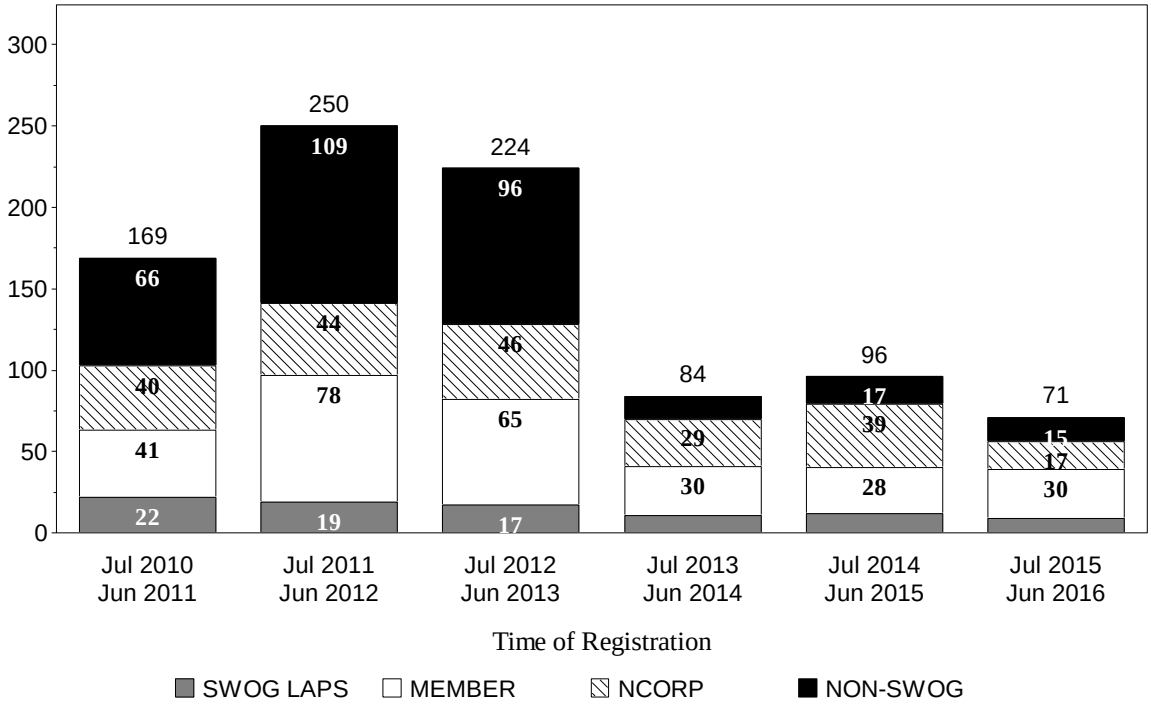
# LYMPHOMA COMMITTEE

# CONTENTS

# Patient Registrations to Studies

By 12 Month Intervals
**LYMPHOMA COMMITTEE**




Screening registrations and registrations to Biologic only studies are excluded

# Patient Registrations by Study and Arm

## LYMPHOMA COMMITTEE

| | Jan 2016 Jun 2016 | Jul 2015 Dec 2015 | Jan 2015 Jun 2015 | All Patients |
|---|---|---|---|---|
| **S1001 DLBCL, I-II, PET-Adapted Therapy** | | | | |
| **Initial registration** | | | | |
| R-CHOP x 3 | 11 | 20 | 20 | 155 |
| R-CHOP x 6 | 3 | 0 | 0 | 4 |
| | 14 | 20 | 20 | 159 |
| **PET-Directed Therapy** | | | | |
| Continued R-CHOP | 19 | 17 | 14 | 134 |
| IFRT + Zevalin | 1 | 0 | 0 | 12 |
| | 20 | 17 | 14 | 146 |
| **9177 NHL, Dose-adj. EPOCH+/-Rituximab*** | | | | |
| Total Registrations | 0 | 1 | 0 | 19 |
| **C51101 CNS, Myelo/Non-myelo Chemo, PhII*** | | | | |
| Total Registrations | 0 | 0 | 2 | 5 |
| **E1411 MCL, RB+R, RBV+R, RB+LR, RBV+LR*** | | | | |
| Total Registrations | 9 | 18 | 17 | 82 |
| **E1412 DLBCL, R2CHOP vs RCHOP*** | | | | |
| Total Registrations | 9 | 0 | 18 | 35 |

* 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)

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

**Date Activated:**
07/15/2011

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

**Date Closed:**
06/01/2016

**Statisticians:**
M LeBlanc, H Li

**Data Coordinator:**
J Jardine

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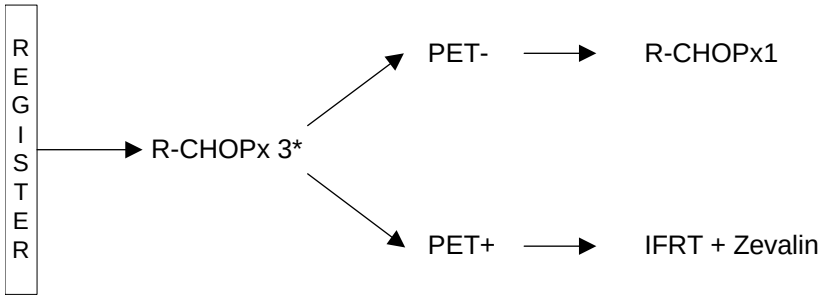
## SCHEMA




*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 described by advanced stage based on local review of the baseline PET/CT: yes vs no.

