology, supporting smooth transitions to best supportive care (9). However, data from prospective clinical trials have been lacking.

We therefore conducted a multisite randomized clinical trial to compare the effectiveness of PCDH in adults with advanced cancer, with a particular focus on quality of life and other patient-centred outcomes. We hypothesized that, compared with traditional outpatient palliative care clinics, PCDH would be associated with improved patient quality of life, better emotional symptom control, more accurate prognosis perception, higher satisfaction with care, and less aggressive end-of-life care.

Methods

Design and participants

We conducted a prospective, nonblinded, randomized superiority trial comparing PCDHs (intervention arm) with traditional outpatient palliative care clinics (standard arm) for patients with advanced cancer at six French centres between September 28, 2020, and July 18, 2023. The initial Eastern Cooperative Oncology Group (ECOG) performance status criterion of 0–2 was later expanded to include all ECOG levels. Patients newly referred to outpatient palliative care were screened daily for eligibility. Eligible participants were adults (≥18 years) with advanced solid tumors and an estimated life expectancy of 2–12 months, as determined by their primary oncologist (10). Patients could designate a primary caregiver for the caregiver needs assessment. Exclusion criteria were inadequate French literacy, severe psychiatric disorders, inability to attend follow-up visits, pregnancy, or childbearing potential without adequate contraception. The study protocol has been published previously (11).

Randomisation

Written informed consent to participate was obtained from all of the participants in the study. Patients were randomly assigned 1:1 to the intervention or standard arm using a web-based minimization procedure, stratified by cancer centre, caregiver status, and estimated life expectancy (2–6 vs 6–12 months). Stratification by cancer centre ensured balance in local care practices and resources; stratification by caregiver status accounted for the potential impact of informal support on patient outcomes and service use; and stratification by estimated life expectancy controlled for baseline prognostic differences that could influence quality-of-life trajectories and end-of-life care intensity.

Intervention delivery

The PCDH is an acute outpatient clinic within tertiary centres that delivers comprehensive, intensive, interdisciplinary palliative care in a single ambulatory visit. Consultations are jointly led by a specialized palliative care physician and nurse, with input from other supportive care professionals and relevant medical specialists, including the patient's oncologist during the same visit when needed. Patients may receive procedures for symptom relief, imaging, systemic pain therapies, parenteral nutrition, or transfusions, as clinically indicated. The core components of the PCDH model have been described previously (7).

Outcomes

The primary outcome was health-related quality of life (HRQOL) deterioration-free survival, assessed monthly for 6 months with the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), targeting three dimensions: global health status, emotional functioning, and fatigue (12).

Secondary outcomes included other HRQOL dimensions, as well as depression and anxiety, assessed at baseline and at months 3 and 6 using the Hospital Anxiety and Depression Scale (HADS) (13). Satisfaction with care was assessed at months 2, 4, and 6 using the EORTC Patient Satisfaction Core 33 and the Out-Patient Satisfaction 7 questionnaires (PATSAT-C33 and OUT-PATSAT7) (14,15). Indicators of aggressive end-of-life care, based on Earle *et al.* (16), comprised receipt of systemic anticancer therapy with non-curative intent in the last month or last two weeks of life, at least one emergency department visit, intensive care unit stay, or hospital admission in the last month of life, and hospice admission in the final three days of life. Additional secondary outcomes were overall survival and caregivers' supportive care needs, the latter assessed at baseline and at months 2, 4, and 6 with the Supportive Care Needs Survey for Partners and Caregivers (SCNS-P&C) among participants who had designated a primary caregiver (17,18).

Exploratory outcomes comprised advance care planning discussions and patients' perception of prognosis and treatment goals, assessed using two dichotomous items from the Prognosis and Treatment Perceptions Questionnaire (PTPQ) (19).

Data were collected using CleanWEB, a secure electronic data capture system compliant with regulatory requirements. Participants completed questionnaires on paper or electronically via CleanWEB on the same day, after their scheduled protocol visit.

