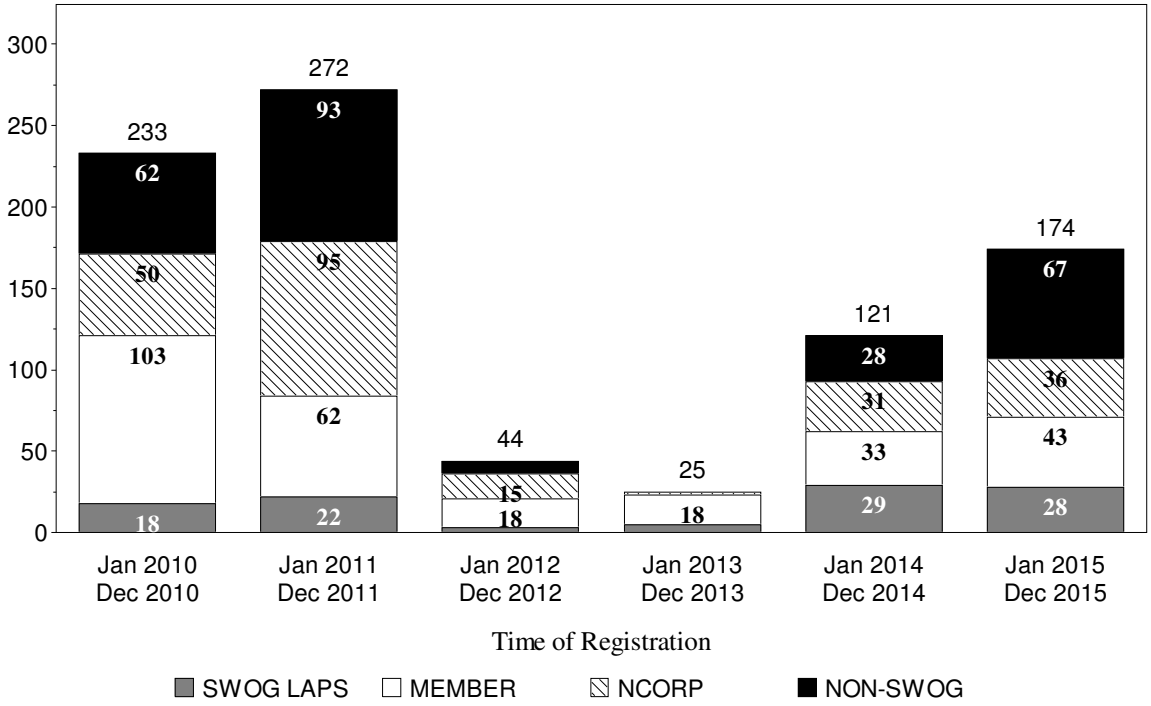
MYELOMA COMMITTEE

CONTENTS

S0777 Phase III....5
S1204 Surveillance....13
S1211 Phase I-II....15
S1304 Phase II....21
E1A11 Phase III SWOG Supported CTSU Study....29
E3A06 Phase III SWOG Supported CTSU Study....31

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

MYELOMA COMMITTEE

	Jul 2015 - Dec 2015	Jan 2015 - Jun 2015	Jul 2014 - Dec 2014	All Patients
S1211 MM, High Risk, RVD +/- ELO				
RVD/Elo Dose Level 1	0	0	0	8
RVD	19	19	11	57
RVD/Elo	19	15	10	51
	38	34	21	116
S1304 MM, relapsed/refractory, Car + Dex				
Initial Registration				
Dex + Low Dose Carfilzomib	17	25	19	72
Dex + High Dose Carfilzomib	13	27	17	71
	30	52	36	143
Cross Over				
Dex + High Dose Carfilzomib	6	9	5	20
E1A11 MM, frontline, BLD vs CLD*				
Total Registrations	3	6	13	28
E3A06 AMM, Lenalidomide vs Observation*				
Total Registrations	6	5	4	28

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

S0777 Phase III

Coordinating Group: SWOG

A Phase III Trial of CC-5013 (Lenalidomide) and Low Dose Dexamethasone (LLD) versus Bortezomib, Lenalidomide, and Low Dose Dexamethasone (BLLD) for Induction, in Patients with Previously Untreated Multiple Myeloma Without an Intent for Immediate Autologous Stem Cell Transplant

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

Study Chairs:
B Durie, M Abidi, B Barlogie

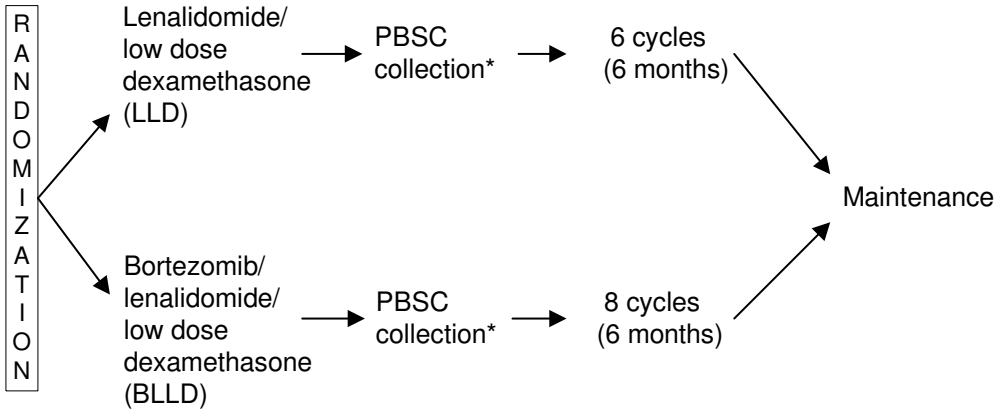
Statisticians:
A Hoering, R Sexton

Data Coordinator:
T Maher

Date Activated:
04/01/2008

Date Closed:
02/02/2012

SCHEMA



* According to institutional guidelines (based on "intent to transplant")

Objectives

To compare progression-free survival (PFS) in patients with newly diagnosed myeloma treated with lenalidomide plus low dose dexamethasone (LLD) versus bortezomib plus lenalidomide and low dose dexamethasone (BLLD).

To assess response to this regimen, using the new international response criteria.

To bank specimens for future translational medicine research.

To follow patients to assess overall survival (OS) and other long-term outcomes, stratified by intent to transplant at progression.

To verify the reported benefit of bortezomib in promoting bone repair/healing by comparing and contrasting the bone healing as determined by achievement of MRI-CR in patients receiving this regimen.

To evaluate custom and genome-wide single nucleotide polymorphisms in correlation with biology, prognosis and outcome for each treatment regimen.

Patient Population

Patients must have newly diagnosed multiple myeloma with measurable M-protein. Patients with non-secretory MM will be eligible only if the baseline serum Freelite is elevated. Patients must have received no prior chemotherapy, and no prior radiotherapy to a large area of the pelvis, for this disease. Prior steroid treatment is allowed provided treatment was not more than two weeks in duration. Patients must have adequate bone marrow function and a Zubrod performance status of 0-2. Zubrod performance status of 3 is acceptable if there is documentation from the treating physician that the patient's multiple myeloma is the central cause of the disability.

