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™

NRG Oncology NCORP Org Chart

NRG NCORP Cancer Prevention and Control Priorities

- Improvement or delay in decline of neurocognitive function
- Reducing of gender-specific symptoms including lymphedem 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

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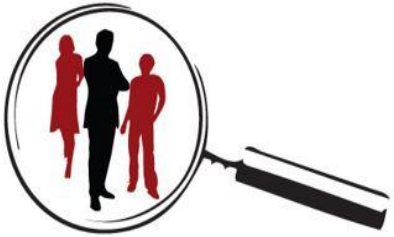

Call for New Concepts

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

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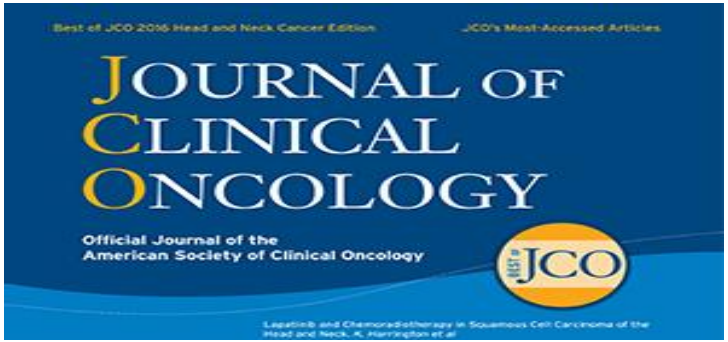
NCORP CPC Recent Publications

- NRG CC001
  - Brown, PB, Gondi V, et al. **Hippocampal Avoidance d**uring Whole-Brain Radiotherapy **Plus Memantine** for Patients with Brain Metastases: Phase III Trial NRG Oncology CC001. J Clin Oncol. 2020 38:10, 1019-1029



- RTOG 1203
  - Yeung AR, Pugh SL, Klopp AH, et al. **Improvement in Patient-Reported Outcomes With Intensity-Modulated Radiotherapy** (RT) Compared with Standard RT: A Report from the NRG Oncology RTOG 1203 Study. J Clin Oncol. 2020;38(15):1685-1692. doi:10.1200/JCO.19.02381

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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

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NCORP Liaisons

Disease Site	Liaison
Brain	Natosha Gatson (HDC)
Breast	Mylin Torres (CPC)
Cervix	Dana Chase (CPC)
GI colorectal/noncolorectal	Jordan Kharofa (CPC)
GU	Bridget Koontz (CPC)
H&N	Beth Beadle (CPC)
Lung	Nitin Ohri (CCDR)
Ovarian	Kathryn Pennington (CPC)
Uterine Corpus	Victoria Bae-Jump (HDC)

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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

	NSABP P1 (BCPT)	NSABP P2 (STAR)
Buffy coat and Plasma	73,218 specimens	286,159 specimens
Fasting lips	500 specimens	N/A
Tissue blocks (FFPE)	11,432 specimens	16,197 specimen

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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 compare to placebo*

Fisher, B, et al & National Surgical Adjuvant Breast, Bowel Project Investigators, Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study, *JNCI: Journal of the National Cancer Institute,* 90(18) 16 Sept 1998, Pages 1371–1388, https://doi.org/10.1093/jnci/90.18.1371

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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 stratified by age, race/ethnicity, history of 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.*

Vogel VG, et al. Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. JAMA. 2006;295(23):2727-2741. doi:10.1001/jama.295.23.joc60074

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.

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Questions

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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

NRG ONCOLOGY™

Symptom Science and QOL Implementation Priorities

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

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NRG Oncology
July 16, 2020

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

CIPN Clinical Trials Planning Meeting 2017

OXFORD

JNCI J Natl Cancer Inst (2019) 111(6): djz011

doi: 10.1093/jnci/djz011
First published online January 31, 2019
Commentary

COMMENTARY

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

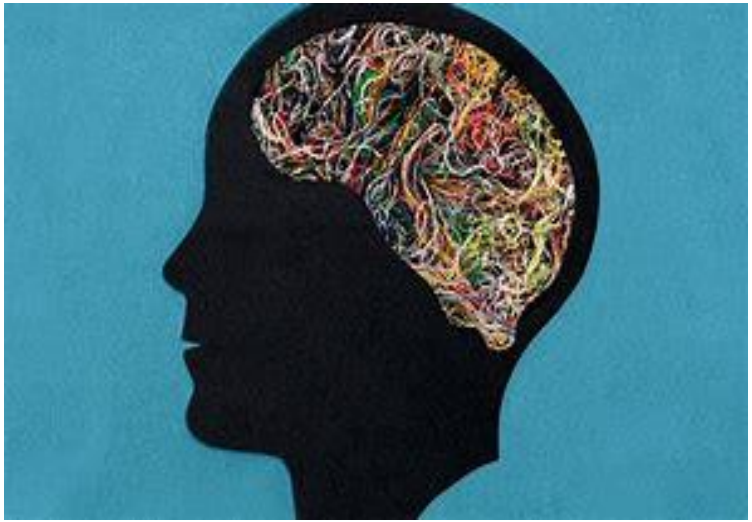
Susan G. Dorsey, Ian R. Kleckner, Debra Barton, Karen Mustian, Ann O'Mara, Diane St. Germain, Guido Cavaletti, Suzanne C. Danhauer, Dawn L. Hershman, Andrea G. Hohmann, Ahmet Hoke, Judith O. Hopkins, Katherine P. Kelly, Charles L. Loprinzi, Howard L. McLeod, Supriya Mohile, Judith Paice, Julia H. Rowland, Daniela Salvemini, Rosalind A. Segal, Ellen Lavoie Smith, Worta McCaskill Stevens, Michelle C. Janelsins

