RTOG 0839

Report Based on Data Through: 02/28/2019

Randomized Phase II Study Of Pre-Operative Chemoradiotherapy +/- Panitumumab (IND #110152) Followed By Consolidation Chemotherapy In Potentially Operable Locally Advanced (Stage IIIA, N2+) Non-Small Cell Lung Cancer

RANDOMIZE

Arm 1: Induction Chemoradiation
Paclitaxel & Carboplatin: 1x/week for 6 weeks
Concurrent RT: 2 Gy/day, 5x/week, for 6 weeks, for a total of 60 Gy

Arm 2: Induction Chemoradiation and Panitumumab
Panitumumab 1x/week for 6 weeks
Paclitaxel & Carboplatin: 1x/week for 6 weeks
Concurrent RT: 2 Gy/day, 5x/week, for 6 weeks, for a total of 60 Gy

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All Patients

Reassessment
4 weeks after Induction treatment

↙ ↘

Resectable Patients with No Disease Progression
Surgery within 2 weeks of reassessment and within 6 weeks of completion of induction treatment

Inoperable Patients (inoperable for medical, anatomical, or other reasons) with No Disease Progression
Patient proceeds to consolidation treatment within 6 weeks of completion of induction treatment

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Arms 1 and 2: Consolidation Chemotherapy
Paclitaxel & Carboplatin: q21 days x 2

Study Chairs:

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Quynh-Thu Le, M.D.	(Radiation Oncology)
Jessica Donington, M.D.	(Thoracic Surgery)
Warren D. D'Souza, Ph.D.	(Medical Physics)
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Adam Dicker, MD, Ph.D.	(Translational Research)

Protocol Statisticians: Chen Hu, Ph.D.
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Research Associates: Jeff Serianni, B.S.
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Dosimetrist: Jennifer Presley, R.T. (R)(M)(T)

Activated: 11/30/2010

Suspended: 06/26/2013 (*protocol-specified adverse event review*)

Reopened: 07/03/2013

Suspended: 09/30/2013 (*protocol-specified adverse event review*)

Reopened: 02/24/2014

Closed: 08/03/2015

Status: Follow-up, primary endpoint published

- **Study Description**
  This is a two-armed randomized phase II study designed to assess whether the addition of panitumumab to induction chemoradiation will improve the rate of mediastinal nodal clearance for patients with potentially operable locally advanced (stage IIIA, N2+) non-small cell lung cancer. The primary endpoint for this study is mediastinal nodal clearance following completion of induction chemoradiation.

- **Patient Accrual**
  Accrual was activated on November 30, 2010, and permanently closed on August 3, 2015, following the NRG Data Monitoring Committee review of toxicity data and the interim analysis. Total accrual was 71 (Table 1); monthly accrual was lower than projected. Median time of follow-up for vital status is 39.8 months.

- **Adverse Events**
  Adverse events (AEs) were graded with CTCAE version 4. As of February 28, 2019 and regardless of attribution to treatment, there have been 4 (18.2%) grade 4 and 0 (0.0%) grade 5 AEs reported on Induction Chemoradiation, and 6 (15.8%) grade 4 and 4 (10.5%) grade 5 AEs reported on Induction Chemoradiation and Panitumumab (Table 2). Adverse events with at least one reported grade 4 or grade 5 event are shown in Table 3. The four grade 5 AEs are lung infection (1), treatment related secondary malignancy (1), bronchopulmonary hemorrhage (1) and respiratory failure (1). There is no noticeable difference among arms in grade 4 adverse events within any system organ class.

Table 1
RTOG 0839 Accrual/Eligibility - Data as of 02/28/2019

	Induction Chemoradiation	Induction Chemoradiation and Panitumumab	Total
Randomized	24	47	71
Ineligible	1	9	10
Eligible	23	38	61

1 patient received no study treatment and is not included in adverse event tables.

