LYMPHOMA COMMITTEE

CONTENTS

Patient Registrations to Studies

By 12 Month Intervals
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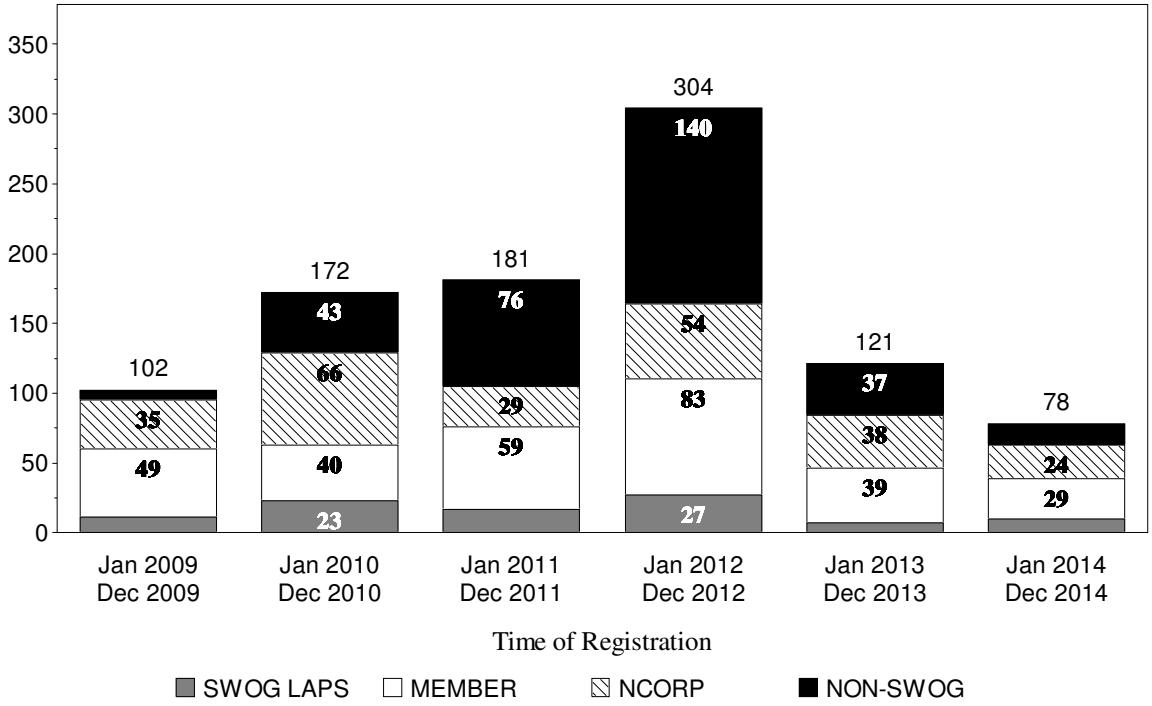

Screening registrations and registrations to Biologic only studies are excluded

Patient Registrations by Study and Arm

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	Jul 2014 Dec 2014	Jan 2014 Jun 2014	Jul 2013 Dec 2013	All Patients
S0806 NHL, Adv, R-CHOP + SAHA				
Initial registration				
R-CHOP+SAHA (400mg D1-9)	0	0	0	11
R-CHOP+SAHA	0	0	10	72
	0	0	10	83
S1001 DLBCL, I-II, PET-Adapted Therapy				
Initial registration				
R-CHOP x 3	22	19	17	104
R-CHOP x 6	0	1	0	1
	22	20	17	105
PET-Directed Therapy				
Continued R-CHOP	23	13	13	84
IFRT + Zevalin	2	4	2	11
	25	17	15	95
S1106 NHL, Adv, R-HCVAD/R-Benda+PBSCT				
Transplant				
Stem Cell Transplant	0	3	7	26
9177 NHL, Dose-Adj. EPOCH+/-Rituximab*				
Total Registrations	2	0	8	18
C51101 CNS, Myelo/Non-Myelo Chemo*				
Total Registrations	0	3	0	3
E1411 MCL, RB+R, RBV+R, RB+LR, RBV+LR*				
Total Registrations	9	14	9	37
E1412 DLBCL, R2CHOP vs RCHOP*				
Total Registrations	5	3	0	8

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

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 and ECOG-ACRIN

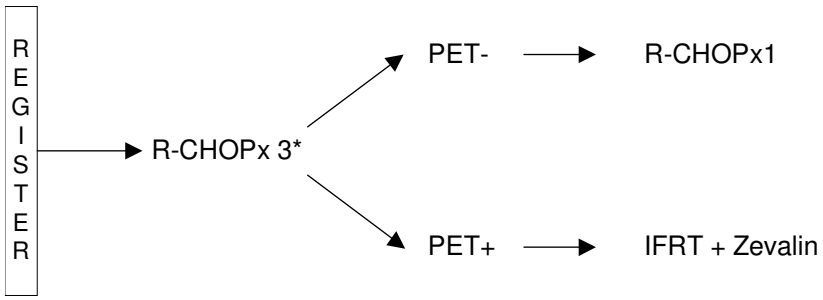
Date Activated:
07/15/2011

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 have adequate renal, hepatic, cardiac and hematologic function. Patients must have a Zubrod performance status of 0-2. 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, 2014, 105 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 ineligible for initial registration, one due to low grade B-cell lymphoma in the bone marrow and one due to no baseline specimens submitted for pathology review.

Ninety-seven 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 14 patients who had early stage DLBCL have experienced Grade 4 hematologic toxicities, one of whom also experienced Grade 4 febrile neutropenia.

Ninety-five patients have been registered to PET-directed therapy, 84 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.

Among 76 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. Seven additional patients on this arm have experienced treatment-related Grade 4 hematologic toxicities, one of who also experienced Grade 4 secondary leukemia.

One of the eleven patients assessed for toxicities on the IFRT + Zevalin arm experienced Grade 4 thrombocytopenia.

