LUNG COMMITTEE

CONTENTS

Patient Registrations to Studies

by 12 Month Intervals
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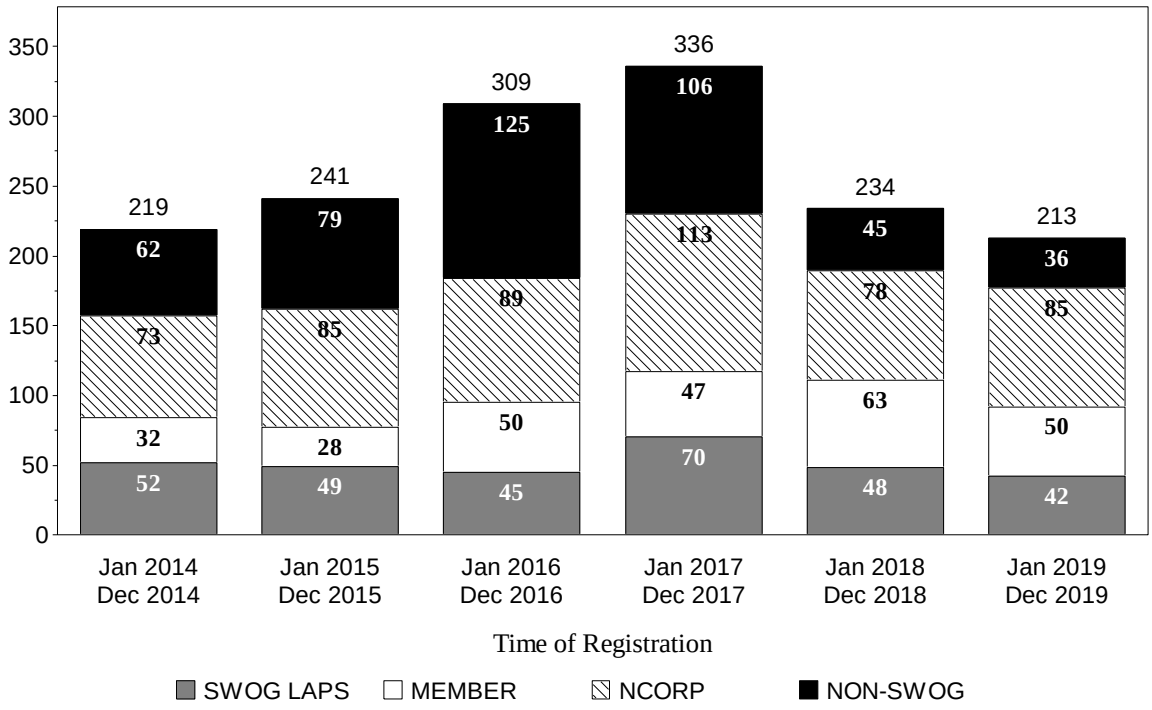

Screening registrations and registrations to Biologic only studies are excluded.

Patient Registrations by Study and Arm

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	Jul 2019 Dec 2019	Jan 2019 Jun 2019	Jul 2018 Dec 2018	All Patients
S1400 SCCA, Advanced, Biomarker Master Protocol				
Screening/Pre-Screening				
Specimen Submission	0	9	155	1,864
LUNGMAP NSCLC, Advanced, Biomarker Master Protocol				
Registration				
Specimen Submission	543	319	0	862
S1400F Non-Match: MEDI4736 + Tremelimumab				
Registration				
MEDI4736 + Tremelimumab	2	15	28	66
S1400K c-Met: ABBV-399 (Process II)				
Registration				
ABBV-399 (Process II)	0	0	13	28
S1800A Non-Match: Ramucirumab + Pembrolizumab vs SoC				
Randomization				
Standard of Care (Investigator Choice)	32	1	0	33
Ramucirumab + Pembrolizumab	27	3	0	30
	59	4	0	63
S1900A LOH and/or BRCA: Rucaparib				
Registration				
Rucaparib	32	7	0	39
S1619 Mesothelioma, Stage I-III, Neoadjuvant Chemotherapy/Atezolizumab -> Atezolizumab + SOC				
Neoadjuvant Therapy				
Chemotherapy + Atezolizumab	8	10	7	25
Surgery				
Surgery	5	7	1	13
Maintenance				
Maintenance	5	5	1	11
S1701 Thymic Advanced, Carboplatin/Paclitaxel/Ramucirumab vs. Carboplatin/Paclitaxel				
Randomization				
Ramucirumab + Carbo/Paclitaxel	1	1	0	2
Carboplatin + Paclitaxel	0	0	0	0
	1	1	0	2

Non-SWOG Studies with SWOG-Credited Registrations

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Studies with Accrual from July 2018 - December 2019

		SWOG Accrual				
	SWOG Champion	**Jul 2019 Dec 2019**	**Jan 2019 Jun 2019**	**Jul 2018 Dec 2018**	**SWOG Total**	**Total Accrued**
A151216 ALCHEMIST, NSCLC, Stage IIIA, II, IB - Screening Date Activated: 02/06/14 *Most Recent Progress Report*	D Gandara	59	85	105	785	5258
A081105 ALCHEMIST, EGFR-mut, Erlotinib Date Activated: 01/02/14 *Most Recent Progress Report*	K Kelly	4	10	6	59	349
C30610 SCLC, Thoracic RT Date Activated: 03/21/08 Date Closed: 12/01/19 *Most Recent Progress Report*		0	1	0	57	732
E4512 ALCHEMIST2, ALK mut, Crizotinib Date Activated: 08/18/14 *Most Recent Progress Report*		2	1	3	14	99
EA5142 ALCHEMIST3, Non-match, Nivolumab Date Activated: 05/16/16 Date Closed: 10/01/19 *Most Recent Progress Report*		11	29	26	121	935
EA5161 Lung, ED-SCLC, Cis/Carbo and Eto +/- Nivo Date Activated: 05/02/18 Date Closed: 12/07/18 *Most Recent Progress Report*		0	0	18	19	160
EA5163 NSCLC, Immunotherapy +/- 2nd line therapy Date Activated: 02/28/19 *Most Recent Progress Report*	A Chiang	12	2	0	14	91
NRGCC003 SCLC, PCI or HA-PCI Date Activated: 12/07/15 *Most Recent Progress Report*	L Gaspar	0	0	0	4	265
NRGLU002 LUNG, Limited Met NSCLC, MST vs LCT + MST Date Activated: 04/07/17 *Most Recent Progress Report*	D Gomez	1	0	0	1	96
NRGLU005 LUNG, LS-SCLC, ChemoRT v ChemoRT+Atezolizumab Date Activated: 05/28/19 *Most Recent Progress Report*	C Hsu	1	0	0	1	37

LUNGMAP Master Protocol – FDA Registration Trial

Coordinating Group: SWOG

A Master Protocol to Evaluate Biomarker-Driven Therapies and Immunotherapies in Previously-Treated Non-Small Cell Lung Cancer (Lung-MAP Screening Study)

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

Date Activated:
01/28/2019

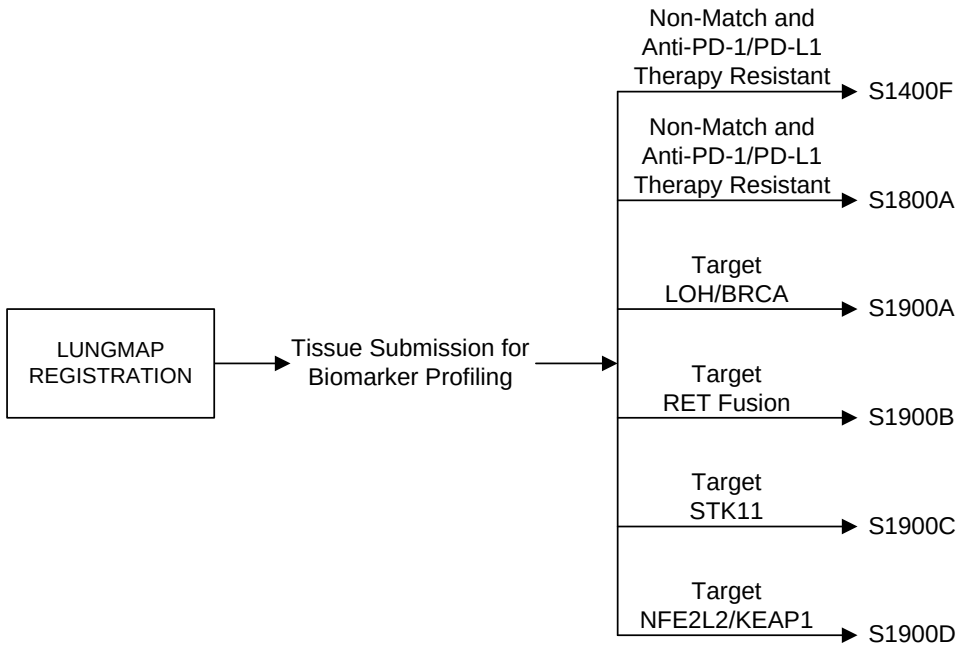
Study Chairs:
R Herbst, D Gandara, K Dragnev (Alliance), J Patel (Alliance), J Neal (ECOG-ACRIN), L Horn (ECOG-ACRIN), M Edelman (NRG), S Waqar (NRG)

Statisticians:
M Redman, K Minichiello, J Miao, J Moon, L Qian

Project Manager:
A Lee

Data Coordinators:
L Everhart, L Highleyman

SCHEMA



Objectives

To test patient specimens to determine eligibility for participation in the biomarker-driven and non-matched sub-studies included within the Lung-MAP umbrella protocol.

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

To evaluate circulating tumor DNA (ctDNA) and compare to the FMI Foundation tissue molecular profiling results in patients who submit a new biopsy for screening.

To establish a tissue/blood repository.

Patient Population

LUNGMAP is an expansion on the previous umbrella protocol S1400. LUNGMAP allows all histologic types of non-small cell lung cancer (NSCLC).

Patients must have pathologically proven NSCLC confirmed by tumor biopsy and/or fine-needle aspiration. Disease must be Stage IV or recurrent. 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). If archival tumor material is exhausted, then a new fresh tumor biopsy that is formalin-fixed and paraffin-embedded must be obtained. Patients must agree to have this tissue submitted to Foundation Medicine for common broad platform CLIA biomarker profiling, PD-L1 IHC, and c-MET IHC. Patients must not have EGFR sensitizing mutations, EGFR T790M mutations, ALK gene fusions, ROS1 gene rearrangements, or BRAF V600E mutations unless they have progressed following all standard of care targeted therapy.

Patients can either be screened upon progression on prior treatment or pre-screened prior to progression on current treatment. Patients screened at progression must have received at least one line of systemic therapy for any stage of disease and must have progressed during or following their most recent line of therapy. For patients whose prior systemic therapy was for Stage I-III disease only, progression on platinum-based chemotherapy must have occurred within one year from their last day of that therapy. For patients treated with consolidation anti-PD-1 or anti-PD-L1 therapy for Stage III disease, progression must have occurred within one year from the date of initiation of therapy. For patients whose prior therapy was for Stage IV or recurrent disease, the patient must have received at least one line of a platinum-based chemotherapy regimen or anti-PD-1/PD-L1 therapy, alone or in combination. To be eligible for pre-screening, current treatment must be for Stage IV or recurrent 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 or anti-PD-1/PD-L1 therapy, alone or in combination.

Patients must have a Zubrod performance status of 0-1 and be willing to provide prior smoking history.

Patients who need a fresh biopsy must also submit whole peripheral blood for ctDNA testing. Patients must agree to have any tissue that remains after testing retained for the use in sub-study Translational Medicine studies. Patients must also be offered participation in banking for future use of specimens.

Accrual Goals

This study is intended to be a long-term ongoing project to establish a National Clinical Trials Network (NCTN) mechanism for genomic screening of a large lung cancer population and subsequently assigning and accruing simultaneously to multiple sub-studies. Each sub-study will have its own accrual goal. It is estimated that about 1,000 patients will be screened per year, with 40%-50% of patients registering to a sub-study.

Summary Statement

The LUNGMAP protocol opened to accrual on January 28, 2019. This protocol replaced the original screening protocol, S1400, which permanently closed to accrual on January 28, 2019.

Patients screened under S1400 are allowed to enroll onto sub-studies opened under the new screening protocol, provided they meet the eligibility criteria.

Under the Lung-MAP umbrella (S1400 and LUNGMAP), thirteen sub-studies have been activated and of them, nine have closed.

Open sub-studies:

S1900A (LOH/BRCA1/BRCA2) activated on January 28, 2019 and is studying rucaparib.

S1800A (Non-match) activated on May 17, 2019 and is studying ramucirumab + MK3475 (pembrolizumab) vs. investigator's choice standard of care.

S1900C (STK11) activated on January 16, 2020 and is studying talazoparib + avelumab.
S1900B (RET fusion) activated on February 10, 2020 and is studying LOXO-292.

Closed sub-studies:
S1400A (Non-match) activated on June 16, 2014 and closed on December 18, 2015 and was studying MEDI4736.
S1400B (PI3K) activated on June 16, 2014 and closed on December 12, 2016 and was studying taselisib.
S1400C (CCGA) activated on June 16, 2014 and closed on September 1, 2016 and was studying palbociclib.
S1400D (FGFR) activated on June 16, 2014 and closed on October 31, 2016 and was studying AZD4547.
S1400E (c-MET) activated on June 16, 2014 and closed on November 26, 2014 and was studying erlotinib vs. erlotinib + rilotumumab.
S1400F (Non-match) activated on October 2, 2017 and was studying MEDI4736 + tremelimumab. The acquired resistance cohort closed on November 6, 2019. The primary resistance cohort closed on March 24, 2020.
S1400G (HRRD) activated on February 7, 2017 and closed on July 23, 2018 and was studying talazoparib.
S1400I (Non-match) activated on December 18, 2015 and closed on April 23, 2018 and was studying nivolumab vs. nivolumab + ipilimumab.
S1400K (c-MET) activated on February 5, 2018 and closed on December 21, 2018 and was studying ABBV-399 (Process II).

As of December 31, 2019, 862 patients have been registered. Seven (0.8%) are currently ineligible due to the following reasons: lack of tissue submission (3), not progressing on standard of care for ALK fusion (2), did not have Stage IV or recurrent disease (1), and not progressing within one year from last chemotherapy for Stage I-III disease (1).

Three hundred sixty-six patients received an assignment to a sub-study. Eight patients progressed on their current sub-study and received a new assignment. Thirty-three patients have requested to be re-assigned to a different sub-study.

Ninety-six patients enrolled to a sub-study.

Four hundred five Notice of Intention Not to Register (NINTR) forms have been submitted. The most common reason (40%) is patients were not eligible for any sub-study. Sixteen (4%) patients submitted the NINTR with the classification of "Other". The most common reasons included: no sub-study available for patient (2) and sub-study not open at site (2).

