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Title of Protocol:
A randomized controlled trial testing the effects of an acupressure intervention on appetite and weight in patients with gastric, esophageal, and pancreatic cancer: a pilot and feasibility study

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SPONSOR: National Center for Complementary and Integrative Health KL2 Grant (July 6, 2023 – February 28, 2026)

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PROTOCOL SYNOPSIS

Protocol Title	A randomized controlled trial testing the effects of an acupressure intervention on appetite and weight in gastric, esophageal, and pancreatic cancer patients: a pilot and feasibility study
Protocol Number	IRB20046
Protocol Sponsor	National Center for Complementary and Integrative Health
Trial Phase	Pilot
Trial Type	Randomized Controlled Pilot Trial
Clinical Indication	Cancer anorexia
Study Objectives	**Primary** To assess feasibility, as assessed by recruitment, adherence, retention, fidelity, and acceptability of an 8-week auricular acupressure intervention with usual care compared to usual care alone. **Secondary** To examine the feasibility of collecting preliminary data on appetite and body weight of an 8-week auricular acupressure intervention compared to usual care control. **Exploratory** To examine the feasibility of collecting preliminary data on circulating inflammatory cytokines and quality of life of an 8-week auricular acupressure intervention compared to usual care control.
Study Design	Randomized Controlled Feasibility Trial (2 arms)
Population	Up to 66 patients between 18-65yo with stage II-IV gastric, esophageal, and pancreatic cancer with planned ≥60 days of any chemotherapy regimen and experience low appetite.
Primary Endpoints	Recruitment and accrual rate, adherence, retention, fidelity, and acceptability
Secondary Endpoints	1. Cancer anorexia and appetite scores (Functional Assessment of Anorexia and Cachexia Treatment – Trial Outcome Index [FAACT-TOI]) 2. Body weight (kg)
Exploratory Endpoints	1. Circulating inflammatory cytokines (IL-1β, IL-4, and TNFα) 2. Quality of life (FACT-General Scale)
Type of control	Waitlist control – receives no acupuncture or acupressure for appetite during 8-week intervention period
Dose	Acupressure: 8 treatments (4 administered in clinic, 4 self-administered at home)
Regimen	Stimulation of ear seeds for 3 minutes bilaterally 3x/day. Ear seeds will be maintained for 5 days following application.
Treatment Groups	Arm 1: Auricular acupressure + usual care. Auricular acupressure applied in clinic every other week alternating with at-home application on alternating weeks (i.e., 8 acupressure treatments over 8 weeks). Arm 2: Waitlist control/usual care. Four bi-weekly auricular acupressure interventions will be provided after completion of the trial.
Treatment Schedule	Application once weekly x 8 weeks, maintained for 5 days following treatment and at least two days of rest between treatments.
Number of trial subjects	N=66
Estimated duration of trial	15 months
Duration of Participation	2 months

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ABBREVIATIONS
Include a table of abbreviations as needed.

AE	Adverse event
AES	Acupuncture Expectancy Scale
CDS	Collaborative Data Services
CHF	Congestive heart failure
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CRF	Case report form
EC	Ethics Committee
eCRF	Electronic case report form
EMR	Electronic medical record
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30
FAACT	Functional Assessment of Anorexia and Cachexia Treatment
FACT-ACS	Functional Assessment of Cancer Therapy - Anorexia/Cachexia Subscale
FACT-G	Functional Assessment of Cancer Therapy - General Scale
FDA	United States Food and Drug Administration
GI	Gastrointestinal
IL-1β	Interleukin 1-beta
IL-4	Interleukin 4
IL-6	Interleukin 6
IRB	Institutional Review Board
ITHS	Institute for Translational Health Sciences
OTC	Over the counter
SAE	Serious adverse event
TCM	Traditional Chinese Medicine
TNFα	Tumor necrosis factor-alpha
TOI	Trial Outcome Index
UW	University of Washington
VAS	Visual Analog Scale

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1.0 GENERAL INFORMATION

This document is a clinical research protocol, and the described study will be conducted in compliance with the IRB approved protocol, associated Federal regulations and all applicable IRB requirements. Pilot data collected from this clinical trial will provide preliminary data to inform the design of future trial testing the effectiveness of auricular acupressure for appetite in gastric, esophageal, and pancreatic cancers, which could serve as a new adjunct therapy for supportive oncology care.

Overview of Study Design

The pilot study will enroll up to 66 stage II-IV gastric, esophageal, and pancreatic cancer patients with low appetite. Recruitment, study activities, and data collection procedures will be conducted by highly trained research staff. Eligible participants will complete baseline assessments and be randomized to two study arms using a permuted block randomization procedure, stratified by cancer site: **Arm 1** – intervention, or **Arm 2** – waitlist control.

Arm 1 auricular acupressure will be delivered by trained nurses or advance practice providers following randomization at baseline (week 0), week 2, midpoint (week 4), and week 6 using taped *Vaccaria* ear seeds with clinical follow-up at closeout (week 8). Arm 1 participants will be instructed on how to apply ear seeds at home on other weeks (i.e., week 1, week 3, week 5, and week 7). Arm 2 will continue to receive usual care but instructed to not receive acupuncture or acupressure until data collection is completed at 8-weeks. A follow-up assessment will take place and baseline assessments will be repeated at closeout (week 8).

1.1 Protocol Title

A randomized controlled trial testing the effects of an acupressure intervention on appetite and weight in patients with gastric, esophageal, and pancreatic cancer: a pilot and feasibility study

1.2 Sponsor Information

National Center for Complementary and Integrative Health (3KL2TR002317-07W2 – 7/6/23-2/28/26)

1.3 Investigator Information

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2.0 INTRODUCTION TO THE PROTOCOL

2.1 Introduction

Cancer anorexia, the abnormal loss of appetite, directly leads to cancer cachexia through malnourishment, reduced caloric intake from tumor impingement, treatment side-effects, and other modifiable risk factors.[1,2] Cachexia is implicated in 20% of cancer-related deaths[1] and affects up to 87% of patients with gastric and pancreatic cancer[3]; 62,210 new pancreatic and 26,300 new gastric cancer cases are projected this year in the United States alone.[4] Cachexia prolongs length of hospital stay for patients, poses a significant cost burden to the hospital system,[7] negatively impacts treatment tolerance and adherence,[8,9] and reduces overall patient quality of life.[9,10] Inflammation, pain, nausea and vomiting, and depression from a reduced quality of life all influence the development of anorexia, malnourishment, and progression to cachexia.[1,11,12] Medications to address anorexia pose a financial challenge to hospitals and patients alike,[13] may be toxic patients, and may not be tolerated with concurrent nausea.[14] Further, direct approaches to reverse malnutrition through artificial nutritional supplementation have demonstrated limited benefit to patients' quality or length of life.[15,16]

2.2 Clinical Data on Acupuncture and Acupressure in Oncology Patient Populations

Auricular acupuncture and acupressure are efficacious in modifying pain,[19-23] reducing chemotherapy-induced nausea and vomiting,[24,25] and improving quality of life in both cancer and non-cancer settings.[26,27] Preliminary evidence suggests auricular acupuncture and full body acupuncture may provide benefits to appetite in patients with cancer anorexia.[28,29] A pilot trial of auricular acupressure for chronic low

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back pain demonstrated significant improvements in pain and overall physical function, increases in anti-inflammatory cytokines (e.g., IL-4), and a within-group reduction in pro-inflammatory cytokines (e.g., TNFα).[19] As IL-1β and TNFα have been implicated in pain, depression, and cancer anorexia, exploring this potential mechanistic interface in a new population is vital.

The research exploring Traditional Chinese Medicine (TCM) therapies focuses primarily on acupuncture in uncontrolled designs or in windows of intervention without long-term follow-up.[28,29] These studies support the hypothesis that auricular acupressure could be an appetite-promoting intervention that improves weight maintenance/gain and physical performance; however, no studies have been conducted (except on acupuncture alone) on the feasibility of a longer-term auricular acupressure intervention in a population at risk for malnourishment in an outpatient setting.

Auricular acupressure is a form of micro-acupuncture that exerts its effect by stimulating the central nervous system using adhesive taped pellets (most commonly the plant seed *Vaccaria segetalis*) applied to specific locations on the external ear.[30-32] The use of *Vaccaria* ear seeds to deliver acupressure has been shown to improve pain, fatigue, insomnia, nausea and vomiting, depression, and quality of life in both cancer and non-cancer settings.[20-27,33-37] Auricular acupressure can be delivered by nurses and advanced practice providers and is a safe, inexpensive, and non-invasive approach to addressing cancer-related symptoms and treatment side-effects.[21,27,35,36]

2.3 Risks/Benefits

Auricular acupressure has yet to be tested in addition to usual care for low appetite in cancer over an 8-week period. However, it is recognized that low appetite poses a risk for negative health outcomes and quality of life in patients with cancer. As there are few complementary treatments outside pharmaceutical management, minimization and reversal of appetite loss is necessary in this population.

Risks

- Discomfort. There may be some discomfort in completing questionnaires about cancer. Participants can decline to complete a survey or skip questions at their own discretion. Participants may additionally experience discomfort during phlebotomy and have slight risk for infection, local bleeding, and bruising.
- Local irritation and pain. Research related injuries are minimal due to the low-risk nature of this study; however, there is a risk of local irritation of ear seeds.
- Inconvenience. The timing and frequency of the in-person clinical visits may provide an inconvenience to participants' schedules.

