NRG Cancer Prevention and Control Meeting

Lisa Kachnic, MD, Cancer Control Chair
Douglas A. Levine, MD, Prevention Chair
Debra Barton, PhD, Cancer Control Vice-Chair
Julie Bauman, MD, Prevention Vice-Chair

July 16, 2020
NRG Oncology NCORP Org Chart

NRG Executive Committee
NCORP PIs: Deb Bruner (contact PI) & Joan Walker
Assoc. Chair: Lisa Kachnic
NRG Group Chairs, NCORP Comm Chairs, NCORP Stats

NRG NCORP Steering Committee
NCORP PIs, Comm Chairs/Vice Chairs, Stats, Community MDs, New Investigator Liaisons, PT Advocates, Admin

Ca Prevention and Control Research (CPCR)
Co-Chairs:
L Kachnic, D Levine
Vice Chairs:
D Barton, J Bauman
- Neurocognitive Function
- Gender-specific Symptom Mgmt
- Dose Alterations
- Ca Risk Reduction

Cancer Care Delivery Research (CCDR)
Chair: M Cooley
Vice Chair: M Hudson
- Ca Survivorship
- Implement EBP in Symptom Mgmt

Health Disparities Research (HDR)
Chair: K Yeager
Vice Chair: C Hughes
- Racial/Ethnic Minorities
- Elderly
- Rural Populations

Patient Centered Outcomes Research (PCOR)
Chair: B. Movsas/Vice Chairs
L. Wenzel, P Ganz
- PROs tx trials
- Consult on PROs in CCC, CPC, CCD, HDC trials

NRG NCORP Operations Committee

NRG NCORP Finance Committee
NRG NCORP Cancer Prevention and Control Priorities

- Improvement or delay in decline of neurocognitive function
- Reducing of gender-specific symptoms including lymphedema and sexual function
- Testing therapeutic delivery modifications to improve QoL and cost-effectiveness in localized cancers while maintaining efficacy
- Reducing cancer risk through optimal screening, biomarker evaluation and risk reduction strategies and
- Assessing behavioral interventions to decrease cancer risk and mitigate cancer treatment-related symptoms
Call for New Concepts

- CPC is always soliciting new concepts
- Please contact Erica Field fielde@nrgoncology.org
NCORP CPC Recent Publications

• NRG CC001

• RTOG 1203
Announcements
CPC Committee Members

Hanna Bandos
Jennifer Bea
Beth Beadle
Jeanne Carter
Reena Cecchini
Dana Chase
Tracy Crane
Jennifer Dorth
Danielle Enserro
Britt Erickson
Carolyn Fang
Vinai Gondi
Elizabeth Hile
Jordan Kharofa
Bridget Koontz
Rachel Kupets
Lindsay Kuroki
Simon Lo
Julie Nangia
Joshua Palmer
Frank Panedo
Kathryn Pennington
Steven Plaxe
Laurel Pracht*
Stephanie Pugh
Erika Radake
Lindsay Romak
Diane Rose*
Alison Stopek
Nicole Stout
Mylin Torres
Minh Tam Truong
C. Jillian Tsai
Lana Uhrig
Kathleen Yost

*patient advocate
## NCORP Liaisons

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<th>Disease Site</th>
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<tr>
<td>Brain</td>
<td>Natosha Gatson (HDC)</td>
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<td>Mylin Torres (CPC)</td>
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<td>Cervix</td>
<td>Dana Chase (CPC)</td>
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<td>Jordan Kharofa (CPC)</td>
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<td>GU</td>
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<td>H&amp;N</td>
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<tr>
<td>Lung</td>
<td>Nitin Ohri (CCDR)</td>
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<tr>
<td>Ovarian</td>
<td>Kathryn Pennington (CPC)</td>
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<tr>
<td>Uterine Corpus</td>
<td>Victoria Bae-Jump (HDC)</td>
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BCPT and STAR Biospecimens Available

Biospecimens are available for research from two prevention trials that accrued 13,000 and 19,000 participants

<table>
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<tr>
<th>Specimen Type</th>
<th>NSABP P1 (BCPT)</th>
<th>NSABP P2 (STAR)</th>
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<tr>
<td>Buffy coat and Plasma</td>
<td>73,218 specimens</td>
<td>286,159 specimens</td>
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<tr>
<td>Fasting lips</td>
<td>500 specimens</td>
<td>N/A</td>
</tr>
<tr>
<td>Tissue blocks (FFPE)</td>
<td>11,432 specimens</td>
<td>16,197 specimen</td>
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</table>
Tamoxifen Breast Cancer Prevention Trial (BCPT): the National Surgical Adjuvant Breast and Bowel Project P-1 Study

Historic BCPT enrolled 13,388 pre-and postmenopausal women aged 35 years and older who were at an increased risk for breast cancer to receive tamoxifen or placebo for 5 years (1992 – 1997)

- Stratified by age, race, history of lobular carcinoma in situ, and breast cancer relative risk (Gail Model)
- Extensive behavioral data were collected at study entry (diet, exercise, alcohol, tobacco) as well as BMI
- Baseline and longitudinal data on health-related quality of life outcomes was collected at regular intervals during the course of the study
- Primary outcome was incidence of invasive breast cancer
- Secondary endpoints: DVT, pulmonary embolus, stroke, myocardial infarction, fracture, other cancers
- **Results:** Tamoxifen was shown to significantly reduce the incidence of invasive and non-invasive breast cancer compared to placebo

Study of Tamoxifen and Raloxifene (STAR) P-2 Study

STAR enrolled 19,490 women at least 35 years of age and postmenopausal at increased risk for breast cancer to receive tamoxifen or raloxifene for 5 years (1999 - 2004)

• Stratified by age, race/ethnicity, history of lobular carcinoma in situ, and 5-year predicted risk (Gail Model) of breast cancer (<2.5%, 2.5%-3.9%, and ≥4.0%)
• Primary Outcome: determine if raloxifene was non-inferior to tamoxifen in the prevention of breast cancer in high risk, postmenopausal women
• Secondary end points: endometrial cancer, in situ breast cancer, cardiovascular disease, stroke, pulmonary embolism, DVT, transient ischemic attack, osteoporotic fracture, cataracts, death, and quality of life
• Results: Raloxifene was found to be as effective as tamoxifen in reducing invasive breast cancers but not non-invasive breast cancer. There was a lower risk of thrombo-embolic events and uterine cancer with raloxifene.