Registration by Network Groups

Registrations ending December 31, 2019

Institutions	Total Reg
SWOG	494
ALLIANCE	182
ECOG-ACRIN	108
NRG	78
Total (4 Network Groups)	**862**

Registration by Institution

Registrations ending December 31, 2019

Institutions	Total Reg
University of Pittsburgh Cancer Institute (UPCI (PA015)	41
Missouri Baptist Medical Center (MO046)	23
Mercy Medical Center (OH064)	20
University of Oklahoma Health Sciences Center (OK003)	17
Mercy Hospital Saint Louis (MO021)	16
University of New Mexico Cancer Center (NM004)	16
University of Rochester (NY167)	16
Northside Hospital (GA031)	15
Essentia Health Cancer Center (MN024)	14
Palo Alto Medical Foundation-Santa Cruz (CA791)	14
Good Samaritan Hospital - Cincinnati (OH073)	13
Regions Hospital (MN001)	12
Roswell Park Cancer Institute (NY158)	12
Illinois CancerCare-Peoria (IL101)	11
Anne Arundel Medical Center (MD042)	10
Ascension Providence Hospitals - Southfield (MI006)	10
Edwards Comprehensive Cancer Center (WV046)	10
Northwestern University (IL036)	10
University of Kentucky/Markey Cancer Center (KY010)	10
Baystate Medical Center (MA004)	9
Lowell General Hospital (MA134)	9
Northeast Georgia Medical Center-Gainesville (GA024)	9
The Mark H Zangmeister Center (OH124)	9
Eastern Maine Medical Center Cancer Care (ME040)	8
FirstHealth of the Carolinas-Moore Regional Hos (NC081)	8
Gundersen Lutheran Medical Center (WI029)	8
IHA Hematology Oncology Consultants-Ann Arbor (MI349)	8
Medical Oncology Hematology Consultants PA (DE038)	8
Olathe Medical Center (KS020)	8
Parkview Regional Medical Center (IN181)	8
Saint Alphonsus Cancer Care Center-Caldwell (ID027)	8
University of California Davis Comprehensive Ca (CA189)	8
University of Vermont Medical Center (VT003)	8
AnMed Health Cancer Center (SC064)	7
Baptist Memorial Hospital and Fowler Family Can (AR019)	7
IHA Hematology Oncology Consultants-Brighton (MI350)	7
Katmai Oncology Group (AK015)	7
Marshfield Medical Center-Marshfield (WI031)	7

Institutions	Total Reg
Memorial Regional Hospital/Joe DiMaggio Childre (FL023)	7
Veterans Affairs Connecticut Healthcare System- (CT063)	7
Western Maryland Regional Medical Center (MD031)	7
Aspirus Regional Cancer Center (WI028)	6
Baptist Memorial Hospital and Cancer Center-Mem (TN029)	6
Lahey Hospital and Medical Center (MA017)	6
Saint Joseph Hospital East (KY106)	6
Stamford Hospital/Bennett Cancer Center (CT033)	6
Arnot Ogden Medical Center/Falck Cancer Center (NY367)	5
Aultman Health Foundation (OH100)	5
Duke University Medical Center (NC010)	5
Illinois CancerCare-Bloomington (IL352)	5
NorthShore University HealthSystem-Evanston Hos (IL018)	5
Palo Alto Medical Foundation Health Care (CA138)	5
Saint Mary's Medical Center (WV010)	5
Salina Regional Health Center (KS029)	5
Sparrow Hospital (MI039)	5
Springfield Regional Cancer Center (OH325)	5
Virginia Cancer Institute (VA067)	5
All Other Institutions	315
Total (225 Institutions)	**862**

Registration, Eligibility, and Evaluability

Classified by Initial Screening Type

Registrations ending December 31, 2019; Data as of February 12, 2020

	TOTAL	Screened at Progression	Pre-screened Prior to Progression
NUMBER REGISTERED	862	345	517
INELIGIBLE	7	1	6
ELIGIBLE	855	344	511
Analyzable, Pend. Elig.	157	65	92

Patient Characteristics

Registrations ending December 31, 2019; Data as of February 12, 2020

	Total (n=855)	
AGE		
Median	66.8	
Minimum	27.7	
Maximum	92.3	
SEX		
Males	458	54%
Females	397	46%
HISPANIC		
Yes	15	2%
No	827	97%
Unknown	13	2%
RACE		
White	763	89%
Black	60	7%
Asian	17	2%
Pacific Islander	2	0%
Native American	1	0%
Multi-Racial	1	0%
Unknown	11	1%
PERFORMANCE STATUS		
0	253	30%
1	591	69%
Data pending	11	1%
SMOKING HISTORY		
Current	257	30%
Former	523	61%
Never	65	8%
Data pending	10	1%
WEIGHT LOSS PAST 6 MONTHS		
< 5%	570	67%
5 - < 10%	126	15%
10 - < 20%	94	11%
>= 20%	7	1%
Data pending	58	7%
HISTOLOGY		
Adenocarcinoma	538	63%
Large Cell	10	1%
Squamous Cell Carcinoma	254	30%
Mixed ≥ 50% Squamous Cell Carcinoma	9	1%
Mixed < 50% Squamous Cell Carcinoma	5	0.6%
Other non-small cell, NOS	33	4%
Data pending	6	0.7%

Sub-Study Assignments

Classified by Initial Screening Type

Registrations ending December 31, 2019; Data as of February 12, 2020

	Screened at Progression (n=271)		Pre-screened Prior to Progression (n=95)	
ASSIGNED SUB-STUDY				
S1400F (Non-match)	15	6%	2	2%
S1800A (Non-match)	208	77%	80	84%
S1900A (LOH/BRCA)	48	18%	13	14%

New Sub-Study Assignments

Patients Receiving New Sub-Study Assignments After Progression

Registrations ending December 31, 2019; Data as of February 12, 2020

	Total (n=8)	
ASSIGNED SUB-STUDY		
S1400F (Non-match)	2	25%
S1800A (Non-match)	6	75%

Notice of Intention Not to Register

Registrations ending December 31, 2019; Data as of February 12, 2020

	Screened at Progression (n=226)		Pre-Screened Prior to Progression (n=179)	
PRIMARY REASON				
Patient is not eligible for any of the sub-studies	119	53%	40	22%
Tissue sample was inadequate for biomarker profiling	16	7%	40	22%
Death	24	11%	48	27%
Symptomatic deterioration	16	7%	16	9%
Investigator decision	16	7%	12	7%
Patient refused	10	4%	4	2%
Preference to receive Standard of Care therapy off study	8	4%	5	3%
Patient is not eligible for the screening study	4	2%	5	3%
Preference to receive an investigational therapy off study	3	1%	0	0%
Other	8	4%	8	5%
Data pending	2	1%	1	0.6%

S1400F Phase II – FDA Registration Trial

Coordinating Group: SWOG

A Phase II Study of MEDI4736 (Durvalumab) plus Tremelimumab as Therapy for Patients with Previously Treated Anti-PD-1/PD-L1 Resistant Stage IV Squamous Cell Lung Cancer (Lung-MAP Non-Match Sub-Study)

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

Study Chairs:
N Leighl (CCTG), N Rizvi

Statisticians:
M Redman, K Minichiello

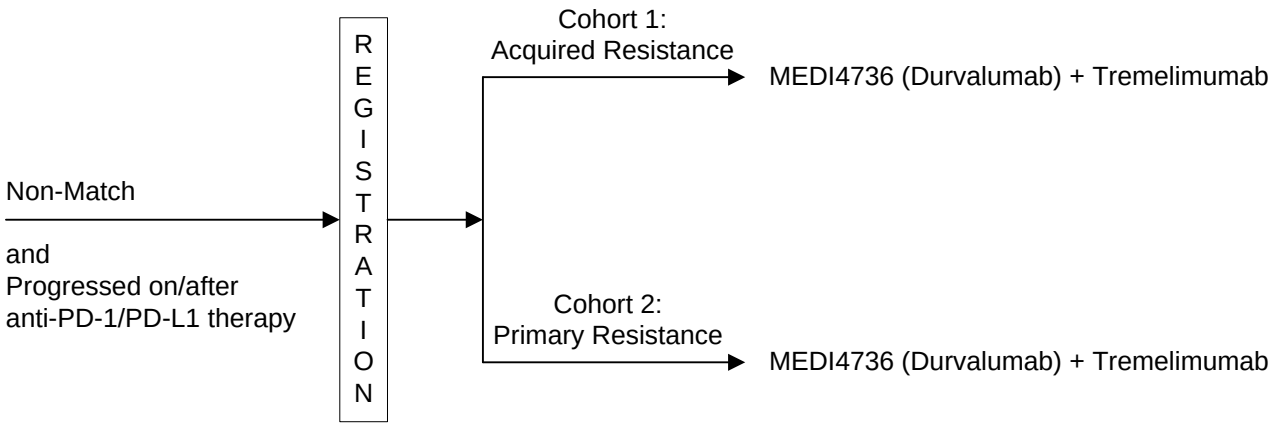
Project Manager:
A Lee

Data Coordinators:
L Everhart, L Highleyman

Date Activated:
10/02/2017

Date Closed:
11/06/2019 (Acquired Resistance Cohort)
03/24/2020 (Primary Resistance Cohort)

SCHEMA



Objectives

This study will enroll patients into two parallel and independently evaluated cohorts as depicted in the schema:

To evaluate the objective response rate (confirmed and unconfirmed, complete and partial) by RECIST 1.1 among patients treated with MEDI4736 (Durvalumab) plus tremelimumab.

To estimate the duration of response (DoR) among patients who achieve a complete response (CR) or partial response (PR) (confirmed and unconfirmed) by RECIST 1.1.

To estimate the duration of response (DoR) per protocol-defined immune-related response criteria among patients who achieve a complete response (CR) or partial response (PR) (confirmed and unconfirmed) by RECIST 1.1.

To evaluate overall survival (OS) among patients treated with MEDI4736 (Durvalumab) plus tremelimumab.

To evaluate investigator-assessed progression-free survival (IA-PFS) among patients treated with MEDI4736 (Durvalumab) plus tremelimumab.

To evaluate IA-PFS assessed per protocol-defined immune-related response criteria (irRC-IA-PFS) among patients treated with MEDI4736 (Durvalumab) plus tremelimumab.

To evaluate the frequency and severity of toxicities associated with MEDI4736 (Durvalumab) plus tremelimumab.

Patient Population

Patients must have been eligible for the screening study and must have been assigned to the S1400F sub-study based on biomarker profiling results. Patients must have experienced disease progression during or after prior anti-PD-1 or anti-PD-L1 antibody monotherapy as their most recent line of treatment. Patients must have measurable disease by CT or MRI. Patients must not have leptomeningeal disease, spinal cord compression or brain metastases unless both (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, and prior to registration, and (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least 24 hours prior to sub-study registration.

Prior exposure to PD-1/PD-L1 in combination with other therapies or CTLA-4 inhibitors is not permitted. Patients must not have received any immunosuppressive medication within 28 days prior to sub-study registration and must not be planning to receive these medications while on protocol therapy. Patients must not have received nitrosoureas or mitomycin-c within 42 days prior to sub-study registration. Patients must not have received any prior systemic therapy within 21 days prior to sub-study registration. Patients must have fully recovered from the effects of surgery at least 14 days prior to sub-study registration. Patients must not be planning to receive any concurrent chemotherapy, immunotherapy, biologic or hormonal therapy for cancer treatment.

Patients must have a Zubrod performance status of 0-1 and adequate hepatic, cardiac, hematologic, thyroid and renal function. Patients must not have experienced a Grade 3 or worse immune-related adverse event (irAE) or any unresolved irAE Grade 2, nor have experienced a toxicity that led to permanent discontinuation of prior anti-PD-1/PD-L1 immunotherapy. Patients must not have any history of organ transplant that requires use of immunosuppressives. Patients must not have clinical signs or symptoms of active tuberculosis infection. Patients must not have received a live attenuated vaccination within 28 days prior to sub-study registration. Patients must not have known HIV, or a known positive test for Hepatitis B virus surface antigen, or Hepatitis C virus ribonucleic acid. Patients with a positive Hepatitis C antibody with a negative viral load are allowed. Patients must not have any prior documented autoimmune or inflammatory disease within three years prior to sub-study registration. Patients with vitiligo, immune-mediated alopecia, Grave's disease, or psoriasis requiring systemic treatment within the past two years are not eligible. Patients with hypothyroidism who are stable on hormone replacement therapy are eligible. Patients must not have any history of primary immunodeficiency.

Stratification/Descriptive Factors

Patients will be stratified into two cohorts:

Acquired resistance: Patients with a history of 24 weeks or more of disease control (complete response, partial response or stable disease) after initiation of

single agent anti-PD-1/PD-L1 therapy that have subsequently progressed after 24 weeks.

Primary resistance: Patients with a history of disease progression within 24 weeks of initiation of single agent anti-PD-1/PD-L1 therapy.

Total accrual goal is 66 patients per cohort to achieve 60 eligible patients per cohort. The study design includes interim analyses within each cohort upon 20 and 40 patients evaluable for response.

Summary Statement

The first interim analysis was performed on each cohort. The acquired resistance cohort (ARC) was placed in temporary closure on February 22, 2019 for the determination of the interim analysis decision. The ARC permanently closed to accrual on November 6, 2019. The primary resistance cohort (PRC) was placed in temporary closure on May 15, 2019 for the determination of the interim analysis decision. The PRC re-opened to accrual on November 6, 2019 and was permanently closed to accrual on March 24, 2020 due to study feasibility.

As of December 31, 2019, 179 S1400 patients and 19 LUNGMAP patients have been assigned to S1400F. Sixty-six patients have been enrolled, six of which are from LUNGMAP.

Of the 132 who did not register, 79 patients were not eligible, 12 patients were investigator decision, eight patients were not eligible for the screening study, seven patients refused, seven patients had symptomatic deterioration, four patients passed away, one had prior exposure to PD-1/PD-L1 in combination with CTLA-4 inhibitor on S1400I, one was a Canadian patient where the study was not open, and one could not delay treatment any longer. The remaining 12 patients have not yet submitted the Notice of Intention Not to Register.

Of the 66 registered patients, six are ineligible due to not receiving anti-PD-L1 monotherapy as their most recent line of treatment and one is ineligible due to baseline CT scans not done within 28 days prior to registration. Additionally, two patients are not analyzable due to passing away prior to receiving any treatment and withdrawing consent prior to receiving any treatment (1 each). Thus, these nine will not be included in any analysis.

Fifty-seven patients have been assessed for adverse events. There has been two treatment-related deaths. One was due to pneumonitis. The exact cause of death could not be determined for the second case (coded “Death NOS”) but was reported as possibly related to pneumonitis. The pneumonitis patient also experienced Grade 4 dyspnea. Additionally, three patients experienced Grade 4 adverse events due to the following: lymphocyte count reduction (1), platelet count reduction (1), and white blood cell reduction (1).

