RTOG 1119

Report Based on Data Through: 04/30/2019

Phase II Randomized Study of Whole Brain Radiotherapy in Combination with Concurrent Lapatinib in Patients with Brain Metastasis from Her2-Positive Breast Cancer: A Collaborative Study of RTOG and KROG

S T R A T I F Y	Graded Prognostic Assessment (GPA): 1.5-2 vs. 2.5-3 vs. 3.5-4 Use of Non-CNS–Penetrating HER2 Blockade at Study Entry: No vs. Yes: trastuzumab ± pertuzumab RT to Be Used: WBRT vs. SRS		**R A N D O M I Z E**	**Arm A** Radiation (WBRT or SRS) Versus **Arm B** Radiation (WBRT or SRS) Plus Lapatinib

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Activated: 07/26/2012

Status: Accruing

- **Study Description**
  This is a randomized phase II study designed to assess the efficacy of lapatinib as a treatment for patients with brain metastasis from Her2-positive breast cancer. All eligible patients must have pathologically (histologically or cytologically) proven diagnosis of invasive HER2-overexpressing breast cancer (3+ staining by immunohistochemistry or HER2 gene amplification by FISH or SISH ≥ 2.2). Patients must have at least 1 measurable unirradiated parenchymal brain metastasis. Patients who are to undergo SRS must have no more than 10 brain metastases. There is no limit on number of brain metastases for WBRT. The minimum size as measured on T1-weighted gadolinium-enhanced MRI must be as follows: ≥ 10 mm if solitary lesion and if ≥ 2 metastasis then at least two must be ≥ 5 mm. Patients may also have the following: 1) progressive parenchymal brain metastases following stereotactic radiosurgery for 1-3 brain metastases, with at least 1 new measurable lesion or 2) progressive parenchymal brain metastases following surgical resection of 1-3 brain metastases, with at least 1 brain metastasis is measurable. Prior lapatinib is allowed as long as the last dose received was > 21 days prior to study entry and provided the patient has not received it at any time after the diagnosis of brain metastasis. The primary endpoint for this study is complete response (CR) rate in the brain at 12 weeks post whole brain irradiation (WBRT) or stereotactic radiosurgery (SRS) as determined by MRI scan of the brain.

- **Patient Accrual**
  Accrual was activated on July 26, 2012 and, as of April 30, 2019, 140 patients have been randomized. Accrual is lower than projected (Table 1 and Figure 1). As of April 30, 2019, the median time of follow-up for vital status is 12.3 months. There are no planned interim analyses for this study. The primary endpoint analysis is planned for fall 2019.

- **Patient and Tumor Characteristics**
  There are 7 ineligible patients on the RT arm and 0 on the RT + Lapatinib arm (Table 2). Out of eligible patients, 9 patients subsequently withdrew consent, 4 on the RT arm and 5 on the RT + Lapatinib arm. The distribution by patient and tumor characteristics is shown in Table 3. Median (min-max) age is 55 years (31-84). The majority of patients have no to minor neurologic symptoms (77.1%) and have a graded prognostic factor of 2.5-3 (53.4%).

- **Adverse Events**
  AEs were graded with CTCAE version 4. As of April 30, 2019, there have been 15 patients (26.3%) with reported grade 3 events, 3 (5.3%) with reported grade 4 events, and 4 (7.0%) with reported grade 5 events on the RT arm compared to 30 (44.8%), 6 (9.0%), and 2 (3.0%), respectively, on the RT + Lapatinib arm (Table 4). There are 14 (20.9%) and 11 (16.4%) patients with reported grade ≥ 3 investigations and metabolism and nutrition disorders, respectively, on the RT + Lapatinib arm compared to 3 (5.3%) and 2 (3.5%) patients on the RT arm. Table 5 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. Nine patients (13.4%) on the RT + Lapatinib arm have grade 3 diarrhea reported compared to no patients on the RT arm. Three out of the four grade 5 events on the RT arm are the following: colonic obstruction, thromboembolic event, and cardiac arrest; all reported as unrelated to protocol treatment and none are new as of this report. The other grade 5 on the RT arm is general disorders and administration site conditions - other, specify and is unlikely related to treatment; this grade 5 event is new as of this report. The 2 grade 5 events on the RT + Lapatinib arm are the following: lung infection reported as unrelated to treatment and encephalopathy reported as unlikely related to protocol treatment. Neither of these grade 5 events are new as of this report.

