NRG Cancer Prevention and Control Meeting

Lisa Kachnic, MD, Cancer Control Chair
Warner Huh, MD, Prevention Chair
Debra Barton, PhD, Cancer Control Vice-Chair
Julie Bauman, MD, Prevention Vice-Chair

February 10, 2022

NRG Oncology NCORP Org Chart

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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

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Announcements

Call for NRG NCORP Pilot Projects

NRG Oncology NCORP is soliciting PILOT projects for applications focused on:

- cancer prevention and cancer control investigation aimed at understanding and/or ameliorating symptoms and toxicity related to neurocognitive function, gender specific symptom reduction, behavioral interventions, treatment dose alterations or delivery, cancer risk reduction, chemotherapy induced peripheral neuropathy

Goal: provide data that will directly lead to future Phase II-III CPC concepts

Watch NRG broadcast for announcement late February 2022!

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NRG-CC004 Publication

Debra Barton, PhD, FAAN, RN
NRG-CC004 Study Chair
NRG Cancer Control Vice-Chair

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NRG-CC004

Phase II Double Blind Dose Finding Trial of Bupropion versus Placebo for Sexual Desire in Women with Breast or Gynecologic Cancer

PI: Deb Barton, PhD

The team: Stephanie L. Pugh, PhD; Patricia A. Ganz, MD; Steven C. Plaxe, MD; Bridget F. Koontz, MD; Jeanne Carter, PhD; Natalya Greyz-Yusupov, MD; Seth J. Page, MD; Kendrith M. Rowland Jr, MD; Ernie P. Balcueva, MD; Sobia Nabeel, MD; Jack B. Basil, MD; Matthew L. Hill, DO; Carolyn Y. Muller, MD; Maria C. Bell, MD; Snehal Deshmukh, MS; NRG leadership: Lisa A. Kachnic, Deb Bruner; Pt. Advocate Laurel Pracht; DCP; BCRF,

all the women who participated

Disclosures

- None

Background

- **Declining sexual health continues to be a critical gap in cancer care. The prevalence in female cancer survivors of distressing sexual problems in some studies is as high as over 90%.**

- **Decreased sexual health, particularly for women with estrogen sensitive tumors due to estrogen deprivation, is a prevalent consequence of treatment in some types of cancer.**
  - **Data provides evidence that estrogen deprivation is associated with loss of dopamine.**

- **Bupropion is a dopaminergic agent with promise to improve sexual desire in women with a history of cancer.**
  - **There have been several studies of bupropion in women <u>without</u> cancer with decreases in sexual desire**
  - (References for these statements are on reference slide at end of presentation.)

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NRG-CC004

PRIMARY OBJECTIVE

- To evaluate the ability of two dose levels of bupropion (150 vs. 300 mg of extended release) to improve sexual desire more than a placebo at 9 weeks (8 weeks on the target dose) as measured by the desire subscale of the Female Sexual Function Index.

Barton et al. Randomized controlled phase II…NRG CC004, JCO, 2021, DOI:10.1200/JCO.21.01473

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NRG-CC004

Some Secondary Objectives

- To evaluate the side effects of 150 and 300 mg bupropion extended release and differentiate these side effects from those in the placebo arm.

- To evaluate the effect of 150 and 300 mg of bupropion extended release on other aspects of sexual function as well as fatigue.

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Schema

STEP 1
REGISTRATION

- Post-menopausal women
- History of breast or gynecologic cancer
- Completed surgery, chemotherapy, and/or radiation at least 6 months prior
- Completion of PHQ4 and FSFI

STEP 2
RANDOMIZATION

STRATIFY

Arm A
- Bupropion 150 mg XL in a.m. x 1 week
- Bupropion 150 mg XL (one 150 mg XL and one placebo capsule) PO in a.m. x 8 weeks
- Placebo one capsule in a.m. x 1 week (titration off)

Arm B
- Bupropion 150 mg XL in a.m. x 1 week
- Bupropion 300 mg XL (two 150 mg XL capsules) PO in a.m. x 8 weeks (target dose)
- Bupropion 150 mg XL in a.m. x 1 week (titatration off)

Arm C
- Placebo 1 capsule in a.m. x 1 week
- Placebo (2 placebo capsules) PO in a.m. x 8 weeks
- Placebo 1 capsule in a.m. daily x 1 week (titration off)
- Arm C Optional: Open label bupropion at 150 mg XL once per day, may increase to 300 mg XL (two 150 mg XL at same time) if desired week 2 preference/response

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Main Eligibility Criteria

- Diagnosis of breast or gynecologic cancer (all types, but not stage IV)
- Completed definitive therapy consisting of surgery, chemotherapy, radiotherapy 180 days prior to registration
- Post-menopausal
- For breast cancer patients only, endocrine therapies are allowed (such as aromatase inhibitors, but not current tamoxifen. Prior tamoxifen is permitted with a 30 day wash out period).
- Vaginal treatments including estrogen were allowed

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Analysis

- Powered to detect 0.45 Cohen's D effect size with 62 women per arm.

- Used t-tests and chi square comparisons to look at differences between arms.

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Accrual and Demographics (≠ 100% due to rounding)

Characteristic	Placebo N=77	150 mg buprop N=79	300 mg buprop N=74
Mean Age	58	55	55
White Black Asian American Indian/ Alaska Native Other (Native Hawaiian, >1 race) Unknown-not reported	67 (87%) 3 (4%) 3 (4%) 1 (1%) 0 3 (4%)	74 (94%) 0 1 (1%) 1 (1%) 2 (3%) 1 (1%)	70 (95%) 3 (1%) 0 0 0 1 (1%)
Hispanic-Latino	3 (4%)	3 (4%)	5 (7%)
SSRI - Yes	11 (14%)	10 (13%)	5 (7%)
Aromatase Inhibitor - Yes	35 (46%)	35 (44%)	37 (50%)

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Participating Sites

72 different locations – primarily NCORPs

- Kaiser Permanente NCORP
- University of Oklahoma Health Sciences Center
- Carle Cancer Center
- Cancer Center of Kansas
- Iowa-Wide Oncology Research Coalition NCORP
- Michigan Cancer Research Consortium NCORP
- New Mexico Minority Underserved NCORP
- Sanford NCI Community Oncology Research Program of the North Central Plains
- Good Samaritan Hospital Cincinnati
- Cancer Research Consortium of West Michigan
- Georgia NCORP
- Metro Minnesota Community Oncology Research Consortium
- Cancer Research for the Ozarks
- Catholic Health Initiatives NCORP
- Northwell Health NCORP
- Wichita CCOP

Many others: Hawaii, Upstate Carolina, LA, WI

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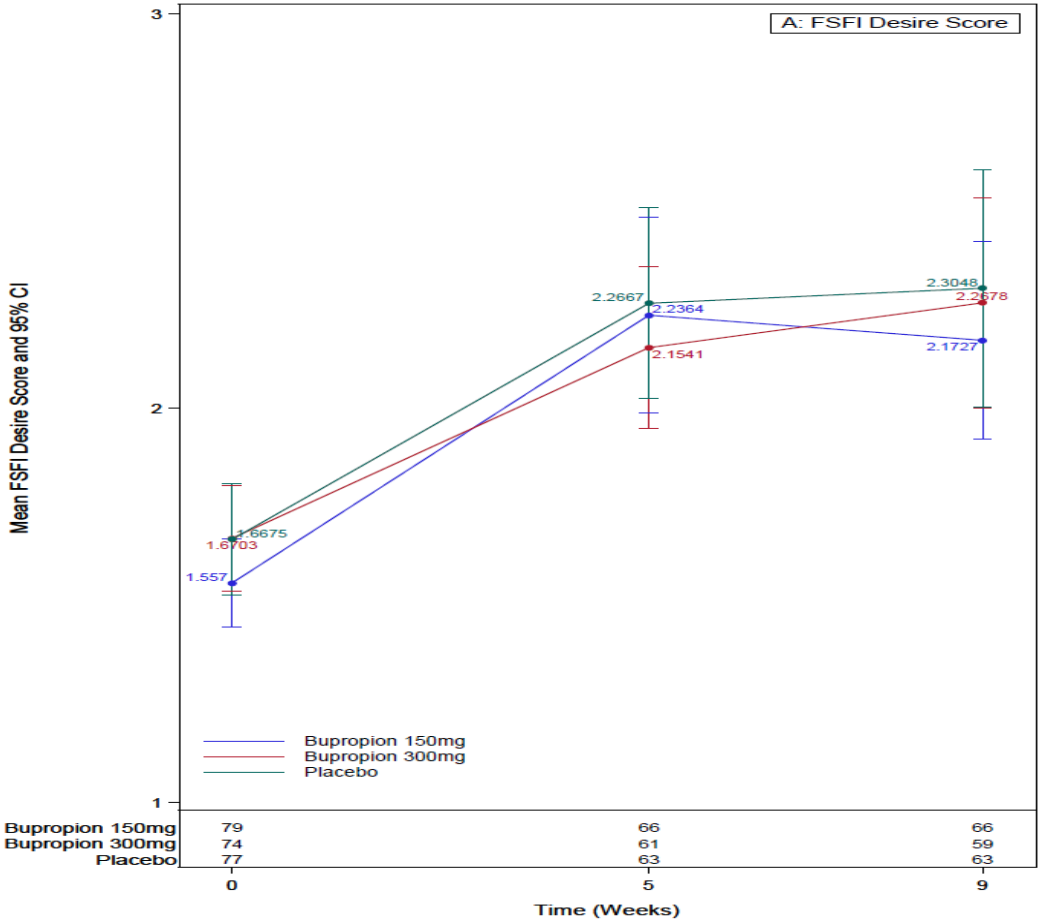
Desire Subscale FSFI (1.2 – 6)



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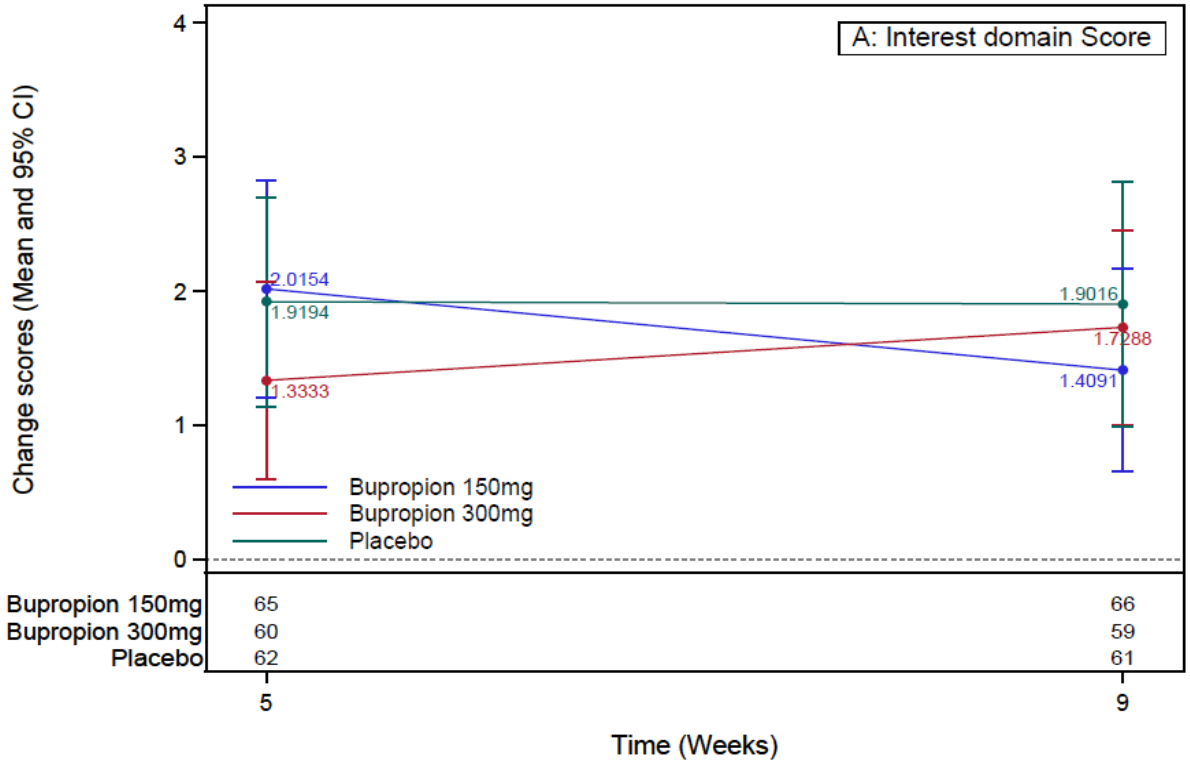
PROMIS Interest



