S1400 Master Protocol

Coordinating Group: SWOG

A Biomarker-Driven Master Protocol for Previously Treated Squamous Cell Lung Cancer

(Lung-MAP)

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

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

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

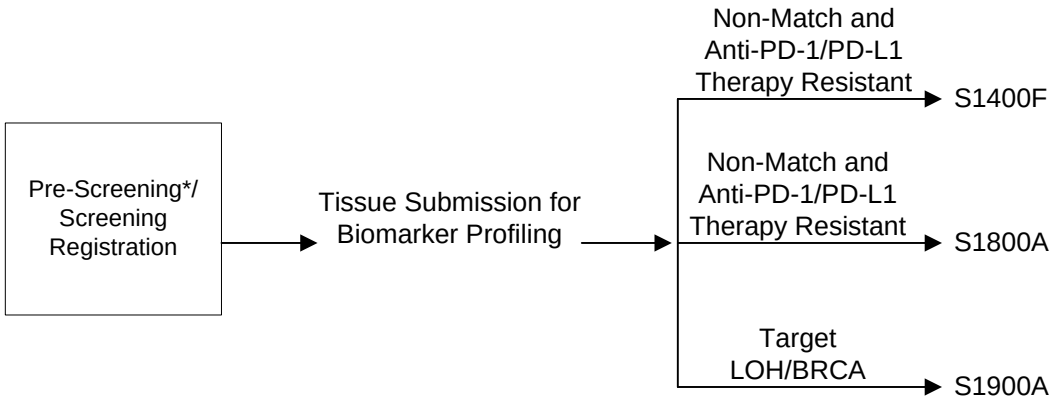
Project Manager:
S Basse

Data Coordinators:
L Everhart, L Highleyman

Date Activated:
06/15/2014

Date Closed:
01/28/2019

SCHEMA



*Patients must progress on current treatment to receive sub-study assignment.

Objectives

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

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

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

Patient Population

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

Patients must either be eligible to be screened at progression on prior treatment or to be pre-screened prior to progression on current treatment. To be eligible for screening at progression, patients must have received at least one line of systemic therapy for any stage of disease. At least one of these lines of therapy must have been a platinum-based chemotherapy regimen or checkpoint inhibitor therapy, and patients must have progressed following the most recent line of therapy. To be eligible for pre-screening, current treatment must be for Stage IV 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 checkpoint inhibitor therapy. Prior to Revision #2, activated May 26, 2015, patients were only allowed to receive at most one prior chemotherapy regimen for Stage IV disease.

Patients must have a Zubrod performance status of 0-1. Prior to Revision #3, activated December 18, 2015, patients were allowed to have a Zubrod performance status of 0-2.

Accrual Goals

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

Summary Statement

As of January 28, 2019, this study was permanently closed to accrual and replaced by a new screening protocol, LUNGMAP. This new screening protocol was activated on the same day and expands eligibility from squamous histology alone to all types of previously-treated stage IV or recurrent non-small cell lung cancer.

Patients enrolled to 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), ten sub-studies have been activated and of them, eight have closed.

Open sub-studies:

S1400F (Non-match) activated on 10/02/17 and is studying MEDI4736 + tremelimumab.

S1900A (LOH/BRCA1/BRCA2) activated on 01/28/19 and is studying rucaparib.

Closed sub-studies:

S1400A (Non-match) activated on 06/16/14 and closed on 12/18/15 and was studying MEDI4736.

S1400B (PI3K) activated on 06/16/14 and closed on 12/12/16 and was studying taselisib.

S1400C (CCGA) activated on 06/16/14 and closed on 09/01/16 and was studying palbociclib.

S1400D (FGFR) activated on 06/16/14 and closed on 10/31/16 and was studying AZD4547.
S1400E (c-MET) activated on 06/16/14 and closed on 11/26/14 and was studying erlotinib vs. erlotinib + rilotumumab.
S1400G (HRRD) activated on 02/07/17 and closed on 07/23/18 and was studying talazoparib.
S1400I (Non-match) activated on 12/18/15 and closed on 04/23/18 and was studying nivolumab vs. nivolumab + ipilimumab.
S1400K (c-MET) activated on 02/05/18 and closed on 12/21/18 and was studying ABBV-399 (Process II).

