DEVELOPING AND IMPLEMENTING CLINICAL TRIALS AND INFRASTRUCTURE: THE CARG GERIATRIC ONCOLOGY TREATMENT OPTIMIZATION (GOTO) PROGRAM FUNDED BY THE RISING TIDE FOUNDATION

National Program Leader:
William Dale, MD, PhD
City of Hope

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Infrastructure Grant
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Grant Overview: CARG GOTO Program

This program will serve as a national model on conducting clinical trials focused on our vulnerable elders, and serve as the foundation for future ground-breaking research and innovative clinical care to improve the lives of older adults with cancer.

- We use a common Geriatric Assessment (GA) tool across projects that has been developed, validated, and used widely by CARG and others to assess older adults with cancer, the CARG-GA.
- The 5 trials will evaluate interventions and patient-centered outcomes that are focused closely on older adults' expressed concerns that will personalize treatment decisions.
- To foster coordination, quality assurance, and standard conduct of the 5 trials, we have created a centralized data coordination plan that will be managed through by City of Hope's Center for Cancer and Aging and CARG.

$4.25 million to support the conduct of 5 patient-centered geriatric oncology RCTs
($2.25M from RT + $2M in matching funds; grant period: 2022-2028)

Patient Engagement

- Continued collaboration with SCOREboard (Stakeholders for Care in Oncology and Research for our Elders board), a patient advocacy group of older adults with cancer
- SCOREboard has partnered with CARG for over a decade, providing active, ongoing collaboration from the beginning of planning for the study, and ongoing through the entirety of the projects.
- Each study will have at least 2 assigned patient advocates/partners, matched to the content of each study, and affiliated as full partners in the creation, design, and implementation of this proposal

Beverly Canin
SCOREboard Co-Chair
Based in New York

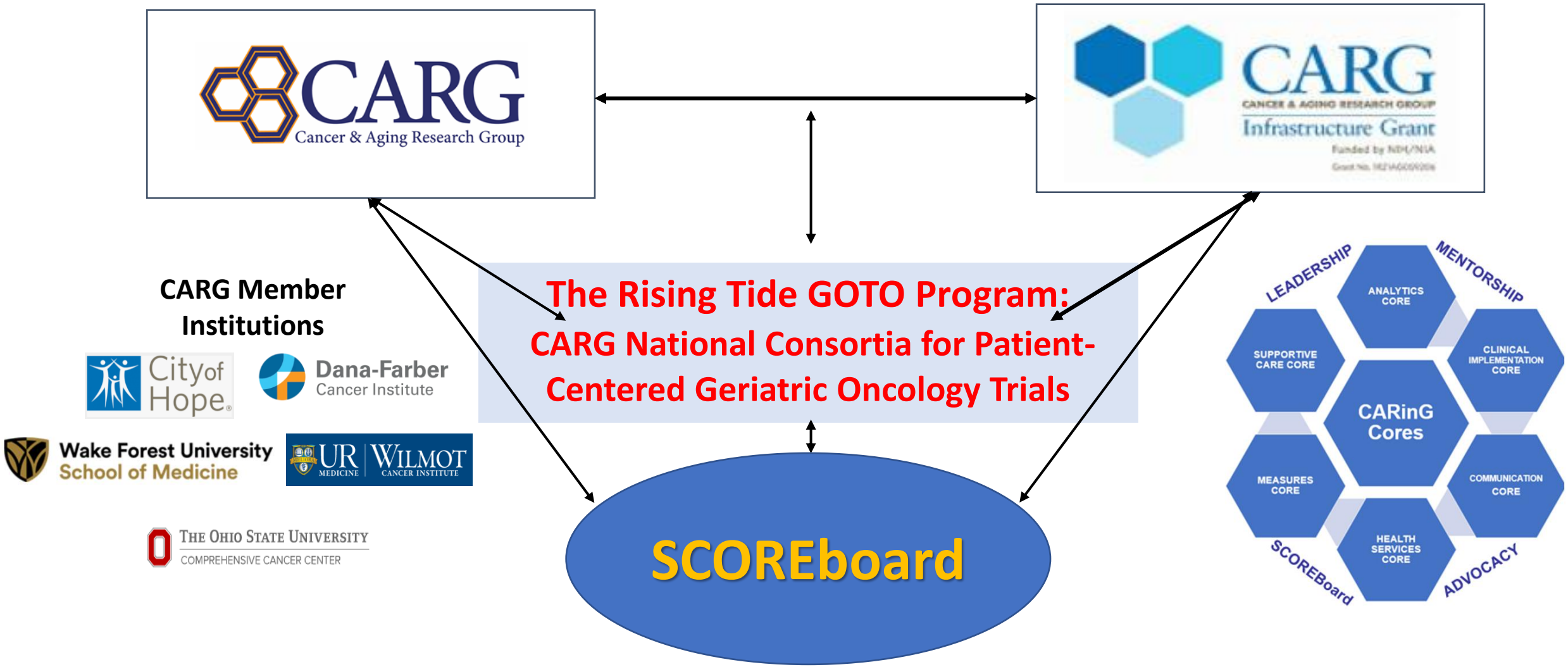
Chuck O'Shea
SCOREboard Co-Chair
Based in California

