BMJ Open

An integrated communication support program for oncologists, caregivers, and patients with rapidly progressing advanced cancer to promote patient-centered communication: J-SUPPORT 1904 study protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036745
Article Type:	Protocol
Date Submitted by the Author:	04-Jan-2020
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Keywords:	Adult oncology < ONCOLOGY, Adult palliative care < PALLIATIVE CARE, MENTAL HEALTH, SOCIAL MEDICINE

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INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

TITLE: An integrated communication support program for oncologists, caregivers, and patients with rapidly progressing advanced cancer to promote patient-centered communication: J-SUPPORT 1904 study protocol for a randomized controlled trial

RUNNING TITLE: Integrated communication program for advanced cancer patients and oncologists

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Word count: 3716 words, excluding title page, abstract, references, figures, and tables

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ABSTRACT

Introduction

Communication is an essential aspect of care for patients with progressive serious illnesses. This study aims to evaluate the efficacy of an integrated patient-centered communication support program involving caregivers, oncologists, and patients with rapidly progressing advanced cancer.

Methods and Analysis

The proposed integrated communication support program is in the randomized control trial stage. It comprises a cluster of oncologists from comprehensive cancer center hospitals in a metropolitan area in Japan. A total of 20 oncologists, 200 patients with advanced pancreatic cancer, and the patients' caregivers are enrolled in this study as of the writing of this protocol report. Oncologists are randomly assigned to the intervention group (IG) or control group (CG). Patients and caregivers are allocated to the same group as their oncologists. The IG oncologists receive a 2.5-hour individual communication skills training, and patients and caregivers receive a half-hour coaching intervention to facilitate prioritizing and discussing questions and concerns; the CG participants do not receive any training. Follow-up data will be collected quarterly for 6 months and annually

for up to three years. The primary endpoint is the intergroup difference between before- and after-intervention patient-centered communication behaviors during oncology visits.

Ethics and dissemination

This study is conducted in accordance with the ethical guidelines for clinical studies published by Japan's Ministry of Education, Cultural, Sports, Science, and Technology, the Ministry of Health, Labour, and Welfare (MHLW), and the ethical principles established for research on humans stipulated in the Declaration of Helsinki and further amendments thereto. The protocol was approved by the Institutional Review Board of National Cancer Center, Japan on July 4, 2018 (ID: 2017-474).

Trial status

This study is currently enrolling participants; enrollment period ends July 31, 2020; estimated follow-up date is March 31, 2023.

Trial registration number

UMIN Clinical Trial Registry: UMIN000033612; Pre-results.

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(290 words)

Keywords: Advance Care Planning, Caregivers, Communication, Decision making, Empathy, End-of-life care, Patient-centered care, Patient-physician relationship, Quality of life

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ARTICLE SUMMARY

Trial registration: The protocol registered on 2nd August, 2018 at UMIN Clinical Trial Registry. The registration number is UMIN000033612.

Data statement: Study protocol, data definition tables, and dataset will be uploaded to the UMIN- Individual Case Data Repository, https://www.umin.ac.jp/icdr/index-j.html.

Protocol version: The protocol version is 1.4 on 20th December, 2019.

Strengths and limitations of this study:

- A strength of this study is the use of a large group of patients, caregivers, and oncologists in the real-world scenario for which the intervention is being tested.
- The use of multicenter participant samples, controls, and patient follow-up allows for reliable study results.
- This study includes oncologists, patients, and caregivers for intervention.
- The intervention program is complex, consisting of multiple factorial components making it difficult to determine which interventions and components are most efficacious or beneficial; however, participants provide assessments of the

intervention components.

- The study only involves pancreatic cancer so the generalization potential for other cancers is unknown. However, as pancreatic cancer is one of the most rapidly progressing, the intervention may be effective for patients with other these cancers.

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INTRODUCTION

Pancreatic cancer is the fourth leading cause of death in Japan with approximately 35,000 new cases diagnosed per year, matching the approximate annual number of deaths from the disease nationally.[1] Over 40% of patients with pancreatic cancer are stage IV at diagnosis and the 5-year survival rate is 7%.[2] Although the initial treatment goal for pancreatic cancer is to cure, even prolonged survival and maintenance of QOL are difficult to achieve.

Most patients with advanced cancer prefer to discuss their prognosis and treatments with their physicians.[3] However, physicians may feel burdened by open discussions for fear of patients losing hope or they may face resistance from caregivers; [4] therefore, these discussions rarely occur.[5] Consequently, patients often overestimate prognoses, underestimate disease severity, and have unrealistic expectations for a cure.[6] Patients who have not discussed prognosis and treatment choices with their oncologists are 3 to 8 times more likely to receive aggressive treatments in their last week of life.[5, 7] Although oncologists and patients find prognostic discussions can be stressful for doctors and patients alike, unnecessary expenses and actual harm to the patient may result from uninformed decisions.[8] Additionally, it has been shown that open discussions do not cause hopelessness or increased fear inpatients, and well-informed patients make

more appropriate treatment choices.[9,10] Hence, oncologists need to provide adequate information regarding cancer treatment decisions for patients approaching the end of life and their caregivers, confirm their understanding, and achieve shared decision making about treatment and care based on patients' personal values, life goals, and treatment preferences.

Patients go from diagnosis to discontinuation of anti-cancer drug treatment (mainly pancreatic cancer patients) desire more "empathic paternalistic communication" from oncologists.[11] Oncologists' empathic communication reduces patients' psychological distress,[12] increases trust in the oncologist,[12] and enhances information recall.[13] Empathic communication is essential, especially for patients with rapidly progressing serious illnesses. Therefore, communication skills training (CST) programs have been developed for physicians to facilitate communication behaviors that strengthen relationships with patients.[14] CST is a learner-centered workshop held in small groups, including role-play with simulated patients (SPs).[15] It is strongly recommended that medical professionals train communication skills in American Society of Clinical Oncology Consensus Guideline in patient-clinician communication. [16]

We conducted a prior survey clarifying the four factors of oncologists' communication skills preferred by patients, referred to as SHARE: "Setting", "How to

deliver the bad news", "Additional information", and "Reassurance and Emotional support."[17,18] A two-day SHARE-CST program for oncologists was developed based on these preferences.[19] Our previous randomized controlled trial (RCT) showed that oncologists who participated in SHARE-CST improved their confidence and behavior in patient-centered communication and their patients experienced a low level of psychological distress and a high level of trust in the oncologist.[12]

In Japan, SHARE-CST was implemented as a 10-year project commissioned by the MHLW for physicians nationwide after the enactment of the National Cancer Control Act. Participants reported that empathic communication attitudes and abilities improved;[20] however, it was difficult for most oncologists to participate in two-day CST group workshops because of busy clinical oncology settings.

Patient-centered approaches using question prompt lists (QPLs) have also been proposed for improving patient-physician communication. A QPL is an inexpensive communication tool employing a structured question list to encourage patient question-asking and participation during consultations.[21] The provision of a QPL and communication interventions with QPL before a consultation is effective in promoting patient question-asking behavior and participation in the consultation, and decreasing patients' anxiety.[22] Our previous RCT trial showed that QPS might be useful for

advanced cancer patients, however, it failed to promote patient question-asking behavior,[23] in part because Japanese patients tend to wait for physicians to encourage them to ask questions.[24] Therefore, in Japan, integrated interventions combining CST for oncologists and QPL-coaching for patients might increase patient questioning behavior and improve patient-centered communication in consultations.[25,26]

Based on the previous trials' results, this study aims to evaluate the efficacy of a new integrated communication support program promoting patient-centered communication regarding treatment and care after standard chemotherapy during first-line chemotherapy among oncologists, caregivers, and patients with rapidly progressing advanced cancer. We hypothesize that, compared to treatment as usual (TAU), the intervention will increase patients' question-asking behaviors, improve patient well-being and patient-centered communication behaviors, and improve health services utilization by reducing aggressive interventions and increasing use of palliative care.

METHODS and ANALYSIS

This protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and SPIRIT PRO Extension Guidelines.[27, 28]

Study design

This study is a single-blind cluster RCT conducted in four metropolitan cancer-treatment hospitals: the National Cancer Center Hospital, the National Cancer Center Hospital East, the Cancer Institute Hospital, and the Kanagawa Cancer Center Hospital. This study protocol has been reviewed and approved by the protocol review committee of Japan Supportive, Palliative, and Psychosocial Oncology Group as J-SUPPORT 1704 study, and the Institutional Review Boards at each participating institution.

An independent data center provides computer-generated random allocation sequences. The assignment sequence is centrally managed; assignment results are automatically sent to a clinical research coordinator (CRC) electronically. The oncologist participants are randomly assigned to an intervention group (IG) or control group (CG), after baseline phase and patient/caregiver participants are randomized by proxy to intervention with TAU or control (TAU alone). A stratified block-randomization scheme is used to assure balanced assignment by site. Within each site, oncologists are randomly assigned approximately evenly across the treatment and control conditions. Because participants in intervention group provided intervention in addition to TAU, and are unblinded.

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Intervention

Oncologist

We modified the original SHARE-CST design,[12] adopting a 2.5-hour individual program consisting of lecture with a textbook and role-play/discussion with a facilitator and SP (See Table 1). The lecture cites evidence of the most important and common patient preferences regarding communication—empathic responses and encouragement to ask questions—variability of patients' preferences in discussing prognoses and being/not being dispassionate, and demonstrates how to check and elicit patient preferences. Additionally, the lecture explains the QPL and discusses frequently asked questions from patients about information related to treatment and care after standard treatment that relates to patients' personal values, life goals, and preferences of patients and caregivers. During the role-playing and discussion, participants are required to consider a patient's emotions and concerns caused by bad news, recognition of his/ her disease, social situations, and information that he/ she would want to know, by empathizing with him/ her. Roleplay also includes dealing with patients who bring QPLs.

Facilitators provide a lecture, lead the role-playing, and discuss patients' potential emotions and communication-related preferences. Facilitators include

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Table 1. Components of CST Program Based on SHARE Model

Component	Description
Conceptual communication skills model: SHARE	
S	Setting up supportive environment for interview (eg, greeting patient cordially, looking at patient's eyes and face)
H	Considering how to deliver bad news (eg, not beginning bad news without preamble, checking to see whether talk is fast paced)
A	Discussing additional information that patient would like to know (eg, answering patient's questions fully, explaining second opinion)
RE	Providing reassurance and addressing patient's emotions with empathic responses (eg, remaining silent out of concern for patient's feelings, accepting patient's expression of emotions)
Module	
Lecture	Introduction, communication skills model, evidence of preferences of patients with cancer regarding communication
Role playing	Simurated consultation with simurated patient using communication skills with scenarios, discussing with facilitator, summary
Scenarios	Discontinuing chemotherapy
	Dealing with patient asking questions
Setting	1 participant
	1 facilitator
	1 simulated patient
Schedule	Orientation (10 minutes)
	Lecture (20 minutes)
	Role playing with peer discussion (45 minutes X 2)

Abbreviation: CST, communication skills training.

psychiatrists, psychologists, and oncologists, all of whom have had 3 years or more of clinical experience in oncology and participated in specialized 30-hour training workshops for facilitating communication skills in oncology. The SPs have also participated in train-the-trainer workshops and a 15-hour SP training.

Patient and Caregiver

Communication coaching for patients was developed to facilitate communication with physicians using a 63-question QPL based on in-depth focus-group interviews with 18 participants (5 pancreatic cancer patients, 3 caregivers patients with pancreatic cancer, 4 bereaved people who had known a patient with pancreatic cancer, and 6 pancreatic oncologists), and previous QPS studies.[23,24,29] The QPL is a 10-page A4 sheet containing 63 questions grouped into 8 topics (diagnosis and stage of the disease, current and future treatments, management of current/possible future symptoms, daily life activities, care and prognosis post standard treatment, caregivers' needs, psychological distress and management, and values) and a space for free questions. Patient communication coaching using the QPL is a half-hour individual program consisting of reading the list to select personally relevant questions, prioritizing selected questions, discussing encouraging their oncologist to ask some high priority questions at their next

oncology visit, discussing difficulties in asking, and practicing asking their oncologist these questions. The intervention is to be provided by clinical psychologists and nurses who have participated in a 10-hour intensive training workshop using an intervention manual. All intervention sessions are noted, summarized, and reported to each oncologist before patients' visits. Intervention providers hold weekly conferences to review their coaching sessions.

Control condition

CG oncologists are provided neither training nor educational materials. Patients/caregivers in the CG are provided TAU.

Participants

Oncologists

Enrolled oncologists must (1) be mainly engaged in anticancer drug treatment of the pancreatic cancer patients; (2) have provided written informed consent for trial participation.

Patients

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Enrolled patients must (1) have a diagnosis of pancreatic cancer (adenocarcinoma); (2) have unresectable pancreatic cancer (UICC stage III or IV) or postoperative recurrence; (3) receive a first-line chemotherapy and be scheduled for a second course; (4) be aged 20 years or older; (5) have a ECOG performance status score of 0 or 1; (6) regularly visit an enrolled oncologist; (7) provide written informed consent for trial participation; (8) be able to read, write, understand, and speak Japanese.

Patients are excluded if they are (1) judged by their oncologist to have cognitive impairment; (2) unable to complete an electronic Patient Reported Outcome (e-PRO) Questionnaire; (3) judged unsuitable for participation by their oncologist.

Caregivers

Enrolled caregivers must (1) be aged 20 years or older; (2) regularly accompany an enrolled patient as primary caregiver; (3) provide written informed consent to trial participation; (4) be able to read, write, understand, and speak Japanese.

Caregivers are excluded if they are unable to complete an electronic Patient Reported Outcome (e-PRO) Questionnaire.

Procedures

This study consists of 3 phases, a baseline phase, an intervention phase, and a follow-up phase (Figure 1). The schedule for outcome measurement is shown in Table 2. After completing the intervention phase, data analysis will ensue. After this study has closed, oncologists in the control group will be provided with the intervention on demand.

Baseline phase

This phase involves oncologist and patients/ caregiver recruitment, and pre-randomization data collection of oncologists' communication behaviors as baseline data for using as a covariate in the RCT analysis. In this phase, 3 to 5 patients and their caregivers (if available) will be recruited for each oncologist. Participants will be asked to be audio recorded at one oncology visit and provide some feedback as to study measures for potential use as covariates in the RCT analyses.

Intervention phase

This phase involves oncologists' randomization, intervention for participants in IG, and follow-up assessment. After oncologists are randomly assigned to the IG or CG, those in the IG will receive an individual intervention.

Next, 10 patients and their caregivers (if available) who regularly visit the

oncologist are recruited and assigned to the IG or CG. After the IG patients and their caregivers receive an intervention or 2 weeks to 1month after baseline in the CG, the conversation of the patient/caregiver and the oncologist audio record at their next consultation. After the visit, patients/caregivers and the oncologists rate the consultation using a follow-up assessment.

Long-term follow-up phase

Patients and their caregivers will be encouraged to provide long-term follow-up assessments at 3, 6, 12, 24, and 36 months after the first follow-up assessment. Caregivers regarding are also asked to provide another assessment at 2 to 6 months post patient death.

Data management, central monitoring, data monitoring, and auditing

We will collect all data, except for audio recorded data, through electronic data capture (EDC) and electronic-patient reported outcomes (ePRO) system or paper-based PRO questionnaires (pPRO) in case of patients' physical limitation. If participants fail to respond to ePRO or pPRO, a CRC blinded to the assignment will elicit subjects' answers to avoid the missing data. Data management and central monitoring will be performed using EDC VIEDOC 4 (PCG Solutions, Sweden) by J-SUPPORT Data Science Team.

Auditing is not also planned for this study.

Concomitant treatments

There is no restriction on concomitant treatments.

Stopping rules for participants

If a participant meets any of the following conditions, the research team can discontinue the intervention. However, the participant will not be considered to have dropped out of the trial at that stage and will receive the assessments: (1) the participant wishes to stop the intervention; (2) the research team judges that the risk of the intervention is greater than the benefit for any reason; (3) the research team judges that it is difficult to continue the intervention because of clinical deterioration; and (4) the research team judges that it is inappropriate to continue the intervention for any reason.

Stopping assessment

If a participant withdraws consent for assessment, he or she will not be followed up. Subjects will be excluded from the intention-to-treat (ITT) cohort of the trial only if they are found to meet any exclusion criteria at baseline (e.g., age under 20 years) after

participation.

Assessment measures

Table 2 shows the schedule for outcome measurement.

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Table 2. Schedule for outcome measurement

		Baseline Phase	Intervention Phase		Follow-up Phase	
		Day 28 of 1st line chemotherapy	Day 28 of 1st line chemothera	Day 42 of 1st line chemothera	3, 6, 12, 24, 36 months after	After post-mortem of the patient
Patient	SHARE RIAS	○				
	Charactaristics	○				
	Evaluation on consultation	○				
	SHARE RIAS			○		
	HADS		○	○	○	
	FACT		○	○	○	
	Short version of CoQOLo		○	○	○	
	TiOS		○	○	○	
	CSQ		○	○	○	
	PEACE		○	○	○	
	Evaluation on consultation, QPL, intervention, oncologist			○		
	PTPQ		○	○	○	
	Charactaristics		○			
	End-of-life Medical care			○	○	
Caregiver	SHARE RIAS	○				
	Charactaristics	○				
	SHARE RIAS			○		
	EQ- D- L		○	○	○	○
	K6		○	○	○	○
	CSQ		○	○	○	
	Charactaristics					
	End-of-life Medical care		○			
	PTPQ		○	○	○	
	Evaluation on consultation, QPL, intervention, oncologist			○		
	Short version of Good Death Inventory					○
Oncologist	SHARE, RIAS	○		○		
	Oncologist's charactaristics		○			
	Evaluation on intervention, QPL			○		
	Evaluation on consultation	○		○		

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Primary outcome measure

Patient-centered communication behaviors

The audio-recorded oncology visits for all participants will be coded for each of the four factors of communication behaviors based on patient preference, referred to as SHARE: setting, delivery of information, additional information, and reassurance and emotional support (see Table 1). [19] The SHARE-RE factor is used as a primary outcome to measure empathic communication between patient/caregiver and oncologist after intervention for both.

