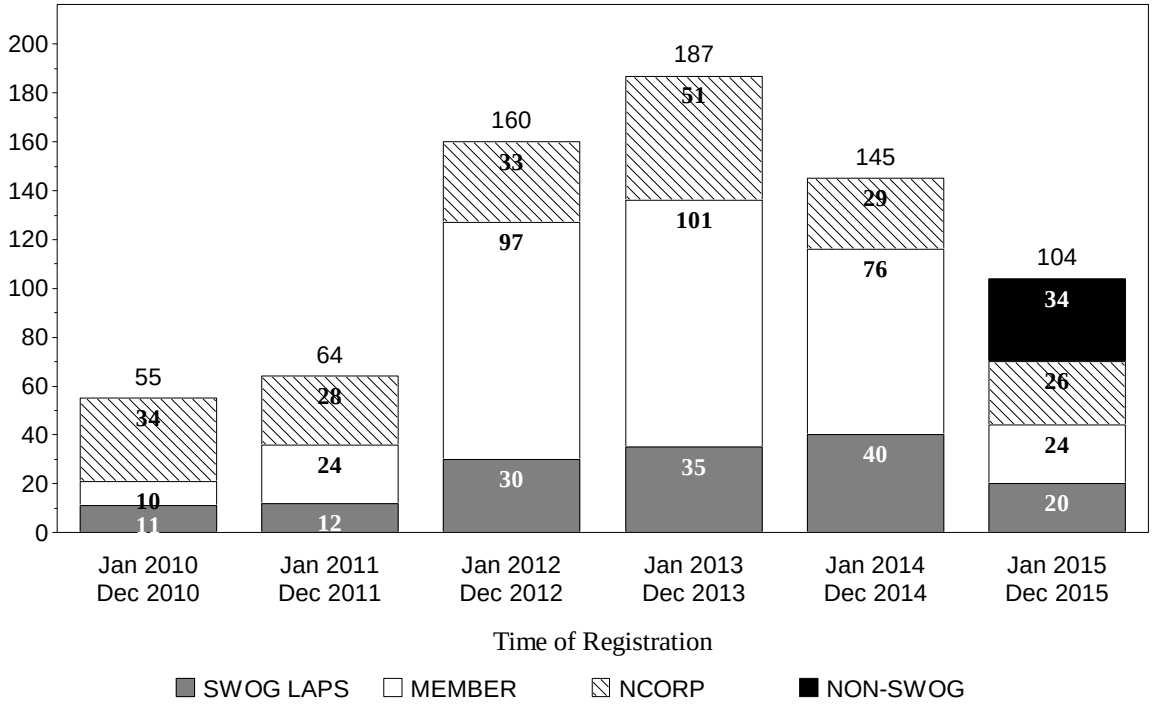
MELANOMA COMMITTEE

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 2015 Dec 2015	Jan 2015 Jun 2015	Jul 2014 Dec 2014	All Patients
S1221 Adv, Dabrafenib + Trametinib + GSK2141795				
Phase I Registrations				
Dabrafenib + GSK2141795 50mg	0	0	0	3
Dabrafenib + GSK2141795 75mg	2	0	1	9
Dabrafenib + Trametinib 1.5mg + GSK2141795 25mg	0	4	0	4
Dabrafenib + Trametinib 1.5mg + GSK2141795 50 mg	3	0	0	3
Dabrafenib + Trametinib 1.5mg + GSK2141795 75 mg	3	0	0	3
	8	4	1	22
S1320 Adv, BRAF Mut, Intermittent vs Continuous Dabrafenib and Trametinib				
Lead-in Continuous Dosing	42	39	6	87
Randomization				
Continuous Dosing	23	13	0	36
Intermittent Dosing	20	13	1	34
	43	26	1	70
S1404 Adj, HD-IFN vs MK-3475				
Tissue for PD-L1 testing	8	0	0	8
Randomization				
High Dose Interferon Alfa-2b	2	0	0	2
MK-3475 (Pembrolizumab)	2	0	0	2
	4	0	0	4
E1609 Adjuvant Ipilimumab vs Interferon*				
Total Registrations	0	0	36	500
E2607 Adv, Dasatinib in KIT+ Patients*				
Total Registrations	1	0	0	5
E3612 Adv, Ipilimumab ± Bevacizumab*				
Total Registrations	1	3	0	4
EA6134 Adv, Dabrafenib/Trametinib=>Ipilimumab/Nivolumab vs Ipilimumab/Nivolumab=>Dabrafenib/Trametinib				
Total Registrations	2	0	0	2

* 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

Objectives

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

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

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

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

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

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

Patient Population

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

Patients must be 18 years of age or older. Patients must have had their blood drawn for viral status testing for HIV, HBV and HCV or provide acceptable viral status documentation prior to registration, as defined in the protocol. Note that

patients must have blood drawn for testing prior to registration for any of the three viruses not covered by the documentation. Patients are allowed to participate in other clinical trials.

Accrual Goals

A total of 3,061 patients will be accrued to achieve 3,000 eligible patients.

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

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

Statisticians:
J Moon, M Othus

Data Coordinator:
J Barrett

Date Activated:
07/12/2013

Date Closed*:
02/02/2016

*Temporary closure

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.

To explore potential drug interactions between dabrafenib and GSK2141795 via pharmacokinectic sampling of patients enrolled on 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 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 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 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 either progressed on a single agent BRAF inhibitor or BRAF inhibitor plus MEK inhibitor 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 be able to swallow capsules and 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 can be enrolled on 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.

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

On February 2, 2016, this study was placed in temporary closure by the NCI due to drug supply issues. No new patients may be enrolled until further notice. However, drug supplies are sufficient enough so that patients currently enrolled can continue to receive protocol treatment.

Doublet Regimen:

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 completed. No dose limiting toxicities (DLT) were observed. Therefore, per protocol, the second cohort of patients to be treated at the dose level of 75 mg GSK2141795 was opened to accrual on February 3, 2014.