Table 1
RTOG 1119 Accrual Summary - Data as of 04/30/2019

Date activated to accrual:	July 26, 2012
Targeted sample size:	143
Projected monthly accrual:	6.0 *
Average monthly accrual over last 6 months:	1.7
Projected accrual as of 04/30/2019:	143
Total accrual as of 04/30/2019:	140
Percent of projected accrual achieved as of 04/30/2019:	97.90%
Percent of total targeted accrual as of 04/30/2019:	97.90%
Projected completion date based on last 6 months accrual:	June 2019

* 0/month for first 6 months.

Table 2
RTOG 1119 Accrual/Eligibility - Data as of 04/30/2019

	RT	RT + Lapatinib	Total
Randomized	72	68	140
Ineligible	7	0	7
Eligible	65	68	133

Table 3
Patient and Tumor Characteristics for Eligible Patients with On-Study Data in RTOG 1119 - Data as of 04/30/2019

	RT		RT + Lapatinib		Total	
Patient or Tumor Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
Age (years)						
≤ 39	3	4.8	8	11.8	11	8.4
40 - 49	19	30.2	16	23.5	35	26.7
50 - 59	23	36.5	26	38.2	49	37.4
60 - 69	12	19.0	12	17.6	24	18.3
≥ 70	6	9.5	6	8.8	12	9.2
Gender						
Female	63	100.0	68	100.0	131	100.0
Race						
American Indian or Alaska Native	1	1.6	0	0.0	1	0.8
Asian	19	30.2	21	30.9	40	30.5
Black or African American	3	4.8	6	8.8	9	6.9
White	39	61.9	40	58.8	79	60.3

Table 3
Patient and Tumor Characteristics for Eligible Patients with On-Study Data in RTOG 1119 - Data as of 04/30/2019

	RT		RT + Lapatinib		Total	
Patient or Tumor Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
More than one race	1	1.6	0	0.0	1	0.8
Unknown	0	0.0	1	1.5	1	0.8
Ethnicity						
Hispanic or Latino	7	11.1	3	4.4	10	7.6
Not Hispanic or Latino	56	88.9	64	94.1	120	91.6
Unknown	0	0.0	1	1.5	1	0.8
Karnofsky Performance Status						
60	9	14.3	2	2.9	11	8.4
70	14	22.2	9	13.2	23	17.6
80	14	22.2	16	23.5	30	22.9
90	18	28.6	26	38.2	44	33.6
100	8	12.7	15	22.1	23	17.6
Neurologic Function						
No neurologic symptoms; fully active at home / work without assistance	19	30.2	30	44.1	49	37.4
Minor neurologic symptoms	26	41.3	26	38.2	52	39.7
Moderate neurologic symptoms/fully active at home	10	15.9	7	10.3	17	13.0
Moderate neurologic symptoms/less than fully active at home	7	11.1	5	7.4	12	9.2
Severe neurologic symptoms	1	1.6	0	0.0	1	0.8
Tumor Laterality						
Right	21	33.3	13	19.1	34	26.0
Left	10	15.9	13	19.1	23	17.6
Bilateral	31	49.2	42	61.8	73	55.7
Unknown	1	1.6	0	0.0	1	0.8
Graded Prognostic Factor (GPA)						
1.5-2	5	7.9	4	5.9	9	6.9
2.5-3	34	54.0	36	52.9	70	53.4
3.5-4	24	38.1	28	41.2	52	39.7
Use of Non-CNS Penetrating HER2 Blockade at Study Entry						
No (None)	22	34.9	27	39.7	49	37.4
Yes (Trastuzumab +/- Pertuzumab)	41	65.1	41	60.3	82	62.6

Table 3
Patient and Tumor Characteristics for Eligible Patients with On-Study Data in RTOG 1119 - Data as of 04/30/2019

