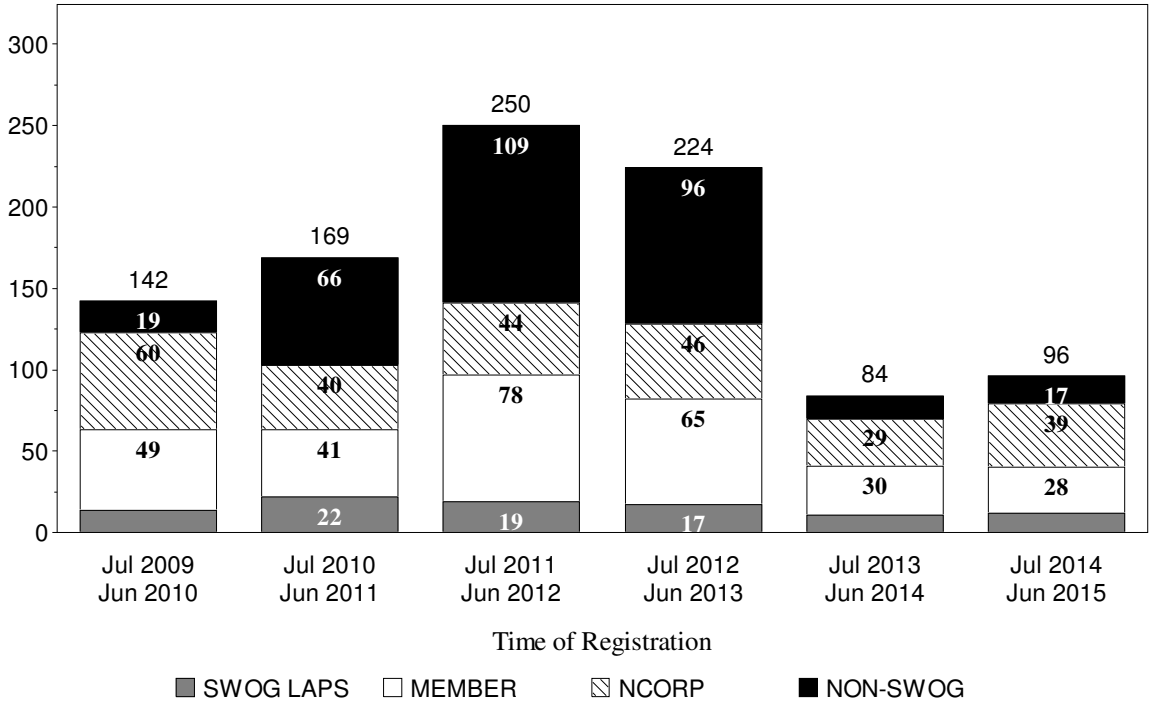
# LYMPHOMA COMMITTEE

# 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 2015 Jun 2015 | Jul 2014 Dec 2014 | Jan 2014 Jun 2014 | All Patients |
|---|---|---|---|---|
| **S1001 DLBCL, I-II, PET-Adapted Therapy** | | | | |
| **Initial registration** | | | | |
| R-CHOP x 3 | 20 | 22 | 19 | 124 |
| R-CHOP x 6 | 0 | 0 | 1 | 1 |
| | 20 | 22 | 20 | 125 |
| **PET-Directed Therapy** | | | | |
| Continued R-CHOP | 14 | 23 | 13 | 98 |
| IFRT + Zevalin | 0 | 2 | 4 | 11 |
| | 14 | 25 | 17 | 109 |
| **S1106 NHL, Adv, R-HCVAD/R-Benda+PBSCT** | | | | |
| **Transplant** | | | | |
| Stem Cell Transplant | 0 | 0 | 3 | 26 |
| **9177 NHL, Dose-Adj. EPOCH+/-Rituximab*** | | | | |
| Total Registrations | 0 | 2 | 0 | 18 |
| **C51101 CNSMyelo/Non-myelo chemo, PhII*** | | | | |
| Total Registrations | 2 | 0 | 3 | 5 |
| **E1411 MCL, RB+R, RBV+R, RB+LR, RBV+LR*** | | | | |
| Total Registrations | 17 | 10 | 14 | 55 |
| **E1412 DLBCL, R2CHOP vs RCHOP*** | | | | |
| Total Registrations | 18 | 5 | 3 | 26 |

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

# S0410 Phase II

## Coordinating Group: SWOG

# Tandem Autologous Stem Cell Transplantation for Patients with Primary Progressive or Recurrent Hodgkin's Disease (a BMT Study), Phase II

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**Participants:**
SWOG, BMT CTN

**Study Chairs:**
E Smith, P Stiff, L Constine, L Rimsza, G Laport (BMT CTN)

**Statisticians:**
H Li, M LeBlanc

**Data Coordinators:**
M Toth, J Jardine

**Date Activated:**
10/15/2005

**Date Closed:**
02/01/2009

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**Objectives**

To assess the two-year progression-free survival for patients with primary progressive or recurrent Hodgkin's lymphoma treated with a tandem transplant program.