How to Apply for Access to Use Biospecimens from P-1 or P-2 Breast Cancer Prevention Trials

Complete and submit the Letter of Intent (LOI) to NRG Oncology (as directed on the NRG website: https://www.nrgoncology.org/Scientific-Program/Biospecimen-Access)

Upon receipt of the LOI, NRG will assign a staff member to work with the investigator.

The LOI will be reviewed by NRG and if determined to be feasible, the investigator will be instructed to complete the NCTN CCSC Proposal Submission Form and submit with all letters of collaboration to NRG to prepare for submission to NCTN CCSC.

The NCTN CCSC will review the proposal for scientific merit and alignment with goals. If approved, the investigator will work with NRG to complete regulatory/legal documentation prior to biospecimen distribution.

Investigators are required to notify NRG Oncology of any publications that result from the use of NRG Oncology biospecimens.
Questions
to our
Distinguished NCI Department of Cancer Prevention Speakers
Cecilia Lee, Dr.P.H., R.N.
NCI DCP NCORP Program Director

Symptom management implementation priorities for community oncology/NCORP setting
Symptom Science and QOL Implementation Priorities

Cecilia Lee, DrPH, RN
Nurse Consultant/Program Director
Division Cancer Prevention
Objectives

- Provide an overview of SxQoL SC High Priorities
- Current and past activities supporting SxQoL SC priorities
  - Clinical Trial Planning Meetings
- NCI funding opportunities
  - Mechanism of therapy induced adverse sequelae
  - NIH HEAL Initiative
  - Cannabis
First Tier SxQoL SC High Priority

I. Cognitive Impairment
II. Neurotoxicity
III. Cardiovascular Toxicity
IV. Fatigue
V. Cancer Specific Pain
Second Tier SxQoL SC High Priority

I. Sleep Disorders
II. Bone Health Toxicity
III. Metabolic Toxicity
IV. Psychological Distress
Status of Reviewed Concepts 8/1/14 to 6/14/19 (n=31)

- Approved = 12
  - First submission=2
  - Pending=12
    - Final approval=10
    - Disapproved=1
    - In review=1
- Disapproved = 18
Submitted Concepts by Symptom
All RBs 8/1/14 to 6/14/19 (n=31)

- Neurocognition (5)
- Cardiovascular (4)
- HR QoL (4)
- Sexual health (3)
- Dermatologic (3)
- Nausea/vomiting (2)
- Lymphedema (1)
- Psychosocial (1)

- Fatigue (1)
- End of life (1)
- Nutrition (1)
- Hot flashes (1)
- Peripheral neuropathy (1)
- Surgical complications (1)
- Stomatitis (1)
- Multiple symptoms (1)
NCI Clinical Trials Planning Meeting

- Identify key groups of patients that could be studied
- Build upon a multidisciplinary team of investigators to answer translation questions
- Identify gaps in the literature on disease groups and treatment phenotypes
- Identify and prioritize key biomarkers (integral/integrated)
- Utilize best measurement practices
- Identify 2 interventions that can be moved forward into an NCI protocol concept/Phase III trial
COMMENTARY

The National Cancer Institute Clinical Trials Planning Meeting for Prevention and Treatment of Chemotherapy-Induced Peripheral Neuropathy

Current Gaps Identified on CIPN

1. Conduct more basic research to understand the mechanism of CIPN
2. Recommend to use patient reported CIPN-20 questionnaire to streamline data collection
3. Identify/support trials focused on prevention of CIPN
4. Investigate behavioral, psychological and other non-pharmacological approaches
5. Promising and understudied interventions for prevention and treating CIPN e.g. Exercise, Duloxetine for CIPN prevention
NCI Cancer Related Cognitive Impairment Clinical Trials Planning Meeting 2021

- Invitation only
- 1.5 Day forum
- Date: TBD
- Participants:
  - CRCI Content experts
  - Senior/Junior clinical research investigators
  - NCORP investigators
  - Basic scientists in the field of CRCI
Clinical Characterization of Cancer Therapy-induced Adverse Sequelae and Mechanism-based Interventional Strategies (R01 Clinical Trial Optional)

- Cancer treatment can result in acute, chronic, and/or progressive toxicities
  - Adverse effects often persist after completion of therapy or develop as late effects

- Cancer survivorship and adverse effects will significantly increase in the next couple of decades

- Little is known about the rates of adverse events related to new therapies

- Development of biomarkers and/or mitigation or prevention strategies are limited by:
  - Lack of mechanistic understanding of adverse events
  - Lack of accurate reporting and archiving of adverse event data
  - Difficulties in objectively measuring treatment-related toxic effects
  - Insufficient characterization of the clinical phenotypes
  - Insufficient studies validating pre-clinical biomarkers in the clinical setting
Purpose of the PAR (R01, Clinical Trials Optional)