Registration by Institution

Institutions	Total Reg	Institutions	Total Reg
Georgia NCORP	6	Oklahoma, Univ of	1
Heartland NCORP	6	Oregon Hlth Sci Univ	1
Southeast COR NCORP	6	Providence Hosp	1
New Mexico MU-NCORP	3	Rochester, Univ of	1
Kentucky, U of	2	VAMC Kansas City	1
MAVERIC	2	Wayne State Univ	1
PIH Health Hosp/Irvine, U of CA	2	Wichita NCORP	1
Colorado, U of	1	Yale University	1
Eisenhower Med Ctr/San Diego, U of CA	1	ALLIANCE	12
Harrington CC	1	NRG	7
MD Anderson CC	1	ECOG-ACRIN	6
Michigan CRC NCORP	1	**Total (24 Institutions)**	**66**
Michigan, U of	1		

Registration, Eligibility, and Evaluability

Classified by Resistance

Data as of February 3, 2020

	TOTAL	Acquired Resistance	Primary Resistance
NUMBER REGISTERED	66	30	36
INELIGIBLE	7	0	7
ELIGIBLE	59	30	29
Analyzable, Pend. Elig.	1	0	1
Not Analyzable	2	0	2
RESPONSE ASSESSMENT			
Determinable	54	30	24
Not Determinable	1	0	1
Too Early	2	0	2
ADVERSE EVENT ASSESSMENT			
Evaluable	57	30	27

Patient Characteristics

Classified by Resistance

Data as of February 3, 2020

	Acquired Resistance (n=30)		Primary Resistance (n=27)	
AGE				
Median	67.8		67.5	
Minimum	46.6		49.7	
Maximum	84.0		89.8	
SEX				
Males	18	60%	18	67%
Females	12	40%	9	33%
HISPANIC				
Yes	3	10%	1	4%
No	26	87%	26	96%
Unknown	1	3%	0	0%
RACE				
White	26	87%	23	85%
Black	3	10%	3	11%
Native American	0	0%	1	4%
Unknown	1	3%	0	0%
PRIOR LINES OF TREATMENT FOR STAGE IV DISEASE				
0	2	7%	2	7%
1	10	33%	7	26%
2	14	47%	15	56%
3	3	10%	2	7%
4	1	3%	1	4%
PERFORMANCE STATUS				
0	10	33%	7	26%
1	20	67%	20	74%
WEIGHT LOSS PAST 6 MONTHS				
< 5%	22	73%	19	70%
5 - < 10%	6	20%	6	22%
10 - < 20%	2	7%	1	4%
>=20%	0	0%	1	4%

Treatment Summary

Classified by Resistance

Data as of February 3, 2020

	TOTAL	Acquired Resistance	Primary Resistance
NUMBER ON PROTOCOL TREATMENT	2	0	2
NUMBER OFF PROTOCOL TREATMENT	55	30	25
REASON OFF TREATMENT			
Treatment completed as planned	0	0	0
Adverse Event or side effects	8	4	4
Refusal unrelated to adverse event	0	0	0
Progression/relapse	42	23	19
Death	4	3	1
Other - not protocol specified	0	0	0
Reason under review	1	0	1
MAJOR PROTOCOL DEVIATIONS	0	0	0
LOST TO FOLLOW-UP	0	0	0
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	2	1	1

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

Adverse Events Unlikely or Not Related to Treatment Excluded

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

Data as of February 3, 2020

	MEDI4736 + Tremelimumab (n=57) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
Atrial flutter	56	1	0	0
Chills	56	1	0	0
Confusion	56	1	0	0
Creatinine increased	56	1	0	0
Death NOS	56	0	0	1
Dehydration	54	3	0	0
Diarrhea	53	4	0	0
Dyspnea	53	3	1	0
Encephalopathy	56	1	0	0
Febrile neutropenia	56	1	0	0
Generalized muscle weakness	56	1	0	0
Hyperglycemia	56	1	0	0
Hypoxia	55	2	0	0
Lung infection	56	1	0	0
Lymphocyte count decreased	54	2	1	0
Nausea	56	1	0	0
Neutrophil count decreased	56	1	0	0
Platelet count decreased	54	2	1	0
Pneumonitis	55	1	0	1
Rash maculo-papular	56	1	0	0
Vomiting	56	1	0	0
White blood cell decreased	56	0	1	0
MAX. GRADE ANY ADVERSE EVENT	39	13	3	2

S1800A Phase II – FDA Registration Trial

Coordinating Group: SWOG

A Phase II Randomized Study of Ramucirumab plus MK3475 (Pembrolizumab) versus Standard of Care for Patients Previously Treated with Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Non-Matched Sub-Study)

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

Date Activated:
05/17/2019

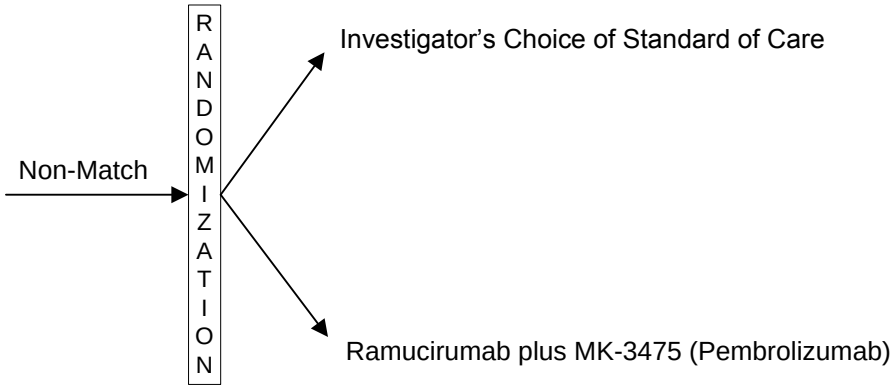
Study Chairs:
K Reckamp, K Dragnev (Alliance)

Statisticians:
M Redman, K Minichiello

Project Manager:
A Lee

Data Coordinators:
L Everhart, L Highleyman

SCHEMA



Objectives

To compare overall survival (OS) between patients previously treated with platinum-based chemotherapy and immunotherapy for Stage IV or recurrent non-small cell lung cancer randomized to ramucirumab plus MK-3475 (pembrolizumab) versus standard of care.

To compare response rates between the arms, including complete response (CR) and partial response (PR) (confirmed and unconfirmed).

To compare the disease control rate (CR, PR, confirmed and unconfirmed, and stable disease).

To evaluate the duration of response among responders within each arm.

To evaluate the frequency and severity of toxicities within each arm.

To compare investigator-assessed progression-free survival (IA-PFS) between the arms.

To evaluate the clinical outcomes (OS, IA-PFS, response) by randomization stratification factors by comparing outcomes within the ramucirumab and MK-3475 (pembrolizumab) arm, performing a sub-group analysis of the arms, and by evaluating an interaction between the factors and treatment arm.

Patient Population

Patients must have been eligible for the screening study and must have been assigned to the S1800A sub-study based on biomarker profiling results. Patients must have received exactly one line of anti-PD-1 or anti-PD-L1 therapy as their most recent line of therapy, either alone or in combination with platinum-based chemotherapy and must have experienced disease progression during or after this regimen more than 84 days following initiation. Patients whose most recent line of therapy was anti-PD-1 or anti-PD-L1 monotherapy must have also experienced disease progression during or after prior platinum-based chemotherapy. Patients must have measurable disease documented by CT or MRI. Patients must not have leptomeningeal disease, spinal cord compression or brain metastases unless they meet the criteria in the protocol. Patients must not have EGFR sensitizing mutations, EGFR T790M mutations, ALK gene fusions, ROS1 gene rearrangements, or BRAF V600E mutations unless they have progressed following all standard of care targeted therapy.

Patients must not have received nitrosoureas or mitomycin-c within 42 days prior to sub-study randomization. Patients must not have received any prior systemic therapy within 21 days prior to sub-study randomization. Patients must have recovered (≤ Grade 1) from any side effects of prior therapy. Patients must not have received systemic treatment with corticosteroids or other immunosuppressive medications within seven days prior to sub-study randomization. Patients must not have received any radiation therapy within 14 days prior to sub-study randomization or lung radiation therapy of > 30 Gy within six months prior to first planned dose. Patients must not have undergone major surgery within 28 days prior to sub-study randomization, or subcutaneous venous access device placement within 7 days prior to randomization. Patients must not be planning to receive any concurrent therapy for cancer while receiving treatment on this study.

Patients must have Zubrod performance status of 0-1 and adequate hepatic, cardiac, coagulation, hematologic, renal, and gastrointestinal function. Patients must not have experienced a Grade 3 or worse immune-related adverse event (irAE) or any unresolved irAE Grade 2, nor have experienced a toxicity that led to permanent discontinuation of prior anti-PD-1/PD-L1 immunotherapy. Patients must not have any history of organ transplant that requires use of immunosuppressives. Patients must not have clinical signs or symptoms of active tuberculosis infection or received a live attenuated vaccination within 28 days prior to sub-study randomization. Patients must not have history of non-infectious pneumonitis that required steroids or current pneumonitis/interstitial lung disease. Patients must not have had a serious or nonhealing wound, ulcer, or bone fracture within 28 days prior to sub-study randomization. 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, an adequate CD4 count, must not require prophylaxis for any opportunistic infections, and must not be newly diagnosed within the last 12 months. Patients must not have gross hemoptysis within two months of sub-study randomization. Patients must not have an active autoimmune disease that has required systemic treatment in the past two years or have any history of primary immunodeficiency.

Patients must agree to have blood specimens submitted for circulating tumor DNA. Patients must be offered participation in banking and in the correlative studies for collection and future use of specimens.

Stratification/Descriptive Factors

Randomization will be stratified by the following factors: (1) PD-L1 status: negative (<1%) vs positive (≥1%) or unknown; and (2) histology: squamous (including mixed histology with any squamous component) vs non-squamous; and (3) if patient is randomized to standard of care arm, does the planned treatment include ramucirumab?: yes vs no.

Accrual Goals

The accrual goal is 144 patients to achieve 130 eligible patients. The first interim analysis will be

performed when at least 24 weeks have elapsed since the 18th eligible patient was randomized to the investigational arm. The second interim analysis will be performed when at least 45 (50%) of the expected deaths have occurred.

Summary Statement

As of December 31, 2019, 27 S1400 patients and 294 LUNGMAP patients have been assigned to S1800A. Sixty-three patients have been enrolled, 59 of which are from LUNGMAP.

Of the 258 who have not registered, 117 patients were not eligible, 22 were investigator decisions, 19 patients passed away, 14 patients had symptomatic deterioration, 13 patients preferred to receive standard of care therapy outside of the study, eight patients refused, five patients were not eligible for the screening study, two patients preferred to receive investigational therapy outside of the study, and 11 had other reasons. The remaining 47 patients have not yet submitted the Notice of Intention Not to Register.

Of the 33 patients registered to the standard of care arm, five patients were ineligible due to the following reasons: not progressing from platinum-based chemotherapy (2), brain metastases requiring continued steroid treatment beyond the time of registration (1), not receiving and progressing on all standard of care targeted therapies for an oncogenic alteration driver (1), and not progressing at least 84 days after initiation of anti-PD-1/PD-L1 therapy (1).

Of the 30 patients registered to the investigational arm, three patients were ineligible due to the following reasons: not receiving and progressing on anti-PD-1/PD-L1 therapy per protocol-specified timeframe (2) and not progressing after platinum-based chemotherapy (1).

On the standard of care arm, 26 patients have been assessed for adverse events. There has been one treatment-related death due to sepsis. An additional five patients have experienced treatment-related Grade 4 events with the most due to neutrophil count reduction (4) and white blood cell reduction (3). The adverse event listed as Gastrointestinal disorders – Other was due to ischemic bowel.

On the investigational arm, 26 patients have been assessed for adverse events. One patient has experienced a treatment-related Grade 4 adverse event due to dyspnea.

Registration by Institution

Registrations ending December 31, 2019

Institutions	Total Reg	Institutions	Total Reg
Southeast COR NCORP	6	Arnot Ogden Med Ctr/Rochester, Univ of	1
Heartland NCORP	5	Cotton O'Neil CC	1
Michigan CRC NCORP	4	CRC West MI NCORP	1
Upstate NCORP	3	Mississippi, Univ of	1
Arkansas, U of	2	Oklahoma, Univ of	1
CORA NCORP	2	Rochester, Univ of	1
Georgia NCORP	2	Salem Hospital	1
Kaiser Perm NCORP	2	Wisconsin NCORP	1
Kansas MU-NCORP	2	ALLIANCE	7
Kentucky, U of	2	ECOG-ACRIN	7
Lahey Hosp & Med Ctr	2	NRG	5
MAVERIC	2	**Total (24 Institutions)**	**63**
Montana NCORP	2		

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2019; Data as of February 14, 2020

	TOTAL	Standard of Care (Inv. Choice)	Ramucirumab + Pembrolizumab
NUMBER REGISTERED	63	33	30
INELIGIBLE	8	5	3
ELIGIBLE	55	28	27
Analyzable, Pend. Elig.	20	16	4
RESPONSE ASSESSMENT			
Determinable	31	12	19
Not Determinable	2	2	0
Too Early	22	14	8
ADVERSE EVENT ASSESSMENT			
Evaluable	52	26	26
Too Early	3	2	1

Patient Characteristics

Registrations ending December 31, 2019; Data as of February 14, 2020

	Standard of Care (Inv. Choice) (n=28)		Ramucirumab + Pembrolizumab (n=27)	
AGE				
Median	65.0		68.5	
Minimum	48.9		46.8	
Maximum	92.9		85.3	
SEX				
Males	16	57%	15	56%
Females	12	43%	12	44%
HISPANIC				
No	28	100%	27	100%
RACE				
White	25	89%	24	89%
Black	2	7%	3	11%
Multi-Racial	1	4%	0	0%
PD-L1 Status				
Negative (<1%)	9	32%	12	44%
Positive (>=1%)	16	57%	12	44%
Unknown	3	11%	3	12%
HISTOLOGY				
Squamous Cell Carcinoma	12	43%	13	48%
Adenocarcinoma	16	57%	14	52%
PLANNED SOC TREATMENT TO INCLUDE RAMUCIRUMAB				
Yes	17	61%	16	59%
No	11	39%	11	41%
PRIOR LINES OF TREATMENT FOR STAGE IV DISEASE				
0	3	11%	0	0%
1	14	50%	15	56%
2	8	29%	7	26%
3	1	4%	2	7%
4	1	4%	1	4%
5	0	0%	1	4%
Data pending	1	4%	1	4%
PERFORMANCE STATUS				
0	2	7%	6	22%
1	25	89%	20	74%
Data pending	1	4%	1	4%
WEIGHT LOSS PAST 6 MONTHS				
< 5%	20	71%	17	63%
5 - < 10%	4	14%	5	19%
10 - < 20%	2	7%	3	11%
Data pending	2	7%	2	7%

Investigator's Choices of Standards of Care

Registrations ending December 31, 2019; Data as of February 14, 2020

	Standard of Care (Inv. Choice) (n=28)	
Ramucirumab + Docetaxel + Dexamethasone	15	54%
Gemcitabine + Dexamethasone	3	11%
Pemetrexed + Dexamethasone	3	11%
Docetaxel	2	7%
Gemcitabine Alone	2	7%
Data pending	3	11%

Treatment Summary

Registrations ending December 31, 2019; Data as of February 14, 2020

	Total
NUMBER ON PROTOCOL TREATMENT	36
NUMBER OFF PROTOCOL TREATMENT	19
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	1
Refusal unrelated to adverse event	1
Progression/relapse	7
Death	1
Other - not protocol specified	0
Reason under review	9
MAJOR PROTOCOL DEVIATIONS	0
LOST TO FOLLOW-UP	0
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	0

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

Adverse Events Unlikely or Not Related to Treatment Excluded
Adverse Events with No Entries for Grades 3 to 5 Have Been Suppressed
Registrations ending December 31, 2019; Data as of February 14, 2020

