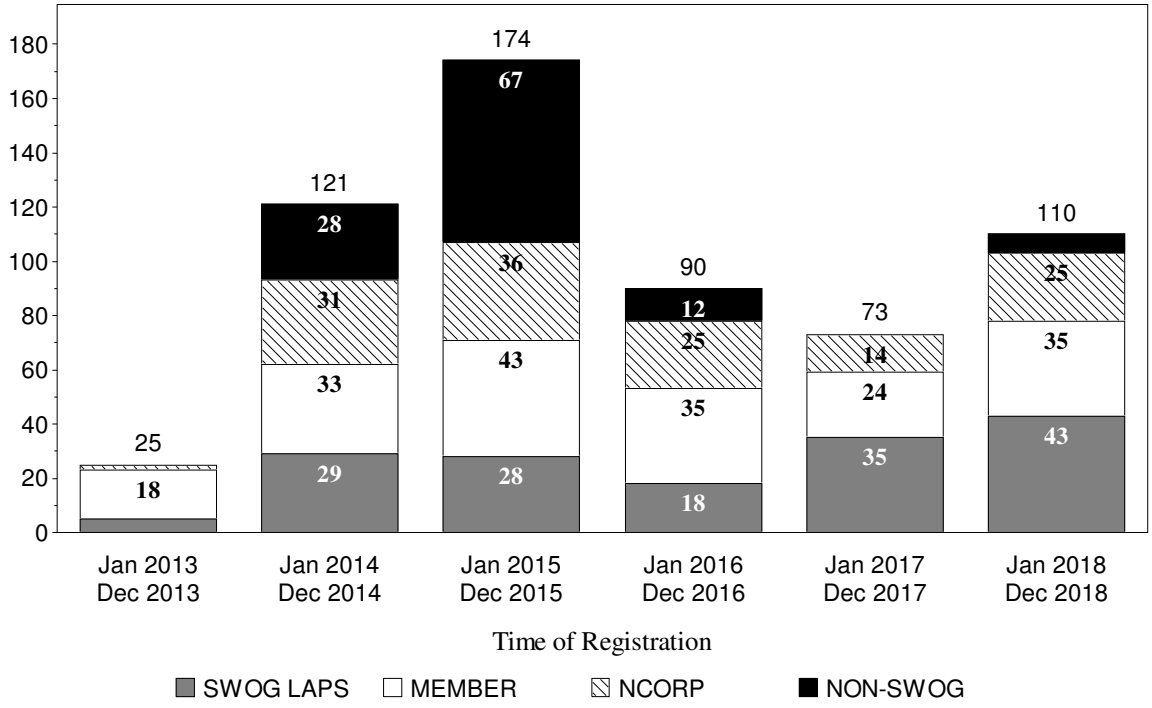
MYELOMA COMMITTEE

CONTENTS

Patient Registrations to Studies

by 12 Month Intervals
MYELOMA COMMITTEE



Screening registrations and registrations to Biologic only studies are excluded.

Patient Registrations by Study and Arm

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	Jul 2018 Dec 2018	Jan 2018 Jun 2018	Jul 2017 Dec 2017	All Patients
S1702 AL Amyloidosis, Relapsed, Isatuximab				
Initial Registration				
Isatuximab	13	3	0	16

Non-SWOG Studies with SWOG-Credited Registrations

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Studies with Accrual from July 2017 - December 2018

		SWOG Accrual				
	SWOG Champion	Jul 2018 Dec 2018	Jan 2018 Jun 2018	Jul 2017 Dec 2017	SWOG Total	Total Accrued
E1A11 MM, frontline, BLD vs CLD	J. Zonder	46	48	33	252	1,056
Date Activated: 11/22/13						
Most Recent Progress Report						
E3A06 AMM, Lenalidomide vs Observation	M Dhodapkar	0	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

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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 the type of 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 and ECOG-ACRIN)

