LEUKEMIA COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
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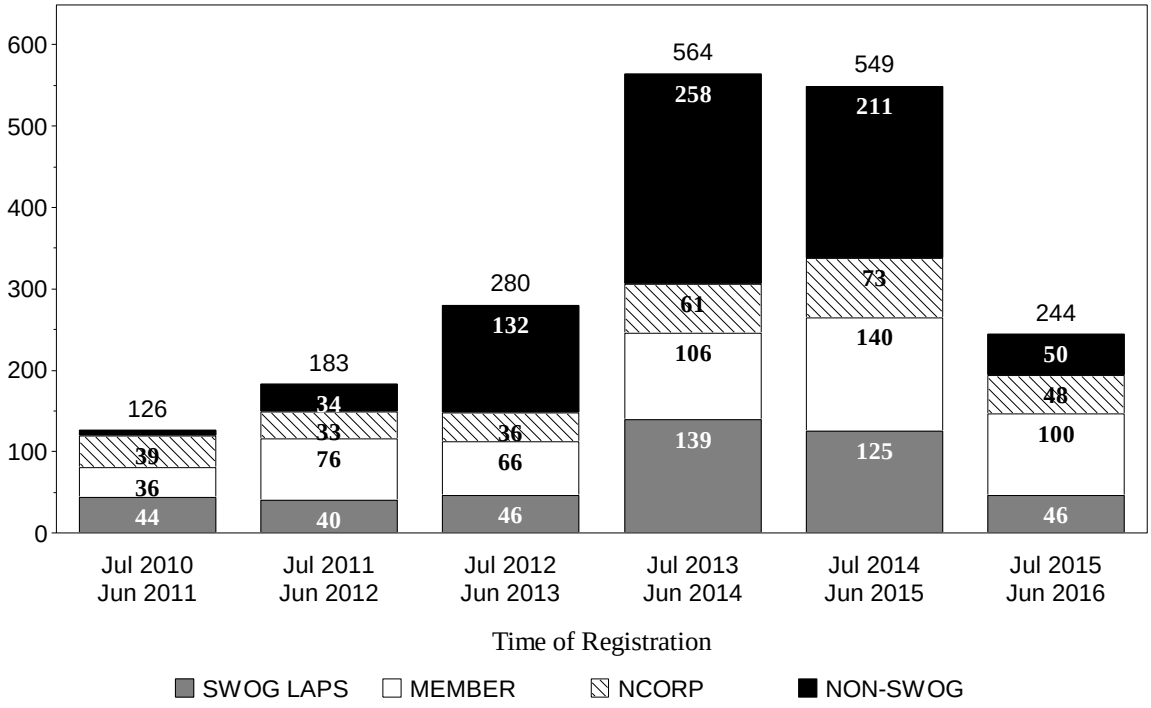

Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

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	Jan 2016 Jun 2016	Jul 2015 Dec 2015	Jan 2015 Jun 2015	All Patients
S0919 Rel AML: Pravastatin+Ida+Ara-C				
Induction				
Pravastatin+Idarubicin+Ara-C	4	3	3	104
S1203 AML, Age 18-60, 7+3/IA/IA+V				
Randomization				
AraC + Daunorubicin	0	44	51	263
AraC + Idarubicin	0	45	49	267
Vorinostat + AraC + Idarubicin	0	0	48	224
	0	89	148	754
S1312 ALL, CD22+, REL/REF, Inotuzumab+CVP				
Initial Registration				
CVP + Inotuzumab dose level 1	0	0	0	5
CVP + Inotuzumab dose level 2	0	0	4	5
CVP + Inotuzumab dose level 3	2	6	3	11
CVP + Inotuzumab dose level 4	1	0	0	1
	3	6	7	22
S1318 ALL, Age 65+, Ph±, Blinatumomab				
Initial registration				
Induction: Ph-negative	4	2	1	7
Induction: Ph-positive	2	0	0	2
	6	2	1	9
A041202 CLL, 65+, Ben+Rtx vs Ibrut±Rtx*				
Registration				
Total Registrations	4	30	30	99
E1910 BCR-ABL-neg, B ALL, Blinatumomab*				
Registration				
Total Registrations	8	9	5	37
E1912 CLL, Age 18-70, Ibrutinib vs FCR*				
Registration				
Total Registrations	37	27	31	130

	Jan 2016 Jun 2016	Jul 2015 Dec 2015	Jan 2015 Jun 2015	All Patients
E2905 MDS, Len vs Len + Epo*				
Registration				
Total Registrations	9	7	5	81

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

S0919 Phase II

A Phase II Study of Idarubicin and Ara-C in Combination with Pravastatin for Poor-risk Acute Myelogenous Leukemia (AML)

Study Chairs:
A Advani, L Michaelis

Date Activated:
08/15/2009

Statisticians:
M Othus, A Moseley

Data Coordinator:
L Highleyman

Objectives

To test whether the complete remission (CR) rate (including CR with incomplete recovery [CRi]) in poor-risk patients with acute myeloid leukemia (AML) treated with a combination of chemotherapy and pravastatin is sufficiently high to warrant Phase III investigation. This will be tested independently in two groups of patients: (1) patients with MDS transformed to AML, and (2) refractory or relapsed patients with previous remission < 6 months.

To estimate relapse-free survival and overall survival rates in these two groups of patients.

To estimate the frequency and severity of toxicities of this regimen in these two groups of patients.

To evaluate in a preliminary manner whether prestudy cytogenetic features correlate with response in these two groups of patients.

Patient Population

MDS transformed to AML cohort (Cohort 1):

Patients must have a previous morphologically confirmed diagnosis of MDS/CMML. Patients may have received previous non-intensive therapy (e.g. azacitidine, decitabine, low-dose cytarabine (LDAC), lenalidomide) given for treatment of MDS/CMML (with up to 20% blasts). At the time of registration patients must have a morphologically confirmed diagnosis of acute myeloid leukemia (AML).

Relapsed/Refractory Cohort (Cohort 2):

Patients must have a previous morphologically confirmed diagnosis of acute myeloid leukemia (AML). Relapse or refractory disease must be documented by a bone marrow examination demonstrating > 5% blasts in the bone marrow not attributable to another cause.

Patients must have received at least one prior induction chemotherapy regimen for their AML and they may have received any type of chemotherapy. Patients must not have received chemotherapy within 14 days prior to registration. Relapsed patients must have achieved CR or CRi, lasting less than six months with their last induction regimen. Primary refractory patients are eligible if, on Day 14 of their previous chemotherapy regimen, they have significant residual disease. Refractory patients who received only hypomethylating agent or low dose therapy for induction are not eligible.

All patients:

Patients with acute promyelocytic leukemia (APL, FAB M3) or blastic transformation of chronic myelogenous leukemia are not eligible.

Patients who have received autologous or allogeneic stem cell transplantation are not eligible.

Patients must have adequate cardiac function as defined in the protocol. Patients must be at least 18 years of age, must have a Zubrod performance status of 0, 1, or 2, and must have adequate renal and hepatic function. Patients must not have clinical evidence of leptomeningeal disease and must not have a systemic fungal, bacterial, viral or other infection that is not controlled. Patients who are known to be HIV+ may be eligible providing they meet all of the criteria in the protocol.

Stratification/Descriptive Factors

Patients will be stratified according to disease status: patients with MDS transformed to AML vs refractory or relapsed patients with previous remission < 6 months.

Accrual Goals

Seventy-four eligible patients will be accrued to the two additional poor-risk cohorts, 37 in each cohort.

Summary Statement

On July 1, 2012, the study was temporarily closed to accrual to relapsed patients with previous remission of longer than three months. Final results for this cohort of 36 patients were reported in the Spring 2013 Report of Studies and are not included in this report. On April 1, 2013, the study was re-opened to two additional poor-risk cohorts: patients with MDS transformed AML, and refractory or relapsed patients with previously remission less than six months. The following tables, other than 'Registration by Institution' show accrual only for these two poor-risk cohorts.

Relapsed/Refractory Cohort:

The study was closed to accrual for refractory/relapsed AML patients on November 24, 2014, after meeting the accrual goal with 50 patients registered. Three patients are ineligible: one due to prior stem cell transplantation and two due to previous remission longer than six months. One patient had a cardiac event prior to starting treatment causing a decline in performance status. This patient did not receive any protocol therapy and is not included in any analyses. A major protocol deviation is coded for one patient who received an extra dose of Ara-C.

Forty-six relapsed/refractory AML patients have been assessed for adverse events. Four treatment related deaths occurred: one due to sepsis (reported as Inf, Unk ANC: blood), another due to hypotension, a third due to beta strep Group B (reported as Inf, 3-4 ANC: blood), and a fourth due to respiratory failure (reported as DLCO). An additional 11 patients experienced treatment-related Grade 4 non-hematologic toxicities.

Two patients accrued to the refractory/relapsed cohort are ineligible for consolidation therapy because the patients are ineligible for the induction step. An additional patient who relapsed prior to consolidation treatment began is not evaluable for toxicities. No Grade 3 or higher toxicity has been reported for consolidation therapy.

MDS Transformed to AML Cohort:

As of June 30, 2016, 18 patients have been accrued to the MDS transformed to AML cohort. Among the 12 patients assessed for adverse events, one patient died from respiratory failure possibly related to treatment (reported as DLCO). Two additional patients reported treatment-related Grade 4 non-hematologic toxicities.

Registration by Institution

Initial Registration

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Stanford University	24	Wichita NCORP	4
Cleveland Clinic OH	23	Birmingham, U of AL	3
Rochester, Univ of	14	PCRC NCORP	2
H Lee Moffitt CC	11	LSU-Shreveport/Gulf South MU-NCORP	1
Colorado, U of	6	Mississippi, Univ of	1
Baylor College	5	Tulane Univ MBCCOP	1
New Mexico MU-NCORP	5	**Total (14 Institutions)**	**104**
Loyola University	4		

Registration, Eligibility, and Evaluability

Classified by Disease status

Initial Registration

Registrations from April 1, 2013 through June 30, 2016; Data as of July 1, 2016

	TOTAL	MDS transformed to AML	Refractory or relapsed with previous remission < 6 months
NUMBER REGISTERED	68	18	50
INELIGIBLE	3	0	3
ELIGIBLE	65	18	47
Analyzable, Pend. Elig.	2	2	0
Not Analyzable	1	0	1
RESPONSE ASSESSMENT			
Determinable	55	15	40
Not Determinable	6	0	6
Too Early	3	3	0
ADVERSE EVENT ASSESSMENT			
Evaluable	58	12	46
Too Early	6	6	0

Patient Characteristics

Classified by Disease status

Initial Registration

Registrations from April 1, 2013 through June 30, 2016; Data as of July 1, 2016

	MDS transformed to AML (n=18)		Refractory or relapsed with previous remission < 6 months (n=46)	
AGE				
Median	64.3		57.3	
Minimum	21.8		23.1	
Maximum	71.9		75.0	
SEX				
Males	10	56%	24	52%
Females	8	44%	22	48%
HISPANIC				
Yes	0	0%	4	9%
No	17	94%	38	83%
Unknown	1	6%	4	9%
RACE				
White	17	94%	35	76%
Black	1	6%	2	4%
Asian	0	0%	6	13%
Multi-Racial	0	0%	3	7%

Treatment Summary

Classified by Disease status

Initial Registration

Registrations from April 1, 2013 through June 30, 2016; Data as of July 1, 2016

	TOTAL	MDS transformed to AML	Refractory or relapsed with previous remission < 6 months
NUMBER ON PROTOCOL TREATMENT	2	2	0
NUMBER OFF PROTOCOL TREATMENT	62	16	46
REASON OFF TREATMENT			
Treatment completed as planned	55	16	39
Adverse Event or side effects	1	0	1
Refusal unrelated to adverse event	1	0	1
Progression/relapse	0	0	0
Death	5	0	5
Other - not protocol specified	0	0	0
Reason under review	0	0	0
MAJOR PROTOCOL DEVIATIONS	1	0	1