	Standard of Care (Inv. Choice) (n=26) Grade				Ramucirumab + Pembrolizumab (n=26) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
ALT increased	25	0	1	0	26	0	0	0
AST increased	25	0	1	0	26	0	0	0
Acidosis	25	0	1	0	26	0	0	0
Acute kidney injury	25	0	1	0	25	1	0	0
Adrenal insufficiency	26	0	0	0	25	1	0	0
Anemia	25	1	0	0	26	0	0	0
Anorexia	25	1	0	0	26	0	0	0
Colonic perforation	25	0	1	0	26	0	0	0
Dehydration	25	1	0	0	26	0	0	0
Delirium	26	0	0	0	25	1	0	0
Diarrhea	25	1	0	0	26	0	0	0
Dizziness	25	1	0	0	26	0	0	0
Dyspnea	25	1	0	0	25	0	1	0
Fatigue	24	2	0	0	25	1	0	0
GI disorders-Other, specify	25	0	1	0	26	0	0	0
Hypertension	26	0	0	0	25	1	0	0
Hypotension	24	1	1	0	26	0	0	0
Hypoxia	24	1	1	0	26	0	0	0
Lung infection	23	3	0	0	26	0	0	0
Lymphocyte count decreased	23	2	1	0	26	0	0	0
Mucositis oral	24	1	1	0	26	0	0	0
Multi-organ failure	25	0	1	0	26	0	0	0
Muscle weakness lower limb	25	1	0	0	26	0	0	0
Nausea	25	1	0	0	26	0	0	0
Neutrophil count decreased	20	2	4	0	26	0	0	0
Pleural effusion	25	1	0	0	26	0	0	0
Sepsis	24	1	0	1	26	0	0	0
Thromboembolic event	25	1	0	0	26	0	0	0
Vomiting	25	1	0	0	26	0	0	0
Wheezing	26	0	0	0	25	1	0	0
White blood cell decreased	19	4	3	0	26	0	0	0
MAX. GRADE ANY ADVERSE EVENT	14	6	5	1	23	2	1	0

S1900A Phase II – FDA Registration Trial

Coordinating Group: SWOG

A Phase II Study of Rucaparib in Patients with Genomic LOH High and/or Deleterious BRCA1/2 Mutation Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Sub-Study)

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

Date Activated:
01/28/2019

Study Chairs:
J Riess, P Wheatley-Price (CCTG)

Statisticians:
M Redman, K Minichiello

Project Manager:
A Lee

Data Coordinators:
L Highleyman, L Everhart

Objectives

To evaluate the overall response rate (confirmed and unconfirmed, complete and partial) associated with rucaparib in genomic LOH high and/or deleterious BRCA1/2 mutations within cohort 1: patients with squamous cell histology; and cohort 2: patients with non-squamous histology (adenocarcinoma, large cell, or NSCLC NOS, or mixed histology with any non-squamous component).

To evaluate investigator assessed progression-free survival and overall survival associated with rucaparib within each cohort.

To evaluate duration of response among responders within each cohort.

To evaluate the frequency and severity of toxicities associated with rucaparib among all patients enrolled on the study (combining cohorts).

Patient Population

Patients must have been eligible for screening (S1400 or LUNGMAP) and must have been assigned to the S1900A sub-study based on biomarker eligibility defined as LOH high and/or deleterious BRCA1/2 mutation. Patients must have progressed following the most recent line of therapy. Patients must have measurable disease by CT or MRI. Patients must not have leptomeningeal disease, spinal cord compression, or brain metastases unless they meet the criteria in the protocol. Patients must not have EGFR sensitizing mutations, EGFR T790M mutations, ALK gene fusions, ROS1 gene rearrangements, or BRAF V600E mutations unless they have progressed following all standard of care targeted therapy.

Patients must not have had prior treatment with any PARP inhibitor. Patients must not have received any prior systemic therapy within 21 days prior to sub-study registration and must have recovered (≤ Grade 1) from any side effects of prior therapy. Patients must not have received any radiation therapy or had a major surgery within 14 days prior to sub-study

registration. Patients must have fully recovered from the effects of prior surgery. Patients must not be planning to receive any concurrent therapy for cancer while receiving treatment on this study.

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 with a known history of HIV seropositivity must have undetectable viral load, an adequate CD4 count, must not require prophylaxis for any opportunistic infections, and must not be newly diagnosed within 12 months prior to sub-study registration. Patients must be able to take oral medications.

Patients must agree to have blood specimens submitted for circulating tumor DNA. Patients must be offered participation in banking and in the correlative studies for collection and future use of specimens.

Stratification/Descriptive Factors

Patients will be stratified into two cohorts based on their histology.

Cohort 1:
Squamous: Patients with squamous cell lung cancer.

Cohort 2:
Non-squamous: Patients with non-squamous cell lung cancer (adenocarcinoma, large cell, NSCLC NOS, mixed histology with any non-squamous component).

Accrual Goals

The accrual goal is 44 patients per cohort to achieve 40 eligible patients per cohort. An interim analysis will take place when 20 patients are evaluable for response.

Summary Statement

As of December 31, 2019, 19 S1400 patients and 61 LUNGMAP patients have been assigned to S1900A. Thirty-nine patients have been enrolled, 31 of which are from LUNGMAP.

Of the 41 who have not registered, 11 patients had symptomatic deterioration, seven patients were not eligible, five patients passed away, five patients refused, one patient preferred to receive investigational therapy outside of the study, and one patient was ineligible for the screening study. The remaining 11 patients have not yet submitted the Notice of Intention Not to Register.

Of the 39 registered patients, three are ineligible due to lab values outside protocol acceptable range and one is ineligible due to receiving chemotherapy within 21 days prior to registration. Additionally, one patient is not analyzable due to algorithmic changes in FMI's process for evaluating LOH biomarker. Thus, these five will not be included in any analysis.

One patient who went off treatment listed as “Other – not protocol specified” in the table below was due to the site losing contact with the patient.

Thirty-three patients have been assessed for adverse events. There have been no Grade 5 treatment-related adverse events. There has been one patient in the squamous cohort who experienced treatment-related Grade 4 platelet count reduction. There have been two patients in the non-squamous or mixed histology cohort who experienced treatment-related Grade 4 adverse events due to: neutrophil count reduction (1) and platelet count reduction (1).

Registration by Institution

Registrations ending December 31, 2019

Institutions	Total Reg	Institutions	Total Reg
Heartland NCORP	5	Columbia MU-NCORP	1
Columbus NCORP	3	CORA NCORP	1
Baptist MU-NCORP	2	CRC West MI NCORP	1
Davis, U of CA	2	MAVERIC	1
Georgia NCORP	2	New Mexico MU-NCORP	1
Henry Ford Hospital	2	Rochester, Univ of	1
Kansas MU-NCORP	2	ALLIANCE	3
Michigan CRC NCORP	2	NRG	3
Southeast COR NCORP	2	ECOG-ACRIN	2
Wisconsin NCORP	2	**Total (20 Institutions)**	**39**
Arnot Ogden Med Ctr/Rochester, Univ of	1		

Registration, Eligibility, and Evaluability

Classified by Histology

Registrations ending December 31, 2019; Data as of February 6, 2020

	TOTAL	Squamous	Non-squamous or mixed histology
NUMBER REGISTERED	39	16	23
INELIGIBLE	4	1	3
ELIGIBLE	35	15	20
Analyzable, Pend. Elig.	1	1	0
Not Analyzable	1	1	0
RESPONSE ASSESSMENT			
Determinable	26	11	15
Not Determinable	1	1	0
Too Early	7	2	5
ADVERSE EVENT ASSESSMENT			
Evaluable	33	13	20
Too Early	1	1	0

Patient Characteristics

Classified by Histology

Registrations ending December 31, 2019; Data as of February 6, 2020

	Squamous (n=14)		Non-squamous or mixed histology (n=20)	
AGE				
Median	60.9		63.8	
Minimum	50.4		54.0	
Maximum	83.6		77.5	
SEX				
Males	7	50%	10	50%
Females	7	50%	10	50%
HISPANIC				
No	14	100%	19	95%
Unknown	0	0%	1	5%
RACE				
White	13	93%	17	85%
Black	1	7%	2	10%
Unknown	0	0%	1	5%
PRIOR LINES OF TREATMENT FOR STAGE IV DISEASE				
1	3	21%	8	40%
2	8	57%	7	35%
3	2	14%	3	15%
4	1	7%	1	5%
6	0	0%	1	5%
PERFORMANCE STATUS				
0	2	14%	6	30%
1	12	86%	14	70%
WEIGHT LOSS PAST 6 MONTHS				
< 5%	8	57%	15	75%
5 - < 10%	4	29%	3	15%
10 - < 20%	2	14%	2	10%

Biomarker Data

Classified by Histology

Registrations ending December 31, 2019; Data as of February 6, 2020

	Squamous (n=14)	Non-squamous or mixed histology (n=20)
BIOMARKER		
LOH	10	17
BRCA1	0	3
BRCA2	5	2

Treatment Summary

Classified by Histology

Registrations ending December 31, 2019; Data as of February 6, 2020

	TOTAL	Squamous	Non-squamous or mixed histology
NUMBER ON PROTOCOL TREATMENT	12	6	6
NUMBER OFF PROTOCOL TREATMENT	22	8	14
REASON OFF TREATMENT			
Treatment completed as planned	0	0	0
Adverse Event or side effects	4	0	4
Refusal unrelated to adverse event	1	0	1
Progression/relapse	15	6	9
Death	1	1	0
Other - not protocol specified	1	1	0
Reason under review	0	0	0
MAJOR PROTOCOL DEVIATIONS	0	0	0
LOST TO FOLLOW-UP	0	0	0
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	1	0	1

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

Classified by Histology

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2019; Data as of February 6, 2020

	Squamous (n=13) Grade						Non-squamous or mixed histology (n=20) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	10	2	0	1	0	0	17	1	1	1	0	0
AST increased	8	4	1	0	0	0	16	1	2	1	0	0
Alkaline phosphatase increased	10	2	0	1	0	0	18	2	0	0	0	0
Anemia	6	1	2	4	0	0	12	4	2	2	0	0
Anorexia	12	1	0	0	0	0	17	2	1	0	0	0
Blood bilirubin increased	11	2	0	0	0	0	19	1	0	0	0	0
Cheilitis	13	0	0	0	0	0	19	0	1	0	0	0
Cholesterol high	10	2	1	0	0	0	19	1	0	0	0	0
Chronic kidney disease	12	0	0	1	0	0	20	0	0	0	0	0
Confusion	13	0	0	0	0	0	19	0	1	0	0	0
Constipation	9	3	1	0	0	0	20	0	0	0	0	0
Cough	13	0	0	0	0	0	18	1	1	0	0	0
Creatinine increased	10	1	2	0	0	0	17	3	0	0	0	0
Dehydration	12	0	1	0	0	0	20	0	0	0	0	0
Diarrhea	12	1	0	0	0	0	16	4	0	0	0	0
Dizziness	13	0	0	0	0	0	19	0	1	0	0	0
Dysarthria	13	0	0	0	0	0	19	1	0	0	0	0
Dysesthesia	12	1	0	0	0	0	20	0	0	0	0	0
Dysgeusia	10	1	2	0	0	0	15	4	1	0	0	0
Dyspepsia	12	1	0	0	0	0	19	0	1	0	0	0
Dyspnea	11	1	1	0	0	0	18	2	0	0	0	0
Fatigue	8	3	2	0	0	0	9	5	5	1	0	0
Generalized muscle weakness	12	1	0	0	0	0	20	0	0	0	0	0
Hand-Foot syndrome	12	0	1	0	0	0	20	0	0	0	0	0
Headache	13	0	0	0	0	0	19	0	1	0	0	0
Hyperglycemia	13	0	0	0	0	0	19	1	0	0	0	0
Hyperhidrosis	13	0	0	0	0	0	19	0	1	0	0	0
Hypertension	13	0	0	0	0	0	18	0	2	0	0	0
Hypoalbuminemia	12	1	0	0	0	0	19	0	1	0	0	0
Hypokalemia	12	0	0	1	0	0	19	1	0	0	0	0
Hyponatremia	13	0	0	0	0	0	18	2	0	0	0	0
Lethargy	13	0	0	0	0	0	19	0	1	0	0	0
Lymphocyte count decreased	10	1	1	1	0	0	18	0	2	0	0	0
Mucositis oral	11	2	0	0	0	0	20	0	0	0	0	0
Myalgia	12	1	0	0	0	0	20	0	0	0	0	0
Nausea	8	5	0	0	0	0	10	5	5	0	0	0
Neutrophil count decreased	12	1	0	0	0	0	17	1	1	0	1	0
Pain in extremity	13	0	0	0	0	0	19	0	1	0	0	0
Photosensitivity	12	1	0	0	0	0	20	0	0	0	0	0
Platelet count decreased	8	2	1	1	1	0	17	2	0	0	1	0
Sore throat	13	0	0	0	0	0	19	0	1	0	0	0
Thromboembolic event	12	0	1	0	0	0	20	0	0	0	0	0
Vomiting	12	1	0	0	0	0	17	3	0	0	0	0
Weight loss	13	0	0	0	0	0	19	1	0	0	0	0
White blood cell decreased	11	0	2	0	0	0	18	0	0	2	0	0
MAX. GRADE ANY ADVERSE EVENT	2	2	2	6	1	0	3	2	11	2	2	0

S1900B Phase II – FDA Registration Trial

Coordinating Group: SWOG

A Phase II Study of LOXO-292 in Patients with RET Fusion-Positive Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Sub-Study)

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

Date Activated:
02/10/2020

Study Chairs:
Y Elamin, J Gray

Statisticians:
M Redman, K Minichiello

Project Manager:
A Lee

Data Coordinators:
L Highleyman, L Everhart

Objectives

To evaluate the objective response rate (confirmed complete or partial response) by blinded independent centralized review (BICR) associated with LOXO-292 in patients with previously-treated Stage IV or recurrent RET fusion-positive non-small cell lung cancer (NSCLC).

To evaluate the duration of BICR-assessed response among BICR responders.

To evaluate the frequency and severity of toxicities.

To evaluate the investigator-assessed objective response rate (confirmed complete or partial response).

To evaluate duration of investigator-assessed response among patients with a response as determined by the local investigator.

To evaluate investigator-assessed progression-free survival (IA-PFS).

To evaluate BICR-assessed PFS.

To evaluate overall survival.

Among patients with brain metastases at baseline:

To evaluate the central nervous system (CNS) response rate (confirmed CR).

To evaluate the duration of intracranial response among patients with a CNS response.

Patient Population

Patients must have been eligible for the screening study (LUNGMAP) and must have been assigned to the S1900B sub-study based on biomarker eligibility defined as RET fusion-positive NSCLC. Testing for RET fusion done outside of LUNGMAP may be used as described in the protocol. Patients must be negative for all validated oncogenic drivers that could cause resistance to LOXO-292, including EGFR sensitizing mutations, EGFR T790M mutations, ALK gene fusions, ROS1 gene fusions, KRAS activating mutations, BRAF V600E mutations, and MET exon 14 skipping mutations or high-level amplifications and expressions. Patients must have progressed following the most recent line of therapy. Patients

must have measurable disease by CT or MRI and 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 they meet the criteria in the protocol.

