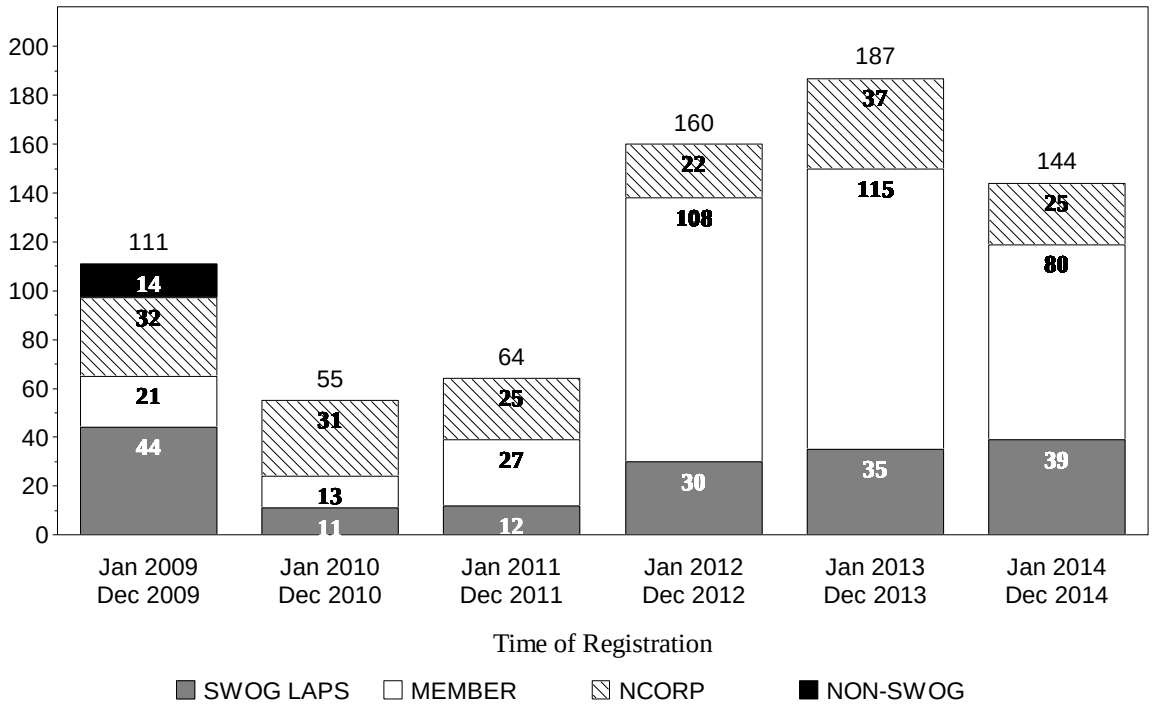
MELANOMA COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
MELANOMA COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

MELANOMA COMMITTEE

	Jul 2014 Dec 2014	Jan 2014 Jun 2014	Jul 2013 Dec 2013	All Patients
S1221 Melan, Adv, Dabrafenib + Trametinib + GSK2141795				
Phase I Registration				
Dabrafenib/GSK2141795 50mg	0	0	3	3
Dabrafenib/GSK2141795 75mg	1	6	0	7
	1	6	3	10
S1320 Melan, Adv, BRAF-mt, Intermittent vs Continuous Dosing with Dabrafenib + Trametinib				
Lead In Registration				
Lead-in Continuous Dosing	6	0	0	6
Randomization				
Intermittent Dosing	1	0	0	1
E1609 Melan, Adjuvant Ipilimumab vs Interferon*				
Total Registrations	36	95	88	499
E2607 Melan, Adv, Dasatinib in KIT+ Patients*				
Total Registrations	0	0	0	0

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

S1204 Surveillance

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

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

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

Date Activated:
08/29/2013

Date Closed*:
12/15/2014

*Temporary Closure

Objectives

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

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

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

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

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

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

Patient Population

Patients must be presenting for evaluation or treatment for the first diagnosis of a new cancer malignancy (including hematologic). Confirmed pathologic diagnosis must be within 120 days of registration. Patients presenting for "second opinions" of confirmed malignancies are eligible, including those who have started cancer treatment at other facilities. Individuals are ineligible if they have been diagnosed with a malignancy other than the current malignancy within the past five years, with the exception of basal cell or squamous cell skin cancer, in situ cervical cancer, or in situ breast cancer. Individuals are eligible if they have had no evidence of disease for a prior malignancy, except as noted above, for at least five years prior to randomization.

