LYMPHOMA COMMITTEE

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Patient Registrations to Studies

By 12 Month Intervals
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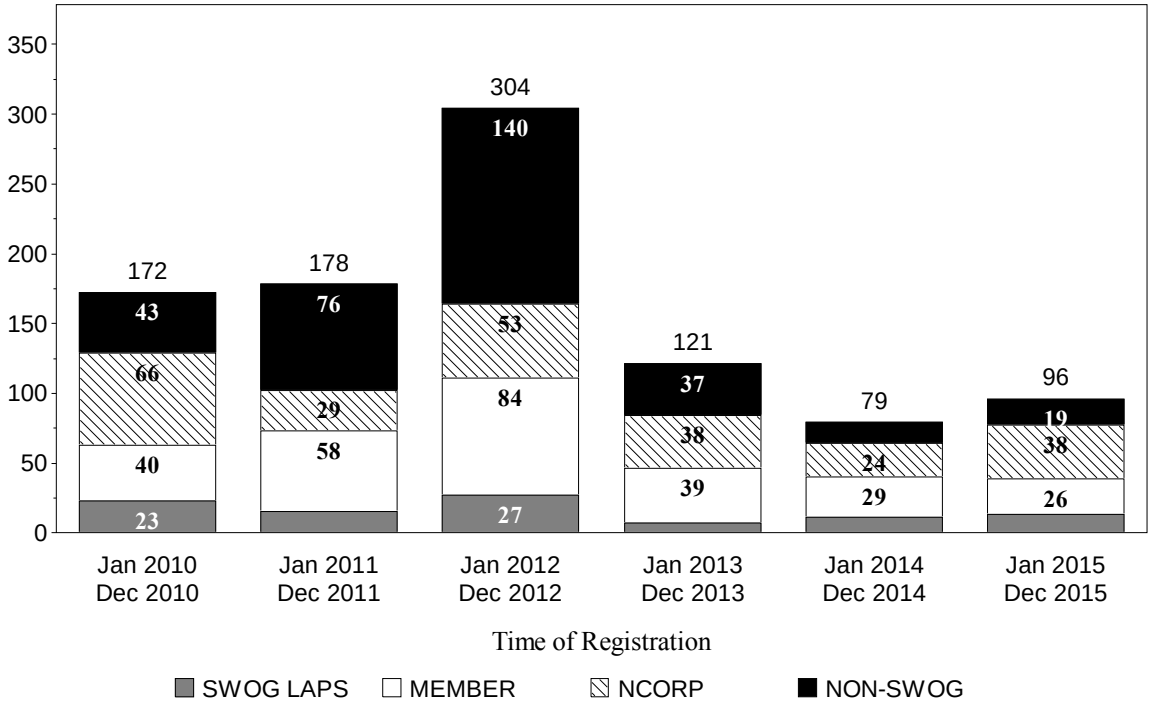

Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

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	Jul 2015 Dec 2015	Jan 2015 Jun 2015	Jul 2014 Dec 2014	All Patients
S1001 DLBCL, I-II, PET-Adapted Therapy				
Initial registration				
R-CHOP x 3	20	20	22	144
R-CHOP x 6	0	0	0	1
	20	20	22	145
PET-Directed Therapy				
Continued R-CHOP	17	14	23	115
IFRT + Zevalin	0	0	2	11
	17	14	25	126
9177 NHL, dose-adj. EPOCH+/-Rituximab*				
Total Registrations	1	0	2	19
C51101 CNS, Myelo/Non-myelo Chemo, PhII*				
Total Registrations	0	2	0	5
E1411 MCL, RB+R, RBV+R, RB+LR, RBV+LR*				
Total Registrations	18	17	10	73
E1412 DLBCL, R2CHOP vs RCHOP*				
Total Registrations	0	18	5	26

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

S0806 Phase I-II

A Phase I/II Trial of Vorinostat (SAHA) in Combination with Rituximab-CHOP in Patients with Newly Diagnosed Advanced Stage Diffuse Large B-cell Lymphoma (DLBCL)

Study Chairs:
D Persky, T Miller

Statisticians:
H Li, M LeBlanc

Data Coordinator:
I Syquia

Date Activated:
11/15/2010

Date Closed:
10/01/2013

Objectives

This study will be conducted in two phases:

Phase I:

To find a safe dose of vorinostat to be used in combination with R-CHOP.

Phase II:

To estimate the two-year progression-free survival rate in patients with newly diagnosed diffuse large B-cell lymphoma (DLBCL) treated with vorinostat and R-CHOP therapy.

To estimate the response rate (complete and partial) and two-year overall survival rate.

To evaluate the toxicity of vorinostat-R-CHOP in patients with newly diagnosed DLBCL.

To assess if acetylation status of MHC class II genes and percentage of CD8+ tumor infiltrating lymphocytes (TIL) correlate with progression-free survival.

To explore whether pretreatment with vorinostat increases acetylation, expression of MHC class II proteins and percentage of CD8+ tumor infiltrating lymphocytes (TIL).

To explore whether tissue acetylation status correlates with whole blood acetylation status.

To explore whether the change in systemic levels of immune cytokines with vorinostat and R-CHOP correlates with lymphoma symptoms, response, progression-free or overall survival.

Patient Population

Patients must have biopsy-proven newly diagnosed diffuse large B-cell lymphoma (DLBCL) with Stage II bulky, Stage III or Stage IV disease, with an International Prognostic Index (IPI) or revised IPI (R-IPI) score greater than 0, and which is positive for CD20. All patients must have measurable disease. Patients with clinical or laboratory evidence of central nervous system involvement by lymphoma are not eligible.

Patients must not have received prior chemotherapy, radiation, or antibody therapy for lymphoma. Steroid pre-medication for IV contrast allergy is allowed. Patients must not have received valproic acid (a HDAC inhibitor) within twenty-eight days prior to registration.

Patients must have a Zubrod performance status of 0-2, be at least age 18, and have adequate cardiac and hematologic function. Patients known to be HIV-positive are not eligible.

Accrual Goals

For the Phase I portion of this study, the first patients enrolled will be treated at 400 mg vorinostat. If that dose is not well tolerated, then lower doses will be evaluated in patients subsequently enrolled. Ten patients will be evaluated at the recommended dose prior to opening the Phase II portion.

The Phase II portion of this study will accrue 65 eligible patients.

Summary Statement

This study was closed to accrual on October 1, 2013, after meeting its accrual goals. A total of 83 patients were registered.

The Phase I portion of this study was activated in a limited number of SWOG institutions on November 15, 2010. The study was temporarily closed on August 26, 2011, with 11 patients registered. One Phase I patient is ineligible due to incorrect histology per pathology review. An additional patient who did not receive any protocol treatment is not analyzable for any endpoint.

Five of the nine Phase I patients went off protocol treatment early due to the following reasons: adverse event (3), patient refusal, and delay of protocol treatment for more than two weeks.

Adverse events have been assessed in all nine analyzable Phase I patients. One patient died of sepsis less than one week after completing all eight cycles of protocol therapy. After review, this was found to be related to protocol treatment. This patient also experienced Grade 4 hematologic toxicities, Grade 4 visceral arterial ischemia, multi-organ failure, and disseminated intravascular coagulation (DIC). Six additional Phase I patients have experienced Grade 4 hematologic toxicities. One of these patients also experienced Grade 4 sepsis, another also experienced Grade 4 hypophosphatemia and hypokalemia, and a third also experienced Grade 4 febrile neutropenia, sepsis, elevated creatinine, and hypokalemia.

Two of the nine Phase I patients experienced an adverse event qualifying as a dose-limiting toxicity: one experienced Grade 3 febrile neutropenia, and another experienced Grade 4 hypokalemia, both in the second week of treatment. This toxicity profile was considered acceptable, and the Phase II dose and schedule of SAHA was established at 400 mg on Days 1-9 of each cycle.

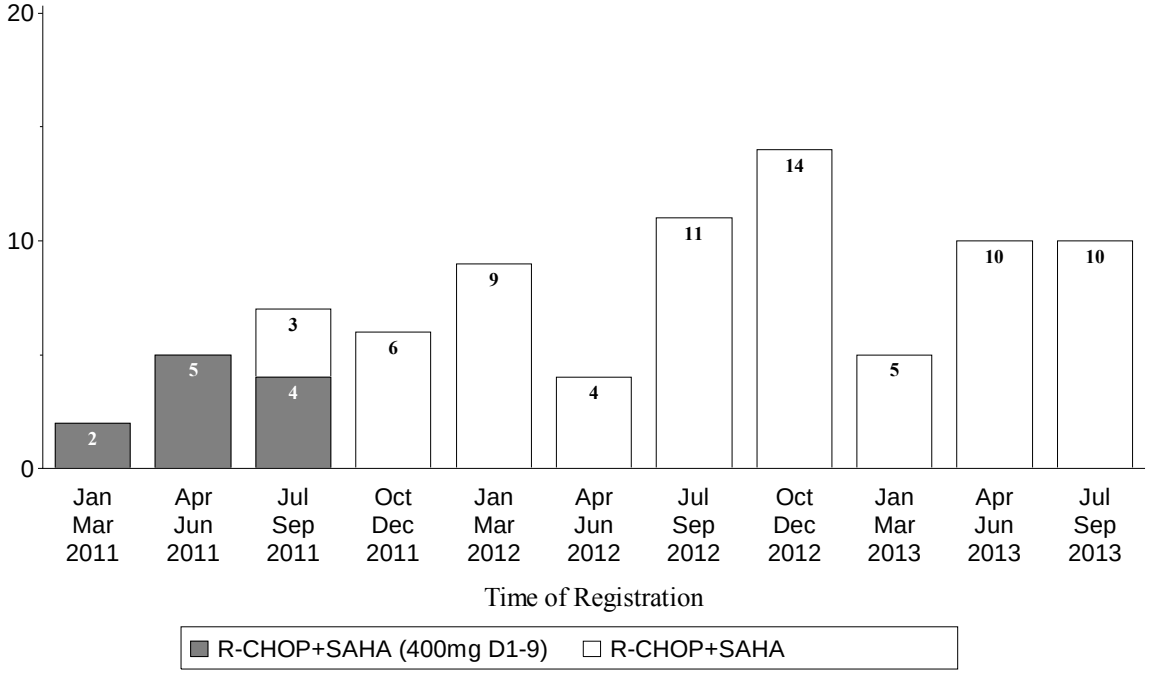
The Phase II portion of this study was activated on September 7, 2011, and closed to accrual on October 1, 2013. A total of 72 patients were registered. Seven patients are ineligible due to the following reasons: incorrect histology per pathology review (3), inadequate pathologic material for diagnosis, no required tissue submission for pathology review, stage II but not bulky disease, and platelet count less than eligibility requirement (1 patient each). An additional two patients who withdrew consent and did not receive any protocol treatment are not analyzable for any endpoint.

Among 63 Phase II patients assessed for adverse events, 36 experienced Grade 4 adverse events, primarily hematologic (31). Grade 4 non-hematologic toxicities have been reported in 17 patients, including sepsis (11), febrile neutropenia (4), myocardial infarction (2), atrial fibrillation, LV systolic dysfunction, duodenal perforation, jejunal perforation, ECG QT corrected interval prolonged, hypokalemia, hypotension, and respiratory failure (one each). Eighteen additional patients experienced Grade 3 toxicities as maximum degree, primarily hematologic.

The first scheduled disease assessment was at the end of the 4th cycle of treatment (week 12), then disease was restaged after completion of 8 cycles of treatment (week 26). After completion of treatment, disease was assessed every six months for two years then annually for a maximum of five years on protocol or until disease progression. Two patients who died early prior to the first scheduled disease assessment, and 10 patients who could not have their exact response determined due to inadequate assessments are assumed to be non-responders for the purpose of response rate estimation. Out of 63 Phase II evaluable patients, 32 complete responses and 19 partial responses were observed, for an estimated response rate of 81% (95% CI: 69.1%, 89.8%).

The median length of follow-up among Phase II patients last known alive is 30 months (range 20.4 - 50.4 months). Twenty-one patients have either progressed or died, for an estimated 2-year progression-free survival of 73% (95%CI: 59.6%, 81.9%). There have been 14 deaths, for an estimated 2-year overall survival of 86% (95%CI: 74.3%, 92.3%).

Initial Registrations By 3 Month Intervals



Registration by Institution

Phase I Patients

Institutions	Total Reg
City of Hope Med Ctr	3
Rochester, Univ of	3
Wichita NCORP	3
Arizona MC, U of	2
Total (4 Institutions)	**11**

Registration, Eligibility, and Evaluability

Phase I Patients

Data as of February 17, 2016

	R-CHOP+SAHA (400mg D1-9)
NUMBER REGISTERED	11
INELIGIBLE	1
ELIGIBLE	10
Not Analyzable	1
ADVERSE EVENT ASSESSMENT	
Evaluable	9

Patient Characteristics

Phase I Patients

Data as of February 17, 2016

	R-CHOP+SAHA (400mg D1-9) (n=9)	
AGE		
Median	66.9	
Minimum	46.4	
Maximum	83.8	
SEX		
Males	6	67%
Females	3	33%
HISPANIC		
Yes	3	33%
No	6	67%
RACE		
White	9	100%

Treatment Summary

Phase I Patients

Data as of February 17, 2016

	R-CHOP+SAHA (400mg D1-9)
NUMBER ON PROTOCOL TREATMENT	0
NUMBER OFF PROTOCOL TREATMENT	9
REASON OFF TREATMENT	
Treatment completed as planned	4
Adverse Event or side effects	3
Refusal unrelated to adverse event	1
Other - not protocol specified	1
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0

