RTOG 1106

Report Based on Data Through: 04/30/2019

Randomized Phase II Trial of Individualized Adaptive Radiotherapy Using During-Treatment FDG-PET/CT and Modern Technology in Locally Advanced Non-Small Cell Lung Cancer (NSCLC)

[1]All Patients: Baseline FDG-PET/CT scan within 4 weeks prior to registration

[2]Subset of Patients: Baseline FMISO-PET/CT scan within 28 days prior to start of treatment, but not on same day as FDG-PET/CT scan. FMISO PET/CT must be done after subject has been registered.
(FMISO sub-study closed to accrual on November 24, 2015)

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STRATIFY		[3]RANDOMIZE	
	Stage 1. IIIA 2. IIIB **Primary Tumor Size** 1. > 5 cm 2. ≤ 5 cm **Histology** 1. Squamous 2. Non-Squamous		**Arm 1: Concurrent Chemoradiotherapy** RT to 50 Gy in 25 fractions (nominally 5 fx/week) [4]Carboplatin and paclitaxel weekly **Arm 2: Concurrent Chemoradiotherapy** RT to 46.2 Gy in 21 fractions (nominally 5 fx/week) [4]Carboplatin and paclitaxel weekly

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ALL PATIENTS: During-RT FDG-PET/CT Scan between fractions 18 and 19 for Both Arms
For Arm 2, re-simulation with CT scan at fractions 18-19

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Arm 1: Continuation of radiotherapy, per the initial plan, not based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles. No adaptation is allowed.

A total of 60 Gy in 30 daily fractions (nominally 5 fx/week)

Arm 2: Adaptive radiotherapy, based on during-RT FDG-PET/CT scan and resimulation with CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

19.8-34.2 Gy in 9 fractions; overall total of up to 80.4 Gy in 30 daily fractions
Individualized to MLD 20 Gy

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ALL PATIENTS: Consolidative Chemotherapy

Arms 1 and 2: Carboplatin and paclitaxel q21 days X 3

IGRT is mandatory for this study (see Section 5.1 of protocol).

[1] All patients will undergo FDG PET/CT at baseline for staging and RT planning and during RT for treatment response assessment and adaptive planning. This baseline scan should be performed within 4 weeks prior to registration, while the during-RT scan should be performed between fractions 18 and 19 for both arms. Patients who have already undergone staging FDG-PET/CT at the time of enrollment may need to repeat the FDG-PET/CT in a treatment planning position due to time lapse or image quality issues. PET/CT will be performed on a flat table top, after at least 4 hours fasting, with controlled blood glucose levels (< 200 mg/dL) and start of imaging acquisition at 50-70 minutes after injection of 8-20 mCi of FDG, in accordance with manufacturer recommendations FDG-PET/CT will be performed in accordance with the protocol and with ECOG-ACRIN Imaging Standards for PET, http://www.acrin.org/CORELABS/PETCORELABORATORY/PETSOPS.aspx. If the baseline FDG-PET/CT is not performed on a flat palette in treatment planning position, it can still be used as the baseline scan only if all of the following conditions are met:

1. done within 4 weeks prior to registration
2. acceptable imaging parameters: 4 hour fast, blood glucose < 200 mg/dl, 8-20 mCi F-18 FDG dose, injection to scan interval 50-70 minutes
3. conducted on an ACR Imaging Core Laboratory ACRIN qualified scanner, which is the same scanner or same model to be used for the mid-treatment FDG PET/CT imaging
4. can be acceptably registered to the simulation CT; the simulation CT must also be submitted as a reference scan for registration