	RT		RT + Lapatinib		Total	
Patient or Tumor Characteristic	**n**	**%**	**n**	**%**	**n**	**%**
Previous Stereotactic Radiosurgery or Surgical Resection[†]	42		47		89	
No	37	88.1	41	87.2	78	87.6
Yes	5	11.9	6	12.8	11	12.4
RT to be used (WBRT or SRS) [‡]						
WBRT	16	25.4	17	25.0	33	25.2
SRS	5	7.9	4	5.9	9	6.9
WBRT (before October 2016 amendment)	42	66.7	47	69.1	89	67.9
Consented to tissue collection						
No	15	23.8	24	35.3	39	29.8
Yes	48	76.2	44	64.7	92	70.2
Consented to blood collection						
No	19	30.2	28	41.2	47	35.9
Yes	44	69.8	40	58.8	84	64.1
Total	63	100.0	68	100.0	131	100.0

2 eligible patients did not have on-study data and are excluded from this table.
[†] Stratification factor removed in October 2016 amendment.
[‡] Stratification factor added in October 2016 amendment.

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

Table 4
Distribution of RTOG 1119 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	RT (n=57)					RT + Lapatinib (n=67)				
	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	4 (7.0)	25 (43.9)	15 (26.3)	3 (5.3)	4 (7.0)	6 (9.0)	16 (23.9)	30 (44.8)	6 (9.0)	2 (3.0)
Blood and lymphatic system disorders	2 (3.5)	2 (3.5)	0 (0.0)	1 (1.8)	0 (0.0)	12 (17.9)	5 (7.5)	3 (4.5)	0 (0.0)	0 (0.0)
Cardiac disorders	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)	1 (1.8)	3 (4.5)	0 (0.0)	2 (3.0)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	8 (14.0)	2 (3.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	2 (3.0)	1 (1.5)	0 (0.0)	0 (0.0)
Endocrine disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	7 (12.3)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	12 (17.9)	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	16 (28.1)	9 (15.8)	2 (3.5)	0 (0.0)	1 (1.8)	17 (25.4)	24 (35.8)	12 (17.9)	0 (0.0)	0 (0.0)
General disorders and administration site conditions	11 (19.3)	16 (28.1)	3 (5.3)	0 (0.0)	1 (1.8)	18 (26.9)	18 (26.9)	6 (9.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations	0 (0.0)	0 (0.0)	5 (8.8)	0 (0.0)	0 (0.0)	0 (0.0)	8 (11.9)	0 (0.0)	2 (3.0)	1 (1.5)
Injury, poisoning and procedural complications	2 (3.5)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	4 (6.0)	5 (7.5)	4 (6.0)	0 (0.0)	0 (0.0)
Investigations	3 (5.3)	2 (3.5)	3 (5.3)	0 (0.0)	0 (0.0)	13 (19.4)	10 (14.9)	11 (16.4)	3 (4.5)	0 (0.0)
Metabolism and nutrition disorders	9 (15.8)	4 (7.0)	1 (1.8)	1 (1.8)	0 (0.0)	13 (19.4)	7 (10.4)	9 (13.4)	2 (3.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	7 (12.3)	8 (14.0)	5 (8.8)	0 (0.0)	0 (0.0)	12 (17.9)	9 (13.4)	5 (7.5)	0 (0.0)	0 (0.0)
Nervous system disorders	12 (21.1)	18 (31.6)	6 (10.5)	1 (1.8)	0 (0.0)	21 (31.3)	13 (19.4)	9 (13.4)	0 (0.0)	1 (1.5)
Psychiatric disorders	8	2	1	0	0	10	12	2	0	0

Table 4
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For All Reported Adverse Events without Regard to Attribution

