Research Center Update
July 2023

Mitch Machtay, M.D.,
NRG Deputy Chair for Research/Chief Scientific Officer
Endowed Professor and Associate Dean for Clinical Oncology Research, Penn State
Remind that Fall 2023 Call for Application for Membership to Committees.
Dose-Escalated Radiotherapy Alone or in Combination With Short-Term Androgen Deprivation for Intermediate-Risk Prostate Cancer: Results of a Phase III Multi-Institutional Trial

Effect of Brachytherapy With External Beam Radiation Therapy Versus Brachytherapy Alone for Intermediate-Risk Prostate Cancer: NRG Oncology RTOG 0232 Randomized Clinical Trial

Pembrolizumab plus Chemotherapy in Advanced Endometrial Cancer

Sustained Preservation of Cognition and Prevention of Patient-Reported Symptoms With Hippocampal Avoidance During Whole-Brain Radiation Therapy for Brain Metastases: Final Results of NRG Oncology CC001

Ten-year Update: NRG Oncology/NSABP B-42 Randomized Trial: Extended Letrozole Therapy in Early-stage Breast Cancer

Stereotactic Radiosurgery vs Conventional Radiotherapy for Localized Vertebral Metastases of the Spine Phase 3 Results of NRG Oncology/RTOG 0631

Krauss DJ; Michalski J; Mileshkin LR; Gondi V; Eskander RN; TMamounas E; Ryu S
NRG Protocol Development

Since birth of NRG (3/1/2014): 83 CTEP; 10 NCORP; + 7 Intergroup Co-led (Grand Total = 100)
### New NRG Trials and their Themes: 1st Half 2023

<table>
<thead>
<tr>
<th>Study Theme</th>
<th>Gender Based</th>
<th>M0 (or Oligo-M1)</th>
<th>Novel Biomarker</th>
<th>Novel RT/Surg</th>
<th>QOL/PRO</th>
<th>Rare Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EAY191-N2</strong></td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>ComboMATCH: Phase II Fulvestrant and Binimetinib for HR+ metastatic breast CA with NF1 mutation/del.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EAY191-N4</strong></td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>ComboMATCH: Phase IIR Selumetinib +/- Olaparib for recurrent Ovarian or Endometrial CA with Ras pathway mutation.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GY028</strong></td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase IB – IIR: Megace +/- Ipatasertib for recurrent/metastatic endometrial CA.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BR008</strong></td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase III Radiation vs. no Radiation for ‘low risk’ HER2 positive breast CA.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LU008</strong></td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase III Standard chemoradiation vs. SBRT followed by chemoradiation for selected stage III NSCLC.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Targeted Therapy Directed by Genetic Testing in Treating Patients with Locally Advanced or Advanced Solid Tumors, The ComboMATCH Screening Trial

https://ecog-acrin.org/clinical-trials/eay191-combomatch/

STATUS: ACTIVE

- EAY 191-N2: Fulvestrant + Binimetinib in HR+ Breast CA with NF1 mutation/deletion
- EAY 191-N4: Selumetinib + Olaparib in GYN cancers with RAS pathway mutations
- EAY 191-E4: Paclitaxel + Nilotinib in cancers resistant to prior taxane therapy
- EAY 191-S3: Paclitaxel + Ipatasertib in cancers with AKT mutations

NCTN Goal: ~20 active ComboMATCH studies at any given time
RT Technology: NRG Lung Trial LU-008 Activated!

Eligibility
• Stage III (or N+ stage II)
• Inoperable
• Primary tumor < 7 cm
  • >2 cm from node(s)
• PS 0-2
• Eligible for post-CRT immunotherapy

Based on a phase I/II study of 55 pts (NCT03141359)
With median f/u of 13.8 mo. there are only 2 regional failures and 0 local failures
(Heinzerling, ASCO 2020, Pract Radiat Oncol 2023)

PI’s: Charles Simone MD and John Heinzerling MD
RT Technology: NRG Brain Met BN009 Relaunched!

Eligibility
- Recurrent brain metastases
- Prior radiosurgery
- New met velocity rate > 4 per year.
- Lung, breast, melanoma, GI or renal CA

Stratify
- Velocity of new BM’s
- Immunotherapy use
- DS-GPA score

Salvage radiosurgery

Hippocampal-Sparing whole brain RT (plus optional SRS boost)

Randomization is 1:1

1º endpoint: 1-yr Neurologic Death Rate

Sample Size: 350 pts

PI’s: Vinai Gondi MD (Northwestern); Michael Chan (Wake Forest)
NRG Developing Trials – Currently N=28

- Brain: 3
- Breast: 1 (1 NCI-approved)
- GI: 2
- GU: 3 (1 NCI-approved)
- GYN: 5 (2 NCI-approved)
- DT GYN 2 (2 NCI-approved)
- H&N : 5 (2 NCI-approved)
- DT Combo-Match 2 (1 NCI-approved)
- NCORP: 5 (2 NCI approved with R01)
Selected NRG Research Center Projects

- Preparing 2024 NRG Grant.
- Advancing Themes:
  - ‘Right-sizing’ Intensity of Therapy
  - Optimizing Diversity and Inclusion
  - ‘Curing’ Oligometastatic Cancer
  - Developing new ComboMATCH arms
- Organizing Working Groups in each Committee
- Streamlining:
  - Protocol eligibility requirements
  - Pragmatic designs
  - Modality QA reviews
- Novel Ancillary Projects, e.g. AI discovery and validation
Ancillary Projects (AP’s)

Thank you to our top APC ‘Peer Reviewers’

- Steve Braunstein (UCSF)
- Paul Brown (Mayo)
- Steve Chang (Henry Ford)
- Stephen Chun (MDAH)
- Paul DiSilvestro (Women & Infants)
- Christina Henson (Oklahoma U)
- Sophia Kamran (MGH)
- Bridget Koontz (GenesisCare/ECU)
- Simon Lo (Univ. Wash.)
- Rimas Lukas (Northwestern)
- Nitin Ohri (Einstein/Montefiore)
- Michael Vogelbaum (Moffitt)
- Trisha Wise-Draper (U Cincinnati)

APC Chair
Suzanne Baldwin
APC Admin Manager
apc@nrgoncology.org
Thank you for Joining our NRG Meeting!

Questions, including PI requests to attend RSC meeting (Wed. 7/26)
• Mitch Machtay: mmachtay@pennstatehealth.psu.edu
• Ronnie Alvarez: Ronald.Alvarez@vumc.org
• Jame Abraham: abrahaj5@ccf.org

Thank you to the 3 Research Centers in Pennsylvania, Led by:

• Nancy Soto
• Kia Neff
• Francy Fonzi