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

Classified by Disease status

Initial Registration

Adverse Events Unlikely or Not Related to Treatment Excluded

Non-Hematologic Adverse Events Only

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

Registrations from April 1, 2013 through June 30, 2016; Data as of July 1, 2016

	MDS transformed to AML (n=12) Grade				Refractory or relapsed with previous remission < 6 months (n=46) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
ALT	11	1	0	0	44	2	0	0
AST	10	2	0	0	45	1	0	0
Alkaline phosphatase	12	0	0	0	45	1	0	0
Cardiac ischemia/infarction	11	0	1	0	46	0	0	0
Colitis, infectious	12	0	0	0	45	1	0	0
Creatinine	11	1	0	0	44	2	0	0
DLCO	10	0	1	1	45	0	0	1
Diarrhea	11	1	0	0	38	8	0	0
Dyspnea	12	0	0	0	44	1	1	0
Edema-limb	11	1	0	0	46	0	0	0
Fatigue	12	0	0	0	44	2	0	0
Febrile neutropenia	4	8	0	0	14	27	5	0
GI Inf, 3-4 ANC: stomach	12	0	0	0	45	1	0	0
GI Pain: abdomen	11	1	0	0	46	0	0	0
GI Pain: esophagus	12	0	0	0	45	1	0	0
GI Pain: oral cavity	12	0	0	0	43	3	0	0
GU Inf, 3-4 ANC: kidney	12	0	0	0	45	1	0	0
Hypoalbuminemia	11	1	0	0	40	6	0	0
Hypocalcemia	10	2	0	0	43	2	1	0
Hypokalemia	10	2	0	0	43	3	0	0
Hyponatremia	12	0	0	0	45	1	0	0
Hypophosphatemia	11	1	0	0	44	2	0	0
Hypotension	11	0	1	0	45	0	0	1
Hypoxia	12	0	0	0	43	3	0	0
Inf, 3-4 ANC: blood	11	0	1	0	39	1	5	1
Inf, Unk ANC: blood	11	0	1	0	42	0	3	1
Lung Hemorrhage: bronchopulm.	12	0	0	0	45	0	1	0
Lung Hemorrhage: nose	12	0	0	0	45	1	0	0
Lung Inf, 3-4 ANC: bronchus	12	0	0	0	45	1	0	0
Lung Inf, 3-4 ANC: lung	11	1	0	0	40	5	1	0
Lung Inf, Unk ANC: mucosa	12	0	0	0	45	1	0	0
Mucositis, clin: oral cavity	12	0	0	0	45	1	0	0
Mucositis, clin: pharynx	12	0	0	0	45	0	1	0
Mucositis, funct: oral cav.	12	0	0	0	45	1	0	0
Musculo. Pain: bone	12	0	0	0	45	1	0	0
Musculo. Pain: limb	12	0	0	0	45	1	0	0
Nausea	12	0	0	0	43	3	0	0
Neuro Inf, 3-4 ANC: mening.	12	0	0	0	45	0	1	0
Opportunistic infection	12	0	0	0	44	2	0	0

	MDS transformed to AML (n=12) Grade				Refractory or relapsed with previous remission < 6 months (n=46) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
Rash	12	0	0	0	45	1	0	0
Renal failure	12	0	0	0	44	0	2	0
Skin Inf, 3-4 ANC: skin	11	1	0	0	46	0	0	0
Typhlitis	12	0	0	0	45	1	0	0
Ulceration	12	0	0	0	45	1	0	0
Vomiting	11	1	0	0	46	0	0	0
Weight Loss	12	0	0	0	44	2	0	0
MAX. GRADE ANY ADVERSE EVENT	1	8	2	1	3	28	11	4

S1203 Phase III

Coordinating Group: SWOG

A Randomized Phase III Study of Standard Cytarabine plus Daunorubicin (7+3) Therapy or Idarubicin with High Dose Cytarabine (IA) Versus IA with Vorinostat (NSC-701852) (IA+V) in Younger Patients with Previously Untreated Acute Myeloid Leukemia (AML)

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

Study Chairs:
G Garcia-Manero, J Pagel, D Rizzieri (Alliance), M Savoie (CCTG), S Strickland (ECOG-ACRIN)

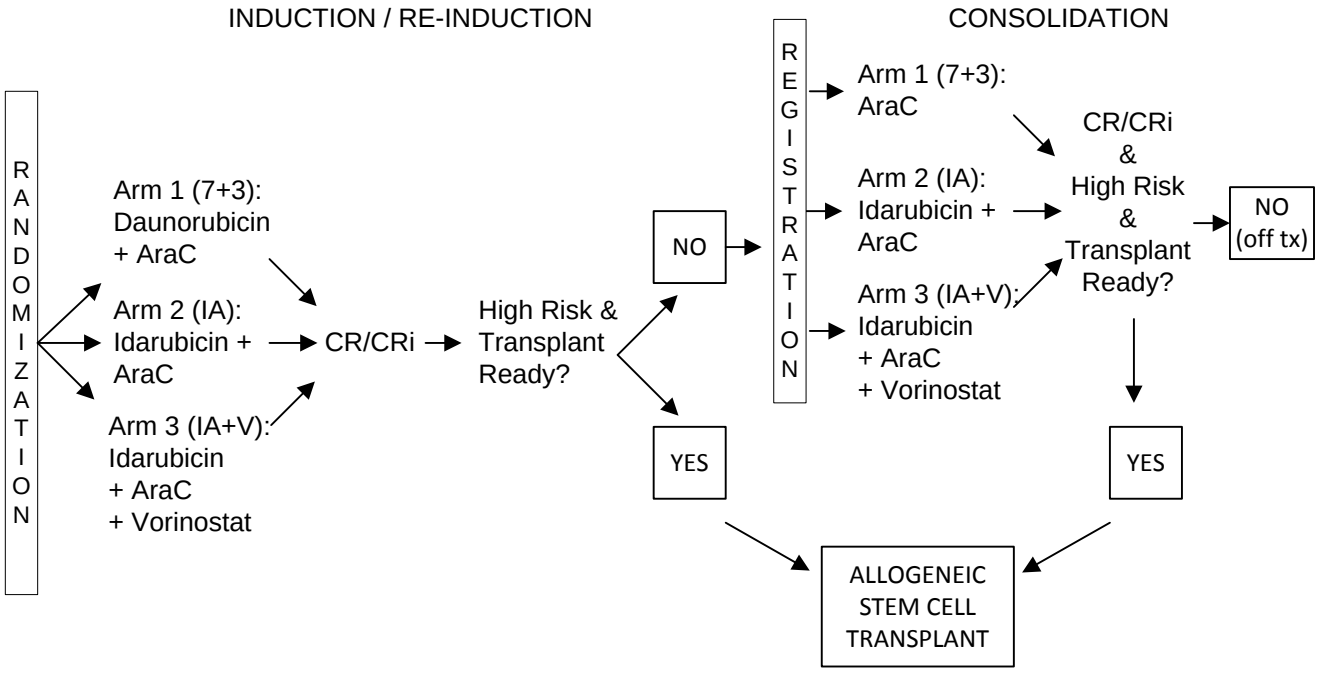
Statisticians:
M Othus, A Moseley

Data Coordinators:
T Maher, L Kingsbury, L Highleyman

Date Activated:
02/08/2013

Date Closed:
11/04/2015

SCHEMA



Objectives

To compare event-free survival (EFS) between patients with AML who receive standard 7+3 or idarubicin and high-dose cytarabine (IA) to patients who receive IA + vorinostat.

To determine whether it is possible to get 60% or more of adults with high-risk AML (by cytogenetics) in first complete remission (CR1) to allogeneic hematopoietic cell transplantation (HCT).

To estimate the frequency and severity of toxicities of the three regimens in this patient population.

To estimate disease-free survival (DFS) among patients who receive transplant.

To compare event-free survival (EFS) between patients who receive standard 7+3 to patients who receive IA.

To estimate the prevalence of the mutations NPM1, IDH1, IDH2, TET2 and DMT3A and the cytogenetic risk distribution of patients on this study and to evaluate the association between these and overall survival (OS), event-free survival (EFS), disease-free survival (DFS), and complete remission rate.

To compare the complete response rate, disease-free survival (DFS), and overall survival (OS) between patients who receive standard 7+3 therapy or IA to patients who receive IA + vorinostat.

Future planned studies will include testing of histone H3 acetylation, induction of gammaH2AX, analysis of ROS resistance and DNA methylation profiles.

Patient Population

Patients must have morphologically confirmed newly diagnosed acute myelogenous leukemia (AML) with blood or bone marrow disease, as defined in the protocol. Patients with only extramedullary disease in the absence of bone marrow or blood involvement are not eligible.

Patients must not have received any prior induction chemotherapy for AML or MDS. Temporary prior measures such as apheresis or hydroxyurea are allowed. Prior anthracycline therapy is allowed, but must not exceed a dose of 200 mg/m^2 daunorubicin or equivalent. Prior ATRA for suspected APL and prior methotrexate for CNS involvement are allowed. Patients with prior history of MDS must not have received azacitidine, decitabine, lenalidomide or vorinostat.

Patients must be between 18 and 60 (inclusive) years of age. Patients must have Zubrod performance status of 3 or lower. Patients must have adequate cardiac function. Patients must not have prolonged QTc interval or cardiac disease. Patients with a prior malignancy are eligible providing they do not require concurrent therapy other than hormonal therapy. Patients must not be receiving valproic acid. Patients who are known to be HIV+ are eligible providing they meet additional criteria in the protocol. Patients with known Hepatitis B or Hepatitis C infection may be eligible providing they have viral load below 800,000 IU/mL.

Stratification/Descriptive Factors

At randomization, patients will be stratified as follows: (1) age at registration: < 40 years vs ⩾ 40 years; (2) onset of leukemia: de novo vs treatment related and/or AML arising from antecedent hematologic disease.

Accrual Goals

The initial accrual goal of this study was 705 eligible patients (235 eligible patients per arm). Arm 3 (Idarubicin +AraC +Vorinostat) was permanently closed to accrual on May 22, 2015, with a total of 224 patients enrolled. Arm 1 (AraC + Daunorubicin) and Arm 2 (AraC + Idarubicin) remain open to accrual until 235 eligible patients enrolled on each arm. Up to five interim analyses will be completed. The first analysis will check for harm and the second analysis will test for futility. The third, fourth, and fifth interim analyses will include both futility and efficacy analyses.

Summary Statement

The study was temporarily closed to accrual on May 22, 2015, due to the outcome of an interim analysis reviewed by the SWOG Data Safety and Monitoring Committee (DSMC) on May 1, 2015. The DSMC analysis showed futility for Arm 3 (Idarubicin +AraC +Vorinostat) showing superiority to either Arm 1 (AraC + Daunorubicin) or Arm 2 (AraC + Idarubicin). The DSMC recommended the closure of Arm 3. Patients currently receiving treatment on Arm 3 who choose to continue protocol treatment may do so with or without vorinostat. If a patient chooses to remain on Arm 3 without vorinostat, the treatment schedule should follow that of Arm 2. The study was reactivated on June 19, 2015 with randomization to either Arm 1 or Arm 2.

The study was permanently closed to accrual on November 4, 2015 with 754 patients registered. Sixteen patients are ineligible due to the following reasons: insufficient blasts (7), no evidence of AML (3), positive Philadelphia chromosome in bone marrow, having APL, receiving valproic acid at the time of registration, being intubated prior to registration, inadequate cardiac function, and testing positive for TB (1 patient each). Seven eligible patients who did not receive any protocol treatment, coded as major protocol deviations, are not evaluable for adverse events. One additional patient was coded as a major protocol deviation, having been given Ara-C at the wrong dose. Eighty-four patients went off protocol therapy for "Other" reasons, the majority of which were physician discretion and/or lack of treatment efficacy.

Seven hundred twenty-two patients were assessed for adverse events on protocol induction treatment. Six treatment-related deaths occurred on the 7+3 arm (AraC + Daunorubicin) due to the following reasons: cardiac arrest, platelet decreased (coded as Death NOS), venous occlusive disease (coded as Hepatobil disorders-Other), multi-organ failure, respiratory failure, and typhlitis (one each). An additional 34 patients on the 7+3 arm experienced Grade 4 non-hematologic toxicities as maximum degree, including one patient with Aspergillus pneumonia, stenotrophomonas, and central line E. coli (coded as Infections/infestations-Other).

Eighteen treatment-related deaths occurred on the IA arm (AraC + Idarubicin) due to the following reasons: sepsis (6), respiratory failure (3), cardiac arrest (2), and one case each of multi-organ failure, unspecified death, ARDS, gastric hemorrhage, hematoma, bronchopulmonary hemorrhage with cardiac arrest, and brain herniation (coded as Nervous sys disorders-Other) with sepsis. One patient who died of sepsis also experienced Grade 4 ischemic bowel and another patient who died of respiratory failure also experienced Grade 4 necrosis of the colon (both coded as GI disorders-Other). One patient who died of sepsis and brain herniation also experienced Grade 4 septic shock and septic emboli (coded as Infections/infestations-Other). An additional 34 patients experienced Grade 4 non-hematologic toxicities as maximum degree, including one patient with heart failure (coded as Cardiac disorder-Other), three patients with monocyte count decrease (coded as Investigations-Other), one patient with hematocrit decrease (coded as Investigations-Other), and one patient with acute renal failure (coded as Renal/urinary disorders-Other).

Sixteen treatment-related deaths occurred on the IA+V arm (AraC + Idarubicin + Vorinostat) due to the following reasons: sepsis (7), respiratory failure (5), multi-organ failure (2), and one case each of bronchopulmonary hemorrhage, cardiac arrest, and intracranial hemorrhage. One patient who died of multi-organ failure also experienced Grade 4 bradycardia (coded as Cardiac disorder-Other). An additional 38 patients experienced Grade 4 non-hematologic toxicities as maximum degree, including one patient with sepsis (coded as Infections/infestations-Other), one patient with monocyte count decrease (coded as Investigations-Other), and one patient with lactate (coded as Investigations-Other).