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

Phase I Patients

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of February 17, 2016

	R-CHOP+SAHA (400mg D1-9) (n=9) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	8	1	0	0	0	0
AST increased	7	2	0	0	0	0
Abdominal pain	7	0	1	1	0	0
Allergic rhinitis	8	1	0	0	0	0
Alopecia	4	2	3	0	0	0
Anemia	0	3	2	3	1	0
Anorexia	4	1	3	1	0	0
Back pain	8	1	0	0	0	0
Bloating	8	1	0	0	0	0
Blurred vision	8	1	0	0	0	0
Bone pain	6	3	0	0	0	0
Bruising	7	2	0	0	0	0
Chest wall pain	8	0	1	0	0	0
Chills	8	0	1	0	0	0
Colitis	8	0	0	1	0	0
Constipation	5	0	4	0	0	0
Cough	6	3	0	0	0	0
Creatinine increased	8	0	0	0	1	0
DIC	8	0	0	0	1	0
Dehydration	7	0	0	2	0	0
Depression	7	1	0	1	0	0
Diarrhea	2	2	3	2	0	0
Dizziness	6	2	0	1	0	0
Dry eye	8	0	1	0	0	0
Dry mouth	6	1	2	0	0	0
Dysgeusia	6	1	2	0	0	0
ECG QT corrected int prolong	8	0	0	1	0	0
Edema face	7	1	1	0	0	0
Edema limbs	8	1	0	0	0	0
Erythema multiforme	7	1	1	0	0	0
Fatigue	1	2	3	3	0	0
Febrile neutropenia	6	0	0	2	1	0
Fever	8	1	0	0	0	0
GI disorders-Other, specify	7	2	0	0	0	0
Gait disturbance	8	0	1	0	0	0
Generalized muscle weakness	4	3	0	2	0	0
Headache	7	1	1	0	0	0
Hematuria	8	0	0	1	0	0
Hot flashes	8	1	0	0	0	0
Hyperglycemia	8	1	0	0	0	0
Hyperhidrosis	8	0	1	0	0	0
Hyperkalemia	8	0	1	0	0	0
Hypertension	8	0	1	0	0	0
Hypoalbuminemia	6	2	0	1	0	0

	R-CHOP+SAHA (400mg D1-9) (n=9) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Hypocalcemia	7	0	1	1	0	0
Hypokalemia	6	1	0	0	2	0
Hyponatremia	6	3	0	0	0	0
Hypophosphatemia	8	0	0	0	1	0
Hypotension	8	1	0	0	0	0
Infections/infestations-Other	8	0	0	1	0	0
Insomnia	5	2	2	0	0	0
Investigations-Other, specify	8	1	0	0	0	0
Lung infection	8	0	1	0	0	0
Lymphocyte count decreased	2	0	3	1	3	0
Metab/nutrition disorders-Oth	8	1	0	0	0	0
Mucosal infection	8	0	1	0	0	0
Mucositis oral	8	0	0	1	0	0
Multi-organ failure	8	0	0	0	1	0
Muscle weakness upper limb	8	1	0	0	0	0
Myalgia	8	0	0	1	0	0
Nail discoloration	7	2	0	0	0	0
Nausea	1	5	2	1	0	0
Neutrophil count decreased	1	0	0	2	6	0
Oral pain	8	1	0	0	0	0
Pain	7	1	1	0	0	0
Pain in extremity	7	0	2	0	0	0
Paresthesia	6	1	2	0	0	0
Peripheral motor neuropathy	4	2	2	1	0	0
Peripheral nerve infection	8	0	1	0	0	0
Peripheral sensory neuropathy	6	2	1	0	0	0
Photophobia	8	1	0	0	0	0
Platelet count decreased	1	3	1	2	2	0
Postnasal drip	8	1	0	0	0	0
Rash maculo-papular	7	1	1	0	0	0
Rectal mucositis	8	0	1	0	0	0
Renal/urinary disorders-Other	8	1	0	0	0	0
Resp/thoracic/mediastinal ds	8	1	0	0	0	0
Rhinitis infective	8	0	1	0	0	0
Sepsis	6	0	0	0	2	1
Skin/subq tissue ds-Other	8	1	0	0	0	0
Urinary frequency	6	3	0	0	0	0
Urine output decreased	8	0	0	1	0	0
Visceral arterial ischemia	8	0	0	0	1	0
Vomiting	5	3	1	0	0	0
Weight gain	8	1	0	0	0	0
Weight loss	7	2	0	0	0	0
White blood cell decreased	1	0	1	3	4	0
MAX. GRADE ANY ADVERSE EVENT	0	0	1	1	6	1

Registration by Institution

Phase II Patients

Institutions	Total Reg	Institutions	Total Reg
Rochester, Univ of	16	Columbus NCORP	1
Arizona MC, U of	7	Evergreen Hem & Onc/PCRC NCORP	1
Dayton NCORP	6	Fowler Family Center/Baptist MU-NCORP	1
Kaiser Perm NCORP	6	Hawaii MU-NCORP	1
City of Hope Med Ctr	5	Lahey Hosp & Med Ctr	1
Loyola University	5	Ozarks NCORP	1
So Calif, U of	5	PCRC NCORP	1
CRC West MI NCORP	3	St Joseph Med Ctr/PCRC NCORP	1
Kansas City NCORP	3	Wichita NCORP	1
Kansas, U of	2	Yale University	1
Southeast COR NCORP	2	**Total (22 Institutions)**	**72**
Upstate Carolina	2		

Registration, Eligibility, and Evaluability

Phase II Patients

Data as of February 17, 2016

	R-CHOP+SAHA
NUMBER REGISTERED	72
INELIGIBLE	7
Insufficient Documentation	1
Irreversible	1
ELIGIBLE	65
Not Analyzable	2
RESPONSE ASSESSMENT	
Determinable	52
Not Determinable	11
ADVERSE EVENT ASSESSMENT	
Evaluable	63

Patient Characteristics

Phase II Patients

Data as of February 17, 2016

	R-CHOP+SAHA (n=63)	
AGE		
Median	64.1	
Minimum	19.6	
Maximum	80.8	
SEX		
Males	36	57%
Females	27	43%
HISPANIC		
Yes	4	6%
No	59	94%
RACE		
White	54	86%
Black	3	5%
Asian	5	8%
Unknown	1	2%

Treatment Summary

Phase II Patients

Data as of February 17, 2016

	R-CHOP+SAHA
NUMBER ON PROTOCOL TREATMENT	0
NUMBER OFF PROTOCOL TREATMENT	63
REASON OFF TREATMENT	
Treatment completed as planned	34
Adverse Event or side effects	16
Refusal unrelated to adverse event	8
Other - not protocol specified	1
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0

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

Phase II Patients

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of February 17, 2016

	R-CHOP+SAHA (n=63) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	49	12	1	1	0	0
AST increased	52	9	1	1	0	0
Abdominal distension	62	1	0	0	0	0
Abdominal pain	48	8	4	3	0	0
Acute kidney injury	61	0	1	1	0	0
Alkaline phosphatase increased	56	7	0	0	0	0
Allergic reaction	62	0	1	0	0	0
Allergic rhinitis	62	1	0	0	0	0
Alopecia	42	9	12	0	0	0
Anemia	12	18	11	20	2	0
Anorexia	39	10	12	2	0	0
Anxiety	59	1	3	0	0	0
Arterial injury	62	0	1	0	0	0
Arthralgia	57	1	5	0	0	0
Atelectasis	62	1	0	0	0	0
Atrial fibrillation	62	0	0	0	1	0
Back pain	58	4	1	0	0	0
Bladder infection	62	0	1	0	0	0
Bladder spasm	62	0	0	1	0	0
Bloating	60	2	1	0	0	0
Blood bilirubin increased	59	3	1	0	0	0
Blood/lymph disorder-Other	61	2	0	0	0	0
Blurred vision	56	5	2	0	0	0
Body odor	62	1	0	0	0	0
Bone marrow hypocellular	62	0	1	0	0	0
Bone pain	60	2	1	0	0	0
Bronchial infection	61	0	1	1	0	0
Bruising	61	2	0	0	0	0
CD4 lymphocytes decreased	59	2	1	1	0	0
CPK increased	62	0	0	1	0	0
Chest pain - cardiac	61	0	2	0	0	0
Chest wall pain	62	1	0	0	0	0
Chills	54	9	0	0	0	0
Chronic kidney disease	62	0	1	0	0	0
Cognitive disturbance	62	0	1	0	0	0
Confusion	62	0	1	0	0	0
Constipation	40	14	9	0	0	0
Cough	53	9	1	0	0	0
Creatinine increased	57	3	3	0	0	0
Cystitis noninfective	62	0	0	1	0	0
Cytokine release syndrome	62	1	0	0	0	0
DLCO decreased	62	0	0	1	0	0
Dehydration	55	0	4	4	0	0
Depression	60	0	3	0	0	0

	R-CHOP+SAHA (n=63) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Diarrhea	36	16	9	2	0	0
Dizziness	47	8	8	0	0	0
Dry mouth	57	5	1	0	0	0
Dry skin	60	3	0	0	0	0
Duodenal perforation	62	0	0	0	1	0
Dysgeusia	55	6	2	0	0	0
Dyspepsia	61	2	0	0	0	0
Dysphagia	62	0	0	1	0	0
Dyspnea	51	8	3	1	0	0
ECG QT corrected int prolong	59	3	0	0	1	0
Ear pain	61	2	0	0	0	0
Edema limbs	48	13	2	0	0	0
Enterocolitis infectious	62	0	1	0	0	0
Epistaxis	62	1	0	0	0	0
Fall	62	1	0	0	0	0
Fatigue	17	21	16	9	0	0
Febrile neutropenia	39	0	0	20	4	0
Fecal incontinence	62	0	0	1	0	0
Fever	43	14	6	0	0	0
Flatulence	61	2	0	0	0	0
Flu like symptoms	61	1	1	0	0	0
Flushing	62	1	0	0	0	0
GERD	62	0	1	0	0	0
GI disorders-Other, specify	60	1	1	1	0	0
Gait disturbance	61	2	0	0	0	0
Gastritis	62	0	1	0	0	0
Gastrointestinal pain	61	0	2	0	0	0
Gen disorders/admin site cond	62	1	0	0	0	0
Generalized muscle weakness	52	7	2	2	0	0
Glucose intolerance	62	1	0	0	0	0
Hand-Foot syndrome	61	1	1	0	0	0
Headache	48	10	5	0	0	0
Hematuria	59	4	0	0	0	0
Hemorrhoids	60	1	2	0	0	0
Hiccups	59	2	1	1	0	0
Hoarseness	62	1	0	0	0	0
Hot flashes	58	4	1	0	0	0
Hypercalcemia	62	1	0	0	0	0
Hyperglycemia	55	2	2	4	0	0
Hyperhidrosis	61	2	0	0	0	0
Hypermagnesemia	61	2	0	0	0	0
Hypernatremia	62	1	0	0	0	0
Hypertension	59	2	2	0	0	0
Hyperuricemia	62	1	0	0	0	0
Hypoalbuminemia	44	7	9	3	0	0
Hypocalcemia	45	14	4	0	0	0
Hypoglycemia	61	2	0	0	0	0
Hypokalemia	45	8	2	7	1	0
Hypomagnesemia	59	4	0	0	0	0
Hyponatremia	44	13	0	6	0	0
Hypophosphatemia	58	1	2	2	0	0

	R-CHOP+SAHA (n=63) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Hypotension	56	3	1	2	1	0
INR increased	62	0	1	0	0	0
Ileus	62	0	1	0	0	0
Infections/infestations-Other	59	0	1	3	0	0
Infusion related reaction	61	0	2	0	0	0
Insomnia	57	5	1	0	0	0
Jejunal perforation	62	0	0	0	1	0
LV systolic dysfunction	62	0	0	0	1	0
Lethargy	62	0	1	0	0	0
Leukocytosis	62	0	0	0	1	0
Localized edema	62	1	0	0	0	0
Lung infection	59	0	0	4	0	0
Lymph node pain	62	1	0	0	0	0
Lymphocyte count decreased	34	3	6	10	10	0
MS/connective tissue disorder	62	1	0	0	0	0
Malaise	60	1	2	0	0	0
Metab/nutrition disorders-Oth	62	1	0	0	0	0
Mucosal infection	60	1	1	1	0	0
Mucositis oral	41	11	8	3	0	0
Muscle weakness lower limb	61	0	2	0	0	0
Myalgia	56	3	2	2	0	0
Myocardial infarction	61	0	0	0	2	0
Nail discoloration	60	3	0	0	0	0
Nail loss	60	3	0	0	0	0
Nasal congestion	61	2	0	0	0	0
Nausea	22	23	15	3	0	0
Neck pain	61	2	0	0	0	0
Nervous sys disorders-Other	62	1	0	0	0	0
Neutrophil count decreased	20	2	4	11	26	0
Non-cardiac chest pain	62	1	0	0	0	0
Obstruction gastric	62	0	0	1	0	0
Oral pain	62	0	1	0	0	0
Pain	58	3	1	1	0	0
Pain in extremity	62	1	0	0	0	0
Palpitations	61	2	0	0	0	0
Paronychia	62	0	0	1	0	0
Peripheral motor neuropathy	59	4	0	0	0	0
Peripheral sensory neuropathy	45	14	4	0	0	0
Platelet count decreased	26	8	7	6	16	0
Pneumonitis	59	0	3	1	0	0
Productive cough	61	2	0	0	0	0
Proteinuria	57	4	2	0	0	0
Pruritus	61	1	1	0	0	0
RLNP	62	0	0	1	0	0
RPLS	62	0	1	0	0	0
Rash maculo-papular	60	2	1	0	0	0
Rectal pain	62	0	1	0	0	0
Repro system/breast ds-Oth	62	1	0	0	0	0
Respiratory failure	62	0	0	0	1	0
Rhinitis infective	61	0	2	0	0	0
Sepsis	52	0	0	0	11	0

	R-CHOP+SAHA (n=63) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Sinus tachycardia	56	6	0	1	0	0
Sinusitis	61	0	1	1	0	0
Skin infection	60	1	2	0	0	0
Skin ulceration	62	1	0	0	0	0
Skin/subq tissue ds-Other	62	1	0	0	0	0
Small intestinal obstruction	62	0	0	1	0	0
Somnolence	62	0	1	0	0	0
Sore throat	60	2	1	0	0	0
Stoma site infection	62	0	0	1	0	0
Stomach pain	60	1	2	0	0	0
Syncope	59	0	0	4	0	0
Thromboembolic event	61	1	1	0	0	0
Tumor pain	62	1	0	0	0	0
Urinary frequency	59	3	1	0	0	0
Urinary incontinence	62	1	0	0	0	0
Urinary tract infection	58	0	2	3	0	0
Urinary tract pain	61	0	0	2	0	0
Urinary urgency	61	1	1	0	0	0
Urine discoloration	62	1	0	0	0	0
Vasc disorders-Other, spec	62	1	0	0	0	0
Vasovagal reaction	62	0	0	1	0	0
Vomiting	43	15	3	2	0	0
Weight gain	60	3	0	0	0	0
Weight loss	52	5	3	3	0	0
White blood cell decreased	20	5	6	12	20	0
MAX. GRADE ANY ADVERSE EVENT	0	2	7	18	36	0

