参加報告ー放射線治療G

群馬大学腫瘍放射線学
群馬大学重粒子線医学研究センター
岡本　雅彦

Radiation Oncology Committee Meeting Agenda
CENTER OF INNOVATION IN RADIATION ONCOLOGY (CIRO)

Date:	Friday, July 21, 2023
Start and End Time:	8:00am- 10:00am Eastern Time
Chair:	Evan Wuthrick, MD
Co-Chairs:	Ivy Petersen, MD and Charles Simone II, MD

Meeting Description:

1. Provide information on the latest developments related to the Imaging and Radiation Oncology Core (IROC) Group and NRG Oncology. Learn about mechanisms of quality assurance and protocol development as they relate to innovative technology in radiation oncology.
2. Describe different aspects of the field of medical physics such as credentialing for advanced technologies.
3. Discuss the most recent findings and technological advances in radiation oncology for multiple NRG clinical disease sites.

Eastern Standard Time

8:00 – 8:05	**Welcome / Introduction**	Evan Wuthrick, MD
8:05 – 8:15	**NCI/NCTN Updates** • **NCI Communications** • **NCTN Medical Physics**	Ceferino Obcemea, PhD/Ying Xiao, PhD
8:15 – 8:20	**NRG RO Medical Physics Subcommittee Updates**	Ying Xiao PhD
8:20 – 8:25	**NRG RO Particle Therapy Workgroup Updates**	Charles Simone, MD
8:25 – 8:30	**Imaging Committee**	Amy Fowler, MD/ Dan Pryma, MD
8:30 – 8:45	**Imaging and Radiation Oncology Core (IROC)** • IROC Houston • IROC Philadelphia • IROC (Contouring & Dosimetry)	 Stephen Kry, PhD Denise Manfredi, BS., R.T.(T) Ying Xiao, PhD
8:45 – 9:49	**Disease Site Reports – (Updates on concepts near development) (8mins)**	
	a. H&N	Jimmy Caudell, MD / Jason Chan, MD
	b. Brain	Christina Tsien, MD / Tony Wang, MD
	d. Gyn	Mark Bernard, MD / Eric Donnelly, MD
	e. GI	Evan Wuthrick, MD / Emma Holliday, MD
	f. GU	Dan Krauss, MD / Hiram Gay, MD
	g. Lung	Pamela Samson, MD / Stephen Chun, MD
	h. Sarcoma	Philip Wong, MD / Dian Wang, MD
	c. Breast	Steven Chmura, MD / Simona Shaitelman, MD
9:49 – 10:00	**NRG NCORP Concept Testing Temporarily Modulated Pulsated RT (TMPRT) GMB**	Jiayi Huang, MD, MSCI

agenda

Radiation Oncology Committee Meeting Agenda
CENTER OF INNOVATION IN RADIATION ONCOLOGY (CIRO)

Date:	Friday, July 21, 2023
Start and End Time:	8:00am- 10:00am Eastern Time
Chair:	Evan Wuthrick, MD
Co-Chairs:	Ivy Petersen, MD and Charles Simone II, MD

Meeting Description:

1. Provide information on the latest developments related to the Imaging and Radiation Oncology Core (IROC) Group and NRG Oncology. Learn about mechanisms of quality assurance and protocol development as they relate to innovative technology in radiation oncology.
2. Describe different aspects of the field of medical physics such as credentialing for advanced technologies.
3. Discuss the most recent findings and technological advances in radiation oncology for multiple NRG clinical disease sites.

Eastern Standard Time

8:00 – 8:05	**Welcome / Introduction**	Evan Wuthrick, MD
8:05 – 8:15	**NCI/NCTN Updates** • **NCI Communications** • **NCTN Medical Physics**	Ceferino Obcemea, PhD/Ying Xiao, PhD
8:15 – 8:20	**NRG RO Medical Physics Subcommittee Updates**	Ying Xiao PhD
8:20 – 8:25	**NRG RO Particle Therapy Workgroup Updates**	Charles Simone, MD
8:25 – 8:30	**Imaging Committee**	Amy Fowler, MD/ Dan Pryma, MD
8:30 – 8:45	**Imaging and Radiation Oncology Core (IROC)** • IROC Houston • IROC Philadelphia • IROC (Contouring & Dosimetry)	 Stephen Kry, PhD Denise Manfredi, BS., R.T.(T) Ying Xiao, PhD
8:45 – 9:49	**Disease Site Reports – (Updates on concepts near development) (8mins)**	
	a. H&N	Jimmy Caudell, MD / Jason Chan, MD
	b. Brain	Christina Tsien, MD / Tony Wang, MD
	d. Gyn	Mark Bernard, MD / Eric Donnelly, MD
	e. GI	Evan Wuthrick, MD / Emma Holliday, MD
	f. GU	Dan Krauss, MD / Hiram Gay, MD
	g. Lung	Pamela Samson, MD / Stephen Chun, MD
	h. Sarcoma	Philip Wong, MD / Dian Wang, MD
	c. Breast	Steven Chmura, MD / Simona Shaitelman, MD
9:49 – 10:00	**NRG NCORP Concept Testing Temporarily Modulated Pulsated RT (TMPRT) GMB**	Jiayi Huang, MD, MSCI

agenda

Topics

CIRO
Center for Innovation in Radiation Oncology
NRG Oncology

- Concepts and Protocols
- Disease Site Templates
- Special Projects
- Special Project Highlights
- CIRO Website Updates

NRG ONCOLOGY™

Concepts and Protocols

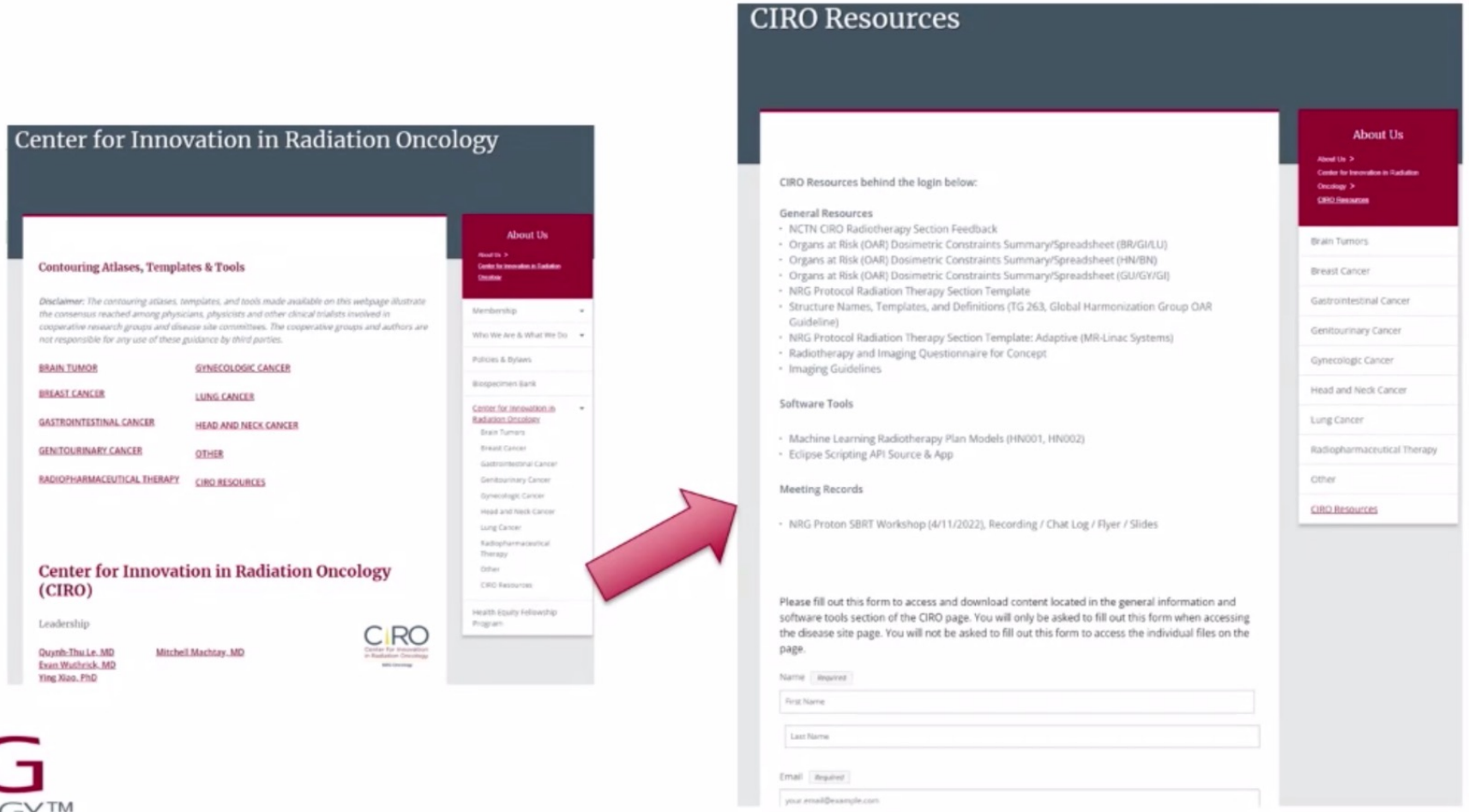
- Concept Review: RT/Imaging
  - •BN2315/TMPRT
  - •HN2317/HN2316/HN2303/HN2115-HN1936-HN2139
  - •LU2301
  - •GI2319-GI2128/GI2312
  - •GU2318/GU2311
  - •UC2304/CV2322/OV2307/CV2220/CV2221
  - •CC2327/CC2325/CC2233

- Medical Physics for developing/amending protocols
  - Consistency with the templates from the CIRO website
  - Verify technical accuracy and consistency
  - •BN012
  - •BR009
  - •HN012
  - •GU009/GU010/GU013/GU002
  - •GY032/GY027
  - •LU008
  - •ETCTN-10642

NRG ONCOLOGY™

CIRO Website Updates

https://www.nrgoncology.org/About-Us/Center-for-Innovation-in-Radiation-Oncology



NRG ONCOLOGY™

NRG ONCOLOGY

Advancing Research. Improving Lives.™

NRG Oncology Imaging Committee

July 17,2023

@NRGOnc NRG Oncology

NCI National Clinical Trials Network
a National Cancer Institute program

NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

NRG ONCOLOGY

Advancing Research. Improving Lives.™

NRG ONCOLOGY IMAGING COMMITTEE MEETING AGENDA

Date:	**Monday July 17, 2023**
Start and End Time:	**1:30PM-3:30PM Eastern/12:30PM-2:30PM Central/ 10:30PM-12:30PM Pacific**
Chair	**Daniel Pryma, MD**
Vice Chair	**Amy Fowler, MD, PhD**

(Eastern Times - PM)

MEETING AGENDA

1:30 - 1:35	**Greetings**	**Amy Fowler, MD, PhD**
1:35 - 1:45	**Update from IROC PHL for NRG Oncology Trials**	**Michael Boss, PhD**
1:45 - 1:55	**Update on RPT Trials**	**Ying Xiao, PhD**
1:55 - 2:30	**Disease Site Updates since last meeting**	

- H&N: Cynthia Wu, MD/ Min Yao, MD
- Brain: Tammy Benzinger, MD
- Breast: Amy Fowler, MD, PhD
- Gyn: Karthik Sundaram, MD
- GI: Aoife Kilcoyne, MD
- GU: Ashesh Jani MD / Bill Hall, MD
- Lung: Andrew Baschnagel, MD
- Sarcoma: Dan Pryma, MD