Geriatric Assessment Measures Across the Studies

- Aligning the CARG GOTO Studies GA Measures with the ASCO Pragmatic Geriatric Assessment (PGA) currently under development
  - Considerations when reconciling the Geriatric Assessment measures:
    - Aligning the CARG GA with the measures proposed by the ASCO PGA
      - Main differences were seen with the psychosocial and cognition measures proposed
    - Disease-specific considerations
    - Understanding scoring and cut-offs for any new measures

Thank you to the Rising Tide program members who are also on the ASCO Geri Onc Guidelines Update Panel, including SCOREboard members John Simmons and Mary Whitehead!

Overarching Infrastructure



Development of a CARG Clinical Trial Infrastructure: Current Initiative

PEOPLE	PROCESSES	POLICIES
Experts from the field leading each study	Formation of a Centralized Data Coordination Center for CARG	Creation of Standard Operating Procedures (SOPs) for screening and data collection, authorship, etc.
Program Manager, Statistical Team, and Clinical Research Assistants lead the COH GOTO data coordinating center	Regulatory: Utilization of single IRB (WIRB) to expedite multi-center approvals	Harmonization of data/measures used across studies (collaboration w/ Measures Core)
Patient Engagement (collaboration with SCOREboard): 2 Patient Partners collaborating with each study team	Multi-Center Databases: REDCap (collaboration with Analytics Core)	Opportunities for Collaborations: Creation of workflows for… - Future Substudies - Criteria to add new participating sites

Long-Term Impact: Creation of the CARG National Consortia of Clinical Trials which will supporting new multi-center studies focused on older adults with cancer

CARG GOTO Clinical Trial Infrastructure

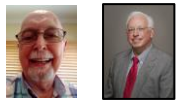
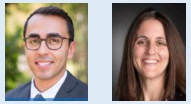
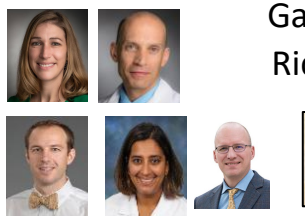
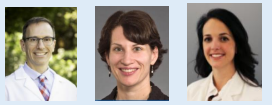
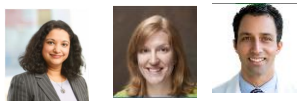
- Utilization of REDCap databases across all 5 clinical trials
- Creating standard processes for:
  - GA data collection
  - GA results and recommendations report
  - Tracking implementation of recommendations based on the GA results
  - Toxicity forms and SOPs for toxicity collection across sites

CARG GOTO Data Coordinating Team





Rising Tide CARG GOTO Studies

Area of Focus	Rising Tide Study Title	Study PIs	SCOREboard Patient Partner(s)
All Cancers: Creating or Optimizing geriatric-assessment decision-making and communication	GA-Driven Interventions with Supportive Care (**GAIN-S**): Telemedicine to Increase Goal Concordant Care for Older Adults with Cancer in the Community	Dr. William Dale Dr. Tanyanika Phillips Dr. Camille Adeimy (City of Hope) 	Lester Wakefield Lewis Mustian 
Breast Cancer: Establishing optimal dosing of agents in vulnerable patients	**DOROTHY**: DOse Reduction Of doceTaxol-based cHemotherapY in vulnerable older women with early-stage breast cancer	Dr. Mina Sedrak (COH) Dr. Rachel Freedman (Dana Farber) 	Mary Whitehead Beverly Canin 
Prostate Cancer: Optimizing treatment initiation (avoiding undertreatment and overtreatment)	PreServing pHysIcal and meNtal hEalth in Men with Prostate Cancer (**SHINE**)	Dr. Alicia Morgans (Dana Farber) Dr. Anthony D'Amico (Dana Farber) Dr. Michael Goodman (Wake Forest) Dr. Sindhuja Kadambi (U of Rochester) Dr. William Dale (COH) 	Gary Wallach Richard Gelb 
Hematological Cancer: Using geriatric assessment guided interventions to optimize treatment tolerance during intensive therapies	Geriatric (G) Assessment Guided Optimization (O) to Accelerate Functional Recovery after Chimeric Antigen Receptor T-cell (CAR-T) Therapy for Patients 60 Years and Older with B-cell Non-Hodgkin Lymphoma or Multiple Myeloma (**GOCART**)	Dr. Andrew Artz (COH) Dr. Ashley Rosko (OSU) Dr. Heidi Klepin (Wake Forest) 	Chuck O'Shea John Simmons 
Lung Cancer: Determining the predictive role of geriatric assessment-guided interventions	Geriatric Assessment and Management (GAM) for Older Adults with Non-Small Cell Lung Cancer Receiving Chemotherapy Radiation Therapy (**GAM-CRT**)	Dr. Supriya Mohile (U of Rochester) Dr. Carolyn Presley (OSU) Dr. Arya Amini (COH) 	Tomma Hargaves Ann Pennella 