Statistical analysis

We assumed an improvement in median HRQOL deterioration-free survival from 1 to 2 months (H0: HR=1; H1: HR=0.5), with a two-sided type I error of 0.0166 (three targeted dimensions), 90% power, and a 1:1 allocation ratio. Under a 12-month accrual and 12-month follow-up, 115 patients (114 events) were required. Accounting for 20% attrition, the target sample size was 144 patients (72 per arm). Baseline characteristics were summarized by arm using means (standard deviations) for quantitative variables and counts (percentages) for qualitative variables. Analyses were conducted in the intent-to-treat population, with exploratory per-protocol analyses. Minimal important differences were defined as 10 points for QLQ-C30 and 1.5 points for HADS; none are established for the other instruments. HRQOL deterioration-free survival was defined as the time from randomization to the first clinically meaningful definitive deterioration from baseline in the relevant score, or death from any cause, whichever occurred first. Deterioration was considered definitive if maintained at all subsequent assessments (20). Patients without a baseline score were censored at baseline. Longitudinal QLQ-C30, HADS, SCNS-P&C, PATSAT-C33, and OUT-PATSAT7 data were analyzed using mixed models for repeated measures. For QLQ-C30, HADS, and SCNS-P&C, models were fitted to change from baseline and included fixed effects for time, treatment, and their interaction, adjusted for baseline score, with patient-level random effects. For PATSAT-C33 and OUT-PATSAT7, models were fitted to absolute scores with the same fixed and random effects structure. Adjusted means and 95% confidence intervals (CI) were reported by arm. Overall survival was defined as the time from randomization to death from any cause; participants who were alive were censored at the date they were last known to be alive. Health-related quality of life deterioration-free survival and overall survival were estimated using the Kaplan–Meier method and compared between arms using the log-rank test, and the association between treatment arm and time-to-event endpoints was assessed using Cox proportional hazards models. All tests were two-sided, with a type I error of 0.016 for the primary endpoint (Bonferroni adjustment for three dimensions) and 0.05 for secondary endpoints. Analyses were performed using SAS version 9.4.

Ethics

Ethics approval was obtained from the Comité de Protection des Personnes Ouest III, University Hospital of Poitiers (2 March 2020; SI CNRIPH 20.01.07.62640). Written information was provided to participants and caregivers, and informed consent was obtained from all participants before data collection.

Results

Participants

Of 315 eligible patients, 139 were randomized (69 standard arm, 70 intervention arm) between 28/09/2020 and 18/07/2023. Reasons for non-participation are shown in **Figure 1**. As shown in **Table 1**, participants' mean age was 66.7 years (SD 12.5), and 97 (69.8%) were women. Most patients had hormone-sensitive breast cancer (n=33, 23.9%), an estimated life expectancy of 6–12 months (n=80, 57.6%), and an ECOG performance status ≥2 (n=124, 89.2%). Thirty-four participants (48.7%) in the intervention arm and 33 participants (47.1%) in the standard arm designated a caregiver. Most designated caregivers (33 standard arm, 34 intervention arm) were spouses or partners (n=47; 70.1%).

Table 1. Baseline participants' characteristics.

Variable	Standard arm	Intervention arm
	Participants	
	(N=69)	**(N=70)**
Age (years), mean (SD)	65.8 (12.7)	67.7 (12.3)
Female, No. (%)	47 (68.1)	50 (71.4)
Travel time hospital-home (min), mean (SD)	42.9 (30.8)	46.4 (42.7)
Relationship status, No. (%)		
Married/Partnered	48 (70.6)	45 (64.3)
Single	20 (29.4)	25 (35.7)
Missing	1	0
Socio-professional category [a], No. (%)		
Craftsmen, merchants, company managers	4 (6.0)	1 (1.5)
Executives and higher intellectual professions	13 (19.4)	20 (30.3)
Intermediate professions	7 (10.4)	3 (4.5)
Employees	8 (11.9)	10 (15.2)
Workers	3 (4.5)	3 (4.5)
Retired	30 (44.8)	27 (40.9)
Unemployed	2 (3.0)	2 (3.0)
Missing	2	4
Cancer type, No. (%)		
Breast cancer	21 (30.4)	22 (31.4)
Lung cancer	15 (21.7)	20 (28.6)
GI cancer	7 (10.1)	6 (8.6)
GU cancer	3 (4.3)	3 (4.3)
Gynecologic cancer	7 (10.1)	13 (18.6)
Melanoma	1 (1.4)	1 (1.4)
Sarcoma	12 (17.4)	3 (4.3)
Other [b]	2 (2.9)	2 (2.9)
Missing	1 (1.4)	0 (0)