- Support preclinical and clinical research projects which seek to:
  1. Clinically characterize adverse sequelae
  2. Translate the mechanistic understanding into therapeutic approaches to prevent or minimize the development of long-term sequelae
  3. Identify mechanisms of new therapy-induced adverse sequelae

- Applications should prospectively identify the specific adverse effects and/or cluster of effects under evaluation
- Collaborations between clinical and non-clinical investigators are encouraged to couple the mechanistic knowledge with the clinical phenotype
- Emphasis should be on translating mechanistic knowledge into approaches or interventions to prevent or mitigate adverse sequelae

NIH HEAL Initiative

- $500M/year Trans-NIH effort
  - Over $945M obligated in FY2019
- 12 NIH Institute and Centers currently leading 26 HEAL research projects
  - Over 20 collaborating Institutes, Centers and Offices
  - From prevention research, basic and translational research, clinical trials, to implementation science
  - Multiple projects integrating research into new settings
- Released 40+ funding announcements for FY2019
- Issued over 375 awards
- https://heal.nih.gov/funding/open (Clinical Trials Optional/Allowed)
Enhancing Pain Management

Improving Treatments for Misuse and Addiction

- Novel Medication Options
- New Prevention & Treatment Strategies
- Translating Research into Practice
- Enhanced Outcomes for Affected Newborns
- Pre-Clinical/Translation Research in Pain Management
- Clinical Research in Pain Management

HEAL Initiative Research Overview
The symposium will highlight the state of the science in cannabis, its chemical constituents (e.g. cannabinoids) and cancer research, including cancer epidemiology, its use in cancer patients, cancer biology and prevention, pre-clinical and clinical cancer symptom and treatment side-effect management, as well as the use of cannabis and cannabinoids as cancer therapeutics. The symposium will also address current barriers to research and strategies to navigate these hurdles to ensure feasibility of rigorous studies designed to address gaps in knowledge as well as potential research opportunities in the area of cannabis cancer-related research.
Acknowledgement

• Thanks to Dr. Alexis Bakos and Diane St. Germaine for contributing to the slides
Sandra Russo, M.D., Ph.D., M.P.H.
NCI Community Oncology & Prevention Trials Research Group Program Director

NCI/DCP Cancer Prevention and Control update
NRG Oncology NCORP Prevention Protocols

• NRG-CC005 (GI) – FORTE (Five or Ten Year Colonoscopy for 1-2 Non-Advanced Adenomatous Polyps)
  Status: Pre-Activation Amendment Awaiting CIRB Approval
  Accrual Goal: 15,000

• NRG-CC008 (GYN) - A Non-Randomized Prospective Clinical Trial Comparing the Non-Inferiority of Salpingectomy to Salpingo-Oophorectomy to Reduce the Risk of Ovarian Cancer Among BRCA1 Carriers (SOROCK)
  Status: Activated, 6/23/20
  Accrual Goal: 2,262
NCORP Research Base Cancer Prevention Chairs Virtual Meeting

July 10, 2020

- Each of the 5 NCTN Research Base Prevention Chairs presented Developing Prevention Trial Concepts
- The Value of Cross Research Base Collaborations in Prevention Trials
- Potential Challenges in Prevention Trials
## NCORP Research Base Prevention Chairs

<table>
<thead>
<tr>
<th>NCORP RB</th>
<th>NCORP RB Prevention Chairs</th>
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</table>
| Alliance NCORP Research Base                                  | Marie E. Wood, MD.  
University of Vermont Medical Center  
Isabelle Bedrosian, MD, FACS  
MD Anderson Cancer Center                                      |
| Children’s Oncology Group (COG) NCORP Research Base           | Brad H. Pollock, PhD, MPH  
Philadelphia, PA                                                                 |
| ECOG-ACRIN NCORP Research Base                                | John M. Kirkwood, MD (Chair)  
University of Pittsburgh School of Medicine                                                  |
| NRG Oncology NCORP Research Base                              | Douglas Levine, MD (Chair)  
Perlmutter Cancer Center, NYU Langone Health  
Julie E. Bauman, MD, PhD (Vice Chair)  
University of Arizona Cancer Center                             |
| SWOG NCORP Research Base                                      | Marian L. Neuhauser, PhD, RD  
Fred Hutchinson Cancer Research Center  
Banu Arun, MD  
MD Anderson Cancer Center                                      |
CROSS RESEARCH BASE (RB) COLLABORATIONS/PARTNERSHIPS

- Each of the 5 NCTN RBs have unique strengths in the development of large prevention trials
- Large clinical prevention trials can take years to develop

Maximize Shared Interests
- RB collaborations could enhance clinical trials goals and optimal outcomes
  - Incorporate the scientific expertise of more than 1 RB
  - Produce superior trial design
  - Benefit from the infrastructure strengths of each collaborating RB
  - Decrease trial development time
- Diminish overlap of RBs efforts on similar trial development in specific disease sites
  - May be able to incorporate several RBs initiatives into one large collaborative prevention trial
  - Increase the ability to accrue patients
- Rapid clinical trial accrual leading to early publication of practice changing results
CROSS RESEARCH BASE (RB) COLLABORATIONS/PARTNERSHIPS

POTENTIAL BENEFITS

- Broad scientific expertise
- Maximize infrastructure strength
- Decrease development time
- Superior trial design
- Increase trial accrual
- Faster dissemination of results
- Early practice change

GOALS

- Transparency
  - Shared collegial recognition
    - RBs and Investigators
Potential Challenges in Prevention Trials

- Eligible patients often not seen in oncology clinics
- Infrastructure required to track patients enrolled
  - Non-oncology clinics may lack access to clinical research infrastructure
- Lack of trial champion in settings where patients present
- Representative accrual of minority and underserved populations
1. **Purpose**

Outline the NCORP Concept/Protocol Efficiency timelines and processes for monitoring, oversight, and implementation of these timelines.