2:30 – 3:30 NRG Imaging and Medical Physics Joint Seminar

Cardiac Sub-Structure Definition for Radiotherapy Toxicity Avoidance

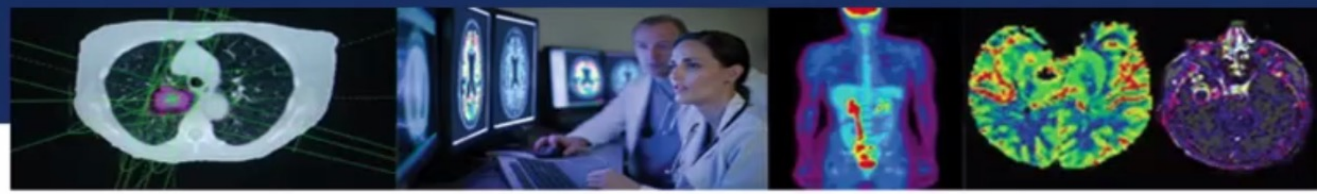
2:30 – 2:55	**Importance of Cardiac Substructure Evaluation in Cancer Therapies**	**Carmen Bergom, MD, PhD**
2:55 – 3:20	**Employing Advanced Technologies for Personalized Evaluation of Cardiac Substructures**	**Carri Glide-Hurst, PhD, DABR, FAAPM**
3:20 – 3:30	**Panel discussion / Q&A**	

NRG ONCOLOGY™

3:30 Meeting Adjourned

RT QA Summary and Projects

Ying Xiao, Ph.D., Dir. IROC Phila. RT



IROC®
IMAGING AND
RADIATION ONCOLOGY CORE
Global Leaders in Clinical Trial Quality Assurance

ACR
AMERICAN COLLEGE OF RADIOLOGY

a National Cancer Institute program

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

Projects for IROC

- AI/Machine learning for case review
- Radiomics extension for MiMSoftware
- Radiopharmaceutical Voxel Dosimetry
- De-ID: Defacing Evaluation
- CodeX

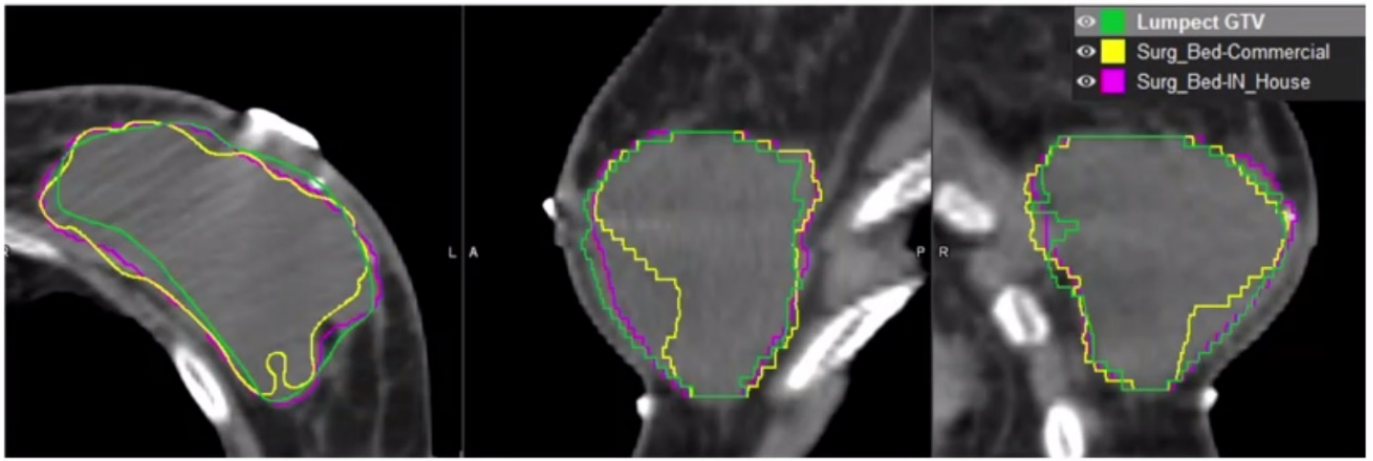
KBP for Plan QA

Disease Site	Trial Name	Target	Technique	KBP Model Status
BN	BN001	Glioblastoma	Photon, Hypo	2B In Use
			Photon, Conventional	In Use
			IMPT	In Use
BR	BR51	Whole Breast	3D or IMRT	2B Built
	BR001	Multiple Mets	SBRT	2B Built
	BR002	Oligomets	SBRT	2B Built
GI	GI006	Esophagus	IMRT	2B Built
			IMPT	2B in Use
	GI0822	Rectal Cancer	3D or IMRT	In Use
	GI002	Rectal Cancer	3D or IMRT	In Use
GU	GU0621	Prostatectomy Bed	3D or IMRT	In Use
	GU0938	Intact Prostate	Cyberknife,IMRT	2B In Use
			IMPT	2B Built
GY	GY006	Cervix	IMRT/Brachy	In Use
HN	HN001	Nasopharyngeal	IMRT	In Use
			IMPT	In Use
	HN002	Oropharyngeal	IMRT	In Use
			IMPT	2B Built
LU	LU1308	NSCLC	Photon	In Use
			IMPT	In Use
CC	CC0631	Spinal Mets	SRS	In Use

OAR Auto-segmentation Models

Site	Existing models				Missing models
	In House model	Carina	TheraPanacea	Clinical trial	Structures
HN	BrainStem, Larynx, Bone_Mandible, OralCavity, Parotids, SpinalCord, and Pharynx, Esophagus_S, Lips, GTV	BrainStem,Chiasm,Mandible,OpticNerves,Parotids,Glnd_Submand, Eyes, MidEars,Innerears, Larynx, Cavity_Oral, Thyroid, Esophagus, BrachialPlexus, Lips, Pharynx, TemporalLobes, Cerebellums, Lens, Cochlea, Brain, Lymph nodes I-VII	BrachialPlexus,BrainStem,Cerebellum,Cochlea,Esophagus,Eyes,Lenses,Larynx,Lips,Mandible,Parotid,OpticChiasm,OpticNerves,Cavity_Oral,SpinalCord,Glnd_Submand, Thryoid,Joint_TM, Cervical lymph nodes I-VII	HN005	
BN	Brainstem, SpinalCord	Brain, Brainstem, Lens, OpticChiasm, OpticNerves, Cerebellums, Lens,Brain, SpinalCord		BN005	
LU	Esophagus, Heart, Lung, and SpinalCord	SpinalCord, Lungs, Heart, Esophagus, Trachea, BronchialTree, Spleen, Kidneys, Stomach, Liver, Pancreas	Breasts, Bronchial Tree, Esophagus, Heart, Humeral Heads, Liver, Lungs, SpinalCord, Trachea, IMC nodes, Interpectoral nodes Level L1-L3, supraclavicular nodes	LU006	
BR	Breasts, Esophagus, Heart, Lung, SpinalCord, Surg_Bed	SpinalCord, Lungs, Heart, Esophagus, Trachea, BronchialTree, Axillary nodes, IMN nodes, supraclavicular nodes		BR007	
GI	SpinalCord, Esophagus, Heart	AdrenalGlands, Esophagus, GallBladder, Kidneys, Liver, Pancreas, PortalVein, Spleen, Stomach	Bag_Bowel, Femoral_Heads, Kidneys, Liver, PenileBulb, Prostate, Rectum, SeminalVes, Colon_Sigmoid, Bladder, CTV_LNPelv	GI007	
GU	Bladder, Femurs, PenileBulb, Rectum, and SeminalVesicle, Urethra	Bladder, FemoralHeads,PenileBulb, Prostate, SeminalVesicle, Rectum		GU008	
				GU009	
				GU010	

BR007 Surg_Bed Segmentation



Surg_Bed	HD (mm)	MDA (mm)	Dice
In House Model	42.3±65.1	5.8±10.5	0.66±0.23
Incremental Model	41.8±59.0	10.4±17.1	0.57±0.24

150 surgical bed contours from patients' data submitted to previous breast trials were used to train the in-house model and the incremental model on commercial platform. The two models were applied on 33 testing cases for comparison.

IROC™
IMAGING AND
RADIATION ONCOLOGY CORE
Global Leaders in Clinical Trial Quality Assurance

AI Assisted QA Workflow

MIM Workflow

Calculated Indices | Screen Capture

↓

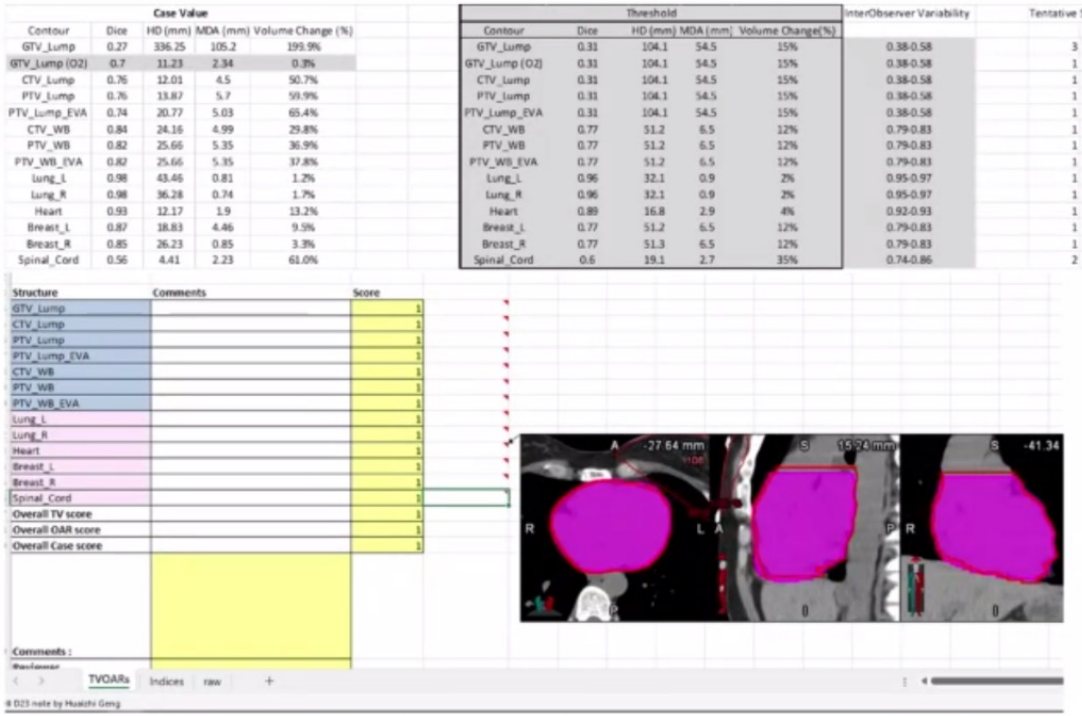
Python Code

Fill Indices to QA Forms | Attach Captures to QA Forms

↓

Filled QA Forms

Tentative QA Scores | Screen Capture for Reference



	Case Value				Threshold					InterObserver Variability	Tentative Score
Contour	Dice	HD (mm)	MDA (mm)	Volume Change (%)	Contour	Dice	HD (mm)	MDA (mm)	Volume Change(%)		
GTV_Lump	0.27	336.25	105.2	199.9%	GTV_Lump	0.31	104.1	54.5	15%	0.38-0.58	3
GTV_Lump (O2)	0.7	11.23	2.34	0.3%	GTV_Lump (O2)	0.31	104.1	54.5	15%	0.38-0.58	1
CTV_Lump	0.76	12.01	4.5	50.7%	CTV_Lump	0.31	104.1	54.5	15%	0.38-0.58	1
PTV_Lump	0.76	13.87	5.7	59.9%	PTV_Lump	0.31	104.1	54.5	15%	0.38-0.58	1
PTV_Lump_EVA	0.74	20.77	5.03	65.4%	PTV_Lump_EVA	0.31	104.1	54.5	15%	0.38-0.58	1
CTV_WB	0.84	24.16	4.99	29.8%	CTV_WB	0.77	51.2	6.5	12%	0.79-0.83	1
PTV_WB	0.82	25.66	5.35	36.9%	PTV_WB	0.77	51.2	6.5	12%	0.79-0.83	1
PTV_WB_EVA	0.82	25.66	5.35	37.8%	PTV_WB_EVA	0.77	51.2	6.5	12%	0.79-0.83	1
Lung_L	0.98	43.46	0.81	1.2%	Lung_L	0.96	32.1	0.9	2%	0.95-0.97	1
Lung_R	0.98	36.28	0.74	1.7%	Lung_R	0.96	32.1	0.9	2%	0.95-0.97	1
Heart	0.93	12.17	1.9	13.2%	Heart	0.89	16.8	2.9	4%	0.92-0.93	1
Breast_L	0.87	18.83	4.46	9.5%	Breast_L	0.77	51.2	6.5	12%	0.79-0.83	1
Breast_R	0.85	26.23	0.85	3.3%	Breast_R	0.77	51.3	6.5	12%	0.79-0.83	1
Spinal_Cord	0.56	4.41	2.23	61.0%	Spinal_Cord	0.6	19.1	2.7	35%	0.74-0.86	2