To evaluate the response rate and toxicitiy in patients with primary progressive or recurrent Hodgkin's lymphoma treated with this regimen.

**Patient Population**

Patients must have histologically or cytologically confirmed Hodgkin's disease that has relapsed after or is refractory to multiagent chemotherapy. Patients must have normal cytogenetics, as determined from a bone marrow aspirate. Patients with CNS disease involvement are ineligible.

Patients must have received systemic chemotherapy as all or part of their treatment for Hodgkin's disease.

Patients must have a Zubrod performance status of 0, 1 or 2. Patients must be at least 15 and no more than 70 years of age. Patients must have adequate hematologic, renal and pulmonary function. Patients must be free of active bacterial, fungal, or viral infection. Patients must not require therapy for coronary artery disease, cardiomyopathy, congestive heart failure or arrythmia, or have known HIV or AIDS.

**Accrual Goals**

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

**Summary Statement**

This study was closed to accrual on February 1, 2009, after meeting its accrual goal. A total of 98 patients were registered. Six patients are ineligible due to the following reasons: inadequate pulmonary function (1), diagnosis cannot be confirmed by pathology review (2), and insufficient baseline documentation (3). Three eligible patients who did not receive any protocol treatment are not analyzable for any of the study endpoints and excluded from the tables.

Eighty-two patients completed protocol treatment as planned. Seven patients went off protocol treatment early due to the following reasons: poor engraftment (1), patient declined TBI (1), disease progression (1), and greater than 60 days between first and second cycle of HDT (4).

Eighty-nine patients have been assessed for toxicities. Seventy patients reported treatment-related Grade 4 adverse events, primarily hematologic (69). One patient who did not experience Grade 4 hematologic toxicity experienced Grade 4 hypotension. Among patients who experienced Grade 4 hematologic toxicities, fourteen patients also experienced Grade 4 non-hematologic toxicities, including febrile neutropenia (3), hypophosphatemia (3), hypokalemia (2), mucositis, clinical: oral cavity (2), mucositis, functional: oral cavity(2), and one case each of dyspnea, esophagitis, fatigue, GI pain: oral cavity, hyperuricemia, hypotension, hypoxia, blood infection, catheter-related infection, foreign body infection, and upper airway lung infection.

Among 84 patients assessed for response, there were 18 (21%) complete responses, 10 (12%) partial responses, one (1%) unconfirmed complete response, and one (1%) unconfirmed partial response were observed. Twenty-four (29%) patients who could not have their exact response determined due to inadequate assessments are included in the denominator as non-responders. The estimated overall response rate is 36% (95% CI: 25.6% - 46.9%).

The median of follow-up among those last known alive is 6.7 years (range 2 - 7.8 years). Forty patients have either progressed or died. The Kaplan-Meier estimate of 2-year progression-free survival is 63% (95% CI: 52%, 72%). There have been 16 deaths, the Kaplan-Meier estimate of 2-year overall survival is 91% (95% CI: 83%, 95%).

## Registration by Institution

| Institutions | Total Reg | Institutions | Total Reg |
|---|---|---|---|
| City of Hope Med Ctr | 52 | Wichita NCORP | 2 |
| PCRC NCORP | 20 | Dayton NCORP | 1 |
| BMTCTN | 9 | Prov Portland MC/PCRC NCORP | 1 |
| Loyola University | 5 | St Luke's Mt State/PCRC NCORP | 1 |
| Tulane University | 4 | **Total (10 Institutions)** | **98** |
| Davis, U of CA | 3 | | |

## Registration, Eligibility, and Evaluability

Data as of August 27, 2015

| | 2 cyc HDT + auto PBSCT |
|---|---|
| NUMBER REGISTERED | 98 |
| INELIGIBLE | 6 |
| Insufficient Documentation | 3 |
| Irreversible | 3 |
| ELIGIBLE | 92 |
| Not Analyzable | 3 |
| RESPONSE ASSESSMENT | |
| Determinable | 60 |
| Not Determinable | 24 |
| Not Applicable | 5 |
| ADVERSE EVENT ASSESSMENT | |
| Evaluable | 89 |