Benefits

- Knowledge gained. Because risks to subjects in this study are minor, the risks are most reasonable in relation to the expected benefits.
- Financial compensation. They will also receive up to $120 in compensation in the form of electronically-delivered gift cards at baseline ($30), midpoint ($40), and closeout ($50) to compensate for time and potential discomfort associated with trial procedures.
- Other benefits. There are no other direct benefits of this research to a given study participant. However, the data from the study will be used to direct future intervention efforts targeting similar populations.

3.0 OVERVIEW OF CLINICAL TRIAL

3.1 Study Objectives

The overall objective for this pilot study is to establish feasibility of implementation and data collection of an 8-week auricular acupressure intervention on appetite, weight, and underlying mechanisms of diminished appetite (i.e., systemic inflammation and quality of life) in patients with stage II-IV gastric, esophageal, and pancreatic cancer.

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3.1.1 **Primary Objective.** To assess feasibility as assessed by recruitment, adherence, retention, fidelity, and acceptability of an 8-week auricular acupressure intervention plus usual care compared to usual care alone.

3.1.2 **Secondary Objectives.** To examine the feasibility of collecting primary data on 1) cancer anorexia (low appetite) and 2) body weight following an 8-week auricular acupressure intervention.

3.1.3 **Exploratory Objectives.** To examine the feasibility of collecting primary data on 1) circulating inflammatory cytokines (i.e., IL-1β, IL-4, and TNFα) and 2) quality of life (i.e., FACT-G) following an 8-week auricular acupressure intervention.

3.2 Study Population

Our target population are patients with stage II-IV gastric, esophageal, or pancreatic cancer with low appetite (n=66) who are 18-65 years old undergoing chemotherapeutic treatment for their cancer for ≥60 days.

3.3 Study Design

This is a pilot, randomized, controlled pilot study testing the feasibility and effect estimation of an 8-week auricular acupressure intervention on appetite in stage II-IV gastric, esophageal, and pancreatic cancer.

3.3.1 **Primary Endpoint.** To assess feasibility measured by recruitment (accrual rate), adherence (attendance and ear seed stimulation), retention (completion of all study assessments), fidelity (provider and participant adherence to procedures), and acceptability (exit interview).

3.3.2 **Secondary Endpoints.** To examine the feasibility of collecting primary data on:

- Appetite using the Functional Assessment for Anorexia/Cachexia Treatment Subscale (FAACT) and FAACT Trial Outcome Index (TOI). A cut-off of 37 points has been validated to predict anorexia in this population with a similar degree of accuracy to the more simplified visual analog scale, which will be used to screen patients for eligibility.[39]
- Body weight (kg)

3.3.3 **Exploratory Endpoints.** To examine the feasibility of collecting primary data on biomarkers of systemic inflammation and quality of life measures.

- Blood will be analyzed for circulating inflammatory cytokines (IL-1β, IL-4, and TNFα).
- Quality of life measures will be analyzed from the Functional Assessment for Cancer Therapy-General (FACT-G).

3.3.4 **Hypotheses**

- The intervention and data collection are feasible and acceptable as outlined in 3.3.1.
- The intervention design is feasible for collecting data on appetite (FAACT and TOI) and body weight (kg).
- The intervention design is feasible for collecting mechanistic data related to cancer anorexia, including circulating inflammatory cytokine levels (IL-1β, IL-4, and TNFα) and quality of life (FACT-G).

3.4 Study Approach

3.4.1 **Recruitment strategies.**

Data request to for electronic medical records (EMR). The Fred Hutch Clinical Analytics team is able to collate data from the shared UW and Fred Hutch EMR system. Study investigators will create a list of variables based on eligibility criteria and will submit a data request or be trained in the processes of data collation. Prior to initiating recruitment, all Fred Hutch GI Oncology physicians

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will be introduced to the study and it will be requested that all of their eligible patients be approached by study staff for study participation.

3.5 Estimated Accrual

Sixty-six patients will be enrolled, 33 randomized to each arm. Current reports estimate an average of 102 unique patients per month at Fred Hutch with pancreatic, gastric, or esophageal cancer, and 33 unique patients per month at UW. As an estimated 50-80% of patients with pancreatic cancer,[40] and 30-80% of patients with advanced cancer of any kind,[41] experience weight loss during cancer management, it is reasonable to achieve target recruitment of 66 patients within the proposed 15-month accrual period.

3.6 Name of Sponsor/Funding Source

National Center for Complementary and Integrative Health (3KL2TR002317-07W2)

4.0 SUBJECT ELIGIBLITY

4.1 Inclusion Criteria

4.1.1 Demographic Data

- 18-65 years of age

4.1.2 Disease Related Criteria

- Stage II-IV gastric, esophageal, or pancreatic cancer
- Appetite score on visual analog scale ≤70/100 (see 3.3.2)

4.1.3 Prior/Current Treatment Related Criteria

- At least 60 days of planned systemic treatment (i.e., chemotherapy, endocrine/hormone therapy, or immunotherapy), whether already initiated or scheduled to be initiated

4.1.4 Accessibility Criteria

- Access to phone and electronic device for study contacts and questionnaires
- Willing and able to attend 4 in-person auricular acupressure treatments at the Fred Hutch South Lake Union Clinic
- Willing and able to perform 4 at-home self-applied treatments of auricular acupressure

4.1.5 Clinical/Laboratory Criteria

- Participants must not have received acupressure or acupuncture for low appetite within last 30 days
- Participants must not be actively using corticosteroids, mirtazapine (Remeron), olanzapine (Zyprexa), or Marinol for appetite stimulation at baseline
- Participants must be able to intake food orally and not require sole or supplemental intravenous nutrition at baseline
- Participants must not have a history of physiological eating disorders (e.g., anorexia nervosa) in the last 3 years
- Participants must not have a current known or diagnosed immunodeficiency
- Participants must have an intact auricular pinna

4.1.6 Ability to understand and the willingness to sign a written informed consent document

- Able to understand and willing to sign written informed consent in English

5.0 SUBJECT REGISTRATION

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Subjects will be registered by the study team and their data will be entered into OnCore CTMS and a secure REDCap™ database. A signed study consent and a signed HIPAA consent are required for registration.

6.0 TREATMENT PLAN

6.1 Treatment Plan and Data Collection Overview

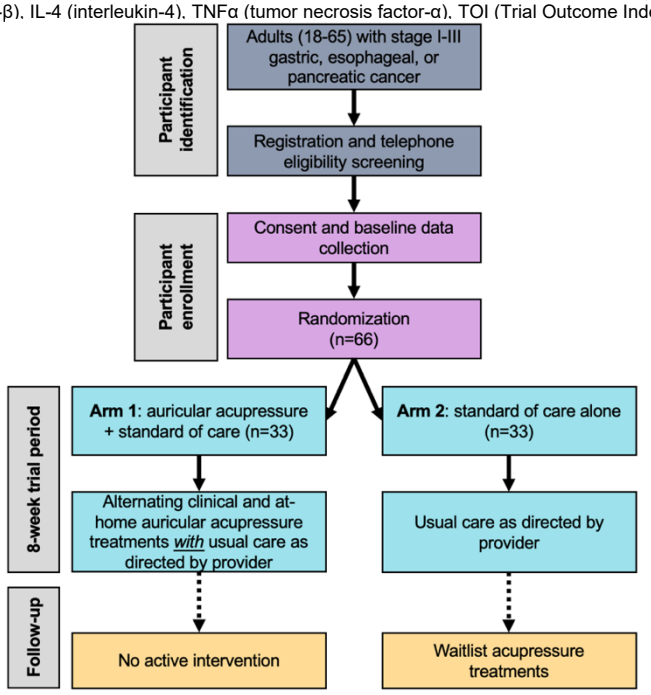
Sixty-six patients will be randomized 1:1 to the intervention arm (n=33) of auricular acupressure plus usual care or the waitlist control arm (n=33) of usual care alone (Figure 1 and Table 1).