Stratification/Descriptive Factors

Treatment randomization will be stratified by the following factors: (1) ISS Stage: I vs II vs III; and (2) intent to transplant at relapse: Yes vs No.

Accrual Goals

A total of 440 eligible patients will be accrued to this trial. Two formal interim analyses are planned after 1/3 (92) and 2/3 (184) of the total expected progressions have occurred. The first interim analysis will be at approximately 36 months (three years), after approximately 75% of patients have been accrued. The second interim analysis will be at approximately 54 months (4 and a half years), after all patients have been accrued.

Summary Statement

This study opened for accrual on April 1, 2008 and closed to accrual on February 2, 2012, after 525 patients had been enrolled. Fifty-two patients, 31 randomized to LLD and 21 randomized to BLLD, have been determined to be ineligible due to the following reasons: missing, insufficient or early or late baseline labs (41), not meeting requirements of measurable disease (6), inadequate marrow function (1), inadequate creatinine clearance (1), having received prior therapy (1), and having received more than 2 weeks of prior steroid therapy (1), and prior malignancy (1). Two patients are not analyzable for survival endpoints due to withdrawal of informed consent prior to beginning therapy (1) and invalid consent, wherein the patient consented, but was under guardianship (1). There have been four major protocol deviations: one patient on the LLD arm did not start treatment per physician's discretion, two patients on the LLD arm were hospitalized before starting treatment, and one patient on the BLLD arm died on the day of first scheduled treatment prior to receiving any treatment. These four patients who did not begin treatment are not evaluable for adverse events. Among the 471 patients who had measurable disease at baseline, 26 on the BLLD arm and 15 on the LLD arm, were removed from study prior to the first disease assessment and are not assessable for response. Among the 85 patients who went off treatment due to “Other Reasons”, the most common reasons cited were intent to pursue non-protocol therapy, most commonly autologous stem cell transplant, and treatment delay greater than that which the protocol allowed. Among the 24 patients who refused further treatment, the most common reasons cited were intent to pursue non-protocol treatment, most commonly autologous stem cell transplant, noncompliance, and concerns regarding quality of life. There have been five treatment-related deaths on the study, one on the LLD arm in which a patient died due to conduction abnormality and four on the BLLD arm (one patient died due to multi-organ failure, one patient experienced Grade 5 hyperglycemia and was also reported as "Death, NOS", one patient died due to colitis, and one patient died due to lung infection).

Fifty-two of the 226 patients assessed for toxicity on the LLD arm and 55 of the 241 patients assessed on

the BLLD arm experienced Grade 4 adverse events as maximum degree. Among non-hematologic Grade 4 adverse events, metabolic (12), vascular (5), and neurologic (3) were most common on the LLD arm, and metabolic (9), pulmonary and upper respiratory (6), infection (5), vascular (4), neurologic (4), and gastrointestinal (3) were most common on the BLLD arm.

At the time of the primary endpoint analysis, 471 patients were eligible and analyzable for survival endpoints. The pre-specified one-sided stratified log-rank test supported the hypothesis that PFS is improved for patients assigned to BLLD compared to those assigned to LLD. The stratified hazard ratio (HR) was 0.712 (96% Wald confidence interval: 0.560, 0.906), and the one-sided stratified log-rank p-value (0.0018) fell well below the protocol-specified one-sided 0.02 significance level. OS was also improved for patients assigned to BLLD versus LLD (stratified HR = 0.709, two-sided log-rank p-value = 0.0250). The final results of this study were presented at the December 2015 conference for the American Society of Hematology. A manuscript is currently being finalized for submission.

Registration by Institution

Institutions	Total Reg	Institutions	Total Reg
ECOG-ACRIN	158	Dayton NCORP	6
Alliance	67	Kansas City NCORP	6
Southeast COR NCORP	34	Montana NCORP	6
Cleveland Clinic OH	20	Providence Hosp	6
Michigan CRC NCORP	19	St Jude Medical Ctr/Irvine, U of CA	6
Wichita NCORP	17	NRG	5
Baylor College	15	St Luke's-Roosevelt/Columbia University	5
Hawaii MU-NCORP	13	CTSU-nos	4
Rochester, Univ of	13	MD Anderson CC	4
Kaiser Perm NCORP	12	Tennessee, U of	4
Nevada CRF NCORP	12	Weissman Cancer Ctr/H Lee Moffitt CC	4
Wayne State Univ	12	Prov Portland MC/PCRC NCORP	3
Heartland NCORP	8	Stormont-Vail Health/Kansas, U of	3
Sinai Hospital/San Antonio, U of TX	8	Arizona MC, U of	2
Upstate Carolina	8	Arkansas, U of	2
New Mexico MU-NCORP	7	CRC West MI NCORP	2
St Joseph Med Ctr/PCRC NCORP	7	Mississippi, Univ of	2
St Louis CCOP	7	All Other Institutions	12
Colorado, U of	6	**Total (48 Institutions)**	**525**

Registration, Eligibility, and Evaluability

Data as of November 5, 2015

	TOTAL	Lenalidomide /Dex	Bortezomib /Lenalidomide /Dex
NUMBER REGISTERED	525	261	264
INELIGIBLE	52	31	21
Insufficient Documentation	41	27	14
ELIGIBLE	473	230	243
Not Analyzable	2	1	1
BASELINE DISEASE STATUS			
Measurable	471	229	242
ADVERSE EVENT ASSESSMENT			
Evaluable	467	226	241
Not Evaluable	4	3	1

Patient Characteristics

Data as of November 5, 2015

	Lenalidomide /Dex (n=229)		Bortezomib /Lenalidomide /Dex (n=242)	
AGE				
Median	63.4		63.3	
Minimum	28.9		35.4	
Maximum	87.4		86.0	
SEX				
Males	122	53%	153	63%
Females	107	47%	89	37%
HISPANIC				
Yes	15	7%	22	9%
No	202	88%	209	86%
Unknown	12	5%	11	5%
RACE				
White	181	79%	191	79%
Black	34	15%	32	13%
Asian	4	2%	7	3%
Pacific Islander	3	1%	2	1%
Native American	1	0%	2	1%
Unknown	6	3%	8	3%
ISS STAGE				
I	59	26%	71	29%
II	91	40%	93	38%
III	79	34%	78	32%
TRANSPLANT INTENT				
Yes	156	68%	168	69%
No	73	32%	74	31%

Treatment Summary

Data as of November 5, 2015

	TOTAL	Lenalidomide /Dex	Bortezomib /Lenalidomide /Dex
NUMBER ON PROTOCOL TREATMENT	66	26	40
NUMBER OFF PROTOCOL TREATMENT	405	203	202
REASON OFF TREATMENT			
Treatment completed as planned	0	0	0
Adverse Event or side effects	135	49	86
Refusal unrelated to adverse event	24	17	7
Progression/relapse	145	91	54
Death	16	6	10
Other - not protocol specified	85	40	45
Reason under review	0	0	0
MAJOR PROTOCOL DEVIATIONS	4	3	1