2. **Timelines**

Category 1 = Studies with concepts: Time from concept receipt to protocol activation
- Target = 475 days
- Absolute = 525 days* *(60 days notice at 465 days)*

Category 2 = Studies without concepts: Time from protocol receipt to protocol activation
- Target = 265 days
- Absolute* = 315 days *(60 days notice at 255 days)*

* Absolute goal includes an extra 50 days to accommodate one additional revision.
## NCORP CONCEPT/PROTOCOL EFFICIENCY TIMELINES

**Effective 8/1/18**

**Category 1 = Studies with concepts:** Time from concept receipt to protocol activation

**Target = 475 days**

**Absolute = 525 days**

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<tr>
<th>Study</th>
<th>Title</th>
<th>Concept Receipt Date</th>
<th>CPSC Review</th>
<th>Current Status</th>
<th>Days from Concept Receipt to Protocol Activation</th>
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<td>NRG-CC008</td>
<td>A Non-Randomized Prospective Clinical Trial Comparing the Non-Inferiority of Salpingectomy to Salpingo-Oophorectomy to Reduce the Risk of Ovarian Cancer Among BRCA1 Carriers (SOROck)</td>
<td>2/12/19</td>
<td>4/9/19</td>
<td>Activated- 6/23/20</td>
<td>468 days</td>
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COVID-19

- Research staff were furloughed or transferred to other departments.
- Everyone is cautiously optimistic that research teams will be able to normalize within four to six months.
- There is concern within hospital administrations as to the future status of furloughed employees.
- Research staff are slowly coming back into the offices, but it will be some time before workflow returns to pre-COVID-19 levels.
- What will be the impact of telemedicine on clinical oncology trials?
NCORP Accrual for “Intervention” Step in NCORP Trials by Lead Research Base Week February 3, 2020 to June 28, 2020 (CTSU OPEN Data)

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UPCOMING VIRTUAL MEETINGS

- **NCORP Annual Meeting**
  - **Part I:** August 31, 2020 12:00 PM – 5:45 PM EST
  - **Part II:** October 6, 2020 2:00 PM – 4:45 PM EST

- **Translational Advances in Cancer Prevention Agent Development**
  —Sponsored by the Division of Cancer Prevention, National Cancer Institute and the Office of Disease Prevention
  - [https://events.cancer.gov/cadrg/tacpad](https://events.cancer.gov/cadrg/tacpad)
  - **August 27-28, 2020**

- **Primary Care Alliance in Research Trials Involving NCORP Sites (PARTNRS)**
  - **September 18, 2020**
Questions & Discussion
Congratulations
Buprenorphine a less toxic opioid substitute in treatment of radiation induced mucositis pain in Head and Neck cancer patients

Aditya Varnam Shreenivas MD, MS
Medical College of Wisconsin
CPC Trials
## Opened NRG CPC Trials

**accrual as of June 30, 2020**

<table>
<thead>
<tr>
<th>Study No</th>
<th>Disease Site</th>
<th>Description</th>
<th>Date Activated</th>
<th>Target Accrual</th>
<th>Total Accrual</th>
<th>NCORP Accrual (%)</th>
<th>Expected Closure Date</th>
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<tbody>
<tr>
<td>GOG 0278</td>
<td>Cervix</td>
<td>Physical function/QoL before and after non-radical surgical therapy for stage IA1 (LVS1+) and IA2-IBI (=2CM) cervical cancer</td>
<td>10/1/12</td>
<td>220</td>
<td>212</td>
<td>&lt;1%</td>
<td>December 2020</td>
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<tr>
<td>NRG CC003</td>
<td>Lung</td>
<td>Seamless phase II/III PCI vs. PCI with hippocampal sparing for cognitive fx preservation in small cell lung cancer</td>
<td>12/7/15</td>
<td>172 (II) 302 (III)</td>
<td>176 of 172 (II) 204 of 302 (III)</td>
<td>28%</td>
<td>Temporarily closure 5/28/20; amendment submitted to increase accrual</td>
</tr>
<tr>
<td>NRG CC008</td>
<td>Ovarian</td>
<td>Non-rand. prospective trial comparing non-inferiority of Salpingectomy to salpingo-Oophorectomy to Reduce risk of Ovarian Ca among BRCA1 carriers (SOROck)</td>
<td>6/23/2020</td>
<td>2262</td>
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</table>
Women with IA1-IB1 (≤2cm) carcinoma of the cervix who have been consented for surgery will be approached for study participation. Pre-entry cone biopsy/LEEP (depth of invasion ≤ 10mm)

Study Entry

Pre-operative QOL Study Survey

**Fertility Preservation Group:**
Conization with pelvic lymphadenectomy (If the lateral margins were positive on the first cone biopsy/LEEP, patients must have a second cone biopsy/LEEP at the time of the pelvic lymphadenectomy)

If depth of invasion (sum of the pre and post entry biopsies) is ≤10 mm, only ECC is required.

If any of the following criteria are met, patient will be followed for survival only:
- Depth of invasion (sum of the pre and post entry biopsies) is >10 mm
- Positive pelvic lymph nodes on final pathology
- Adjuvant therapy required

**No Wish for Future Fertility Group:** Simple hysterectomy with pelvic lymphadenectomy (If the lateral margins were positive on the first cone biopsy/LEEP, patients must have a second cone biopsy/LEEP prior to hysterectomy)

If depth of invasion (sum of the pre and post entry biopsies) is ≤10 mm, proceed to hysterectomy.