Table 1. Overview of Trial Data Collection

Procedure	*Screening*	*Baseline (week 0)*	*Home Application (weeks 1, 3, 5, and 7)*	*Follow-up (weeks 2 and 6)*	*Midpoint (week 4)*	*Closeout (week 8)*	*Follow-up (week 16)*
Eligibility Screen	X						
Consent	X	X					
Safety and AE Monitor (intervention arm only + waitlist controls using vouchers)		X		X	X	X	X
Acupressure Intervention							
Clinic intervention		X		X	X		
At-home intervention			X				
Fidelity assurance			*Conducted throughout trial*				
Aim 1. Feasibility and Acceptability							
Acceptability questionnaires (intervention arm only)						X	
Adherence (diary, intervention arm only)			*Conducted throughout trial*				
Retention/Attrition				X	X	X	
Acupuncture Expectancy Scale		X					
Aim 2. Effect on Appetite and Weight Loss							
FAACT TOI		X			X	X	X
Body Weight		X			X	X	
Aim 3. Exploration of Underlying Mechanisms							
Blood Draw (IL-1β , IL-4, and TNFα)		X				X	
FACT-G		X			X	X	X

AE (adverse event), AES (Acupressure Expectancy Scale), FAACT (Functional Assessment of Anorexia/Cachexia Treatment), FACT-G (Functional Assessment of Cancer Therapy- General), IL-1β (interleukin-1-β), IL-4 (interleukin-4), TNFα (tumor necrosis factor-α), TOI (Trial Outcome Index)

Figure 1. Flow of Study Procedures

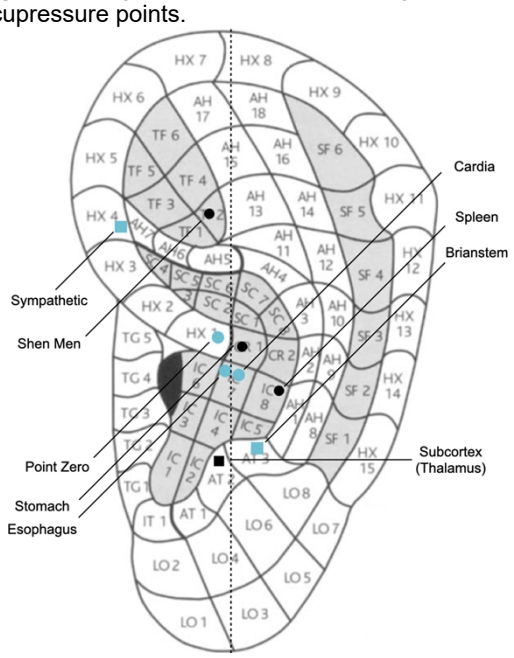


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6.2 Auricular Acupressure Intervention

The intervention group will receive auricular acupressure with non-colored, non-latex adhesive application of *Vaccaria* ear seeds applied *bilaterally* on 4-6 points (Figure 2 and Table 2) to address appetite as well as potential underlying mechanisms of cancer anorexia (e.g., pain). Acupressure points were determined through: 1) review of available literature on addressing anorexia,[28,29] pain,[19,20] nausea and vomiting,[25] and quality of life improvement,[21,25,27,37] by using the most common and overlapping auricular acupressure points; followed by 2) iterative consensus building between the PI and three skilled clinical oncology acupuncturists at Fred Hutch with at least 5 years of experience using auricular acupuncture and acupressure. Participants will be provided ear seeds to take home with verbal and written instructions including paper ear diagrams to apply self-administered auricular acupressure on alternate weeks between in-person visits (e.g., between baseline and week 2).

Figure 2. Diagram of model ear with targeted acupressure points.



Providers (RN, ARNP, and LAc providers) will apply ear seeds every other week to Shenmen, Stomach, Spleen, and Subcortex to every participant. Providers may apply up to two additional points at in-person visits according to the individual participant symptom presentation. These additional points (Figure 2, in teal) may be interchanged between visits and will include Sympathetic for pain, Cardia for nausea, Brainstem for vomiting, Esophagus for difficulty swallowing, and Point Zero for low quality of life. If a participant experiences more than two symptoms of pain, nausea, vomiting, difficulty swallowing, and/or low quality of life concurrently, the two symptoms the patients would most like to be addressed will be targeted by the appropriate point. Patients will self-apply the standard protocol (i.e., Shenmen, Stomach, Spleen, and Subcortex) on weeks between in-person visits. Acupressure points will first be cleaned using 70% isopropyl alcohol before seed placement.

Table 3. Auricular Acupressure Point Protocol and Modifications

	Points
Standard Protocol	Shenmen, Stomach, Spleen, Subcortex
Patient-Reported Symptom-Specific Points (up to 2 points)	
Pain	Sympathetic
Nausea	Cardia
Vomiting	Brainstem
Difficulty Swallowing	Esophagus
Low Quality of Life	Point Zero

Acupressure points will be stimulated three times per day for three minutes each and maintained for five days for seven cycles over eight weeks, consistent with the majority of auricular acupressure protocols in cancer settings.[25] Participants will be instructed to stimulate each seed by gently massaging one point for 10 presses, repeating the pattern on all seeds, until 3 minutes of consistent stimulation has been reached. Participants can stimulate seeds bilaterally for the 3-minute period at the same time, or can stimulate the seeds unilaterally for 3 minutes on each side. Taped seeds will be removed at home by participants after five days. Participants will have an estimated two days between cycles of ear seeds. Handouts describing acupressure procedures and ear seed care instructions will be provided to participants (Appendix A).

If a participant misses a scheduled in-person clinic visit (baseline, week 2, midpoint, week 6, closeout), it will not be made up; however, all participants who miss an in-person visit will be instructed to perform the standard protocol as directed for alternating weeks.

6.3 Waitlist Control

To support recruitment and retention, all those who are enrolled will receive acupressure treatment. Participants assigned to the control group (usual care) will receive regular care as deemed appropriate by their clinician during the active phase of the trial. Evidence suggests the use of “sham” acupuncture and acupressure may exert an action that can potentially mask results of the true intervention, most notably in chronic pain.[42] As this proposal assesses impact on inflammatory cytokines, this pilot study will use usual care comparisons.[43] For those allocated to the usual care waitlist control group, four bi-weekly auricular

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acupressure interventions will be provided per the study protocol immediately following their participation (8 weeks) to support participant recruitment, retention, and beneficence in the context of auricular acupressure as a potential therapy to reduce symptom burden in patients.

6.4 Concomitant Medication and Supportive Care Guidelines

Use of systemic (oral or intravenous) steroids and immunomodulators, appetite stimulants (e.g., Marinol, mirtazapine, olanzapine), and supplemental nutritional delivery (e.g., total parenteral nutrition or percutaneous endoscopic gastrostomy) at baseline for appetite stimulation will deem participants ineligible. However, systemic corticosteroids, immunomodulators, and supplemental nutritional delivery are considered standard-of-care options for appetite management and will be allowed on this study. Standard-of-care supporting care is recommended for other symptoms related to cancer or chemotherapy treatment.

6.5 Duration of Therapy

The intervention will be delivered over 8 weeks, concurrently with systemic cancer therapy (with or without radiation).

6.6 Duration of Follow-Up

Patients in the intervention arm will be followed up 8 weeks after active treatment ends to assess for carryover effects on appetite quality of life. Participants in the usual care/waitlist control arm will not be followed after active treatment with the exception of collection of data during waitlist control auricular acupressure visits if these are pursued.

6.7 Dosing Delays/Dose Modifications

Dose modifications, hold, and other alterations to planned chemotherapy will be at the discretion of the treating physician. Auricular acupressure teatments will only be adjusted within a 3-day window following the 2-day minimum “rest” period between treatments. If a participant discontinues chemotherapy, they may continue to receive auricular acupressure as protocolized.

6.8 Tools to Promote Treatment Adherence

Adherence will be monitored by daily electronic diary using the MyCap platform via REDCap™ (Section 7.6). MyCap additionally has the capacity to send automated reminders and notifications to patients via an app or email while maintaining confidentiality (Section 13.0). Reminder calls from study staff may be implemented upon request to support patient adherence.

6.9 End of Treatment (EOT) Visit Schedule and Procedures

The EOT visits for the intervention arm who discontinue from the study should ideally occur within 1 week (7 days) of their week 7 self-applied auricular acupressure treatment and is permitted in the range of 3-7 days after the last auricular acupressure treatment. The EOT visit for the usual care/waitlist control arm should occur within the range of 3-7 days after 8 weeks from their baseline visit. Procedures to be performed during the EOT visit include:

- Weight measurement (kg)
- Administration of the final FAACT measure
- Administration of the acceptability questionnaire
- AE assessment
- Blood draw

As per **6.6**, patients in the usual care/waitlist control arm and choose to use auricular acupressure coupons (Appendices H and I) will have the official EOT for uniform data collection, but will also have limited data collected at the time of each auricular acupressure session to note any AEs or major symptoms at the time of each follow-up visit.

7.0 SUBJECT EVALUATION

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7.1 In-Person Clinical Evaluations

Clinical evaluations take place according to the Study Calendar (Section 6.1). The window between the closeout clinical evaluation visit and all in-clinic ear seed applications visits should be as close to the scheduled day (i.e., 7 days following prior treatment) as possible. Delays in treatment within 3 days are permitted and will not be considered a deviation from protocol or require cessation of protocol therapy.

- Vitals
  - Body weight (kg)
- Appetite Measurement
  - Visual Analog Scale
  - Functional Assessment Anorexia/Cachexia Treatment (FAACT)
- Quality of Life Measurement
  - Functional Assessment of Cancer Therapy (General Scale – FACT-G)
- Labs
  - Hematology/serology: inflammatory cytokines (IL-1β, IL-4, and TNFα)
- Concomitant Symptom Checklist
  - Visual Analog Scale
- Acupressure Diary
- Clinical Adverse Event Attribution (see Section 10.0)
  - CTCAE version 5.0

7.2 Patient-Reported Outcome (Appetite and Quality of Life) Assessments

These assessments will be administered at screening (7.2.1), baseline (7.2.2, 7.2.3), midpoint (7.2.2, 7.2.3), and closeout (7.2.2, 7.2.3) before receiving auricular acupressure treatment. At each time point, the FAACT (including FACT-G; Appendices C and D) will be used to assess appetite and quality of life.

7.2.1 Visual Analog Scale (VAS) for Appetite

The VAS has been validated in oncology patients undergoing chemotherapy to predict anorexia.[39] A cut-off of ≤70/100 predicts anorexia with 76% sensitivity and 83% specificity. The VAS will be administered as a preliminary screening tool (Appendix B).

