

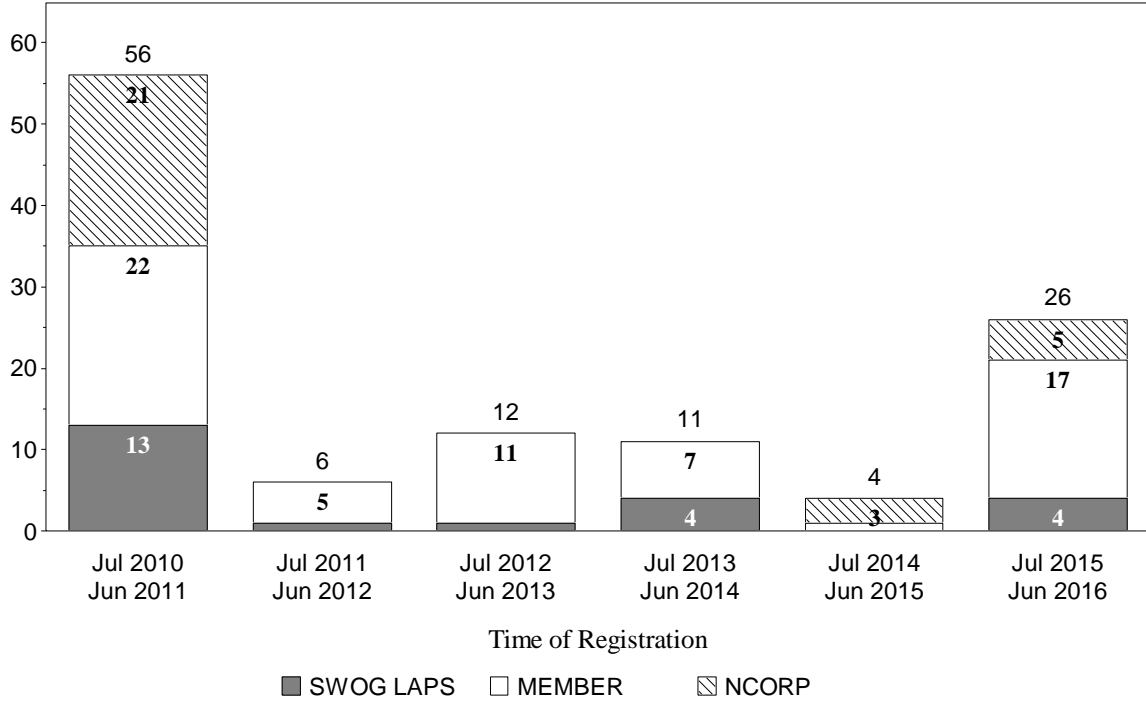
EARLY THERAPEUTICS AND RARE CANCERS COMMITTEE

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Patient Registrations to Studies

By 12 Month Intervals
EARLY THERAPEUTICS AND RARE CANCERS COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

EARLY THERAPEUTICS AND RARE CANCERS COMMITTEE

	Jan 2016 Jun 2016	Jul 2015 Dec 2015	Jan 2015 Jun 2015	All Patients
A071102 GBM, adj TMZ +/- Veliparib*				
Total Registrations	10	8	4	22
A071401 Prog. Meningiomas, SMO/AKT/NF2 Inhib*				
Total Registrations	4	0	0	4
ARST1321 Non Rhabdo STS, Pazopanib (PAZNTIS)*				
Total Registrations	1	1	0	2
EAY131 MATCH*				
Total Registrations	2	0	0	2

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

S1609 Phase II

Coordinating Group: SWOG

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

Participants:

SWOG, CTSU

Study Chairs:

S Patel, Y Chae

Statisticians:

M Othus, M Plets

Data Coordinator:

L Kingsbury

Objectives

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

To evaluate toxicities in each cohort.

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

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

Patient Population

Patients must have enrolled in EAY131, NCI-MATCH, and were either not matched to a molecularly guided therapy or progressed on molecularly matched therapy and have no further molecularly matched treatment recommendations per EAY131. Patients must have measurable disease and histologically confirmed rare cancer and/or cancer of unknown primary specified on the list of eligible rare cancer histologic cohorts in the S1609 protocol. Patients who do not qualify for one of the histologic cohorts may be considered for registration in the "Not

Otherwise Categorized" Rare Tumors cohort with confirmation of the study chairs.