# Patient Characteristics

Data as of August 27, 2015

| | 2 cyc HDT + auto PBSCT (n=89) | |
|---|---|---|
| AGE | | |
| Median | 34.4 | |
| Minimum | 18.2 | |
| Maximum | 60.3 | |
| SEX | | |
| Males | 48 | 54% |
| Females | 41 | 46% |
| HISPANIC | | |
| Yes | 2 | 2% |
| No | 53 | 60% |
| Unknown | 34 | 38% |
| RACE | | |
| White | 75 | 84% |
| Black | 6 | 7% |
| Asian | 4 | 4% |
| Unknown | 4 | 4% |
| LYMPHOMA DISEASE STATUS | | |
| Recurrent | 49 | 55% |
| Refractory | 40 | 45% |
| HISTOLOGY | | |
| Nodular Sclerosis | 77 | 87% |
| Mixed Cellularity | 5 | 6% |
| Lymphocyte Predominant | 2 | 2% |
| Other Hodgkins | 5 | 6% |
| PERFORMANCE STATUS | | |
| 0 | 64 | 72% |
| 1 | 25 | 28% |
| CURRENT STAGE OF DISEASE | | |
| I | 1 | 1% |
| II | 10 | 11% |
| III | 53 | 60% |
| IV | 21 | 24% |
| Unknown | 4 | 4% |
| SYMPTOMS | | |
| A | 52 | 58% |
| B | 37 | 42% |

## Treatment Summary

Data as of August 27, 2015

| | 2 cyc HDT + auto PBSCT |
|---|---|
| NUMBER ON PROTOCOL TREATMENT | 0 |
| NUMBER OFF PROTOCOL TREATMENT | 89 |
| REASON OFF TREATMENT | |
| Treatment completed as planned | 82 |
| Adverse Event or side effects | 0 |
| Refusal unrelated to adverse event | 1 |
| Progression/relapse | 1 |
| Death | 0 |
| 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

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of August 27, 2015

| | 2 cyc HDT + auto PBSCT (n=89) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| ALT | 44 | 28 | 11 | 6 | 0 | 0 |
| AST | 43 | 38 | 4 | 4 | 0 | 0 |
| Acne | 87 | 1 | 1 | 0 | 0 | 0 |
| Alkaline phosphatase | 65 | 21 | 3 | 0 | 0 | 0 |
| Allergic reaction | 85 | 0 | 1 | 3 | 0 | 0 |
| Allergy-other | 88 | 1 | 0 | 0 | 0 | 0 |
| Alopecia | 60 | 5 | 24 | 0 | 0 | 0 |
| Anorexia | 37 | 20 | 13 | 19 | 0 | 0 |
| Ascites | 88 | 1 | 0 | 0 | 0 | 0 |
| Atelectasis | 88 | 1 | 0 | 0 | 0 | 0 |
| Auditory/Ear-other | 87 | 1 | 1 | 0 | 0 | 0 |
| Bicarbonate, serum-low | 53 | 34 | 2 | 0 | 0 | 0 |
| Bilirubin | 84 | 4 | 0 | 1 | 0 | 0 |
| Bronchospasm | 85 | 2 | 2 | 0 | 0 | 0 |
| Bruising | 87 | 2 | 0 | 0 | 0 | 0 |
| Cardiac General-other | 87 | 2 | 0 | 0 | 0 | 0 |
| Cheilitis | 88 | 0 | 1 | 0 | 0 | 0 |
| Cholesterol | 84 | 4 | 1 | 0 | 0 | 0 |
| Colitis, infectious | 87 | 0 | 2 | 0 | 0 | 0 |
| Cond. Abn.: NOS | 88 | 1 | 0 | 0 | 0 | 0 |
| Confusion | 88 | 0 | 0 | 1 | 0 | 0 |
| Constipation | 66 | 22 | 1 | 0 | 0 | 0 |
| Constitutional Symptoms-other | 87 | 1 | 0 | 1 | 0 | 0 |
| Cough | 62 | 25 | 1 | 1 | 0 | 0 |
| Creatinine | 72 | 15 | 2 | 0 | 0 | 0 |