As of December 31, 2015, nine patients have been enrolled to the cohort investigating GSK2141795 at

the dose level of 75 mg. One patient is currently ineligible, due uncontrolled hypertension. In addition, three eligible patients did not receive any protocol treatment and are not evaluable for any of the study endpoints. Of the remaining five patients, one did not meet the protocol-specified criteria to be considered evaluable for DLTs. As of February 12, 2016, there have been no DLTs reported for the first four evaulable patients on the 75 mg cohort. Once this study is re-opened to accrual, this cohort will continue until six patients evaluable for DLTs have been enrolled.

Triplet Regimen:

The Phase I portion of this trial investigating the three drug combination of GSK2141795 + dabrafenib + trametinib was activated on February 13, 2015. The first cohort of patients treated at the dose level of 1.5 mg of trametinib and 25 mg of GSK2141795 has been completed. One of these patients did not meet the protocol-specified criteria to be considered evaluable for DLTs and was replaced. No DLT were observed among the three evaluable patients. Therefore, per protocol, the second cohort of patients to be treated at the dose level of 1.5 mg trametinib and 50 mg GSK2141795 was opened to accrual on August 28, 2015.

The second cohort of three patients treated at the dose level of 1.5 mg trametinib and 50 mg GSK2141795 has been completed. No dose limiting toxicities (DLT) were observed. Therefore, per protocol, the third cohort of patients to be treated at the dose level of 1.5 mg trametinib and 75 mg GSK2141795 was opened to accrual on December 15, 2015.

As of December 31, 2015, three patients have been enrolled to the third cohort. One of these patients did not meet the protocol-specified criteria to be considered evaluable for DLTs and will need to be replaced once the study is re-opened to accrual.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg
Colorado, U of	5
Los Angeles, U of CA	5
Ohio State Univ	5
Michigan, U of	3
Prov Portland MC/PCRC NCORP	2
San Francisco, U-CA	1
Sutter Cancer RC	1
Total (7 Institutions)	**22**

Registration, Eligibility, and Evaluability

Patients Enrolled on the Doublet Regimen

Registrations ending December 31, 2015; Data as of February 16, 2016

	TOTAL	Dabrafenib + GSK2141795 50mg	Dabrafenib + GSK2141795 75mg
NUMBER REGISTERED	12	3	9
INELIGIBLE	1	0	1
ELIGIBLE	11	3	8
Not Analyzable	3	0	3
BASELINE DISEASE STATUS			
Measurable	8	3	5
RESPONSE ASSESSMENT			
Determinable	8	3	5
ADVERSE EVENT ASSESSMENT			
Evaluable	8	3	5
DOSE-LIMITING TOXICITIES			
Evaluable	7	3	4
Not Evaluable	1	0	1

Registration, Eligibility, and Evaluability

Patients Enrolled on the Triplet Regimen

Registrations ending December 31, 2015; Data as of February 16, 2016

	TOTAL	Dabrafenib + Trametinib 1.5mg + GSK2141795 25mg	Dabrafenib + Trametinib 1.5mg + GSK2141795 50mg	Dabrafenib + Trametinib 1.5mg + GSK2141795 75mg
NUMBER REGISTERED	10	4	3	3
ELIGIBLE	10	4	3	3
Not Analyzable	1	1	0	0
BASELINE DISEASE STATUS				
Measurable	8	3	3	2
Non Measurable	1	0	0	1
RESPONSE ASSESSMENT				
Determinable	6	3	3	0
Too Early	2	0	0	2
Not Applicable	1	0	0	1
ADVERSE EVENT ASSESSMENT				
Evaluable	9	3	3	3
DOSE-LIMITING TOXICITIES				
Evaluable	6	3	3	0
Not Evaluable	1	0	0	1
Too Early	2	0	0	2

Patient Characteristics

Registrations ending December 31, 2015; Data as of February 16, 2016

	Total (n=18)	
AGE		
Median	59.8	
Minimum	18.5	
Maximum	70.3	
SEX		
Males	12	67%
Females	6	33%
HISPANIC		
No	17	94%
Unknown	1	6%
RACE		
White	17	94%
Unknown	1	6%
PRIOR BRAF INHIBITOR		
Yes	11	61%
No	7	39%
TYPE OF CANCER		
Melanoma	15	83%
Lung	2	11%
Thyroid	1	6%

Treatment Summary

Patients Enrolled on the Doublet Regimen

Registrations ending December 31, 2015; Data as of February 16, 2016

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

Treatment Summary

Patients Enrolled on the Triplet Regimen

Registrations ending December 31, 2015; Data as of February 16, 2016

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

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

Patients Enrolled on the Doublet Regimen

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2015; Data as of February 16, 2016

	Total (n=8) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Alopecia	7	1	0	0	0	0
Anemia	7	0	1	0	0	0
Anorexia	5	2	1	0	0	0
Arthralgia	7	1	0	0	0	0
Chills	6	2	0	0	0	0
Constipation	7	1	0	0	0	0
Cough	7	1	0	0	0	0
Diarrhea	7	0	1	0	0	0
Dizziness	6	2	0	0	0	0
Dry skin	7	1	0	0	0	0
Edema limbs	6	2	0	0	0	0
Fatigue	3	5	0	0	0	0
Fever	5	2	1	0	0	0
Flu like symptoms	7	1	0	0	0	0
Flushing	7	1	0	0	0	0
Gen disorders/admin site cond	7	1	0	0	0	0
Hand-Foot syndrome	6	2	0	0	0	0
Headache	6	2	0	0	0	0
Hyperglycemia	7	0	0	1	0	0
Hyperhidrosis	7	1	0	0	0	0
Hypernatremia	7	1	0	0	0	0