ECOG performance status [c], No. (%)		
0	2 (2.9)	0 (0.0)
1	7 (10.1)	6 (8.6)
2	52 (75.4)	54 (77.1)
3	8 (11.6)	10 (14.3)
4	0 (0)	0 (0)
Estimated life expectancy, No. (%)		
[2;6[months	28 (40.6)	31 (44.3)
[6;12] months	41 (59.4)	39 (55.7)
EORTC QLQ-C30, mean (SD)		
Global health status	48 (19.0)	49 (20.0)
Fatigue	57 (26.2)	64 (26.4)
Emotional functioning	70 (25.0)	65 (25.9)
	Designated primary caregivers	
	(N=33)	**(N=34)**
Age (years), mean (SD)	61.4 (15.4)	66.0 (14.5)
Women, No. (%)	18 (54.5)	19 (55.9)
Relationship, No. (%)		
Spouse/Partner	23 (69.7)	24 (70.6)
Siblings	1 (3.0)	3 (8.8)
Parent/Child	7 (21.2)	5 (14.7)
Other member of the family	2 (6.1)	0
Friend	0	2 (5.9)

Abbreviations: EOL: End-of-life; ECOG = Eastern Cooperative Oncology Group ; EORTC: European Organisation for Research and Treatment of Cancer; GI: Gastrointestinal; GU: Genitourinary; Receptor; QLQ-C30: Core Quality of Life questionnaire; SD: Standard deviation.

[a] The socio-professional categories are a French classification system established by *National Institute of Statistics and Economic Studies* (INSEE) to group the population based on their occupation, hierarchical position, and employment status.

[b] Other cancer types included head and neck cancers, and carcinoma with unknown primary.

[c] ECOG performance status was classified as follows: 0 = fully active, no restrictions; 1 = able to carry out light work; 2 = unable to work and in bed <50% of the day; 3 = capable of only limited self-care and in bed >50% of the day; 4 = completely disabled, unable to perform any self-care, and totally confined to bed or chair.

Intervention delivery

In the standard arm, 11 patients (15.7%) had at least one PCDH visit, whereas in the intervention arm, 50 patients (71.4%) attended the PCDH at least once. The main reasons for PCDH visits in the standard arm were patient request and technical needs, while the absence of PCDH visits among some patients in the intervention arm reflected a lack of complex medico-psychosocial needs (no requirement for additional healthcare professionals beyond the palliative care team, interventional or technical procedures, or imaging). Completion rates for patients' and caregivers' questionnaires are detailed in **Additional file 1.**

Primary outcome

The HRQOL deterioration-free survival did not differ between arms for any of the three targeted dimensions in either the intent-to-treat or per-protocol analyses: global health status (HR 1.04, 95% CI 0.64–1.68; p=0.86, and HR 1.09, 95% CI 0.64–1.87; p=0.67), emotional functioning (HR 0.84, 95% CI 0.51–1.38; p=0.41, and HR 0.92, 95% CI 0.53–1.59; p=0.70), and fatigue (HR 0.91, 95% CI 0.56–1.46; p=0.62, and HR 1.03, 95% CI 0.61–1.77; p=0.88) respectively (**Figure 2**).

Secondary outcomes

Secondary outcome measures are summarized in **Table 2**. There were no statistically significant differences between the standard and intervention arms across most HRQOL domains over time. However, the intervention arm showed a greater reduction in depression scores than the standard arm (mean difference −2.30, 95% CI −4.57 to −0.04; p=0.046), whereas anxiety scores did not differ significantly between groups (p=0.363). Regarding needs among caregivers, the standard arm reported significantly lower psychological and emotional needs (estimated mean difference 0.50, 95% CI 0.15–0.99; p=0.044) and communication and family support needs (estimated mean difference 0.27, 95% CI 0.01–0.52; p=0.043) compared with the intervention arm, with no significant between-group differences for work and social security needs or health care service and information needs. No significant differences were observed between arms in satisfaction with doctors, nurses, overall care, or ambulatory care (continuity, convenience, transition). The proportion of patients receiving at least one aggressive end-of-life intervention was similar in the standard and intervention arms (10/29 [34.5%] *vs* 8/26 [30.8%]; p=0.550). Overall survival also did not differ significantly between arms (3.9 *vs* 5.3 months; HR 1.11, 95% CI 0.77–1.60; p=0.57; **Figure 3**).