System Organ Class	RT (n=57)					RT + Lapatinib (n=67)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(14.0)	(3.5)	(1.8)	(0.0)	(0.0)	(14.9)	(17.9)	(3.0)	(0.0)	(0.0)
Renal and urinary disorders	0	0	0	0	0	4	4	2	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(6.0)	(6.0)	(3.0)	(0.0)	(0.0)
Reproductive system and breast disorders	0	0	0	0	0	2	2	0	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(3.0)	(3.0)	(0.0)	(0.0)	(0.0)
Respiratory, thoracic and mediastinal disorders	6	5	2	0	0	8	6	4	1	0
	(10.5)	(8.8)	(3.5)	(0.0)	(0.0)	(11.9)	(9.0)	(6.0)	(1.5)	(0.0)
Skin and subcutaneous tissue disorders	8	14	1	0	0	16	20	7	0	0
	(14.0)	(24.6)	(1.8)	(0.0)	(0.0)	(23.9)	(29.9)	(10.4)	(0.0)	(0.0)
Social circumstances	0	0	0	0	0	1	0	0	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)	(0.0)	(0.0)
Vascular disorders	4	2	4	0	1	8	7	6	0	0
	(7.0)	(3.5)	(7.0)	(0.0)	(1.8)	(11.9)	(10.4)	(9.0)	(0.0)	(0.0)

Adverse events were graded with CTCAE version 4.

Table 5
Distribution of RTOG 1119 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	RT (n=57)					RT + Lapatinib (n=67)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
BLOOD AND LYMPHATIC SYSTEM DISORDERS	2	2	0	1	0	12	5	3	0	0
	(3.5)	(3.5)	(0.0)	(1.8)	(0.0)	(17.9)	(7.5)	(4.5)	(0.0)	(0.0)
Anemia	2	2	0	0	0	11	5	2	0	0
	(3.5)	(3.5)	(0.0)	(0.0)	(0.0)	(16.4)	(7.5)	(3.0)	(0.0)	(0.0)
Febrile neutropenia	0	0	0	1	0	0	0	0	0	0
	(0.0)	(0.0)	(0.0)	(1.8)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
Leukocytosis	0	0	0	0	0	0	0	1	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)
CARDIAC DISORDERS	1	0	1	0	1	3	0	2	0	0
	(1.8)	(0.0)	(1.8)	(0.0)	(1.8)	(4.5)	(0.0)	(3.0)	(0.0)	(0.0)
Atrial fibrillation	0	0	0	0	0	0	0	1	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)

Table 5
Distribution of RTOG 1119 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	RT (n=57)					RT + Lapatinib (n=67)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Cardiac arrest	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Left ventricular systolic dysfunction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)
Sinus tachycardia	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.5)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)
EAR AND LABYRINTH DISORDERS	8 (14.0)	2 (3.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	2 (3.0)	1 (1.5)	0 (0.0)	0 (0.0)
External ear inflammation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)
EYE DISORDERS	7 (12.3)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	12 (17.9)	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
Keratitis	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
GASTROINTESTINAL DISORDERS	16 (28.1)	9 (15.8)	2 (3.5)	0 (0.0)	1 (1.8)	17 (25.4)	24 (35.8)	12 (17.9)	0 (0.0)	0 (0.0)
Colonic obstruction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhea	3 (5.3)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	16 (23.9)	6 (9.0)	9 (13.4)	0 (0.0)	0 (0.0)
Mucositis oral	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (6.0)	4 (6.0)	1 (1.5)	0 (0.0)	0 (0.0)
Nausea	14 (24.6)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	16 (23.9)	17 (25.4)	4 (6.0)	0 (0.0)	0 (0.0)
Vomiting	7 (12.3)	1 (1.8)	2 (3.5)	0 (0.0)	0 (0.0)	13 (19.4)	7 (10.4)	2 (3.0)	0 (0.0)	0 (0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	11 (19.3)	16 (28.1)	3 (5.3)	0 (0.0)	1 (1.8)	18 (26.9)	18 (26.9)	6 (9.0)	0 (0.0)	0 (0.0)
Fatigue	11 (19.3)	13 (22.8)	2 (3.5)	0 (0.0)	0 (0.0)	20 (29.9)	15 (22.4)	4 (6.0)	0 (0.0)	0 (0.0)
Gait disturbance	1 (1.8)	2 (3.5)	1 (1.8)	0 (0.0)	0 (0.0)	3 (4.5)	6 (9.0)	0 (0.0)	0 (0.0)	0 (0.0)
General disorders and administration site conditions - Other	1	0	0	0	1	0	0	2	0	0

