MYELOMA COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
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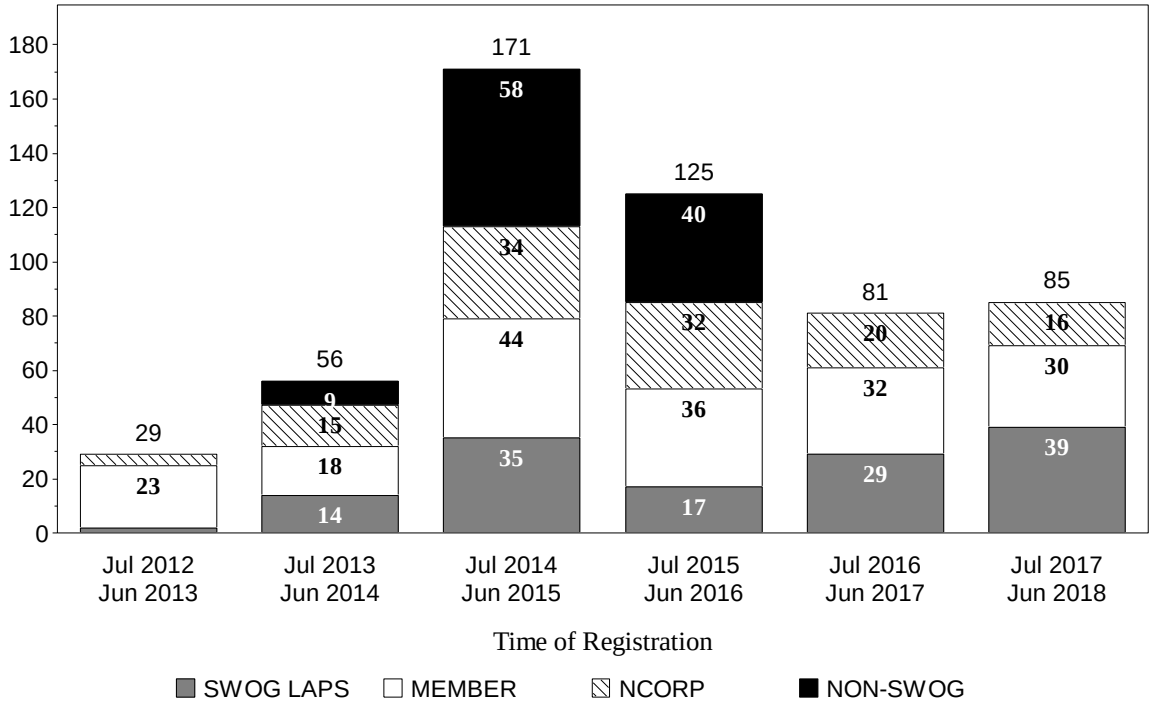

Screening registrations and registrations to Biologic only studies are excluded.

Patient Registrations by Study and Arm

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	Jan 2018 Jun 2018	Jul 2017 Dec 2017	Jan 2017 Jun 2017	All Patients
S1702 AL Amyloidosis, Relapsed, Isatuximab				
Initial Registration				
Isatuximab	3	0	0	3

Non-SWOG Studies with SWOG-Credited Registrations

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Studies with Accrual from January 2017 - June 2018

	SWOG Champion	SWOG Accrual Jan 2018 Jun 2018	SWOG Accrual Jul 2017 Dec 2017	SWOG Total	Total Accrued
E1A11 MM, frontline, BLD vs CLD	J Zonder	48	33	208	911
Date Activated: 11/22/13					
Most Recent Progress Report					
E3A06 AMM, Lenalidomide vs Observation	M Dhodapkar	0	1	35	226
Date Activated: 11/08/10 Date Closed: 07/14/17					
Most Recent Progress Report					

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, D Hershman

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

Date Activated:
08/29/2013

Date Closed:
02/15/2017

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, describe the timing and type of treatments received (if any), both for the viral infections and the cancers.

Describe type adverse events possibly attributable to the patient's viral status in patients with HIV, HBV, and/or HCV infection.

Using simulation modeling that is directly informed by the data obtained from this study, determine the cost-effectiveness (expressed as cost per infection detected and cost per year of life gained) 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.

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.