Based on previous study methods,[19] the impressions of conversations from consultations will be assessed using the 8 SHARE-RE categories of the 27 SHARE categories for analysis, in a random order, by two blinded coders who have been trained for 30 hours or more for some tasks independently on two occasions with a rating manual.

Secondary outcome measure

Patient-preferred communication behavior

Patient-preferred communication will be analyzed using impression ratings from two blinded coders, as described above. The analysis will include the audio-recorded oncology visits for all participants using the total score of the 27 SHARE

categories.[18,19] On the basis of previous study methods,[19] the 40 categories of the Rote intention analysis system (RIAS) will also be used in assessing patient-centered communications. [30]

Patient-reported outcome measures

Several scales will be used to produce a comprehensive profile of each patient participant. These include the Hospital Anxiety and Depression Scale (HADS);[31] the Physical well-being and Functional well-being subscale of the Functional Assessment of Cancer Therapy (FACT- Physical & Functional);[32] the Short version of the Comprehensive Quality of Life Outcome inventory (CoQOLo);[33] the Trust in Oncologists Scale (TiOS).[34] Satisfaction with their oncologist and experience with the disease will be measured with the Client Satisfaction Questionnaire (CSQ);[35] the Peace, Equanimity, and Acceptance in the Cancer Experience (PEACE) questionnaire;[36] and the Prognosis and Treatment Perceptions Questionnaire (PTPQ).[37]

Patients' relevant medical and sociological background information includes stage, diagnosis date, treatment status, treatment history, comorbidities, sex, age, job status, household income, household size, social support, marital status, educational experience, treatment, and care preference at the end of life. Medical utilization at the end

of life will be determined by the date of death, any chemotherapy agent given within 14 days of death, any new chemotherapeutic regimen started within 30 days of death, and involvement of hospice; and palliative care services; all of this information is obtained from medical fee information.[26]

A patients' assessment survey of the intervention's usefulness includes "Did you understand how to use the QPL and did you actually use it?" "Do you think you will continue the intervention?" "Was the intervention useful to you?" Their assessment of Oncologists includes "Did the oncologist talk about the QPL?" and "How did the oncologist respond to your questions?", their assessment of QPL includes "Did the QPL helped you ask the oncologist questions?" "Is the QPL useful?" "Did you read the QPL before the visit?" and "Do you think you will read the QPL in the future?" as well as whether they asked selected questions to oncologist after the visit, which questions they selected, and "How much you have discussed with your oncologist in the visit?"

Caregiver survey measures

Several scales will also be used for a comprehensive view of caregivers, including the K6 nonspecific psychological distress scale;[38] and the 5 Dimension EuroQol (EQ-5D).[39] Satisfaction with the oncologist is measured with the CSQ. After

the patient's death, the caregiver's QOL as the bereaved is measured with the Short version of Good Death Inventory (GDI).[40]

Caregivers' relevant sociological background information includes sex, age, relationship with the patient, job status, household income, household size, social support, marital status, educational experience, and treatment and care preferences at the end of life).

After the first post-intervention visit, caregivers in the IG will evaluate the intervention, the oncologist, and the QPL and report any selected questions used with the oncologist.

Oncologist survey measures

The relevant data concerning the oncologists include their sociological background (sex, age, clinical experience). The oncologists' medical utilization will be determined by their recollection of the dates and circumstances of the post-intervention consultations with patients/caregivers.

The usefulness of the intervention will also be measured using evaluations provided by the oncologists in the IG.

Harms

No specific and serious adverse events are presumed for participants of this study. However, by participating in the interventions, some participants may potentially experience psychological distress from imagining their situation after standard treatment. The patients/ caregivers and oncologists will also be subjected to time burdens of a half-hour and 2.5 hours for the intervention, and 10–30 minutes for each baseline and follow-up assessment. Therefore, we will give patients/caregivers a reward of 500 Japanese yen for each participant assessment. There are no financial risks associated with study participation.

Compensation

If participants develop unexpected health issues due to study participation during or after completion of this study, treatment will be adequately provided per standard medical care, covered by the National Health Insurance.

Sample size estimation

Our previous study revealed that the effect size of SHARE-RE scores was 1.9 at post-intervention. [12] For a sample size based on 80% power to detect a significant

difference at a significance level of 0.05 (two-sided), 10 oncologists and 70–100 participants (7–10 per oncologist) would be required for each arm in the follow-up phase, assuming some participant drop out and data loss. Assuming that 80% of patients will be accompanied by caregivers at doctor visits, a total of 112–160 participants would be required. Based on previous studies, a total of 60–150 patients (3 to 5 per oncologist) are needed in the baseline phase.[26]

Patient and public involvement statement

This study protocol was co-designed by a patient with pancreatic cancer and a family member of a pancreatic cancer patient who participated as researchers. They spoke with other patients to help determine recommendations for when patients' preferences and/or opinions should be considered. They will play a similar role in the implementation of this study. Thus, patients were and will continue to be involved in this study. The results of this study will be available via a study website.

Data analysis

Primary analyses

To examine the intervention effect parameters of all randomly assigned subjects

in the primary analysis set according to the ITT principle, we will analyze the primary outcome with SHARE-RE as an indicator of enhanced empathic communication using a generalized linear model. The primary outcome of interest is the difference in SHARE-RE scores between the two groups after intervention. A two-sided p value < 0.05 will be used to indicate statistical significance.

Secondary analyses

We will perform secondary analyses to supplement our primary analysis and obtain a clearer understanding of our clinical questions. The secondary analyses will use models similar to that of the primary analysis and will examine data for the secondary outcome measures. These analyses will be conducted for exploratory purposes.

Interim analyses

No interim analysis is planned.

Publication policy

The protocol and study results will be submitted to peer-reviewed journals. The first author of the main paper will be a member of the steering committee (authors of the

protocol paper). Another person could be the first author if approved by the steering committee. The list of coauthors will be determined before submitting each paper.

Study period

This study period of this trial is April 2017 to March 2023; the registration period is August 2018 to July 2020.

Ethics and dissemination

The present study is subject to ethical guidelines for clinical studies published by Japan's Ministry of Education, Science and Technology and Ministry of Health, Labour, and Welfare and the modified Act on the Protection of Personal Information as well as the ethical principles established for research on humans stipulated in the Declaration of Helsinki and further amendments thereto. If important protocol modifications are needed, the investigators will discuss them and report to the review board for approval. Regarding dissemination, the results obtained will be submitted for publication in peer-reviewed journals. The main and relevant findings will be presented at conferences.

DISCUSSION

This study is a multi-site randomized controlled trial to evaluate the efficacy of an integrated communication support program for rapidly progressive advanced cancer patients, caregivers, and oncologists to promote patient-centered communication. The intervention program is unique in intervening with both oncologists and patients/caregivers for a brief time at the time of first-line chemotherapy before they are critically ill.

In clinical oncology, the introduction of personalized precision medicine has allowed great therapeutic progress. While patient-oncologist communication is uncertain and complex, and busy oncologists often find it difficult to take extra time with their patients. As a result, personalized and precise communication between a patient and an oncologist may not be achieved. If empathic communication between patients and oncologists can be improved, including shared decision making based on patient values and preferences about the use of evidence-based medicine, the result can be an effective integration of best practices and patient values, allowing for better use of clinical expertise available resources.

In this study, it is essential that intervention facilitators and SPs be well trained to maintain the quality of the intervention. In the future, it may be possible to reduce costs

by developing internet-based programs. Regarding QPL, clinical benefits may increase when it is possible to link medical records with data from wearable devices. Above all, the use of electronic media is expected to make implementation of the intervention program easier.

Strengths and limitations of this study

This study has two methodological limitations. First, we involve both oncologists and patients/caregivers. The intervention program for both is complex, consisting of multiple factorial components. Thus, if the interventions prove superior to usual care, we cannot determine which interventions and components are most efficacious or beneficial in promoting their communication. Second, patient intervention will be applied only with patients with pancreatic cancer. The generalization potential for other cancers is unknown. However, because pancreatic cancer is one of most rapidly progressive, the intervention may be effective in other cancers.

Acknowledgements

We thank Ms. T Mashiko and Ms. M Kurosaki for their data management support. We also thank members of PanCan Japan, Ms. S Furutani, Dr M Mori, Dr Y

Shirai, Dr S Umezawa, Ms. N Inomata, Mr. M Umehashi, Dr M Okamura, Dr M Odawara, Dr A Hanai, Mr. R Soga, Ms. R Sugihara, Ms. T Akiyama and Ms. M Kanamaru for their support for this study.

Contributors

MF is a principal investigator. MY participated in this study as a patient and a caregiver. MF and YU developed the CST program. MF, AS, SJ, TO, YM and YU developed the QPL. MF, TO, TY, MI, MU, MO, KT, TM, YM and YU participated in the design of this study. All authors prepared the protocol and agree of final protocol and revisions. MF, AS, SJ, MT prepared of investigators brochure (IB) and CRFs. TY played a chief role in the statistical parts. TM played roles in the data management. MF drafted the manuscript. All authors participated in, read and approved the final manuscript.

Funding

This study is supported by a Grant-in-Aid for Japan Agency for Medical Research and Development (JP 17ck0106237h0001) and in part by The National Cancer Center Research and Development Fund (30-A-11). This funding source had no role in the design of this study and will not have any role during its execution, analyses,

interpretation of the data, or decision to submit results.

Sponsor

None

Competing interests

All authors declare that they have no competing interests regarding this work. TO has received research funding from Ono Pharmaceutical, Kowa, Dainippon Sumitomo Pharma, Chugai Pharmaceutical, Novartis, Yakult Honsha, AstraZeneca, Eizai, Lilly, Bristol-Myers Squibb. TY received consulting fees from Ono Pharmaceutical, Kowa, Japan Tobacco, Chugai Pharmaceutical, Tsumura & CO, CAC Croit, Asahi Intecc, Asahi Kasei Pharma and Clinical Trial. MI has received honoraria from Novartis Pharma, Bayer Yakuhin, Bristol-Myers Squibb, Abbott Japan, Eisai, Taiho Pharmaceutical, Eli Lilly Japan, Daiichi-Sankyo, Yakult, Otsuka Pharmaceutical, Nobelpharma, EA Pharma and Teijin Pharma, research funding from Bayer Yakuhin, Kyowa Hakko Kirin, Yakult, Taiho Pharmaceutical, Eli Lilly Japan, Ono Pharmaceutical, Eisai, AstraZeneca, Zeria Pharmaceutical, Chugai, Bristol Myers Sqiibb, Merck Serono, Kowa, Nano Carrier, ASLAN, Daiichi-Sankyo., Sumitomo Dainippon, Novartis Pharma, Baxalta, Boehringer Ingelheim and Takara Bio. He is a consulting or advisory role for Nano Carrier, Bayer

Yakuhin, Eisai, Kyowa Hakko Kirin, Novartis Pharma, Shire, MSD, Bristol Myers Sqiibb, Eli Lilly Japan, Sumitomo Dainippon, Daiichi-Sankyo, Teijin Pharma, Takara Bio and a board member of ASLAN, Chugai. MU has received honoraria from Taiho Pharmaceutical, Yakult Honsha, AstraZeneca, Novartis, Lilly, Teijin Pharma, Shire, Ono Pharmaceutical, and Merck Serono, and research funding from Taiho Pharmaceutical, Shire, Daiichi Sankyo, Eisai, AstraZeneca, Ono Pharmaceutical, MSD, Merck Serono, NanoCarrier, Dainippon Sumitomo Pharma, Incyte, ASLAN Pharmaceuticals, and Yakult Honsha. MO has received lecture fees from Taiho Pharmaceutical and honoraria from Taiho Pharmaceutical, Yakult, Bayer, Pfizer and Novartis.

Patient consent for publication

Not required.

Ethics approval

The protocol was reviewed and approved by the Institutional Review Board of National Cancer Center on 4 July 2018 (ID: 2014-474) as well as by the J-SUPPORT Scientific Advisory Board.

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Provenance and peer review

Not commissioned; externally peer reviewed.

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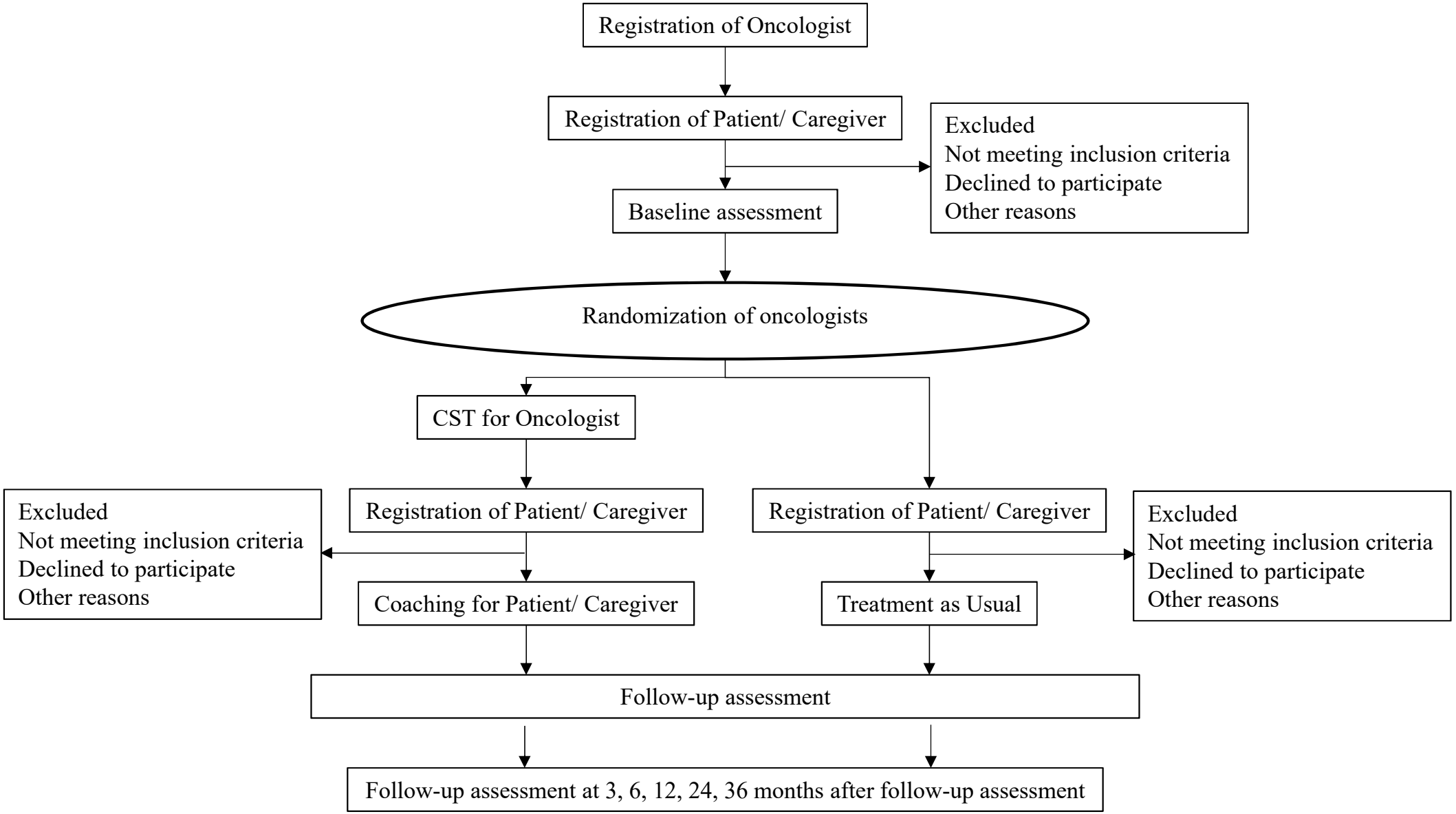

Figure 1. Participant flow diagram

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Appendices A

Informed Consent Form for Oncologists

医師用説明文書

医師への質問を支援する研究へのご協力のお願い

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はじめに

国立がん研究センターでは、患者さんのために最新の医療を提供するとともに、よりよい診断方法や治療方法、そしてがんに関するさまざまな症状を和らげる方法を開発するための取り組みをおこなっています。

このたび説明いたしますのは、すい臓がんに対する化学療法を受けている方を対象とし、患者さんやご家族から医療者に対してよくある質問を箇条書きにした具体的質問集を用いることによって、患者さん・ご家族、医師とのコミュニケーションが促進されるか否かを確認するための研究です。

本研究の内容について説明文書を読まれ、今回私たちが計画している研究の主旨をご理解いただき、その上でこの研究にご参加いただけましたら幸いに存じます。

１． 本研究の目的と意義

本研究では患者さん・ご家族と医師のコミュニケーションを促進するために、介入者（心理士、看護師、相談員）による質問支援を治療早期から導入することにより、治療選択がよりご本人の価値観に沿うものとなり、生活の質に良い影響を及ぼすかどうかを明らかにすることを目的としています。

医師は患者さん・ご家族に医療に関する説明を十分に行い、理解を確認し、患者さんご自身の自由意思に基づいた治療選択を求める必要があります。また、患者さん・ご家族は医師からの共感的行動を必要としていることが、これまでの研究において示されています。また、このような望ましいコミュニケーションが患者さんの健康の保持・増進、ストレスや前向きさによい影響を及ぼすということが明らかにされています。このように治療を行っていく過程において、患者さん・ご家族と医師の間のコミュニケーションは重要です。

そこで本研究では、患者さん・ご家族に対する質問支援プログラムを開発し、患者さん・ご家族－医師間の共感的コミュニケーション促進への有効性を検証します。このプログラムが有用であった場合には、治療早期から患者さん一人一人の自由意思に沿った医療の提供を促す支援法が実用化され、がん患者さんの生活の質を向上させるだけでなく、医師の負担を減らすことができます。一方、有用でなかった際にも、効果がなかった原因等を分析することで、今後有用と考えられる仕組みを作りあげることに役立つものと考えます。