Structure	Comments	Score
GTV_Lump		1
CTV_Lump		1
PTV_Lump		1
PTV_Lump_EVA		1
CTV_WB		1
PTV_WB		1
PTV_WB_EVA		1
Lung_L		1
Lung_R		1
Heart		1
Breast_L		1
Breast_R		1
Spinal_Cord		1
Overall TV score		1
Overall OAR score		1
Overall Case score		1
Comments :		

TVOARs | Indices | raw

The workflow enables QA forms to be generated in batch mode. 55 QA forms for BR007 and 70 forms for GU010 were generated and waiting to be compared with PI reviews as pilot study.

Radiation Oncology Committee Meeting Agenda
CENTER OF INNOVATION IN RADIATION ONCOLOGY (CIRO)

Date:	Friday, July 21, 2023
Start and End Time:	8:00am- 10:00am Eastern Time
Chair:	Evan Wuthrick, MD
Co-Chairs:	Ivy Petersen, MD and Charles Simone II, MD

Meeting Description:

1. Provide information on the latest developments related to the Imaging and Radiation Oncology Core (IROC) Group and NRG Oncology. Learn about mechanisms of quality assurance and protocol development as they relate to innovative technology in radiation oncology.
2. Describe different aspects of the field of medical physics such as credentialing for advanced technologies.
3. Discuss the most recent findings and technological advances in radiation oncology for multiple NRG clinical disease sites.

Eastern Standard Time

8:00 – 8:05	**Welcome / Introduction**	Evan Wuthrick, MD
8:05 – 8:15	**NCI/NCTN Updates** • **NCI Communications** • **NCTN Medical Physics**	Ceferino Obcemea, PhD/Ying Xiao, PhD
8:15 – 8:20	**NRG RO Medical Physics Subcommittee Updates**	Ying Xiao PhD
8:20 – 8:25	**NRG RO Particle Therapy Workgroup Updates**	Charles Simone, MD
8:25 – 8:30	**Imaging Committee**	Amy Fowler, MD/ Dan Pryma, MD
8:30 – 8:45	**Imaging and Radiation Oncology Core (IROC)** • IROC Houston • IROC Philadelphia • IROC (Contouring & Dosimetry)	 Stephen Kry, PhD Denise Manfredi, BS., R.T.(T) Ying Xiao, PhD
8:45 – 9:49	**Disease Site Reports – (Updates on concepts near development) (8mins)** a. H&N b. Brain d. Gyn e. GI f. GU g. Lung h. Sarcoma c. Breast	 Jimmy Caudell, MD / Jason Chan, MD Christina Tsien, MD / Tony Wang, MD Mark Bernard, MD / Eric Donnelly, MD Evan Wuthrick, MD / Emma Holliday, MD Dan Krauss, MD / Hiram Gay, MD Pamela Samson, MD / Stephen Chun, MD Philip Wong, MD / Dian Wang, MD Steven Chmura, MD / Simona Shaitelman, MD
9:49 – 10:00	**NRG NCORP Concept Testing Temporarily Modulated Pulsated RT (TMPRT) GMB**	Jiayi Huang, MD, MSCI

agenda

NRG ONCOLOGY

Advancing Research. Improving Lives.™

Head and Neck Updates

July 2023 Meeting

@NRGOnc NRG Oncology

NCI National Clinical Trials Network
a National Cancer Institute program

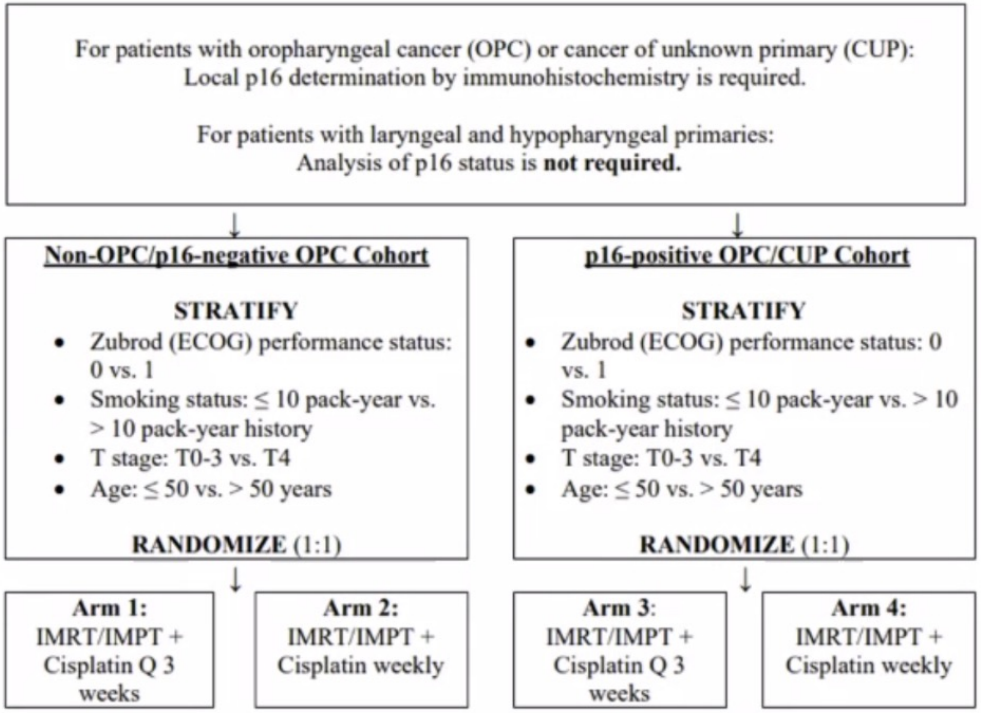
NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

IMS Operator

H & N Active Studies

Protocol	Ph	Title	PI	Activation	Accrual	Disease
HN001	II/III	Randomized Phase II/III Studies of Individualized Treatment for NPC Based on Biomarker Epstein Barr Virus (EBV) DNA	Nancy Lee, MD	04/21/14	154/170 detectable EBV 512/632 undetectable EBV	EBV+ NPC
HN005	II/III	Randomized Phase II/III Trial of Reduced-Dose Reduced-Field Radiation Therapy Alone or in Combo with Chemotherapy or Immunotherapy for Patients with p16-Positive, Non-Smoking-Associated, Locoregionally Advanced OPC	Sue Yom, MD PhD	07/10/19	355/382 Ph II	p16+ OPC
HN006	II/III	Randomized Phase II/III Trial of Sentinel Lymph Node Biopsy Versus Elective Neck Dissection for Early-Stage Oral Cavity Cancer	Stephen Y. Lai, MD	07/08/20	157/228 Ph II	Early-stage Oral Cavity
HN008	I	Phase I Trial with Expansion Cohort of DNA-PK Inhibition and IMRT in Cisplatin-Ineligible Patients with Stage 3-4 Local-Regionally Advanced Head and Neck Squamous Cell Carcinoma (HNSCC)	Maura Gillison, MD PhD	12/10/20	9/42	Cisplatin-Ineligible LA-HNSCC
HN009	II/III	Randomized Phase II/III Trial of Radiation with High-Dose Cisplatin (100 mg/m2) Every Three Weeks Versus Radiation with Low-Dose Weekly Cisplatin (40 mg/m2) for Patients with Locoregionally Advanced HNSCC	Paul Harari, MD	10/27/21	p16 neg 59/230 Ph II p16 pos 83/234 Ph II	LA-HNSCC
HN010	II	NRG-HN010: Docetaxel plus trastuzumab (TH) versus ado-trastuzumab emtansine (T-DM1) for recurrent/metastatic HER2 positive salivary gland cancer	Alan L. Ho, MD PhD	09/30/22	3/116	R/M SDC
RTOG 1216	II/III	Randomized Phase II/III Trial of Adjuvant Radiation Therapy with Cisplatin, Docetaxel-Cetuximab, or Cisplatin-Atezolizumab in Pathologic High-Risk, HPV-Negative Head and Neck Cancer	Paul Harari, MD	03/18/13	303/613 Ph III	Post-op, +SM or ENE
RTOG 3507	II	A Randomized Phase II Study of Pembrolizumab Plus Stereotactic Re-irradiation versus SBRT Alone for Locoregionally Recurrent or Second Primary Head and Neck Carcinoma	Stuart J. Wong, MD	11/14/18	44/102	R/Second Primary HNSCC

NRG-HN009: Randomized Phase II/III Trial of Radiation with High-Dose Cisplatin (100 mg/m2) Every Three Weeks Versus Radiation with Low-Dose Weekly Cisplatin (40 mg/m2) for Patients with Locoregionally Advanced HNSCC



59/230

83/234

Phase II: To determine whether radiation with cisplatin weekly is superior in terms of acute toxicity, as measured by the T-scores (TAME method), to radiation with cisplatin every 3 weeks

Phase III:

1.To determine whether radiation with cisplatin weekly is non-inferior to radiation with cisplatin every 3 weeks in terms of overall survival (OS)

2.To determine whether radiation with cisplatin weekly is superior in terms of acute toxicity, as measured by the T-scores (TAME method), to radiation with cisplatin every 3 weeks

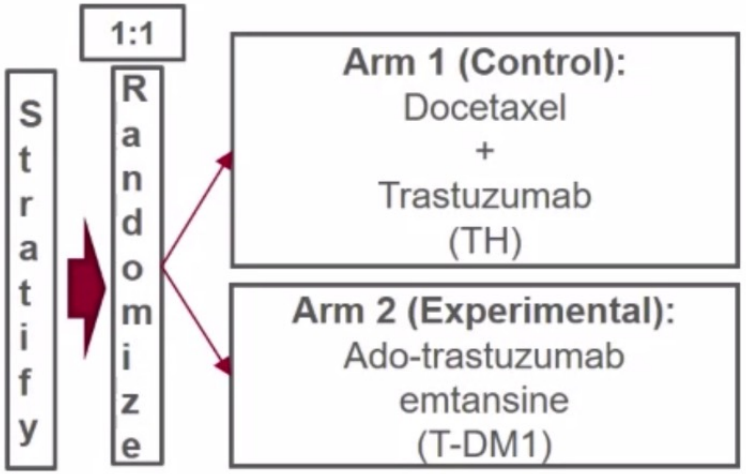
NRG ONCOLOGY™

2021/10 open

PI: Paul Harari

NRG-HN010: Docetaxel plus trastuzumab (TH) versus ado-trastuzumab emtansine (T-DM1) for recurrent/metastatic HER2 positive salivary gland cancer