7.2.2 Functional Assessment of Anorexia/Cachexia Treatment (FAACT)

The Functional Assessment of Anorexia/Cachexia Treatment (FAACT) is a 39-item scale that contains the Functional Assessment of Cancer Therapy – General (FACT-G) and an Anorexia-Cachexia Subscale (ACS).[44] The FACT-G and its additional modules (FAACT) have been validated in United States cohorts of patients with cancer.[45-47] The additional ACS module explores individual patient circumstances surrounding anorexia, including food aversion, eating and weight loss worry, eating difficulties, loss of control, and physical decline. A FACT-ACS cut-off of 37 points has been identified to predict anorexia in this population with a similar degree of accuracy to the more simplified VAS tool.[39] This tool will be used to comprehensively assess participant experiences of anorexia and the changes during the trial.

7.2.3 Quality of Life Assessments - FACT-G

The FACT-G is a multiple item Likert scale questionnaire which highlights domains of physical, social/family, emotional, and functional well-being. Compared with other tools that explore quality of life in interventional cancer research, such as the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-C30,[48] the FACT-G has comparable internal consistency, internal structure, convergent validity, and support for interpretation.[49-51]

7.3 Blood-Based Biomarkers of Inflammation

Quantitative serum biomarkers of inflammation, including IL-1β, IL-4, and TNFα, will be assessed at baseline before receiving auricular acupressure treatment and at closeout. Samples will be drawn, processed, and stored in Fred Hutch biorepositories. Samples will be analyzed using the multiplex immunoassay Luminex® 200™ system (Invitrogen, Carlsbad, CA, USA) at the UW Department of

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Laboratory Medicine and Pathology. The UW Department of Laboratory Medicine has regularly and successfully used the Luminex® system for clinical research studies. The intra-assay coefficient for variation (CV) of Luminex® immunnoassays are estimated to be 2.6, 4.9, and 3.7, and 12.7, 19.5. and 17.2 for inter-assay CV, for IL-1β, IL-4, and TNFα, respectively.

7.4 Acupressure Expectancy Scale (AES)

A version of the Acupuncture Expectancy Scale modified for acupressure will be administered at baseline to assess the impact patient expectations have on potential effects of auricular acupressure (Appendix E). This scale has been validated to assess acupuncture expectancy and measures a participant's expectations for benefit to their illness, coping ability, symptomatic presentation, and energy levels.[52] To reduce potential bias due to the knowledge of randomization assignment, this measure will be assessed prior to randomization in all study participants.

7.5 Concomitant Symptom Checklist

The auricular acupressure treatment can be modified at all in-person clinical visits to address up to two additional complaints known to affect appetite in patients with cancer (i.e., pain, nausea, vomiting, dysphagia, and low quality of life or depression). These assessments will be administered at baseline, week 2, midpoint, and week 6 visits before receiving auricular acupressure treatment.

7.5.1 Visual Analog Scale (VAS) for Symptom Interference

The VAS is a simple tool that may be administered to patients as a tool to visually identify which symptoms pose the greatest interference with patient daily life. A multi-component VAS (Appendix F) will be given to the patient to identify the level of interference for each of these symptoms within the last 7 days. The two symptoms with greatest interference will be added to the in-person auricular acupressure treatment. If no or only one symptom is identified, no additional ear seeds or one additional ear seed will be applied to the respective location. If more than two symptoms equally interfere according to VAS score, the patient will self-elect which symptom and respective ear seed will be placed.

7.6 Acupressure Diary

Assessment of self-stimulation of ear seeds at the prescribed duration and frequency will be collected through self-report electronically (Appendix G). Participants will be provided an electronic adherence monitoring form during the first five days of post-baseline treatment using MyCap via REDCap™. This form will assess full, partial, or non-compliance to the intervention. Physical forms will be provided as needed for participants upon request. For participants who are partially- or non-compliant, the research team will provide reminders through text message, email, or by reviewing recommendations for reminder alarms. The treatment adherence form will be provided again following week 1 at-home, midpoint in-office, and week 5 at-home procedures. Additional information on implementing adherence support tools can be found in Section 12.0.

8.0 SUBJECT DISCONTINUATION OF ACTIVE TREATMENT (WITHDRAWAL)

Subjects may be removed from this study at any time at their discretion. Subjects may also elect to be removed from this protocol if they develop any untoward side effects (e.g., local discomfort, rash, or irritation) from the study procedures (i.e., auricular acupressure).

If a subject withdraws consent to participate in the study or aspects of the study, attempts should be made to obtain permission to record survival data up to the protocol-described end of the subject follow-up period. Documentation in the medical record should state that the subject is withdrawing from the study and what, if any, selected data the subject will permit the investigator to obtain.

If a subject withdraws consent and has received less than one auricular acupressure treatment, an additional patient will be recruited.

An explanation for discontinuing treatment is recorded for each subject discontinuing treatment on the appropriate CRF/eCRF. The PI must be notified immediately if a subject discontinues treatment. All

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subjects, irrespective of treatment status, will continue to be followed for survival. Treatment in this study must be discontinued for any of the following reasons:

- at Investigator's discretion;
- at the subject's request;
- if the subject enrolls in a trial of another investigational agent which does not permit concurrent treatment;
- if the patient misses first (baseline) auricular acupressure sessions, in which they may be reconsented;
- Grade 4 or life-threatening toxicity (See Section 10.0, Adverse Events) attributable to the study intervention.

If a patient discontinues a prescribed chemotherapy regimen, he/she may continue to receive acupuncture as protocolized until the completion of 2 months duration of auricular acupressure treatment.

9.0 CONCOMITANT MEDICATIONS/THERAPIES

Participants will be asked during the Baseline questionnaire about recent and current medication use and acupuncture/acupressure treatments. Changes in medications during time in the trial will be queried at trial closeout. Medications will be recorded for name (brand or generic, as applicable), dose (according to amount taken), frequency, historical duration of use, and whether the medication is prescribed or over-the-counter (OTC). Any OTC medications that are not taken on a consistent or regular basis will not be recorded.

Example medication query to be included:

Medication Name		Dose	Frequency	Duration	Additional Notes
Ondansetron	[ ] brand [X] generic	4mg	Twice daily	2 years	
Vitamin D3	[ ] brand [X] generic	5,000 IU	Daily	6 months	
Valtrex (valacyclovir)	[X] brand [ ] generic	1,000mg	Daily	5 years	

Concomitant medication limitations are described in section 6.4.

10.0 ADVERSE EVENTS

10.1 Adverse Events

This is a low-risk study with no pharmacologic intervention agent. Any adverse events will be recorded in the Adverse Event Summary Form and reported (Section 10.2).

10.2 Adverse Event Grading Scale

0 = No Adverse Event or within normal limits
1 = Mild Severity: Transient laboratory test alterations; discomforts noted but no disruption of daily activities; no therapy, or only symptomatic therapy required
2 = Moderate Severity: Laboratory test alterations indicating injury without long-term risk; discomfort sufficient to modify normal daily activity; specific therapy required (i.e., more than symptomatic)
3 = Serious Severity: Laboratory test indicating a serious health threat or permanent injury; incapacity, inability to work, inability to perform normal daily activity; hospitalization required or prolonged; emergency treatment required; life-threatening events; death

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10.3 Adverse Event Reporting Requirements

Plan for unanticipated AE reporting: All unanticipated AEs related to the study procedures that are severe or serious will be reported by Dr. Blake Langley to the IRB within 7 days of notification of the investigator.

Plan for anticipated AE reporting: All serious anticipated AEs related to the study procedures will be reported by Dr. Blake Langley to the IRB within 7 days of notification of the investigator.

Plan for ongoing review of results: The PIs will be notified within 24 hours by the research manager of any early terminations due to an adverse event.

Plan for safety review: The PI will perform a cumulative review of all adverse events and premature terminations review every 6 months after study initiation or after completion of 50% of participant visits, whichever occurs first.

Plan for annual reporting: A summary of the investigation including all adverse events and how they were handled, enrollment, drop-outs and reason for discontinuation and any protocol modifications will be provided to the IRB on an annual basis.

Annual Reports will contain:

- The number of adverse events and an explanation of how each event was handled
- The number of complaints and how each complaint was handled
- The number of subject withdrawals and an explanation of why the subject withdrew or was withdrawn
- The number of protocol deviations and how each was handled

The occurrence of any serious and unexpected event may prompt changes in study protocol. Any such change will be approved by the IRB before implementation.

10.4 Serious Adverse Event (SAE)

An adverse event should be classified as an SAE if it meets one of the following criteria:

Fatal	Adverse event results in death.
Life threatening	The adverse events placed the subject at immediate risk of death. This classification did not apply to an adverse event that hypothetically might cause death if it were more severe.
Hospitalization	It required or prolonged inpatient hospitalization. Hospitalizations for elective medical or surgical procedures or treatments planned before enrollment in the treatment plan or routine check-ups are not SAEs by this criterion. Admission to a palliative unit or hospice care facility is not considered to be a hospitalization.
Disabling/incapacitating	Resulted in a substantial and permanent disruption of the subject's ability to carry out normal life functions.
Congenital anomaly or birth defect	An adverse outcome in a child or fetus of a subject exposed to the molecule or treatment plan regimen before conception or during pregnancy.
Medically significant	The adverse event did not meet any of the above criteria but could have jeopardized the subject and might have required medical or surgical intervention to prevent one of the outcomes listed above.

