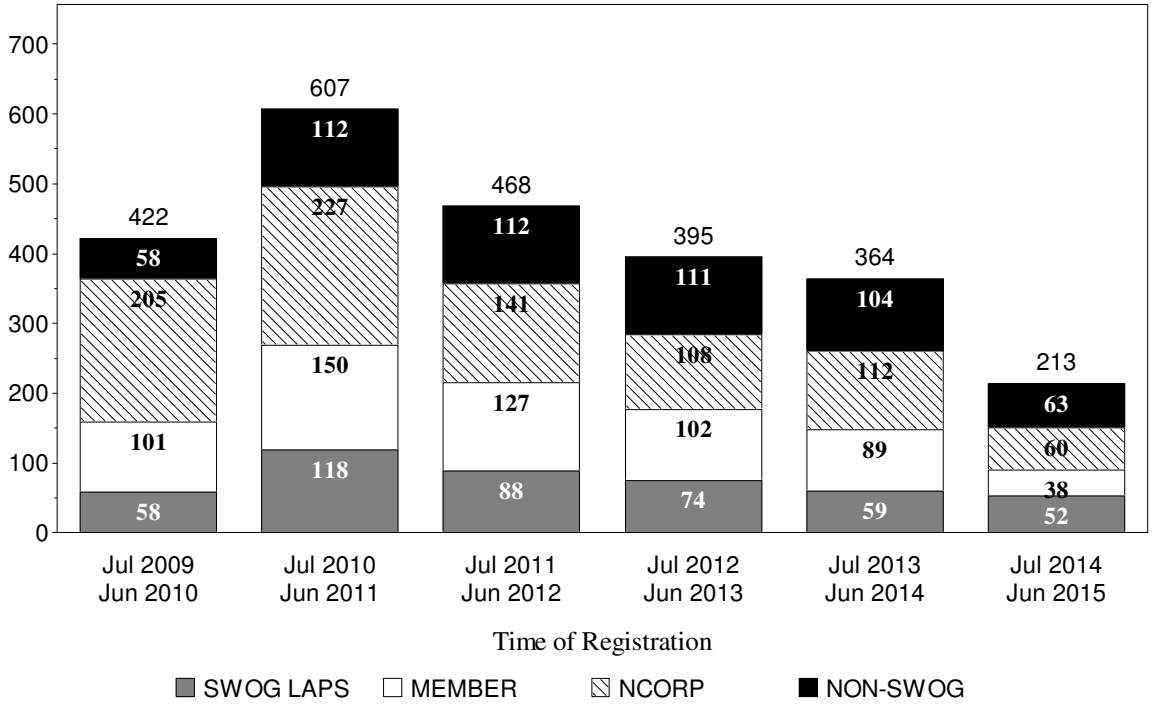
LUNG COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
LUNG COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

LUNG COMMITTEE

	Jan 2015 Jun 2015	Jul 2014 Dec 2014	Jan 2014 Jun 2014	All Patients
S0819 NSCLC, Adv, Chemo/Bevacizumab ± Cetuximab				
Randomization				
Chemotherapy ± Bevacizumab	0	0	58	671
Chemotherapy ± Bevacizumab + Cetuximab	0	0	53	662
	0	0	111	1,333
S0905 Mesothelioma, Cediranib + Chemotherapy				
Randomization				
Pemetrexed + CDDP + blinded drug	10	3	6	44
Pemetrexed + CDDP + blinded drug	10	7	4	44
	20	10	10	88
S1206 NSCLC, Stage III, Chemoradiotherapy + ABT-888				
Phase I Registration				
Radiotherapy + Paclitaxel + Carboplatin + ABT-888 40mg	0	0	2	8
Radiotherapy + Paclitaxel + Carboplatin + ABT-888 80mg	1	4	2	7
	1	4	4	15
Re-Evaluation & Consolidation				
Paclitaxel + Carboplatin + ABT-888 80mg	2	3	2	9
S1400 SCCA, Adv, Biomarker Master Protocol				
Screening Registration				
Specimen Submission	178	134	0	312
S1400A Non-Match: MEDI4736 vs Docetaxel				
Registration				
MEDI4736	38	10	0	48
Docetaxel	28	10	0	38
	66	20	0	86
S1400B P13K: GDC-0032 vs Docetaxel				
Randomization				
GDC-0032	3	2	0	5
Docetaxel	3	2	0	5
	6	4	0	10
S1400C CDK4/6: Palbociclib vs Docetaxel				
Randomization				
Palbociclib	6	6	0	12
Docetaxel	6	4	0	10
	12	10	0	22
S1400D FGFR: AZD4547 vs Docetaxel				
Randomization				
AZD4547	5	0	0	5
Docetaxel	3	3	0	6
	8	3	0	11
S1400E HGF: Erlotonib ± Rilotumumab				
Randomization				
Rilotumumab + Erlotinib	0	4	0	4
Erlotinib	0	5	0	5
	0	9	0	9
S1403 Adv, EGFR-mut, Afatinib ± Cetuximab				
Randomization				
Afatinib + Cetuximab	2	0	0	2
Afatinib	3	0	0	3
	5	0	0	5

	Jan 2015 Jun 2015	Jul 2014 Dec 2014	Jan 2014 Jun 2014	All Patients
A151216 ALCHEMIST - Screening*				
Total Registrations	15	1	0	16
A081105 ALCHEMIST, EGFR mut, Erlotinib*				
Total Registrations	1	0	0	1
C140503 NSCL, Lobectomy vs Sublobar Resection*				
Total Registrations	0	1	3	20
C30610 SCLC, Thoracic RT*				
Total Registrations	1	1	2	49
C30901 Mesothelioma, Maintenance Pemetrexed vs Observation*				
Total Registrations	0	1	0	2
E2511 ESCLC, CDDP + Etoposide + Blinded Drug*				
Total Registrations	5	3	0	8
E5508 NSCL, Adv, Maintenance Bevacizumab vs Pemetrexed vs Bevacizumab + Pemetrexed*				
Total Registrations	10	9	9	52
R1306 NSCLC, Adv, ALK/EGFR, Target Agents*				
Total Registrations	1	2	3	6

* For non-SWOG coordinated studies only SWOG registrations are shown.

S0905 Phase I-II

A Phase I/Randomized Phase II Study of Cediranib (NSC #732208) versus Placebo in Combination with Cisplatin and Pemetrexed in Chemonaive Patients with Malignant Pleural Mesothelioma

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Study Chairs:
A Tsao, N Vogelzang, I Wistuba

Date Activated:
03/15/2010

Statisticians:
M Redman, J Moon, J Miao

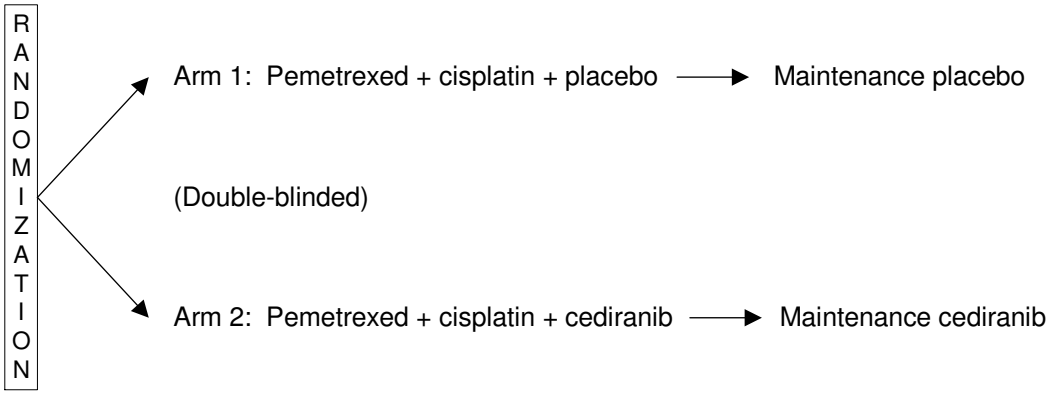
Data Coordinator:
B Zeller

SCHEMA

Phase I portion
(open to limited institutions)*:

Pemetrexed + cisplatin + cediranib at assigned dose
↓
Maintenance cediranib at assigned dose
↓
Temporary closure to assess the dose for Phase II

Phase II portion
(open to all SWOG institutions):



*NOTE: Phase I patients do NOT continue on to the Phase II portion of the study.

Objectives
This study will be conducted in two different parts:

Phase I portion:

To establish the maximum tolerated dose (MTD) and the recommended Phase II dose of cediranib in combination with cisplatin and pemetrexed.

To assess the safety and toxicity of the regimen.

Phase II portion:

To assess whether cisplatin/pemetrexed plus cediranib as compared to cisplatin/pemetrexed plus placebo improves progression-free survival in patients with malignant pleural mesothelioma.

To collect specimens for banking for use in future research studies.

To compare overall survival in patients treated with cisplatin/pemetrexed plus cediranib to those treated with cisplatin/pemetrexed plus placebo.

To assess the safety profile of the regimen.

To assess response rate (confirmed and unconfirmed, complete and partial responses) and disease control rate (response or stable disease) in the subset of patients with measurable disease as defined by RECIST 1.1.

To assess response rate and disease control rate using Modified RECIST for Pleural Tumors in the subset of patients with measurable disease as defined by Modified RECIST for Pleural Tumors.

To assess the rate of agreement between local and central pathology review of mesothelioma and its histologic subtypes.

Patient Population
Patients must have histologically confirmed diagnosis of malignant pleural mesothelioma. Patients may have measurable or non-measurable disease by either RECIST 1.1 or modified RECIST for pleural tumors.

Patients must not have received any prior systemic therapy (chemotherapy or other biologic therapy). Patients may have received prior surgery (e.g. pleurectomy or pleurodesis) or prior radiation therapy.

Patients must have adequate hepatic, hematologic, renal and cardiac function and must have a Zubrod performance status $\leq$ 2. Patients must not be receiving any medications that may markedly affect renal function, such as vancomycin, amphotericin, or pentamidine. Patients must not have a history of clinically significant hemoptysis. Patients must not have known HIV infection. Patients must be able to swallow oral medications.

Institutions must seek additional patient consent for the banking and future use of specimens.

Stratification/Descriptive Factors
For the Phase II portion of this study, patient randomization will be stratified by the following: (1) performance status: 0-1 vs 2; (2) histologic subtype: epithelioid vs biphasic or sarcomatoid.

Accrual Goals
The Phase I portion of this study will be a limited dose de-escalation study with two possible doses of cediranib. The first patients will receive 30 mg of cediranib. If that dose is not well-tolerated, then subsequently enrolled patients will receive 20 mg of cediranib. Ten patients will be evaluated at the recommended dose prior to opening the Phase II portion.

The Phase II portion of this study will accrue 96 eligible patients, approximately 48 per arm. An interim analysis will be performed after 50% of the expected events on the control arm have occurred.

Summary Statement
The Phase I portion of this study has been completed. The recommended Phase II dose for cediranib is 20 mg.

The phase II portion of the trial was opened to accrual on September 15, 2011. As of June 30, 2015, 88 patients have been registered. Two patients are currently ineligible: one due to inadequate renal function and one due to inadequate hematologic function. One eligible patient did not receive any protocol treatment (coded as a major deviation) and is not evaluable for adverse events.

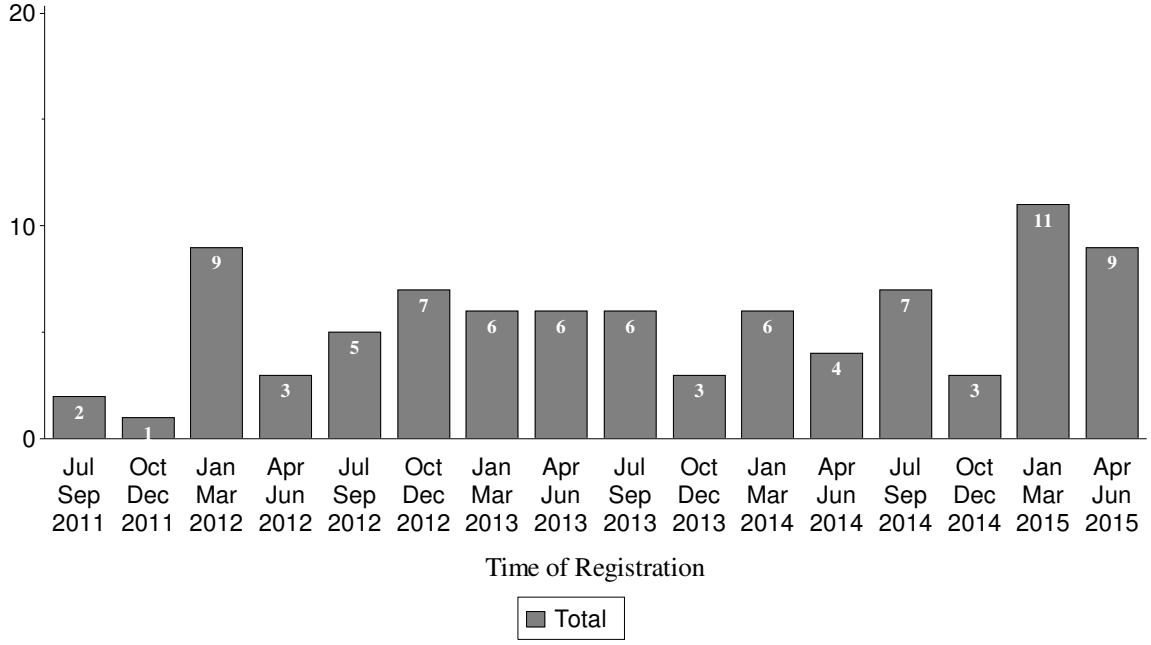
Eighty-one patients have been assessed for adverse events. There have been four treatment-related deaths: one due to dyspnea, one due to respiratory failure and two for whom the exact cause of death could not determined (coded as "Death, NOS" and

"Sudden death, NOS"). Seven additional patients have reported Grade 4 adverse events.

Institutions are reminded that in addition to reporting tumor assessments per RECIST 1.1 guidelines, six pleural thickness measurements are required at each assessment so that disease can also be assessed by the Modified RECIST for Pleural Tumors.

Initial Registrations By 3 Month Intervals

Phase II Patients



Registration by Institution

Phase II Patients

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
MD Anderson CC	38	Michigan CRC NCORP	2
Kaiser Vallejo NCORP	8	NE Georgia Med Ctr/Mississippi, Univ of	2
Heartland NCORP	7	So Calif, U of	2
Wayne State Univ	5	St Joseph Med Ctr/PCRC NCORP	2
Henry Ford Hosp	3	UF Cancer Center/Arkansas, U of	2
Michigan, U of	3	Davis, U of CA	1
Montana NCORP	3	Harrison Bremerton/Harrison Medical Ctr	1
Singing River Hosp/Mississippi, Univ of	3	Highline Medical Ctr/Franciscan Res Ctr	1
Southeast COR NCORP	3	**Total (18 Institutions)**	**88**
Greenville NCORP	2		

Registration, Eligibility, and Evaluability

Phase II Patients

Registrations ending June 30, 2015; Data as of August 17, 2015

	Total
NUMBER REGISTERED	88
INELIGIBLE	2
ELIGIBLE	86
Analyzable, Pend. Elig.	6
BASELINE DISEASE STATUS, RECIST 1.1	
Measurable	55
Non Measurable	23
Too Early	8
RESPONSE ASSESSMENT. RECIST 1.1	
Determinable	45
Not Determinable	7
Too Early	11
Not Applicable	23
BASELINE DISEASE STATUS, MODIFIED RECIST	
Measurable	57
Non Measurable	20
Too Early	7
RESPONSE ASSESSMENT, MODIFIED RECIST	
Determinable	46
Not Determinable	5
Too Early	13
Not Applicable	20
ADVERSE EVENT ASSESSMENT	
Evaluable	81
Not Evaluable	1
Too Early	4

Patient Characteristics

Phase II Patients

Registrations ending June 30, 2015; Data as of August 17, 2015

	Total (n=86)	
AGE		
Median	72.1	
Minimum	45.5	
Maximum	85.3	
SEX		
Males	74	86%
Females	12	14%
HISPANIC		
Yes	4	5%
No	80	93%
Unknown	2	2%
RACE		
White	80	93%
Black	4	5%
Unknown	2	2%
PERFORMANCE STATUS		
0-1	80	93%
2	6	7%
HISTOLOGY		
Epithelioid or Mesothelioma, NOS	61	71%
Biphasic or Sarcomatoid	25	29%

Treatment Summary

Phase II Patients

Registrations ending June 30, 2015; Data as of August 17, 2015

	Total
NUMBER ON PROTOCOL TREATMENT	8
NUMBER OFF PROTOCOL TREATMENT	78
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	12
Refusal unrelated to adverse event	3
Progression/relapse	34
Death	9
Other - not protocol specified	12
Reason under review	8
MAJOR PROTOCOL DEVIATIONS	1

Number of Patients with a Given Type and Grade of Adverse Event

Phase II Patients

Adverse Events Unlikely or Not Related to Treatment Excluded

Adverse Events with No Entries for Grades 3 to 5 or Unknown Have Been Suppressed

Registrations ending June 30, 2015; Data as of August 17, 2015

	Total (n=81) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Acute coronary syndrome	80	0	0	1	0	0
Anemia	40	14	21	5	1	0
Anorexia	45	13	14	9	0	0
Atrial fibrillation	79	1	0	1	0	0
Atrial flutter	79	0	0	2	0	0
Chest pain - cardiac	80	0	0	1	0	0
Chest wall pain	80	0	0	1	0	0
Creatinine increased	64	11	5	1	0	0
Death NOS	80	0	0	0	0	1
Dehydration	61	3	12	5	0	0
Delirium	80	0	0	1	0	0
Diarrhea	55	16	9	1	0	0
Duodenal hemorrhage	80	0	0	1	0	0
Dyspnea	68	5	5	2	0	1
Fall	80	0	0	1	0	0
Fatigue	29	15	27	10	0	0
Gen disorders/admin site cond	79	0	1	1	0	0
Generalized muscle weakness	72	2	5	2	0	0
Glucose intolerance	80	0	0	1	0	0
Headache	77	3	0	1	0	0

	Total (n=81) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Hearing impaired	78	1	0	2	0	0
Hyperglycemia	75	2	3	1	0	0
Hypertension	58	2	12	9	0	0
Hypocalcemia	74	3	2	1	1	0
Hypokalemia	72	8	0	0	1	0
Hypomagnesemia	54	18	7	2	0	0
Hyponatremia	67	9	0	5	0	0
Hypotension	76	0	2	3	0	0
Intracranial hemorrhage	80	0	0	0	1	0
Lung infection	77	0	1	3	0	0
Lymphocyte count decreased	69	1	8	3	0	0
Mucositis oral	70	5	4	2	0	0
Nausea	28	21	24	8	0	0
Neutrophil count decreased	58	6	6	7	4	0
Non-cardiac chest pain	77	3	0	1	0	0
Peripheral sensory neuropathy	71	7	2	1	0	0
Platelet count decreased	66	7	4	3	1	0
Pneumonitis	80	0	0	1	0	0
Renal/urinary disorders-Other	80	0	0	1	0	0
Respiratory failure	80	0	0	0	0	1
Sinus bradycardia	79	0	0	2	0	0
Sudden death NOS	80	0	0	0	0	1
Supraventricular tachycardia	80	0	0	1	0	0
Syncope	80	0	0	1	0	0
Thromboembolic event	72	2	2	1	4	0
Urinary tract infection	79	0	1	1	0	0
Vomiting	59	11	9	2	0	0
Weight loss	60	11	6	4	0	0
White blood cell decreased	57	10	8	4	2	0
Wound dehiscence	80	0	0	1	0	0
MAX. GRADE ANY ADVERSE EVENT	5	4	23	38	7	4

S1013 Pilot

A Prospective Study of Epidermal Growth Factor Receptor (HER-1/EGFR) Inhibitor-Induced Dermatologic Toxicity: Validation of the Functional Assessment of Cancer Therapy-EGFRI 18 (FACT-EGFRI 18) Questionnaire for EGFRI-Induced Skin Toxicities

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Study Chairs:
S Wong, C Moinpour, J Wade

Date Activated:
11/15/2011

Statisticians:
J Unger, K Arnold

Data Coordinator:
D Marrah

Objectives

To establish psychometric properties for the Functional Assessment of Cancer Therapy Epidermal Growth Factor Receptor Inhibitor (FACT-EGFRI 18) module (based on criterion validity, known group's validity, internal consistency reliability, and responsiveness to change) as a patient-reported outcome (PRO) measure of EGFRI-induced skin-related toxicity.

