NRG-GU006

Report Based on Data Through: 04/30/2019

A PHASE II, DOUBLE-BLINDED, PLACEBO-CONTROLLED RANDOMIZED TRIAL OF SALVAGE RADIOTHERAPY WITH OR WITHOUT ENHANCED ANTI-ANDROGEN THERAPY WITH APALUTAMIDE IN RECURRENT PROSTATE CANCER

SCHEMA

STEP 1 REGISTRATION
Submission of tissue for Decipher analysis
Note: Decipher analysis results must be completed before Step 2 randomization can occur. If Decipher results have already been obtained, in lieu of tissue, results must be submitted to GenomeDx for validation.

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STEP 2 REGISTRATION

STRATIFY
Surgical Margins: Positive vs. Negative
Pre-SRT PSA: <0.5 ng/mL vs ≥0.5-1.0 ng/mL
PAM50 Molecular Subtype (per Decipher analysis): Luminal B vs (Luminal A/Basal/Unknown)

Randomize 1:1

↓

Arm 1 (Blinded)
External Beam Radiation:
64.8 to 70.2, 1.8 Gy/36-39 fractions
Plus

Blinded placebo daily for 6 months (~180 days) to start on Day 1 of radiation therapy (+/- 2 weeks)

↓

Arm 2 (Blinded)
External Beam Radiation:
64.8 to 70.2, 1.8 Gy/36-39 fractions
Plus

Blinded apalutamide daily for 6 months (~180 days) to start on Day 1 of radiation therapy (+/- 2 weeks)

Abbreviations: PSA, prostate specific antigen; SRT, salvage radiation therapy

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Activated:	April 27, 2018	
Status:	Open to Accrual	

- **Study Description**
  This is a double-blinded, placebo-controlled two-armed randomized phase II study designed to determine whether, in men with post-prostatectomy PSA recurrences, salvage radiation (SRT) with enhanced anti-androgen therapy with apalutamide will improve biochemical progression-free survival (bPFS) compared to SRT alone. The primary endpoint is biochemical progression-free survival (bPFS). BPFS is defined as time from randomization to first occurrence of clinical/radiographic local, regional, or distant metastases, death from any cause or a rise in PSA ≥0.2ng/ml from nadir PSA, with a second PSA measurement confirmation. Key secondary endpoints are overall survival, cancer-specific mortality, metastasis-free survival, distant metastasis, local/regional progression, salvage hormone therapy and PSA nadir during first year of treatment. The study will also evaluate an integral biomarker (molecular subtype) to determine whether a subsequent phase III trial (if warranted) should utilize a biomarker-enrichment design, biomarker-stratified design, or a standard design that eliminates the biomarker from consideration.

- **Patient Accrual**
  NRG-GU006 opened to accrual on April 27, 2018. The targeted number to be enrolled is 324 with a projected accrual rate of 7.5 patients per month after an initial 6 month period of no accrual. As of April 30, 2019, 81 patients have been enrolled which is more than the 47 patients projected (Table 1 and Figure 1). The median time of follow-up for vital status is 3.4 months. The first (and only) interim analysis of bPFS is projected to occur in December, 2022.

- **Patient and Tumor Characteristics**
  Of the 97 screened patients, 81 have been randomized (Table 2). Table 3 shows the distribution of patient and tumor characteristics for all randomized eligible patients. The median (min-max) age is 66 years (47-79). Most patients are white (84.0%), have a combined Gleason of 7 (72.8%), are luminal A/Basal/unknown (55.6%) and a Karnofsky performance status of 100 (59.3%). Three patients have withdrawn consent, one prior to randomization and one per arm post randomization.

- **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. Two patients (3.9%) have reported a grade 3 event, 1 patient (2.0%) reported a grade 4 event and zero have reported a grade 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 one grade 4 event was a blood and lymphatic system disorder (with definite attribution to protocol treatment).

Table 1
NRG GU006 Accrual Summary - Data as of 04/30/2019

Date activated to accrual:	April 27, 2018
Targeted sample size:	324
Projected monthly accrual*:	7-8
Average monthly accrual over last 6 months:	9.8
Total accrual:	81
Projected accrual as of 04/30/2019:	47
Percent of projected accrual achieved as of 04/30/2019:	172.34%
Percent of total targeted accrual as of 04/30/2019:	25%
Projected completion date based on last 6 months accrual:	May 2021

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

Table 2
NRG GU006 Accrual/Eligibility - Data as of 04/30/2019

	Blinded RX	Blinded RX	Total
Screened	-	-	97
Randomized	35	46	81
Ineligible	0	0	0
Eligible	35	46	81

Table 3
Patient and Tumor Characteristics for All Randomized Patients in NRG GU006 - Data as of 04/30/2019

	Blinded RX		Blinded RX		Total	
Patient or Tumor Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
Age (years)						
≤ 49	1	2.9	1	2.2	2	2.5
50 - 59	6	17.1	11	23.9	17	21.0
60 - 69	13	37.1	23	50.0	36	44.4
≥ 70	15	42.9	11	23.9	26	32.1