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GA-DRIVEN INTERVENTIONS WITH SUPPORTIVE CARE: TELEMEDICINE TO INCREASE GOAL CONCORDANT CARE FOR OLDER ADULTS WITH CANCER IN THE COMMUNITY (GAIN-S)

William Dale, MD, PhD
City of Hope – Duarte

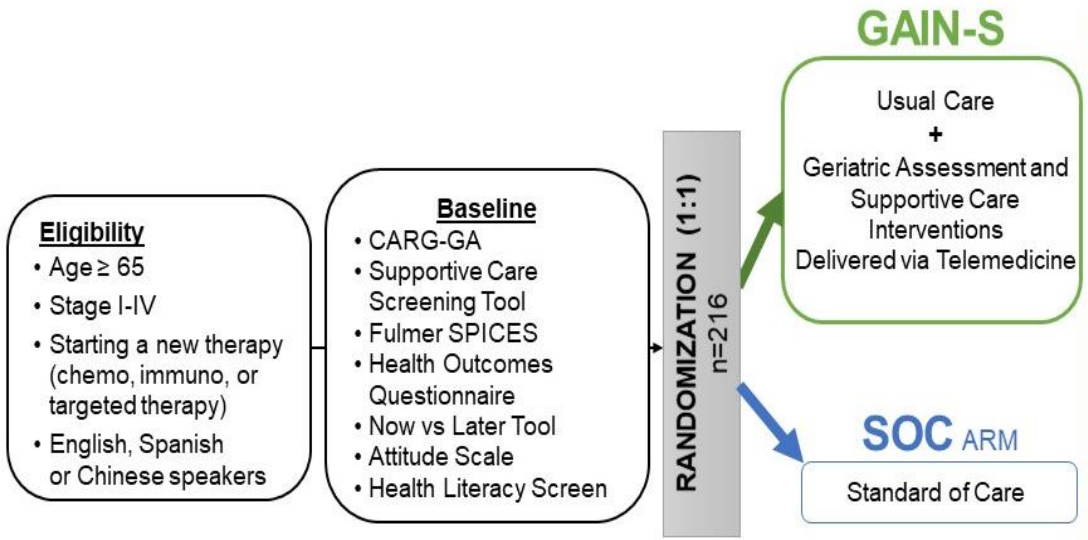
Tanyanika Phillips, MD, MPH
City of Hope – Antelope Valley

Camille Adeimy, MD
City of Hope - Upland

STUDY SCHEMA & OBJECTIVES

Overall Study Objective:

To implement GA-driven MDT supportive care interventions (GAIN-S) through telemedicine to improve communication between the primary care team and patients and caregivers in a remote community setting to increase prognostic discussions and goal concordant care in older patients with advanced cancer



*Prior to study initiation, each site will be quantitatively evaluated utilizing the evidence-based *Association of Community Cancer Centers (ACCC) Geriatric Oncology Gap Assessment tool*; each site would be reassessed at the end of the study for evaluation of process improvement.

Follow Study Procedures Conducted at 3 and 6 months

- CARG-GA
- Supportive Care Screening Tool
- Fulmer SPICES

Primary endpoints:

- Advance Directive Completion
- Documented Prognostic and Goals of Concordant Care Discussions (medical chart review)
- Direct inpatient cost

Secondary endpoints:

- Grade 3+ Toxicities
- Dose Modifications
- Was It Worth It Questionnaire
- Patient-Defined Treatment Goals and Preferences (Health Outcomes Questionnaire, Now vs. Later, Attitude Scale)

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OUTCOMES

- **Primary endpoints:**
  - Implement GA-driven MDT supportive care interventions (GAIN-S) through telemedicine to:
    1) improve communication between the primary care team (oncologist, nurses) and patients and caregivers in a remote community setting to increase prognostic discussions and goal concordant care (primary outcome: advanced directive completion)
    2) to improve cost-saving (primary outcome: direct inpatient cost) in older patients with cancer.

- **Secondary endpoints:**
  - Determine whether GAIN-S implemented in a community setting will lead to a decrease in treatment toxicity.
  - To examine whether GAIN-S intervention will lead to improvement in. hospitalizations, dose delays, dose reduction and discontinuation
  - To compare patient satisfaction using the "Was It Worth It" (WIWI) between the 2 arms at the 3 and/or 6 month timepoint.
  - To compare patient preferences at baseline, using the validated patient-defined treatment preference and goals measures between the 2 arms and longitudinal change, at 3 and/or 6 month timepoint.

