NRG-GU005

Report Based on Data through: 04/30/2019

Phase III IGRT and SBRT vs IGRT and Hypofractionated IMRT for localized intermediate risk prostate cancer

SCHEMA

PATIENT POPULATION

Previously untreated localized intermediate-risk prostate cancer

STRATIFICATION

Risk Group
1. Gleason score 7(3+4) with PSA <10 ng/mL
2. Gleason score 7(3+4) with 10 ng/mL <= PSA < 20 ng/mL
3. Gleason score 6(3+3) with 10 ng/mL < PSA < 20 ng/mL

Use of rectal manipulation
1. No
2. Rectal balloon
3. SpaceOAR
4. SpaceOAR and rectal balloon

RANDOMIZATION

Arm 1: IMRT

70 Gy in 28 fractions of 2.5 Gy to the prostate +/- proximal 1cm of seminal vesicles

Minimal Margins:
8 mm uniform in expansion,
5 mm posteriorly

Arm 2: SBRT

36.25 Gy in 5 fractions of 7.25 Gy to the prostate +/- proximal 1 cm of seminal vesicles

Minimal Margins:
5 mm superior inferior & laterally,
3 mm anterior & posterior

Prostate specific antigen (PSA); Gray (Gy)

Study Chairs:	Rodney J. Ellis, MD	(Principal Investigator/Radiation Oncology)
	Felix Feng, MD	(Translational Science)
	Robert L. Grubb, III, MD	(Urology)
	Robert E. Wallace, PhD	(Medical Physics)
	James Yu,	(Radiation Oncology/ Quality of Life)
	Andre A. Konski, MD, MBA, MA, FACR	(Comparative Effectiveness)
	Cynthia Menard, MD	(MR)
Protocol Statisticians:	Stephanie Pugh, PhD	
	Joseph Rodgers, MS	
Research Associates:	Roseann Bonanni, CTR, CCRP	
	Margaret Kennish AS, CCRC	
Dosimetrist:	Joanne C. Hunter, BS, RT(T)(R)	
Activated:	11/16/2017	
Status:	Accruing	

- **Study Description**
  This is a two-armed randomized phase III study designed to determine whether SBRT can be shown to be superior to hypofractionated IMRT in terms of genitourinary (GU) and gastrointestinal (GI) toxicity in untreated localized intermediate-risk prostate cancer patients. The co-primary endpoints are patient-reported GI and GU toxicity, as measured by EPIC-26 bowel and urinary irritation domains, respectively, at 24 months post completion of therapy, and disease free survival (DFS), defined as time to biochemical failure (Phoenix definition), local failure, regional failure, distant metastasis, or death from any cause. Since the EPIC-26 is only validated in certain languages, patients must speak English, French, or Spanish. Key secondary endpoints include health-related quality of life, biochemical failure, distant metastasis, overall survival, prostate cancer specific survival, and local/regional failures.

- **Patient Accrual**
  NRG-GU005 opened to accrual on November 16, 2017. The projected accrual rate is 15 patients per month after an initial 6 months period of no accrual. As of April 30, 2019, 130 patients have been enrolled which is less than the 173 patients projected (Table 1 and Figure 1). The median time of follow-up for vital status is 2.3 months. The interim analysis for GI/GU toxicity and DFS is projected to occur in the summer and fall of 2022, respectively.

- **Patient and Tumor Characteristics**
  Of the 130 randomized patients, all are eligible (62 on the IMRT arm and 68 on the SBRT arm) (Table 2). Table 3 shows the distribution of patient and tumor characteristics for all eligible patients. The median (min-max) age is 69 years (42-79). Most patients are white (81.5%), in the Gleason score 7 (3+4) with PSA less than or equal to 10 ng/ml risk group (73.1%), have either SpaceOAR only for rectal manipulation (43.1%) or no rectal manipulation (43.1%), have a T-Stage of T1 (76.2%) and a Zubrod performance status of 0 (86.9%). Two patients on the IMRT arm have withdrawn consent.

- **Adverse Events**
  Adverse events (AEs) were graded with CTCAE version 5.0. AEs by highest grade AE by system organ class, without regard to attribution are displayed in Table 4. On the IMRT arm, there have been 3 patients (6.7%) with a reported grade 3 adverse events. No patients have reported grade 4 or 5 events. On the SBRT arm, no

patients have reported a grade 3, 4 or 5 event. Table 5 shows the distribution of patients by highest grade AE and by specific AE term without regard to attribution. This table only includes system organ classes and terms with at least one grade 3, 4 or 5 event. The grade 3 events on the IMRT arm are erectile dysfunction (reported as unrelated to treatment) and hypertension (2 patients; reported as unrelated and unlikely to be related to treatment).

Table 1
NRG GU005 Accrual Summary - Data as of 4/30/2019

Date activated to accrual:	November 16, 2017
Targeted sample size:	622
Projected monthly accrual*:	15
Average monthly accrual over last 6 months:	12.2
Total accrual as of 4/30/2019:	130
Projected accrual as of 4/30/2019:	173
Percent of projected accrual achieved as of 4/30/2019:	75.14%
Percent of total targeted accrual as of 4/30/2019:	46.1%
Projected completion date based on last 6 months accrual:	September 2022

*No accrual was expected for the first 6 months of this study.