Table 5
Distribution of RTOG 1119 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	RT (n=57)					RT + Lapatinib (n=67)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(1.8)	(0.0)	(0.0)	(0.0)	(1.8)	(0.0)	(0.0)	(3.0)	(0.0)	(0.0)
INFECTIONS AND INFESTATIONS	0 (0.0)	0 (0.0)	5 (8.8)	0 (0.0)	0 (0.0)	0 (0.0)	8 (11.9)	0 (0.0)	2 (3.0)	1 (1.5)
Bladder infection	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)
Endocarditis infective	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations - Other	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lung infection	0 (0.0)	0 (0.0)	3 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)
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 (3.0)	0 (0.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (3.5)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	4 (6.0)	5 (7.5)	4 (6.0)	0 (0.0)	0 (0.0)
Fall	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (4.5)	2 (3.0)	2 (3.0)	0 (0.0)	0 (0.0)
Fracture	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	1 (1.5)	0 (0.0)	0 (0.0)
Hip fracture	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)
INVESTIGATIONS	3 (5.3)	2 (3.5)	3 (5.3)	0 (0.0)	0 (0.0)	13 (19.4)	10 (14.9)	11 (16.4)	3 (4.5)	0 (0.0)
Alanine aminotransferase increased	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	8 (11.9)	2 (3.0)	2 (3.0)	1 (1.5)	0 (0.0)
Alkaline phosphatase increased	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	6 (9.0)	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
Aspartate aminotransferase increased	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (10.4)	2 (3.0)	0 (0.0)	1 (1.5)	0 (0.0)
Blood bilirubin increased	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	3 (4.5)	4 (6.0)	1 (1.5)	1 (1.5)	0 (0.0)
GGT increased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)
Lymphocyte count decreased	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	7 (10.4)	4 (6.0)	6 (9.0)	0 (0.0)	0 (0.0)
Neutrophil count decreased	0	0	0	0	0	1	1	1	0	0

Table 5
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For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	RT (n=57)					RT + Lapatinib (n=67)				
	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)	(0.0)	(0.0)	(1.5)	(1.5)	(1.5)	(0.0)	(0.0)
Platelet count decreased	1	0	1	0	0	6	2	2	2	0
	(1.8)	(0.0)	(1.8)	(0.0)	(0.0)	(9.0)	(3.0)	(3.0)	(3.0)	(0.0)
Weight loss	1	1	1	0	0	2	3	2	0	0
	(1.8)	(1.8)	(1.8)	(0.0)	(0.0)	(3.0)	(4.5)	(3.0)	(0.0)	(0.0)
White blood cell decreased	1	0	0	0	0	8	0	3	0	0
	(1.8)	(0.0)	(0.0)	(0.0)	(0.0)	(11.9)	(0.0)	(4.5)	(0.0)	(0.0)
METABOLISM AND NUTRITION DISORDERS	9	4	1	1	0	13	7	9	2	0
	(15.8)	(7.0)	(1.8)	(1.8)	(0.0)	(19.4)	(10.4)	(13.4)	(3.0)	(0.0)
Anorexia	9	2	1	0	0	9	8	2	0	0
	(15.8)	(3.5)	(1.8)	(0.0)	(0.0)	(13.4)	(11.9)	(3.0)	(0.0)	(0.0)
Dehydration	0	0	0	0	0	0	1	4	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(6.0)	(0.0)	(0.0)
Hyperglycemia	1	1	0	1	0	6	2	2	0	0
	(1.8)	(1.8)	(0.0)	(1.8)	(0.0)	(9.0)	(3.0)	(3.0)	(0.0)	(0.0)
Hyperkalemia	1	0	0	0	0	1	0	1	0	0
	(1.8)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(1.5)	(0.0)	(0.0)
Hypocalcemia	1	0	0	0	0	3	1	2	0	0
	(1.8)	(0.0)	(0.0)	(0.0)	(0.0)	(4.5)	(1.5)	(3.0)	(0.0)	(0.0)
Hypokalemia	0	0	0	0	0	5	1	2	1	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(7.5)	(1.5)	(3.0)	(1.5)	(0.0)
Hyponatremia	1	0	0	0	0	5	0	3	1	0
	(1.8)	(0.0)	(0.0)	(0.0)	(0.0)	(7.5)	(0.0)	(4.5)	(1.5)	(0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	7	8	5	0	0	12	9	5	0	0
	(12.3)	(14.0)	(8.8)	(0.0)	(0.0)	(17.9)	(13.4)	(7.5)	(0.0)	(0.0)
Back pain	3	2	0	0	0	4	2	1	0	0
	(5.3)	(3.5)	(0.0)	(0.0)	(0.0)	(6.0)	(3.0)	(1.5)	(0.0)	(0.0)
Bone pain	0	1	0	0	0	1	1	1	0	0
	(0.0)	(1.8)	(0.0)	(0.0)	(0.0)	(1.5)	(1.5)	(1.5)	(0.0)	(0.0)
Chest wall pain	1	0	0	0	0	0	0	1	0	0
	(1.8)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)
Generalized muscle weakness	0	4	2	0	0	6	4	1	0	0
	(0.0)	(7.0)	(3.5)	(0.0)	(0.0)	(9.0)	(6.0)	(1.5)	(0.0)	(0.0)
Muscle weakness left-sided	1	1	1	0	0	1	0	0	0	0
	(1.8)	(1.8)	(1.8)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)	(0.0)	(0.0)
Muscle weakness lower limb	1	3	1	0	0	2	4	0	0	0