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FUTURE IMPACT

- Will provide community oncologists and patients with much-needed expertise from a geriatric-trained multidisciplinary team via telemedicine to help identify the most vulnerable older adults for whom targeted interventions could be implemented to improve QoL and end-of-life care
- This study has the potential to provide a roadmap for others providing geriatric oncology multidisciplinary care in a community setting for an aging oncology population.
- Positive findings from this clinical trial has the potential to be adapted across the 30+ clinical sites within the COH network and provide a model of care for similar community clinical networks to follow in order to improve the care of older patients with cancer.
- Infrastructure:
  - Developing and testing workflows to administer the geriatric assessment remotely and provide standardized reports to the treating providers summarizing GA results and recommendations based on needs identified

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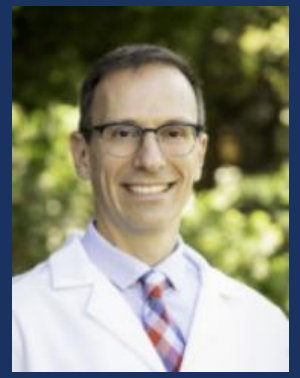
GERIATRIC (G) ASSESSMENT GUIDED OPTIMIZATION (O) TO ACCELERATE FUNCTIONAL RECOVERY AFTER CHIMERIC ANTIGEN RECEPTOR T-CELL (CAR-T) THERAPY FOR PATIENTS 60 YEARS & OLDER WITH B-CELL NON-HODGKIN LYMPHOMA OR MULTIPLE MYELOMA (GOCART)