To document minimally important differences over time for the FACT-EGFRI 18 by comparing mean changes in this PRO measure to the patient's direct assessment of change using two anchor items (change in skin condition severity and impact).

To examine the association between toxicity profiles (severity and time to onset), and treatment profiles (e.g., delays and discontinuation) and the FACT-EGFRI 18 scores.

To assess degree of concordance between FACT-EGFRI 18 ratings and study site physician CTCAE Version 4.0 EGFRI-Induced Dermatologic Toxicity Grading Assessment ratings.

To evaluate feasibility outcomes.

Patient Population

Patients must have a diagnosis of colorectal or lung cancer and be planning to receive one of the following HER1/EGFR inhibitor therapies listed below for at least 6 weeks: (a) cetuximab 400 mg/m^2 loading dose, 250 mg/m^2 weekly; (b) cetuximab 500 mg/m^2 every 2 weeks; (c) panitumumab 6 mg/kg every 2 weeks; (d) erlotinib 100-150 mg daily. Other HER1/EGFR inhibitor therapies, schedules, or doses of the above listed agents are not allowed.

Concurrent chemotherapy and other anti-cancer therapies (such as carboplatin, paclitaxel, and bevacizumab) are allowed EXCEPT for the following chemotherapeutic agents which are known to cause skin rash that could interfere with EGFRI-induced skin toxicity assessment: gemcitabine, capecitabine, and topical fluorouracil. Patients may have had prior HER1/EGFR inhibitor therapy but must have fully recovered from any skin toxicities prior to registration. Patients must not have any of the serious concomitant skin disorders specified in the protocol that, in the investigator's opinion, could interfere with assessment of EGFRI induced skin toxicity. Patients must not be planning to receive any of the concomitant medications specified in the protocol that can cause skin rash or other dermatologic reactions that could interfere with the EGFRI-induced skin toxicity assessments, for the duration of the study. Patients must not be planning to receive

concurrent external beam radiation therapy, including prophylactic cranial radiation.

Patients must have a Zubrod performance status of 0-2. Patients must be able to complete questionnaires in English. Patients may concurrently participate in other therapeutic clinical trials. Patients must have completed the baseline S1013 FACT-EGFRI 18 within seven days prior to registration.

Accrual Goals

This study will enroll 112 analyzable patients.

Summary Statement

For the current status of this study, please refer to the Symptom Control and QOL chapter.

S1204 Surveillance

A Sero-Epidemiologic Survey and Cost-Effectiveness Study of Screening for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Among Newly Diagnosed Cancer Patients

Study Chairs:
S Ramsey, R Loomba, R Chugh, D Hershman, J Hwang

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

Date Activated:
08/29/2013

Objectives

Among newly diagnosed cancer patients presenting to SWOG-affiliated community and academic oncology clinics, estimate the prevalence of human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV) infection.

Evaluate known sociodemographic, clinical, and behavioral factors that are significantly associated with previously undiagnosed HIV, HBV, and/or HCV infection in a population of people with newly diagnosed cancer.

Among patients who are identified as having HIV, HBV, and/or HCV, evaluate the timing and type of treatments received, both for the viral infections and the cancers.

Evaluate type and rate of cancer treatment-related adverse events in patients with HIV, HBV, and/or HCV infection.

Determine the cost-effectiveness of (1) routine, universal screening and (2) risk factor-directed screening of newly diagnosed cancer patients for HIV, HBV and/or HCV versus current care.

Create a biorepository of stored serum for future translational medicine studies that may include identifying genomic and viral factors that increase the risk of serious adverse effects among participants infected with HIV, HBV, and/or HCV being treated for invasive cancers.

Patient Population

Patients must be presenting for evaluation or treatment for the first diagnosis of a new solid or hematologic cancer malignancy. Confirmed diagnosis date must be within 120 days prior to first clinic visit as a newly diagnosed cancer patient at the registering clinic. Patients presenting for "second opinions" of confirmed malignancies are eligible, including those who have started cancer treatment at other facilities. Patients must be registered within 90 days after their first clinic visit. Patients must not have been diagnosed with a malignancy other than the current malignancy within the past five years, with the exception of basal cell or squamous cell skin cancer, in situ cervical cancer, or in situ breast cancer. Patients must have no evidence of disease for a prior malignancy for at least five years prior to randomization except as noted above.

Patients must be 18 years of age or older. Patients must have had their blood drawn for viral status testing for HIV, HBV and HCV or provide acceptable viral status documentation prior to registration, as defined in the protocol. Note that patients must have blood drawn for testing prior to registration for any of the three viruses not covered by the documentation. Patients are allowed to participate in other clinical trials.

Accrual Goals
A total of 3,000 eligible patients will be accrued.

Summary Statement
For the current status of this study, please refer to the Cancer Care Delivery chapter.

S1206 Phase I-II

A Dose Finding Study Followed by a Phase II Randomized, Placebo-Controlled Study of Veliparib ABT-888 Added to Chemoradiotherapy with Carboplatin and Paclitaxel for Unresectable Stage III Non-Small Cell Lung Cancer (NSCLC)

Study Chairs:
A Argiris, M Cristea, A Chen

Statisticians:
J Miao, J Moon, M Redman

Data Coordinators:
V Green, L Kaye

Date Activated:
01/02/2013

SCHEMA

Phase I portion (open to limited institutions)*:

XRT + PC + ABT-888 at assigned dose

↓

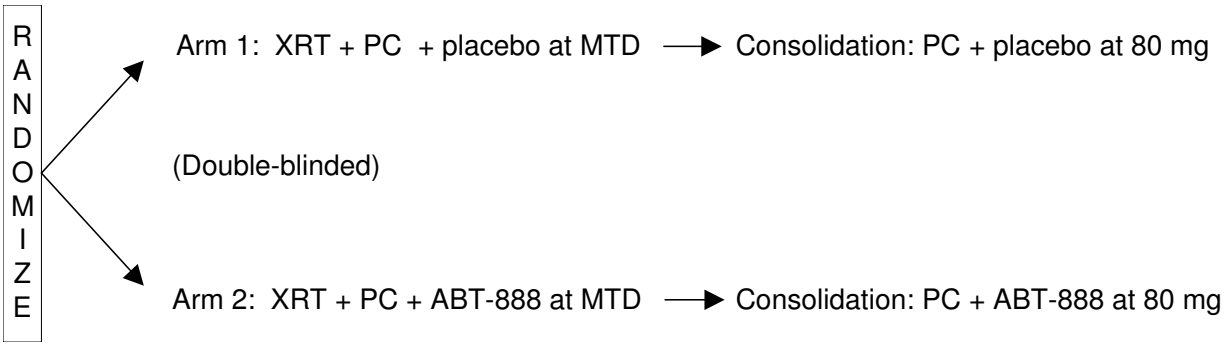
Consolidation: PC + ABT-888 at 80 mg

↓

Temporary closure to assess the dose for Phase II

**NOTE: Phase I patients do NOT continue on to the Phase II portion of the study.*

Phase II portion (open to all SWOG institutions):



Objectives
This study will be conducted in two different parts:

Phase I portion:

To establish the maximum tolerated dose (MTD) and the recommended Phase II dose of ABT-888 when given concurrently with standard carboplatin/paclitaxel and radiotherapy in patients with unresectable Stage III non-small cell lung cancer (NSCLC).

Phase II portion:

To assess whether ABT-888 when given concurrently with standard carboplatin/paclitaxel and radiotherapy improves progression-free survival in patients with unresectable Stage III NSCLC when compared to standard carboplatin/paclitaxel and radiotherapy plus placebo.

To compare overall survival in patients treated with carboplatin/paclitaxel and radiotherapy plus ABT-888 to those treated with carboplatin/paclitaxel and radiotherapy plus placebo.

To assess the response rate (confirmed and unconfirmed, complete and partial responses) and disease control rate (stable disease or better) in the subset of patients with measurable disease.

To assess the safety and toxicity profile of the regimen.

To collect tumor tissue from pretreatment biopsies (archival samples or repeat optional biopsy by bronchoscopy) and a second optional biopsy (by bronchoscopy) for biomarker studies, including peripheral blood mononuclear cell (PARP) activity by measuring the levels of poly-ADP-ribose, y-H2AX, and mRNA expression levels of DNA repair enzymes such as ERCC1/XRCC1.

To collect blood samples for evaluation of PARP and y-H2AX (circulating tumor cells) and other relevant future studies.

Patient Population
Patients must have histologically or cytologically proven new diagnosis of unresectable Stage III non-small cell lung cancer. Patients must have a baseline CT/MRI to rule out CNS disease. Patients may have measurable or non-measurable disease.

Patients must not have received prior systemic therapy (chemotherapy or other biologic therapy) or chest radiation for NSCLC. Patients must not have had a previous surgical resection. However, an exploratory thoracotomy, mediastinoscopy, excisional biopsy or similar surgery for the purpose of determining the diagnosis, stage or potential resectability of newly diagnosed lung tumor is allowed.

Patients must have adequate hematologic, renal, hepatic, and pulmonary function and a Zubrod performance status of 0-1. Patients must not have Grade 1 or worse symptomatic sensory neuropathy, any known immune deficiencies, or a history of seizures or allergic reactions attributed to compounds of similar chemical or biologic composition to ABT-888, carboplatin, paclitaxel or other agents used in this study. Patients must not have had more than a 10% weight loss during the previous six months. Patients must be able to swallow whole capsules. Patients must be offered participation in correlative studies.

Stratification/Descriptive Factors
For the Phase II portion of this study, patient randomization will be stratified by the following: (1) Stage: IIIA vs IIIB; (2) histologic subtype: squamous cell vs non-squamous.

Accrual Goals
Patient enrollment will follow the traditional "3+3" algorithm until the MTD for ABT-888 is reached or the highest dose tested is judged tolerable. At least six patients will be evaluated at the recommended dose prior to opening the Phase II portion.

The Phase II portion of this study will accrue 104 eligible patients, approximately 52 per arm. An interim analysis will be performed after 50% of the expected events have occurred.

Summary Statement
The Phase I portion of the study will evaluate up to four dose levels in four separate cohorts. The initial dose level is ABT-888 at 40 mg with a possible decrease to 20 mg or increase to 80 mg in the next cohort. If the 80 mg dose level is reached, a further increase to 120 mg is possible.

The initial dose level of ABT-888 at 40 mg has completed accrual. Eight patients were registered. Two patients did not receive enough treatment to meet the protocol-specified criteria to be considered evaluable for dose limiting toxicities (DLT) and were

replaced. Of the six evaluable patients in the 40 mg cohort, one experienced a DLT due to Grade 3 dysphagia, esophagitis, and esophageal pain. Therefore, as specified in the protocol, the next dose level of ABT-888 at 80 mg was opened to accrual.

The second cohort evaluating ABT-888 at 80 mg has also completed accrual. Seven patients were registered. One of these patients experienced a Grade 3 drug-infusion reaction and per protocol was replaced. Six patients have been evaluated for DLTs. One patient experienced a DLT due to Grade 3 dehydration and esophagitis. Therefore, as specified in the protocol, the next dose level of ABT-888 at 120 mg was opened to accrual on May 28, 2015.

As of June 30, 2015, there have been no patients registered to the current cohort evaluating ABT-888 at 120 mg.

A total of 15 patients have been evaluated for adverse events related to concurrent chemoradiation. Three patients, two on the 40 mg cohort and one on the 80 mg cohort, have experienced Grade 4 adverse events. All of these events have been hematologic.

Nine patients have gone on to receive consolidation chemotherapy. Eight of these patients have been assessed for adverse events related to consolidation therapy. There has been one treatment-related death due to sepsis. Three additional patients have experienced Grade 4 adverse events. All of these events have been hematologic.

Registration by Institution

Institutions	Total Reg
Davis, U of CA	5
Yale University	4
Arizona MC, U of	3
City of Hope Med Ctr	2
Henry Ford Hosp	1
Total (5 Institutions)	**15**

Registration, Eligibility, and Evaluability

Concurrent Chemoradiotherapy
Data as of August 7, 2015

	TOTAL	Radiotherapy + Paclitaxel + Carboplatin + ABT-888 40mg	Radiotherapy + Paclitaxel + Carboplatin + ABT-888 80mg
NUMBER REGISTERED	15	8	7
ELIGIBLE	15	8	7
BASELINE DISEASE STATUS			
Measurable	15	8	7
RESPONSE ASSESSMENT			
Determinable	14	8	6
Too Early	1	0	1
ADVERSE EVENT ASSESSMENT			
Evaluable	15	8	7
DOSE-LIMITING TOXICITY ASSESSMENT			
Evaluable	12	6	6
Not Evaluable	3	2	1

Patient Characteristics

Concurrent Chemoradiotherapy

Data as of August 7, 2015

	Total (n=15)	
AGE		
Median	67.0	
Minimum	57.6	
Maximum	80.9	
SEX		
Males	9	60%
Females	6	40%
HISPANIC		
No	15	100%
RACE		
White	13	87%
Black	1	7%
Asian	1	7%
STAGE		
IIIA	10	67%
IIIB	5	33%
HISTOLOGY		
Squamous cell	6	40%
Non-squamous cell	9	60%
BASELINE LDH		
Normal	9	60%
Elevated	3	20%
Data pending	3	20%
PERFORMANCE STATUS		
0	7	47%
1	8	53%
SMOKING STATUS		
Current Smoker	1	7%
Former Smoker	12	80%
Never Smoker	2	13%
WEIGHT LOSS PAST 6 MONTHS		
< 5%	9	60%
5 - 10%	6	40%

Number of Patients with a Given Type and Grade of Adverse Event

Concurrent Chemoradiotherapy

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of August 7, 2015

	Radiotherapy + Paclitaxel + Carboplatin + ABT-888 40mg (n=8) Grade						Radiotherapy + Paclitaxel + Carboplatin +ABT-888 80mg (n=7) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	8	0	0	0	0	0	6	0	1	0	0	0
AST increased	8	0	0	0	0	0	6	0	1	0	0	0
Abdominal pain	8	0	0	0	0	0	6	1	0	0	0	0
Allergic reaction	7	0	1	0	0	0	7	0	0	0	0	0
Anemia	2	3	2	1	0	0	4	2	1	0	0	0
Anorexia	6	2	0	0	0	0	5	1	1	0	0	0
Arthralgia	7	1	0	0	0	0	6	0	1	0	0	0
Back pain	7	1	0	0	0	0	7	0	0	0	0	0
Bone pain	7	0	1	0	0	0	7	0	0	0	0	0
CD4 lymphocytes decreased	7	1	0	0	0	0	7	0	0	0	0	0
Creatinine increased	7	1	0	0	0	0	7	0	0	0	0	0
Dehydration	7	0	1	0	0	0	5	0	1	1	0	0
Dermatitis radiation	6	2	0	0	0	0	3	2	2	0	0	0
Diarrhea	7	1	0	0	0	0	6	1	0	0	0	0
Dizziness	7	1	0	0	0	0	7	0	0	0	0	0
Dry skin	7	1	0	0	0	0	6	1	0	0	0	0
Dysgeusia	7	1	0	0	0	0	3	4	0	0	0	0
Dyspepsia	8	0	0	0	0	0	4	2	1	0	0	0
Dysphagia	6	1	0	1	0	0	6	1	0	0	0	0
Dyspnea	7	0	1	0	0	0	7	0	0	0	0	0
Epistaxis	7	1	0	0	0	0	6	1	0	0	0	0
Esophageal pain	7	0	0	1	0	0	6	0	1	0	0	0
Esophagitis	3	0	4	1	0	0	2	1	2	2	0	0
Fatigue	5	1	0	2	0	0	3	2	2	0	0	0
Febrile neutropenia	8	0	0	0	0	0	6	0	0	1	0	0
GERD	8	0	0	0	0	0	6	1	0	0	0	0
GI disorders-Other, specify	7	1	0	0	0	0	5	2	0	0	0	0
Generalized muscle weakness	7	1	0	0	0	0	7	0	0	0	0	0
Hoarseness	8	0	0	0	0	0	5	2	0	0	0	0
Hypercalcemia	7	1	0	0	0	0	7	0	0	0	0	0
Hyperglycemia	8	0	0	0	0	0	5	0	0	2	0	0
Hypermagnesemia	7	1	0	0	0	0	6	1	0	0	0	0
Hypernatremia	8	0	0	0	0	0	6	1	0	0	0	0
Hypertension	8	0	0	0	0	0	6	1	0	0	0	0
Hypoalbuminemia	6	0	2	0	0	0	7	0	0	0	0	0
Hypokalemia	5	2	0	1	0	0	6	1	0	0	0	0
Hypomagnesemia	6	1	1	0	0	0	7	0	0	0	0	0
Hyponatremia	6	2	0	0	0	0	6	1	0	0	0	0
Hypotension	7	1	0	0	0	0	7	0	0	0	0	0
Infusion related reaction	8	0	0	0	0	0	6	0	0	1	0	0
Lung infection	7	0	0	1	0	0	7	0	0	0	0	0
Lymphocyte count decreased	3	0	1	3	1	0	2	0	0	4	1	0
Mucositis oral	8	0	0	0	0	0	6	0	1	0	0	0
Myalgia	6	2	0	0	0	0	7	0	0	0	0	0
Nausea	5	3	0	0	0	0	4	2	1	0	0	0
Neutrophil count decreased	5	1	0	1	1	0	3	0	0	4	0	0
Non-cardiac chest pain	8	0	0	0	0	0	6	1	0	0	0	0
Papulopustular rash	8	0	0	0	0	0	6	1	0	0	0	0
Paresthesia	8	0	0	0	0	0	6	1	0	0	0	0
Peripheral sensory neuropathy	7	1	0	0	0	0	7	0	0	0	0	0
Platelet count decreased	6	2	0	0	0	0	6	1	0	0	0	0

	Radiotherapy + Paclitaxel + Carboplatin + ABT-888 40mg (n=8) Grade						Radiotherapy + Paclitaxel + Carboplatin +ABT-888 80mg (n=7) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Presyncope	7	0	1	0	0	0	7	0	0	0	0	0
Productive cough	8	0	0	0	0	0	6	1	0	0	0	0
Pruritus	7	1	0	0	0	0	7	0	0	0	0	0
Rash acneiform	7	1	0	0	0	0	7	0	0	0	0	0
Rash maculo-papular	6	1	1	0	0	0	6	1	0	0	0	0
Sinus tachycardia	7	1	0	0	0	0	6	1	0	0	0	0
Skin infection	7	0	1	0	0	0	7	0	0	0	0	0
Skin/subq tissue ds-Other	7	1	0	0	0	0	7	0	0	0	0	0
Sore throat	7	0	1	0	0	0	6	1	0	0	0	0
Vomiting	8	0	0	0	0	0	6	1	0	0	0	0
Weight loss	7	1	0	0	0	0	6	1	0	0	0	0
White blood cell decreased	2	3	1	0	2	0	2	1	1	3	0	0
MAX. GRADE ANY ADVERSE EVENT	1	1	0	4	2	0	0	0	0	6	1	0