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

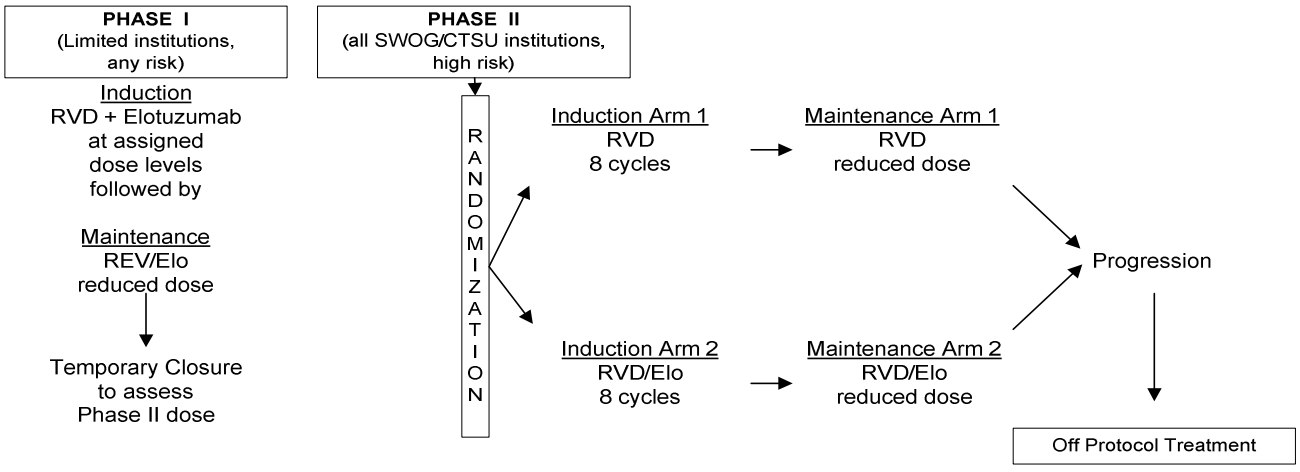
Statisticians:
R Sexton, A Hoering

Data Coordinators:
S O'Bryan

Date Activated:
10/27/2012

Date Closed:
05/15/2018

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 temporarily closed on June 2, 2016. On May 15, 2018, the closure became permanent. As 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.

Fourteen patients went off study due to "other" reasons; the reasons cited include intent to transplant (6), physician discretion (7), 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 February 4, 2019

	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 February 4, 2019

	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 February 4, 2019

	Phase II
NUMBER ON PROTOCOL TREATMENT	13
NUMBER OFF PROTOCOL TREATMENT	91
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	14
Reason under review	1
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 February 4, 2019

	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	22	7	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	45	7	2	0	0	0	34	12	2	2	0	0
Gastrointestinal disorders	14	15	18	7	0	0	12	11	24	3	0	0
General disorders and administ	15	15	15	9	0	0	7	12	21	7	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	40	0	10	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	12	8	10	19	5	0	11	5	8	17	9	0
Metabolism and nutrition disor	24	12	13	5	0	0	16	7	17	8	2	0
Musculoskeletal and connective	26	9	15	3	1	0	24	11	9	6	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	51	2	0	1	0	0	45	3	2	0	0	0
Respiratory, thoracic and medi	34	9	8	1	2	0	25	15	6	3	1	0
Skin and subcutaneous tissue d	34	13	4	3	0	0	28	16	3	3	0	0
Vascular disorders	33	3	11	4	3	0	24	5	15	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 $\geq$ 28 days prior to registration and have stable disease at time of registration. Patients with metastatic brain parenchymal disease must have been treated and 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)