Recurrent/Metastatic (R/M) or unresectable HER2 overexpressed and/or amplified SGC Patients
- No prior systemic therapy for R/M or unresectable disease (prior hormonal therapy allowed)
- RECIST v1.1 measurable and non-measurable disease



- **Treat until progression, unacceptable AE, withdraw of consent, death, intercurrent illness or other change that makes treatment unacceptable.**
- **Crossover allowed**

STRATIFY BY:
- Prior HER2 targeted therapy in the adjuvant or neoadjuvant setting (Yes vs. No);

Primary Endpoint: PFS determined by local assessment
Secondary Endpoints: ORR, OS, Toxicity (CTCAE), QOL (PRO-CTCAE)
Exploratory Endpoints: ORR with cross-over to T-DM1 and TH, correlative tissue study endpoints

Accrual 3/116

Overall sample size = 116 pts (assuming 5% dropout)
1-sided alpha=0.10, 80% power, HR=0.65, 1:1 randomization

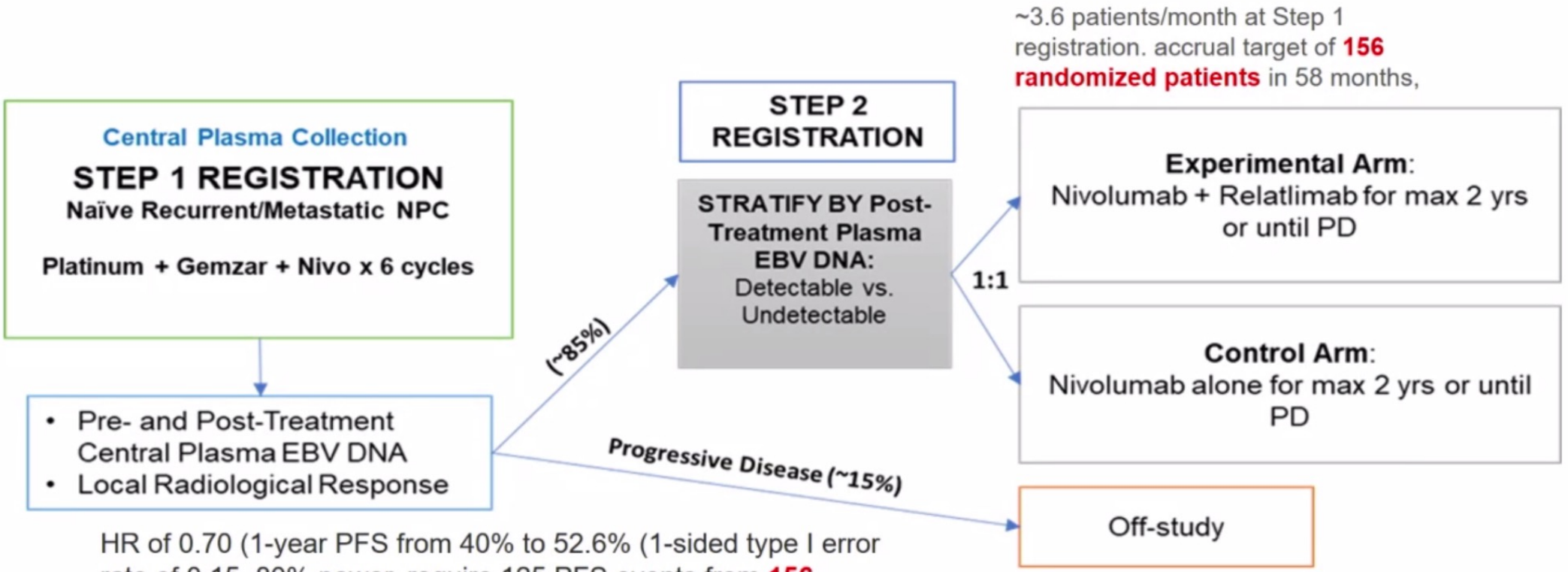
NRG ONCOLOGY™

PI: Alan Ho

H & N Studies In Development

Protocol	Title/Concept	PI	Activation
HN011 (HN007 replacement)	1st line treatment of R/M NPC: Ph II maintenance nivolumab vs. nivolumab + relatlimab following platinum-gemcitabine-nivolumab (RE-MAIN)	Brigette Ma, MD	Q4 2023
HN012 (HN004 replacement)	Randomized Phase II/III Trial of Radiotherapy with Concurrent Xevinapant vs. Cetuximab in Patients with Stage III-IVB Head and Neck Cancer with a Contraindication to Cisplatin (XCELSIOR)	Loren Mell, MD	Q4 2023
RTOG 3521	A Phase II Study of Toripalimab in Combination with Cisplatin and Gemcitabine in Recurrent Metastatic Non-Endemic Nasopharyngeal Carcinoma Systemic Treatment Naïve Patients (TRANSPARENT)	Anna Spreafico, MD	Q1 2024
HN2139 (formerly HN2115)	Chemo-immunotherapy vs. immunotherapy in recurrent/persistent PD-L1 enriched SCCHN undergoing salvage surgery	Nabil Saba, MD	Pending development
HN2316	Randomized Phase III Trial of Immunotherapy with Response-adjusted Surgery versus Standard-of-Care (SOC) Surgery for Resectable Stage III/IV Cutaneous Squamous Cell Carcinoma (CSCC)	Neil Gross, MD	Pending development

NRG-HN011, Strategy for Optimal Maintenance Therapy for EBV+ Recurrent/Metastatic Nasopharyngeal Carcinoma

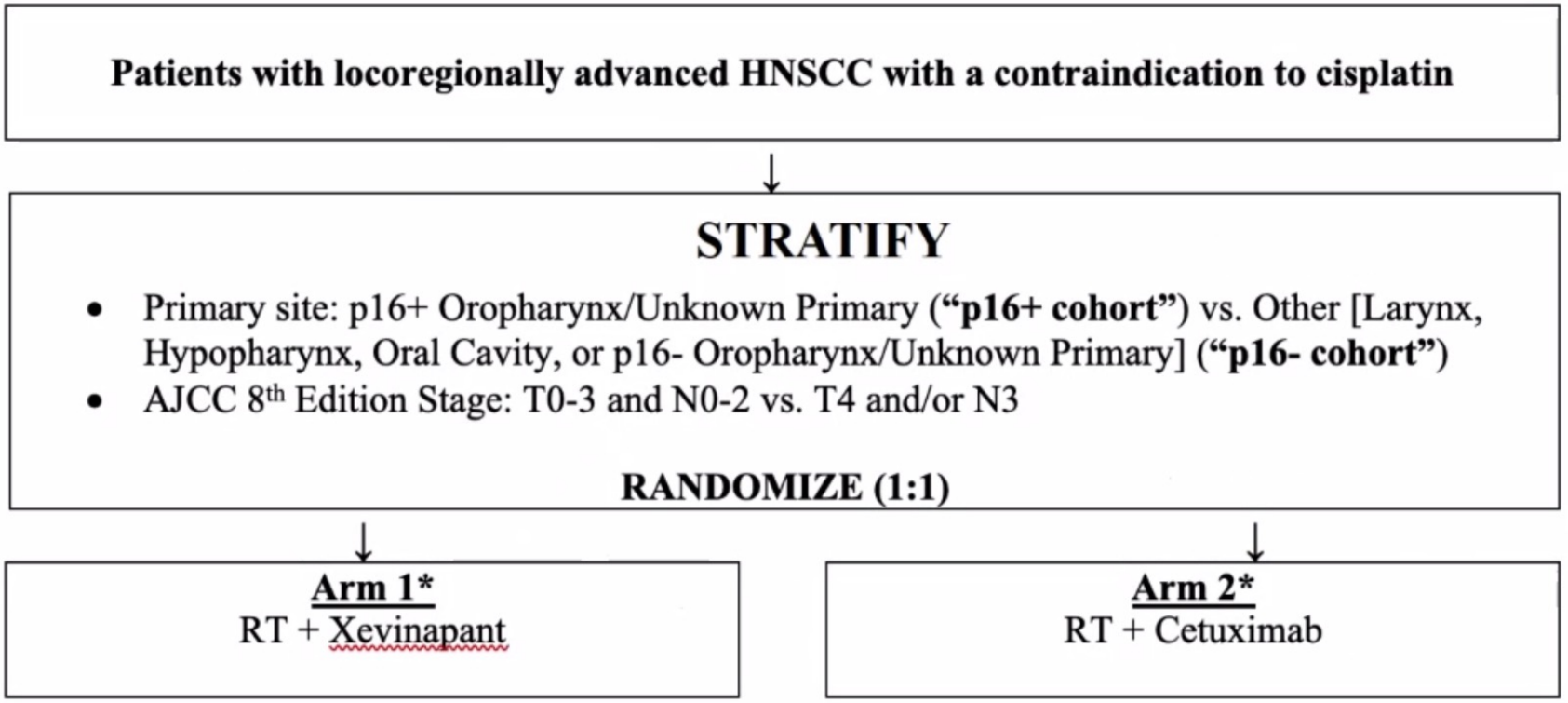


HR of 0.70 (1-year PFS from 40% to 52.6% (1-sided type I error rate of 0.15, 80% power, require 125 PFS events from **156 randomized patients**, after adjusting for a 5% dropout rate

NRG ONCOLOGY™

PI: Brigette Ma

NRG-HN012: RANDOMIZED PHASE III TRIAL OF RADIOTHERAPY WITH CONCURRENT XEVINAPANT VS. CETUXIMAB FOR LOCOREGIONALLY ADVANCED HEAD AND NECK CANCER PATIENTS WITH A CISPLATIN CONTRAINDICATION (XCELSIOR)

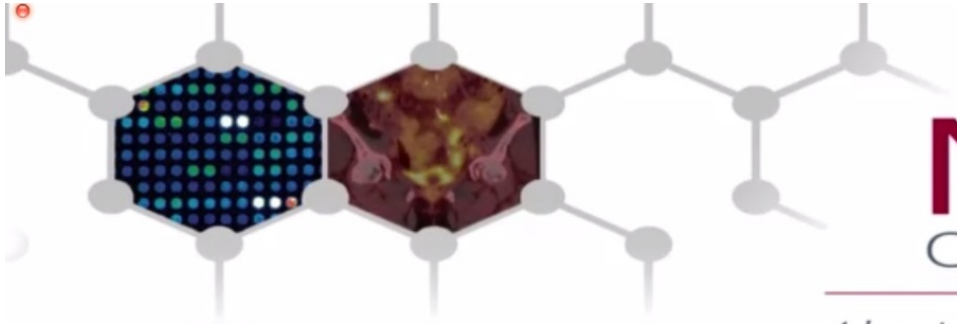


Xevinapant: 200 mg/day orally or enterally for 14 days in **six** 21-day cycles beginning day 1 of RT

Cetuximab: 400 mg/m^2 intravenously (IV) 5-7 days prior to day 1 of RT x **one** cycle, then 250 mg/m^2 IV weekly x **seven** cycles concurrent with RT