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

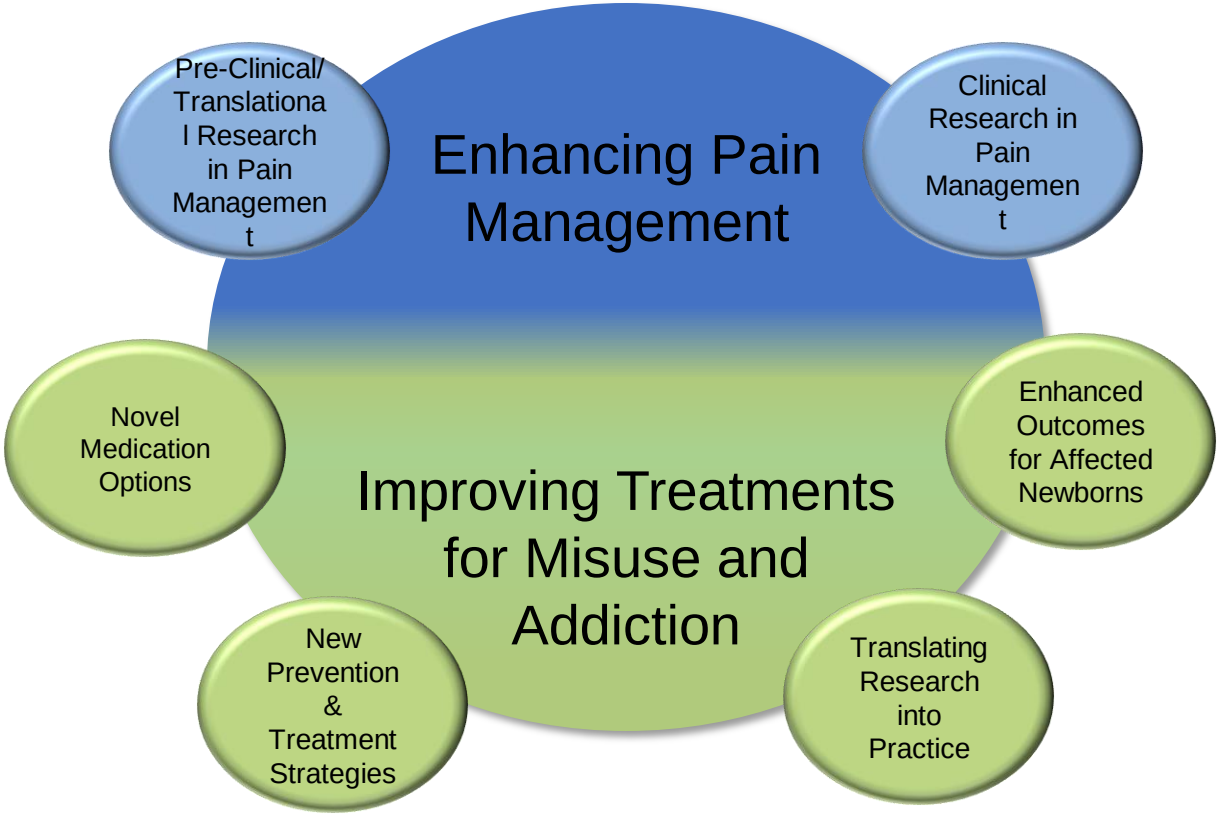
- Applications should prospectively identify the specific adverse effects and/or cluster of effects under evaluation
- Collaborations between clinical and non-clinical investigators are encouraged to couple the mechanistic knowledge with the clinical phenotype
- Emphasis should be on translating mechanistic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

- https://grants.nih.gov/grants/guide/pa-files/par-19-325.html

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)

HEAL Initiative Research Overview



NCI Cannabis, Cannabinoids and Cancer Research Symposium

(Virtual Meeting)

December 15-18, 2020

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

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NCI Community Oncology Research Program

Cancer Prevention and Control Meeting

July 16, 2020

Sandra Russo, M.D., Ph.D., M.P.H.
Community Oncology and Prevention Trials Research Group
Division of Cancer Prevention

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NCI Community Oncology Research Program

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 BRCA1Carriers (SOROCk)**
  Status: Activated, 6/23/20
  Accrual Goal: 2,262

NCI Community Oncology Research Program

A program of the National Cancer Institute of the National Institutes of Health

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**

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NCORP Research Base Prevention Chairs

NCORP RB	NCORP RB Prevention Chairs
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. Neuhouser, 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

NCORP CONCEPT/PROTOCOL EFFICIENCY TIMELINES
Effective 8/1/18

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

Study	Title	Concept Receipt Date	CPSC Review	Current Status	Days from Concept Receipt to Protocol Activation
NRG-CC008	A Non-Randomized Prospective Clinical Trial Comparing the Non-Inferiority of Salpingectomy to Salpingo-Oophorectomy to Reduce the Risk of Ovarian Cancer Among BRCA1Carriers (SOROCk)	2/12/19	4/9/19	Activated- 6/23/20	468 days

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)

NCORP Research Base	2/3 - 2/9	2/10 - 2/16	2/17 - 2/23	2/24 - 3/1	3/2 - 3/8	3/9 - 3/15	3/16 - 3/22	3/23 - 3/29	3/30 - 4/3	4/6 - 4/10	4/13 - 4/17	4/20 - 4/23	4/27 - 5/1	5/4 - 5/8	5/11 – 5/17	5/18 – 5/24	5/25 – 5/31	6/1 – 6/7	6/8 – 6/14	6/15 – 6/21	6/22 – 6/28	% Change Last Week vs Weekly Avg 2/3 – 3/15
ALLIANCE	16	15	4	24	9	18	8	4	2	0	1	5	3	3	3	4	2	4	4	7	11	-22%
COG	0	0	0	1	1	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	-100%
ECOG-ACRIN	115	140	116	118	144	124	68	3	2	5	0	1	5	19	26	39	34	60	81	106	91	-28%
NRG	4	3	4	1	9	4	3	0	2	1	1	1	2	3	3	3	6	3	1	2	3	-29%
SWOG	10	5	2	7	5	2	3	2	1	1	3	2	1	3	2	2	1	2	1	2	2	-62%
URCC	10	6	12	5	9	3	4	1	4	2	1	2	5	3	3	7	1	5	2	7	3	-63%
WAKE	15	21	19	10	14	10	2	0	2	1	1	0	1	1	0	0	2	1	1	0	3	-80%
TOTAL	170	190	157	166	191	162	88	10	13	11	7	11	18	32	37	55	46	75	90	124	113	-35%

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
  - **August 27-28, 2020**

- Primary Care Alliance in Research Trials Involving NCORP Sites (PARTNRS)
  - **September 18, 2020**

Questions & Discussion

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Congratulations

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2020 Pilot Project Awardee

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

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CPC Trials

NRG ONCOLOGY™

Opened NRG CPC Trials

****accrual as of June 30, 2020**

Study No	Disease Site	Description	Date Activated	Target Accrual	Total Accrual	NCORP Accrual (%)	Expected Closure Date
GOG 0278	Cervix	Physical function/QoL before and after non-radical surgical therapy for stage IA1 (LVSI+) and IA2-IBI (=2CM) cervical cancer	10/1/12	220	212	<1%	December 2020
NRG CC003	Lung	Seamless phase II/III PCI vs. PCI with hippocampal sparing for cognitive fx preservation in small cell lung cancer	12/7/15	172 (II) 302 (III)	176 of 172 (II) 204 of 302 (III)	28%	Temporarily closure 5/28/20; amendment submitted to increase accrual
NRG CC008	Ovarian	Non-rand. prospective trial comparing non-inferiority of **S**alpingectomy to salpingo-**O**ophorectomy to **R**educe risk of **O**varian **C**a among *BRCA1* carriers (**SOROCk**)	6/23/2020	2262			

GOG 0278
PI Covens

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)

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, 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

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 Surveys1 4-6 weeks Post-Op and every 6 months (6, 12, 18, 24) for two years