Patients must be 18 years of age or older. Patients must have had their blood drawn for testing for HIV, HBV and HCV prior to registration. Patients who have had HIV, HBV and/or HCV testing within 60 days prior to registration and who do not wish to be retested are eligible, provided supporting documents can be obtained confirming viral test results for all three viruses. Patients who are viral positive for either HIV, HBV, and/or HCV and who do not wish to be retested are eligible, provided documentation of viral load within 120 days prior to registration can be obtained. Note that these patients must be tested for

or provide current viral load for all three viruses to be eligible. All documentation must be obtained prior to registration. Patients are allowed to participate in other clinical trials.

Cancer Control Credits
No cancer control credits are awarded for this study.

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

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

S1221 Phase I-II
Phase I/II Study of the Safety and Efficacy of the AKT Inhibitor GSK2141795 in Combination with Dabrafenib and Trametinib in Patients with BRAF Mutant Cancer

Study Chairs:
A Ribas, A Algazi, B Chmielowski, R Lo

Statisticians:
J Moon, M Othus

Data Coordinator:
J Barrett

Date Activated:
07/12/2013

Objectives

Phase I Portion:

The Phase I portion will be performed in two parts. Part 1 will investigate the doublet combination of dabrafenib and GSK2141795. Part 2 will investigate the triplet combination of dabrafenib, trametinib and GSK2141795.

Part 1:

To assess the safety of dabrafenib in combination with GSK2141795 and select the optimal dose of GSK2141795 for the Phase II portion in patients with BRAF mutant cancer, should it ever be pursued in the future.

To explore potential drug interactions between dabrafenib and GSK2141795 via pharmacokinectic sampling of patients enrolled on this part of the Phase I portion.

Part 2:

To assess the safety of dabrafenib and trametinib in combination with GSK2141795 and select the optimal dose of the combination for the Phase II portion in patients with BRAF mutant cancer.

To explore potential drug interactions between dabrafenib, trametinib and GSK2141795 via pharmacokinectic sampling of patients enrolled on this part of the Phase I portion.

Phase II Portion:

The Phase II portion will only investigate the triplet combination of dabrafenib, trametinib and GSK2141795.

To evaluate the objective response rate (confirmed and unconfirmed complete and partial responses) in patients with Stage IV or unresectable Stage III $BRAF^{v600}$ mutant metastatic melanoma who have who have acquired resistance to BRAF inhibitor-based therapy treated with the triplet combination of dabrafenib, trametinib and GSK2141795

To estimate overall survival and progression-free survival.

To assess the toxicity profile of the recommended Phase II dose.

To explore the molecular mechanisms of acquired resistance to BRAF inhibitor therapy in patients with $BRAF^{v600}$ mutant metastatic melanoma.

Patient Population
Phase I portion:

Patients may have any type of locally advanced unresectable Stage IIIC or Stage IV cancer, irrespective of the histology or prior therapy. Patients may have measurable or non-measurable disease. Patients with melanoma must have a serum LDH performed at baseline.

Patients must either be naïve to BRAF inhibitor therapy or must have progressed on either a single agent BRAF inhibitor or BRAF inhibitor plus MEK inhibitor therapy.

Patients must have a Zubrod performance status ≤ 1.

Phase II portion:

Patients must have histologically confirmed melanoma that is Stage IIIC or Stage IV. Patients must have a serum LDH performed at baseline and must have measurable disease.

Patients must have either progressed on a single agent BRAF inhibitor or BRAF inhibitor plus MEK inhibitor therapy.

Patients must have a Zubrod performance status ≤ 2.

All Patients:

Patients must have $BRAF^{V600}$ mutant metastatic cancer documented by a CLIA-certified laboratory. All patients must have a CT or MRI of the brain. Patients with brain metastases are eligible only if they are asymptomatic or they have been previously treated and are stable (i.e. not requiring corticosteroids).

Patients may have received prior systemic therapy (chemotherapy, immunotherapy, biologic therapy, or combination regimens), surgery, or radiation therapy.

Patients must have adequate hematologic, hepatic, renal, cardiac and ocular function. Patients must be able to retain oral medication. Patients who have feeding tubes must be able to take whole capsules without modifying them. Patients must not have an active Hepatitis B or Hepatitis C infection. Patients requiring therapeutic anticoagulation must have approval from physician to use therapeutic dosing of warfarin and they must have close monitoring of PT/INR during the trial. Patients must not be receiving any medications or substances that are strong inhibitors or inducers of CYP3A or CYP2C8 or P-glycoprotein (Pgp) or breast cancer resistance protein 1 (Bcrp1), or using herbal remedies. Patients must not have any history of allergic reactions to compounds of similar chemical or biologic composition to dabrafenib or GSK2141795. Patients with HIV are eligible if they are not on antiviral agents and have adequate CD4 counts. Women of childbearing potential must have a negative pregnancy test within 14 days prior to registration.