Table 2
NRG GU005 Accrual/Eligibility - Data as of 4/30/2019

	IMRT	SBRT	Total
Randomized	62	68	130
Ineligible	0	0	0
Eligible	62	68	130

Table 3
Patient and Tumor Characteristics for All Eligible Patients in NRG GU005 - Data as of 4/30/2019

	IMRT		SBRT		Total	
Patient or Tumor Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
Age (years)						
≤ 49	1	1.6	0	0.0	1	0.8
50 - 59	4	6.5	7	10.3	11	8.5
60 - 69	39	62.9	22	32.4	61	46.9
≥ 70	18	29.0	39	57.4	57	43.8
Race						
American Indian or Alaska Native	0	0.0	1	1.5	1	0.8
Asian	0	0.0	1	1.5	1	0.8

Table 3
Patient and Tumor Characteristics for All Eligible Patients in NRG GU005 - Data as of 4/30/2019

	IMRT		SBRT		Total	
Patient or Tumor Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
Black or African American	12	19.4	6	8.8	18	13.8
White	48	77.4	58	85.3	106	81.5
More than one race	1	1.6	0	0.0	1	0.8
Unknown	1	1.6	2	2.9	3	2.3
Ethnicity						
Hispanic or Latino	2	3.2	1	1.5	3	2.3
Not Hispanic or Latino	60	96.8	67	98.5	127	97.7
Risk Group						
Gleason score 7 (3+4) with PSA less than 10 ng/ml	44	71.0	51	75.0	95	73.1
Gleason score 7 (3+4) with PSA greater than or equal to 10 ng/ml	16	25.8	9	13.2	25	19.2
Gleason score 6 (3+3) with PSA greater than 10 ng/ml	2	3.2	8	11.8	10	7.7
Rectal Manipulation						
No	26	41.9	30	44.1	56	43.1
Rectal Balloon	1	1.6	1	1.5	2	1.5
SpaceOAR	29	46.8	27	39.7	56	43.1
SpaceOAR and rectal balloon	6	9.7	10	14.7	16	12.3
Combined Gleason Score						
6	2	3.2	8	11.8	10	7.7
7	60	96.8	60	88.2	120	92.3
T-Stage						
T1	48	77.4	51	75.0	99	76.2
T2	14	22.6	17	25.0	31	23.8
N-Stage						
N0	62	100.0	68	100.0	130	100.0
Zubrod PS						
0	54	87.1	59	86.8	113	86.9
1	8	12.9	9	13.2	17	13.1
Total	62	100.0	68	100.0	130	100.0

Table 4
Distribution of NRG-GU005 Patients by Highest Grade Adverse Event
by System Organ Class - Data as of 4/30/2019
For All Reported Adverse Events without Regard to Attribution

System Organ Class	IMRT (n=45)					SBRT (n=49)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Overall Highest Grade	20 (44.4)	17 (37.8)	3 (6.7)	0 (0.0)	0 (0.0)	23 (46.9)	21 (42.9)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	20 (44.4)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	13 (26.5)	4 (8.2)	0 (0.0)	0 (0.0)	0 (0.0)
General disorders and administration site conditions	23 (51.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (22.4)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injury, poisoning and procedural complications	1 (2.2)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Investigations	1 (2.2)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metabolism and nutrition disorders	2 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nervous system disorders	3 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (6.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Psychiatric disorders	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders	25 (55.6)	12 (26.7)	0 (0.0)	0 (0.0)	0 (0.0)	24 (49.0)	13 (26.5)	0 (0.0)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders	5 (11.1)	1 (2.2)	1 (2.2)	0 (0.0)	0 (0.0)	5 (10.2)	3 (6.1)	0 (0.0)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
Skin and subcutaneous tissue disorders	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Surgical and medical procedures	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	3 (6.7)	4 (8.9)	2 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	4 (8.2)	0 (0.0)	0 (0.0)	0 (0.0)

Adverse events were graded with CTCAE version 5.0.

Table 5
Distribution of NRG-GU005 Patients by Highest Grade Adverse Event
by Specific Adverse Event Term - Data as of 4/30/2019
For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	IMRT (n=45)					SBRT (n=49)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	5 (11.1)	1 (2.2)	1 (2.2)	0 (0.0)	0 (0.0)	5 (10.2)	3 (6.1)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	1 (2.2)	1 (2.2)	1 (2.2)	0 (0.0)	0 (0.0)	4 (8.2)	2 (4.1)	0 (0.0)	0 (0.0)	0 (0.0)
VASCULAR DISORDERS	3 (6.7)	4 (8.9)	2 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	4 (8.2)	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension	0 (0.0)	4 (8.9)	2 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	4 (8.2)	0 (0.0)	0 (0.0)	0 (0.0)

Adverse events were graded with CTCAE version 5.
Only includes system organ classes and terms with at least one Grade 3, Grade 4 or Grade 5.

Figure 1
Cumulative Accrual for NRG-GU005 - Data as of 4/30/2019