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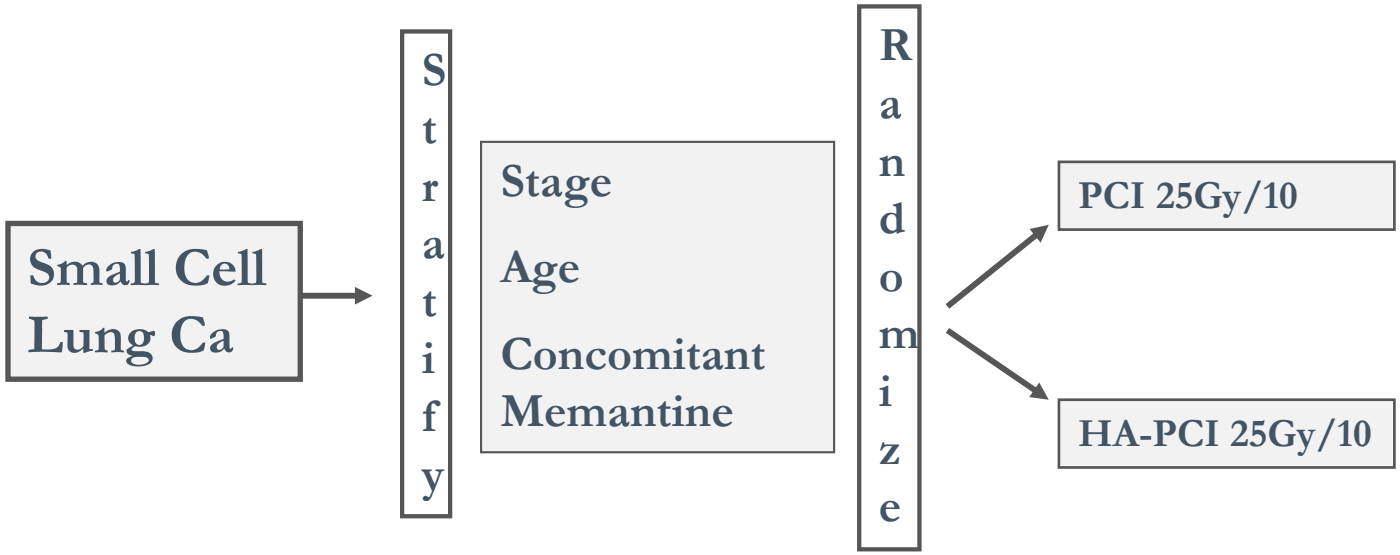
NRG CC003: Phase IIR/III Trial Prophylactic Cranial Irradiation with or without Hippocampal Avoidance for Small Cell Lung Cancer

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 endpts: 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

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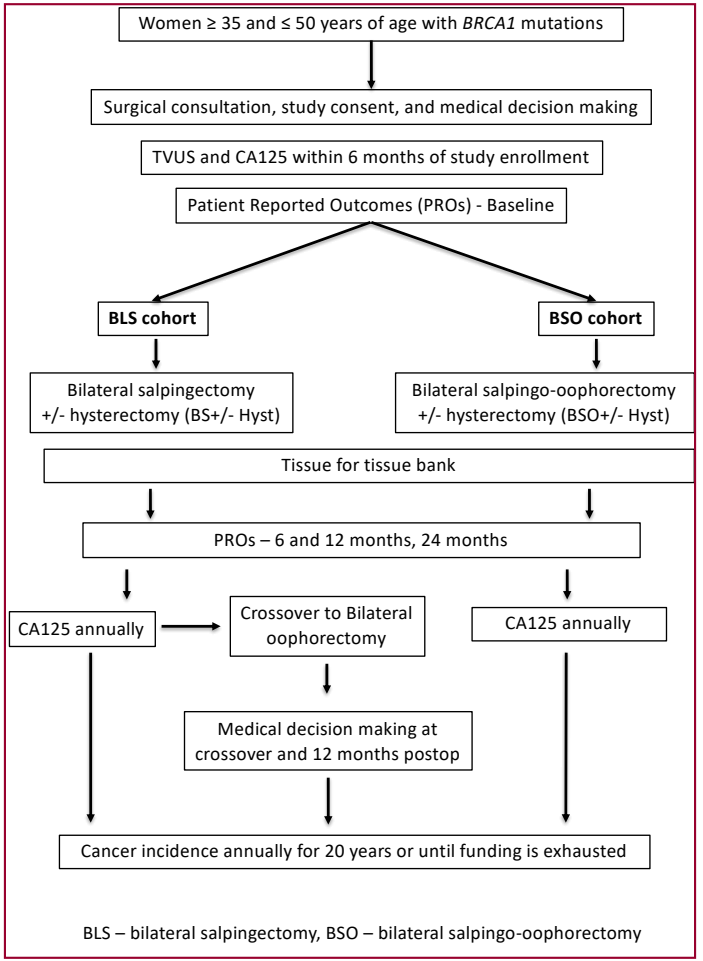
NRG CC008 SOROCk
PI Levine

- *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!

Study Champions

Study	Protocol Title	Accrual	Comments
S1820	Testing Diet Intervention vs. Non-Diet Intervention for Management of Bowel Symptoms in Rectal Cancer Survivors (PI Sun)	9/126	Tracy Crane is the NRG Study Champion
S0820	Double Blind Placebo-Controlled Trial to Prevent Recurrence of High Risk Adenomas and Second Primary Colorectal Cancers (PACES) - (PI Zell)	278/491	Jenny Dorth is the NRG Study Champion
EA1151	Tomosynthesis Mammographic Imaging Screening Trial (TMIST) – (PI Pisano)	26,823/ 164,946	NRG is a study champion; enrolled 2,461 participants

