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NRG-CC012CD: Managing Symptoms and Psychological Distress During Oral Anti-Cancer Treatment

Alla Sikorskii, PhD; Terry Badger, PhD; Tracy Crane, PhD

Overview/Training
July 26, 2024

This NRG-Oncology protocol is being conducted in collaboration with NIH/NCI R01 #1R01CA279472-01 funding to Drs. Sikorskii MPI (contact), Badger (MPI) and Crane (MPI).



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NRG Oncology



Study Team Contacts

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NRG Oncology Headquarters Contacts

Data Management For questions concerning eligibility or data submission	Lisa Abate
Protocol Development For questions concerning protocol and informed consent versions & amendments	Erica Field, MPH, MHA
Project Managers For questions concerning patient recruitment, data collection, and interventions.	Jamillah Gross-Caldwell Michigan State University 517-884-7662 Grey Freylersythe University of Miami 305-243-9832 Shared Inbox: SYMON@miami.edu



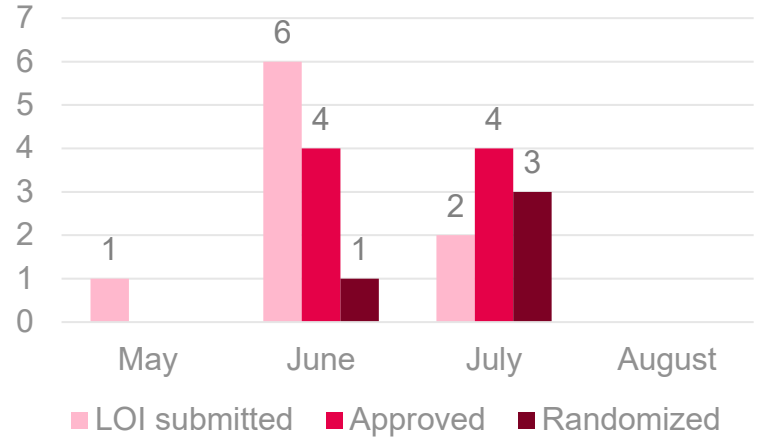
Study Updates

Site Enrollment

Study Activation May 1, 2024

Interested Sites: 21



















- Approved: 8
 - Randomized: 4







TIP-C Interveners

- Centrally contracted social workers identified
 - 1 randomized site will utilize this service
- 5 of 8 approved sites can provide own TIP-C intervener

Sites Distribution

-  Cancer Research of Wiscons...
-  Puerto Rico Minority Unders...
-  Upstate Carolina NCORP
-  Carle Cancer Center NCORP
-  Ozarks NCORP
-  Lake Regional Health Syste...
-  NCORP of the Carolinas
-  Georgia Cares Minority Unde...
-  Delaware /Christiana Care N...
-  Southeast Clinical Oncology ...
-  Cancer Research Consortiu...
-  Hawaii Minority Underserved...
-  Pacific Cancer Research Con...
-  Gulf South Minority Underse...
-  Columbus NCORP
-  Nevada Research Foundatio...
-  Stroger Hospital of Cook Co...
-  New Mexico Minority Unders...



-  Approved
-  ATSM+TIPC Intervention
-  Expressed Interest
-  IVR Active Control



Study Background and Rationale

Study Background

- There are currently more than 50 U.S. Food and Drug Administration (FDA)-approved oral anticancer agents, and their use is increasing
- Patients on oral agents must self-manage their symptoms (e.g., fatigue, anxiety, skin rash) with less interactions with on oncology team compared to infusion treatment
- Telemonitoring and management of symptoms are key for reducing symptom burden, emergency department [ED] or urgent care visits, hospitalizations, and treatment interruptions

Study Rationale

- This is a confirmatory trial of the adaptive Automated Telephone Symptom Management (ATSM) + Telephone Interpersonal Counseling (TIPC) in real world of community-based oncology practices
- Comparison condition: telephone interactive voice response (IVR) symptom monitoring.
- Data will inform future implementation of this telehealth symptom monitoring strategy, including acceptability, appropriateness, cost, and cost savings due to reductions in unscheduled health service use.
- Practices provide usual care and are not asked to alter their practice as part of the trial.

Primary Objective

To test the effectiveness of Automated Telephone System Management (ATSM) + Telephone Interpersonal Counseling (TIPC) versus active control (IVR) on patient-level outcome of the summary toxicity index of 24 symptoms commonly experienced during oral anti-cancer treatment over weeks 1-12 (immediate effect) and 13-17 (sustained effect).