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System Organ Class/Term	RT (n=57)					RT + Lapatinib (n=67)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(1.8)	(5.3)	(1.8)	(0.0)	(0.0)	(3.0)	(6.0)	(0.0)	(0.0)	(0.0)
Muscle weakness right-sided	0	1	1	0	0	1	0	0	0	0
	(0.0)	(1.8)	(1.8)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)	(0.0)	(0.0)
Neck pain	2	0	0	0	0	1	0	2	0	0
	(3.5)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(3.0)	(0.0)	(0.0)
NERVOUS SYSTEM DISORDERS	12	18	6	1	0	21	13	9	0	1
	(21.1)	(31.6)	(10.5)	(1.8)	(0.0)	(31.3)	(19.4)	(13.4)	(0.0)	(1.5)
Central nervous system necrosis	0	0	0	0	0	0	0	1	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)
Cognitive disturbance	2	1	0	0	0	1	0	1	0	0
	(3.5)	(1.8)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(1.5)	(0.0)	(0.0)
Dizziness	4	3	0	0	0	12	4	1	0	0
	(7.0)	(5.3)	(0.0)	(0.0)	(0.0)	(17.9)	(6.0)	(1.5)	(0.0)	(0.0)
Dysphasia	1	0	1	0	0	1	0	0	0	0
	(1.8)	(0.0)	(1.8)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)	(0.0)	(0.0)
Edema cerebral	0	0	0	1	0	0	0	0	0	0
	(0.0)	(0.0)	(0.0)	(1.8)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
Encephalopathy	0	0	0	0	0	0	0	0	0	1
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)
Headache	13	8	2	0	0	15	8	3	0	0
	(22.8)	(14.0)	(3.5)	(0.0)	(0.0)	(22.4)	(11.9)	(4.5)	(0.0)	(0.0)
Leukoencephalopathy	0	0	0	0	0	0	0	1	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)
Memory impairment	7	3	1	0	0	7	1	1	0	0
	(12.3)	(5.3)	(1.8)	(0.0)	(0.0)	(10.4)	(1.5)	(1.5)	(0.0)	(0.0)
Nervous system disorders - Other	3	0	1	0	0	2	0	0	0	0
	(5.3)	(0.0)	(1.8)	(0.0)	(0.0)	(3.0)	(0.0)	(0.0)	(0.0)	(0.0)
Peripheral sensory neuropathy	4	2	0	0	0	5	3	1	0	0
	(7.0)	(3.5)	(0.0)	(0.0)	(0.0)	(7.5)	(4.5)	(1.5)	(0.0)	(0.0)
Seizure	1	0	1	0	0	0	2	1	0	0
	(1.8)	(0.0)	(1.8)	(0.0)	(0.0)	(0.0)	(3.0)	(1.5)	(0.0)	(0.0)
Stroke	0	0	0	0	0	0	0	1	0	0
	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(1.5)	(0.0)	(0.0)
Syncope	0	0	2	0	0	0	0	0	0	0
	(0.0)	(0.0)	(3.5)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
PSYCHIATRIC DISORDERS	8	2	1	0	0	10	12	2	0	0
	(14.0)	(3.5)	(1.8)	(0.0)	(0.0)	(14.9)	(17.9)	(3.0)	(0.0)	(0.0)
Confusion	1	0	1	0	0	2	3	1	0	0
	(1.8)	(0.0)	(1.8)	(0.0)	(0.0)	(3.0)	(4.5)	(1.5)	(0.0)	(0.0)