Fourteen patients are currently ineligible for consolidation due to the following reasons: not meeting protocol defined remission (7), being ineligible for induction (5), persistent leukemia cutis, and evidence of residual extramedullary disease. One patient on the IA arm who did not receive any consolidation treatment, coded as a major protocol deviation, is not evaluable for adverse events. Two other patients are coded as major protocol deviations: one on the IA arm who progressed after registration to consolidation therapy and before treatment started and one on the IA+V arm who never returned for treatment after consolidation was delayed due to fatty liver.

Two possibly treatment-related deaths occurred during consolidation on the 7+3 arm: one due to seizure and one is reported as both respiratory/thoracic/mediastinal disorder and Death NOS. Twenty-six additional patients on the 7+3 consolidation arm experienced Grade 4 non-hematologic toxicities as maximum degree.

One treatment-related death occurred during consolidation on the IA arm due to sepsis. Twenty-five additional patients experienced Grade 4 non-hematologic toxicities during consolidation as maximum degree.

Five treatment-related deaths occurred on the IA+V consolidation arm due to the following reasons: respiratory failure (2), sepsis (2), lung infection, and intracranial hemorrhage. Twenty-six additional patients experienced Grade 4 non-hematologic toxicities during consolidation as maximum degree.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Alliance	218	Dayton NCORP	6
ECOG-ACRIN	161	MD Anderson CC	5
Stanford University	47	New Mexico MU-NCORP	4
Cleveland Clinic OH	27	Northwestern Univ	4
Kansas, U of	27	Prov Portland MC/PCRC NCORP	4
Birmingham, U of AL	25	Providence Hosp	4
CCTG	24	Florida, Univ of/Yale University	3
Rochester, Univ of	22	Heartland NCORP	3
Davis, U of CA	17	Montana NCORP	3
Yale University	15	Upstate Carolina	3
MUSC MU-NCORP	13	Wayne State Univ	3
NRG	13	Baylor College	2
Oregon Hlth Sci Univ	13	Kansas City NCORP	2
Kentucky, U of	12	Michigan, U of	2
Loyola University	10	PCRC NCORP	2
Mississippi, Univ of	9	San Diego, U of CA	2
Oklahoma, Univ of	9	CTSU	1
City of Hope Med Ctr	8	Michigan CRC NCORP	1
Irvine, U of CA	8	Ozarks NCORP	1
H Lee Moffitt CC	7	Southeast COR NCORP	1
Arizona MC, U of	6	St Luke's Mt State/PCRC NCORP	1
CRC West MI NCORP	6	**Total (43 Institutions)**	**754**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2016; Data as of July 1, 2016

	TOTAL	AraC + Daunorubicin	AraC + Idarubicin	Vorinostat + AraC + Idarubicin
NUMBER REGISTERED	754	263	267	224
INELIGIBLE	16	2	6	8
ELIGIBLE	738	261	261	216
RESPONSE ASSESSMENT				
Determinable	696	254	244	198
Not Determinable	41	6	17	18
Too Early	1	1	0	0
ADVERSE EVENT ASSESSMENT				
Evaluable	722	257	257	208
Not Evaluable	7	0	2	5
Too Early	9	4	2	3

Patient Characteristics

Registrations ending June 30, 2016; Data as of July 1, 2016

	AraC + Daunorubicin (n=261)		AraC + Idarubicin (n=261)		Vorinostat + AraC + Idarubicin (n=216)	
AGE						
Median	48.3		51.4		48.9	
Minimum	19.2		18.8		19.6	
Maximum	60.8		60.9		61.0	
< 40 years	68.0	26%	65.0	25%	55.0	25%
⩾ 40 years	193.0	74%	196.0	75%	161.0	75%
SEX						
Males	130	50%	134	51%	114	53%
Females	131	50%	127	49%	102	47%
HISPANIC						
Yes	19	7%	22	8%	21	10%
No	226	87%	217	83%	185	86%
Unknown	16	6%	22	8%	10	5%
RACE						
White	218	84%	217	83%	178	82%
Black	19	7%	19	7%	17	8%
Asian	6	2%	4	2%	7	3%
Pacific Islander	2	1%	1	0%	0	0%
Native American	3	1%	0	0%	3	1%
Multi-Racial	1	0%	1	0%	0	0%
Unknown	12	5%	19	7%	11	5%
ONSET						
De novo	236	90%	236	90%	193	89%
Treatment related and/or AML arising from antecedent hematologic disease	25	10%	25	10%	23	11%

Treatment Summary

Registrations ending June 30, 2016; Data as of July 1, 2016

	Total
NUMBER ON PROTOCOL TREATMENT	0
NUMBER OFF PROTOCOL TREATMENT	738
REASON OFF TREATMENT	
Treatment completed as planned	579
Adverse Event or side effects	17
Refusal unrelated to adverse event	19
Progression/relapse	4
Death	34
Other - not protocol specified	84
Reason under review	1
MAJOR PROTOCOL DEVIATIONS	8

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Non-Hematologic Adverse Events Only

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

Registrations ending June 30, 2016; Data as of July 1, 2016

	AraC + Daunorubicin (n=257) Grade				AraC + Idarubicin (n=257) Grade				Vorinostat + AraC + Idarubicin (n=208) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
ALT increased	245	11	1	0	240	17	0	0	188	19	1	0
ARDS	256	0	1	0	254	1	1	1	204	0	4	0
AST increased	249	7	1	0	243	14	0	0	196	11	1	0
AV block complete	257	0	0	0	256	1	0	0	208	0	0	0
Abdominal distension	256	1	0	0	257	0	0	0	207	1	0	0
Abdominal infection	256	1	0	0	256	0	1	0	207	1	0	0
Abdominal pain	253	4	0	0	251	6	0	0	200	8	0	0
Acidosis	256	0	1	0	256	1	0	0	206	1	1	0
Acute kidney injury	255	0	2	0	252	2	3	0	204	2	2	0
Alkaline phosphatase increased	255	2	0	0	255	2	0	0	207	1	0	0
Alkalosis	256	1	0	0	256	1	0	0	206	2	0	0
Allergic reaction	257	0	0	0	257	0	0	0	206	2	0	0
Anal hemorrhage	257	0	0	0	257	0	0	0	207	1	0	0
Anal pain	257	0	0	0	256	1	0	0	208	0	0	0
Anal ulcer	257	0	0	0	257	0	0	0	207	1	0	0
Anorectal infection	257	0	0	0	257	0	0	0	204	4	0	0
Anorexia	252	4	1	0	242	15	0	0	196	12	0	0
Atelectasis	257	0	0	0	257	0	0	0	207	1	0	0
Atrial fibrillation	257	0	0	0	254	0	3	0	207	0	1	0
Atrial flutter	257	0	0	0	256	1	0	0	207	1	0	0
Blood bilirubin increased	248	8	1	0	242	12	3	0	187	17	4	0
Bone infection	256	1	0	0	257	0	0	0	208	0	0	0
Bone pain	257	0	0	0	256	1	0	0	208	0	0	0
Bronchopulmonary hemorrhage	256	1	0	0	256	0	0	1	205	1	1	1
Bullous dermatitis	257	0	0	0	255	2	0	0	208	0	0	0
Cardiac arrest	256	0	0	1	254	0	0	3	206	0	1	1
Cardiac disorder-Other, spec	256	1	0	0	256	0	1	0	207	0	1	0
Cardiac troponin I increased	257	0	0	0	256	1	0	0	208	0	0	0
Catheter related infection	255	2	0	0	250	7	0	0	204	4	0	0
Chills	256	1	0	0	257	0	0	0	208	0	0	0
Chronic kidney disease	257	0	0	0	255	1	1	0	208	0	0	0
Cognitive disturbance	257	0	0	0	257	0	0	0	207	1	0	0
Colitis	254	3	0	0	248	9	0	0	203	3	2	0
Colonic hemorrhage	255	2	0	0	257	0	0	0	207	1	0	0
Colonic perforation	257	0	0	0	257	0	0	0	207	0	1	0
Conduction disorder	256	0	1	0	257	0	0	0	208	0	0	0
Confusion	257	0	0	0	255	2	0	0	208	0	0	0
Conjunctivitis	256	1	0	0	257	0	0	0	208	0	0	0
Constipation	257	0	0	0	256	1	0	0	208	0	0	0
Constrictive pericarditis	256	1	0	0	257	0	0	0	208	0	0	0
Creatinine increased	256	1	0	0	251	4	2	0	204	3	1	0
DIC	255	2	0	0	256	1	0	0	207	1	0	0
Death NOS	256	0	0	1	256	0	0	1	208	0	0	0
Dehydration	256	1	0	0	257	0	0	0	205	3	0	0

	AraC + Daunorubicin (n=257) Grade				AraC + Idarubicin (n=257) Grade				Vorinostat + AraC + Idarubicin (n=208) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
Dental caries	256	1	0	0	257	0	0	0	208	0	0	0
Device related infection	256	1	0	0	254	3	0	0	208	0	0	0
Diarrhea	242	15	0	0	237	20	0	0	170	37	1	0
Dry mouth	257	0	0	0	256	1	0	0	208	0	0	0
Dry skin	257	0	0	0	255	2	0	0	208	0	0	0
Duodenal hemorrhage	256	0	1	0	257	0	0	0	208	0	0	0
Dyspepsia	256	1	0	0	257	0	0	0	208	0	0	0
Dysphagia	256	1	0	0	256	1	0	0	208	0	0	0
Dyspnea	254	2	1	0	251	3	3	0	200	5	3	0
ECG QT corrected int prolong	257	0	0	0	255	1	1	0	206	2	0	0
Edema cerebral	257	0	0	0	257	0	0	0	207	0	1	0
Edema limbs	257	0	0	0	254	3	0	0	206	2	0	0
Ejection fraction decreased	255	1	1	0	251	5	1	0	204	4	0	0
Encephalopathy	257	0	0	0	256	1	0	0	208	0	0	0
Enterocolitis	256	1	0	0	251	4	2	0	203	5	0	0
Enterocolitis infectious	256	1	0	0	253	4	0	0	204	4	0	0
Epistaxis	255	2	0	0	256	1	0	0	206	2	0	0
Erythema multiforme	256	1	0	0	257	0	0	0	208	0	0	0
Erythroderma	257	0	0	0	257	0	0	0	207	1	0	0
Esophageal hemorrhage	257	0	0	0	257	0	0	0	207	1	0	0
Esophageal pain	256	1	0	0	256	1	0	0	208	0	0	0
Esophagitis	254	3	0	0	255	2	0	0	207	1	0	0
Eye infection	257	0	0	0	256	1	0	0	208	0	0	0
Fatigue	243	14	0	0	239	18	0	0	195	13	0	0
Febrile neutropenia	108	143	6	0	98	149	10	0	95	108	5	0
Fever	253	3	1	0	250	7	0	0	202	5	1	0
GERD	256	1	0	0	257	0	0	0	208	0	0	0
GGT increased	254	3	0	0	255	2	0	0	204	4	0	0
GI disorders-Other, specify	256	1	0	0	252	3	2	0	207	1	0	0
Gait disturbance	257	0	0	0	257	0	0	0	207	1	0	0
Gastric hemorrhage	257	0	0	0	255	1	0	1	205	2	1	0
Gastritis	256	1	0	0	257	0	0	0	208	0	0	0
Gen disorders/admin site cond	257	0	0	0	254	2	1	0	207	1	0	0
Generalized muscle weakness	255	2	0	0	256	1	0	0	206	2	0	0
Genital edema	257	0	0	0	257	0	0	0	207	1	0	0
Glucose intolerance	256	1	0	0	257	0	0	0	208	0	0	0
Gum infection	256	1	0	0	257	0	0	0	208	0	0	0
Hand-Foot syndrome	257	0	0	0	255	2	0	0	208	0	0	0
Headache	255	2	0	0	255	2	0	0	204	4	0	0
Heart failure	254	3	0	0	255	2	0	0	205	1	2	0
Hematoma	257	0	0	0	256	0	0	1	208	0	0	0
Hematuria	257	0	0	0	255	2	0	0	208	0	0	0
Hepatic failure	256	0	1	0	257	0	0	0	208	0	0	0
Hepatic infection	256	1	0	0	256	1	0	0	208	0	0	0
Hepatobil disorders-Other	256	0	0	1	257	0	0	0	207	1	0	0
Hyperglycemia	253	4	0	0	247	8	2	0	192	15	1	0
Hyperhidrosis	256	1	0	0	256	1	0	0	208	0	0	0
Hyperkalemia	257	0	0	0	256	0	1	0	207	1	0	0
Hypermagnesemia	257	0	0	0	256	1	0	0	208	0	0	0
Hypernatremia	257	0	0	0	257	0	0	0	207	0	1	0