２． 本研究の対象となる方について

すい臓がんと診断され、抗がん剤治療を受けている、満 20 歳以上の、日本語が理解できる患者さんの担当医が対象となります。また、患者さんとそのご家族の方自体も本研究の対象となっています。

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３． 本研究の内容と方法

本研究では、コミュニケーション・コーチングを受けるグループ（介入群）と受けないグループ（対照群）のどちらかにご参加頂きます。グループは無作為に割り当て、コミュニケーション・コーチングを受けるグループに割り当たった場合には、皆様のご都合のよい時間に、約 3 時間の講義とロールプレイを受けていただきます。コミュニケーション・コーチングを受けないグループに割り当たった場合には、通常通りの診察をおこなっていただきます。

どちらのグループに参加することになった場合にも、診察の様子を２回録音させていただきます。1 回目は同意取得後、２回目は、介入群は適格基準を満たす患者さん・ご家族が質問支援を受けられた次の週の診察後/対照群は通常診療の診察（T1）です。また T0（介入群がコミュニケーション・コーチングを受ける前）と T1 両方のタイミングで質問票を用いた調査にご協力頂きます。

本研究に参加して頂ける皆様には、個別の番号をつけさせていただき、研究で集めたデータは個別の番号がわからなければ個人が特定できないようにしたうえで、データセンター（国立がん研究センター社会と健康研究センター健康支援研究部）に集めます。本研究は、平成 30 年 4 月より平成 35 年 3 月までの間に行われます。最終の質問票を用いた調査を行った時点で、参加終了となります。一回の調査にかかる時間は 30 分程度です。

スケジュール

同意取得後	T0	介入	T1
両グループ： 診察場面の録音	両グループ： 質問票を用いた調査	介入群のみ： 介入者による質問支援 3 時間程度（※支援を受けるグループに割り当たった場合のみ）	両グループ： 診察場面の録音 その後、質問票を用いた調査

４． 研究への参加により予想される利益と不利益、評価調査終了後の対応

本研究に参加されても、通常診療と比べ、皆様が職務上、経済上の特別な利益を得られることはありません。

また、原則として皆様に不利益は生じないと考えておりますが、質問票の記入やコミュニケーション・コーチングが診療業務を行う上でご負担となる可能性があります。この研究への参加を、もしご負担に感じられるようでしたら、いつでもこの研究へのご協力を中止していただいてかまいません。

５． 健康被害が発生した場合の対応・補償について

本研究のコミュニケーション・コーチング による介入は投薬や処置といった治療行為

を含まないため、本研究によって有害事象が発生することは原則ないと考えられますが、万が一、本研究に関わる何らかの理由により、健康を害する状況が発生した場合には、適切な医療機関で対応させていただきます。これらの場合、用いられる保険は通常のあなたが加入されている医療保険となり、この研究からの補償金は発生いたしませんこと、予めご了承ください。

６． 参加いただかない場合でも不利益を受けないこと

本研究への参加は、皆様の自由意思にもとづくものであり、参加に同意されない場合でも皆様の今後の職務上において不利益を受けることは一切ありません。

７． 同意した後にいつでもこれを撤回できること

本研究への同意をいただいた後でも、いつでもこれを撤回することができます。参加への同意を撤回された場合でも、皆様の職務上において不利益を受けることは一切ありません。同意を撤回される場合には、お手数ですが、研究代表者までお知らせください。同意撤回時点までに集めたデータの研究利用も不可とするかどうかのご判断をいただくため、同意撤回文書のご提出をお願いいたします。

８． 研究にご参加いただいた場合の経済的な負担

本研究では、参加いただいた場合に皆様に特別な経済的負担はありません。

９． プライバシーの保護と個人の人権の擁護

本研究で得られた録音した IC レコーダー、解析の過程で生じるテキスト化したデータ及び書類等は、施錠可能なスペースで保管します。皆様のプライバシーに関する情報は、研究期間終了後５年間保存した後に、シュレッダー等を用いて破棄します。

また、当院の別の部署の担当者が、本研究が正しく行われているかを監査するために皆様の記録を見ることがありますが、この場合にも皆様のプライバシーは厳重に守られます。

１０.本研究に関する情報公開

本研究に関する情報については、大学病院医療情報ネットワーク臨床試験登録システム(UMIN-CTR)に登録し、公開いたします。

１１.データの二次利用について

本研究で得られたデータを二次利用することがあります。この場合は、個人を識別する情報と結びつかないよう匿名化した上、がん患者さんの生活の質の向上に役立てる目的に

限り、データを利用いたします。なお、本研究において提供された個人情報の管理責任者は、研究代表者/研究責任者の藤森麻衣子(項目 16 参照)となります。

１２.本研究の倫理審査について

本研究は、国立がん研究センター研究倫理審査委員会の審査を受け、内容や方法が適切であり、皆様の人権が守られていることが確認され、実施について承認を受け、国立がん研究センター理事長の研究許可を得たものです。

１３.参加いただく期間と研究全体の実施予定期間、予定参加人数

この研究は平成 30 年 4 月より平成 35 年 3 月まで行い、その後の結果の分析は平成 36 年 3 月までに行う予定です。研究全体の参加予定人数は約 560 名（医師　約 20 名・患者約 300 名・患者家族　約 240 名）を予定しております。

１４.本研究の資金と利益相反について

臨床研究における利益相反とは、研究者が企業等から経済的な利益の提供を受け、その利益の存在により臨床研究の結果に影響を及ぼす可能性がある状況のことをいいます。

本研究は、国立研究開発法人日本医療研究開発機構 平成 29 年度革新的がん医療実用化研究事業 領域 5 の研究（研究代表者：藤森麻衣子、課題管理番号：17ck0106237h0001）であり、その他の特定の団体からの資金提供や物品等の無償提供は受けておらず、研究組織全体に関して起こりうる利益相反はありません。

本研究に関する研究者の利益相反の管理は、参加施設それぞれが自施設の研究者に関して行っています。当センターにおける利益相反の管理は、国立がん研究センター利益相反委員会が行っていますので、詳細をお知りになりたい場合は、研究代表者までお問い合わせください。

１５.本研究に対して分からないことがある場合

本研究に関しまして、質問や疑問がありましたら、いつでも遠慮なく研究事務局までお問い合わせください。また、本研究への参加に同意しない場合でも、質問がありましたらお申し出ください。

１６.担当者の連絡先、研究代表者、研究責任者、研究事務局

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INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

【共同研究機関の研究責任者】

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国立がん研究センター東病院	肝胆膵内科	池田公史
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がん研究会有明病院	消化器内科	尾阪将人
東京女子医科大学病院	消化器内科	高山敬子

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TEL：03-3547-2511（PHS6032）

【説明者】

説明者名：（　　）

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

同 意 文 書

国立がん研究センター中央病院　病院長　殿

「医師への質問を支援する研究」
国立研究開発法人日本医療研究開発機構 平成 29 年度革新的がん医療実用化研究事業 領域 5
研究代表者：藤森麻衣子、課題管理番号：17ck0106237h0001

1. 本研究の目的と意義
2. 本研究の対象となる方について
3. 本研究の内容と方法
4. 研究への参加により予想される利益と不利益、評価調査終了後の対応
5. 健康被害が発生した場合の対応・補償について
6. 参加いただかない場合でも不利益を受けないこと
7. 同意した後にいつでもこれを撤回できること
8. 研究にご参加いただいた場合の経済的な負担
9. プライバシーの保護と個人の人権の擁護
10. 本研究に関する情報公開
11. データの二次利用について
12. 本研究の倫理審査について
13. 参加いただく期間と研究全体の実施予定期間、予定参加人数
14. 本研究の資金と利益相反について
15. 本研究に対して分からないことがある場合
16. 担当者の連絡先、研究代表者、研究事務局

私は、本臨床研究について以上の項目を説明しました。

説明日：　平成　　年　　月　　日
説明者氏名：＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿(自署)

私はこの臨床研究に参加するにあたり、試験の内容について担当者より十分な説明を受けました。試験の内容を理解しましたので、参加することについて同意します。

同意日：　平成　　年　　月　　日

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

氏名： _____（自署）

Appendices B

Informed Consent Form for Patients and Caregivers

患者さん・同伴者の方用説明文書

医師とのコミュニケーションを支援する研究へのご協力のお願い

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

はじめに

国立がん研究センターでは、患者さんのために最新の医療を提供するとともに、よりよい診断方法や治療方法、そしてよりよいケアを開発するための取り組みをおこなっています。

このたび説明いたしますのは、すい臓がんに対する化学療法を受けている方を対象とし、医療に関わる人達（医師、看護師、心理士、相談員等）に対してよくある質問を箇条書きにした具体的質問集を用いて患者さん、同伴者の方、医師とのコミュニケーションが促進されるか否かを確認するための研究です。

本研究の内容について説明文書を読まれ、今回私たちが計画している研究の主旨をご理解いただき、その上でこの研究にご参加いただけましたら幸いに存じます。

1. **本研究の目的と意義**

本研究では患者さん・同伴者の方と担当医師間のコミュニケーションの改善が、患者さんの生活の質に良い影響を及ぼすかどうかを明らかにすることを目的としています。本研究では、患者さんから医師へのよくある質問集を用いて患者さんが担当医師への質問をしやすくするお手伝いを治療早期から導入します。

患者さん・同伴者の方―医師のコミュニケーションは治療を進めていく上でとても重要です。医師は患者さん・同伴者の方に医療に関する説明を十分に行い、理解を確認し、患

者さんご自身の自由意思に基づいた治療選択を求める必要があります。また過去の研究で、患者さん・ご家族は医師からの共感的行動を必要としていることが示されています。このような治療についての十分な説明と共感的行動を含む望ましいコミュニケーションが患者さんの健康の保持・増進、ストレスや前向きさによい影響を及ぼすということが明らかにされています。

そこで本研究では、患者さん・同伴者の方に対して具体的な質問集を用いて医師への質問をしやすくするプログラムを開発し、患者さん・同伴者の方－医師間の共感的コミュニケーション促進への有効性を検証します。このプログラムが有用であった場合には、治療早期からお一人お一人の自由意思に沿った医療の提供を促す支援方法が実用化され、がん患者さんの生活の質を向上させることができます。一方、有用でなかった際にも、効果がなかった原因等を分析することで、今後有用と考えられる仕組みを作りあげることに役立つものと考えます。

2. 本研究の対象となる方の病状と治療について

すい臓がんと診断され、抗がん剤治療を受けている、満 20 歳以上の、日本語が理解できる患者さんと同伴者の方、担当医が対象となります。

3. 本研究の内容と方法

本研究では、皆様に３つのグループ（グループ１、グループ２－１、グループ２－２）

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のいずれかに入っていただきます。グループ１、グループ２のどちらに入るのかは、調査の時期によって、調査者からお願いさせていただきます。

グループ１では、参加に同意を頂きましたら、診察場面の録音をさせていただき、質問票への回答をお願いいたします。

グループ２では、具体的な質問集を用い医師への質問をしやすくするお手伝い（以下、コミュニケーション支援と呼びます）を受けるグループ２－１と、受けないグループ２－２のどちらかに入っていただきます。２－１と２－２どちらのグループに入るかは、患者さんご自身のご希望や担当医の判断で決まるのではなく、「ランダム化」という方法で、コンピューターを使って、五分五分の確率でどちらかに入ります。コミュニケーション支援を受けるグループ２－１に入った場合には、次回の抗がん剤の治療の待ち時間、あるいは治療中（皆様のご都合のよい時間）にコミュニケーション支援を行うトレーニングを受けた者（心理士等）からコミュニケーション支援を受けていただきます。コミュニケーション支援を受けないグループ２－２に入った場合には、通常通りの診療になります。どちらのグループも、ご参加頂いた時(第 1 週)と第 3 週、3 か月後、6 か月後、1 年後、2 年後、3 年後に質問票を用いた調査にご協力頂くことになります。3か月以降の調査につきましては、事前に改めてお電話にてご依頼をさせていただきます。また、第 3 週目の診察の様子を録音させて頂きます（下記、スケジュールをご参照ください)。

さらに、診察予約状況、現在受けられている治療に関するカルテ記載を担当の医師の許

可を得て使用させて頂きます。また、皆様の診療内容や医療費に関する情報を把握するために、診療情報（介護保険、診療報酬明細書の情報を含む）を閲覧させて頂きます。

本研究に参加頂くことに同意していただきましたら、皆様には個別の番号をつけさせていただきます。すべてのデータは、個別の番号がわからなければ個人が特定できないようにしたうえで、データセンター（国立がん研究センター社会と健康研究センター健康支援研究部）に集めます。

本研究は、平成 30 年 4 月より平成 35 年 3 月までの間に行われます。最終の質問票の調査を行った時点で、参加終了となります。

スケジュール

<グループ 1 の場合>

同意取得後
医師の診察の録音 質問票を用いた調査

<グループ 2 – 1 の場合>

同意取得後	第 2 週	第 3 週	3，6，12，24，36 か月後

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第一回目の質問票を用いた調査 10 分～30 分程度	医師より質問集配布。 具体的な質問集を用いたコミュニケーション支援。 40 分～60 分程度	医師の診察の録音。 質問票を用いた調査 10 分～30 分程度	フォローアップのための質問票を用いた調査 これらの調査は、来院時に実施します。転院された場合は郵送にて実施させていただきます。 10 分～30 分程度

＜グループ２－２の場合＞

同意取得後	第 2 週	第 3 週	3，6，12，24，36 か月後
第一回目の質問票を用いた調査 10 分～30 分程度	通常通りの診療	医師の診察の録音。 質問票を用いた調査 10 分～30 分程度	フォローアップのための質問票を用いた調査 これらの調査は、来院時に実施します。転院された場合は郵送にて実施させていただきます。 10 分～30 分程度

4. 研究への参加により予想される利益と不利益、評価調査終了後の対応

本研究に参加されても、通常診療と比べ、患者さんが診療上、経済上の特別な利益を得られることはありません。

質問票の記入や面談が体調や気持ちの上でご負担となる場合があります。この研究への参加を、もしご負担に感じられるようでしたら、いつでもこの研究へのご協力を中止していただいてかまいません。なお、調査は個人差もありますが、１回 30 分程度の時間を要するため、グループ 1 に参加頂いた方には、調査終了後 500 円分のクオカードを差し上げま

す。また、グループ２－１、グループ２－２に参加頂いた方には、1 回目の調査時にはトートバックとボールペン、2 回目以降の調査では１回につき 500 円分のクオカードを差し上げます。

5. 健康被害が発生した場合の対応・補償について

本研究は投薬や処置といった治療行為を含まないため、本研究によって有害事象が発生することは原則ないと考えられますが、万が一質問票を用いた調査や面談により、気分の落ち込みや不安など、ご不快な状況が発生した場合には、外来・病棟スタッフまたは当院の精神腫瘍科チームが対応させていただきます。これらの場合、用いられる保険は通常のあなたが加入されている医療保険となり、この研究からの補償金は発生いたしませんこと、予めご了承ください。

6. 参加いただかない場合でも不利益を受けないこと

本研究への参加は、皆様の自由意思にもとづくものであり、参加に同意されない場合でも、患者さんご自身の今後の治療において不利益を受けることは一切ありません。

7. 同意した後にいつでもこれを撤回できること

本研究への同意をいただいた後でも、いつでもこれを撤回することができます。参加への同意を撤回することで不利益を受けることは一切ありません。同意を撤回される場合に

は、お手数ですが、担当医または研究代表者までお知らせください。同意を撤回する時点までに集めたデータの研究利用も不可とするかどうかのご判断をいただくため、同意撤回文書のご提出をお願いいたします。

8. 研究にご参加いただいた場合の経済的な負担

本研究にご参加いただくことで皆様の費用負担が通常より増えることはありません。

9. プライバシーの保護と個人の人権の擁護

本研究で得られた録音した IC レコーダー、診療情報（介護保険、診療報酬明細書の情報を含む）、解析の過程で生じるテキスト化したデータ及び書類等は、施錠可能なスペースで保管します。皆様のプライバシーに関する情報は、研究期間終了後 5 年間保存した後に、紙媒体はシュレッダー、電子媒体はデータの完全消去などにて破棄します。

また、当院の別の部署の担当者が、本研究が正しく行われているかを監査するために皆様の記録を見ることがありますが、この場合にも皆様のプライバシーは厳重に守られます。

10. 本研究に関する情報公開

本研究に関する情報については、大学病院医療情報ネットワーク臨床試験登録システム(UMIN-CTR)に登録し、公開いたします。

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11. データの二次利用について

本研究で得られたデータを二次利用することがあります。この場合は、個人を識別する情報と結びつかないよう匿名化した上、がん患者さんの生活の質の向上に役立てる目的に限り、データを利用いたします。なお、本研究において提供された個人情報の管理責任者は、研究代表者/研究責任者の藤森麻衣子(項目 16 参照)となります。

12. 本研究の倫理審査について

本研究は、国立がん研究センター研究倫理審査委員会の審査を受け、内容や方法が適切であり、皆様の人権が守られていることが確認され、実施について承認を受け、国立がん研究センター理事長の研究許可を得たものです。

13. 参加いただく期間と研究全体の実施予定期間、予定参加人数

この研究は平成 30 年 4 月より平成 35 年 3 月まで行い、その後の結果の分析は平成 36 年 3 月までに行う予定です。研究全体の参加予定人数は約 560 名を予定しております。

14. 本研究の資金と利益相反について

臨床研究における利益相反とは、研究者が企業等から経済的な利益の提供を受け、その利益の存在により臨床研究の結果に影響を及ぼす可能性がある状況のことをいいます。

本研究は、国立研究開発法人日本医療研究開発機構 平成 29 年度革新的がん医療実用化

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

研究事業 領域 5 の研究（研究代表者：藤森麻衣子、課題管理番号：17ck0106237h0001）であり、その他の特定の団体からの資金提供や物品等の無償提供は受けておらず、研究組織全体に関して起こりうる利益相反はありません。