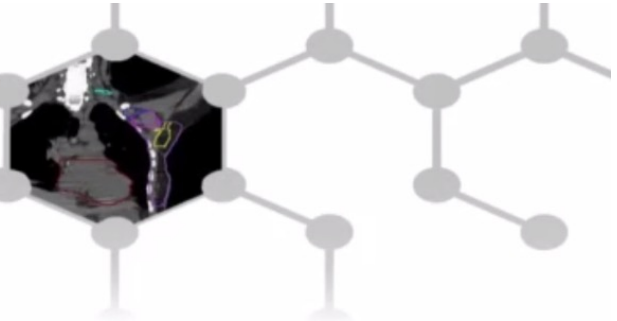
NRG ONCOLOGY™

PI: Loren Mell



NRG ONCOLOGY

Advancing Research. Improving Lives.™



GI Studies

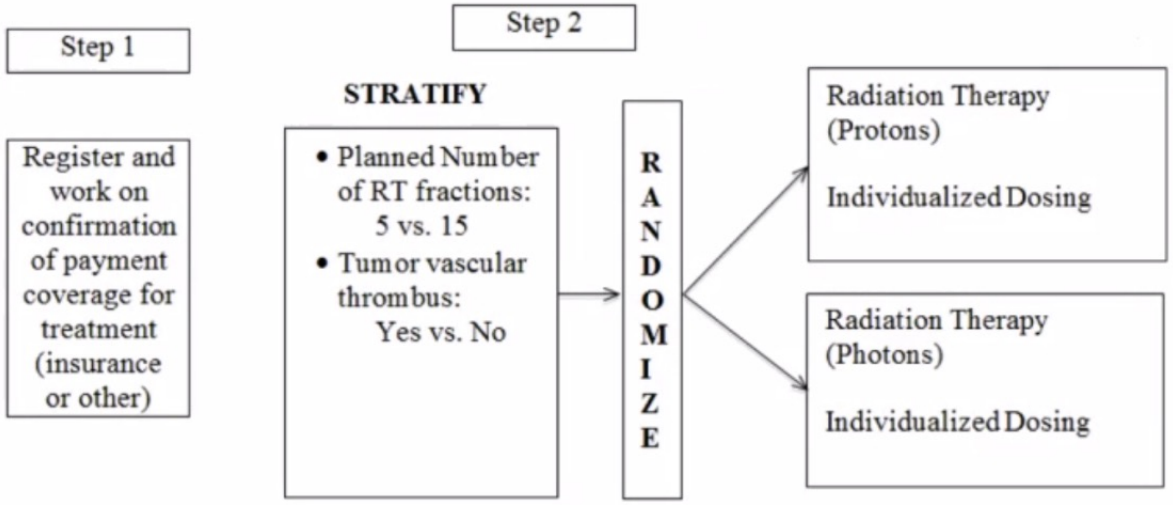
@NRGOnc NRG Oncology

NCI National Clinical Trials Network
a National Cancer Institute program

NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

IMS Operator

GI003 Ph III Protons vs. Photons for HCC



Key Eligibility:
>1cm mass, 3 or fewer tumors, <15 cm single lesion or <10 cm if 2 lesions, <6 cm if 3 lesions

PTV Dose:
5 fxns: 30-50Gy
15 fxns: 37.5-67.5Gy
Depending on mean liver-GTV dose

Activated: 6/21/17
Current Accrual = 86
Target Accrual = 167
Accrual / month = 1.8
17 sites open

NRG ONCOLOGY™

GI006 Ph III Protons vs IMRT for Esophageal

STEP 1 REGISTRATION
Documentation of financial clearance or confirmation of insurance coverage for Proton Therapy (PBT)

↓

STEP 2 REGISTRATION

STRATIFY

- Histology (adenocarcinoma vs. squamous cell carcinoma)
- Stage (I-II vs. III)
- Disease Potentially Resectable (Yes vs. No)
- Induction chemotherapy (Yes vs. No)

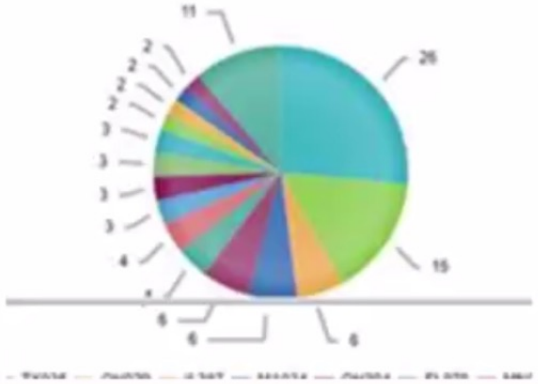
RANDOMIZE*

Arm 1	Arm 2
PBT [50.4 Gy (RBE)] + Carboplatin/Paclitaxel for 28 d	IMRT (50.4 Gy) + Carboplatin/Paclitaxel for 28 d
Followed by surgery 4-8 weeks after completion of radiation	Followed by surgery 4-8 weeks after completion of radiation

Key Eligibility:
Financial clearance and/or insurance authorization for protons must be confirmed prior to registration

PTV Dose:
50.4Gy in 28 fractions with concurrent carbo/taxol

Patient Intervention Accrual by site



Activated 3/16/19
Current Accrual = 126
Target Accrual = 300
Accrual / month = 3
77 sites open

NRG ONCOLOGY™

GI007 Ph I Trial of OBP-301 (Telomelysin) and CRT for inop esoph/gastroesoph cancer

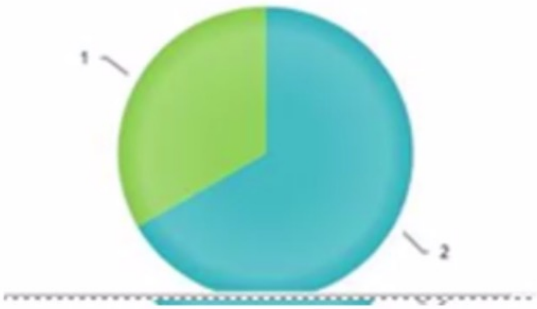
Treatment Regimen with Initial OBP-301 Dose Level:OBP-301 injection must start Thursday or Friday. Chemoradiation must start Monday or Tuesday.

		Week 1	Week 2		Week 3	Week 4		Week 5
	Day -3 (+/- 1 day)	Day 1 (+/- 1 day)	Day 8 (+/- 2 day)	Day 12 (+/- 1 day)	Day 15 (+/- 2 day)	Day 22 (+/- 1 day)	Day 26 (+/- 1 day)	Day 29 (+/- 1 day)
OBP-301 by EGD 1 x10^{12} vp/mL (q14d ±1 day)	×			×			×	
CarboplatinAUC 2		×	×		×	×		×
Paclitaxel 50mg/m^2		×	×		×	×		×
Radiation 1.8 Gy/fraction		Daily Monday-Friday for 5 ½ weeks (28 fractions)						

Key Eligibility:
Not a candidate for surgery, esoph or Siewert I-II GEJ, T2-4 and/or N+

PTV Dose:
50.4Gy in 28 fractions with concurrent carbo/taxol and OBP-301

Patient Intervention Accrual by site



Activated 6/29/20
Current Accrual = 7
Target Accrual = 6-21
Accrual / month = 0.5

Temporarily closed to accrual April 21, 2023 for approximately 3 months for a protocol-specified toxicity analysis.

NRG ONCOLOGY™

Developing Concepts

GI2312: Randomized Phase III Study of Atezolizumab/Bevacizumab versus Stereotactic Body Radiation Therapy followed by Atezolizumab/Bevacizumab in Hepatocellular Cancer (n=380)

Presented to liver TF, survey and final comments being accumulated

NRG ONCOLOGY™

Developing Concepts

NRG 2319: A Phase II Randomized Trial of Dose Escalated Radiation in Locally Advanced Pancreas Cancer (LAPC) Patients (n = 180)

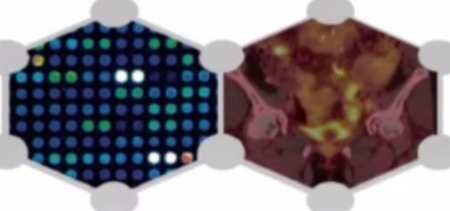
Will be reviewed by pancreatic TF 7/24/23

NRG ONCOLOGY™

Developing Concepts

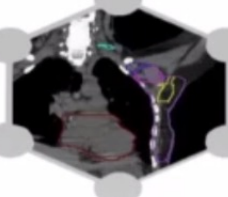
GI2125: HER2 + Esophageal & GE junction adenocarcinoma building on RTOG 1010- arms of the study still being worked out

NRG ONCOLOGY™



NRG ONCOLOGY

Advancing Research. Improving Lives.™



Current and Planned NRG Genitourinary Cancer Trials

Hiram Gay, MD
GU Liaison
NRG Oncology

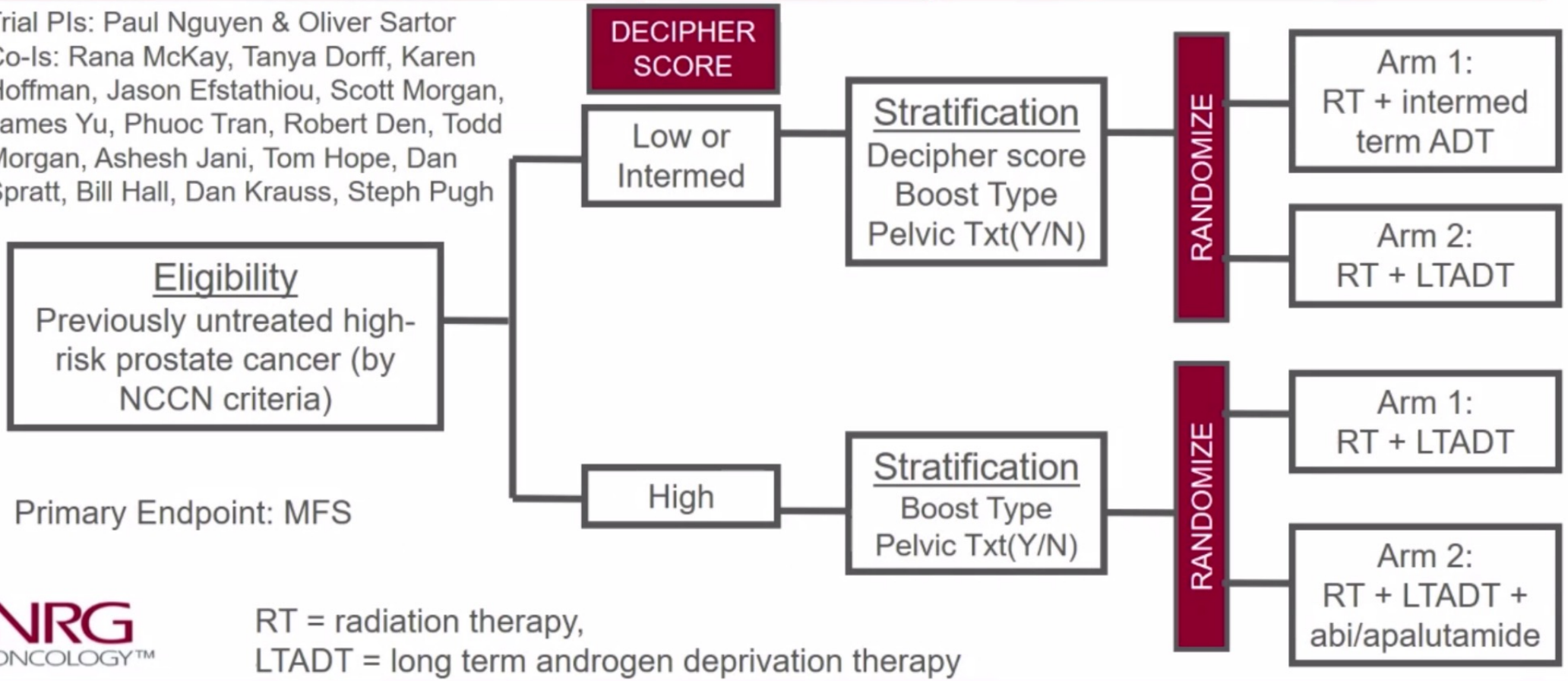
Localized Prostate Cancer Trials

Disease State	Trial	Status
Unfavorable Intermediate Risk	NRG GU010 (GUIDANCE)	Accruing ~11/mo **de**-intensification ~28/mo intensification
High Risk	NRG GU009 (PREDICT-RT)	Accruing ~36/mo **de**-intensification ~22/mo intensification
Higher Risk	NRG GU007	Accruing ~1/month Nearly complete accrual on phase I