As of December 31, 2018, 1,855 patients have been registered. Seventy-two patients (4%) are currently ineligible due to the following reasons: inadequate tissue for biomarker profiling (25), prior treatment (17), histology (13), inadequate Zubrod performance status (5), registering prior to progression on first-line therapy prior to amendment allowing pre-screening (3), ineligible staging (3), lack of tissue submission (2), patient was already deceased at the time of registration (2), lack of baseline forms and path report submission (1), and consent withdrawal prior to registration (1). An additional patient is not analyzable due to mixed histology found by an outside institution after registration.

One thousand three hundred fifty-two patients received sub-study assignments for a total of 1,474 initial assignments, re-assignments, and new assignments following progression on a sub-study. One thousand two hundred thirty-nine patients received one assignment. Of the 106 patients with two assignments, 64 received re-assignments and 42 received new assignments following progression on a sub-study. Of the five patients with three assignments, four received re-assignments with a new assignment following progression on a sub-study and one received two new assignments following progression on two sub-studies. Of the two patients with three assignments, both received a re-assignment as well as two new assignments following progression on two sub-studies.

Of the 730 pre-screening patients, 366 have submitted the Notice of Progression and been assigned to a sub-study. One hundred and six pre-screening patients have not submitted the Notice of Progression and could potentially be assigned to a sub-study in the future. The other 258 patients without an assignment have either passed away, submitted a Notice of Intention Not to Register form, did not have adequate tissue for successful biomarker results, or had no sub-studies to which they could be assigned.

Six hundred thirty-seven patients enrolled to at least one sub-study for a total of 663 sub-study registrations. Six hundred twelve registered to one sub-study, 24 registered to two sub-studies, and one patient registered to three sub-studies.

One thousand one hundred twenty-six patients have submitted the Notice of Intention Not to Register (NINTR) form. The reasons for not registering are described in the Notice of Intention Not to Register table. The most common reason (36%) is patients were not eligible for any sub-study. Thirty-five (3%) patients submitted the NINTR with the classification of "Other". The reasons included: sub-study closed (10), patient location to site (5), proceeded with different treatment instead (6), did not want to wait for progression (2), sub-study drug not available (2), previous treatment on S1400I (2), screening tissue inadvertently discarded, so no biomarker results obtained (1), CT scans not covered by insurance (1), failed post-sequencing analysis (1), enrolled on different study (1), consent withdrawal (1), uncontrolled atrial fibrillation (1), accidental enrollment (1), and high creatinine levels (1).

Registration by Network Groups

Registrations ending December 31, 2018

Institutions	Total Reg
SWOG	910
ALLIANCE	399
ECOG-ACRIN	325
NRG	203
CCTG	18
Total (5 Network Groups)	**1855**

Registration by Institution

Registrations ending December 31, 2018

Institutions	Total Reg
Roswell Park Cancer Institute (NY158)	45
Duke University Medical Center (NC010)	39
Northside Hospital (GA031)	28
University of Pittsburgh Cancer Ins (PA015)	24
M D Anderson Cancer Center (TX035)	23
University of Pennsylvania/Abramson (PA075)	21
Yale University (CT018)	21
University of California Davis Comp (CA189)	20
University of Wisconsin Hospital an (WI020)	20
University of Rochester (NY167)	19
Veterans Affairs Connecticut Health (CT063)	19
Fox Chase Cancer Center (PA086)	18
Baptist Health Lexington (KY026)	17
Indiana University/Melvin and Bren (IN007)	17
Froedtert and the Medical College o (WI013)	16
University of Maryland/Greenebaum C (MD015)	16
Ascension Providence Hospitals - So (MI006)	15
City of Hope Comprehensive Cancer C (CA043)	15
Wayne State University/Karmanos Can (MI020)	15
Cancer Center of Kansas - Wichita (KS034)	14
Cookeville Regional Medical Center (TN144)	14
Northeast Georgia Medical Center-Ga (GA024)	14
Washington University School of Med (MO011)	14
University of Washington Medical Ce (WA020)	13
Vanderbilt University/Ingram Cancer (TN008)	13
Dartmouth-Hitchcock Medical Center/ (NH012)	12
Essentia Health Cancer Center (MN024)	12
Geisinger Medical Center (PA052)	12
Illinois CancerCare-Peoria (IL101)	12
Richard L. Roudebush Veterans Affai (IN004)	12
UC San Diego Moores Cancer Center (CA249)	12
University of Oklahoma Health Scien (OK003)	12
WellSpan Health-York Hospital (PA047)	12
Medical Oncology Hematology Consult (DE038)	11