Table 2
Distribution of RTOG 0839 Patients by Highest Grade Adverse Event
by System Organ Class - Data as of 02/28/2019
For All Reported Adverse Events without Regard to Attribution

System Organ Class	Induction Chemoradiation (n=22) n and (%) of Patients by Grade					Induction Chemoradiation and Panitumumab (n=38) n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Overall Highest Grade	0 (0.0)	2 (9.1)	16 (72.7)	4 (18.2)	0 (0.0)	1 (2.6)	10 (26.3)	17 (44.7)	6 (15.8)	4 (10.5)
Blood and lymphatic system disorders	7 (31.8)	6 (27.3)	2 (9.1)	0 (0.0)	0 (0.0)	11 (28.9)	6 (15.8)	3 (7.9)	0 (0.0)	0 (0.0)
Cardiac disorders	3 (13.6)	8 (36.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.3)	3 (7.9)	2 (5.3)	1 (2.6)	0 (0.0)
Ear and labyrinth disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	2 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	3 (13.6)	10 (45.5)	6 (27.3)	0 (0.0)	0 (0.0)	11 (28.9)	19 (50.0)	6 (15.8)	0 (0.0)	0 (0.0)
General disorders and administration site conditions	6 (27.3)	12 (54.5)	2 (9.1)	0 (0.0)	0 (0.0)	16 (42.1)	15 (39.5)	4 (10.5)	0 (0.0)	0 (0.0)
Immune system disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	1 (2.6)	0 (0.0)	1 (2.6)	0 (0.0)
Infections and infestations	0 (0.0)	6 (27.3)	3 (13.6)	1 (4.5)	0 (0.0)	1 (2.6)	1 (2.6)	4 (10.5)	2 (5.3)	1 (2.6)
Injury, poisoning and procedural complications	6 (27.3)	1 (4.5)	1 (4.5)	0 (0.0)	0 (0.0)	3 (7.9)	1 (2.6)	0 (0.0)	1 (2.6)	0 (0.0)
Investigations	3 (13.6)	1 (4.5)	11 (50.0)	3 (13.6)	0 (0.0)	7 (18.4)	7 (18.4)	5 (13.2)	6 (15.8)	0 (0.0)

Table 2
Distribution of RTOG 0839 Patients by Highest Grade Adverse Event
by System Organ Class - Data as of 02/28/2019
For All Reported Adverse Events without Regard to Attribution

System Organ Class	Induction Chemoradiation (n=22)					Induction Chemoradiation and Panitumumab (n=38)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Metabolism and nutrition disorders	5 (22.7)	10 (45.5)	2 (9.1)	1 (4.5)	0 (0.0)	14 (36.8)	5 (13.2)	8 (21.1)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	5 (22.7)	8 (36.4)	0 (0.0)	0 (0.0)	0 (0.0)	5 (13.2)	5 (13.2)	3 (7.9)	0 (0.0)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)	1 (2.6)
Nervous system disorders	9 (40.9)	4 (18.2)	3 (13.6)	0 (0.0)	0 (0.0)	14 (36.8)	6 (15.8)	2 (5.3)	1 (2.6)	0 (0.0)
Psychiatric disorders	4 (18.2)	3 (13.6)	0 (0.0)	0 (0.0)	0 (0.0)	7 (18.4)	5 (13.2)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders	2 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (10.5)	4 (10.5)	0 (0.0)	1 (2.6)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	8 (36.4)	4 (18.2)	7 (31.8)	2 (9.1)	0 (0.0)	9 (23.7)	12 (31.6)	4 (10.5)	2 (5.3)	2 (5.3)
Skin and subcutaneous tissue disorders	4 (18.2)	7 (31.8)	0 (0.0)	0 (0.0)	0 (0.0)	13 (34.2)	16 (42.1)	5 (13.2)	0 (0.0)	0 (0.0)
Surgical and medical procedures	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	5 (22.7)	0 (0.0)	3 (13.6)	1 (4.5)	0 (0.0)	4 (10.5)	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)

Adverse events were graded with CTCAE version 4.0.

