RTOG 0938

Report Based on Data Through: 03/14/2019

Randomized Phase II Trial of Hypofractionated Radiotherapy for Favorable Risk Prostate Cancer

STRATIFY	RANDOMIZE
Treatment techniques/machine 1. All linear accelerator based treatment (excluding Cyberknife) 2. Cyberknife 3. Protons	**Arm 1** 36.25 Gy in 5 fractions of 7.25 Gy over two and a half weeks (in 15-17 days)* **Arm 2** 51.6 Gy in 12 daily fractions of 4.3 Gy over two and a half weeks (in 16-18 days)*

*For proton doses, see protocol Section 6.1.4.

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Activated: 09/29/2011

Closed: 02/10/2014

Status: Follow-up, primary endpoint published

- **Study Description**
  This is a two-armed randomized phase II study designed to determine if one or both of the hypofractionation regimens are beneficial. Patients must have histologically confirmed diagnosis of adenocarcinoma of the prostate within 365 days (1 year) of randomization; Gleason scores 2-6; Clinical stage T1-2a and PSA < 10 ng/mL (PSA should not be obtained within 10 days after prostate biopsy). The primary endpoint for this study is to demonstrate that 1-year health-related quality of life (HRQOL) for at least one hypofractionated arm is not significantly lower than baseline as measured by the Bowel and Urinary domains of the Expanded Prostate Cancer Index Composite (EPIC) instrument.

- **Patient Accrual**
  Accrual was activated on September 29, 2011 and completed on February 10, 2014 with 255 patients randomized (Table 1). The median time of follow-up for vital status is 5 years.

- **Adverse Events**
  Adverse events (AEs) were graded with CTCAE version 4. As of March 14, 2019 there have been 5 patients (4.2%) with grade 3 events and 1 patient (0.8%) with a grade 4 event (sepsis) reported in the 5 fractions arm compared to 12 patients (9.9%) with grade 3 events and 1 patient (0.8%) with a grade 4 event (lung infection) in 12 fractions arm regardless of attribution to treatment (Tables 1, 2). There have not been any grade 5 events reported to date. Table 3 shows the distribution of patients by highest grade AE 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.

Table 1
RTOG 0938 Accrual/Eligibility - Data as of 03/14/2019

	5 Fractions	12 Fractions	Total
Randomized	127	128	255
Ineligible	8	7	15
Eligible	119	121	240

Table 2
Distribution of RTOG 0938 Patients by Highest Grade Adverse Event by System Organ Class - Data as of 03/14/2019
For All Reported Adverse Events without Regard to Attribution

System Organ Class	5 Fractions (n=119) n and (%) of Patients by Grade					12 Fractions (n=121) n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Overall Highest Grade	33 (27.7)	63 (52.9)	5 (4.2)	1 (0.8)	0 (0.0)	38 (31.4)	56 (46.3)	12 (9.9)	1 (0.8)	0 (0.0)
Blood and lymphatic system disorders	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)

Table 2
Distribution of RTOG 0938 Patients by Highest Grade Adverse Event
by System Organ Class - Data as of 03/14/2019
For All Reported Adverse Events without Regard to Attribution

System Organ Class	5 Fractions (n=119)					12 Fractions (n=121)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Ear and labyrinth disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	1 (0.8)	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)
Gastrointestinal disorders	42 (35.3)	21 (17.6)	2 (1.7)	0 (0.0)	0 (0.0)	44 (36.4)	18 (14.9)	4 (3.3)	0 (0.0)	0 (0.0)
General disorders and administration site conditions	27 (22.7)	6 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	31 (25.6)	6 (5.0)	1 (0.8)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations	1 (0.8)	3 (2.5)	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)	5 (4.1)	1 (0.8)	1 (0.8)	0 (0.0)
Injury, poisoning and procedural complications	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Investigations	2 (1.7)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metabolism and nutrition disorders	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	4 (3.4)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	7 (5.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nervous system disorders	3 (2.5)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Psychiatric disorders	13 (10.9)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	8 (6.6)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders	58 (48.7)	31 (26.1)	2 (1.7)	0 (0.0)	0 (0.0)	53 (43.8)	41 (33.9)	3 (2.5)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders	23 (19.3)	33 (27.7)	2 (1.7)	0 (0.0)	0 (0.0)	21 (17.4)	28 (23.1)	1 (0.8)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Skin and subcutaneous tissue disorders	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (4.1)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	1	0	1	0	0	1	1	3	0	0

Table 2
Distribution of RTOG 0938 Patients by Highest Grade Adverse Event
by System Organ Class - Data as of 03/14/2019
For All Reported Adverse Events without Regard to Attribution

System Organ Class	5 Fractions (n=119)					12 Fractions (n=121)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(0.8)	(0.0)	(0.8)	(0.0)	(0.0)	(0.8)	(0.8)	(2.5)	(0.0)	(0.0)

Adverse events were graded with CTCAE version 4.