**Post-Operative**
Follow-up Visits 4-6 weeks Post-op and every 3 months (3, 6, 9, 12) for 1 year then every 6 months (18, 24, 30, 36) for 2 years and QOL Study Surveys 4-6 weeks Post-Op and every 6 months (6, 12, 18, 24) for two years
NRG CC003: Phase IIR/III Trial Prophylactic Cranial Irradiation with or without Hippocampal Avoidance for Small Cell Lung Cancer

PIs: Minesh Mehta (Miami Cancer Institute) + Vinai Gondi (Northwestern)

Basic Eligibility: Small cell lung cancer; PR or CR to chemo; ECOG PS ≤ 70; MRI scan

Sample Size: Phase IIR: 172 patients; Phase III: 302 patients

Primary endpoints:
- Phase IIR: Intracranial relapse rate at 12 months
- Phase III: HVLT-R delayed recall deterioration at 6 months

Statistical Design:
- Phase IIR: Non-inferiority margin of >20% difference. 164 analyzable pts.
- Phase III: 29% with PCI vs. 14.5% with HA-PCI. 198 analyzable pts
NRG CC008 SOROCk  
PI Levine

- **BRCA1** carriers will self-select surgical arm
  - Copy of genetic test report required
- Normal preoperative CA125 and TVUS required, per parameters in protocol
- Tissue will remain at local site in virtual tissue bank unless invasive cancer or precursor lesion is found at surgery
- Follow-up can be in person or remote
- Annual CA125 is required (local or remote)

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Not confidential – Please post!
<table>
<thead>
<tr>
<th>Study</th>
<th>Protocol Title</th>
<th>Accrual</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1820</td>
<td>Testing Diet Intervention vs. Non-Diet Intervention for Management of Bowel Symptoms in Rectal Cancer Survivors (PI Sun)</td>
<td>9/126</td>
<td>Tracy Crane is the NRG Study Champion</td>
</tr>
<tr>
<td>S0820</td>
<td>Double Blind Placebo-Controlled Trial to Prevent Recurrence of High Risk Adenomas and Second Primary Colorectal Cancers (PACES) - (PI Zell)</td>
<td>278/491</td>
<td>Jenny Dorth is the NRG Study Champion</td>
</tr>
<tr>
<td>EA1151</td>
<td>Tomosynthesis Mammographic Imaging Screening Trial (TMIST) – (PI Pisano)</td>
<td>26,823/164,946</td>
<td>NRG is a study champion; enrolled 2,461 participants</td>
</tr>
</tbody>
</table>
SWOG 1820: Testing Diet Intervention vs. Non-Diet Intervention for Management of Bowel Symptoms in Rectal Cancer Survivors

Rectal cancer survivors (N=94, 47 per arm)
- Between 6-24 months post-treatment completion
- Low anterior resection syndrome (LARS) score of 21-42 (minor/major symptoms)
- English-speaking
- 18 years and older

Intervention Arm (AIMS-RC)*
- 10 telephone coaching calls over 4 months (about 20-40 minutes)
  - Goal setting
  - Identifying and overcoming challenges
  - Food and symptom diary
  - Motivational interviewing and problem-solving (MAPS)
  - AIMS-RC resource manual
  - Personalized text/email messaging support between calls

Attention Control Arm (Healthy Living Education)*
- 10 telephone calls over 4 months (about 20-40 minutes)
  - Sleep, sun safety, food safety, skin care, active wear, bone health, physical activity, clinical trials, evaluating online resources, screening & surveillance
  - Attention control resource manual
  - Automated, standard text/email messaging support between calls

Outcomes:
- Bowel Function (MSKCC-BFI)
- QOL (COH-QOL-CRC), LARS score, self-efficacy (PROMIS), motivation, positive/negative affect (PANAS), diet quality, feasibility and acceptability

*Centrally-administered by trained health coaches at the University of Arizona

Week 18 follow-up (PROs)

Week 26 follow-up (PROs)
SWOG 0820: Double Blind Placebo-Controlled Trial to Prevent Recurrence of High Risk Adenomas and Second Primary Colorectal Cancers (PACES)

**Inclusion:**
- Stage 0-III colorectal adenocarcinoma
- s/p partial colectomy, polypectomy, TAE +/− chemo(RT)
- Register 6 mo -15 mo postop, ≥30 d post chemo(RT)
- NED at colonoscopy +/− CT scan ≥ 6 mo postop

**Exclusion:**
- No high CV risk
- No hearing loss
- No high-dose NSAID
- No GI ulcer
- No family hx FAP, HNPCC, IBD

*Stratify by stage/adjuvant tx*

**Randomize**
- Placebo X 3y
- Eflornithine 500mg/d + Sulindac 150mg/d X 3y

**Year 3**
- Colonoscopy
- Audiogram

1° endpoint = 3y event rate high-risk adenomas + 2nd primary CRCs

Stats: 80% power for event rate 27% → 13.5%

**Year 8**
- Colonoscopy at years 3 and 8

F/U schedule:
q3mo X 1y → q6mo X 2y → q1y X 5y
TMIST Cohort
Women Ages 45-74 Presenting for Breast Screening

Digital Mammography (DM)
- Annual DM Screening¹ (Baseline, 12-, 24-, 36-, 48-
  Months, or Until Cancer Detected)
- Biennial DM Screening²

Tomosynthesis (TM)
- Annual TM Screening¹ (Baseline 12-, 24-, 36-, 48-
  Months, or Until Cancer Detected)
- Biennial TM Screening² (Baseline, 24-, 48-
  Months or Until Cancer Detected)