Patients must not have had prior treatment with selective anti-RET inhibitors. For patients whose prior therapy was for Stage IV or recurrent disease, the patient must have received at least one line of a platinum-based chemotherapy regimen. For patients whose prior systemic therapy was for Stage I-III disease only, disease progression on platinum-based chemotherapy must have occurred within one year from the last date that the patient received that therapy. Prior anti-PD-1/PD-L1 therapy, alone or in combination, is allowed. Patients must not have received any prior systemic therapy within 14 days prior to sub-study registration and must have recovered from any side effects of prior therapy. Patients must not have received any radiation therapy or had a major surgery within 14 days prior to sub-study registration. Patients must have fully recovered from the effects of prior surgery. Patients must not be planning to receive any concurrent therapy for cancer while receiving treatment on this study. Patients must not be planning to receive any strong inhibitors or inducers of CYP3A4 at least 14 days prior to sub-study registration and throughout protocol treatment. Patients must not be planning to use proton pump inhibitors at least one week prior to sub-study registration and throughout protocol treatment.

Patients must have a Zubrod performance status of 0-1, adequate hematologic, hepatic, cardiac, renal, and gastrointestinal function, and be able to swallow capsules. Patients must not have any clinically significant uncontrolled systemic illness. Patients with hepatitis B or C, or HIV may be eligible provided they meet the criteria in the protocol.

Patients must agree to have blood specimens submitted for circulating tumor DNA. Patients must be offered participation in banking and in correlative studies for collection and future use of specimens.

Accrual Goals

The accrual goal is 124 patients to achieve 100 eligible and evaluable patients in the primary analysis population and 112 in the safety analysis population defined as all eligible patients who receive at least one dose of study drug.

S1900C Phase II – FDA Registration Trial

Coordinating Group: SWOG

A Phase II Study of Talazoparib Plus Avelumab in Patients with Stage IV or Recurrent Non-Squamous Non-Small Cell Lung Cancer Bearing Pathogenic *STK11* Genomic Alterations (Lung-MAP Sub-Study)

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

Date Activated:
01/16/2020

Study Chairs:
F Skoulidis, J Suga

Statisticians:
M Redman, K Minichiello

Project Manager:
A Lee

Data Coordinators:
L Highleyman, L Everhart

Objectives

To evaluate the objective response rate (confirmed and unconfirmed, complete and partial) with talazoparib plus avelumab in patients with Stage IV or recurrent non-squamous non-small cell lung cancer bearing pathogenic ***STK11*** genomic alterations that were previously treated with anti-PD-1/PD-L1 therapy and platinum-based chemotherapy.

To evaluate disease control rate at 12 weeks after registration.

To evaluate investigator assessed progression-free survival.

To evaluate overall survival.

To evaluate duration of response among responders.

To evaluate the frequency and severity of toxicities.

Patient Population

Patients must have been eligible for the screening study (LUNGMAP) and must have been assigned to the S1900C sub-study based on biomarker eligibility defined as ***STK11*** positive. Patients must have histologically or cytologically confirmed Stage IV or recurrent non-squamous, mixed squamous/non-squamous, or non-small cell lung cancer not otherwise specified. Patients must have progressed following the most recent line of therapy. Patients must have measurable disease by CT or MRI and 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 they meet the criteria in the protocol.

Patients must have received at least one line of anti-PD-1 or anti-PD-L1 therapy for Stage III, IV, or recurrent disease. Any number of additional, non-platinum-based chemotherapy or targeted therapy regimens for recurrent or metastatic disease are allowed provided they meet the criteria in the protocol. Patients who received prior adjuvant platinum-based therapy post-surgical resection for Stage I-III disease must have had disease progression

during or after platinum-based chemotherapy that occurred less than 365 days from the last date that the patient received that therapy. Patients must not have had prior treatment with any PARP inhibitor. Patients must not have received any prior systemic immunotherapy or any prior systemic therapy within timeframe in the protocol and must have recovered from any side effects. Patients must not be taking, nor plan to take while on protocol treatment strong P-gp inhibitors, P-gp inducers, or strong breast cancer resistance protein inhibitors. Patients must not have received systemic treatment with corticosteroids or other immunosuppressive medications, any radiation therapy, or had a major surgery within 14 days prior to sub-study registration. Patients must have fully recovered from the effects of prior surgery.

Patients must have a Zubrod performance status of 0-1 and adequate hematologic, hepatic, cardiac, renal, and gastrointestinal function and able to swallow capsules whole. Patients must not have a history of prior organ transplantation. Patients with hepatitis B or C, or HIV may be eligible provided they meet the criteria in the protocol. Patients must not have known prior or suspected hypersensitivity to monoclonal antibodies, or any history of anaphylaxis or uncontrolled asthma. Patients must not have experienced any immune-related adverse event. Patients must not have evidence of active infection requiring systemic therapy. Patients must not have received any live attenuated vaccinations within 28 days prior to sub-study registration.

Patients must agree to have blood specimens submitted for circulating tumor DNA. Patients must be offered participation in banking and in the correlative studies for collection and future use of specimens.

Accrual Goals

The accrual goal is 44 patients to achieve 40 eligible patients. An interim analysis is planned for when 20 patients are evaluable for response.

S1900D Phase II – FDA Registration Trial

Coordinating Group: SWOG

A Randomized Phase II Study of TAK228 (MLN0128, Sapanisertib) Plus Docetaxel Versus Standard of Care in Patients with Previously-Treated *NFE2L2* or *KEAP1*-Positive Stage IV or Recurrent Squamous Cell Lung Cancer (ECOG-ACRIN Lung-MAP Sub-Study)

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

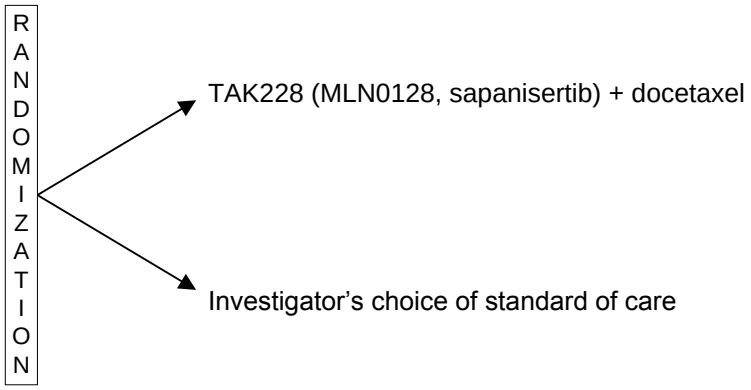
Study Chairs:
P Paik (ECOG-ACRIN), M Edelman (ECOG-ACRIN)

Statisticians:
M Redman, K Minichiello

Project Manager:
A Lee

Data Coordinators:
L Highleyman, L Everhart

SCHEMA



Objectives

To compare the investigator-assessed progression-free survival (IA-PFS) between patients with *NFE2L2* or *KEAP1*-positive Stage IV or recurrent squamous cell lung cancer randomized to TAK228 (MLN0128, sapanisertib) + docetaxel versus standard of care therapy.

To compare overall response rate by RECIST 1.1 between the treatment arms.

To compare overall survival (OS) between the treatment arms.

To evaluate duration of response among responders within each treatment arm.

To evaluate and compare the frequency and severity of toxicities associated within each treatment arm.

To evaluate outcomes of IA-PFS, OS, and response in the subsets of patients eligible based on the presence of *NFE2L2* versus *KEAP1* alterations.

Patient Population

Patients must have been eligible for screening (S1400 or LUNGMAP) and must have been assigned to the S1900D sub-study based on biomarker eligibility defined as a *NFE2L2* mutation or *KEAP1* alteration. Patients must have a histologically or cytologically confirmed Stage IV or recurrent pure squamous cell lung cancer. Patients must have progressed following the most recent line of therapy. Patients must have measurable disease by CT or MRI and 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 they meet the criteria in the protocol. Patients must not have EGFR sensitizing mutations, EGFR T790M mutations, ALK gene fusions, ROS1 gene rearrangements, or BRAF V600E mutations unless they have progressed following all standard of care targeted therapy.

Patients must not have received any radiation therapy or had a major surgery within 14 days prior to sub-study randomization. Patients must have recovered from the effects of prior therapy and surgery. Patients must not have previously received treatment with PI3K, AKT, PI3K/mTOR inhibitors, TORC1/2 inhibitors or TORC1 inhibitors. Patients must not be planning to receive any concurrent therapy for cancer while receiving treatment on this study.

Patients must have a Zubrod performance status of 0-1, adequate hematologic, hepatic, cardiac, renal, and gastrointestinal function, and be able to swallow oral medications. Patients must be able to safely receive at least one of the investigator's choice of standard of care regimens. Patients with hepatitis B or C, or HIV may be eligible provided they meet the criteria in the protocol. Patients must not have any uncontrolled illnesses, including diabetes, or have received any live attenuated vaccinations within 28 days prior to sub-study randomization.

Patients must agree to have blood specimens submitted for circulating tumor DNA. Patients must be offered participation in banking and in the correlative studies for collection and future use of specimens.

Stratification/Descriptive Factors

Randomization will be stratified according to the following factors: (1) prior taxane treatment: yes vs no; (2) planned choice of standard of care: docetaxel alone vs docetaxel + ramucirumab; and (3) presence of *NFE2L2*: yes vs no.

Accrual Goals

The accrual goal is 94 patients to achieve 84 eligible patients. An interim analysis is planned for when 50% IA-PFS events have been reported.

S1415CD Phase III

Coordinating Group: SWOG

Pragmatic Trial to Evaluate a Guideline-Based Colony Stimulating Factor Standing Order Intervention and to Determine the Effectiveness of Colony Stimulating Factor Use as Prophylaxis for Patients Receiving Chemotherapy with Intermediate Risk for Febrile Neutropenia – Trial Assessing CSF Prescribing Effectiveness and Risk (TrACER)

Participants:
SWOG, CTSU

Date Activated:
09/01/2016

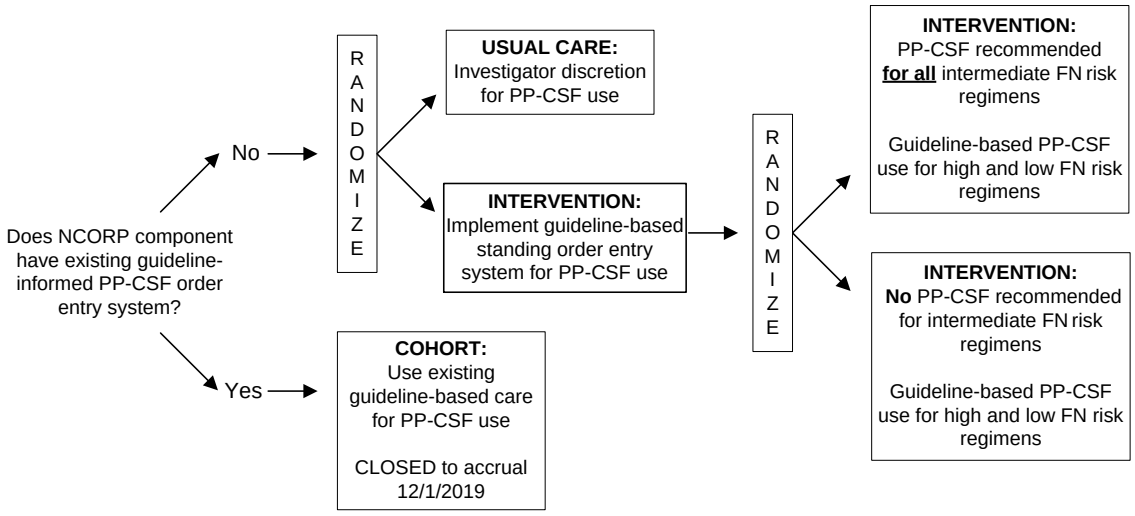
Study Chairs:
S Ramsey, D Hershman

Statisticians:
A Bansal, W Barlow, K Arnold

Project Manager:
K Watabayashi

Data Coordinator:
K Carvalho

SCHEMA



Randomization is at the NCORP component level. All patients at participating components will be subject to the PP-CSF use care as determined by component assignment (Usual Care, Intervention, or Cohort). Only consented patients registered to the study will participate in the data collection.

Objectives

To compare the use of primary prophylactic colony stimulating factor (PP-CSF) according to recommended clinical practice guidelines among patients registered at Intervention components versus Usual Care components.

To compare the rate of febrile neutropenia (FN) among patients registered at Intervention components versus Usual Care components.

To compare the rate of FN among intermediate risk patients registered at Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare the rate of FN among low-risk patients registered at Intervention components versus Usual Care components.

To compare the FN-related health-related quality of life (HRQL) among low-risk patients registered at Intervention components versus Usual Care components.

To compare patient adherence to PP-CSF prescribing among patients registered at Intervention components versus Usual Care components.

To compare patient knowledge of the indications for, efficacy of, and side effects associated with PP-CSF between the initiation and conclusion of the first cycle of myelosuppressive systemic therapy among patients registered at Intervention components versus Usual Care components.

To compare the proportion of patients completing the initial systemic therapy regimen at planned duration and at planned dose intensity among patients registered at Intervention components versus Usual Care components.

To compare antibiotic use both as prophylaxis and as treatment for FN among patients registered at Intervention components versus Usual Care components.

To compare the rate of FN-related emergency department visits and hospitalizations among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare the FN-related health-related quality of life (HRQL) among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

To compare overall survival among intermediate risk patients registered to Intervention components by component treatment assignment (administer PP-CSF to intermediate risk patients versus not).

Patient Population

Patients must have a current diagnosis of breast cancer, non-small cell lung cancer, or colorectal cancer. Cancer may be metastatic or non-metastatic.

Patients must be planning to receive one of the study-allowed regimens as their initial treatment for their current cancer diagnosis. Patients must be registered prior to or on the same day as their first cycle of chemotherapy. Patient must not have had any systemic therapy (chemotherapy or combination regimens) in the 180 days just prior to registration. Prior biologic therapy, immunotherapy, tyrosine kinase inhibitors, and hormonal therapy are allowed. Patients must not be receiving or planning to receive concurrent radiation therapy during systemic treatment. Patients must not have any known contraindication to CSFs, including prior hypersensitivity to *E. coli*-derived proteins, filgrastim, pegfilgrastim, or tbo-filgrastim.

Patients must be able to understand and provide information for the patient-completed study forms in either English or Spanish. Patients may have had a prior malignancy. Patients must not be participating or plan to participate in other clinical trials that involve investigational systemic cancer treatments or investigational uses of CSF during their first six months after registration.

Stratification/Descriptive Factors

NCORP components eligible for randomization will be randomly assigned to Usual Care or Intervention with stratification by component size (number of patients at that component) and type of NCORP component (minority/underserved vs not).

Accrual Goals

A total of 3,960 patients will be accrued to achieve 3,600 eligible patients. The Intervention components will accrue 2,376 patients, the Usual Care components will accrue 792 patients and the Cohort components will accrue 792 patients.

One interim analysis will be conducted when 360 patients in the intermediate risk group at Intervention components have complete outcome information. A second interim analysis will be conducted when 650 patients in the intermediate risk group at Intervention components have complete outcome information. Complete outcome is defined as an assessment of FN after six months of follow-up after treatment commences.

Summary Statement

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

S1609 Phase II

Coordinating Group: SWOG

DART: Dual Anti-CTLA-4 and Anti-PD-1 Blockade in Rare Tumors

Participants:
SWOG, CTSU

Date Activated:
01/13/2017

Study Chairs:
S Patel, Y Chae

Statisticians:
M Othus, M Plets, E Mayerson

Data Coordinators:
C Magner, S Gurung

Objectives

To evaluate the RECIST 1.1 overall response rate (ORR) in subsets of patients with advanced rare cancers treated with ipilimumab plus nivolumab combination immunotherapy.