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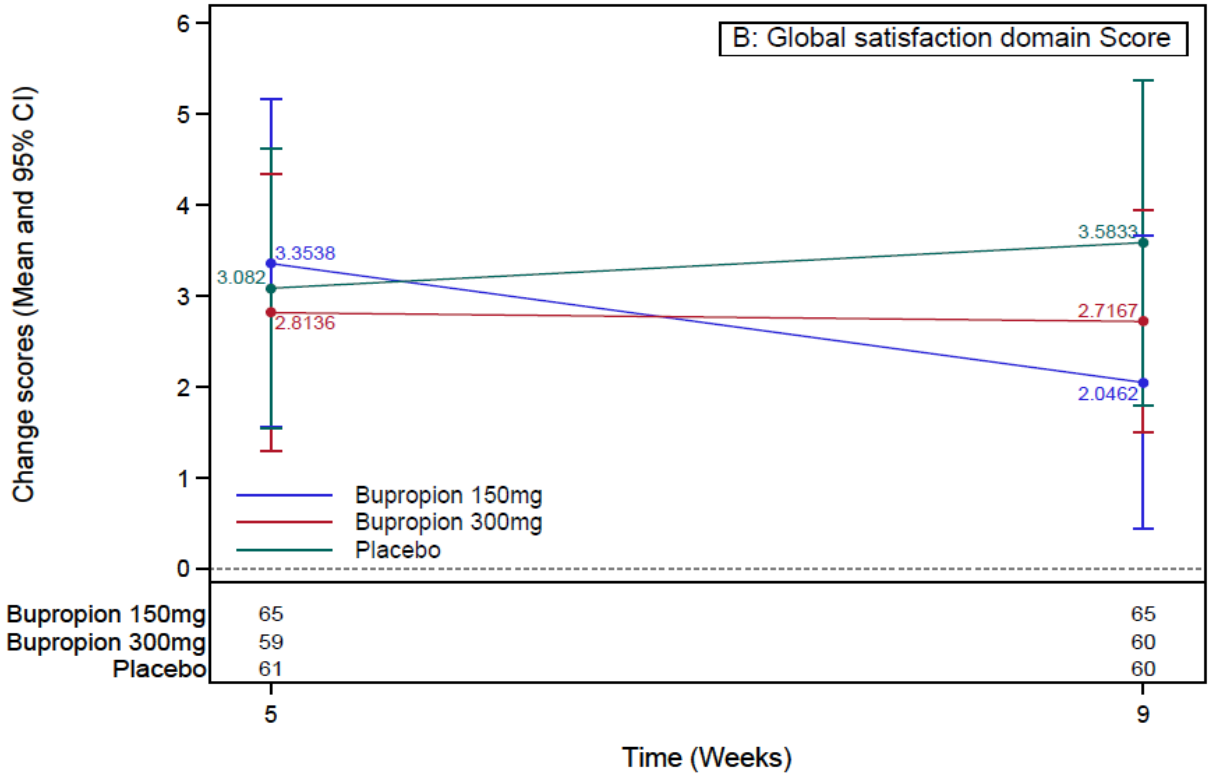
PROMIS Satisfaction



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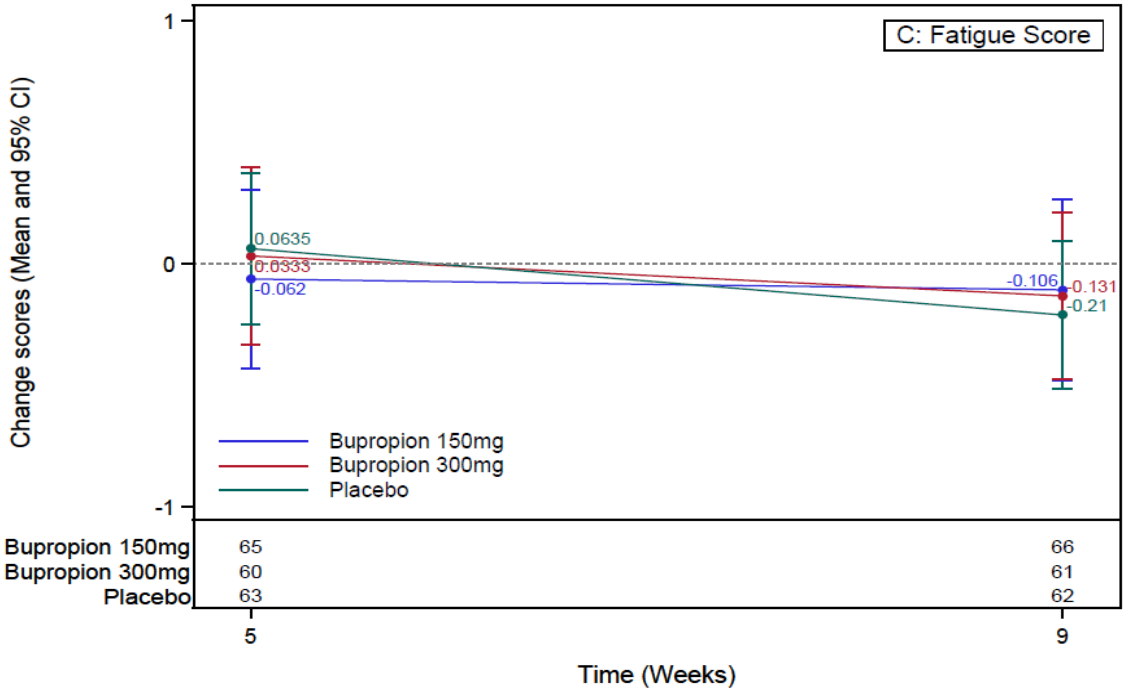
PROMIS Fatigue



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Side Effects - Tolerability

- **CTCAE**
  - no grade 4/5
  - 1 gr3 headache (150 mg and placebo arm)
  - 1 gr3 insomnia (150 mg)
  - 1 gr3 hypertension (300 mg)
- **PRO-CTCAE**
  - 7 weeks:
    - sign. diff. headache 29% (300 mg) vs 10% (P)
    - ↓ appetite 8.6% (P) vs 0 (150mg)
    - insomnia 37.9% (P) vs 20% (150mg)
  - 9 weeks:
    - sign. diff. dry mouth 44.6% (P) vs 25% (150 mg)
    - insomnia 64.3% (P) vs 42.1% (150 mg)

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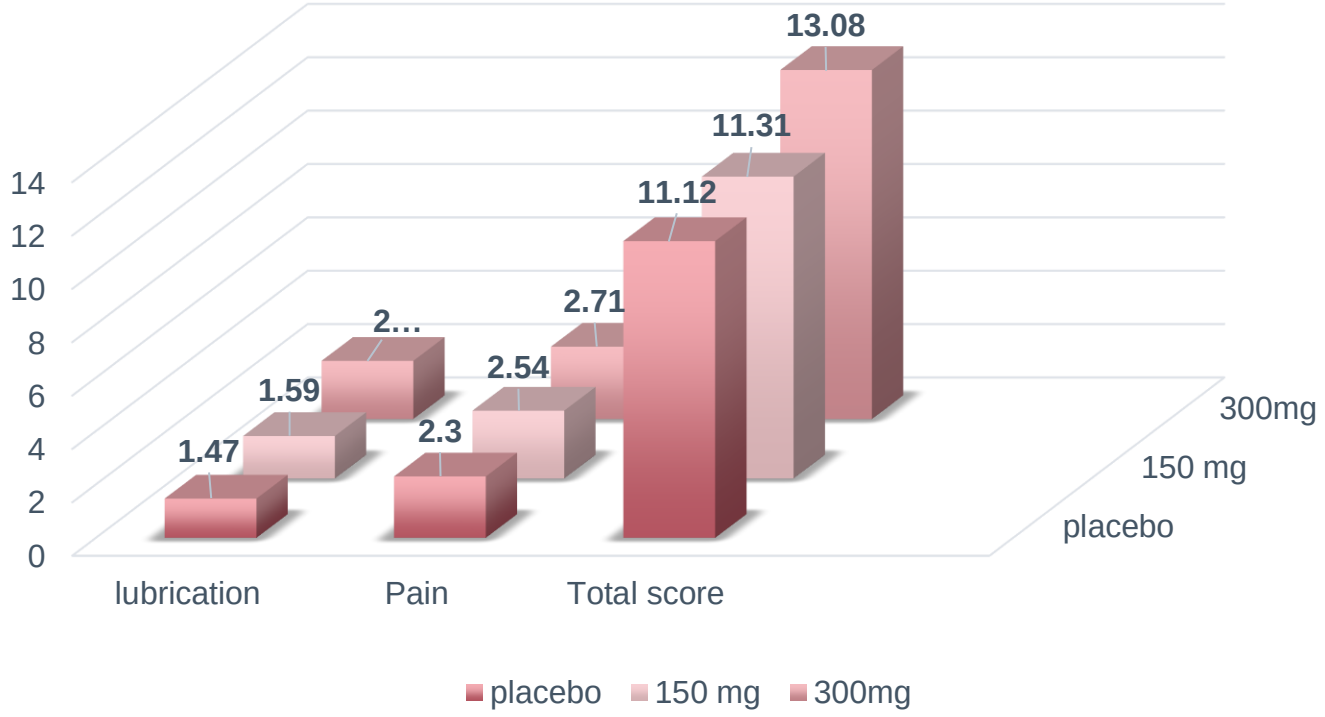
FSFI Scores



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Thoughts, Lessons – Next Steps

- Sexual health scores were extremely low indicating THIS IS A PROBLEM AREA.
- Placebo response was higher than expected.
- Editorial comments on two libido studies – It's complicated.
- In progress: a multi-component intervention that includes treating vulvo-vaginal atrophy (pharmacologic) and libido and self image (behavioral) A partner intervention for communication and satisfaction is also in feasibility testing stages.

References

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CPC Trials

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4 Open NRG CPC Trials (accrual as of 2/9/22)

Study No	Disease Site	Description	Date Activated	Target Accrual	Total Accrual	NCORP Accrual (%)	Expected Closure Date
NRG-CC003	Lung	Seamless Ph II/III PCI vs. PCI with Hippocampal Sparing for Cognitive Fx	12/7/15	172 (II) 392 (III)	176 of 172 (II) 379 of 392 (III)	30%	June 2022
NRG-CC005	GI	FORTE – Five- or Ten-Year Colonoscopy for 1-2 Non-advanced Adenomatous Polyps	10/6/2021	9500	1	100%	December 2024
NRG-CC008	Ovarian	Non-randomized Prospective Trial Comparing Non-inferiority of **S**alpingectomy to Salpingo-**O**ophorectomy to **R**educe the Risk of **O**varian **C**a among *BRCA1* Carriers (SOROCk)	6/23/20	2262	121	21%	July 2040
NRG-CC009	Brain	SRS vs. HA-WBRT for 10 or Fewer Brain Metastases from Small Cell Lung Cancer	2/24/21	200	16	53%	July 2030

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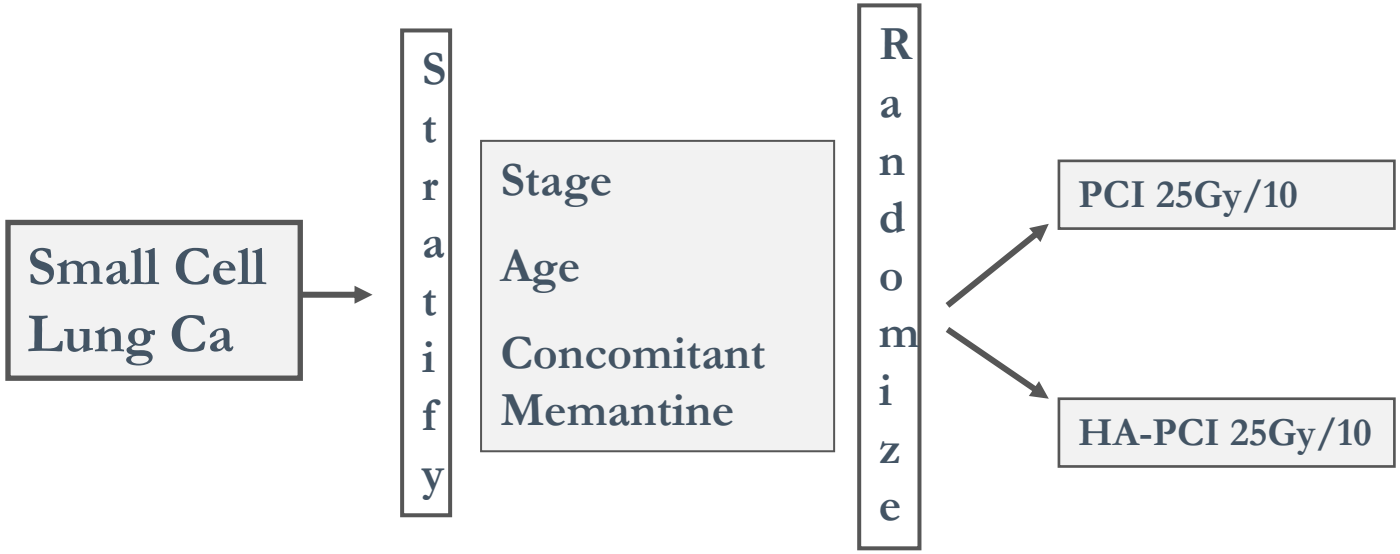
NRG CC003: Phase IIR/III Trial Prophylactic Cranial Irradiation with or without Hippocampal Avoidance for Small Cell Lung Cancer

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:392 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. 196 analyzable pts