[2] (FMISO sub-study closed to accrual on November 24, 2015)
Baseline FMISO-PET/CT will be performed only on a subset of patients (n=58) and at institutions with access to the radiopharmaceutical that agree to participate in this imaging component. If the site opts to participate, all patients enrolled by the site must receive the FMISO-PET/CT (when FMISO is available). The baseline FMISOPET/CT will be performed on a different day than FDG-PET/CT, and within 28 days prior to the start of radiotherapy. FMISO PET/CT must be done after subject has been registered. If pre-treatment FDG-PET/CT is repeated, then FMISO and FDG-PET/CT may be performed in either sequence but must be performed on different days. Institutions that have access to FMISO should participate in the advanced hypoxia imaging of the substudy until target accrual has been reached. **Refer to Sections 6.10–6.13 for detailed information on FMISO and FMISO-PET/CT and Sections 6.14–6.17 for FDG and FDG-PET/CT.**

[3] The randomization of experimental and standard arms is set as 2:1, with stratification by MLD and PreGTV. The 2:1 randomization will allow more patients to be treated on the experimental arm (Arm 2).

[4] Chemotherapy will begin the same week as radiation therapy and will be given on the same day each week.

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Activated:	02/22/2012	
Closed:	03/08/2017	
Status:	Follow-up, pending primary outcome analysis	

- **Study Description**
  This is a two-armed randomized phase II study designed to assess whether the local-regional progression-free rate is improved when adaptive radiation therapy planning is used for patients with stage IIIA or IIIB non-operable non-small cell lung cancer. The primary endpoint for this study is the local-regional progression-free rate at 2 years. The randomization of experimental and standard arms is set as 2:1.

- **Patient Accrual**
  Accrual was activated on February 22, 2012 and closed March 8, 2017. Total accrual as of study closure was 138 (Table 1); monthly accrual was slower than projected. Median time of follow-up for vital status is 24.9 months. The final analysis is planned to occur in fall 2019.

- **Patient and Tumor Characteristics**
  Four patients on Standard RT and 4 on Adaptive RT are not eligible for analysis (Table 2); reasons are listed in Table 3. The distribution by patient and tumor characteristics is shown in Table 4. Median (min-max) age is 64 years (24-82). Most patients are female (52.7%), white (71.3%), not Hispanic or Latino (88.4%), and had a Zubrod Performance Status of 1 (57.4%) As of April 30, 2019, 6 patients on Standard RT and 6 patients on Adaptive RT have withdrawn consent to follow-up.

- **Adverse Events**
  Adverse events (AEs) were graded with CTCAE version 4. As of April 30, 2019 and regardless of attribution to treatment, there have been 11 patients (26.2%) with grade 4 and 2 (4.8%) patients with grade 5 AEs reported on Standard RT, and 15 patients (18.3%) with grade 4 and 5 (6.1%) patients with grade 5 AEs reported on Adaptive RT (Table 5). There are no notable differences in grade 4-5 rates by system organ class. All adverse events, regardless of attribution to protocol treatment, for which at least one grade 4 or grade 5 event has been reported are shown in Table 6. Comparing with the last report, there were no changes in the incidences of grade 4 or higher AEs, regardless of attributions. There are no notable differences in grade 4-5 rates by term.

Table 1
RTOG 1106 Accrual Summary - Data as of 04/30/2019

Date activated to accrual:	February 2, 2012
Targeted sample size:	138
Projected monthly accrual*:	6
Average monthly accrual over last 6 months:	3.2
Total accrual:	138

*Little to no accrual was anticipated during the first 6 months of the trial.

Table 2
RTOG 1106 Accrual/Eligibility - Data as of 04/30/2019

	Standard RT	Adaptive RT	Total
Randomized	48	90	138
Ineligible	4	4	8
Eligible	44	86	130

Table 3
RTOG 1106 Cases Excluded - Data as of 04/30/2019

	Standard RT (n=4)		Adaptive RT (n=4)		Total (n=8)	
Reason	**n**	**%**	**n**	**%**	**n**	**%**
Ineligible - HGB < 10.0 g/dl at registration	1	25.0	1	25.0	2	25.0
Ineligible - DLCO not evaluated prior to registration	0	0.0	1	25.0	1	12.5
Ineligible - PET/MR used for staging rather than PET/CT	1	25.0	0	0.0	1	12.5
Ineligible - pre-registration PFTs and CBCs evaluated outside of required timeframe	0	0.0	1	25.0	1	12.5
Ineligible - pre-registration PFTs evaluated outside of required timeframe	1	25.0	0	0.0	1	12.5
Ineligible - pre-registration creatinine clearance evaluated outside of required timeframe	1	25.0	0	0.0	1	12.5
Ineligible - prior invasive malignancy within 3 years prior to registration	0	0.0	1	25.0	1	12.5