| | 2 cyc HDT + auto PBSCT (n=89) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Cystitis | 88 | 1 | 0 | 0 | 0 | 0 |
| DLCO | 88 | 0 | 1 | 0 | 0 | 0 |
| Dehydration | 82 | 0 | 1 | 6 | 0 | 0 |
| Dermatology-other | 67 | 21 | 0 | 1 | 0 | 0 |
| Diarrhea | 26 | 40 | 16 | 7 | 0 | 0 |
| Distension | 81 | 7 | 1 | 0 | 0 | 0 |
| Dizziness | 60 | 25 | 4 | 0 | 0 | 0 |
| Dry eye | 88 | 1 | 0 | 0 | 0 | 0 |
| Dry mouth | 72 | 15 | 1 | 1 | 0 | 0 |
| Dry skin | 81 | 8 | 0 | 0 | 0 | 0 |
| Dysphagia | 77 | 6 | 1 | 5 | 0 | 0 |
| Dyspnea | 71 | 9 | 4 | 4 | 1 | 0 |
| Ear Pain: external ear | 87 | 2 | 0 | 0 | 0 | 0 |
| Edema-head and neck | 85 | 4 | 0 | 0 | 0 | 0 |
| Edema-larynx | 88 | 0 | 1 | 0 | 0 | 0 |
| Edema-limb | 69 | 16 | 3 | 1 | 0 | 0 |
| Esophagitis | 78 | 2 | 5 | 3 | 1 | 0 |
| Eye Op Inj: cornea | 88 | 0 | 1 | 0 | 0 | 0 |
| Eye Pain: eye | 87 | 2 | 0 | 0 | 0 | 0 |
| FEV1 | 86 | 1 | 2 | 0 | 0 | 0 |
| Fatigue | 28 | 27 | 30 | 3 | 1 | 0 |
| Febrile neutropenia | 43 | 0 | 0 | 43 | 3 | 0 |
| Fever | 57 | 14 | 16 | 2 | 0 | 0 |
| Flu-like syndrome | 86 | 1 | 2 | 0 | 0 | 0 |
| Flushing | 78 | 8 | 3 | 0 | 0 | 0 |
| GGT | 84 | 4 | 1 | 0 | 0 | 0 |
| GI Hemorrhage: rectum | 88 | 1 | 0 | 0 | 0 | 0 |
| GI Hemorrhage: upper GI | 88 | 1 | 0 | 0 | 0 | 0 |
| GI Inf, 3-4 ANC: abdomen, NOS | 88 | 0 | 0 | 1 | 0 | 0 |
| GI Inf, 3-4 ANC: rectum | 87 | 0 | 1 | 1 | 0 | 0 |
| GI Inf, 3-4 ANC: stomach | 88 | 0 | 0 | 1 | 0 | 0 |
| GI Pain: abdomen | 60 | 23 | 6 | 0 | 0 | 0 |
| GI Pain: anus | 86 | 2 | 1 | 0 | 0 | 0 |
| GI Pain: esophagus | 87 | 2 | 0 | 0 | 0 | 0 |
| GI Pain: oral cavity | 70 | 12 | 5 | 1 | 1 | 0 |
| GI Pain: rectum | 81 | 6 | 2 | 0 | 0 | 0 |
| GI Pain: stomach | 79 | 9 | 1 | 0 | 0 | 0 |
| GI-other | 82 | 7 | 0 | 0 | 0 | 0 |
| GU Hemorrhage: urinary | 84 | 4 | 1 | 0 | 0 | 0 |
| GU Hemorrhage: vagina | 87 | 1 | 1 | 0 | 0 | 0 |
| GU Inf, Unk ANC: UTI | 88 | 0 | 1 | 0 | 0 | 0 |
| GU Obstruction: bladder | 88 | 0 | 1 | 0 | 0 | 0 |
| GU Pain: bladder | 86 | 3 | 0 | 0 | 0 | 0 |
| Gait/walking | 88 | 1 | 0 | 0 | 0 | 0 |
| Gastritis | 84 | 1 | 4 | 0 | 0 | 0 |
| Hand-foot | 85 | 1 | 3 | 0 | 0 | 0 |
| Hearing (w/o monit. prog.) | 87 | 0 | 2 | 0 | 0 | 0 |
| Heartburn | 61 | 24 | 4 | 0 | 0 | 0 |
| Hematoma | 87 | 2 | 0 | 0 | 0 | 0 |
| Hemoglobin | 23 | 2 | 43 | 20 | 1 | 0 |
| Hemorrhage-other | 83 | 5 | 0 | 1 | 0 | 0 |