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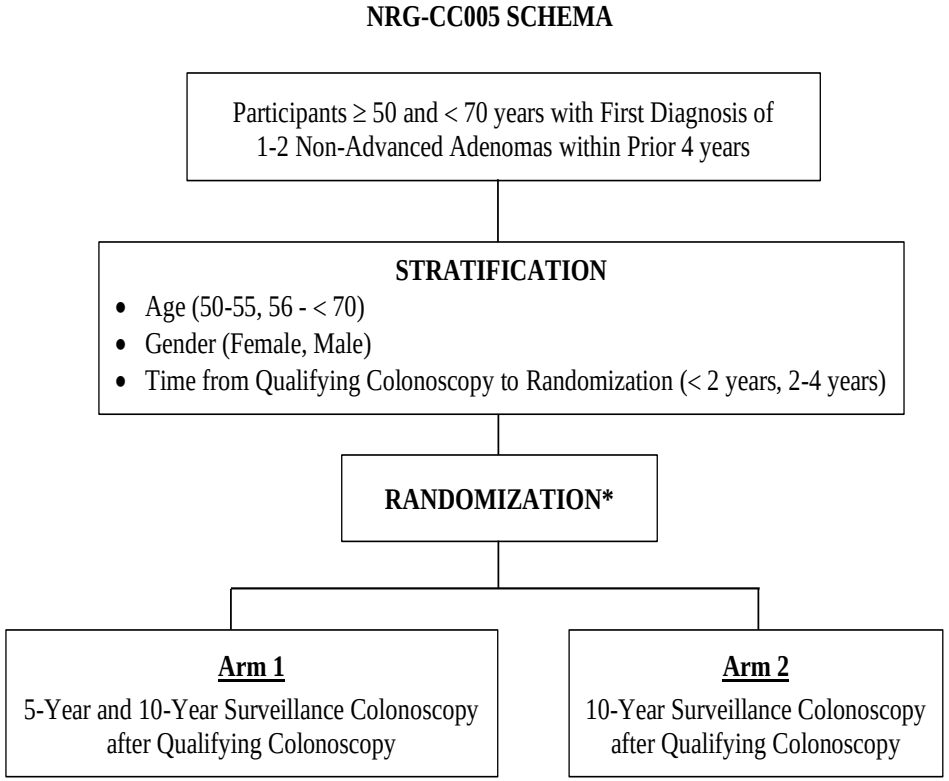
NRG-CC005/FORTE

PI: Robert Schoen, MD

Sample size = 9500

Biospecimen collection:

- Streck tube (1)
- Stool sample (3)
- FFPE tissue



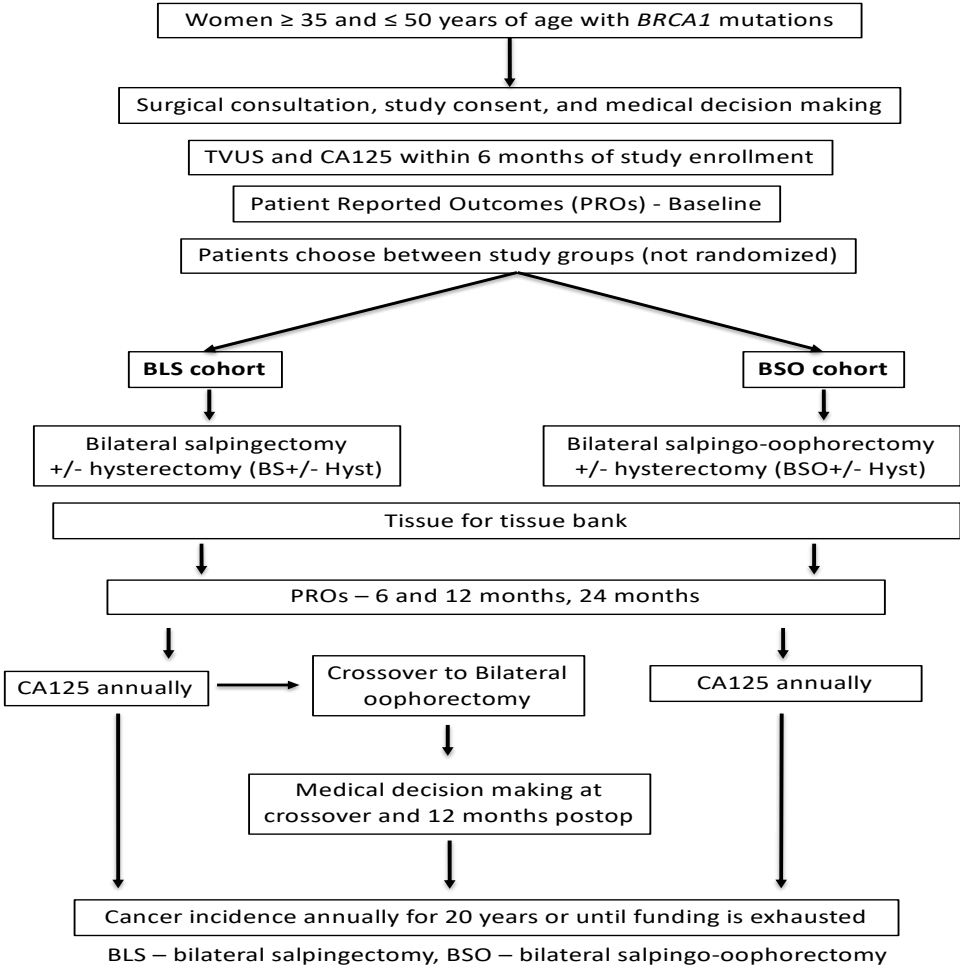
* Randomization is 1:1.

NRG-CC008

Co-PIs: Joan Walker, MD; Warner Huh, MD; Kathryn Pennington, MD

Sample size = 2262

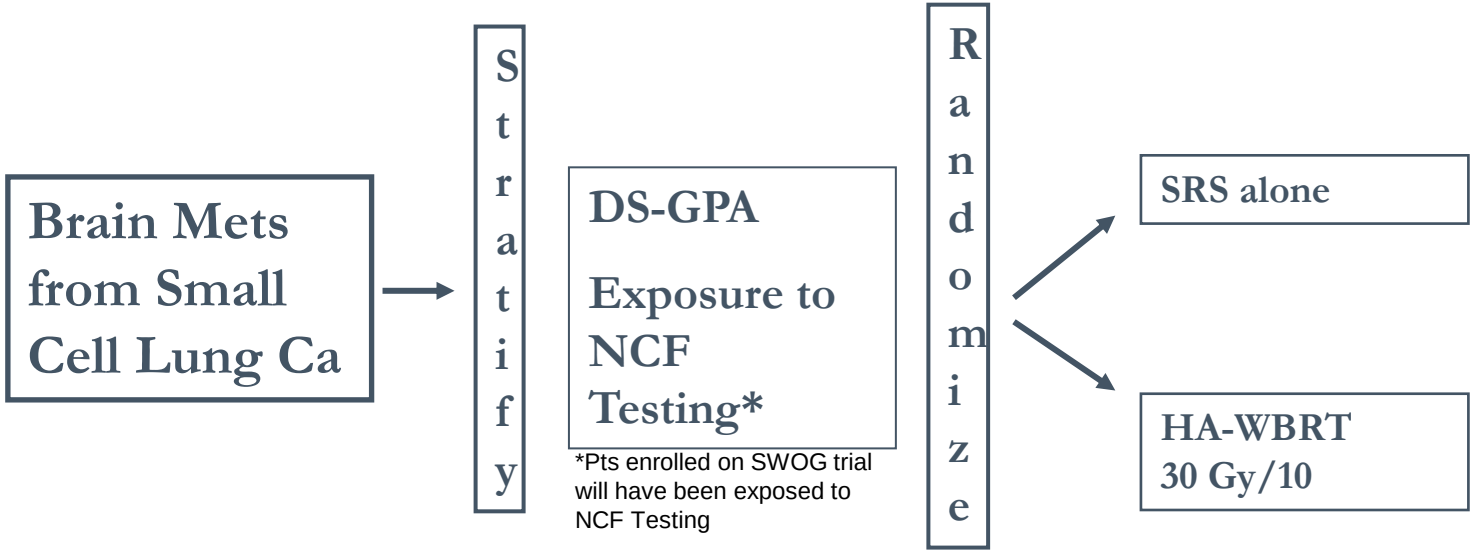
Primary objective: To compare the non-inferiority BLS with delayed oophorectomy to BSO to reduce the risk of ovarian cancer among women with deleterious *BRCA1* germline mutations



NRG CC009: Phase III Trial Stereotactic Radiosurgery versus Hippocampal-Avoidant Whole-Brain Radiotherapy for 10 or Fewer Brain Metastases from Small Cell Lung Cancer

PIs: Chad Rusthoven (Univ of Colorado) + Vinai Gondi (Northwestern)

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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Questions

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Study Champions

Study	Protocol Title	Accrual (1/20/22)	Comments
S1820	Testing Diet Intervention vs. Non-Diet Intervention for Management of Bowel Symptoms in Rectal Cancer Survivors (PI Sun)	79/126	Tracy Crane is the NRG study champion; NRG has enrolled ~25% of participants
S0820	Double Blind Placebo-Controlled Trial to Prevent Recurrence of High-Risk Adenomas and Second Primary Colorectal Cancers (PACES) (PI Zell)	327/491	Jennifer Dorth is the NRG study champion for this trial and enrolled ~10% of participants
EA1151	Tomosynthesis Mammographic Imaging Screening Trial (TMIST) (PI Pisano)	62,726/164946	NRG is a champion for this trial and enrolled ~6% of participants
A221805	Duloxetine To Prevent Oxaliplatin-Induced CIPN: Rand. Double-Bind, Placebo-Controlled Phase II To Phase III Study (PI Smith)	82/327	Jordan Kharofa is the NRG study champion for this trial. NRG has enrolled 10% of participants
EA2185	Comparing the Clinical Impact of Pancreatic Cyst Surveillance Programs	106/4606	Aasma Shaukat is the NRG Study Champion; NRG has enrolled ~13% of participants

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Developing NRG NCORP Trials

Study No.	Disease	Comments
NRG-CC010 Ed Tanner, MD	Impact of Sentinel Lymph Node Mapping on Patient Reported Lower Extremity Limb Dysfunction in Endometrial Cancer	Protocol submitted to DCP December 2021
NRG-CC2047 Deb Bruner, PhD	Gynecologic Cancer Therapy: The Vaginal Microbiome and Patient Symptom Experience	Pending R01 submission
NRG-CC2204 Diane Von Ah	Cognitive Training for Cancer-related Cognitive Impairment: A Multi-Center Randomized Controlled Trial	R01 submission Feb 2022

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Concepts in Development

Concept	Disease	Comments
Rand. Blinded, Placebo Controlled Phase 2 Trial of Concurrent ChemoRT w/ and w/out the BMX-001 in Patients with H&N Cancer (D. Brizel/S. Yom)	Head & Neck	
Preoperative RT to Improve Cosmetic Outcomes in Breast Ca Pts (S. Shaitelman)	Breast	Collaborative NCORP RB concept
Endometrial cancer prevention in women with obesity with the levonorgestrel-releasing intrauterine system (L. Bernard)	Gyn/Endometrial	Developed from pre-LOI from
Stereotactic Pelvic Radiotherapy in Uterine Cancers (SPARTACUS) III (E. Leung)	Uterine	
Cyrocompression for prevention of paclitaxel-induced peripheral neuropathy (K. Pennington)	Breast & Gyn	Intergroup trial

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NRG-CC010: A Phase III trial of the Impact of Sentinel Lymph Node Mapping on Patient Reported Lower Extremity Limb Dysfunction in Endometrial Cancer

Edward Tanner, MD

NRG-CC010 Study Chair

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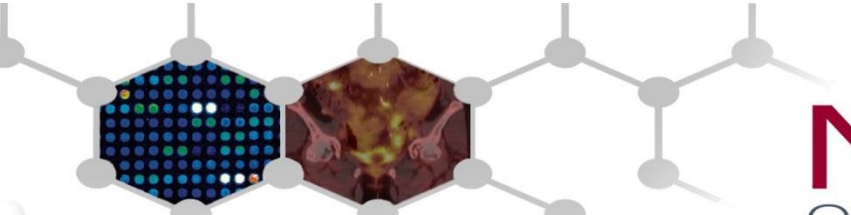

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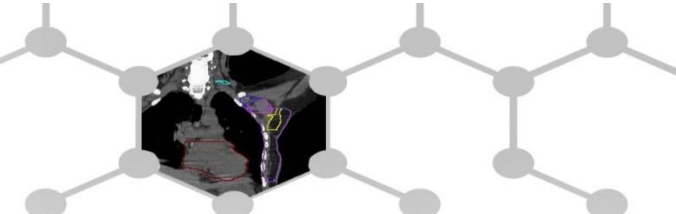

NRG-CC010: A Phase III trial of the Impact of Sentinel Lymph Node Mapping on Patient Reported Lower Extremity Limb Dysfunction in Endometrial Cancer

Edward Tanner, MD

February 10, 2022

Disclosures

- None

Study Objectives

Primary Objective: To compare the rates of lower extremity limb dysfunction (defined as a ≥4-point increase in GCLQ score from baseline) in patients with apparent uterine confined endometrial cancer randomized to one of two lymphatic assessment strategies at time of hysterectomy:
Arm 1: SLN mapping followed by side-specific lymphadenectomy on sides without a SLN identified according to an NCCN Guidelines approved algorithm.
Arm 2: SLN mapping according to an NCCN Guidelines approved algorithm followed by bilateral pelvic +/- para-aortic lymphadenectomy.