Table 4
Patient and Tumor Characteristics for All Eligible Patients with On-Study Data in RTOG 1106 - Data as of 04/30/2019

	Standard RT		Adaptive RT		Total	
Patient or Tumor Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
Age (years)						
≤ 49	2	4.7	6	7.0	8	6.2
50 - 59	8	18.6	22	25.6	30	23.3
60 - 69	23	53.5	34	39.5	57	44.2
≥ 70	10	23.3	24	27.9	34	26.4
Gender						
Male	25	58.1	36	41.9	61	47.3
Female	18	41.9	50	58.1	68	52.7
Race						
American Indian or Alaskan Native	2	4.7	0	0.0	2	1.6
Asian	1	2.3	2	2.3	3	2.3
Black or African American	6	14.0	10	11.6	16	12.4
White	32	74.4	60	69.8	92	71.3
Unknown	2	4.7	14	16.3	16	12.4
Ethnicity						
Hispanic or Latino	0	0.0	2	2.3	2	1.6
Not Hispanic or Latino	42	97.7	72	83.7	114	88.4
Unknown	1	2.3	12	14.0	13	10.1
Zubrod Performance Status						
0	17	39.5	38	44.2	55	42.6
1	26	60.5	48	55.8	74	57.4
Histology						
Squamous cell carcinoma	17	39.5	36	41.9	53	41.1
Non-squamous cell carcinoma	26	60.5	50	58.1	76	58.9
AJCC Stage						
Stage IIIA	24	55.8	46	53.5	70	54.3
Stage IIIB	19	44.2	40	46.5	59	45.7
Primary tumor size						
> 5 cm	17	39.5	34	39.5	51	39.5
≤ 5 cm	26	60.5	52	60.5	78	60.5
Consented to tissue collection						

Table 4
Patient and Tumor Characteristics for All Eligible Patients with On-Study Data in RTOG 1106 - Data as of 04/30/2019

	Standard RT		Adaptive RT		Total	
Patient or Tumor Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
No	6	14.0	13	15.1	19	14.7
Yes	37	86.0	73	84.9	110	85.3
Consented to blood collection						
No	6	14.0	16	18.6	22	17.1
Yes	37	86.0	70	81.4	107	82.9
Total	43	100.0	86	100.0	129	100.0

1 eligible patient does not have on-study data and are excluded from this table.

6 patients received no study treatment and are not included in adverse event tables.

Table 5
Distribution of RTOG 1106 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

	Standard RT (n=42)					Adaptive RT (n=82)				
System Organ Class	**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	0 (0.0)	10 (23.8)	15 (35.7)	11 (26.2)	2 (4.8)	2 (2.4)	16 (19.5)	44 (53.7)	15 (18.3)	5 (6.1)
Blood and lymphatic system disorders	9 (21.4)	6 (14.3)	3 (7.1)	1 (2.4)	0 (0.0)	20 (24.4)	22 (26.8)	7 (8.5)	1 (1.2)	0 (0.0)
Cardiac disorders	3 (7.1)	1 (2.4)	1 (2.4)	0 (0.0)	0 (0.0)	7 (8.5)	4 (4.9)	2 (2.4)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	2 (4.8)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Endocrine disorders	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	2 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	8 (19.0)	20 (47.6)	6 (14.3)	0 (0.0)	0 (0.0)	16 (19.5)	46 (56.1)	11 (13.4)	1 (1.2)	0 (0.0)
General disorders and administration site conditions	9 (21.4)	20 (47.6)	6 (14.3)	1 (2.4)	1 (2.4)	22 (26.8)	33 (40.2)	14 (17.1)	0 (0.0)	0 (0.0)
Immune system disorders	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)	0 (0.0)	1 (1.2)	0 (0.0)
Infections and infestations	0	5	4	0	0	1	9	9	2	1