Exploratory Outcomes

For exploratory outcomes, there were no significant differences between groups in patients' perceptions of the goal of therapy or the curability of their cancer, and advance care planning documentation –

including do-not-resuscitate orders, prognostic awareness, treatment goals, and end-of-life discussions – was comparable between arms, with no statistically significant differences (**Table 2**).

Discussion

This first multisite randomized trial showed that, in patients with advanced cancer referred to outpatient palliative care, a comprehensive, intensive PCDH model did not improve HRQOL deterioration-free survival compared with a traditional outpatient clinic. However, the intervention was associated with a greater reduction in depressive symptoms, and caregivers in the intervention arm reported higher psychological, emotional, and communication needs than those in the standard arm.

Our cohort was similar to a previous retrospective series of 116 PCDH patients, showing comparable follow-up duration (3.13 months, 95% CI 2.6–4.0), and better functional impairment (mean ECOG 2.8) (21). In our cohort with a median overall survival between 3.9 and 5.3 months, we observed that HRQOL declined during the final two months of follow-up in both arms. This pattern of late decline is consistent with prior work showing accelerated deterioration in global quality of life in the last 2-3 months of life (22–24). Quality of life was selected as the primary outcome because enhancing patients' quality of life is a central goal and core indicator of palliative care practice and research (25,26). However, using quality of life measured in the last months of life as a primary endpoint presents important methodological challenges, including high attrition, missing data due to clinical deterioration, difficulties with repeated self-report in very frail patients, and uncertainty about how to interpret changes close to death (27,28). Our findings suggest that depressive symptoms decreased in the intervention arm, whereas anxiety remained relatively stable. Although anxiety and depression are strongly linked in advanced cancer (29), depression may have been more responsive to the PCDH model because it is often more amenable to established pharmacological and psychosocial treatments and easier access to psychiatric input. In contrast, existential and death-related anxiety is frequently more refractory (30,31) and may require longer-term, specialized psychological interventions beyond routine outpatient contacts. The higher caregivers' needs in the PCDH arm may reflect greater recognition and articulation of unmet needs rather than indicating worse outcomes. The PCDH model, with its longer, interdisciplinary visits and explicit inclusion of caregivers (7), likely created more opportunities to explore caregiver concerns, validate their experiences, and normalize help-seeking. However, further research, particularly qualitative studies, would be valuable.

Compared with earlier early palliative care trials, which typically enrolled patients with ECOG 0–2 and reported median survival beyond 8 months (32–35), our cohort had a much shorter median overall survival (3.9 and 5.3 months in the intervention and standard arms). This suggests a frailer population than is usually seen in traditional outpatient clinics and may explain why some patients in the standard arm required additional PCDH visits.

Suboptimal intervention delivery is therefore a key limitation and suggests that PCDH is unlikely to benefit all palliative outpatients. These findings may help refine patient selection, indicating that PCDH

should be reserved for individuals with higher symptom burden, complex psychosocial or technical needs, and a clear requirement for more intensive palliative care prior to scheduling the visit. Additionally, we did not reach the planned sample size, and high attrition due to disease progression limited follow-up, which may have affected the robustness and statistical power of our study to detect clinically meaningful differences between arms.

While the PCDH model did not show superiority over traditional outpatient clinics in delaying the HRQOL deterioration-free survival, it provided benefits in managing depression symptoms. This approach may represent a robust intervention for supporting complex adult cancer patients in outpatient palliative care. An ancillary medico-economic analysis is underway to assess its impact on healthcare resources.

Abbreviations

ECOG = Eastern Cooperative Oncology Group; EORTC = European Organization for Research and Treatment; HADS = Hospital anxiety depression scale; HRQoL = Health-related quality of life; OUT-PATSAT7 = Out-patient satisfaction 7 questionnaire; PATSAT-C33 = Patient Satisfaction Core 33 questionnaire; PCDH = Palliative care day hospital; PTPQ = Prognosis and treatment perceptions questionnaire; QLQ-C30 = Quality of Life Questionnaire Core 30; SCNS-P&C = Supportive Care Needs Survey for Partners and Caregivers questionnaire.

Declarations

Ethical approval and consent to participate

This study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki, and French Good Clinical Practice. Ethical approval was not needed, according to French law (Article L1121-1, Law no. 2011– 2012 29 December 2011 - art. 5). However the study was submitted and approved to a local ethics committee, the Comité de Protection des Personnes Ouest III belonging to University Hospital of Poitiers (date: 2 March 2020, committee reference number: SI CNRIPH 20.01.07.62640).