Registration by Institution

Initial Registration

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Alliance	23	Loyola University	3
Rochester, Univ of	23	St Luke's Mt State/PCRC NCORP	2
ECOG-ACRIN	14	Virginia Mason MC/Northwest NCORP	2
Upstate Carolina	7	Fred Hutchinson CRC	1
Arizona MC, U of	6	Greenville NCORP	1
Michigan CRC NCORP	5	Hawaii MU-NCORP	1
Kansas City NCORP	4	Montana NCORP	1
Wichita NCORP	4	NRG	1
Yale University	4	**Total (18 Institutions)**	**105**
Kentucky, U of	3		

Registration, Eligibility, and Evaluability

Initial Registration

Registrations ending December 31, 2014; Data as of February 26, 2015

	TOTAL	R-CHOP x 3	R-CHOP x 6
NUMBER REGISTERED	105	104	1
INELIGIBLE	2	2	0
Insufficient Documentation	1	1	0
Irreversible	1	1	0
ELIGIBLE	103	102	1
Analyzable, Pend. Elig.	96	95	1
RESPONSE ASSESSMENT			
Determinable	87	86	1
Not Determinable	1	1	0
Too Early	15	15	0
ADVERSE EVENT ASSESSMENT			
Evaluable	97	96	1
Too Early	6	6	0

Patient Characteristics

Initial Registration

Registrations ending December 31, 2014; Data as of February 26, 2015

	R-CHOP x 3 (n=102)		R-CHOP x 6 (n=1)	
AGE				
Median	61.6		74.3	
Minimum	18.5		74.3	
Maximum	85.5		74.3	
SEX				
Males	53	52%	0	0%
Females	49	48%	1	100%
HISPANIC				
Yes	5	5%	0	0%
No	96	94%	1	100%
Unknown	1	1%	0	0%
RACE				
White	88	86%	1	100%
Black	6	6%	0	0%
Asian	6	6%	0	0%
Native American	1	1%	0	0%
Unknown	1	1%	0	0%
PET UPSTAGED				
Yes	0	0%	1	100%
No	102	100%	0	0%

Treatment Summary

Initial Registration

Registrations ending December 31, 2014; Data as of February 26, 2015

	TOTAL	R-CHOP x 3	R-CHOP x 6
NUMBER ON PROTOCOL TREATMENT	13	13	0
NUMBER OFF PROTOCOL TREATMENT	90	89	1
REASON OFF TREATMENT			
Treatment completed as planned	88	87	1
Adverse Event or side effects	0	0	0
Refusal unrelated to adverse event	0	0	0
Other - not protocol specified	1	1	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

Initial Registration

Adverse Events Unlikely or Not Related to Treatment Excluded

Registrations ending December 31, 2014; Data as of February 26, 2015

	R-CHOP x 3 (n=96) Grade						R-CHOP x 6 (n=1) Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	86	9	1	0	0	0	1	0	0	0	0	0
AST increased	89	7	0	0	0	0	1	0	0	0	0	0
Abdominal pain	94	2	0	0	0	0	1	0	0	0	0	0
Agitation	95	0	1	0	0	0	1	0	0	0	0	0
Alkaline phosphatase increased	92	3	1	0	0	0	1	0	0	0	0	0
Allergic reaction	90	1	5	0	0	0	1	0	0	0	0	0
Alopecia	54	13	29	0	0	0	0	0	1	0	0	0
Anal hemorrhage	95	1	0	0	0	0	1	0	0	0	0	0
Anemia	50	34	9	3	0	0	0	1	0	0	0	0
Anorexia	82	10	4	0	0	0	0	1	0	0	0	0
Anxiety	92	1	3	0	0	0	1	0	0	0	0	0
Arthralgia	92	3	1	0	0	0	1	0	0	0	0	0
Back pain	93	2	1	0	0	0	1	0	0	0	0	0
Bloating	94	0	2	0	0	0	1	0	0	0	0	0
Blurred vision	94	2	0	0	0	0	1	0	0	0	0	0
Bone pain	88	4	4	0	0	0	1	0	0	0	0	0
CD4 lymphocytes decreased	93	0	1	2	0	0	1	0	0	0	0	0
Chills	91	4	1	0	0	0	1	0	0	0	0	0
Confusion	95	1	0	0	0	0	1	0	0	0	0	0
Constipation	64	24	8	0	0	0	0	0	1	0	0	0
Cough	90	4	1	1	0	0	1	0	0	0	0	0
Creatinine increased	94	2	0	0	0	0	1	0	0	0	0	0
Dehydration	90	1	5	0	0	0	1	0	0	0	0	0
Depression	95	0	1	0	0	0	1	0	0	0	0	0
Diarrhea	84	8	1	3	0	0	1	0	0	0	0	0
Dizziness	90	6	0	0	0	0	1	0	0	0	0	0
Dry mouth	90	6	0	0	0	0	1	0	0	0	0	0
Dry skin	96	0	0	0	0	0	0	1	0	0	0	0
Dysgeusia	86	5	5	0	0	0	1	0	0	0	0	0
Dyspepsia	84	6	6	0	0	0	1	0	0	0	0	0
Dyspnea	86	7	2	1	0	0	0	1	0	0	0	0
Edema face	95	1	0	0	0	0	1	0	0	0	0	0
Edema limbs	88	6	1	1	0	0	0	1	0	0	0	0
Epistaxis	95	1	0	0	0	0	1	0	0	0	0	0
Eye disorders - Other, specify	94	2	0	0	0	0	1	0	0	0	0	0
Eye pain	95	1	0	0	0	0	1	0	0	0	0	0
Fatigue	30	51	13	2	0	0	0	1	0	0	0	0
Febrile neutropenia	88	0	0	6	2	0	1	0	0	0	0	0
Fever	86	9	1	0	0	0	1	0	0	0	0	0
Flatulence	94	2	0	0	0	0	1	0	0	0	0	0
Flu like symptoms	95	0	1	0	0	0	1	0	0	0	0	0
GERD	92	3	1	0	0	0	1	0	0	0	0	0
GI disorders-Other, specify	94	2	0	0	0	0	1	0	0	0	0	0
Gastritis	95	0	1	0	0	0	1	0	0	0	0	0