Response

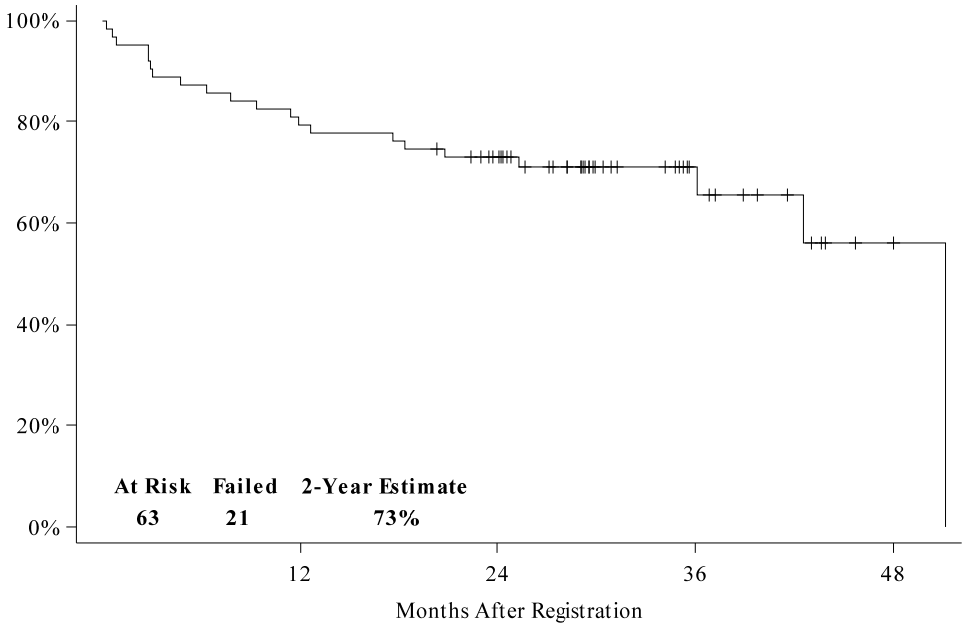
Data as of February 17, 2016

	R-CHOP+SAHA	
	N	**%**
Complete Response	32	51
Partial Response	19	30
PR Non-measurable Disease	0	0
Unconfirmed Complete Response	0	0
Unconfirmed Partial Response	0	0
Unconfirmed PR NM Disease	0	0
Early Death	2	3
Assessment Inadequate	10	16
Total	63	100

Progression-Free Survival

Phae II Patients

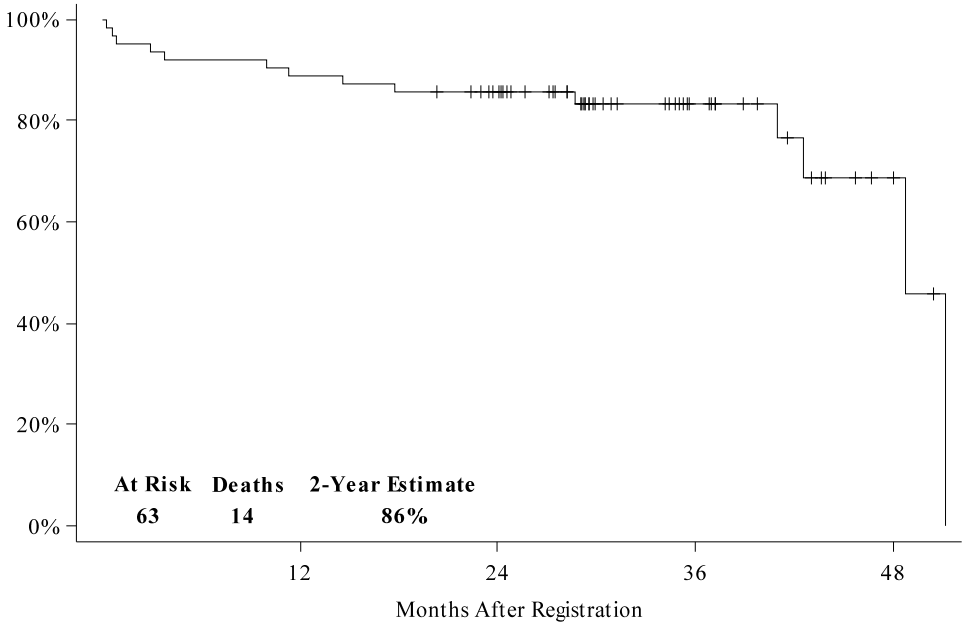
Data as of February 17, 2016



Overall Survival

Phase II Patients

Data as of February 17, 2016



S1001 Phase II

Coordinating Group: SWOG

A Phase II Trial of PET-Directed Therapy for Limited Stage Diffuse Large B-Cell Lymphoma (DLBCL)

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

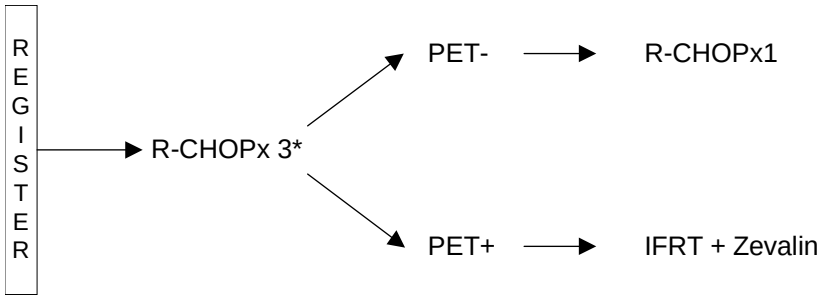
Date Activated:
07/15/2011

Study Chairs:
D Persky, T Miller, S Park (Alliance), L Swinnen (ECOG-ACRIN)

Statisticians:
M LeBlanc, H Li

Data Coordinator:
J Jardine

SCHEMA



*All patients who are early stage by CT but advanced stage by PET/CT at baseline will receive R-CHOPx6

Objectives

To assess the five-year progression-free survival (PFS) rate in patients with newly diagnosed limited stage diffuse large B-cell lymphoma using PET scan to direct therapy after three cycles of R-CHOP.

To evaluate progression-free survival within the PET+ and PET- subgroups of patients with newly diagnosed limited stage diffuse large B-cell lymphoma (DLBCL).

To evaluate the toxicity of this treatment regimen in this patient population.

To evaluate the response probability in this patient population.

To evaluate overall survival (OS) in the overall population, and within the PET+ and PET- subgroups.

To estimate the rate of upstaging at baseline by PET among patients newly diagnosed with limited stage diffuse large B-cell lymphoma by CT imaging and describe outcomes in patients upstaged by PET at baseline to advanced DLBCL.

To evaluate the association of germinal center B-cell subtype (GCB) vs stromal-1 vs stromal-2 gene expression signatures with PFS and OS.

Patient Population

Patients must have non-bulky Stage I or II de-novo diffuse large B-cell non-Hodgkin's lymphoma (DLBCL) which is positive for CD20. Patients who have Stage I or II non-bulky disease based on diagnostic CT scan, but are upstaged to Stage III or IV based on FDG-PET evaluation, are also eligible. Patients with primary mediastinal lymphoma, testicular lymphoma, prior or simultaneous diagnosis of indolent lymphoma, or post-transplant lymphoproliferative disorder with DLBCL morphology are not eligible. Patients may have either measurable or evaluable limited-stage DLBCL. Patients rendered free of measurable or evaluable disease by virtue of biopsy (resection) are also eligible. Patients with CNS involvement are not eligible.

Patients must not have received prior chemotherapy, radiation therapy, or antibody therapy for lymphoma.

Patients must be at least 18 years of age and have a Zubrod performance status of 0-2. Patients must have adequate renal, hepatic, cardiac and hematologic function. Patients known to be HIV-positive are not eligible.

Stratification/Descriptive Factors

For registration step 1, patients will be stratified by advanced stage based on local review of the baseline PET/CT: yes vs no.

For registration step 2, patients will be stratified by the positive PET/CT after three cycles of R-CHOP based on centralized review: yes vs no.

Accrual Goals

Assuming an ineligibility rate of 10%, we anticipate needing to accrue 155 patients in order to obtain 140 eligible patients. Assuming that 15% of eligible patients will have been upstaged at baseline by PET, we expect that 120 patients will receive PET-directed therapy. We further expect that 30 of these patients will be PET-positive, assuming a PET-positive rate of 25%. If the actual rate of PET-positivity is less than 25%, accrual will continue until 30 eligible patients in the FDG-PET-positive subgroup are enrolled.

Summary Statement

As of December 31, 2015, 145 patients had been registered to this study, including one patient who was upstaged to advanced stage DLBCL based on local review of the baseline PET/CT. Two patients are currently ineligible for initial registration, one due to incorrect histology and one due to no required baseline specimens submitted for pathology review.

One hundred thirty-nine patients have been assessed for toxicities on initial R-CHOP therapy. One patient died of sepsis five days after the last date of treatment during the first cycle of treatment. After review, this was found to be probably related to protocol treatment. This patient also experienced Grade 4 hematologic toxicities and febrile neutropenia. An additional 24 patients experienced Grade 4 hematologic toxicities, three of whom also experienced Grade 4 non-hematologic toxicities: febrile neutropenia (2), hyponatremia, and sepsis.

One hundred twenty-six patients have been registered to PET-directed therapy, 115 of whom were PET-negative and registered to the continued R-CHOP therapy, and 11 of whom were PET-positive and registered to the IFRT + Zevalin therapy. One patient is ineligible due to being ineligible at step 1. A major protocol deviation is coded for one PET-negative patient who did not received any PET-directed R-CHOP therapy, this patient is not evaluable for toxicities.

Among 109 patients on the continued R-CHOP arm that have been evaluated for toxicities, one patient died from hypoxia, which was possibly attributable to treatment, and had also experienced Grade 4 neutropenia and respiratory, thoracic and mediastinal disorders. Eleven additional patients on this arm experienced treatment-related Grade 4 hematologic toxicities, one of whom also experienced Grade 4 secondary leukemia. Two of the 11 patients assessed for toxicities on the IFRT + Zevalin arm experienced Grade 4 hematologic toxicities: thrombocytopenia and neutropenia (1 patient each).

Registration by Institution

Initial Registration

Registrations ending December 31, 2015

Institutions	Total Reg	Institutions	Total Reg
Alliance	37	City of Hope Med Ctr	2
Rochester, Univ of	26	Greenville NCORP	2
ECOG-ACRIN	19	Northwest NCORP	2
Michigan CRC NCORP	8	St Luke's Mt State/PCRC NCORP	2
Upstate Carolina	7	Virginia Mason MC/Northwest NCORP	2
Arizona MC, U of	6	Essentia Hlth NCORP	1
Kansas City NCORP	6	Fred Hutchinson CRC	1
Yale University	6	Montana NCORP	1
Hawaii MU-NCORP	4	NRG	1
Loyola University	4	Southeast COR NCORP	1
Wichita NCORP	4	**Total (22 Institutions)**	**145**
Kentucky, U of	3		

Registration, Eligibility, and Evaluability

Initial Registration

Registrations ending December 31, 2015; Data as of February 17, 2016

	TOTAL	R-CHOP x 3	R-CHOP x 6
NUMBER REGISTERED	145	144	1
INELIGIBLE	2	2	0
Insufficient Documentation	1	1	0
Irreversible	1	1	0
ELIGIBLE	143	142	1
Analyzable, Pend. Elig.	135	134	1
RESPONSE ASSESSMENT			
Determinable	121	120	1
Not Determinable	2	2	0
Too Early	20	20	0
ADVERSE EVENT ASSESSMENT			
Evaluable	139	138	1
Too Early	4	4	0

Patient Characteristics

Initial Registration

Registrations ending December 31, 2015; Data as of February 17, 2016

	R-CHOP x 3 (n=142)		R-CHOP x 6 (n=1)	
AGE				
Median	61.6		74.3	
Minimum	18.5		74.3	
Maximum	85.5		74.3	
SEX				
Males	73	51%	0	0%
Females	69	49%	1	100%
HISPANIC				
Yes	6	4%	0	0%
No	130	92%	1	100%
Unknown	6	4%	0	0%
RACE				
White	123	87%	1	100%
Black	6	4%	0	0%
Asian	10	7%	0	0%
Native American	1	1%	0	0%
Unknown	2	1%	0	0%
PET UPSTAGED				
Yes	0	0%	1	100%
No	142	100%	0	0%

Treatment Summary

Initial Registration

Registrations ending December 31, 2015; Data as of February 17, 2016

	TOTAL	R-CHOP x 3	R-CHOP x 6
NUMBER ON PROTOCOL TREATMENT	14	14	0
NUMBER OFF PROTOCOL TREATMENT	129	128	1
REASON OFF TREATMENT			
Treatment completed as planned	122	121	1
Adverse Event or side effects	1	1	0
Refusal unrelated to adverse event	0	0	0
Other - not protocol specified	1	1	0
Reason under review	4	4	0
MAJOR PROTOCOL DEVIATIONS	0	0	0

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

Initial Registration

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2015; Data as of February 17, 2016