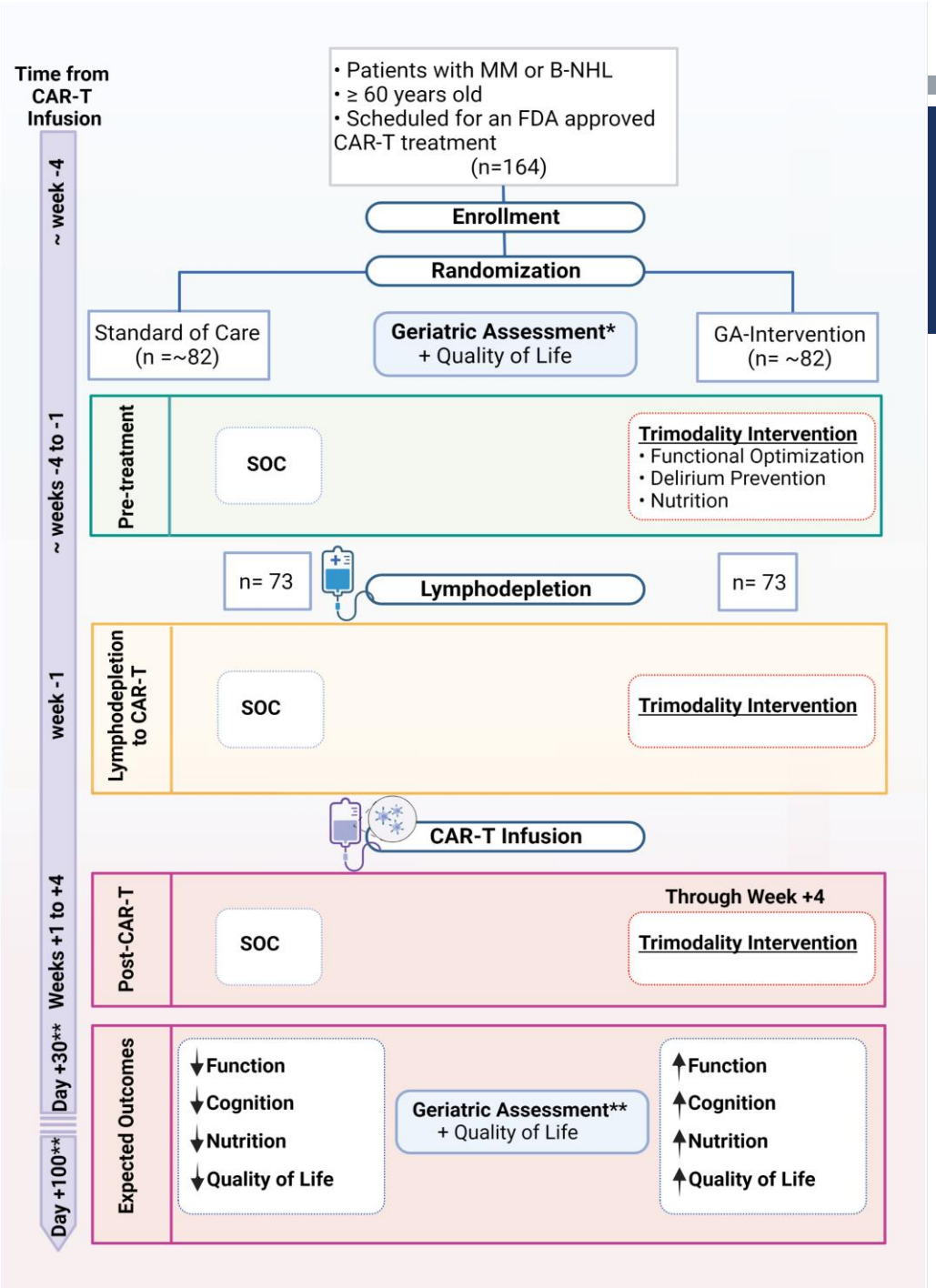
Andrew Artz, MD, MS
City of Hope

Ashley Rosko, MD
The Ohio State University

Heidi Klepin, MD, MS
Wake Forest University

STUDY SCHEMA & OBJECTIVES

Study Objective: Evaluate the effects of a GA-informed intervention in attenuating physical function decline among older patients receiving CAR-therapy at day +30 post-CAR-T infusion



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OUTCOMES

- ***Primary Endpoint(s):***
  - Changes in Short Physical Performance Battery (SPPB) from baseline to day 30 after CAR-T infusion
- ***Secondary Endpoint(s):***
  - Trimodality optimization coordination success requires physical or virtual visits addressing functional optimization, delirium prevention and nutrition before lymphodepletion
  - Frailty Progression
  - Cognitive impairment (MoCA)
  - Malnourishment will be operationalized as weight loss
  - CAR-T-related neurotoxicities will be assessed using ASTCT Consensus Grading for Cytokine Release Syndrome and IEC-associated neurotoxicity syndrome (ICANS) (Lee, et al BBMT 2019). The time to neurotoxicity, the maximum grade, and duration of neurotoxicity will be recorded.
  - Overall Survival, response rate and progression-free survival through one year.

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FUTURE IMPACT

- First randomized interventional study of resilience in the high-toxicity setting hematologic malignancies
- CAR-T and other adoptive cellular therapies one of the fastest growing and promising areas of cancer treatment
- Paradigm shifting approach in mitigating toxicity for cellular therapy-focus on the patient rather than the therapy
- Exportable design promotes immediately changing standard of care if successful

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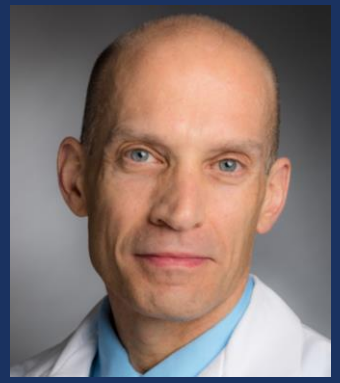
PRESERVING PHYSICAL AND MENTAL HEALTH IN MEN WITH PROSTATE CANCER (SHINE)

National PI:
Alicia Morgans, MD



Anthony D'Amico, MD, PhD

William Dale, MD, PhD
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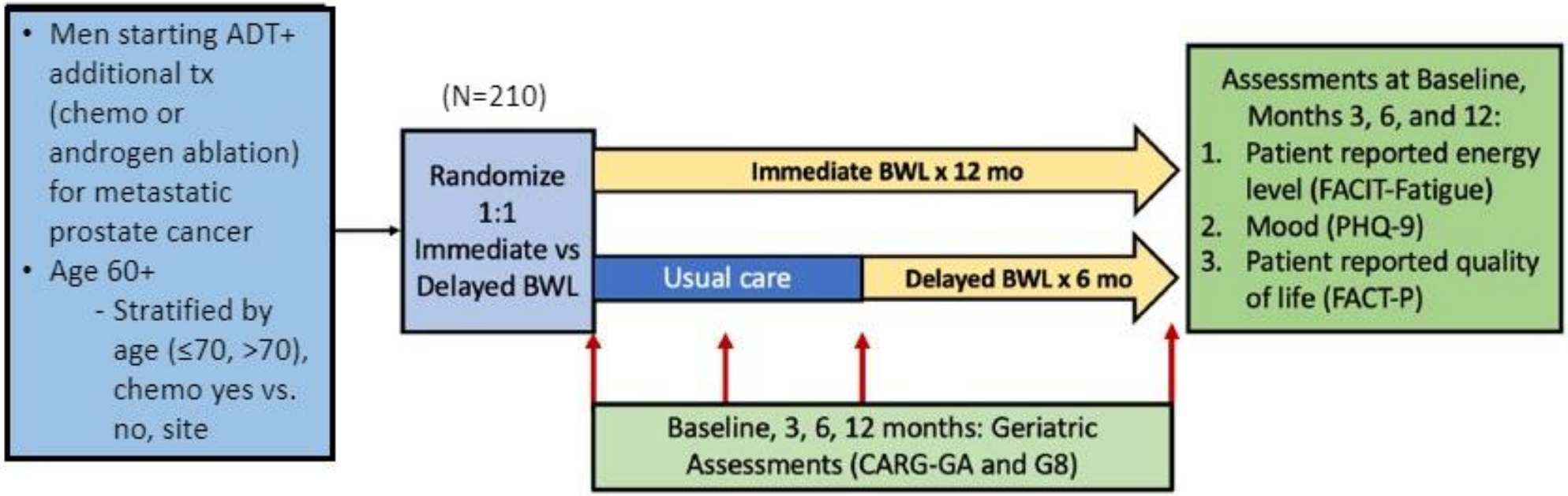
University of Rochester