	Total (n=8) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Hypokalemia	7	1	0	0	0	0
Hyponatremia	7	0	0	1	0	0
Hypophosphatemia	7	0	1	0	0	0
Hypotension	7	1	0	0	0	0
Inj/poisoning/proced comp-Other	7	1	0	0	0	0
Insomnia	7	1	0	0	0	0
Lymphocyte count decreased	5	2	1	0	0	0
Myalgia	7	1	0	0	0	0
Nail ridging	7	1	0	0	0	0
Nausea	4	4	0	0	0	0
Non-cardiac chest pain	7	1	0	0	0	0
Pain	7	1	0	0	0	0
Pain in extremity	7	1	0	0	0	0
Pain of skin	7	1	0	0	0	0
Platelet count decreased	7	1	0	0	0	0
Rash maculo-papular	7	1	0	0	0	0
Renal/urinary disorders-Other	7	1	0	0	0	0
Skin/subq tissue ds-Other	5	2	0	1	0	0
Tremor	7	1	0	0	0	0
Vasc disorders-Other	7	0	0	1	0	0
Vomiting	6	2	0	0	0	0
Weight loss	6	1	1	0	0	0
MAX. GRADE ANY ADVERSE EVENT	1	3	2	2	0	0

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

Patients Enrolled on the Triplet Regimen

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2015; Data as of February 16, 2016

	Total (n=9) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	8	1	0	0	0	0
AST increased	8	1	0	0	0	0
Abdominal pain	8	1	0	0	0	0
Dehydration	8	1	0	0	0	0
Diarrhea	7	2	0	0	0	0
Dry skin	8	1	0	0	0	0
Dyspepsia	8	1	0	0	0	0
Fatigue	7	2	0	0	0	0
Fever	7	0	2	0	0	0
Hypertension	8	0	1	0	0	0
Hyponatremia	7	0	0	2	0	0
Joint effusion	8	1	0	0	0	0
Lymphocyte count decreased	8	0	0	1	0	0
Myalgia	8	1	0	0	0	0

	Total (n=9) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Nausea	7	2	0	0	0	0
Neutrophil count decreased	8	1	0	0	0	0
Rash acneiform	8	0	1	0	0	0
Tumor pain	8	1	0	0	0	0
Vomiting	8	0	0	1	0	0
Weight loss	8	1	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	1	2	2	4	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

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

Study Chairs:
A Algazi, A Daud, R Lo

Statisticians:
M Othus, J Moon, M Wu

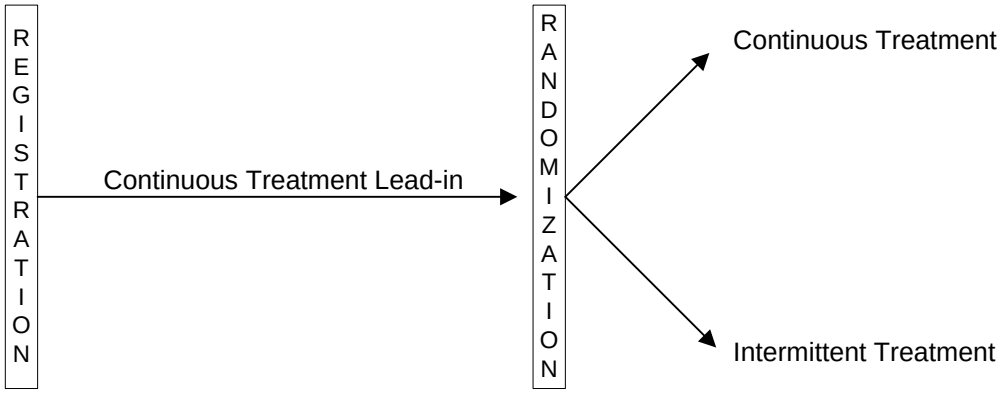
Data Coordinator:
J Barrett

Date Activated:
07/22/2014

Date Closed*:
02/02/2016

*Temporary closure

SCHEMA



Objectives

To compare progression-free survival with intermittent dosing versus continuous dosing of dabrafenib and trametinib among patients with metastatic BRAFV600E/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. BRAFV600 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 7 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

On February 2, 2016, this study was placed in temporary closure by the NCI due to drug supply issues. Drug supplies are sufficient so that patients currently enrolled can continue on treatment and may also register to the randomization step. However, no new patients may be enrolled to receive lead-in continuous dosing until further notice.

Accrual to this study has been slower then anticipated. In an effort to increase accrual, a proposed amendment would allow BRAF mutation to be documented by any assay as long as it is performed in a CLIA-certified laboratory.

As of December 31, 2015, 87 patients have been registered. Three patients are currently ineligible: one due to having a Zubrod performance status of 2 at the time of enrollment, one due to inadequate cardiac function, and one due to untreated brain metastases In addition, one eligible patient who refused protocol treatment and was never randomized, is not evaluable for any of the study endpoints.

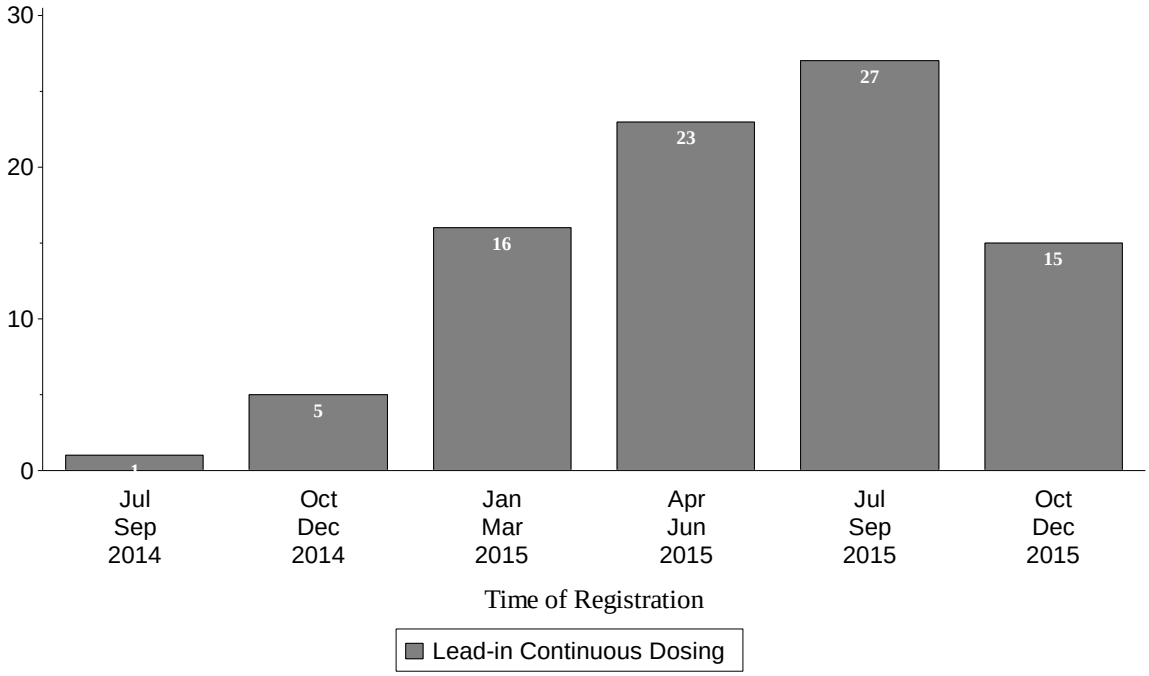
Eighty patients have been assessed for adverse events related to lead-in continuous dosing. There has been one treatment-related death due to sepsis.