	AraC + Daunorubicin (n=257) Grade				AraC + Idarubicin (n=257) Grade				Vorinostat + AraC + Idarubicin (n=208) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
Hypertension	250	7	0	0	251	6	0	0	203	4	1	0
Hyperuricemia	257	0	0	0	256	1	0	0	207	0	1	0
Hypoalbuminemia	252	4	1	0	249	8	0	0	200	8	0	0
Hypocalcemia	250	6	1	0	243	13	1	0	184	21	3	0
Hypoglycemia	257	0	0	0	257	0	0	0	207	1	0	0
Hypokalemia	239	15	3	0	237	20	0	0	184	22	2	0
Hypomagnesemia	257	0	0	0	257	0	0	0	207	1	0	0
Hyponatremia	238	17	2	0	238	19	0	0	200	8	0	0
Hypophosphatemia	236	18	3	0	226	27	4	0	178	28	2	0
Hypotension	254	3	0	0	246	7	4	0	199	4	5	0
Hypoxia	255	1	1	0	253	3	1	0	199	5	4	0
Ileus	257	0	0	0	256	1	0	0	206	2	0	0
Infections/infestations-Other	240	16	1	0	240	16	1	0	194	13	1	0
Infective myositis	256	1	0	0	257	0	0	0	208	0	0	0
Inj/poisoning/proced comp-Oth	256	1	0	0	257	0	0	0	208	0	0	0
Intracranial hemorrhage	257	0	0	0	257	0	0	0	207	0	0	1
Investigations-Other, specify	256	1	0	0	251	2	4	0	205	1	2	0
Irregular menstruation	256	1	0	0	257	0	0	0	208	0	0	0
Jejunal obstruction	257	0	0	0	257	0	0	0	207	1	0	0
Kidney infection	257	0	0	0	256	1	0	0	208	0	0	0
LV systolic dysfunction	255	2	0	0	254	3	0	0	208	0	0	0
Laryngeal edema	256	1	0	0	257	0	0	0	208	0	0	0
Laryngeal mucositis	257	0	0	0	257	0	0	0	207	1	0	0
Lipase increased	257	0	0	0	257	0	0	0	206	2	0	0
Lower GI hemorrhage	257	0	0	0	256	1	0	0	205	3	0	0
Lung infection	237	20	0	0	236	17	4	0	195	11	2	0
MS/connective tissue disorder	257	0	0	0	256	1	0	0	207	1	0	0
Menorrhagia	256	1	0	0	257	0	0	0	208	0	0	0
Metab/nutrition disorders-Oth	256	1	0	0	256	1	0	0	208	0	0	0
Middle ear inflammation	256	1	0	0	257	0	0	0	208	0	0	0
Mucosal infection	256	1	0	0	257	0	0	0	207	1	0	0
Mucositis oral	238	18	1	0	240	17	0	0	197	11	0	0
Multi-organ failure	256	0	0	1	254	0	2	1	203	1	2	2
Myalgia	257	0	0	0	257	0	0	0	207	1	0	0
Nausea	250	7	0	0	243	14	0	0	203	5	0	0
Neck edema	257	0	0	0	257	0	0	0	207	1	0	0
Nervous sys disorders-Other	257	0	0	0	256	0	0	1	208	0	0	0
Non-cardiac chest pain	256	1	0	0	257	0	0	0	207	1	0	0
Oral pain	252	5	0	0	252	5	0	0	208	0	0	0
Pain	256	1	0	0	257	0	0	0	208	0	0	0
Pain in extremity	256	1	0	0	257	0	0	0	207	1	0	0
Papulopustular rash	257	0	0	0	256	1	0	0	208	0	0	0
Paresthesia	257	0	0	0	257	0	0	0	207	1	0	0
Pericardial effusion	257	0	0	0	257	0	0	0	207	1	0	0
Pericardial tamponade	257	0	0	0	257	0	0	0	207	0	1	0
Periorbital edema	257	0	0	0	256	1	0	0	208	0	0	0
Peripheral sensory neuropathy	257	0	0	0	257	0	0	0	207	1	0	0
Pharyngeal mucositis	256	1	0	0	257	0	0	0	208	0	0	0
Pharyngitis	256	1	0	0	257	0	0	0	208	0	0	0
Pleural effusion	256	1	0	0	257	0	0	0	207	1	0	0

	AraC + Daunorubicin (n=257) Grade				AraC + Idarubicin (n=257) Grade				Vorinostat + AraC + Idarubicin (n=208) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
Pneumonitis	256	1	0	0	253	3	1	0	206	2	0	0
Pruritus	257	0	0	0	256	1	0	0	207	1	0	0
Pulmonary edema	256	1	0	0	255	1	1	0	203	4	1	0
Purpura	257	0	0	0	256	1	0	0	208	0	0	0
Rash acneiform	256	1	0	0	256	1	0	0	208	0	0	0
Rash maculo-papular	246	11	0	0	231	26	0	0	198	10	0	0
Rectal hemorrhage	256	1	0	0	257	0	0	0	208	0	0	0
Rectal pain	256	1	0	0	257	0	0	0	207	1	0	0
Renal/urinary disorders-Other	257	0	0	0	256	0	1	0	208	0	0	0
Resp/thoracic/mediastinal ds	256	1	0	0	254	2	1	0	206	1	1	0
Respiratory failure	254	0	2	1	249	0	5	3	194	0	9	5
Restrictive cardiomyopathy	256	1	0	0	257	0	0	0	208	0	0	0
Salivary duct inflammation	256	1	0	0	257	0	0	0	208	0	0	0
Scrotal infection	257	0	0	0	257	0	0	0	207	0	1	0
Scrotal pain	257	0	0	0	257	0	0	0	207	1	0	0
Seizure	256	1	0	0	257	0	0	0	207	1	0	0
Sepsis	241	0	16	0	232	0	18	7	176	0	25	7
Sinus bradycardia	257	0	0	0	257	0	0	0	207	1	0	0
Sinus tachycardia	257	0	0	0	255	2	0	0	206	2	0	0
Sinusitis	255	2	0	0	257	0	0	0	208	0	0	0
Skin infection	252	5	0	0	256	1	0	0	205	3	0	0
Skin ulceration	257	0	0	0	257	0	0	0	207	1	0	0
Skin/subq tissue ds-Other	257	0	0	0	255	2	0	0	207	1	0	0
Soft tissue infection	256	0	1	0	257	0	0	0	208	0	0	0
Sore throat	256	1	0	0	255	2	0	0	206	2	0	0
Stomach pain	256	1	0	0	257	0	0	0	208	0	0	0
Stroke	257	0	0	0	256	1	0	0	207	0	1	0
Supraventricular tachycardia	257	0	0	0	256	1	0	0	207	1	0	0
Syncope	255	2	0	0	255	2	0	0	205	3	0	0
TTP	254	1	2	0	257	0	0	0	207	1	0	0
Testicular disorder	257	0	0	0	256	1	0	0	208	0	0	0
Thromboembolic event	256	1	0	0	257	0	0	0	208	0	0	0
Tooth infection	256	1	0	0	257	0	0	0	208	0	0	0
Tumor lysis syndrome	253	4	0	0	249	8	0	0	199	9	0	0
Typhlitis	249	7	0	1	244	13	0	0	185	22	1	0
Upper GI hemorrhage	256	1	0	0	257	0	0	0	207	1	0	0
Upper respiratory infection	255	2	0	0	256	1	0	0	206	2	0	0
Urinary incontinence	257	0	0	0	257	0	0	0	207	1	0	0
Urinary tract infection	252	5	0	0	255	2	0	0	202	6	0	0
Urine output decreased	257	0	0	0	257	0	0	0	207	1	0	0
Vaginal hemorrhage	257	0	0	0	257	0	0	0	206	2	0	0
Vascular access complication	257	0	0	0	255	2	0	0	207	0	1	0
Vasovagal reaction	257	0	0	0	256	1	0	0	207	0	1	0
Ventricular tachycardia	257	0	0	0	256	1	0	0	208	0	0	0
Vomiting	254	3	0	0	251	6	0	0	204	4	0	0
Weight loss	255	2	0	0	257	0	0	0	206	2	0	0
Wound infection	256	1	0	0	257	0	0	0	208	0	0	0
MAX. GRADE ANY ADVERSE EVENT	68	149	34	6	49	156	34	18	37	117	38	16

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

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.

S1312 Phase I

A Phase I Study of Inotuzumab (NSC-772518) in Combination with CVP (Cyclophosphamide, Vincristine, Prednisone) for Patients with Relapsed/Refractory CD22-Positive Acute Leukemia (including B-ALL, Mixed Phenotypic Leukemia, and Burkitt's Leukemia)

Study Chairs:
A Advani, M Liedtke

Date Activated:
04/01/2014

Statisticians:
M Othus, A Moseley

Data Coordinator:
L Highleyman

Objectives

To assess the safety of inotuzumab in combination with cyclophosphamide, vincristine and prednisone (CVP) and to determine the maximum tolerated dose (MTD) of inotuzumab in this regimen for patients with relapsed or refractory CD22-positive acute leukemia (B-ALL, mixed phenotype, and Burkitt's).

To estimate the preliminary activity [response rate: complete remission (CR) + complete remission with incomplete count recovery (CRi)] of this combination in the expansion cohort.

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

Patient Population

Patients must have a diagnosis of relapsed or refractory CD22-positive acute leukemia including B-ALL, mixed phenotype leukemia (bilineal and biphenotypic), or Burkitt's leukemia based on WHO classification. Patients with bilineal leukemia are excluded. Patients must have evidence of acute leukemia in their peripheral blood or bone marrow. Patients must have ≥ 5% blasts in the peripheral blood or bone marrow. At least ≥ 20% of those blasts must be CD22-positive (surface) based on local immunophenotyping and histopathology. Patients must be refractory or have relapsed following prior induction therapy.

Patients may have received prior allogeneic transplant or autologous transplant. Patients with prior allogeneic bone marrow transplant will be eligible only if the conditions stated in the protocol are met. Patients known to have Ph+ ALL must have either failed treatment or been intolerant to treatment with at least one second or third generation tyrosine kinase inhibitor. Patients must not have received prior treatment with inotuzumab. Previous treatment with other anti-CD22 antibodies must have been completed at least 90 days prior to registration. Patients must not have received any chemotherapy, investigational agents, or undergone major surgery within 14 days prior to registration with the following exceptions: (1) Monoclonal antibodies must not have been received for one week prior to registration; (2) Chimeric antigen receptor (CAR) T-cells must not have been received for 28 days prior to registration; (3) Steroids, hydroxyurea, vincristine, 6-mercaptopurine, methotrexate, thioguanine and intrathecal chemotherapy are permitted within any time frame prior to registration. FDA-approved tyrosine kinase inhibitors may also be administered until one day prior to start of study therapy (C1, D1). All drug-related toxicities must have resolved to ≤ Grade 2. Treatment with hydroxyurea and steroids is permitted to bring down peripheral blast count.

Patients must be at least 18 years of age and have Zubrod performance status of 0-2. Patients must not have a systemic bacterial, fungal, or viral infection that is not controlled. Patients must not have active

CNS involvement. Patients must have < Grade 2 neuropathy (sensory/motor). Patients must not have a history of chronic or active hepatitis B or C infection. Patients must not have evidence or history of veno-occlusive disease or sinusoidal obstruction syndrome. Patients who are known to be HIV+ are eligible providing they meet all of the criteria in the protocol. Patients with a history of a serious allergic or anaphylactic reaction to humanized monoclonal antibodies are not eligible. Patients must have adequate hematologic, renal, hepatic and cardiac function.

Accrual Goals

Patient enrollment will follow the traditional "3+3" algorithm until the MTD for inotuzumab is reached or the highest dose tested is judged tolerable. This study will accrue 3-30 eligible and evaluable patients in the Phase I portion and six additional eligible patients in the expansion cohort.

Summary Statement

The study will evaluate up to five dose levels of inotuzumab.

The initial dose level of 0.4 mg/m^2 inotuzumab completed accrual on November 1, 2014 with five eligible patients registered. The second dose level evaluating inotuzumab at 0.6 mg/m^2 on day 1 and 0.4 mg/m^2 on day 15 was closed to accrual on May 15, 2015 with five patients registered. One patient was ineligible due to inadequate liver function, leaving four eligible patients in this dose level. The third dose level evaluating inotuzumab at 0.8 mg/m^2 on day 1 and 0.4 mg/m^2 on day 15 was closed to accrual on April 15, 2016 with 11 patients registered. One patient was ineligible due to inadequate liver function, leaving 10 eligible patients in this dose level.

There were no dose limiting toxicities (DLT) in either the first or second dose level.

Four of the 10 eligible patients in the third dose level were not evaluable for DLT: two patients were removed from treatment before prolonged myelosuppression could be assessed, one patient died and did not receive a full cycle of treatment, and one patient continued to take tyrosine kinase inhibitor (TKI) while on protocol and is coded as a major protocol deviation. One of the first three evaluable patients experienced DLT (prolonged myelosuppression), so three additional slots were opened on this dose level on November 5, 2015. None of these additional patients experienced a DLT. One patient went off treatment after cycle 3 to receive a transplant. Among 10 patients assessed for toxicity, one patient experienced Grade 4 hyperglycemia.