Patients must have available and must be willing to submit blood and tissue samples as outlined in the protocol.

Stratification/Descriptive Factors
Patients enrolled on the Phase I portion will be stratified by planned treatment regimen: dabrafenib and GSK2141795 (D + G) vs dabrafenib, trametinib and GSK2141795 (D + T + G).

Accrual Goals
The study will be conducted in two sequential parts. Patients enrolled to the Phase I portion will not be included in the analysis of the Phase II portion.

Both the doublet regimen and the triplet regimen will be investigated during the Phase I portion. Within each stratum, patient enrollment will follow the traditional "3+3" algorithm until the MTD for GSK2141795 is reached or the highest dose tested is judged tolerable. At least six patients will be evaluated at the recommended dose within each stratum.

Only the triplet regimen will be investigated in the Phase II portion. A two-stage design will be used. Initially, ten eligible patients will be registered. If at least two responses are observed, an additional 23 eligible patients will be registered.

Summary Statement
This study was amended to add a third drug, trametinib, to the two drug combination currently being investigated in the Phase I portion of the trial. The Phase I portion investigating the doublet combination will continue until its conclusion. Effective February 13, 2015, patients may be enrolled on either the doublet regimen (dabrafenib and GSK2141795) or the triplet regimen (dabrafenib, trametinib and GSK2141795). Patients with melanoma are encouraged to be enrolled on the triplet regimen. At the conclusion of the Phase I

portion, the Phase II portion will evaluate the efficacy of the three drug combination in patients with melanoma. The Phase II evaluation of the two-drug combination will no longer be pursued.

The Phase I portion of this trial, investigating the two drug combination of GSK2141795 + dabrafenib, was activated on July 1, 2013. The first cohort of three patients treated at the dose level of 50 mg GSK2141795 has been enrolled and evaluated for toxicity. No dose limiting toxicities (DLT) were observed.

The second cohort of patients, to be treated at the dose level of 75 mg GS2141795, was opened to accrual on February 3, 2014, and has been expanded to target an accrual goal of six patients evaluable for DLT. As of December 31, 2015, seven patients have been enrolled on the 75 mg cohort. However, three of these patients did not meet the protocol-specified criteria to be considered evaluable for DLTs, including two eligible patients who did not receive any protocol treatment and are not evaluable for any of the study endpoints (coded as a major protocol deviation). As of February 13, 2015, there have been no DLTs reported for the first four evaluable patients on the 75 mg cohort.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg
Los Angeles, U of CA	3
Ohio State Univ	3
Colorado, U of	2
Prov Portland MC/PCRC NCORP	2
Total (4 Institutions)	**10**

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2014; Data as of February 13, 2015

	TOTAL	Dabrafenib + GSK2141795 50mg	Dabrafenib + GSK2141795 75mg
NUMBER REGISTERED	10	3	7
ELIGIBLE	10	3	7
Not Analyzable	2	0	2
BASELINE DISEASE STATUS			
Measurable	7	3	4
Non Measurable	1	0	1
RESPONSE ASSESSMENT			
Determinable	7	3	4
Not Applicable	1	0	1
ADVERSE EVENT ASSESSMENT			
Evaluable	8	3	5
DOSE-LIMITING TOXICITY ASSESSMENT			
Evaluable	7	3	4
Not Evaluable	1	0	1

Patient Characteristics

Registrations ending December 31, 2014; Data as of February 13, 2015

	Total (n=8)	
AGE		
Median	59.8	
Minimum	40.5	
Maximum	70.2	
SEX		
Males	7	88%
Females	1	13%
HISPANIC		
No	8	100%
RACE		
White	8	100%
PRIOR BRAF INHIBITOR		
Yes	5	63%
No	2	25%
Data pending	1	13%
TYPE OF CANCER		
Melanoma	5	63%
Lung	2	25%
Thyroid	1	13%

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2014; Data as of February 13, 2015