Table 5
Distribution of RTOG 1106 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	Standard RT (n=42) n and (%) of Patients by Grade					Adaptive RT (n=82) n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(0.0)	(11.9)	(9.5)	(0.0)	(0.0)	(1.2)	(11.0)	(11.0)	(2.4)	(1.2)
Injury, poisoning and procedural complications	13 (31.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	26 (31.7)	6 (7.3)	1 (1.2)	0 (0.0)	0 (0.0)
Investigations	4 (9.5)	6 (14.3)	9 (21.4)	9 (21.4)	0 (0.0)	9 (11.0)	12 (14.6)	26 (31.7)	11 (13.4)	0 (0.0)
Metabolism and nutrition disorders	6 (14.3)	12 (28.6)	7 (16.7)	0 (0.0)	0 (0.0)	26 (31.7)	18 (22.0)	13 (15.9)	3 (3.7)	0 (0.0)
Musculoskeletal and connective tissue disorders	7 (16.7)	10 (23.8)	2 (4.8)	0 (0.0)	0 (0.0)	21 (25.6)	18 (22.0)	2 (2.4)	0 (0.0)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)
Nervous system disorders	16 (38.1)	10 (23.8)	3 (7.1)	0 (0.0)	0 (0.0)	34 (41.5)	18 (22.0)	8 (9.8)	1 (1.2)	0 (0.0)
Psychiatric disorders	4 (9.5)	5 (11.9)	2 (4.8)	0 (0.0)	0 (0.0)	16 (19.5)	9 (11.0)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders	3 (7.1)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	6 (7.3)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	10 (23.8)	15 (35.7)	4 (9.5)	0 (0.0)	1 (2.4)	19 (23.2)	25 (30.5)	16 (19.5)	2 (2.4)	3 (3.7)
Skin and subcutaneous tissue disorders	7 (16.7)	9 (21.4)	0 (0.0)	0 (0.0)	0 (0.0)	16 (19.5)	13 (15.9)	2 (2.4)	0 (0.0)	0 (0.0)
Vascular disorders	3 (7.1)	1 (2.4)	1 (2.4)	0 (0.0)	0 (0.0)	4 (4.9)	10 (12.2)	6 (7.3)	0 (0.0)	1 (1.2)

Adverse events were graded with CTCAE version 4.0.

Table 6
Distribution of RTOG 1106 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	Standard RT (n=42) n and (%) of Patients by Grade					Adaptive RT (n=82) n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
BLOOD AND LYMPHATIC SYSTEM DISORDERS	9 (21.4)	6 (14.3)	3 (7.1)	1 (2.4)	0 (0.0)	20 (24.4)	22 (26.8)	7 (8.5)	1 (1.2)	0 (0.0)
Anemia	10 (23.8)	7 (16.7)	2 (4.8)	0 (0.0)	0 (0.0)	19 (23.2)	22 (26.8)	6 (7.3)	1 (1.2)	0 (0.0)
Disseminated intravascular coagulation	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
GASTROINTESTINAL DISORDERS	8 (19.0)	20 (47.6)	6 (14.3)	0 (0.0)	0 (0.0)	16 (19.5)	46 (56.1)	11 (13.4)	1 (1.2)	0 (0.0)
Ileus	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 (1.2)	0 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	9 (21.4)	20 (47.6)	6 (14.3)	1 (2.4)	1 (2.4)	22 (26.8)	33 (40.2)	14 (17.1)	0 (0.0)	0 (0.0)
Death NOS	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infusion related reaction	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.4)	0 (0.0)	1 (1.2)	2 (2.4)	2 (2.4)	0 (0.0)	0 (0.0)
IMMUNE SYSTEM DISORDERS	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)	0 (0.0)	1 (1.2)	0 (0.0)
Allergic reaction	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)	0 (0.0)	1 (1.2)	0 (0.0)
INFECTIONS AND INFESTATIONS	0 (0.0)	5 (11.9)	4 (9.5)	0 (0.0)	0 (0.0)	1 (1.2)	9 (11.0)	9 (11.0)	2 (2.4)	1 (1.2)
Infections and infestations - Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)	3 (3.7)	0 (0.0)	1 (1.2)
Sepsis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)	0 (0.0)
Urinary tract infection	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.7)	1 (1.2)	1 (1.2)	0 (0.0)
INVESTIGATIONS	4 (9.5)	6 (14.3)	9 (21.4)	9 (21.4)	0 (0.0)	9 (11.0)	12 (14.6)	26 (31.7)	11 (13.4)	0 (0.0)
CD4 lymphocytes decreased	0	1	0	1	0	1	2	1	0	0