For registration step 2, patients will be described 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**

This study was closed to accrual on June 1, 2016, after a total accrual of 159 patients, 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 incorrect histology and one due to no required baseline specimens submitted for pathology review.

One hundred fifty-one patients have been assessed for toxicities on initial R-CHOPx3 therapy. One patient died of sepsis five days after the last date of treatment during the first cycle of treatment. Upon review, this was found to be probably related to protocol treatment. This patient also experienced Grade 4 hematologic toxicities and febrile neutropenia. An additional 26 patients experienced Grade 4 hematologic toxicities, three of whom also experienced Grade 4 non-hematologic toxicities: febrile neutropenia (2), hyponatremia, and sepsis.

The patient on R-CHOPx6 therapy did not experience Grade 3 or greater toxicities.

One hundred forty-six patients have been registered to PET-directed therapy, 134 of whom were interim PET-negative and registered to the continued R-CHOP therapy, and 12 of whom were interim PET-positive and registered to the IFRT + Zevalin therapy. One PET-negative patient is ineligible due to being ineligible at Step 1. Major protocol deviations are coded for two PET-negative patients who did not received any PET-directed R-CHOP therapy; these two patients are not evaluable for toxicities related to PET-directed therapy.

Among 123 patients on the continued R-CHOP arm that have been assessed 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.

## Registration by Institution

Initial Registration

Registrations ending June 30, 2016

| Institutions | Total Reg | Institutions | Total Reg |
|---|---|---|---|
| Alliance | 40 | Kentucky, U of | 3 |
| Rochester, Univ of | 28 | Fred Hutchinson CRC | 2 |
| ECOG-ACRIN | 20 | Greenville NCORP | 2 |
| Michigan CRC NCORP | 8 | Northwest NCORP | 2 |
| Arizona MC, U of | 7 | NRG | 2 |
| Upstate Carolina | 7 | St Luke's Mt State/PCRC NCORP | 2 |
| Kansas City NCORP | 6 | Virginia Mason MC/Northwest NCORP | 2 |
| Wichita NCORP | 6 | Essentia Hlth NCORP | 1 |
| Yale University | 6 | Montana NCORP | 1 |
| Loyola University | 5 | Southeast COR NCORP | 1 |
| City of Hope Med Ctr | 4 | **Total (22 Institutions)** | **159** |
| Hawaii MU-NCORP | 4 | | |

## Registration, Eligibility, and Evaluability

Initial Registration

Registrations ending June 30, 2016; Data as of July 18, 2016

| | TOTAL | R-CHOP x 3 | R-CHOP x 6 |
|---|---|---|---|
| NUMBER REGISTERED | 159 | 158 | 1 |
| INELIGIBLE | 2 | 2 | 0 |
| Insufficient Documentation | 1 | 1 | 0 |
| Irreversible | 1 | 1 | 0 |
| ELIGIBLE | 157 | 156 | 1 |
| Analyzable, Pend. Elig. | 151 | 150 | 1 |
| RESPONSE ASSESSMENT | | | |
| Determinable | 137 | 136 | 1 |
| Not Determinable | 2 | 2 | 0 |
| Too Early | 18 | 18 | 0 |
| ADVERSE EVENT ASSESSMENT | | | |
| Evaluable | 152 | 151 | 1 |
| Too Early | 5 | 5 | 0 |

## Patient Characteristics

Initial Registration

Registrations ending June 30, 2016; Data as of July 18, 2016

| | R-CHOP x 3 (n=156) | | R-CHOP x 6 (n=1) | |
|---|---|---|---|---|
| AGE | | | | |
| Median | 61.6 | | 74.3 | |
| Minimum | 18.5 | | 74.3 | |
| Maximum | 85.7 | | 74.3 | |
| SEX | | | | |
| Males | 80 | 51% | 0 | 0% |
| Females | 76 | 49% | 1 | 100% |
| HISPANIC | | | | |
| Yes | 7 | 4% | 0 | 0% |
| No | 142 | 91% | 1 | 100% |
| Unknown | 7 | 4% | 0 | 0% |
| RACE | | | | |
| White | 136 | 87% | 1 | 100% |
| Black | 6 | 4% | 0 | 0% |
| Asian | 10 | 6% | 0 | 0% |
| Native American | 1 | 1% | 0 | 0% |
| Unknown | 3 | 2% | 0 | 0% |
| PET UPSTAGED | | | | |
| Yes | 0 | 0% | 1 | 100% |
| No | 156 | 100% | 0 | 0% |