	Dabrafenib + GSK2141795 50mg (n=3) Grade						Dabrafenib + GSK2141795 75mg (n=5) Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	3	0	0	0	0	0	4	1	0	0	0	0
AST increased	3	0	0	0	0	0	4	1	0	0	0	0
Alkaline phosphatase increased	3	0	0	0	0	0	4	0	1	0	0	0
Anemia	3	0	0	0	0	0	4	0	1	0	0	0
Anorexia	2	0	1	0	0	0	2	3	0	0	0	0
Arthralgia	3	0	0	0	0	0	4	1	0	0	0	0
Back pain	3	0	0	0	0	0	4	1	0	0	0	0
Chills	3	0	0	0	0	0	2	3	0	0	0	0
Constipation	2	1	0	0	0	0	4	1	0	0	0	0
Diarrhea	3	0	0	0	0	0	3	1	1	0	0	0
Dizziness	2	1	0	0	0	0	4	1	0	0	0	0
Dry mouth	3	0	0	0	0	0	4	1	0	0	0	0
Dry skin	3	0	0	0	0	0	4	1	0	0	0	0
Dysgeusia	3	0	0	0	0	0	4	1	0	0	0	0

	Dabrafenib + GSK2141795 50mg (n=3)						Dabrafenib + GSK2141795 75mg (n=5)					
	Grade						Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Edema limbs	2	1	0	0	0	0	4	1	0	0	0	0
Fatigue	1	2	0	0	0	0	2	2	1	0	0	0
Fever	1	1	1	0	0	0	3	2	0	0	0	0
Flu like symptoms	2	1	0	0	0	0	5	0	0	0	0	0
Flushing	3	0	0	0	0	0	3	1	0	1	0	0
Gen disorders/admin site cond	3	0	0	0	0	0	4	1	0	0	0	0
Hand-Foot syndrome	2	1	0	0	0	0	4	1	0	0	0	0
Headache	3	0	0	0	0	0	3	2	0	0	0	0
Hyperglycemia	2	0	0	1	0	0	5	0	0	0	0	0
Hyperhidrosis	2	1	0	0	0	0	5	0	0	0	0	0
Hypernatremia	3	0	0	0	0	0	4	1	0	0	0	0
Hypokalemia	2	1	0	0	0	0	5	0	0	0	0	0
Hyponatremia	2	0	0	1	0	0	5	0	0	0	0	0
Hypophosphatemia	2	0	1	0	0	0	5	0	0	0	0	0
Hypotension	2	1	0	0	0	0	5	0	0	0	0	0
Insomnia	2	1	0	0	0	0	5	0	0	0	0	0
Lymphocyte count decreased	1	1	1	0	0	0	4	1	0	0	0	0
Myalgia	2	1	0	0	0	0	5	0	0	0	0	0
Nausea	1	2	0	0	0	0	2	3	0	0	0	0
Non-cardiac chest pain	3	0	0	0	0	0	4	1	0	0	0	0
Pain	3	0	0	0	0	0	4	1	0	0	0	0
Pain in extremity	3	0	0	0	0	0	4	1	0	0	0	0
Pain of skin	2	1	0	0	0	0	5	0	0	0	0	0
Platelet count decreased	3	0	0	0	0	0	4	1	0	0	0	0
Rash maculo-papular	3	0	0	0	0	0	4	1	0	0	0	0
Renal/urinary disorders-Other	3	0	0	0	0	0	4	1	0	0	0	0
Sinus tachycardia	3	0	0	0	0	0	4	0	1	0	0	0
Skin induration	3	0	0	0	0	0	4	1	0	0	0	0
Skin/subq tissue ds-Other	2	0	0	1	0	0	2	3	0	0	0	0
Tremor	3	0	0	0	0	0	4	1	0	0	0	0
Vasc disorders-Other	2	0	0	1	0	0	5	0	0	0	0	0
Vomiting	1	2	0	0	0	0	5	0	0	0	0	0
Weight loss	2	0	1	0	0	0	4	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	0	1	0	2	0	0	1	1	2	1	0	0

S1320 Phase II

Coordinating Group: SWOG

A Randomized Phase II Trial of Intermittent versus Continuous Dosing of Dabrafenib (NSC-763760) and Trametinib (NSC-763093) in BRAF$^{V600E/K}$ Mutant Melanoma