Michael Goodman, MD
Wake Forest University

Dana Farber Cancer Institute

STUDY SCHEMA & OBJECTIVES

Study Objective: To assess whether exposure to bright white light (BWL) is associated with less treatment related fatigue at 3 months than no exposure to BWL in men with prostate cancer starting combination ADT treatment



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OUTCOMES

- **Primary Endpoint:**
  - Comparison of patient-reported fatigue at 3 months between men treated with immediate vs. delayed bright white light (BWL) therapy
- **Secondary Endpoints:**
  - Compare additional QOL assessments including mood, geriatric assessments, and overall quality of life between immediate and delayed BWL treatment arms
- **Exploratory Objectives:**
  - Comparing the longitudinal trajectory of fatigue, mood, geriatric assessments and overall QOL between immediate and delayed BWL treatment arms

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FUTURE IMPACT

- We hypothesize that bright white light (BWL) exposure will be associated with superior mood, geriatric assessment, and overall quality of life at 3 months in men with prostate cancer receiving combination androgen deprivation therapy than no BWL exposure.
- Patients will have the opportunity to avoid both undertreatment and overtreatment, optimizing cancer and quality of life outcomes with a non-pharmacologic intervention.
- Infrastructure
  - REDCap resources – automated processes for patient registration and randomization for this multi-center study

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DOSE REDUCTION OF DOCETAXOL-BASED CHEMOTHERAPY IN VULNERABLE OLDER WOMEN WITH EARLY-STAGE BREAST CANCER (DOROTHY)

Mina Sedrak, MD, MS
City of Hope

Rachel Freedman, MD, MPH
Dana Farber Cancer Institute

STUDY SCHEMA & OBJECTIVES

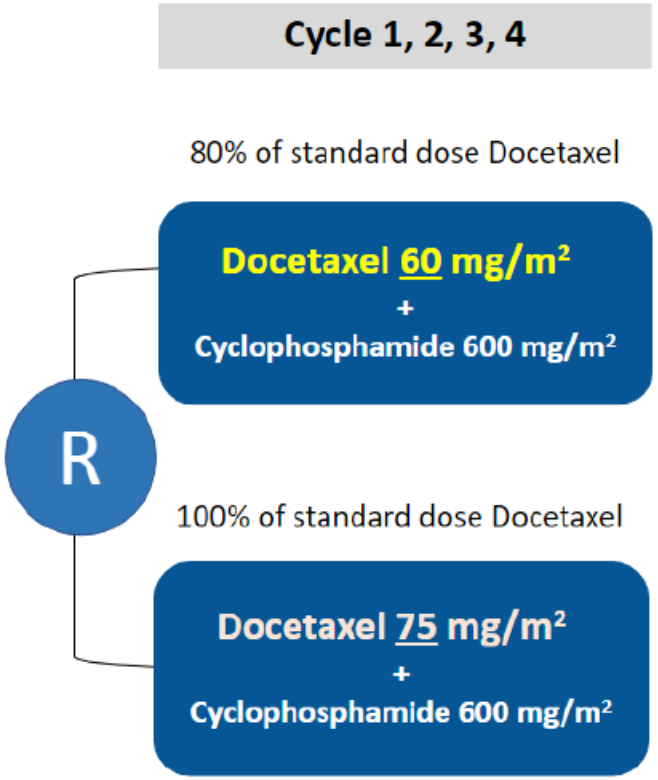
A pragmatic, noninferiority, randomized controlled trial to compare reduced-dose vs. standard-dose docetaxel (T) when combined with cyclophosphamide (C) in the setting of neo/adjuvant 'TC' in vulnerable older patients with early stage HER2-negative breast cancer

Study Objective:

Compare the RDI of two different dosing strategies of docetaxel for the TC regimen in adults age >65 with stage I-III HER2-negative breast cancer, considered as vulnerable (CARG-BC score ≥6)

Eligibility

- Age ≥ 65
- Stage I-III BC
- HER2-neg
- Neo/Adj TC chemo per physician and patient decision
- *CARG-BC score ≥6*
- Baseline GA



*Beyond Cycle 1, TC dose de-escalation is allowed per discretion of the treating physician. Dose escalation of docetaxel in intervention arm is **not** allowed for cycles 2, 3, and 4.*