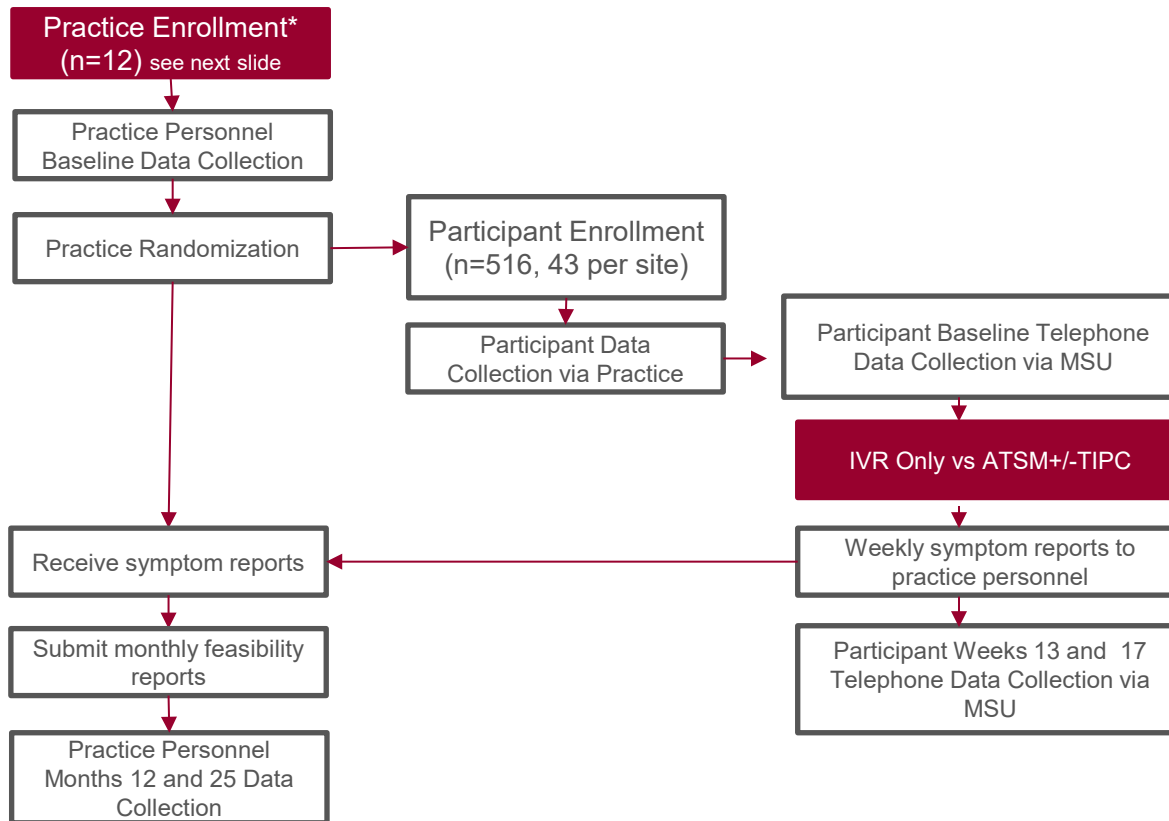
Secondary Objective

Test the effectiveness of ATSM+TIPC versus active control (IVR) on patient-level outcome of unscheduled health services use (hospitalizations, ED or urgent care visits) over weeks 1-12 and 13-17.