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For Selected Adverse Events without Regard to Attribution

System Organ Class/Term	RT (n=57)					RT + Lapatinib (n=67)				
	n and (%) of Patients by Grade					n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
Hallucinations	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)
Insomnia	3 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (11.9)	4 (6.0)	1 (1.5)	0 (0.0)	0 (0.0)
RENAL AND URINARY DISORDERS	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (6.0)	4 (6.0)	2 (3.0)	0 (0.0)	0 (0.0)
Acute kidney injury	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	1 (1.5)	1 (1.5)	0 (0.0)	0 (0.0)
Chronic kidney disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	1 (1.5)	0 (0.0)	0 (0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	6 (10.5)	5 (8.8)	2 (3.5)	0 (0.0)	0 (0.0)	8 (11.9)	6 (9.0)	4 (6.0)	1 (1.5)	0 (0.0)
Dyspnea	3 (5.3)	2 (3.5)	2 (3.5)	0 (0.0)	0 (0.0)	5 (7.5)	4 (6.0)	3 (4.5)	1 (1.5)	0 (0.0)
Hypoxia	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	1 (1.5)	0 (0.0)	0 (0.0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	8 (14.0)	14 (24.6)	1 (1.8)	0 (0.0)	0 (0.0)	16 (23.9)	20 (29.9)	7 (10.4)	0 (0.0)	0 (0.0)
Erythroderma	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)
Palmar-plantar erythrodysesthesia syndrome	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	3 (4.5)	1 (1.5)	1 (1.5)	0 (0.0)	0 (0.0)
Pruritus	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	3 (4.5)	1 (1.5)	1 (1.5)	0 (0.0)	0 (0.0)
Rash acneiform	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (16.4)	4 (6.0)	1 (1.5)	0 (0.0)	0 (0.0)
Rash maculo-papular	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	5 (7.5)	3 (4.5)	2 (3.0)	0 (0.0)	0 (0.0)
Skin ulceration	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)
VASCULAR DISORDERS	4 (7.0)	2 (3.5)	4 (7.0)	0 (0.0)	1 (1.8)	8 (11.9)	7 (10.4)	6 (9.0)	0 (0.0)	0 (0.0)
Hypertension	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	3 (4.5)	4 (6.0)	0 (0.0)	0 (0.0)
Hypotension	0	0	1	0	0	1	1	0	0	0

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System Organ Class/Term	RT (n=57) n and (%) of Patients by Grade					RT + Lapatinib (n=67) n and (%) of Patients by Grade				
	1	2	3	4	5	1	2	3	4	5
	(0.0)	(0.0)	(1.8)	(0.0)	(0.0)	(1.5)	(1.5)	(0.0)	(0.0)	(0.0)
Thromboembolic event	0	0	2	0	1	0	1	3	0	0
	(0.0)	(0.0)	(3.5)	(0.0)	(1.8)	(0.0)	(1.5)	(4.5)	(0.0)	(0.0)
Vascular disorders - Other	0	0	1	0	0	0	0	0	0	0
	(0.0)	(0.0)	(1.8)	(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.

Figure 1
Cumulative Accrual for RTOG 1119 - Data as of 04/30/2019