Long-term Follow-up
## Developing NRG NCORP Trials

<table>
<thead>
<tr>
<th>Study No</th>
<th>Disease</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRG-CC005</td>
<td>Forte – Five or Ten Year Colonoscopy for 1-2 Non-advanced Adenomatous Polyps (R. Schoen)</td>
<td>Pre-activation revision submitted to DCP</td>
</tr>
<tr>
<td>NRG-CC009</td>
<td>SRS vs. HA-WBRT for 10 or Fewer Brain Metastases from Small Cell Lung Cancer (V. Gondi)</td>
<td>Protocol – 1st circulation</td>
</tr>
<tr>
<td>NRG-CC1925</td>
<td>Smoking Cessation and Relapse Prevention in Newly Diagnosed Cervical Cancer Patients (T. Crane)</td>
<td>R01 resubmission fall 2020</td>
</tr>
</tbody>
</table>

### NCORP Concept Review – July 2020

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gynecologic Cancer Therapy: The Vaginal Microbiome and Patient Symptom Experience (D. Bruner)</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td>Impact of Sentinel Lymph Node Mapping on Patient Reported Lower Extremity Limb Dysfunction in Endometrial Cancer (U1603), (E. Tanner)</td>
<td>Pending</td>
</tr>
</tbody>
</table>
FORTE – 5,10 vs 10 Year Colonoscopy for Non-Advanced Adenomas

Robert E. Schoen, MD, MPH
Professor of Medicine & Epidemiology
PI, FORTE Trial
University of Pittsburgh | UPMC
Pittsburgh, PA
“Recent” Multi-Society Task Force Surveillance Recommendations

<table>
<thead>
<tr>
<th>Neoplasia found</th>
<th>No polyps, or hyperplastic polyps in rectum/sigmoid</th>
<th>Neoplasia found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fontcolor-blue</td>
<td>Repeat in 10 years</td>
<td>Repeat in 10 years</td>
</tr>
<tr>
<td>Serrated polyposis</td>
<td>Repeat in 1 year</td>
<td>Repeat in 1 year</td>
</tr>
<tr>
<td>Hight risk adenomas</td>
<td>&gt; 10 Adenomas Repeat in less than 3 years</td>
<td>&gt; 10 Adenomas Repeat in less than 3 years</td>
</tr>
<tr>
<td>≥ 10 mm or With dysplasia or traditional serrated adenoma</td>
<td>3–10 Adenomas Repeat in 3 years</td>
<td>3–10 Adenomas Repeat in 3 years</td>
</tr>
<tr>
<td>Villous adenoma(s) or tubular adenoma(s) ≥ 10 mm Repeat in 3 years</td>
<td>1–2 Tubular adenomas &lt; 10 mm Repeat in 5–10 years</td>
<td>1–2 Tubular adenomas &lt; 10 mm Repeat in 5–10 years</td>
</tr>
<tr>
<td>&lt; 10 mm in Proximal colon and without dysplasia Repeat in 5 years</td>
<td>Adenoma(s) with high grade dysplasia Repeat in 3 years</td>
<td>Adenoma(s) with high grade dysplasia Repeat in 3 years</td>
</tr>
</tbody>
</table>

These recommended intervals assume a complete exam to cecum, adequate bowel prep, and complete removal of polyps at the baseline exam.
PLCO Trial: Long-term CRC Incidence

No cancer difference in NAA vs NA: ?? Can delay surveillance for 10 y

RR = 1.2 (0.8-1.7)

Click. JAMA 2018:319:2021
Pathology Report
1-2 non-advanced adenomas

N = 15000
Colonoscopies up to 4 years ago

Schema

Colonoscopies up to 4 years ago

Secondary endpoint: Advanced Adenoma

Randomized

Surveillance Colonoscopy

5 Yr.

10 Yr.

End Point: CRC Incidence

Secondary endpoint: Advanced Adenoma
1. \( \geq 50 < 70 \), with first time diagnosis of 1-2 non-advanced tubular adenomas
2. Complete to cecum/adequate preparation
3. Complete excision of polyps
4. Exclude high risk genetic syndromes, IBD, life expectancy \(<10\)y

- NO path/lab submissions
- F/U in out years remote
Identifying Patients to Enroll

Retrospective:

- Colonoscopy report – 1 or 2 <1cm polyps
- Pathology report – tubular or serrated adenomas
- Age 50-69
- ~ Diagnosed in up to 4.0 yrs ago
- No prior adenomas – first time diagnosis
- No other cancer in previous 5 years
- No Family history of CRC <60, no IBD, etc.

Prospective:

- Active colonoscopy practices
Widespread recognition that surveillance colonoscopy requires further study

Surveillance is costly and of uncertain benefit

FORTE is an understandable, appropriate trial design with straightforward requirements

Currently at CIRB; estimated to open in early September
NRG CC009
Phase III Trial of Stereotactic Radiosurgery versus Hippocampal Avoidant WBRT for Small Cell Lung Cancer Brain Metastases

PIs: Chad Rusthoven MD and Vinai Gondi MD
Alliance: Steven Schild, MD Med Onc: D. Ross Camidge, MD
Neurocog: Jeffrey Wefel, PhD QOL: Terri Armstrong, PhD
Imaging: Joshua Palmer, MD and Joe Bovi, MD
Rad Onc: Paul Brown, MD Comp Effectiveness: Mark Mishra, MD
Stats: Stephanie Pugh, PhD
Background

• Whole-brain radiotherapy is standard of care for small-cell lung cancer brain metastases
  – Prior brain metastasis trials of SRS vs WBRT or HA-WBRT did not include small-cell lung cancer

• Cognitive toxicity from WBRT
  – Mitigated with SRS, memantine, hippocampal avoidance
  – Historic objections to SRS in small-cell related to concern for short interval CNS progression impacting OS
Background