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

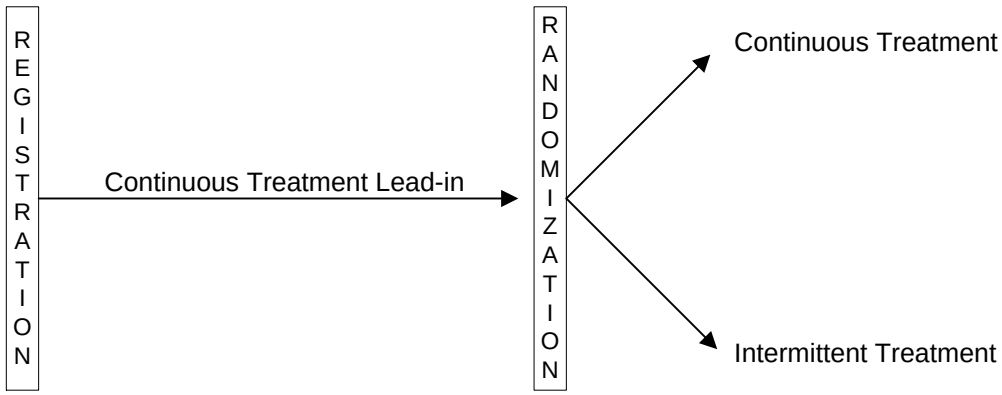
Date Activated:
07/22/2014

Study Chairs:
A Algazi, A Daud, R Lo

Statisticians:
M Othus, J Moon, M Wu

Data Coordinator:
J Barrett

SCHEMA



Objectives

To compare progression-free survival with intermittent dosing versus continuous dosing of dabrafenib and trametinib among patients with metastatic BRAF$^{V600E/K}$ mutant melanoma.

To compare the response rate (complete and partial response, confirmed and unconfirmed), overall survival, and survival after progression between the two dosing schedules.

To compare the frequency and severity of fever greater than Grade 1 (per CTCAE 4.0) of the two dosing schedules.

To estimate the frequency and severity of toxicities of the two dosing schedules.

To bank tissue and whole blood in anticipation of future studies to evaluate molecular events associated with clinical benefit and disease progression in patients treated with continuous versus intermittent dabrafenib and trametinib.

Patient Population

Patients must have histologically or cytologically confirmed Stage IV or unresectable Stage III melanoma. Patients must have BRAF mutation-positive melanoma (i.e., V600E or V600K) as determined via Sanger sequencing or an FDA-approved BRAF mutation detection assay. $BRAF^{V600}$ mutant status must be documented by a CLIA-certified laboratory. Patients must have measurable disease as defined by RECIST 1.1. Contrast-enhanced CT scans of the neck, chest, abdomen and pelvis are required. A whole body PET/CT scan with diagnostic quality images and intravenous iodinated contrast may be used in lieu of a contrast enhanced CT of the neck, chest, abdomen and pelvis. Contrast may be omitted if the treating investigator believes that exposure to contrast poses an excessive risk to the patient. Patients must not have brain metastases unless brain metastases have been treated and patient is asymptomatic with no residual neurological dysfunction and has not received enzyme-reducing anti-epileptic drugs or corticosteroids for at least seven days prior to registration. Patients must have serum LDH obtained prior to registration for treatment randomization stratification and accurate staging.

Patients must not have received a prior BRAF or MEK inhibitor. Prior surgery, radiotherapy, immunotherapy, or chemotherapy are allowed.

Patients must have adequate hematologic, hepatic, cardiac, and renal function and a Zubrod performance status of 0-1. Patients must not have a known history or current evidence of retinal vein occlusion (RVO) or central serous retinopathy (CSR). Patients must not have any predisposing factors for RVO or CSR such as uncontrolled glaucoma, ocular hypertension, uncontrolled systemic hypertension, diabetes mellitus, or a history of hyperviscosity or hypercoagulability syndromes. An ophthalmic exam is required for all patients. Patients must not have evidence of optic disc cupping, visual field defects, or an intraocular pressure greater than 21 mmHg. Patients must be able to take oral medications and must not have any impairment of gastrointestinal disease that may significantly alter the absorption of protocol treatment. Patients must discontinue treatment with therapeutic warfarin prior to registration. Patients must not have a history of pneumonitis or interstitial lung disease. Patients with known hepatitis B, or hepatitis C are not eligible. Patients known to be HIV positive must have CD4 cells $\geq$ 500 uL, a serum HIV viral load < 25,000 IU/ml and must be able to discontinue antiretroviral therapy. Patients must have a dermatology exam within 28 days prior to registration.

Patients must be offered the opportunity to participate in specimen banking.

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following: (1) prestudy serum LDH: elevated (> IULN) vs normal; (2) known prior exposure to immune checkpoint inhibitors targeting CTLA-4, PD-1, or PD-L1: yes vs no.

Accrual Goals

The accrual goal is 226 eligible patients. An interim analysis testing for harm will be performed when 78 progression events have occurred.