	R-CHOP x 3 (n=96)						R-CHOP x 6 (n=1)					
	Grade						Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Generalized muscle weakness	89	5	1	1	0	0	1	0	0	0	0	0
Headache	90	6	0	0	0	0	1	0	0	0	0	0
Hematuria	95	1	0	0	0	0	1	0	0	0	0	0
Hemoglobin increased	95	1	0	0	0	0	1	0	0	0	0	0
Hoarseness	95	1	0	0	0	0	0	1	0	0	0	0
Hot flashes	95	1	0	0	0	0	1	0	0	0	0	0
Hyperglycemia	83	7	3	3	0	0	1	0	0	0	0	0
Hyperhidrosis	94	1	1	0	0	0	1	0	0	0	0	0
Hyperkalemia	95	0	1	0	0	0	1	0	0	0	0	0
Hypernatremia	95	1	0	0	0	0	1	0	0	0	0	0
Hypertension	92	2	0	2	0	0	1	0	0	0	0	0
Hypoalbuminemia	87	4	5	0	0	0	0	1	0	0	0	0
Hypocalcemia	87	6	3	0	0	0	1	0	0	0	0	0
Hypokalemia	92	3	0	1	0	0	1	0	0	0	0	0
Hypomagnesemia	92	4	0	0	0	0	1	0	0	0	0	0
Hyponatremia	94	2	0	0	0	0	1	0	0	0	0	0
Hypophosphatemia	95	0	1	0	0	0	1	0	0	0	0	0
Hypotension	93	1	2	0	0	0	1	0	0	0	0	0
Infusion related reaction	86	1	9	0	0	0	1	0	0	0	0	0
Injection site reaction	95	0	1	0	0	0	1	0	0	0	0	0
Insomnia	86	6	4	0	0	0	1	0	0	0	0	0
Localized edema	95	1	0	0	0	0	1	0	0	0	0	0
Lower GI hemorrhage	95	1	0	0	0	0	1	0	0	0	0	0
Lung infection	95	0	0	1	0	0	1	0	0	0	0	0
Lymphocyte count decreased	62	14	9	10	1	0	0	0	1	0	0	0
Lymphocyte count increased	95	0	0	1	0	0	1	0	0	0	0	0
Memory impairment	94	2	0	0	0	0	1	0	0	0	0	0
Mucositis oral	80	11	4	1	0	0	0	1	0	0	0	0
Myalgia	92	4	0	0	0	0	1	0	0	0	0	0
Nasal congestion	95	1	0	0	0	0	1	0	0	0	0	0
Nausea	46	37	12	1	0	0	0	1	0	0	0	0
Neck pain	95	0	1	0	0	0	1	0	0	0	0	0
Neutrophil count decreased	60	4	7	10	15	0	1	0	0	0	0	0
Oral pain	95	0	0	1	0	0	1	0	0	0	0	0
Pain	92	0	4	0	0	0	1	0	0	0	0	0
Paresthesia	95	1	0	0	0	0	1	0	0	0	0	0
Peripheral motor neuropathy	93	2	1	0	0	0	1	0	0	0	0	0
Peripheral nerve infection	95	0	1	0	0	0	1	0	0	0	0	0
Peripheral sensory neuropathy	75	17	3	1	0	0	1	0	0	0	0	0
Phlebitis	95	0	1	0	0	0	1	0	0	0	0	0
Platelet count decreased	81	9	3	3	0	0	0	1	0	0	0	0
Proteinuria	95	1	0	0	0	0	1	0	0	0	0	0
Pruritus	93	2	1	0	0	0	1	0	0	0	0	0
Rash acneiform	95	1	0	0	0	0	1	0	0	0	0	0
Rash maculo-papular	91	4	1	0	0	0	0	1	0	0	0	0
Renal/urinary disorders-Other	95	1	0	0	0	0	1	0	0	0	0	0
Repro system/breast ds-Oth	95	1	0	0	0	0	1	0	0	0	0	0
Resp/thoracic/mediastinal ds	95	1	0	0	0	0	1	0	0	0	0	0
Scalp pain	95	1	0	0	0	0	1	0	0	0	0	0
Sepsis	95	0	0	0	0	1	1	0	0	0	0	0
Sinus tachycardia	95	1	0	0	0	0	1	0	0	0	0	0

	R-CHOP x 3 (n=96) Grade						R-CHOP x 6 (n=1) Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Sinusitis	95	0	1	0	0	0	1	0	0	0	0	0
Skin infection	94	2	0	0	0	0	1	0	0	0	0	0
Skin/subq tissue ds-Other	93	3	0	0	0	0	1	0	0	0	0	0
Sore throat	92	3	1	0	0	0	1	0	0	0	0	0
Stomach pain	95	0	1	0	0	0	1	0	0	0	0	0
Superficial thrombophlebitis	95	0	1	0	0	0	1	0	0	0	0	0
Thromboembolic event	95	0	1	0	0	0	1	0	0	0	0	0
Upper respiratory infection	91	0	5	0	0	0	1	0	0	0	0	0
Urinary frequency	90	5	1	0	0	0	1	0	0	0	0	0
Urinary incontinence	95	1	0	0	0	0	1	0	0	0	0	0
Urinary tract infection	87	0	6	3	0	0	1	0	0	0	0	0
Urine discoloration	95	1	0	0	0	0	1	0	0	0	0	0
Vaginal infection	95	0	1	0	0	0	1	0	0	0	0	0
Voice alteration	94	1	1	0	0	0	1	0	0	0	0	0
Vomiting	86	7	3	0	0	0	0	1	0	0	0	0
Watering eyes	95	1	0	0	0	0	1	0	0	0	0	0
Weight gain	94	2	0	0	0	0	0	1	0	0	0	0
Weight loss	90	5	1	0	0	0	1	0	0	0	0	0
Wheezing	95	1	0	0	0	0	1	0	0	0	0	0
White blood cell decreased	60	10	8	9	9	0	0	0	1	0	0	0
MAX. GRADE ANY ADVERSE EVENT	2	12	40	27	14	1	0	0	1	0	0	0

Registration, Eligibility, and Evaluability

PET-Directed Therapy

Registrations ending December 31, 2014; Data as of February 26, 2015

	TOTAL	Continued R-CHOP	IFRT + Zevalin
NUMBER REGISTERED	95	84	11
INELIGIBLE	1	1	0
Insufficient Documentation	1	1	0
Irreversible	1	1	0
ELIGIBLE	94	83	11
Analyzable, Pend. Elig.	90	79	11
RESPONSE ASSESSMENT			
Determinable	73	68	5
Too Early	21	15	6
ADVERSE EVENT ASSESSMENT			
Evaluable	87	76	11
Too Early	7	7	0

Treatment Summary

PET-Directed Therapy

Registrations ending December 31, 2014; Data as of February 26, 2015

	TOTAL	Continued R-CHOP	IFRT + Zevalin
NUMBER ON PROTOCOL TREATMENT	9	9	0
NUMBER OFF PROTOCOL TREATMENT	85	74	11
REASON OFF TREATMENT			
Treatment completed as planned	83	72	11
Adverse Event or side effects	0	0	0
Refusal unrelated to adverse event	0	0	0
Other - not protocol specified	0	0	0
Reason under review	2	2	0
MAJOR PROTOCOL DEVIATIONS	0	0	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, 2014; Data as of February 26, 2015