Seventy patients have been randomized between intermittent and continuous dosing. Three patients are currently ineligible: two that were ineligible for the trial at the initial registration, and one patient who

had disease progression during the lead-in continuous phase.

Sixty patients have been assessed for adverse events during the randomized portion of the trial. One patient has experienced a Grade 4 treatment-related adverse event due to fever.

Initial Registrations By 3 Month Intervals



Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
ECOG-ACRIN	23	Kansas, U of	2
Kaiser Perm NCORP	9	Los Angeles, U of CA	2
San Francisco, U-CA	7	Loyola University	2
Alliance	5	Michigan, U of	2
Ohio State Univ	5	Ozarks NCORP	2
Utah, U of	5	Wichita NCORP	2
Arkansas, U of	3	Boston Medical Ctr	1
Heartland NCORP	3	Lahey Hosp & Med Ctr	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	3	Nevada CRF NCORP	1
NRG	3	PCRC NCORP	1
Southeast COR NCORP	3	**Total (22 Institutions)**	**87**
Arizona MC, U of	2		

Registration, Eligibility, and Evaluability

Lead-In Continuous Dosing

Registrations ending December 31, 2015; Data as of February 16, 2016

	Lead-in Continuous Dosing
NUMBER REGISTERED	87
INELIGIBLE	3
ELIGIBLE	84
Not Analyzable	1
ADVERSE EVENT ASSESSMENT	
Evaluable	80
Too Early	3

Treatment Summary

Registrations ending December 31, 2015; Data as of February 16, 2016

	Lead-in Continuous Dosing
NUMBER ON PROTOCOL TREATMENT	3
NUMBER OFF PROTOCOL TREATMENT	80
REASON OFF TREATMENT	
Treatment completed as planned	69
Adverse Event or side effects	3
Refusal unrelated to adverse event	1
Progression/relapse	4
Death	2
Other - not protocol specified	0
Reason under review	1
MAJOR PROTOCOL DEVIATIONS	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 or Unknown Have Been Suppressed

Registrations ending December 31, 2015; Data as of February 16, 2016

	Lead-in Continuous Dosing (n=80) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**
AST increased	77	3	0	0
Acute kidney injury	78	1	1	0
Anorexia	79	1	0	0
Blood bilirubin increased	79	1	0	0
Blood/lymph disorder-Other	79	1	0	0
Cardiac troponin T increased	79	1	0	0
Dehydration	76	4	0	0
Diarrhea	79	1	0	0
ECG QT corrected int prolong	79	1	0	0
Ejection fraction decreased	79	0	1	0
Epistaxis	79	1	0	0
Erythema multiforme	79	1	0	0
Febrile neutropenia	79	1	0	0
Fever	79	1	0	0
Hyponatremia	78	2	0	0
Hypoxia	79	1	0	0
Lipase increased	79	1	0	0
Lymphocyte count decreased	79	1	0	0
Mucositis oral	79	1	0	0
Nausea	79	1	0	0
Neutrophil count decreased	79	1	0	0
Proteinuria	79	1	0	0
Rash acneiform	79	1	0	0
Rash maculo-papular	79	1	0	0
Sepsis	79	0	0	1
Urinary tract infection	79	1	0	0
Vasc disorders-Other	79	1	0	0
MAX. GRADE ANY ADVERSE EVENT	60	19	0	1

Registration, Eligibility, and Evaluability

Randomization

Registrations ending December 31, 2015; Data as of February 16, 2016

	TOTAL	Continuous Dosing	Intermittent Dosing
NUMBER REGISTERED	70	36	34
INELIGIBLE	3	2	1
ELIGIBLE	67	34	33
Analyzable, Pend. Elig.	3	3	0
RESPONSE ASSESSMENT			
Determinable	49	25	24
Too Early	18	9	9
ADVERSE EVENT ASSESSMENT			
Evaluable	60	29	31
Too Early	7	5	2

Patient Characteristics

Randomization

Registrations ending December 31, 2015; Data as of February 16, 2016

	Continuous Dosing (n=34)		Intermittent Dosing (n=33)	
AGE				
Median	62.1		65.0	
Minimum	24.5		26.3	
Maximum	81.3		82.0	
SEX				
Males	23	68%	24	73%
Females	11	32%	9	27%
HISPANIC				
No	34	100%	33	100%
RACE				
White	34	100%	32	97%
Multi-Racial	0	0%	1	3%
PERFORMANCE STATUS				
0	22	65%	21	64%
1	12	35%	12	36%
PRIMARY TYPE				
Cutaneous	28	82%	22	67%
Unknown primary	4	12%	10	30%
Data pending	2	6%	1	3%