## Treatment Summary

Initial Registration

Registrations ending June 30, 2016; Data as of July 18, 2016

| | TOTAL | R-CHOP x 3 | R-CHOP x 6 |
|---|---|---|---|
| NUMBER ON PROTOCOL TREATMENT | 9 | 9 | 0 |
| NUMBER OFF PROTOCOL TREATMENT | 148 | 147 | 1 |
| REASON OFF TREATMENT | | | |
| Treatment completed as planned | 143 | 142 | 1 |
| Adverse Event or side effects | 2 | 2 | 0 |
| Refusal unrelated to adverse event | 0 | 0 | 0 |
| Other - not protocol specified | 1 | 1 | 0 |
| Reason under review | 1 | 1 | 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 June 30, 2016; Data as of July 18, 2016

| | R-CHOP x 3 (n=151) Grade | | | | | | R-CHOP x 6 (n=1) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| ALT increased | 128 | 20 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| AST increased | 135 | 15 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Abdominal pain | 146 | 4 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Agitation | 149 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Alkaline phosphatase increased | 145 | 5 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Allergic reaction | 145 | 1 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Alopecia | 88 | 20 | 43 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Anal hemorrhage | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Anemia | 72 | 59 | 12 | 8 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Anorexia | 131 | 14 | 5 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Anxiety | 145 | 2 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Arthralgia | 143 | 6 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Back pain | 147 | 3 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Bloating | 148 | 1 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Blood bilirubin increased | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Blurred vision | 148 | 3 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Bone pain | 138 | 7 | 5 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| CD4 lymphocytes decreased | 148 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Catheter related infection | 150 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Chills | 143 | 7 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Concentration impairment | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Confusion | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Constipation | 96 | 42 | 12 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Cough | 143 | 6 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Creatinine increased | 147 | 4 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dehydration | 144 | 1 | 6 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Depression | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Diarrhea | 133 | 14 | 1 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dizziness | 139 | 12 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dry mouth | 142 | 9 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dry skin | 148 | 3 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Dysgeusia | 134 | 12 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dyspepsia | 135 | 8 | 8 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dyspnea | 138 | 8 | 2 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Edema face | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Edema limbs | 142 | 7 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Endocrine disorders-Other | 150 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Epistaxis | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Eye disorders - Other, specify | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Eye pain | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Facial pain | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Fall | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Fatigue | 45 | 81 | 21 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Febrile neutropenia | 137 | 0 | 0 | 11 | 3 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |

| | R-CHOP x 3 (n=151) Grade | | | | | | R-CHOP x 6 (n=1) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| Fever | 138 | 11 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Flank pain | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Flatulence | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Flu like symptoms | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| GERD | 145 | 4 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| GI disorders-Other, specify | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Gastritis | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Gen disorders/admin site cond | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Generalized muscle weakness | 142 | 6 | 2 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Headache | 139 | 12 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hematuria | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hemoglobin increased | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hemorrhoids | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hiccups | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hoarseness | 149 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Hot flashes | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hyperglycemia | 132 | 10 | 5 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hyperhidrosis | 148 | 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hyperkalemia | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypernatremia | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypertension | 144 | 2 | 2 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypoalbuminemia | 135 | 8 | 8 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Hypocalcemia | 140 | 8 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypokalemia | 140 | 7 | 2 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypomagnesemia | 146 | 5 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hyponatremia | 143 | 7 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypophosphatemia | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypotension | 147 | 2 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Infusion related reaction | 134 | 2 | 15 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Injection site reaction | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Insomnia | 132 | 12 | 7 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Irregular menstruation | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lip infection | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Localized edema | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lower GI hemorrhage | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lung infection | 149 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lymphocyte count decreased | 86 | 24 | 20 | 16 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Memory impairment | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Menorrhagia | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Mucosal infection | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Mucositis oral | 128 | 16 | 6 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Myalgia | 144 | 7 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Nail discoloration | 148 | 3 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Nasal congestion | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Nausea | 80 | 50 | 20 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Neck pain | 148 | 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Neutrophil count decreased | 96 | 5 | 11 | 13 | 26 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Oral pain | 148 | 0 | 2 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Pain | 146 | 1 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Pain of skin | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Papulopustular rash | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |

| | R-CHOP x 3 (n=151) Grade | | | | | | R-CHOP x 6 (n=1) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| Paresthesia | 147 | 4 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Peripheral motor neuropathy | 146 | 4 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Peripheral nerve infection | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Peripheral sensory neuropathy | 116 | 30 | 4 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Phlebitis | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Platelet count decreased | 126 | 17 | 3 | 3 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Postnasal drip | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Presyncope | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Productive cough | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Proteinuria | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Pruritus | 147 | 3 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Rash acneiform | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Rash maculo-papular | 143 | 7 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Renal/urinary disorders-Other | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Repro system/breast ds-Oth | 149 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Resp/thoracic/mediastinal ds | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Scalp pain | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sepsis | 149 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sinus bradycardia | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sinus tachycardia | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sinusitis | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Skin infection | 148 | 2 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Skin/subq tissue ds-Other | 146 | 5 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sore throat | 145 | 5 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Stomach pain | 149 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Stroke | 150 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Superficial thrombophlebitis | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Thromboembolic event | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Upper respiratory infection | 144 | 0 | 7 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urinary frequency | 142 | 8 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urinary incontinence | 149 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urinary retention | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urinary tract infection | 142 | 0 | 6 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urinary urgency | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urine discoloration | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Vaginal infection | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Voice alteration | 149 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Vomiting | 138 | 8 | 5 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Watering eyes | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Weight gain | 149 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Weight loss | 144 | 6 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Wheezing | 150 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| White blood cell decreased | 94 | 16 | 10 | 17 | 14 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Wound infection | 150 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| **MAX. GRADE ANY ADVERSE EVENT** | 1 | 21 | 64 | 38 | 26 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |

## Registration, Eligibility, and Evaluability

PET-Directed Therapy

Registrations ending June 30, 2016; Data as of July 18, 2016

| | TOTAL | Continued R -CHOP | IFRT + Zevalin |
|---|---|---|---|
| NUMBER REGISTERED | 146 | 134 | 12 |
| INELIGIBLE | 1 | 1 | 0 |
| Insufficient Documentation | 1 | 1 | 0 |
| Irreversible | 1 | 1 | 0 |
| ELIGIBLE | 145 | 133 | 12 |
| Analyzable, Pend. Elig. | 139 | 127 | 12 |
| RESPONSE ASSESSMENT | | | |
| Determinable | 121 | 115 | 6 |
| Not Determinable | 1 | 1 | 0 |
| Too Early | 23 | 17 | 6 |
| ADVERSE EVENT ASSESSMENT | | | |
| Evaluable | 134 | 123 | 11 |
| Not Evaluable | 2 | 2 | 0 |
| Too Early | 9 | 8 | 1 |

## Treatment Summary

PET-Directed Therapy

Registrations ending June 30, 2016; Data as of July 18, 2016

| | TOTAL | Continued R -CHOP | IFRT + Zevalin |
|---|---|---|---|
| NUMBER ON PROTOCOL TREATMENT | 13 | 12 | 1 |
| NUMBER OFF PROTOCOL TREATMENT | 132 | 121 | 11 |
| REASON OFF TREATMENT | | | |
| Treatment completed as planned | 130 | 119 | 11 |
| Adverse Event or side effects | 1 | 1 | 0 |
| Refusal unrelated to adverse event | 1 | 1 | 0 |
| Other - not protocol specified | 0 | 0 | 0 |
| Reason under review | 0 | 0 | 0 |
| MAJOR PROTOCOL DEVIATIONS | 2 | 2 | 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 June 30, 2016; Data as of July 18, 2016

| | Continued R-CHOP (n=123) Grade | | | | | | IFRT + Zevalin (n=11) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| ALT increased | 112 | 10 | 0 | 1 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| AST increased | 116 | 7 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Abdominal pain | 122 | 0 | 0 | 1 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Alkaline phosphatase increased | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Allergic rhinitis | 122 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Alopecia | 98 | 8 | 17 | 0 | 0 | 0 | 9 | 0 | 2 | 0 | 0 | 0 |
| Anemia | 78 | 31 | 12 | 2 | 0 | 0 | 6 | 3 | 1 | 1 | 0 | 0 |
| Anorexia | 120 | 1 | 1 | 1 | 0 | 0 | 8 | 2 | 1 | 0 | 0 | 0 |
| Anxiety | 123 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Arthralgia | 120 | 2 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Arthritis | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Blurred vision | 122 | 1 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Bone pain | 121 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Chills | 122 | 1 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Constipation | 117 | 6 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Cough | 119 | 3 | 1 | 0 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| Creatinine increased | 120 | 2 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Dehydration | 123 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Depression | 123 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Dermatitis radiation | 123 | 0 | 0 | 0 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| Diarrhea | 119 | 4 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Dizziness | 123 | 0 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Dry mouth | 120 | 3 | 0 | 0 | 0 | 0 | 9 | 0 | 2 | 0 | 0 | 0 |
| Dysgeusia | 118 | 2 | 3 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Dyspepsia | 121 | 2 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Dysphagia | 123 | 0 | 0 | 0 | 0 | 0 | 9 | 1 | 1 | 0 | 0 | 0 |
| Dyspnea | 117 | 4 | 2 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Ear pain | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Edema limbs | 120 | 3 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Ejection fraction decreased | 122 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Esophagitis | 123 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Eye disorders - Other, specify | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Eye pain | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Fall | 122 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Fatigue | 76 | 38 | 8 | 1 | 0 | 0 | 5 | 5 | 1 | 0 | 0 | 0 |
| Febrile neutropenia | 121 | 0 | 0 | 2 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Fever | 121 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Flu like symptoms | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| GERD | 118 | 4 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Gastric ulcer | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Gastritis | 122 | 1 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Gen disorders/admin site cond | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Generalized muscle weakness | 120 | 1 | 2 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Gum infection | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |

| | Continued R-CHOP (n=123) Grade | | | | | | IFRT + Zevalin (n=11) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| Headache | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hearing impaired | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hot flashes | 120 | 3 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypercalcemia | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hyperglycemia | 117 | 3 | 2 | 1 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Hyperhidrosis | 123 | 0 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Hyperkalemia | 121 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypertension | 117 | 4 | 0 | 2 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hyperuricemia | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypoalbuminemia | 120 | 3 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypocalcemia | 120 | 2 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypoglycemia | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypokalemia | 118 | 2 | 1 | 2 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypomagnesemia | 122 | 1 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Hyponatremia | 120 | 2 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypotension | 122 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypoxia | 121 | 0 | 0 | 1 | 0 | 1 | 11 | 0 | 0 | 0 | 0 | 0 |
| Infections/infestations-Other | 122 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Insomnia | 121 | 2 | 0 | 0 | 0 | 0 | 9 | 0 | 2 | 0 | 0 | 0 |
| Irregular menstruation | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Laryngeal edema | 123 | 0 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Leukocytosis | 122 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Localized edema | 122 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Lymphedema | 122 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Lymphocyte count decreased | 79 | 19 | 17 | 8 | 0 | 0 | 7 | 2 | 0 | 2 | 0 | 0 |
| Malaise | 122 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Memory impairment | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Mucositis oral | 117 | 5 | 1 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Muscle weakness lower limb | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Muscle weakness upper limb | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Myalgia | 121 | 2 | 0 | 0 | 0 | 0 | 9 | 1 | 1 | 0 | 0 | 0 |
| Nail discoloration | 121 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nail loss | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nail ridging | 121 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nasal congestion | 121 | 0 | 2 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nausea | 111 | 12 | 0 | 0 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| Neoplasms, all | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nervous sys disorders-Other | 122 | 0 | 0 | 1 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Neutrophil count decreased | 107 | 2 | 3 | 3 | 8 | 0 | 6 | 1 | 2 | 1 | 1 | 0 |
| Oral pain | 121 | 1 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Pain | 120 | 3 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Pain in extremity | 119 | 2 | 2 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Paresthesia | 121 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Peripheral motor neuropathy | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Peripheral sensory neuropathy | 99 | 21 | 2 | 1 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| Pharyngitis | 122 | 0 | 1 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Phlebitis | 122 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Platelet count decreased | 107 | 12 | 0 | 2 | 2 | 0 | 7 | 0 | 1 | 2 | 1 | 0 |
| Productive cough | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Pruritus | 121 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Rash acneiform | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |

| | Continued R-CHOP (n=123) Grade | | | | | | IFRT + Zevalin (n=11) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| Renal calculi | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Resp/thoracic/mediastinal ds | 121 | 1 | 0 | 0 | 1 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Secondary Leukemia | 122 | 0 | 0 | 0 | 1 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Sinus bradycardia | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Sinus tachycardia | 121 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Skin infection | 120 | 1 | 1 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Skin/subq tissue ds-Other | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Small intestine infection | 122 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Sore throat | 122 | 0 | 1 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Telangiectasia | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Thromboembolic event | 122 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Upper respiratory infection | 120 | 0 | 3 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Urinary frequency | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Urinary tract infection | 121 | 0 | 2 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Urine discoloration | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Voice alteration | 122 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Vomiting | 122 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Weight gain | 120 | 2 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Weight loss | 120 | 1 | 1 | 1 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| White blood cell decreased | 94 | 16 | 3 | 5 | 5 | 0 | 6 | 1 | 2 | 2 | 0 | 0 |
| **MAX. GRADE ANY ADVERSE EVENT** | 11 | 34 | 48 | 18 | 11 | 1 | 1 | 4 | 2 | 2 | 2 | 0 |

# S1204 Surveillance

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

**Study Chairs:**
S Ramsey, D Hershman

**Date Activated:**
08/29/2013

**Statisticians:**
J Unger, K Arnold

**Data Coordinator:**
M Yee

**Objectives**

Among newly diagnosed cancer patients presenting to SWOG-affiliated community and academic oncology clinics, estimate the prevalence of human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV) infection.

Evaluate known sociodemographic, clinical, and behavioral factors that are significantly associated with previously undiagnosed HIV, HBV, and/or HCV infection in a population of people with newly diagnosed cancer.

Among patients who are identified as having HIV, HBV, and/or HCV, evaluate the timing and type of treatments received, both for the viral infections and the cancers.

Evaluate type and rate of cancer treatment-related adverse events in patients with HIV, HBV, and/or HCV infection.

Determine the cost-effectiveness of (1) routine, universal screening and (2) risk factor-directed screening of newly diagnosed cancer patients for HIV, HBV and/or HCV versus current care.