本研究に関する研究者の利益相反の管理は、参加施設それぞれが自施設の研究者に関して行っています。当センターにおける利益相反の管理は、国立がん研究センター利益相反委員会が行っています。詳細をお知りになりたい場合は、担当医までお問い合わせください。

15. 本研究に対して分からないことがある場合

本研究に関しまして、質問や疑問がありましたら、いつでも遠慮なく研究事務局までお問い合わせください。また、本研究への参加に同意しない場合でも、質問がありましたらお申し出ください。

16. 担当者の連絡先、研究代表者、研究責任者、共同研究機関の研究責任者、研究事務局

【研究代表者/研究責任者】 藤森麻衣子

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【共同研究機関の研究責任者】

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

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がん研究会有明病院	消化器内科	尾阪将人
東京女子医科大学病院	消化器内科	高山敬子

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【説明者】

説明者名：（　　）

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

同 意 文 書

国立がん研究センター中央病院　病院長　殿

「医師とのコミュニケーションを支援する研究」

国立研究開発法人日本医療研究開発機構 平成 29 年度革新的がん医療実用化研究事業 領域 5

研究代表者：藤森麻衣子、課題管理番号：17ck0106237h0001

1. 本研究の目的と意義

2. 本研究の対象となる方の病状と治療について

3. 本研究の内容と方法

グ ル ー プ 1：□診察場面の録音・□質問票を用いた調査・□診療情報の収集

グループ２－１：□質問票を用いた調査・介入：□診察場面の録音・□診療情報の収集

グループ２－２：□質問票を用いた調査：□診察場面の録音・□診療情報の収集

4. 研究への参加により予想される利益と不利益、評価調査終了後の対応

5. 健康被害が発生した場合の対応・補償について

6. 参加いただかない場合でも不利益を受けないこと

7. 同意した後にいつでもこれを撤回できること

8. 研究にご参加いただいた場合の経済的な負担

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

9. プライバシーの保護と個人の人権の擁護

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15. 本研究に対して分からないことがある場合

16. 担当者の連絡先、研究代表者、研究責任者、共同研究機関の研究責任者、研究事務局

私は、本臨床研究について以上の項目を説明しました。

説明日： 平成 年 月 日

説明者氏名： （自署）

私はこの臨床研究に参加するにあたり、試験の内容について担当者より十分な説明を受けました。試験の内容を理解しましたので、参加することについて同意します。

同意日： 平成 年 月 日

氏名： （自署）

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Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	7
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	7
Protocol version	#3	Date and version identifier	7
Funding	#4	Sources and types of financial, material, and other support	31
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	31
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	32
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	31
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		other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
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Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	9
Objectives	#7	Specific objectives or hypotheses	12
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	13
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	13

Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	16
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Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	19
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	19
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	27
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	27
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	27
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further	19

		details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	27
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	25
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	32
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Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	13
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	28

Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	18
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	42
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Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	32
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	7
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	25
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	28

Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	28
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	7
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Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

BMJ Open

An integrated communication support program for oncologists, caregivers, and patients with rapidly progressing advanced cancer to promote patient-centered communication: J-SUPPORT 1904 study protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036745.R1
Article Type:	Protocol
Date Submitted by the Author:	12-Jun-2020
Complete List of Authors:	Fujimori, Maiko; National Cancer Center Japan, Division of Health Care Research, Behavioral Science and Survivorship Research Group, Center for Public Health Sciences, National Cancer Center Japan Sato, Ayako; National Cancer Center Japan, Division of Health Care Research, Behavioral Science and Survivorship Research Group, Center for Public Health Sciences Jinno, Sayaka; National Cancer Center Japan, Division of Health Care Research, Behavioral Science and Survivorship Research Group, Center for Public Health Sciences Okusaka, Takuji; National Cancer Center Hospital, Hepatobiliary and Pancreatic Oncology Division Yamaguchi, Takuhiro; Tohoku University Graduate School of Medicine Department of Medical Biochemistry, Division of Biostatistics Ikeda, Masafumi; National Cancer Center-Hospital East, Department of Hepato-bliary Pancreatic Oncology Ueno, Makoto; Kanagawa Cancer Center, Department of Gastroenterology, Hepatobiliary and Pancreatic Medical Oncology Division Ozaka, Masato; Public Interest Incorporated Foundation Cancer Institute Hospital of JFCR, Department of Hepatobiliary and Pancreatic Medical Oncology Takayama, Yukiko; Tokyo Women's Medical University Hospital, Department of Medicine, Institute of Gastroenterology Miyaji, Tempei; Tokyo Medical University School of Medicine Graduate School of Medicine, Department of Clinical Trial Data Management Majima, Yoshiyuki; Pancreatic Cancer Action Network Uchitomi , Yosuke; Innovation Center for Supportive, Palliative and Psychosocial Care, National Cancer Center Hospital, & Behavioral and Survivorship Research Group, Center for Public Health Sciences
Primary Subject Heading:	Communication
Secondary Subject Heading:	Oncology, Palliative care, Patient-centred medicine
Keywords:	Adult oncology < ONCOLOGY, Adult palliative care < PALLIATIVE CARE, MENTAL HEALTH, SOCIAL MEDICINE

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INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

TITLE: An integrated communication support program for oncologists, caregivers, and patients with rapidly progressing advanced cancer to promote patient-centered communication: J-SUPPORT 1904 study protocol for a randomized controlled trial

RUNNING TITLE: Integrated communication program for advanced cancer patients and oncologists

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Word count: 3716 words, excluding title page, abstract, references, figures, and tables

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

ABSTRACT

Introduction

Communication is an essential aspect of care for patients with progressive serious illnesses. This study aims to evaluate the efficacy of a new, integrated communication support program for oncologists, patients with rapidly progressing advanced cancer and their caregivers.

Methods and Analysis

The proposed integrated communication support program is in the randomized control trial stage. It comprises a cluster of oncologists from comprehensive cancer center hospitals in a metropolitan area in Japan. A total of 20 oncologists, 200 patients with advanced pancreatic cancer, and the patients' caregivers are enrolled in this study as of the writing of this protocol report. Oncologists are randomly assigned to the intervention group (IG) or control group (CG). Patients and caregivers are allocated to the same group as their oncologists. The IG oncologists receive a 2.5-hour individual communication skills training, and patients and caregivers receive a half-hour coaching intervention to facilitate prioritizing and discussing questions and concerns; the CG participants do not receive any training. Follow-up data will be collected quarterly for 6 months for a year

and then annually for up to three years. The primary endpoint is the intergroup difference between before- and after-intervention patient-centered communication behaviors during oncology visits.

Ethics and dissemination

This study is conducted in accordance with the ethical guidelines for clinical studies published by Japan's Ministry of Education, Cultural, Sports, Science, and Technology, the Ministry of Health, Labour, and Welfare (MHLW), and the ethical principles established for research on humans stipulated in the Declaration of Helsinki and further amendments thereto. The protocol was approved by the Institutional Review Board of National Cancer Center, Japan on July 4, 2018 (ID: 2017-474).

Trial status

This study is currently enrolling participants; enrollment period ends July 31, 2020; estimated follow-up date is March 31, 2023.

Trial registration number

UMIN Clinical Trial Registry: UMIN000033612; Pre-results.

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

(299 words)

Keywords: Advance Care Planning, Caregivers, Communication, Decision making, Empathy, End-of-life care, Patient-centered care, Patient-physician relationship, Quality of life

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

ARTICLE SUMMARY

Trial registration: The protocol registered on 2nd August, 2018 at UMIN Clinical Trial Registry. The registration number is UMIN000033612.

Data statement: Study protocol, data definition tables, and dataset will be uploaded to the UMIN- Individual Case Data Repository, https://www.umin.ac.jp/icdr/index-j.html.

Protocol version: The protocol version is 1.4 on 20th December, 2019.

Strengths and limitations of this study:

- A strength of this study is the use of a large group of patients, caregivers, and oncologists in the real-world scenario for which the intervention is being tested.
- The use of multicenter participant samples, controls, and patient follow-up allows for reliable study results.
- This study includes oncologists, patients, and caregivers for intervention.
- The intervention program is complex, consisting of multiple factorial components, which makes it difficult to determine which interventions and components are most efficacious or beneficial; however, participants provide subjective

assessments of the intervention components.

- The study only involves pancreatic cancer, so the generalization potential for other cancers is unknown. However, as pancreatic cancer is one of the most rapidly progressing cancers, the intervention may also be effective for patients with other cancers.

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

INTRODUCTION

Pancreatic cancer is the fourth leading cause of death in Japan, with approximately 35,000 new cases diagnosed per year, matching the approximate annual number of deaths from the disease nationally.[1] Over 40% of patients with pancreatic cancer are stage IV at diagnosis, and the 5-year survival rate is 7%.[2] Although the initial treatment goal for pancreatic cancer is to cure, even prolonged survival and maintenance of QOL are difficult to achieve.

Most patients with advanced cancer prefer to discuss their prognosis and treatments with their physicians.[3] However, physicians may feel burdened by open discussions for fear of patients losing hope, or they may face resistance from caregivers;[4] therefore, these discussions rarely occur.[5] Consequently, patients often overestimate the hopefulness of prognoses, underestimate disease severity, and have unrealistic expectations for a cure.[6] Patients who have not discussed prognosis and treatment choices with their oncologists are 3 to 8 times more likely to receive aggressive treatments in their last week of life.[5,7] Although oncologists and patients find that prognostic discussions can be stressful, unnecessary expenses and actual harm to the patient may result from uninformed decisions.[8] Additionally, it has been shown that open discussions do not cause hopelessness or increased fear in patients and that well-

informed patients make more appropriate treatment choices.[9,10] Hence, oncologists need to provide adequate information regarding cancer treatment decisions for patients and their caregivers approaching the end of life, confirm patients' and caregivers' understanding, and achieve shared decision making about treatment and care based on patients' personal values, life goals, and treatment preferences.

In previous study, patients from the diagnosis to the discontinuation of anti-cancer drug treatment stage (mainly pancreatic cancer patients) showed to desire more "empathic communication" from oncologists.[11] Empathic communication by oncologists reduces patients' psychological distress,[12] increases trust in the oncologist,[12] and enhances information recall.[13] Empathic communication is essential especially for patients with rapidly progressing serious illnesses. Therefore, communication skills training (CST) programs have been developed to help physicians to facilitate communication behaviors that strengthen relationships with patients.[14] CST involves learner-centered workshop held in small groups and including role-play with simulated patients (SPs).[15] It is strongly recommended that medical professionals train themselves in communication skills based on American Society of Clinical Oncology Consensus Guidelines for patient–clinician communication.[16] Learning tools (e.g., www.vitaltalk.org) are available to medical practitioners to support this learning.

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

We conducted a prior survey clarifying the four elements of communication skills patients prefer oncologists to have, referred to as SHARE: "setting," "how to deliver the bad news," "additional information," and "reassurance and emotional support."[17,18] A two-day SHARE-CST program for oncologists was developed based on these preferences.[19] The program is a small-group workshop including the above-mentioned modules; it employs role-play with simulated patients and immediate feedback[15] to allow learners to practice discussing serious news with cancer patients and caregivers, such as transition to palliative care when chemotherapy is failing. The program emphasizes that physicians respect the values of each patient and provide reassurance and emotional support in Asian culture.[20] Our previous randomized controlled trial (RCT) of physicians, including oncologists treating pancreatic cancer, showed that oncologists who participated in SHARE-CST improved their behavior in terms of patient-preferred communication as well as their self-confidence in communication with patients and that their patients experienced a relatively low level of psychological distress and a high level of trust in the oncologist.[12] In Japan, SHARE-CST was implemented as a 10-year project commissioned by the MHLW for physicians nationwide after the enactment of the National Cancer Control Act. Participants reported that their empathic communication attitudes and abilities had improved;[21] however, it

was difficult for most oncologists to participate in two-day CST group workshops because of the busy clinical oncology settings in which they worked.

Patient-centered approaches using question prompt lists (QPLs) have also been proposed for the improvement of patient-physician communication. A QPL is an inexpensive communication tool employing a structured question list to encourage patient question-asking and participation during consultations.[22] The provision of a QPL and implementation of communication interventions with QPL before consultation is effective in promoting patient question-asking behavior and participation in the consultation and in decreasing patients' anxiety.[23] Our previous RCT of patients with advanced gastric, colorectal, esophageal, and lung cancer showed that QPL was useful in making initial treatment decisions for them but failed to promote patient question-asking behavior,[24] in part because Japanese patients tend to wait for physicians to encourage them to ask questions.[25] The number of patients asking their physician questions was median 1, compared to mean/median 8.5 to 14 in studies in Western countries.[23,24] In Japan, it has been reported that cancer patients have preference of not being burden to others and of "omakase" (leaving the decision-making to a medical expert), and it is difficult to elicit the patient's preference.[26] Thus, in Japan, integrated interventions combining CST for oncologists and communication coaching with QPL for patients

might increase patient questioning behavior and improve patient-centered communication in consultations.[27,28]

Based on the results of previous trials, this study aims to evaluate the efficacy of a new, integrated communication support program, consisting of a CST for oncologists and communication coaching with QPL for patients with rapidly progressing advanced cancer and their caregivers, promoting oncologists' patient-centered communication behaviors. We hypothesize that, compared to treatment as usual (TAU), the intervention will increase oncologists' patient-centered communication behaviors, increase patients' question-asking behaviors, and improve patient well-being and health services utilization by reducing aggressive interventions and increasing use of palliative care.

METHODS and ANALYSIS

This protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and SPIRIT PRO Extension Guidelines.[29,30]

Study design

This study is a single-blind cluster RCT conducted in four metropolitan cancer-

treatment hospitals: the National Cancer Center Hospital, the National Cancer Center Hospital East, the Cancer Institute Hospital, and the Kanagawa Cancer Center Hospital. This study protocol has been reviewed and approved by the protocol review committee of the Japan Supportive, Palliative, and Psychosocial Oncology Group as J-SUPPORT 1704 and by the Institutional Review Boards at each participating institution.

An independent data center provides computer-generated random allocation sequences. The assignment sequence is centrally managed; assignment results are automatically sent to a clinical research coordinator (CRC), electronically. The oncologist participants are randomly assigned to an intervention group (IG) or control group (CG) after the baseline phase; patient/caregiver participants are assigned to the same group as their oncologists. A stratified block-randomization scheme is used to assure balanced assignment by site. Within each site, oncologists are randomly assigned approximately evenly across IG and CG. Participants in IG provide intervention in addition to TAU, and are unblinded.

Intervention

Oncologists

We modified the original SHARE-CST design,[12] adopting a 2.5-hour

individual program with a facilitator and a simulated patient (SP), consisting of lecture with a textbook (30 min) and 2 role-plays with immediate feedback (see Table 1). The original SHARE-CST is a small group consisting of 4 oncologists, 2 facilitators and 2 SPs, and included a lecture and 8 role-plays (twice per oncologist) with immediate feedback. The lecture cites evidence of the most important and common patient preferences regarding communication—empathic responses and encouragement to ask questions—and the variability of patients' preferences in discussing prognoses and being/not being dispassionate; it also demonstrates how to check and elicit patient preferences. Additionally, the lecture explains the QPL and discusses frequently asked questions from patients about information related to treatment and care after standard treatment that relates to patients' personal values, life goals, and preferences, as well as those of their caregivers. During the role-playing and discussion, participants are required to consider a patient's emotions and concerns caused by bad news, recognition of their disease, social situations, and information that they would want to know, and to empathize with the patient. Role-play also includes dealing with patients who bring QPLs.

Facilitators provide a lecture, lead the role-play, and discuss patients' potential emotions and communication-related preferences. Facilitators include psychiatrists, psychologists, and oncologists, all of whom have had 3 years or more of clinical

experience in oncology and participated in specialized 30-hour training workshops facilitating communication skills in oncology. The SPs have also participated in train-the-trainer workshops and 15 hours of SP training.

Patient and Caregiver

Communication coaching for patients was developed to facilitate communication with physicians using a 63-question QPL based on in-depth focus-group interviews with 18 participants (5 pancreatic cancer patients, 3 caregivers patients with pancreatic cancer, 4 bereaved people who had lost a family with pancreatic cancer, and 6 pancreatic oncologists), and previous QPL studies.[23,24,31] The QPL is a 10-page A4 sheet containing 63 questions grouped into 8 topics (diagnosis and stage of the disease, current and future treatments, management of current/possible future symptoms, daily life activities, care and prognosis post standard treatment, caregivers' needs, psychological distress and management, and values) and a space for free questions. Patient communication coaching using the QPL is a half-hour program, conducted individually or with a caregiver, consisting of reading the list to select personally relevant questions, prioritizing selected questions, discussing difficulties in asking the questions to their one's oncologist at their next oncology visit, and practicing asking their one's oncologist these

questions. The intervention is to be provided to patients individually or with caregivers by clinical psychologists and nurses who have participated in a 10-hour intensive training workshop using an intervention manual. All intervention sessions are noted and summarized. Before patients' visits, the oncologist is told which the questions the patient chose to ask from the QPL and the summary of the intervention. Intervention providers hold weekly conferences to review their coaching sessions.

Control condition

CG oncologists are provided neither training nor educational materials. Patients/caregivers in the CG are provided TAU.

Participants

Oncologists

Enrolled oncologists must (1) be mainly engaged in anticancer drug treatment of pancreatic cancer patients; (2) have provided written informed consent for trial participation.

Patients

Enrolled patients must (1) have a diagnosis of pancreatic cancer (adenocarcinoma); (2) have unresectable pancreatic cancer (UICC stage III or IV) or postoperative recurrence; (3) receive a first-line chemotherapy and be scheduled for a second course; (4) be aged 20 years or older; (5) have a ECOG performance status score of 0 or 1; (6) regularly visit an enrolled oncologist; (7) provide written informed consent for trial participation; and (8) be able to read, write, understand, and speak Japanese.

Patients are excluded if they are (1) judged by their oncologist to have cognitive impairment; (2) unable to complete an electronic Patient Reported Outcome (e-PRO) Questionnaire; or (3) judged unsuitable for participation by their oncologist.