Written informed consent to participate was obtained from all of the participants in the study

Consent for publication

Not applicable

Availability of data and materials

Data are available from the principal investigator Carole Bouleuc upon reasonable request and with appropriate justification.

Competing interest

The authors have no competing interests to declare that are relevant to the content of this article.

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Authors' contributions

Conceptualization: LM, AA, AM, CB; Methodology: LM, MT, AA, AM, CB; Data collection: LTM, MT, AM, SM, EG, DH, EK, OS, CB; Statistical Analysis: AA; Writing: LM, MT, AA, CB, MT; Supervision: CM, MDS. All authors read and approved the final manuscript.

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Table

Table 2 is available in the supplementary files section

Figures

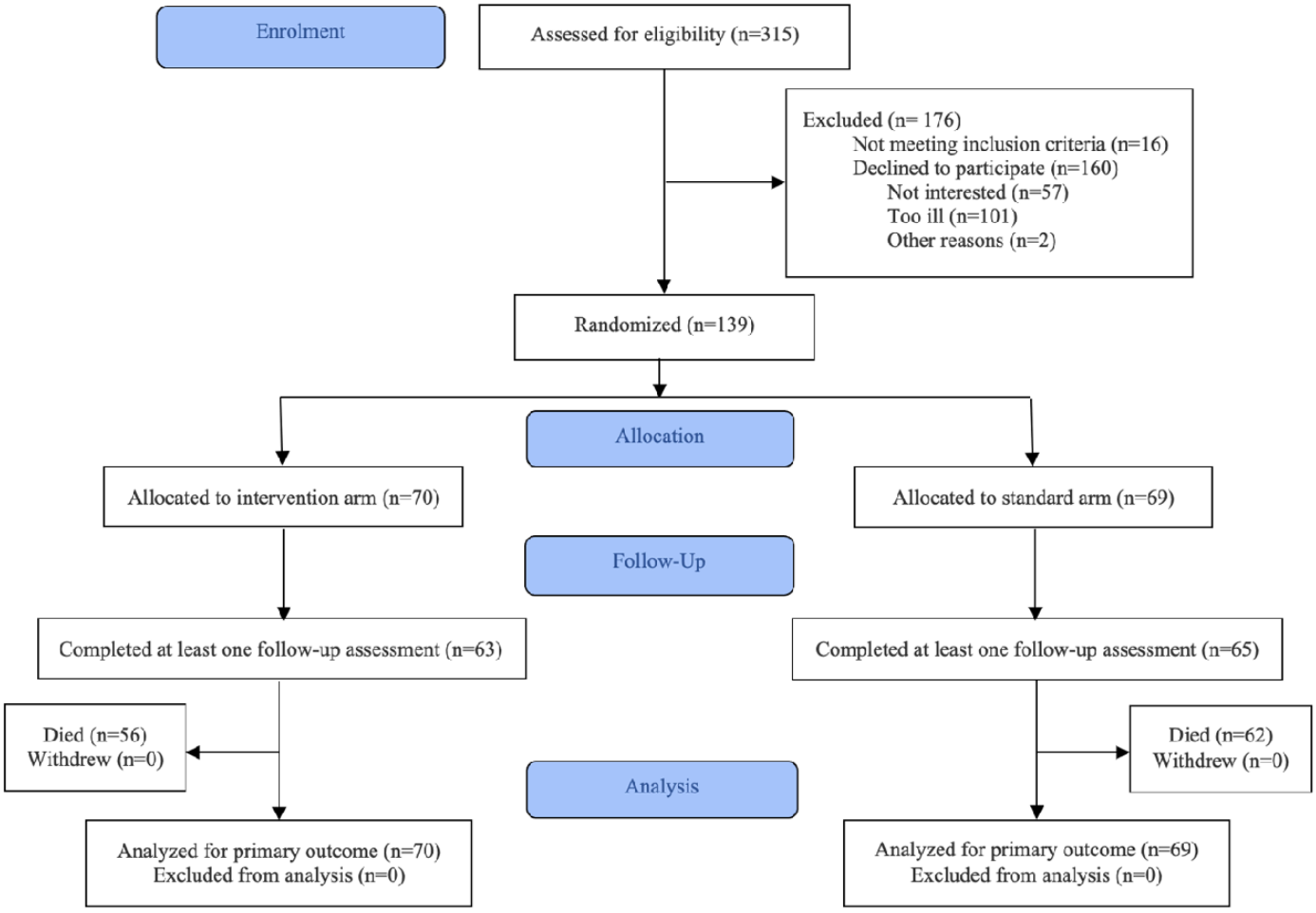

Figure 1

Flow of participants through a trial of intervention arm *versus* standard arm.