| | 2 cyc HDT + auto PBSCT (n=89) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Hemorrhoids | 84 | 1 | 4 | 0 | 0 | 0 |
| Hiccoughs | 82 | 1 | 6 | 0 | 0 | 0 |
| Hot flashes | 85 | 3 | 1 | 0 | 0 | 0 |
| Hypercalcemia | 80 | 9 | 0 | 0 | 0 | 0 |
| Hyperglycemia | 40 | 12 | 32 | 5 | 0 | 0 |
| Hypermagnesemia | 85 | 3 | 0 | 1 | 0 | 0 |
| Hypernatremia | 88 | 1 | 0 | 0 | 0 | 0 |
| Hyperpigmentation | 78 | 10 | 1 | 0 | 0 | 0 |
| Hypertension | 78 | 10 | 1 | 0 | 0 | 0 |
| Hypertriglyceridemia | 83 | 4 | 2 | 0 | 0 | 0 |
| Hyperuricemia | 82 | 6 | 0 | 0 | 1 | 0 |
| Hypoalbuminemia | 36 | 30 | 23 | 0 | 0 | 0 |
| Hypocalcemia | 38 | 30 | 20 | 1 | 0 | 0 |
| Hypoglycemia | 83 | 6 | 0 | 0 | 0 | 0 |
| Hypokalemia | 36 | 40 | 0 | 11 | 2 | 0 |
| Hypomagnesemia | 62 | 22 | 5 | 0 | 0 | 0 |
| Hyponatremia | 51 | 27 | 0 | 11 | 0 | 0 |
| Hypophosphatemia | 45 | 5 | 14 | 22 | 3 | 0 |
| Hypotension | 47 | 11 | 21 | 9 | 1 | 0 |
| Hypoxia | 80 | 0 | 5 | 3 | 1 | 0 |
| Incontinence, anal | 87 | 2 | 0 | 0 | 0 | 0 |
| Inf, 0-2 ANC: blood | 87 | 0 | 0 | 2 | 0 | 0 |
| Inf, 0-2 ANC: cath.-related | 88 | 0 | 0 | 1 | 0 | 0 |
| Inf, 3-4 ANC: blood | 87 | 0 | 0 | 1 | 1 | 0 |
| Inf, 3-4 ANC: cath-related | 88 | 0 | 0 | 0 | 1 | 0 |
| Inf, 3-4 ANC: foreign body | 88 | 0 | 0 | 0 | 1 | 0 |
| Inf, Unk ANC: blood | 88 | 0 | 0 | 1 | 0 | 0 |
| Infection-other | 75 | 6 | 3 | 5 | 0 | 0 |
| Injection site reaction | 87 | 2 | 0 | 0 | 0 | 0 |
| Insomnia | 54 | 27 | 8 | 0 | 0 | 0 |
| Leukocytes | 25 | 0 | 0 | 0 | 64 | 0 |
| Lung Hemorrhage: nose | 81 | 5 | 1 | 2 | 0 | 0 |
| Lung Hemorrhage: resp. tract | 88 | 1 | 0 | 0 | 0 | 0 |
| Lung Inf, 0-2 ANC: up. airway | 88 | 0 | 1 | 0 | 0 | 0 |
| Lung Inf, 3-4 ANC: lung | 85 | 0 | 1 | 3 | 0 | 0 |
| Lung Inf, 3-4 ANC: pharynx | 88 | 0 | 1 | 0 | 0 | 0 |
| Lung Inf, 3-4 ANC: sinus | 87 | 0 | 1 | 1 | 0 | 0 |
| Lung Inf, 3-4 ANC: up. airway | 88 | 0 | 0 | 0 | 1 | 0 |
| Lung Inf, Unk ANC: sinus | 88 | 0 | 1 | 0 | 0 | 0 |
| Lung Pain: chest wall | 80 | 9 | 0 | 0 | 0 | 0 |
| Lung Pain: chest/thorax | 80 | 8 | 1 | 0 | 0 | 0 |
| Lung Pain: sinus | 87 | 2 | 0 | 0 | 0 | 0 |
| Lung Pain: throat/phar/lar | 62 | 20 | 4 | 3 | 0 | 0 |
| Lymphatic Pain: lymph node | 88 | 1 | 0 | 0 | 0 | 0 |
| Lymphatics-other | 88 | 0 | 0 | 1 | 0 | 0 |
| Lymphopenia | 38 | 1 | 1 | 2 | 47 | 0 |
| Metabolic/Lab-other | 85 | 0 | 4 | 0 | 0 | 0 |
| Mood alteration: agitation | 84 | 5 | 0 | 0 | 0 | 0 |
| Mood alteration: anxiety | 59 | 22 | 8 | 0 | 0 | 0 |
| Mood alteration: depression | 79 | 3 | 5 | 2 | 0 | 0 |
| Mucositis, clin: oral cavity | 62 | 10 | 8 | 7 | 2 | 0 |