To evaluate the overall response rate (ORR) in patients with gestational trophoblastic tumors treated with ipilimumab plus nivolumab combination immunotherapy.

To evaluate the RECIST 1.1 overall response rate (ORR) in patients PD-L1 amplified cancers treated with nivolumab immunotherapy.

To evaluate toxicities in each cohort.

To estimate overall survival (OS), progression-free survival (PFS), clinical benefit rate; and to estimate immune-related ORR (irORR), and immune-related PFS (irPFS) by unidimensional immune-related response criteria.

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

Patient Population

Patients must have histologically confirmed rare cancer and/or cancer of unknown primary specified on the list of eligible rare cancer histologic cohorts in the S1609 protocol or with PD-L1 amplification only. As of September 11, 2017, patients are no longer required to have been enrolled in EAY131 (NCI-MATCH) to be eligible for this study.

Patients must have measurable disease and have progressed following at least one line of standard systemic therapy and there must not be other approved/standard therapy available that has been shown to prolong overall survival. Patients are also eligible if no standard treatment exists that has been shown to prolong overall survival. Patients in one of the histologically defined rare cancer cohorts may have received either prior anti-CTLA-4 or other prior anti-PD-1/anti-PD-L1 therapy, but not both, provided that it is completed at least 4 weeks prior to registration. Patients in the PD-L1 amplification cohort must not have received anti-PD-1/anti-PD-L1 therapy; prior anti-CTLA-4 is allowed provided that it is completed at least 4 weeks prior to registration. Patients who had a prior immune-related adverse event with prior immunotherapy are not eligible. Patients with brain metastases or primary brain tumors must have completed treatment, surgery or radiation therapy at least 28 days prior to registration and have stable disease at time of registration. Patients with metastatic brain parenchymal disease must have been treated and off steroids for seven days prior to registration. Patients must have been off all other systemic anti-cancer therapy at least seven

days prior to registration and any therapy-induced toxicity must have recovered to Grade 1 or less.

Patients must have a Zubrod performance status of 0-2 and have adequate hematologic, hepatic, renal, thyroid, and adrenal axis function. Patients must not have active autoimmune disease that has required systemic treatment in the past two years or any uncontrolled intercurrent illness. Patients must not have known active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection at time of registration. Patients with HBV or HCV that have an undetectable viral load, or in the opinion of the treating investigator is well controlled, are eligible. Patients who are known to be HIV-positive at registration are eligible if they meet the conditions outlined in the protocol.

Stratification/Descriptive Factors

Patients will be described by histologic cohorts, with the exception of PD-L1 amplification patients.

Accrual Goals

The maximum accrual for this study is 818 patients. A two-stage design will be used for all cohorts, with the exception of the "Not Otherwise Categorized" (NOC) and "Cancer of Unknown Primary" (CuP) cohorts. Initially, six eligible patients will be registered to each histologic cohort. If at least one response is observed within a cohort, an additional 10 eligible patients will be registered to that cohort. Up to 16 eligible patients will be registered to the CuP cohort with no formal first stage response assessment. Up to 60 eligible patients will be enrolled to the NOC cohort, and data may be used to open additional cohorts.

Summary Statement

For the current status of this study, please refer to the Early Therapeutics and Rare Cancers chapter.

S1614 Phase III

Coordinating Group: SWOG

A Phase III Randomized Trial of Prophylactic Antiviral Therapy in Patients with Current or Past Hepatitis B Virus (HBV) Infection Receiving Anti-Cancer Therapy for Solid Tumors

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

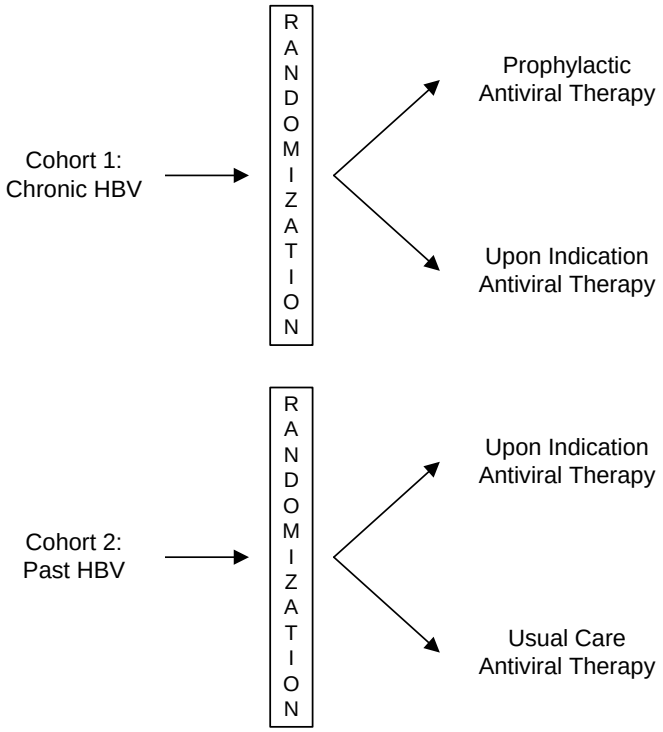
Date Activated:
02/21/2019

Study Chairs:
J Hwang, A Lok, E Mitchell (ECOG-ACRIN)

Statisticians:
J Unger, E Mayerson

Data Coordinators:
S Dzingle, R Topacio

SCHEMA



Objectives
Co-primary objectives:

To compare the effect of prophylactic tenofovir alafenamide (TAF) therapy versus upon indication TAF therapy on time-to-adverse liver outcomes of liver failure or liver-related death in patients with chronic HBV infection (HBsAg+ and anti-HBc+) receiving anti-cancer therapy for solid tumors.

To compare the effect of upon indication TAF therapy versus usual care on time-to-adverse liver outcomes of liver failure or liver-related death in patients with past HBV infection (HBsAg- and anti-HBc+) receiving anti-cancer therapy for solid tumors.

Secondary objectives:

Using time-to-event analysis, to compare the effect of TAF therapy versus upon indication TAF therapy on HBV reactivation, on the combined endpoint of adverse liver outcomes (liver failure or liver-related death) and HBV reactivation, and on HBV flare by arm in patients with chronic HBV infection receiving anti-cancer therapy for solid tumors.

Using time-to-event analysis, to compare the effect of upon indication TAF therapy versus usual care on HBV reactivation, on the combined endpoint of adverse liver outcomes (liver failure or liver-related death) and HBV reactivation, and on HBV flare by arm in patients with past HBV infection receiving anti-cancer therapy for solid tumors.

Patient Population
Patients must be diagnosed with Stage I-III solid tumor malignancy not involving the liver. Patients must have HBV infection as indicated through positive HBsAG or anti-HBc tests. Patients must not have lymphoma, leukemia, or myeloma. Patients must not have primary liver cancer or evidence of any malignancy that involves the liver.

Patients must be planning to receive a new regimen of systemic anti-cancer therapy for their solid tumor malignancy and must have discontinued all previous therapies. Patients must not have received anti-CD20 cancer therapy regimens nor had a hematopoietic stem cell transplant. Patients must have discontinued any antiviral medications active against HBV at least 90 days prior to registration, and discontinue any contraindicated medications as identified in the protocol at time of registration.

Patients must have a Zubrod performance status of 0-2, and have adequate liver, renal, and coagulation function. Patients must not have known cirrhosis, known hepatitis-C infection, or history of human immunodeficiency infection proven by an HIV test within the past 365 days. Patients must have complete results for HBsAg, anti-HBc, anti-HBs, and HBV DNA lab tests as specified in the protocol. Patients must be able to take oral medications.

Patients must be willing to submit specimens for ongoing testing of HBV reactivation. Patients must be offered the opportunity to participate in the translational medicine studies.

Stratification/Descriptive Factors
Patients with chronic HBV infection will be randomized within Cohort 1, with randomization balanced by planned cancer therapy type: any cytotoxic therapy vs immunotherapy alone vs targeted therapy alone vs immunotherapy and targeted therapy.

Patients with past HBV infection will be randomized within Cohort 2 with randomization balanced by the following factors: (1) planned cancer therapy type: any cytotoxic therapy vs immunotherapy alone vs targeted therapy alone vs immunotherapy and targeted therapy; and (2) anti-HBs status: positive vs negative.

Accrual Goals
The accrual goal for this study is 444 patients, 222 patients per cohort to achieve 200 eligible patients per cohort. A single formal interim analysis for efficacy for each cohort will be conducted when one half of patients have reached one year of follow-up.

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

S1619 Pilot

Coordinating Group: SWOG

A Feasibility Trial of Neoadjuvant Cisplatin-Pemetrexed with Atezolizumab in Combination and in Maintenance for Resectable Malignant Pleural Mesothelioma

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Participants:
SWOG, CTSU

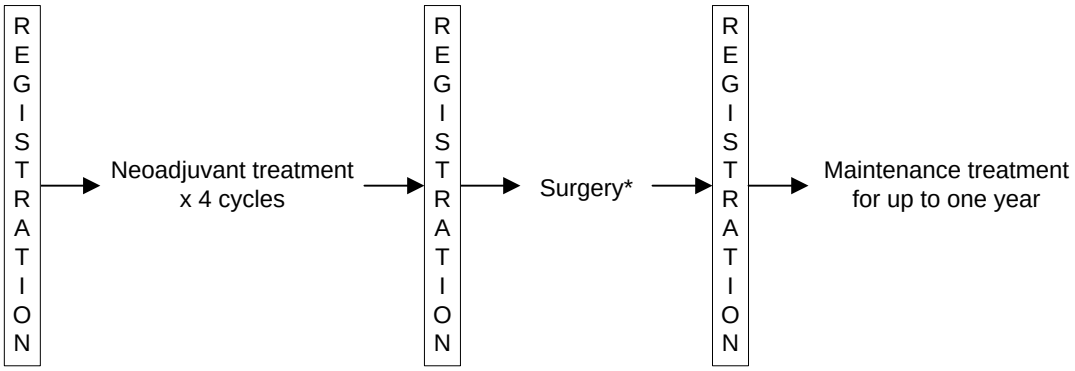
Date Activated:
11/03/2017

Study Chairs:
A Tsao, J Cetnar, B Sepesi, D Gomez

Statisticians:
L Qian, M Redman

Data Coordinator:
J Harris

SCHEMA



*Patients will undergo either extrapleural pneumonectomy (EPP) and optional radiation therapy or pleurectomy/decortication (P/D). The type of surgery performed is determined by the treating investigator.

Objectives

To evaluate if the regimen of neoadjuvant cisplatin-pemetrexed-atezolizumab, surgery +/- radiation, then maintenance atezolizumab is feasible and safe (as defined in Section 11.1) for patients with resectable malignant pleural mesothelioma.

To evaluate progression free survival (both by RECIST 1.1 and also using a Modified RECIST for Pleural Tumors) in patients with resectable malignant pleural mesothelioma treated with a regimen of neoadjuvant cisplatin-pemetrexed-atezolizumab, surgery +/- radiation, followed by one year of maintenance atezolizumab.

To evaluate overall survival in patients with resectable malignant pleural mesothelioma treated with a regimen of neoadjuvant cisplatin-pemetrexed-atezolizumab, surgery +/- radiation, followed by one year of maintenance atezolizumab.

To evaluate response rate (confirmed and unconfirmed, complete and partial, both by RECIST 1.1 and also using a Modified RECIST for Pleural Tumors) in the subset of this patient population with measurable disease.

Patient Population

Patients must have non-measurable or measurable Stage I-III malignant pleural mesothelioma that is deemed resectable and must be planning to undergo pleurectomy decortication (P/D) or extrapleural pneumonectomy (EPP). Patients must have epithelioid or biphasic histology (sarcomatoid histology is excluded). Patients must have undergone extended surgical staging including mediastinoscopy or endobronchial ultrasound. Patients must undergo video-assisted thoracoscopic surgery and diagnostic laparoscopy.

Patients must not have had prior immunotherapy or chemotherapy for malignant pleural mesothelioma. Patients must not have had any major surgery, radiation, anticancer therapy, or investigational agent within 28 days prior to registration. Patients must not have undergone prior allogeneic bone marrow transplantation or prior solid organ transplantation.

Patients must have a Zubrod performance status 0-1 and adequate hematologic, renal, hepatic, and hearing function. Patients must not have a history of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins. Patients must not have a known hypersensitivity or allergy to biopharmaceuticals produced in Chinese hamster ovary cells or any component of the atezolizumab formulation. Patients must not have severe infections, active tuberculosis or active autoimmune disease that has required systemic treatment in the past two years. Patients must not have a history of idiopathic pulmonary fibrosis, pneumonitis, organizing pneumonia, or evidence of active pneumonitis. Patients must not have active hepatitis B, hepatitis C, or a known positive test for HIV. Patients must not have significant cardiovascular disease. Patients must not receive live, attenuated influenza vaccine within four weeks prior to registration or plan to at any time during the study.

Additional clinical and laboratory requirements must be met prior to surgery and maintenance therapy.

Stratification/Descriptive Factors

Patients will be placed into defined cohorts by the planned type of surgery: extrapleural pneumonectomy (EPP) vs pleurectomy/decortication (P/D).

Accrual Goals

Enrollment will proceed independently in two separate cohorts. In each cohort, the accrual goal is 14 patients to achieve 12 eligible patients.

Summary Statement

As of December 31, 2019, 25 patients have registered, 21 in the pleurectomy/decortication (P/D) cohort and four in the extrapleural pneumonectomy (EPP) cohort. Of the 25 registered patients, 2 patients were ineligible for the following reasons: registering after receiving protocol treatment (1), and no hepatitis testing performed and surgical consultation outside the required time window (1). Twenty-three patients have been assessed for adverse events related to neoadjuvant therapy. One patient died of treatment-related sepsis.

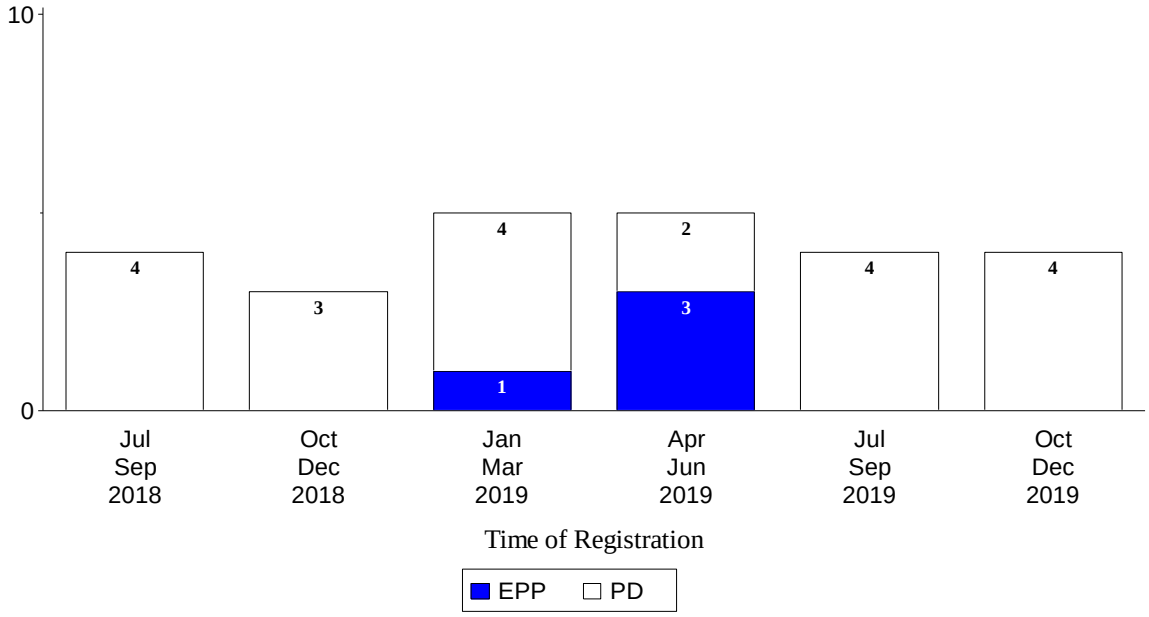
Thirteen patients have registered to the surgery treatment. One patient was ineligible due to no pulmonary function test done before surgery. Eleven patients have received P/D and one patient has received EPP. Ten patients have been assessed for adverse events related to surgery. No treatment-related adverse events greater than Grade 3 have been reported.