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of November 5, 2015

	Lenalidomide/Dex (n=226) Grade						Bortezomib/Lenalidomide/Dex (n=241) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Allergy/immunology	209	12	5	0	0	0	228	7	4	2	0	0
Auditory/Ear	208	1	17	0	0	0	232	1	8	0	0	0
Blood/Bone Marrow	47	25	50	70	34	0	51	27	49	73	41	0
Cardiac Arrhythmia	214	5	3	4	0	0	229	7	2	3	0	0
Cardiac General	194	13	11	8	0	0	190	15	18	18	0	0
Coagulation	223	0	0	3	0	0	236	0	0	5	0	0
Constitutional symptoms	48	60	83	35	0	0	45	60	89	46	1	0
Death	226	0	0	0	0	0	239	0	0	0	0	2
Dermatology/Skin	135	61	21	9	0	0	142	50	42	6	1	0
Endocrine	207	11	8	0	0	0	224	5	12	0	0	0
Gastrointestinal	60	84	65	17	0	0	39	64	85	49	3	1
Hemorrhage/Bleeding	212	12	2	0	0	0	224	7	3	7	0	0
Hepatobiliary/Pancreas	224	0	0	2	0	0	239	0	0	2	0	0
Infection	166	1	28	29	2	0	174	2	31	28	5	1
Lymphatics	150	56	18	2	0	0	146	66	24	5	0	0
Metabolic/Laboratory	54	54	55	51	12	0	68	50	60	53	9	1
Musculoskeletal/Soft Tissue	165	25	22	13	1	0	170	20	28	22	1	0
Neurology	79	78	44	21	3	1	47	42	72	76	4	0
Ocular/Visual	187	19	8	12	0	0	182	37	16	6	0	0
Pain	146	44	27	9	0	0	113	55	44	29	0	0
Pulmonary/Upper Respiratory	150	42	25	8	1	0	149	55	16	15	6	0
Renal/Genitourinary	212	2	3	8	1	0	225	8	3	5	0	0

	Lenalidomide/Dex (n=226) Grade						Bortezomib/Lenalidomide/Dex (n=241) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Secondary Malignancy	222	0	0	3	1	0	239	0	0	1	1	0
Sexual/Reproductive Function	223	1	1	1	0	0	238	2	1	0	0	0
Syndromes	224	0	0	2	0	0	235	1	2	3	0	0
Vascular	201	0	4	16	5	0	210	1	8	18	4	0
MAX. GRADE ANY ADVERSE EVENT	11	8	38	116	52	1	7	7	29	139	55	4

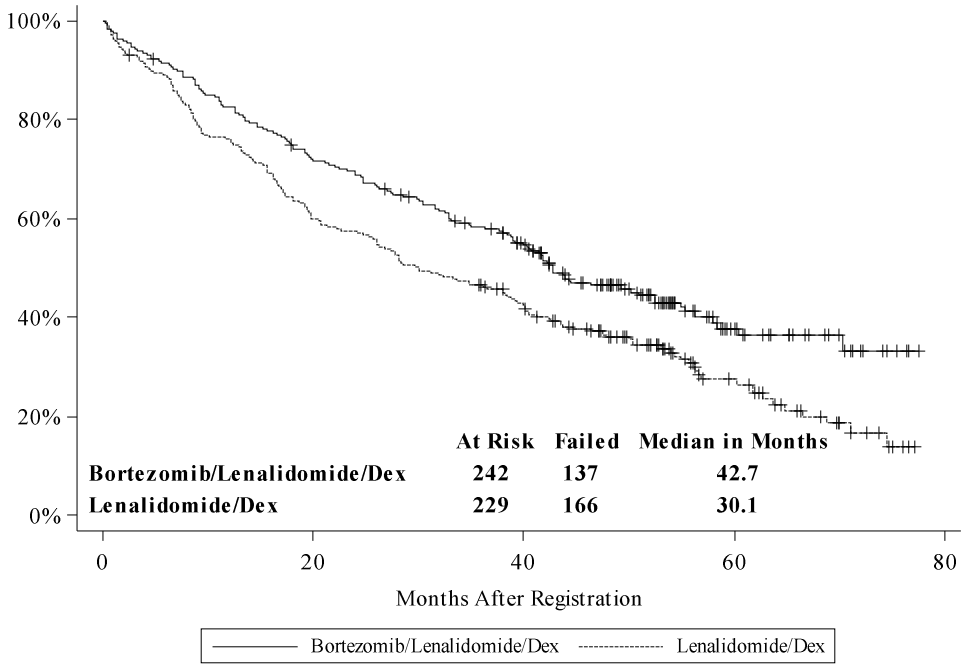
Response

Data as of November 5, 2015

	Lenalidomide/Dex		Bortezomib/Lenalidomide/Dex	
	N	**%**	**N**	**%**
Stringent Complete Response	0	0	1	0
Complete Response	18	8	32	13
Very Good Partial Response	46	20	55	23
Partial Response	80	35	79	33
Unc Stringent Complete Response	0	0	1	0
Unconfirmed Complete Response	4	2	5	2
Unconfirmed Very Good Partial Response	5	2	3	1
Unconfirmed Remission	0	0	0	0
Unconfirmed Partial Remission	10	4	20	8
Stable/No Remission	42	18	14	6
Increasing Disease	9	4	3	1
Early Death	0	0	3	1
Assessment Inadequate	15	7	26	11
Total	229	100	242	100

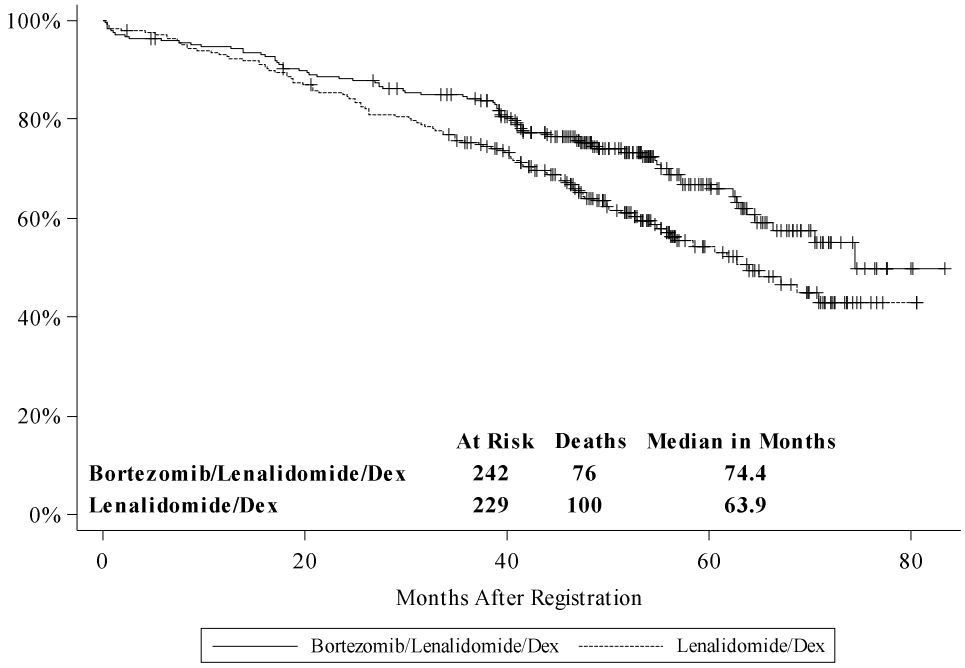
Progression-Free Survival

Data as of November 5, 2015



Overall Survival

Data as of November 5, 2015



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

Date Activated:
08/29/2013

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

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.