Registration, Eligibility, and Evaluability

Consolidation Chemotherapy
Data as of August 7, 2015

	Paclitaxel + Carboplatin + ABT-888 80mg
NUMBER REGISTERED	9
ELIGIBLE	9
ADVERSE EVENT ASSESSMENT	
Evaluable	8
Too Early	1

Treatment Summary

Consolidation Chemotherapy
Data as of August 7, 2015

	Paclitaxel + Carboplatin + ABT-888 80mg
NUMBER ON PROTOCOL TREATMENT	3
NUMBER OFF PROTOCOL TREATMENT	6
REASON OFF TREATMENT	
Treatment completed as planned	6
Adverse Event or side effects	0
Refusal unrelated to adverse event	0
Progression/relapse	0
Death	0
Other - not protocol specified	0
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0

Number of Patients with a Given Type and Grade of Adverse Event

Consolidation Chemotherapy

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of August 7, 2015

	Paclitaxel + Carboplatin + ABT-888 80mg (n=8) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	7	1	0	0	0	0
AST increased	7	1	0	0	0	0
Alopecia	5	2	1	0	0	0
Anemia	4	3	1	0	0	0
Anorexia	6	2	0	0	0	0
Arthralgia	6	1	1	0	0	0
Bone pain	6	0	1	1	0	0
Dizziness	7	1	0	0	0	0
Dry mouth	7	0	1	0	0	0
Dysgeusia	6	1	1	0	0	0
Dyspepsia	6	2	0	0	0	0
Esophagitis	5	1	2	0	0	0
Fatigue	5	0	3	0	0	0
GI disorders-Other	7	1	0	0	0	0
Hoarseness	7	1	0	0	0	0
Hypernatremia	7	1	0	0	0	0
Hypoglycemia	7	1	0	0	0	0
Hypotension	7	0	0	1	0	0
Lymphocyte count decreased	5	1	1	1	0	0
Myalgia	7	1	0	0	0	0
Nausea	5	3	0	0	0	0
Neutrophil count decreased	3	0	0	1	4	0
Pain	7	1	0	0	0	0
Peripheral sensory neuropathy	5	2	1	0	0	0
Platelet count decreased	5	2	1	0	0	0
Rash maculo-papular	7	1	0	0	0	0
Sepsis	7	0	0	0	0	1
Sore throat	6	2	0	0	0	0
White blood cell decreased	4	0	2	1	1	0
MAX. GRADE ANY ADVERSE EVENT	0	0	3	1	3	1

S1300 Phase II

Coordinating Group: SWOG

A Randomized, Phase II Trial of Crizotinib Plus Pemetrexed versus Pemetrexed Monotherapy in Alk-Positive Non-Squamous NSCLC Patients Who Have Progressed Systemically after Previous Clinical Benefit from Crizotinib Monotherapy

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Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, NCIC CTG, NRG)

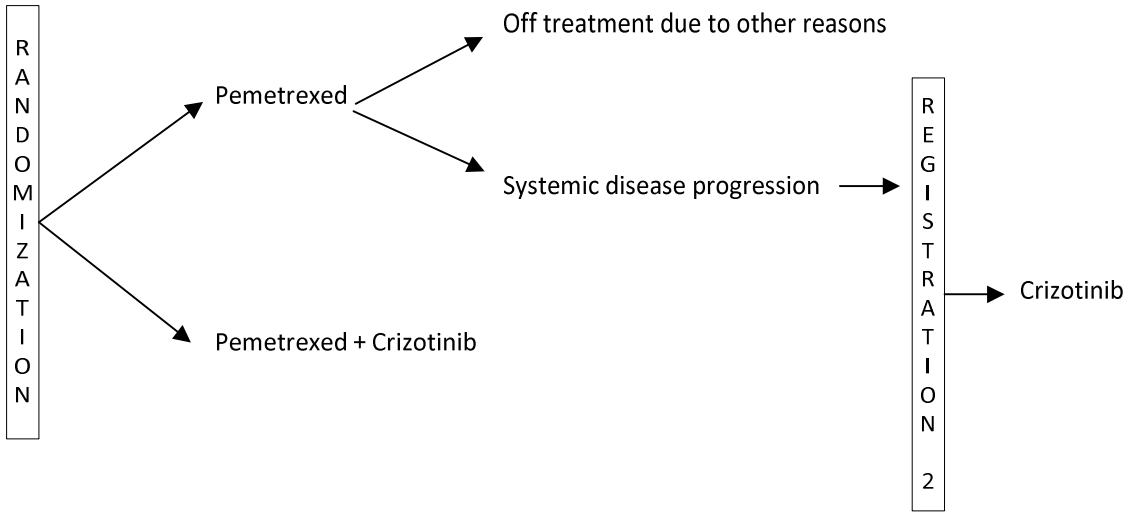
Date Activated:
08/01/2014

Study Chairs:
R Camidge, T Li, R Doebele

Statisticians:
M Redman, J Moon, J Miao

Data Coordinator:
B Zeller

SCHEMA



Objectives

To compare progression-free survival (PFS) between the combination of crizotinib and pemetrexed versus pemetrexed monotherapy in ALK+ non-squamous non-small cell lung cancer (NSCLC) patients who achieved clinical benefit with crizotinib monotherapy and subsequently progressed systemically.

To compare the response rate (confirmed and unconfirmed, complete and partial responses) in patients randomized to receive pemetrexed monotherapy to historical data.

To assess overall survival in both arms.

To evaluate the patterns of failure (CNS, extra-CNS) of the combination of crizotinib and pemetrexed and of pemetrexed monotherapy in ALK+ non-squamous NSCLC after progression on crizotinib monotherapy.

To evaluate the frequency and severity of toxicities resulting from the administration of crizotinib and pemetrexed compared to pemetrexed monotherapy.

To evaluate PFS and the response rate in patients treated with crizotinib following progression on the pemetrexed monotherapy arm.

Translational Medicine Objectives:

To compare progression-free survival and response rates between ALK dominant and ALK non-dominant patients in the subset of patients who have tissue submitted from a rebiopsy, both overall and within each treatment arm.

To evaluate if the magnitude of difference in these outcomes between ALK dominant and ALK non-dominant patients varies by treatment arm.

To assess blood biomarkers of sensitivity and resistance to crizotinib and pemetrexed in an exploratory manner. The blood biomarkers include cell free circulating DNA, microRNA before treatment, during treatment (after 2 cycles) and at treatment progression.

To assess pharmacogenomic factors in peripheral blood that might affect the drug level and treatment outcomes in an exploratory manner.

To assess proteomic/immunologic parameters that might affect the treatment outcomes in an exploratory manner.

To evaluate the frequency of individual mechanisms of resistance (CNG, mutation, alternateoncogene).

To identify previously unknown and alternative driver mechanisms for ALK FISH+ non-small cell lung cancer.

Patient Population

Patients must have histologically or cytologically proven primary non-squamous non-small cell lung cancer (adenocarcinoma, large cell carcinoma, adenocarcinoma in situ, mixed histology with < 50% squamous or unspecified). Patients with tumors having squamous cell components of 50% or more are not eligible. Disease must be Stage IV. Patients must have documented ALK positivity at the time of initial crizotinib monotherapy using the Vysis Break-Apart FISH assay (or other FDA-approved diagnostic test). Samples are deemed to be FISH-positive if greater than or equal to 15% of scored tumor cells had split ALK 5' and 3' probe signals or had isolated 3' signal. Patients must have measurable disease per RECIST 1.1. All patients must have a CT or MRI scan of the brain. Patients must not have brain metastases unless the patient is asymptomatic and has no residual neurological dysfunction off corticosteroids or anti-convulsants for at least 14 days, or the brain metastases have been treated and have remained controlled for at least 14 days.

Patients must have received crizotinib monotherapy at 250 mg BID on a continuous dosing schedule for at least 90 days and must have achieved clinical benefit and subsequently have systemically progressed. Clinical benefit is defined as having stable disease for at least 90 days or achieving a confirmed partial or complete response per RECIST 1.1. Systemic progression is defined as progressive disease per RECIST 1.1 excluding progression based on brain/CNS metastases alone.

Patients must be pemetrexed-naïve. Patients may have received any number of prior chemotherapy or molecularly targeted agents. Patients may have received palliative radiotherapy. Patients must not have received any major surgery within 28 days prior to registration. Patients must not have had any prior exposure to HSP90 inhibitors (such as IPI-504 or ganetespib) or non-crizotinib ALK inhibitors (such as AP26113 or LDK378). Patients must have adequate hematologic, hepatic, cardiac, and renal function and a Zubrod performance status of 0-2. Patients must be able to swallow capsules. Male patients must have free and total testosterone level obtained prior to registration.

All patients must be offered participation in translational medicine studies. Patients with biopsy accessible disease must be offered participation in additional translational medicine studies comparing ALK dominant and ALK non-dominant disease.

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following: (1) prior platinum exposure: yes vs no; (2) Zubrod performance status: 0-1 vs 2; (3) prior history of brain metastases: yes vs no.

Accrual Goals

The accrual goal is 108 eligible patients. Assuming an ineligibility rate of 5%, this would require 114 total patients. In addition, the target number of patients to be included in this analysis of ALK dominance versus ALK non-dominance is 60 evaluable patients. This will require approximately 86 patients to submit to a re-biopsy. An interim analysis for futility and/or harm alone will be performed when 49 progression events have been observed. This analysis is expected to occur at about 17 months after study activation, at approximately 74% accrual (80 of 108 eligible patients).

Summary Statement

This study was activated on August 1, 2014. As of June 30, 2015, there have been no patients registered. An amendment is planned to address issues that may be hurting accrual to this study. Proposed changes to the protocol will include opening up the study to patients who have failed prior treatment with any ALK tyrosine kinase inhibitor instead of only crizotinib, and adding a platinum agent of the treating investigators choice to each treatment arm.

S1400 Master Protocol

Coordinating Group: SWOG

A Biomarker-Driven Master Protocol for Second Line Therapy of Stage IV Squamous Cell Lung Cancer (Lung-MAP)

Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, NRG)

Date Activated:
06/15/2014

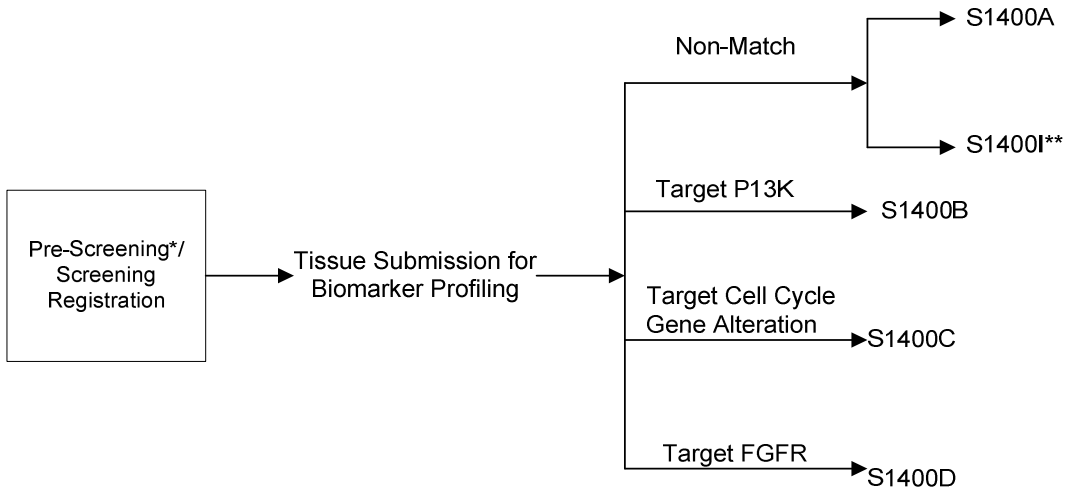
Study Chairs:
V Papadimitrakopoulou, F Hirsch, P Mack, R Herbst, L Schwartz, D Gandara, E Vokes (Alliance), S Ramalingam (ECOG-ACRIN), J Bradley (NRG)

Statisticians:
M Redman, S McDonough, J Miao, J Moon

Project Manager:
M Yee

Data Coordinators:
L Highleyman, K Amber

SCHEMA



*Patients must progress on current treatment to receive sub-study assignment.
**S1400I will activate once S1400A completes accrual.

Objectives

To establish a National Clinical Trials Network (NCTN) mechanism for genomically screening large but homogeneous cancer populations and subsequently assigning and accruing simultaneously to a multi-sub-study "Master Protocol". Each of the biomarker-driven sub-studies in this protocol will evaluate a targeted therapy (TT) or targeted therapy combination (TTC) based on a designated therapeutic biomarker-drug combination, with the ultimate goal being approval of new targeted therapies in this setting. Non-match sub-studies will evaluate non-match therapies (NMT) in patients not eligible for any of the biomarker-driven sub-studies, also with the goal of approval.

To evaluate the screen success rate defined as the percentage of screened patients that register for a therapeutic sub-study.

To establish a tissue/ blood repository from patients with refractory squamous cell cancer.

Patient Population

Patients must have pathologically proven Stage IV squamous cell carcinoma (SCCA) of the lung confirmed by tumor biopsy and/or fine-needle aspiration. The primary diagnosis of squamous cell carcinoma should be established using the current WHO/IASLC-classification of Thoracic Malignancies and must be based on H&E stained slides with or without specific defined IHC characteristics (p40/p63 positive, TTF1 negative). Mixed histologies are not allowed. Patients must have adequate tumor tissue available (defined as at least 20% tumor cells and at least 0.2 mm^3 tumor size as confirmed by the treating institution's local pathologist) and must agree to have this tissue submitted to Foundation Medicine for common broad platform CLIA biomarker profiling. Patients must not have a known EGFR mutation or ALK fusion. Patients whose biomarker profiling results indicate the presence of an EGFR mutation or ALK fusion will be notified that they are not eligible for any of the sub-studies.

Patients must either be eligible to be screened at progression on prior treatment or to be pre-screened prior to progression on current treatment. To be eligible for screening at progression, patients must have received at least one line of systemic therapy for any stage of disease. At least one of these lines of therapy must have been a platinum-based chemotherapy regimen, and patients must have progressed following the most recent line of therapy. To be eligible for pre-screening, current treatment must be for Stage IV disease and patient must have received at least one dose of the current regimen. Patients must have previously received or currently be receiving a platinum-based chemotherapy regimen.

Patients must have a Zubrod performance status of 0-1.

Accrual Goals

This study is intended to be a long-term ongoing project to establish a National Clinical Trials Network (NCTN) mechanism for genomically screening large but homogeneous cancer populations and subsequently assigning and accruing simultaneously to multiple sub-studies. Each sub-study will have its own accrual goal. It is assumed that 500-800 patients will be screened per year, with 50%-70% of patients eventually enrolling onto a sub-study.

Summary Statement

As of June 30, 2015, 312 patients have been registered. Thirty patients are currently ineligible due to the following reasons: inadequate tissue for biomarker profiling (17), prior treatment (5), histology (4), registering prior to progression on first-line therapy prior to amendment allowing pre-screening (2), patient withdrawal prior to registration (1), and inadequately treated basal cell carcinoma (1). One additional patient withdrew prior to data and/or tissue submission and is not included in any analyses.

As of June 30, 2015, 243 eligible patients have been assigned to a sub-study based on their biomarker results, and 138 patients have been enrolled to their assigned sub-study.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	61	Hawaii MU-NCORP	3
ECOG-ACRIN	43	Methodist Hospital	3
NRG	42	Michigan, U of	3
Heartland NCORP	15	Presbyterian Hosp/Irvine, U of CA	3
Yale University	10	Providence Hosp	3
Kaiser Vallejo NCORP	8	Tulane University	3
Rochester, Univ of	8	Arkansas, U of	2
Columbus NCORP	7	Cleveland Clinic OH	2
Michigan CRC NCORP	7	Harrington CC	2
Ozarks NCORP	7	Kansas, U of	2
Southeast COR NCORP	7	Kentucky, U of	2
Cookeville Reg MC	6	Northwest NCORP	2
Montana NCORP	6	St Jude Medical Ctr/Irvine, U of CA	2
MD Anderson CC	5	Sutter Cancer RC	2
City of Hope Med Ctr	4	Upstate Carolina	2
Davis, U of CA	4	Wayne State Univ	2
Henry Ford Hosp	4	Wichita NCORP	2
Lahey Hosp & Med Ctr	4	All Other Institutions	20
San Diego, U of CA	4	**Total (56 Institutions)**	**312**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of August 10, 2015

	Total
NUMBER REGISTERED	312
INELIGIBLE	30
ELIGIBLE	282
Analyzable, Pend. Elig.	22
Not analyzable	1

Patient Characteristics

Registrations ending June 30, 2015; Data as of August 10, 2015

	Total (n=281)	
AGE		
Median	66.9	
Minimum	35.2	
Maximum	91.7	
SEX		
Males	188	67%
Females	93	33%
HISPANIC		
Yes	10	4%
No	265	94%
Unknown	6	2%
RACE		
White	234	83%
Black	23	8%
Asian	9	3%
Pacific Islander	2	1%
Native American	3	1%
Multi-Racial	2	1%
Unknown	8	3%
PERFORMANCE STATUS		
0	75	27%
1	148	53%
2	47	17%
Data pending	11	4%
SMOKING HISTORY		
Current	91	32%
Former	171	61%
Never	10	4%
Data pending	9	3%
WEIGHT LOSS PAST 6 MONTHS		
< 5%	198	70%
5 - <10%	45	16%
10 - < 20%	23	8%
>=20%	4	1%
Data pending	11	4%

Biomarker Data and Sub-Study Assignments

Registrations ending June 30, 2015; Data as of August 10, 2015

	Total (n=243)	
CELL CYCLE GENE ALTERATION		
Negative	197	81%
Positive	46	19%
FGFR		
Negative	211	87%
Positive	32	13%
MET IHC		
Negative	24	10%
Positive	32	13%
PI3K		
Negative	218	90%
Positive	25	10%
ASSIGNED SUB-STUDY		
S1400A (non-match)	149	61%
S1400B (PI3K)	17	7%
S1400C (Cell Cycle Gene Alteration)	38	16%
S1400D (FGFR)	23	9%
S1400E (c-MET)	16	7%

S1400A Phase II

Coordinating Group: SWOG

A Phase II Study of MEDI4736 and Docetaxel for Previously Treated Patients with Stage IV Squamous Cell Lung Cancer and No Matching Biomarkers (Lung-MAP Sub-Study)

Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, NRG)

Date Activated:
06/15/2014

Study Chairs:
V Papadimitrakopoulou, H Borghaei (ECOG-ACRIN)

Statisticians:
M Redman, S McDonough, J Miao, J Moon

Project Manager:
M Yee

Data Coordinators:
L Highleyman, K Amber

SCHEMA

Note: Docetaxel arm has been removed as it closed to accrual per Revision #2, 04-22-15.

Objectives

To assess the response rate (confirmed and unconfirmed, complete and partial) among patients treated with MEDI4736.

To assess the response rate (confirmed and unconfirmed, complete and partial) among PD-L1 positive patients treated with MEDI4736.

To assess investigator-assessed progression-free survival (IA-PFS) among patients treated with MEDI4736.

To assess IA-PFS among PD-L1 positive patients treated with MEDI4736.

To assess overall survival (OS) in patients treated with MEDI4736.

To assess OS in PD-L1 positive patients treated with MEDI4736.

To evaluate the frequency and severity of toxicities associated with MEDI4736.

To assess immune-related IA-PFS using a modified response criteria adapted for immunotherapy (irRC-IA-PFS) in all patients and in the subset of patients determined to be PD-L1 positive treated with MEDI4736.

To compare IA-PFS, irRC-IA-PFS, OS, toxicity and response rates between patients randomized to MEDI4736 versus docetaxel.

To identify additional predictive or prognostic tumor/blood biomarkers beyond the chosen biomarker.

To identify potential resistance biomarkers at disease progression.

To establish a tissue/blood repository from patients with refractory squamous cell cancer.