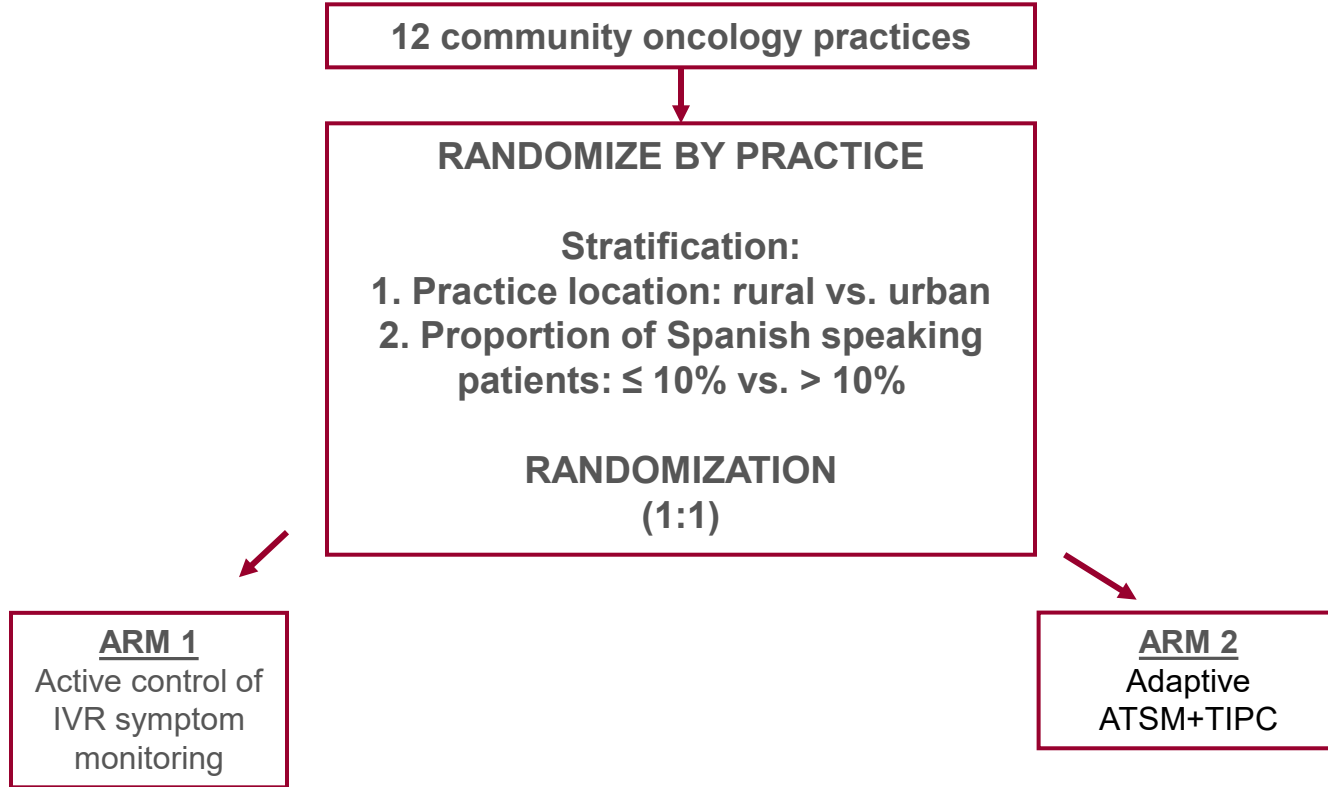
Exploratory Objectives

- Estimate delivery cost of the ATSM+TIPC and active control (IVR) and cost savings for the ATSM+TIPC versus active control as a result of reduced unscheduled health services use
- Estimate the effect of the ATSM+TIPC versus active control (IVR) on patient-reported financial burden
- Evaluate implementation outcomes at the practice personnel level including feasibility, actions on symptom reports, treatment fidelity, and perceptions of intervention acceptability and appropriateness