Caregivers

If an enrolled patient is accompanied by a caregiver, the caregiver is also approached. Enrolled caregivers must (1) be aged 20 years or older; (2) regularly accompany an enrolled patient as primary caregiver; (3) provide written informed consent to trial participation; (4) be able to read, write, understand, and speak Japanese.

Caregivers are excluded if they are unable to complete an electronic Patient Reported Outcome (e-PRO) Questionnaire.

Procedures

This study consists of 3 phases: a baseline phase, an intervention phase, and a follow-up phase (Figure 1). The schedule for outcome measurement is shown in Table 2. After completing the intervention phase, data analysis will ensue. After this study has closed, oncologists in the control group will be provided with the intervention on demand.

Baseline phase

This phase involves oncologist and patient/caregiver recruitment as well as pre-randomization data collection on oncologists' communication behaviors as baseline data for use as a covariate in the RCT analysis. In this phase, 3 to 5 patients and their caregivers (if available) will be recruited for each oncologist. Participants will be asked to allow themselves to be audio-recorded at one oncology visit for primary and secondary communication behavior outcomes and to provide some evaluation on consultation as to study measures for potential use as covariates in the RCT analyses (Table 2).

Intervention phase

This phase involves oncologist randomization, intervention for participants in IG, and follow-up assessment. After oncologists are randomly assigned to the IG or CG, those

in the IG receive an individual intervention.

Next, 10 patients and their caregivers (if available) who regularly visit the oncologist are recruited and assigned to the IG or CG. After the IG patients and their caregivers receive an intervention, or 2 weeks to 1 month after baseline in the CG, the conversation between the patient/caregiver and the oncologist at their next consultation is audio-recorded. After the visit, patients/caregivers and the oncologists rate the consultation using a follow-up assessment.

Long-term follow-up phase

Patients and their caregivers will be encouraged to provide long-term follow-up assessments at 3, 6, 12, 24, and 36 months after the first follow-up assessment to evaluate effects on patient's physical and psychological condition and medical utilization at end of life. Caregivers are also asked to provide another assessment at 2 to 6 months post–patient death.

Data management, central monitoring, data monitoring, and auditing

We will collect all data, except for audio-recorded data, through electronic data capture (EDC) and electronic patient reported outcomes (ePRO) systems or paper-based

PRO questionnaires (pPRO) if patients are prevented from using the electronic approach. If participants fail to respond to ePRO or pPRO, a CRC blinded to the assignment will elicit their answers to avoid missing data. Data management and central monitoring will be performed using EDC VIEDOC 4 (PCG Solutions, Uppsala, Sweden) by the J-SUPPORT Data Science Team. Auditing is not planned for this study.

Concomitant treatments

There is no restriction on concomitant treatments.

Stopping rules for participants

If a participant meets any of the following conditions, the research team can discontinue the intervention; however, the participant will not be considered to have dropped out of the trial at that stage and will still receive the assessments: (1) the participant wishes to stop the intervention; (2) the research team judges that the risk of the intervention is greater than the benefit for any reason; (3) the research team judges that it is difficult to continue the intervention because of clinical deterioration; and (4) the research team judges that it is inappropriate to continue the intervention for any reason.

Stopping assessment

If a participant withdraws consent for assessment, he or she will not be followed up. Subjects will be excluded from the intention-to-treat (ITT) cohort of the trial only if they are found to meet any exclusion criteria at baseline after participation.

Assessment measures

Table 2 shows the schedule for outcome measurement.

Primary outcome measure

Oncologist's patient-centered communication behaviors

The audio-recorded oncology visits for all participants will be coded for each of the four factors of communication behaviors based on patient preference, referred to as SHARE: setting, delivery of information, additional information, and reassurance and emotional support (see Table 1).[19] The SHARE-RE factor is used as a primary outcome to measure empathic communication between patient/caregiver and oncologist after intervention for both.

Following previous study methods,[19] impressions of conversations from consultations will be assessed using the SHARE-RE factor score, consisting of 8 categories for analysis, in a random order, by two blinded coders who have been trained

for 30 hours or more on two occasions with a rating manual.

Secondary outcome measure

Oncologist's Patient-preferred communication behavior

Patient-preferred communication will be analyzed using impression ratings from two blinded coders, as described above. The analysis will include the audio-recorded oncology visits for all participants using the total SHARE score, for all 27 categories.[18,19] Following previous study methods,[19] the 40 categories of the Roter Intention Analysis System (RIAS) will also be used in assessing patient-preferred communications.[32]

Patient's and caregiver's communication behavior

Following previous study methods,[19] the 40 categories of the Roter Intention Analysis System (RIAS) will also be used in assessing patient's and caregiver's communications behavior, for example question-asking.[32]

Patient-reported outcome measures

Several scales will be used to produce a comprehensive profile of each patient

participant. These include the Hospital Anxiety and Depression Scale (HADS);[33] the Physical and Functional Well-being subscales of the Functional Assessment of Cancer Therapy (FACT-Physical & Functional);[34] the Short version of the Comprehensive Quality of Life Outcome inventory (CoQoLo);[35] the Trust in Oncologists Scale (TiOS);[36] the Client Satisfaction Questionnaire (CSQ);[37] the Peace, Equanimity, and Acceptance in the Cancer Experience (PEACE) questionnaire;[38] and the Prognosis and Treatment Perceptions Questionnaire (PTPQ).[39]

Patients' relevant medical and sociological background information includes stage, diagnosis date, treatment status, treatment history, comorbidities, sex, age, job status, household income, household size, social support, marital status, educational experience, treatment, and care preference at the end of life. Medical utilization at the end of life will be determined by the date of death, any chemotherapy agent given within 14 days of death, any new chemotherapeutic regimen started within 30 days of death, and involvement of hospice and palliative care services; all of this information is obtained from medical fee information and the caregivers post–patient death.[27]

A patients' assessment of the intervention's usefulness includes "Did you understand how to use the QPL and did you actually use it?" "Do you think you will continue the intervention?" and "Was the intervention useful to you?" Their assessment

of oncologists includes “Did the oncologist talk about the QPL?" and “How did the oncologist respond to your questions?” Their assessment of QPL includes “Did the QPL help you ask the oncologist questions?” “Is the QPL useful?” “Did you read the QPL before the visit?” and “Do you think you will read the QPL in the future?” as well as whether they asked selected questions to oncologist after the visit, which questions they selected, and “How much you have discussed with your oncologist in the visit?” in the intervention phase.

Caregiver survey measures

Several scales will also be used to gain a comprehensive view of caregivers, including the K6 nonspecific psychological distress scale (K6);[40] the 5 Dimension EuroQol (EQ-5D);[41] and the CSQ.[37] After the patient’s death, the caregiver’s QOL as the bereaved is measured with the Short version of the Good Death Inventory (GDI).[42]

Caregivers’ relevant sociological background information includes sex, age, relationship with the patient, job status, household income, household size, social support, marital status, educational experience, and treatment and care preferences at end of life.

After the first post-intervention visit, caregivers in the IG will evaluate the

intervention, the oncologist, and the QPL and report any selected questions used with the oncologist.

Oncologist survey measures

The relevant data concerning the oncologists include their sociological background (sex, age, and clinical experience). The oncologists' evaluation of medical utilization by the patient will be set by their recollection of the dates.

The usefulness of the intervention will also be measured using evaluations provided by the oncologists in the IG.

Harms

No specific and serious adverse events are presumed for participants in this study. However, by participating in the interventions, some participants may potentially experience psychological distress from imagining their situation after standard treatment. The patients/ caregivers and oncologists will also be subjected to time burdens of a half-hour and 2.5 hours for the intervention, and 10–30 minutes for each baseline and follow-up assessment. Therefore, we will give patients/caregivers a reward of 500 Japanese yen for each participant assessment. There are no reward for the intervention and no financial

risks associated with study participation.

Compensation

If participants develop unexpected health issues due to study participation during or after completion of this study, treatment will be adequately provided per standard medical care, covered by the National Health Insurance.

Sample size estimation

Our previous study revealed that the effect size of SHARE-RE score was 1.9 at post-intervention.[12] For a sample size based on 80% power to detect a significant difference at a significance level of 0.05 (two-sided), 10 oncologists and 70–100 participants (7–10 per oncologist) would be required for each arm in the follow-up phase, assuming some participant drop out and data loss. Assuming that 80% of patients will be accompanied by caregivers at doctor visits, a total of 112–160 participants would be required. Based on previous studies, a total of 60–150 patients (3 to 5 per oncologist) are then needed in the baseline phase.[27]

Although the total time devoted to CST for the oncologists in this study is reduced from the original SHARE-CST program, the role-plays for individual

participants are performed the same time, and communication coaching with QPL for the patients is added. Therefore the effect size from the previous study was adopted for sample size calculation, and 20 oncologists, 3 patients per oncologist, a total of 60 patients in the baseline phase, and 10 patients per oncologist, for a total of 200 patients, are enrolled in the follow-up phase (Figure 1).

Patient and public involvement statement

This study protocol was co-designed by a patient with pancreatic cancer and a family member of a pancreatic cancer patient who participated as researchers. They spoke with other patients to help develop recommendations for when patients' preferences and/or opinions should be considered. They will play a similar role in the implementation of the study. Thus, patients were and will continue to be involved in the study. The results of this study will be available via a study website.

Data analysis

Primary analyses

To examine the intervention effect parameters of all randomly assigned subjects in the primary analysis set according to the ITT principle, we will analyze the primary

outcome with SHARE-RE as an indicator of enhanced empathic communication using a generalized linear model. The primary outcome of interest is the difference in SHARE-RE scores between the two groups after intervention. A two-sided p value < 0.05 will be used to indicate statistical significance.

Secondary analyses

We will perform secondary analyses to supplement our primary analysis and obtain a clearer understanding of our clinical questions. The secondary analyses will use models similar to that of the primary analysis and will examine data for the secondary outcome measures. These analyses will be conducted for exploratory purposes.

Interim analyses

No interim analysis is planned.

Publication policy

The protocol and study results will be submitted to peer-reviewed journals. The first author of the main paper will be a member of the steering committee (the authors of the protocol paper). Another person could be the first author if approved by the steering

committee. The list of coauthors will be determined before submitting each paper.

Study period

This study period of this trial is April 2017 to March 2023; the registration period is August 2018 to July 2020.

Ethics and dissemination

The present study is subject to ethical guidelines for clinical studies published by Japan's Ministry of Education, Science and Technology and Ministry of Health, Labour, and Welfare and the modified Act on the Protection of Personal Information as well as the ethical principles established for research on humans stipulated in the Declaration of Helsinki and further amendments thereto. If important protocol modifications are needed, the investigators will discuss them and report to the review board for approval. Regarding dissemination, the results obtained will be submitted for publication in peer-reviewed journals. The main and/or relevant findings will be presented at conferences.

DISCUSSION

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This study is a multi-site randomized controlled trial to evaluate the efficacy of an integrated communication support program for rapidly progressive advanced cancer patients, caregivers, and oncologists to promote patient-centered communication. The intervention program is unique in intervening with both oncologists and patients/caregivers for a brief time at the point of first-line chemotherapy, before they are critically ill.

In clinical oncology, the introduction of personalized precision medicine has allowed great therapeutic progress. Patient-oncologist communication is uncertain and complex, and busy oncologists often find it difficult to take extra time with their patients. As a result, personalized and precise communication between a patient and an oncologist may not be achieved. If empathic communication between patients and oncologists can be improved, including shared decision making based on patient values and preferences about the use of evidence-based medicine, the result can be an effective integration of best practices and patient values, allowing for better use of clinical expertise and available resources.

In this study, it is essential that intervention facilitators and SPs be well trained to maintain the quality of the intervention. In the future, it may be possible to reduce costs by developing internet-based programs. Regarding QPL, clinical benefits may increase

when it is possible to link medical records with data from wearable devices. Above all, the use of electronic media is expected to make implementation of the intervention program easier.

Strengths and limitations

This study has two methodological limitations. First, we involve both oncologists and patients/caregivers. The intervention program for both is complex, consisting of multiple factorial components. Thus, if the interventions prove superior to usual care, we will not be able to determine which interventions and components are most efficacious or beneficial in promoting communication. Second, patient intervention will be applied only to patients with pancreatic cancer. The generalization potential of the approach for other cancers is thus unknown. However, because pancreatic cancer is one of most rapidly progressive cancers, the intervention may be effective in other cancers too.

Figure 1 caption

Participant flow diagram

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Acknowledgements

We thank Ms. T Mashiko and Ms. M Kurosaki for their data management support. We also thank members of PanCan Japan, Ms. S Furutani, Dr M Mori, Dr Y Shirai, Dr S Umezawa, Ms. N Inomata, Mr. M Umehashi, Dr M Okamura, Dr M Odawara, Dr A Hanai, Mr. R Soga, Ms. R Sugihara, Ms. T Akiyama and Ms. M Kanamaru for their support for this study.

Contributors

MF is a principal investigator. MF and YU developed the CST program. MF, AS, SJ, TO, YM and YU developed the QPL. MF, TO, TY, MI, MU, MO, KT, TM, YM and YU participated in the design of this study. All authors prepared the protocol and agree of final protocol and revisions. MF, AS, SJ, MT prepared of investigators brochure (IB) and CRFs. TY played a chief role in the statistical parts. TM played roles in the data management. MF drafted the manuscript. All authors participated in, read and approved the final manuscript.

Funding

This study is supported by a Grant-in-Aid for Japan Agency for Medical

Research and Development (JP 17ck0106237h0001) and in part by The National Cancer Center Research and Development Fund (30-A-11). This funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Sponsor

None

Competing interests

All authors declare that they have no competing interests regarding this work. TO has received research funding from Ono Pharmaceutical, Kowa, Dainippon Sumitomo Pharma, Chugai Pharmaceutical, Novartis, Yakult Honsha, AstraZeneca, Eizai, Lilly, Bristol-Myers Squibb. TY received consulting fees from Ono Pharmaceutical, Kowa, Japan Tobacco, Chugai Pharmaceutical, Tsumura & CO, CAC Croit, Asahi Intecc, Asahi Kasei Pharma and Clinical Trial. MI has received honoraria from Novartis Pharma, Bayer Yakuhin, Bristol-Myers Squibb, Abbott Japan, Eisai, Taiho Pharmaceutical, Eli Lilly Japan, Daiichi-Sankyo, Yakult, Otsuka Pharmaceutical, Nobelpharma, EA Pharma and Teijin Pharma, research funding from Bayer Yakuhin, Kyowa Hakko Kirin, Yakult, Taiho Pharmaceutical, Eli Lilly Japan, Ono Pharmaceutical, Eisai, AstraZeneca, Zeria

Pharmaceutical, Chugai, Bristol Myers Sqiibb, Merck Serono, Kowa, Nano Carrier, ASLAN, Daiichi-Sankyo., Sumitomo Dainippon, Novartis Pharma, Baxalta, Boehringer Ingelheim and Takara Bio. He is a consulting or advisory role for Nano Carrier, Bayer Yakuhin, Eisai, Kyowa Hakko Kirin, Novartis Pharma, Shire, MSD, Bristol Myers Sqiibb, Eli Lilly Japan, Sumitomo Dainippon, Daiichi-Sankyo, Teijin Pharma, Takara Bio and a board member of ASLAN, Chugai. MU has received honoraria from Taiho Pharmaceutical, Yakult Honsha, AstraZeneca, Novartis, Lilly, Teijin Pharma, Shire, Ono Pharmaceutical, and Merck Serono, and research funding from Taiho Pharmaceutical, Shire, Daiichi Sankyo, Eisai, AstraZeneca, Ono Pharmaceutical, MSD, Merck Serono, NanoCarrier, Dainippon Sumitomo Pharma, Incyte, ASLAN Pharmaceuticals, and Yakult Honsha. MO has received lecture fees from Taiho Pharmaceutical and honoraria from Taiho Pharmaceutical, Yakult, Bayer, Pfizer and Novartis.

Patient consent for publication

Not required.

Ethics approval

The protocol was reviewed and approved by the Institutional Review Board of

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National Cancer Center on 4 July 2018 (ID: 2014-474) as well as by the J-SUPPORT Scientific Advisory Board.

Provenance and peer review

Not commissioned; externally peer reviewed.

Open access

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Table 1. Components of CST Program Based on SHARE Model

	Description
Conceptual communication skills model: SHARE	
S	Setting up supportive environment for interview, including fundamental communication skills (e.g., greeting patient cordially, looking at patient's eyes and face)
H	Considering how to deliver bad news (e.g., not beginning bad news without preamble, checking to see whether talk is fast paced)
A	Discussing additional information that patient would like to know (e.g., answering patient's questions fully, explaining second opinion)
RE	Providing reassurance and addressing patient's emotions with empathic responses (e.g., remaining

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	silent out of concern for patient's feelings, accepting patient's expression of emotions)
Component Lecture Role playing	Introduction, communication skills model, evidence on preferences of patients with cancer regarding communication Simurated consultation with simurated patient using communication skills with scenarios, discussing with facilitator, summary
Scenarios on communication in advanced care	Discontinuing chemotherapy Dealing with patient asking questions
Setting	1 participant 1 facilitator 1 simulated patient
Schedule	Orientation and lecture (30 minutes)

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	Role playing with immediate feedback (60 minutes X 2)

Abbreviation: CST, communication skills training.