11.0 DATA AND SAFETY MONITORING PLAN

A data safety and monitoring committee is not needed as this is not a Phase 3 clinical trial. Dr. Blake Langley will oversee the data safety and monitoring for this project. He will meet with the study staff to discuss protocols and procedures to ensure participant safety and the validity and integrity of the study data. All staff members will attend trainings on these procedures and will be given information on the importance of reporting any adverse event immediately. Dr. Langley, and the IRB will be alerted about any adverse events immediately. Dr. Langley will discuss any adverse effects and examine available data to assess

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whether safety is compromised. Action to resolve the adverse event will be discussed with IRB prior to implementation. The team will enact any actions recommended by the IRB.

In addition, protocols are reviewed at least annually and as needed by the Fred Hutch Scientific Review Committee (SRC) and the Fred Hutch/University of Washington Cancer Consortium Institutional Review Board (IRB). The review committees evaluate accrual, adverse events, stopping rules, and adherence to the applicable data and safety monitoring plan for studies actively enrolling or treating subjects. The IRB reviews the study progress and safety information to assess continued acceptability of the risk-benefit ratio for human subjects. Approval of committees as applicable is necessary to continue the study.

The trial will comply with the standard guidelines set forth by these regulatory committees and other institutional, state and federal guidelines.

12.0 STATISTICAL CONSIDERATIONS

12.1 Study Design

This is a pilot, randomized, controlled pilot study testing the feasibility of an 8-week auricular acupressure intervention on appetite in stage II-IV esophageal, and pancreatic cancer.

12.2 Primary/Secondary Endpoints and Analytical Methods

12.2.1 Primary Endpoints

Feasibility is the primary endpoint of this trial, assessed in terms of accrual, retention, intervention adherence, intervention fidelity, and acceptability. Accrual will be measured by the average rate of participants-per-month enrolled into both groups with the goal of an average of 5 patients/month over a 15-month period. Retention will be measured by the number of participants who remain in the trial and provide data at the closeout visit. Adherence will be measured in the intervention group by the number of applied auricular acupressure treatments, with the total possible being 8. Fidelity will be assessed by study team adherence to symptom query and appropriate ear seed point modifications to the standard protocol (see Section 7.5.1) and accuracy of seed placement according to photographic analysis. Acceptability will be assessed for participants in the intervention arm following trial completion or early withdrawal, for participants in the waitlist control arm who follow through with treatment, and for providers through semi-structured interviews.

12.2.2 Secondary Endpoints

The secondary endpoints include appetite as measured by the FAACT TOI and/or the FACT-ACS, and body weight (kg).

12.2.3 Exploratory Endpoints

The exploratory endpoints include inflammatory cytokine levels (IL-1β, IL-4, and TNFα) and quality of life as measured by the FACT-G.

12.3 Sample Size and Power

With a sample size of 33 participants in each arm, and with the projection of up to 20% attrition, the trial should still be sufficient to establish the feasibility of the intervention as defined by the domains above. For example, using the definition of adherence described above, if the true adherence rate is 90%, then with 33 patients the probability of an observed adherence rate in excess of 80% is 0.96. On the other hand, if the true adherence rate is 70%, the probability of an observed adherence rate in excess of 80% 0.09. Data generated in this trial will provide important and useful information to inform the design of future trials.

12.4 Randomization

Following baseline data collection, participants will be randomized 1:1 to auricular acupressure plus standard care or standard care alone (n=66). Participants will be randomized to the intervention or waitlist control using a permuted block design with random block sizes stratified on cancer site.

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12.5 Statistical Analysis

Primary endpoints will assess feasibility by: 1) meeting target accrual rate, 2) ≥70% retention in the treatment arm with <20% difference in retention compared to the standard care/waitlist control group, 3) ≥67% adherence to self-stimulation of acupressure and >75% attendance at in-person treatment visits beyond baseline (week 2, midpoint, week 6, week 8), 4) >75% provider adherence appropriate ear seed point modifications to the standard protocol (see Section 7.5.1) and >75% accuracy of provider-applied ear seed placements, and 5) a majority of participants and providers reporting positive acceptability responses to treatment. The ability to accrue and retain, have participants remain adherent and attend visits, and have providers adhere and accurately apply measures in the protocol will be the main considerations for determining feasibility as outlined by the parameters above.

Secondary and exploratory endpoints will include describing group-specific parameter changes over the 8-week intervention period. Analyses will assess change in each outcome as a change from baseline to week 8 and observe temporal changes at week 4 for patient-reported outcomes associated with our exploratory aim. Secondary endpoints include appetite (FAACT and/or the TOI) and body weight (kg). Exploratory endpoints include circulating inflammatory cytokine levels, nausea and vomiting, and quality of life. Average change within groups will be described using descriptive statistics. Within each group, the change over the 8-week intervention period will be assessed using a one-sample t-test, as appropriate, depending on the observed distributions. No formal comparisons will be made between groups.

The FAACT questionnaire has identified two acceptable assessments of treatment effects through the Trial Outcome Index (TOI) or the FAACT score. The TOI is composed of the Physical Well-Being and Emotional Well-Being subscales of the FACT-G in addition to the Anorexia/Cachexia Subscale, while the FAACT composite score is composed of all FACT-G and FACT-ACS domains. These scores will be considered for additional exploratory analysis.

12.6 Ethnic and Gender Distribution Chart

Enrollment in the trial will be open to all people diagnosed with pancreatic, gastric, and esophageal cancers. We will actively enroll patients with pancreatic, gastric, and esophageal cancer who seek care at the Fred Hutchinson Cancer Center (Fred Hutch) and the University of Washington. These cancers affect men at a higher rate than women, estimated at 55.1% to 44.9% within the Fred Hutch system, respectively (extracted from Tableau). Additional data reflects 67.2% of all patients diagnosed with these cancers are white, 15.4% are of unknown or mixed race, 9.8% are Asian, 4.2% are Black or African, 2.3% are American Indian or Alaska Native, and roughly 1.0% are Hawaiian or other Pacific Islander. We will aim to recruit a population reflective of the demographics seen in the Fred Hutch and University of Washington medical systems.

Projected Target Accrual

ETHNIC AND GENDER DISTRIBUTION CHART

Table 3. TARGETED / PLANNED ENROLLMENT: Number of Subjects

Ethnic Category	Sex / Gender		
	Females	Males	Total
Hispanic or Latino	2	2	4
Not Hispanic or Latino	33	28	62
Ethnic Category Total of All Subjects*	36	30	66
Racial Category			
American Indian / Alaska Native	1	1	2
Asian	3	3	6
Native Hawaiian or Other Pacific Islander	1	1	2
Black or African American	2	1	2

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White	24	20	44
More Than One Race	2	2	4
Unknown	3	2	5
Racial Categories: Total of All Subjects*	36	30	66

13.0 DATA MANAGEMENT/CONFIDENTIALITY

Collaborative Data Services (CDS) Shared Resource

CDS will use REDCap™ to track, collect and maintain study data. REDCap™ is a web-based research-centric electronic data capture system supported through a federally funded consortium led by Vanderbilt University. The system is fully supported by CDS, which maintains the REDCap™ installation and provides a secure system with high reliability and availability. CDS will design, build, and maintain the REDCap™ data forms that will be used for data capture, including screening, participant questionnaires, and staff forms for participant tracking. CDS will provide programming extensions to REDCap when necessary to improve efficiency.

Specific to this study, CDS or the study team will build an automated bi-directional text message interface (e.g., MyCap via REDCap™) where participants will report their adherence to at-home study procedures, and the REDCap™ system will send automated motivational responses as provided by the study team. However, CDS will not monitor participant responses. All bidirectional communication with participants will take place with designated research staff only overseen by Dr. Langley. This interface will also include an integrated messaging system to send appointment reminders via email or text messaging (based on the participant's choice) that will be used to improve participant retention rates. All staff have will maintain active Human Subject Research and HIPAA training as appropriate to their role. All data will be stored in a secure password protected computer folder, which only authorized research staff will have access to.

14.0 INVESTIGATOR OBLIGATIONS

The PI is responsible for the conduct of the clinical trial at the site and is responsible for personally overseeing the treatment of all study subjects. The PI must assure that all study site personnel, including sub-Investigators and other study staff members, adhere to the study protocol and to all applicable regulations and guidelines regarding clinical trials both during and after study completion. All subjects are informed of the nature of the program, it is possible hazards, and their right to withdraw at any time, and each subject signs a form indicating their consent to participate prior to receiving any study-related procedures.

15.0 ADMINISTRATIVE AND REGULATORY CONSIDERATIONS

15.1 Pre-Study Documentation

The following documentation will be filed prior to initiation of the trial: curricula vitae of the PI and all Sub-Investigators; copy of the correspondence from the IRB/EC indicating approval of the protocol and Informed Consent Forms, signed by the IRB/EC chairperson or designee; an IRB/EC membership list containing the names and occupations of the IRB/EC members; copy of the Informed Consent Forms that were reviewed and approved by the IRB/EC.