Eleven patients have registered to receive maintenance treatment. One patient enrolled on maintenance treatment is ineligible due to inadequate hematologic function. Nine patients have been assessed for adverse events related to maintenance therapy. No treatment-related adverse events greater than Grade 3 have been reported.

Please note prior to receiving surgery and maintenance treatment, patients must be registered in OPEN.

Initial Registrations by 3 Month Intervals

Divisions by Planned Type of Surgery
Initial Registration



Registration by Institution

Initial Registration
Registrations ending December 31, 2019

Institutions	Total Reg
MD Anderson CC	12
MUSC MU-NCORP	5
Fred Hutchinson CRC	2
City of Hope Med Ctr	1
ECOG-ACRIN	3
ALLIANCE	1
NRG	1
Total (7 Institutions)	**25**

Registration, Eligibility, and Evaluability

Initial Registration

Registrations ending December 31, 2019; Data as of February 26, 2020

	Chemotherapy + Atezolizumab
NUMBER REGISTERED	25
INELIGIBLE	2
ELIGIBLE	23
BASELINE DISEASE STATUS by RECIST 1.1	
Measurable	13
Non Measurable	10
RESPONSE ASSESSMENT by RECIST 1.1	
Determinable	12
Not Determinable	1
Not Applicable	10
BASELINE DISEASE STATUS by Modified RECIST	
Measurable	17
Non Measurable	6
RESPONSE ASSESSMENT by Modified RECIST	
Determinable	17
Not Applicable	6
ADVERSE EVENT ASSESSMENT	
Evaluable	23

Patient Characteristics

Initial Registration

Registrations ending December 31, 2019; Data as of February 26, 2020

	Chemotherapy + Atezolizumab (n=23)	
AGE		
Median	66.8	
Minimum	49.9	
Maximum	77.3	
SEX		
Males	17	74%
Females	6	26%
HISPANIC		
No	23	100%
RACE		
White	20	87%
Asian	3	13%
SURGERY COHORT		
EPP	3	13%
PD	20	87%
PERFORMANCE STATUS		
0	11	48%
1	11	48%
Data pending	1	4%

	Chemotherapy + Atezolizumab (n=23)	
WEIGHT LOSS PAST 6 MONTHS		
< 5%	18	78%
5 - <10%	3	13%
Data pending	2	9%

Treatment Summary

Initial Registration
Neoadjuvant Treatment
Registrations ending December 31, 2019; Data as of February 26, 2020

	Chemotherapy + Atezolizumab
NUMBER ON PROTOCOL TREATMENT	1
NUMBER OFF PROTOCOL TREATMENT	22
REASON OFF TREATMENT	
Treatment completed as planned	18
Adverse Event or side effects	1
Refusal unrelated to adverse event	0
Progression/relapse	2
Death	1
Other - not protocol specified	0
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0
LOST TO FOLLOW-UP	0
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	0

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

Initial Registration
Neoadjuvant Treatment
Adverse Events Unlikely or Not Related to Treatment Excluded
Registrations ending December 31, 2019; Data as of February 26, 2020

	Chemotherapy + Atezolizumab (n=23) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	21	2	0	0	0	0
AST increased	22	1	0	0	0	0
Acute kidney injury	22	0	0	0	1	0
Anemia	16	4	2	1	0	0
Anorexia	16	5	2	0	0	0
Arthralgia	22	1	0	0	0	0
Blood/lymph disorder-Other	22	1	0	0	0	0
Constipation	19	2	1	1	0	0
Creatinine increased	21	2	0	0	0	0
Diarrhea	22	0	0	1	0	0
Dizziness	22	1	0	0	0	0
Dry skin	22	1	0	0	0	0
Dysgeusia	21	2	0	0	0	0
Fatigue	11	8	4	0	0	0
GERD	21	0	2	0	0	0
Generalized muscle weakness	22	1	0	0	0	0
Hearing impaired	22	0	1	0	0	0
Hiccups	21	1	1	0	0	0
Hypocalcemia	22	1	0	0	0	0
Hypokalemia	22	0	0	1	0	0
Hypomagnesemia	22	1	0	0	0	0
Hyponatremia	18	4	0	1	0	0
Hypotension	22	0	1	0	0	0
Infusion related reaction	21	0	2	0	0	0
Lung infection	22	0	0	1	0	0
Lymphocyte count decreased	20	1	0	2	0	0
Malaise	22	1	0	0	0	0
Myalgia	22	1	0	0	0	0
Nasal congestion	22	1	0	0	0	0
Nausea	8	8	7	0	0	0
Neutrophil count decreased	15	3	4	1	0	0
Paronychia	22	1	0	0	0	0
Peripheral sensory neuropathy	22	1	0	0	0	0
Platelet count decreased	22	1	0	0	0	0
Pneumonitis	22	0	0	1	0	0
Rash acneiform	21	2	0	0	0	0
Rash maculo-papular	21	1	1	0	0	0
Respiratory failure	22	0	0	0	1	0
Sepsis	22	0	0	0	0	1
Sore throat	22	1	0	0	0	0
Tinnitus	22	1	0	0	0	0
Vomiting	20	3	0	0	0	0
White blood cell decreased	18	1	4	0	0	0
MAX. GRADE ANY ADVERSE EVENT	3	2	11	6	0	1

Registration, Eligibility, and Evaluability

Surgery

Registrations ending December 31, 2019; Data as of February 26, 2020

	Surgery
NUMBER REGISTERED	13
INELIGIBLE	1
ELIGIBLE	12
Analyzable, Pend. Elig.	1
ADVERSE EVENT ASSESSMENT	
Evaluable	10
Too Early	2

Treatment Summary

Surgery

All eligible and selected ineligible patients included

Registrations ending December 31, 2019; Data as of February 26, 2020

	Surgery
NUMBER ON PROTOCOL TREATMENT	1
NUMBER OFF PROTOCOL TREATMENT	11
REASON OFF TREATMENT	
Treatment completed as planned	10
Adverse Event or side effects	0
Refusal unrelated to adverse event	0
Progression/relapse	0
Death	1
Other - not protocol specified	0
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0
LOST TO FOLLOW-UP	0
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	0

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

Surgery

Adverse Events Unlikely or Not Related to Treatment Excluded

All Eligible and Selected Ineligible Patients Included

Registrations ending December 31, 2019; Data as of February 26, 2020

	Surgery (n=10) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Anemia	8	1	1	0	0	0
Atrial fibrillation	9	0	1	0	0	0
Dyspnea	9	0	1	0	0	0
Non-cardiac chest pain	9	1	0	0	0	0
Pain	8	1	1	0	0	0
Peripheral sensory neuropathy	9	0	1	0	0	0
Weight loss	9	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	6	1	3	0	0	0

Registration, Eligibility, and Evaluability

Maintenance

Registrations ending December 31, 2019; Data as of February 26, 2020

	Maintenance
NUMBER REGISTERED	11
INELIGIBLE	1
ELIGIBLE	10
ADVERSE EVENT ASSESSMENT	
Evaluable	10

Treatment Summary

Maintenance

All eligible and selected ineligible patients included

Registrations ending December 31, 2019; Data as of February 26, 2020

	Maintenance
NUMBER ON PROTOCOL TREATMENT	6
NUMBER OFF PROTOCOL TREATMENT	3
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	0
Refusal unrelated to adverse event	0
Progression/relapse	3
Death	0
Other - not protocol specified	0
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0
LOST TO FOLLOW-UP	0
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	0

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

Maintenance

Adverse Events Unlikely or Not Related to Treatment Excluded

All Eligible and Selected Ineligible Patients Included

Registrations ending December 31, 2019; Data as of February 26, 2020

	Maintenance (n=9) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Anemia	8	1	0	0	0	0
Constipation	7	2	0	0	0	0
Creatinine increased	8	0	1	0	0	0
Fatigue	6	3	0	0	0	0
Hypothyroidism	8	1	0	0	0	0
Nausea	8	1	0	0	0	0
Rash acneiform	8	1	0	0	0	0
Tinnitus	8	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	4	4	1	0	0	0

S1701 Phase II

Coordinating Group: SWOG

A Randomized Phase II Trial of Carboplatin-Paclitaxel With or Without Ramucirumab in Patients with Unresectable Locally Advanced, Recurrent, or Metastatic Thymic Carcinoma

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

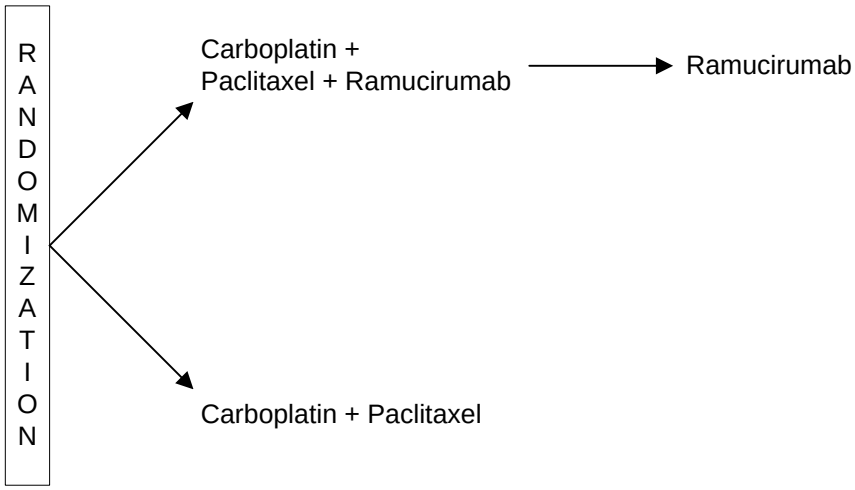
Date Activated:
08/09/2018

Study Chairs:
A Tsao, M Koczywas, M Edelman (ECOG-ACRIN)

Statisticians:
Y Zhao, L Qian

Data Coordinator:
L Kaye

SCHEMA



Objectives

The primary study objective is to compare progression-free survival between patients with incurable unresectable locally advanced, or recurrent, or metastatic thymic carcinoma randomized to carboplatin-paclitaxel with or without ramucirumab.

To evaluate the frequency and severity of toxicity of carboplatin-paclitaxel with or without ramucirumab in this patient population.

To compare the response rate (complete response, partial response, confirmed and unconfirmed) between treatment arms.

To compare disease control rate (complete response, partial response, confirmed or unconfirmed, stable disease) between treatment arms.

To compare overall survival between treatment arms.

Patient Population

Patients must have histologically or cytologically confirmed, unresectable thymic carcinoma as defined in the protocol, that is either locally advanced, recurrent, or metastatic. Patients must not be candidates for localized surgery. Patients must have measurable disease. Patient must not have brain metastases unless (1) metastases have been treated and have remained controlled for at least two weeks following treatment, and (2) patient has no residual neurological dysfunction off corticosteroids for at least one day prior to randomization.

Patients must not have undergone surgery within 28 days prior to randomization or minor surgery/subcutaneous venous access device placement within seven days prior to randomization. Patients must not have had prior systemic anti-cancer therapy for locally advanced or metastatic unresectable thymic carcinoma. Prior adjuvant or neoadjuvant therapy is allowed. Patients must not be candidates for radiation therapy with curative intent.

Patients must have a Zubrod performance status of 0-2 and adequate hematologic, coagulation, hepatic and renal function. Patients must not have experienced any Grade 3 or above GI bleeding, a history of deep vein thrombosis (DVT), pulmonary embolism (PE), or any other significant thromboembolism within 84 days prior to randomization. Patients must not have cirrhosis at a level of Child-Pugh B (or worse), cirrhosis and a history of hepatic encephalopathy, or clinically meaningful ascites resulting from cirrhosis. Patients must not have experienced any arterial thromboembolic events. Patients must not have a history of uncontrolled or poorly-controlled hypertension. Patients must not have experienced hemoptysis within two months prior to randomization or with radiographic evidence of intratumor cavitation or has radiologically documented evidence of major blood vessel invasion or encasement by cancer. Patients must not have a prior history of gastrointestinal perforation/fistula or risk factors for perforation. Patients must not have a serious or nonhealing wound, ulcer, or bone fracture within 28 days prior to randomization. Patients must not be receiving chronic antiplatelet therapy within seven days prior to randomization.

Patients must be offered the opportunity to participate in banking of specimens for future research.

Accrual Goals

The accrual goal is 66 patients to achieve 60 eligible patients. Interim analyses will be performed when 50% of the expected PFS events have been observed.

Summary Statement

The study accrual had been slower than expected due to the difficulty of definitive diagnosis of thymic carcinoma. On January 3, 2020, eligible pathologic cancer types were amended. Thymic carcinoma may be defined as "thymic epithelial malignancy, consistent with thymic carcinoma", or "WHO Type C thymic epithelial tumor", or "thymic epithelial malignancy" with radiographic imaging consistent with thymic carcinoma.

As of December 31, 2019, two patients have enrolled to the study. Both patients have been assessed for adverse events. No treatment-related adverse events greater than Grade 3 have been reported.

Registration by Institution

Registrations ending December 31, 2019

Institutions	Total Reg
City of Hope Med Ctr	1
Davis, U of CA	1
Total (2 Institutions)	**2**

S1714 Observational Cohort

Coordinating Group: SWOG

A Prospective Observational Cohort Study to Develop a Predictive Model of Taxane-Induced Peripheral Neuropathy in Cancer Patients

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Participants:
SWOG, CTSU

Date Activated:
03/01/2019

Study Chairs:
M Trivedi, D Hershman

Statisticians:
J Unger, A Darke

Data Coordinators:
K Carvalho, M Yee

Objectives

To develop and validate a clinical risk prediction model using clinical factors for the development of peripheral neuropathy in patients receiving taxane-based chemotherapy regimens.

To examine patient-reported outcomes (PROs) and objective measures of chemotherapy induced peripheral neuropathy (CIPN) to better define the phenotype of peripheral neuropathy in this patient population.

To assess the incidence of CIPN within one year in this patient population.

To identify predictors of treatment dose reductions, delays, and discontinuations associated with CIPN symptoms in this patient population.

Patient Population

Patients must have Stage I, II, or III primary non-small cell lung, primary breast, or primary ovarian/fallopian tube cancer.

Patients must plan to start treatment with one of the study-approved taxane-based chemotherapy regimens within 14 days after registration, and must not have received a taxane, platinum, vinca alkaloid, or bortezomib-based chemotherapy regimen prior to registration.

Patients may have pre-existing neuropathy.