Summary Statement

As of December 31, 2014, six patients have been enrolled and one patient has been randomized.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg
San Francisco, U-CA	4
Kaiser NCORP	1
KaiserPermanenteSCAL/Kaiser NCORP	1
Total (3 Institutions)	**6**

S1404 Phase III

Coordinating Group: SWOG

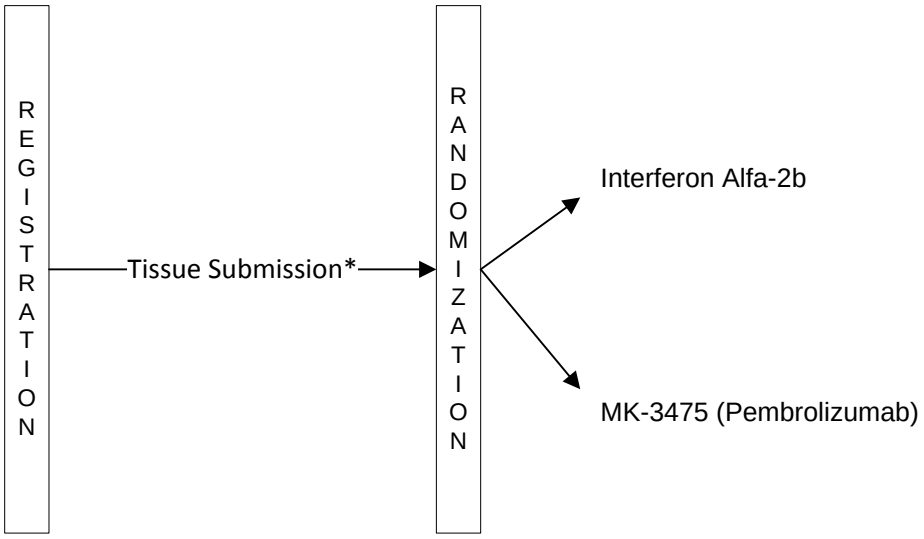
A Phase III Randomized Trial Comparing High Dose Interferon to MK-3475 (Pembrolizumab) in Patients with High Risk Resected Melanoma

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

Study Chairs:
K Grossmann, S Patel, A Tarhini (ECOG-ACRIN)

Statisticians:
M Othus, J Moon, M Wu

SCHEMA



*PD-L1 status determined by central laboratory

Objectives

To compare overall survival with high dose interferon alfa-2b to MK-3475 (pembrolizumab) among patients with resected Stage III and IV melanoma.

To compare relapse-free survival between the two regimens among all patients and within PD-L1 positive and negative subgroups.

To compare overall survival between the two regimens within PD-L1 positive and negative subgroups.

To assess the safety and tolerability of the two regimens.

To bank tissue and whole blood.

To evaluate PD-L1 expression through immunohistochemistry assay.

Patient Population

Patients must have histologically confirmed selected Stage III or Stage IV melanoma of cutaneous or mucosal origin or unknown primary. Patients must not have melanoma of ocular origin. Patients are eligible for this trial either at initial presentation of their melanoma, at time of first detected nodal, satellite/in-transit, distant metastases or recurrent disease in prior lymphadenectomy or distant site. Patients must not have a history of brain metastases. Patients who have multiple regional nodal basin involvement are eligible. Gross or microscopic extracapsular nodal extension is permitted. All disease must have been completely resected with negative pathologic margins and no clinical, radiologic, or pathologic evidence of any incompletely resected melanoma.

Patients may have received prior radiotherapy, including after the surgical resection that rendered the patient disease-free. Patients must not have received prior therapy with interferon alfa-2b, pegylated interferon, or any anti-PD-1 or anti-PD-L1 agents. Patients may have received other forms of treatment for melanoma, including chemotherapy, immunotherapy, interleukins, ipilimumab, or anti-tumor vaccine provided these were last received at least 42 days prior to enrollment and prior to the surgery(s) performed to render the patient free of disease. Patients must be registered within 98 days of the last surgery performed to render the patient free of disease.

Patients must have a Zubrod performance status of 0-1, and have adequate renal, hepatic, hematologic, and cardiac function. Patients must not have autoimmune disorders, conditions of immunosuppression or treatment with corticosteroids. Patients known to be HIV positive must have adequate CD4 counts and low viral load. Patients must not have known active hepatitis B or C infections. Patients must not have received live vaccines within 42 days prior to enrollment. Women of childbearing potential must have a negative pregnancy test within 28 days prior to randomization.

Patients must have available and be willing to submit adequate tissue for PD-L1 testing. The results of the PD-L1 testing will be used to stratify treatment randomization. Patients must be offered the opportunity to participate in specimen banking

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following: (1) surgically resected AJCC stage: IIIA(N2a) vs IIIB vs IV; (2) PD-L1 status: positive vs negative vs unknown.

Accrual Goals

The accrual goal of this study is to randomize 1,240 eligible patients. Up to two formal interim analyses will be performed when 50% and 75% of the expected deaths across both arms combined have been observed.