15.2 Study Site Training

Before initiation of the study, the PI or his designated representatives will review and discuss the following items with the Investigator and clinic staff: the protocol, study procedures, record keeping and administrative requirements, drug accountability, AE reporting, Good Clinical Practice guidelines, CRF/eCRF

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completion guidelines, monitoring requirements, and the ability of the site to satisfactorily complete the protocol. Additional documents with instructions for study compliance and CRF/eCRF completion will be provided.

15.3 Documentation

The PI and study staff will maintain a comprehensive and centralized filing system containing all study-related documentation. These files must be suitable for inspection by any applicable regulatory agencies/competent authorities at any time and should consist of the following elements: subject files (complete medical records, laboratory data, supporting source documentation, and the Informed Consent); study files (the protocol with all amendments, copies of all pre-study documentation, and all correspondence between the Competent Authorities, IRB/EC, etc.).

15.4 Access to Source Data

The PI will permit applicable regulatory authorities to monitor the study as needed. The CRF/eCRF and related source documents will be reviewed in detail by applicable regulatory authorities as needed. Only original source documents are acceptable for review. This review includes inspection of data acquired as a requirement for participation in this study and other medical records as required to confirm information contained in the CRF/eCRF, such as past history, secondary diagnoses, and concomitant medications. Other study records, such as correspondence with Competent Authorities, and IRB/EC and screening logs will also be inspected. All source data and study records must also be available for inspection by representatives of regulatory agencies.

15.5 Data Collection

Data will be collected and stored in an electronic database. Any changes or corrections made to the CRF/eCRF must be subsequently reviewed and signed by the PI. All data fields in the CRF/eCRF must be completed.

15.6 Protocol Interpretation and Compliance

The procedures defined in the protocol are carefully reviewed by the PI and his staff prior to the time of study initiation to ensure accurate representation and implementation. Protocol amendments, if any, are reviewed and implemented promptly following IRB/EC and relevant Competent Authorities approval.

15.7 Disclosure of Data/Publication

Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties other than those noted below is prohibited. Such medical information may be given to the subject's personal physician or to other appropriate medical personnel responsible for the subject's welfare. Data generated as a result of this study are to be available for inspection on request by regulatory agencies, the Sponsor or its designee and by the IRB/EC. It is anticipated that the results of this study will be submitted to a peer-reviewed scientific journal. Authorship on such a paper will be acknowledged with customary scientific practice.

15.8 Ethical Considerations

The Investigator agrees to conduct this study in accordance with applicable United States FDA clinical trial regulations and guidelines, applicable United States FDA clinical trial regulations and guidelines, the ICH (E6) GCP guidelines, the IRB/EC and local legal requirements and with the Declaration of Helsinki (1989). The Investigator will conduct all aspects of this study in accordance with all national, state, and local laws of the applicable regulatory agencies.

15.9 Informed Consent

The PI assumes the responsibility of obtaining written Informed Consent for each subject or the subject's legally authorized representative before any study-specific procedures are performed. Subjects meeting the criteria set forth in the protocol will be offered the opportunity to participate in the study. To avoid introduction of bias, the Investigator must exercise no selectivity regarding offering eligible subjects the opportunity to participate in the study. Subjects or parents/legal guardians of all candidate subjects will receive a comprehensive explanation of the proposed treatment, including the nature of the therapy,

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alternative therapies available, any known previously experienced adverse reactions, the investigational status of the study treatment, and other factors that are part of obtaining a proper Informed Consent. Subjects will be given the opportunity to ask questions concerning the study, and adequate time to consider their decision to or not to participate.

Informed Consent will be documented using a written Consent Form that includes all the elements required by FDA regulations and ICH guidelines. The form is to be signed and dated by the subject or subject's legally authorized representative and by the person who administers the consent process. A copy of the signed form will be given to the person who signed it, the original signed Consent Form will be filed with the subject's medical records, and copy maintained with the subject's study records. The date and time of time of the Informed Consent must be recorded in the source documents.

If an amendment to the protocol changes the subject participation schedule in scope or activity, or increases the potential risk to the subject, the Informed Consent Form must be amended. Any amended Informed Consent must be approved by the IRB/EC prior to use. The revised Informed Consent Form must be used to obtain re-consent from any subjects currently enrolled in the study if the subject is affected by the amendment and must be used to document consent from any new subjects enrolled after the approval date of the amendment.

15.10 Institutional Review Board/Ethics Committee

The PI will assure that an appropriately constituted IRB/EC that complies with the requirements of 21 CFR Section 56 or written assurance of compliance with ICH (E6) guidelines will be responsible for the initial and continuing review and approval of the clinical study. Before initiation of the study, the PI or designee will forward copies of the protocol and Consent Form to be used for the study to the IRB/EC for its review and approval.

The PI or designee will also assure that all changes in the research activity and all unanticipated problems involving risks to human subjects or others will be reported promptly to the IRB/EC, and that no changes will be made to the protocol without prior Sponsor and IRB/EC approval, except where necessary to eliminate apparent immediate hazards to human subjects.

The Investigator or designee will be responsible for submitting periodic progress reports to the IRB/EC at intervals appropriate to the degree of subject risk involved in the study, but not less than once per year and at the completion or termination of the study.

15.11 Subject Privacy

The Investigators affirm and uphold the principle of the subject's right to privacy. The Investigators shall comply with applicable national and local privacy laws.

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16.0 REFERENCES

1. Ni J, Zhang L. Cancer Cachexia: Definition, Staging, and Emerging Treatments. *Cancer Manag Res*. 2020;12:5597-5605. doi:10.2147/CMAR.S261585
2. Liu Y, Zhang PY, Na J, et al. Prevalence, intensity, and prognostic significance of common symptoms in terminally ill cancer patients. *J Palliat Med*. Jul 2013;16(7):752-7. doi:10.1089/jpm.2013.0028
3. Dewys WD, Begg C, Lavin PT, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. *Am J Med*. Oct 1980;69(4):491-7. doi:10.1016/s0149-2918(05)80001-3
4. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. *CA Cancer J Clin*. 01 2022;72(1):7-33. doi:10.3322/caac.21708
5. Barajas Galindo DE, Vidal-Casariego A, Calleja-Fernández A, et al. Appetite disorders in cancer patients: Impact on nutritional status and quality of life. *Appetite*. 07 01 2017;114:23-27. doi:10.1016/j.appet.2017.03.020
6. Andreae C, Strömberg A, Årestedt K. Prevalence and associated factors for decreased appetite among patients with stable heart failure. *J Clin Nurs*. Jun 2016;25(11-12):1703-12. doi:10.1111/jocn.13220
7. Arthur ST, Van Doren BA, Roy D, Noone JM, Zacherle E, Blanchette CM. Cachexia among US cancer patients. *J Med Econ*. Sep 2016;19(9):874-80. doi:10.1080/13696998.2016.1181640
8. Shragge JE, Wismer WV, Olson KL, Baracos VE. The management of anorexia by patients with advanced cancer: a critical review of the literature. *Palliat Med*. Sep 2006;20(6):623-9. doi:10.1177/0269216306070322
9. Bozzetti F. Forcing the vicious circle: sarcopenia increases toxicity, decreases response to chemotherapy and worsens with chemotherapy. *Ann Oncol*. Sep 01 2017;28(9):2107-2118. doi:10.1093/annonc/mdx271
10. Keller HH. Nutrition and health-related quality of life in frail older adults. *J Nutr Health Aging*. 2004;8(4):245-52.
11. Ezeoke CC, Morley JE. Pathophysiology of anorexia in the cancer cachexia syndrome. *J Cachexia Sarcopenia Muscle*. Dec 2015;6(4):287-302. doi:10.1002/jcsm.12059
12. Peixoto da Silva S, Santos JMO, Costa E Silva MP, Gil da Costa RM, Medeiros R. Cancer cachexia and its pathophysiology: links with sarcopenia, anorexia and asthenia. *J Cachexia Sarcopenia Muscle*. 06 2020;11(3):619-635. doi:10.1002/jcsm.12528
13. Gupta A, Nshuti L, Grewal US, et al. Financial Burden of Drugs Prescribed for Cancer-Associated Symptoms. *JCO Oncol Pract*. 02 2022;18(2):140-147. doi:10.1200/OP.21.00466
14. Tuca A, Jimenez-Fonseca P, Gascón P. Clinical evaluation and optimal management of cancer cachexia. *Crit Rev Oncol Hematol*. Dec 2013;88(3):625-36. doi:10.1016/j.critrevonc.2013.07.015
15. Good P, Cavenagh J, Mather M, Ravenscroft P. Medically assisted nutrition for palliative care in adult patients. *Cochrane Database Syst Rev*. Oct 08 2008;(4):CD006274. doi:10.1002/14651858.CD006274.pub2
16. Roeland EJ, Bohlke K, Baracos VE, et al. Management of Cancer Cachexia: ASCO Guideline. *J Clin Oncol*. 07 20 2020;38(21):2438-2453. doi:10.1200/JCO.20.00611
17. Muscaritoli M, Corsaro E, Molfino A. Awareness of Cancer-Related Malnutrition and Its Management: Analysis of the Results From a Survey Conducted Among Medical Oncologists. *Front Oncol*. 2021;11:682999. doi:10.3389/fonc.2021.682999
18. Henrikson NB, Shankaran V. Improving Price Transparency in Cancer Care. *J Oncol Pract*. Jan 2016;12(1):44-7. doi:10.1200/JOP.2015.006171
19. Lin WC, Yeh CH, Chien LC, Morone NE, Glick RM, Albers KM. The Anti-Inflammatory Actions of Auricular Point Acupressure for Chronic Low Back Pain. *Evid Based Complement Alternat Med*. 2015;2015:103570. doi:10.1155/2015/103570
20. Yeh CH, Chien LC, Chiang YC, Ren D, Suen LK. Auricular point acupressure as an adjunct analgesic treatment for cancer patients: a feasibility study. *Pain Manag Nurs*. Jun 2015;16(3):285-93. doi:10.1016/j.pmn.2014.08.005
21. Yeh CH, Chien LC, Lin WC, Bovbjerg DH, van Londen GJ. Pilot Randomized Controlled Trial of Auricular Point Acupressure to Manage Symptom Clusters of Pain, Fatigue, and Disturbed Sleep in Breast Cancer Patients. *Cancer Nurs*. 2016 Sep-Oct 2016;39(5):402-10. doi:10.1097/NCC.0000000000000303