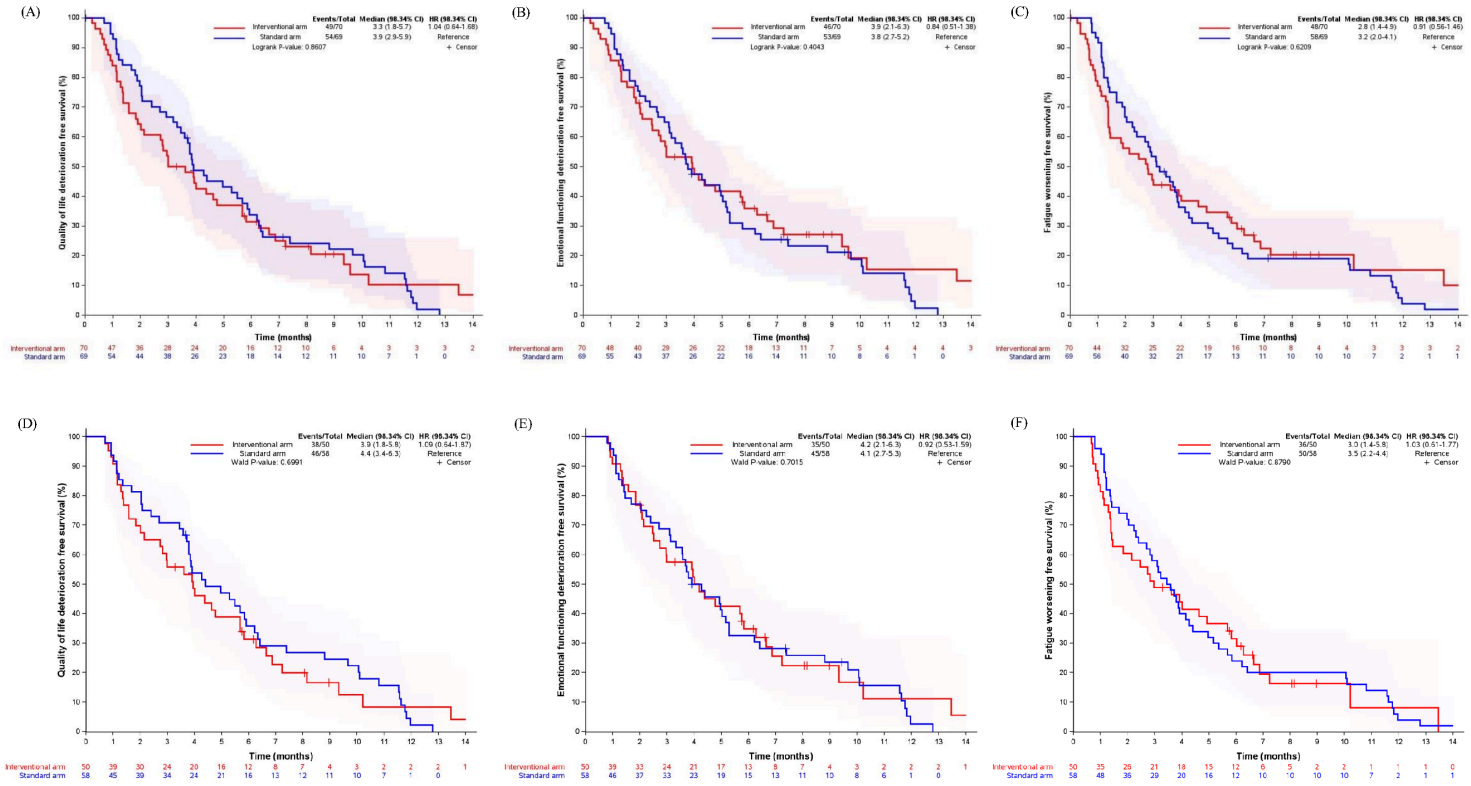

Figure 2

Health-related quality-of-life deterioration-free survival in intent-to-treat and per-protocol populations.