	R-CHOP x 3 (n=138) Grade						R-CHOP x 6 (n=1) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	120	16	2	0	0	0	1	0	0	0	0	0
AST increased	125	13	0	0	0	0	1	0	0	0	0	0
Abdominal pain	134	3	1	0	0	0	1	0	0	0	0	0
Agitation	136	1	1	0	0	0	1	0	0	0	0	0
Alkaline phosphatase increased	132	5	1	0	0	0	1	0	0	0	0	0
Allergic reaction	132	1	5	0	0	0	1	0	0	0	0	0
Alopecia	83	18	37	0	0	0	0	0	1	0	0	0
Anal hemorrhage	137	1	0	0	0	0	1	0	0	0	0	0
Anemia	68	50	12	8	0	0	0	1	0	0	0	0
Anorexia	120	13	4	1	0	0	0	1	0	0	0	0
Anxiety	132	2	4	0	0	0	1	0	0	0	0	0
Arthralgia	131	6	1	0	0	0	1	0	0	0	0	0
Back pain	134	3	1	0	0	0	1	0	0	0	0	0
Bloating	136	0	2	0	0	0	1	0	0	0	0	0
Blood bilirubin increased	136	2	0	0	0	0	1	0	0	0	0	0
Blurred vision	135	3	0	0	0	0	1	0	0	0	0	0
Bone pain	128	6	4	0	0	0	1	0	0	0	0	0
CD4 lymphocytes decreased	135	0	1	2	0	0	1	0	0	0	0	0
Chills	130	7	1	0	0	0	1	0	0	0	0	0
Concentration impairment	137	1	0	0	0	0	1	0	0	0	0	0
Confusion	137	1	0	0	0	0	1	0	0	0	0	0
Constipation	88	38	11	1	0	0	0	0	1	0	0	0
Cough	132	4	1	1	0	0	1	0	0	0	0	0
Creatinine increased	135	3	0	0	0	0	1	0	0	0	0	0
Dehydration	131	1	6	0	0	0	1	0	0	0	0	0
Depression	137	0	1	0	0	0	1	0	0	0	0	0
Diarrhea	122	12	1	3	0	0	1	0	0	0	0	0
Dizziness	129	9	0	0	0	0	1	0	0	0	0	0
Dry mouth	130	8	0	0	0	0	1	0	0	0	0	0
Dry skin	138	0	0	0	0	0	0	1	0	0	0	0
Dysgeusia	124	9	5	0	0	0	1	0	0	0	0	0
Dyspepsia	123	8	7	0	0	0	1	0	0	0	0	0
Dyspnea	125	8	2	3	0	0	0	1	0	0	0	0
Edema face	137	1	0	0	0	0	1	0	0	0	0	0
Edema limbs	129	7	1	1	0	0	0	1	0	0	0	0
Endocrine disorders-Other	137	0	0	1	0	0	1	0	0	0	0	0
Epistaxis	137	1	0	0	0	0	1	0	0	0	0	0
Eye disorders - Other, specify	136	2	0	0	0	0	1	0	0	0	0	0
Eye pain	137	1	0	0	0	0	1	0	0	0	0	0
Facial pain	136	2	0	0	0	0	1	0	0	0	0	0
Fatigue	41	75	19	3	0	0	0	1	0	0	0	0
Febrile neutropenia	125	0	0	10	3	0	1	0	0	0	0	0
Fever	125	11	2	0	0	0	1	0	0	0	0	0
Flank pain	137	1	0	0	0	0	1	0	0	0	0	0

	R-CHOP x 3 (n=138) Grade						R-CHOP x 6 (n=1) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Flatulence	136	2	0	0	0	0	1	0	0	0	0	0
Flu like symptoms	137	0	1	0	0	0	1	0	0	0	0	0
GERD	132	3	3	0	0	0	1	0	0	0	0	0
GI disorders-Other, specify	136	2	0	0	0	0	1	0	0	0	0	0
Gastritis	137	0	1	0	0	0	1	0	0	0	0	0
Gen disorders/admin site cond	136	2	0	0	0	0	1	0	0	0	0	0
Generalized muscle weakness	130	6	1	1	0	0	1	0	0	0	0	0
Headache	126	12	0	0	0	0	1	0	0	0	0	0
Hematuria	137	1	0	0	0	0	1	0	0	0	0	0
Hemoglobin increased	137	1	0	0	0	0	1	0	0	0	0	0
Hemorrhoids	137	1	0	0	0	0	1	0	0	0	0	0
Hiccups	137	1	0	0	0	0	1	0	0	0	0	0
Hoarseness	136	1	1	0	0	0	0	1	0	0	0	0
Hot flashes	136	2	0	0	0	0	1	0	0	0	0	0
Hyperglycemia	120	10	4	4	0	0	1	0	0	0	0	0
Hyperhidrosis	136	1	1	0	0	0	1	0	0	0	0	0
Hyperkalemia	137	0	1	0	0	0	1	0	0	0	0	0
Hypernatremia	137	1	0	0	0	0	1	0	0	0	0	0
Hypertension	131	2	2	3	0	0	1	0	0	0	0	0
Hypoalbuminemia	123	7	8	0	0	0	0	1	0	0	0	0
Hypocalcemia	127	8	3	0	0	0	1	0	0	0	0	0
Hypokalemia	128	6	2	2	0	0	1	0	0	0	0	0
Hypomagnesemia	134	4	0	0	0	0	1	0	0	0	0	0
Hyponatremia	132	5	0	0	1	0	1	0	0	0	0	0
Hypophosphatemia	137	0	1	0	0	0	1	0	0	0	0	0
Hypotension	135	1	2	0	0	0	1	0	0	0	0	0
Infusion related reaction	123	2	13	0	0	0	1	0	0	0	0	0
Injection site reaction	137	0	1	0	0	0	1	0	0	0	0	0
Insomnia	122	10	6	0	0	0	1	0	0	0	0	0
Localized edema	137	1	0	0	0	0	1	0	0	0	0	0
Lower GI hemorrhage	137	1	0	0	0	0	1	0	0	0	0	0
Lung infection	136	0	0	2	0	0	1	0	0	0	0	0
Lymphocyte count decreased	82	22	16	13	5	0	0	0	1	0	0	0
Memory impairment	136	2	0	0	0	0	1	0	0	0	0	0
Menorrhagia	137	1	0	0	0	0	1	0	0	0	0	0
Mucositis oral	116	15	6	1	0	0	0	1	0	0	0	0
Myalgia	131	7	0	0	0	0	1	0	0	0	0	0
Nail discoloration	136	2	0	0	0	0	1	0	0	0	0	0
Nasal congestion	137	1	0	0	0	0	1	0	0	0	0	0
Nausea	77	44	16	1	0	0	0	1	0	0	0	0
Neck pain	135	2	1	0	0	0	1	0	0	0	0	0
Neutrophil count decreased	89	5	10	10	24	0	1	0	0	0	0	0
Oral pain	135	0	2	1	0	0	1	0	0	0	0	0
Pain	134	0	4	0	0	0	1	0	0	0	0	0
Paresthesia	136	2	0	0	0	0	1	0	0	0	0	0
Peripheral motor neuropathy	134	3	1	0	0	0	1	0	0	0	0	0
Peripheral nerve infection	137	0	1	0	0	0	1	0	0	0	0	0
Peripheral sensory neuropathy	109	25	3	1	0	0	1	0	0	0	0	0
Phlebitis	137	0	1	0	0	0	1	0	0	0	0	0
Platelet count decreased	117	13	3	3	2	0	0	1	0	0	0	0
Presyncope	137	0	1	0	0	0	1	0	0	0	0	0

	R-CHOP x 3 (n=138) Grade						R-CHOP x 6 (n=1) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Proteinuria	137	1	0	0	0	0	1	0	0	0	0	0
Pruritus	135	2	1	0	0	0	1	0	0	0	0	0
Rash acneiform	137	1	0	0	0	0	1	0	0	0	0	0
Rash maculo-papular	131	6	1	0	0	0	0	1	0	0	0	0
Renal/urinary disorders-Other	137	1	0	0	0	0	1	0	0	0	0	0
Repro system/breast ds-Oth	136	1	1	0	0	0	1	0	0	0	0	0
Resp/thoracic/mediastinal ds	137	1	0	0	0	0	1	0	0	0	0	0
Scalp pain	137	1	0	0	0	0	1	0	0	0	0	0
Sepsis	136	0	0	0	1	1	1	0	0	0	0	0
Sinus tachycardia	137	1	0	0	0	0	1	0	0	0	0	0
Sinusitis	137	0	1	0	0	0	1	0	0	0	0	0
Skin infection	135	2	0	1	0	0	1	0	0	0	0	0
Skin/subq tissue ds-Other	134	4	0	0	0	0	1	0	0	0	0	0
Sore throat	133	4	1	0	0	0	1	0	0	0	0	0
Stomach pain	136	1	1	0	0	0	1	0	0	0	0	0
Stroke	137	0	0	1	0	0	1	0	0	0	0	0
Superficial thrombophlebitis	137	0	1	0	0	0	1	0	0	0	0	0
Thromboembolic event	137	0	1	0	0	0	1	0	0	0	0	0
Upper respiratory infection	131	0	7	0	0	0	1	0	0	0	0	0
Urinary frequency	130	7	1	0	0	0	1	0	0	0	0	0
Urinary incontinence	137	1	0	0	0	0	1	0	0	0	0	0
Urinary tract infection	129	0	6	3	0	0	1	0	0	0	0	0
Urine discoloration	137	1	0	0	0	0	1	0	0	0	0	0
Vaginal infection	137	0	1	0	0	0	1	0	0	0	0	0
Voice alteration	136	1	1	0	0	0	1	0	0	0	0	0
Vomiting	125	8	5	0	0	0	0	1	0	0	0	0
Watering eyes	137	1	0	0	0	0	1	0	0	0	0	0
Weight gain	136	2	0	0	0	0	0	1	0	0	0	0
Weight loss	131	6	1	0	0	0	1	0	0	0	0	0
Wheezing	137	1	0	0	0	0	1	0	0	0	0	0
White blood cell decreased	87	15	8	14	14	0	0	0	1	0	0	0
Wound infection	137	0	1	0	0	0	1	0	0	0	0	0
MAX. GRADE ANY ADVERSE EVENT	1	20	58	34	24	1	0	0	1	0	0	0

Registration, Eligibility, and Evaluability

PET-Directed Therapy

Registrations ending December 31, 2015; Data as of February 17, 2016

	TOTAL	Continued R -CHOP	IFRT + Zevalin
NUMBER REGISTERED	126	115	11
INELIGIBLE	1	1	0
Insufficient Documentation	1	1	0
Irreversible	1	1	0
ELIGIBLE	125	114	11
Analyzable, Pend. Elig.	117	106	11
RESPONSE ASSESSMENT			
Determinable	106	100	6
Not Determinable	1	1	0
Too Early	18	13	5
ADVERSE EVENT ASSESSMENT			
Evaluable	120	109	11
Not Evaluable	1	1	0
Too Early	4	4	0

Treatment Summary

PET-Directed Therapy

Registrations ending December 31, 2015; Data as of February 17, 2016

	TOTAL	Continued R -CHOP	IFRT + Zevalin
NUMBER ON PROTOCOL TREATMENT	11	11	0
NUMBER OFF PROTOCOL TREATMENT	114	103	11
REASON OFF TREATMENT			
Treatment completed as planned	112	101	11
Adverse Event or side effects	1	1	0
Refusal unrelated to adverse event	0	0	0
Other - not protocol specified	0	0	0
Reason under review	1	1	0
MAJOR PROTOCOL DEVIATIONS	1	1	0

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

PET-Directed Therapy

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2015; Data as of February 17, 2016

	Continued R-CHOP (n=109) Grade						IFRT + Zevalin (n=11) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	102	6	0	1	0	0	10	1	0	0	0	0
AST increased	105	4	0	0	0	0	10	1	0	0	0	0
Abdominal pain	108	0	0	1	0	0	10	1	0	0	0	0
Allergic rhinitis	108	0	1	0	0	0	11	0	0	0	0	0
Alopecia	88	7	14	0	0	0	9	0	2	0	0	0
Anemia	68	27	12	2	0	0	6	3	1	1	0	0
Anorexia	106	1	1	1	0	0	8	2	1	0	0	0
Anxiety	109	0	0	0	0	0	10	0	1	0	0	0
Arthralgia	107	1	1	0	0	0	11	0	0	0	0	0
Arthritis	108	1	0	0	0	0	11	0	0	0	0	0
Blurred vision	108	1	0	0	0	0	10	1	0	0	0	0
Bone pain	108	1	0	0	0	0	11	0	0	0	0	0
Chills	108	1	0	0	0	0	10	1	0	0	0	0
Constipation	104	5	0	0	0	0	10	1	0	0	0	0
Cough	105	3	1	0	0	0	9	2	0	0	0	0
Creatinine increased	106	2	1	0	0	0	11	0	0	0	0	0
Dehydration	109	0	0	0	0	0	10	0	1	0	0	0
Depression	109	0	0	0	0	0	10	0	1	0	0	0
Dermatitis radiation	109	0	0	0	0	0	9	2	0	0	0	0
Diarrhea	106	3	0	0	0	0	10	1	0	0	0	0
Dizziness	109	0	0	0	0	0	10	1	0	0	0	0
Dry mouth	106	3	0	0	0	0	9	0	2	0	0	0
Dysgeusia	105	2	2	0	0	0	10	0	1	0	0	0
Dyspepsia	107	2	0	0	0	0	10	1	0	0	0	0
Dysphagia	109	0	0	0	0	0	9	1	1	0	0	0
Dyspnea	103	4	2	0	0	0	11	0	0	0	0	0
Ear pain	108	1	0	0	0	0	11	0	0	0	0	0
Edema limbs	106	3	0	0	0	0	11	0	0	0	0	0
Ejection fraction decreased	108	0	0	1	0	0	11	0	0	0	0	0
Esophagitis	109	0	0	0	0	0	10	0	1	0	0	0
Eye disorders - Other, specify	108	1	0	0	0	0	11	0	0	0	0	0
Eye pain	108	1	0	0	0	0	11	0	0	0	0	0
Fall	108	0	0	1	0	0	11	0	0	0	0	0
Fatigue	70	33	5	1	0	0	5	5	1	0	0	0
Febrile neutropenia	107	0	0	2	0	0	11	0	0	0	0	0
Fever	108	1	0	0	0	0	11	0	0	0	0	0
Flu like symptoms	108	1	0	0	0	0	11	0	0	0	0	0
GERD	105	3	1	0	0	0	11	0	0	0	0	0
Gastritis	109	0	0	0	0	0	10	1	0	0	0	0
Generalized muscle weakness	106	1	2	0	0	0	10	1	0	0	0	0
Gum infection	108	1	0	0	0	0	11	0	0	0	0	0
Headache	108	1	0	0	0	0	11	0	0	0	0	0
Hearing impaired	108	1	0	0	0	0	11	0	0	0	0	0
Hot flashes	108	1	0	0	0	0	11	0	0	0	0	0