The fourth dose level was opened to accrual on June 7, 2016 and has accrued one patient as of June 30, 2016.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg
Cleveland Clinic OH	8
City of Hope Med Ctr	5
Rochester, Univ of	4
Baylor College	3
Stanford University	2
Total (5 Institutions)	**22**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2016; Data as of July 5, 2016

	TOTAL	CVP + Inotuzumab dose level 1	CVP + Inotuzumab dose level 2	CVP + Inotuzumab dose level 3	CVP + Inotuzumab dose level 4
NUMBER REGISTERED	22	5	5	11	1
INELIGIBLE	2	0	1	1	0
ELIGIBLE	20	5	4	10	1
Analyzable, Pend. Elig.	1	0	0	0	1
RESPONSE ASSESSMENT					
Determinable	17	5	4	8	0
Not Determinable	2	0	0	2	0
Too Early	1	0	0	0	1
ADVERSE EVENT ASSESSMENT					
Evaluable	19	5	4	10	0
Too Early	1	0	0	0	1
DLT ASSESSMENT					
Evaluable	12	3	3	6	0
Not Evaluable	7	2	1	4	0
Too Early	1	0	0	0	1

Patient Characteristics

Registrations ending June 30, 2016; Data as of July 5, 2016

	CVP + Inotuzumab dose level 1 (n=5)		CVP + Inotuzumab dose level 2 (n=4)		CVP + Inotuzumab dose level 3 (n=10)		CVP + Inotuzumab dose level 4 (n=1)	
AGE								
Median	48.9		42.3		42.8		33.1	
Minimum	22.4		20.7		22.4		33.1	
Maximum	73.7		56.4		75.4		33.1	
SEX								
Males	4	80%	0	0%	6	60%	0	0%
Females	1	20%	4	100%	4	40%	1	100%
HISPANIC								
Yes	2	40%	2	50%	2	20%	1	100%
No	3	60%	2	50%	7	70%	0	0%
Unknown	0	0%	0	0%	1	10%	0	0%
RACE								
White	4	80%	3	75%	6	60%	1	100%
Black	1	20%	1	25%	2	20%	0	0%
Unknown	0	0%	0	0%	2	20%	0	0%

Treatment Summary

Registrations ending June 30, 2016; Data as of July 5, 2016

	TOTAL	CVP + Inotuzumab dose level 1	CVP + Inotuzumab dose level 2	CVP + Inotuzumab dose level 3	CVP + Inotuzumab dose level 4
NUMBER ON PROTOCOL TREATMENT	2	0	0	1	1
NUMBER OFF PROTOCOL TREATMENT	18	5	4	9	0
REASON OFF TREATMENT					
Treatment completed as planned	3	1	2	0	0
Adverse Event or side effects	2	0	0	2	0
Refusal unrelated to adverse event	0	0	0	0	0
Progression/relapse	6	1	1	4	0
Death	1	0	0	1	0
Other - not protocol specified	6	3	1	2	0
Reason under review	0	0	0	0	0
MAJOR PROTOCOL DEVIATIONS	1	0	0	1	0

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Hematologic Adverse Events Only

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

Registrations ending June 30, 2016; Data as of July 5, 2016

	CVP + Inotuzumab dose level 1 (n=5) Grade				CVP + Inotuzumab dose level 2 (n=4) Grade				CVP + Inotuzumab dose level 3 (n=10) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
Anemia	4	0	1	0	3	1	0	0	6	4	0	0
Lymphocyte count decreased	4	0	1	0	3	1	0	0	7	2	1	0
Neutrophil count decreased	3	0	2	0	1	2	1	0	4	1	5	0
Platelet count decreased	3	0	2	0	2	0	2	0	7	1	2	0
White blood cell decreased	2	0	3	0	0	2	2	0	2	2	6	0
MAX. GRADE ANY ADVERSE EVENT	2	0	3	0	0	1	3	0	2	2	6	0

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

Adverse Events Unlikely or Not Related to Treatment Excluded

Non-Hematologic Adverse Events Only

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

Registrations ending June 30, 2016; Data as of July 5, 2016

	CVP + Inotuzumab dose level 1 (n=5) Grade				CVP + Inotuzumab dose level 2 (n=4) Grade				CVP + Inotuzumab dose level 3 (n=10) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
Febrile neutropenia	5	0	0	0	3	1	0	0	8	2	0	0
Fever	5	0	0	0	3	1	0	0	10	0	0	0
GI disorders-Other, specify	5	0	0	0	3	1	0	0	10	0	0	0
Gastric hemorrhage	4	1	0	0	4	0	0	0	10	0	0	0
Headache	5	0	0	0	3	1	0	0	10	0	0	0
Hyperglycemia	5	0	0	0	4	0	0	0	8	1	1	0
Hypertension	5	0	0	0	4	0	0	0	9	1	0	0
Hypocalcemia	5	0	0	0	4	0	0	0	9	1	0	0
Intracranial hemorrhage	4	1	0	0	4	0	0	0	10	0	0	0
MAX. GRADE ANY ADVERSE EVENT	3	2	0	0	3	1	0	0	4	5	1	0

S1318 Phase II

Coordinating Group: SWOG

A Phase II Study of Blinatumomab and POMP (Prednisone, Vincristine, Methotrexate, 6-Mercaptopurine) for Elderly Patients (≥ 65 Years of Age) with Newly Diagnosed Acute Lymphoblastic Leukemia (ALL)

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

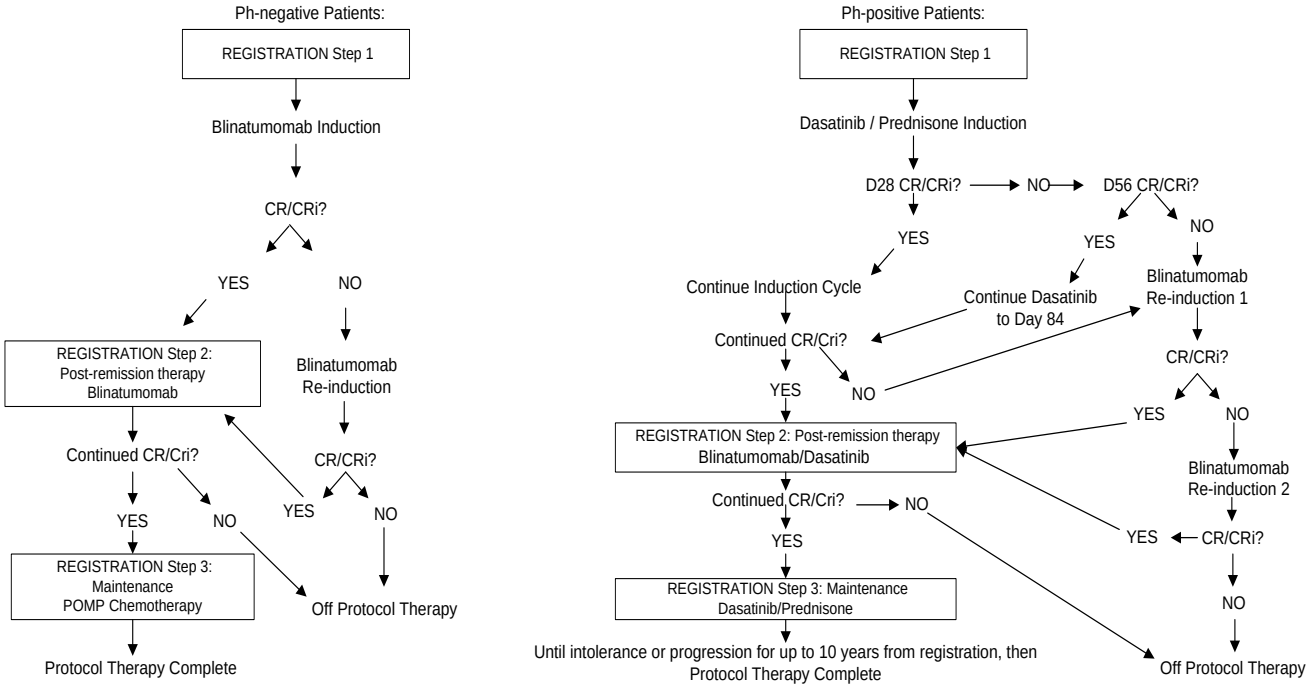
Date Activated:
01/12/2015

Study Chairs:
A Advani, K O'Dwyer, M Wiedewult (Alliance), J Park (ECOG-ACRIN)

Statisticians:
M Othus, A Moseley

Data Coordinator:
T Maher

SCHEMA



Objectives

To evaluate the three-year survival rate in elderly patients with newly diagnosed Philadelphia chromosome (Ph) negative ALL treated with blinatumomab followed by POMP maintenance.

To evaluate in a preliminary manner (feasibility study) the safety of dasatinib-steroid based induction followed by blinatumomab treatment in combination with dasatinib followed by dasatinib-based maintenance in elderly patients with newly diagnosed Ph-positive ALL, relapsed/refractory Ph-positive ALL, and Ph-like DSMKF ALL (newly-diagnosed relapsed or refractory).

To evaluate toxicities in these patient populations treated with these regimens.

To estimate the rates of complete response (CR), complete response with incomplete count recovery (CRi), and disease-free survival in Ph-negative patients.

To estimate disease-free and overall survival in Ph-positive ALL and Ph-like DSMKF ALL.

To estimate in each cohort the rate of minimal residual disease (MRD) negativity, and the time to achieve MRD negativity (exploratory analysis).

To determine whether anti-idiotype antibodies directed against blinatumomab develop with blinatumomab treatment in this study.

Patient Population

Patients must have a new morphologic diagnosis of precursor B cell acute lymphoblastic leukemia (ALL) (non-T cell) based on WHO criteria as defined in protocol. Patients with Burkitts (L3) are not eligible for this study. Patients with Ph-positive or Ph-like ALL with dasatinib-sensitive mutations or kinase fusions (DSMKF) may have relapsed or refractory diagnoses. Patients must have a diagnosis of Ph-negative ALL or Ph-positive ALL by cytogenetics, FISH or polymerase chain reaction (PCR). If not already known, BCR-ABL status (p190 or p210) must be evaluated in Ph-positive patients by PCR. To be registered under the Ph-like DSMKF criterion, the patient must have a known or presumed activating Ph-like signature and dasatinib-sensitive mutation or kinase fusion as defined in the protocol. Patients must have evidence of ALL in their marrow or peripheral blood with at least 20% lymphoblasts (at least 5% for relapsed/refractory patients) within 14 days prior to registration. At registration, relapsed/refractory patients must submit pathology and cytogenetics reports from time of original diagnosis. Immunophenotyping of the blood or marrow lymphoblasts must be performed to determine lineage within 14 days prior to registration. Patients with only extramedullary disease in the absence of bone marrow or blood involvement are not eligible. Patients must not have testicular involvement.

Patients must not have received any prior chemotherapy, radiation therapy, or other therapy for the treatment of ALL (other than those noted below) and must not be receiving any immunosuppressive therapy. Patients must not have received any prior investigational therapy within 28 days prior to registration. Patients may have received the following within any time prior to registration: low dose chemotherapy, TKI therapy, steroids, hydroxyurea, leukapheresis, intrathecal chemotherapy, or vincristine. Patients must not have received any monoclonal antibody therapy within 42 days of registration.

Patients must be at least 65 years of age and have a Zubrod performance status of 0-2. Patients must have adequate hepatic, cardiac and renal function. Patients must not have a history or presence of clinically relevant CNS pathology and must have a lumbar puncture to determine CNS involvement of ALL within 14 days prior to registration. Patients must not have systemic fungal, bacterial, viral or other infection that is not controlled. Patients must not have Grade 2 or higher neuropathy (cranial, motor or sensory) within 14 days prior to registration. Patients known to be positive for HIV may be eligible, providing they meet the criteria in the protocol. Patients must not be candidates for allogeneic hematopoietic stem cell transplant. Patients must not have any known autoimmune disease. Ph-negative patients must have PT/PTT/INR/fibrinogen and neurologic assessment tests within 28 days prior to registration. Ph-positive patients must not have active pericardial effusion, ascites or pleural effusion of any grade.

Stratification/Descriptive Factors

Patients are stratified by Registration Cohort (1 and 2).

Accrual Goals

This study will accrue up to 26 eligible Ph-negative patients. An interim analysis will be performed among the first 11 of these patients. If at least five complete remissions (CR or CRi) are observed, then

the study will continue to full accrual. The study will continue accruing while the remission data is being reviewed.

This study will initially accrue six eligible and evaluable Ph-positive/Ph-like DSMKF patients. If the regimen is considered safe, then the study will accrue nine additional eligible Ph-positive/Ph-like DSMKF patients.

Summary Statement

The study was activated on January 12, 2015. As of June 30, 2016, seven patients have been enrolled to the Ph-negative cohort and two have been enrolled to the Ph-positive/Ph-like DSMKF cohort.