Concurrent immunotherapy is allowed

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OUTCOMES

- **Primary Endpoint:**
  - Relative Dose Intensity
- **Secondary Endpoints:**
  - Proportion of treatment success
  - Patient-reported symptomatic toxicities (PRO-CTCAE)
  - Clinician-reported toxicities (CTCAE)
  - Patient satisfaction (Was It Worth It)
  - Changes in function and health status over time
  - Survival

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FUTURE IMPACT

- This is one of the first studies to examine a tailored, personalized dosing strategy to optimize delivery of chemotherapy in a vulnerable population, a subgroup of older patients in urgent need of prospective evidence to guide their care.
- This is a pragmatic trial, with dosing modifications after cycle 1 left to the discretion of the clinician, giving more flexibility to clinicians to manage patients as per their standard practice.
- By the end of this study, we will have determined whether an alternate dosing strategy of chemotherapy can be delivered as effectively as standard dosing but with more tolerability in vulnerable older adults with high-risk early breast cancer.

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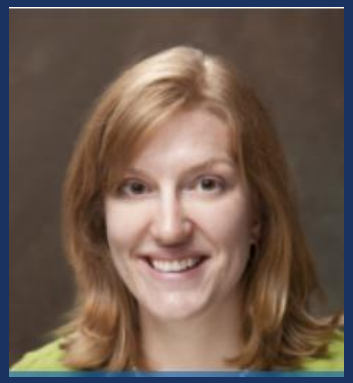
GERIATRIC ASSESSMENT AND MANAGEMENT (GAM) FOR OLDER ADULTS WITH NON-SMALL CELL LUNG CANCER RECEIVING CHEMOTHERAPY RADIATION THERAPY (GAM-CRT)



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Supriya Mohile, MD, MS
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Arya Amini, MD
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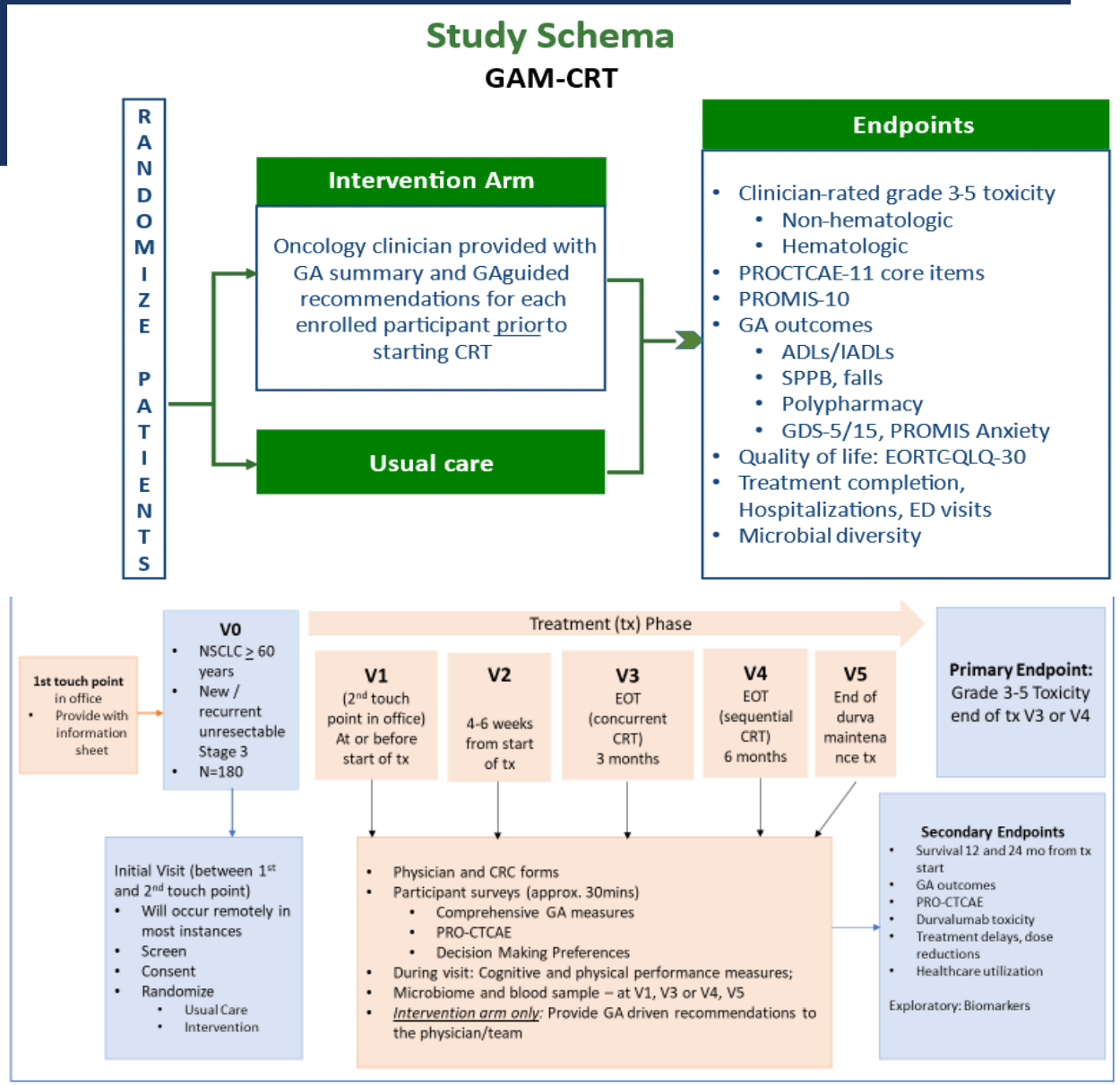
Co-Is:
Daniel Spakowicz, PhD MS
(The Ohio State University)
Consultants:
Melisa Wong, MD MS (UCSF),
Noam VanderWalde, MD MS
(West Cancer Center)