Table 2. Schedule for outcome measurement

			Baseline Phase		Intervention Phase		Follow-up Phase	
	Outcome	Measurement	Day 28 of 1st line chemotherapy	Day 42 of 1st line chemotherapy	Day 28 of 1st line chemotherapy	Day 42 of 1st line chemotherapy	3, 6, 12, 24, 36 months after	After post-mortem of the patient
Patient in baseline phase	Patient's communication behavior	RIAS		○				
	Patient's medical and sociological background	Cancer stage, diagnosis date, treatment status, treatment history, comorbidities, sex, age, work status, household income, household size, social support, marital status, educational	○					

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		experience, treatment, and care preference at the end of life						
	Patient's evaluation of consultation	"How did the oncologist respond to your questions?""Did you ask selected questions during consultation?" "How much have you discussed with your oncologist in the visit?"		○				
Patient in intervention and follow-up phase	Patient's communication behavior	RIAS				○		
	Patient's psychological distress	HADS			○	○	○	
	Patient's physicial and functional QOL	FACT-Physical & Functional			○	○	○	
	Patient's comprehensive QOL	Short version of CoQOLo			○	○	○	
	Patient's trust in oncologist	TiOS			○	○	○	
	Patient's satisfaction with oncologist	CSQ			○	○	○	

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	Patient's acceptance in cancer experience	PEACE			○	○	○		
	Patient's prognosis and treatment perception	PTPQ			○	○	○		
	Patient's evaluation of consultation	"How did the oncologist respond to your questions?" "Did you ask selected questions during consultation?" "How much have you discussed with your oncologist in the visit?" "Did you understand how to use the QPL and did you actually use it?"				○			
	Patient's evaluation of intervention and QPL in intervention group	"Do you think you will continue the intervention?" "Was the intervention useful to you?" "Did the oncologist talk about the QPL?"				○			

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	Patient's medical and sociological background	"Did the QPL helped you ask the oncologist questions?" "Is the QPL useful?" "Did you read the QPL before the visit?" "Do you think you will read the QPL in the future?" Cancer stage, diagnosis date, treatment status, treatment history, comorbidities, sex, age, job status, household income, household size, social support, marital status, educational experience, treatment, and care preference at the end of life			○			
	Patient's medical utilization at the end of life	The date of death, any chemotherapy agent given within 14 days						○

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		of death, any new chemotherapeutic regimen started within 30 days of death, and involvement of hospice and palliative care services						
Caregiver in baseline phase	Caregiver's communication behavior	RIAS		○				
	Caregiver's charactaristics	Sex, age, relationship with the patient, job status, household income, household size, social support, marital status, educational experience, and treatment and care preferences at the end of life	○					
	Caregiver's evaluation of consultation	"How did the oncologist respond to your questions?" "Did you ask selected questions during consultation?" "How much		○				

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		have you discussed with your oncologist in the visit?"						
Caregiver in intervention and follow-up phase	Caregiver's communication behavior	RIAS				○		
	Caregiver's psychological distress	K6			○	○	○	○
	Caregiver's QOL	EQ-5D			○	○	○	○
	Caregiver's satisfaction with oncologist	CSQ			○	○	○	
	Caregiver's sociological background	Sex, age, relationship with the patient, job status, household income, household size, social support, marital status, educational experience, and treatment and care preferences at the end of life						
	Caregiver's prognosis and treatment perception	PTPQ			○	○	○	

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	Caregiver's evaluation of consultation	"How did the oncologist respond to your questions?" "Did you ask selected questions during consultation?" "How much have you discussed with your oncologist in the visit?"				○			
	Caregiver's evaluation of intervention and QPL in intervention group	"Did you understand how to use the QPL and did you actually use it?" "Do you think you will continue the intervention?" "Was the intervention useful to you?" "Did the oncologist talk about the QPL?" "Did the QPL help you ask the oncologist questions?" "Is the QPL useful?" "Did you read the QPL before the visit?" "Do				○				

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		you think you will read the QPL in the future?"						
	Short version of Good Death Inventory	Short version of Good Death Inventory						○
Oncologist	Oncologist's Patient-centered communication behaviors	SHARE-RE		○		○		
	Oncologist's Patient-preferred communication behavior	SHARE-total		○		○		
	Oncologist's Patient-preferred communication behavior	RIAS		○		○		
	Oncologist's sociological background	Sex, age, clinical experience	○					
	Oncologist's evaluation of medical utilization by patient	The date of management		○		○		
	Oncologist's evaluation of intervention	The usefulness of the intervention				○		

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Abbreviation: RIAS, Roter intention analysis system

HADS, Hospital Anxiety and Depression Scale

FACT-Physical & Functional, Physical well-being and Functional well-being subscales of the Functional Assessment of Cancer Therapy

CoQOLo, Comprehensive Quality of Life Outcome inventory

TiOS, Trust in Oncologists Scale

CSQ, Client Satisfaction Questionnaire

PEACE, Peace, Equanimity, and Acceptance in the Cancer Experience questionnaire

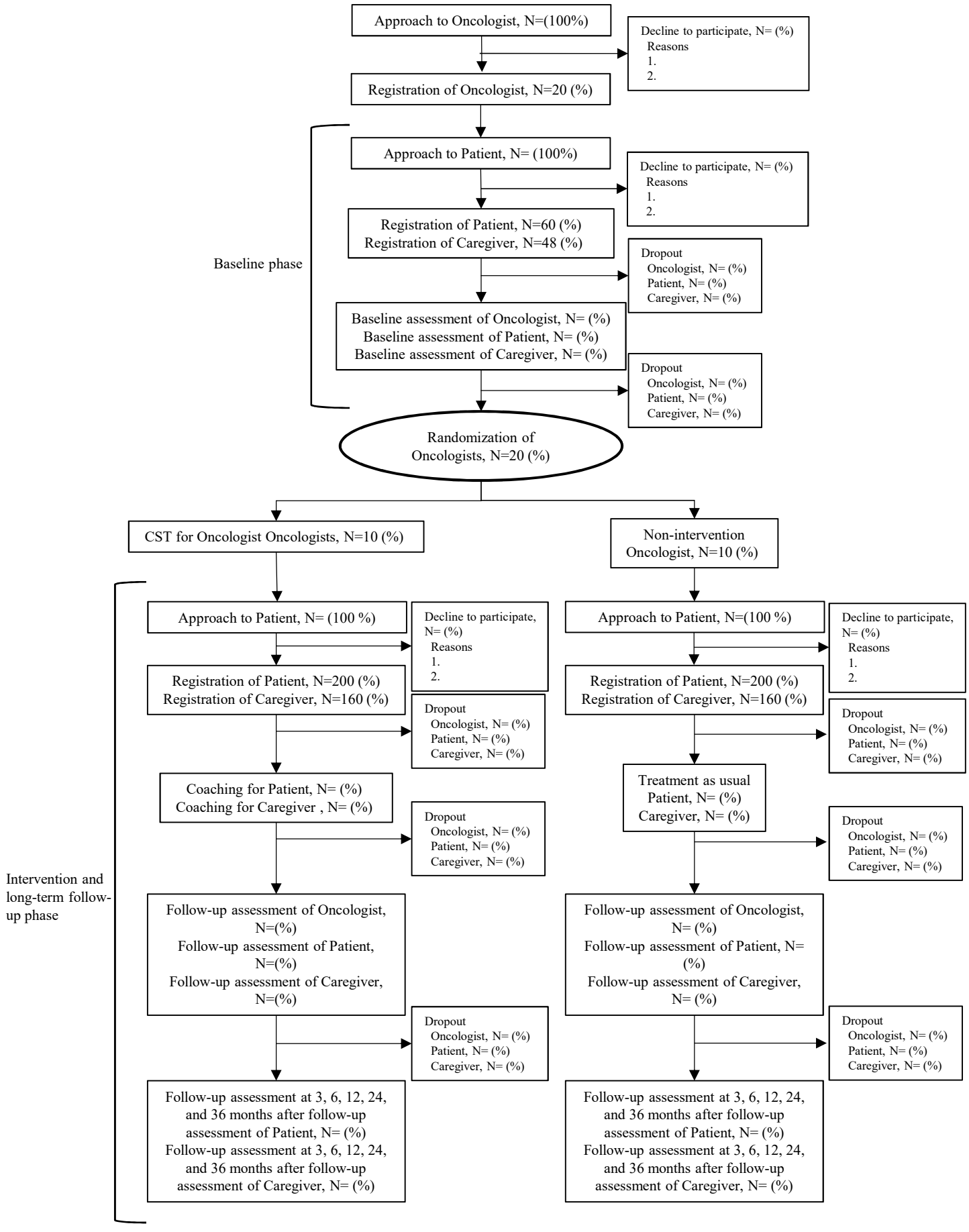
PTPQ, Prognosis and Treatment Perceptions Questionnaire

K6, K6 nonspecific psychological distress scale

EQ-5D, 5 Dimension EuroQol

GDI, Good Death Inventory

IG, Intervention Group


Approach to Oncologist, N=(100%)
Decline to participate, N= (%)
Reasons
1.
2.
Registration of Oncologist, N=20 (%)
Approach to Patient, N= (100%)
Decline to participate, N= (%)
Reasons
1.
2.
Registration of Patient, N=60 (%)
Registration of Caregiver, N=48 (%)
Baseline phase
Dropout
Oncologist, N= (%)
Patient, N= (%)
Caregiver, N= (%)
Baseline assessment of Oncologist, N= (%)
Baseline assessment of Patient, N= (%)
Baseline assessment of Caregiver, N= (%)
Dropout
Oncologist, N= (%)
Patient, N= (%)
Caregiver, N= (%)
Randomization of Oncologists, N=20 (%)
CST for Oncologist Oncologists, N=10 (%)
Non-intervention Oncologist, N=10 (%)
Approach to Patient, N= (100 %)
Decline to participate, N= (%)
Reasons
1.
2.
Approach to Patient, N=(100 %)
Decline to participate, N= (%)
Reasons
1.
2.
Registration of Patient, N=200 (%)
Registration of Caregiver, N=160 (%)
Dropout
Oncologist, N= (%)
Patient, N= (%)
Caregiver, N= (%)
Registration of Patient, N=200 (%)
Registration of Caregiver, N=160 (%)
Dropout
Oncologist, N= (%)
Patient, N= (%)
Caregiver, N= (%)
Coaching for Patient, N= (%)
Coaching for Caregiver , N= (%)
Dropout
Oncologist, N= (%)
Patient, N= (%)
Caregiver, N= (%)
Treatment as usual
Patient, N= (%)
Caregiver, N= (%)
Dropout
Oncologist, N= (%)
Patient, N= (%)
Caregiver, N= (%)
Intervention and long-term follow-up phase
Follow-up assessment of Oncologist, N=(%)
Follow-up assessment of Patient, N=(%)
Follow-up assessment of Caregiver, N=(%)
Follow-up assessment of Oncologist, N= (%)
Follow-up assessment of Patient, N= (%)
Follow-up assessment of Caregiver, N= (%)
Dropout
Oncologist, N= (%)
Patient, N= (%)
Caregiver, N= (%)
Dropout
Oncologist, N= (%)
Patient, N= (%)
Caregiver, N= (%)
Follow-up assessment at 3, 6, 12, 24, and 36 months after follow-up assessment of Patient, N= (%)
Follow-up assessment at 3, 6, 12, 24, and 36 months after follow-up assessment of Caregiver, N= (%)
Follow-up assessment at 3, 6, 12, 24, and 36 months after follow-up assessment of Patient, N= (%)
Follow-up assessment at 3, 6, 12, 24, and 36 months after follow-up assessment of Caregiver, N= (%)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	7
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	7
Protocol version	#3	Date and version identifier	7
Funding	#4	Sources and types of financial, material, and other support	31
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	31
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	32
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	31
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and	31

		other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	9
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	9
Objectives	#7	Specific objectives or hypotheses	12
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	13
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	13

Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	16
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	13
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	13
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	13
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	20
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	21

Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	18
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	26
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	17
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	13
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque,	13

		sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	13
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	13
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	13
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	19

Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	19
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	19
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	27
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	27
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	27
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further	19

		details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	27
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	25
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	32
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	13
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	28

Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	18
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	42
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	28
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	32
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	7
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	25
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	28

Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	28
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	7
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Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	1
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

BMJ Open

An integrated communication support program for oncologists, caregivers, and patients with rapidly progressing advanced cancer to promote patient-centered communication: J-SUPPORT 1904 study protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036745.R2
Article Type:	Protocol
Date Submitted by the Author:	23-Jul-2020
Complete List of Authors:	Fujimori, Maiko; National Cancer Center Japan, Division of Health Care Research, Behavioral Science and Survivorship Research Group, Center for Public Health Sciences, National Cancer Center Japan Sato, Ayako; National Cancer Center Japan, Division of Health Care Research, Behavioral Science and Survivorship Research Group, Center for Public Health Sciences Jinno, Sayaka; National Cancer Center Japan, Division of Health Care Research, Behavioral Science and Survivorship Research Group, Center for Public Health Sciences Okusaka, Takuji; National Cancer Center Hospital, Hepatobiliary and Pancreatic Oncology Division Yamaguchi, Takuhiro; Tohoku University Graduate School of Medicine Department of Medical Biochemistry, Division of Biostatistics Ikeda, Masafumi; National Cancer Center-Hospital East, Department of Hepato-bliary Pancreatic Oncology Ueno, Makoto; Kanagawa Cancer Center, Department of Gastroenterology, Hepatobiliary and Pancreatic Medical Oncology Division Ozaka, Masato; Public Interest Incorporated Foundation Cancer Institute Hospital of JFCR, Department of Hepatobiliary and Pancreatic Medical Oncology Takayama, Yukiko; Tokyo Women's Medical University Hospital, Department of Medicine, Institute of Gastroenterology Miyaji, Tempei; Tokyo Medical University School of Medicine Graduate School of Medicine, Department of Clinical Trial Data Management Majima, Yoshiyuki; Pancreatic Cancer Action Network Uchitomi , Yosuke; Innovation Center for Supportive, Palliative and Psychosocial Care, National Cancer Center Hospital, & Behavioral and Survivorship Research Group, Center for Public Health Sciences
Primary Subject Heading:	Communication
Secondary Subject Heading:	Oncology, Palliative care, Patient-centred medicine
Keywords:	Adult oncology < ONCOLOGY, Adult palliative care < PALLIATIVE CARE, MENTAL HEALTH, SOCIAL MEDICINE

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INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

TITLE: An integrated communication support program for oncologists, caregivers, and patients with rapidly progressing advanced cancer to promote patient-centered communication: J-SUPPORT 1904 study protocol for a randomized controlled trial

RUNNING TITLE: Integrated communication program for advanced cancer patients and oncologists

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Word count: 3716 words, excluding title page, abstract, references, figures, and tables

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

ABSTRACT

Introduction

Communication is an essential aspect of care for patients with progressive serious illnesses. This study aims to evaluate the efficacy of a new, integrated communication support program for oncologists, patients with rapidly progressing advanced cancer and their caregivers.

Methods and Analysis

The proposed integrated communication support program is in the randomized control trial stage. It comprises a cluster of oncologists from comprehensive cancer center hospitals in a metropolitan area in Japan. A total of 20 oncologists, 200 patients with advanced pancreatic cancer, and the patients' caregivers are enrolled in this study as of the writing of this protocol report. Oncologists are randomly assigned to the intervention group (IG) or control group (CG). Patients and caregivers are allocated to the same group as their oncologists. The IG oncologists receive a 2.5-hour individual communication skills training, and patients and caregivers receive a half-hour coaching intervention to facilitate prioritizing and discussing questions and concerns; the CG participants do not receive any training. Follow-up data will be collected quarterly for 6 months for a year

and then annually for up to three years. The primary endpoint is the intergroup difference between before- and after-intervention patient-centered communication behaviors during oncology visits.

Ethics and dissemination

This study is conducted in accordance with the ethical guidelines for clinical studies published by Japan's Ministry of Education, Cultural, Sports, Science, and Technology, the Ministry of Health, Labour, and Welfare (MHLW), and the ethical principles established for research on humans stipulated in the Declaration of Helsinki and further amendments thereto. The protocol was approved by the Institutional Review Board of National Cancer Center, Japan on July 4, 2018 (ID: 2017-474).

Trial status

This study is currently enrolling participants; enrollment period ends July 31, 2020; estimated follow-up date is March 31, 2023.

Trial registration number

UMIN Clinical Trial Registry: UMIN000033612; Pre-results.

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

(299 words)

Keywords: Advance Care Planning, Caregivers, Communication, Decision making, Empathy, End-of-life care, Patient-centered care, Patient-physician relationship, Quality of life

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

ARTICLE SUMMARY

Trial registration: The protocol registered on 2nd August, 2018 at UMIN Clinical Trial Registry. The registration number is UMIN000033612.

Data statement: Study protocol, data definition tables, and dataset will be uploaded to the UMIN- Individual Case Data Repository, https://www.umin.ac.jp/icdr/index-j.html.

Protocol version: The protocol version is 1.4 on 20th December, 2019.

Strengths and limitations of this study:

- A strength of this study is the use of a large group of patients, caregivers, and oncologists in the real-world scenario for which the intervention is being tested.
- The use of multicenter participant samples, controls, and patient follow-up allows for reliable study results.
- This study includes oncologists, patients, and caregivers for intervention.
- The intervention program is complex, consisting of multiple factorial components, which makes it difficult to determine which interventions and components are most efficacious or beneficial; however, participants provide subjective

assessments of the intervention components.

- The study only involves pancreatic cancer, so the generalization potential for other cancers is unknown. However, as pancreatic cancer is one of the most rapidly progressing cancers, if the intervention is effective for patients with pancreatic cancer who have severe physical and psychological conditions, it may be applied to patients with other cancers as well.

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

INTRODUCTION

Pancreatic cancer is the fourth leading cause of death in Japan, with approximately 35,000 new cases diagnosed per year, matching the approximate annual number of deaths from the disease nationally.[1] Over 40% of patients with pancreatic cancer are stage IV at diagnosis, and the 3-year survival rate for stage III and IV is 11.9% and 2.5%, respectively.[2] Although the initial treatment goal for pancreatic cancer is to cure, even prolonged survival and maintenance of QOL are difficult to achieve.

Most patients with advanced cancer prefer to discuss their prognosis and treatments with their physicians.[3] However, physicians may feel burdened by open discussions for fear of patients losing hope, or they may face resistance from caregivers;[4] therefore, these discussions rarely occur.[5] Consequently, patients often overestimate the hopefulness of prognoses, underestimate disease severity, and have unrealistic expectations for a cure.[6] Patients who have not discussed prognosis and treatment choices with their oncologists are 3 to 8 times more likely to receive aggressive treatments in their last week of life.[5,7] Although oncologists and patients find that prognostic discussions can be stressful, unnecessary expenses and actual harm to the patient may result from uninformed decisions.[8] Additionally, it has been shown that open discussions do not cause hopelessness or increased fear in patients and that well-

informed patients make more appropriate treatment choices.[9,10] Hence, oncologists need to provide adequate information regarding cancer treatment decisions for patients and their caregivers approaching the end of life, confirm patients' and caregivers' understanding, and achieve shared decision making about treatment and care based on patients' personal values, life goals, and treatment preferences.