Patients must not have received prior anti-PD-1 or anti-PD-L1 therapy. Other immunotherapy is permitted, provided that it is completed at least seven days prior to registration. Patients who had prior immune-related adverse event with prior immunotherapy are not eligible. Patients with brain metastases or primary brain tumors must have completed treatment, surgery or radiation therapy \geq 28 days prior to registration and have stable disease at time of registration. Patients with metastatic brain parenchymal disease must have been treated and patients must be off steroids for seven days prior to registration. Patients must have been off all other systemic anti-cancer therapy at least seven days prior to registration and any therapy-induced toxicity must have recovered to \leq Grade 1.

Patients must have a Zubrod performance status of 0-2 and have adequate hematologic, hepatic, renal, thyroid, and adrenal axis function. Patients must not have active autoimmune disease that has required systemic treatment in past two years or any uncontrolled intercurrent illness. Patients must not have known active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection at time of registration. Patients with HBV or HCV that have an undetectable viral load, or in the opinion of the

treating investigator is well controlled, are eligible. Patients who are known to be HIV-positive at registration are eligible if they meet the conditions outlined in the protocol.

Stratification/Descriptive Factors

Patients will be described by histologic cohorts.

Accrual Goals

The accrual goal for this study is 334 patients to achieve 300 eligible patients. A two-stage design will be used. Initially, six eligible patients will be registered to each histologic cohort. If at least one response is observed within a cohort, an additional 10 eligible patients will be registered to that cohort.

A071102 Phase II-III SWOG Supported CTSU Study

Coordinating Group: Alliance

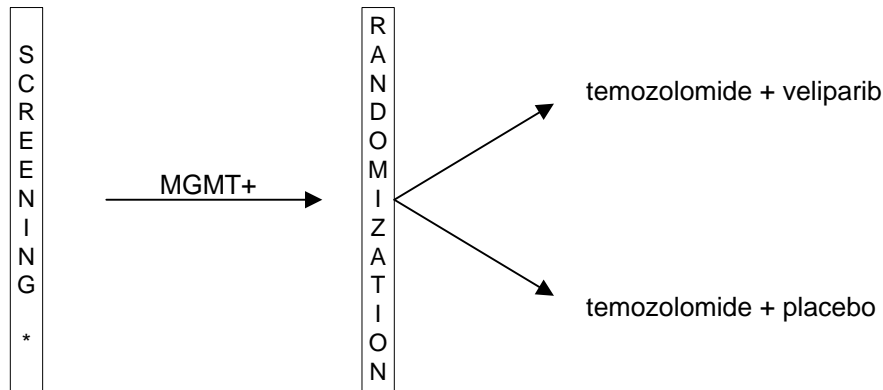
A Phase II/III Randomized Trial of Veliparib or Placebo in Combination with Adjuvant Temozolomide in Newly Diagnosed Glioblastoma with MGMT Promoter Hypermethylation

Participants:
Alliance, CTSU

Date Activated:
09/19/2014

Study Chairs:
J Sarkaria (Alliance), D Piccioni (SWOG)

SCHEMA



*Central pathology review and central laboratory MGMT testing.

Objectives

Test whether the experimental combination of ABT-888 (veliparib) combined with temozolomide (TMZ), compared to the control of placebo combined with TMZ, significantly extends overall survival in newly diagnosed GBM patients with tumor MGMT promoter hypermethylation.

Test whether the experimental treatment significantly extends progression-free survival.

Test whether the experimental treatment improves objective tumor response.

Test whether the experimental treatment is associated with significantly greater rates of grade 3 or higher adverse events.

Patient Population

Patients must have newly diagnosed Grade IV intracranial glioblastoma or gliosarcoma that has been confirmed by central pathology review and must have sufficient tissue available for MGMT methylation status evaluation. Patients who have had local MGMT testing and results revealed an unmethylated tumor status are not eligible. Patients may have measurable or non-measurable disease, but patients must not have progressive disease.