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22. Yeh CH, Lukkahatai N, Campbell C, et al. Preliminary Effectiveness of Auricular Point Acupressure on Chemotherapy-Induced Neuropathy: Part 1 Self-Reported Outcomes. *Pain Manag Nurs*. 12 2019;20(6):614-622. doi:10.1016/j.pmn.2019.04.005
23. Yeh CH, Lukkahatai N, Campbell C, et al. Preliminary Effectiveness of Auricular Point Acupressure on Chemotherapy-Induced Neuropathy: Part 2 Laboratory-Assessed and Objective Outcomes. *Pain Manag Nurs*. 12 2019;20(6):623-632. doi:10.1016/j.pmn.2019.04.004
24. Tan JY, Liu J, Suen LKP, Molassiotis A, Wang T. Development and validation of an evidence-based auricular acupressure intervention for managing chemotherapy-induced nausea and vomiting in breast cancer patients. *Complement Ther Med*. Aug 2020;52:102502. doi:10.1016/j.ctim.2020.102502
25. Eghbali M, Yekaninejad MS, Varaei S, Jalalinia SF, Samimi MA, Sa'atchi K. The effect of auricular acupressure on nausea and vomiting caused by chemotherapy among breast cancer patients. *Complement Ther Clin Pract*. Aug 2016;24:189-94. doi:10.1016/j.ctcp.2016.06.006
26. Lin L, Zhang Y, Qian HY, et al. Auricular acupressure for cancer-related fatigue during lung cancer chemotherapy: a randomised trial. *BMJ Support Palliat Care*. Mar 2021;11(1):32-39. doi:10.1136/bmjspcare-2019-001937
27. Vallim ETA, Marques ADCB, Coelho RCFP, Guimarães PRB, Felix JVC, Kalinke LP. Auricular acupressure in the quality of life of women with breast cancer: a randomized clinical trial. *Rev Esc Enferm USP*. 2019;53:e03525. doi:10.1590/S1980-220X2018043603525
28. Yoon SL, Grundmann O, Williams JJ, Carriere G. Novel intervention with acupuncture for anorexia and cachexia in patients with gastrointestinal tract cancers: a feasibility study. *Oncol Nurs Forum*. Mar 2015;42(2):E102-9. doi:10.1188/15.ONF.E102-E109
29. Sun L, Mao JJ, Liu Q, Yang Y, He B. Effects of auricular acupuncture on appetite in patients with advanced cancer: a pilot randomized controlled trial. *Ann Palliat Med*. Jul 2020;9(4):1804-1811. doi:10.21037/apm.2020.04.24
30. Wang SM, Peloquin C, Kain ZN. The use of auricular acupuncture to reduce preoperative anxiety. *Anesth Analg*. Nov 2001;93(5):1178-80, table of contents. doi:10.1097/00000539-200111000-00024
31. Qu F, Zhang D, Chen LT, et al. Auricular acupressure reduces anxiety levels and improves outcomes of in vitro fertilization: a prospective, randomized and controlled study. *Sci Rep*. May 22 2014;4:5028. doi:10.1038/srep05028
32. Nomenclature WGoAA. World Health Organization Report of the Working Group on Auricular Nomenclature. In: Unit WHOTM, editor. Geneva: World Health Organization; 1990.
33. Chen L, Wu X, Chen X, Zhou C. Efficacy of Auricular Acupressure in Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Patients with Cancer: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med*. 2021;2021:8868720. doi:10.1155/2021/8868720
34. Kuo HC, Tsao Y, Tu HY, Dai ZH, Creedy DK. Pilot randomized controlled trial of auricular point acupressure for sleep disturbances in women with ovarian cancer. *Res Nurs Health*. 10 2018;41(5):469-479. doi:10.1002/nur.21885
35. Lin L, Jing X, Zhang Y, Qian H, Xu J, Tian L. Factors Influencing Compliance with Auricular Acupressure Therapy in Patients with Cancer-Related Fatigue. *Patient Prefer Adherence*. 2020;14:1275-1281. doi:10.2147/PPA.S261466
36. Tsao Y, Creedy DK. Auricular acupressure: reducing side effects of chemotherapy in women with ovarian cancer. *Support Care Cancer*. Nov 2019;27(11):4155-4163. doi:10.1007/s00520-019-04682-8
37. Xiao B, Liu ZH. Efficacy on depression in breast cancer treated with acupuncture and auricular acupressure. *Zhongguo Zhen Jiu*. Oct 2014;34(10):956-60.
38. Organization WH. Guidelines on basic training and safety in acupuncture. Geneva1999.
39. Blauwhoff-Buskermolen S, Ruijgrok C, Ostelo RW, et al. The assessment of anorexia in patients with cancer: cut-off values for the FAACT-A/CS and the VAS for appetite. *Support Care Cancer*. Feb 2016;24(2):661-666. doi:10.1007/s00520-015-2826-2
40. Hendifar AE, Petzel MQB, Zimmers TA, et al. Pancreas Cancer-Associated Weight Loss. *Oncologist*. 05 2019;24(5):691-701. doi:10.1634/theoncologist.2018-0266
41. Hariyanto TI, Kurniawan A. Appetite problem in cancer patients: Pathophysiology, diagnosis, and treatment. *Cancer Treat Res Commun*. 2021;27:100336. doi:10.1016/j.ctarc.2021.100336
42. Vickers AJ, Cronin AM, Maschino AC, et al. Acupuncture for chronic pain: individual patient data meta-analysis. *Arch Intern Med*. Oct 22 2012;172(19):1444-53. doi:10.1001/archinternmed.2012.3654

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43. Avins AL. Needling the status quo. *Arch Intern Med*. Oct 22 2012;172(19):1454-5. doi:10.1001/archinternmed.2012.4198
44. Meregaglia M, Borsoi L, Cairns J, Tarricone R. Mapping health-related quality of life scores from FACT-G, FAACT, and FACIT-F onto preference-based EQ-5D-5L utilities in non-small cell lung cancer cachexia. *Eur J Health Econ*. Mar 2019;20(2):181-193. doi:10.1007/s10198-017-0930-6
45. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol*. Mar 1993;11(3):570-9. doi:10.1200/JCO.1993.11.3.570
46. Ribaudo JM, Cella D, Hahn EA, et al. Re-validation and shortening of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire. *Qual Life Res*. 2000;9(10):1137-46. doi:10.1023/a:1016670403148
47. Abraham M, Kordatou Z, Barriuso J, et al. Early recognition of anorexia through patient-generated assessment predicts survival in patients with oesophagogastric cancer. *PLoS One*. 2019;14(11):e0224540. doi:10.1371/journal.pone.0224540
48. Machingura A, Taye M, Musoro J, et al. Clustering of EORTC QLQ-C30 health-related quality of life scales across several cancer types: Validation study. *Eur J Cancer*. 07 2022;170:1-9. doi:10.1016/j.ejca.2022.03.039
49. Luckett T, King MT, Butow PN, et al. Choosing between the EORTC QLQ-C30 and FACT-G for measuring health-related quality of life in cancer clinical research: issues, evidence and recommendations. *Ann Oncol*. Oct 2011;22(10):2179-90. doi:10.1093/annonc/mdq721
50. Miller J, Wells L, Nwulu U, Currow D, Johnson MJ, Skipworth RJE. Validated screening tools for the assessment of cachexia, sarcopenia, and malnutrition: a systematic review. *Am J Clin Nutr*. 12 01 2018;108(6):1196-1208. doi:10.1093/ajcn/nqy244
51. Molfino A, de van der Schueren MAE, Sánchez-Lara K, et al. Cancer-associated anorexia: Validity and performance overtime of different appetite tools among patients at their first cancer diagnosis. *Clin Nutr*. 06 2021;40(6):4037-4042. doi:10.1016/j.clnu.2021.02.016
52. Mao JJ, Armstrong K, Farrar JT, Bowman MA. Acupuncture expectancy scale: development and preliminary validation in China. *Explore (NY)*. 2007 Jul-Aug 2007;3(4):372-7. doi:10.1016/j.explore.2006.12.003

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17.0 APPENDICES

17.1 Appendix A: Acupressure Instructions for Stimulation and Ear Seed Care

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Home Care for Your Acupressure Ear Seed Treatment

Treatments with acupressure ear seeds involve placing small seeds on specific points of the ear and stimulating them with pressure to help relieve symptoms. Seeds are applied to the skin with stick-on adhesive similar to medical tape. These acupressure ear seeds are applied topically only. The skin is not punctured and there is no needle inserted. Acupressure ear seeds are used in this study as the primary form of treatment.