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)

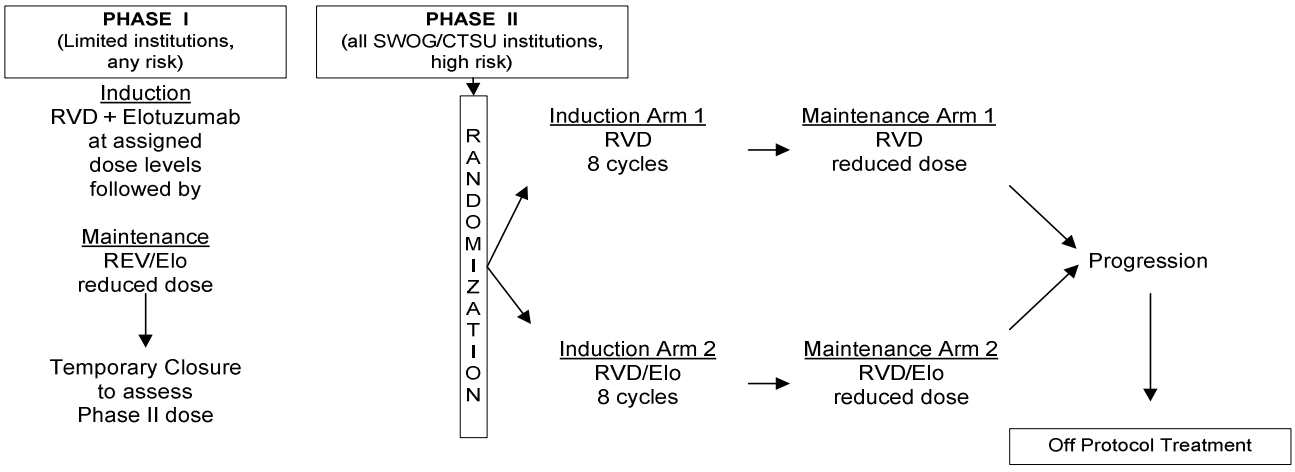
Date Activated:
10/27/2012

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

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. As of December 31, 2015, 116 patients had been enrolled to the trial. The Phase I portion of the trial is now complete and Dose Level 1 (10 mg/kg) has been established as the appropriate dose level for the Phase II portion of the trial.

The Phase II portion of the trial was temporarily closed on January 6, 2016 pending the approval of an amendment to accrue a total of 130 patients to ensure that the target accrual of 100 eligible patients is reached. The amendment has been approved and the study was reactivated on February 2, 2016.

Among the 108 patients enrolled to the Phase II portion of the trial, 57 were randomized to the RVD arm and 51 were randomized to the RVD/Elo arm. Ten patients on the RVD arm and five patients on the RVE/Elo arm are ineligible due to the following reasons: missing, insufficient, or early or late baseline labs (9), prior therapy not completed at least 56 days prior to registration (2), criteria for measurable disease not met (3), and criteria for high risk not met (1). There has been one major protocol deviation: a patient on the RVD/Elo arm withdrew consent prior to receiving any treatment. This patient is not evaluable for response or adverse events.

Five patients on the Phase II portion of the trial went of study due to "other" reasons; the reasons cited include physician discretion (1) and intent to transplant (4). Five of the 44 patients on the RVD arm and six of the 41 patients on the RVD/Elo arm who have been assessed for toxicities have

experienced Grade 4 adverse events as maximum degree. The non-hematologic Grade 4 adverse events reported were thromboembolic event (2), respiratory failure (1), and sepsis (1) on the RVD arm and infusion-related reaction (1), respiratory failure (1), sepsis (1), and stroke (1) on the RVD/Elo arm. No treatment-related deaths have been reported.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
ECOG-ACRIN	23	Wayne State Univ	3
Kansas, U of	12	Loyola University	2
Carolinas Med Ctr/San Antonio, U of TX	11	So Calif, U of	2
Cleveland Clinic OH	10	Southeast COR NCORP	2
MD Anderson CC	10	CRC West MI NCORP	1
Alliance	6	Dayton NCORP	1
City of Hope Med Ctr	5	Essentia Hlth NCORP	1
Michigan CRC NCORP	5	Kansas City NCORP	1
Rochester, Univ of	5	Oklahoma, Univ of	1
Providence Hosp	4	Sinai Hospital/San Antonio, U of TX	1
Columbus NCORP	3	Stormont-Vail Health/Kansas, U of	1
Heartland NCORP	3	**Total (24 Institutions)**	**116**
NRG	3		

Registration, Eligibility, and Evaluability

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

	TOTAL	RVD/Elo Dose Level 1	RVD	RVD/Elo
NUMBER REGISTERED	116	8	57	51
INELIGIBLE	17	2	10	5
Insufficient Documentation	11	2	5	4
ELIGIBLE	99	6	47	46
Analyzable, Pend. Elig.	3	0	1	2
Not Analyzable	1	1	0	0
RESPONSE ASSESSMENT				
Determinable	57	5	26	26
Not Determinable	1	0	0	1
Too Early	40	0	21	19
ADVERSE EVENT ASSESSMENT				
Evaluable	90	5	44	41
Not Evaluable	1	0	0	1
Too Early	7	0	3	4

Patient Characteristics

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

	RVD/Elo Dose Level 1 (n=5)		RVD (n=47)		RVD/Elo (n=46)	
AGE						
Median	66.9		63.6		62.1	
Minimum	56.1		36.2		40.0	
Maximum	79.3		84.6		78.7	
SEX						
Males	2	40%	29	62%	28	61%
Females	3	60%	18	38%	18	39%
HISPANIC						
Yes	0	0%	1	2%	2	4%
No	5	100%	43	91%	43	93%
Unknown	0	0%	3	6%	1	2%
RACE						
White	2	40%	40	85%	39	85%
Black	1	20%	7	15%	5	11%
Unknown	2	40%	0	0%	2	4%
PCL AND/OR HIGH LDH						
Yes	0	0%	8	17%	7	15%
No	5	100%	39	83%	39	85%

Treatment Summary

Classified by phase

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

	TOTAL	Phase I	Phase II
NUMBER ON PROTOCOL TREATMENT	60	3	57
NUMBER OFF PROTOCOL TREATMENT	38	2	36
REASON OFF TREATMENT			
Treatment completed as planned	1	0	1
Adverse Event or side effects	16	0	16
Refusal unrelated to adverse event	1	0	1
Progression/relapse	9	0	9
Death	1	0	1
Other - not protocol specified	7	2	5
Reason under review	3	0	3
MAJOR PROTOCOL DEVIATIONS	1	0	1