To evaluate response rates (confirmed or unconfirmed, complete and partial responses) among patients re-treated with MEDI4736.

To estimate median IA-PFS from the date of re-treatment among patients re-treated with MEDI4736.

Patient Population

Patients must have been eligible for the S1400 screening study and must have been assigned to the S1400A sub-study based on biomarker profiling results.

Patients must have progressed on most recent line of systemic therapy. Patients must have measurable disease per RECIST 1.1. Patients must not have leptomeningeal disease, spinal cord compression, or brain metastases unless: (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, AND (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least one day prior to registration. Patients must not have any active or prior documented autoimmune or inflammatory disease (including inflammatory bowel disease, diverticulitis with the exception of diverticulosis, celiac disease, irritable bowel disease; Wegner syndrome; Hashimoto syndrome) within three years prior to registration. Patients must not have had vitiligo, alopecia, Grave's disease, or psoriasis requiring systemic treatment within three years prior to registration.

Patients must not have received any prior systemic chemotherapy or investigational drug within 21 days prior to registration. Patients must have recovered from any side effects of prior therapy. Localized palliative radiation therapy is allowed for symptom management, provided treatment is completed at least 14 days prior to registration. All other types of radiation must be completed at least 28 days prior to registration. Patients must have fully recovered from the effects of surgery at least 14 days prior to registration. Patients must not have any prior exposure to immunotherapy such as, but not limited to anti-PD-1 or anti-PD-L1 antibodies (anti-CTLA-4 antibodies, live attenuated vaccines, anti-EGFR agents, and GM-GSF are allowed). Patients must not have received nitrosoureas or mitomycin-c within 42 days prior to registration.

Patients must have a Zubrod performance status of 0-1 and adequate hematologic, hepatic, cardiac, and renal function. Patients must not have documented evidence of acute hepatitis or have an active or uncontrolled infection. Patients must not have known HIV, Hepatitis B or Hepatitis C positivity. Patients must not have any history of primary immunodeficiency, tuberculosis, or organ transplant that requires use of immunosuppressives. Patients must not have any known allergy or reaction to any

component of the MEDI4736 formulation. Patients must not have received a live attenuated vaccination or any immunosuppressive medication within 28 days prior to registration. However, intranasal and inhaled corticosteroids or systemic corticosteroids at physiologic doses not to exceed 10 mg/day of prednisone or equivalent are allowed. Patients must not have any prior immune-related adverse event (irAE) of Grade 3 or worse or any unresolved irAE greater than Grade 1.

Stratification/Descriptive Factors

Prior to Revision #2, treatment randomization was stratified by the following: (1) Zubrod performance status: 0-1 vs 2; (2) gender: male vs female; (3) smoking status: current vs former or never.

Randomization and stratification are no longer required as this has been modified to a single arm study.

Accrual Goals

The accrual goal is 100 eligible patients and 30 PD-L1 positive patients treated with MEDI4736.

Summary Statement

Under Revision #2, S1400A was re-designed into a single arm study; the docetaxel arm was permanently closed to accrual. Patients on the docetaxel arm will not be included in the primary analyses, but are included in the tables below for completeness. Seven patients receiving docetaxel came off protocol treatment per Revision #2 and are coded as 'Other' in the Treatment Summary table.

As of June 30, 2015, 149 patients (61% of eligible patients screened on S1400) have been assigned to S1400A and 86 patients have been enrolled.

Of the 48 patients assigned to MEDI4736, two patients are currently ineligible due to Hepatitis C positivity and inadequate baseline data (1 patient each). One additional patient did not receive any protocol treatment due to symptomatic deterioration and is not included in any analyses.

Of the 38 patients assigned to docetaxel, two patients are ineligible due to no evidence of measurable disease and brain metastases (1 patient each). Five additional patients did not receive any protocol treatment due to: patient withdrawal (3), restarting corticosteroids for brain metastases (1), and death (1). All five are excluded from analyses.

On the MEDI4736 arm, 43 patients have been assessed for adverse events. There has been one treatment-related death due to bronchopulmonary hemorrhage. Two additional patients experienced Grade 4 treatment related adverse events including dyspnea and hyponatremia.

On the docetaxel arm, 30 patients have been assessed for adverse events. There has been one treatment related death due to sepsis. Nine additional patients experienced Grade 4 treatment related adverse events including hematemesis (reported as ‘GI disorders-Other’) and hemoptysis (reported as ‘Resp/thoracic/mediastinal ds’).

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
NRG	15	Wayne State Univ	2
Alliance	10	Wichita NCORP	2
ECOG-ACRIN	10	Yale University	2
MD Anderson CC	4	Cleveland Clinic OH	1
Michigan CRC NCORP	4	Columbus NCORP	1
City of Hope Med Ctr	3	Greenville NCORP	1
Cookeville Reg MC	3	Gulf South MU-NCORP	1
Kaiser Vallejo NCORP	3	Henry Ford Hosp	1
Davis, U of CA	2	Kentucky, U of	1
Hawaii MU-NCORP	2	Northwest NCORP	1
Heartland NCORP	2	Ozarks NCORP	1
Lahey Hosp & Med Ctr	2	Presbyterian Hosp/Irvine, U of CA	1
Michigan, U of	2	San Diego, U of CA	1
Montana NCORP	2	St Charles Hlth Sys/PCRC NCORP	1
Providence Hosp	2	St Joseph Med Ctr/PCRC NCORP	1
Rochester, Univ of	2	**Total (31 Institutions)**	**86**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of August 12, 2015

	TOTAL	MEDI4736	Docetaxel
NUMBER REGISTERED	86	48	38
INELIGIBLE	4	2	2
ELIGIBLE	82	46	36
Analyzable, Pend. Elig.	4	4	0
Not Analyzable	6	1	5
BASELINE DISEASE STATUS			
Measurable	69	39	30
Too Early	7	6	1
ADVERSE EVENT ASSESSMENT			
Evaluable	73	43	30
Too Early	3	2	1

Patient Characteristics

Registrations ending June 30, 2015; Data as of August 12, 2015

	MEDI4736 (n=45)		Docetaxel (n=31)	
AGE				
Median	63.4		71.0	
Minimum	35.3		50.2	
Maximum	91.8		83.0	
HISPANIC				
Yes	1	2%	0	0%
No	44	98%	31	100%
RACE				
White	35	78%	28	90%
Black	5	11%	1	3%
Asian	4	9%	1	3%
Multi-Racial	0	0%	1	3%
Unknown	1	2%	0	0%

Biomarker Data

Registrations ending June 30, 2015; Data as of August 12, 2015

	MEDI4736 (n=45)		Docetaxel (n=31)	
CELL CYCLE GENE ALTERATION				
Negative	45	100%	31	100%
FGFR				
Negative	42	93%	30	97%
Positive	3	7%	1	3%
PI3K				
Negative	44	98%	30	97%
Positive	1	2%	1	3%

Treatment Summary

Registrations ending June 30, 2015; Data as of August 12, 2015

	TOTAL	MEDI4736	Docetaxel
NUMBER ON PROTOCOL TREATMENT	24	22	2
NUMBER OFF PROTOCOL TREATMENT	52	23	29
REASON OFF TREATMENT			
Treatment completed as planned	0	0	0
Adverse Event or side effects	7	3	4
Refusal unrelated to adverse event	0	0	0
Progression/relapse	30	16	14
Death	4	1	3
Other - not protocol specified	8	0	8
Reason under review	3	3	0
MAJOR PROTOCOL DEVIATIONS	0	0	0

Number of Patients with a Given Type and Grade of Adverse Event

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending June 30, 2015; Data as of August 12, 2015

	MEDI4736 (n=43) Grade					Docetaxel (n=30) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
ALT increased	3	0	2	0	0	0	0	1	0	0
AST increased	1	1	2	0	0	1	1	0	0	0
Abdominal pain	1	0	1	0	0	0	0	0	0	0
Agitation	0	0	0	0	0	1	0	0	0	0
Alcohol intolerance	0	1	0	0	0	0	0	0	0	0
Alkaline phosphatase increased	3	0	2	0	0	1	0	0	0	0
Allergic rhinitis	0	0	0	0	0	1	1	0	0	0
Alopecia	0	0	0	0	0	3	6	0	0	0
Anemia	8	2	2	0	0	6	7	5	0	0
Anorexia	4	2	0	0	0	4	5	0	0	0
Arthralgia	0	1	0	0	0	1	1	0	0	0
Back pain	1	2	0	0	0	0	0	0	0	0
Bloating	1	0	0	0	0	0	0	0	0	0
Blood bilirubin increased	1	0	0	0	0	1	0	0	0	0
Blood/lymph disorder-Other	2	0	0	0	0	0	0	0	0	0
Bone pain	0	0	1	0	0	0	0	0	0	0
Bronchopulmonary hemorrhage	0	0	0	0	1	1	0	0	0	0
Bruising	1	0	0	0	0	0	0	0	0	0
Cardiac disorder-Other, spec	0	0	0	0	0	0	1	0	0	0
Chills	2	0	0	0	0	1	0	0	0	0
Cholecystitis	0	0	1	0	0	0	0	0	0	0
Cholesterol high	1	0	0	0	0	0	0	0	0	0
Chronic kidney disease	0	1	0	0	0	0	0	0	0	0
Confusion	0	0	0	0	0	0	1	0	0	0
Constipation	2	1	0	0	0	5	1	0	0	0

	MEDI4736 (n=43) Grade					Docetaxel (n=30) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Cough	2	1	0	0	0	2	1	0	0	0
Creatinine increased	4	1	0	0	0	1	0	0	0	0
Dehydration	1	1	0	0	0	0	0	1	0	0
Diarrhea	3	3	1	0	0	3	1	1	0	0
Dizziness	2	0	0	0	0	1	0	0	0	0
Dry eye	0	0	0	0	0	1	0	0	0	0
Dry mouth	2	0	0	0	0	0	0	0	0	0
Dry skin	0	0	0	0	0	1	0	0	0	0
Dysgeusia	3	1	0	0	0	3	2	0	0	0
Dyspepsia	1	0	0	0	0	1	0	0	0	0
Dysphagia	1	0	0	0	0	0	0	0	0	0
Dyspnea	1	1	3	1	0	5	2	2	0	0
Edema limbs	2	1	0	0	0	1	2	0	0	0
Endocrine disorders-Other	1	0	0	0	0	0	0	0	0	0
Erythema multiforme	1	0	0	0	0	1	0	0	0	0
Eye disorders - Other, specify	1	0	0	0	0	0	0	0	0	0
Fatigue	8	7	1	0	0	4	11	5	0	0
Febrile neutropenia	0	0	0	0	0	0	0	2	1	0
Fever	3	0	0	0	0	1	0	0	0	0
Flashing lights	1	0	0	0	0	0	0	0	0	0
Flu like symptoms	0	0	0	0	0	1	0	0	0	0
GERD	1	0	0	0	0	0	1	0	0	0
GI disorders-Other, specify	1	0	0	0	0	1	0	0	1	0
Gastritis	1	0	0	0	0	0	1	0	0	0
Gastrointestinal pain	0	1	0	0	0	0	0	0	0	0
Gen disorders/admin site cond	0	0	0	0	0	1	2	0	0	0
Generalized muscle weakness	1	0	0	0	0	1	3	1	0	0
Glucose intolerance	1	0	0	0	0	0	0	0	0	0
Headache	1	0	0	0	0	0	0	0	0	0
Hiccups	0	0	0	0	0	1	0	0	0	0
Hot flashes	1	0	0	0	0	0	0	0	0	0
Hypercalcemia	2	0	0	0	0	0	0	0	0	0
Hyperglycemia	3	0	0	0	0	0	0	1	0	0
Hyperhidrosis	1	0	0	0	0	0	0	0	0	0
Hyperkalemia	1	0	0	0	0	0	0	0	0	0
Hypertension	2	0	0	0	0	0	0	0	0	0
Hyperthyroidism	6	0	0	0	0	0	0	0	0	0
Hypertriglyceridemia	1	0	0	0	0	0	0	0	0	0
Hypoalbuminemia	0	1	0	0	0	1	4	0	0	0
Hypocalcemia	1	0	0	0	0	0	0	0	0	0
Hypokalemia	0	0	0	0	0	1	0	0	0	0
Hypomagnesemia	0	0	0	0	0	2	0	0	0	0
Hyponatremia	2	0	2	1	0	1	0	1	0	0
Hypotension	1	0	0	0	0	0	0	0	0	0
Hypothyroidism	2	2	0	0	0	1	0	0	0	0
Hypoxia	0	0	2	0	0	0	0	0	1	0
Immune sys disorders-Other	0	0	0	0	0	0	0	1	0	0
Infusion related reaction	0	1	1	0	0	0	0	0	0	0
Injection site reaction	0	0	0	0	0	1	0	0	0	0
Insomnia	0	0	0	0	0	1	1	0	0	0
Leukocytosis	0	0	1	0	0	0	0	0	0	0

	MEDI4736 (n=43) Grade					Docetaxel (n=30) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Lung infection	0	0	1	0	0	0	1	2	0	0
Lymphocyte count decreased	2	2	1	0	0	0	4	5	0	0
MS/connective tissue disorder	1	0	0	0	0	1	0	0	0	0
Malaise	0	0	0	0	0	2	1	0	0	0
Mucositis oral	0	0	0	0	0	1	3	1	0	0
Muscle weakness lower limb	0	1	0	0	0	0	0	0	0	0
Myalgia	2	0	0	0	0	2	3	0	0	0
Nail discoloration	0	0	0	0	0	3	0	0	0	0
Nail ridging	0	0	0	0	0	1	0	0	0	0
Nasal congestion	1	0	0	0	0	0	0	0	0	0
Nausea	9	0	1	0	0	6	4	0	0	0
Nervous sys disorders-Other	1	0	0	0	0	0	0	0	0	0
Neutrophil count decreased	1	0	0	0	0	0	0	2	8	0
Pain	0	4	0	0	0	0	0	0	0	0
Pain in extremity	0	1	0	0	0	0	1	0	0	0
Palpitations	1	0	0	0	0	0	0	0	0	0
Paresthesia	0	0	0	0	0	1	0	0	0	0
Peripheral motor neuropathy	0	0	0	0	0	0	1	0	0	0
Peripheral sensory neuropathy	4	0	0	0	0	5	1	0	0	0
Phlebitis	0	0	0	0	0	0	1	0	0	0
Platelet count decreased	2	0	0	0	0	4	1	0	0	0
Pneumonitis	0	0	0	0	0	0	1	1	0	0
Proteinuria	1	0	0	0	0	0	1	0	0	0
Pruritus	0	0	0	0	0	2	0	0	0	0
Rash acneiform	1	0	0	0	0	1	0	0	0	0
Rash maculo-papular	5	2	0	0	0	1	0	0	0	0
Renal/urinary disorders-Other	1	0	0	0	0	0	0	0	0	0
Resp/thoracic/mediastinal ds	0	0	0	0	0	0	0	0	1	0
Sepsis	0	0	0	0	0	0	0	0	1	1
Sinus tachycardia	1	1	0	0	0	0	0	0	0	0
Sinusitis	0	1	0	0	0	0	1	0	0	0
Sore throat	0	0	0	0	0	1	0	0	0	0
Stevens-Johnson syndrome	0	0	0	0	0	0	0	1	0	0
Syncope	0	0	1	0	0	0	0	0	0	0
Upper respiratory infection	0	1	0	0	0	0	0	0	0	0
Urinary tract infection	0	0	1	0	0	0	1	0	0	0
Urticaria	1	0	0	0	0	0	0	0	0	0
Vaginal inflammation	1	0	0	0	0	0	0	0	0	0
Voice alteration	1	0	0	0	0	0	0	0	0	0
Vomiting	1	0	0	0	0	5	0	0	0	0
Watering eyes	2	0	0	0	0	1	0	0	0	0
Weight gain	0	0	0	0	0	1	0	0	0	0
Weight loss	4	1	1	0	0	1	1	0	0	0
White blood cell decreased	1	0	0	0	0	3	1	4	1	0
MAX. GRADE ANY ADVERSE EVENT	12	12	13	2	1	4	5	11	9	1

S1400B Phase II-III

Coordinating Group: SWOG

A Phase II/III Study of Taselisib for Previously Treated PI3K Positive Patients with Stage IV Squamous Cell Lung Cancer (Lung-MAP Sub-Study)

Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, NRG)

Date Activated:
06/15/2014

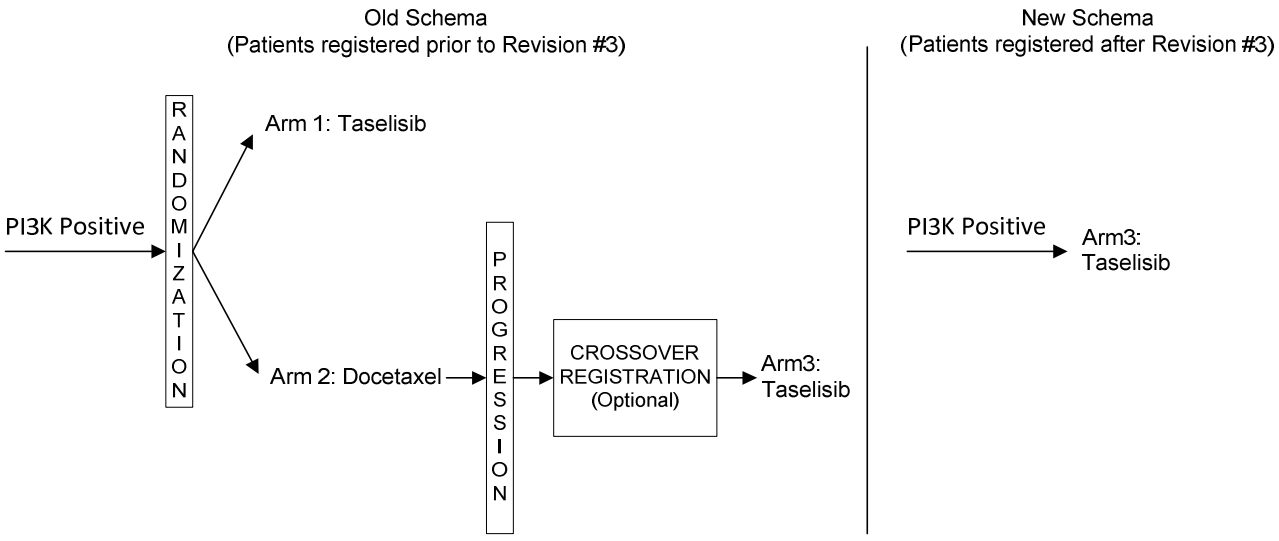
Study Chairs:
J Engelman (Alliance), C Langer (NRG)

Statisticians:
M Redman, S McDonough, J Miao, J Moon

Project Manager:
M Yee

Data Coordinators:
L Highleyman, K Amber

SCHEMA



Objectives

Patients are assigned to the S1400 sub-study using a definition of PI3K-positivity based on the Foundation Medicine (FMI) criteria. The primary analysis of this study will be performed first within a subset of patients who fulfill Genentech's more restrictive definition of PI3K-postivity (GNE PI3K-positive) followed by an evaluation using all of the patients who fulfill the FMI criteria.

Phase II component:

To evaluate if there is sufficient evidence to continue to the Phase III component by evaluating the objective response rate (ORR) for PI3K GNE-positive patients registered to S1400B treated with taselisib.

To evaluate investigator-assessed progression free survival (IA-PFS) and overall survival (OS) in both the subset of patients defined to be PI3K GNE-positive and the entire S1400B (PI3K FMI positive) study population treated with taselisib.

To evaluate ORR in the entire S1400B (PI3K FMI positive) study population treated with taselisib.

To evaluate the duration of response (DoR) in both the subset of patients defined to be PI3K GNE-positive and the entire S1400B (PI3K FMI positive) study population treated with taselisib who achieve a CR or PR (confirmed and unconfirmed) by RECIST 1.1.