You will have non-metallic seeds from the *Vaccaria* plant placed on up to six (6) acupoints in the upper part of each ear. These acupressure ear seeds are safe if left on during imaging (such as CT, MRI, X-Ray, or PET scans).

Instructions for applying ear seeds:

1. Locate the correct point using the guides on the following pages.
2. Clean ear by gently wiping across each point location using the provided 70% alcohol wipes.
3. Wait for the skin to dry.
4. Remove ear seed from package using fingernail.
5. Apply ear seed on each point.
6. Press on the ear seed to make sure it is adhered to the point.

Instructions for massaging ear seeds:

- Gently stimulate the seeds by applying **10 presses** with light to moderate pressure using your fingertips or thumb pads. Slowly and consistently apply and release pressure before moving to the next seed.
- Repeat this process, then continue again to the each of the seeds on both ears.
- Rotate stimulation between all points for at least **three (3) minutes, three (3) times daily**.
- Document this using the MyCap application.

What should this feel like?

It is common to feel some pressure or tenderness when stimulating the seeds.

Instructions for ear seed care:

The acupressure seeds do not require any special care, but there are some guidelines and precautions:

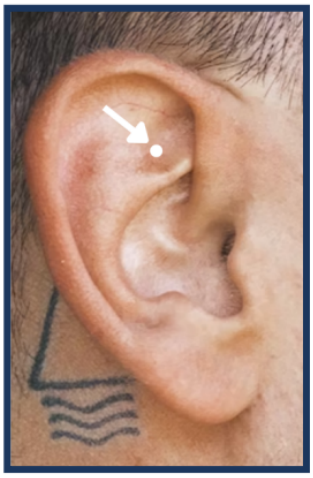
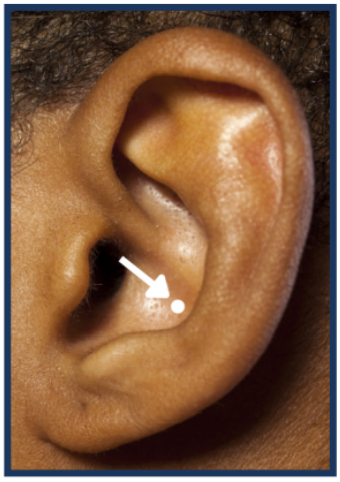
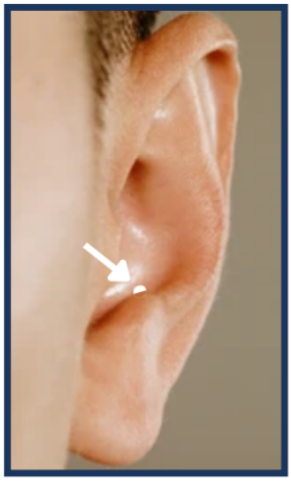
- All acupressure seeds should be removed after on day 5 each week.
- If the acupressure seeds become painful or the surrounding skin becomes red, itchy or sore gently remove the tape and seed and c lean the area with soap and water.
- Do not replace a <u>used</u> acupressure seed if it comes off accidentally. You can use a <u>new</u> ear seed from your packet and reapply to the same spot following the instructions above.
- Acupressure seeds can be disposed of in the trash.

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Acupressure Ear Seed Instructions and Care
RG1123492 (PI: Langley)

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Shen Men Finding the point: near the outer corner of the hollow area at the top of the ear 	**Stomach** Finding the point: on the ridge just next to the center of the ear 
Spleen Finding the point: just below the outer end of the hard central ridge 	**Subcortex** Finding the point: just central to the top point of the cartilage above the ear lobe 

Watch a video to help you locate each point:
[[PLACEHOLDER for bit.ly and QR code]]

Don't forget – you can refer to the photo you took on your first day!

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17.2 Appendix B: Visual Analog Scale for Appetite

Over the past 7 days, I would say...

I had no appetite at all — My appetite was very good

(Place a mark on the scale above)

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17.3 Appendix C: Functional Assessment of Cancer Therapy – Anorexia/Cachexia Subscale

FAACT (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
C6	I have a good appetite	0	1	2	3	4
ACT1	The amount I eat is sufficient to meet my needs	0	1	2	3	4
ACT2	I am worried about my weight	0	1	2	3	4
ACT3	Most food tastes unpleasant to me	0	1	2	3	4
ACT4	I am concerned about how thin I look	0	1	2	3	4
ACT6	My interest in food drops as soon as I try to eat	0	1	2	3	4
ACT7	I have difficulty eating rich or "heavy" foods	0	1	2	3	4
ACT9	My family or friends are pressuring me to eat	0	1	2	3	4
O2	I have been vomiting	0	1	2	3	4
ACT10	When I eat, I seem to get full quickly	0	1	2	3	4
ACT11	I have pain in my stomach area	0	1	2	3	4
ACT13	My general health is improving	0	1	2	3	4

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17.4 Appendix D: Functional Assessment of Cancer Therapy – General

FAACT (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.**

	PHYSICAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

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FAACT (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.

	EMOTIONAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	**Not at all**	**A little bit**	**Some-what**	**Quite a bit**	**Very much**
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

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17.5 Appendix E: Adapted Acupressure Expectancy Scale

For each statement, please choose the closest answer.

Please note: the answers you provide will not affect the group you are assigned to.

Every individual may have different expectation of the effects of acupressure. If we use the following statements to describe your expectation of acupressure's effect on your treatment side effects after the entire course of acupressure therapy, how much do you agree?

	Do Not Agree At all	Agree A Little	Moderately Agree	Mostly Agree	Completely Agree
1) **My treatment side effects will improve a lot.** * must provide value	○	○	○	○	○
2) **I will be able to cope with my treatment side effects better.** * must provide value	○	○	○	○	○
3) **The symptoms of my treatment side-effects will disappear.** * must provide value	○	○	○	○	○
4) **My energy level will increase.** * must provide value	○	○	○	○	○

5) **Which of the two treatment assignments do you prefer?**

* must provide value

- ○ Waitlist, with the option of receiving ear acupressure after 8 weeks
- ○ Ear acupressure during treatment

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17.6 Appendix F: Multi-Component Visual Analog Scale for Concomitant Symptoms (delivered through MyCap)

Please indicate how you felt over the past 7 days for each of the following...

Pain	I had no pain at all	I had a lot of significant pain
	(Place a mark on the scale above)	
Nausea	I had no nausea at all	I had a lot of significant nausea
	(Place a mark on the scale above)	
Vomiting	I had no vomiting at all	I had a lot of significant vomiting
	(Place a mark on the scale above)	
Difficulty Swallowing	I had no difficulty swallowing at all	I had a lot of significant difficulty swallowing
	(Place a mark on the scale above)	
Mood	I had no issues with mood/depression at all	I had a lot of significant issues with mood/depression
	(Place a mark on the scale above)	

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17.7 Appendix G: Acupressure Diary (delivered through MyCap)

Daily Acupressure Diary

Please complete the survey below.

Thank you!

Please indicate the number of times you massages all acupressure points on each ear for the required 3 minutes.

Is today a rest day when you do not have ear seeds placed?

- ◯ Yes, today is a rest day
- ◯ No, I have ear seeds placed today

What day of the treatment cycle is this?

- ◯ Day 1
- ◯ Day 2
- ◯ Day 3
- ◯ Day 4
- ◯ Day 5

Remember! Today is your Day 5 and final day of this cycle. Please remove your ears seeds after applying the treatment as recommended.

Number of times ear seeds pressed on each side throughout the day.

- ◯ None
- ◯ Once
- ◯ Twice
- ◯ Three times
- ◯ More than three times

Average length of pressure applied to ear seeds during each session

- ◯ Less than 1 minute
- ◯ 1-2 minutes
- ◯ 2-3 minutes
- ◯ 3 minutes as recommended
- ◯ More than 3 minutes

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17.8 Appendix H: Waitlist Acupuncture Voucher

Fred Hutch IRB Approved 12/28/2023

PI: Langley, IR#20046

Fred Hutch Cancer Center

Acupressure Voucher

Thank you for participating in the "Pilot acupressure as a complementary therapy for anorexia in cancer" study!

You are eligible to receive up to four (4) auricular acupressure sessions at no charge:

- All acupressure sessions are scheduled as a series of treatments every other week.
- The acupressure seeds do not require any specific care, but there are some guidelines and precautions that will be reviewed by the provider at your visit.
- If you need to cancel your appointment, please notify the scheduling team at least 24 hours before your appointment by calling (206) 667-3481.

When you are ready to schedule your series of acupressure sessions, please:

1. Contact the Principal Investigator, Blake Langley, to begin the scheduling process at the phone number or email address listed below.
2. The scheduling team will then contact you to schedule your acupressure treatments.
3. The acupressure appointments will take place in the GI Care Neighborhood.
4. If you are scheduled in the Wellness Center, you will receive directions and parking information for acupressure appointments.
5. All of your acupressure appointments will need to be completed within 6 months after you complete your study participation.
6. Missed acupressure visits will not be rescheduled/
7. **Your voucher will expire on**: _____

If you have any questions, please call Blake Langley at (206) 667-3481 or email blangley@fredhutch.org.

Thank you for your study participation!