RTOG 0926

Report Based on Data Through: 04/30/2019

A Phase II Protocol for Patients with Stage T1 Bladder Cancer to Evaluate Selective Bladder Preserving Treatment by Radiation Therapy Concurrent with Radiosensitizing Chemotherapy Following a Thorough Transurethral Surgical Re-staging

Institutional TURBT for re-staging →	**Full-dose Radiation* and Concurrent Chemotherapy** →**	**Cystoscopic Surveillance 8-10 weeks after treatment; if negative, q 3 months for the 1st year, q 4 months for year 2, q 6 months for years 3, 4, and 5*** and then annually**
Stage T1 (T1G2 or T1G3)	* Total dose of 61.2 Gy in 34 daily fractions ** Cisplatin 3 days/week during Weeks 1, 3, and 5 **-OR-** Mitomycin day 1 and 5-fluorouracil Weeks 1 and 4	***For T1 and Tcis tumor recurrence, recommend early salvage cystectomy. For Ta tumor recurrence, recommend either appropriate conservative treatment or cystectomy.

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Activated: 11/11/2009

Closed: 12/20/2017

Status: Follow-up, pending primary outcome analysis

- **Study Description**
  This is a one-armed phase II study to evaluate selective bladder preserving concurrent radiation and chemotherapy treatment after transurethral surgical re-staging. Patients must be operable with non-muscle invading tumors and with at least one being a high grade Stage T1 urothelial carcinoma for whom radical cystectomy is being considered as the next conventional step in therapy by standard urologic guidelines. Patients must have AJCC Stages T1, NX or N0, M0 with only transitional cell histology. Patients must be restaged by a urologist in the participating institution with an aggressive, visibly complete TURBT with muscularis propria in the specimen but with no evidence of its invasion by tumor. Patients must have failed standard treatment with, or be medically ineligible for, intravesical biological therapy or chemotherapy. There must be no evidence of prostatic stromal invasion by tumor. The primary endpoint for this study is the three-year rate of freedom from radical cystectomy.

- **Patient Accrual**
  Accrual was activated on November 11, 2009 and completed on December 20, 2017 with 37 patients enrolled (Table 1 and Figure 1). Accrual to this study was slower than anticipated. As of April 30, 2019, the median time of follow-up for vital status is 5.4 months. The primary analysis will occur in December 2020, after all patients have been followed for a minimum of 3 years.

- **Patient and Tumor Characteristics**
  There are 3 ineligible patients, two of which did not receive protocol treatment (Tables 2 and 3). Ineligible patients are excluded from analysis. From the remaining patients, two subsequently withdrew consent. The distribution by patient and tumor characteristics is shown in Table 4. Median (min-max) age is 71 years (53-86). Most patients are male (91.2%), white (94.1%), and have a Zubrod performance status = 0 (85.3%).

- **Adverse Events**
  AEs were graded with CTCAE version 4. As of April 30, 2019, there have been 20 patients (58.8%) with reported grade 3 events, 1 patient (2.9%) with a reported grade 4 event, and 1 patient (2.9%) with a reported grade 5 event (Table 5). Table 6 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 event. The most common grade 3 events were reported for the investigations (23.5%) system organ class, with decreases in lymphocyte counts as the cause. The one grade 4 AE was a thromboembolic event reported as unlikely related to treatment. Another patient had a grade 4 blood and lymphatic system disorder, as well as a grade 5 chronic kidney disease, which was reported as unrelated to treatment (Table 6). There have been no new grade 5 AEs since the last report.

Table 1
RTOG 0926 Accrual Summary - Data as of 04/30/2019

Targeted sample size:	37
Date activated to accrual:	November 11, 2009
Projected monthly accrual:	1.0 *
Average monthly accrual over the last 6 months:	0.5
Total Accrual:	37

* 0 in first 6 months.