**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: NCI

# 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

**Participants:**
NCI, CTSU

**Date Activated:**
05/15/2012

**Study Chairs:**
K Dunleavy (NCI), 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**

NCI reported a total accrual of 148 patients as of June 30, 2016, including 19 SWOG registrations. The complete November 2015 summary of this study from NCIMet is available on the SWOG web site.

## Registration by Institution

Registrations ending June 30, 2016

| 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** |

# A051301 Phase III SWOG Supported CTSU Study

**Coordinating Group: Alliance**

# A Randomized Double-Blind Phase III Study of Ibrutinib During and Following Autologous Stem Cell Transplantation Versus Placebo in Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma of the Activated B-cell Subtype

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**Participants:**
Alliance, CTSU

**Date Activated:**
07/06/2016

**Study Chairs:**
C Andreadis (Alliance), P Stiff (SWOG)

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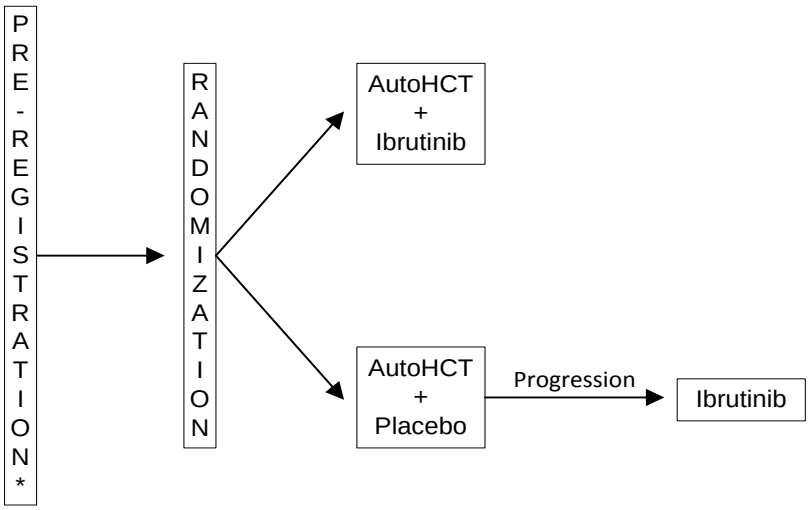
## SCHEMA




*Determination of ABC subtype will be performed by central review.

**Objectives**

To evaluate the ability of ibrutinib to improve 24-month progression free survival (PFS) compared to placebo.

To evaluate the ability of ibrutinib to improve overall survival (OS) compared to placebo.

To evaluate the ability of ibtutinib to improve post-transplant response rates compared to placebo.

To evaluate time to hematopoietic recovery in the two arms.

To evaluate the safety and tolerability of ibrutinib compared to placebo.

To evaluate the incidence of secondary malignancies in the two arms.

To evaluate immune reconstitution in the two arms.

**Patient Population**

Patients must have a diagnosis of WHO diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma not otherwise specified (NOS), or B-cell lymphoma, unclassifiable (BCLU), with features intermediate between DLBCL and Burkitt lymphoma. Patients must have ABC subtype determined by central review. Patients must have chemosensitive disease as defined by at least a partial response to salvage therapy at their latest assessment. Patients must have progressed or be refractory to prior anthracycline-containing chemotherapy. Patients must not have active central nervous system or meningeal involvement by lymphoma or any evidence of myelodysplasia or cytogenetic abnormality indicative of myelodysplasia on any bone marrow biopsy prior to initiation of therapy.

Patients must be deemed eligible to proceed with high-dose chemotherapy and autologous stem cell transplantation. Patients must not have more than three prior regimens for large cell component. Prior use of ibrutinib is allowed unless patient has had disease progression while receiving ibrutinib. Patients must not have had major surgery within seven days prior to registration or minor surgery within three days prior to registration. Patients should not require chronic use of strong CYP3A inhibitors or inducers, or concurrent therapeutic dose of steroids except as listed in the protocol. Steroids should be discontinued for 14 days before starting protocol treatment. Patients must not have requirement for warfarin or similar vitamin K antagonists.

Patients must have an ECOG performance status of 0-2, be at least 18 years of age, and have adequate cardiac, renal, pulmonary, and hepatic function to proceed to transplant. Women of childbearing potential must have a negative serum pregnancy test. HIV infected patients are eligible with restrictions. Patients must have no known bleeding diathesis, no history of stroke or intracranial hemorrhage within six months before treatment, no active and clinically significant hepatic impairment, and no serologic status reflecting active hepatitis B or C infection.

**Stratification/Descriptive Factors**

Patient randomization will be stratified by the following factors: (1) type of transplant regimen planned: CBV vs BEAM; and (2) time to relapse: $\leq$ 12 months vs > 12 months.

**Accrual Goals**

Patients will be assigned to one of the following groups at study entry: 1) Early safety assessment or 2) Double-blinded randomization.

This study will accrue 302 patients, including a cohort of 6 patients to investigate the safety of ibrutinib. A total of 296 patients will be randomized. Two formal interim analyses are planned for when 140 and 210 patients have at least two years of follow-up.