Study Schema

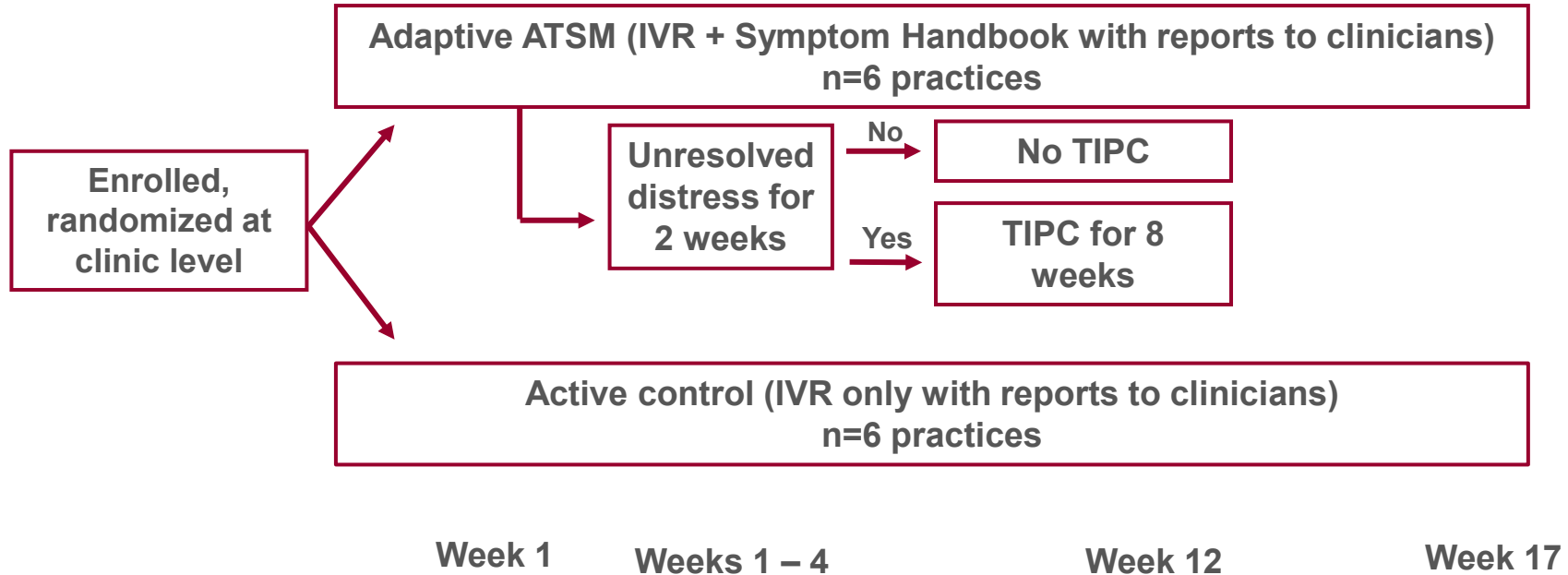


Practice Enrollment



IVR = Interactive Voice Response
ATSM = Automated Telephone System Management
TIPC = Telephone Interpersonal Counseling

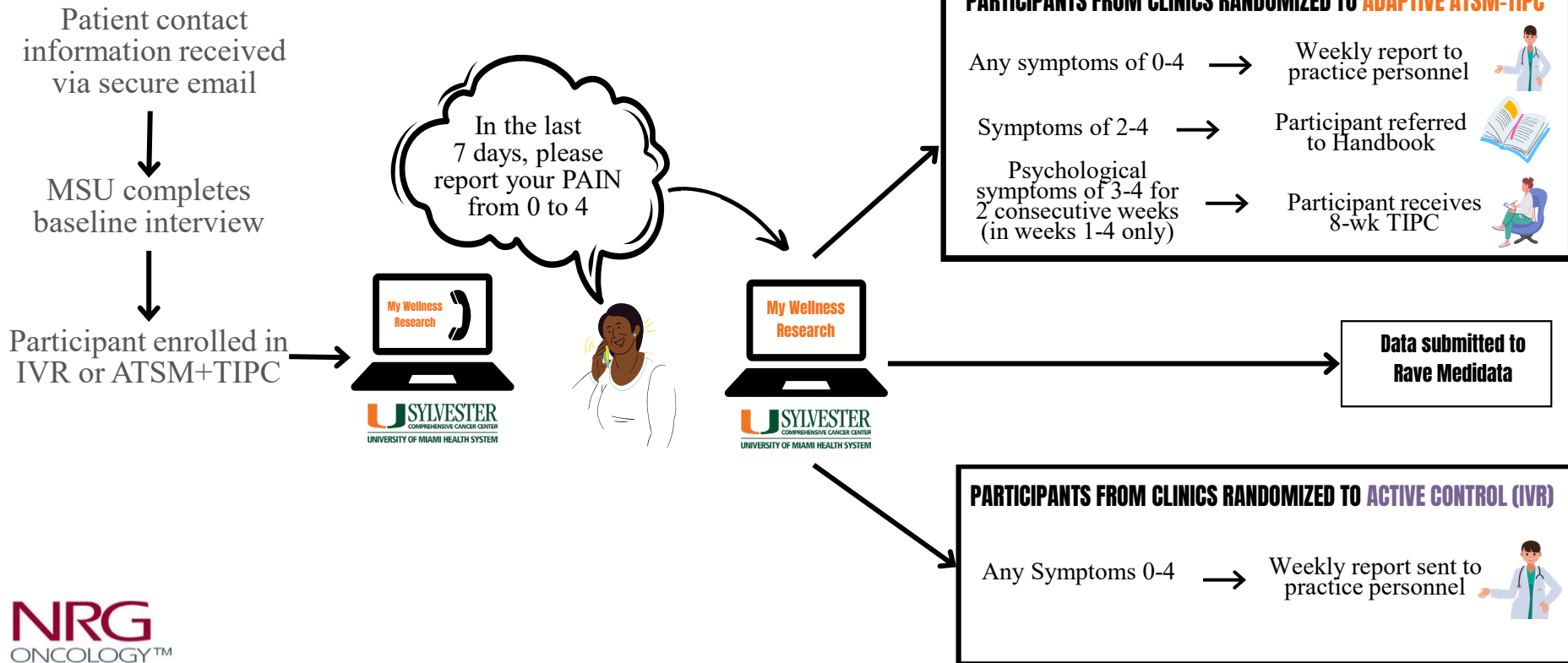
Participant Intervention



Symptoms Assessed

- 24 symptoms will be assessed via IVR weekly for 17 weeks using Patient-Reported Outcomes Common Terminology Criteria for Adverse Events (PRO-CTCAE)
- Symptom severity is rated as 0=none, 1=mild, 2=moderate, 3=severe, 4=very severe
- Weekly summary for each patient is sent to practice (any person or people identified by practice)
- Practice personnel are not required to do anything specific based on the report, but report recipient(s) will be asked monthly what was done