	Continued R-CHOP (n=109) Grade						IFRT + Zevalin (n=11) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Hypercalcemia	108	1	0	0	0	0	11	0	0	0	0	0
Hyperglycemia	103	3	2	1	0	0	10	1	0	0	0	0
Hyperhidrosis	109	0	0	0	0	0	10	1	0	0	0	0
Hyperkalemia	107	2	0	0	0	0	11	0	0	0	0	0
Hypertension	104	3	0	2	0	0	11	0	0	0	0	0
Hyperuricemia	108	1	0	0	0	0	11	0	0	0	0	0
Hypoalbuminemia	106	3	0	0	0	0	11	0	0	0	0	0
Hypocalcemia	107	1	0	1	0	0	11	0	0	0	0	0
Hypoglycemia	108	1	0	0	0	0	11	0	0	0	0	0
Hypokalemia	104	2	1	2	0	0	11	0	0	0	0	0
Hypomagnesemia	108	1	0	0	0	0	10	1	0	0	0	0
Hyponatremia	107	1	0	1	0	0	11	0	0	0	0	0
Hypotension	108	0	0	1	0	0	11	0	0	0	0	0
Hypoxia	107	0	0	1	0	1	11	0	0	0	0	0
Infections/infestations-Other	108	0	1	0	0	0	11	0	0	0	0	0
Insomnia	108	1	0	0	0	0	9	0	2	0	0	0
Laryngeal edema	109	0	0	0	0	0	10	1	0	0	0	0
Leukocytosis	108	0	0	1	0	0	11	0	0	0	0	0
Lymphedema	108	0	1	0	0	0	11	0	0	0	0	0
Lymphocyte count decreased	68	17	17	7	0	0	7	2	0	2	0	0
Malaise	108	0	1	0	0	0	11	0	0	0	0	0
Memory impairment	108	1	0	0	0	0	11	0	0	0	0	0
Mucositis oral	105	3	1	0	0	0	10	0	1	0	0	0
Muscle weakness lower limb	108	1	0	0	0	0	11	0	0	0	0	0
Muscle weakness upper limb	108	1	0	0	0	0	11	0	0	0	0	0
Myalgia	107	2	0	0	0	0	9	1	1	0	0	0
Nail discoloration	108	1	0	0	0	0	11	0	0	0	0	0
Nail loss	108	1	0	0	0	0	11	0	0	0	0	0
Nail ridging	107	2	0	0	0	0	11	0	0	0	0	0
Nasal congestion	107	0	2	0	0	0	11	0	0	0	0	0
Nausea	99	10	0	0	0	0	9	2	0	0	0	0
Neoplasms, all	108	1	0	0	0	0	11	0	0	0	0	0
Nervous sys disorders-Other	108	0	0	1	0	0	10	1	0	0	0	0
Neutrophil count decreased	93	2	3	3	8	0	6	1	2	1	1	0
Oral pain	107	1	1	0	0	0	11	0	0	0	0	0
Pain	107	2	0	0	0	0	11	0	0	0	0	0
Pain in extremity	106	2	1	0	0	0	10	0	1	0	0	0
Paresthesia	107	2	0	0	0	0	11	0	0	0	0	0
Peripheral motor neuropathy	108	1	0	0	0	0	11	0	0	0	0	0
Peripheral sensory neuropathy	89	17	2	1	0	0	9	2	0	0	0	0
Pharyngitis	108	0	1	0	0	0	10	0	1	0	0	0
Phlebitis	108	0	1	0	0	0	11	0	0	0	0	0
Platelet count decreased	93	12	0	2	2	0	7	0	1	2	1	0
Productive cough	108	1	0	0	0	0	11	0	0	0	0	0
Renal calculi	108	1	0	0	0	0	11	0	0	0	0	0
Resp/thoracic/mediastinal ds	107	1	0	0	1	0	11	0	0	0	0	0
Secondary Leukemia	108	0	0	0	1	0	11	0	0	0	0	0
Sinus tachycardia	108	1	0	0	0	0	11	0	0	0	0	0
Skin infection	107	1	1	0	0	0	11	0	0	0	0	0
Skin/subq tissue ds-Other	108	1	0	0	0	0	11	0	0	0	0	0
Small intestine infection	108	0	0	1	0	0	11	0	0	0	0	0

	Continued R-CHOP (n=109) Grade						IFRT + Zevalin (n=11) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Sore throat	108	0	1	0	0	0	10	1	0	0	0	0
Telangiectasia	108	1	0	0	0	0	11	0	0	0	0	0
Thromboembolic event	108	0	0	1	0	0	11	0	0	0	0	0
Upper respiratory infection	106	0	3	0	0	0	11	0	0	0	0	0
Urinary frequency	108	1	0	0	0	0	11	0	0	0	0	0
Urinary tract infection	107	0	2	0	0	0	10	0	1	0	0	0
Urine discoloration	108	1	0	0	0	0	11	0	0	0	0	0
Voice alteration	108	0	1	0	0	0	11	0	0	0	0	0
Vomiting	108	1	0	0	0	0	11	0	0	0	0	0
Weight gain	106	2	1	0	0	0	11	0	0	0	0	0
Weight loss	107	0	1	1	0	0	9	2	0	0	0	0
White blood cell decreased	80	16	3	5	5	0	6	1	2	2	0	0
MAX. GRADE ANY ADVERSE EVENT	10	29	42	16	11	1	1	4	2	2	2	0

S1106 Phase II

Coordinating Group: SWOG

A Randomized Phase II Trial of R-HCVAD/MTX/ARA-C Induction Followed by Consolidation with an Autologous Stem Cell Transplant vs. R-Bendamustine Induction Followed by Consolidation with an Autologous Stem Cell Transplant for Patients ≤ 65 Years of Age with Previously Untreated Mantle Cell Lymphoma

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

Study Chairs:
R Chen, S Bernstein, S Forman, T Shea (Alliance), T Fenske (ECOG-ACRIN)

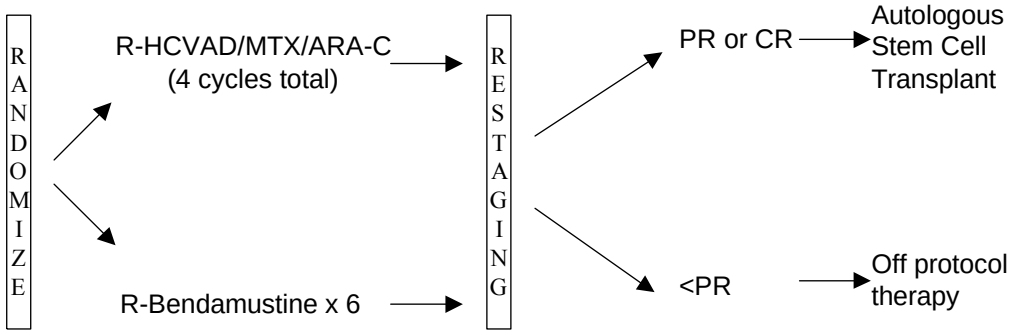
Statisticians:
M LeBlanc, H Li

Data Coordinator:
I Syquia

Date Activated:
10/01/2011

Date Closed:
06/26/2013

SCHEMA



Objectives

To estimate the two-year progression-free survival (PFS) in patients with newly diagnosed mantle cell lymphoma (MCL) treated with R-HCVAD/MTX/ARA-C + autologous stem cell transplant or R-bendamustine + autologous stem cell transplant and to select a regimen for further development.

To assess the response rate and overall survival of patients with newly diagnosed MCL treated with these regimens.

To assess the toxicitiy and tolerability of these regimens in patients with newly diagnosed MCL.

To determine the prognostic value of quantitative minimal residual disease (MRD) monitoring in the peripheral blood of MCL patients after induction therapy and serially after high-dose chemotherapy and autologous stem cell transplant on treatment outcome.

To bank diagnostic tissue sections, and peripheral blood prior to treatment, after induction therapy, before transplant and after transplant for future translational research studies.

Patient Population

Patients must have previously untreated Stage III, IV, or bulky Stage II mantle cell lymphoma. A diagnosis of MCL must be confirmed by histopathological diagnosis including immunohistochemistry and flow cytometry documenting both of the following phenotypes: 1) CD19+ or CD20+ and 2) Cyclin D1+ or evidence of the t(11;14) translocation by cytogenetics or fluorescence in situ hybridization (FISH). Patients must have bidimensionally measurable disease, with no evidence of CNS involvement.

Patients must not have received prior chemotherapy, radiation, or antibody therapy for lymphoma.

Patients must be at least 18 and no more than 65 years old and have a Zubrod performance status of 0, 1 or 2. Patients must have adequate cardiac, renal, and hepatic function. Patients known to be HIV positive or who have a history of solid organ transplantation are not eligible. Patients with active hepatitis are not eligible.

Stratification/Descriptive Factors

Patient randomization will be stratified by risk classification by Mantle Cell Lymphoma International Prognostic Index (MIPI) score: Low Risk vs Intermediate/High Risk.

Accrual Goals

Planned accrual was 160 eligible patients (approximately 80 per arm).

Summary Statement

This study was permanently closed to accrual on June 26, 2013, due to meeting the study's primary objective as evaluated by CTEP. The final accrual was 53 eligible patients, including 18 patients on the R-HCVAD/R-MTX/ARA-C arm and 35 patients on the R-Bendamustine arm. The R-HCVAD/R-MTX/ARA-C arm was permanently closed to accrual on January 24, 2013, due to toxicity (failure of stem cell collection and/or delay of therapy due to hematological toxicity). One patient on this arm who did not receive any protocol treatment is not analyzable for any endpoint.

On the R-HCVAD/R-MTX/ARA-C arm, 12 patients discontinued protocol treatment early for the following reasons: adverse events including thrombocytopenia (3), decreased platelet count, and delayed pancytopenia (1 patient each); failure to collect stem cells (5); withdrew consent due to the out-of-pocket cost of stem cell collection/transplant (1); and patient refusal (1).

On the R-Bendamustine arm, seven patients discontinued protocol treatment early for the following reasons: adverse events including bendamustine allergy, persistent decreased ANC, and seizures while receiving Zofran (1 patient each); patient refusal (3); and insurance reason (1).

Among 17 patients on the R-HCVAD/R-MTX/ARA-C arm assessed for adverse events, 13 patients reported Grade 4 hematologic toxicities. There have been no Grade 4 or higher non-hematologic adverse events reported.

Among 35 patients on the R-Bendamustine arm assessed for adverse events, 15 patients reported Grade 4 hematologic toxicities and additonal 15 patients reported Grade 3 toxicities as maximum degree, primarily hematologic (14). There have been no Grade 4 or higher non-hematologic adverse events reported.

Twenty-six patients were registered to receive the stem cell transplant, including five patients from the R-HCVAD/R-MTX/ARA-C arm and 21 patients from the R-Bendamustine arm. Among 26 eligible patients assessed for adverse events, 20 patients reported Grade 4 hematologic toxicities. Three of these also experienced Grade 4 non-hematologic toxicities, including one with febrile neutropenia, one with blood bilirubin increased, and another one with ARDS, diarrhea, enterocolitis infectious, hypocalcemia, and hypotension.

Among 17 patients treated with R-HCVAD/R-MTX/ARA-C followed by autologous stem cell transplant, 6 (35%) patients achieved a complete response and 10 (59%) patients achieved a partial response. One patient who could not have exact response determined due to inadequate assessments is assumed to be a non-responders for the purpose of

response rate estimation. The estimated response rate is 94.1% (95% CI: 71.3%, 99.9%).

Among 35 patients treated with R-Bendamustine followed by autologous stem cell transplant, 14 (40%) patients achieved a complete response and 15 (43%) patients achieved a partial response. Six (17%) patients who could not have their exact response determined due to inadequate assessments are as assumed to be non-responders for the purpose of response rate estimation. The estimated response rate is 82.9% (95% CI: 66.4%, 93.4%).

The median length of follow-up among those treated with R-HCVAD/R-MTX/ARA-C followed by autologous stem cell transplant and last known alive is 36 months (range 10 - 41 months). The median length of follow-up among those treated with R-Bendamustine followed by autologous stem cell transplant and last known alive is 32 months (range 1 - 45 months). The estimated 2-year progression-free survival (PFS) probabilities were 82% (95% CI: 53.0%, 93.7%) on the R-HCVAD/R-MTX/ARA-C followed by autologous stem cell transplant arm and 81% (95% CI: 62.7%, 91.1%) on the R-Bendamustine followed by autologous stem cell transplant arm. The estimated 2-year overall survival (OS) probabilities were 88% (95% CI: 59.5%, 96.8%) on the R-HCVAD/R-MTX/ARA-C followed by autologous stem cell transplant arm and 87% (95% CI: 69.8%, 95.1%) on the R-Bendamustine followed by autologous stem cell transplant arm.

Registration by Institution

Initial Registration

Institutions	Total Reg	Institutions	Total Reg
Alliance	23	Kentucky, U of	2
ECOG-ACRIN	7	Davis, U of CA	1
Rochester, Univ of	7	Prov Portland MC/PCRC NCORP	1
Dayton NCORP	3	St Louis University	1
City of Hope Med Ctr	2	Wayne State Univ	1
Greenville NCORP	2	Wichita NCORP	1
KaiserPermanenteCOL/Kaiser Perm NCORP	2	**Total (13 Institutions)**	**53**

Registration, Eligibility, and Evaluability

Initial Registration

Data as of February 10, 2016

	TOTAL	R-HCVAD/MTX /Ara-C	R-Bendamustine
NUMBER REGISTERED	53	18	35
ELIGIBLE	53	18	35
Not Analyzable	1	1	0
RESPONSE ASSESSMENT			
Determinable	45	16	29
Not Determinable	7	1	6
ADVERSE EVENT ASSESSMENT			
Evaluable	52	17	35

Patient Characteristics

Initial Registration

Data as of February 10, 2016

	R-HCVAD/MTX /Ara-C (n=17)		R-Bendamustine (n=35)	
AGE				
Median	58.8		56.6	
Minimum	43.6		33.0	
Maximum	65.7		64.1	
SEX				
Males	9	53%	32	91%
Females	8	47%	3	9%
HISPANIC				
No	16	94%	35	100%
Unknown	1	6%	0	0%
RACE				
White	13	76%	32	91%
Black	1	6%	2	6%
Asian	1	6%	0	0%
Unknown	2	12%	1	3%
MIPI SCORE				
low risk	11	65%	22	63%
intermediate/high risk	6	35%	13	37%

Treatment Summary

Induction

Data as of February 10, 2016

	TOTAL	R-HCVAD/MTX /Ara-C	R-Bendamustine
NUMBER ON PROTOCOL TREATMENT	0	0	0
NUMBER OFF PROTOCOL TREATMENT	52	17	35
REASON OFF TREATMENT			
Treatment completed as planned	32	5	27
Adverse Event or side effects	8	5	3
Refusal unrelated to adverse event	4	1	3
Other - not protocol specified	7	6	1
Reason under review	0	0	0
MAJOR PROTOCOL DEVIATIONS	0	0	0