To evaluate the frequency and severity of toxicities associated with taselisib.

To identify additional predictive tumor/blood biomarkers that may modify response or define resistance to taselisib beyond the chosen biomarker for biomarker-driven sub-studies.

To identify potential resistance biomarkers at disease progression.

To establish a tissue/blood repository from patients with refractory squamous cell cancer.

Phase III component:

If the study meets the criteria specified in **S1400** Section 11.2, the study will be amended to include a follow-on randomized Phase III trial.

Patient Population

Patients must have been eligible for the S1400 screening study and must have been assigned to the S1400B sub-study based on biomarker profiling results.

Patients must have progressed on most recent line of systemic therapy. Patients must have measurable disease per RECIST 1.1. Patients must not have leptomeningeal disease, spinal cord compression, or brain metastases unless: (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, AND (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least one day prior to registration.

Patients must not have received any prior systemic chemotherapy or investigational drug within 21 days prior to registration. Patients must have recovered from any side effects of prior therapy. Localized palliative radiation therapy is allowed for symptom management, provided treatment is completed at least 14 days prior to registration. All other types of radiation must be completed at least 28 days prior to registration. Patients must have fully recovered from the effects of surgery at least 14 days prior to registration. Patients must not be taking, nor plan to take while on protocol treatment and for 14 days post the last dose of study treatment, drugs, herbal supplements or foods that are known to be strong/moderate CYP3A4 substrates.

Patients must have a Zubrod performance status of 0-1 and adequate hematologic, hepatic, cardiac, and renal function. Patients must not have Type 1 or 2 diabetes which requires insulin and must have HbA1c < 7% and a fasting glucose < 125 mg/dL. Patients must not have documented evidence of acute hepatitis or have an active or uncontrolled infection. Patients must not have active or a known history of small or large intestine inflammation such as Crohn's disease or ulcerative colitis, and must not have any impairment of gastrointestinal function or gastrointestinal disease that may significantly alter the absorption of taselisib. Patients must be able to take oral medications. Patients must not require daily supplemental oxygen. Patients with a known history of HIV seropositivity must have undetectable viral load using standard HIV assays in clinical practice, must have a CD4 count of at least 400/mcL, must not require prophylaxis for any opportunistic infections (i.e. fungal, mAC, or PCP), and must not be newly diagnosed within the last 12 months.

Stratification/Descriptive Factors
Prior to Revision #3, treatment randomization was stratified by the following: (1) Zubrod performance status: 0-1 vs 2; (2) gender: male vs female; (3) number of prior therapies: one vs two or more; (4) GNE PI3K status: positive vs negative.

As the design and objectives have been modified to a single arm Phase II, followed by a randomized Phase III, randomization is not required for the Phase II component. Patients will continue to be stratified by GNE PIK3CA mutation status to achieve the minimum number of GNE+ patients required for the primary objective.

Accrual Goals
The Phase II accrual goal is 56 eligible patients to include 40 GNE PI3K-positive patients treated with taselisib.

Summary Statement
Under Revision #3, S1400B will be re-designed to a single arm Phase II study; the docetaxel arm will permanently close to accrual. Patients on the docetaxel arm will not be included in analyses, but are included in the tables below for completeness.

As of June 30, 2015, 17 patients (7% of eligible patients screened on S1400) have been assigned to S1400B and 10 patients have been enrolled.

Of the five patients assigned to the taselisib arm, one patient died prior to treatment start and is not included in any analyses. Of the five patients assigned to the docetaxel arm, one patient withdrew prior to receiving protocol treatment and is not included in any analyses.

Four patients on the taselisib arm have been assessed for adverse events. One patient experienced Grade 4 treatment related respiratory failure. Two additional patients experienced Grade 3 treatment related events.

Four patients on the docetaxel arm have been assessed for adverse events. One patient experienced Grade 4 treatment related neutropenia. Three additional patients experienced Grade 3 treatment related events.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
Alliance	4
NRG	3
ECOG-ACRIN	1
Henry Ford Hosp	1
Montana NCORP	1
Total (5 Institutions)	**10**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of August 27, 2015

	TOTAL	Taselisib	Docetaxel
NUMBER REGISTERED	10	5	5
ELIGIBLE	10	5	5
Not Analyzable	2	1	1
BASELINE DISEASE STATUS			
Measurable	7	4	3
Too Early	1	0	1
ADVERSE EVENT ASSESSMENT			
Evaluable	8	4	4

Patient Characteristics

Registrations ending June 30, 2015; Data as of August 27, 2015

	Taselisib (n=4)		Docetaxel (n=4)	
AGE				
Median	78.2		67.8	
Minimum	63.8		44.5	
Maximum	79.1		73.2	
HISPANIC				
Yes	0	0%	1	25%
No	4	100%	3	75%
RACE				
White	1	25%	3	75%
Black	1	25%	0	0%
Asian	1	25%	0	0%
Pacific Islander	0	0%	1	25%
Native American	1	25%	0	0%
PERFORMANCE STATUS				
0-1	4	100%	4	100%
2	0	0%	0	0%
GENDER				
Male	2	50%	2	50%
Female	2	50%	2	50%
NUMBER OF PRIOR THERAPIES				
One	2	50%	3	75%
Two or more	2	50%	1	25%
PI3K GNE				
Positive	3	75%	4	100%
Negative	1	25%	0	0%

Additional Biomarker Data

Registrations ending June 30, 2015; Data as of August 27, 2015

	Taselisib (n=4)		Docetaxel (n=4)	
CELL CYCLE GENE ALTERATION				
Negative	2	50%	4	100%
Positive	2	50%	0	0%
FGFR				
Negative	4	100%	4	100%

Treatment Summary

Registrations ending June 30, 2015; Data as of August 27, 2015

	TOTAL	Taselisib	Docetaxel
NUMBER ON PROTOCOL TREATMENT	3	3	0
NUMBER OFF PROTOCOL TREATMENT	5	1	4
REASON OFF TREATMENT			
Treatment completed as planned	0	0	0
Adverse Event or side effects	0	0	0
Refusal unrelated to adverse event	0	0	0
Progression/relapse	3	0	3
Death	1	1	0
Other - not protocol specified	0	0	0
Reason under review	1	0	1
MAJOR PROTOCOL DEVIATIONS	0	0	0

Number of Patients with a Given Type and Grade of Adverse Event

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending June 30, 2015; Data as of August 27, 2015

	Taselisib (n=4) Grade					Docetaxel (n=4) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Alkaline phosphatase increased	0	1	0	0	0	0	0	0	0	0
Alopecia	0	0	0	0	0	1	2	0	0	0
Anemia	0	1	0	0	0	0	2	0	0	0
Anorexia	0	1	0	0	0	1	0	1	0	0
Anxiety	0	0	0	0	0	1	0	0	0	0
Constipation	0	0	0	0	0	1	0	0	0	0
Creatinine increased	1	0	0	0	0	0	0	0	0	0
Dehydration	0	0	1	0	0	0	1	0	0	0
Diarrhea	1	0	1	0	0	1	0	0	0	0
Dysgeusia	0	0	0	0	0	1	0	0	0	0
Dyspepsia	0	0	0	0	0	1	0	0	0	0
Dyspnea	0	0	0	0	0	0	0	1	0	0
Edema limbs	0	0	0	0	0	2	0	0	0	0
Fatigue	0	1	0	0	0	1	1	0	0	0
Flu like symptoms	0	0	0	0	0	0	1	0	0	0
Generalized muscle weakness	0	0	0	0	0	0	1	0	0	0
Hand-Foot syndrome	0	0	0	0	0	0	1	0	0	0
Headache	0	0	0	0	0	1	0	0	0	0
Hyperglycemia	1	1	0	0	0	1	1	0	0	0
Hypertension	0	0	1	0	0	0	0	0	0	0
Hypoalbuminemia	0	1	0	0	0	1	1	0	0	0
Hypomagnesemia	0	0	0	0	0	2	0	0	0	0
INR increased	0	0	0	0	0	0	0	1	0	0
Lung infection	0	0	1	0	0	0	0	0	0	0
Lymphocyte count decreased	0	0	1	0	0	0	1	0	0	0
Mucosal infection	0	0	0	0	0	0	1	0	0	0
Mucositis oral	0	0	0	0	0	1	0	0	0	0

	Taselisib (n=4) Grade					Docetaxel (n=4) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Nausea	0	0	0	0	0	1	0	0	0	0
Neutrophil count decreased	0	0	0	0	0	1	1	0	1	0
Pain	0	0	0	0	0	1	0	0	0	0
Peripheral motor neuropathy	0	0	0	0	0	0	1	0	0	0
Resp/thoracic/mediastinal ds	0	0	0	0	0	0	0	1	0	0
Respiratory failure	0	0	0	1	0	0	0	0	0	0
Weight loss	0	0	0	0	0	1	0	0	0	0
White blood cell decreased	0	0	0	0	0	2	0	2	0	0
MAX. GRADE ANY ADVERSE EVENT	1	0	2	1	0	0	0	3	1	0

S1400C Phase II-III

Coordinating Group: SWOG

A Phase II/III Study of Palbociclib for Previously Treated Cell Cycle Gene Alteration Positive Patients with Stage IV Squamous Cell Lung Cancer (Lung-MAP Sub-Study)

Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, NRG)

Date Activated:
06/15/2014

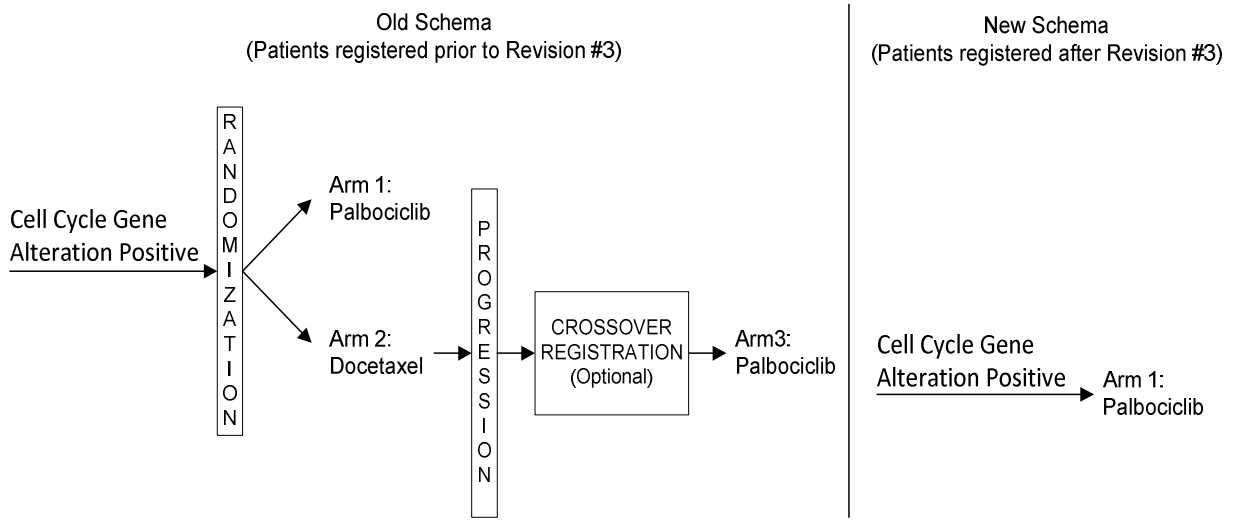
Study Chairs:
M Edelman (NRG), K Albain

Statisticians:
M Redman, S McDonough, J Miao, J Moon

Project Manager:
M Yee

Data Coordinators:
L Highleyman, K Amber

SCHEMA



Objectives
Phase II component:

To evaluate if there is sufficient evidence to continue to the Phase III component by evaluating the objective response rate (ORR) (confirmed and unconfirmed, complete and partial) for cell cycle gene alteration positive patients registered to S1400C treated with palbociclib.

To evaluate investigator-assessed progression-free survival (IA-PFS) and overall survival (OS) in cell cycle gene alteration-positive patients treated with palbociclib.

To evaluate the duration of response (DoR) in cell cycle gene alteration positive patients treated with palbociclib who achieve a CR or PR (confirmed and unconfirmed) by RECIST 1.1.

To evaluate the frequency and severity of toxicities associated with palbociclib.

To identify additional predictive tumor/blood biomarkers that may modify response or define resistance to palbociclib beyond the chosen biomarker for biomarker-driven sub-studies.

To identify potential resistance biomarkers at disease progression.

To establish a tissue/blood repository from patients with refractory squamous cell carcinoma (SCCA) of the lung.

Phase III component:

If the study meets the criteria specified in **S1400** Section 11.2, the study will be amended to include a follow-on randomized Phase III trial.

Patient Population
Patients must have been eligible for the S1400 screening study and must have been assigned to the S1400C sub-study based on biomarker profiling results.

Patients must have progressed on most recent line of systemic therapy. Patients must have measurable disease by CT or MRI per RECIST 1.1. Patients must not have leptomeningeal disease, spinal cord compression or brain metastases unless: (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, AND (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least one day prior to registration.

Patients must not have received any prior systemic chemotherapy or investigational drug within 21 days prior to registration. Patients must have recovered from any side effects of prior therapy. Localized palliative radiation therapy is allowed for symptom management, provided treatment is completed at least 14 days prior to registration. All other types of radiation must be completed at least 28 days prior to registration. Patients must have fully recovered from the effects of surgery at least 14 days prior to registration. Patients must not be taking within 7 days prior to registration, nor plan to take while on protocol treatment and for 14 days after the last dose of study treatment, strong CYP3A4 inhibitors and/or strong CYP3A4 inducers. Patients must not be taking within 7 days prior to registration, nor plan to take while on protocol treatment, drugs that are known to prolong the QT interval.

Patients must have a Zubrod performance status of 0-1 and adequate hematologic, hepatic, cardiac, and renal function. Patients must have electrolytes (Na, K, Cl, Ca, Mg) within institutional limits. Patients must not have any family or personal history of long or short QT syndrome, Brugada syndrome or known history of QTc prolongation, or Torsade de Pointes. Patients must be able to take oral medications and must not have any impairment of gastrointestinal function or gastrointestinal disease that may significantly alter the absorption of palbociclib. Patients must not have documented evidence of acute hepatitis or have an active or uncontrolled infection. Patients with a known history of HIV seropositivity must have undetectable viral load using standard HIV assays in clinical practice, must have a CD4 count of at least 400/mcL, must not require prophylaxis for any opportunistic infections (i.e. fungal, mAC, or PCP), and must not be newly diagnosed within the last 12 months.

Stratification/Descriptive Factors
Prior to Revision #3, treatment randomization was stratified by the following: (1) Zubrod performance status: 0-1 vs 2; (2) gender: male vs female; (3) number of prior therapies: one vs two or more.

As the design and objectives have been modified to a single arm Phase II, followed by a randomized Phase III, randomization and stratification are not required for the Phase II component.

Accrual Goals
The Phase II accrual goal is 40 eligible patients treated with palbociclib.

Summary Statement
Under Revision #3, S1400C will be re-designed to a single arm Phase II study; the docetaxel arm will permanently close to accrual. Patients on the docetaxel arm will not be included in analyses, but are included in the tables below for completeness.

As of June 30, 2015, 38 patients (16% of eligible patients screened on S1400) have been assigned to S1400C and 22 patients have been enrolled.

Of the 12 patients assigned to palbociclib, 4 patients are ineligible due to inadequate baseline lab values (one patient was also on a drug known to prolong QT interval).

Of the 10 patients assigned to the docetaxel arm, three patients are ineligible due to receiving a drug known to prolong QT interval (2) and no evidence of measurable disease (1).

On the palbociclib arm, eight patients have been assessed for adverse events and one has experienced Grade 4 neoplasms that are deemed to be related to treatment. Three additional patients have experienced Grade 3 treatment related adverse events.

On the docetaxel arm, seven patients have been assessed for adverse events and four patients have experienced Grade 3 treatment related adverse events.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	5	Harrington CC	1
Kaiser Vallejo NCORP	3	Hem-Onc Consultants/Loyola University	1
Davis, U of CA	2	Michigan, U of	1
ECOG-ACRIN	2	NRG	1
Montana NCORP	2	Utah, U of	1
Beaumont NCORP	1	Yale University	1
Columbus NCORP	1	**Total (13 Institutions)**	**22**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of August 11, 2015

	TOTAL	Palbociclib	Docetaxel
NUMBER REGISTERED	22	12	10
INELIGIBLE	7	4	3
ELIGIBLE	15	8	7
BASELINE DISEASE STATUS			
Measurable	15	8	7
ADVERSE EVENT ASSESSMENT			
Evaluable	15	8	7

Patient Characteristics

Registrations ending June 30, 2015; Data as of August 11, 2015

	Palbociclib (n=8)		Docetaxel (n=7)	
AGE				
Median	63.3		64.4	
Minimum	54.2		46.9	
Maximum	78.2		76.3	
HISPANIC				
No	8	100%	7	100%
RACE				
White	7	88%	6	86%
Black	1	13%	0	0%
Native American	0	0%	1	14%
PERFORMANCE STATUS				
0-1	8	100%	6	86%
2	0	0%	1	14%
GENDER				
Male	5	63%	4	57%
Female	3	38%	3	43%
NUMBER OF PRIOR THERAPIES				
One	3	38%	0	0%
Two or more	5	63%	7	100%

Additional Biomarker Data

Registrations ending June 30, 2015; Data as of August 11, 2015

	Palbociclib (n=8)		Docetaxel (n=7)	
FGFR				
Negative	8	100%	6	86%
Positive	0	0%	1	14%
PI3K				
Negative	6	75%	7	100%
Positive	2	25%	0	0%

Treatment Summary

Registrations ending June 30, 2015; Data as of August 11, 2015

	TOTAL	Palbociclib	Docetaxel
NUMBER ON PROTOCOL TREATMENT	3	1	2
NUMBER OFF PROTOCOL TREATMENT	12	7	5
REASON OFF TREATMENT			
Treatment completed as planned	0	0	0
Adverse Event or side effects	1	1	0
Refusal unrelated to adverse event	2	1	1
Progression/relapse	8	4	4
Death	1	1	0
Other - not protocol specified	0	0	0
Reason under review	0	0	0
MAJOR PROTOCOL DEVIATIONS	0	0	0

Number of Patients with a Given Type and Grade of Adverse Event

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending June 30, 2015; Data as of August 11, 2015

	Palbociclib (n=8) Grade					Docetaxel (n=7) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Alkaline phosphatase increased	0	1	0	0	0	2	0	0	0	0
Alopecia	0	0	0	0	0	2	2	0	0	0
Anemia	2	1	2	0	0	3	2	0	0	0
Anorexia	1	0	0	0	0	0	1	1	0	0
Bronchial infection	0	0	0	0	0	0	1	0	0	0
Bruising	1	0	0	0	0	0	0	0	0	0
Chills	2	0	0	0	0	0	0	0	0	0
Constipation	1	0	0	0	0	2	0	0	0	0
Creatinine increased	1	0	0	0	0	0	0	0	0	0
Dehydration	0	0	0	0	0	0	3	1	0	0
Diarrhea	1	0	0	0	0	1	1	1	0	0
Dizziness	0	0	0	0	0	2	1	0	0	0
Dry eye	0	0	0	0	0	1	0	0	0	0
Dry mouth	1	0	0	0	0	0	0	0	0	0
Dry skin	1	0	0	0	0	0	0	0	0	0
Dysgeusia	1	0	0	0	0	1	0	0	0	0
Dyspnea	0	1	1	0	0	0	0	0	0	0
Edema trunk	0	0	0	0	0	0	0	1	0	0
Epistaxis	1	0	0	0	0	0	0	0	0	0
Fatigue	3	0	1	0	0	1	2	1	0	0
Fever	0	0	0	0	0	1	0	0	0	0
Flatulence	1	0	0	0	0	0	0	0	0	0
GERD	0	1	0	0	0	0	0	0	0	0
Generalized muscle weakness	1	0	0	0	0	0	1	1	0	0
Hiccups	0	0	0	0	0	0	0	1	0	0