In previous study, patients from the diagnosis to the discontinuation of anti-cancer drug treatment stage (mainly pancreatic cancer patients) showed to desire more "empathic communication" from oncologists.[11] Empathic communication by oncologists reduces patients' psychological distress,[12] increases trust in the oncologist,[12] and enhances information recall.[13] Empathic communication is essential especially for patients with rapidly progressing serious illnesses. Therefore, communication skills training (CST) programs have been developed to help physicians to facilitate communication behaviors that strengthen relationships with patients.[14] CST involves learner-centered workshop held in small groups and including role-play with simulated patients (SPs).[15] It is strongly recommended that medical professionals train themselves in communication skills based on American Society of Clinical Oncology Consensus Guidelines for patient–clinician communication.[16] Learning tools (e.g., www.vitaltalk.org) are available to medical practitioners to support this learning.

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

We conducted a prior survey clarifying the four elements of communication skills patients prefer oncologists to have, referred to as SHARE: "setting," "how to deliver the bad news," "additional information," and "reassurance and emotional support."[17,18] A two-day SHARE-CST program for oncologists was developed based on these preferences.[19] The program is a small-group workshop including the above-mentioned modules; it employs role-play with simulated patients and immediate feedback[15] to allow learners to practice discussing serious news with cancer patients and caregivers, such as transition to palliative care when chemotherapy is failing. The program emphasizes that physicians respect the values of each patient and provide reassurance and emotional support and has been implemented in several Asian countries.[20] Our previous randomized controlled trial (RCT) of physicians, including oncologists treating pancreatic cancer, showed that oncologists who participated in SHARE-CST improved their behavior in terms of patient-preferred communication as well as their self-confidence in communication with patients and that their patients experienced a relatively low level of psychological distress and a high level of trust in the oncologist.[12] In Japan, SHARE-CST was implemented as a 10-year project commissioned by the MHLW for physicians nationwide after the enactment of the National Cancer Control Act. Participants reported that their empathic communication

attitudes and abilities had improved;[21] however, it was difficult for most oncologists to participate in two-day CST group workshops because of the busy clinical oncology settings in which they worked.

Patient-centered approaches using question prompt lists (QPLs) have also been proposed for the improvement of patient-physician communication. A QPL is an inexpensive communication tool employing a structured question list to encourage patient question-asking and participation during consultations.[22] The provision of a QPL and implementation of communication interventions with QPL before consultation is effective in promoting patient question-asking behavior and participation in the consultation and in decreasing patients' anxiety.[23] Our previous RCT of patients with advanced gastric, colorectal, esophageal, and lung cancer showed that QPL was useful in making initial treatment decisions for them but failed to promote patient question-asking behavior,[24] in part because Japanese patients tend to wait for physicians to encourage them to ask questions.[25] The number of patients asking their physician questions was median 1, compared to mean/median 8.5 to 14 in studies in Western countries.[23,24] In Japan, it has been reported that cancer patients have preference of not being burden to others and of "omakase" (leaving the decision-making to a medical expert), and it is difficult to elicit the patient's preference.[26] Thus, in Japan, integrated interventions

combining CST for oncologists and communication coaching with QPL for patients might increase patient questioning behavior and improve patient-centered communication in consultations.[27,28]

Based on the results of previous trials, this study aims to evaluate the efficacy of a new, integrated communication support program, consisting of a CST for oncologists and communication coaching with QPL for patients with rapidly progressing advanced cancer and their caregivers, promoting oncologists' patient-centered communication behaviors. We hypothesize that, compared to treatment as usual (TAU), the intervention will increase oncologists' patient-centered communication behaviors, increase patients' question-asking behaviors, and improve patient well-being and health services utilization by reducing aggressive interventions and increasing use of palliative care.

METHODS and ANALYSIS

This protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and SPIRIT PRO Extension Guidelines.[29,30]

Study design

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

This study is a single-blind cluster RCT conducted in four metropolitan cancer-treatment hospitals: the National Cancer Center Hospital, the National Cancer Center Hospital East, the Cancer Institute Hospital, and the Kanagawa Cancer Center Hospital. This study protocol has been reviewed and approved by the protocol review committee of the Japan Supportive, Palliative, and Psychosocial Oncology Group as J-SUPPORT 1704 and by the Institutional Review Boards at each participating institution.

An independent data center provides computer-generated random allocation sequences. The assignment sequence is centrally managed; assignment results are automatically sent to a clinical research coordinator (CRC), electronically. The oncologist participants are randomly assigned to an intervention group (IG) or control group (CG) after the baseline phase; patient/caregiver participants are assigned to the same group as their oncologists. A stratified block-randomization scheme is used to assure balanced assignment by site. Within each site, oncologists are randomly assigned approximately evenly across IG and CG. Participants in IG provide intervention in addition to TAU, and are unblinded.

Intervention

Oncologists

INTEGRATED COMMUNICATION PROGRAM FOR ADVANCED CANCER PATIENTS AND ONCOLOGISTS

We modified the original SHARE-CST design,[12] adopting a 2.5-hour individual program with a facilitator and a simulated patient (SP), consisting of lecture with a textbook (30 min) and 2 role-plays with immediate feedback (see Table 1). The original SHARE-CST is a small group consisting of 4 oncologists, 2 facilitators and 2 SPs, and included a lecture and 8 role-plays (twice per oncologist) with immediate feedback. The lecture cites evidence of the most important and common patient preferences regarding communication—empathic responses and encouragement to ask questions—and the variability of patients' preferences in discussing prognoses and being/not being dispassionate; it also demonstrates how to check and elicit patient preferences. Additionally, the lecture explains the QPL and discusses frequently asked questions from patients about information related to treatment and care after standard treatment that relates to patients' personal values, life goals, and preferences, as well as those of their caregivers. During the role-playing and discussion, participants are required to consider a patient's emotions and concerns caused by bad news, recognition of their disease, social situations, and information that they would want to know, and to empathize with the patient. Role-play also includes dealing with patients who bring QPLs.

Facilitators provide a lecture, lead the role-play, and discuss patients' potential emotions and communication-related preferences. Facilitators include psychiatrists,

psychologists, and oncologists, all of whom have had 3 years or more of clinical experience in oncology and participated in specialized 30-hour training workshops facilitating communication skills in oncology. The SPs have also participated in train-the-trainer workshops and 15 hours of SP training.

Patient and Caregiver

Communication coaching for patients was developed to facilitate communication with physicians using a 63-question QPL based on in-depth focus-group interviews with 18 participants (5 pancreatic cancer patients, 3 caregivers patients with pancreatic cancer, 4 bereaved people who had lost a family with pancreatic cancer, and 6 pancreatic oncologists), and previous QPL studies.[23,24,31] The QPL is a 10-page A4 sheet containing 63 questions grouped into 8 topics (diagnosis and stage of the disease, current and future treatments, management of current/possible future symptoms, daily life activities, care and prognosis post standard treatment, caregivers' needs, psychological distress and management, and values) and a space for free questions. Patient communication coaching using the QPL is a half-hour program, conducted individually or with a caregiver, consisting of reading the list to select personally relevant questions, prioritizing selected questions, discussing difficulties in asking the questions to their one's

oncologist at their next oncology visit, and practicing asking their one's oncologist these questions. The intervention is to be provided to patients individually or with caregivers by clinical psychologists and nurses who have participated in a 10-hour intensive training workshop using an intervention manual. The intervention providers note and summarize the content of all intervention sessions, that is, the information that the patient want to know and their preferences of treatment and care. Before patients' visits, the oncologist is told which the questions the patient chose to ask from the QPL and the summary of the intervention. Intervention providers hold weekly conferences to review their coaching sessions.

Control condition

CG oncologists are provided neither training nor educational materials. Patients/caregivers in the CG are provided TAU.

Participants

Oncologists

Enrolled oncologists must (1) be mainly engaged in anticancer drug treatment of pancreatic cancer patients; (2) have provided written informed consent for trial

participation.

Patients in baseline phase and intervention and long-term follow-up phase

Enrolled patients must (1) have a diagnosis of pancreatic cancer (adenocarcinoma); (2) have unresectable pancreatic cancer (UICC stage III or IV) or postoperative recurrence; (3) receive a first-line chemotherapy and be scheduled for a second course; (4) be aged 20 years or older; (5) have a ECOG performance status score of 0 or 1; (6) regularly visit an enrolled oncologist; (7) provide written informed consent for trial participation; and (8) be able to read, write, understand, and speak Japanese.

Patients are excluded if they are (1) judged by their oncologist to have cognitive impairment; (2) unable to complete an electronic Patient Reported Outcome (e-PRO) Questionnaire; or (3) judged unsuitable for participation by their oncologist.

Caregivers in baseline phase and intervention and long-term follow-up phase

If an enrolled patient is accompanied by a caregiver, the caregiver is also approached. Enrolled caregivers must (1) be aged 20 years or older; (2) regularly accompany an enrolled patient as primary caregiver; (3) provide written informed consent to trial participation; (4) be able to read, write, understand, and speak Japanese.

Caregivers are excluded if they are unable to complete an electronic Patient Reported Outcome (e-PRO) Questionnaire.

Procedures

This study consists of 3 phases: a baseline phase, an intervention phase, and a follow-up phase (Figure 1). The schedule for outcome measurement is shown in Table 2. After completing the intervention phase, data analysis will ensue. After this study has closed, oncologists in the control group will be provided with the intervention on demand.

Baseline phase

This phase involves oncologist and patient/caregiver recruitment as well as pre-randomization data collection on oncologists' communication behaviors as baseline data for use as a covariate in the RCT analysis. In this phase, 3 to 5 patients and their caregivers (if available) will be recruited for each oncologist. Participants will be asked to allow themselves to be audio-recorded at one oncology visit and to provide the evaluation of consultation for primary and secondary outcomes as covariates in the analyses (Table 2).

Intervention phase

This phase involves oncologist randomization, intervention for participants in IG, and follow-up assessment. After oncologists are randomly assigned to the IG or CG, those in the IG receive an individual intervention.

Next, 10 patients and their caregivers (if available) who regularly visit the oncologist are recruited and assigned to the IG or CG. After the IG patients and their caregivers receive an intervention, or 2 weeks to 1 month after baseline in the CG, the conversation between the patient/caregiver and the oncologist at their next consultation is audio-recorded. After the consultation, patients/caregivers and the oncologists rate the consultation using a follow-up assessment.

Long-term follow-up phase

Patients and their caregivers will be encouraged to provide long-term follow-up assessments at 3, 6, 12, 24, and 36 months after the first follow-up assessment to evaluate effects on patient's physical and psychological condition and medical utilization at end of life. Caregivers are also asked to provide another assessment at 2 to 6 months post–patient death.

Data management, central monitoring, data monitoring, and auditing

We will collect all data, except for audio-recorded data, through electronic data capture (EDC) and electronic patient reported outcomes (ePRO) systems or paper-based PRO questionnaires (pPRO) if patients are prevented from using the electronic approach. If participants fail to respond to ePRO or pPRO, a CRC blinded to the assignment will elicit their answers to avoid missing data. Data management and central monitoring will be performed using EDC VIEDOC 4 (PCG Solutions, Uppsala, Sweden) by the J-SUPPORT Data Science Team. Auditing is not planned for this study.

Concomitant treatments

There is no restriction on concomitant treatments.

Stopping rules for participants

If a participant meets any of the following conditions, the research team can discontinue the intervention; however, the participant will not be considered to have dropped out of the trial at that stage and will still receive the assessments: (1) the participant wishes to stop the intervention; (2) the research team judges that the risk of the intervention is greater than the benefit for any reason; (3) the research team judges that it is difficult to continue the intervention because of clinical deterioration; and (4) the

research team judges that it is inappropriate to continue the intervention for any reason.

Stopping assessment

If a participant withdraws consent for assessment, he or she will not be followed up. Subjects will be excluded from the intention-to-treat (ITT) cohort of the trial only if they are found to meet any exclusion criteria at baseline after participation.

Assessment measures

Table 2 shows the schedule for outcome measurement.

Primary outcome measure

Oncologist's patient-centered communication behaviors

The audio-recorded oncology visits for all participants will be coded for each of the four factors of communication behaviors based on patient preference, referred to as SHARE: setting, delivery of information, additional information, and reassurance and emotional support (see Table 1).[19] The SHARE-RE factor is used as a primary outcome to measure empathic communication between patient/caregiver and oncologist after intervention for both.

Following previous study methods,[19] impressions of conversations between

patient/caregiver and oncologist from consultations will be assessed using the SHARE-RE factor score, consisting of 8 categories for analysis, in a random order, by two blinded coders who have been trained for 30 hours or more on two occasions with a rating manual.

Secondary outcome measure

Oncologist's Patient-preferred communication behavior

Patient-preferred communication will be analyzed using impression ratings from two blinded coders, as described above. The analysis will include the audio-recorded oncology visits for all participants using the total SHARE score, for all 27 categories.[18,19] Following previous study methods,[19] the 40 categories of the Roter Intention Analysis System (RIAS) will also be used in assessing patient-preferred communications.[32]

Patient's and caregiver's communication behavior

Following previous study methods,[19] the 40 categories of the Roter Intention Analysis System (RIAS) will also be used in assessing patient's and caregiver's communications behavior, for example question-asking.[32]

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Patient-reported outcome measures

Several scales will be used to produce a comprehensive profile of each patient participant. These include the Hospital Anxiety and Depression Scale (HADS);[33] the Physical and Functional Well-being subscales of the Functional Assessment of Cancer Therapy (FACT-Physical & Functional);[34] the Short version of the Comprehensive Quality of Life Outcome inventory (CoQoLo);[35] the Trust in Oncologists Scale (TiOS);[36] the Client Satisfaction Questionnaire (CSQ);[37] the Peace, Equanimity, and Acceptance in the Cancer Experience (PEACE) questionnaire;[38] and the Prognosis and Treatment Perceptions Questionnaire (PTPQ).[39]

Patients' relevant medical and sociological background information includes stage, diagnosis date, treatment status, treatment history, comorbidities, sex, age, job status, household income, household size, social support, marital status, educational experience, treatment, and care preference at the end of life. Medical utilization at the end of life will be determined by the date of death, any chemotherapy agent given within 14 days of death, any new chemotherapeutic regimen started within 30 days of death, and involvement of hospice and palliative care services; all of this information is obtained from medical fee information and the caregivers post–patient death.[27]

A patients' assessment of the intervention's usefulness includes "Did you

understand how to use the QPL and did you actually use it?" "Do you think you will continue the intervention?" and "Was the intervention useful to you?" Their assessment of oncologists includes "Did the oncologist talk about the QPL?" and "How did the oncologist respond to your questions?" Their assessment of QPL includes "Did the QPL help you ask the oncologist questions?" "Is the QPL useful?" "Did you read the QPL before the visit?" and "Do you think you will read the QPL in the future?" as well as whether they asked selected questions to oncologist after the consultation, which questions they selected, and "How much you have discussed with the oncologist in the visit?" in the intervention phase.

Caregiver survey measures

Several scales will also be used to gain a comprehensive view of caregivers, including the K6 nonspecific psychological distress scale (K6);[40] the 5 Dimension EuroQol (EQ-5D);[41] and the CSQ.[37] After the patient's death, the caregiver's QOL as the bereaved is measured with the Short version of the Good Death Inventory (GDI).[42]

Caregivers' relevant sociological background information includes sex, age, relationship with the patient, job status, household income, household size, social support,

marital status, educational experience, and treatment and care preferences at end of life.

After the first post-intervention visit, caregivers in the IG will evaluate the intervention, the oncologist, and the QPL and report any selected questions used with the oncologist.

Oncologist survey measures

The relevant data concerning the oncologists include their sociological background (sex, age, and clinical experience). The oncologists' evaluation of medical utilization by the patient will be set by their recollection of the dates.

The usefulness of intervention will also be measured using evaluations provided by the oncologists in the IG.

Harms

No specific and serious adverse events are presumed for participants in this study. However, by participating in the interventions, some participants may potentially experience psychological distress from imagining their situation after standard treatment. The patients/ caregivers and oncologists will also be subjected to time burdens of a half-hour and 2.5 hours for the intervention, and 10–30 minutes for each baseline and follow-

up assessment. Therefore, we will give patients/caregivers a reward of 500 Japanese yen for each participant assessment. There are no reward for the intervention and no financial risks associated with study participation.

Compensation

If participants develop unexpected health issues due to study participation during or after completion of this study, treatment will be adequately provided per standard medical care, covered by the National Health Insurance.

Sample size estimation

Our previous study revealed that the effect size of SHARE-RE score was 1.9 at post-intervention.[12] For a sample size based on 80% power to detect a significant difference at a significance level of 0.05 (two-sided), 10 oncologists and 70–100 participants (7–10 per oncologist) would be required for each arm in the follow-up phase, assuming some participant drop out and data loss. Assuming that 80% of patients will be accompanied by caregivers at doctor visits, a total of 112–160 participants would be required. Based on previous studies, a total of 60–150 patients (3 to 5 per oncologist) are then needed in the baseline phase.[27]

Although the total time devoted to CST for the oncologists in this study is reduced from the original SHARE-CST program, the role-plays for individual participants are performed the same time, and communication coaching with QPL for the patients is added. Therefore the effect size from the previous study was adopted for sample size calculation, and 20 oncologists, 3 patients per oncologist, a total of 60 patients in the baseline phase, and 10 patients per oncologist, for a total of 200 patients, are enrolled in the follow-up phase (Figure 1).