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

Induction

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of February 10, 2016

	R-HCVAD/MTX/Ara-C (n=17) Grade						R-Bendamustine (n=35) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	9	6	1	1	0	0	27	7	1	0	0	0
APTT prolonged	17	0	0	0	0	0	34	1	0	0	0	0
AST increased	13	2	1	1	0	0	27	8	0	0	0	0
Abdominal distension	17	0	0	0	0	0	33	0	2	0	0	0
Abdominal pain	15	2	0	0	0	0	34	0	1	0	0	0
Acute kidney injury	17	0	0	0	0	0	34	0	1	0	0	0
Agitation	17	0	0	0	0	0	34	1	0	0	0	0
Alkaline phosphatase increased	14	3	0	0	0	0	31	4	0	0	0	0
Allergic reaction	17	0	0	0	0	0	32	1	2	0	0	0
Allergic rhinitis	17	0	0	0	0	0	34	1	0	0	0	0
Alopecia	9	2	6	0	0	0	32	2	1	0	0	0
Anemia	2	0	5	9	1	0	10	18	4	3	0	0
Anorexia	11	3	3	0	0	0	23	9	3	0	0	0
Anxiety	17	0	0	0	0	0	33	2	0	0	0	0
Arthralgia	15	2	0	0	0	0	29	3	2	1	0	0
Back pain	15	1	1	0	0	0	33	1	1	0	0	0
Bloating	15	0	2	0	0	0	35	0	0	0	0	0
Blood bilirubin increased	17	0	0	0	0	0	31	3	1	0	0	0
Blurred vision	17	0	0	0	0	0	33	2	0	0	0	0
Bone pain	16	0	1	0	0	0	30	3	2	0	0	0
Bruising	16	0	1	0	0	0	34	1	0	0	0	0
CD4 lymphocytes decreased	15	0	0	1	1	0	33	0	0	1	1	0
Catheter related infection	16	0	0	1	0	0	34	0	0	1	0	0
Chest wall pain	17	0	0	0	0	0	34	1	0	0	0	0
Chills	15	2	0	0	0	0	32	2	1	0	0	0
Cognitive disturbance	16	1	0	0	0	0	35	0	0	0	0	0
Conjunctivitis	16	1	0	0	0	0	35	0	0	0	0	0
Constipation	5	10	2	0	0	0	20	14	1	0	0	0
Cough	15	1	1	0	0	0	29	4	2	0	0	0
Creatinine increased	16	1	0	0	0	0	32	2	1	0	0	0
Cytokine release syndrome	16	0	1	0	0	0	35	0	0	0	0	0
DLCO decreased	16	1	0	0	0	0	35	0	0	0	0	0
Dehydration	16	0	0	1	0	0	34	1	0	0	0	0
Depression	17	0	0	0	0	0	33	2	0	0	0	0
Diarrhea	10	3	3	1	0	0	29	5	1	0	0	0
Dizziness	14	3	0	0	0	0	31	4	0	0	0	0
Dry eye	16	0	1	0	0	0	35	0	0	0	0	0
Dry mouth	17	0	0	0	0	0	34	1	0	0	0	0
Dry skin	17	0	0	0	0	0	32	3	0	0	0	0
Duodenal ulcer	16	0	1	0	0	0	35	0	0	0	0	0
Dysesthesia	17	0	0	0	0	0	34	1	0	0	0	0
Dysgeusia	15	1	1	0	0	0	32	3	0	0	0	0
Dyspepsia	16	0	1	0	0	0	34	0	1	0	0	0
Dysphagia	17	0	0	0	0	0	34	1	0	0	0	0

	R-HCVAD/MTX/Ara-C (n=17) Grade						R-Bendamustine (n=35) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Dyspnea	16	1	0	0	0	0	30	3	2	0	0	0
ECG QT corrected int prolong	17	0	0	0	0	0	34	1	0	0	0	0
Ear pain	16	1	0	0	0	0	35	0	0	0	0	0
Edema face	16	1	0	0	0	0	35	0	0	0	0	0
Edema limbs	16	1	0	0	0	0	31	3	1	0	0	0
Enterocolitis infectious	17	0	0	0	0	0	34	0	0	1	0	0
Epistaxis	14	0	2	1	0	0	34	0	1	0	0	0
Facial pain	16	1	0	0	0	0	35	0	0	0	0	0
Fatigue	6	5	6	0	0	0	2	22	10	1	0	0
Febrile neutropenia	12	0	0	5	0	0	30	0	0	5	0	0
Fever	17	0	0	0	0	0	27	6	2	0	0	0
Flushing	16	1	0	0	0	0	35	0	0	0	0	0
GERD	17	0	0	0	0	0	33	0	2	0	0	0
GI disorders-Other, specify	17	0	0	0	0	0	34	0	1	0	0	0
Generalized muscle weakness	14	1	2	0	0	0	33	1	1	0	0	0
Headache	13	2	2	0	0	0	32	1	2	0	0	0
Hematuria	17	0	0	0	0	0	34	1	0	0	0	0
Hemorrhoids	15	1	1	0	0	0	34	0	1	0	0	0
Hiccups	17	0	0	0	0	0	34	1	0	0	0	0
Hot flashes	17	0	0	0	0	0	34	1	0	0	0	0
Hypercalcemia	17	0	0	0	0	0	34	1	0	0	0	0
Hyperglycemia	9	1	5	2	0	0	24	7	4	0	0	0
Hyperkalemia	17	0	0	0	0	0	33	2	0	0	0	0
Hypermagnesemia	17	0	0	0	0	0	34	1	0	0	0	0
Hypernatremia	17	0	0	0	0	0	34	1	0	0	0	0
Hypertension	17	0	0	0	0	0	31	1	3	0	0	0
Hyperuricemia	16	1	0	0	0	0	31	4	0	0	0	0
Hypoalbuminemia	10	4	3	0	0	0	30	1	3	1	0	0
Hypocalcemia	10	3	4	0	0	0	30	3	2	0	0	0
Hypokalemia	11	1	0	5	0	0	29	1	3	2	0	0
Hypomagnesemia	16	1	0	0	0	0	33	2	0	0	0	0
Hyponatremia	13	4	0	0	0	0	30	5	0	0	0	0
Hypophosphatemia	12	0	1	4	0	0	32	1	1	1	0	0
Hypotension	15	2	0	0	0	0	30	3	2	0	0	0
Infections/infestations-Other	17	0	0	0	0	0	31	1	2	1	0	0
Infusion related reaction	14	1	2	0	0	0	31	0	3	1	0	0
Insomnia	16	0	1	0	0	0	33	2	0	0	0	0
Investigations-Other, specify	17	0	0	0	0	0	34	0	1	0	0	0
Irritability	16	1	0	0	0	0	35	0	0	0	0	0
Localized edema	17	0	0	0	0	0	34	1	0	0	0	0
Lymphocyte count decreased	6	1	0	3	7	0	6	1	1	15	12	0
MS/connective tissue disorder	17	0	0	0	0	0	34	1	0	0	0	0
Malaise	17	0	0	0	0	0	34	1	0	0	0	0
Metab/nutrition disorders-Oth	17	0	0	0	0	0	34	1	0	0	0	0
Mucositis oral	10	5	2	0	0	0	33	1	1	0	0	0
Myalgia	16	1	0	0	0	0	31	1	2	1	0	0
Nail ridging	16	1	0	0	0	0	34	1	0	0	0	0
Nasal congestion	17	0	0	0	0	0	33	1	1	0	0	0
Nausea	8	6	2	1	0	0	14	17	4	0	0	0
Neuralgia	17	0	0	0	0	0	34	1	0	0	0	0
Neutrophil count decreased	6	0	0	0	11	0	17	2	4	3	9	0

	R-HCVAD/MTX/Ara-C (n=17) Grade						R-Bendamustine (n=35) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Non-cardiac chest pain	17	0	0	0	0	0	34	1	0	0	0	0
Oral pain	17	0	0	0	0	0	34	1	0	0	0	0
Pain	17	0	0	0	0	0	31	2	2	0	0	0
Pain in extremity	17	0	0	0	0	0	32	2	0	1	0	0
Pain of skin	16	1	0	0	0	0	35	0	0	0	0	0
Papulopustular rash	17	0	0	0	0	0	34	1	0	0	0	0
Paresthesia	17	0	0	0	0	0	34	0	1	0	0	0
Pelvic pain	17	0	0	0	0	0	34	1	0	0	0	0
Peripheral motor neuropathy	15	1	1	0	0	0	35	0	0	0	0	0
Peripheral sensory neuropathy	13	3	1	0	0	0	34	1	0	0	0	0
Pharyngeal mucositis	17	0	0	0	0	0	34	1	0	0	0	0
Platelet count decreased	2	2	1	0	12	0	12	14	3	5	1	0
Pleural effusion	16	0	1	0	0	0	34	0	1	0	0	0
Presyncope	16	0	1	0	0	0	35	0	0	0	0	0
Productive cough	17	0	0	0	0	0	34	0	1	0	0	0
Pruritus	16	0	1	0	0	0	33	1	0	1	0	0
ROM decreased	17	0	0	0	0	0	34	1	0	0	0	0
Rash acneiform	16	1	0	0	0	0	34	1	0	0	0	0
Rash maculo-papular	15	1	0	1	0	0	29	4	1	1	0	0
Rhinitis infective	17	0	0	0	0	0	34	0	1	0	0	0
Scalp pain	16	1	0	0	0	0	35	0	0	0	0	0
Sinus bradycardia	17	0	0	0	0	0	33	2	0	0	0	0
Sinus tachycardia	14	2	1	0	0	0	32	3	0	0	0	0
Skin infection	17	0	0	0	0	0	34	0	1	0	0	0
Skin/subq tissue ds-Other	17	0	0	0	0	0	32	2	1	0	0	0
Sore throat	15	2	0	0	0	0	33	1	0	1	0	0
Syncope	16	0	0	1	0	0	35	0	0	0	0	0
Thromboembolic event	17	0	0	0	0	0	34	0	1	0	0	0
Tumor pain	17	0	0	0	0	0	34	0	0	1	0	0
Upper respiratory infection	17	0	0	0	0	0	33	0	2	0	0	0
Urinary frequency	17	0	0	0	0	0	33	2	0	0	0	0
Urinary incontinence	16	0	1	0	0	0	35	0	0	0	0	0
Urinary tract infection	17	0	0	0	0	0	34	0	0	1	0	0
Urticaria	17	0	0	0	0	0	34	0	1	0	0	0
Vascular access complication	17	0	0	0	0	0	34	0	0	1	0	0
Vomiting	13	3	1	0	0	0	28	4	3	0	0	0
Weight gain	17	0	0	0	0	0	34	1	0	0	0	0
Weight loss	16	1	0	0	0	0	31	3	1	0	0	0
White blood cell decreased	6	0	1	0	10	0	11	5	5	9	5	0
MAX. GRADE ANY ADVERSE EVENT	0	0	3	1	13	0	0	2	3	15	15	0

Registration, Eligibility, and Evaluability

Stem Cell Transplant

Data as of February 10, 2016

	Stem Cell Transplant
NUMBER REGISTERED	26
ELIGIBLE	26
RESPONSE ASSESSMENT	
Determinable	25
Not Determinable	1
ADVERSE EVENT ASSESSMENT	
Evaluable	26

Treatment Summary

Stem Cell Transplant

Data as of February 10, 2016

	Stem Cell Transplant
NUMBER ON PROTOCOL TREATMENT	0
NUMBER OFF PROTOCOL TREATMENT	26
REASON OFF TREATMENT	
Treatment completed as planned	26
Adverse Event or side effects	0
Refusal unrelated to adverse event	0
Progression/relapse	0
Death	0
Other - not protocol specified	0
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0

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

Stem Cell Transplant

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of February 10, 2016

	Stem Cell Transplant (n=26) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	19	6	1	0	0	0
ARDS	25	0	0	0	1	0
AST increased	20	5	1	0	0	0
Abdominal pain	25	0	1	0	0	0
Acidosis	25	0	0	1	0	0
Alkaline phosphatase increased	22	4	0	0	0	0
Allergic rhinitis	25	0	1	0	0	0
Alopecia	19	1	6	0	0	0
Anemia	5	1	11	9	0	0
Anorexia	14	6	5	1	0	0
Anxiety	25	1	0	0	0	0
Arthralgia	25	1	0	0	0	0
Atrial flutter	25	0	1	0	0	0
Blood bilirubin increased	22	1	1	1	1	0
Catheter related infection	25	0	0	1	0	0
Chills	25	1	0	0	0	0
Constipation	22	4	0	0	0	0
Cough	24	2	0	0	0	0
Creatinine increased	24	2	0	0	0	0
Dehydration	25	1	0	0	0	0
Device related infection	25	0	0	1	0	0
Diarrhea	5	12	5	3	1	0
Dry mouth	24	2	0	0	0	0
Dysgeusia	22	3	1	0	0	0
Dyspepsia	25	0	1	0	0	0
Dysphagia	25	1	0	0	0	0
Dyspnea	25	0	1	0	0	0
Edema limbs	23	2	1	0	0	0
Enterocolitis	25	0	0	1	0	0
Enterocolitis infectious	25	0	0	0	1	0
Fatigue	11	12	3	0	0	0
Febrile neutropenia	13	0	0	12	1	0
Fecal incontinence	25	0	1	0	0	0
Fever	22	4	0	0	0	0
Flank pain	25	1	0	0	0	0
Flushing	25	1	0	0	0	0
GERD	24	0	2	0	0	0
Gallbladder infection	25	0	0	1	0	0
Gastrointestinal pain	25	1	0	0	0	0
Generalized muscle weakness	24	1	1	0	0	0
Headache	24	2	0	0	0	0
Hematuria	25	1	0	0	0	0
Hemorrhoids	25	0	1	0	0	0
Hiccups	25	1	0	0	0	0