S1211 Phase I-II

Coordinating Group: SWOG

A Randomized Phase I/II Study of Optimal Induction Therapy of Bortezomib, Dexamethasone and Lenalidomide with or without Elotuzumab (NSC-764479) for Newly Diagnosed High Risk Multiple Myeloma

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

Date Activated:
10/27/2012

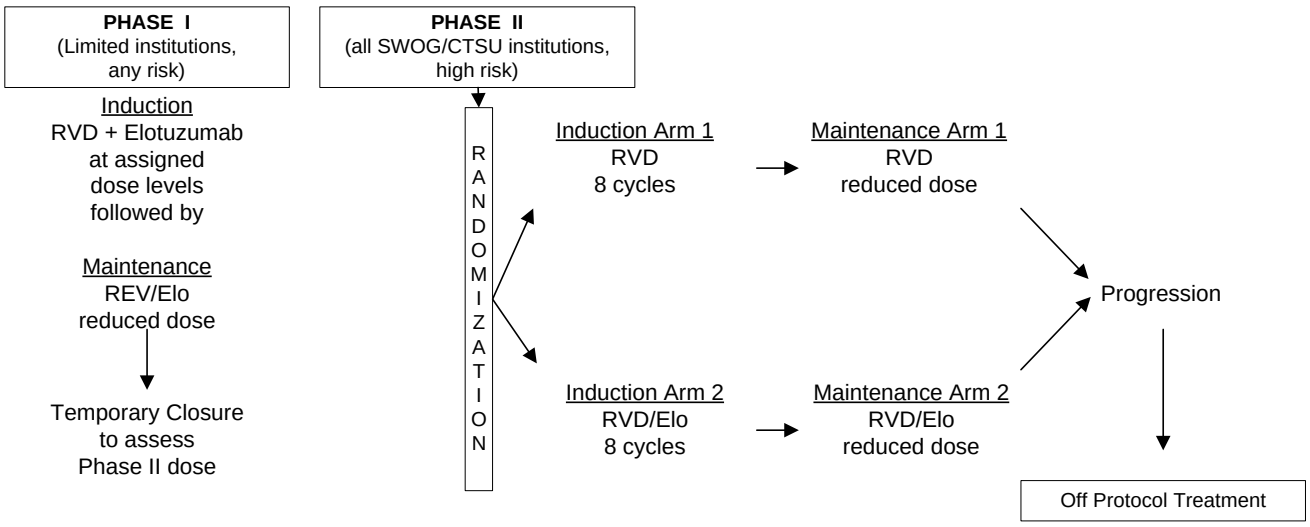
Study Chairs:
S Usmani, S Ailawadhi, J Shah, T Zimmerman (Alliance), N Callander (ECOG-ACRIN)

Date Closed:
06/02/2016

Statisticians:
R Sexton, A Hoering

Data Coordinator:
J Jardine

SCHEMA



*Patients will be enrolled into either the Phase I portion OR the Phase II portion, not both.

Objectives

Phase I Run-in

To determine the appropriate Phase II dose of elotuzumab to use in combination with lenalidomide, bortezomib and dexamethasone for patients with multiple myeloma.

Phase II Trial

To assess whether incorporation of elotuzumab into the treatment algorithm of high risk multiple myeloma will improve progression-free survival.

To estimate the frequency and severity of toxicities of this treatment strategy in this patient population.

Patient Population

Patients must have measurable, newly diagnosed active multiple myeloma. Non-secretory disease is not allowed.

For the Phase II portion, patients must be high risk by high GEP-70 genomic signature, specified FISH features, presence of plasma cell leukemia, or elevated LDH.

Patients on the Phase I portion may not have received any prior chemotherapy. Patients on the Phase II portion may have received one prior cycle of any noninvestigational chemotherapy. Patients may have received prior radiotherapy for symptomatic localized bone lesions or impending spinal cord compression only.

Patients must have adequate marrow, hepatic and renal function and must not have involvement of the central nervous system. Patients must have Zubrod performance status 0-2, must be at least 18 years of age, and must not have POEMS or clinically significant illness.

Stratification/Descriptive Factors

Patients in the Phase II portion of the study will be stratified as follows: primary plasma cell leukemia (PCL) and/or high LDH vs everyone else.