E1609 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

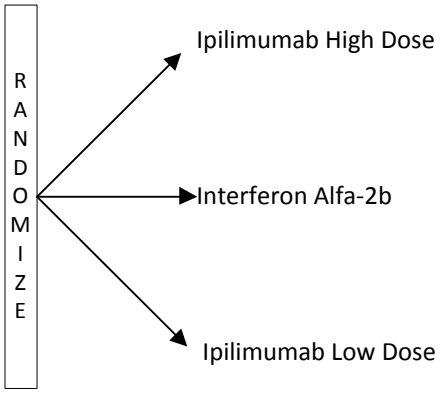
A Phase III Randomized Study of Adjuvant Ipilimumab Anti-CTLA4 Therapies Versus High-Dose Interferon Alfa-2b for Resected High-Risk Melanoma

Participants:
ECOG-ACRIN, CTSU

Date Activated:
06/08/2011

Study Chairs:
A Tarhini (ECOG-ACRIN), L Flaherty (SWOG)

SCHEMA



Objectives

First co-primary endpoint:

To evaluate recurrence-free survival (RFS) between patients randomized to receive post-operative adjuvant ipilimumab given at either 10 mg/kg (high dose ipilimumab; HIP) or 3 mg/kg (low dose ipilimumab; LIP) versus those randomized to receive high dose interferon alfa-2b (HDI) utilizing a heirarchical design assessing HIP versus HDI first and LIP versus HDI second (if the first comparison is significant).

Second co-primary endpoint:

To evaluate overall survival (OS) between patients randomized receive post-operative adjuvant HIP or LIP versus those randomized to receive HDI utilizing a heirarchical design assessing HIP versus HDI first and LIP versus HDI second (if the first comparison is significant).

Secondary endpoints:

To evaluate safety and tolerability of post-operative adjuvant ipilimumab therapy given at either 10 mg/kg or 3 mg/kg.

Among patients enrolled by CCOPs, to compare the global QOL between the ipilimumab arms versus HDI using FACT-G form and to evaluate the effect of treatment-related side effects that may have an impact on the health-related domains of QOL using FACITD and FACT-BRM.

Patient Population

Patients must have one of the following: selected Stage III (IIIB/IIIC) or selected Stage IV (M1a/M1b) melanoma of cutaneous origin; unknown primary melanoma presenting with cutaneous, subcutaneous, nodal and/or lung metastases with LDH within the institutional upper limit of normal; recurrence in a regional lymph node basin following resection of an original cutaneous primary; recurrence in the form of satellite/in-transit, distant skin/subcutaneous, nodal or lung metastases following resection of an original cutaneous primary or unknown primary melanoma; recurrence in a regional lymph node basin following a prior complete lymph node dissection and resection of an original cutaneous primary or unknown primary melanoma. All disease must be completely resected with free margins. Patients rendered free of disease by non-surgical means are not eligible. Patients with disease recurrence are eligible provided all relapsed disease has been completely resected with free margins. Patients must be randomized within 12 weeks of their most recent surgical procedure required to render the patient disease-free.

Patients must not have received any adjuvant treatment (chemotherapy, biotherapy, or limb perfusion). Previous radiation is allowed, including radiation following complete resection of disease. Patients must not have received any prior treatment with anti-CTLA4 monoclonal antibodies, CTLA-4 inhibitors/agonists, CD137 agonists, or interferon-alpha. Other forms of prior treatment for melanoma (e.g. IL-2, anti-tumor vaccine, chemotherapy) are allowed if completed prior to the resection(s) performed to render the patient free of disease.

Patients must have adequate hematologic, renal, and hepatic function and an ECOG performance status of 0-1. All females of childbearing potential must have a blood test or urine study to rule out pregnancy. Patients must not have any active infections requiring current treatment with parental antibiotics, autoimmmune disorders or conditions that require ongoing treatment with systemic corticosteroids, or a documented history of inflammatory bowel disease (including ulcerative colitis and Crohn's disease) or diverticulitis. Patients must not have had any infectious disease vaccination (e.g. standard influenza, H1N1 influenza, pneumococcal, meningococcal, tetanus toxoid) within the past four weeks prior to randomization. Patients must not have active or chronic infection with HIV, hepatitis B, or Hepatitis C. All patients must have negative testing for HIV, HBV, and HCV within four weeks prior to randomization.

Patients must submit tissue samples for central pathology review.

Stratification/Descriptive Factors

Treatment randomization will be stratified by AJCC Stage: IIIB vs IIIC vs M1a vs M1b.

Cancer Control Credits

The NCI Division of Cancer Prevention has not assigned up cancer control credits for registration to this study. There are potential cancer control credits for quality of life.