Patient and public involvement statement

This study protocol was co-designed by a patient with pancreatic cancer and a family member of a pancreatic cancer patient who participated as researchers. They spoke with other patients to help develop recommendations for when patients' preferences and/or opinions should be considered. They will play a similar role in the implementation of the study. Thus, patients were and will continue to be involved in the study. The results of this study will be available via a study website.

Data analysis

Primary analyses

To examine the intervention effect parameters of all randomly assigned subjects in the primary analysis set according to the ITT principle, we will analyze the primary outcome with SHARE-RE as an indicator of enhanced empathic communication using a generalized linear model. The primary outcome of interest is the difference in SHARE-RE scores between the two groups after intervention. A two-sided p value < 0.05 will be used to indicate statistical significance.

Secondary analyses

We will perform secondary analyses to supplement our primary analysis and obtain a clearer understanding of our clinical questions. The secondary analyses will use models similar to that of the primary analysis and will examine data for the secondary outcome measures. These analyses will be conducted for exploratory purposes.

Interim analyses

No interim analysis is planned.

Publication policy

The protocol and study results will be submitted to peer-reviewed journals. The

first author of the main paper will be a member of the steering committee (the authors of the protocol paper). Another person could be the first author if approved by the steering committee. The list of coauthors will be determined before submitting each paper.

Study period

This study period of this trial is April 2017 to March 2023; the registration period is August 2018 to July 2020.

Ethics and dissemination

The present study is subject to ethical guidelines for clinical studies published by Japan's Ministry of Education, Science and Technology and Ministry of Health, Labour, and Welfare and the modified Act on the Protection of Personal Information as well as the ethical principles established for research on humans stipulated in the Declaration of Helsinki and further amendments thereto. If important protocol modifications are needed, the investigators will discuss them and report to the review board for approval. Regarding dissemination, the results obtained will be submitted for publication in peer-reviewed journals. The main and/or relevant findings will be presented at conferences.

DISCUSSION

This study is a multi-site randomized controlled trial to evaluate the efficacy of an integrated communication support program for rapidly progressive advanced cancer patients, caregivers, and oncologists to promote patient-centered communication. The intervention program is unique in intervening with both oncologists and patients/caregivers for a brief time at the point of first-line chemotherapy, before they are critically ill.

In clinical oncology, the introduction of personalized precision medicine has allowed great therapeutic progress. Patient-oncologist communication is uncertain and complex, and busy oncologists often find it difficult to take extra time with their patients. As a result, personalized and precise communication between a patient and an oncologist may not be achieved. If empathic communication between patients and oncologists can be improved, including shared decision making based on patient values and preferences about the use of evidence-based medicine, the result can be an effective integration of best practices and patient values, allowing for better use of clinical expertise and available resources.

In this study, it is essential that intervention facilitators and SPs be well trained

to maintain the quality of the intervention. In the future, it may be possible to reduce costs by developing internet-based programs. Regarding QPL, clinical benefits may increase when it is possible to link medical records with data from wearable devices. Above all, the use of electronic media is expected to make implementation of the intervention program easier.

Strengths and limitations

This study has two methodological limitations. First, the intervention program for both oncologists and patients/caregivers is complex, consisting of multiple factorial components. Thus, if the interventions prove superior to usual care, we will not be able to determine which interventions and components are most efficacious or beneficial in promoting communication. Second, patient intervention will be applied only to patients with pancreatic cancer. The generalization potential of the approach for other cancers is thus unknown. However, as pancreatic cancer is one of the most rapidly progressing cancers, if the intervention is effective for patients with pancreatic cancer who have severe physical and psychological conditions, it may be applied to patients with other cancers as well.

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Figure 1 caption

Participant flow diagram

Abbreviation: CST, communication skills training

Acknowledgements

We thank Ms. T Mashiko and Ms. M Kurosaki for their data management support. We also thank members of PanCan Japan, Ms. S Furutani, Dr M Mori, Dr Y Shirai, Dr S Umezawa, Ms. N Inomata, Mr. M Umehashi, Dr M Okamura, Dr M Odawara, Dr A Hanai, Mr. R Soga, Ms. R Sugihara, Ms. T Akiyama and Ms. M Kanamaru for their support for this study.

Contributors

MF is a principal investigator. MF and YU developed the CST program. MF, AS, SJ, TO, YM and YU developed the QPL. MF, TO, TY, MI, MU, MO, KT, TM, YM and YU participated in the design of this study. All authors prepared the protocol and agree of final protocol and revisions. MF, AS, SJ, MT prepared of investigators brochure (IB) and CRFs. TY played a chief role in the statistical parts. TM played roles in the data management. MF drafted the manuscript. All authors participated in, read and approved

the final manuscript.

Funding

This study is supported by a Grant-in-Aid for Japan Agency for Medical Research and Development (JP 17ck0106237h0001) and in part by The National Cancer Center Research and Development Fund (30-A-11). This funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Sponsor

None

Competing interests

All authors declare that they have no competing interests regarding this work. TO has received research funding from Ono Pharmaceutical, Kowa, Dainippon Sumitomo Pharma, Chugai Pharmaceutical, Novartis, Yakult Honsha, AstraZeneca, Eizai, Lilly, Bristol-Myers Squibb. TY received consulting fees from Ono Pharmaceutical, Kowa, Japan Tobacco, Chugai Pharmaceutical, Tsumura & CO, CAC Croit, Asahi Intecc, Asahi Kasei Pharma and Clinical Trial. MI has received honoraria from Novartis Pharma,

Bayer Yakuhin, Bristol-Myers Squibb, Abbott Japan, Eisai, Taiho Pharmaceutical, Eli Lilly Japan, Daiichi-Sankyo, Yakult, Otsuka Pharmaceutical, Nobelpharma, EA Pharma and Teijin Pharma, research funding from Bayer Yakuhin, Kyowa Hakko Kirin, Yakult, Taiho Pharmaceutical, Eli Lilly Japan, Ono Pharmaceutical, Eisai, AstraZeneca, Zeria Pharmaceutical, Chugai, Bristol Myers Sqiibb, Merck Serono, Kowa, Nano Carrier, ASLAN, Daiichi-Sankyo., Sumitomo Dainippon, Novartis Pharma, Baxalta, Boehringer Ingelheim and Takara Bio. He is a consulting or advisory role for Nano Carrier, Bayer Yakuhin, Eisai, Kyowa Hakko Kirin, Novartis Pharma, Shire, MSD, Bristol Myers Sqiibb, Eli Lilly Japan, Sumitomo Dainippon, Daiichi-Sankyo, Teijin Pharma, Takara Bio and a board member of ASLAN, Chugai. MU has received honoraria from Taiho Pharmaceutical, Yakult Honsha, AstraZeneca, Novartis, Lilly, Teijin Pharma, Shire, Ono Pharmaceutical, and Merck Serono, and research funding from Taiho Pharmaceutical, Shire, Daiichi Sankyo, Eisai, AstraZeneca, Ono Pharmaceutical, MSD, Merck Serono, NanoCarrier, Dainippon Sumitomo Pharma, Incyte, ASLAN Pharmaceuticals, and Yakult Honsha. MO has received lecture fees from Taiho Pharmaceutical and honoraria from Taiho Pharmaceutical, Yakult, Bayer, Pfizer and Novartis.

Patient consent for publication

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Not required.

Ethics approval

The protocol was reviewed and approved by the Institutional Review Board of National Cancer Center on 4 July 2018 (ID: 2014-474) as well as by the J-SUPPORT Scientific Advisory Board.

Provenance and peer review

Not commissioned; externally peer reviewed.

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Table 1. Components of CST Program Based on SHARE Model

	Description
Conceptual communication skills model: SHARE	
S	Setting up supportive environment for interview, including fundamental communication skills (e.g., greeting patient cordially, looking at patient's eyes and face)
H	Considering how to deliver bad news (e.g., not beginning bad news without preamble, checking to see whether talk is fast paced)
A	Discussing additional information that patient would like to know (e.g., answering patient's questions fully, explaining second opinion)
RE	Providing reassurance and addressing patient's emotions with empathic responses (e.g., remaining silent out of concern for patient's feelings, accepting patient's expression of emotions)
Component	
Lecture	Introduction, communication skills model, evidence on preferences of patients with cancer regarding communication
Role playing	Simurated consultation with simurated patient using communication skills with scenarios, discussing with facilitator, summary
Scenarios on communication in advanced care	Discontinuing chemotherapy Dealing with patient asking questions
Setting	1 participant 1 facilitator 1 simulated patient
Schedule	Orientation and lecture (30 minutes) Role playing with immediate feedback (60 minutes X 2)

Abbreviation: CST, communication skills training.

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Table 2. Schedule for outcome measurement

	Outcome	Measurement	Baseline Phase		Intervention Phase		Follow-up Phase	
			Day 28 of 1st line chemotherapy	Day 42 of 1st line chemotherapy	Day 28 of 1st line chemotherapy	Day 42 of 1st line chemotherapy	3, 6, 12, 24, 36 months after	After post-mortem of the patient
Patient in baseline phase	Patient's communication behavior	RIAS		○				
	Patient's medical and sociological background	Cancer stage, diagnosis date, treatment status, treatment history, comorbidities, sex, age, work status, household income, household size, social support, marital status, educational experience, treatment, and care preference at the end of life	○					
	Patient's evaluation of consultation	"How did the oncologist respond to your questions?" "Did you ask selected questions during consultation?" "How much have you discussed with the oncologist t in the visit?"		○				
Patient in intervention and follow-up phase	Patient's communication behavior	RIAS				○		
	Patient's psychological distress	HADS			○	○	○	
	Patient's physical and functional QOL	FACT-Physical & Functional			○	○	○	
	Patient's comprehensive QOL	Short version of CoQOLo			○	○	○	
	Patient's trust in oncologist	TiOS			○	○	○	
	Patient's satisfaction with oncologist	CSQ			○	○	○	
	Patient's acceptance in cancer experience	PEACE			○	○	○	
	Patient's prognosis and treatment perception	PTPQ			○	○	○	
	Patient's evaluation of consultation	"How did the oncologist respond to your questions?" "Did you ask selected questions during consultation?" "How much have you discussed with the oncologist in the visit?"				○		
	Patient's evaluation of intervention in the IG	"Did you understand how to use the QPL and did you actually use it?" "Do you think you will continue the intervention?" "Was the intervention useful to you?" "Did the oncologist talk about the QPL?" "Did the QPL helped you ask the oncologist questions?" "Is the QPL useful?" "Did you read the QPL before the visit?" "Do you think you will read the QPL in the future?"				○		
	Patient's medical and sociological background	Cancer stage, diagnosis date, treatment status, treatment history, comorbidities, sex, age, job status, household income, household size, social support, marital status, educational experience, treatment, and care preference at the end of life			○			
	Patient's medical utilization at the end of life	The date of death, any chemotherapy agent given within 14 days of death, any new chemotherapeutic regimen started within 30 days of death, and involvement of hospice and palliative care services						○
Caregiver in baseline phase	Caregiver's communication behavior	RIAS		○				
	Caregiver's characteristics	Sex, age, relationship with the patient, job status, household income, household size, social support, marital status, educational experience, and preferences on treatment and care for the patient at the end of life	○					
	Caregiver's evaluation of consultation	"How did the oncologist respond to your questions?" "Did you ask selected questions during consultation?" "How much have you discussed with your oncologist in the visit?"		○				
Caregiver in intervention and follow-up phase	Caregiver's communication behavior	RIAS				○		
	Caregiver's psychological distress	K6			○	○	○	○
	Caregiver's QOL	EQ-5D			○	○	○	○
	Caregiver's satisfaction with oncologist	CSQ			○	○	○	
	Caregiver's sociological background	Sex, age, relationship with the patient, job status, household income, household size, social support, marital status, educational experience, and preferences on treatment and care for the patient at the end of life						
	Caregiver's prognosis and treatment perception	PTPQ			○	○	○	

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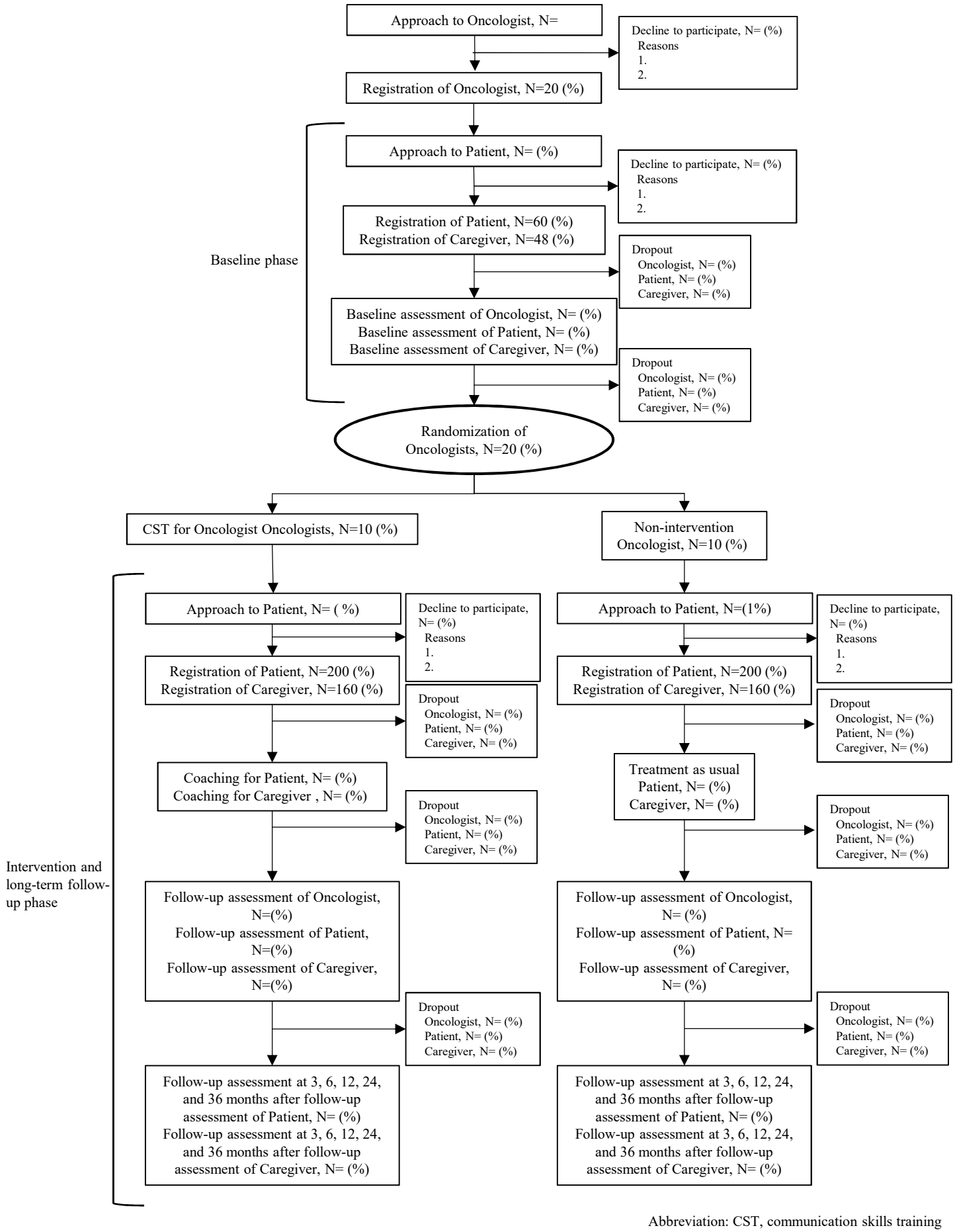
	Caregiver's evaluation of consultation	"How did the oncologist respond to your questions?" "Did you ask selected questions during consultation?" "How much have you discussed with the oncologist in the visit?"				○		
	Caregiver's evaluation of intervention in the IG	"Did you understand how to use the QPL and did you actually use it?" "Do you think you will continue the intervention?" "Was the intervention useful to you?" "Did the oncologist talk about the QPL?" "Did the QPL help you ask the oncologist questions?" "Is the QPL useful?" "Did you read the QPL before the visit?" "Do you think you will read the QPL in the future?"				○		
	Patient's comprehensive end-of-life QOL	Short version of GDI						○
Oncologist	Oncologist's Patient-centered communication behaviors	SHARE-RE		○		○		
	Oncologist's Patient-preferred communication behavior	SHARE-total		○		○		
	Oncologist's Patient-preferred communication behavior	RIAS		○		○		
	Oncologist's sociological background	Sex, age, clinical experience	○					
	Oncologist's evaluation of medical utilization by patient	The date of management		○		○		
	Oncologist's evaluation of intervention	The usefulness of intervention				○		

Abbreviation: RIAS, Roter intention analysis system
HADS, Hospital Anxiety and Depression Scale
QOL, quality of life
FACT-Physical & Functional, Physical well-being and Functional well-being subscales of the Functional Assessment of Cancer Therapy
CoQOLo, Comprehensive Quality of Life Outcome inventory
TiOS, Trust in Oncologists Scale
CSQ, Client Satisfaction Questionnaire
PEACE, Peace, Equanimity, and Acceptance in the Cancer Experience questionnaire
PTPQ, Prognosis and Treatment Perceptions Questionnaire
K6, K6 nonspecific psychological distress scale
EQ-5D, 5 Dimension EuroQol
GDI, Good Death Inventory
IG, intervention group



Abbreviation: CST, communication skills training

Figure 1. Participant flow diagram

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	7
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	7
Protocol version	#3	Date and version identifier	7
Funding	#4	Sources and types of financial, material, and other support	31
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	31
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	32
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	31
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and	31

		other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	9
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	9
Objectives	#7	Specific objectives or hypotheses	12
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	13
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	13

Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	16
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	13
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	13
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	13
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	20
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	21

Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	18
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	26
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	17
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	13
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque,	13

		sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	13
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	13
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	13
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	19

Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	19
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	19
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	27
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	27
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	27
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further	19

		details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	27
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	25
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	32
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	13
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	28

Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	18
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	42
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	28
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	32
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	7
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	25
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	28

Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	28
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	7
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	1
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a