Institutions	Total Reg
Missouri Baptist Medical Center (MO046)	11
Olathe Medical Center (KS020)	11
Saint Joseph Mercy Hospital (MI013)	11
University of Chicago Comprehensive (IL057)	11
FirstHealth of the Carolinas-Moore (NC081)	10
Lahey Hospital and Medical Center (MA017)	10
Massachusetts General Hospital Canc (MA034)	10
Moffitt Cancer Center (FL065)	10
Oklahoma Cancer Specialists and Res (OK037)	10
University of Michigan Comprehensiv (MI014)	10
UT Southwestern/Simmons Cancer Cent (TX011)	10
West Virginia University Healthcare (WV025)	10
Beth Israel Deaconess Medical Cente (MA038)	9
Cancer Care Specialists of Illinois (IL185)	9
Cancer Center of Kansas-Wichita Med (KS067)	9
Eisenhower Medical Center (CA076)	9
Fowler Family Center for Cancer Car (AR019)	9
Harold Alfond Center for Cancer Car (ME037)	9
Henry Ford Hospital (MI026)	9
Mary Imogene Bassett Hospital (NY143)	9
Mission Hospital Inc-Memorial Campu (NC031)	9
PeaceHealth Saint Joseph Medical Ce (WA069)	9
Saint Mary's Medical Center (WV010)	9
Sparrow Hospital (MI039)	9
Spartanburg Medical Center (SC024)	9
The Don and Sybil Harrington Cancer (TX068)	9
University Health Network-Princess (11030)	9
University of Kansas Cancer Center (KS004)	9
Guthrie Medical Group PC-Robert Pac (PA062)	8
Kansas City Veterans Affairs Medica (MO029)	8
Mercy Medical Center (OH064)	8
Mount Sinai Medical Center (FL036)	8
Ochsner Medical Center Jefferson (LA007)	8
Temple University Hospital (PA093)	8
University of Alabama at Birmingham (AL002)	8
University of Kentucky/Markey Cance (KY010)	8
University of Texas Health Science (TX059)	8
Frederick Memorial Hospital (MD036)	7
John B Amos Cancer Center (GA045)	7
Loma Linda University Medical Cente (CA078)	7
Mercy Hospital Saint Louis (MO021)	7
MetroHealth Medical Center (OH036)	7
Northwestern University (IL036)	7
Ohio State University Comprehensive (OH007)	7
Oregon Health and Science Universit (OR010)	7
Presbyterian Intercommunity Hospita (CA030)	7
ProMedica Flower Hospital (OH012)	7
Springfield Clinic (IL194)	7
University of Miami Miller School o (FL028)	7
University of Vermont College of Me (VT004)	7
Western Maryland Regional Medical C (MD031)	7
Baptist Memorial Hospital and Cance (TN029)	6
Bon Secours Saint Francis Medical C (VA175)	6
Central Vermont Medical Center (VT019)	6