Accrual Goals

Phase I Run-In

Six patients (high or low risk) will be treated with bortezomib, lenalidomide, dexamethasone per protocol and elotuzumab at 10 mg/kg. If one or fewer patients experience a DLT this dose level of elotuzumab will be considered safe and the Phase II portion of the trial will be done using this dose level. If two or more patients experience a DLT, this dose level will be deemed too toxic and an additional six patients will be accrued and treated at a lower dose level of elotuzumab.

Phase II Trial

One hundred eligible patients will be accrued to this trial. An interim analysis for futility is planned after approximately half (32) of the total expected progressions have occurred, at approximately three years and seven months.

Summary Statement

This study opened for accrual on October 27, 2012. The study reached full accrual and closed on June 2, 2016. At this time, 142 patients had been enrolled to the trial. The Phase I portion of the trial was completed on September 24, 2012 and Dose Level 1 (10 mg/kg) was established as the appropriate dose level for the Phase II portion of the trial. The following summary contains only Phase II patients with the exception of the Registration by Institution table.

Among the 134 patients enrolled to the Phase II portion of the trial, 68 were randomized to the RVD arm and 66 were randomized to the RVD/Elo arm. Fourteen patients on the RVD arm and 15 patients on the RVD/Elo arm are ineligible due to the following reasons: missing, insufficient, or early or late baseline labs (21), prior therapy not completed at least 56 days prior to registration (3), criteria for measurable disease not met (3), uncontrolled diabetes (1), and criteria for high risk not met (1). One patient on the RVD/Elo arm withdrew consent prior to receiving any treatment. This patient is not evaluable for survival, response, or adverse events.

Twelve patients went off study due to "other" reasons; the reasons cited include intent to transplant (6), physician discretion (5), and recurrence of endometrial cancer (1). There has been one treatment-related death: a patient on the RVD/Elo arm died due to multi-organ failure. Ten of the 54 patients on the RVD arm and 11 of the 50 patients on the RVD/Elo arm who have been assessed for toxicities have experienced Grade 4 adverse events as maximum degree. The most common non-hematologic Grade 4 adverse events reported were

thromboembolic event (2), sepsis (2) and respiratory failure (2) on the RVD arm, and alanine transaminase (ALT) increased (2), aspartate transaminase (AST) increased (2), and infusion-related reaction (2) on the RVD/Elo arm.

Registration by Institution

Phase I and Phase II

Institutions	Total Reg	Institutions	Total Reg
Carolinas Med Ctr/San Antonio, U of TX	12	Ozarks NCORP	2
Kansas, U of	12	So Calif, U of	2
Cleveland Clinic OH	10	Cotton O'Neil CC/Kansas, U of	1
MD Anderson CC	10	CRC West MI NCORP	1
City of Hope Med Ctr	7	Dayton NCORP	1
Rochester, Univ of	7	Essentia Hlth NCORP	1
Michigan CRC NCORP	5	Kansas City NCORP	1
Columbus NCORP	4	Oklahoma, Univ of	1
Providence Hosp	4	Tulane University	1
Southeast COR NCORP	4	ECOG-ACRIN	31
Heartland NCORP	3	ALLIANCE	10
Loyola University	3	NRG	3
Sinai Hospital/San Antonio, U of TX	3	**Total (26 Institutions)**	**142**
Wayne State Univ	3		

Registration, Eligibility, and Evaluability

Classified by arm

Phase II patients only

Data as of August 2, 2018

	TOTAL	RVD	RVD/Elo
NUMBER REGISTERED	134	68	66
INELIGIBLE	29	14	15
Insufficient Documentation	21	9	12
Irreversible	21	9	12
ELIGIBLE	105	54	51
Not Analyzable	1	0	1
RESPONSE ASSESSMENT			
Determinable	101	52	49
Not Determinable	3	2	1
ADVERSE EVENT ASSESSMENT			
Evaluable	104	54	50

Patient Characteristics

Classified by arm
Phase II patients only
Data as of August 2, 2018

	RVD (n=54)		RVD/Elo (n=50)	
AGE				
Median	65.0		62.3	
Minimum	36.1		40.0	
Maximum	84.5		78.6	
SEX				
Males	33	61%	29	58%
Females	21	39%	21	42%
HISPANIC				
Yes	1	2%	2	4%
No	49	91%	47	94%
Unknown	4	7%	1	2%
RACE				
White	46	85%	43	86%
Black	8	15%	6	12%
Unknown	0	0%	1	2%
PCL AND/OR HIGH LDH				
Yes	9	17%	6	12%
No	45	83%	44	88%