	Continued R-CHOP (n=76) Grade						IFRT + Zevalin (n=11) Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	71	5	0	0	0	0	10	1	0	0	0	0
AST increased	74	2	0	0	0	0	10	1	0	0	0	0
Abdominal pain	75	0	0	1	0	0	10	1	0	0	0	0
Allergic rhinitis	75	0	1	0	0	0	11	0	0	0	0	0
Alopecia	62	5	9	0	0	0	9	0	2	0	0	0
Anemia	49	18	7	2	0	0	7	2	1	1	0	0
Anorexia	74	0	1	1	0	0	9	1	1	0	0	0
Anxiety	76	0	0	0	0	0	10	0	1	0	0	0
Arthralgia	75	1	0	0	0	0	11	0	0	0	0	0
Arthritis	75	1	0	0	0	0	11	0	0	0	0	0
Blurred vision	76	0	0	0	0	0	10	1	0	0	0	0
Chills	75	1	0	0	0	0	10	1	0	0	0	0
Constipation	73	3	0	0	0	0	10	1	0	0	0	0
Cough	72	3	1	0	0	0	9	2	0	0	0	0
Creatinine increased	73	2	1	0	0	0	11	0	0	0	0	0
Dehydration	76	0	0	0	0	0	10	0	1	0	0	0
Depression	76	0	0	0	0	0	10	0	1	0	0	0
Dermatitis radiation	76	0	0	0	0	0	9	2	0	0	0	0
Diarrhea	74	2	0	0	0	0	10	1	0	0	0	0
Dizziness	76	0	0	0	0	0	10	1	0	0	0	0

	Continued R-CHOP (n=76)						IFRT + Zevalin (n=11)					
	Grade						Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Dry mouth	74	2	0	0	0	0	9	0	2	0	0	0
Dysgeusia	72	2	2	0	0	0	10	0	1	0	0	0
Dyspepsia	74	2	0	0	0	0	10	1	0	0	0	0
Dysphagia	76	0	0	0	0	0	9	1	1	0	0	0
Dyspnea	73	2	1	0	0	0	11	0	0	0	0	0
Ear pain	75	1	0	0	0	0	11	0	0	0	0	0
Edema limbs	74	2	0	0	0	0	11	0	0	0	0	0
Ejection fraction decreased	75	0	0	1	0	0	11	0	0	0	0	0
Esophagitis	76	0	0	0	0	0	10	0	1	0	0	0
Eye disorders - Other, specify	75	1	0	0	0	0	11	0	0	0	0	0
Eye pain	75	1	0	0	0	0	11	0	0	0	0	0
Fall	75	0	0	1	0	0	11	0	0	0	0	0
Fatigue	50	22	3	1	0	0	5	5	1	0	0	0
Febrile neutropenia	74	0	0	2	0	0	11	0	0	0	0	0
Fever	75	1	0	0	0	0	11	0	0	0	0	0
Flu like symptoms	75	1	0	0	0	0	11	0	0	0	0	0
GERD	73	3	0	0	0	0	11	0	0	0	0	0
Gastritis	76	0	0	0	0	0	10	1	0	0	0	0
Generalized muscle weakness	73	1	2	0	0	0	10	1	0	0	0	0
Gum infection	75	1	0	0	0	0	11	0	0	0	0	0
Hearing impaired	75	1	0	0	0	0	11	0	0	0	0	0
Hot flashes	75	1	0	0	0	0	11	0	0	0	0	0
Hypercalcemia	75	1	0	0	0	0	11	0	0	0	0	0
Hyperglycemia	71	3	1	1	0	0	10	1	0	0	0	0
Hyperhidrosis	76	0	0	0	0	0	10	1	0	0	0	0
Hyperkalemia	74	2	0	0	0	0	11	0	0	0	0	0
Hypertension	73	2	0	1	0	0	11	0	0	0	0	0
Hyperuricemia	75	1	0	0	0	0	11	0	0	0	0	0
Hypoalbuminemia	74	2	0	0	0	0	11	0	0	0	0	0
Hypocalcemia	74	1	0	1	0	0	11	0	0	0	0	0
Hypoglycemia	75	1	0	0	0	0	11	0	0	0	0	0
Hypokalemia	73	1	1	1	0	0	11	0	0	0	0	0
Hypomagnesemia	75	1	0	0	0	0	10	1	0	0	0	0
Hypotension	75	0	0	1	0	0	11	0	0	0	0	0
Hypoxia	75	0	0	0	0	1	11	0	0	0	0	0
Insomnia	76	0	0	0	0	0	9	0	2	0	0	0
Laryngeal edema	76	0	0	0	0	0	10	1	0	0	0	0
Leukocytosis	75	0	0	1	0	0	11	0	0	0	0	0
Lymphocyte count decreased	45	14	11	6	0	0	7	2	0	2	0	0
Malaise	75	0	1	0	0	0	11	0	0	0	0	0
Memory impairment	75	1	0	0	0	0	11	0	0	0	0	0
Mucositis oral	72	3	1	0	0	0	10	0	1	0	0	0
Muscle weakness lower limb	75	1	0	0	0	0	11	0	0	0	0	0
Muscle weakness upper limb	75	1	0	0	0	0	11	0	0	0	0	0
Myalgia	75	1	0	0	0	0	9	1	1	0	0	0
Nail discoloration	75	1	0	0	0	0	11	0	0	0	0	0
Nail loss	75	1	0	0	0	0	11	0	0	0	0	0
Nail ridging	74	2	0	0	0	0	11	0	0	0	0	0
Nasal congestion	74	0	2	0	0	0	11	0	0	0	0	0
Nausea	71	5	0	0	0	0	9	2	0	0	0	0
Nervous sys disorders-Other	75	0	0	1	0	0	10	1	0	0	0	0

	Continued R-CHOP (n=76)						IFRT + Zevalin (n=11)					
	Grade						Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
Neutrophil count decreased	65	2	1	2	6	0	7	1	2	1	0	0
Oral pain	75	1	0	0	0	0	11	0	0	0	0	0
Pain	74	2	0	0	0	0	11	0	0	0	0	0
Pain in extremity	74	1	1	0	0	0	10	0	1	0	0	0
Paresthesia	74	2	0	0	0	0	11	0	0	0	0	0
Peripheral motor neuropathy	75	1	0	0	0	0	11	0	0	0	0	0
Peripheral sensory neuropathy	67	7	1	1	0	0	9	2	0	0	0	0
Pharyngitis	75	0	1	0	0	0	10	0	1	0	0	0
Phlebitis	75	0	1	0	0	0	11	0	0	0	0	0
Platelet count decreased	68	7	0	1	0	0	9	0	0	1	1	0
Productive cough	75	1	0	0	0	0	11	0	0	0	0	0
Resp/thoracic/mediastinal ds	74	1	0	0	1	0	11	0	0	0	0	0
Secondary Leukemia	75	0	0	0	1	0	11	0	0	0	0	0
Sinus tachycardia	75	1	0	0	0	0	11	0	0	0	0	0
Skin infection	74	1	1	0	0	0	11	0	0	0	0	0
Skin/subq tissue ds-Other	75	1	0	0	0	0	11	0	0	0	0	0
Small intestine infection	75	0	0	1	0	0	11	0	0	0	0	0
Sore throat	75	0	1	0	0	0	10	1	0	0	0	0
Telangiectasia	75	1	0	0	0	0	11	0	0	0	0	0
Thromboembolic event	75	0	0	1	0	0	11	0	0	0	0	0
Upper respiratory infection	73	0	3	0	0	0	11	0	0	0	0	0
Urinary tract infection	74	0	2	0	0	0	10	0	1	0	0	0
Voice alteration	75	0	1	0	0	0	11	0	0	0	0	0
Weight gain	73	2	1	0	0	0	11	0	0	0	0	0
Weight loss	74	0	1	1	0	0	9	2	0	0	0	0
White blood cell decreased	55	11	3	5	2	0	8	1	0	2	0	0
MAX. GRADE ANY ADVERSE EVENT	5	19	30	14	7	1	1	4	3	2	1	0