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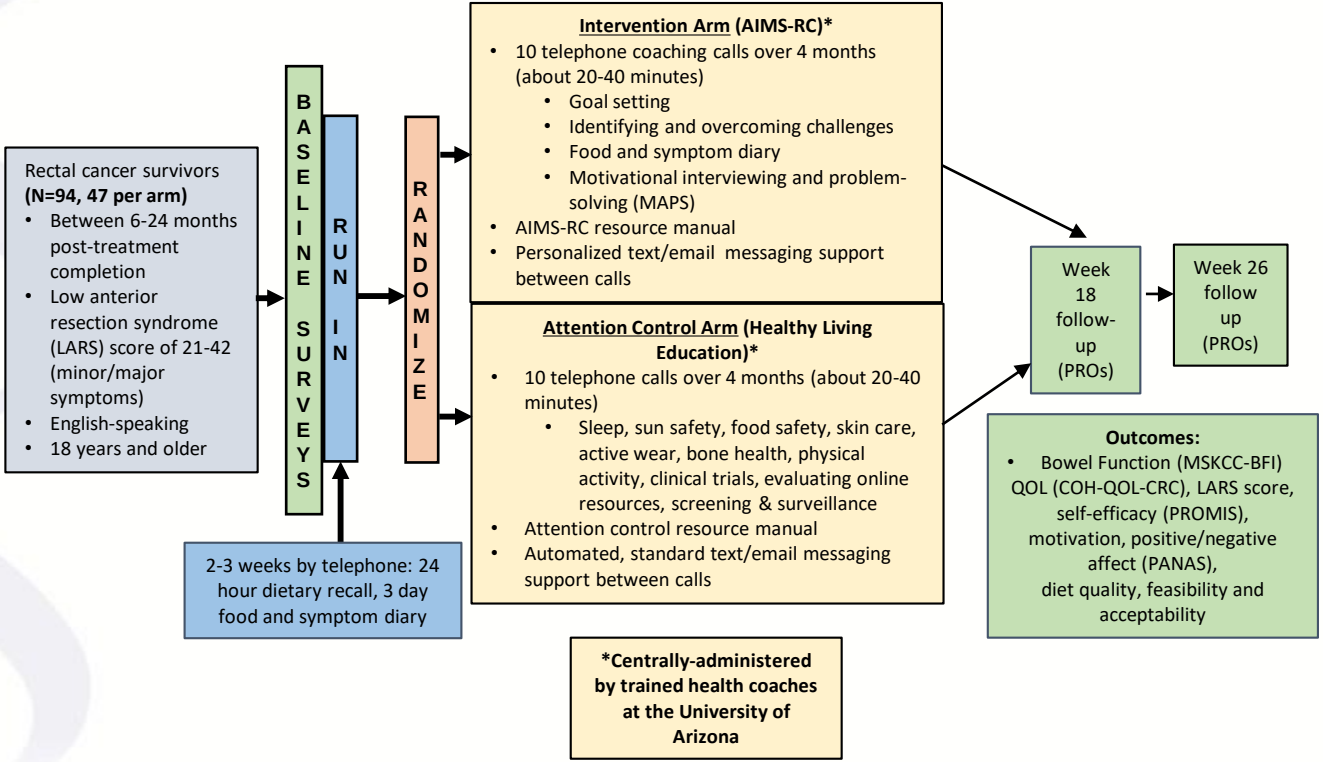
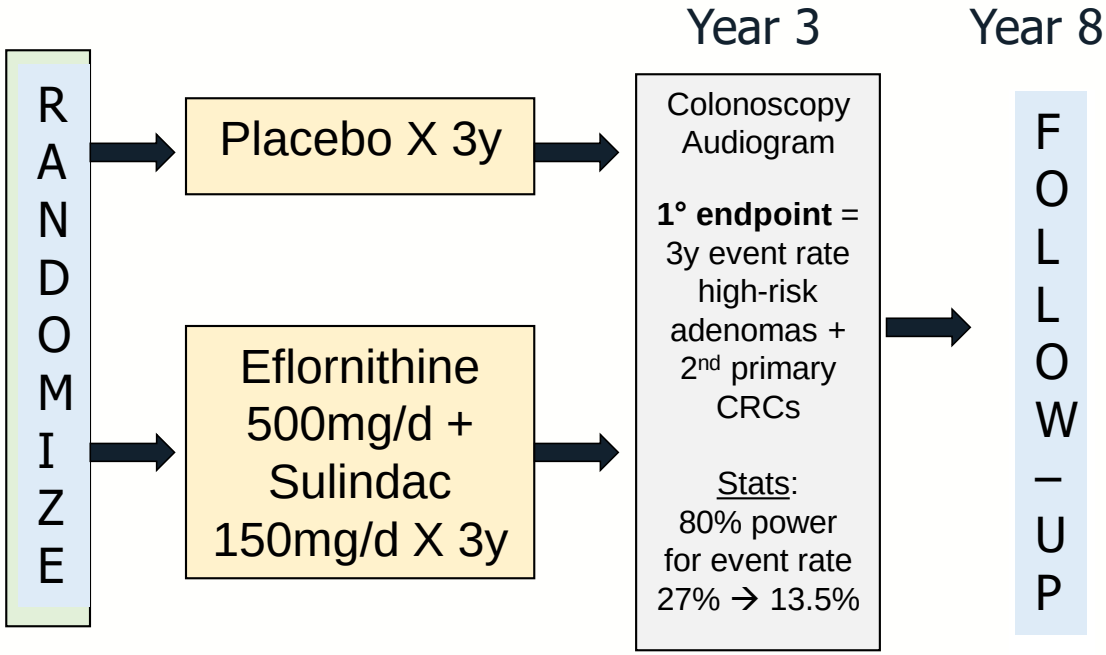
SWOG 1820: Testing Diet Intervention vs. Non-Diet Intervention for Management of Bowel Symptoms in Rectal Cancer Survivors



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 adenoCa
- 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

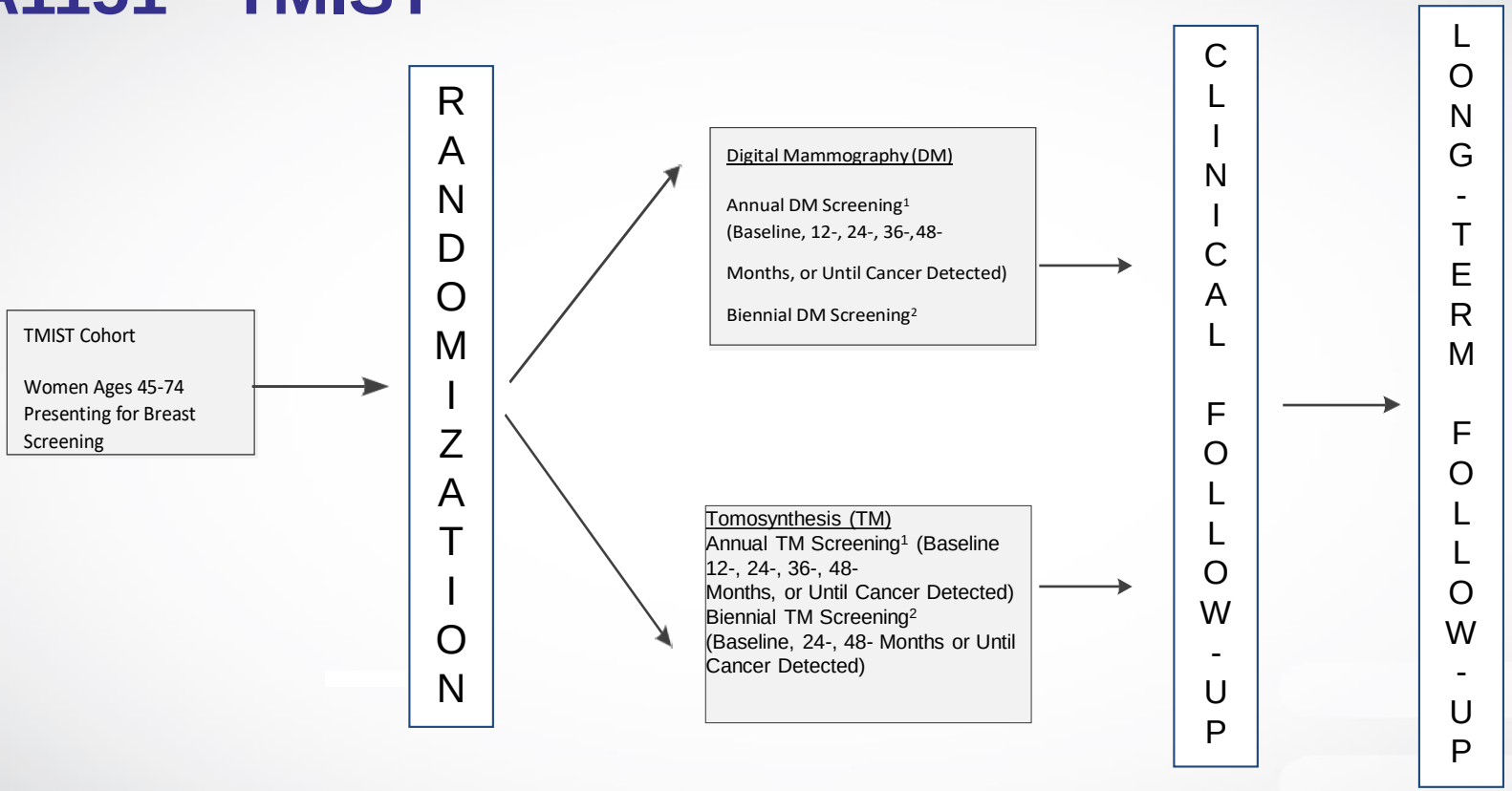
Exclusion:
- No high CV risk
- No hearing loss
- No high-dose NSAID
- No GI ulcer
- No family hx FAP, HNPCC, IBD