Table 3
Distribution of RTOG 0839 Patients by Highest Grade Adverse Event
by Specific Adverse Event Term - Data as of 02/28/2019
For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	Induction Chemoradiation (n=22)					Induction Chemoradiation and Panitumumab (n=38)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
CARDIAC DISORDERS	3	8	0	0	0	2	3	2	1	0

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	1	2	3	4	5	1	2	3	4	5
	(13.6)	(36.4)	(0.0)	(0.0)	(0.0)	(5.3)	(7.9)	(5.3)	(2.6)	(0.0)
Cardiac arrest	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 (2.6)	0 (0.0)
IMMUNE SYSTEM DISORDERS	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	1 (2.6)	0 (0.0)	1 (2.6)	0 (0.0)
Anaphylaxis	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 (2.6)	0 (0.0)
INFECTIONS AND INFESTATIONS	0 (0.0)	6 (27.3)	3 (13.6)	1 (4.5)	0 (0.0)	1 (2.6)	1 (2.6)	4 (10.5)	2 (5.3)	1 (2.6)
Lung infection	0 (0.0)	2 (9.1)	3 (13.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.3)	2 (5.3)	1 (2.6)
Pleural infection	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)
Sepsis	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (7.9)	0 (0.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	6 (27.3)	1 (4.5)	1 (4.5)	0 (0.0)	0 (0.0)	3 (7.9)	1 (2.6)	0 (0.0)	1 (2.6)	0 (0.0)
Postoperative thoracic procedure complication	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 (2.6)	0 (0.0)
INVESTIGATIONS	3 (13.6)	1 (4.5)	11 (50.0)	3 (13.6)	0 (0.0)	7 (18.4)	7 (18.4)	5 (13.2)	6 (15.8)	0 (0.0)
Lymphocyte count decreased	0 (0.0)	2 (9.1)	6 (27.3)	1 (4.5)	0 (0.0)	2 (5.3)	2 (5.3)	4 (10.5)	3 (7.9)	0 (0.0)
Neutrophil count decreased	1 (4.5)	0 (0.0)	7 (31.8)	0 (0.0)	0 (0.0)	1 (2.6)	3 (7.9)	4 (10.5)	2 (5.3)	0 (0.0)
Platelet count decreased	6 (27.3)	2 (9.1)	1 (4.5)	1 (4.5)	0 (0.0)	5 (13.2)	1 (2.6)	1 (2.6)	1 (2.6)	0 (0.0)
White blood cell decreased	3 (13.6)	3 (13.6)	4 (18.2)	2 (9.1)	0 (0.0)	2 (5.3)	4 (10.5)	6 (15.8)	1 (2.6)	0 (0.0)
METABOLISM AND NUTRITION DISORDERS	5 (22.7)	10 (45.5)	2 (9.1)	1 (4.5)	0 (0.0)	14 (36.8)	5 (13.2)	8 (21.1)	0 (0.0)	0 (0.0)
Hypocalcemia	2 (9.1)	1 (4.5)	0 (0.0)	1 (4.5)	0 (0.0)	6 (15.8)	2 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)

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	1	2	3	4	5	1	2	3	4	5
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)	1 (2.6)
Treatment related secondary malignancy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)	1 (2.6)
NERVOUS SYSTEM DISORDERS	9 (40.9)	4 (18.2)	3 (13.6)	0 (0.0)	0 (0.0)	14 (36.8)	6 (15.8)	2 (5.3)	1 (2.6)	0 (0.0)
Nervous system disorders - Other	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 (2.6)	0 (0.0)
RENAL AND URINARY DISORDERS	2 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (10.5)	4 (10.5)	0 (0.0)	1 (2.6)	0 (0.0)
Acute kidney injury	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	8 (36.4)	4 (18.2)	7 (31.8)	2 (9.1)	0 (0.0)	9 (23.7)	12 (31.6)	4 (10.5)	2 (5.3)	2 (5.3)
Aspiration	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 (2.6)	0 (0.0)
Bronchopleural fistula	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)	1 (2.6)	0 (0.0)
Bronchopulmonary hemorrhage	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)
Dyspnea	10 (45.5)	4 (18.2)	2 (9.1)	0 (0.0)	0 (0.0)	9 (23.7)	3 (7.9)	4 (10.5)	1 (2.6)	0 (0.0)
Hypoxia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	1 (2.6)	1 (2.6)	0 (0.0)
Pleural hemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumonitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.3)	4 (10.5)	1 (2.6)	2 (5.3)	0 (0.0)

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	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Respiratory failure	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	1 (2.6)
VASCULAR DISORDERS	5 (22.7)	0 (0.0)	3 (13.6)	1 (4.5)	0 (0.0)	4 (10.5)	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)
Thromboembolic event	1 (4.5)	0 (0.0)	2 (9.1)	1 (4.5)	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 4 or Grade 5.