Of the six patients evaluable for toxicity, one patient in the Ph-negative cohort died due to respiratory failure possibly related to treatment. One other patient in the Ph-negative cohort experienced Grade 4 lung infection possibly related to treatment. No Grade 4 or higher non-hematologic adverse events have been reported in the Ph-positive/Ph-like DSMKF cohort.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg
Alliance	3
Cleveland Clinic OH	2
City of Hope Med Ctr	1
ECOG-ACRIN	1
New Mexico MU-NCORP	1
Rochester, Univ of	1
Total (6 Institutions)	**9**

Registration, Eligibility, and Evaluability

Registrations ending June 30, 2016; Data as of July 25, 2016

	TOTAL	Induction: Ph -negative	Induction: Ph -positive
NUMBER REGISTERED	9	7	2
ELIGIBLE	9	7	2
Analyzable, Pend. Elig.	1	1	0
RESPONSE ASSESSMENT			
Determinable	4	3	1
Not Determinable	1	1	0
Too Early	4	3	1
ADVERSE EVENT ASSESSMENT			
Evaluable	6	4	2
Too Early	3	3	0

Patient Characteristics

Registrations ending June 30, 2016; Data as of July 25, 2016

	Induction: Ph -negative (n=7)		Induction: Ph -positive (n=2)	
AGE				
Median	76.2		73.3	
Minimum	66.3		73.0	
Maximum	79.2		73.6	
SEX				
Males	5	71%	0	0%
Females	2	29%	2	100%
HISPANIC				
Yes	1	14%	0	0%
No	6	86%	2	100%
RACE				
White	7	100%	2	100%

Treatment Summary

Registrations ending June 30, 2016; Data as of July 25, 2016

	TOTAL	Induction: Ph -negative	Induction: Ph -positive
NUMBER ON PROTOCOL TREATMENT	5	3	2
NUMBER OFF PROTOCOL TREATMENT	4	4	0
REASON OFF TREATMENT			
Treatment completed as planned	3	3	0
Adverse Event or side effects	0	0	0
Refusal unrelated to adverse event	0	0	0
Progression/relapse	0	0	0
Death	1	1	0
Other - not protocol specified	0	0	0
Reason under review	0	0	0
MAJOR PROTOCOL DEVIATIONS	0	0	0

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

Adverse Events Unlikely or Not Related to Treatment Excluded
Non-Hematologic Adverse Events Only
Adverse Events with No Entries for Grades 3 to 5 Have Been Suppressed
Registrations ending June 30, 2016; Data as of July 25, 2016

	Induction: Ph-negative (n=4) Grade				Induction: Ph-positive (n=2) Grade			
ADVERSE EVENTS	**⩽2**	**3**	**4**	**5**	**⩽2**	**3**	**4**	**5**
Diarrhea	4	0	0	0	1	1	0	0
Dyspnea	3	0	1	0	2	0	0	0
Febrile neutropenia	4	0	0	0	1	1	0	0
Hyperglycemia	3	1	0	0	2	0	0	0
Infections/infestations-Other	3	1	0	0	2	0	0	0
Infusion related reaction	3	1	0	0	2	0	0	0
Joint infection	3	1	0	0	2	0	0	0
Lung infection	3	0	1	0	2	0	0	0
Pneumonitis	3	1	0	0	2	0	0	0
Respiratory failure	3	0	0	1	2	0	0	0
MAX. GRADE ANY ADVERSE EVENT	0	2	1	1	1	1	0	0

A041202 Phase III SWOG Supported CTSU Study

Coordinating Group: Alliance

A Randomized Phase III Study of Bendamustine plus Rituximab Versus Ibrutinib plus Rituximab Versus Ibrutinib Alone In Untreated Older Patients (⩾ 65 Years of Age) With Chronic Lymphocytic Leukemia (CLL)

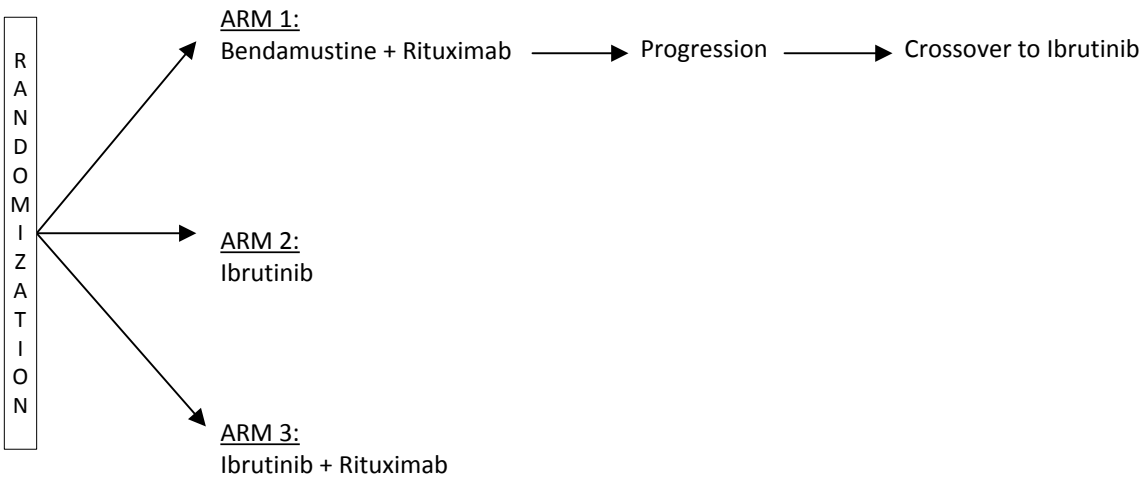
Participants:
Alliance, CTSU

Date Activated:
12/10/2013

Study Chairs:
J Woyach (Alliance), S Coutre (SWOG)

Date Closed:
12/28/2015

SCHEMA



Objectives

To determine whether progression free survival (PFS) is superior after therapy with bendamustine in combination with rituximab, ibrutinib alone, or ibrutinib in combination with rituximab in patients age 65 or older with previously untreated CLL.

To determine 2-year PFS in each of the three treatment arms.

To determine which treatment arm produces superior overall survival (OS).

To determine the complete response (CR) rate, complete and nodular partial response (CR/nPR) rate, and overall response (PR+nPR+CR) rate (ORR) among the three treatment arms and compare these arms.

To determine the impact of MRD-negative disease at time of CR documentation and at 2 years on PFS and OS in each of the treatment arms.

To determine duration of response after each of the three treatments and compare these treatment arms.

To determine toxicity and tolerability of the three treatment regimens.

To determine response and PFS of patients initially on the bendamustine in combination with rituximab arm who cross over to ibrutinib.

To determine whether baseline cytogenetic markers, Zap-70 methylation, IgVH mutational status, or select DNA mutations predict outcomes or time to response in these three arms.

To determine whether local FISH results for del(11q22.3) and del(17p13.1) are consistent with central analysis.

To determine whether baseline microRNA and gene expression markers are correlated with clinical outcomes of interest (e.g. progression-free and alive at 2 years versus not), as well as to explore changes in microRNA expression from baseline to post-treatment time points, with a focus on those with persistent lymphocytosis and relapse.

To determine whether eradication of MRD predicts longer duration of response with standard therapy and ibrutinib-based regimens.

To describe the baseline functional status, comorbid medical conditions, and number of medications of older CLL patients who meet criteria for therapy.

To determine how functional status changes with therapy using baseline to 3-month evaluation and end-of-study/2-year evaluation; to determine whether this change is different among the treatment groups.

To determine whether geriatric assessment variables known to be associated with chemotherapy toxicity in other disease groups can also predict therapy-associated toxicity in the CLL population.

To assess whether the FCGR3A polymorphism (rs396991) is correlated with depth of response (MRD status) to ibrutinib plus rituximab after six cycles, with secondary endpoints CR rate, rapidity of response, and progression-free survival (PFS).

To assess whether C1QA polymorphism (rs172378) is correlated with MRD status, CR rate, rapidity of response, and PFS.

Patient Population

Patients must be diagnosed with CLL in accordance with IWCLL 2008 criteria as defined in the protocol. Patients must have intermediate or high-risk Rai stage CLL. Patients must not have any history of Richter's transformation or prolymphocytic leukemia.

Patients must not have had prior therapy for CLL (except palliative steroids or treatment of autoimmune complications of CLL with rituximab or steroids). Treatment with rituximab and/or high dose corticosteroids for autoimmune complications of CLL must be completed at least four weeks prior to enrollment. Palliative steroids must be at a dose not higher than 20 mg/day of prednisone or equivalent corticosteroid at the time of registration. Patients must not be receiving active systemic anticoagulation with heparin or warfarin. Patients must be off warfarin therapy for at least 30 days prior to enrollment. Patients must not have had major surgery within ten days or minor surgery within seven days of enrollment.

Patients must be at least 65 years of age and have ECOG performance status of 0-2. Patients with active hepatitis B are not eligible. Patients with a positive hepatitis B core antibody but with negative hepatitis B DNA may participate, but must have hepatitis serologies and hepatitis B DNA monitored periodically. Patients must not have uncontrolled active systemic infection requiring intravenous antibiotics. Patients must have adequate hematologic, renal, cardiac and hepatic function. Patients with known HIV are eligible if their CD4 count is $\geq$ 350 cells/mm^3 and if they are not taking prohibited CYP-interacting medications. Patients must not have a known allergy to mannitol or prior significant hypersensitivity to rituximab.

Stratification/Descriptive Factors

Patients are stratified by (1) Rai stage: intermediate vs high; (2) presence or absence of del(11q22.3) or del(17p13.1) on FISH; and (3) methylation of CpG 3 on Zap-70: < 20% vs $\geq$ 20%. In the event that a sample does not yield a Zap-70 methylation status, data will be input based on IgVH mutation status: > 20 if IgVH mutated or < 20 for unmutated.

Accrual Goals

A total of 498 evaluable patients will be accrued to this study. The study will conduct three interim analyses taking place after approximately 33%, 50% and 75% of events have occurred.

Summary Statement

This study closed to pre-registration on December 28, 2015 and closed to registration on May 16, 2016. The final enrollment was 548 registered patients, including 99 registrations from SWOG institutions.

The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Kaiser Perm NCORP	17	PIH Health Hosp/Irvine, U of CA	2
KaiserPermanenteSCAL/Kaiser Perm NCORP	13	Columbus NCORP	1
Rochester, Univ of	10	Fowler Family Center/Baptist MU-NCORP	1
City of Hope Med Ctr	7	KaiserPermanenteCOL/Kaiser Perm NCORP	1
Cleveland Clinic OH	7	MAVERIC	1
Stanford University	6	McLaren Cancer Inst/Wayne State Univ	1
Yale University	6	Poudre Valley Hosp/Colorado, U of	1
Kansas, U of	5	Sacred Heart Hosp/Arkansas, U of	1
Arizona MC, U of	3	San Antonio, U of TX	1
Orange Reg Med Ctr	3	St Luke's Mt State/PCRC NCORP	1
Boston Medical Ctr	2	Stormont-Vail Health/Kansas, U of	1
CORA NCORP	2	Sutter Cancer RC	1
Lahey Hosp & Med Ctr	2	Wayne State Univ	1
Northwestern Univ	2	**Total (27 Institutions)**	**99**

E1910 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Phase III Randomized Trial of Blinatumomab for Newly Diagnosed BCR-ABL-negative B Lineage Acute Lymphoblastic Leukemia in Adults

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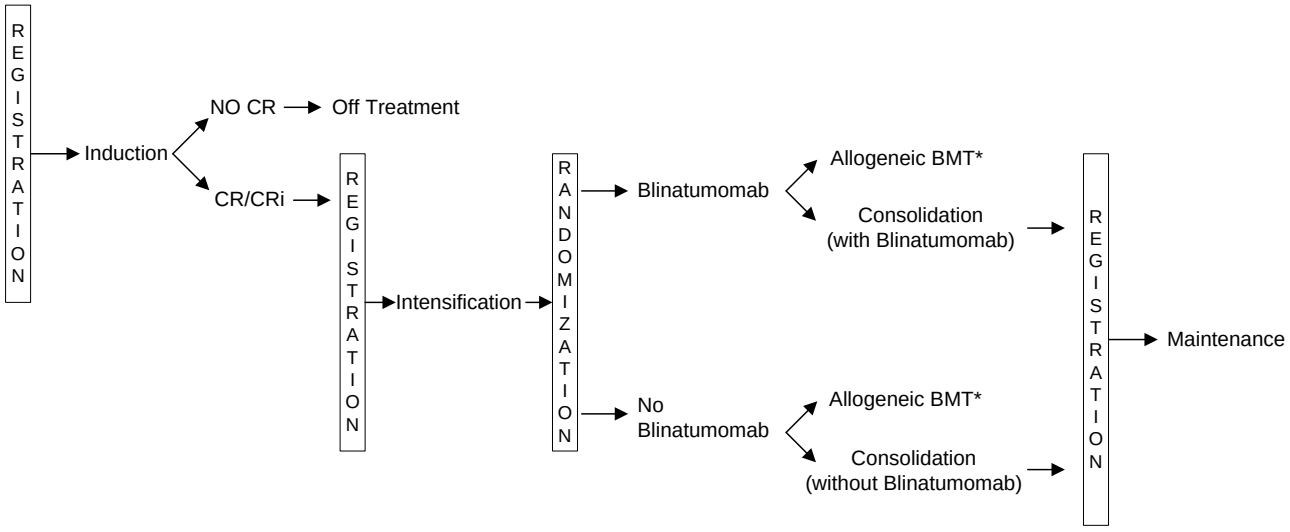
Participants:
ECOG-ACRIN, CTSU

Date Activated:
12/23/2013

Study Chairs:
M Litzow (ECOG-ACRIN), M Liedtke (SWOG)

SCHEMA



*For those patients with a suitable donor who elect to proceed to BMT, patients may receive up to 2 cycles of consolidation chemotherapy prior to transplant.