NRG ONCOLOGY™

NRG GU009: Parallel Phase III Randomized Trials for High Risk Prostate Cancer Testing Treatment De-Intensification for Men with Lower Genomic Risk and Treatment Intensification for Men with Higher Genomic Risk (PREDICT-RT)

Trial PIs: Paul Nguyen & Oliver Sartor
Co-Is: Rana McKay, Tanya Dorff, Karen Hoffman, Jason Efstathiou, Scott Morgan, James Yu, Phuoc Tran, Robert Den, Todd Morgan, Ashesh Jani, Tom Hope, Dan Spratt, Bill Hall, Dan Krauss, Steph Pugh



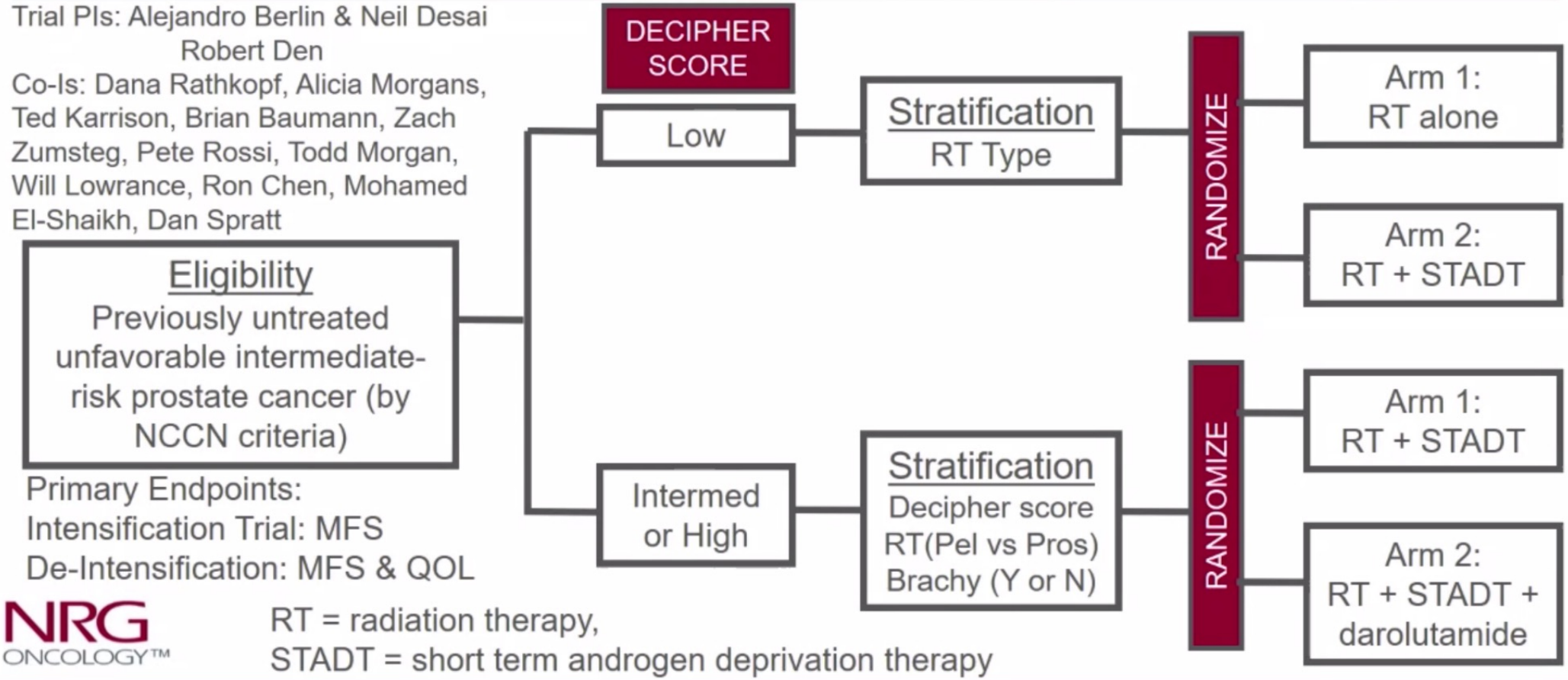
Primary Endpoint: MFS

NRG ONCOLOGY™

RT = radiation therapy,
LTADT = long term androgen deprivation therapy

NRG GU010: Genomic-Risk Stratified Unfavorable Intermediate Risk Prostate Cancer: De-intensification and Intensification Clinical Trial (GUIDANCE)

Trial PIs: Alejandro Berlin & Neil Desai
Robert Den
Co-Is: Dana Rathkopf, Alicia Morgans, Ted Karrison, Brian Baumann, Zach Zumsteg, Pete Rossi, Todd Morgan, Will Lowrance, Ron Chen, Mohamed El-Shaikh, Dan Spratt



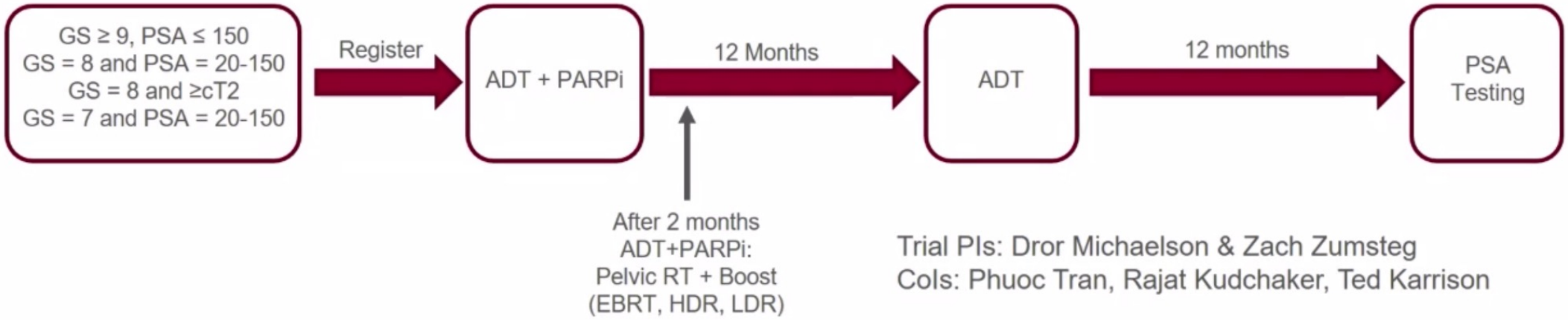
Primary Endpoints:
Intensification Trial: MFS
De-Intensification: MFS & QOL

NRG ONCOLOGY™

RT = radiation therapy,
STADT = short term androgen deprivation therapy

NRG GU007: Phase I & Randomized Phase II Trial of Niraparib with Radiotherapy and Androgen Deprivation Therapy (ADT) in High Risk Prostate Cancer

Phase I Schema



Trial PIs: Dror Michaelson & Zach Zumsteg
CoIs: Phuoc Tran, Rajat Kudchaker, Ted Karrison

Dose Escalation Levels:
- Level 1: Niraparib 100mg PO daily for 12 months, before, during, and after RT
- Level 2: Niraparib for 12 months; 200mg PO daily before and after RT; 100mg PO daily during RT
- Level 3: Niraparib 200mg PO daily for 12 months, before, during, and after RT

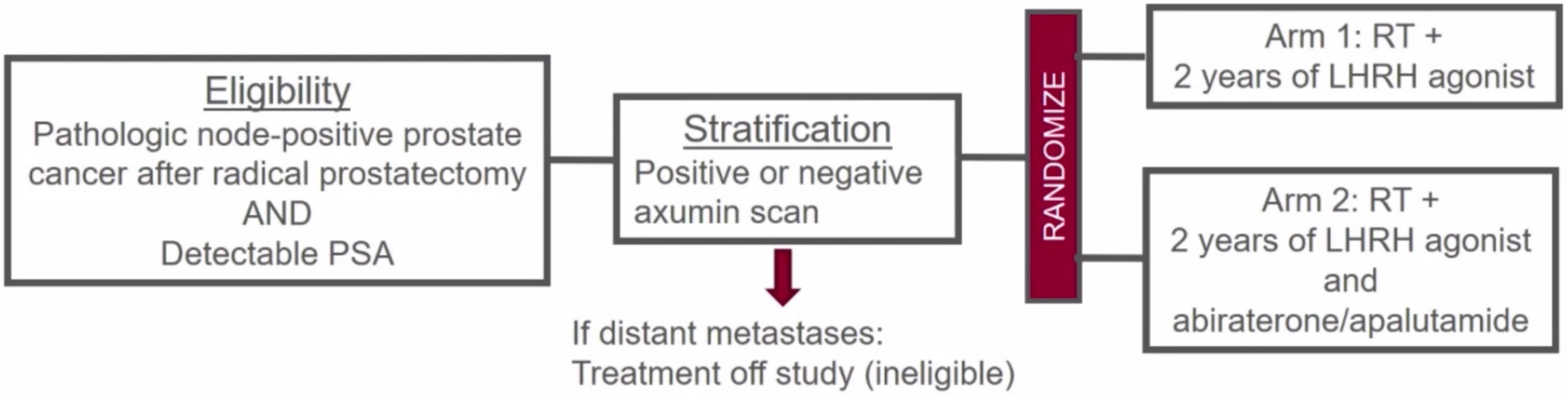
NRG ONCOLOGY™

Post-Operative Prostate Cancer Trials

Disease State	Trial	Status
Node-Positive	NRG GU008	Accruing ~5/month
Oligometastatic (after initial treatment to the prostate)	NRG GU011	Accruing ~2/month

NRG ONCOLOGY™

NRG GU008: Incorporating abiraterone/apalutamide and advanced imaging into salvage treatment for patients with node-positive prostate cancer after radical prostatectomy: A phase III randomized trial



Primary Endpoint: Metastases-Free Survival

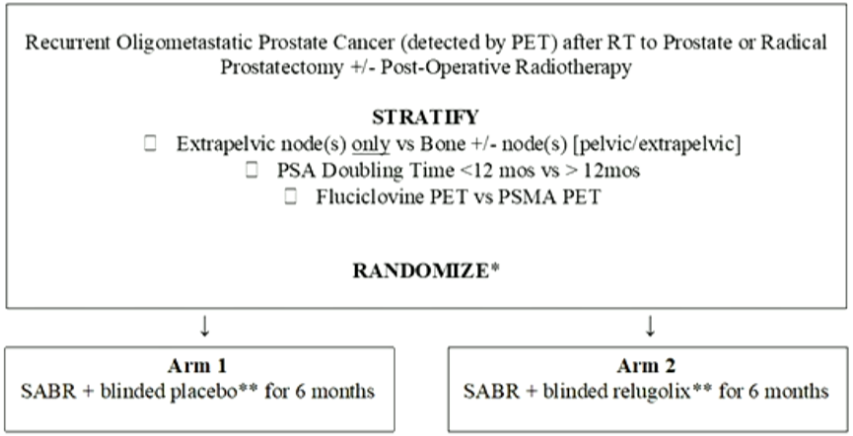
Trial PI: Ron Chen
Cols: Efstathiou, Colleen Lawton, Ashesh Jani, Ed Posadas, Paul Nguyen, David Schuster, Michael Seider, Andre Konski, Bill Hall, Hala Borno, Mihaela Rosu-Bubulac, Neha Vapiwala, Ted Karrison