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

Statisticians:
A Hoering, K Chansky

Data Coordinator:
S O'Bryan

Date Activated:
03/08/2018

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

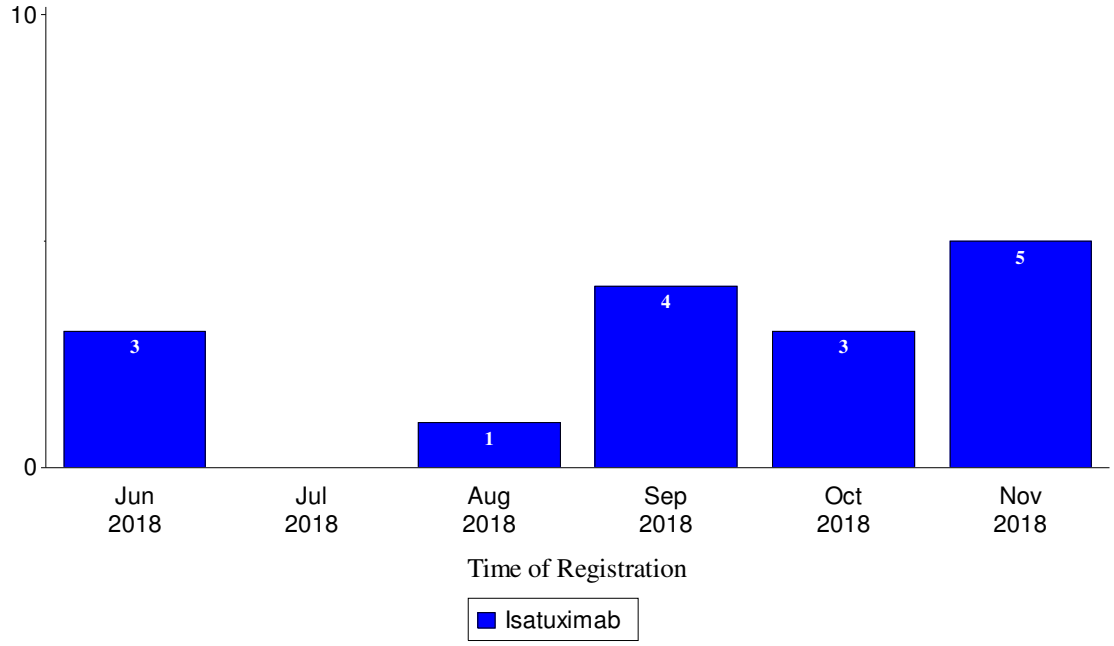
Thirty-nine patients are expected to be enrolled to achieve 35 eligible patients. Initially, 20 eligible, evaluable patients will be accrued. If two or more hematologic responses (partial or better) are observed, then an additional 15 eligible patients will be enrolled.

Summary Statement

The study opened on March 8, 2018. As of December 31, 2018, 16 patients had been registered to the study. One patient is ineligible due to the timing of baseline assessments, which are outside of the study-specified window. All patients are still on treatment. Five patients have been evaluated for response, and the requisite number of responses have been observed to allow continuing on to the second stage of accrual without a temporary closure. Among the 14 patients evaluated for toxicity, two patients have experienced Grade 3 adverse events (anemia and fatigue), and one patient has experienced a Grade 4 event (decreased lymphocytes). There have been no treatment-related deaths. Seven infusion-related reactions have been observed, all Grade 2.

Initial Registrations by 1 Month Intervals

Divisions by ARM



Registration by Institution

Registrations ending December 31, 2018

Institutions	Total Reg	Institutions	Total Reg
Boston Medical Ctr	2	Wayne State Univ	1
Columbia MU-NCORP	1	Yale University	1
CORA NCORP	1	ECOG-ACRIN	4
Heartland NCORP	1	NRG	2
Loyola University	1	ALLIANCE	1
Oregon Hlth Sci Univ	1	**Total (11 Institutions)**	**16**

Registration, Eligibility, and Evaluability

Registrations ending December 31, 2018; Data as of February 15, 2019

	Isatuximab
NUMBER REGISTERED	16
INELIGIBLE	1
Insufficient Documentation	1
Irreversible	1
ELIGIBLE	15
Analyzable, Pend. Elig.	7
RESPONSE ASSESSMENT	
Determinable	5
Too Early	10
ADVERSE EVENT ASSESSMENT	
Evaluable	14
Too Early	1

Patient Characteristics

Registrations ending December 31, 2018; Data as of February 15, 2019

	Isatuximab (n=15)	
AGE		
Median	71.5	
Minimum	50.7	
Maximum	79.5	
SEX		
Males	6	40%
Females	9	60%
HISPANIC		
No	14	93%
Unknown	1	7%
RACE		
White	13	87%
Asian	1	7%
Unknown	1	7%