Health-related quality-of-life deterioration-free survival in the intent-to-treat population for (A) global health status, (B) emotional functioning, and (C) fatigue, and in the per-protocol population for (D) global health status, (E) emotional functioning, and (F) fatigue.

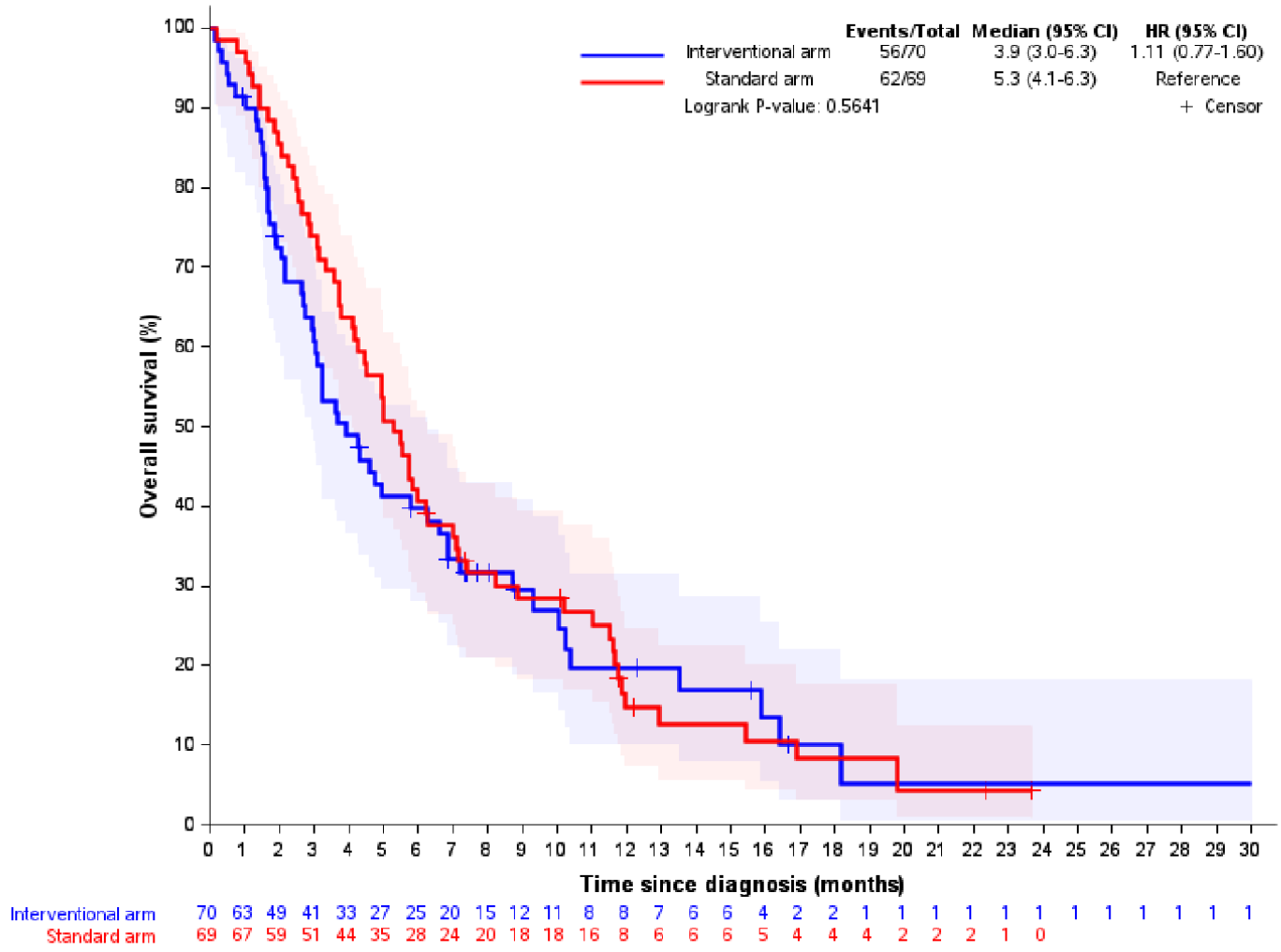

Figure 3

Kaplan-Meier reverse method of overall survival from study enrollment.

Supplementary Files

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- Additionalfile1.xlsx
- Table2.xlsx