NRG ONCOLOGY™

NRG GU 011 (PROMETHEAN)

- Patients with oligometastatic (1-5 sites) prostate cancer identified on fluciclovine or PSMA PET
  - Tc-99 bone scan negative
- Primary endpoint: radiological PFS
- Accrual: n = 4/260

NRG-GU011
SCHEMA



*Randomization is 1:1

NRG ONCOLOGY
Advancing Research. Improving Lives.™

Renal Cancer Trials

Disease State	Trial	Status
Metastatic	GU012	Accrued 1 patient

NRG ONCOLOGY™

Stereotactic Ablative RT for Metastatic Unresected RenAl Cell Receiving Immunotherapy

Schema Phase IIR "SAMURI" Trial:

- Metastatic RCC
- At least 1 IMDC risk factors
- Selected for treatment with immunotherapy
- 10 cm or less primary lesion
- Amenable to treatment with SBRT to the primary lesion (DVH based inclusion criteria)

Stratify:

1. Metastatic treatment planned to all distant sites (physician declares intent)
2. Planned Immunotherapy Type (IO-VEGF versus IO-IO)

RANDOMIZE

Total 132

Control

Standard Immunotherapy (dealers choice any IO, per protocol):

Options:
- Nivolumab and ipilimumab
- Pembrolizumab and Axitinib
- Avelumab and axitinib

(Allow for cytoreductive nephrectomy)

44

Experimental

SBRT followed by Standard immunotherapy (dealers choice any IO, per protocol):

Options:
- Nivolumab and ipilimumab
- Pembrolizumab and Axitinib
- Avelumab and axitinib

(Allow for cytoreductive nephrectomy)

88

PRIMARY ENDPOINT: Radiographic Progression free survival (PFS)
SECONDARY ENDPOINTs:

1. Radiographic PFS in predefined histological subgroups
2. Safety/Toxicity/Tolerability of SABR
3. Response (RECIST)
4. Time to second line therapy
5. Overall Survival
6. Use of cytoreductive nephrectomy

PI: Bill Hall
Cols: Rana McKay, Todd Morgan, Felix Feng

NRG ONCOLOGY

Trials in Queue for Development

Disease State	Trial	Design
High-Risk Treatment Naïve Prostate Cancer	GU013 Hi-FIVE Trial (K. Hoffman)	SBRT vs multi-week RT (conventional or moderate hypofx)
Muscle Invasive Bladder Cancer	GU2311 (S. Delacroix, H. Nagar)	Hypofractionated and Adaptive Ultra-Hypofractionated RT for Muscle Invasive Bladder Cancer
Recurrent High-Grade T1 Bladder Cancer	GU2318 (B. Baumann, S. Delacroix)	Pembrolizumab and RT vs. RT and concurrent Chemo (PARRC Trial)
Unfavorable Intermediate-Risk Prostate Cancer	GU2124 (B. Baumann)	Whole-gland RT plus Microboost Ablative RT given Concurrently to ≤2 MR-detected intraprostatic lesions vs. standard whole-gland (MARC-2)

NRG ONCOLOGY™

GU 2216: High-Five
>**GU013**

- Successor concept to NRG GU 005 (accrual completed)
- 5-fraction SBRT for prostate cancer +/- “microboost” to MR-dominant lesions
- Phase IIIR concept looking to accrue > 1200 patients
- Being submitted for GUSC review

NRG ONCOLOGY
Advancing Research. Improving Lives.™

GU 005
低～中リスク前立腺がん
IMRTとSBRTを比較する試験

IMRT arm : 60Gy/20fx or 70Gy/28fx　vs
SBRT arm : 36.25Gy/5fx

Radiation Oncology Committee Meeting Agenda
CENTER OF INNOVATION IN RADIATION ONCOLOGY (CIRO)

Date:	Friday, July 21, 2023
Start and End Time:	8:00am- 10:00am Eastern Time
Chair:	Evan Wuthrick, MD
Co-Chairs:	Ivy Petersen, MD and Charles Simone II, MD

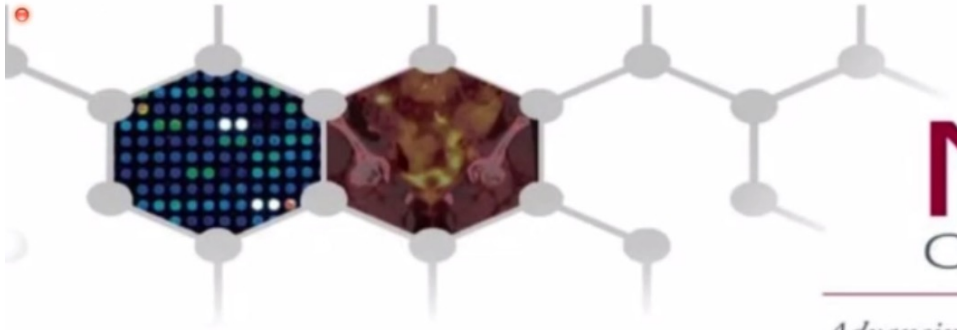
Meeting Description:

1. Provide information on the latest developments related to the Imaging and Radiation Oncology Core (IROC) Group and NRG Oncology. Learn about mechanisms of quality assurance and protocol development as they relate to innovative technology in radiation oncology.
2. Describe different aspects of the field of medical physics such as credentialing for advanced technologies.
3. Discuss the most recent findings and technological advances in radiation oncology for multiple NRG clinical disease sites.

Eastern Standard Time

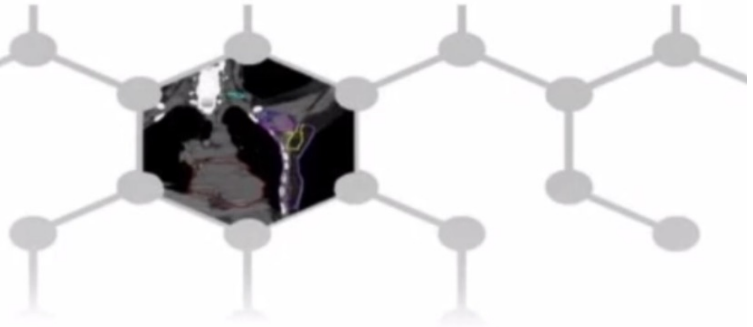
8:00 – 8:05	**Welcome / Introduction**	Evan Wuthrick, MD
8:05 – 8:15	**NCI/NCTN Updates** • **NCI Communications** • **NCTN Medical Physics**	Ceferino Obcemea, PhD/Ying Xiao, PhD
8:15 – 8:20	**NRG RO Medical Physics Subcommittee Updates**	Ying Xiao PhD
8:20 – 8:25	**NRG RO Particle Therapy Workgroup Updates**	Charles Simone, MD
8:25 – 8:30	**Imaging Committee**	Amy Fowler, MD/ Dan Pryma, MD
8:30 – 8:45	**Imaging and Radiation Oncology Core (IROC)** • IROC Houston • IROC Philadelphia • IROC (Contouring & Dosimetry)	 Stephen Kry, PhD Denise Manfredi, BS., R.T.(T) Ying Xiao, PhD
8:45 – 9:49	**Disease Site Reports – (Updates on concepts near development) (8mins)**	
	a. H&N	Jimmy Caudell, MD / Jason Chan, MD
	b. Brain	Christina Tsien, MD / Tony Wang, MD
	d. Gyn	Mark Bernard, MD / Eric Donnelly, MD
	e. GI	Evan Wuthrick, MD / Emma Holliday, MD
	f. GU	Dan Krauss, MD / Hiram Gay, MD
	g. Lung	Pamela Samson, MD / Stephen Chun, MD
	h. Sarcoma	Philip Wong, MD / Dian Wang, MD
	c. Breast	Steven Chmura, MD / Simona Shaitelman, MD
9:49 – 10:00	**NRG NCORP Concept Testing Temporarily Modulated Pulsated RT (TMPRT) GMB**	Jiayi Huang, MD, MSCI

agenda



NRG ONCOLOGY

Advancing Research. Improving Lives.™



A randomized phase 3 study comparing temporally-modulated pulsed radiation therapy (TMPRT) versus standard radiation therapy with temozolomide for elderly patients with newly diagnosed MGMT-unmethylated glioblastoma to prolong symptom deterioration-free survival

NRG-CC2325

Jiayi Huang MD MSCI

Washington University in St. Louis

Temporally-modulated pulsed radiation therapy (TMPRT)

- **TMPRT** (also know as pulsed low-dose rate RT): 0.2Gy pulses, delivered in 10 pulses, with 3 min interval for a total of 2 Gy per day.

  ⟺ FLASH radiotherapy (40-100Gy/secの高線量率で有害事象を低減させる)

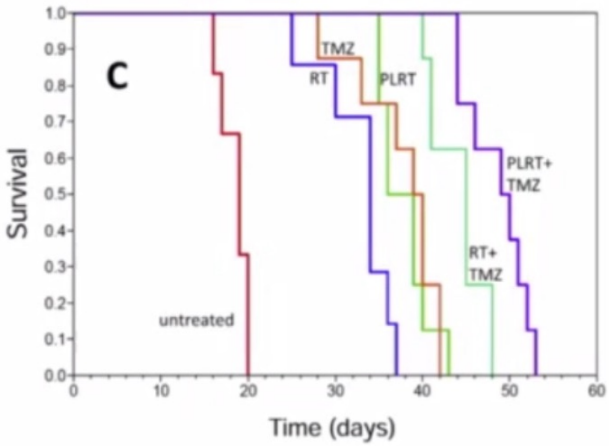
- **Preclinical Data from murine models**: (1) increases radiosensitivity of tumor cell by not activating G2/M arrest, (2) induces less bone-marrow derived immunosuppressive myeloid cells into tumor, (3) reduces radiation-related vascular injury, (4) reduces neuronal death.

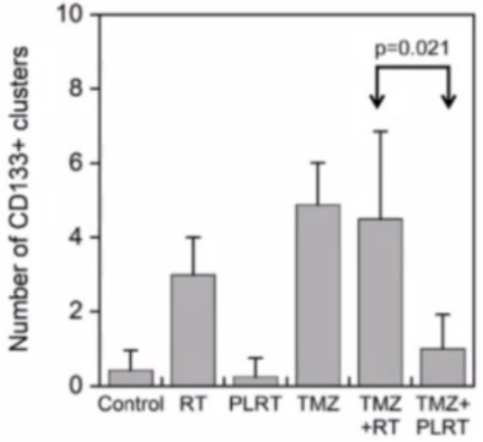
- **Clinical Feasibility:** 352 recurrent GBM or brain tumor patients have been re-irradiated using TMPRT across at least 12 retrospective reports from multiple institutions, including GBM patients with age 71 – 79.