Table 6
Distribution of RTOG 1106 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	Standard RT (n=42) n and (%) of Patients by Grade					Adaptive RT (n=82) n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(0.0)	(2.4)	(0.0)	(2.4)	(0.0)	(1.2)	(2.4)	(1.2)	(0.0)	(0.0)
Lymphocyte count decreased	0 (0.0)	2 (4.8)	7 (16.7)	7 (16.7)	0 (0.0)	5 (6.1)	6 (7.3)	16 (19.5)	7 (8.5)	0 (0.0)
Neutrophil count decreased	1 (2.4)	6 (14.3)	1 (2.4)	2 (4.8)	0 (0.0)	2 (2.4)	8 (9.8)	9 (11.0)	2 (2.4)	0 (0.0)
Platelet count decreased	11 (26.2)	4 (9.5)	2 (4.8)	1 (2.4)	0 (0.0)	14 (17.1)	2 (2.4)	5 (6.1)	4 (4.9)	0 (0.0)
White blood cell decreased	1 (2.4)	11 (26.2)	7 (16.7)	0 (0.0)	0 (0.0)	14 (17.1)	9 (11.0)	15 (18.3)	1 (1.2)	0 (0.0)
METABOLISM AND NUTRITION DISORDERS	6 (14.3)	12 (28.6)	7 (16.7)	0 (0.0)	0 (0.0)	26 (31.7)	18 (22.0)	13 (15.9)	3 (3.7)	0 (0.0)
Acidosis	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 (1.2)	0 (0.0)
Hyperglycemia	2 (4.8)	2 (4.8)	3 (7.1)	0 (0.0)	0 (0.0)	6 (7.3)	9 (11.0)	4 (4.9)	1 (1.2)	0 (0.0)
Hypokalemia	4 (9.5)	2 (4.8)	1 (2.4)	0 (0.0)	0 (0.0)	7 (8.5)	1 (1.2)	4 (4.9)	1 (1.2)	0 (0.0)
Hypophosphatemia	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	2 (2.4)	0 (0.0)	1 (1.2)	0 (0.0)
NERVOUS SYSTEM DISORDERS	16 (38.1)	10 (23.8)	3 (7.1)	0 (0.0)	0 (0.0)	34 (41.5)	18 (22.0)	8 (9.8)	1 (1.2)	0 (0.0)
Depressed level of consciousness	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 (1.2)	0 (0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (23.8)	15 (35.7)	4 (9.5)	0 (0.0)	1 (2.4)	19 (23.2)	25 (30.5)	16 (19.5)	2 (2.4)	3 (3.7)
Bronchopulmonary hemorrhage	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)
Hypoxia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)	1 (1.2)	0 (0.0)
Pneumonitis	1 (2.4)	1 (2.4)	1 (2.4)	0 (0.0)	1 (2.4)	2 (2.4)	3 (3.7)	1 (1.2)	1 (1.2)	0 (0.0)
Pulmonary fibrosis	0	0	0	1	0	2	1	0	0	0