	Continuous Dosing (n=34)		Intermittent Dosing (n=33)	
STAGE				
III	3	9%	5	15%
IV	31	91%	28	85%
SITE(S) OF DISTANT METASTASES				
Bone	4	12%	6	18%
Brain/CNS	2	6%	1	3%
Liver	9	26%	6	18%
Lymph node, skin, soft tissue	18	53%	14	42%
Lung	16	47%	17	52%
Other, visceral	7	21%	8	24%
Other non-visceral	7	21%	5	15%
Data pending	3	9%	5	15%
LDH				
Elevated (>IULN)	15	44%	15	45%
Normal	19	56%	18	55%
PRIOR THERAPY WITH IMMUNE CHECKPOINT INHIBITOR				
Yes	10	29%	8	24%
No	24	71%	25	76%
PRIOR BIOLOGIC THERAPY				
No	11	32%	15	45%
Yes	1	3%	1	3%
Data pending	22	65%	17	52%
PRIOR CHEMOTHERAPY				
No	12	35%	12	36%
Yes	2	6%	3	9%
Data pending	20	59%	18	55%
PRIOR IMMUNOTHERAPY				
No	10	29%	11	33%
Yes	6	18%	5	15%
Data pending	18	53%	17	52%
PRIOR RADIATION THERAPY				
No	32	94%	21	64%
Yes	2	6%	12	36%
PRIOR SURGERY				
No	8	24%	7	21%
Yes	26	76%	26	79%

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, 2015; Data as of February 16, 2016

	Continuous Dosing (n=29) Grade						Intermittent Dosing (n=31) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	28	1	0	0	0	0	27	3	1	0	0	0
AST increased	26	1	0	2	0	0	25	5	0	1	0	0
AV block first degree	29	0	0	0	0	0	30	1	0	0	0	0
Abdominal pain	29	0	0	0	0	0	29	2	0	0	0	0
Alkaline phosphatase increased	23	5	1	0	0	0	27	3	1	0	0	0
Alopecia	28	1	0	0	0	0	30	1	0	0	0	0
Anemia	21	7	1	0	0	0	27	3	1	0	0	0
Anorexia	26	2	1	0	0	0	29	1	1	0	0	0
Arthralgia	27	1	1	0	0	0	28	1	2	0	0	0
Blood bilirubin increased	29	0	0	0	0	0	30	1	0	0	0	0
Blood/lymph disorder-Other	29	0	0	0	0	0	30	1	0	0	0	0
Blurred vision	29	0	0	0	0	0	30	1	0	0	0	0
CPK increased	28	0	1	0	0	0	31	0	0	0	0	0
Chills	24	3	2	0	0	0	24	3	3	1	0	0
Concentration impairment	29	0	0	0	0	0	30	1	0	0	0	0
Constipation	27	2	0	0	0	0	28	3	0	0	0	0
Creatinine increased	28	1	0	0	0	0	30	0	1	0	0	0
Dehydration	25	3	0	1	0	0	31	0	0	0	0	0
Depression	28	0	1	0	0	0	31	0	0	0	0	0
Diarrhea	23	4	2	0	0	0	27	4	0	0	0	0
Dizziness	28	1	0	0	0	0	29	2	0	0	0	0
Dry eye	29	0	0	0	0	0	30	1	0	0	0	0
Dry mouth	27	1	1	0	0	0	30	1	0	0	0	0
Dry skin	28	1	0	0	0	0	30	1	0	0	0	0
Dysgeusia	26	3	0	0	0	0	29	1	1	0	0	0
Dyspepsia	27	1	1	0	0	0	31	0	0	0	0	0
Dyspnea	29	0	0	0	0	0	29	2	0	0	0	0
ECG QT corrected int prolong	28	1	0	0	0	0	31	0	0	0	0	0
Edema face	29	0	0	0	0	0	30	1	0	0	0	0
Edema limbs	27	2	0	0	0	0	31	0	0	0	0	0
Ejection fraction decreased	27	0	2	0	0	0	27	0	2	2	0	0
Fatigue	12	11	6	0	0	0	17	8	5	1	0	0
Fever	18	5	5	1	0	0	27	2	1	0	1	0
Fibr deep connect tissue	28	0	0	1	0	0	31	0	0	0	0	0
Flu like symptoms	23	4	1	1	0	0	30	0	1	0	0	0
Flushing	29	0	0	0	0	0	30	1	0	0	0	0
GERD	28	1	0	0	0	0	31	0	0	0	0	0
Gait disturbance	29	0	0	0	0	0	30	1	0	0	0	0
Gen disorders/admin site cond	29	0	0	0	0	0	28	2	1	0	0	0
Generalized muscle weakness	28	0	1	0	0	0	29	2	0	0	0	0
Glucose intolerance	28	1	0	0	0	0	31	0	0	0	0	0
Hand-Foot syndrome	29	0	0	0	0	0	30	0	1	0	0	0
Headache	27	2	0	0	0	0	26	5	0	0	0	0
Heart failure	28	1	0	0	0	0	31	0	0	0	0	0