• Emerging evidence re: SRS for SCLC brain mets

  – FIRE-SCLC\(^1\): SRS (n=710) vs WBRT
    Median OS 8.5 mo, median time to CNS prog 8.1 mo
    WBRT assoc with improved time to CNS prog, but no OS advantage

  – Serizawa et al\(^2\): SRS SCLC n=34 vs. NSCLC n=211
    Comparable OS, CNS control, neurologic death

  – Yomo, Hayashi\(^3\): SRS SCLC n=70 (46 without prior PCI/WBRT)
    Med OS 7.8 mos

  – NCDB\(^4\): N=200 SRS vs. WBRT for SCLC brain mets
    Favorable OS with SRS overall and in matched data

  – Cifarelli et al\(^5\): N=293 SRS (61 without prior PCI/WBRT)
    Median OS 7.5 mo with upfront SRS, necrosis rate 5%

\(^1\)Rusthoven, *JAMA Oncology* 2020
\(^2\)Serizawa, *JNS* 2002
\(^3\)Yomo, *BMC Cancer* 2015
\(^4\)Robin, *Lung Cancer* 2018
\(^5\)Cifarelli, *Neurosurgery* 2019,
First-line Radiosurgery vs Whole-Brain Radiotherapy for Small Cell Lung Cancer Brain Metastases: The FIRE-SCLC Cohort Study
Rusthoven et al., *JAMA Oncology*. 2020 Jun 4

- Retrospective (28 centers in Asia, North America, Europe)
- 710 patients treated with first-line SRS without prior PCI or WBRT
- Propensity score matched analyses demonstrated superior time to CNS progression with WBRT, but no OS advantage
- After SRS, 34% underwent salvage SRS vs 16% salvage WBRT
- Leptomeningeal progression (10.8%), neurological mortality (12.4%)
Background

- Practice-changing evidence re: WBRT

RTOG 0614\(^1\):
Hazard ratio of memantine = 0.78

NRG CC001\(^2\):
Hazard ratio of hippocampal avoidance added to memantine = 0.74

\(^1\)Brown et al. Neuro-Onc 2013 \(^2\)Brown, Gondi et al. JCO 2020
NRG CC009 Schema

Basic Eligibility: Small cell lung cancer; ≤10 brain mets ≤3cm; total vol 30cc; KPS≥70

Brain Mets from Small Cell Lung Ca

DS-GPA Exposure to NCF Testing*

SRS alone
HA-WBRT 30 Gy/10

Sample Size: 200 patients

Primary endpt: Time to cognitive failure--HVLT-R, COWA, and TMT A and B

Basic Statistical Design:
Cognitive fxn failure 58.8% at 6 mos with HA-WBRT+mem vs. 41.8% at 6 mos with SRS. 150 analyzable pts

*Pts enrolled on SWOG trial will have been exposed to NCF Testing
Summary/Status

• Secondary endpoints:
  – PROs: MDASI-BT, PROMIS cognition
  – Cumulative incidence of brain mets, # of salvage therapies
  – Overall survival, cumulative incidence of neurologic death
  – Adverse events

• Collaboration:
  – Support from SWOG, Alliance
  – SWOG MRI surveillance +/- PCI trial: brain met failures on observation arm can dual-enroll

• 5/26/20: Concept approved by DCP SxQOL Committee
  – Protocol under development
  – 9/8/20: Protocol submission to NCI
CC-1925
Smoking Cessation and Relapse Prevention in Newly Diagnosed Cervical Cancer Patients

Tracy Crane, PhD, RDN (PI)
University of Arizona
Diandra Ayala-Peacock, MD, Jennifer Vidrine, PhD,
Cynthia Thomson, PhD, RDN, Alla Sikorskii, PhD, Austin Miller, PhD
Rationale

1. Nearly 50% of cervical cancer patients report smoking at the time of diagnosis.
2. Cervical cancer patients who smoke have worse health outcomes than non-smokers.
   2. Survival is significantly impacted for those who continue to smoke after receiving a cancer diagnosis.
3. Relapse rates are **3 times** higher for cancer survivors compared to other quitters.
4. Integrate and build on lessons learned from NCI C3I moonshot to evaluate the impact of cessation on treatment toxicities and disease outcomes.
CC-1925 Concept History

- Approved and fully endorsed by the NCORP Steering Mock Review Process Summer 2017
- R01 submitted March 2018, New submission R01 submitted February 2019 – Score: 38
- Change to sequential multiple assignment randomized trial (SMART) Design
- R01 re-submission Fall 2020
Figure 3. CRANE NRG-CC-1925: Adaptive intervention sequences to facilitate smoking cessation during cancer treatment—study schematic

- Newly diagnosed cervical cancer patient with chemoradiation as part of tx plan and current smoker

**First Randomization**

- Motivation and Problem Solving (MAPS) weekly calls x 6 weeks, followed by patient-directed calls x 10 months (n = 136)

- Smoking Cessation (SC) Intervention weekly calls x 6 weeks (n = 408)

**Second Randomization**

- Quit
  - SC Monthly Calls x 10 months (n = 122)
  - SC Weekly x 4 wks → monthly calls x 9 months (n = 143)

- Not Quit
  - MAPS Weekly x 4 wks → Participant-directed x 9 months (n = 143)

**Flowchart Details**

- Current Smokers (n=544)
- Surgery consult and Radiation Planning Phase
  - Consent pts at surgery appointment or radiation consult or planning visit

- Radiation Treatment Phase ≤556 days
  - Repeat weekly assessment coinciding with pt radiation treatment visits

- Post-Radiation Treatment Phase
  - Repeat assessment coinciding with pt care visits 3, 6, 9, 12 and 18 months

**Systemic Treatment Phase**

**TIME**

- Baseline Assessment
- Mid-tx response ~6 weeks post enrollment
Specific Aims

• **Aim 1:** Determine if the rate of biochemically-verified 7-day smoking abstinence (primary outcome) is higher among **responders** randomized to MAPS as compared to SC at 18 months, and if secondary outcomes of treatment toxicity and quality of life are improved with MAPS compared to SC at 3, 6, 9, 12, and 18 months.