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

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

	RVD (n=44) Grade						RVD/Elo (n=41) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	37	6	1	0	0	0	36	3	1	1	0	0
AST increased	40	4	0	0	0	0	37	3	0	1	0	0
Agitation	44	0	0	0	0	0	38	1	1	1	0	0
Allergic reaction	44	0	0	0	0	0	40	0	0	1	0	0
Anemia	24	4	12	4	0	0	30	4	5	2	0	0
Atrial fibrillation	42	0	0	2	0	0	39	1	0	1	0	0
Back pain	41	1	2	0	0	0	33	5	2	1	0	0
Bone pain	43	1	0	0	0	0	38	0	2	1	0	0
Diarrhea	33	4	4	3	0	0	34	4	2	1	0	0
Dyspnea	35	6	3	0	0	0	31	5	4	1	0	0
Edema limbs	26	9	7	2	0	0	25	11	5	0	0	0
Encephalopathy	43	0	0	1	0	0	41	0	0	0	0	0
Fall	41	2	0	1	0	0	41	0	0	0	0	0
Fatigue	23	11	6	4	0	0	18	14	7	2	0	0
Febrile neutropenia	43	0	0	0	1	0	40	0	0	1	0	0
Fracture	44	0	0	0	0	0	40	0	0	1	0	0
Generalized muscle weakness	40	1	3	0	0	0	30	6	4	1	0	0
Hyperglycemia	41	1	0	2	0	0	31	5	4	1	0	0
Hyperkalemia	42	1	0	1	0	0	39	1	1	0	0	0
Hypertension	39	1	3	1	0	0	39	1	1	0	0	0
Hypokalemia	41	2	1	0	0	0	34	4	1	2	0	0
Hyponatremia	41	1	0	2	0	0	34	6	0	1	0	0
Hypotension	42	0	2	0	0	0	36	0	4	1	0	0
Infections/infestations-Other	42	0	1	1	0	0	40	0	0	1	0	0
Infusion related reaction	44	0	0	0	0	0	39	0	0	1	1	0
Insomnia	37	6	1	0	0	0	30	7	3	1	0	0
Lung infection	43	0	1	0	0	0	38	0	0	3	0	0
Lymphocyte count decreased	27	3	5	8	1	0	30	1	4	5	1	0
Muscle weakness lower limb	40	1	2	1	0	0	37	1	3	0	0	0
Nausea	32	8	3	1	0	0	31	6	4	0	0	0
Neuralgia	44	0	0	0	0	0	39	1	0	1	0	0
Neutrophil count decreased	31	1	5	6	1	0	33	3	2	3	0	0
Peripheral motor neuropathy	40	3	1	0	0	0	33	3	3	2	0	0
Peripheral sensory neuropathy	21	15	5	3	0	0	16	11	12	2	0	0
Platelet count decreased	26	6	5	6	1	0	21	7	5	5	3	0
Pneumonitis	43	0	1	0	0	0	40	0	0	1	0	0
Pulmonary edema	43	0	0	1	0	0	41	0	0	0	0	0
Rash acneiform	42	1	0	1	0	0	40	1	0	0	0	0
Rash maculo-papular	35	7	1	1	0	0	32	5	1	3	0	0
Resp/thoracic/mediastinal ds	44	0	0	0	0	0	40	0	0	1	0	0
Respiratory failure	43	0	0	0	1	0	40	0	0	0	1	0
Sepsis	43	0	0	0	1	0	40	0	0	0	1	0

	RVD (n=44) Grade						RVD/Elo (n=41) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Skin infection	43	0	1	0	0	0	40	0	0	1	0	0
Stroke	44	0	0	0	0	0	40	0	0	0	1	0
Syncope	43	0	0	1	0	0	41	0	0	0	0	0
Thromboembolic event	39	0	1	2	2	0	37	0	3	1	0	0
Urinary tract infection	43	0	0	1	0	0	39	0	2	0	0	0
Urine output decreased	44	0	0	0	0	0	40	0	0	1	0	0
White blood cell decreased	29	2	10	2	1	0	30	5	4	2	0	0
MAX. GRADE ANY ADVERSE EVENT	1	5	13	20	5	0	0	4	13	18	6	0

S1304 Phase II

Coordinating Group: SWOG

A Phase II Randomized Study Comparing Two Doses of Carfilzomib (NSC-756640) with Dexamethasone for Multiple Myeloma Patients with Relapsed or Refractory Disease

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

Study Chairs:
S Ailawadhi, M Abidi, S Lentzsch, P Voorhees (Alliance), A Cohen (ECOG-ACRIN)

Statisticians:
R Sexton, A Hoering

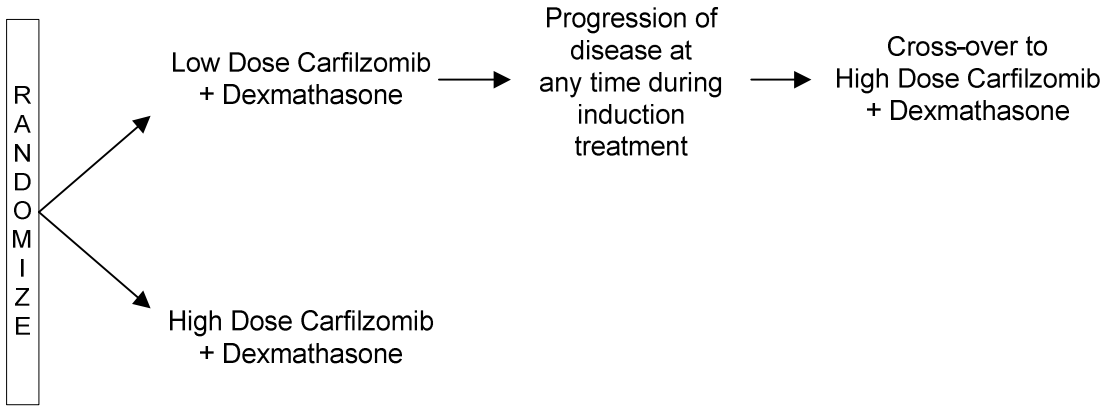
Data Coordinator:
J Jardine

Date Activated:
10/18/2013

Date Closed*:
11/06/2015

*Temporary Closure

SCHEMA



Objectives

To evaluate and compare progression free survival of two different doses of carfilzomib with dexamethasone in multiple myeloma (MM) patients with relapsed or refractory disease.

To evaluate and compare response rates for each arm.

To evaluate response rates for patients that relapse on low dose carfilzomib and subsequently cross-over to high dose carfilzomib.

To evaluate the safety of this combination for this patient population.

To evaluate overall survival.

To explore the molecular variability in MM cells obtained from extramedullary bone marrow relapse sites.

To explore the role of PET scanning in assessing disease burden and as a tool to assess treatment response.