	Continuous Dosing (n=29) Grade						Intermittent Dosing (n=31) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Hematuria	28	1	0	0	0	0	31	0	0	0	0	0
Hemoglobin increased	28	1	0	0	0	0	31	0	0	0	0	0
Hyperglycemia	26	2	0	1	0	0	27	0	4	0	0	0
Hyperhidrosis	28	1	0	0	0	0	31	0	0	0	0	0
Hyperkalemia	28	1	0	0	0	0	31	0	0	0	0	0
Hypersomnia	28	1	0	0	0	0	31	0	0	0	0	0
Hypertension	26	1	2	0	0	0	29	0	1	1	0	0
Hypoalbuminemia	25	3	1	0	0	0	27	4	0	0	0	0
Hypocalcemia	26	3	0	0	0	0	31	0	0	0	0	0
Hypoglycemia	28	1	0	0	0	0	31	0	0	0	0	0
Hypokalemia	28	1	0	0	0	0	31	0	0	0	0	0
Hyponatremia	28	1	0	0	0	0	27	4	0	0	0	0
Hypophosphatemia	29	0	0	0	0	0	29	0	2	0	0	0
Hypotension	28	0	1	0	0	0	30	1	0	0	0	0
Hypothyroidism	29	0	0	0	0	0	30	0	1	0	0	0
Infections/infestations-Other	29	0	0	0	0	0	30	0	0	1	0	0
Insomnia	29	0	0	0	0	0	30	1	0	0	0	0
Investigations-Other, specify	29	0	0	0	0	0	29	2	0	0	0	0
Lipase increased	25	3	1	0	0	0	27	0	2	2	0	0
Localized edema	28	0	1	0	0	0	31	0	0	0	0	0
Lymphocyte count decreased	28	0	1	0	0	0	31	0	0	0	0	0
Lymphocyte count increased	28	0	1	0	0	0	31	0	0	0	0	0
MS/connective tissue disorder	28	0	1	0	0	0	31	0	0	0	0	0
Metab/nutrition disorders-Other	28	1	0	0	0	0	31	0	0	0	0	0
Mucositis oral	26	2	0	1	0	0	31	0	0	0	0	0
Myalgia	28	1	0	0	0	0	29	1	1	0	0	0
Nausea	20	7	2	0	0	0	23	6	2	0	0	0
Neutrophil count decreased	24	2	1	2	0	0	29	2	0	0	0	0
Non-cardiac chest pain	29	0	0	0	0	0	30	1	0	0	0	0
Pain	28	1	0	0	0	0	31	0	0	0	0	0
Pain in extremity	28	1	0	0	0	0	30	1	0	0	0	0
Peripheral sensory neuropathy	28	1	0	0	0	0	30	1	0	0	0	0
Personality change	28	0	1	0	0	0	31	0	0	0	0	0
Platelet count decreased	25	3	0	1	0	0	30	1	0	0	0	0
Proteinuria	27	1	1	0	0	0	31	0	0	0	0	0
Pruritus	29	0	0	0	0	0	28	2	1	0	0	0
Purpura	28	1	0	0	0	0	31	0	0	0	0	0
Rash acneiform	24	4	1	0	0	0	26	5	0	0	0	0
Rash maculo-papular	24	2	3	0	0	0	28	2	1	0	0	0
Serum amylase increased	29	0	0	0	0	0	27	2	1	1	0	0
Sinus tachycardia	29	0	0	0	0	0	30	0	1	0	0	0
Sinusitis	28	0	1	0	0	0	31	0	0	0	0	0
Skin infection	28	1	0	0	0	0	31	0	0	0	0	0
Skin/subq tissue ds-Other	27	1	0	1	0	0	27	4	0	0	0	0
Thromboembolic event	28	0	0	1	0	0	31	0	0	0	0	0
Upper respiratory infection	28	0	1	0	0	0	31	0	0	0	0	0
Urinary frequency	28	1	0	0	0	0	31	0	0	0	0	0
Urinary urgency	28	1	0	0	0	0	31	0	0	0	0	0
Vomiting	26	2	1	0	0	0	29	2	0	0	0	0
Weight loss	27	1	1	0	0	0	27	3	1	0	0	0

	Continuous Dosing (n=29) Grade						Intermittent Dosing (n=31) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
White blood cell decreased	21	3	3	2	0	0	28	3	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	5	5	11	8	0	0	2	7	13	8	1	0

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

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

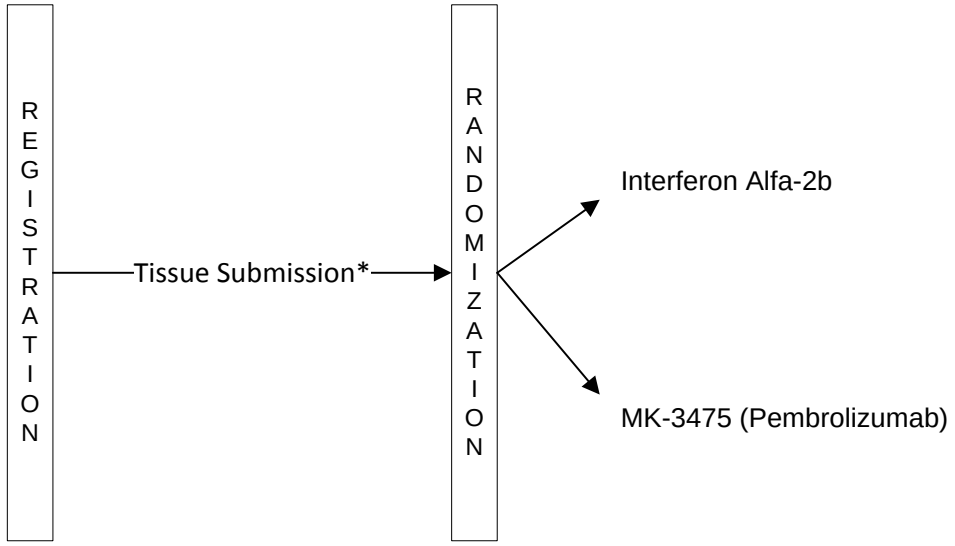
Date Activated:
10/15/2015

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

Statisticians:
M Othus, H Li, J Moon

Data Coordinators:
D Heaney, J Barrett

SCHEMA



*PD-L1 status determined by central laboratory

Objectives

Co-Primary Objectives:

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

To compare overall survival between the two regimens within the PD-L1 positive subgroup in this population.

To compare relapse-free survival between the two regimens among all patients and within the PD-L1 positive subgroup in this population.

Secondary Objectives:

To estimate overall survival and relapse-free survival for patients who are PD-L1 negative or PD-L1 indeterminate in this population.

To compare overall survival and relapse-free between the two regimens within the PD-L1 positive and PD-L1 negative subgroups and to investigate the interaction between PD-L1 status (positive versus negative) and treatment arm.

To assess the safety and tolerability of the two regimens.

To bank tissue and whole blood.

To evaluate PD-L1 expression through immunohistochemistry assay.