Patients must be able and willing to complete questionnaires in English or Spanish, agree to submit all required specimens for translational research, and be offered the opportunity to submit additional optional specimens for banking.

Stratification/Descriptive Factors

Patients will be classified by the following factors: (1) primary cancer: lung vs breast vs ovarian/fallopian tube, and (2) planned taxane regimen: paclitaxel vs docetaxel.

Accrual Goals

A total of 1050 patients will be accrued to achieve 1000 eligible patients. When 525 patients have been accrued to the paclitaxel or docetaxel group, that group will be closed to further accrual. When 250 lung cancer patients have been accrued, the lung cancer category will be closed to further accrual.

Summary Statement

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

S1827 Phase III

Coordinating Group: SWOG

A Randomized Phase III Trial of MRI Surveillance with or without Prophylactic Cranial Irradiation (PCI) in Small-Cell Lung Cancer

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Participants:
SWOG, CTSU (Supported by Alliance, NRG)

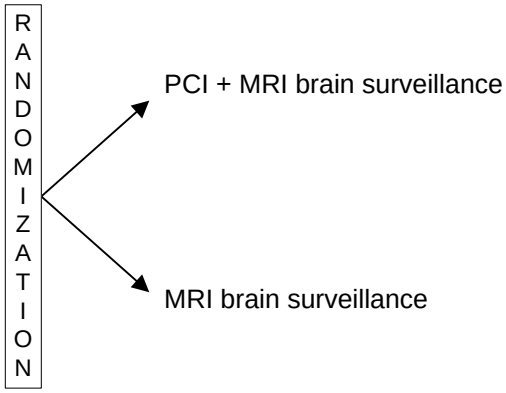
Date Activated:
01/10/2020

Study Chairs:
C Rusthoven, P Brown, J Patel (Alliance), D Gelblum (NRG)

Statisticians:
M Redman, J Miao, L Qian

Data Coordinators:
L Kaye, J Harris

SCHEMA



Objectives

To evaluate whether overall survival (OS) with MRI surveillance alone is not inferior to MRI surveillance combined with prophylactic cranial irradiation (PCI) for the treatment of small-cell lung cancer (SCLC).

To compare cognitive failure-free survival (CFFS) rate up to 12 months after randomization between the arms.

To compare brain metastasis-free survival between the arms.

To compare OS between the arms within the subgroups of patients with limited-stage and extensive-stage disease.

To compare cognitive failure-free survival (CFFS) rates at the assessment times between the arms.

To compare the cumulative incidence of cognitive failure, with death as a competing risk, between the arms.

To compare the frequency and severity of toxicities between the two arms.

Patient Population

Patients must have a histologically confirmed diagnosis of SCLC. Patients must have an MRI of the brain performed within 28 days prior to registration documenting no evidence of brain metastases or leptomeningeal disease. Patients also must not have a history of brain metastases or leptomeningeal disease.

Patients with limited-stage SCLC must have completed platinum-based chemotherapy and either definitive thoracic radiotherapy or definitive surgical resection; thoracic radiation in addition to definitive surgical resection is allowed. Patients with extensive-stage SCLC must have completed platinum-based chemotherapy either with or without thoracic radiotherapy. Immunotherapy concurrent with and/or adjuvant to first-line therapy is allowed. Patients must have had a response to first-line therapy and no evidence of progression in opinion of the treating investigator. No more than 8 weeks may have elapsed between day 1 of the last cycle of chemotherapy and randomization. Patients must not have received prior radiotherapy to the brain or whole brain radiotherapy.

Patients must be at least 18 years of age and have a Zubrod performance status of 0-2 with adequate hepatic, cardiac, respiratory, renal, and hematologic function. Patients must not have a contraindication to MR imaging or gadolinium contrast. Patients must not have any severe active comorbidities. Patients with known HIV positive are eligible provided they meet criteria as described in the protocol.

Patients who speak and understand English or French must agree to participate in cognitive function testing. Patients must be offered the opportunity to have specimens submitted for translational medicine studies.

Stratification/Descriptive Factors

Patients will be randomized between MRI surveillance with or without prophylactic cranial irradiation using a dynamic balancing algorithm. Patients will be stratified on the following factors: (1) stage: limited vs extensive; (2) immune checkpoint inhibitor therapy part of first-line regimen: yes vs no; and (3) Zubrod performance status: 0 or 1 vs 2.

Accrual Goals

The accrual goal is 600 eligible patients. Three interim monitoring are planned at approximately 36, 48 and 60 months.

S1914 Phase III – FDA Registration Trial

Coordinating Groups: SWOG and NRG

A Randomized Phase III Trial of Induction/Consolidation Atezolizumab (NSC #783608) + SBRT Versus SBRT Alone in High-risk, Early Stage NSCLC

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

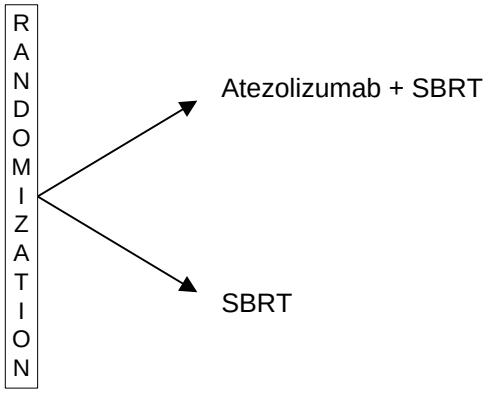
Date Activated:
03/25/2020

Study Chairs:
M Daly, C Simone (NRG), C Steuer (ECOG-ACRIN)

Statisticians:
J Moon, J Miao, M Redman

Data Coordinators:
L Everhart, L Highleyman

SCHEMA



Objectives

To compare overall survival in patients with inoperable, early stage non-small cell lung cancer (NSCLC) randomized to stereotactic body radiation therapy (SBRT) with or without atezolizumab.

To compare investigator-assessed progression-free survival (IA-PFS) between the arms.

To compare PFS by blinded independent centralized review between the arms in a random subset of patients.

To evaluate distant, locoregional, and local failure rates within each treatment arm.

To evaluate the frequency and severity of toxicities within each treatment arm.

Patient Population

Patients must have histologically or cytologically proven Stage I-IIA or limited T3N0M0 NSCLC). Patients may have T3 disease with the exclusion of multifocal tumors and pericardial involvement. Disease must have one or more of the following high-risk features: (1) tumor diameter ≥ 2 cm as assessed by diagnostic CT, (2) tumor $SUV_{max} \geq 6.2$ as assessed by FDG PET/CT, or (3) moderately differentiated, poorly differentiated, or undifferentiated histology. Patients must have adequate pre-registration diagnostic imaging within the timeframe in the protocol. Patients must not have evidence of hilar or mediastinal nodal involvement. Patients must be medically or surgically inoperable according to the protocol.

Patients must not have received any prior treatment for NSCLC or undergone prior radiation to overlapping regions of the chest. Patients must not have received treatment with systemic immunostimulatory or immunosuppressive agents, including corticosteroids, within 14 days prior to randomization.

Patients must have a Zubrod performance status of 0-2 with adequate hepatic, cardiac, renal and hematologic functions. Patients must not have an active autoimmune disease that has required systemic treatment in past two years or a recent severe infection. Patients must be tested for both hepatitis B virus (HBV) and hepatitis C virus (HCV) infection. Patients with known HIV positive are eligible provided they meet criteria as described in the protocol. Patient must not have a history of clinically significant interstitial lung disease or evidence of active pneumonitis on the screening chest CT.

Patients must agree to have specimens submitted for translational medicine and banking.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) tumor size: < 4 cm versus ≥ 4 cm; (2) tumor location: central vs peripheral; and (3) Zubrod performance status: 0/1 vs 2.

Accrual Goals

The accrual goal is 480 patients to achieve 432 eligible patients. Four interim analyses are planned at approximately 36, 48, 60, and 72 months.

S1929 Phase II

Coordinating Group: SWOG

Phase II Randomized Study of Maintenance Atezolizumab Versus Atezolizumab in Combination with Talazoparib in Patients with SLFN11 Positive Extensive Stage Small Cell Lung Cancer (ES-SCLC)

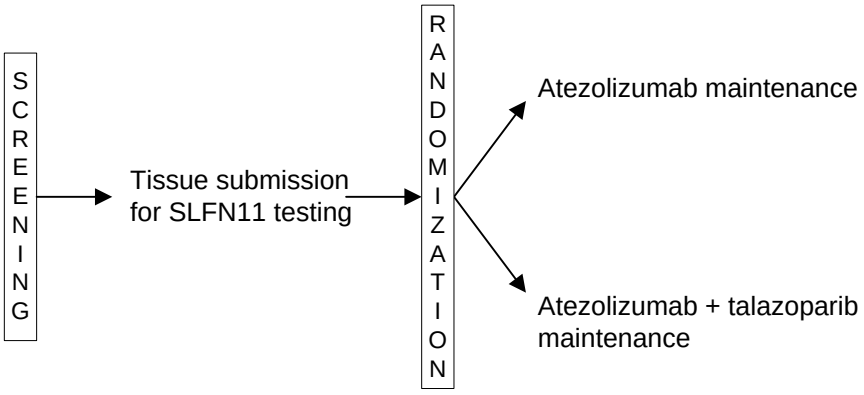
Participants:
SWOG, CTSU (Supported by Alliance, ECOG-ACRIN)

Study Chairs:
N Karim, K Reckamp, W Petty (Alliance), K Mehta (ECOG-ACRIN)

Statisticians:
Y Zhao, L Qian

Data Coordinator:
J Harris

SCHEMA



Objectives

To compare progression free survival among participants with Schlafen family member 11 (SLFN11) positive extensive stage small cell lung cancer (ES-SCLC) randomized to atezolizumab or atezolizumab plus talazoparib as maintenance therapy

To compare overall survival between the arms.

To compare objective response rate among participants with measurable disease between the arms, including complete response and partial response (confirmed and unconfirmed) by RECIST 1.1.

To evaluate the frequency and severity of adverse events within each treatment arm.

Patient Population

Patients must have histologic or pathologic confirmed ES-SCLC that is SLFN11 positive as determined centrally. Patients with brain metastases are eligible provided imaging after CNS-directed therapy shows no evidence of progression. Patients must not have had disease disease progression based on post-induction imaging.

Patients must have completed front-line induction therapy as described in the protocol. Patients must not have received any immunotherapy for SCLC prior to starting induction treatment. Patients may have received prior radiation treatment or prophylactic cranial irradiation. Patients must not have experienced any unresolved Grade 2 or any Grade 3 or higher immune-related adverse event during induction therapy or any event that led to permanent discontinuation of prior anti-PD-1/PD-L1 immunotherapy. Patients must not have undergone prior allogeneic bone marrow or solid organ transplantation, nor can they be taking or plan to take strong P-gp inhibitors, P-gp inducers or breast cancer resistance protein inhibitors as described in the protocol. Patients must not have received any investigational agents prior to registration.

Patients must have a Zubrod performance status of 0-2 and adequate hepatic, cardiac, renal and hematologic function. Patients must not have known active tuberculosis, diabetes, end stage renal disease, clinically significant liver disease, or other serious medical illness. Patients must not have active pneumonitis or pulmonary history as described in the protocol. Patients must be able to swallow capsules whole and not be on corticosteroids as described in the protocol. Patients with hepatitis B, hepatitis C or HIV infection may be eligible provided they meet the criteria in the protocol.

Patients must be offered the opportunity to have specimens submitted for banking.

Stratification/Descriptive Factors

Patient randomization will be stratified according to following factors: (1) Zubrod performance status: 0-1 vs 2; and (2) received radiation therapy: yes vs no.

Accrual Goals

The accrual goal is 323 patients screened for SLFN 11 to achieve 84 eligible and randomized patients. An interim analysis is planned when 50% of the expected PFS events have been observed.

S1933 Phase II

Coordinating Group: SWOG

A Phase II Feasibility Trial of Hypofractionated Radiotherapy Followed by Atezolizumab Consolidation in Stage II or III NSCLC Patients with Borderline Performance Status

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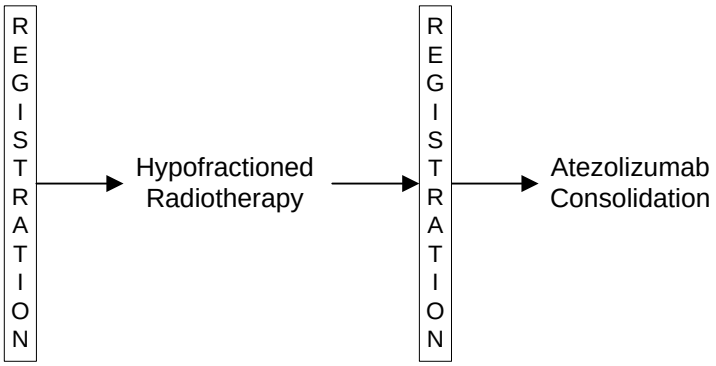
Participants:
SWOG, CTSU

Study Chairs:
R Aljumaily, T Mitin, A Wozniak, R Decker

Statisticians:
M Redman, J Miao

Data Coordinator:
L Kaye

SCHEMA



Objectives

To evaluate the rate of Grade 3-5 Treatment-Related Adverse Events (TRAEs) in patients who are not candidates for surgery or concurrent chemoradiation and who have either performance status 0-2 and Stage II or performance status 2 and Stage III non-small cell lung cancer (NSCLC), treated with hypofractionated thoracic radiotherapy followed by atezolizumab.

To evaluate response rate (confirmed and unconfirmed, complete and partial by RECIST 1.1) from Registration Step 2 in the subset of patients with measurable disease.

To evaluate response rate (confirmed and unconfirmed, complete and partial by RECIST 1.1) during radiation therapy in the subset of patients with measurable disease.

To evaluate progression free survival (PFS) from Registration Step 2 by RECIST 1.1.

To evaluate overall survival (OS) from Registration Step 2.

To evaluate the frequency and severity of toxicities.

Patient Population

Patients must have pathologic (cytological or histological) proof of non-small cell lung cancer (NSCLC). Patients must have Stage III NSCLC with Zubrod Performance Status of 2 or Stage II NSCLC with Zubrod Performance Status of 0-2. Patients must not be candidates for surgical resection in the opinion of the treating investigator. Patients must not be candidates for concurrent chemoradiation in the opinion of the treating investigator. Patients' disease must fit within the radiation constraints as described in the protocol.

Patients may have received prior treatment for their lung cancer, including surgery, chemotherapy, targeted agents, and/or radiation treatment at least 12 months prior to Registration Step 1. Patients must not have received any chemotherapy, biologic agent, or any investigational agent within 14 days prior to Registration Step 1. Patients may have had prior radiation therapy as long as the irradiated area does not overlap with the radiation field targeted for this study.

Patients must be at least 18 years of age with adequate hepatic, cardiac, liver, renal and hematologic functions Patients must have an MRI or CT scan of the brain with contrast within 28 days prior to Registration Step 1. Patients must have recovered from any adverse effects of prior major surgery to the satisfaction of the treating physician. Patients with known HIV or HBV infection must have undetectable viral load and under related therapy. Patients with a history of HCV infection must have been treated and cured.

Stratification/Descriptive Factors

This study does not include any stratification factors.

Accrual Goals

The accrual goal is 47 patients. An interim analysis will take place when 20 patients are evaluable for toxicity in the safety analysis population.