Study Enrollment and Preoperative Assessment

Disability assessment (GCLQ score)
General health assessment (EQ-5D)
Lower extremity limb circumference measurements
Bioimpedence assessment (subset only)

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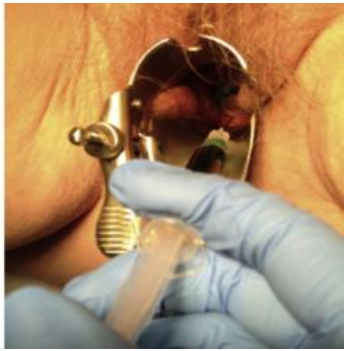
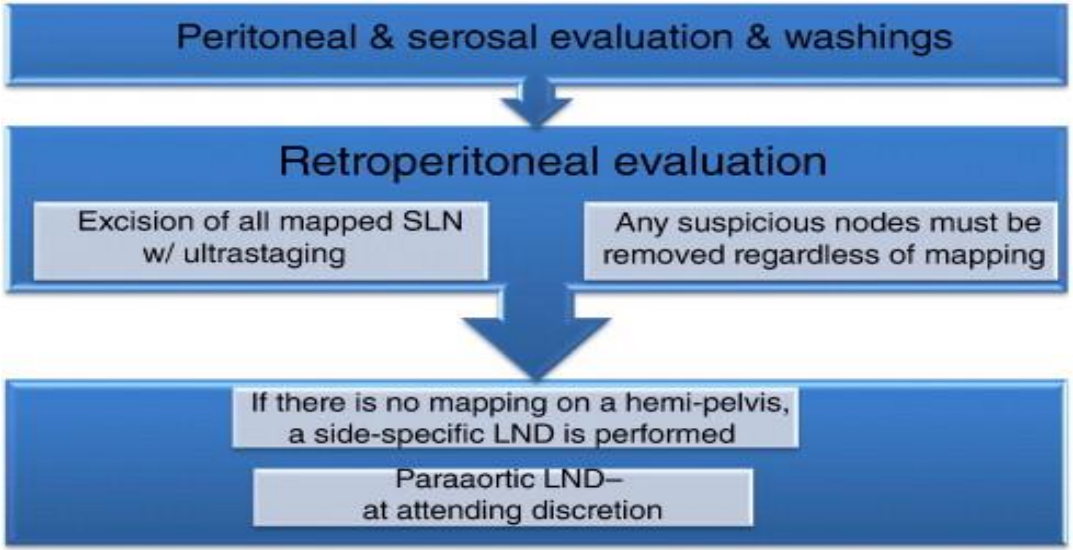
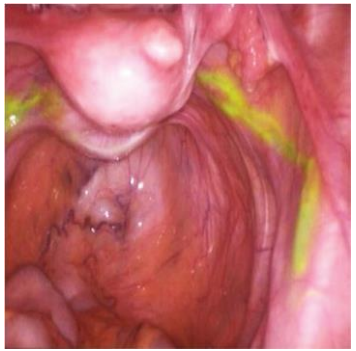
Study Intervention

- SLN mapping has been approved as alternative to lymphadenectomy by NCCN without prospective evaluation of impact on lymphedema







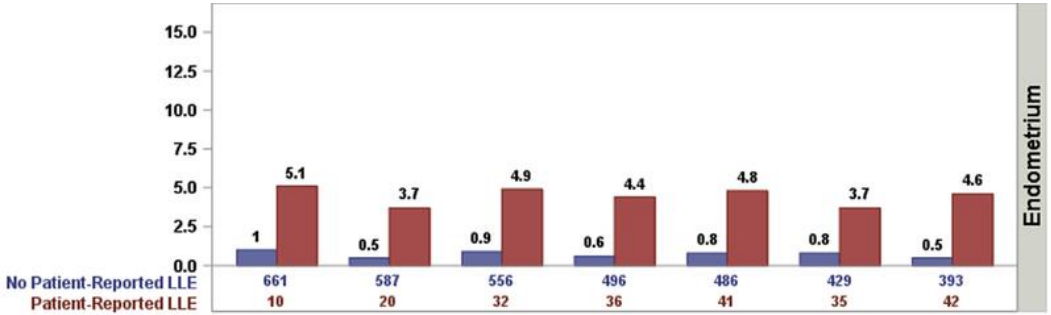

Study Enrollment and Preoperative Assessment:
EQ-5D-5L and Gynecologic Cancer Lymphedema Questionnaires (GCLQ)
Circumferential limb measurements
Minimally Invasive Surgery for Endometrial Cancer Including SLN Mapping
In OR prior to incision, surgeon states intention to perform para-aortic lymphadenectomy if assigned to Arm 2
Cervical injection of ICG followed by removal of SLNs according to NCCN algorithm (see Section 5.2)
Randomization assignment revealed to surgeon upon completion of SLN mapping
RANDOMIZATION 1:1
Study Arm 1: On any side without a SLN identified, side-specific pelvic lymphadenectomy*; omentectomy for appropriate histologies
Study Arm 2: Pelvic lymphadenectomy performed bilaterally; para-aortic lymphadenectomy if planned; omentectomy for appropriate histologies
Clinician-selected adjuvant therapy (NCCN guideline directed therapies recommended)
Data Collection at 3, 6, 9, 12, and 18 Months after Surgery:
Provider lymphedema assessment
PRO questionnaires: GCLQ and EQ-5D-5L
Circumferential limb measurements
Lower extremity bioimpedance (subset of sites)
Patient Questionnaire for lymphedema-associated costs
Recurrence and survival data (24 months)

Patient Population

- Women with apparent uterine confined endometrial cancer
- Appropriate candidate for minimally invasive hysterectomy and pelvic lymphadenectomy
- Patients stratified by tumor grade:
  - Grade 1-2 endometrioid versus grade 3 endometrioid/type II histologies
- Sample size: 428 enrolled, 342 evaluable patients
  - At least 20% Black women enrolled
- Surgeon eligibility: at least 10 SLN mapping cases → no learning curve cases

Primary Study Endpoint

- Patient-reported lower extremity limb dysfunction: a 4+ point increase in GCLQ score from baseline during 18 months of follow up
- GOG 244: 4+ point increase in GCLQ score closely linked to clinician reported lymphedema



- Instrument is validated and only 20 questions (*goal*: reduce dropout)
- 35% of patients with a 4+ point increase in GCLQ score in GOG 244

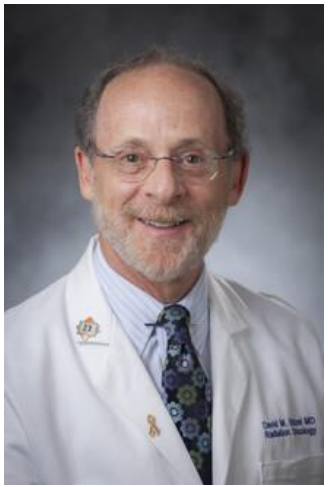
Additional Objectives

- To compare the following outcomes between Arm 1 and Arm 2:
  - Changes in lower extremity limb circumference
  - Changes in lower extremity bioimpedance (subset)
  - PFS and OS
- To validate the test characteristics of a SLN mapping algorithm including SLN detection rates, rate of identifying lymphatic metastases, and detection of micrometastases using pathologic ultra-staging as well as rate of periop complications
- To compare adjuvant therapy decisions in patients with apparent uterine confined endometrial cancer randomized to one of two lymphatic assessment strategies at time of hysterectomy
- To explore impact of patient characteristics (age, BMI, race), extent of lymph node dissection, and adjuvant therapy decisions (radiation, chemotherapy) on the development of lower extremity limb dysfunction – as well as their interaction with lymph node assessment strategies.
- To evaluate cost-effectiveness of SLN mapping with or without completion lymphadenectomy for endometrial cancer

Questions?

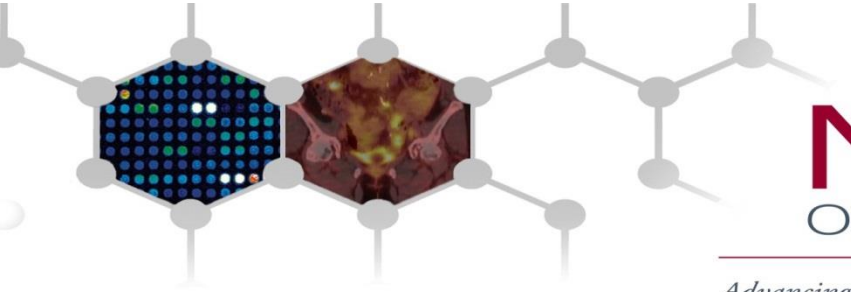
Developing Concept

Randomized, blinded, placebo-controlled phase II trial of concurrent chemoRT w/ and w/out BMX-001 for H&N squamous cancer



David Brizel, MD

Study Chair



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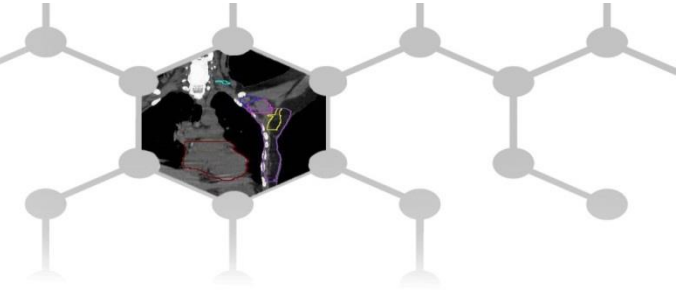

A Randomized, Blinded, Placebo-Controlled Phase II Trial of Concurrent Chemoradiation +/-the Radioprotector BMX-001 in Patients with Head and Neck Squamous Cell Carcinoma

David M. Brizel, MD

NRG Winter Conference
February 10-11, 2022

Disclosures

- Up to Date Oncology: Section Editor Head and Neck Cancer
- Biomimetix LLC: NCI SBIR for Clinical Trials Support

Why Is this Study Needed?

- Severe oral mucositis(SOM): frequent, debilitating acute toxicity of chemoradiation in HNC (65-69%)
  - Impairment of nutrition, hydration, swallowing, QOL, RT delivery
  - No FDA approved pharmacologic strategies in solid tumors

- Effective management of SOM constitutes an unmet medical need

- BMX-001 as adjunct to RT/CDDP may protect against acute and chronic toxicities and significantly mitigate impairment of QOL
  - Efficacy for both mucositis and xerostomia
  - Practical 2x/week subcutaneous administration
  - Strong safety profile

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Background:
Manganese (MN) Porphyrin Compounds

- Potent anti-inflammatory agents
- Catalytically inactivate many ROS including peroxynitrite and superoxide anion
- BMX-001 (MnTnBuOE-2-PyP^{5+}) amongst the most potent metalloporphyrins
  - Eliminates ROS to inactivate stress response pathways
  - Inhibits transcription factors including HIF-1, NFκB,SP-1, AP-1
- C57BL/6J mice with orthotopic HNSCC: 13 Gy RT +/-concurrent BMX-001
  - Less mucositis 10 days post-RT with BMX-001
  - Preservation of saliva production 6 weeks post-RT (Ashcraft, et al. 2015)
- FaDu xenograft model:
  - Absence of tumor protection: longer survival w/ RT+BMX than RT+ vehicle: (Birer, et al. 2017)

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Background: BMX-001 in Locally Advanced HNC (ASTRO 2021)

- **Safety endpoints (n=29)**
  - Levels 1&2: (6/6) received 100% of planned dose; 19/23(83%) at level 3
  - Transient grade 1 injection site skin reaction: 100%
  - Grade 1 QT prolongation (n=2): at level 3 only with loading dose
  - SAE (grade 3): Hypotension (1), fever/pancytopenia (1), hyponatremia (1)
- **Therapeutic endpoints**
  - SOM (grade 3 mucositis) incidence: 41%
  - SOM time to onset (median): 43 days
  - SOM duration (median): 25 days
  - Grade $\geq$2 xerostomia: 18%, 8%, 9% at 1, 6, 12 months respectively post-CRT
  - 1-yr PFS: 97% (1 recurrence)

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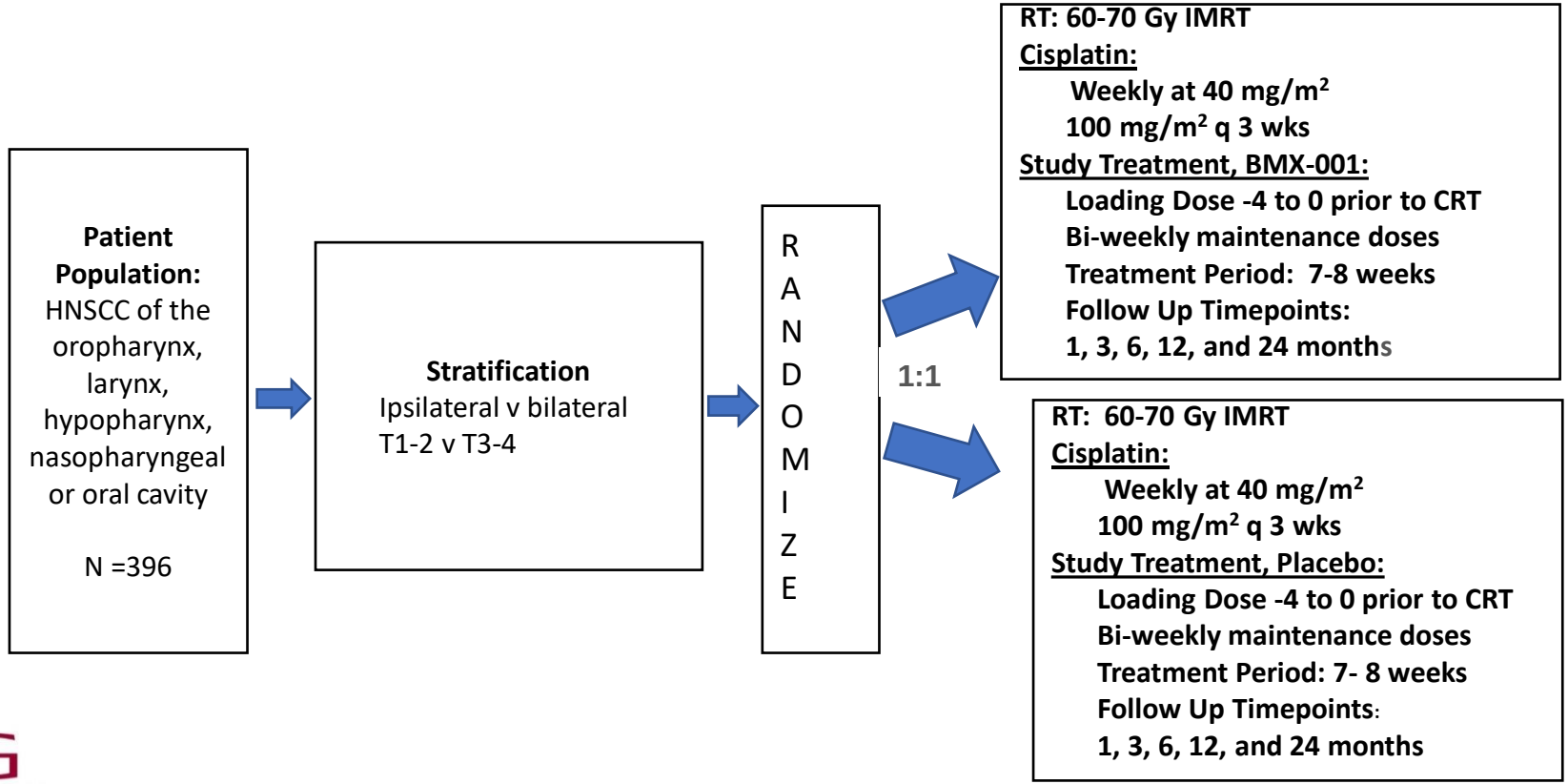
Overarching Rationale