	Palbociclib (n=8) Grade					Docetaxel (n=7) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Hyperglycemia	0	0	1	0	0	2	1	0	0	0
Hypoalbuminemia	0	0	0	0	0	1	1	1	0	0
Hypocalcemia	0	0	0	0	0	0	1	0	0	0
Hypokalemia	0	0	0	0	0	1	0	0	0	0
Hyponatremia	1	0	0	0	0	0	0	1	0	0
Hypophosphatemia	0	0	0	0	0	0	0	1	0	0
Hypotension	0	0	0	0	0	0	1	0	0	0
Infusion related reaction	0	0	0	0	0	0	1	0	0	0
Insomnia	0	0	0	0	0	1	1	0	0	0
Lymphocyte count decreased	0	0	2	0	0	0	2	2	0	0
Malaise	0	0	0	0	0	1	0	0	0	0
Mucositis oral	0	0	0	0	0	1	0	0	0	0
Myalgia	1	0	0	0	0	1	1	0	0	0
Nausea	2	1	0	0	0	1	2	0	0	0
Neoplasms, all	0	0	0	1	0	0	0	0	0	0
Neutrophil count decreased	0	1	1	0	0	0	0	1	0	0
Pain	1	0	0	0	0	0	0	0	0	0
Peripheral sensory neuropathy	0	0	0	0	0	2	0	0	0	0
Platelet count decreased	1	0	1	0	0	0	0	0	0	0
Productive cough	1	0	0	0	0	0	0	0	0	0
Restlessness	0	1	0	0	0	1	0	0	0	0
Skin/subq tissue ds-Other	0	0	0	0	0	1	0	0	0	0
Sore throat	1	0	0	0	0	0	0	0	0	0
Ventricular tachycardia	0	0	0	0	0	0	1	0	0	0
Vomiting	1	0	0	0	0	1	0	0	0	0
Weight loss	0	1	0	0	0	0	0	0	0	0
White blood cell decreased	1	3	0	0	0	0	0	1	0	0
MAX. GRADE ANY ADVERSE EVENT	0	3	3	1	0	0	3	4	0	0

S1400D Phase II-III

Coordinating Group: SWOG

A Phase II/III Study of AZD4547 for Previously Treated FGFR-Positive Therapy Patients with Stage IV Squamous Cell Lung Cancer (Lung-MAP Sub-Study)

Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, NRG)

Date Activated:
06/15/2014

Study Chairs:
C Aggarwal (ECOG-ACRIN), P Lara

Statisticians:
M Redman, S McDonough, J Miao, J Moon

Project Manager:
M Yee

Data Coordinators:
L Highleyman, K Amber

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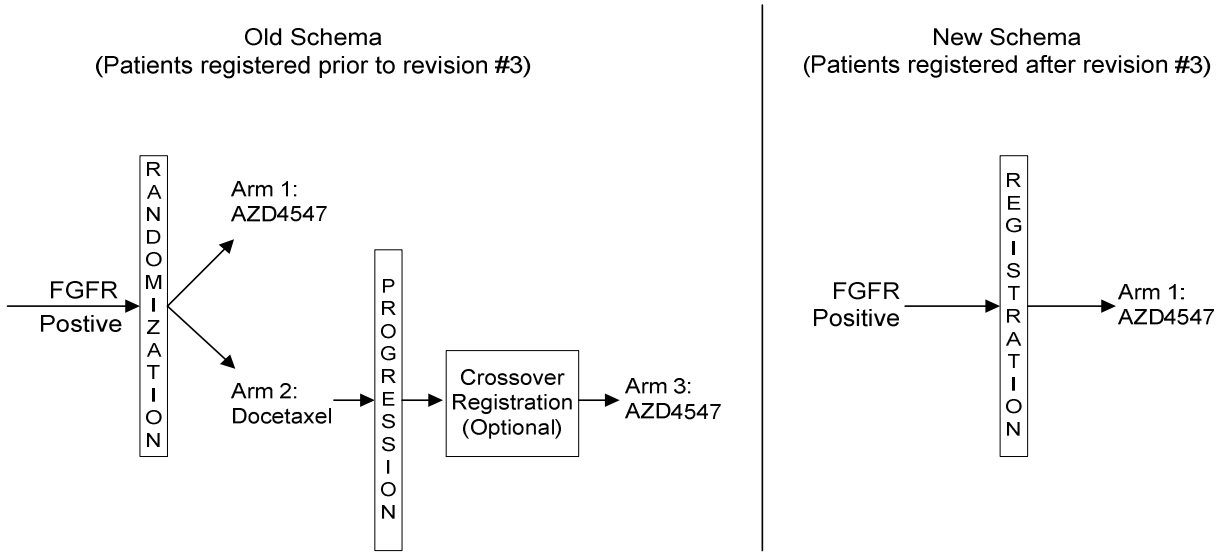


Objectives
Phase II component:

To evaluate if there is sufficient evidence to continue to the Phase III component by evaluating the objective response rate (ORR) (confirmed and unconfirmed, complete and partial) with AZD4547 in FGFR-positive patients.

To evaluate investigator-assessed progression-free survival (IA-PFS) and overall survival (OS) in FGFR-positive patients treated with AZD4547.

To evaluate the duration of response (DoR) in FGFR positive patients treated with AZD4547 who achieve a CR or PR (confirmed and unconfirmed) by RECIST 1.1.

To evaluate the frequency and severity of toxicities associated with AZD4547.

To identify additional predictive tumor/blood biomarkers that may modify response or define resistance to AZD4547 beyond the chosen biomarker for biomarker-driven sub-studies.

To identify potential resistance biomarkers at disease progression.

To establish a tissue/blood repository from patients with refractory squamous cell carcinoma (SCCA) of the lung.

Phase III component:

If the study meets the criteria specified in **S1400** Section 11.2, the study will be amended to include a follow-on randomized Phase III trial.

Patient Population
Patients must have been eligible for the S1400 screening study and must have been assigned to the S1400D sub-study based on biomarker profiling results.

Patients must have progressed on most recent line of systemic therapy. Patients must have measurable disease by CT or MRI per RECIST 1.1. Patients must not have leptomeningeal disease, spinal cord compression, or brain metastases unless: (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, AND (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least one day prior to registration.

Patients must not have received any prior systemic chemotherapy or investigational drug within 21 days prior to registration. Patients must have recovered from the side effects of prior therapy. Localized palliative radiation therapy is allowed for symptom management, provided treatment is completed at least 14 days prior to registration. All other types must be completed at least 28 days prior to registration. Patients must have fully recovered from the effects of surgery at least 14 days prior to registration. Patients must not be taking, nor plan to take while on protocol treatment and for 14 days after the last dose of study treatment, drugs, herbal supplements or foods that are known to be strong/moderate CYP3A4 or CYP2D6 substrates. Patients must not have received nitrosourea or mitomycin C within 42 days prior to registration. Patients must not have received any agent with FGFR inhibition as its primary pharmacology.

Patients must have a Zubrod performance status of 0-1 and adequate hematologic, hepatic, cardiac, renal and ophthalmological function and must be at least 25 years of age. Patients must be able to take oral medications and must not have any impairment of gastrointestinal function or gastrointestinal disease that may significantly alter the absorption of AZD4547. Patients must not have a history of hypersensitivity to active or inactive excipients of AZD4547 or drugs with a similar chemical structure or class to AZD4547. Patients must have calcium and phosphate levels within institutional limits. Patients must not have documented evidence of acute hepatitis or have an active or uncontrolled infection. Patients with a known history of HIV seropositivity must have undetectable viral load using standard HIV assays in clinical practice, must have a CD4 count of at least 400/mcL, must not require prophylaxis for any opportunistic infections (i.e. fungal, mAC, or PCP), and must not be newly diagnosed within the last 12 months.

Stratification/Descriptive Factors
Prior to Revision #3, treatment randomization was stratified by the following: (1) Zubrod performance status: 0-1 vs 2; (2) gender: male vs female; (3) number of prior therapies: one vs two or more.

As the design and objectives have been modified to a single arm Phase II, followed by a randomized Phase III, randomization and stratification are not required for the Phase II component.

Accrual Goals
The Phase II accrual goal is 40 eligible patients treated with AZD4547.

Summary Statement
Under Revision #3, S1400D will be re-designed to a single arm Phase II study; the docetaxel arm will permanently close to accrual. Patients on the docetaxel arm will not be included in analyses, but are included in the tables below for completeness.

As of June 30, 2015, 23 patients (9% of eligible patients screened on S1400) have been assigned to

S1400D and eleven patients have been enrolled.

Of the 5 patients assigned to AZD4547, one patient is ineligible due to insufficient lab values.

On the AZD4547 arm, four patients have been assessed for adverse events and one patient experienced Grade 4 treatment related sepsis. No other Grade 3 or higher adverse events have been reported.

On the docetaxel arm, six patients have been assessed for adverse events and one patient has experienced Grade 4 treatment related hematologic adverse events. Three additional patients have reported Grade 3 treatment related adverse events.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	2	Kaiser Vallejo NCORP	1
NRG	2	Kentucky, U of	1
Arkansas, U of	1	Ozarks NCORP	1
ECOG-ACRIN	1	Sinai Hospital/San Antonio, U of TX	1
Heartland NCORP	1	**Total (9 Institutions)**	**11**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2015; Data as of August 11, 2015

	TOTAL	AZD4547	Docetaxel
NUMBER REGISTERED	11	5	6
INELIGIBLE	1	1	0
ELIGIBLE	10	4	6
Analyzable, Pend. Elig.	1	1	0
BASELINE DISEASE STATUS			
Measurable	9	3	6
Too Early	1	1	0
ADVERSE EVENT ASSESSMENT			
Evaluable	10	4	6

Patient Characteristics

Registrations ending June 30, 2015; Data as of August 11, 2015

	AZD4547 (n=4)		Docetaxel (n=6)	
AGE				
Median	68.2		60.3	
Minimum	51.6		51.9	
Maximum	87.8		79.3	
HISPANIC				
No	4	100%	6	100%
RACE				
White	3	75%	5	83%
Black	1	25%	1	17%
PERFORMANCE STATUS				
0-1	4	100%	6	100%
2	0	0%	0	0%
GENDER				
Male	4	100%	4	67%
Female	0	0%	2	33%
NUMBER OF PRIOR THERAPIES				
One	1	25%	2	33%
Two or more	3	75%	4	67%

Additional Biomarker Data

Registrations ending June 30, 2015; Data as of August 11, 2015

	AZD4547 (n=4)		Docetaxel (n=6)	
CELL CYCLE GENE ALTERATION				
Negative	4	100%	6	100%
PI3K				
Negative	4	100%	6	100%

Treatment Summary

Registrations ending June 30, 2015; Data as of August 11, 2015

	TOTAL	AZD4547	Docetaxel
NUMBER ON PROTOCOL TREATMENT	2	2	0
NUMBER OFF PROTOCOL TREATMENT	8	2	6
REASON OFF TREATMENT			
Treatment completed as planned	0	0	0
Adverse Event or side effects	1	0	1
Refusal unrelated to adverse event	1	0	1
Progression/relapse	4	2	2
Death	0	0	0
Other - not protocol specified	2	0	2
Reason under review	0	0	0
MAJOR PROTOCOL DEVIATIONS	0	0	0

Number of Patients with a Given Type and Grade of Adverse Event

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending June 30, 2015; Data as of August 11, 2015

	AZD4547 (n=4) Grade					Docetaxel (n=6) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
ALT increased	1	0	0	0	0	0	0	0	0	0
AST increased	0	1	0	0	0	0	0	0	0	0
Alkaline phosphatase increased	0	0	0	0	0	1	0	0	0	0
Alopecia	0	0	0	0	0	1	2	0	0	0
Anemia	0	1	0	0	0	2	1	2	0	0
Anorexia	0	2	0	0	0	1	1	0	0	0
Confusion	0	0	0	0	0	0	1	0	0	0
Cough	0	0	0	0	0	1	0	0	0	0
Creatinine increased	0	0	0	0	0	1	0	0	0	0
Dehydration	0	0	0	0	0	0	1	0	0	0
Depression	0	0	0	0	0	1	0	0	0	0
Diarrhea	0	0	0	0	0	1	0	0	0	0
Dizziness	0	0	0	0	0	1	0	0	0	0
Dry mouth	1	0	0	0	0	1	0	0	0	0
Dry skin	1	0	0	0	0	0	0	0	0	0
Dysgeusia	0	1	0	0	0	1	0	0	0	0
Dyspepsia	0	0	0	0	0	1	0	1	0	0
Dyspnea	0	0	0	0	0	0	1	0	0	0
Epistaxis	1	0	0	0	0	0	0	0	0	0
Fatigue	2	1	0	0	0	3	3	0	0	0
Febrile neutropenia	0	0	0	0	0	0	0	2	0	0
Fever	0	0	0	0	0	1	0	0	0	0
Flu like symptoms	0	0	0	0	0	1	0	0	0	0
Flushing	0	0	0	0	0	1	0	0	0	0
Hot flashes	0	0	0	0	0	1	0	0	0	0

	AZD4547 (n=4) Grade					Docetaxel (n=6) Grade				
ADVERSE EVENTS	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Hypoalbuminemia	0	0	0	0	0	0	1	0	0	0
Hypocalcemia	0	0	0	0	0	1	0	0	0	0
Hypoglycemia	0	0	0	0	0	0	1	0	0	0
Hyponatremia	0	0	0	0	0	1	0	0	0	0
Hypophosphatemia	0	0	0	0	0	1	0	0	0	0
Infusion related reaction	0	0	0	0	0	0	1	0	0	0
Injection site reaction	0	0	0	0	0	1	0	0	0	0
Lymphocyte count decreased	0	0	0	0	0	1	0	1	1	0
MS/connective tissue disorder	1	0	0	0	0	0	0	0	0	0
Metab/nutrition disorders-Oth	1	0	0	0	0	0	0	0	0	0
Mucositis oral	0	0	0	0	0	2	0	0	0	0
Nail discoloration	1	0	0	0	0	0	0	0	0	0
Nausea	0	0	0	0	0	2	1	0	0	0
Neutrophil count decreased	0	0	0	0	0	1	0	0	1	0
Pain in extremity	1	0	0	0	0	1	0	0	0	0
Peripheral sensory neuropathy	0	0	0	0	0	2	0	0	0	0
Phlebitis	0	0	0	0	0	0	1	0	0	0
Pruritus	0	0	0	0	0	1	0	0	0	0
Rash maculo-papular	0	0	0	0	0	1	0	0	0	0
Retinal detachment	1	0	0	0	0	0	0	0	0	0
Sepsis	0	0	0	1	0	0	0	0	0	0
Skin ulceration	0	0	0	0	0	0	1	0	0	0
Skin/subq tissue ds-Other	0	0	0	0	0	1	0	0	0	0
Upper respiratory infection	0	0	0	0	0	0	1	0	0	0
White blood cell decreased	0	0	0	0	0	0	1	1	1	0
MAX. GRADE ANY ADVERSE EVENT	1	2	0	1	0	0	2	3	1	0

S1400I Phase III

Coordinating Group: SWOG

A Phase III Randomized Study of Nivolumab Plus Ipilimumab versus Nivolumab for Previously Treated Patients with Stage IV Squamous Cell Lung Cancer and No Matching Biomarker (LUNG-MAP Sub-Study)

Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN, NRG)

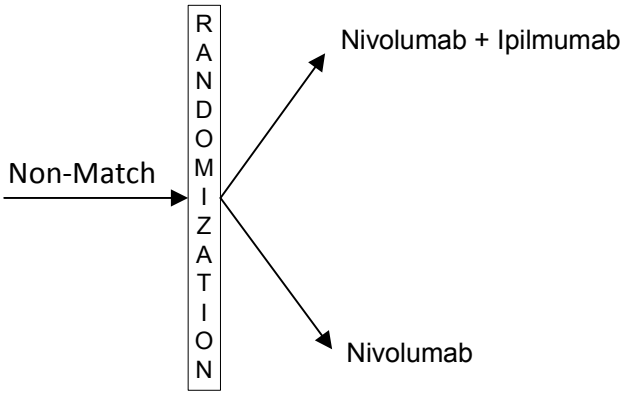
Study Chairs:
S Gettinger, L Bazhenova

Statisticians:
M Redman, S McDonough, J Miao, J Moon

Project Manager:
M Yee

Data Coordinators:
L Highleyman, K Amber

SCHEMA



Objectives

To compare overall survival (OS) in patients with advanced stage refractory SCCA of the lung randomized to nivolumab plus ipilimumab versus nivolumab.

To compare investigator-assessed progression-free survival (IA-PFS) in patients with advanced stage refractory SCCA of the lung randomized to nivolumab plus ipilimumab versus nivolumab.

To compare the response rates (confirmed and unconfirmed, complete and partial) per RECIST 1.1 among patients randomized to receive nivolumab plus ipilimumab versus nivolumab.

To compare the response rates (confirmed only, complete and partial) per RECIST 1.1 among patients randomized to receive nivolumab plus ipilimumab versus nivolumab.

To evaluate the frequency and severity of toxicities associated with nivolumab plus ipilimumab versus nivolumab.

To evaluate if there is a differential treatment effect on OS, IA-PFS, and Response by tumor PD-L1 expression status.

Patient Population

Patients must have been eligible for the S1400 screening study and must have been assigned to the S1400I sub-study based on biomarker profiling results.

Patients must have measurable disease by CT or MRI per RECIST 1.1. Patients must have a CT or MRI scan of the brain to evaluate for CNS disease. Patients must not have leptomeningeal disease, spinal cord compression, or brain metastases unless (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, AND (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least one day prior to registration to S1400I.

Patients must not have received any prior systemic chemotherapy or investigational drug within 21 days prior to S1400I registration. Patients may have received localized palliative radiation provided treatment has been completed at least 14 days prior to S1400I registration. All other types of radiation must be completed more than 28 days prior to S1400I registration. Patients must not have had prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CTLA-4 antibody, or any other antibody or drug specifically targeting T-cell costimulation or immune checkpoint pathways. Patients must not have received systemic treatment with either corticosteroids or other immunosuppressive medications within 14 days prior to registration to S1400I.

Patients must have Zubrod performance status of 0-1 and adequate hematologic, hepatic, cardiac, and renal function. Patients must not have an active, known, or suspected autoimmune disease. Patients must not have a known positive test for HIV, AIDS, hepatitis B, or hepatitis C. Patients with a positive hepatitis C antibody with a negative viral load are allowed. Patients must not have interstitial lung disease that is symptomatic or may interfere with the detection or management of suspected drug-related pulmonary toxicity.

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following: (1) gender: male vs female; (2) number of prior therapies: one vs two or more.

Accrual Goals

The accrual goal is 332 eligible patients. Interim analyses will be performed when 50% and 75% of the expected deaths have been observed.

S1403 Phase II-III

Coordinating Group: SWOG

A Randomized Phase II/III Trial of Afatinib Plus Cetuximab versus Afatinib Alone in Treatment-Naïve Patients with Advanced, EGFR Mutation Positive Non Small Lung Cancer (NSCLC)

Participants:
SWOG, CTSU

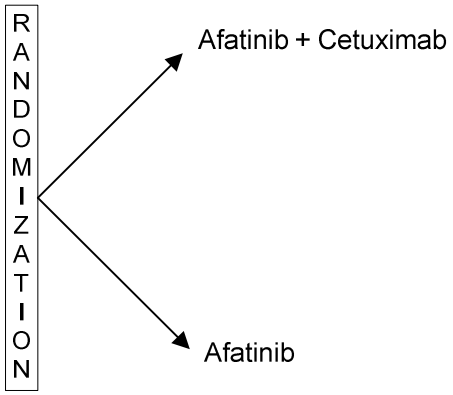
Date Activated:
03/25/2015

Study Chairs:
S Goldberg, R Lilenbaum, K Politi

Statisticians:
M Redman, J Moon, J Miao

Data Coordinator:
B Zeller

SCHEMA



Objectives

Phase II portion:

To evaluate if there is sufficient evidence to continue to the Phase III component by comparing progression-free survival (PFS) between patients randomized to afatinib alone versus afatinib in combination with cetuximab in the first-line treatment of patients with advanced EGFR-mutant NSCLC.