Patients must have completed standard radiotherapy and concomitant TMZ therapy. Patients must not have received any other prior therapy (neo-adjuvant or adjuvant). Patients receiving anticoagulation must be on a stable dose two weeks prior to registration. Patients must not have had a major surgery within 14 days prior to registration.

Patients must have adequate hematologic, renal, and hepatic function and an ECOG performance status of 0-2. Patients must not have a seizure disorder that is uncontrolled at the time of registration, Grade 3 or Grade 4 thromboembolic disease within six months of registration or a known history of prolonged QT syndrome.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) age group: < 70 vs ≥ 70 years; (2) ECOG performance status: 0-1 vs 2; and (3) extent of resection: gross total resection vs subtotal resection or biopsy.

Accrual Goals

A total of 440 patients will be accrued to this study to achieve 400 eligible patients. This includes up to 322 in the Phase II portion and an additional 118 in the Phase III portion. Interim analyses will be performed after 65% information is attained for the Phase II comparison and after 53% information is attained for the Phase III comparison. Accrual will be suspended at the end of the Phase II portion of the trial (once 293 patients have been accrued) until 160 deaths have been observed.

Summary Statement

Alliance reported a total accrual of 189 patients as of June 30, 2016, including 22 SWOG registrations. The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Rochester, Univ of	5	Baylor College	1
San Diego, U of CA	4	Northwestern Univ	1
St Joseph Med Ctr/PCRC NCORP	3	St Jude Medical Ctr/Irvine, U of CA	1
Kaiser Perm NCORP	2	Yale University	1
Ozarks NCORP	2	Total (10 Institutions)	22
Portsmouth Reg Hosp/Lahey Hosp & Med Ctr	2		

A071401 Phase II SWOG Supported CTSU Study

Coordinating Group: Alliance

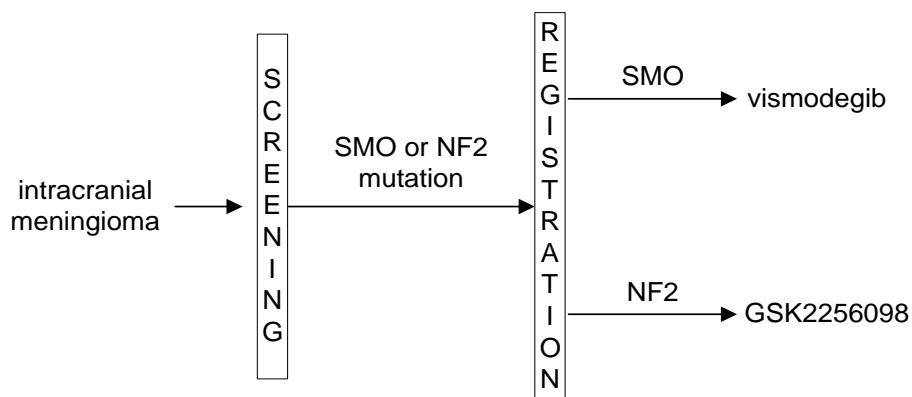
Phase II Trial of SMO/ AKT/ NF2 Inhibitors in Progressive Meningiomas with SMO/ AKT/ NF2 Mutations

Participants:
Alliance, CTSU

Date Activated:
08/06/2015

Study Chairs:
P Brastianos (Alliance), E Galanis (Alliance),
D Piccioni (SWOG)

SCHEMA



Objectives

To determine the activity of a SMO inhibitor in patients with meningiomas harboring SMO mutations as measured by 6-month progression-free survival (PFS) and response rate.

To determine the activity of a FAK inhibitor in patients with meningiomas harboring NF2 mutations as measured by 6-month PFS and response rate.

To determine overall survival and progression-free survival of SMO and FAK inhibitors in patients with meningioma.

To determine adverse event rates of SMO and FAK inhibitors in patients with meningioma.

To evaluate genetic biomarkers in meningioma.

To evaluate dynamic contrast enhanced MRI during treatment with SMO and FAK inhibitors for meningioma.

Patient Population

Patients must have histologically proven intracranial meningioma (any grade) as documented by central pathology and presence of SMO or NF2 mutation. Patients must have residual measurable disease immediately following surgery or progressive measurable disease. Patients must not have metastatic meningioma. Patients with a history of NF and other stable CNS tumors are eligible if lesions have been stable for six months prior to registration.