- **BMX-001 substantially reduces mucositis severity caused by radiation concurrent chemoradiation**

- **Generalizable to the community setting due to ease of use**

BMX-001 in Locally Advanced HNC



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Study Endpoints

- **Primary (QOL)**
  - Difference in OMWQ-HN summary score from pre-CRT to 1 mo post-CRT
- **Secondary**
  - SOM incidence (WHO gr≥3) from start of CRT to 4, 6, 8, and 12 weeks post-CRT
  - Duration of SOM
  - Other toxicities (CTCAE 5.0 and PRO-CTCAE)
  - Incidence and severity of xerostomia and dermatitis
  - Duration of radiation dermatitis
  - DFS and OS
- **Exploratory**
  - Opioid usage

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Statistical Considerations OMWQ-HN

- Double blind, placebo controlled

- Minimally important difference (MID) is 4 (range 0-54)
  - Effect size of 0.33
  - t-test with a 2-sided type I error of 0.05 and 296 patients provides 80% statistical power to detect an effect size of 0.33
  - Increase sample size by 5% due to death, 5% due to consent withdrawal, and 15% due to patient non-compliance
  - Resulting target accrual: 396

- Interim futility analysis when 50% of evaluable patients reach 1 mo post CRT

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Questions?

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Developing Concept

Neoadjuvant partial breast radiotherapy in early-stage breast cancer: A randomized phase III trial to improve cosmetic outcomes

Simona Shaitelman, MD

Study Chair

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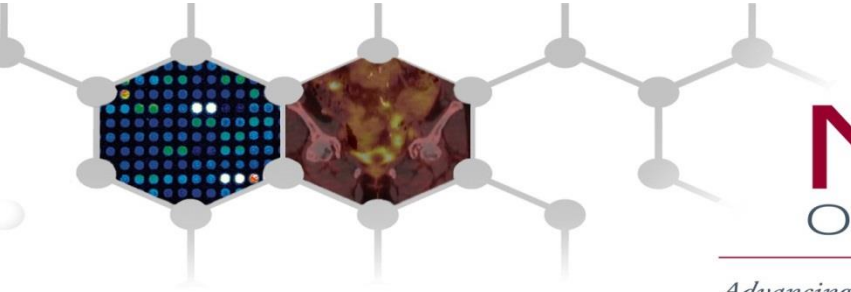

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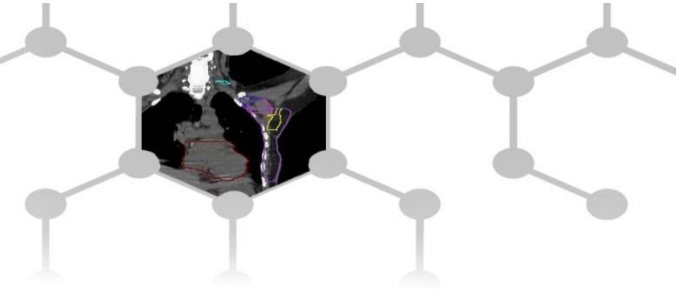

Preoperative Radiation to Improve Cosmetic Outcomes in Breast Cancer

PI Simona Shaitelman, MD, EdM

NRG Winter Conference
February 10-11, 2022

Disclosures

- Grants: NIH, Emerson Collective Foundation, Childress Family Foundation
- Research support: TAE, AlphaTau, Artios Pharmaceuticals

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Study Team

PI: Simona F. Shaitelman, MD, EdM

CPC Chair: Mylin Torres, MD

Health Disparities Chair: Oluwadamilola Oladeru, MD, MA, MBA

Biostatistics: Danielle Enserro, PhD

Medical Oncology Chair: Julie Nangia, MD

Pathology Chair: Hannah Wen, MD

Breast Surgical Oncology Chair: Irene Wapnir, MD

Radiation Oncology Co-Chairs: Elizabeth Nichols, MD; Rachel Blitzblau, MD, PhD

Medical Physics Chair: Leonard Kim, MS, AMusD

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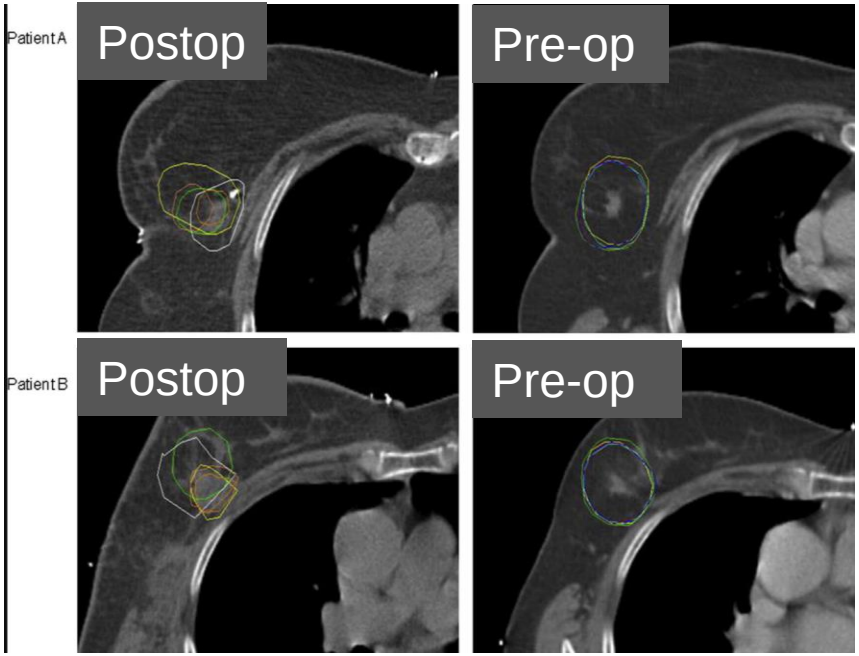
Rationale

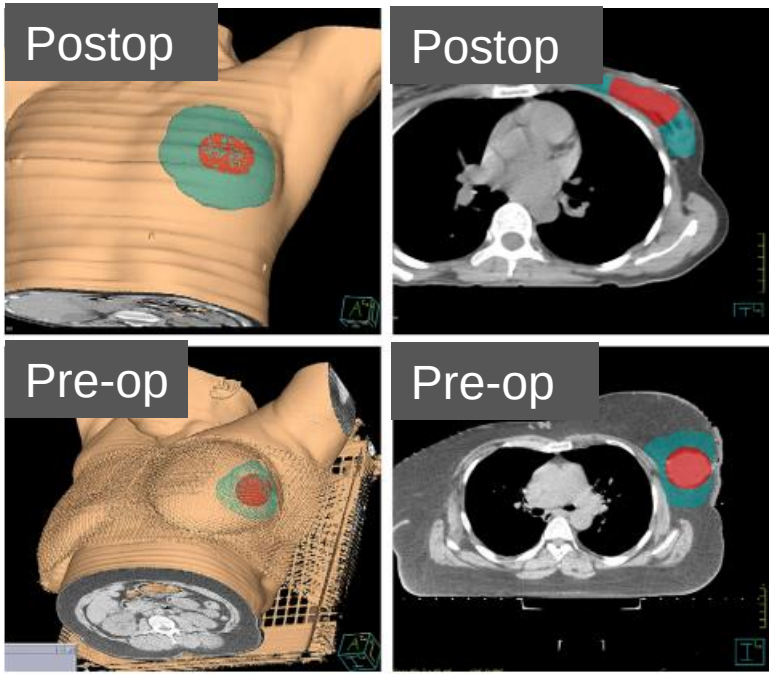
- Significant interest in use of external beam partial breast
  - Local control is outstanding (5yr LRR ~1-2%)
  - Ability to deliver treatments faster (patient-centric)
- HOW to best deliver PBI to improve outcomes compared to with WBI is uncertain
- Still a lot of variability in cosmetic outcomes with breast RT
  - **African American patients** tend to have worse cosmetic results than White patients
  - **Overweight and obese patients** tend to have worse cosmetic results
  - Patients with **large breast cup size** have worse cosmesis

Advantages to Preoperative PBI

More Accurate Tumor Targeting



Smaller Area Targeted



- High dose irradiated area excised (might lead to less fibrosis)

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Van der Leij, Radiother Oncol 2014; Nichols, *IJROBP* 2010

Background: Adjuvant PBI Trials

- NSABP B39/RTOG 0413: 4,216pts randomized to adjuvant WBI or PBI (5 days bid)
  - ~**30%** of pts had **poor-fair cosmetic result** (by pt and by MD assessment – no difference between arms)
- CCTG RAPID: 2,135 pts randomized to adjuvant WBI or PBI (5 days bid)
  - **36%** pts **poor-fair cosmesis** s/p PBI (vs. 15% s/p WBI) at 7yrs by pt assessment
- IMPORT LOW: 2,018 pts randomized to adjuvant WBI or PBI (**once daily x 15 days**)
  - **Moderate-marked** breast **appearance change**: **15%** PBI vs. 27% WBI
- Florence: 520 pts randomized to adjuvant WBI vs. IMRT PBI (5 non-consecutive tx)
  - Patient rated cosmesis 81% good & **18% excellent** s/p PBI (worse with WBI)

Background: Adjuvant PBI Trials

- NSAPB B39/RTOG 0413: 4,216pts
  bid)
  - ~30% of
- These trials primarily reported on a static cosmetic result after treatment and not a delta from baseline.
- Patients' individual views of their breast cosmesis vary at baseline and so ideally patients would serve as their own controls.
- Ideally baseline would be before any local-regional intervention.

consecutive tx)
cellent s/p PBI (worse with WBI)

Background: Adjuvant PBI Trials

- NSABP B-39: among those receiving PBI
  - 17% improved global cosmesis over time
  - 46% stable global cosmesis over time
  - 37% decline in global cosmesis over time
  - Enrollment:
    - 7% African American
    - 4% Hispanic or Latino
    - Accrued 7 patients/month

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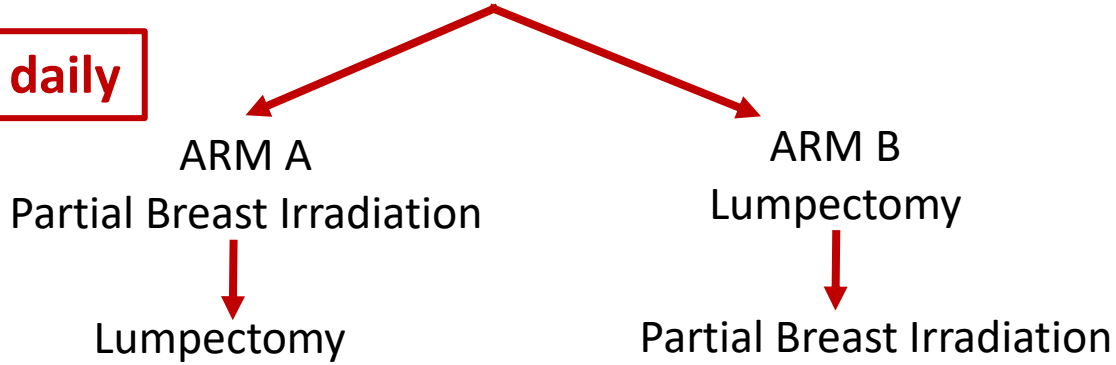
Early Stage, Biologically Favorable Breast Cancer

RT: 26Gy/5fx daily



Null Hypothesis:

There is no difference in the proportion of patients with stable or improved Global Cosmesis Score at 3 years in neoadjuvant vs. adjuvant partial breast irradiation

Alternative Hypothesis:

There is **a difference of 20% (85% vs. 65%)** in the proportion of patients with **stable or improved Global Cosmesis Score** at 3 years with neoadjuvant vs. adjuvant partial breast irradiation.