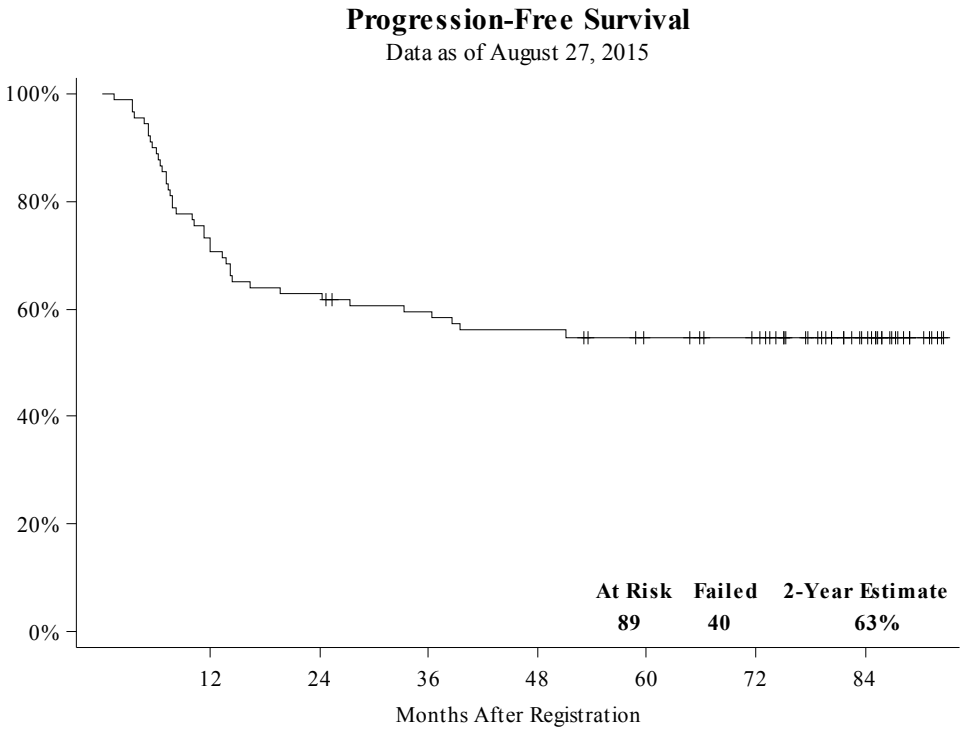
| | 2 cyc HDT + auto PBSCT (n=89) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Mucositis, clin: pharynx | 56 | 15 | 10 | 8 | 0 | 0 |
| Mucositis, funct: esophagus | 88 | 0 | 1 | 0 | 0 | 0 |
| Mucositis, funct: oral cav. | 75 | 4 | 4 | 4 | 2 | 0 |
| Mucositis, funct: pharynx | 66 | 7 | 6 | 10 | 0 | 0 |
| Mucositis, funct: stomach | 88 | 1 | 0 | 0 | 0 | 0 |
| Muscle weakness: whole body | 72 | 12 | 5 | 0 | 0 | 0 |
| Musculo. Pain: back | 64 | 19 | 6 | 0 | 0 | 0 |
| Musculo. Pain: bone | 78 | 6 | 5 | 0 | 0 | 0 |
| Musculo. Pain: joint | 82 | 4 | 1 | 2 | 0 | 0 |
| Musculo. Pain: limb | 83 | 4 | 2 | 0 | 0 | 0 |
| Musculo. Pain: muscle | 83 | 6 | 0 | 0 | 0 | 0 |
| Musculo. Pain: neck | 86 | 1 | 2 | 0 | 0 | 0 |
| Nail changes | 88 | 1 | 0 | 0 | 0 | 0 |
| Nasal/paranasal reactions | 85 | 2 | 2 | 0 | 0 | 0 |
| Nausea | 8 | 19 | 30 | 32 | 0 | 0 |
| Neuro Pain: head/headache | 43 | 27 | 17 | 2 | 0 | 0 |
| Neuro Pain: neuralg/periph nrv | 88 | 0 | 1 | 0 | 0 | 0 |
| Neurop: mot-jaw; sens-facial | 88 | 1 | 0 | 0 | 0 | 0 |
| Neuropathy-motor | 88 | 1 | 0 | 0 | 0 | 0 |
| Neuropathy-sensory | 80 | 8 | 1 | 0 | 0 | 0 |
| Neutrophils | 23 | 0 | 0 | 3 | 63 | 0 |
| Nystagmus | 88 | 0 | 1 | 0 | 0 | 0 |
| Ocular-other | 84 | 4 | 1 | 0 | 0 | 0 |
| Opportunistic infection | 88 | 0 | 0 | 1 | 0 | 0 |
| Pain-other | 63 | 16 | 8 | 2 | 0 | 0 |
| Pain: NOS | 87 | 2 | 0 | 0 | 0 | 0 |
| Pain: tumor pain | 85 | 1 | 3 | 0 | 0 | 0 |
| Palpitations | 88 | 1 | 0 | 0 | 0 | 0 |
| Pericardial effusion | 87 | 2 | 0 | 0 | 0 | 0 |
| Petechiae | 87 | 1 | 1 | 0 | 0 | 0 |
| Photophobia | 88 | 1 | 0 | 0 | 0 | 0 |
| Platelets | 17 | 3 | 0 | 8 | 61 | 0 |
| Pleural effusion | 86 | 2 | 1 | 0 | 0 | 0 |
| Pneumonitis | 76 | 2 | 8 | 3 | 0 | 0 |
| Pruritus | 76 | 9 | 3 | 1 | 0 | 0 |
| Psychosis | 87 | 0 | 1 | 1 | 0 | 0 |
| Pulmonary hypertension | 88 | 0 | 0 | 1 | 0 | 0 |
| Pulmonary-other | 78 | 11 | 0 | 0 | 0 | 0 |
| RT Dermatitis: ChemoRT derm. | 87 | 0 | 2 | 0 | 0 | 0 |
| RT Dermatitis: RT dermatitis | 86 | 3 | 0 | 0 | 0 | 0 |
| Rash | 60 | 9 | 16 | 4 | 0 | 0 |
| Renal-other | 85 | 4 | 0 | 0 | 0 | 0 |
| Restrictive cardiomyopathy | 88 | 0 | 1 | 0 | 0 | 0 |
| Rhinitis | 78 | 7 | 4 | 0 | 0 | 0 |
| Rigors/chills | 54 | 21 | 14 | 0 | 0 | 0 |
| Salivary gland changes | 86 | 3 | 0 | 0 | 0 | 0 |
| Sexual-other | 88 | 1 | 0 | 0 | 0 | 0 |
| Sexual/Repro. Pain: pelvis | 87 | 1 | 1 | 0 | 0 | 0 |
| Sexual/Repro. Pain: penis | 88 | 1 | 0 | 0 | 0 | 0 |
| Sexual/Repro. Pain: prostate | 88 | 0 | 1 | 0 | 0 | 0 |
| Sexual/Repro. Pain: scrotum | 87 | 2 | 0 | 0 | 0 | 0 |