Patient-Specific Study Flow



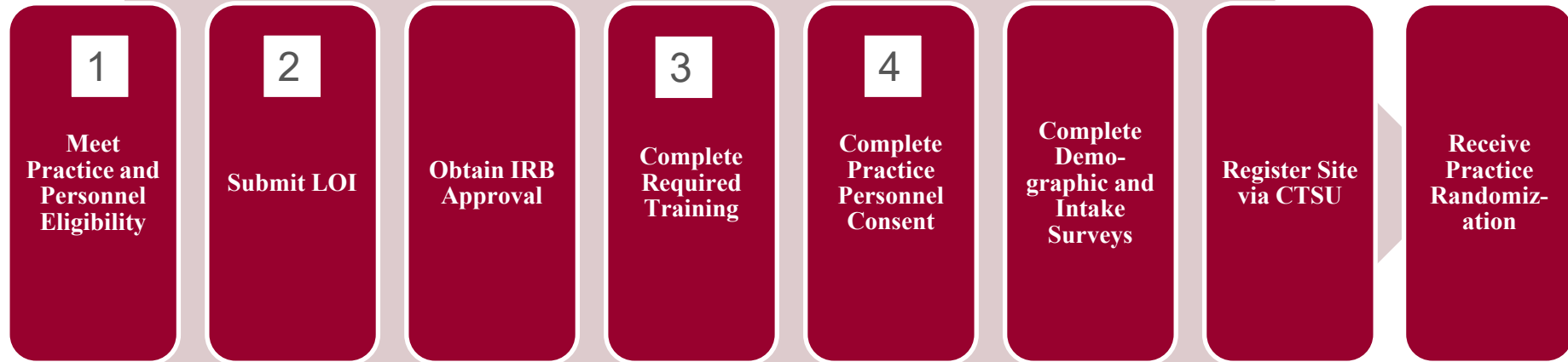


Practice Study Activities

Practice and Staff Characteristics

- Total of 12 practices will be enrolled
 - At least 4 practices must be rural, i.e., having 1+ rural county in the catchment area. Rural county is defined as not containing a core urban area of 50,000 or more population
 - Practices serving Spanish-speaking population will be prioritized
- Approximately 4 personnel will enroll at each practice, not limited
 - Practice personnel eligible to participate are: physicians, nurses, nurse practitioners, advanced practice providers, physician assistants, medical assistants, pharmacists, social workers, and other behavioral health professionals who have the requisite education, licensure or certifications for their roles and are involved in symptom management of patients on trial.

Practice: Opening Study



1a

Practice Key Eligibility Criteria

- Total of 12 practices will be enrolled
 - At least 4 practices must be rural. Practices serving Spanish-speaking population will be prioritized.
- All institutions participating in the practice are NCORP affiliates or sub-affiliates.
 - Practices are defined as a single NCORP affiliate or sub-affiliate; or NCORP affiliate and/or sub-affiliates that share the same physicians/staff but are in different locations.
- Able to participate for 25 months after IRB approval and start-up activities
- Administer oral therapy (other than hormonal) to at least 40 patients per year
- Able to accrue 2 patients per month
- Able to identify a recipient(s) of weekly IVR symptom reports (can be any designated member of practice personnel)
- Practice may or may not have a behavioral health professional who is willing to be trained and deliver TIPC. If not, TIPC intervener will be hired by the study
- At least some personnel must be willing to consent as research participants for implementation aims

1b

Practice Personnel Eligibility Criteria

Practice personnel will be key stakeholders in this research study, themselves consenting to participation, receiving reports, and completing brief monthly questionnaires. The practice personnel must provide study-specific informed consent prior to study entry.

Approximately 4 personnel will enroll at each practice, but not limited

- Practice personnel eligible to participate are: physicians, nurses, nurse practitioners, advanced practice providers, physician assistants, medical assistants, pharmacists, etc. and are involved in symptom management of patients on trial.
- Age \geq 18 years
- Planned to be involved in usual care for at least one enrolled patient during patient's participation in the study
- At least one practice personnel has to receive IVR reports and complete monthly forms (about 30 minutes)
- Social worker/ behavioral health professional who will deliver TIPC intervention, licensure, or eligibility for licensure in behavioral counseling if required by the State or Territory.

Letter of Intent

- Practices interested in participating will submit a Letter of Intent
- LOI will be posted on CTSU website
- Complete LOI and submit it to the CTSU via the Regulatory Submission Portal.