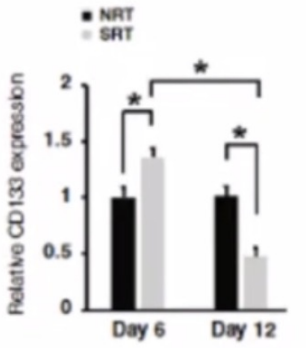
- **Prospective Single-arm Pilot Data**: 20 newly diagnosed non-elderly GBM patients were treated with TMPRT+TMZ, demonstrated promising OS, preservation of QOL and verbal memory.

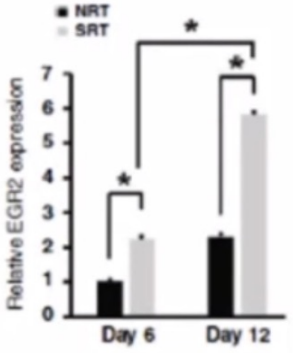
NRG ONCOLOGY™

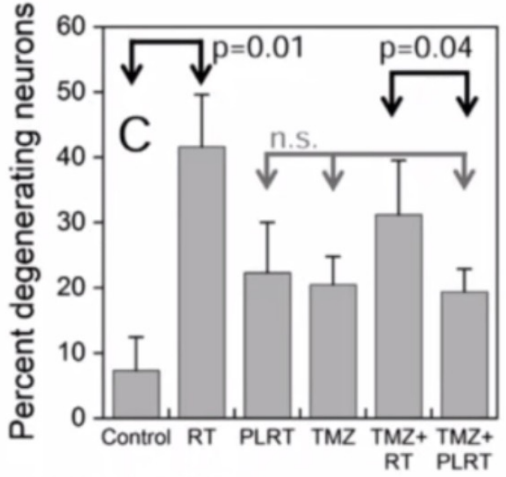
Preclinical: PLRT + TMZ on tumor and TME

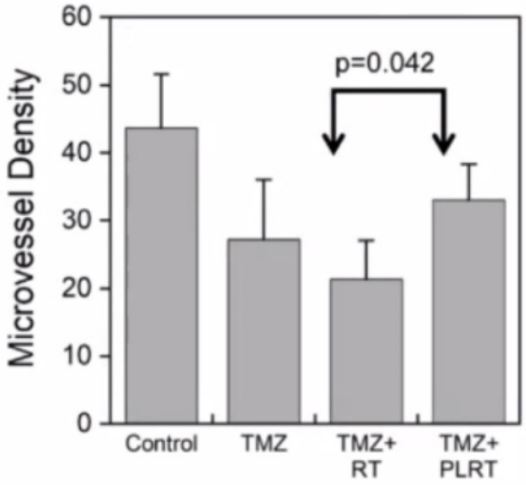


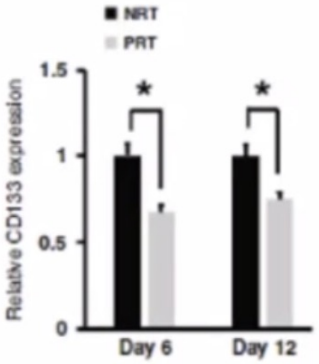


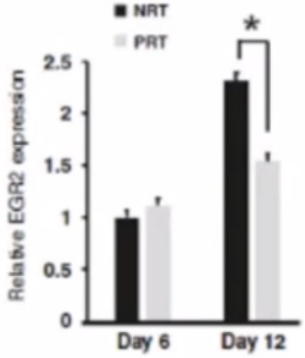










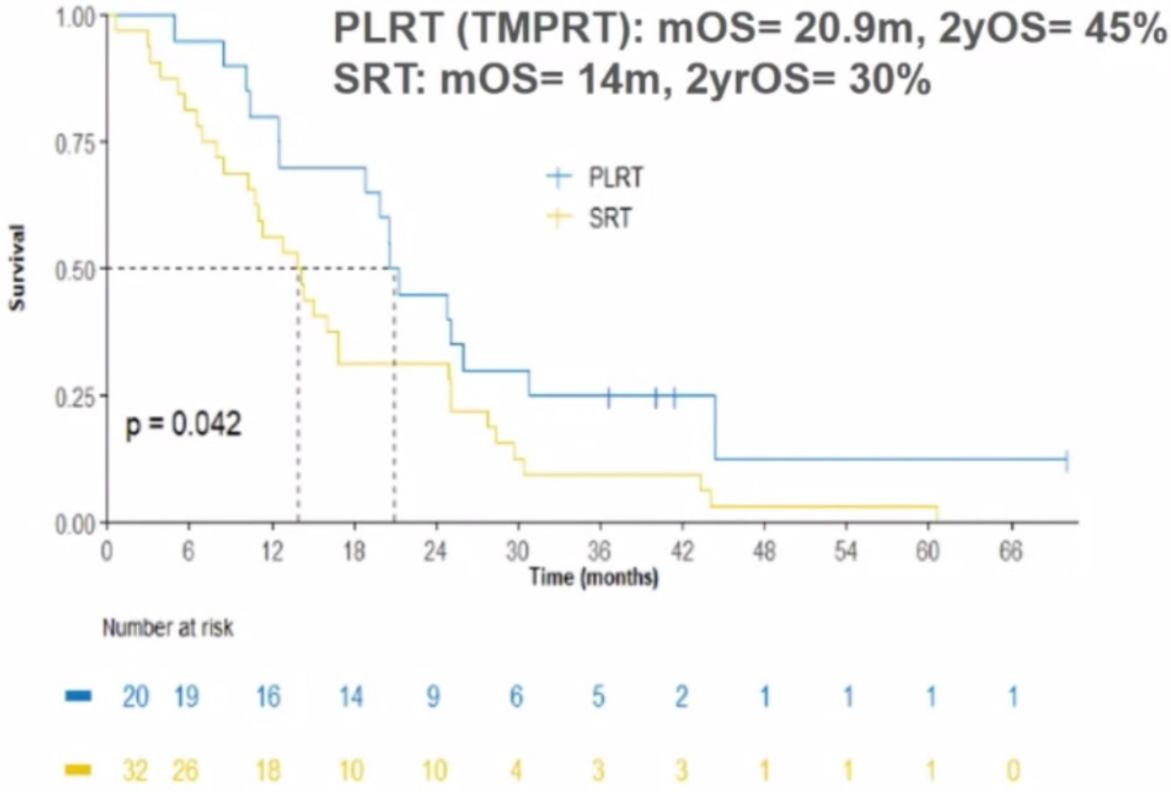


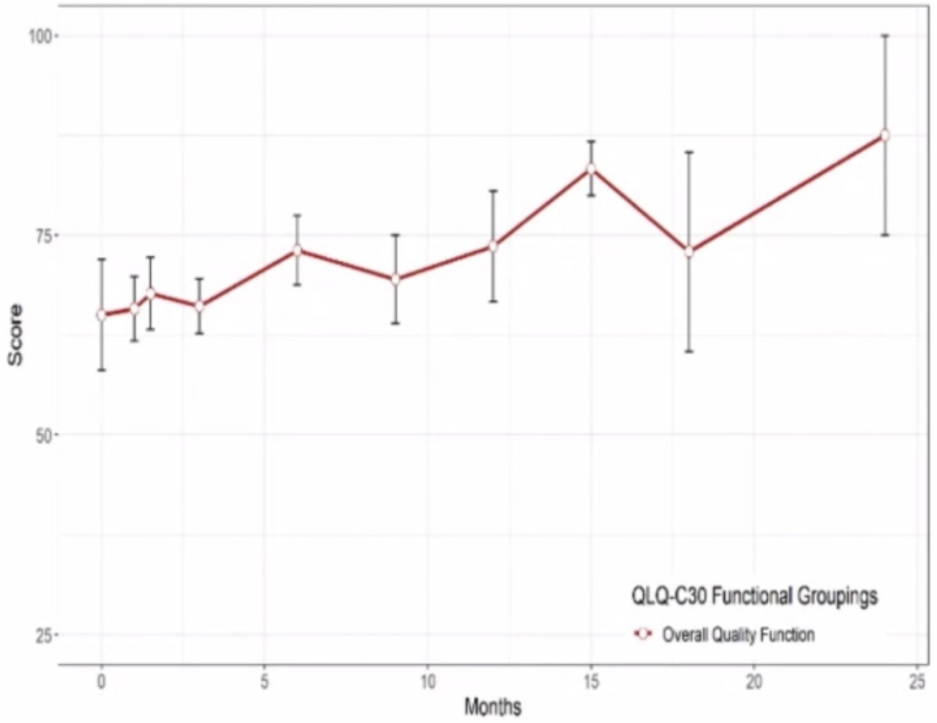
ONCOLOGY™

Lee, Huang, Marples et al, Int J Radiat Oncol Biol Phys 86(5):978-985, 2013.

Parson, Madlambayan et al, British Journal of Cancer 126(6):927-36, 2022.

Prospective Phase 2 Data

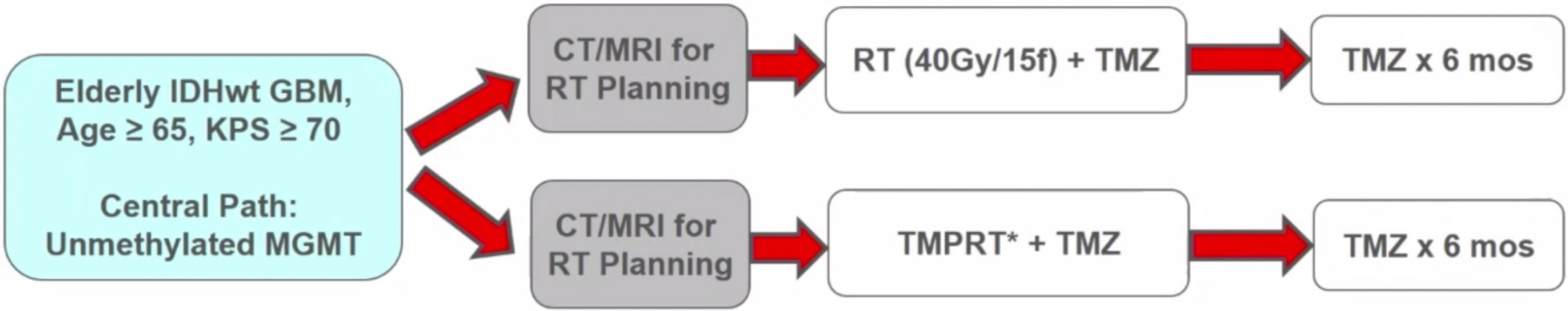




NRG ONCOLOGY™

Almahariq, Chinnaiyan, Dilworth, et al. Neuro-Oncology, 23(3): 447-456, 2021.

Concept: Study Schema



Stratify by:
-RPA: IV vs V
-TTF: Yes vs No vs Undecided
-Symptom burden: <5 vs ≥5

*TMPRT: 0.205Gy x 13 pulses with 3 min interval

PRO: *MDASI-BT, LASA and G8 at baseline, 1 month after RT (month 2), month 4, 6, 9, & 12.*
Proxy Completion Allowed

NRG ONCOLOGY™

Eligibility

- **Inclusion**:
  - IDH-wildtype GBM as per WHO 2021 classification
  - Elderly patient (age ≥ 65)
  - Unmethylated MGMT
  - KPS ≥ 70
  - MDASI-BT baseline symptom burden score < 9
- **Exclusion**:
  - Prior cranial RT (LITT or Gliadel permissible)
  - Other active cancer requiring treatment (allow patients with previously treated cancer in remission or low-risk cancer on observation)
  - Movement disorder that would impede lying flat for 40 min

NRG ONCOLOGY™


10 Years
NRG
ONCOLOGY
2023 SUMMER MEETING