Objectives

To compare the overall survival (OS) of blinatumomab in conjunction with chemotherapy to chemotherapy alone in patients with BCR-ABL-negative B cell precursor ALL who are MRD positive after induction and intensification chemotherapy, based on multiparameter flow cytometric (MFC) assessment of residual blasts.

If superiority of blinatumomab in the MRD positive group is shown, to compare the OS of blinatumomab in conjuction with chemotherapy to chemotherapy alone in patients with BCR-ABL-negative B cell precursor ALL who are MRD negative after induction and intensification chemotherapy, based on MFC assessment of residual blasts.

If superiority of blinatumomab in the MRD positive group is not shown, to compare the OS of blinatumomab in conjunction with chemotherapy to chemotherapy alone in the overall population of patients with BCR-ABL-negative B cell precursor ALL.

To compare the relapse-free survival (RFS) of blinatumomab in conjunction with chemotherapy to chemotherapy alone in MRD positive patients, MRD negative patients and overall population after induction and intensification chemotherapy.

To determine if blinatumomab can convert patients who are MRD positive by MFC assessment of residual blasts after induction and intensification chemotherapy to MRD negativity.

To assess the toxicities of blinatumomab in this patient population.

To assess the toxicities of the modified E2993 chemotherapy regimen in this patient population.

To describe the outcome of patients who proceed to allogeneic blood or marrow transplant after treatment with or without blinatumomab.

To determine differences in MRD kinetics among patient with the BCR/ABL 1-like B-lineage ALL, and assess the efficacy of blinatumomab in each molecular subgroup.

To evaluate the incidence of anti-blinatumomab antibody formation.

Patient Population

Patients must have newly diagnosed, previously untreated BCR-ABL negative B cell precursor acute lymphoblastic leukemia. Patients with mature B ALL (Burkitt's-like leukemia) are not eligible. Patients must be negative for the Philadelphia chromosome.

Patients must not have a concurrent active malignancy for which they are receiving treatment.

Patients must be between the age of 30 and 70 years and have an ECOG performance status of 0-3. Patients must have adequate hepatic and cardiac function. Patients must not have a history of recent myocardial infarction (within three months of registration), uncontrolled congestive heart failure, or uncontrolled cardiac arrhythmia. Patients must not have a history or presence of clinically relevant CNS pathology. Patients must not have intercurrent organ damage or medical problems that will jeopardize the outcome of therapy. Patients must not have an active uncontrolled infection. Patients with known HIV infection are not eligible. Patients must not have an antecedent hematologic disorder.

Stratification/Descriptive Factors

At randomization (Step 3) patients will be stratified by (1) MRD status: positive vs negative; (2) white blood cell counts (WBC) at diagnosis: < 30,000/mcL vs ≥ 30,000/mcL; (3) age: < 55 years vs ≥ 55 years; and (4) whether patients intend to receive HSCT: yes vs no.

Accrual Goals

The accrual goal for this study is 360 eligible patients. Interim analyses will be performed annually beginning when at least 18 events (approximately 30% information) have occurred in the MRD-positive subgroup.

Summary Statement

ECOG-ACRIN reported a total accrual of 129 patients as of June 30, 2016, including 37 registrations from SWOG institutions. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Yale University	8	Arkansas, U of	1
Stanford University	6	Greenville NCORP	1
Kansas, U of	4	Irvine, U of CA	1
Rochester, Univ of	4	Northwestern Univ	1
Cleveland Clinic OH	3	San Diego, U of CA	1
Arizona MC, U of	2	Wayne State Univ	1
Birmingham, U of AL	2	**Total (14 Institutions)**	**37**
Intermountain MC/Northwest NCORP	2		

E1912 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

A Randomized Phase III Study of Ibrutinib (PCI-32765)-based Therapy vs Standard Fludarabine, Cyclophosphamide, and Rituximab (FCR) Chemoimmunotherapy in Untreated Younger Patients with Chronic Lymphocytic Leukemia (CLL)

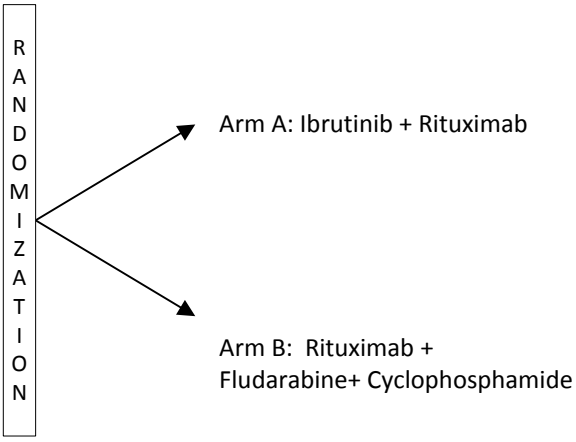
Participants:
ECOG-ACRIN, CTSU

Date Activated:
02/07/2014

Study Chairs:
T Shanafelt (ECOG-ACRIN), S O'Brien (SWOG)

Date Closed:
06/09/2016

SCHEMA



Objectives

The primary objective for the trial is to evaluate the ability of ibrutinib-based induction therapy to prolong progression free survival (PFS) compared to standard FCR chemoimmunotherapy for younger patients with CLL.

To evaluate overall survival (OS) of patients based on treatment arm.

To monitor and assess toxicity of treatment with ibrutinib-based induction relative to standard FCR chemotherapy.

To compare quality of life (QOL) in CLL patients during the first six months of treatment among patients receiving ibrutinib-based induction therapy relative to standard FCR chemoimmunotherapy.

To compare QOL over the long-term in CLL patients receiving continuous therapy using ibrutinib to that of CLL patients who completed FCR therapy.

To determine the effect of pretreatment clinical and biological characteristics on clinical outcomes of the different arms.

To determine if the minimal residual disease (MRD) status as assessed by flow cytometry at different time

points during and after treatment is an effective surrogate marker for prolonged PFS and overall survival.

To compare the genetic abnormalities and dynamics of intra-clonal architecture of CLL patients before and after treatment with CIT and non-CIT approaches and explore relationships with treatment resistance.

To explore the effects of FCR and ibrutinib-based therapy on T-cell immune function.

To conduct confirmatory validation genotyping of single nucleotide polymorphisms (SNPs) associated with the efficacy and toxicity of fludarabine-based therapy as in a prior ECOG GWAS analysis in the E2997 trial.

To evaluate the ability of a prognostic model that incorporates clinical and biologic characters to predict a response to therapy and clinical outcome (PFS, OS).

To evaluate signaling networks downstream of the B-cell receptor in patients receiving ibrutinib-based therapy.

To collect relapse samples to study mechanisms of resistance to both FCR and ibrutinib-based therapy.

Patient Population

Patients must have a diagnosis of CLL according to the NCI/IWCLL criteria or SLL according to the WHO criteria. Patients must meet at least one of the indications for treatment of CLL or small lymphocytic leukemia (SLL) listed in the protocol. Patients must not have deletion of 17p13 on cytogenetic analysis by FISH.

Patients must not have had prior chemotherapy or monoclonal anti-body therapy for treatment of CLL or SLL. Patients must not have had previous use of corticosteroids for autoimmune complications that have developed since the initial diagnosis of CLL. Patients must not have had major surgery within 28 days of first dose of study drug or minor surgery within three days of first dose of study drug. Patients must not have had radiation therapy within four weeks prior to registration. Patients must not have received warfarin or another vitamin K antagonist in the preceding 30 days.

Patients must be between 18 and 70 years of age, life expectancy of at least 12 months, and have an ECOG performance status of 0-2. Patients must have adequate renal, hepatic and cardiac function. Patients must not have active hemolytic anemia requiring immunosuppressive therapy or other pharmacologic treatment. Patients with HIV infection may be eligible provided they meet the criteria listed in the protocol. Patients must not have uncontrolled infection or infection with known chronic, active hepatitis C, or positive serology for hepatitis B. Patients must not have had a cerebral vascular accident or intracranial bleed within the last six months. Patients must not have any known bleeding disorders or any of the gastrointestinal disorders listed in the protocol. Patients must not be vaccinated with live, attenuated vaccines within 4 weeks of first dose of study drug.

Stratification/Descriptive Factors

At randomization, patients will be stratified as follows: (1) age at registration: < 60 years vs ≥ 60 years; (2) ECOG performance status: 0 or 1 vs 2; (3) disease stage: 3 or 4 vs 1 or 2; (4) baseline cytogenetic abnormalities on FISH: deletion 11q22.3(ATM) vs other.

Accrual Goals

The accrual goal of this study is 519 patients: 346 in arm A (Ibrutinib) and 173 patients in arm B (FCR). The first interim analysis will be performed when follow-up is available through the later of five years after the start of accrual or two years after accrual is completed. If this study is not at full information at this time, then interim analyses will be performed annually until full information is reached.

Summary Statement

This study closed to accrual on June 9, 2016 with 529 patients registered, including 130 from SWOG institutions. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
Rochester, Univ of	24	Birmingham, U of AL	1
Kaiser Perm NCORP	20	CORA NCORP	1
Stanford University	20	Greenville NCORP	1
Fred Hutchinson CRC	8	Harrington CC	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	8	Irvine, U of CA	1
Beaumont NCORP	6	KaiserPermanenteCOL/Kaiser Perm NCORP	1
Arkansas, U of	5	Kansas City NCORP	1
Yale University	5	Northwest NCORP	1
Loyola University	3	Orange Reg Med Ctr	1
Montana NCORP	3	Ozarks NCORP	1
UF Cancer Center/Arkansas, U of	3	Providence Hosp	1
Wayne State Univ	3	St Joseph Med Ctr/PCRC NCORP	1
Lahey Hosp & Med Ctr	2	Stanford Cancer Ctr/Stanford University	1
Northwestern Univ	2	Stormont-Vail Health/Kansas, U of	1
San Antonio, U of TX	2	**Total (30 Institutions)**	**130**
Sutter Cancer RC	2		

E2905 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

Randomized Phase III Trial Comparing the Frequency of Major Erythroid Response (MER) to Treatment with Lenalidomide (Revlimid®) Alone and in Combination with Epoetin Alfa (Procrit®) in Subjects with Low- or Intermediate-1 Risk MDS and Symptomatic Anemia

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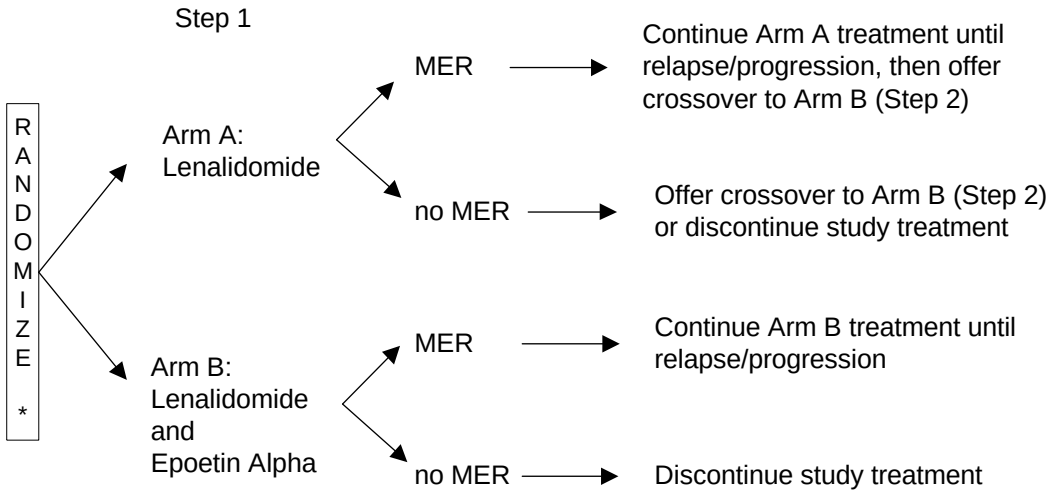
Participants:
ECOG-ACRIN, CTSU

Date Activated:
02/09/2009

Study Chairs:
A List (ECOG-ACRIN), C Schiffer (SWOG)

Date Closed:
05/13/2016

SCHEMA



* Patients with the del 5q31.1 abnormality will not be randomized but will be assigned to Arm A.

Objectives

To compare the rate of major erythroid response (MER) between lenalidomide monotherapy and combined treatment of lenalidomide and epoetin alfa in EPO non-responsive Low/Int-1 risk MDS patients or EPO-treatment naive patients with low probability of EPO benefit.

To compare the time to MER by treatment assignment.

To evaluate the duration of MER by treatment assignment.

To estimate the frequency of MER to salvage combination therapy in patients who fail to experience a MER with lenalidomide monotherapy.

To evaluate and compare the frequency of minor erythroid response by treatment assignment.

To investigate the mechanism and target of lenalidomide action in patients with chromosome 5q31.1 deletion.