Letter of Intent (LOI) for NRG-CC0012CD: Managing Symptoms and Psychological Distress During Oral Anti-Cancer Treatment

Practice Name:

Practice Site(s): Lead CTEP Code Name

CTEP Code Name

CTEP Code Name

CTEP Code Name (copy and paste for additional sites)

Lead Site Study Coordinator: email:

Lead PI: email:

- A practice is defined as a NCORP component and/or subcomponents that share the same physicians and/or staff, but are in different locations. Note: Only 12 practices may participate in this study. Once a site is included in each practice, they are not able to be included in another practice and are not allowed to change practices for the duration of the study regardless of any changes in NRG membership.
- All practices must enroll at least 43 patients and at minimum one practice personnel who is involved in care for at least one patient on trial.

Questions regarding your practice:

1. List all counties in the catchment area of the practice (see section 3 of the protocol for NIH Participant Population Inclusion Policy):
2. Percent of Spanish speakers among patients seen in the practice:
3. Approximate number of patients satisfying this study's eligibility criteria per year:
4. Does your practice have an available social worker or behavioral health professional at the practice?
5. Are social worker(s) or behavioral health professional(s) at your site willing to be trained in the Telephone Interpersonal Counseling (TIPC) intervention?
 - a. If yes, provide name/contact information:

After approval of the LOI to participate in NRG-CC012CD, social worker(s) or other behavioral health professional(s) will have 60 days to complete TIPC intervention training.
6. If a social worker or other behavioral health professional is not available at the practice or unwilling or unable to be trained in and deliver TIPC, are you willing to have a person contracted by the study deliver TIPC to patients in your practice?
7. Identify practice personnel who will receive weekly reports with summaries of symptoms experienced by patients on trial and complete brief monthly assessments about use of these reports. Practice personnel are physicians, nurses, physician assistants, social workers, pharmacists, and other clinicians who provide care to patients during the 17 weeks while on this study. You can identify one practice personnel as a recipient of weekly symptom reports or multiple practice personnel as best for your practice. Practice personnel are not asked to do anything special based on these reports but will be asked monthly what if anything was done as part of patient care. Please provide the name/contact information for practice personnel below:

Practice personnel name: email:

Protocol Training

- Must be completed within 90 days of approval as a participating site.
- At least one designated staff member must complete the training.
 - If staff member leaves, another staff member must complete the training.

Training Options

- NRG Oncology Semi-Annual Meetings – 1 hour in-person training
- Web-based training slides available on CTSU website
 - Recording of past in-person training available at <https://www.nrgoncology.org/Winter-Meeting-2024>

4b

Training Certificate

Training certificate on CTSU must be completed and submitted to the CTSU prior to enrollment of first participant.

**NRG-CC012CD Web-based training
Confirmation of Completion**

Instructions: Submit the completed via the CTSU Regulatory Submission Portal

*This verifies that you have completed viewing the
NRG-CC012CD Training slides.*

• Name _____
(Please type/print)

Your Individual NCI CTEP ID Code: _____

Check one (you are):