Accrual Goals

A total of 1,500 patients will be enrolled.

Summary Statement

This study is open to accrual of adolescent patients (ages 12-17), but remains permanently closed to adult patients after meeting the protocol specified accrual goals for that subgroup. As of December 31, 2014 there have been 1,671 registrations to this study, which include 499 CTSU registrations from SWOG institutions. The complete summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
H Lee Moffitt CC	41	Irvine, U of CA	7
Arkansas, U of	37	Wayne State Univ	7
Ohio State Univ	32	Cleveland Clinic OH	6
Sutter Cancer RC	28	Loyola University	6
Baylor Univ Med Ctr	26	Montana NCORP	6
Colorado, U of	25	Ozarks Reg NCORP	6
Los Angeles, U of CA	22	Sinai Hospital/San Antonio, U of TX	6
Arizona MC, U of	18	Southeast CCC NCORP	6
Kaiser NCORP	17	KaiserPermanenteCOL/Kaiser NCORP	5
Utah, U of	12	Oregon Hlth Sci Univ	5
Michigan, U of	11	Lahey Hosp & Med Ctr	4
Cincinnati MC, U of	10	Mem Hosp, Co Springs/Colorado, U of	4
Kansas, U of	10	Virginia Mason CCOP	4
Puget Sound	10	Yale University	4
Rochester, Univ of	10	Boston MC MBCCOP	3
St Luke's Mt State	10	Greenville NCORP	3
Thompson Ca Surv Ctr/San Antonio, U of TX	10	Hawaii MU-NCORP	3
West Michigan NCORP	9	Kansas City NCORP	3
Carolinas Med Ctr/San Antonio, U of TX	8	San Diego, U of CA	3
Highlands Onc Group/Arkansas, U of	8	St Charles Hlth Sys/Puget Sound	3
Northwest CCOP	8	All Other Institutions	35
UF Cancer Center/Arkansas, U of	8	**Total (69 Institutions)**	**499**

E2607 Phase II SWOG Supported CTSU Study
Coordinating Group: ECOG-ACRIN
A Phase II Trial of Dasatinib in KIT-Positive Patients with Unresectable Locally Advanced or Stage IV Mucosal, Acral and Vulvovaginal Melanomas

Participants:
ECOG-ACRIN, CTSU

Date Activated:
11/22/2011

Study Chairs:
D Lawrence (ECOG-ACRIN), K Margolin (SWOG)

Objectives

To estimate the objective tumor response rate for dasatinib monotherapy in treatment-naive or previously treated KIT-positive patients with advanced or metastatic acral or mucosal melanoma.

To estimate the response duration for dasatinib monotherapy in this patient population.

To estimate the progression-free survival for dasatinib monotherapy.

To evaluate the safety profile of this treatment.

To evaluate the PDGFR expression, and activation of Src Family Kinases in tumor samples and correlate these parameters with response to treatment.

Patient Population

Patients must have histologically or cytologically confirmed unresectable Stage IV melanoma that is one of the following subtypes: acral (defined as occurring on the palms, soles, or subungal sites), mucosal, or arising from the vagina and/or vulva. Patients with ocular primaries are not eligible. Patients with a history or clinical evidence of brain metastases must have completed radiation therapy or surgical treatment of brain lesions and have no evidence of CNS progression. Patients must have measurable disease as defined by RECIST. Patients must be c-KIT positive as determined by local assessment or by central review. See protocol for specific instructions.

Patients may have had prior systemic therapy with the exception that prior treatment with targeted therapies directed to c-KIT/PDGFR are not allowed (e.g. imatinib or sunitinib). Patients may have had prior limb perfusion or radiation therapy.

Patients must have adequate hematologic, renal, hepatic, and cardiac function with a performance status of 0-1. Females of childbearing potential are required to have a pregnancy test. Patients must not be taking cytochrome P450 enzyme-inducing antiepileptic drugs. Patients must have adequate blood coagulation with or without therapeutic warfarin.

Accrual Goals

A two-stage design will be used. Initially 15 KIT-positive patients will be enrolled. If three or more confirmed responses are observed, an additional 15 KIT-positive patients will be enrolled. To enroll 30 KIT-positive patients will require that approximately 250 patients be screened.

Summary Statement

SWOG's support of this study began after it was amended in November, 2011 with a new design which restricted the patient population to c-KIT positive patients. As of December 31, 2014, 20 c-KIT positive patients have been enrolled, including four CTSU registration by SWOG institutions. The complete summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg
Hawaii MU-NCORP	2
Kansas City NCORP	1
Michigan, U of	1
Total (3 Institutions)	**4**