*Stratify by stage/adjuvant tx

F/U schedule:
q3mo X 1y → q6mo X 2y → q1y X 5y
Colonoscopy at years 3 and 8

EA1151 - TMIST



Developing NRG NCORP Trials

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

NCORP Concept Review – July 2020	
Gynecologic Cancer Therapy: The Vaginal Microbiome and Patient Symptom Experience (D. Bruner)	Pending
Impact of Sentinel Lymph Node Mapping on Patient Reported Lower Extremity Limb Dysfunction in Endometrial Cancer (U1603), (E. Tanner)	Pending

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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

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FORTE five ten
A COLORECTAL CANCER PREVENTION TRIAL

NIH NATIONAL CANCER INSTITUTE Community Oncology Research Program (NCORP)

NCI National Clinical Trials Network
a National Cancer Institute program

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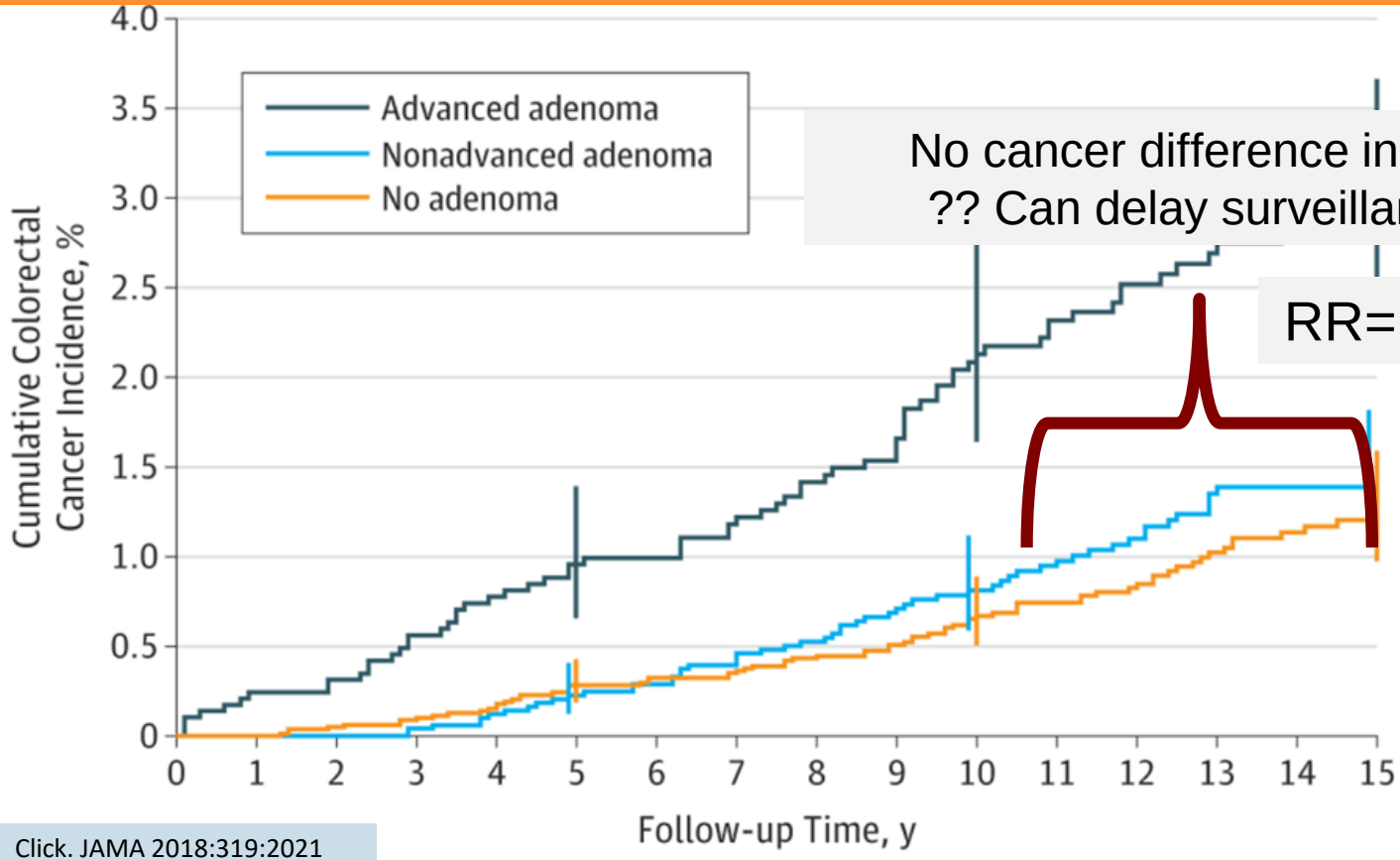
“Recent” Multi-Society Task Force Surveillance Recommendations

FiveFORTenE
A COLORECTAL CANCER PREVENTION TRIAL

No polyps, or hyperplastic polyps in rectum/sigmoid		
Repeat in 10 years		
Neoplasia found		
Serrated polyps/lesions	**High risk adenomas**	**Low risk adenomas**
Serrated polyposis Repeat in 1 year	**> 10 Adenomas** Repeat in less than 3 years	**1–2 Tubular adenomas < 10 mm** Repeat in 5–10 years
≥ 10 mm or With dysplasia or traditional serrated adenoma Repeat in 3 years	**3–10 Adenomas** Repeat in 3 years	
< 10 mm in Proximal colon and without dysplasia Repeat in 5 years	**Villous adenoma(s) or tubular adenoma(s) ≥ 10 mm** Repeat in 3 years	
	Adenoma(s) with high grade dysplasia Repeat in 3 years	

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

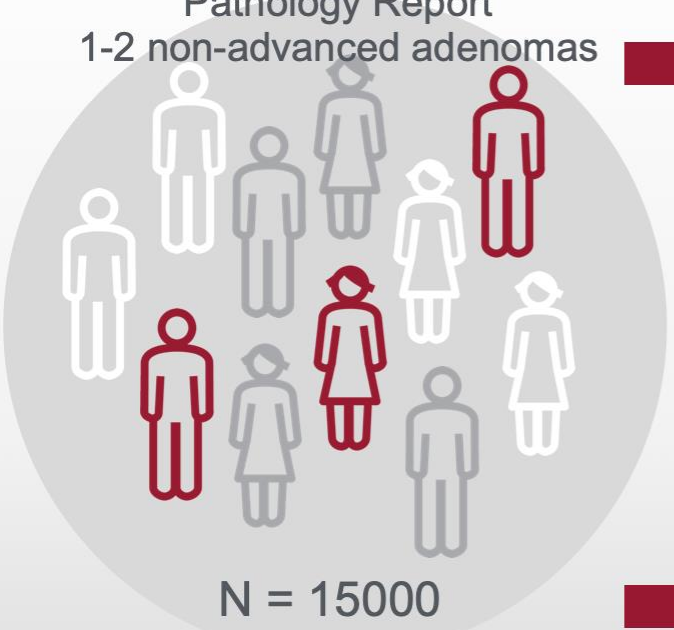
RR=1.2 (0.8-1.7)