To compare treatment-related side effects that may have an impact on the health-related domains of quality of life between the two regimens using the FACT-BRM and the EQ-5D-3L.

To evaluate exposure-response analyses for activity and efficacy, potential pharmacodynmaic biomarkers, and safety of MK-3475 (pembrolizumab) by performing pharmacokinectic (PK) and anti-drug antibody (ADA) testing on patients randomized to receive MK-3475 (pembrolizumab).

Patient Population

Patients must have histologically confirmed selected Stage III (IIIA/N2a, IIIB, IIIC) 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 willing to have blood draws for PK/ADA analysis should the patient be randomized to receive MK-3475 (pembrolizumab). 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 IIIC vs. IV; (2) PD-L1 status: positive vs negative vs indeterminant. The patient's PD-L1 status will be blinded.

Accrual Goals

The accrual goal of this study is to randomize 1,240 eligible patients. Up to two formal interim analyses of overall survival will be performed when 55% and 85% of the expected deaths across both arms combined have been observed. The final analysis of relapse-free survival will be performed when all patients are off protocol therapy (expected to be one year after the last eligible patients is randomized) and 100% of expected events for relapse-free survival have been observed.

Summary Statement

On October 28, 2015, the FDA expanded the approval of ipilimumab in melanoma to include adjuvant treatment of patients with stage III melanoma with pathologic involvement of regional lymph nodes >1 mm who have undergone complete resection including total lymphadenectomy. In response to this development, a proposed amendment to this study has been submitted to the NCI. The amendment would change the control arm of this study to investigator/patient choice between high-dose interferon alfa-2b or ipilimumab.

As of December 31, 2015, a total of eight patients have been screened for PD-L1 status and four patients have been randomized.

Registration by Institution

Initial Registration

Registrations ending December 31, 2015

Institutions	Total Reg
Alliance	2
ECOG-ACRIN	2
Dayton NCORP	1
Heartland NCORP	1
MD Anderson CC	1
NRG	1
Total (6 Institutions)	**8**

Registration, Eligibility, and Evaluability

Initial Registration

Registrations ending December 31, 2015; Data as of January 8, 2016

	Tissue for PD-L1 testing
NUMBER REGISTERED	8
ELIGIBLE	8
Analyzable, Pend. Elig.	8

Registration by Institution

Randomization

Registrations ending December 31, 2015

Institutions	Total Reg
ECOG-ACRIN	2
Alliance	1
Dayton NCORP	1
Total (3 Institutions)	**4**

EA6134 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Randomized Phase III Trial of Dabrafenib plus Trametinib followed by Ipilimumab plus Nivolumab at Progression versus Ipilimumab plus Nivolumab followed by Dabrafenib plus Trametinib at Progression in Patients with Advanced BRAF^{v600} Mutant Melanoma

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Participants:
ECOG-ACRIN, CTSU

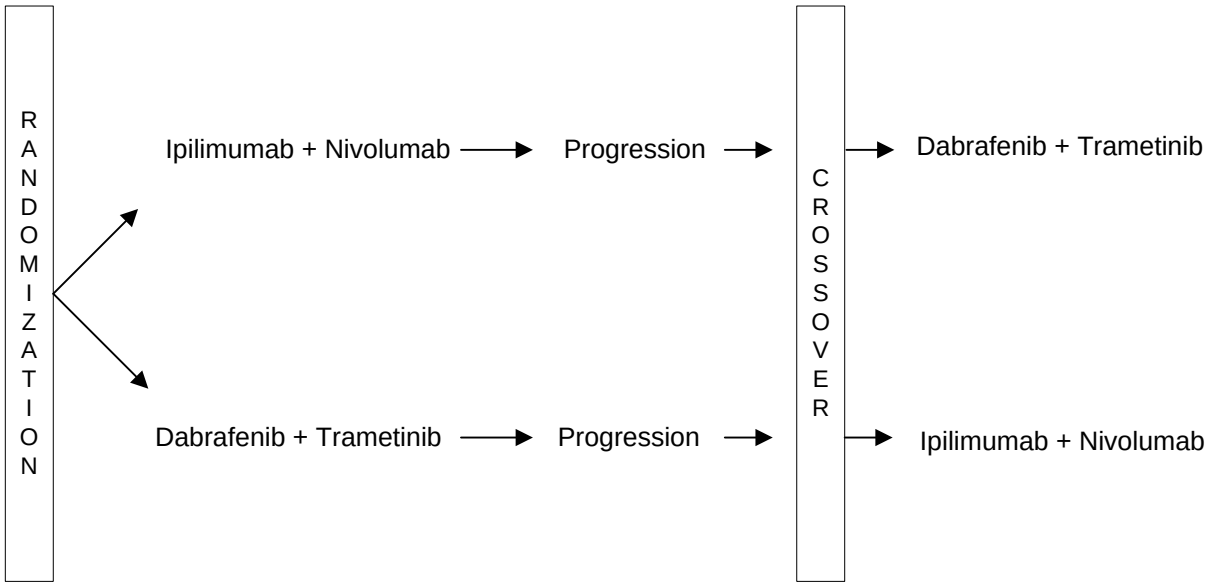
Study Chairs:
M Atkins (ECOG-ACRIN), B Chmielowski (SWOG)

Date Activated:
07/13/2015

Date Closed*:
02/02/2016

*temporary closure

SCHEMA



Objectives

To determine whether initial treatment with either combination ipilimumab + nivolumab (with subsequent dabrafenib in combination with trametinib) or dabrafenib in combination with trametinib (with subsequent ipilimumab + nivolumab) significantly improves 2-year overall survival (OS) in patients with unresectable stage III or stage IV BRAF^{V600} mutant melanoma.

To evaluate the impact of initial treatment on overall survival.

To evaluate the anti-tumor activities (RECIST-defined response rate, median PFS) and safety profiles of ipilimumab + nivolumab and dabrafenib + trametinib.

To evaluate the activity (RECIST-defined response rate, median PFS) and safety of dabrafenib + trametinib in patients who have had disease progression on ipilimumab + nivolumab and in comparison to its activity and safety in ipilimumab + nivolumab naïve patients.