# 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)

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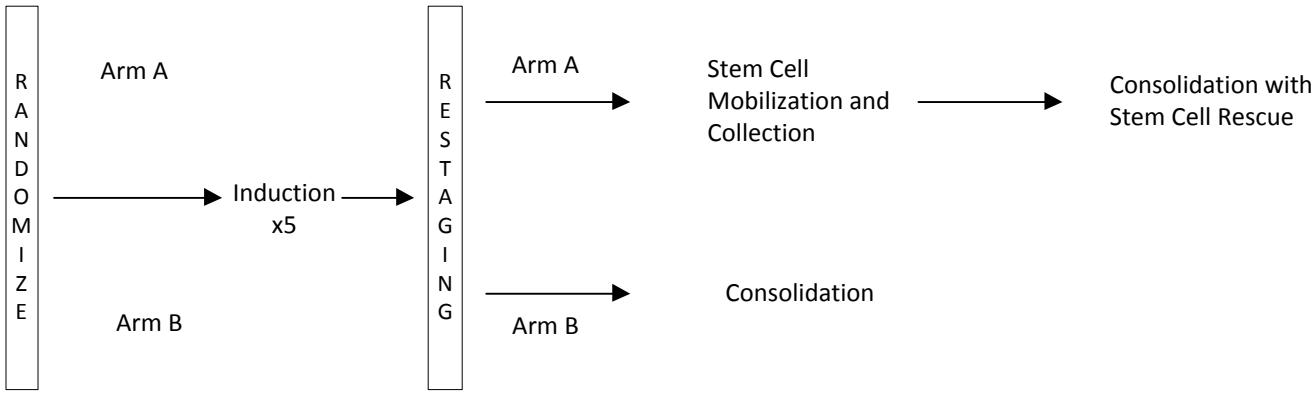
## SCHEMA




**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 ($ADC_{mini}$, $ADC_{25\%}$, and $ADC_{mean}$) 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 73 patients as of June 30, 2016, 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)

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**Participants:**
ECOG-ACRIN, CTSU

**Date Activated:**
06/15/2012

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

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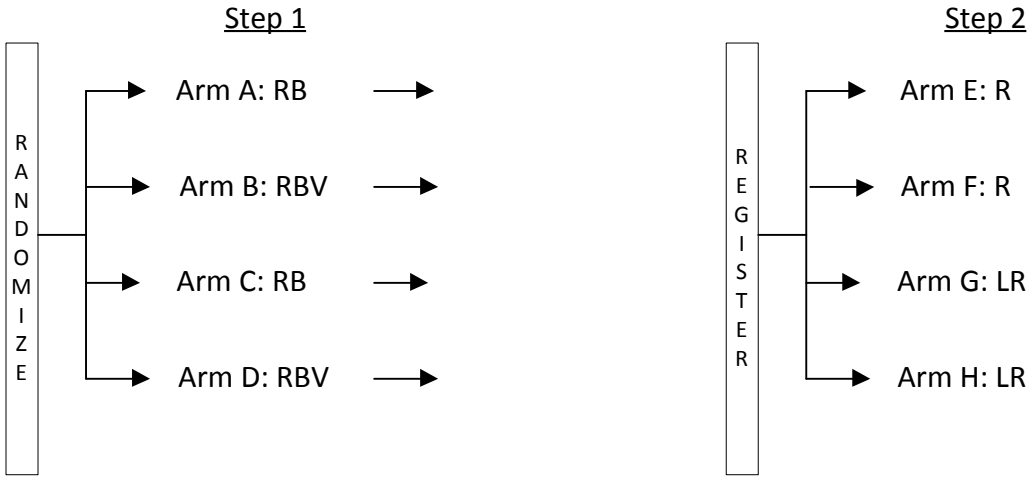
## SCHEMA




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 the objective response rate (ORR) for RB and RBV.

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 $\geq 60$.

**Accrual Goals**

A total of 372 patients will be accrued to this study.

**Summary Statement**

ECOG-ACRIN reported a total accrual of 353 patients as of June 30, 2016, including 82 SWOG registrations. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

# Registration by Institution

Registrations ending June 30, 2016

| Institutions | Total Reg | Institutions | Total Reg |
|---|---|---|---|
| Rochester, Univ of | 22 | Prov Portland MC/PCRC NCORP | 3 |
| Kaiser Perm NCORP | 12 | Dayton NCORP | 2 |
| Cleveland Clinic OH | 9 | KaiserPermanenteCOL/Kaiser Perm NCORP | 2 |
| Oregon Hlth Sci Univ | 5 | Arizona MC, U of | 1 |
| Fred Hutchinson CRC | 4 | Columbia MU-NCORP | 1 |
| Hawaii MU-NCORP | 4 | Southeast COR NCORP | 1 |
| Poudre Valley Hosp/Colorado, U of | 4 | UF Cancer Center/Arkansas, U of | 1 |
| CRC West MI NCORP | 3 | Upstate Carolina | 1 |
| Kansas City NCORP | 3 | Wayne State Univ | 1 |
| Montana NCORP | 3 | **Total (19 Institutions)** | **82** |