| | 2 cyc HDT + auto PBSCT (n=89) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Sexual/Repro. Pain: testicle | 88 | 1 | 0 | 0 | 0 | 0 |
| Sexual/Repro. Pain: vagina | 88 | 1 | 0 | 0 | 0 | 0 |
| Skin Inf, 0-2 ANC: skin | 87 | 0 | 2 | 0 | 0 | 0 |
| Skin Inf, 3-4 ANC: skin | 86 | 0 | 2 | 1 | 0 | 0 |
| Skin Inf, Unk ANC: skin | 88 | 0 | 0 | 1 | 0 | 0 |
| Skin Pain: face | 84 | 5 | 0 | 0 | 0 | 0 |
| Skin Pain: gums | 88 | 1 | 0 | 0 | 0 | 0 |
| Skin Pain: lip | 88 | 1 | 0 | 0 | 0 | 0 |
| Skin Pain: skin | 88 | 1 | 0 | 0 | 0 | 0 |
| Somnolence | 76 | 0 | 13 | 0 | 0 | 0 |
| Supra Arrhyth: Sinus Brady. | 85 | 4 | 0 | 0 | 0 | 0 |
| Supra Arrhyth: Sinus Tachy. | 60 | 26 | 3 | 0 | 0 | 0 |
| Supra Arrhyth: Supra Tachy. | 88 | 0 | 0 | 1 | 0 | 0 |
| Sweating | 79 | 9 | 1 | 0 | 0 | 0 |
| Syndromes-other | 87 | 0 | 0 | 2 | 0 | 0 |
| Taste alteration | 76 | 10 | 3 | 0 | 0 | 0 |
| Thrombosis/embolism | 87 | 0 | 0 | 2 | 0 | 0 |
| Tremor | 87 | 2 | 0 | 0 | 0 | 0 |
| Ulceration | 88 | 0 | 1 | 0 | 0 | 0 |
| Urinary frequency | 85 | 3 | 1 | 0 | 0 | 0 |
| Urinary retention | 88 | 0 | 1 | 0 | 0 | 0 |
| Vaginal discharge | 87 | 1 | 1 | 0 | 0 | 0 |
| Vaginal mucositis | 88 | 0 | 1 | 0 | 0 | 0 |
| Vaginitis | 87 | 0 | 2 | 0 | 0 | 0 |
| Valvular heart disease | 88 | 0 | 1 | 0 | 0 | 0 |
| Vent Arrhyth: Vent Tachy. | 88 | 1 | 0 | 0 | 0 | 0 |
| Vital capacity | 87 | 0 | 2 | 0 | 0 | 0 |
| Vomiting | 20 | 18 | 39 | 12 | 0 | 0 |
| Watery eye | 88 | 1 | 0 | 0 | 0 | 0 |
| Weight Loss | 68 | 15 | 6 | 0 | 0 | 0 |
| Weight gain | 81 | 7 | 1 | 0 | 0 | 0 |
| **MAX. GRADE ANY ADVERSE EVENT** | 2 | 1 | 0 | 16 | 70 | 0 |