S1108 Phase II

Coordinating Group: SWOG

Phase II Trial of the Aurora Kinase A Inhibitor MLN8237, in Relapsed or Refractory Peripheral T-Cell Non-Hodgkin Lymphoma

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

Study Chairs:
P Barr, D Mahadevan, S Horwitz (Alliance), C Flowers (ECOG-ACRIN)

Statisticians:
H Li, M LeBlanc

Data Coordinator:
J Jardine

Date Activated:
10/28/2011

Date Closed:
06/06/2013

Objectives

To estimate the objective response rate after treatment with MLN8237 in patients with relapsed or refractory peripheral T-cell non-Hodgkin lymphoma (PTCL).

To assess overall survival (OS) and progression-free survival (PFS) in this patient population. To evaluate the safety and tolerability of MLN8237 treatment for this patient population.

To explore the association between pre-treatment aurora kinase A expression in tumor biopsies as measured by fluorescence in situ hybridization (FISH) and objective response rate in patients with PTCL treated with MLN8237.

To investigate the copy number, mutational status, expression of aurora kinase (A, B and C) and associated signaling pathways in PTCL utilizing tissue microarray analysis (TMA) before and after treatment with MLN8237.

To investigate changes in the serum cytokine profile before and after aurora kinase inhibitor treatment.

To evaluate serum markers of apoptosis before and after aurora kinase inhibitor treatment as pharmacodynamic markers of efficacy.

Patient Population

Patients must have histologically or cytologically confirmed relapsed/refractory non-Hodgkin lymphoma (NHL) with any of the following T-cell histologies: peripheral T-cell NHL not otherwise specified; anaplastic large cell T-cell lymphoma; angioimmunoblastic T-cell NHL; extranodal NK/T-cell lymphoma, nasal type; enteropathy associated T-cell NHL; hepatosplenic T-cell lymphomas; subcutaneous panniculitis-like T-cell lymphoma; adult T-cell leukemia/lymphoma; unclassifiable PTCL; transformed cutaneous T-cell lymphoma (CTCL) to PTCL with systemic involvement (not local skin transformation). All patients must have bidimensionally measurable disease. Patients with clinical or laboratory evidence of central nervous system involvement by lymphoma are not eligible.

Patients must have received at least one course of prior systemic therapy which may include chemotherapy, antibody therapy, or immunotherapy. Patients may have received prior radiation in combination with systemic therapy. Patients must not have received a previous allogeneic stem cell

transplant or be within 90 days of an autologous stem cell transplant.

Patients must be at least 18 years of age and have a Zubrod performance status of 0, 1 or 2. Patients must have adequate hematologic and hepatic function. Patients known to be HIV-positive must not have multi-drug resistant HIV infection, CD4 counts <150/mcL or other concurrent AIDS-defining conditions.

Accrual Goals

Thirty-five eligible patients will be accrued to this study.

Summary Statement

The study was permanently closed to accrual on June 6, 2013, with a final accrual of 42 patients. Five patients are ineligible: one due to inadequate kidney function, one due to no evidence of lymphoma in the bone marrow upon central pathologic review, one due to immunophenotype with positive T-cell and B-cell markers upon central pathologic review, another two due to inadequate pathologic material to confirm T-cell lymphoma diagnosis.

Five patients went off protocol treatment early due to adverse events: anorexia, skin infection, sub-epidermal bulla, fatigue caused by diffuse eczema with severe pruritis, and thrombocytopenia (one each). One patient withdrew from study after five cycles of protocol treatment. Another five patients went off protocol therapy early for the following reasons not specified in the protocol: progression per institution but not meeting the protocol defined criteria for progression (3), treatment delayed for more than three weeks (1), and clinical error (1).

Thirty-seven patients have been assessed for adverse events. One patient died of sepsis eight days after completing two cycles of protocol therapy, probably treatment-related. Eleven patients have experienced treatment-related Grade 4 adverse events, primarily hematologic (10). One patient who did not experience Grade 4 hematologic toxicity experienced Grade 4 treatment related secondary malignancy. Two patients who experience Grade 4 hematologic toxicities also experienced Grade 4 non-hematologic toxicities: one with febrile neutropenia and another one with toxic epidermal necrolysis and sub-epidermal bulla (coded as "Skin/subq tissue ds-other"). Twelve more patients experienced Grade 3 toxicities, primarily hematologic.

Among 37 eligible patients, two (5%) complete responses and seven (19%) partial responses were observed, for a response rate of 24.3% (95% CI: 11.8%, 41.2%). Seven (19%) patients who could not have their exact response determined due to inadequate assessments are included in the denominators as non-responders. The estimated response rate is significantly greater than the hypothesized value of 10% with exact p-value = 0.009. The median duration of response in nine responders is three months (range 1 - 18 months).

The median of follow-up among those last known alive is 25.2 months (range 19.6 – 27.3 months). Thirty-six patients have either progressed or died, with median PFS of 2.9 months (95% CI 2.2, 4.3). The estimate of 1-year progression-free survival is 8% (95% CI: 2.1%, 19.6%). There have been 30 deaths, with median OS of 7.7 months (95% CI 4.5, 9.5). The estimate of 1-year overall survival is 30% (95% CI: 16.1%, 44.7%).