# 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)

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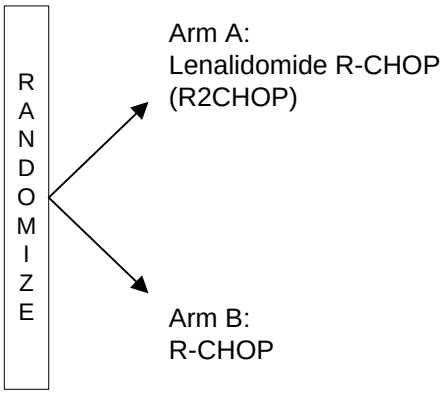
## SCHEMA




**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).

**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**

ECOG-ACRIN reported a total accrual of 295 patients as of June 30, 2016, including 35 SWOG registrations. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.

## Registration by Institution

Registrations ending June 30, 2016

| Institutions | Total Reg | Institutions | Total Reg |
|---|---|---|---|
| Rochester, Univ of | 15 | Arizona MC, U of | 1 |
| Montana NCORP | 4 | Hawaii MU-NCORP | 1 |
| Cincinnati MC, U of | 3 | Kaiser Perm NCORP | 1 |
| Columbia MU-NCORP | 3 | Kansas City NCORP | 1 |
| KaiserPermanenteSCAL/Kaiser Perm NCORP | 3 | Wayne State Univ | 1 |
| Brooke Army Med Ctr | 2 | **Total (11 Institutions)** | **35** |

# EAY131 Master Protocol / Phase II

## Coordinating Group: ECOG-ACRIN

## NCI-MATCH: Molecular Analysis for Therapy Choice

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**Participants:**
ECOG-ACRIN, CTSU

**Date Activated:**
08/12/2015

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

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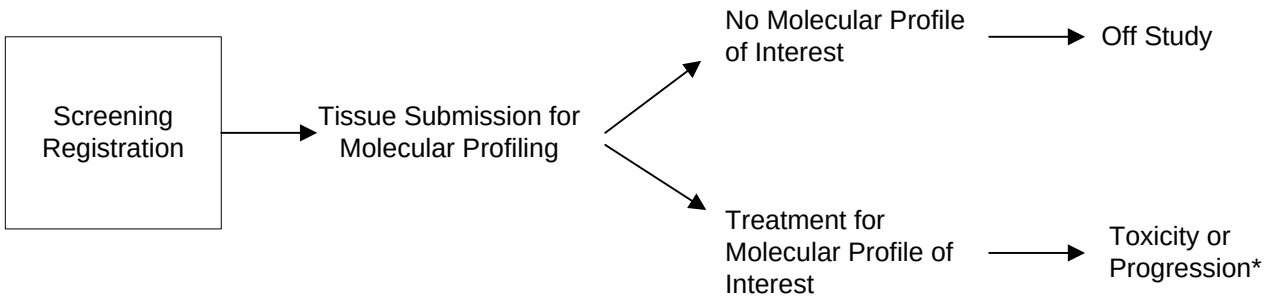
## SCHEMA




*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/multiple myeloma.

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/multiple myeloma.

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 protein and imaging-based assessment platforms.

To assess whether radiomic phenotypes obtained from pre-treatment imaging and changes from pre- through post-therapy imaging can predict objective response and progression free survival and to evaluate the association between pre-treatment radiomic phenotypes and targeted gene mutation patterns of tumor biopsy specimens.

**Patient Population**

Patients must have histologically documented solid tumors or histologically confirmed diagnosis of lymphoma or multiple myeloma 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 and meet one of the criteria in the protocol regarding tissue procurement.

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 start of treatment. Patients must not require the use of full dose coumarin-derivative anticoagulants. Factor X inhibitors are permitted. Patients may receive non-protocol treatment after biopsy (if clinically indicated) until they receive notification of results, but patients may not enroll in another investigational study during this time and the therapy cannot be an arm in this trial.

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. Patients must not have any uncontrolled intercurrent illness. 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 reach 25 patients by the time the overall study screening accrual goal is met, and if 13 patients have been treated and no responses have been observed, then the steering committee may consider terminating accrual in that subgroup due to lack of feasibility. After 500 patients are screened, the study design will be reassessed to assure its appropriateness. 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 January 26, 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 assessment of study design appropriateness was lifted on May 31, 2016, when this study reopened to enrollment with an additional 14 new subprotocols.

Patients with multiple myeloma will be allowed to enroll in the MATCH protocol at a future amendment. The screening sample collection, processing and assay are currently being validated for the marrow specimens for patients with myeloma. Once this is completed, an amendment allowing these patients to enroll will be submitted. Patients with myeloma cannot be entered on the trial until that is completed.

ECOG-ACRIN reported a total of 1,013 screened patients and 29 molecularly matched patients as of June 30, 2016. This includes 139 screened and two molecularly matched SWOG registrations. The complete Spring 2016 summary of this study from ECOG-ACRIN is available on the SWOG web site.