To explore changes in left ventricular ejection fraction in patients with relapsed or refractory multiple myeloma treated with low dose carfilzomib or high dose carfilzomib plus dexamethasone.

Patient Population

Patients must have a confirmed diagnosis of symptomatic myeloma and must be relapsed or refractory. Patients must have measurable disease, must have had a least one, but no more than six prior regimens of therapy for the disease, may not have received any prior carfilzomib and must not be receiving any other concurrent investigational therapy. Patients with non-secretory MM or known amyloidosis are ineligible.

Patients must discontinue specified therapies within 28 days prior to registration.

Patients must be 18 years of age. Patients must have a complete physical, PET scan, ECHO, EKG, and a skeletal survey. Patients must have a Zubrod performance status between 0 and 2, must not have any clinically significant illness or any significant neuropathies, and must have adequate liver and marrow function and creatinine clearance.

Stratification/Descriptive Factors

Patients will be stratified by the following factors: (1) one to three prior therapies vs four to six prior therapies; and (2) refractory to bortezomib vs not refractory to bortezomib.

Accrual Goals

A total of 126 eligible patients will be enrolled. One interim analysis is planned for when one half of the total expected events have occurred, at approximately one year and eight months.

Summary Statement

This study was activated on October 18, 2013. The study was temporarily closed on November 6, 2015 pending the approval of an amendment to accrue a total of 153 patients to ensure that the target accrual of 126 eligible patients is reached. At this time, 143 patients, 72 randomized to low dose carfilzomib (LDC) and 71 randomized to high dose carfilzomib (HDC), had been enrolled to the trial. Eight patients randomized to LDC and 14 patients randomized to HDC were ineligible for the following reasons: missing, insufficient, early or late baseline labs (18), multiple myeloma diagnosis not confirmed (2), criteria for measurable disease not met (1), prior therapy completed less than 28 days prior to registration (1). There has been one major protocol deviation: a patient randomized to HDC withdrew from the study prior to receiving protocol treatment. This patient is not evaluable for adverse events or response.

Three patients went of study due to "other" reasons; the reasons cited include second primary malignancy (1), lack of compliance (1), and intent to transplant (1). Three treatment-related deaths have been reported: two patients, one on each arm, died due to sepsis (the patients on the HDC arms is also indicated as having died due to causes not otherwise specified, Death NOS), and one patient on the LDC arm died due to causes not otherwise specified (Death NOS). Four of the 57 patients assessed for toxicity on the LDC arm and eight of the 55 patients assessed for toxicity on the HDC arm experienced Grade 4 adverse events as maximum grade. The non-hematologic Grade 4 adverse events observed were cardiac arrest (1), increased creatinine (1), respiratory failure (1), and restrictive cardiomyopathy (1) on the LDC arm and acute respiratory distress syndrome (2), acute kidney injury (1), dyspnea (1), hyperglycemia (1), hypocalcemia (1), lung infection (1), and stroke (1) on the HDC arm.

Twenty patients had registered to the Crossover HDC arm (C-HDC), six of whom were ineligible for the following reasons: missing, insufficient, early or late baseline labs from initial registration (3), multiple myeloma diagnosis not confirmed at time of initial registration (1), patient did not progress on initial study treatment (1), crossover occurred less than 14 days after last dose of initial study treatment (1).

Among the 12 patients assessed for toxicity on C-HDC arm, 4 patients experienced Grade 4 adverse events, including the following non-hematologic adverse events: atrial flutter (1), lung infection (1), secondary leukemia (1), and sepsis (1). No treatment-related deaths have been reported.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	33	KaiserPermanenteSCAL/Kaiser Perm NCORP	2
ECOG-ACRIN	21	Montana NCORP	2
So Calif, U of	17	Nevada CRF NCORP	2
NRG	9	Arizona MC, U of	1
Kaiser Perm NCORP	8	Boston MC MBCCOP	1
Michigan CRC NCORP	8	Boston Medical Ctr	1
MD Anderson CC	7	Lahey Hosp & Med Ctr	1
Loyola University	5	Mississippi, Univ of	1
Florida, Univ of/Yale University	4	Northwest NCORP	1
Heartland NCORP	4	Oklahoma, Univ of	1
Providence Hosp	4	Ozarks NCORP	1
Southeast COR NCORP	3	Wichita NCORP	1
Yale University	3	**Total (26 Institutions)**	**143**
Davis, U of CA	2		

Registration, Eligibility, and Evaluability

Classified by arm

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

	TOTAL	Dex+Low Dose Carfilzomib	Dex+High Dose Carfilzomib
NUMBER REGISTERED	143	72	71
INELIGIBLE	22	8	14
Insufficient Documentation	18	7	11
ELIGIBLE	121	64	57
RESPONSE ASSESSMENT			
Determinable	78	40	38
Not Determinable	10	4	6
Too Early	33	20	13
ADVERSE EVENT ASSESSMENT			
Evaluable	112	57	55
Not Evaluable	1	0	1
Too Early	8	7	1

Patient Characteristics

Classified by arm

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

	Dex+Low Dose Carfilzomib (n=64)		Dex+High Dose Carfilzomib (n=57)	
AGE				
Median	65.0		66.6	
Minimum	43.4		44.8	
Maximum	90.0		81.9	
SEX				
Males	33	52%	35	61%
Females	31	48%	22	39%
HISPANIC				
Yes	10	16%	8	14%
No	50	78%	43	75%
Unknown	4	6%	6	11%
RACE				
White	50	78%	42	74%
Black	12	19%	9	16%
Asian	1	2%	3	5%
Native American	1	2%	0	0%
Unknown	0	0%	3	5%
PRIOR THERAPIES				
1-3	51	80%	43	75%
4-6	13	20%	14	25%
REFRACTORY TO BORTEZOMIB				
Yes	30	47%	29	51%
No	34	53%	28	49%

Treatment Summary

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

	Total
NUMBER ON PROTOCOL TREATMENT	36
NUMBER OFF PROTOCOL TREATMENT	85
REASON OFF TREATMENT	
Treatment completed as planned	10
Adverse Event or side effects	27
Refusal unrelated to adverse event	5
Progression/relapse	33
Death	3
Other - not protocol specified	3
Reason under review	4
MAJOR PROTOCOL DEVIATIONS	1