Click. JAMA 2018:319:2021

Schema

FIVE FORT ENE
A COLORECTAL CANCER PREVENTION TRIAL

Pathology Report
1-2 non-advanced adenomas

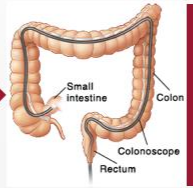


N = 15000

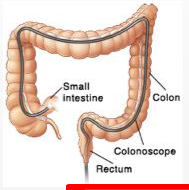
Colonoscopies up to 4 years ago

RANDOMIZED

5 Yr.



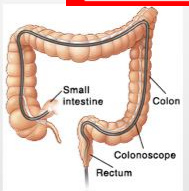
10 Yr.



Surveillance Colonoscopy

End Point:
CRC Incidence

10 Yr.



Secondary endpoint:
Advanced Adenoma

Straightforward Eligibility

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1. ≥ 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 <10y

- NO path/lab submissions
- F/U in out years remote

Identifying Patients to Enroll

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A COLORECTAL CANCER PREVENTION TRIAL

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

Summary/Status

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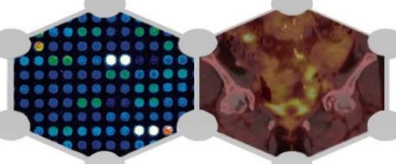
A COLORECTAL CANCER PREVENTION TRIAL

- 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



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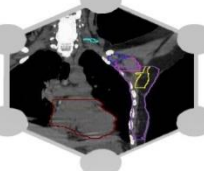

NRG CC009

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%

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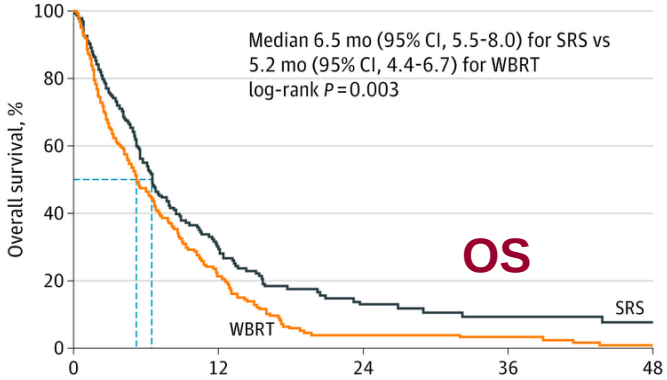
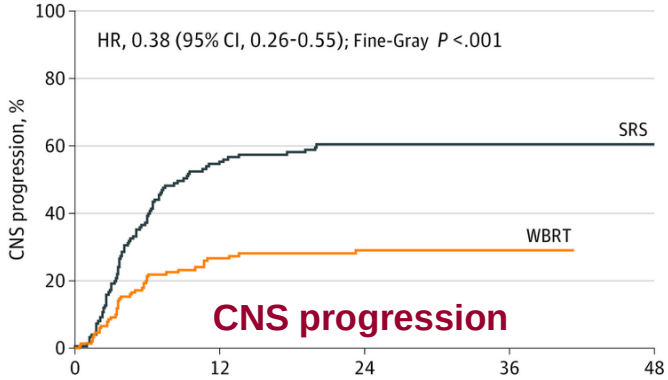
[1]Rusthoven, *JAMA Oncology* 2020 [2]Serizawa, *JNS* 2002, [3]Yomo, *BMC Cancer* 2015,
[4]Robin, *Lung Cancer* 2018, [5]Cifarelli, *Neurosurgery* 2019,

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%)

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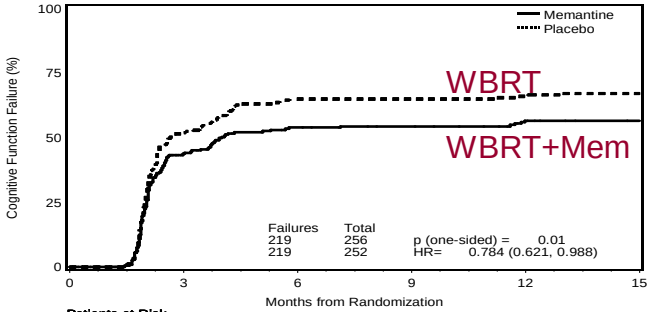
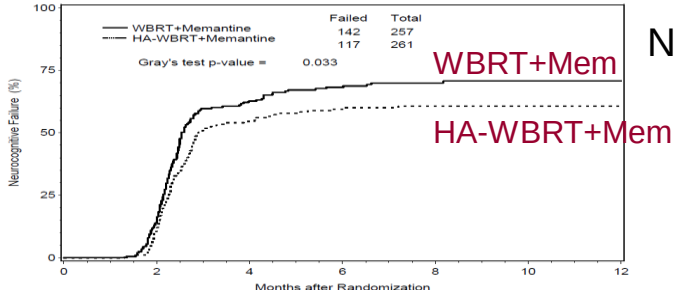
Background

- 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

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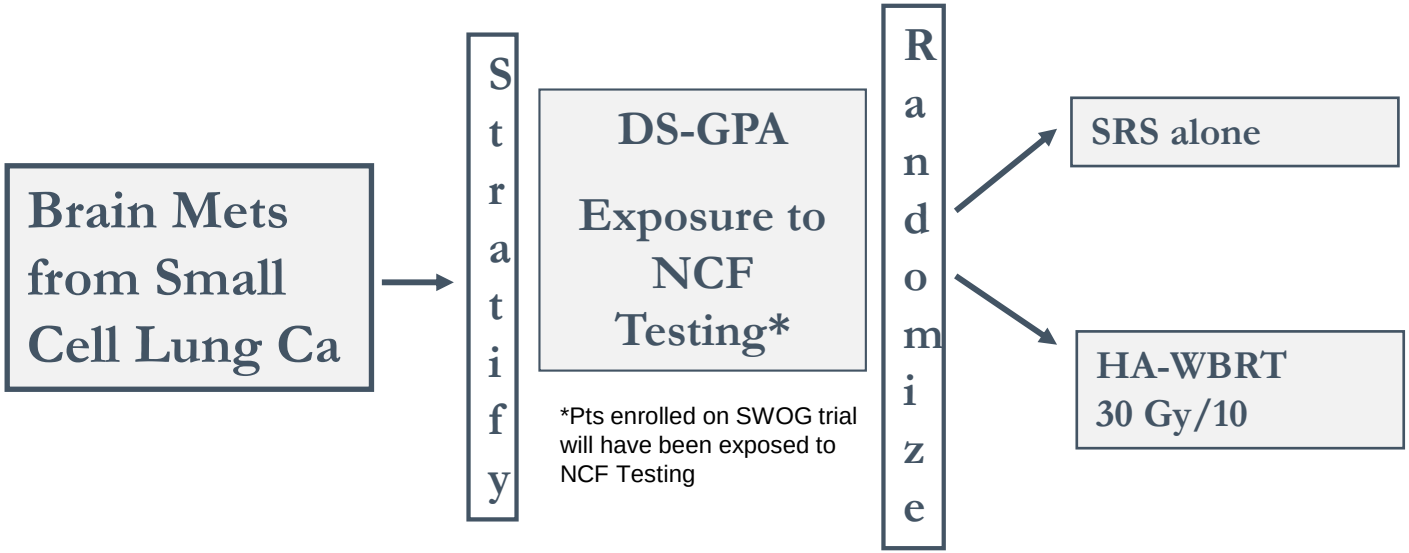
[1]Brown et al. Neuro-Onc 2013 [2]Brown, Gondi et al. JCO 2020