Patients must not have received chemotherapy, other investigational agents or a craniotomy within 28 days prior to registration. Patients who received external beam radiation, interstitial brachytherapy or radiosurgery must have completed therapy more than

24 weeks prior to registration. For those patients receiving steroid therapy, steroid dosing must be stable for at least four days prior to registration. Patients must not be planning to receive concurrent investigational agents or other meningioma-directed therapy while on study.

Patients must have adequate hematologic, renal, cardiac, and hepatic function and an ECOG performance status of 0-2. Patients must not have known active hepatitis B or C, Child Pugh Class B or C liver disease, uncontrolled gastric ulcer disease, uncontrolled diabetes, or uncontrolled hypertension. Patients must not have abdominal fistula, GI perforation, or intra-abdominal abscess within 28 days prior to registration. Patients with an SMO mutation assigned to receive vismodegib must be 30 years of age or older. Patients with an NF2 mutation must be 18 years of age or older.

Stratification/Descriptive Factors

Patients will be described by tumor grade: Grade I vs Grade II/III.

Accrual Goals

A total of 56 patients will be accrued to this study to achieve 12 eligible patients per tumor grade per arm. There is no planned interim analysis.

Summary Statement

Alliance reported a total accrual of 21 patients as of June 30, 2016, including four SWOG registrations. The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

<u>Institutions</u>	<u>Total Reg</u>
San Diego, U of CA	2
Colorado, U of	1
CORA NCORP	1
Total (3 Institutions)	4

ARST1321 Phase II-III SWOG Supported CTSU Study

Coordinating Groups: COG and NRG

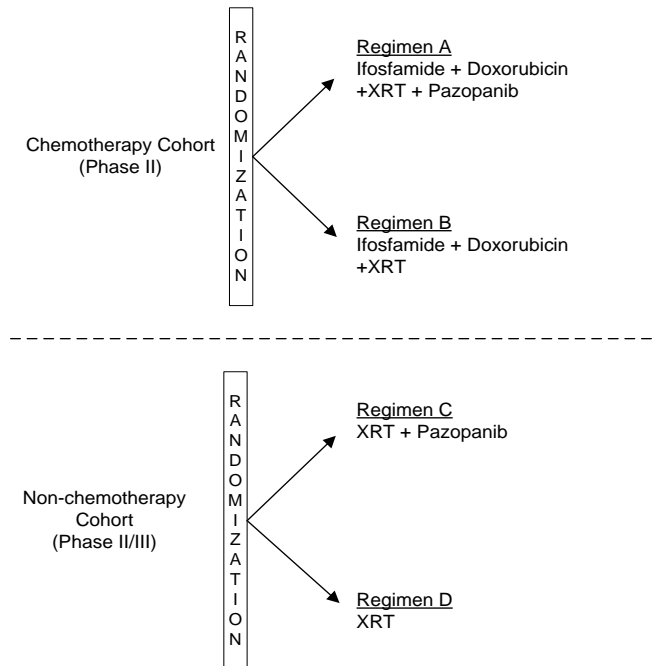
Pazopanib Neoadjuvant Trial in Non-Rhabdomyosarcoma Soft Tissue Sarcomas (PAZNTIS): A Phase II/III Randomized Trial of Preoperative Chemoradiation or Preoperative Radiation Plus or Minus Pazopanib

Participants:
COG, NRG, CTSU

Date Activated:
05/16/2014

Study Chairs:
A Weiss (COG), T Scharschmidt (NRG), Y Chen (NRG),
V Villalobos (SWOG)

SCHEMA



Objectives

To identify the dose of pazopanib that is feasible when given in combination with radiation or chemoradiation in pediatric and adult patients newly diagnosed with unresected intermediate- and high-risk NRSTS.

To compare the rates of near complete pathologic response (> 90% necrosis) with the addition of pazopanib to preoperative chemoradiation versus preoperative chemoradiation alone for potentially resectable > 5 cm, Grade 3 intermediate to high risk chemotherapy-sensitive NRSTS in the Phase II portion of the study for this cohort.