	Stem Cell Transplant (n=26) Grade					
ADVERSE EVENTS	**0**	**1**	**2**	**3**	**4**	**5**
Hyperglycemia	23	3	0	0	0	0
Hypernatremia	25	1	0	0	0	0
Hypertension	25	0	1	0	0	0
Hyperuricemia	24	2	0	0	0	0
Hypoalbuminemia	16	3	7	0	0	0
Hypocalcemia	10	8	6	1	1	0
Hypokalemia	17	6	2	1	0	0
Hypomagnesemia	21	4	0	1	0	0
Hyponatremia	20	5	0	1	0	0
Hypophosphatemia	22	1	0	3	0	0
Hypotension	20	2	3	0	1	0
Hypoxia	25	0	0	1	0	0
Ileus	25	0	1	0	0	0
Injection site reaction	25	1	0	0	0	0
Lung infection	24	0	1	1	0	0
Lymphocyte count decreased	13	0	1	1	11	0
Mucositis oral	13	10	3	0	0	0
Nausea	7	8	9	2	0	0
Neutrophil count decreased	8	1	1	1	15	0
Pain in extremity	25	1	0	0	0	0
Peripheral sensory neuropathy	23	2	1	0	0	0
Pharyngeal mucositis	25	1	0	0	0	0
Platelet count decreased	7	0	0	1	18	0
Pneumonitis	25	0	1	0	0	0
Proteinuria	25	1	0	0	0	0
Pruritus	24	2	0	0	0	0
Rash maculo-papular	24	1	0	1	0	0
Rectal hemorrhage	25	0	0	1	0	0
Sinus bradycardia	25	1	0	0	0	0
Sinus tachycardia	24	2	0	0	0	0
Skin infection	24	0	2	0	0	0
Skin/subq tissue ds-Other	25	1	0	0	0	0
Small intestinal obstruction	24	0	1	1	0	0
Sore throat	25	1	0	0	0	0
Stomach pain	25	1	0	0	0	0
Thromboembolic event	25	0	1	0	0	0
Urinary tract infection	25	0	1	0	0	0
Vomiting	17	5	3	1	0	0
Watering eyes	24	1	1	0	0	0
Weight gain	25	1	0	0	0	0
Weight loss	23	2	1	0	0	0
White blood cell decreased	6	0	0	1	19	0
MAX. GRADE ANY ADVERSE EVENT	0	1	3	2	20	0

Overall Response

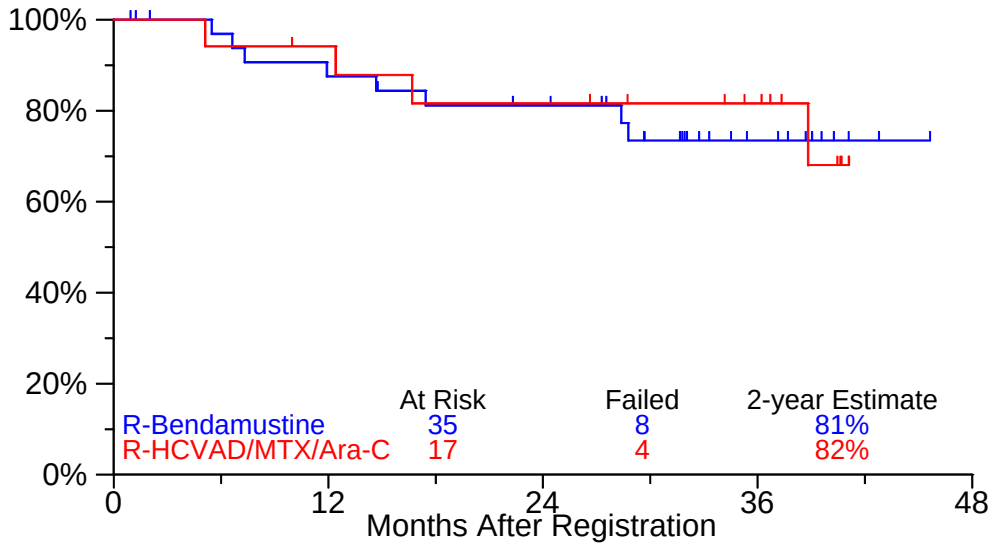
Induction Therapy followed by Stem Cell Transplant

Data as of February 10, 2016

	R-HCVAD/MTX/Ara-C		R-Bendamustine	
	N	%	N	%
Complete Response	6	35	14	40
Partial Response	10	59	15	43
Assessment Inadequate	1	6	6	17
Total	17	100	35	100

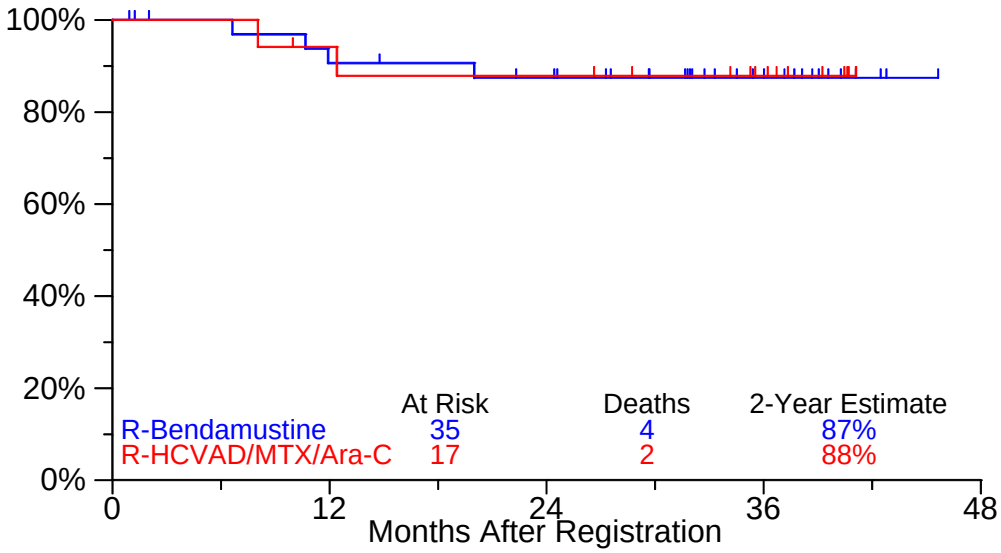
Progression-Free Survival

Data as of February 10, 2016



Overall Survival

Data as of February 10, 2016



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.

9177 Phase II SWOG Supported CTSU Study

Coordinating Group: NCIMet

Phase II Study of Dose-Adjusted EPOCH +/- Rituximab in Adults with Untreated Burkitt Lymphoma, c-MYC Positive Diffuse Large B-Cell Lymphoma and Plasmablastic Lymphoma

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Participants:
NCIMet, CTSU

Date Activated:
05/15/2012

Study Chairs:
K Dunleavy (NCIMet), M Fanale (SWOG)

Objectives

To determine PFS, EFS and OS of risk adaptive DA-EPOCH-R in newly diagnosed Burkitt Lymphoma, c-MYC + DLBCL and DA-EPOCH in c-MYC+ plasmablastic lymphoma ≥ 18 years.

To assess predictive value of early FDG-PET/CT scans on PFS.

To obtain pilot comparative molecular profiling in HIV negative and positive BL and c-MYC + DLBCL, including c-MYC + plasmablastic lymphoma.

To assess the toxicity of risk adaptive DA-EPOCH-R in newly diagnosed Burkitt Lymphoma, c-MYC + DLBCL and DA-EPOCH in c-MYC+ plasmablastic lymphoma ≥ 18 years.

Patient Population

Patients must have histologically documented Burkitt lymphoma or B-cell lymphoma, unclassifiable, with features intermediate between Diffuse Large B-cell lymphoma and Burkitt Lymphoma, c-MYC + DLBCL or c-MYC+ plasmablastic lymphoma with all disease stages. Patients with primary central nervous system (CNS) lymphoma are excluded.

Patients must not have received any prior treatment except limited-field radiotherapy, short course of glucocorticoids and/or cyclophosphamide for an urgent problem at diagnosis and/or a single dose of intrathecal methotrexate at time of the pre-treatment diagnostic lumbar puncture.

Patients must be at least 18 years old and have ECOG performance status 0-4. Patients must have adequate major organ function unless impairment due to lymphoma.

Accrual Goals

A total of 194 patients will be accrued to this study.

Summary Statement

In April 2014, an interim analysis that looked at accrual of the MYC + DLBCL and Burkitt Lymphoma (BL) arms showed that the accrual ceiling in the MYC + DLBCL arm, which included plasmablastic lymphoma and B-cell lymphoma with features intermediate between BL and DLBCL, had been exceeded, therefore, accrual to this arm was suspended. At the same time, the analysis revealed that only 35 patients had been accrued to the BL arm which is significantly short of the initial accrual goal for this arm (96 patients). The study was amended on June 24, 2014, to increase the overall accrual goal to 194 in order to reach the BL arm initial accrual goal.

NCIMet reported a total accrual of 138 patients as of December 31, 2015, including 19 SWOG registrations.

Registration by Institution

Registrations ending December 31, 2015

Institutions	Total Reg
Rochester, Univ of	9
Cleveland Clinic OH	4
Kentucky, U of	4
Kansas City NCORP	1
Tennessee, U of	1
Total (5 Institutions)	**19**

C51101 Phase II SWOG Supported CTSU Study

Coordinating Group: Alliance

A Randomized Phase II Trial of Myeloablative versus Non-myeloablative Consolidation Chemotherapy for Newly Diagnosed Primary CNS-B-cell Lymphoma

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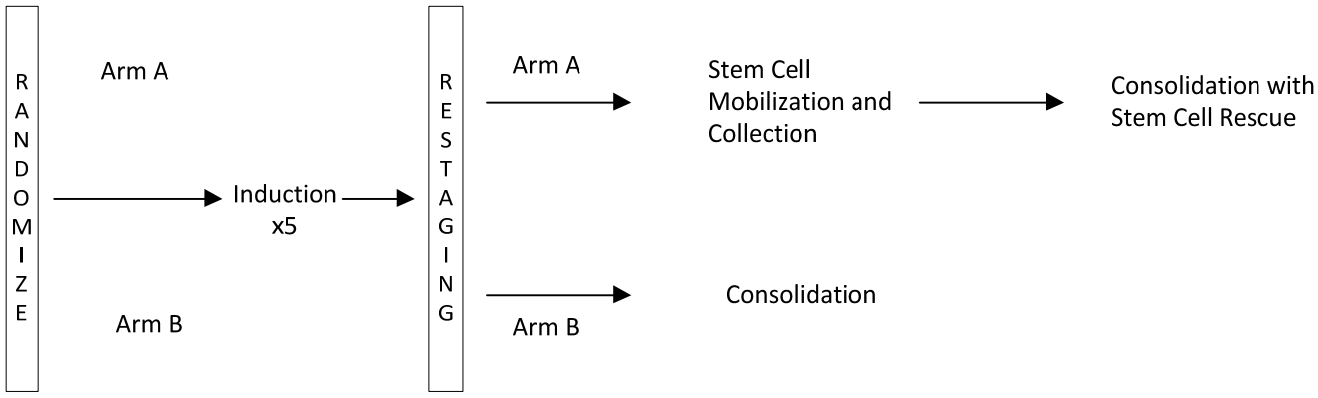
Participants:
Alliance, CTSU

Date Activated:
07/01/2012

Study Chairs:
T Batchelor (Alliance), N Mohile (SWOG)

SCHEMA



Objectives

To compare the two-year progression-free survival (PFS) of patients treated with the myeloablative consolidation treatment strategy of HDT/ASCT versus those treated with non-myeloablative consolidation chemotherapy with cytarabine and etoposide.

To compare the two-year event-free survival (EFS) and the overall survival (OS) of patients treated with consolidation HDT/ASCT versus those treated with consolidation chemotherapy consisting of etoposide and cytarabine.

To assess the toxicities associated with consolidation HDT/ASCT versus consolidation consisting of etoposide and cytarabine.

To determine diffusion MRI metrics (ADCmini, ADC25%, and ADCmean) prior to induction chemotherapy, after one full induction chemotherapy cycle, and at the end of induction chemotherapy as a predictor of response and outcome.

To determine brain FDG-PET metrics (tumor SUV and tumor versus background SUV) prior to induction chemotherapy, after one full induction chemotherapy cycle, and at the end of induction chemotherapy as a predictor of response and outcome.

To determine whether low baseline ADC measurements are associated with shorter PFS and OS.

To determine whether reduction in tumor SUV by > 25% on brain FDGPET/CT after one cycle of induction therapy is associated with improved PFS and OS.

To determine which IHC-based biomarkers are predictive of an adverse prognosis.

To determine which IHC-based biomarkers are predictive of a favorable prognosis for BCL6 (B-cell CLL/lymphoma 6), and STAT 6 (signal transducer and activator of transcription 6, interleukin-4 induced).

To analyze tumor tissue for gene expression profiles, and to correlate these profiles with treatment outcomes.

To determine whether CSF proteome is a predictor of outcomes (prognostic marker) irrespective of treatment arm for IL-10 (interleukin 10) and C3 (complement component 3).

To assess the neurocognitive function of patients treated with consolidation HDT/ASCT versus those treated with consolidation chemotherapy (etoposide and cytarabine) as measured by serial administration of the International PCNSL Collaborative Group (IPCG) neurocognitive battery and evaluate the long-term survivorship differences between the two arms.

To assess the quality of life of patients treated with consolidation HDT/ASCT versus those treated with consolidation etoposide and cytarabine as measured by the EORTC Quality of Life Questionnaire-Core 30/Brain Cancer Module-20 (EORTC-QLQ30/BCM20), and to evaluate the long-term survivorship differences between the two arms.

Patient Population

Patients must have confirmed central nervous system (CNS) diffuse large B-cell lymphoma. Patients must have no evidence or history of non-Hodgkin lymphoma (NHL) outside of CNS. Patients must not have isolated ocular lymphoma .

Patient must not have received any prior chemotherapy or radiation therapy for lymphoma. Patients must have no history of organ transplantation or ongoing immunosuppressant therapy.

Patients must be between 18 to 75 years old and have Karnofsky Performance Scale (KPS) $\geq$ 30 ($\geq$ 50 for patients ages 60-70). Patients must have adequate cardiac, pulmonary, hematologic, renal, and hepatic function. Patients must have negative HIV serology and negative HCV serology (unless HBsAb positive patients have recently received HBV vaccine, in this case HBcAb should be negative).

Stratification/Descriptive Factors

Patient randomization will be stratified by age and KPS score: age < 51 years vs age $\geq$ 51 years and KPS $\geq$ 70 vs age $\geq$ 51 years and KPS < 70.

Accrual Goals

A total of 160 patients will be accrued to this study (80 per arm).

Summary Statement

Alliance reported a total accrual of 61 patients as of December 31, 2015, including 5 SWOG registrations: one from University of California Davis, two from Fred Hutchinson Cancer Research Center, and two from University of Rochester. The complete November 2015 summary of this study from Alliance is available on the SWOG web site.