STUDY SCHEMA & OBJECTIVES

Study Objective:

To demonstrate that providing a GA summary and recommendations for GA-directed interventions to oncology teams (intervention group) as compared to usual care (control group) decreases the proportion of older adults with unresectable, stage III NSCLC who experience any grade 3-5 non-hematologic toxicity (primary outcome) from either concurrent or sequential chemotherapy and radiation treatment.



OUTCOMES

- **Primary endpoint**
  - Grade 3-5 non-hematologic toxicity evaluated by the NCI CTCAE criteria v.5.

    The primary outcome will be at end of definitive intent treatment.
- **Secondary endpoint(s)**
  - Overall toxicity
  - Patient-reported symptomatic toxicities as measured by PRO-CTCAE, PROMIS-10
  - GA outcomes such as function (ADL/IADL), physical performance (SPPB, falls), polypharmacy (reduction in medication burden), mood (GDS 5 and PROMIS Anxiety)
  - Quality of life (EORTC-QLQ-30)
  - Treatment completion, hospitalizations/Emergency Department visit rates.
  - Toxicities from durvalumab after completion of adjuvant treatment (13 cycles or 12 months)
- **Exploratory Endpoint:**
  - Explore microbial diversity and blood components at baseline, and at 6 months from treatment initiation as a potential biomarker of treatment-related toxicity and disease response.

FUTURE IMPACT

- Adds knowledge on how GAM can impact outcomes of older adults with stage III NSCLC cancer, including coordination of care with radiation oncology
- Infrastructure
  - REDCap resources for toxicity assessment and intervention
  - Biospecimens (microbiome and blood)

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Next Steps

- Initiation of monthly study team meetings to prep for launch of the studies once IRB approval is received (anticipate approvals within the next 2-3 months)
- Integration of the CARG GOTO program/Rising Tide grant into new grant proposals
  - NIH R33 Infrastructure Grant Renewals (MPIs: W. Dale, S. Mohile, H. Klepin)
  - Receipt of the COH Excellence Award (PI: W. Dale): $50,000 to support the CARG infrastructure
  - Continued fundraising
- Substudies/Future Analyses
  - Creation of workflows to approve new concepts
  - Funding mechanisms

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Cancer and Aging Clinical Trials Infrastructure

Questions:

- What would you like to see persist as part of the CARG Infrastructure following the completion of the Rising Tide effort?
- Can you suggest ways to improve the coordination across sites through the CARG Infrastructure?
- How can we further lower the barriers to patient accrual to studies through the use of the infrastructure?

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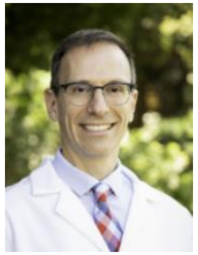
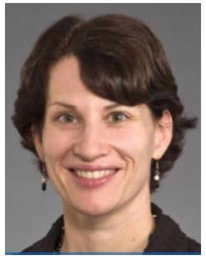
Thank You!

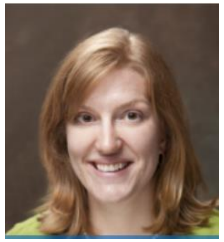
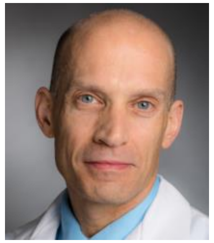
"Growth is never by mere chance;
it is the result of forces working together."
- James Cash Penney





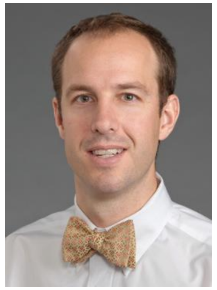











- SCOREboard
- Our Generous Donors
- Administrative and Study Team Members Across all the Sites