To assess the safety of each treatment arm when used in the first-line setting.

Phase III portion:

To determine the efficacy of the combination of afatinib and cetuximab compared to afatinib alone as measured by overall survival (OS) in the first-line treatment of patients with advanced EGFR-mutant NSCLC.

To compare PFS between patients randomized to afatinib alone versus afatinib in combination with cetuximab.

To compare time to treatment failure and time to treatment discontinuation (as defined in the protocol) between patients randomized to afatinib alone versus afatinib in combination with cetuximab.

To evaluate the overall response rate (confirmed and unconfirmed, complete and partial responses) in the subset of patients with measurable disease treated with afatinib plus cetuximab compared to afatinib alone.

To assess the safety of each treatment arm when used in the first-line setting.

To investigate whether the presence of de novo EGFR T790M mutation or other molecular alterations in the pre-treatment tumor are associated with clinical outcomes.

To assess whether the ratio of sensitizing EGFR (EGFRs) mutation to EGFR T790M is associated with clinical outcomes or is altered during treatment.

To evaluate the frequency of known mechanisms of resistance to EGFR-directed therapies in the context of afatinib and afatinib plus cetuximab treatment.

To identify potential novel predictors of response to afatinib plus cetuximab.

To identify potential new mechanisms of resistance to EGFR-directed therapies.

To compare copy number alterations in MET, EGFR, and HER2 between tissue specimens collected after disease progression and pretreatment tissue specimens.

To evaluate the relationship between clinical outcomes and EGFR Immunohistochemistry H-Score in pretreatment tissue specimens.

To compare levels of circulating tumor markers in peripheral blood at pretreatment, during treatment, and after progression, and investigate their relationship with clinical outcomes.

To establish patient-derived xenografts (PDXs) from a subset of patients by re-biopsy at the time of progressive disease for drug testing and genomic analysis.

Patient Population

Patients must have histologically or cytologically confirmed Stage IV non-small cell lung cancer (NSCLC). Patients must have documented presence of a sensitizing EGFR mutation. Patients with mutations known to be resistant to EGFR inhibitors (i.e., most exon 20 insertion mutations) are not eligible. EGFR testing must be performed in a CLIA-certified laboratory. Patients must not have symptomatic brain metastases or evidence of leptomeningeal carcinomatosis, and must have a CT or MRI scan of the brain to evaluate for CNS disease. Patients with asymptomatic brain metastases are eligible if off of steroids for at least 7 days prior to registration without development of symptoms. Patients must not have any known clinically active interstitial lung disease.

Patients must not have received any prior systemic therapy including chemotherapy or EGFR tyrosine kinase inhibitor therapy (including gefitinib, erlotinib, afatinib, or any experimental EGFR TKI agents). Patients may have received prior concurrent chemoradiation or adjuvant therapy with the exception of adjuvant EGFR-directed therapy. Patients may have had prior surgery.

Patients must have adequate hematologic, hepatic, cardiac, and renal function and must have a Zubrod performance status of 0-2. Patients must not have significant gastrointestinal disorders with diarrhea as a major symptom (e.g. Crohn's disease, malabsorption, etc.) and must be able to swallow medication by oral route. Patients must not have a known history of active hepatitis B or hepatitis C infection. Patients who are known to be HIV seropositive are not eligible. Patients must not have a history of allergic reactions attributed to compounds of similar chemical or biologic composition to afatinib or cetuximab.

Patients must have adequate tissue available (as defined in the protocol) and must agree to submission of tissue and blood. In addition, patients enrolled at sites participating in the repeat-biopsy portion of the study (see protocol for details) must agree to submission of tissue obtained by a repeat biopsy at the time of progression.

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following: (1) performance status: 0-1 vs 2; (2)

EGFR mutation type: exon 19 deletion vs other mutations.

Accrual Goals

The accrual goal is 576 eligible patients. The Phase II interim analysis to evaluate for stopping for futility will be performed when 64 progression events have been observed, at which time it is expected that 212 eligible patients will have been accrued. If the study proceeds to the Phase II portion, additional interim analyses will be performed when 50% and 75% of the expected deaths have been observed.

Summary Statement

This study was activated on March 25, 2015. As of June 30, 2015, five patients have been registered. A planned amendment that would add collection of whole blood for additional translational medicine objectives has been submitted to CTEP for approval.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
San Antonio, U of TX	2
Alliance	1
Columbus NCORP	1
ECOG-ACRIN	1
Total (4 Institutions)	**5**

A151216 (ALCHEMIST Screening) SWOG Supported CTSU Study

Coordinating Group: Alliance

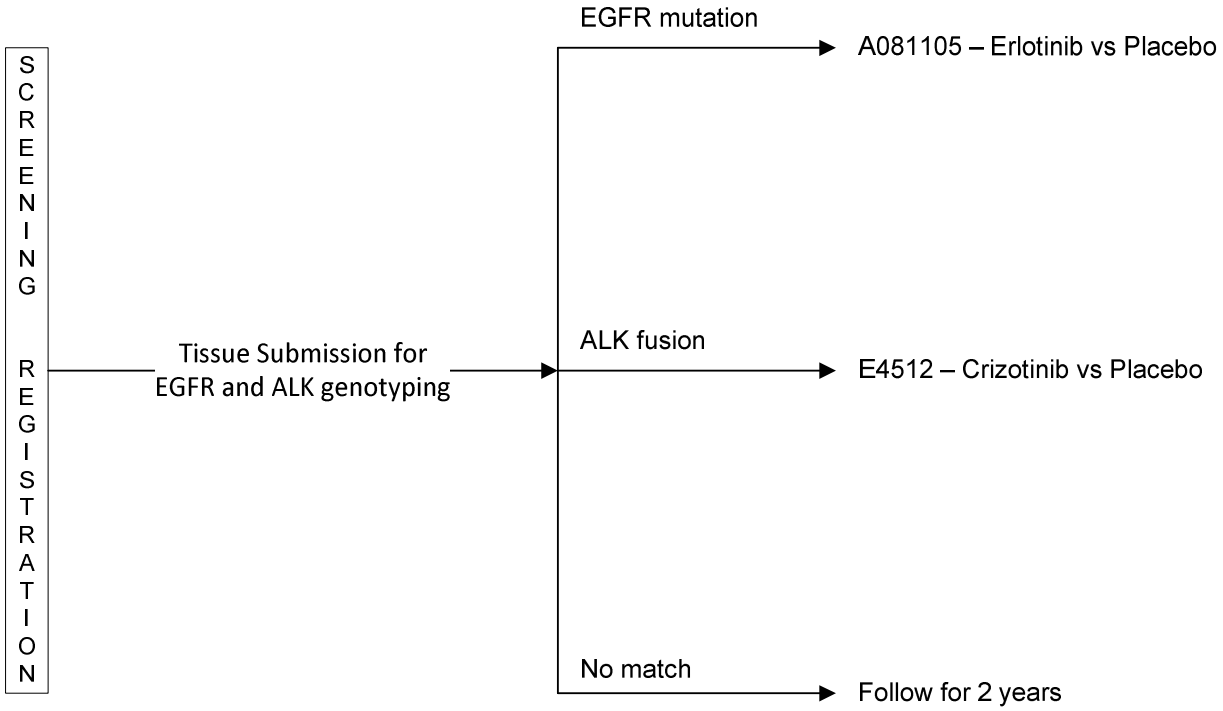
Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST)

Participants:
Alliance, CTSU

Date Activated:
08/18/2014

Study Chairs:
G Oxnard (Alliance), D Gandara (SWOG)

SCHEMA



Objectives

To centrally genotype resected lung adenocarcinomas for EGFR mutations and ALK rearrangements to facilitate accrual to randomized adjuvant studies.

To obtain clinically annotated tumor tissue and patient-matched non-malignant DNA from peripheral blood, as well as detailed epidemiologic and clinical follow-up data, to allow clinically annotated advanced genomic analyses in concert with NCI Center for Cancer Genomics (CCG).

To characterize the natural history of EGFR and ALK wild-type lung cancers to allow subsequent development of targeted therapies against genotype-defined subpopulations in the adjuvant and recurrent settings.

To cross-validate local genotyping assays for EGFR and ALK with a central reference standard.

To study the genomic evolution of lung cancers by comparing genomic characteristics at resection and at recurrence.

Patient Population

Patients must have completely resected non-squamous, non-small cell lung cancer with pathologic stage IIIA, II or large IB (≥ 4cm) in greatest dimension.

Patients must not have received neoadjuvant therapy, or prior treatment with agents targeting EGFR mutation or ALK rearrangement.

Patients must have Zubrod performance status of 0-1.Patients must have adequate FFPE tissue available for central EGFR and ALK genotyping.

Accrual Goals

It is estimated that up to 8000 patients may need to be genotyped in order to fully accrue to the EGFR (estimated prevalence 15%) and ALK (estimated prevalence 5%) randomized adjuvant studies (A081105 and E4512, respectively).

Summary Statement

As of June 30, 2015, there have been 236 registrations to this study, including 16 screening registrations from SWOG institutions. The complete summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
Kaiser Vallejo NCORP	8
Providence Hosp	3
Cleveland Clinic OH	1
KaiserPermanenteSCAL/Kaiser Vallejo NCORP	1
Lahey Hosp & Med Ctr	1
St Jude Medical Ctr/Irvine, U of CA	1
Wayne State Univ	1
Total (7 Institutions)	**16**

A081105 (ALCHEMIST-EGFR) Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

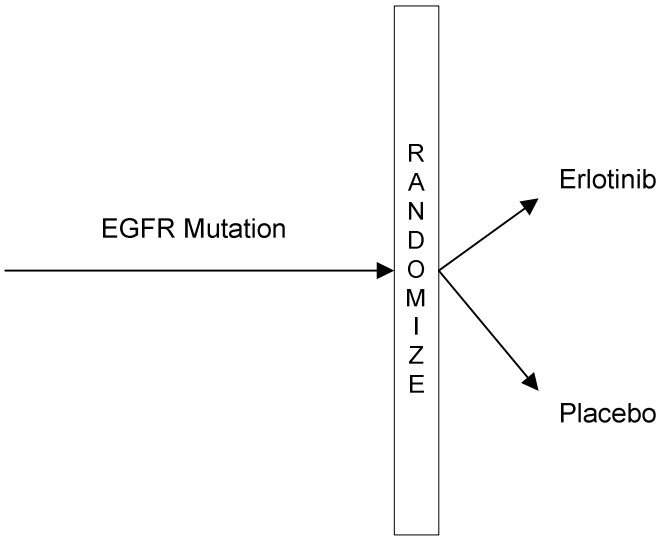
Randomized Double Blind Placebo Controlled Study of Erlotinib or Placebo in Pateints with Completely Resected Epidermal Growth Factor Receptor (EGFR) Mutant Non-small Cell Lung Cancer (NSCLC) (ALCHEMIST-EGFR)

Participants:
Alliance, CTSU

Date Activated:
08/18/2014

Study Chair:
R Govindan (Alliance)

SCHEMA



Objectives

To assess whether adjuvant therapy with erlotinib will result in improved overall survival (OS) over placebo for patients with completely resected stage IB (≥4 cm), II, or IIIA EGFR mutant non-small cell lung cancer (NSCLC, confirmed centrally) following complete resection and standard post-operative therapy.

To assess whether adjuvant therapy with erlotinib will result in improved disease free survival (DFS) over placebo both in the overall study population and within the stage subgroups: IB and II/IIIA.

To evaluate the safety profile of erlotinib in the adjuvant setting.

To assess whether adjuvant therapy with erlotinib will result in improved DFS rate at two years, and improved OS rate at five years over placebo both in the overall study population and within the stage subgroup: IB and II/IIIA.

To assess the primary and secondary objectives in all randomized patients, regardless of central confirmation of the EGFR mutant status.

Patient Population

Patients must have previously registered to A151216, with the result of lung cancer harboring an EGFR exon 19 deletion or L858R mutation. Patients must not have known resistant mutations in the EGFR TK domain (T790M). Patients with both EGFR mutant and ALK rearrangements are to be registered to A081105. Patients must be completely resected stage IB (≥4 cm), II or IIIA non-squamous NSCLC with negative margins.

Patients must have completely recovered from surgery and standard post-operative therapy and have no interstitial fibrosis or lung disease.

Patients must have adequate hematologic, hepatic, and renal function and ECOG performance status of 0-1.

Stratification/Descriptive Factors

Patients will be stratified by the following factors: (1) stage: IB ≥ 4 cm, II vs IIIA; (2) prior chemotherapy: yes vs no; (3) exon 19 deletion: yes vs no; and (4) ECOG performance status: 0 vs 1.

Accrual Goals

The accrual goal for this study is 410 eligible patients. Assuming a 5% rate of patient withdrawal or refusal and 5% of EGFR mutation not confirmed centrally, the total accrual is 450.

Interim analysis will be performed for futility when 50% of the events, or 91 deaths, have been observed.

Summary Statement

As of June 30, 2015, there have been nine registrations to this study, including one registration from a SWOG institution, St. Jude Medical Center/University of California Irvine. The complete summary of this study from Alliance is available on the SWOG web site.

E4512 (ALCHEMIST-ALK) Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

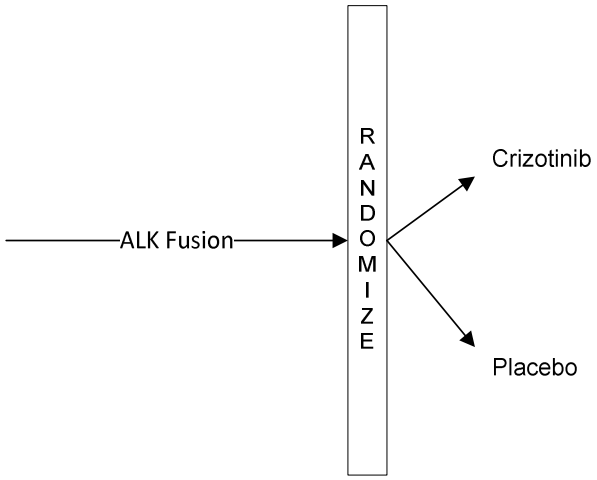
A Phase III Double-Blind Trial for Surgically Resected Early Stage Non-Small Cell Lung Cancer: Crizotinib versus Placebo for Patients with Tumors Harboring the Anaplastic Lymphoma Kinase (ALK) Fusion Protein (ALCHEMIST-ALK)

Participants:
ECOG-ACRIN, CTSU

Date Activated:
08/18/2014

Study Chair:
D Gerber (ECOG-ACRIN)

SCHEMA



Objectives

To evaluate whether adjuvant therapy with crizotinib will result in improved overall survival (OS) over placebo for patients with stage IB ≥4 cm, II and IIIA, ALK-positive NSCLC following surgical resection.

To evaluate and compare disease-free survival (DFS) associated with crizotinib and placebo.

To evaluate the safety profile of crizotinib when given in the adjuvant therapy setting.

To collect tumor tissue and blood specimens for future research.

Patient Population

Patients must be registered to A151216 with the result that tumor is positive for translocation or inversion events involving the ALK gene locus. Patients must have undergone complete surgical resection of their stage IB (≥4 cm), II, or non-squamous IIIA non-small cell lung cancer (NSCLC) and have had negative margins. Patients must not have N3 disease.

Patients must have completed any prior adjuvant chemotherapy or radiation therapy two or more weeks prior to randomization and adequately recovered from surgery at the time of randomization. Patients must not have prior treatment with crizotinib or another ALK inhibitor. Patients must not have received neo-adjuvant chemotherapy or radiation therapy.

Patients must have ECOG performance status of 0-1, and have adequate hematologic, hepatic, cardiac, and renal function. Patients must not have active infection, or other uncontrolled intercurrent illness. Patients must not have known interstitial fibrosis or interstitial lung disease. Patients must not be using any medication, herbals, or foods that are known potent CYP3A4 inhibitors or inducers. All females of childbearing potential must have a negative pregnancy test.

Stratification/Descriptive Factors

Patients will be stratified by the following factors: (1) prior chemotherapy: yes vs no; (2) stage: IB ≥4 cm, II vs IIIA; (3) prior radiation therapy: yes vs no; (4) gender: male vs female.

Accrual Goals

The accrual goal for this study is 378 patients. There will be 10 interim analyses performed, every six months at approximately 6~9% increments in information, starting at roughly 25% information (42 events).

Summary Statement

This study was activated on August 18, 2014. As of June 30, 2015, there have been two registrations to this study, but no registrations from SWOG institutions. The complete summary of this study from Alliance is available on the SWOG web site.

C140503 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Phase III Randomized Trial of Lobectomy versus Sublobar Resection for Small (≤ 2 cm) Peripheral Non-Small Cell Lung Cancer

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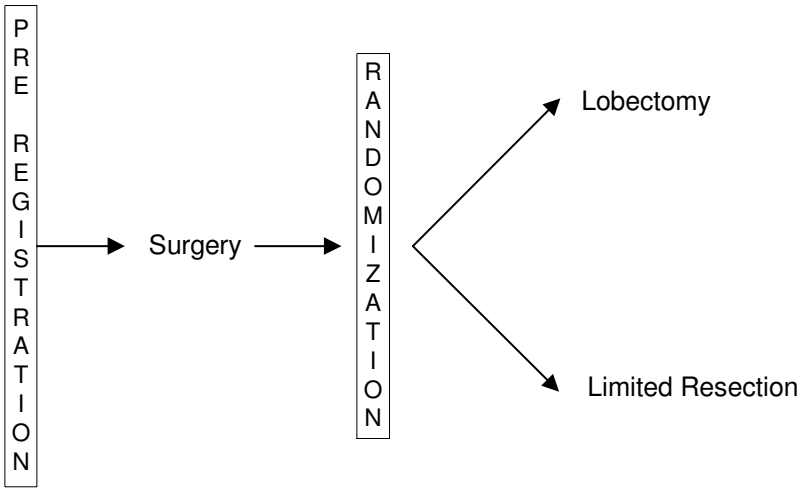
Participants:
Alliance, CTSU

Date Activated:
07/09/2007

Study Chairs:
N Altorki (Alliance), J Mitchell (SWOG)

SCHEMA



Randomization is done intra-operatively after determining patient eligibility. CRA's must be able to access the web-based CALGB registration system during surgery to obtain treatment assignment and inform the surgeon of the assignment at the site.

Objectives

To determine whether disease-free survival after sublobar resection (segmentectomy or wedge) is non-inferior to that after lobectomy.

To determine the rates of loco-regional and systemic recurrence (exclusive of second primaries) after lobar and sublobar resection.

To determine the difference between the two arms of the study in pulmonary function as determined by expiratory flow rates measured at six months post-operatively.

To explore the relationship between characteristics of the primary lung cancer, as revealed by pre-operative CT and PET imaging, and outcomes.

To determine the false-negative rate of pre-operative PET scan for identification of involved hilar and mediastinal lymph nodes.

To assess the utility of annual follow-up CT imaging after surgical resection of small Stage IA non-small cell lung cancer.

Patient Population

Patients must have histologically confirmed NSCLC. Patients must have a peripheral lung nodule ≤ 2 cm on preoperative CT scan which is presumed to be lung cancer. The center of the tumor, as seen on CT, must be located in the outer third of the lung in either transverse, coronal or sagittal plane. Patients with pure ground glass opacities or pathologically confirmed N1 or N2 disease are not eligible. The tumor location must be suitable for either lobar or sublobar resection (wedge or segment). Patients must have no evidence of locally advanced or metastatic disease. Intra-operative confirmation of N0 status by frozen section examination is required. Patients are to be registered and randomized intra-operatively (see protocol for details).