Treatment Summary

Registrations ending December 31, 2018; Data as of February 15, 2019

	Isatuximab
NUMBER ON PROTOCOL TREATMENT	15
NUMBER OFF PROTOCOL TREATMENT	0
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	0
Refusal unrelated to adverse event	0
Progression/relapse	0
Death	0
Other - not protocol specified	0
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0
LOST TO FOLLOW-UP	0
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	0

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, 2018; Data as of February 15, 2019

	Isatuximab (n=14) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	13	1	0	0	0	0
Alkaline phosphatase increased	13	1	0	0	0	0
Alopecia	13	1	0	0	0	0
Anemia	11	2	0	1	0	0
Anorexia	13	1	0	0	0	0
Bronchial infection	13	0	1	0	0	0
Cardiac troponin I increased	13	1	0	0	0	0
Chills	13	1	0	0	0	0
Constipation	13	1	0	0	0	0
Diarrhea	10	3	1	0	0	0
Dizziness	13	0	1	0	0	0
Dry mouth	13	1	0	0	0	0
Dysgeusia	13	1	0	0	0	0
Fatigue	10	2	1	1	0	0
GERD	13	0	1	0	0	0
Headache	12	2	0	0	0	0
Hot flashes	13	0	1	0	0	0
Infusion related reaction	7	0	7	0	0	0
Insomnia	12	1	1	0	0	0
Investigations-Other, specify	12	2	0	0	0	0
Lymphocyte count decreased	10	2	1	0	1	0
Mucositis oral	12	2	0	0	0	0
Muscle cramp	13	1	0	0	0	0
Nausea	12	2	0	0	0	0
Pain	12	2	0	0	0	0
Skin/subq tissue ds-Other	13	0	1	0	0	0
Upper respiratory infection	12	0	2	0	0	0
Vomiting	12	1	1	0	0	0
MAX. GRADE ANY ADVERSE EVENT	0	3	8	2	1	0

S1803 Phase III

Phase III Study of Daratumumab/rHuPH20 (NSC- 810307) + Lenalidomide or Lenalidomide as Post-Autologous Stem Cell Transplant Maintenance Therapy in Patients with Multiple Myeloma Using Minimal Residual Disease to Direct Therapy Duration (DRAMMATIC)

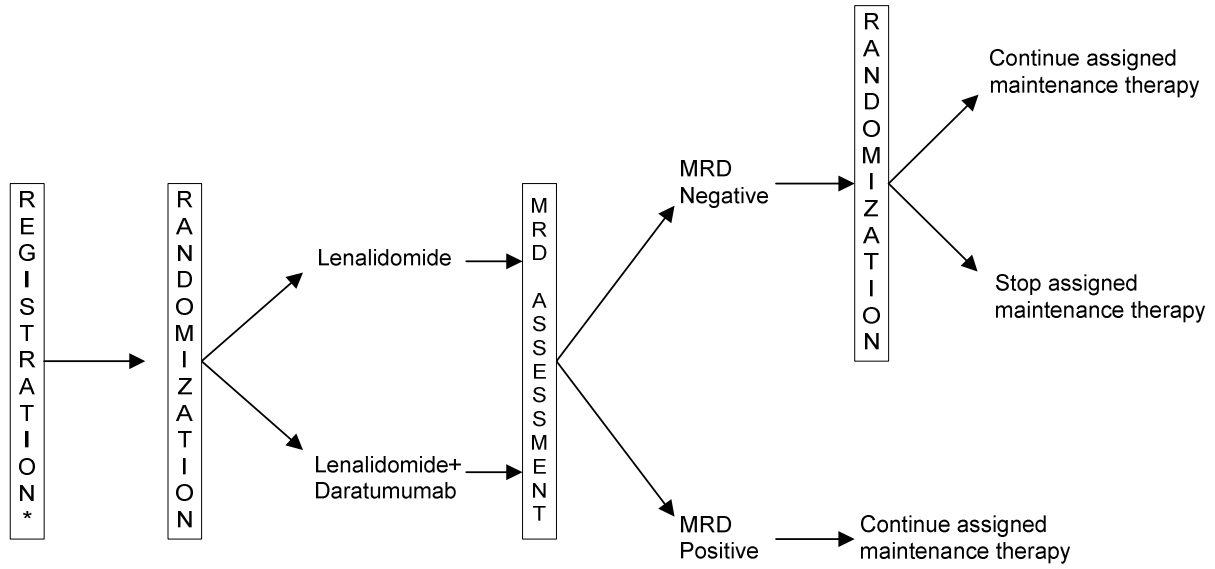
Participants:
SWOG, CTSU (Supported by BMTCTN)