Table 2
RTOG 0926 Accrual/Eligibility - Data as of 04/30/2019

	3D CRT+Cisplatin
Randomized	37
Ineligible	3
Eligible	34

Table 3
RTOG 0926 Cases Excluded - Data as of 04/30/2019

	3D CRT+Cisplatin (n=3)	
Reason	**n**	**%**
No protocol treatment	2	66.7
Ineligible - Not Stage T1	1	33.3

Table 4
Patient and Tumor Characteristics for Eligible Patients in RTOG 0926 - Data as of 04/30/2019

	3D CRT+Cisplatin	
Patient or Tumor Characteristic	**n**	**%**
Age (years)		
<=59	4	11.8
60-69	12	35.3
70-79	14	41.2
80+	4	11.8
Gender		
Male	31	91.2
Female	3	8.8
Race		
Black or African American	2	5.9
White	32	94.1
Ethnicity		
Not Hispanic or Latino	34	100.0

Table 4
Patient and Tumor Characteristics for Eligible Patients in RTOG 0926 - Data as of 04/30/2019

Patient or Tumor Characteristic	3D CRT+Cisplatin n	%
Zubrod Performance Status		
0	29	85.3
1	5	14.7
Consented to tissue collection		
No	1	2.9
Yes	33	97.1
Consented to blood collection		
No	5	14.7
Yes	29	85.3
Consented to urine collection		
No	5	14.7
Yes	29	85.3
Total	34	100.0

3 patients did not have on-study data and are excluded from this table.

Table 5
Distribution of RTOG 0926 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	3D CRT+Cisplatin (n=34) n and (%) of Patients by Grade				
	1	2	3	4	5
Overall Highest Grade	2 (5.9)	9 (26.5)	20 (58.8)	1 (2.9)	1 (2.9)
Blood and lymphatic system disorders	9 (26.5)	5 (14.7)	6 (17.6)	1 (2.9)	0 (0.0)
Cardiac disorders	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	2 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	2 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	21	8	4	0	0

Table 5
Distribution of RTOG 0926 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	3D CRT+Cisplatin (n=34) n and (%) of Patients by Grade				
	1	2	3	4	5
	(61.8)	(23.5)	(11.8)	(0.0)	(0.0)
General disorders and administration site conditions	20 (58.8)	10 (29.4)	2 (5.9)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Immune system disorders	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations	0 (0.0)	5 (14.7)	6 (17.6)	0 (0.0)	0 (0.0)
Injury, poisoning and procedural complications	2 (5.9)	2 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)
Investigations	6 (17.6)	8 (23.5)	8 (23.5)	0 (0.0)	0 (0.0)
Metabolism and nutrition disorders	10 (29.4)	9 (26.5)	7 (20.6)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	9 (26.5)	3 (8.8)	1 (2.9)	0 (0.0)	0 (0.0)
Nervous system disorders	9 (26.5)	2 (5.9)	2 (5.9)	0 (0.0)	0 (0.0)
Psychiatric disorders	6 (17.6)	1 (2.9)	2 (5.9)	0 (0.0)	0 (0.0)
Renal and urinary disorders	10 (29.4)	11 (32.4)	6 (17.6)	0 (0.0)	1 (2.9)
Reproductive system and breast disorders	3 (8.8)	4 (11.8)	1 (2.9)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	12 (35.3)	1 (2.9)	3 (8.8)	0 (0.0)	0 (0.0)
Skin and subcutaneous tissue disorders	5 (14.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	1 (2.9)	4 (11.8)	3 (8.8)	1 (2.9)	0 (0.0)

Adverse events were graded with CTCAE version 4.

Table 6
Distribution of RTOG 0926 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	3D CRT+Cisplatin (n=34) n and (%) of Patients by Grade				
	1	2	3	4	5
BLOOD AND LYMPHATIC SYSTEM DISORDERS	9 (26.5)	5 (14.7)	6 (17.6)	1 (2.9)	0 (0.0)
Anemia	9 (26.5)	6 (17.6)	5 (14.7)	0 (0.0)	0 (0.0)
Blood and lymphatic system disorders - Other	0 (0.0)	0 (0.0)	1 (2.9)	1 (2.9)	0 (0.0)
Febrile neutropenia	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
CARDIAC DISORDERS	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Atrial fibrillation	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
GASTROINTESTINAL DISORDERS	21 (61.8)	8 (23.5)	4 (11.8)	0 (0.0)	0 (0.0)
Diarrhea	15 (44.1)	4 (11.8)	2 (5.9)	0 (0.0)	0 (0.0)
Duodenal ulcer	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Enterocolitis	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Gastrointestinal disorders - Other	4 (11.8)	1 (2.9)	1 (2.9)	0 (0.0)	0 (0.0)
Lower gastrointestinal hemorrhage	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Mucositis oral	3 (8.8)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	20 (58.8)	10 (29.4)	2 (5.9)	0 (0.0)	0 (0.0)
Non-cardiac chest pain	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Pain	3 (8.8)	2 (5.9)	1 (2.9)	0 (0.0)	0 (0.0)
HEPATOBILIARY DISORDERS	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Hepatobiliary disorders - Other	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
INFECTIONS AND INFESTATIONS	0 (0.0)	5 (14.7)	6 (17.6)	0 (0.0)	0 (0.0)
Lung infection	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Tooth infection	0	0	1	0	0