Patients must not have had any prior chemotherapy or radiation therapy for this malignancy.

Patients must have an ECOG performance status of 0-2.

Stratification/Descriptive Factors

Treatment randomization is stratified by: (1) tumor size: < 1 cm vs 1 - 1.5 cm vs > 1.5 - 2.0 cm; (2) histology: squamous cell carcinoma vs adenocarcinoma vs other; (3) smoking status: never vs former vs current.

Accrual Goals

The accrual goal is 1,297 patients.

Summary Statement

As of June 30, 2015, there have been 567 registrations to this study, including 20 CTSU registrations from SWOG institutions. The complete summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
PCRC NCORP	6
Colorado, U of	4
Davis, U of CA	4
Mem Hosp, Co Springs/Colorado, U of	3
Tennessee, U of	2
Arkansas, U of	1
Total (6 Institutions)	**20**

C30610 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

Phase III Comparison of Thoracic Radiotherapy Regimens in Patients with Limited Small Cell Lung Cancer Also Receiving Cisplatin and Etoposide

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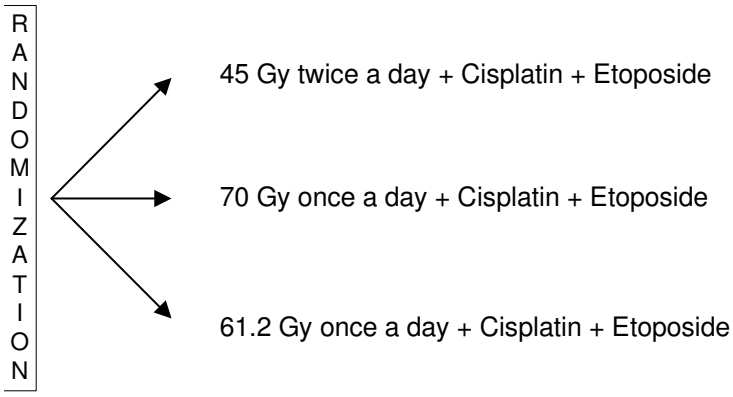
Participants:
Alliance, CTSU

Date Activated:
03/21/2008

Study Chairs:
J Bogart (Alliance), L Gaspar (SWOG)

SCHEMA



Objectives

To determine whether administering high dose thoracic radiotherapy, 70 Gy or 61.2 Gy, will improve median and two-year survival compared with 45 Gy in patients with limited stage small cell lung cancer.

To compare response rates, failure-free survival, and toxicity between these thoracic radiotherapy regimens.

To compare rates of local relapse, distant metastases, and brain metastases.

To compare patients' quality of life between these treatment regimens in terms of their physical symptoms, physical functioning, and psychological state.

To describe the patterns of use of thoracic intensity modulated radiation therapy (IMRT) in patients with limited stage small cell lung cancer.

To examine blood-based biomarkers of response and resistance to cisplatin and etoposide.

Patient Population

Patients must have histologically or cytologically documented limited stage small cell lung cancer. Patients must not have had prior radiotherapy or chemotherapy for limited stage small cell lung cancer. Patients with complete surgical resection of disease are not eligible.

Patients must have adequate hematologic, hepatic, and renal function with an ECOG performance status of 0-2. Patients must be offered participation in the

sub-studies for correlative science (C150712) and quality of life (C7072).

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following factors: (1) gender: male vs female; (2) weight loss during the six months prior to study entry: ≤ 5% vs > 5%; (3) performance status: 0 vs 1 vs 2; (4) radiotherapy technique: IMRT vs 3D.

Accrual Goals

The implementation of the study will be divided into two stages (see protocol for details) and will enroll 670-712 patients.

Summary Statement

As of June 30, 2015, there have been 456 registrations to this study, including 49 registrations from SWOG institutions. The complete summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg	Institutions	Total Reg
Wichita NCORP	13	Columbus NCORP	1
Davis, U of CA	8	Michigan, U of	1
Heartland NCORP	7	Mississippi, Univ of	1
St Elizabeth's MC/Davis, U of CA	3	MUSC MU-NCORP	1
Cincinnati MC, U of	2	NE Georgia Med Ctr/Mississippi, Univ of	1
Highlands Onc Group/Arkansas, U of	2	Stormont-Vail Health/Kansas, U of	1
Kaiser Vallejo NCORP	2	Thompson Ca Surv Ctr/San Antonio, U of TX	1
Providence Hosp	2	Wayne State Univ	1
Sinai Hospital/San Antonio, U of TX	2	**Total (17 Institutions)**	**49**

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

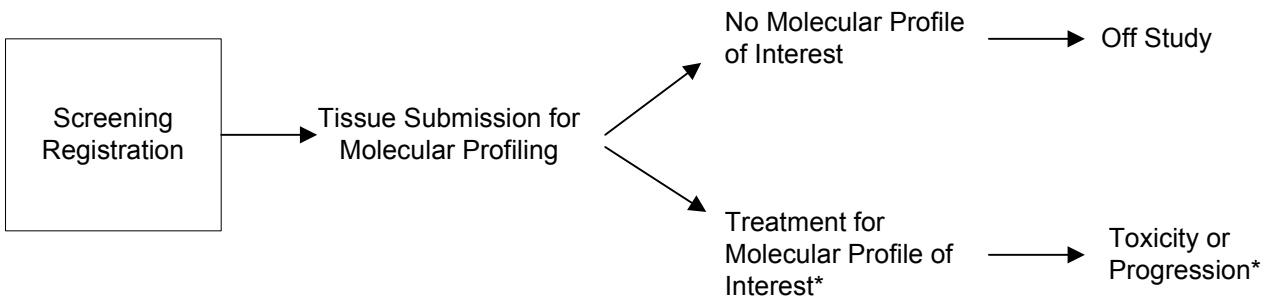
NCI-MATCH: Molecular Analysis for Therapy Choice

Participants:
ECOG-ACRIN, CTSU

Date Activated:
08/12/2015

Study Chairs:
K Flaherty (ECOG-ACRIN), P O'Dwyer (ECOG-ACRIN), A Chen (NCI), B Conley (NCI)

SCHEMA



*Upon progression or inability to tolerate protocol treatment, patients may be re-screened for additional molecular profiles of interest and corresponding protocol treatment.

Objectives

To evaluate the proportion of patients with objective response (OR) to targeted study agent(s) in patients with advanced refractory cancers/lymphomas.

To evaluate the proportion of patients alive and progression free at six months of treatment with targeted study agent in patients with advanced refractory cancers/lymphomas.

To evaluate the time until death or disease progression.

To identify potential predictive biomarkers beyond the genomic alteration by which treatment is assigned or resistance mechanisms using additional genomic, RNA and protein-based assessment platforms.

Patient Population

Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma that has progressed following at least one line of standard systemic therapy and/or for whose disease no standard treatment exists that has been shown to prolong survival. Patients must have measurable disease, have tumor amenable to image guided or direct vision biopsy, and be willing and able to undergo biopsy for molecular profiling.

Patients must not currently be receiving any other investigational agents. Any prior therapy, radiotherapy (except palliative radiation therapy of 30 Gy or less), or major surgery must have been completed at least four weeks prior to treatment on NCI-MATCH and patient must be recovered from adverse events due to prior therapy (except alopecia

and lymphopenia). Palliative radiation therapy must have been completed at least two weeks prior to enrollment on a NCI-MATCH treatment subprotocol, and patient must have recovered from any adverse events of this therapy. Patients with brain metastases or primary brain tumors must have completed treatment , surgery, or radiation therapy at least four weeks prior to initial registration. Patients must not require the use of full dose coumarin-derivative anticoagulants such as warfarin. Low molecular weight heparin is permitted for prophylactic or therapeutic use.

Patients must be at least 18 years of age, have an ECOG performance status of 0 or 1 and must be able to swallow tablets. Patients must have adequate hematologic, hepatic, renal, cardiac and marrow function. HIV-positive patients are eligible provided they meet protocol criteria. Each subprotocol will have additional eligibility criteria that will be outlined in Section 2.0 of the agent-specific subprotocol.

Accrual Goals

The target screening accrual for this study is approximately 3,000 patients, with the goal of accruing 35 patients in each treatment subprotocol. If after screening 500 patients, the total number of patients with actionable tumor alteration (therefore qualifying for treatment) is below 50, results will be presented to the steering committee for consideration of terminating the trial. Within any given subprotocol, if rate of enrollment is such that it is unlikely accrual can be completed in 7.5 years, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. An interim analysis of the assay results will be performed after biopsies from approximately the first 200 patients are processed.

Summary Statement

This study activated on August 12, 2015, with ten subprotocols included in the activation. Only sites utilizing the CIRB as their IRB of record will be able to participate in the trial.

N107C Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Phase III Trial of Post-Surgical Stereotactic Radiosurgery (SRS) Compared with Whole Brain Radiotherapy (WBRT) on Resected Metastatic Brain Disease

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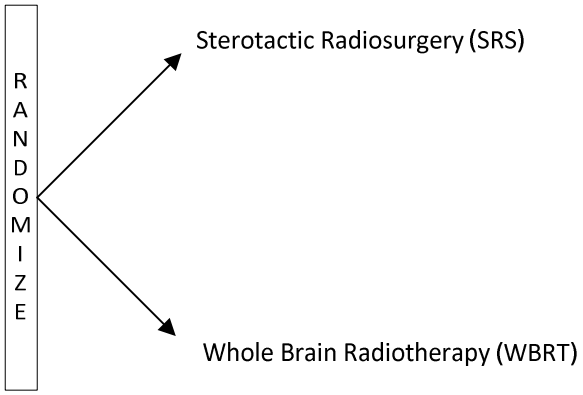
Participants:
Alliance, CTSU

Date Activated:
07/08/2011

Study Chairs:
P Brown (Alliance), L Gaspar (SWOG)

SCHEMA



Objectives

Co-Primary Endpoints:

To ascertain in patients with one to four brain metastases whether there is improved overall survival in patients who receive stereotactic radiosurgery (SRS) to the surgical bed compared to patients who receive whole brain radiotherapy (WBRT).

To ascertain in patients with one to four brain metastases whether there is less neurocognitive progression at six months post-randomization in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

Secondary:

To ascertain whether there is improved QOL in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

To ascertain whether there is improved time to central nervous system failure in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

To ascertain whether there is longer duration of functional independence in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

To ascertain in patients with one to four brain metastases whether there is better long-term neurocognitive status in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

To tabulate and descriptively compare the post-treatment adverse events associated with the interventions.

To evaluate local tumor bed recurrence at six months with post-surgical SRS to the surgical bed in comparison to WBRT.

To evaluate time to local recurrence with post-surgical SRS to the surgical bed in comparison to WBRT.

To evaluate if there is any difference in CNS failure patterns (local, distant, leptomeningeal) in patients who receive SRS to the surgical bed compared to patients who receive WBRT.

Correlative:

To evaluate radiation changes in the limbic system that may correlate with neurotoxicity using brain MRI scans.

To determine if Apo E (i.e. Apo E2, Apo E3, and Apo E4) genotyping may prove to be a predictor of radiation induced neurocognitive decline (or neuroprotection).

To determine if inflammatory markers (i.e. IL-2, IL-6, and TNF-alpha) may prove to be predictors of radiation induced neurocognitive decline.

To determine if oxidative stress biomarkers (i.e. protein carbonyl content, lipid hydroperoxides, and isoprostane levels) may prove to be predictors of radiation induced neurocognitive decline.

To determine if hormone and growth factors [i.e. glucocortcoids (e.g. cortisol), gonal steroids (e.g. estradiol, testosterone, progesterone), growth hormone, human chorionic gonadotropin (hCG), insulin-like growth factor-1 (IGF-1), and neuronal growth factor (NGF)] may prove to be a predictor of radiation induced neurocognitive decline.

Patient Population

Patients must have one to four brain metastases, as defined on a pre-operative brain MRI, with one brain lesion resected. Pathology from the resected brain lesion must be consistent with a non-central nervous system primary site. The resection cavity must measure < 5.0 cm in maximal extent on the post-operative brain MRI (or CT). Any unresected lesions must measure ≤ 3.0 cm in maximal extent on the contrasted pre-operative brain MRI. Patients may have active disease outside of the nervous system. Patients must be an appropriate candidate to be treated with either a gamma knife or a linear accelerator-based radiosurgery system. Patients must not have a brain metastasis that is located ≤ 5 mm of the optic chiasma or within the brainstem. Patients must not have widespread definitive leptomeningeal metastases, primary germ cell tumor, small cell carcinoma, or lymphoma.

Patients must not have received any prior cranial radiation therapy.

Patients must have an ECOG performance status of 0-2 and must be able to complete a neurocognitive examination without assistance. Patients must be willing and able to complete quality of life questionnaires with or without assistance. Patients must be able to complete a MRI with contrast of the head and must not have a known allergy to gadolinium. Patients must be willing to provide mandatory blood and urine samples for correlative research purposes.

The SRS facility must be Radiological Physics Center (RPC) approved and the Neurocognitive Testing examiner must have credentialing confirming completion of the neurocognitive testing training.

Stratification/Descriptive Factors

Patient randomization will be stratified by the following factors: (1) age: < 60 vs ≥ 60; (2) number of months extracranial disease controlled: ≤ 3 vs > 3; (3) number of pre-operative brain-metastases: 1 vs 2-4; (4) histology: lung vs radioresistant (brain metastases from a sarcoma, melanoma, or renal cell carcinoma histology) vs other; (5) resection cavity maximal diameter: ≤ 3cm vs > 3 cm.

Accrual Goals

A total of 192 patients, including an extra 18 to accommodate losses due to cancellations, ineligibility, or major protocol deviations.

Summary Statement

As of June 30, 2015 there have been 182 registrations to this study, but no registrations from SWOG

institutions. The complete summary of this study from Alliance is available on the SWOG web site.

R1306 Phase II SWOG Supported CTSU Study

Coordinating Group: NRG

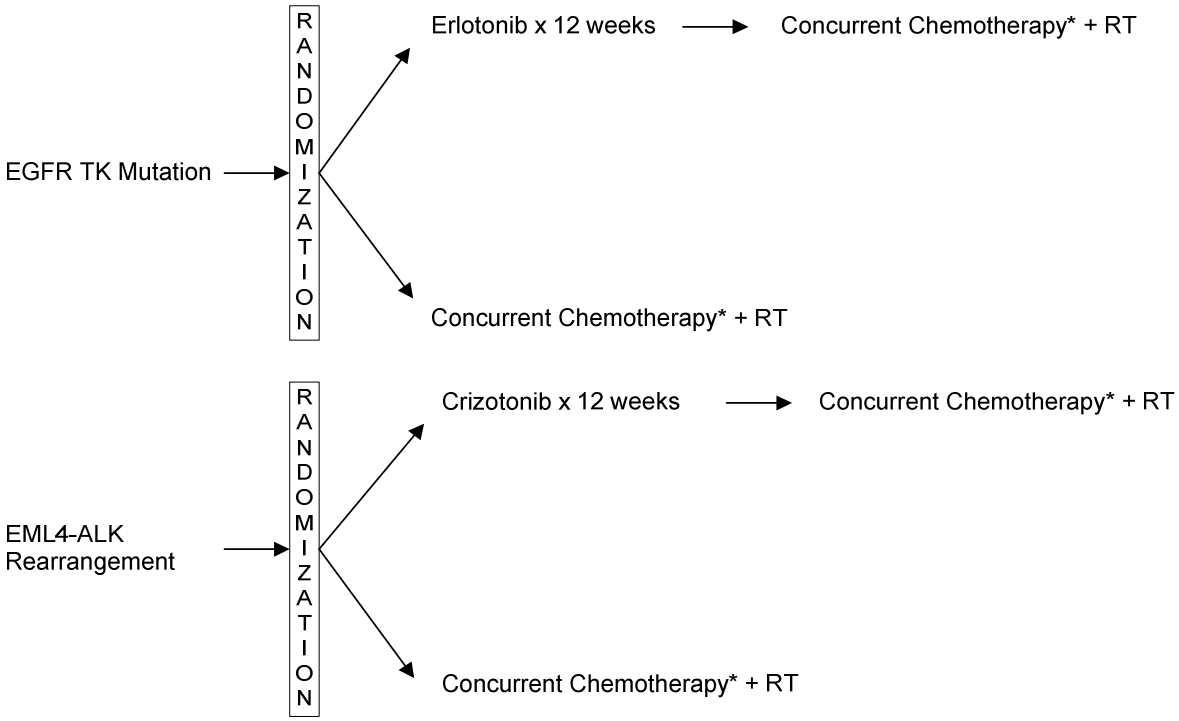
A Randomized Phase II Study of Individualized Combined Modality Therapy for Stage III Non-Small Cell Lung Cancer (NSCLC)

Participants:
NRG, CTSU

Date Activated:
11/04/2013

Study Chairs:
R Govindan (NRG), M Daly (SWOG)

SCHEMA



*Cisplatin/Etoposide or Paclitaxel/Carboplatin, per treating Investigator's discretion.

NOTE: Patients with both an EGFR TK mutation and an EMLF-ALK rearrangement will be placed in the ALK cohort.

Objectives

To assess whether patients with unresectable local-regionally advanced NSCLC treated with targeted agents based on molecular characteristics have a longer progression-free survival (PFS) than those treated with standard care therapy alone.

To evaluate response rates.

To assess toxicity.

To assess overall survival.

To correlate clinical outcomes with tumor molecular aberrations identified from deep sequencing of selected kinomes in patients from whom adequate baseline tissue is available.

Patient Population

Patients must have histologically or cytologically confirmed, newly diagnosed non-squamous NSCLC which is stage IIIA/IIIB and deemed unresectable. Patients may have a pleural effusion, provided it can be seen only on chest CT but not on chest x-ray, is too small to tap, and is transudate, cytologically negative, and non-bloody. Patients must have measurable disease. Patients must have documented presence of a known "sensitive" mutation in the EGFR TK domain (exon 19 deletion, L858) or EML4-ALK fusion rearrangement or both. Patients must also have documented absence of T790M mutation in the EGFR TK domain. All pre-enrollment biomarker screening must have been performed at a CLIA certified lab. The FDA approved Vysis dual color FISH assay must be used for detection of an ALK rearrangement.

Patients must have adequate cardiac, renal, hepatic and hematologic function and a Zubrod performance status of 0-1. Patients must not have atelectasis of the entire lung, COPD exacerbation or any other respiratory illness requiring hospitalization or precluding study therapy. Patients must not be known to have AIDS. Women of childbearing potential must have a serum pregnancy test performed within 14 days prior to enrollment.

Stratification/Descriptive Factors

Patients are stratfied by (1) weight loss: $\leq 5\%$ vs $> 5\%$; (2) stage: IIIA vs IIIB; and (3) planned chemotherapy regimen: cisplatin/etoposide vs paclitaxel/carboplatin.

Accrual Goals

Accrual will proceed separately in two cohorts. Patients with both an EGFR TK mutation and a EML4-ALK rearrangement will be placed in the ALK cohort. For the EGFRTK mutation cohort, 148 eligible patients will be enrolled. For the EML4-ALK rearrangement cohort, 74 eligible patients will be enrolled. In each cohort, an interim analysis for futility will be performed after half of the expected PFS events have occurred (44 for the EGFR TK mutation cohort, 29 for the EML4-ALK rearrangement cohort).

Summary Statement

As of June 30, 2015, there have been 22 registrations to this study, including six registrations by SWOG institutions. The complete summary of this study from NRG is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2015

Institutions	Total Reg
MD Anderson CC	4
Lahey Hosp & Med Ctr	2
Total (2 Institutions)	**6**