Registration by Institution

Institutions	Total Reg	Institutions	Total Reg
Alliance	25	Loyola University	1
Rochester, Univ of	5	LSU-Shreveport/Gulf South MU-NCORP	1
Arizona MC, U of	3	Salem Hospital/Oregon Hlth Sci Univ	1
ECOG-ACRIN	3	San Antonio, U of TX	1
City of Hope Med Ctr	2	**Total (9 Institutions)**	**42**

Registration, Eligibility, and Evaluability

Initial Registration

Data as of March 16, 2015

	MLN8237
NUMBER REGISTERED	42
INELIGIBLE	5
Insufficient Documentation	2
Irreversible	2
ELIGIBLE	37
RESPONSE ASSESSMENT	
Determinable	30
Not Determinable	7
ADVERSE EVENT ASSESSMENT	
Evaluable	37

Patient Characteristics

Initial Registration

Data as of March 16, 2015

	MLN8237 (n=37)	
AGE		
Median	62.0	
Minimum	21.6	
Maximum	86.1	
SEX		
Males	24	65%
Females	13	35%
HISPANIC		
Yes	4	11%
No	32	86%
Unknown	1	3%
RACE		
White	24	65%
Black	10	27%
Asian	1	3%
Unknown	2	5%

Treatment Summary

Initial Registration

Data as of March 16, 2015

	MLN8237
NUMBER ON PROTOCOL TREATMENT	0
NUMBER OFF PROTOCOL TREATMENT	37
REASON OFF TREATMENT	
Treatment completed as planned	2
Adverse Event or side effects	5
Refusal unrelated to adverse event	1
Progression/relapse	20
Death	4
Other - not protocol specified	5
Reason under review	0
MAJOR PROTOCOL DEVIATIONS	0

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

Initial Registration

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of March 16, 2015

	MLN8237 (n=37)					
	Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**
ALT increased	35	2	0	0	0	0
AST increased	32	5	0	0	0	0
Abdominal pain	36	0	0	1	0	0
Alkaline phosphatase increased	30	5	0	2	0	0
Alopecia	28	4	5	0	0	0
Anal hemorrhage	36	1	0	0	0	0
Anal mucositis	36	1	0	0	0	0
Anemia	15	3	7	11	1	0
Anorexia	30	3	3	1	0	0
Back pain	35	0	1	1	0	0
Blood bilirubin increased	32	3	1	1	0	0
Blood/lymph disorder-Other	35	1	1	0	0	0
CD4 lymphocytes decreased	35	0	0	2	0	0
Chills	35	2	0	0	0	0
Cholesterol high	36	0	1	0	0	0
Constipation	34	2	1	0	0	0
Cough	35	1	1	0	0	0
Creatinine increased	33	3	1	0	0	0
Dehydration	35	0	2	0	0	0
Diarrhea	31	4	1	1	0	0
Dizziness	36	0	1	0	0	0

	MLN8237 (n=37)					
	Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**
Dry mouth	36	1	0	0	0	0
Dysgeusia	36	1	0	0	0	0
Dysphagia	36	1	0	0	0	0
Dyspnea	36	1	0	0	0	0
Edema limbs	35	1	1	0	0	0
Epistaxis	36	1	0	0	0	0
Fall	36	1	0	0	0	0
Fatigue	20	8	8	1	0	0
Febrile neutropenia	32	0	0	4	1	0
Fever	30	3	3	1	0	0
Flatulence	36	1	0	0	0	0
GI disorders-Other, specify	36	0	0	1	0	0
Generalized muscle weakness	36	1	0	0	0	0
Headache	34	3	0	0	0	0
Hemorrhoids	36	0	1	0	0	0
Hypercalcemia	35	0	1	1	0	0
Hyperglycemia	36	0	0	1	0	0
Hypernatremia	36	1	0	0	0	0
Hypoalbuminemia	34	0	3	0	0	0
Hypocalcemia	34	1	2	0	0	0
Hypokalemia	36	0	1	0	0	0
Hyponatremia	32	5	0	0	0	0
Hypotension	34	1	1	1	0	0
Infections/infestations-Other	35	0	1	1	0	0
Lethargy	36	1	0	0	0	0
Leukocytosis	36	0	0	1	0	0
Lung infection	36	0	0	1	0	0
Lymph gland infection	36	0	0	1	0	0
Lymphocyte count decreased	25	0	4	5	3	0
Memory impairment	36	1	0	0	0	0
Metab/nutrition disorders-Oth	36	1	0	0	0	0
Mucositis oral	29	2	2	4	0	0
Muscle weakness lower limb	36	1	0	0	0	0
Nasal congestion	36	1	0	0	0	0
Nausea	35	1	1	0	0	0
Neutrophil count decreased	21	2	2	5	7	0
Oral pain	35	1	1	0	0	0
Pain	34	1	0	2	0	0
Pain in extremity	36	0	1	0	0	0
Pharyngolaryngeal pain	36	1	0	0	0	0
Platelet count decreased	20	4	4	2	7	0
Productive cough	36	0	1	0	0	0
Proteinuria	36	0	1	0	0	0
Pruritus	34	2	1	0	0	0
Rash maculo-papular	33	1	1	2	0	0
Sepsis	36	0	0	0	0	1
Sinus tachycardia	36	1	0	0	0	0
Sinusitis	36	0	1	0	0	0
Skin hyperpigmentation	36	1	0	0	0	0
Skin infection	35	0	1	1	0	0
Skin ulceration	36	0	1	0	0	0

	MLN8237 (n=37)					
	Grade					
ADVERSE EVENT	**0**	**1**	**2**	**3**	**4**	**5**
Skin/subq tissue ds-Other	35	1	0	0	1	0
Somnolence	35	1	1	0	0	0
Toxic epidermal necrolysis	36	0	0	0	1	0
Tx related secondary malig	36	0	0	0	1	0
Upper respiratory infection	36	0	1	0	0	0
Vomiting	34	2	1	0	0	0
Weight loss	33	3	1	0	0	0
White blood cell decreased	22	4	4	5	2	0
MAX. GRADE ANY ADVERSE EVENT	5	1	7	12	11	1