Study Chairs:
A Krishnan, P Hari (BMTCTN)

Statisticians:
A Hoering, R Sexton

Data Coordinator:
S O'Bryan

SCHEMA



*Patients may register any time following induction therapy.

Objectives

To compare overall survival (OS) between the two treatment arms with lenalidomide as the comparator arm and lenalidomide + daratumumab/rHuPH20 as the experimental arm in post-autologous transplant multiple myeloma (MM) patients.

To compare the best overall response rate (ORR), including partial remission (PR), very good partial remission (VGPR), and complete remission (CR, sCR) in the subset of patients not in PR at randomization to lenalidomide versus lenalidomide + daratumumab/rHuPH20 in this patient population.

To compare progression-free survival (PFS) between the study arms in this patient population.

To evaluate MRD-negativity on the two treatment arms at randomization (Registration Step 2), and to compare MRD-negativity at 12, 24 (second randomization), 36, and 48 months after first randomization between lenalidomide and lenalidomide + daratumumab/rHuPH20 in this patient population.

To compare toxicities and tolerability of long term therapy between the study arms.

To report the findings of the 12-month MRD analysis once accrual has been completed and all eligible patients have been randomized to indefinite or discontinued treatment in this patient population.

To compare overall survival (OS) between MRD negative patients randomized to continued lenalidomide vs. discontinued lenalidomide from the time of second randomization in this patient population.

To compare overall survival (OS) between MRD negative patients randomized to continued lenalidomide + daratumumab/rHuPH20 vs. discontinued lenalidomide + daratumumab/rHuPH20 from time of second randomization in this patient population.

Patient Population

Patients must have had a confirmed diagnosis of symptomatic multiple myeloma that required systemic induction therapy prior to autologous stem cell transplantation (ASCT). Patients must not have any organ involvement by amyloidosis and must not have progressive disease at any time prior to registration. Patients must not have uncontrolled bacterial, viral or fungal infections or known central nervous system (CNS) involvement. Patients with smoldering MM are not eligible. Patients must have disease appropriately assessed per protocol. Patients must not be refractory or intolerant to either study drug. Patients must have initiated induction therapy within 12 months prior to registration and have received at least two cycles of induction therapy. Patients must not have received any investigational agents within 14 days prior to registration and be willing and able to take DVT prophylaxis.

Patients must be between 18 and 75 years of age and have Zubrod performance status 0-2. Patients must have adequate renal, hepatic and gastrointestinal function and be acceptable for transplant. Patients must not have any uncontrolled intercurrent illness. Patients must submit specimens for MRD and be offered participation in specimen banking.

Prior to first randomization, patients must have completed ASCT within 180 days prior to randomization and must not have had progressive disease between induction and randomization. Patients must have Zubrod performance status 0-2 and have adequate hepatic and renal function. All ASCT-related toxicities must have recovered to $\leq$ Grade 1 (except for alopecia, fatigue and amenorrhea). Females of childbearing potential must have a negative serum or urine pregnancy test.

Prior to second randomization, patients must have completed 24 cycles of protocol maintenance with either L or LD.

Stratification/Descriptive Factors

Patients will be stratified at the time of first randomization based on the following factors: (1) R-ISS stage at time of initial diagnosis: I/II vs III; (2) proteasome inhibitor or daratumumab/rHuPH20 induction therapy: yes vs no; and (3) best clinical response to ASCT: VGPR or better vs all others.

Accrual Goals

A total of 1,100 patients will be accrued to ensure 950 eligible patients randomized. Three formal interim analyses for futility and one interim analysis for efficacy are planned.