Number of Patients:

224pts randomized 1:1 neoadjuvant vs. adjuvant PBI

Anticipate 20% pt drop-out (178 planned evaluable for primary endpoint)

90% power to evaluate if the alternative hypothesis is true with a one-sided alpha of 5%

Accrual:

Anticipate national accrual rate 5pts/month→45months (3.8yrs) months to complete accrual

Total duration of the study: 81mo (6.8yrs) for accrual + f/u period

Aim to attract patients from historically underrepresented populations

Eligibility:

- cT1N0 breast cancer
- ER+, HER2-
- Non-lobular
- No LVSI
- Age ≥ ~~40yrs~~ 60yrs
- Breast cup size ≥ C

Stratification

- Baseline Depression (PROMIS Emotional Distress-Depression – Short Form 4a (>50 vs. ≤ 50)

Secondary Endpoint:

- TGF-β polymorphism

Exploratory Endpoint

- RCB
- ARTIC/POLAR

Strategies to Increase Enrollment of Historically Under-represented Populations

- Start enrollment for 12-18mo at NCORP & NRG sites that primarily serve an African American/Latinx population ahead of opening enrollment broadly
- Establish target cohorts and open broadly but cap once certain targets are filled
- Advertise the study:
  - Letters to MD's at those sites
  - Messaging to targeted patient advocate networks / newsletters / faith-based organizations
  - Social media
- Offer tele-support for clinical trials staff to these targeted NCORP sites, which may be understaffed
- Consent form – translatable into non-English language format
- Provide educational tools to define breast cup size

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Questions?

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Developing Concept

Endometrial cancer prevention in obese women utilizing levonorgestrel-releasing IUD

Laurence Bernard, MD

Study Chair

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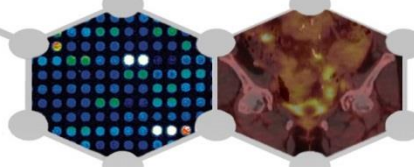

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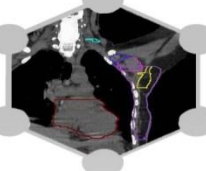

LNG-IUS for Endometrial Cancer Prevention in Women with Obesity: UC2034

Laurence Bernard, MD, MPH
McMaster University
Tracy Crane, PhD, RDN
University of Miami
Hanna Bandos, PhD
University of Pittsburgh
Emma Crosbie, MBChB (Hons), PhD
University of Manchester
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MD Anderson Cancer Centre

NRG ONCOLOGY VIRTUAL SEMIANNUAL MEETING
February 10th 2022

Disclosures

- No disclosures

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Scientific Background

Women with a BMI >30 have 2-10 times the risk of developing an endometrial cancer compared to women with a BMI <25.In the United States, 43.3% of women suffer from obesity (BMI >30), and 9.2% from severe obesity (BMI>40)

Endometrial cancer incidence and mortality rates are rising in high-income countries. Baseline lifetime risk is 1/40.

The levonorgestrel intrauterine system (LNG-IUS) was associated with a 50-78% risk reduction in endometrial cancer in population-based studies.

The use of the LNG-IUS for endometrial protection is biologically plausible and is currently used for EIN hyperplasia/low grade endometrial cancer fertility-preserving treatment.

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Scientific Background

There is strong evidence that following the National Guidelines on Nutrition and Physical Activity can reduce risk of recurrent or new cancers, improve quality of life (QOL) and reduce mortality.

The LNG-IUS would be a cost-effective chemoprophylaxis method in a Canadian setting.

Derbyshire et al. have published a single arm feasibility study of the LNG-IUS for endometrial protection in women with BMI >40. In total, 103 women were approached, 54 were offered a participant information sheet, 35 agreed to participate and 25 received a LNG-IUS. Their median age and BMI were 54 years and 47kg/m2 respectively. Three women (3/35, 9%) were ineligible due to atypical hyperplasia/endometrial cancer on their baseline biopsy. The LNG-IUS was well tolerated and had a positive overall effect on bleeding patterns and mental wellbeing. All but one woman (96%) kept her LNG-IUS.

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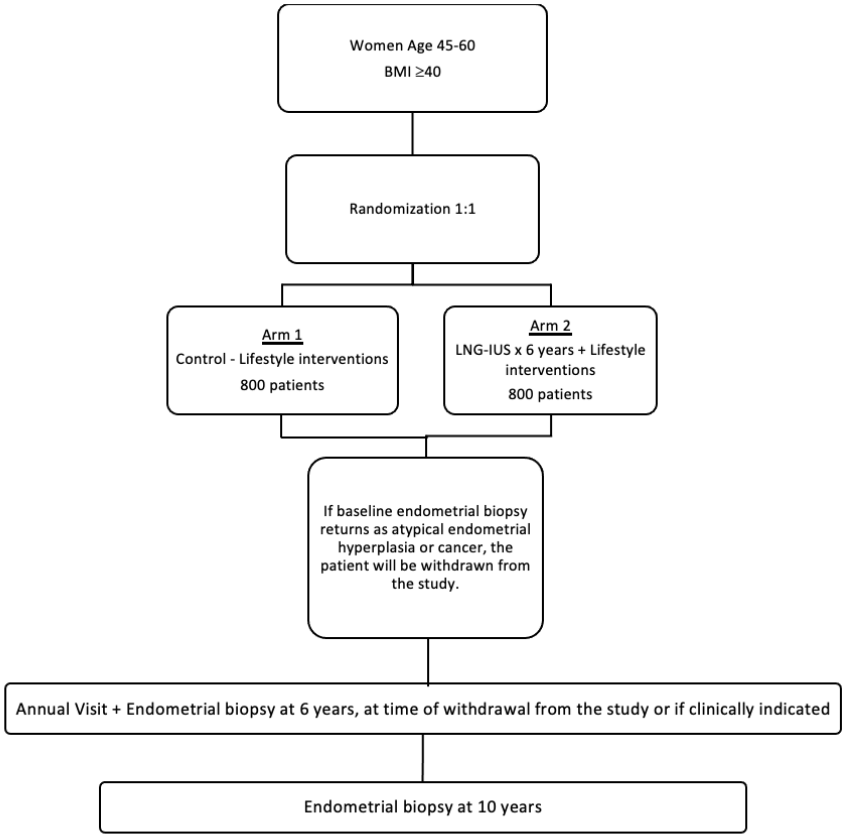
Study Design



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Primary Objective

- Primary objective:
  To determine the effect of LNG-IUS administered for 6 years on the 6-year occurrence of endometrial intraepithelial neoplasia or endometrial cancer (EIN/EC) in a high-risk population.

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Secondary Objectives

- To determine the effect of LNG-IUS administered for 6 years on the 10-year prevalence of EIN or endometrial cancer in a high-risk population
- To determine if health-related quality of life (QOL) is impacted by the LNG-IUS using the Short Form 36 (SF-36)
- To assess adverse events, graded using Common Terminology Criteria for Adverse Events (CTCAE) version (v)5.0
- Enhance racial and ethnic minority trial inclusion and measure difference in outcome between race
- Evaluate the uptake and adherence to the cancer prevention guidelines on diet and physical activity
- Explore the mediating role of self-efficacy in the relationship between lifestyle intervention and weight

<u>Exploratory objective</u>

- Development of predictive biomarkers using endometrial tissue, blood samples, urine samples and vaginal swabs

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Statistical Design

- Randomization (1:1)
  - Control – Lifestyle interventions
  - Therapy – Lifestyle interventions + levonorgestel-releasing intrauterine system (LNG-IUS) inserted for 6 years

- Targeted accrual: 2-arm trial. 800 patients in each groups (total 1600). 60 pts/month x 26 months
- Projected Accrual Dates: Start 2023 End: 2026
- Study duration: 10 years
- 80% power at one-sided alpha 0.05 to detect a RR 0.50
- Masking: None
- Intention-to-treat analysis

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Statistical Design

- Assumptions
  - 6-year rate of AH/EC: 6.8%

- Drop-in rate from the control arm to therapy arm (either to oral contraceptive pill, endometrial ablation, SERM/SPRM, hysterectomy)
  - 10% over 6 years (annual rate = 0.01756)

- Drop-out rate from therapy
  - expulsion – 10% over first two years, but 80% would want the device reinserted, therefore 2% over 2 years (annual rate = 0.0101)
  - due to symptoms – pain, abnormal uterine bleeding – 6% over six years (annual rate = 0.0103)
  - therefore, overall annual drop-out rate for the first 2 years is 0.0204, and for the next 4 years is 0.0103
  - Annual loss to follow-up rate – 0.005

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Inclusion/Exclusion Criteria

Inclusion criteria:

- Women age 45-60
- BMI≥ 40
- Benign (no EIN or cancer) endometrial biopsy at registration
- Has an intact uterus
- Owns a mobile phone and has access to a scale

Exclusion criteria:

- Need for contraception, management of abnormal uterine bleeding or management of menopausal symptoms with hormonal therapy at time of randomization.
- Inability to place the device in an outpatient clinic.
- Inability to obtain endometrial tissue
- History of endometrial ablation
- History of EIN or endometrial cancer
- Persistent hyperplasia without atypia after repeat endometrial biopsy at 3 months.
- Cervical dysplasia
- Contraindication to LNG-IUS

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Lifestyle Intervention

- Scalable, digital program using moderate exercise and healthy diet, as successfully used in three past cooperative group trials, GOG-0225, SW1820 and A011401.
  - Participants randomized to either group will receive 4 weekly calls to introduce them to the study, set them up with the homebased kit, and lay the foundation for study expectations and basic healthy cancer prevention behaviors of diet and physical activity.
  - Participants will then be contacted quarterly for booster sessions with their coach. SMS (text) messages will be sent three times per week at a time that is convenient as indicated by the participant. Messages will 1) motivational message, 2) call to action message (ie how many servings of vegetables did you eat) and 3) supportive message.
  - A home based kit will be provided to participants and include 1 Fitbit, resistance bands and printed materials. Given the battery life of things like the Fitbit, we will send a second homebased kit at year 3 to replace any lost or broken pieces.

Timing	Description	Mode of delivery
Weeks: 1 – 4 (weekly)	Health coaching	telephone
Month: 3, 6, 9 (quarterly)	Health coaching	telephone
Year: 1, 2, 3, 4, 5, 6 (annually)	Health coaching	telephone
3 x per week x 6 years	Interactive messaging	SMS (text)
Baseline and Year 3	Home based kit (resistance bands, fitbit, printed materials)	Mail

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Questions?

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Developing Concept

Stereotactic Pelvic Adjuvant Radiation Therapy in Cancers of the Cervix and Uterus

Eric Leung, MD

Study Chair

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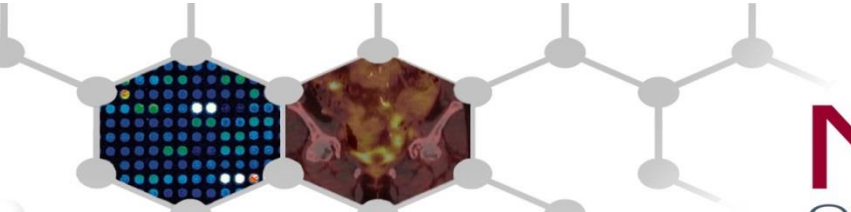

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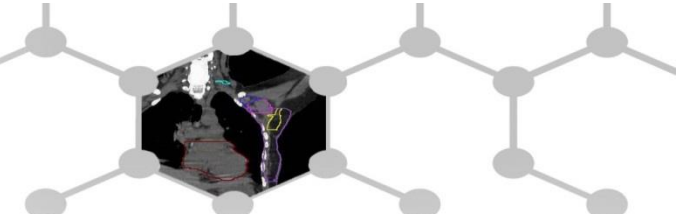

SPARTACUS III
(Stereotactic Pelvic Adjuvant Radiation Therapy in Cancers of the Cervix and Uterus)

PI: Eric Leung
Associate Professor, Department of Radiation Oncology
Sunnybrook Health Sciences Centre, Odette Cancer Centre
University of Toronto

Disclosures

Employment:

Department of Radiation Oncology
Sunnybrook Health Sciences Centre
University of Toronto

No other conflicts to disclose

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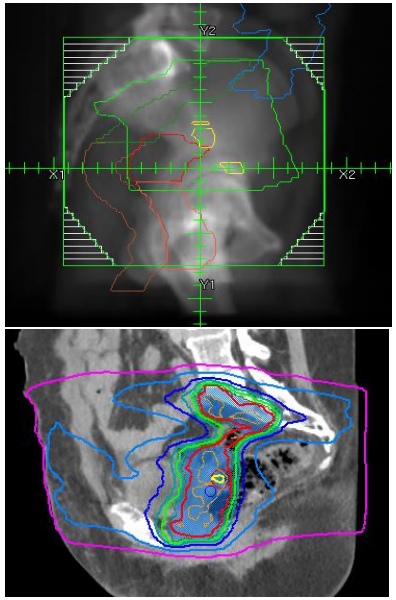
Background

- **Cervical and Uterine Cancers**
  - **4th and 6th most common cancers in women worldwide**
- **Adjuvant Pelvic RT**
  - **Local Control**
  - **Intermediate risk cervix**
    - **GOG 92**
  - **Uterine cancers**
    - **All Stages**



- **Standard Fractionation**
  - 5 weeks
  - 45 – 50.4 Gy in 25 – 28 fractions
- **Treatment Burden**
  - Quality of life
  - Cost
- **COVID – 19 Pandemic**
  - Social Distancing
  - Decrease exposure
- **Hypofractionation**
  - Established in other disease sites
    - Eg. rectum, prostate, breast

1-Rahib L, et al. Cancer Res. 2014 Jun 1;74(11):2913-21.
2-Peters EEM, et al. Int J Gynecol Pathol. 2021 Aug 16.
3-Randall ME, et al. J Clin Oncol. 2019 Jul 20;37(21):1810-1818
4-Klopp, et al. J Clin Oncol. 2018; 36 (24): 2538-2544