Response

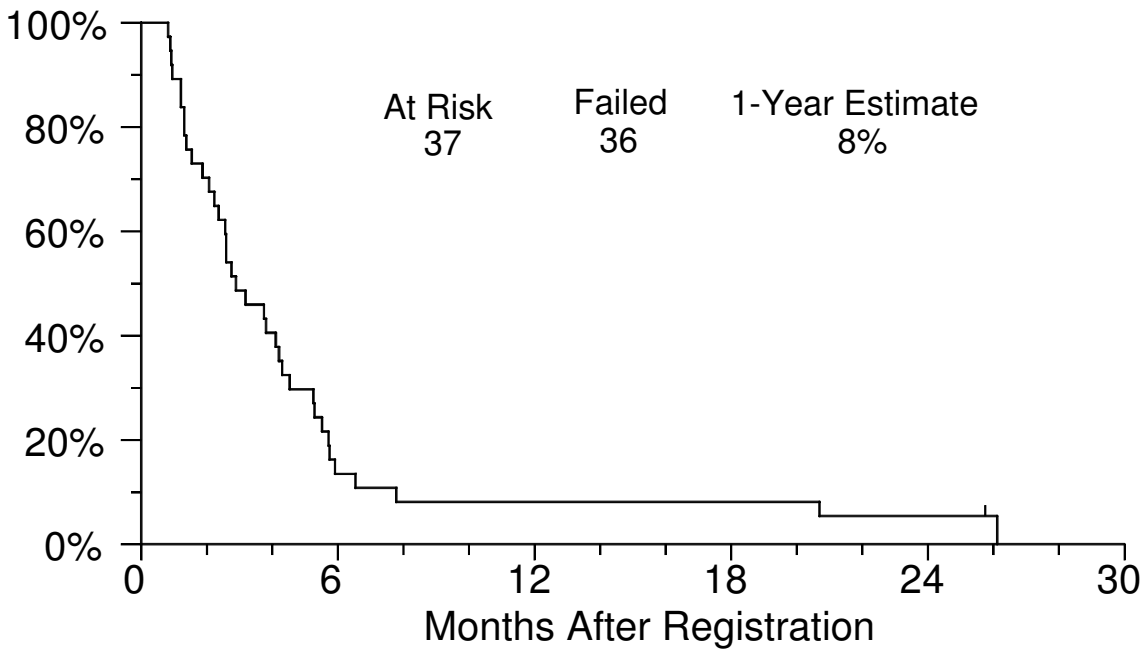
Initial Registration

Data as of March 16, 2015

	MLN8237	
	N	**%**
Complete Response	2	5
Partial Response	7	19
PR Non-measurable Disease	0	0
Unconfirmed Complete Response	0	0
Unconfirmed Partial Response	0	0
Unconfirmed PR NM Disease	0	0
Stable/No Response	7	19
Increasing Disease	14	38
Assessment Inadequate	7	19
Total	37	100

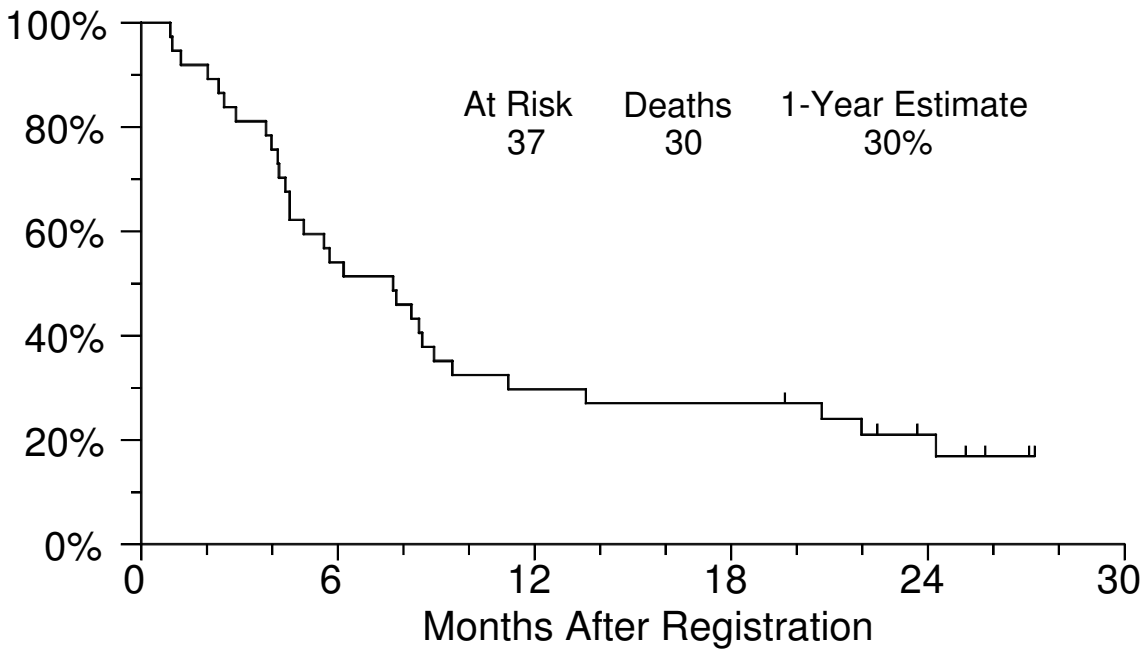
Progression-Free Survival

Data as of March 16, 2015



Overall Survival

Data as of March 16, 2015



S1204 Surveillance

A Sero-Epidemiologic Survey and Cost-Effectiveness Study of Screening for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Among Newly Diagnosed Cancer Patients

Study Chairs:
S Ramsey, R Loomba, R Chugh, D Hershman, J Hwang

Statisticians:
J Unger, K Arnold

Data Coordinator:
M Yee

Date Activated:
08/29/2013

Date Closed*:
12/15/2014

*Temporary Closure

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 cancer malignancy (including hematologic). Confirmed pathologic diagnosis must be within 120 days of registration. Patients presenting for "second opinions" of confirmed malignancies are eligible, including those who have started cancer treatment at other facilities. Individuals are ineligible if they 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. Individuals are eligible if they have had no evidence of disease for a prior malignancy, except as noted above, for at least five years prior to randomization.

Patients must be 18 years of age or older. Patients must have had their blood drawn for testing for HIV, HBV and HCV prior to registration. Patients who have had HIV, HBV and/or HCV testing within 60 days prior to registration and who do not wish to be retested are eligible, provided supporting documents can be obtained confirming viral test results for all three viruses. Patients who are viral positive for

either HIV, HBV, and/or HCV and who do not wish to be retested are eligible, provided documentation of viral load within 120 days prior to registration can be obtained. Note that these patients must be tested for or provide current viral load for all three viruses to be eligible. All documentation must be obtained prior to registration. Patients are allowed to participate in other clinical trials.

Cancer Control Credits

No cancer control credits are awarded for this study.

Accrual Goals

A total of 3,000 eligible patients will be accrued.

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 must not have received any prior treatment except limited-field radiotherapy, short course of glucocorticoids and/or cyclophosphamide for an urgent problem at diagnosis.

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 153 patients will be accrued to this study.