NRG CC009 Schema

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



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

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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

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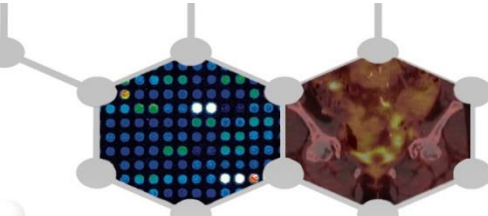

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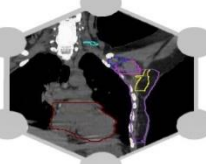

CC-1925
Smoking Cessation and Relapse Prevention in Newly Diagnosed Cervical Cancer Patients

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.
    1. Smoking strongest predictor of toxicity related complications for patients receiving radiation treatment.
    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.

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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

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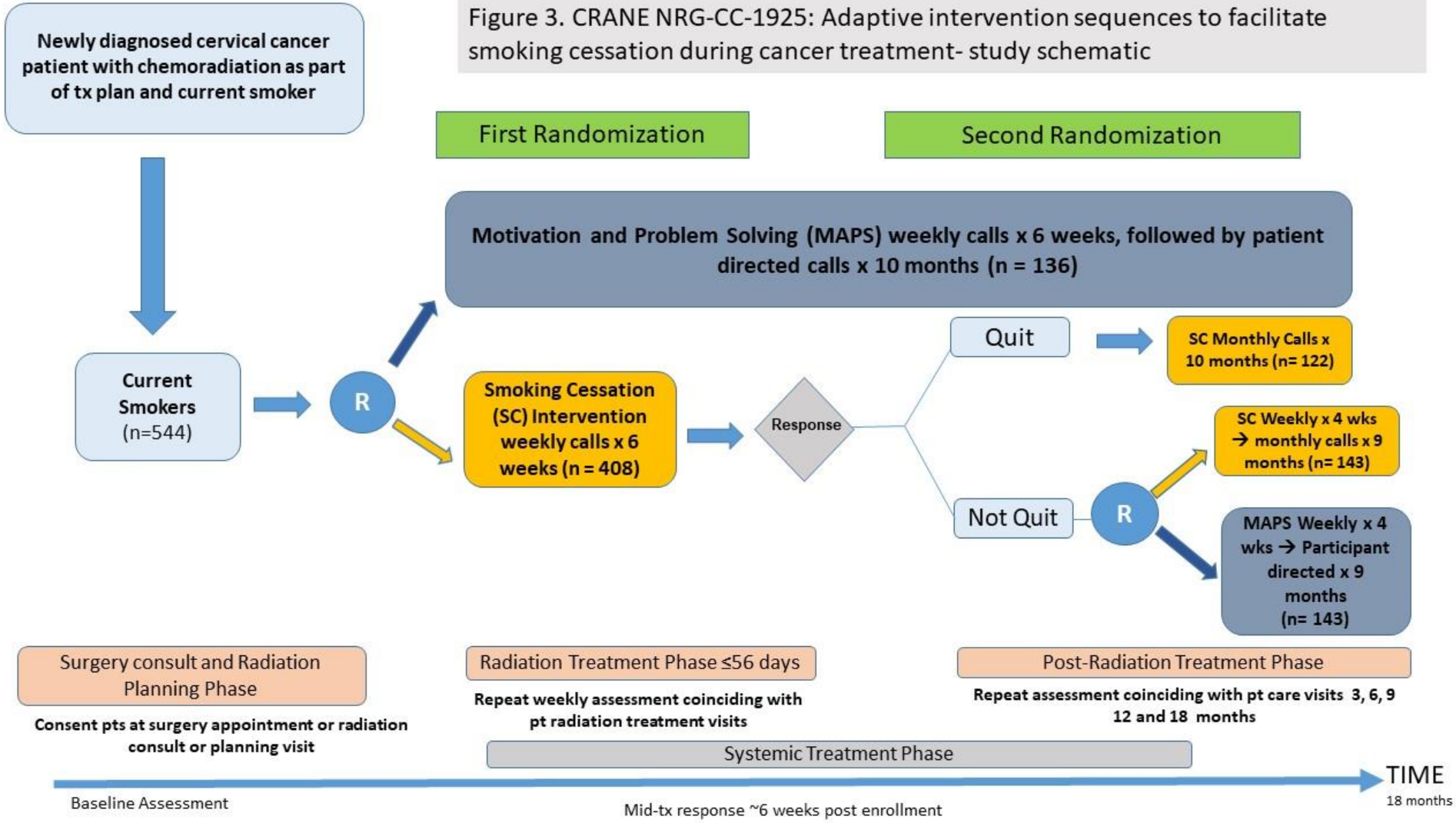
Figure 3. CRANE NRG-CC-1925: Adaptive intervention sequences to facilitate smoking cessation during cancer treatment- study schematic



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.

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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

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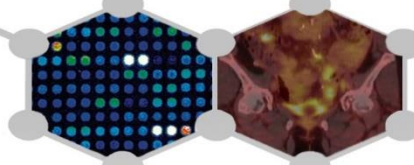

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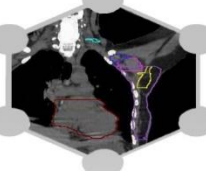


Gynecologic Cancer Therapy, the Vaginal Microbiome and Patient Symptom Experience