Table 3
Patient and Tumor Characteristics for All Randomized Patients in NRG GU006 - Data as of 04/30/2019

Patient or Tumor Characteristic	Blinded RX n	Blinded RX %	Blinded RX n	Blinded RX %	Total n	Total %
Race						
Asian	1	2.9	1	2.2	2	2.5
Black or African American	1	2.9	8	17.4	9	11.1
White	31	88.6	37	80.4	68	84.0
More than one race	1	2.9	0	0.0	1	1.2
Unknown	1	2.9	0	0.0	1	1.2
Ethnicity						
Hispanic or Latino	3	8.6	3	6.5	6	7.4
Not Hispanic or Latino	32	91.4	42	91.3	74	91.4
Unknown	0	0.0	1	2.2	1	1.2
Surgical margins						
Negative	19	54.3	21	45.7	40	49.4
Postivie	16	45.7	25	54.3	41	50.6
Pre-SRT PSA						
< 0.5	32	91.4	41	89.1	73	90.1
0.5 - 1.0	3	8.6	5	10.9	8	9.9
Pam50 Molecular Subtype						
Luminal B	16	45.7	20	43.5	36	44.4
Luminal A/Basal/Unknown	19	54.3	26	56.5	45	55.6
Combined Gleason Score						
7	26	74.3	33	71.7	59	72.8
8	2	5.7	7	15.2	9	11.1
9	7	20.0	6	13.0	13	16.0
T-Stage						
T2	17	48.6	24	52.2	41	50.6
T3	18	51.4	22	47.8	40	49.4
N-Stage						
NX	3	8.6	5	10.9	8	9.9
N0	32	91.4	41	89.1	73	90.1
M-Stage						
M0	35	100.0	46	100.0	81	100.0

Table 3
Patient and Tumor Characteristics for All Randomized Patients in NRG GU006 - Data as of 04/30/2019

Patient or Tumor Characteristic	Blinded RX n	Blinded RX %	Blinded RX n	Blinded RX %	Total n	Total %
Karnofsky Performance Status						
80	0	0.0	2	4.3	2	2.5
90	14	40.0	17	37.0	31	38.3
100	21	60.0	27	58.7	48	59.3
Total	35	100.0	46	100.0	81	100.0

Table 4
Distribution of NRG-GU006 Patients by Highest Grade Adverse Event by System Organ Class - Data as of 04/30/2019
For All Reported Adverse Events without Regard to Attribution

System Organ Class	Blinded RX (n=51) n and (%) of Patients by Grade 1	2	3	4	5
Overall Highest Grade	17 (33.3)	16 (31.4)	2 (3.9)	1 (2.0)	0 (0.0)
Blood and lymphatic system disorders	2 (8.3)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)
Ear and labyrinth disorders	1 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	14 (58.3)	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
General disorders and administration site conditions	17 (70.8)	1 (4.2)	1 (4.2)	0 (0.0)	0 (0.0)
Infections and infestations	1 (4.2)	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Injury, poisoning and procedural complications	5 (20.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Investigations	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metabolism and nutrition disorders	1 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	5	1	0	0	0

Table 4
Distribution of NRG-GU006 Patients by Highest Grade Adverse Event by System Organ Class - Data as of 04/30/2019
For All Reported Adverse Events without Regard to Attribution

System Organ Class	Blinded RX (n=51) n and (%) of Patients by Grade				
	1	2	3	4	5
	(20.8)	(4.2)	(0.0)	(0.0)	(0.0)
Nervous system disorders	6 (25.0)	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)
Renal and urinary disorders	18 (75.0)	5 (20.8)	0 (0.0)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders	4 (16.7)	4 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Skin and subcutaneous tissue disorders	5 (20.8)	4 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	5 (20.8)	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)

Adverse events were graded with CTCAE version 4.0.

Table 5
Distribution of NRG-GU006 Patients by Highest Grade Adverse Event by Specific Adverse Event Term - Data as of 04/30/2019
For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	Blinded RX (n=24) n and (%) of Patients by Grade				
	1	2	3	4	5
BLOOD AND LYMPHATIC SYSTEM DISORDERS	2 (8.3)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)
Blood and lymphatic system disorders - Other	1 (4.2)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	17 (70.8)	1 (4.2)	1 (4.2)	0 (0.0)	0 (0.0)
Fatigue	16 (66.7)	1 (4.2)	1 (4.2)	0 (0.0)	0 (0.0)
NERVOUS SYSTEM DISORDERS	6	0	1	0	0

Table 5
Distribution of NRG-GU006 Patients by Highest Grade Adverse Event
by Specific Adverse Event Term - Data as of 04/30/2019
For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	Blinded RX (n=24)				
	n and (%) of Patients by Grade				
	1	2	3	4	5
	(25.0)	(0.0)	(4.2)	(0.0)	(0.0)
Paresthesia	0	0	1	0	0
	(0.0)	(0.0)	(4.2)	(0.0)	(0.0)

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

Figure 1
Cumulative Accrual for NRG GU006- Data as of 04/30/2019