Treatment Summary

Classified by phase
Phase II patients only
Data as of August 2, 2018

	Phase II
NUMBER ON PROTOCOL TREATMENT	16
NUMBER OFF PROTOCOL TREATMENT	88
REASON OFF TREATMENT	
Treatment completed as planned	1
Adverse Event or side effects	38
Refusal unrelated to adverse event	4
Progression/relapse	31
Death	2
Other - not protocol specified	12
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0

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

Classified by arm

Phase II patients only

Adverse Events Unlikely or Not Related to Treatment Excluded

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

Data as of August 2, 2018

	RVD (n=54) Grade						RVD/Elo (n=50) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Blood and lymphatic system dis	23	6	16	8	1	0	28	5	8	9	0	0
Cardiac disorders	48	3	0	3	0	0	45	4	0	1	0	0
Eye disorders	46	7	1	0	0	0	34	12	2	2	0	0
Gastrointestinal disorders	16	14	17	7	0	0	12	11	24	3	0	0
General disorders and administ	16	14	15	9	0	0	7	12	22	6	2	1
Hepatobiliary disorders	54	0	0	0	0	0	49	0	0	1	0	0
Immune system disorders	54	0	0	0	0	0	49	0	0	1	0	0
Infections and infestations	41	0	9	2	2	0	34	0	8	7	1	0
Injury, poisoning and procedur	48	5	0	1	0	0	47	2	0	1	0	0
Investigations	13	7	10	19	5	0	12	5	8	16	9	0
Metabolism and nutrition disor	26	10	13	5	0	0	17	6	17	8	2	0
Musculoskeletal and connective	26	10	14	3	1	0	24	11	10	5	0	0
Nervous system disorders	7	18	21	8	0	0	8	15	17	9	1	0
Psychiatric disorders	42	10	2	0	0	0	32	10	5	3	0	0
Renal and urinary disorders	50	3	0	1	0	0	45	3	2	0	0	0
Respiratory, thoracic and medi	35	8	8	1	2	0	25	15	6	3	1	0
Skin and subcutaneous tissue d	35	12	4	3	0	0	28	16	3	3	0	0
Vascular disorders	35	1	11	4	3	0	24	6	14	6	0	0
MAX. GRADE ANY ADVERSE EVENT	0	1	15	28	10	0	0	2	9	27	11	1

S1609 Phase II

Coordinating Group: SWOG

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

Participants:
SWOG, CTSU

Date Activated:
01/13/2017

Study Chairs:
S Patel, Y Chae

Statisticians:
M Othus, M Plets, E Mayerson

Data Coordinators:
C McLeod, J Hayward

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 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" (NOC) cohort with confirmation by one of the study chairs. As of September 11, 2017, patients are no longer required to have been enrolled in EAY131 (NCI-MATCH) to be eligible for this study.

Patients must have measurable disease and have progressed following at least one line of standard systemic therapy and there must not be other approved/standard therapy available that has been shown to prolong overall survival. Patients are also eligible if no standard treatment exists that has been shown to prolong overall survival. Patients must not have received either prior anti-CTLA4, 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 a prior immune-related adverse event with prior immunotherapy are not eligible. Patients with brain metastases or primary brain tumors must have completed treatment, surgery or radiation therapy ≥ 28 days prior to registration and have stable disease at time of registration. Patients with metastatic brain parenchymal disease must have been treated and off steroids for seven days prior to registration. Patients must have been off all other systemic anti-cancer therapy at least seven days prior to registration and any therapy-induced toxicity must have recovered to ≤ Grade 1.

Patients must have a Zubrod performance status of 0-2 and have adequate hematologic, hepatic, renal, thyroid, and adrenal axis function. Patients must not have active autoimmune disease that has required systemic treatment in the past two years or any uncontrolled intercurrent illness. Patients must not

have known active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection at time of registration. Patients with HBV or HCV that have an undetectable viral load, or in the opinion of the treating investigator is well controlled, are eligible. Patients who are known to be HIV-positive at registration are eligible if they meet the conditions outlined in the protocol.

Stratification/Descriptive Factors
Patients will be described by histologic cohorts.