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

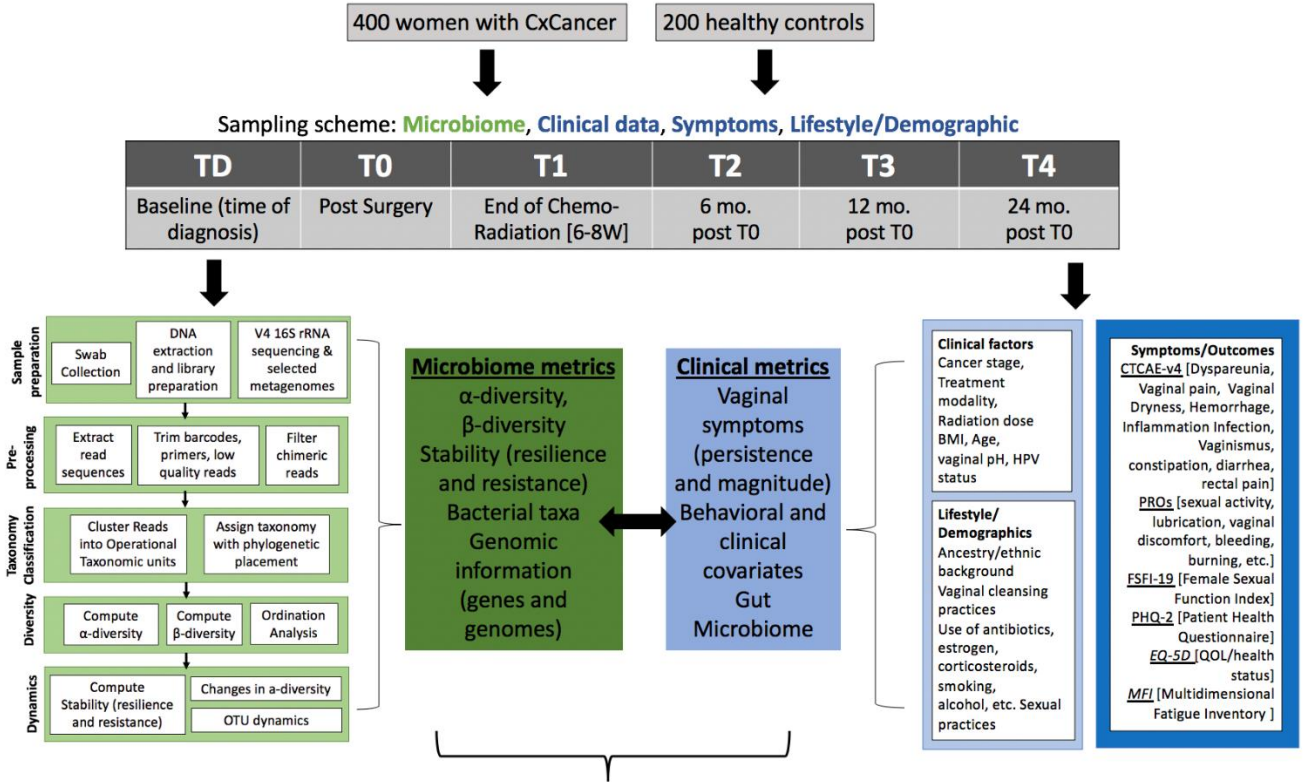
Yijuan Hu, PhD | Emory University

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

Schema



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

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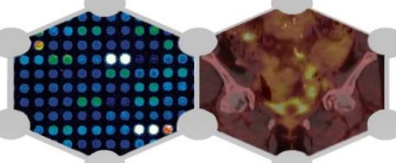

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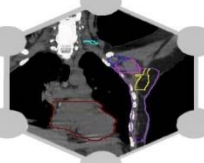
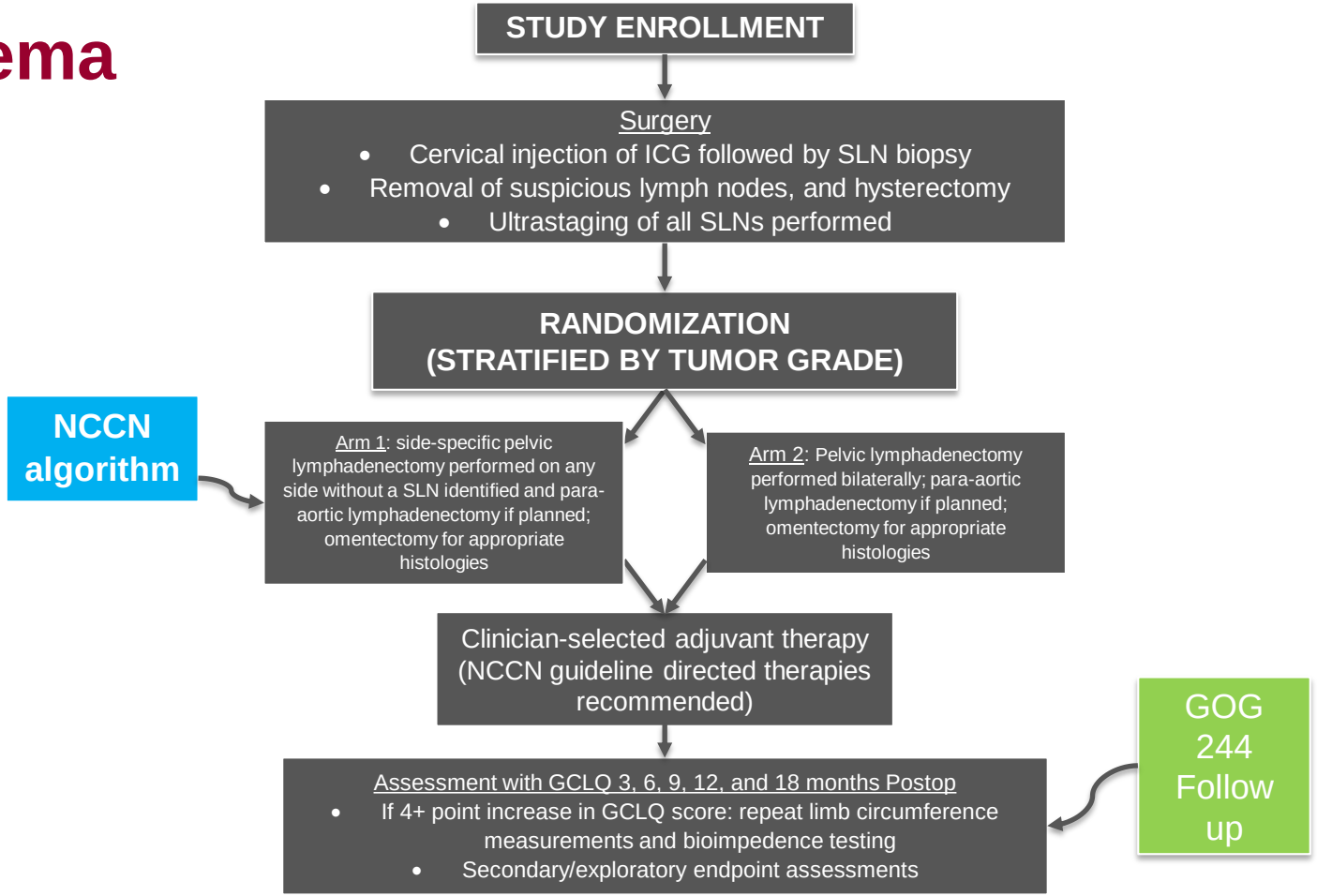


Impact of Sentinel Lymph Node Mapping on Patient Reported Lower Extremity Limb Dysfunction in Endometrial Cancer (U1603)

Edward Tanner, M.D.

Northwestern University

Schema



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NCORP CPC Contact Information

Cancer Control and Symptom Management

Chair: Lisa Kachnic, MD, FASTRO; 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; jebauman@email.arizona.edu

Budgets/Other NCORP Questions

Erica Field, NCORP Administrator; fielde@nrgoncology.org

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