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

Classified by arm

Adverse Events Unlikely or Not Related to Treatment Excluded

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

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

	Dex+Low Dose Carfilzomib (n=57) Grade						Dex+High Dose Carfilzomib (n=55) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ARDS	57	0	0	0	0	0	53	0	0	0	2	0
Abdominal pain	54	2	1	0	0	0	51	2	1	1	0	0
Acute coronary syndrome	57	0	0	0	0	0	54	0	0	1	0	0
Acute kidney injury	56	0	0	1	0	0	53	0	1	0	1	0
Anemia	34	9	8	5	1	0	29	9	9	8	0	0
Anorexia	51	2	4	0	0	0	49	3	2	1	0	0
Back pain	55	1	1	0	0	0	44	5	5	1	0	0
Blurred vision	54	2	0	1	0	0	46	9	0	0	0	0
Cardiac arrest	56	0	0	0	1	0	55	0	0	0	0	0
Cardiac disorder-Other, spec	54	2	0	1	0	0	53	0	1	1	0	0
Chest pain - cardiac	56	0	0	1	0	0	54	1	0	0	0	0
Confusion	57	0	0	0	0	0	53	1	0	1	0	0
Creatinine increased	49	2	4	1	1	0	49	4	1	1	0	0
Death NOS	57	0	0	0	0	0	53	0	0	0	0	2
Dehydration	55	0	1	1	0	0	52	2	1	0	0	0
Delusions	57	0	0	0	0	0	54	0	0	1	0	0
Diarrhea	44	11	2	0	0	0	43	6	5	1	0	0
Dizziness	50	7	0	0	0	0	49	5	0	1	0	0
Dyspnea	47	3	6	1	0	0	39	9	3	3	1	0
Edema limbs	49	4	3	1	0	0	50	4	1	0	0	0
Ejection fraction decreased	55	0	0	2	0	0	55	0	0	0	0	0
Fatigue	33	10	14	0	0	0	28	13	7	7	0	0
Febrile neutropenia	57	0	0	0	0	0	53	0	0	2	0	0

	Dex+Low Dose Carfilzomib (n=57) Grade						Dex+High Dose Carfilzomib (n=55) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Glaucoma	56	0	0	1	0	0	55	0	0	0	0	0
Heart failure	55	0	1	1	0	0	52	1	0	2	0	0
Hiccups	57	0	0	0	0	0	53	1	0	1	0	0
Hyperglycemia	53	3	1	0	0	0	42	10	0	2	1	0
Hypertension	48	5	2	2	0	0	46	2	3	4	0	0
Hypocalcemia	55	1	1	0	0	0	52	0	2	0	1	0
Hypokalemia	51	4	1	1	0	0	53	2	0	0	0	0
Hyponatremia	55	2	0	0	0	0	52	1	0	2	0	0
Hypophosphatemia	56	0	1	0	0	0	52	0	2	1	0	0
Hypotension	56	0	0	1	0	0	54	1	0	0	0	0
Hypoxia	57	0	0	0	0	0	53	0	0	2	0	0
Infections/infestations-Other	55	0	1	1	0	0	51	0	2	2	0	0
Insomnia	50	5	2	0	0	0	45	5	4	1	0	0
Investigations-Other, specify	55	0	1	1	0	0	55	0	0	0	0	0
LV systolic dysfunction	55	0	0	2	0	0	55	0	0	0	0	0
Lung infection	55	0	0	2	0	0	49	0	0	5	1	0
Lymphocyte count decreased	45	5	5	2	0	0	43	5	3	4	0	0
Lymphocyte count increased	56	0	0	1	0	0	55	0	0	0	0	0
Memory impairment	55	2	0	0	0	0	54	0	0	1	0	0
Nausea	40	11	5	1	0	0	42	9	4	0	0	0
Neutrophil count decreased	50	6	1	0	0	0	46	4	3	1	1	0
Pain in extremity	55	2	0	0	0	0	51	2	1	1	0	0
Platelet count decreased	40	12	2	1	2	0	32	7	4	7	5	0
Resp/thoracic/mediastinal ds	57	0	0	0	0	0	54	0	0	1	0	0
Respiratory failure	56	0	0	0	1	0	55	0	0	0	0	0
Restrictive cardiomyopathy	55	0	0	1	1	0	55	0	0	0	0	0
Sepsis	56	0	0	0	0	1	54	0	0	0	0	1
Stroke	57	0	0	0	0	0	54	0	0	0	1	0
Tumor lysis syndrome	56	0	0	1	0	0	55	0	0	0	0	0
Vomiting	47	5	4	1	0	0	51	2	2	0	0	0
Weight loss	56	0	1	0	0	0	52	1	1	1	0	0
White blood cell decreased	44	9	4	0	0	0	38	8	7	2	0	0
MAX. GRADE ANY ADVERSE EVENT	5	13	18	16	4	1	5	6	12	22	8	2

Registration, Eligibility, and Evaluability

Crossover

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

	Crossover
NUMBER REGISTERED	20
INELIGIBLE	6
Insufficient Documentation	3
Irreversible	3
ELIGIBLE	14
Analyzable, Pend. Elig.	1
RESPONSE ASSESSMENT	
Determinable	2
Not Determinable	2
Too Early	10
ADVERSE EVENT ASSESSMENT	
Evaluable	12
Too Early	2

Treatment Summary

Crossover

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

	Crossover
NUMBER ON PROTOCOL TREATMENT	5
NUMBER OFF PROTOCOL TREATMENT	9
REASON OFF TREATMENT	
Treatment completed as planned	0
Adverse Event or side effects	6
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

Crossover

Adverse Events Unlikely or Not Related to Treatment Excluded

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

	Crossover (n=12) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Acute kidney injury	11	0	0	1	0	0
Alkaline phosphatase increased	11	1	0	0	0	0
Anemia	5	2	2	3	0	0
Anxiety	11	0	1	0	0	0
Atrial flutter	11	0	0	0	1	0
Cough	11	1	0	0	0	0
Creatinine increased	10	1	1	0	0	0
Dehydration	11	0	1	0	0	0
Diarrhea	11	1	0	0	0	0
Dizziness	11	1	0	0	0	0
Dysgeusia	11	1	0	0	0	0
Dyspnea	10	2	0	0	0	0
Fatigue	8	3	1	0	0	0
Generalized muscle weakness	11	0	1	0	0	0
Hypercalcemia	11	0	0	1	0	0
Hypertension	11	0	1	0	0	0
Hypoalbuminemia	11	0	1	0	0	0
Insomnia	11	0	1	0	0	0
Lung infection	11	0	0	0	1	0
Lymphocyte count decreased	9	0	1	2	0	0
Myalgia	11	1	0	0	0	0
Nausea	9	3	0	0	0	0
Peripheral sensory neuropathy	11	1	0	0	0	0
Platelet count decreased	7	2	1	1	1	0
Secondary Leukemia	11	0	0	0	1	0
Sepsis	11	0	0	0	1	0
Sinus disorder	11	0	1	0	0	0
Supraventricular tachycardia	11	0	0	1	0	0
White blood cell decreased	9	1	2	0	0	0
MAX. GRADE ANY ADVERSE EVENT	2	1	1	4	4	0