- Investigator on IRB Approval
 Research Associate

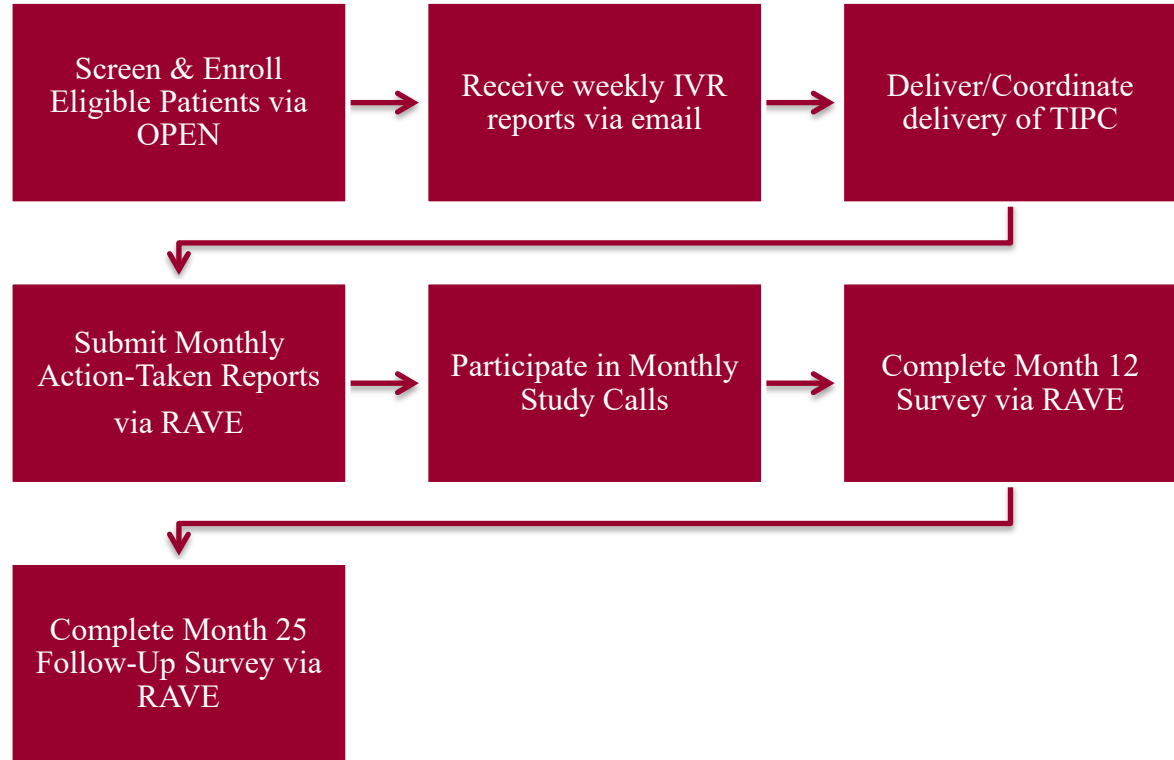
• Institution Name _____

• Institution NCI CTEP ID Code: _____
(list additional institution CTEP ID Codes if you are the Qualified Investigator for additional sites and the sites are also listed on the IRB/REB approval)

• Date completed _____

Signature: _____

Practice: Participating in Study



Patient Key Eligibility Criteria

- Starting a new course of an oral anti-cancer agent (the list of agents is posted to the CTSU website) other than checkpoint immune inhibitors, within 4 weeks after registration or have started an oral anti-cancer agent in the past 4 weeks.
 - Hormone therapies, radiation, infusions, and supportive care treatments and medications can be concomitant
- Age \geq 18 years.
- Able to speak and understand English or Spanish.
- Access to a telephone and ability to answer questions via telephone in English or Spanish.
- Able to provide study-specific informed consent prior to study entry and authorization permitting release of personal health information.

Patient Key Exclusion Criteria

- Treatment with immune checkpoint inhibitor at enrollment
- Only receiving sex hormone inhibitor
- Being in the intervention arm of another symptom management trial at intake into this study. Participation in lifestyle trials with primary outcomes other than symptoms is acceptable.
- Currently receiving regular behavioral counseling for psychological symptoms (at least two counseling sessions within the past two months). Patients who completed behavioral counseling within 2 months prior to registration are eligible. Behavioral counseling for issues other than psychological symptoms (e.g., as part of weight loss or smoking cessation program) is not an exclusion criterion.
- Currently in hospice care

Targeted Patient Enrollment

- The study enrollment goal is $\geq 15\%$ Spanish speakers (defined as participants who prefer information communicated in Spanish)
- The enrollment of Spanish speakers will be monitored via monthly enrollment tracking
- Enrollment of patients who are not Spanish speakers will be closed when their number reaches 85% of the target enrollment of 516 patients, i.e., no more than 438 non-Spanish speaking patients will be enrolled
- Rural determination is at the practice level (serving at least one rural county). No restriction on enrollment of patients residing in rural or urban areas

Patient Enrollment

- Patient registration can only occur after eligibility criteria confirmed, and study site is listed as ‘approved’ in CTSU.
- Complete patient contact form, patient demographics form, patient history form
- Register Patient in OPEN (See section 8.2.1 for OPEN enrollment protocol)
- Email patient contact information to SYMON@miami.edu for UMiami/MSU to start non-practice data collection and IVR delivery.
- Planned enrollment is average of 2 patients per month over 21 months (total of 43 from practice)

Weekly IVR Report for Providers

Recipients of these reports
can be any designated
practice personnel at site

Practice personnel are not
required to action these
reports

Provider Report

Patient Name: Elle Example

MRN: 1234567

Study Start Date: 06/28/2024

Below is a summary of your patient's symptoms reported on [06/29/2024](#)

Severe Symptoms

Cough: 4

Arm or leg swelling: 3

Pain: 4

Vomiting: 4

Moderate Symptoms

Pounding or racing heartbeat (Palpitations): 2

Hand-foot syndrome: 2

Headache: 1

No Symptoms Reported

Shortness of breath: 0

Tingling in Hands or Feet: 0

Dizziness: 0

Problems with concentration: 0

Insomnia: 0

Fatigue: 0

Anxiety: 0

Feeling that nothing could cheer you up: [0](#)

Sad or unhappy feelings: 0

Shivering or shaking chills: 0

Unexpected or excessive sweating: 0

Dry mouth: 0

Mouth or throat sores: [0](#)

Decreased appetite: [0](#)

Nausea: 0

Constipation: 0

Diarrhea: 9 (Refused to answer)