Table 6
Distribution of RTOG 0926 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	3D CRT+Cisplatin (n=34) n and (%) of Patients by Grade				
	1	2	3	4	5
	(0.0)	(0.0)	(2.9)	(0.0)	(0.0)
Urinary tract infection	0 (0.0)	3 (8.8)	4 (11.8)	0 (0.0)	0 (0.0)
INVESTIGATIONS	6 (17.6)	8 (23.5)	8 (23.5)	0 (0.0)	0 (0.0)
Lymphocyte count decreased	2 (5.9)	6 (17.6)	8 (23.5)	0 (0.0)	0 (0.0)
Neutrophil count decreased	1 (2.9)	2 (5.9)	2 (5.9)	0 (0.0)	0 (0.0)
White blood cell decreased	9 (26.5)	2 (5.9)	1 (2.9)	0 (0.0)	0 (0.0)
METABOLISM AND NUTRITION DISORDERS	10 (29.4)	9 (26.5)	7 (20.6)	0 (0.0)	0 (0.0)
Dehydration	0 (0.0)	3 (8.8)	2 (5.9)	0 (0.0)	0 (0.0)
Hyperglycemia	9 (26.5)	5 (14.7)	1 (2.9)	0 (0.0)	0 (0.0)
Hyperkalemia	1 (2.9)	2 (5.9)	1 (2.9)	0 (0.0)	0 (0.0)
Hypoalbuminemia	5 (14.7)	2 (5.9)	1 (2.9)	0 (0.0)	0 (0.0)
Hypomagnesemia	4 (11.8)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Hyponatremia	5 (14.7)	0 (0.0)	2 (5.9)	0 (0.0)	0 (0.0)
Hypophosphatemia	1 (2.9)	2 (5.9)	1 (2.9)	0 (0.0)	0 (0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	9 (26.5)	3 (8.8)	1 (2.9)	0 (0.0)	0 (0.0)
Back pain	2 (5.9)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
NERVOUS SYSTEM DISORDERS	9 (26.5)	2 (5.9)	2 (5.9)	0 (0.0)	0 (0.0)
Stroke	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Syncope	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
PSYCHIATRIC DISORDERS	6 (17.6)	1 (2.9)	2 (5.9)	0 (0.0)	0 (0.0)
Confusion	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Insomnia	4	0	1	0	0

Table 6
Distribution of RTOG 0926 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	3D CRT+Cisplatin (n=34) n and (%) of Patients by Grade				
	1	2	3	4	5
	(11.8)	(0.0)	(2.9)	(0.0)	(0.0)
RENAL AND URINARY DISORDERS	10 (29.4)	11 (32.4)	6 (17.6)	0 (0.0)	1 (2.9)
Chronic kidney disease	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	1 (2.9)
Hematuria	3 (8.8)	3 (8.8)	5 (14.7)	0 (0.0)	0 (0.0)
Renal calculi	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Urinary tract obstruction	0 (0.0)	1 (2.9)	1 (2.9)	0 (0.0)	0 (0.0)
Urinary tract pain	3 (8.8)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	3 (8.8)	4 (11.8)	1 (2.9)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders - Other	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	12 (35.3)	1 (2.9)	3 (8.8)	0 (0.0)	0 (0.0)
Aspiration	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)
Dyspnea	9 (26.5)	1 (2.9)	2 (5.9)	0 (0.0)	0 (0.0)
Hypoxia	0 (0.0)	1 (2.9)	2 (5.9)	0 (0.0)	0 (0.0)
VASCULAR DISORDERS	1 (2.9)	4 (11.8)	3 (8.8)	1 (2.9)	0 (0.0)
Hypotension	1 (2.9)	1 (2.9)	1 (2.9)	0 (0.0)	0 (0.0)
Thromboembolic event	0 (0.0)	2 (5.9)	1 (2.9)	1 (2.9)	0 (0.0)
Vascular disorders - Other	0 (0.0)	0 (0.0)	1 (2.9)	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.

Figure 1
Cumulative Accrual for RTOG 0926 - Data as of 04/30/2019