Table 6
Distribution of RTOG 1106 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	Standard RT (n=42)					Adaptive RT (n=82)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(0.0)	(0.0)	(0.0)	(2.4)	(0.0)	(2.4)	(1.2)	(0.0)	(0.0)	(0.0)
Respiratory failure	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)	2 (2.4)
Respiratory, thoracic and mediastinal disorders - Other	2 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	2 (2.4)	1 (1.2)	0 (0.0)	1 (1.2)
VASCULAR DISORDERS	3 (7.1)	1 (2.4)	1 (2.4)	0 (0.0)	0 (0.0)	4 (4.9)	10 (12.2)	6 (7.3)	0 (0.0)	1 (1.2)
Thromboembolic event	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (6.1)	1 (1.2)	0 (0.0)	1 (1.2)

Adverse events were graded with CTCAE version 4.
Only includes system organ classes and terms with at least one Grade 4 or Grade 5.
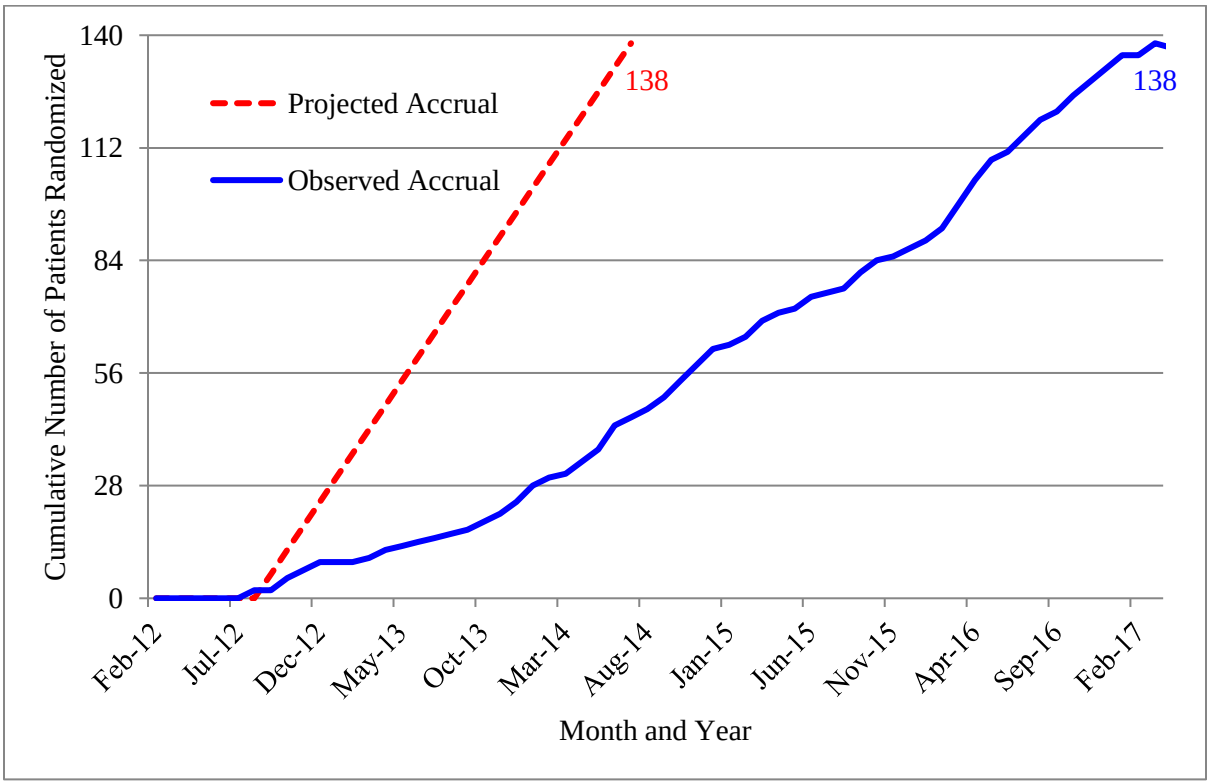
Figure 1
Cumulative Accrual for RTOG 1106 - Data as of 04/30/2019