To compare the rates of near complete pathologic response (> 90% necrosis) with the addition of pazopanib to preoperative radiotherapy versus preoperative radiotherapy alone for potentially resectable intermediate to high risk adult and pediatric NRSTS in the Phase II portion of the study for this cohort (using a Phase II decision rule to go onto the Phase III portion of the study).

To compare the rates of event-free survival (EFS) with the addition of pazopanib to preoperative radiotherapy versus preoperative radiotherapy alone for localized intermediate to high risk adult and pediatric NRSTS in the Phase III portion of the study for this cohort if the Phase II decision rule is passed.

To estimate the rates of local failure, regional failure, distant metastasis free survival, disease-free survival, and overall survival with the addition of pazopanib to preoperative chemoradiation or preoperative radiation in intermediate to high risk adult and pediatric NRSTS.

To compare the pattern of recurrence (local, regional and distant) between preoperative chemoradiation or radiation with the addition of pazopanib for adult and pediatric NRSTS.

To define the toxicities of ifosfamide and doxorubicin chemotherapy and radiation when used in combination with pazopanib in intermediate to high risk adult and pediatric NRSTS.

Patient Population

Patients must have newly diagnosed and histopathologically confirmed, potentially resectable non-rhabdomyosarcoma soft tissue sarcoma (NRSTS) of the extremity or trunk. Patients with non-metastatic and metastatic disease are eligible, but patients with known CNS metastases are not eligible. Sufficient tissue and blood must be available for submission. Patients are eligible for the chemotherapy cohort, the non-chemotherapy cohort or both cohorts based on if the patient is medically deemed able to undergo chemotherapy, tumor histology, size, and grade as defined in the protocol.

Patients must not have received prior anthracycline or ifosfamide chemotherapy, pazopanib or similar multi-targeted TKI, or radiotherapy to tumor-involved sites. Patients must not have had gross total

resection of the primary tumor at any time prior to registration, including if patient has now recurred after the total resection. Within seven days prior to registration, patients must not be chronically receiving CYP3A4 substrates with narrow therapeutic indices or potent CYP3A4 inhibitors. Patients must not be chronically receiving potent CYP3A4 inducers within 14 days prior to registration.

Patients must be at least two years of age at the time of the biopsy that established the diagnosis of NRSTS. Patients must have adequate hematologic, renal, hepatic, cardiac, and pulmonary function. Adult patients must have a Karnofsky performance status ≥ 70 . Patients must not have uncontrolled hypertension and must not have evidence of active bleeding or bleeding diathesis. Patients must not have any condition that may increase the risk of gastrointestinal (GI) bleeding or GI perforation and patients must not be HIV positive.

Stratification/Descriptive Factors

In the chemotherapy cohort, patient randomization will be stratified according to the following factors: (1) age group: < 18 years vs ≥ 18 years; (2) extent of disease: localized vs metastatic; and (3) sarcoma subtype: synovial vs other. In the chemotherapy cohort, patient randomization will be stratified according to the following factors: (1) age group: < 18 years vs ≥ 18 years; (2) Grade: 2 vs 3; and (3) size of primary: < 5 cm vs ≥ 5 cm.

Accrual Goals

A total of 340 patients will be accrued to this study, including 140 in the chemotherapy cohort and 200 in the non-chemotherapy cohort. Interim analyses will be performed in the Phase II chemotherapy cohort when 43% response information is attained and yearly thereafter. Interim analyses will be performed in the non-chemotherapy cohort after 50% information is attained for the Phase II comparison, after 33% information is attained for the Phase III comparison, and yearly thereafter.

Summary Statement

COG and NRG reported a total accrual of 60 patients as of June 30, 2016, including two SWOG registrations. The complete Spring 2016 summary of this study from COG is available on the SWOG web site.