To evaluate the activity of ipilimumab + nivolumab (RECIST-defined response rate, median PFS) and safety in patients who have had disease progression on dabrafenib + trametinib and in comparison to its activity and safety in dabrafenib + trametinib naïve patients.

To assess the feasibility of crossover to the alternative treatment strategy, defined as the percentage of patients who are able to crossover from one arm to the other and complete at least an initial course (12 weeks) of treatment after crossover without intervening symptomatic disease progression or treatment limiting toxicity.

This study also includes objectives related to translational medicine and patient-reported outcomes. Please refer to the protocol for details.

Patient Population

Patients must have histological or cytological confirmation of melanoma which is stage IV or unresectable stage III and clearly progressive. Patients must have $BRAF^{V600E}$ or $BRAF^{V600K}$ mutations, identified by an FDA-approved test at a CLIA-certified lab. Patients must have measurable disease as defined by RECIST 1.1. Patients must not have currently active CNS metastases. Patients may have treated brain metastases (with either surgical resection or stereotactic radiosurgery (SRS)) that have been stable on head MRI or contrast CT scan for at least four weeks following treatment and within four weeks prior to randomization, provided they have not have taken any steroids for the purpose of managing their brain metastases for at least 14 days prior to randomization. Patients with only whole brain irradiation for treatment of CNS metastases are ineligible. Patients with a history of RAS mutation-positive tumors are not eligible. Patients must have aggressive melanoma that results in a serum LDH of more than 10 times the institutional upper limit of normal.

Patients may have had prior systemic therapy in the adjuvant setting; however this adjuvant treatment must not have included a CTLA4 or PD1 pathway blocking antibody or a BRAF/MEK inhibitor. Patients must not have received any prior systemic therapy for stage IV disease. Patients may have received prior radiation therapy or surgery.

Patients must have adequate hematologic, hepatic, and renal function and an ECOG performance status of 0-1. Patients must not have any ongoing or active infections requiring parenteral antibiotics. Patients must not have a history of bleeding diathesis or need for concurrent anticoagulation. Therapeutic level dosing of warfarin can be used with close monitoring of PT/INR. Patients must not have a history of or evidence of cardiovascular risks. Patients must not have evidence of active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection. Patients must no be known to be HIV infected. Patients must not have active autoimmune disease or a history of autoimmune disease that might recur, which may affect vital organ function or require immune suppressive treatment including systemic corticosteroids. Patients with vitiligo, endocrine deficiencies including thyroiditis managed with replacement hormones including physiologic corticosteroids are eligible. Patients with rheumatoid arthritis and other arthropathies, Sjögren's syndrome and psoriasis controlled with topical medication and patients with positive serology, such as antinuclear antibodies (ANA), are eligible provided they do not require systemic immune suppression treatment. Patients must not be taking any medications or substances that are strong inhibitors or inducers of CYP3A or CYP2C8. Patients must not have evidence of interstitial lung disease or pneumonitis, or a history of retinal vein occlusion (RVO) or malabsorption, swallowing difficulty, or other conditions that would interfere with the ingestion or absorption of dabrafenib or trametinib. All females of childbearing potential must have a pregnancy test.

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following: (1) ECOG performance status: 0 vs 1; (2) serum LDH: normal vs elevated (defined as above IULN).

Accrual Goals

The accrual goal is 270 eligible patients.

Summary Statement

On February 2, 2016, this study was placed in temporary closure by the NCI due to drug supply issues. Patients currently enrolled can continue on treatment. However, no new patients may be enrolled until further notice.

As of December 31, 2015, there have been 10 registrations to this study, including two CTSU registrations by SWOG institutions: one by UCLA and one by Sutter Cancer RC. The complete summary of this study is available on the SWOG web site.

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

NCI-MATCH: Molecular Analysis for Therapy Choice

Participants:
ECOG-ACRIN, CTSU

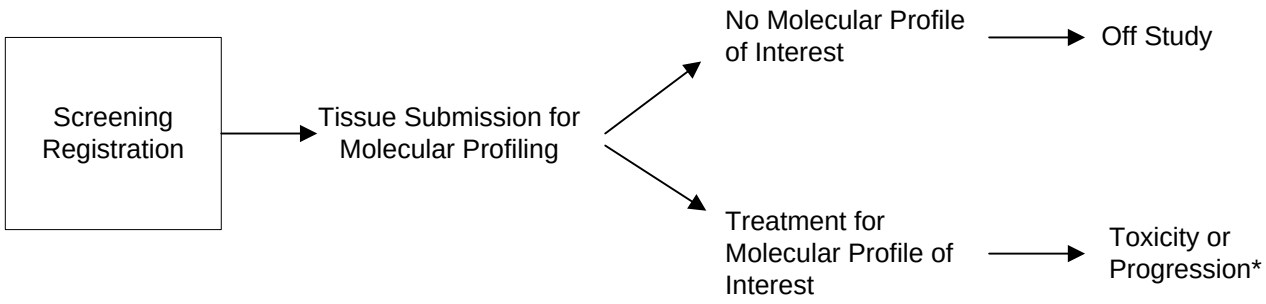
Study Chairs:
K Flaherty (ECOG-ACRIN), P O'Dwyer (ECOG-ACRIN), A Chen (NCI), B Conley (NCI)

Date Activated:
08/12/2015

Date Closed*:
11/11/2015

*temporary closure

SCHEMA



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

Objectives

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

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

To evaluate the time until death or disease progression.

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

Patient Population

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

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

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

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

Accrual Goals

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

Summary Statement

This study activated on August 12, 2015, with 10 subprotocols included in the activation. Only sites utilizing the CIRB as their IRB of record are able to participate in the trial. The study was temporarily closed to accrual on November 11, 2015, after rapid accrual of 795 patients to the screening step in only three months, including 119 SWOG registrations. This pause in patient enrollment for interim analysis and review is expected to lift by May 2016, when an additional 12 to 14 new subprotocols are expected to be open.