E1411 Phase II SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

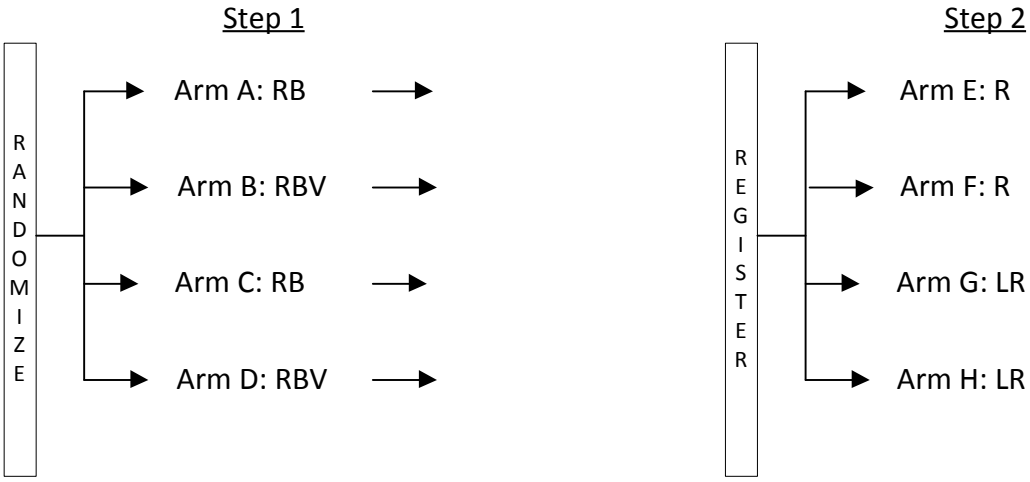
Intergroup Randomized Phase II Four Arm Study in Patients with Previously Untreated Mantle Cell Lymphoma of Therapy with: Arm A = Rituximab + Bendamustine Followed by Rituximab Consolidation (RB → R), Arm B = Rituximab + Bendamustine + Bortezomib Followed by Rituximab Consolidation (RBV → R), Arm C = Rituximab + Bendamustine Followed by Lenalidomide + Rituximab Consolidation (RB → LR) or Arm D = Rituximab + Bendamustine + Bortezomib Followed by Lenalidomide + Rituximab Consolidation (RBV → LR)

Participants:
ECOG-ACRIN, CTSU

Date Activated:
06/15/2012

Study Chairs:
M Smith (ECOG-ACRIN), B Till (SWOG)

SCHEMA



RB: Rituximab + Bendamustine
RBV: Rituximab + Bendamustine + Bortezomib

R: Rituximab
LR: Lenalidomide + Rituximab

Objectives

To determine whether the addition of bortezomib (RBV) to an induction regimen of rituximab bendamustine (RB) improves progression-free survival (PFS) compared to RB alone in patients with previously untreated mantle cell lymphoma.

To determine whether the addition of lenalidomide to a consolidation regimen of rituximab following an induction regimen of RB or RBV improves PFS compared to consolidation rituximab alone in this patient population.

To determine whether the addition of bortezomib to induction therapy improves the PET-documented complete response rate compared to RB alone.

To determine whether the addition of lenalidomide to consolidation therapy improves CR and ORR compared with rituximab alone among patients who do not have PET-documented CR at the end of induction.

To determine overall survival (OS) in the treatment arms.

To determine safety, with attention to the addition of bortezomib in the induction regimen and lenalidomide-rituximab as consolidation therapy.

To determine the extent and severity of neuropathy associated with the addition of bortezomib to induction treatment using patient-reported outcomes data.

To determine the extent of severity of fatigue associated with the addition of lenalidomide to consolidation treatment using patient-reported outcomes data.

To evaluate the effects of the addition of bortezomib and lenalidomide and the effect of bortezomib-related neuropathy on patient-reported health-related quality of life.

To evaluate the response of lymphoma-specific symptoms to treatment.

To describe the trajectory of lymphoma symptoms, neuropathy, fatigue and overall health-related quality of life prior to, during and following treatment among older adults with MCL using longitudinal patient-reported outcomes data.

See protocol for objectives for laboratory correlative studies, imaging correlative studies, and residual disease assessment by molecular and flow cytometric techniques.

Patient Population

Patients must have histologically confirmed untreated mantle cell lymphoma (MCL). Patients must have at least one objective measurable disease parameter. Patients must have no known CNS involvement.

Patients must not have received prior therapy for MCL, except less than two weeks of steroid therapy for symptom control if there is measurable disease outside the radiation portal. Patients may be on chronic steroids for non-malignant disease if on a stable dose equivalent to $\leq$ 20 mg prednisone per day. Patients must not be participating in any other clinical trial or taking any other experimental medications within 14 days prior to registration.

Patients must have ECOG performance status 0-2 and adequate cardiac, hematologic, renal, and hepatic function. Patients must not have Grade 2 or greater peripheral neuropathy. HIV positive patients are not excluded, but may enroll with restrictions. Patients must have no hypersensitivity to bortezomib, boron or mannitol. Patients must agree that if randomized to Arms C or D, and proceed onto Arms G and H, they must register into the mandatory RevAssist program. Patients must have no medical contra-indications to DVT prophylaxis.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) mantle cell lymphoma IPI (MIPI) risk status: low risk vs intermediate risk vs high risk; and (2) age: < 60 vs ≥ 60.

Accrual Goals

A total of 332 patients will be accrued to this study.

Summary Statement

ECOG-ACRIN reported a total accrual of 294 patients as of December 31, 2015, including 73 SWOG registrations. 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
Rochester, Univ of	21	Dayton NCORP	2
Cleveland Clinic OH	9	KaiserPermanenteCOL/Kaiser Perm NCORP	2
Kaiser Perm NCORP	9	Poudre Valley Hosp/Colorado, U of	2
Fred Hutchinson CRC	4	Arizona MC, U of	1
Hawaii MU-NCORP	4	Southeast COR NCORP	1
CRC West MI NCORP	3	UF Cancer Center/Arkansas, U of	1
Kansas City NCORP	3	Upstate Carolina	1
Montana NCORP	3	Wayne State Univ	1
Oregon Hlth Sci Univ	3	**Total (18 Institutions)**	**73**
Prov Portland MC/PCRC NCORP	3		

E1412 Phase II SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

Randomized Phase II Open Label Study of Lenalidomide R-CHOP (R2CHOP) vs. RCHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone) in Patients with Newly Diagnosed Diffuse Large B Cell Lymphoma

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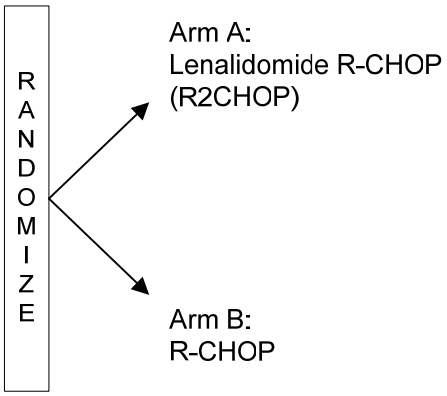
Participants:
ECOG-ACRIN, CTSU

Date Activated:
01/22/2014

Study Chairs:
G Nowakowski (ECOG-ACRIN), J Amengual (SWOG)

SCHEMA



Objectives

To determine progression-free survival (PFS).

To evaluate response rate (RR).

To determine the complete response (CR) rate as defined by PET-CT criteria.

To determine overall survival (OS).

To examine the impact of DLBCL molecular subtype on outcome.

To correlate interim PET scan results to treatment outcome.

Patient Population

Patients must have histologically confirmed diffuse large B-cell non-Hodgkin's lymphoma (DLBCL) expressing CD20 antigen. Patients with transform lymphoma or known primary mediastinal large B-cell lymphoma are excluded. Patients must have Stage II bulky disease, Stage III or IV disease. Patients with Stage I and Stage II non-bulky disease are excluded (Ann Arbor Staging). Patients must not have known CNS lymphoma or cerebrospinal fluid involvement with malignant lymphoma cells. Patients must have

measurable disease as detected by CT or the CT images of the PET/CT.

Patients must be previously untreated and not receiving any other agent that would be considered as a treatment for the lymphoma. Patients must not have history of radiation therapy to 25% or greater of the bone marrow for other diseases or history of anthracycline therapy. Patients must not be receiving erythroid stimulating agents.

Patients must be at least 18 years old and have International Prognostic Index of 2 or greater and ECOG performance status of 0-2. Patients must have adequate cardiac, renal, hepatic and hematologic function. Patients must not have history of myocardial infarction within six months; congestive heart failure requiring use of ongoing maintenance therapy for life-threatening ventricular arrhythmias; history of deep venous thrombosis/embolism, threatening thromboembolism or known thrombophilia (patient may participate if on full anticoagulation); or history of AIDS-related conditions (other than the presenting DLBCL) or post-transplant lymphoproliferative disorder (PTLD) in immunocompromised patients. Patients must not have other active malignancy requiring therapy such as radiation, chemotherapy, or immunotherapy, with exception of localized non-melanotic skin cancer and any cancer that in the judgment of the investigator has been treated with curative intent and will not interfere with the study treatment plan and response assessment.

Stratification/Descriptive Factors

Patient randomization will be stratified according to the following factors: (1) International Prognostic Index (IPI): 2/3 vs 4/5; and (2) age: < 60 years vs ≥ 60 years.

Accrual Goals

The original accrual goal was 220 patients. After interim pathology review, the study was amended to increase accrual to 345 patients.

Summary Statement

This study was temporarily closed to accrual on May 22, 2015, with a total of accrual of 219 patients, to perform interim pathology review and gen expression profiling (GEP) assessment. Based on the pathology review of 107 patients, it was projected that the study will fall short of analysis goals, primarily due to pathology ineligibility and inadequacy of the submitted tissue for GEP. The study was amended to allow a "real time" central pathology eligibility screening process and accrual of an additional 125 patients. The study was re-activated on October 13, 2015, with a final accrual goal of 345 patients.

ECOG-ACRIN reported a total accrual of 230 patients as of December 31, 2015, including 26 SWOG registrations. The complete Fall 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending May 22, 2015

Institutions	Total Reg	Institutions	Total Reg
Rochester, Univ of	11	Cincinnati MC, U of	1
Montana NCORP	4	Hawaii MU-NCORP	1
Columbia MU-NCORP	3	Kaiser Perm NCORP	1
KaiserPermanenteSCAL/Kaiser Perm NCORP	3	Wayne State Univ	1
Brooke Army Med Ctr	1	**Total (9 Institutions)**	**26**

EAY131 Master Protocol / Phase II

Coordinating Group: ECOG-ACRIN

NCI-MATCH: Molecular Analysis for Therapy Choice

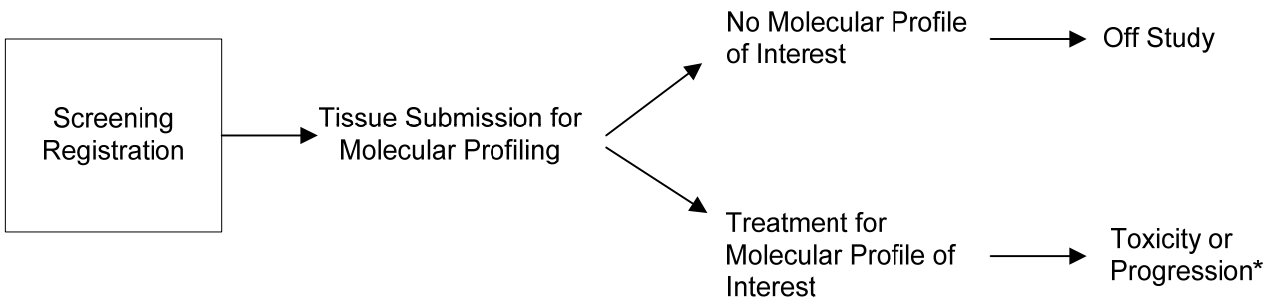
Participants:
ECOG-ACRIN, CTSU

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

Date Activated:
08/12/2015

Date Closed:
11/11/2015

SCHEMA



*Upon progression or inability to tolerate protocol treatment, patients may be re-screened for additional molecular profiles of interest and corresponding protocol treatment.

Objectives

To evaluate the proportion of patients with objective response (OR) to targeted study agent(s) in patients with advanced refractory cancers/lymphomas.

To evaluate the proportion of patients alive and progression free at six months of treatment with targeted study agent in patients with advanced refractory cancers/lymphomas.

To evaluate the time until death or disease progression.

To identify potential predictive biomarkers beyond the genomic alteration by which treatment is assigned or resistance mechanisms using additional genomic, RNA and protein-based assessment platforms.

Patient Population

Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma that has progressed following at least one line of standard systemic therapy and/or for whose disease no standard treatment exists that has been shown to prolong survival. Patients must have measurable disease, have tumor amenable to image guided or direct vision biopsy, and be willing and able to undergo biopsy for molecular profiling.

Patients must not currently be receiving any other investigational agents. Any prior therapy, radiotherapy (except palliative radiation therapy of 30 Gy or less), or major surgery must have been completed at least four weeks prior to treatment on NCI-MATCH and patient must be recovered from adverse events due to prior therapy (except alopecia

and lymphopenia). Palliative radiation therapy must have been completed at least two weeks prior to enrollment on a NCI-MATCH treatment subprotocol, and patient must have recovered from any adverse events of this therapy. Patients with brain metastases or primary brain tumors must have completed treatment , surgery, or radiation therapy at least four weeks prior to initial registration. Patients must not require the use of full dose coumarin-derivative anticoagulants such as warfarin. Low molecular weight heparin is permitted for prophylactic or therapeutic use.

Patients must be at least 18 years of age, have an ECOG performance status of 0 or 1 and must be able to swallow tablets. Patients must have adequate hematologic, hepatic, renal, cardiac and marrow function. HIV-positive patients are eligible provided they meet protocol criteria. Each subprotocol will have additional eligibility criteria that will be outlined in Section 2.0 of the agent-specific subprotocol.

Accrual Goals

The target screening accrual for this study is approximately 3,000 patients, with the goal of accruing 35 patients in each treatment subprotocol. If after screening 500 patients, the total number of patients with actionable tumor alteration (therefore qualifying for treatment) is below 50, results will be presented to the steering committee for consideration of terminating the trial. Within any given subprotocol, if rate of enrollment is such that it is unlikely accrual can be completed in 7.5 years, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. An interim analysis of the assay results will be performed after biopsies from approximately the first 200 patients are processed.

Summary Statement

This study activated on August 12, 2015, with 10 subprotocols included in the activation. Only sites utilizing the CIRB as their IRB of record are able to participate in the trial. The study was temporarily closed to accrual on November 11, 2015, after rapid accrual of 795 patients to the screening step in only three months, including 119 SWOG registrations. This pause in patient enrollment for interim analysis and review is expected to lift by May 2016, when an additional 12 to 14 new subprotocols are expected to be open.