Accrual Goals
The accrual goal for this study is 707 patients to achieve 636 eligible patients. A two-stage design will be used for all cohorts, with the exception of the NOC and "Cancer of Unknown Primary" (CuP) cohorts. Initially, six eligible patients will be registered to each histologic cohort. If at least one response is observed within a cohort, an additional 10 eligible patients will be registered to that cohort. Up to 16 eligible patients will be registered to the CuP cohort with no formal first stage response assessment. Up to 60 eligible patients will be enrolled to the NOC cohort, and data may be used to open additional cohorts.

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

S1702 Phase II

Coordinating Group: SWOG

A Phase II Study of Isatuximab (SARC650984) for Patients with Previously Treated AL Amyloidosis

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

Date Activated:
03/08/2018

Study Chairs:
E Scott, V Sanchorawala, H Landau (Alliance), E Campagnaro (ECOG-ACRIN)

Statisticians:
A Hoering, K Chansky

Data Coordinator:
S O'Bryan

Objectives

To assess the efficacy as measured by the confirmed overall hematologic response rate (partial response or better) of isatuximab in relapsed/refractory systemic light chain (AL) amyloidosis.

To evaluate toxicities in the treatment of relapsed/refractory AL amyloidosis treated with isatuximab.

To evaluate time to hematologic response.

To evaluate duration of response.

To evaluate progression-free survival (PFS).

To evaluate overall survival (OS).

Patient Population

Patients must have a confirmed diagnosis of primary systemic AL amyloidosis and must be relapsed or refractory to at least one prior line of therapy. Patients must have measurable disease, and must have objective organ involvement (renal, cardiac, hepatic, gastrointestinal, nervous system, or soft tissue). The absolute difference between involved and uninvolved serum free light chains must be $\geq$ 4.5 mg/dL. Patients must not have active symptomatic multiple myeloma.

Patients must not have received daratumumab within 56 days prior to registration nor have been refractory to daratumumab.

Patients must be 18 years of age or older. Patients must have bone marrow aspirate including FISH and cytogenetic testing, and echocardiogram. Patients must have adequate liver function, hematologic function, cardiac, and renal function. Patients must not have any clinically significant uncontrolled systemic illness, uncontrolled diabetes, or uncontrolled hypertension. Zubrod performance status must be 0-2.

Accrual Goals

Thirty-nine patients are expected to be enrolled to achieve 35 eligible patients. Initially, 20 eligible, evaluable patients will be accrued. If two or more hematologic responses (partial or better) are observed, then an additional 15 eligible patients will be enrolled.

Summary Statement

The study opened on March 8, 2018. As of June 30, 2018, three patients had been registered to the study.

Registration by Institution

Registrations ending June 30, 2018

Institutions	Total Reg
Heartland NCORP	1
Loyola University	1
Oregon Hlth Sci Univ	1
Total (3 Institutions)	**3**

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

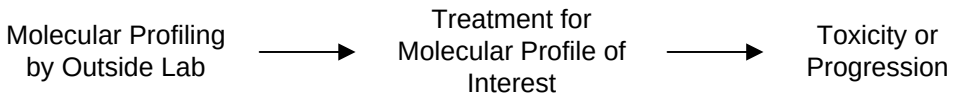
NCI-MATCH: Molecular Analysis for Therapy Choice

Participants:
ECOG-ACRIN, CTSU

Date Activated:
08/12/2015

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

SCHEMA



*As of May 1, 2017, patients must be screened via one of the outside laboratories listed in the protocol and only those patients with an applicable rare variant mutation of interest are eligible for subprotocol enrollment.

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 all adverse events due to prior therapy must have resolved to a Grade 1 or better (except alopecia and lymphopenia) by start of treatment. Palliative radiation therapy must have been completed at least two weeks prior to start of treatment. 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 have discontinued steroids at least one week prior to registration and remain off steroids thereafter, except as permitted in the protocol. Patients with glioblastoma must have been on a stable dose of steroids, or be off steroids, for one week prior to registration to treatment step. Patients must not require the use of full dose coumarin-derivative anticoagulants. Low molecular weight heparin is permitted for prophylactic or therapeutic use. 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, must have a life expectancy of at least 3 months, 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.

Only sites utilizing the CIRB as their IRB of record are able to participate in the trial.

Accrual Goals

The target screening accrual for this study is approximately 6,452 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 trial termination. 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

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