TIPC Intervention

- Practices randomized to Adaptive ATSM+TIPC will identify a TIPC intervener (social worker, behavioral health professional) who can be trained to deliver TIPC
 - If no personnel are available, the study team will work to contract someone licensed to practice in that state
- Practice TIPC intervener will complete an asynchronous online training course and will be reimbursed for their time
- Practice TIPC intervener will be compensated for delivery of TIPC intervention
- A TIPC supervisor at University of Arizona will work closely with TIPC intervener for training and delivery continuity

Study Intervention Modifications

Patients can continue in the study if they are willing to, regardless of oral agent temporary or permanent stoppages, hospitalizations, or hospice (they cannot be in hospice at enrollment, but later is not a reason for modification of study intervention).

Adverse Events

None. The interventions in this study are designed to address symptoms resulting from cancer and its treatment, and weekly IVR symptom reports will be sent to practices for all patients.

Data Management

CTSU

Practice IRB approval

Protocol-specific
training

Site registration
documents

OPEN

Practice Enrollment

Practice Personnel
Enrollment

Patient Enrollment

RAVE

Practice Personnel
Demographics
Questionnaire

Patient Screening Data

Monthly “Action
Taken” Reports

Patient health record
review

Feasibility and
Acceptability
questionnaires (months
12 and 25 only)

CC012CD@miami.edu

LOI (retrieve from CTSU)

Patient Contact Form
(within 1 business day)

Blank Rave forms and Summary of Data
Submission are available on the CTSU website.

Statistical Considerations, Protocol Logistics & Regulatory Requirements

Study Design and Duration

- Primary endpoint: summary toxicity index of 24 PRO-CTCAE symptoms over weeks 1-12 (immediate effect)
- Toxicity index over weeks 13-17 (sustained effect) will also be evaluated
- A total of 516 patients will be enrolled (43 per practice, with 34 analyzed after attrition).
- Each practice will be in the study for approx. 25 months, enrolling patients for approx. 21 months
 - Each patient will be in the study for 17 weeks
- Accrual goal is an average of 2 patients per month
- If fewer than 8 patients are accrued during the first 6 months of practice's participation in the trial or fewer than 2 monthly forms of actions on symptom reports are completed, practice's participation will be discontinued, and another practice will be enrolled.

Regulatory Logistics

- Maintenance of regulatory records is important!
 - Retain correspondence
 - Maintain IRB approval (amendments and continuing reviews)
 - Keep IRB registration current throughout the study
- Keep local staff current with the NCI Registration and Credential Repository (RCR):
 - All staff contributing to NCI sponsored trials will need to register. Questions related to RCR can be directed to RCRHelpDesk@nih.gov

Protocol Deviations

- NCI/CTEP will not issue or approve any waivers for protocol deviations. This applies to all components of the approved protocol, including eligibility criteria, intervention schedule, and statistical aspects.
- NRG recognizes that deviations may occur during a trial and NRG's process is to have sites report all deviations to NRG and to the CIRB
- Sites can report any deviations to NRG by completing a Deviation form in Rave



In Closing

Monthly Study Calls

- There will be monthly calls with sites about accrual, regulatory requirements, and any issues arising during the study.
- Timing of monthly calls yet to be determined; webinar invitations will be sent to all practice personnel.
- Site PIs or designated Physician delegates (must be site co-chairs) must make every effort to attend.
- Site study team (RAs, study nurses, etc.) are required to attend at least once per quarter

- LOI submissions open via CTSU!
- Key study contacts:
 - Jamillah Gross-Caldwell, Michigan State University
 - Grey Freylersythe, University of Miami
- SYMON@miami.edu
- www.craneresearchlab.org/cc012cd



FAQs

What oral treatments are eligible?

The list will be maintained on CTSU, as it will be updating all of the time. We recommend checking eligibility against the version in CTSU every time.

How do changes in a patient's treatment plan affect their participation?

Patients can continue in the study if they are willing to, regardless of oral agent temporary or permanent stoppages, hospitalizations, or initiation of hospice care.

How are deviations handled?

Sites can report any deviations to NRG by completing a Deviation form in Rave. Sites should also report deviations to CIRB where applicable.

What staff are eligible to participate as practice personnel?

Physicians, nurses, nurse practitioners, advanced practice providers, physician assistants, medical assistants, pharmacists, social workers, and other behavioral health professionals who have the requisite education, licensure or certifications for their roles and are involved in symptom management of patients on trial.

How are “rural” practices defined?

Having at least one rural county in their catchment area. Based on the Department of Health and Human Services, rural county is defined as county that is not part of a Metropolitan Statistical Area, i.e., does not contain a core urban area of 50,000 or more population