Institutions	Total Reg
CHI Health Saint Francis (NE022)	6
Cleveland Clinic Foundation (OH027)	6
Cone Health Cancer Center (NC004)	6
Covenant Medical Center-Lakeside (TX054)	6
Crossroads Cancer Center (IL208)	6
Duke Raleigh Hospital (NC213)	6
Greenville Health System Cancer Ins (SC036)	6
Jewish Hospital Medical Center Nort (KY099)	6
Kaiser Permanente Moanalua Medical (HI007)	6
Marshfield Medical Center-Marshfiel (WI031)	6
Memorial Medical Center-Las Cruces (NM039)	6
Montefiore Medical Center-Einstein (NY313)	6
Peninsula Regional Medical Center (MD035)	6
Saint Francis Medical Center (MO009)	6
Salem Hospital (OR021)	6
Sinai Hospital of Baltimore (MD020)	6
United Hospital Center (WV017)	6
University of Cincinnati/Barrett Ca (OH070)	6
University of Iowa/Holden Comprehen (IA018)	6
University of Mississippi Medical C (MS005)	6
University of New Mexico Cancer Cen (NM004)	6
University of Virginia Cancer Cente (VA009)	6
Baystate Medical Center (MA004)	5
Boston Medical Center (MA043)	5
Carle Cancer Center (IL168)	5
Emory University Hospital/Winship C (GA005)	5
Faxton-Saint Luke's Healthcare (NY214)	5
Greater Baltimore Medical Center (MD018)	5
Kaiser Permanente-Bellflower (CA031)	5
Kootenai Cancer Center (ID013)	5
Loyola University Medical Center (IL017)	5
Memorial Regional Hospital/Joe DiMa (FL023)	5
Parkland Memorial Hospital (TX006)	5
Penn State Health Saint Joseph Medi (PA108)	5
Randolph Hospital (NC109)	5
Saint John's Hospital - Healtheast (MN041)	5
Sanford Joe Lueken Cancer Center (MN089)	5
Siouxland Regional Cancer Center (IA034)	5
South Georgia Medical Center/Pearlm (GA069)	5
Spectrum Health at Butterworth Camp (MI132)	5
The Methodist Hospital System (TX036)	5
Trinity Cancer Care Center (ND026)	5
University of Arkansas for Medical (AR006)	5
University of Massachusetts Medical (MA011)	5
All Other Institutions	560
Total (436 Institutions)	**1855**

Registration, Eligibility, and Evaluability

Classified by Screening

Registrations ending December 31, 2018; Data as of February 19, 2019

	TOTAL	Screened at Progression	Pre-screened Prior to Progression
NUMBER REGISTERED	1855	1125	730
INELIGIBLE	72	48	24
ELIGIBLE	1783	1077	706
Analyzable, Pend. Elig.	5	4	1
Not Analyzable	1	0	1

Patient Characteristics

Registrations ending December 31, 2018; Data as of February 19, 2019

	Total (n=1782)	
AGE		
Median	67.0	
Minimum	22.9	
Maximum	91.7	
SEX		
Males	1200	67%
Females	582	33%
HISPANIC		
Yes	46	3%
No	1703	96%
Unknown	33	2%
RACE		
White	1509	85%
Black	169	9%
Asian	42	2%
Pacific Islander	7	0%
Native American	14	1%
Multi-Racial	3	0%
Unknown	38	2%
PERFORMANCE STATUS		
0	471	26%
1	1234	69%
2	74	4%
Data pending	3	0%
SMOKING HISTORY		
Current	616	35%
Former	1093	61%
Never	69	4%
Data pending	4	0%

	Total (n=1782)	
WEIGHT LOSS PAST 6 MONTHS		
< 5%	1264	71%
5 - <10%	294	16%
10 - < 20%	192	11%
>=20%	21	1%
Data pending	11	1%

Complete Number of Sub-Study Assignments

Classified by Initial Screening Type

Including Sub-Studies Closed to Accrual; Including Re-Assignments and New Assignments

Screening Registrations ending December 31, 2018; Data as of February 26, 2019

	Screened at Progression	Pre-screened Prior to Progression	TOTAL
ASSIGNED SUB-STUDY			
S1400A (Non-match)	153	7	160
S1400B (PI3K)	54	13	67
S1400C (Cell Cycle Gene Alteration)	84	10	94
S1400D (FGFR)	87	22	109
S1400E (c-MET)	23	0	23
S1400F (Non-match)	105	56	161
S1400G (HRRD)	46	32	78
S1400I (Non-match)	480	245	725
S1400K (c-MET)	38	19	57
TOTAL NUMBER OF SUB-STUDY ASSIGNMENTS	1070	404	1474
TOTAL NUMBER OF PATIENTS WITH ASSIGNMENTS	986	366	1352
NUMBER OF SUB-STUDY ASSIGNMENTS PER PATIENT			
1	907	332	1239
2	75	31	106
3	3	2	5
4	1	1	2

Notice of Intention Not to Register

Registrations ending December 31, 2018; Data as of February 19, 2019

	Total (n=1126)	
PRIMARY REASON		
Patient not eligible for any sub-study	402	36%
Death	161	14%
Tissue inadequate for biomarker profiling	137	12%
Symptomatic deterioration	132	12%
Patient refused	101	9%
Investigator decision	68	6%
Preference to receive Nivolumab	50	4%
Patient not eligible for screening study	40	4%
Other	35	3%