E1A11 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

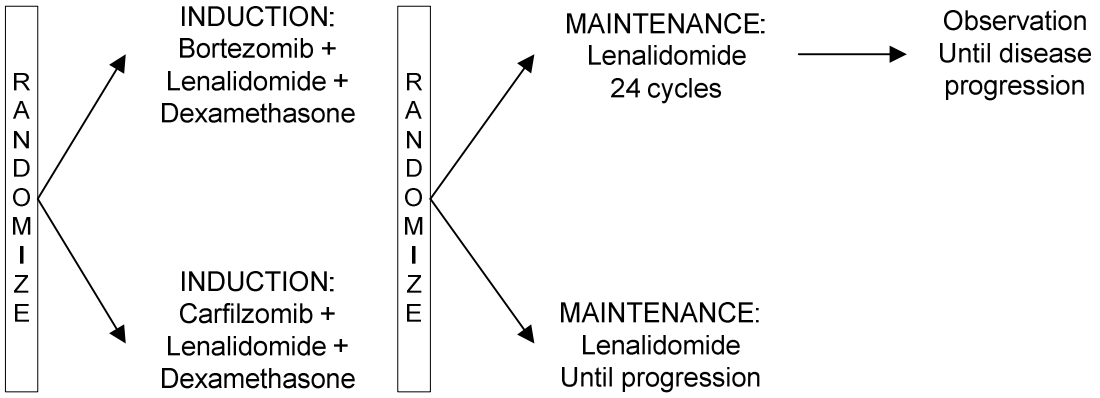
Randomized Phase III Trial of Bortezomib, LENalidomide and Dexamethasone (VRd) Versus Carfilzomib, Lenalidomide and Dexamethasone (CRd) Followed by Limited or Indefinite DURation Lenalidomide MaintenANCE in Patients with Newly Diagnosed Symptomatic Multiple Myeloma (ENDURANCE)

Participants:
ECOG-ACRIN, CTSU

Date Activated:
11/22/2013

Study Chairs:
S Kumar (ECOG-ACRIN), A Cohen, J Zonder (SWOG)

SCHEMA



Objectives

To compare overall survival with the two different lenalidomide maintenance strategies

To compare the progression-free survival and safety of each lenalidomide maintenance approach

To compare the progression-free survival between induction treatments

To compare rates of response, duration of response, time to progression, overall survival, and safety of the induction therapies

Patient Population

Patients must have been diagnosed with symptomatic standard-risk multiple myeloma within the last 90 days and have measurable or evaluable disease.

Patients must not have received lenalidomide, bortezomib, or carfilzomib for the treatment of symptomatic myeloma.

Patients must be at least 18 years of age with an ECOG performance status of 0-2, although 3 is allowed if it is secondary to pain. Patients must have adequate hepatic, renal and hematologic function. Prior malignancies are allowed if treated with curative intent that does not require active therapy. Gluticorticoid use is restricted following registration. Patients must use effective contraception.

Stratification/Descriptive Factors

At registration to induction therapy, patient randomization will be stratified by intent to stem cell transplant at progression: yes vs no. At registration to maintenance therapy, patient randomization will be stratified by induction treatment: Arm A vs Arm B.

Accrual Goals

Seven hundred fifty-six patients will be accrued to this study.

Summary Statement

ECOG-ACRIN reported that 239 patients had registered to this study as of December 31, 2015, including 28 from SWOG institutions. The complete Fall 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
Wayne State Univ	4	Hawaii MU-NCORP	1
Beaumont NCORP	3	Kaiser Perm NCORP	1
KaiserPermanenteCOL/Kaiser Perm NCORP	3	Ozarks NCORP	1
Montana NCORP	3	Sacred Heart Hosp/Arkansas, U of	1
Providence Hosp	3	San Antonio, U of TX	1
Sutter Cancer RC	2	Southeast COR NCORP	1
Baylor College	1	St Jude Medical Ctr/Irvine, U of CA	1
CORA NCORP	1	**Total (16 Institutions)**	**28**
Dayton NCORP	1		

E3A06 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

Randomized Phase III Trial of Lenalidomide versus Observation Alone in Patients with Asymptomatic Smoldering Multiple Myeloma

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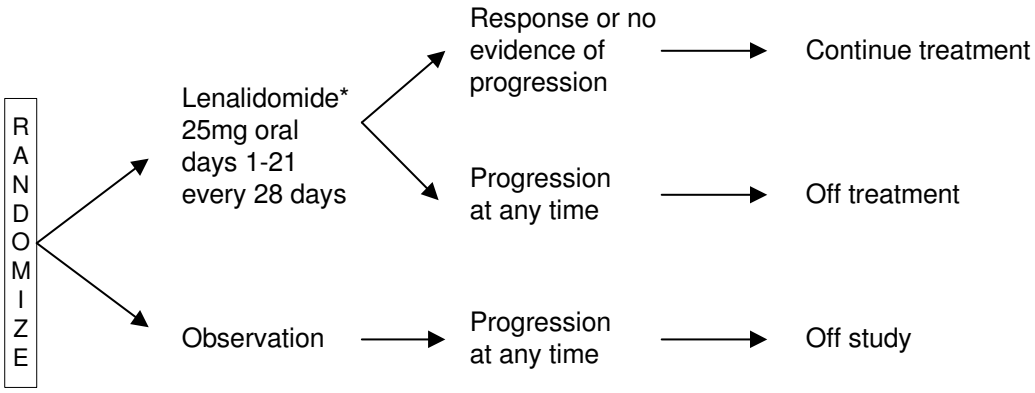
Participants:
ECOG-ACRIN, CTSU

Date Activated:
02/01/2011

Study Chairs:
S Lonial (ECOG-ACRIN), M Dhodapkar (SWOG)

SCHEMA



*Mobilize stem cells following 4 cycles of therapy

Objectives

To compare progression-free survival (where failure is defined as death or the development of symptomatic multiple myeloma requiring therapy) between patients treated with lenalidomide versus observation alone in asymptomatic, smoldering/indolent multiple myeloma.

To compare the response rate, time to progression, one-year progression-free survival rate, duration of response, and overall survival between patients randomized to receive lenalidomide therapy versus observation alone for early-stage multiple myeloma.

To study the effects of lenalidomide on laboratory markers of immune function, evaluate the effect of IgH translocations, and gene expression profiling as predictors of response and risk of progression, and to study the prognostic value of MRI-detected asymptomatic bone disease on outcome.

To evaluate immune function as measured by SOX-2 and correlate to progression-free survival.

Patient Population

Patients must have previously untreated asymptomatic MM diagnosed within one year prior to registration. Patients with smoldering multiple

myeloma (SMM) are eligible. Patients with MGUS are not eligible.

Patients must have received no prior therapy for myeloma or SMM. Prior radiation therapy for the treatment of solitary plasmacytoma is permitted, but more than three months must have elapsed from the last day of radiation.

Patients must be 18 years of age or older. Patients must have an ECOG performance status between 0 and 2 and must not have Grade 2 or higher peripheral neuropathy or active, uncontrolled infection. Patients must not have baseline bone lesions or plasmacytomas.

Accrual Goals

Three hundred thirty-six patients will be randomized with equal allocation to lenalidomide versus observation.

Summary Statement

ECOG-ACRIN reported that 158 patients had registered to this study as of December 31, 2015, including 28 from SWOG institutions. The complete Fall 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
Kansas, U of	12	Ozarks NCORP	1
Greenville NCORP	6	Prov Portland MC/PCRC NCORP	1
Tulane University	2	Providence Hosp	1
Yale University	2	Tennessee, U of	1
Irvine, U of CA	1	**Total (10 Institutions)**	**28**
Montana NCORP	1		