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SPARTACUS I Trial

- **Multi-center Phase I/II Study**
  - **Sunnybrook and London Health Sciences Centre**
  - **Hypothesis**
    - ***Hypofractionated radiotherapy 30 Gy in 5 fractions for adjuvant radiation treatment in uterine cancer will be well tolerated with acceptable acute GI and GU toxicity and quality of life.***

- **Primary Aim:**
  - **Acute GI and GU Toxicities (CTCAE V.5)**
- **Secondary Aims:**
  - **Quality of life - Patient-reported**
    - **EORTC core (QLQ-C30)**
    - **Uterine (EN-24)**
  - *Late toxicity rates*
  - *Local Control*
  - *Disease Free Survival*

Inclusion:
Post-op endometrial cancer for pelvic radiation
- Outer half myometrial invasion
- High grade
- Stage II and III
- Sequential chemo

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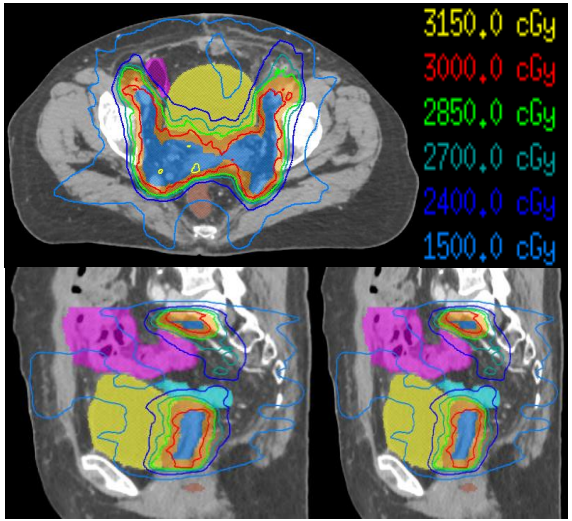
SPARTACUS I Trial

30 Gy in 5 fractions BED

- α/β = 10 (Tumour control/Acute toxicities)
  - EQD_2 = 40 Gy
- α/β = 3 (Late toxicities)
  - EQD_2 = 54 Gy

Five Fraction SBRT Planning

- 40 Gy in 5 fractions to prostate, 25 Gy in 5 fractions to nodes
  - Several phase I/II studies, >140 patients at Sunnybrook OCC
    - Median FU > 4 years, 0% grade 3+ acute or late toxicity



SPARTACUS planning protocol from 5 fraction SBRT

1-Brand DH et al. Lancet Oncol. 2019 20 (11): 1531-1543.
2-Musunuru HB, et al. Int J of Radiat Oncol . 2018 102 (5): 1438 - 1447

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Results

Trial Accrual and Follow-up

- May 2019 to August 2021
- Median follow-up 12 months (3-24)

Demographic and Clinical Characteristic	Total (N = 61)	
Age (years)	66 (51-88)	
Grade		
1	14	(22.95%)
2	15	(24.59%)
3 or High	32	(52.45%)
Stage		
I	39	(63.93%)
II	6	(9.84%)
III	16	(26.23%)
Adjuvant chemotherapy		
No	46	(75.41%)
Yes	15	(24.59%)
Vault brachy		
No	52	(85.25%)
Yes	9	(14.75%)

CTCAE Physician Reported Acute GI/GU Toxicities

N = number of patients

	Worst GI	Worst GU
# Grade 1	34 (56%)	25 (41%)
# Grade 2	7 (11%)	2 (3%)
# Grade 3	1 (1.6%)	0

- Vaginal
  - discharge grade 1 (2 patients) grade 2 (1 patient)
- Lymphedema or MSK toxicities
  - none

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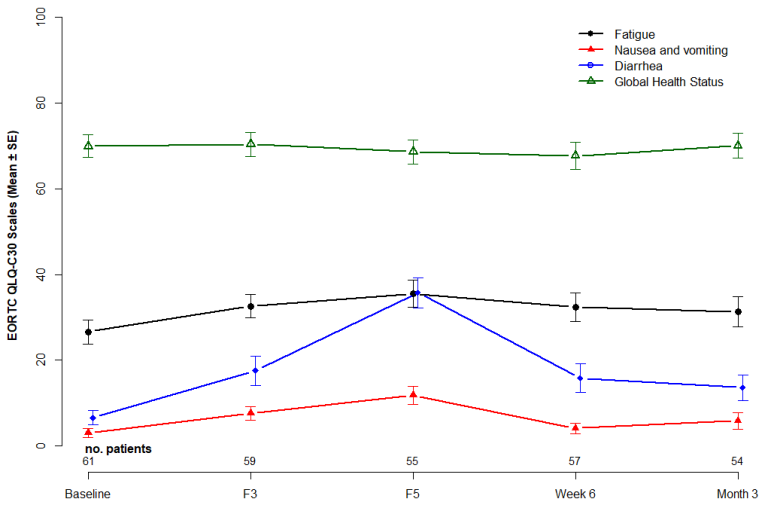
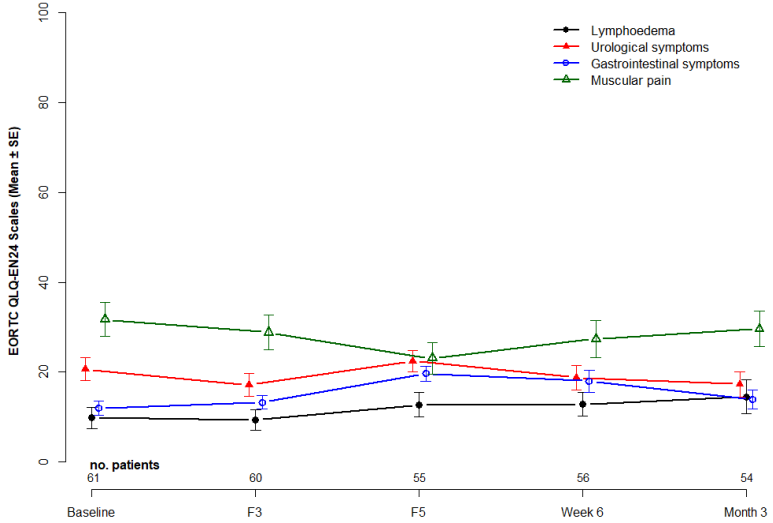
Results

EORTC QLQ-C30 Scores



EORTC EN-24 Scores



- **Only 'Diarrhea' clinically (≥10) and statistically significant change at F5** ($p<0.0001$)

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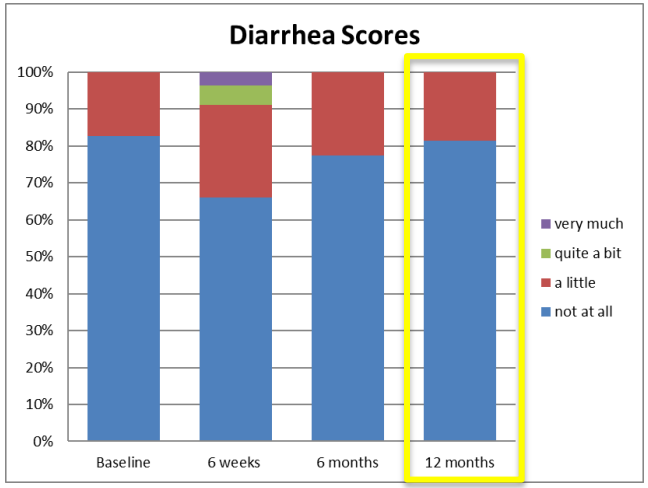
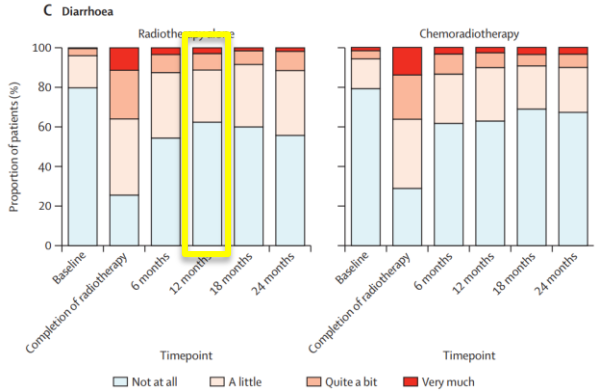
Late Toxicities - Preliminary Results

SPARTACUS I



PORTEC 3



de Boer SM, et al. Lancet Oncol. 2016 Aug;17(8):1114-1126.

SPARTACUS - 1 Year Diarrhea Score = 4.9 (31 patients)
PORTEC 3 - 1 Year Diarrhea Score = 18 (Radiation Alone Arm)

Currently no Grade 3 or higher late toxicities at 12 months median FU (3 -24)

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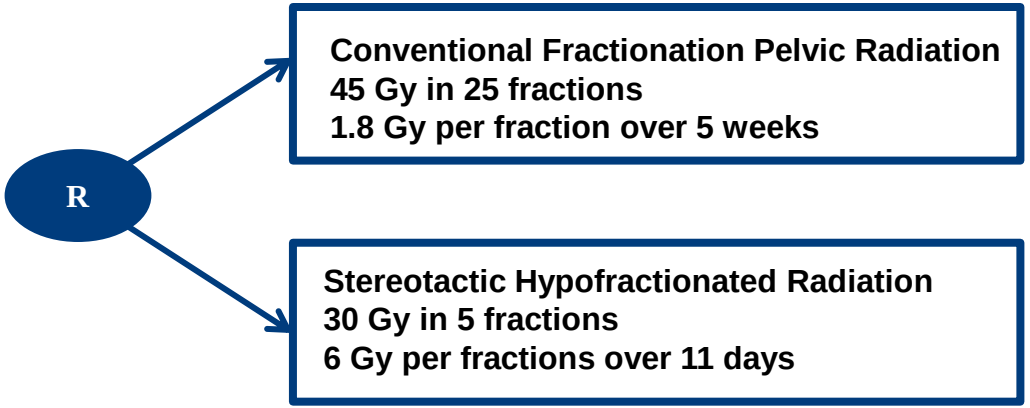
SPARTACUS III: Design Schema

- Phase 2, investigator-led, open-label, multi-site trial, using 1:1 randomization



- Hypothesis: Hypofractionated radiotherapy to a dose of 30 Gy in 5 fractions (6 Gy given every other day) for adjuvant radiation treatment in uterine and cervical cancer leads to similar late gastrointestinal quality of life as conventional fractionated radiation.

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SPARTACUS III: Objectives

Primary:

- To compare the long-term bowel toxicities associated with hypofractionated vs conventional adjuvant pelvic radiation as measured by EORTC C-30 questionnaire for diarrhea at 24 months

Secondary:

- Late and acute bowel and urinary toxicities associated with hypofractionated treatment and conventional fractionation in adjuvant pelvic radiation using EORTC C30 and EN24.
- Late and acute bowel and urinary toxicities associated with hypofractionated treatment and conventional fractionation in adjuvant pelvic radiation CTCAE v5.0
- Late and acute bowel and urinary toxicities associated with hypofractionated treatment and conventional fractionation in adjuvant pelvic radiation using EPIC QOL
- To compare the local-regional failure of hypofractionated treatment and conventional fractionation
- Vulvovaginal symptoms associated with hypofractionated treatment and conventional fractionation in adjuvant pelvic radiation using VAS/VuAS

SPARTACUS III - Inclusion Criteria and Schedule

- **Patient with histologically confirmed endometrial adenocarcinoma, serous or clear cell carcinoma or cervical squamous cell carcinoma or adenocarcinoma.**
- Patient is a candidate for adjuvant pelvic radiation for uterine cancer (+/- vault brachytherapy), meeting one of the following conditions:
  - High grade histology (including serous and clear cell)
- OR
  - Outer-half myometrial invasion and FIGO grade 1-2
- OR
  - FIGO stage II - III
- Patient is a candidate for adjuvant pelvic radiation for cervical cancer with intermediate risk factors including 2 of the following:
  - Lymphovascular space invasion
  - 1/3 or more stromal invasion
  - Larger than 4 cm tumour diameter
- Patients who are to receive adjuvant systemic therapy sequentially in addition to pelvic radiotherapy will be eligible

Assessments	Baseline (Prior to RT)	*Fraction/Week 3 - On treatment	*Fraction/Week 5 - Last treatment	6 weeks post-treatment	12 weeks post-treatment	Clinical follow-up visit**
Medical History Assessment, Including Rectal and Urinary Function Assessment	X					
Toxicity Assessment (CTCAE v5.0)	X	X	X	X	X	X
EORTC	X	X	X	X	X	X
EPIC	X	X	X	X	X	X
VAS/VuAS	X	X	X	X	X	X
ECOG Performance Status	X	X	X	X	X	X
Physical Assessment	X			X	X	X
Bloodwork	X		X	X		

'Fraction' for Arm 2, 'Week' for Arm 1. Timepoint comparison during radiation are based on proportion of treatment that is completed (eg 1 week completed for Arm 1 is equivalent to 1 fraction completed for Arm 2) Clinical follow-up will occur at 6- and 12-weeks post treatment, every 3 months thereafter until 1 year post-treatment, and subsequently every 6 months until 2 years post-treatment.*

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SPARTACUS III - Statistical Design

- Groups will be considered non-inferior if the difference between groups remains within the minimum clinical significance difference (10 points) for the mean diarrhea score based on the EORTC C-30 questionnaire.
- With an Alpha = 0.05, standard deviation of 24, 99 patients in each arm are needed for a power = 0.90.
- With an estimated attrition rate of 15%, 117 patients in each arm (117 x 0.85 = 99.5) or 234 total patients will be required.
- **Safety Analysis**
  - 30 Gy in 5 fraction BED comparable to other hypofractionation doses for microscopic pelvis
  - SPARTACUS I - 1 local recurrence (1.6%) detected at the time of radiation
  - Safety Analysis to determine if hypofractionation local failure > conventional at 50 and 100 patients

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Summary

- SPARTACUS III - Phase II randomized design
  - 30 Gy / 5 fractions vs 45 Gy / 25 fractions
  - SPARTACUS I
    - Acute toxicity data
    - Preliminary late toxicity
  - Primary endpoint late GI QOL (EORTC diarrhea at 2 years)
  - Quality of Life Measures
    - EORTC QOL and EPIC
    - PRO-CTCAE, VAS/VuAS

Questions

1) EORTC QLQ-C30 question 28 measures ‘financial difficulties’ in hypofractionation and conventional fractionation treatments. Would you recommend a more comprehensive evaluation tool such as COST (COmprehensive Score for financial Toxicity)?