• **Aim 2:** Determine if the rate of biochemically-verified 7-day smoking abstinence is higher in **non-responders** randomized to a step-up MAPS as compared to continued SC at 18 months, and if secondary outcomes of treatment toxicity and quality of life are improved with MAPS compared to SC at 3, 6, 9, 12, and 18 months.
Specific Aims cont.

• **Aim 3**: Determine whether the effects of MAPS vs. SC on primary and secondary outcomes, if present, are mediated by motivation and self-efficacy for quitting smoking.

• **Aim 4**: Inform future tailoring in the adaptive intervention sequencing by comparing responders and non-responders at the end of the initial 6-week SC and at 18 months with respect to age, smoking history and nicotine dependence, cancer stage, race/ethnicity, socio-economic status, use of nicotine replacement therapy, and co-morbid conditions.

• **Aim 5**: Explore overall survival and time free of disease progression according to the duration of smoking abstinence (harm reduction).
Questions & Discussion
Gynecologic Cancer Therapy, the Vaginal Microbiome and Patient Symptom Experience

Principal Investigator: Deborah Watkins Bruner, RN, PhD, FAAN | Sr. Vice President of Research, Emory University

Konstantinos Konstantinidis, PhD | Georgia Tech and Emory University
Krish Tewari, MD | University of California, Irvine
Jason D. Wright, MD | Columbia University
Yijuan Hu, PhD | Emory University
Stephanie Shook Pugh, PhD | Associate Director NRG Oncology
Mary S Dolan, MD | Emory Midlife and Menopausal Medicine Center
Carolyn Muller, MD | University of New Mexico Health Sciences Center
400 women with CxCancer  
200 healthy controls

Sampling scheme: Microbiome, Clinical data, Symptoms, Lifestyle/Demographic

<table>
<thead>
<tr>
<th>TD</th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (time of diagnosis)</td>
<td>Post Surgery</td>
<td>End of Chemo-Radiation [6-8W]</td>
<td>6 mo. post T0</td>
<td>12 mo. post T0</td>
<td>24 mo. post T0</td>
</tr>
</tbody>
</table>

**Microbiome metrics**
- α-diversity
- β-diversity
- Stability (resilience and resistance)
- Bacterial taxa
- Genomic information (genes and genomes)

**Clinical metrics**
- Vaginal symptoms (persistence and magnitude)
- Behavioral and clinical covariates
- Gut Microbiome

**Clinical factors**
- Cancer stage
- Treatment modality
- Radiation dose
- BMI, Age, vaginal pH, HPV status

**Lifestyle/Demographics**
- Ancestry/ethnic background
- Vaginal cleansing practices
- Use of antibiotics, estrogen, corticosteroids, smoking, alcohol, etc.

**Symptoms/Outcomes**
- CTCATv4 (Dyspareunia, Vaginal pain, Vaginal Dryness, Hemorrhage, Inflammation, Infection, Vaginitis, constipation, diarrhea, rectal pain)
- PDEs (sexual activity, lubrication, vaginal discomfort, bleeding, burning, etc.)
- FSFI-19 (Female Sexual Function Index)
- PHQ-2 (Patient Health Questionnaire)
- EQ-5D/ISO1(Health status)
- MFI (Multidimensional Fatigue Inventory)

Identification VM metrics (structure & dynamics) with strong associations with CxCa treatment toxicities (severity & persistence) and HPV status and cancer recurrence controlling for demographic, lifestyle and clinical variance

**Exploratory Aim:** Identification of GM metrics with strong associations with patient-reported gastrointestinal symptoms, fatigue and depression
Impact of Sentinel Lymph Node Mapping on Patient Reported Lower Extremity Limb Dysfunction in Endometrial Cancer (U1603)

Edward Tanner, M.D.
Northwestern University
STUDY ENROLLMENT

Surgery
- Cervical injection of ICG followed by SLN biopsy
- Removal of suspicious lymph nodes, and hysterectomy
- Ultrastaging of all SLNs performed

RANDOMIZATION
(STRATIFIED BY TUMOR GRADE)

Arm 1: side-specific pelvic lymphadenectomy performed on any side without a SLN identified and para-aortic lymphadenectomy if planned; omentectomy for appropriate histologies

Arm 2: Pelvic lymphadenectomy performed bilaterally; para-aortic lymphadenectomy if planned; omentectomy for appropriate histologies

Clinic-selected adjuvant therapy (NCCN guideline directed therapies recommended)

Assessment with GCLQ 3, 6, 9, 12, and 18 months Postop
- If 4+ point increase in GCLQ score: repeat limb circumference measurements and bioimpedence testing
- Secondary/exploratory endpoint assessments

NCCN algorithm

GOG 244 Follow up
NCORP CPC Contact Information

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lak2187@cumc.columbia.edu
Vice-Chair: Debra Barton, PhD;
debbartn@med.umich.edu

Cancer Prevention
Chair: Douglas Levine, MD;
Douglas.Levine@nyulangone.org
Vice-Chair: Julie Bauman, MD;
jebaumann@email.arizona.edu

Budgets/Other NCORP Questions
Erica Field, NCORP Administrator;
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