To evaluate the frequency of cytogenetic response and progression, and the relation between cytogenetic pattern and erythroid response.

To evaluate the frequency of bone marrow response (CR+PR).

To evaluate the relationship between erythroid response and laboratory correlates of the following: (a) Pretreatment and onstudy endogenous EPO level (Arm A); (b) To evaluate the effect of CD45 isoform profile on lenalidomide enhancement of EPO-induced STAT5 phosphorylation in CD71Hi erythroid precursors and the relationship to erythroid response; (c) To characterize molecular targets relevant to lenalidomide cytotoxicity in del5q31.1 cells; (d) To evaluate the frequency of cryptic chromosome 5q31.1 deletions in patients with non-del5q31.1 MDS by array-based genomic scan, and to determine the relationship to hematologic response.

Patient Population

Patients must have documented diagnosis of MDS lasting at least three months according to WHO criteria or non-proliferative chronic myelomonocytic leukemia. Patients must have International Prognostic Scoring System (IPSS) categories of Low- or Intermediate-1 risk disease. Patients must have IPSS score determined by cytogenetic analysis prior to randomization. Patients with cytogenetic failure and < 10% marrow blasts will be eligible. Patients with cytogenetic failure must have previous cytogenetic results (FISH is not a substitute) within the last six months post last type of MDS treatment (in this case, not referring to growth factors as type of MDS treatment). Patients must have symptomatic anemia untransfused with hemoglobin < 9.5 g/dL within eight weeks of randomization or with RBC transfusion-dependence (i.e., ≥ 2 units/month) confirmed for a minimum of eight weeks before randomization. Patients must not have proliferative (WBC ≥ 12,000/mcL) chronic myelomonocytic leukemia. Patients must not have MDS secondary to treatment with radiotherapy, chemotherapy, and/or immunotherapy for malignant or autoimmune diseases.

Patients without deletion 5q31.1 must have failed treatment with an erythropoietic growth factor, or have a low probability of response to rhu-erythropoietin as defined in the protocol. Patients must be off all non-transfusion therapy for MDS for 28 days prior to initiation of study treatment, including all types of growth factors. Patients may receive hydrocortisone prophylactically to prevent transfusion reactions. Patients must not have prior therapy with lenalidomide or have used cytotoxic chemotherapeutic agents or experimental agents for the treatment of MDS within eight weeks prior to randomization.

Patients must be at least 18 years of age. Patients must have a serum erythropoietin level documented prior to randomization and ≤ 56 days before day 1 of study treatment. Patients must not have documented iron deficiency and must have documented marrow iron stores. If marrow iron stain is not available, the transferrin saturation must be > 20% or a serum ferritin > 100 ng/mL. Patients must have the following lab values documented on two occasions (separated by at least seven days) within 56 days prior to randomization: platelet count ≥ 50,000/mcL without platelet transfusion, ANC ≥ 500 cells/mcL, serum creatinine ≤ 1.5 x ULN, serum SGOT or SGPT ≤ 2.0 x ULN, serum total bilirubin < 3.0 mg/dL. Patients must not have had prior Grade 3 or higher allergic reactions to thalidomide, must not have had a known allergic reaction to epoetin alfa or human serum albumin, and must not have prior desquamating rash at time of study entry. Patients must not have clinically significant anemia resulting from iron, B12, or folate deficiencies, autoimmune or hereditary hemolysis, or gastrointestinal bleeding. Patients must not have a history of thromboembolic events within three years prior to randomization. Patients must not have known HIV-1 seropositivity, uncontrolled seizure, or uncontrolled hypertension.

Stratification/Descriptive Factors

At randomization patients will be stratified by (1) serum erythropoietin level: ≤ 500 mU/mL vs > 500 mU/mL, and (2) prior erythropoietic growth factor treatment: yes vs no. All patients with del 5q31.1 karyotype will be assigned to treatment with lenalidomide monotherapy (Arm A).

Accrual Goals

The study requires 212 patients without 5q31.1 deletion. The estimated accrual goal is a total of 252 eligible patients.

Summary Statement

The study was activated at ECOG-ACRIN on January 29, 2009. The study closed to accrual on May 13, 2016 after the fifth planned interim analysis called for stopping for efficacy. The study enrolled

240 patients including 81 from SWOG institutions. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending June 30, 2016

Institutions	Total Reg	Institutions	Total Reg
H Lee Moffitt CC	29	Providence Hosp	2
KaiserPermanenteSCAL/Kaiser Perm NCORP	7	Columbia MU-NCORP	1
Greenville NCORP	6	CORA NCORP	1
Yale University	6	Henry Ford Hosp	1
Wayne State Univ	5	Kansas, U of	1
Davis, U of CA	4	Lahey Clinic Med Ctr/Davis, U of CA	1
Montana NCORP	4	Southeast COR NCORP	1
Rochester, Univ of	3	St Luke's Mt State/PCRC NCORP	1
Thompson Ca Surv Ctr/San Antonio, U of TX	3	Winthrop-Univ Hosp/Columbia University	1
Colorado, U of	2	**Total (20 Institutions)**	**81**
Kansas City NCORP	2		

E2906 Phase III SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

Phase III Randomized Trial of Clofarabine as Induction and Post-Remission Therapy vs. Standard Daunorubicin & Cytarabine Induction and Intermediate Dose Cytarabine Post-Remission Therapy, Followed by Decitabine Maintenance vs. Observation in Newly-Diagnosed Acute Myeloid Leukemia in Older Adults (Age ⩾ 60 Years)

Participants:
ECOG-ACRIN, CTSU

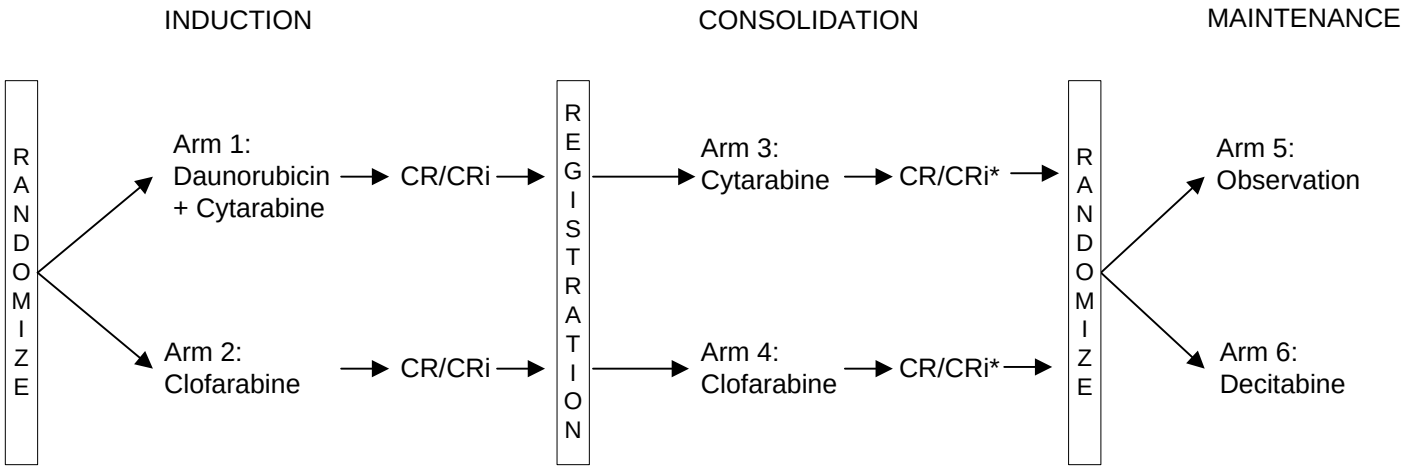
Study Chairs:
J Foran (ECOG-ACRIN), J Godwin (SWOG)

Date Activated:
02/24/2011

Date Closed*:
02/23/2015

*Temporary closure

SCHEMA



*Note: Patients with an HLA matched donor who achieve CR/CRi or morphologic leukemia-free state will proceed to allogeneic Hematopoietic Stem Cell Transplantation after consolidation.

Objectives

To evaluate the effect of clofarabine induction and consolidation therapy on overall survival in comparison with standard therapy (daunorubicin + cytarabine) in newly-diagnosed AML patients age 60 years and older.

To evaluate complete remission (CR) rates, duration of remission, and toxicity/treatment-related mortality of clofarabine in comparison with standard therapy (daunorubicin + cytarabine) in newly-diagnosed AML patients age 60 years and older.

To evaluate the feasibility of consolidation with reduced-intensity conditioning and allogeneic hematopoietic stem cell transplantation from HLA-identical donors in patients who achieve a response to induction therapy, including the incidence of successful engraftment, acute and chronic graft-versus-host disease, transplant-related mortality, and its impact on overall survival in comparison to patients receiving chemotherapy.

To evaluate the duration of remission and disease-free survival of patients in complete remission following completion of consolidation therapy who are subsequently randomized to receive scheduled low-dose decitabine maintenance in comparison with observation.

To perform expression and methylation profiling on all patients receiving decitabine and to correlate their integrated epigenetic signatures with response to decitabine.

To examine the epigenetic profiles of remission marrow in patients randomized to observation vs. decitabine to determine whether epigenetic signature of apparently morphologically normal bone marrow is predictive of relapse or response to decitabine maintenance.

To explore the possible association of response to clofarabine with ABC-transporter P-glycoprotein (Pgp).

To assess the intensity of expression of CXCR4 on diagnostic leukemia cells and to correlate this parameter with other established prognostic factors.

To assess the entire spectrum of somatic mutations and affected pathways at diagnosis of AML and elucidate the association between gene mutation and outcome.

To examine the impact of smoking, obesity, regular acetaminophen use, regular aspirin use, benzene exposure, living in a rural/farm environment and some other underlying exposures and lifestyle factors associated with AML development on OS.

To investigate potential correlative results between array CGH findings and acute myeloid leukemia patient characteristics.

To compare health-related QOL (physical, functional, leukemia-specific well-being) and fatigue in elderly AML patients receiving standard induction therapy with those receiving clofarabine.

To measure the change in health-related QOL that occurs over time (within treatment groups).

To comprehensively assess patient function at the time of study enrollment.

To determine if components of a comprehensive geriatric assessment of QOL scales predict ability to complete AML treatment.

To describe the impact of transplant on QOL in AML patients above age 60.

Patient Population

Patients must have newly-diagnosed AML according to WHO classification and be considered candidates for intensive chemotherapy based upon examination of peripheral blood, bone marrow aspirate specimens, or touch preparations of the bone marrow biopsy. Patients must not have blastic transformation of chronic myelogenous leukemia. Patients with secondary AML are eligible. Patients with documented CNS involvement are not eligible.

Patients must not have received prior chemotherapy for AML with the exception of hydroxurea for increased blast count or leukapheresis for leukocytosis. Patients who have received a limited and short-term exposure of ATRA (all trans retinoic acid) while AML-M3 (Acute Promyelocytic Leukemia) was being ruled out, and which has been discontinued, will be eligible. Patients with confirmed APL will be excluded. Patients who have received previous treatment for antecedent hematologic disorder (AHD) with 5-azacitidine, decitabine, or low dose cytarabine are not eligible.

Patients must have an ECOG performance status 0-3 and reached their 60th birthday. Patients must have adequate cardiac, hepatic, and renal function. Patients must not have a concurrent active malignancy for which they are receiving treatment (other than MDS). Patients with known HIV infection or any active, uncontrolled infection are not eligible.

Stratification/Descriptive Factors

At initial randomization patients will be stratified by (1) age: 60-69 vs $\geq$ 70 years; (2) therapy-related AML: yes vs no; and (3) presence of AHD at the time of diagnosis of AML: yes vs no.

For the randomization to maintenance, treatment randomization will be stratified by (1) age: 60-69 vs ≥ 70 years; (2) cytogenetics: unfavorable vs other; and (3) induction treatment: arm 1 vs arm 2.

Accrual Goals

The accrual goal for this study is 747 patients. Up to nine interim analyses will be performed beginning when approximately 25% of planned full information has occurred. Interim analyses will include both futility and efficacy analyses.

Summary Statement

This study was temporarily closed to accrual on February 23, 2015. The Therapeutic Subcommittee of the ECOG-ACRIN Data Safety Monitoring Committee has recommended that enrollment to this study be suspended due to differences in survival rates favoring standard daunorubicin and cytarabine for induction and consolidation compared to clofarabine induction and consolidation.

ECOG-ACRIN reported a total accrual of 727 patients as of February 23, 2015, including 75 registrations from SWOG institutions. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending February 23, 2015

Institutions	Total Reg	Institutions	Total Reg
Rochester, Univ of	27	Cincinnati MC, U of	3
Loyola University	9	Columbia MU-NCORP	3
Arizona MC, U of	7	Upstate Carolina	3
Kentucky, U of	7	Mississippi, Univ of	1
Dayton NCORP	5	New Mexico MU-NCORP	1
CRC West MI NCORP	4	Winthrop-Univ Hosp/Yale University	1
Florida, Univ of/Yale University	4	**Total (13 Institutions)**	**75**