2) Would you recommend the addition of a health cost-effectiveness measure such as EQ-5D?

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Acknowledgements

Sunnybrook Health Sciences Centre and London Health Sciences Centre

- **Patients**
- **Clinical Trials Team**
- **Radiation Therapy and Physics**

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Radiation Oncology UNIVERSITY OF TORONTO

Sunnybrook ODETTE CANCER CENTRE

London Health Sciences Centre
London Regional Cancer Program

Western UNIVERSITY · CANADA

Questions?

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Developing Intergroup Concept

STOP CIPN: Randomized trial of Limb CryocompreSsion versus ConTinuous cOmPression versus Low Cyclic Compression for the Prevention of Taxane-InduCed perIPheral Neuropathy

Kathryn Pennington, MD

Study Chair

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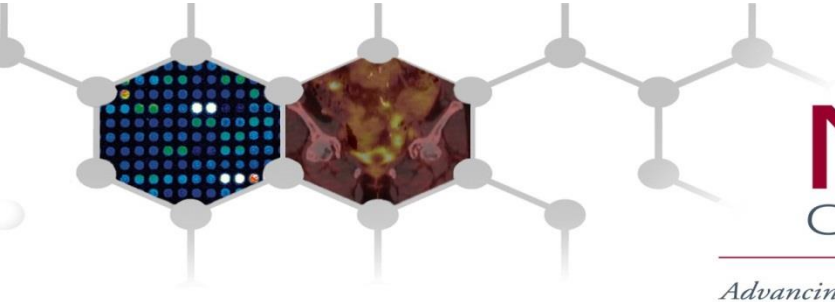

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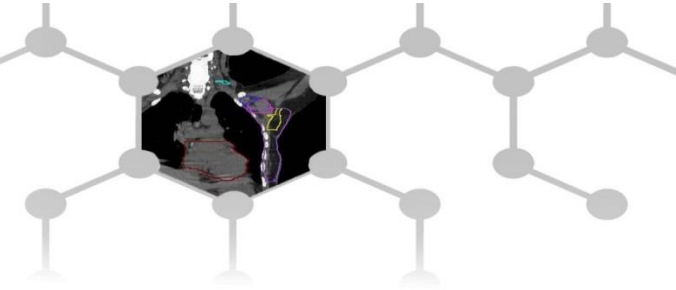

STOP CIPN: Randomized trial of Limb Cryocompre**S**sion versus Con**T**inuous c**O**m**P**ression versus Low Cyclic Compression for the Prevention of Taxane-Indu**C**ed per**IP**heral **N**europathy (SWOG 2205)

Study Chairs: Kathryn Pennington (NRG); Melissa Accordino (SWOG)
Co-I's: Debra Barton (NRG); Dawn Hershman (SWOG); Charles Loprinzi (Alliance)
Statistician: Joesph Unger (SWOG)

NRG Virtual Winter Meeting – Cancer Prevention & Control Workshop
February 10, 2022

Disclosures

- None

Why Is this Study Needed?

- Chemotherapy-induced peripheral neuropathy (CIPN) is a common, long-term, dose-limiting side effect that greatly impacts QoL
- No known CIPN prevention in rigorous RCTs

Cryotherapy (frozen gloves/socks)

- Hanai et al (n=36, pts were own control): less tactile deterioration hands/feet: 25-28% v. 64-81%
- Shigematsu et al (n=44): % with significant CIPN (↓ FACT-NTX by >6pts) 41% vs. 73%
- Sato et al (n=182 [n=40 cryo and n=142 hx controls]): G2+ sensory neuropathy 8% vs 34%
- ***Poorly tolerated or stopped in 32-50%***

Compression therapy

- Tsuyuki et al (n=43, pts were own control): G2+ sensory neuropathy 21% vs 76%
- CONTRoL study (n=63; cryo v. compression v. placebo): stopping criterion met at 17th triplet (n=51), FACT-NTX <5 point ↓ from baseline: compression 65% vs cryo 41% and placebo 41%

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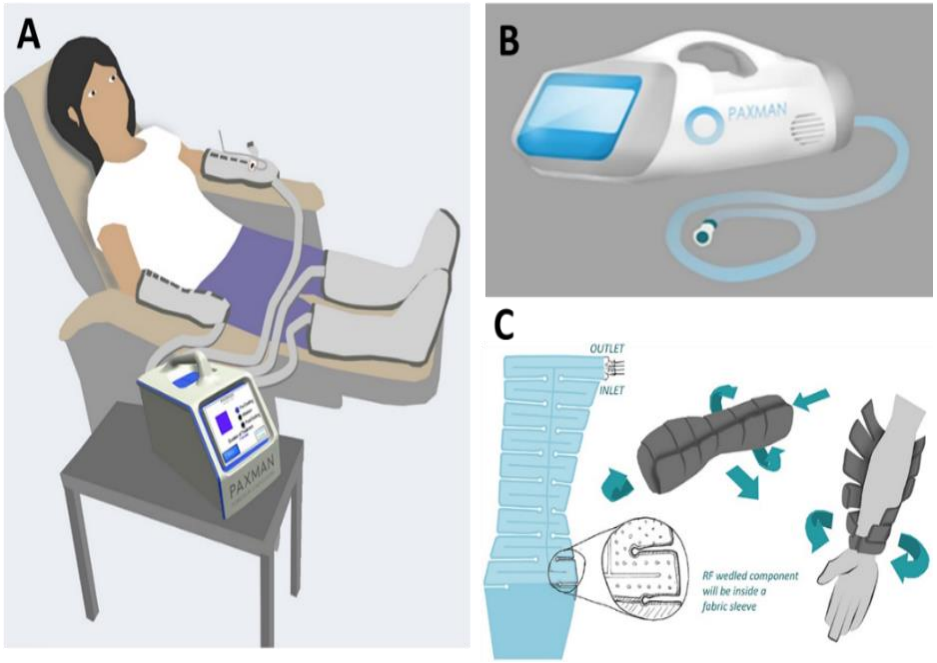
Loprinzi CL et al JCO 2020; Jordan B et al Ann Oncol 2020; Hanai A et al JNCI 2018, Shigematsu H et al J Pharm Health Care Sci 2016, Beijers AJM et al Ann Oncol 2020; Ruddy KJ et al Breast 2019; Tsuyuki S et al BCRT 2016; CONTRoL Trial NCT03873272

“Cryocompression” - Overcomes Prior Limitations

- **Continuous-flow cooling device**
  - Improves rigor (constant/uniform temp)
  - Able to adjust temp
- **Improved tolerability with cyclic compression**
  - Gate control theory of pain
- **Possible improved efficacy as lower temperatures achieved**
  - In pilot: **<u>0% G2+ sensory neuropathy</u>,** 54% grade 1, 46% grade 0



Bandla A et al *Acta Oncol* 2016; Bandla A et al *Supportive Care in Cancer* 2019

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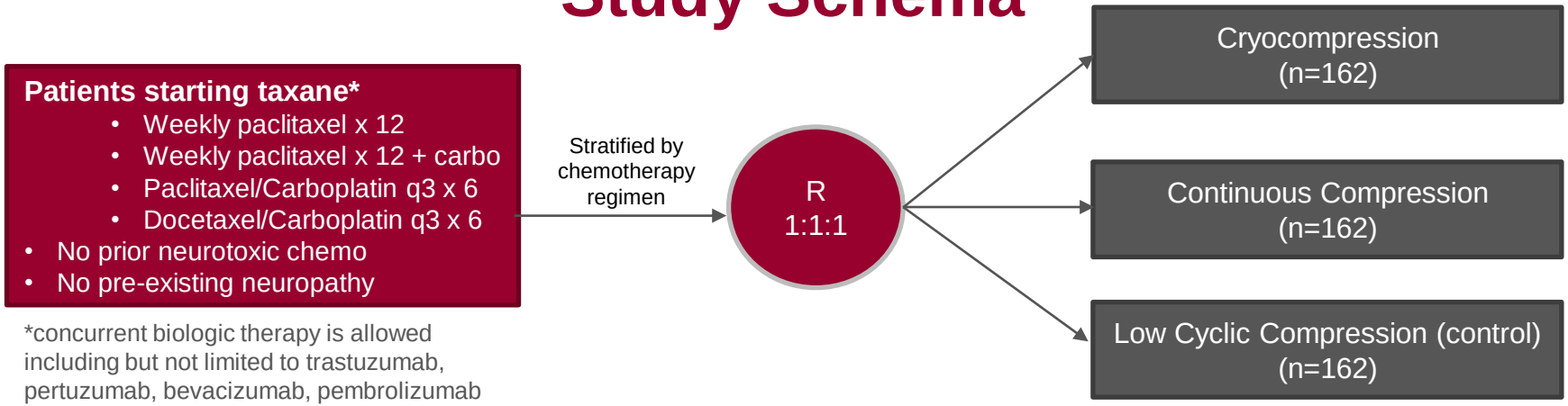
Study Schema



Intervention on all 4 extremities, starts 30 min before taxane and continued until 30 min after taxane completed

- **Cryocompression: temperature 11°C and cyclical pressure 5-15 mmHg (cycles from 5 to 15 mmHg every 5 min)**
- **Continuous Compression: continuous pressure of 25 mmHg**
- **Low Cyclic Compression (control): low cyclical pressure 0-5 mmHg**

Not expected to significantly ↓ blood flow, alter neurotoxic chemotherapy delivery to extremities, or to prevent CIPN

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Study Objectives

Primary Objective: To compare the proportion of participants who develop clinically meaningful CIPN (an absolute increase of ≥8 points over baseline in the CIPN-20 sensory subscale score) at 12 weeks by arm

Secondary Objectives:

- To compare trajectories over time by arm in proportion of participants with clinically meaningful CIPN, using a linear mixed model
- To assess adverse events, graded using CTCAE

Study Objectives

Exploratory Objectives:

- To compare differences by arm at 12 weeks in:
  - mean EORTC CIPN-20 sensory, motor, and autonomic neuropathy subscale scores
  - mean individual PROMIS-29 domain scores
- To compare rates of CTCAE grade 2+ sensory, motor neuropathy at 12 weeks
- To evaluate changes in objective sensory and motor function tests from baseline to 12 weeks (Vibration threshold, Neuropen, Timed Get Up and Go)
- To evaluate tolerability (rate of temperature reductions, interruptions, early discontinuation of device)
- To determine device satisfaction, assessed by patient questionnaire
- To compare taxane dose-reductions, treatment delays/discontinuation due to CIPN, relative taxane dose intensity and total dose received

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Study Assessments

Assessments	Baseline	6 weeks (±2 wks)	12 weeks (±2 wks)	24 weeks (±4 wks)	52 weeks (±4 wks)
Medical History	X				
Concomitant Medications, Chemotherapy Treatment Schedule	X	X	X	X	X
EORTC-QLQ-CIPN20	X	X	X	X	X
PROMIS-29 v2.1	X	X	X	X	X
Device Satisfaction and Comfort			X		
Objective sensory and motor tests: Vibration Threshold Test Neuropen Test (pressure/pain) Timed get up and go	X	X	X	X	X
Device Tolerability	X	X	X	X	X
CTCAE neuropathy CTCAE nail changes	X	X	X	X	X
Blood collection	X		X	X	

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Statistical Considerations

- **<u>Power:</u> N=486 participants provide 81% power to detect absolute 20% reduction in proportion developing CIPN**
  - Design incorporates 20% dropout and 3% ineligibility
  - 3 separate 2-sided (alpha=0.0167) pairwise tests
- **<u>Stratification:</u> by chemotherapy regimen (weekly paclitaxel, weekly paclitaxel + carboplatin, paclitaxel/carboplatin q3 weeks, docetaxel/carbo q3 weeks)**
- **<u>Analysis:</u>**
  - Primary analysis conducted using multivariable logistic regression adjusting for baseline score and stratification factor as covariates
  - Longitudinal analysis of serial measurements (6,12 ,24,52 weeks) assessed using Generalized Estimating Equations
  - Sensitivity analysis includes dropouts (may be positively correlated with CIPN) as failures

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Questions

- **Feasible for sites?**
  - Device training, possible extended time in infusion center
  - Objective sensory testing by staff

- **Control arm: 0-5 mmHg cyclic compression**
  - Consent - Goal of study to determine which study intervention is most effective. Will not share hypothesis.

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Special thank you to Deb Barton for her mentorship

Questions?

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Resources for Concept Development

- NRG NCORP Website
  - https://www.nrgoncology.org/Scientific-Program/NRG-NCORP-Research-Base
  - Slide Deck Orientation: Click link under “Learn more about opportunities and working with NRG NCORP”
- CPC Concept Development Form
  - https://www.nrgoncology.org/Scientific-Program/NRG-NCORP-Research-Base/NCORP-Resources
- CPC Pre-LOI Form
  - Contact Erica Field, fielde@nrgoncology.org

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