Registration by Institution
Registrations ending June 30, 2016

Institutions	Total Reg
Kansas, U of	1
Northwestern Univ	1
Total (2 Institutions)	2

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

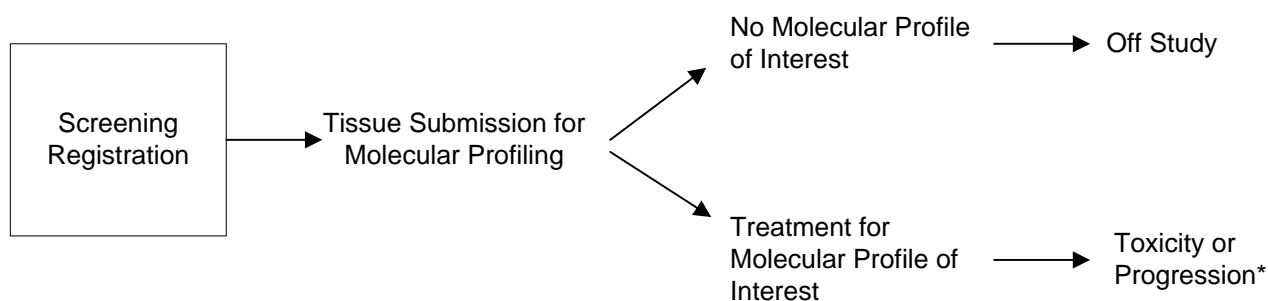
NCI-MATCH: Molecular Analysis for Therapy Choice

Participants:
ECOG-ACRIN, CTSU

Date Activated:
08/12/2015

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

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/multiple myeloma.

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/multiple myeloma.

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 protein and imaging-based assessment platforms.

To assess whether radiomic phenotypes obtained from pre-treatment imaging and changes from pre-through post-therapy imaging can predict objective response and progression free survival and to evaluate the association between pre-treatment radiomic phenotypes and targeted gene mutation patterns of tumor biopsy specimens.

Patient Population

Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma or multiple myeloma 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 and meet one of the criteria in the protocol regarding tissue procurement.

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 start of treatment. Patients must not require the use of full dose coumarin-derivative anticoagulants. Factor X inhibitors are permitted. Patients may receive non-protocol treatment after biopsy (if clinically indicated) until they receive notification of results, but patients may not enroll in another investigational study during this time and the therapy cannot be an arm in this trial.

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. Patients must not have any uncontrolled intercurrent illness. 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 reach 25 patients by the time the overall study screening accrual goal is met, and if 13 patients have been treated and no responses have been observed, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. After 500 patients are screened, the study design will be reassessed to assure its appropriateness. 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 January 26, 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 assessment of study design appropriateness was lifted on May 31, 2016, when this study reopened to enrollment with an additional 14 new subprotocols.

Patients with multiple myeloma will be allowed to enroll in the MATCH protocol at a future amendment. The screening sample collection, processing and assay are currently being validated for the marrow specimens for patients with myeloma. Once this is completed, an amendment allowing these patients to enroll will be submitted. Patients with myeloma cannot be entered on the trial until that is completed.

ECOG-ACRIN reported a total of 1,013 screened patients and 29 molecularly matched patients as of June 30, 2016. This includes 139 screened and two molecularly matched SWOG registrations. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution
 Screening
 Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	25	Beaumont NCORP	2
Henry Ford Hosp	18	Davis, U of CA	2
Wayne State Univ	15	Providence Hosp	2
Intermountain MC/Northwest NCORP	10	Cedars-Sinai Med Ctr	1
Cleveland Clinic OH	9	Cookeville Reg MC	1
Michigan, U of	8	CORA NCORP	1
Colorado, U of	7	Mem Hosp, Co Springs/Colorado, U of	1
KaiserPermanenteCOL/Kaiser Perm NCORP	7	Poudre Valley Hosp/Colorado, U of	1
Sutter Cancer RC	6	San Antonio, U of TX	1
Sutter General Hosp/Sutter Cancer RC	6	Sinai Hospital/San Antonio, U of TX	1
Southeast COR NCORP	4	St Charles Hlth Sys/PCRC NCORP	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	3	Tulane University	1
Ozarks NCORP	3	Total (26 Institutions)	139
S Georgia Med Ctr/Brooke Army Med Ctr	3		

Registration by Institution
 Molecularly Matched
 Registrations ending June 30, 2016

Institutions	Total Reg
Cleveland Clinic OH	1
Colorado, U of	1
Total (2 Institutions)	2