Table 3
Distribution of RTOG 0938 Patients by Highest Grade Adverse Event
by Specific Adverse Event Term - Data as of 03/14/2019
For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	5 Fractions (n=119)					12 Fractions (n=121)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
GASTROINTESTINAL DISORDERS	42 (35.3)	21 (17.6)	2 (1.7)	0 (0.0)	0 (0.0)	44 (36.4)	18 (14.9)	4 (3.3)	0 (0.0)	0 (0.0)
Colonic fistula	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Diarrhea	23 (19.3)	4 (3.4)	1 (0.8)	0 (0.0)	0 (0.0)	22 (18.2)	9 (7.4)	0 (0.0)	0 (0.0)	0 (0.0)
Mucositis oral	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Proctitis	7 (5.9)	10 (8.4)	1 (0.8)	0 (0.0)	0 (0.0)	13 (10.7)	5 (4.1)	3 (2.5)	0 (0.0)	0 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	27 (22.7)	6 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	31 (25.6)	6 (5.0)	1 (0.8)	0 (0.0)	0 (0.0)
Fatigue	26 (21.8)	4 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	28 (23.1)	5 (4.1)	1 (0.8)	0 (0.0)	0 (0.0)
HEPATOBILIARY DISORDERS	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cholecystitis	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
INFECTIONS AND INFESTATIONS	1	3	0	1	0	1	5	1	1	0

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For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	5 Fractions (n=119) n and (%) of Patients by Grade					12 Fractions (n=121) n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(0.8)	(2.5)	(0.0)	(0.8)	(0.0)	(0.8)	(4.1)	(0.8)	(0.8)	(0.0)
Hepatitis viral	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Lung infection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
Sepsis	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
INVESTIGATIONS	2 (1.7)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CPK increased	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
METABOLISM AND NUTRITION DISORDERS	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoalbuminemia	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypophosphatemia	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RENAL AND URINARY DISORDERS	58 (48.7)	31 (26.1)	2 (1.7)	0 (0.0)	0 (0.0)	53 (43.8)	41 (33.9)	3 (2.5)	0 (0.0)	0 (0.0)
Acute kidney injury	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cystitis noninfective	13 (10.9)	3 (2.5)	1 (0.8)	0 (0.0)	0 (0.0)	14 (11.6)	6 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hematuria	7 (5.9)	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	9 (7.4)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)
Renal and urinary disorders - Other	29 (24.4)	3 (2.5)	1 (0.8)	0 (0.0)	0 (0.0)	31 (25.6)	4 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)
Urinary incontinence	11 (9.2)	4 (3.4)	1 (0.8)	0 (0.0)	0 (0.0)	12 (9.9)	10 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Urinary retention	15 (12.6)	6 (5.0)	1 (0.8)	0 (0.0)	0 (0.0)	15 (12.4)	9 (7.4)	2 (1.7)	0 (0.0)	0 (0.0)
Urinary tract obstruction	5 (4.2)	4 (3.4)	1 (0.8)	0 (0.0)	0 (0.0)	4 (3.3)	1 (0.8)	1 (0.8)	0 (0.0)	0 (0.0)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	23 (19.3)	33 (27.7)	2 (1.7)	0 (0.0)	0 (0.0)	21 (17.4)	28 (23.1)	1 (0.8)	0 (0.0)	0 (0.0)

Table 3
Distribution of RTOG 0938 Patients by Highest Grade Adverse Event
by Specific Adverse Event Term - Data as of 03/14/2019
For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	5 Fractions (n=119)					12 Fractions (n=121)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Erectile dysfunction	16 (13.4)	33 (27.7)	2 (1.7)	0 (0.0)	0 (0.0)	15 (12.4)	28 (23.1)	1 (0.8)	0 (0.0)	0 (0.0)
VASCULAR DISORDERS	1 (0.8)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	3 (2.5)	0 (0.0)	0 (0.0)
Hypertension	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	3 (2.5)	0 (0.0)	0 (0.0)
Hypotension	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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