Summary Statement

NCIMet reported a total accrual of 119 patients as of December 31, 2014, including 18 CTSU registrations from SWOG institutions.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg
Rochester, Univ of	9
Kentucky, U of	4
Cleveland Clinic OH	3
Kansas City NCORP	1
Tennessee, U of	1
Total (5 Institutions)	**18**

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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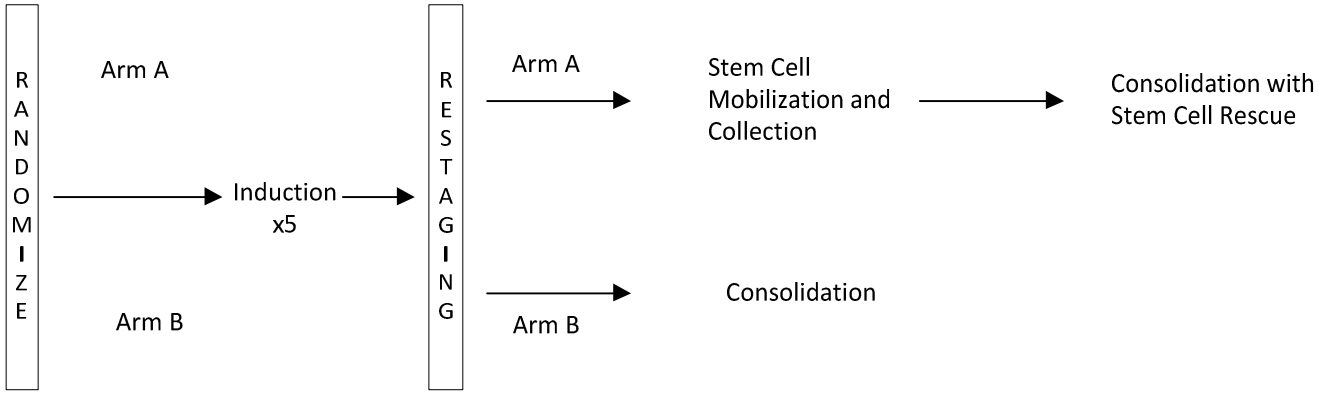
Participants:
Alliance, CTSU

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 or isolated leptomeningeal lymphoma. Patients must have at least one measurable, contrast-enhancing brain lesion (≥ 1 cm in length).

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 70 years old and have Karnofsky Performance Scale (KPS) ≥ 30 (≥ 50 for patients ages 60-70). Patients must have adequate cardiac, pulmonary, hematologic, renal, and hepatic function. Patients must be HIV negative, HBV negative (or HBcAb negative if HBsAb is positive), and HCV negative.

Stratification/Descriptive Factors

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

Cancer Control Credits

The NCI Division of Cancer Prevention has not assigned cancer control credit for registration to this study. There are potential cancer control credits for quality of life.

Accrual Goals

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

Summary Statement

Alliance reported a total accrual of 41 patients as of December 31, 2014, including three CTSU registrations from SWOG institutions, one each from University of California Davis, Fred Hutchinson Cancer Research Center, and University of Rochester. The complete November 2014 summary of this study from Alliance is available on the SWOG web site.

E1411 Phase II SWOG Supported CTSU Study

Coordinating Group: ECOG-ACRIN

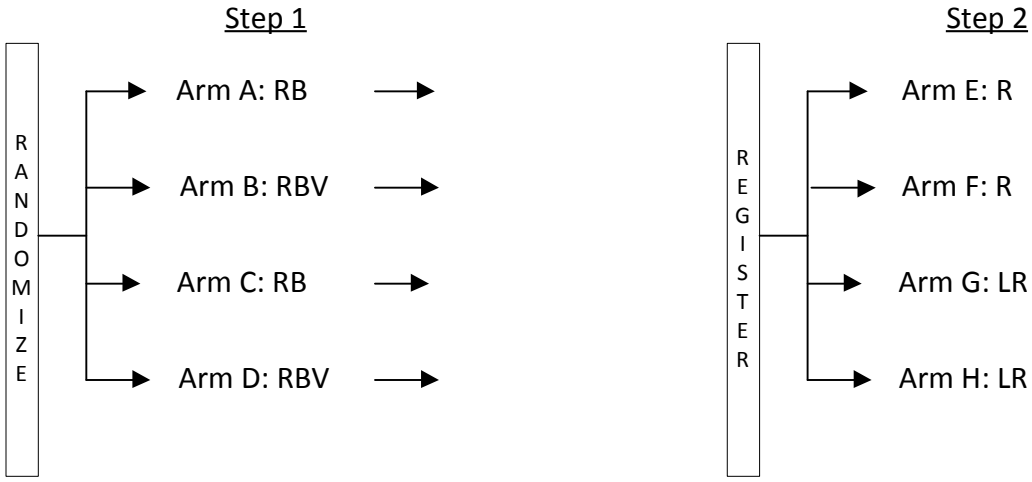
Intergroup Randomized Phase II Four Arm Study In Patients With Previously Untreated Mantle Cell Lymphoma Of Therapy With: Arm A = Rituximab + Bendamustine Followed By Rituximab Consolidation (RB → R), Arm B = Rituximab + Bendamustine + Bortezomib Followed By Rituximab Consolidation (RBV → R), Arm C = 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 > 60 years of age 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 one week of steroid therapy for symptom control. 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.

Cancer Control Credits

The NCI Division of Cancer Prevention has not assigned cancer control credit for registration to this study. There are potential cancer control credits for quality of life.

Accrual Goals

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

Summary Statement

ECOG-ACRIN reported a total accrual of 168 patients as of December 31, 2014, including 37 CTSU registrations from SWOG institutions. The complete Fall 2014 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg	Institutions	Total Reg
Rochester, Univ of	13	Poudre Valley Hosp/Colorado, U of	2
Cleveland Clinic OH	4	KaiserPermanenteCOL/Kaiser NCORP	1
Hawaii MU-NCORP	3	Montana NCORP	1
West Michigan NCORP	3	UF Cancer Center/Arkansas, U of	1
Western Onc CCOP	3	Upstate Carolina	1
Dayton NCORP	2	Wayne State Univ	1
Kaiser NCORP	2	**Total (13 Institutions)**	**37**

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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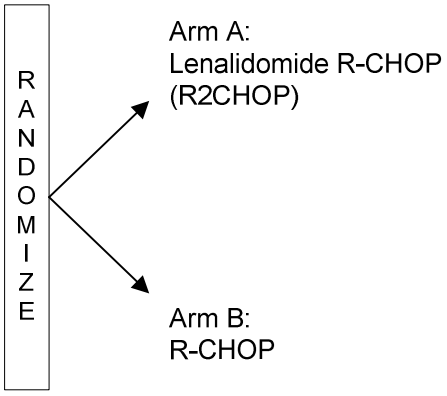
Participants:
ECOG-ACRIN, CTSU

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 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

A total of 220 patients will be accrued to this study. If the total number of ABC subtype is below 100 after a total of 220 patients were accrued, the study will re-open for accruing at a pace of 25 patients each time until 100 eligible ABC patients is achieved. A maximum of 300 patients will be enrolled to the study.

Summary Statement

ECOG-ACRIN reported a total accrual of 139 patients as of December 31, 2014, including 8 CTSU registrations from SWOG institutions. The complete Fall 2014 summary of this study from ECOG-ACRIN is available on the SWOG web site.

Registration by Institution

Registrations ending December 31, 2014

Institutions	Total Reg
Rochester, Univ of	6
Montana NCORP	2
Total (2 Institutions)	**8**