## Response

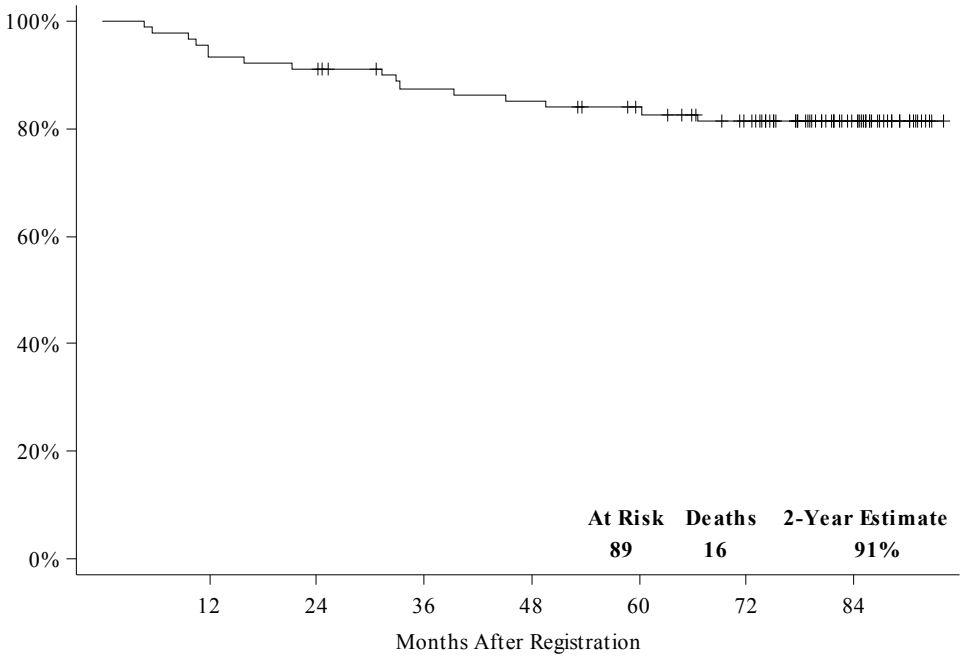
Data as of August 27, 2015

| | 2 cyc HDT +uto PBSCT | |
|---|---|---|
| | **N** | **%** |
| Complete Response | 18 | 21 |
| Partial Response | 10 | 12 |
| Unconfirmed Complete Response | 1 | 1 |
| Unconfirmed Partial Response | 1 | 1 |
| Stable/No Response | 25 | 30 |
| Increasing Disease | 5 | 6 |
| Assessment Inadequate | 24 | 29 |
| **Total** | 84 | 100 |


Progression-Free Survival
Data as of August 27, 2015
100%
80%
60%
40%
20%
0%
At Risk
89
Failed
40
2-Year Estimate
63%
12
24
36
48
60
72
84
Months After Registration

## Overall Survival

Data as of August 27, 2015



# S0601 Phase II

# Phase II Study of Combination Rituximab-CHOP and Bortezomib (Velcade®) Induction Therapy Followed By Bortezomib Maintenance Therapy For Patients With Newly Diagnosed Mantle Cell Lymphoma

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**Study Chairs:**
B Till, R Fisher, L Rimsza

**Statisticians:**
H Li, M LeBlanc

**Data Coordinator:**
J Jardine

**Date Activated:**
08/15/2006

**Date Closed:**
06/01/2008

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**Objectives**

To estimate the 2-year progression-free survival rate in newly diagnosed patients with mantle cell lymphoma treated with rituximab-CHOP-bortezomib induction therapy (R-CHOP-V) followed by bortezomib maintenance therapy (VM).

To estimate the response rate (complete, complete unconfirmed, and partial responses) in newly diagnosed patients with mantle cell lymphoma treated with this regimen.

To evaluate the toxicity of bortezomib maintenance therapy (VM) in newly diagnosed patients with mantle cell lymphoma.

To bank tissue and serum from patients with mantle cell lymphoma for future correlative studies.

**Patient Population**

Patients must have previously untreated Stage III, IV, or bulky Stage II mantle cell lymphoma. Patients must have bidimensionally measurable disease, with no CNS involvement.

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

Patients must be at least 18 years old and have a Zubrod performance status of 0, 1 or 2. Patients known to be HIV positive are not eligible.

**Accrual Goals**

Sixty eligible patients will be accrued to this study.

**Summary Statement**

This study was closed to initial registrations on June 1, 2008, having met its accrual goal. Sixty-eight patients registered to this study. Three patients are ineligible: two patients had incorrect histology based on the central pathology review and one patient had insufficient baseline documentation.

Sixty-one patients completed induction therapy as planned. Four patients went off induction treatment early, one due to progressive disease and three due to adverse events including fatigue and pneumonitis.

All 65 eligible patients have been assessed for toxicities during induction therapy. One patient died from possibly treatment-related complete cardiac atrioventricular block (coded as "Sudden death") on Day 20 after completion of induction therapy; this patient also experienced Grade 4 hematologic toxicities. Thirty-one patients experienced Grade 4 toxicities as maximum degree, primarily hematologic (30). Four patients experienced Grade 4 non-hematologic toxicities: hyperuricemia (1), febrile neutropenia (1), and fatigue (2).

This study was closed to registrations to maintenance therapy on February 25, 2009 after 50 patients had gone on to maintenance therapy. Three patients are ineligible because these patients were ineligible for the initial registration. Eighteen patients did not go

onto maintenance therapy due to the following reasons: progressive disease (5, one patient during induction and four between induction and maintenance), toxicity during induction (3), withdrawal to pursue autologous stem cell transplant (2), neuropathy (2), death that was non-cancer and non-treatment related (2), patient's refusal (2), and other reasons (2).

Twenty-seven patients completed maintenance therapy as planned and 20 patients went off maintenance therapy early due to the following reasons: Grade 3 fatigue (1), withdrew consent due to insurance issues (1), and progressive disease (18). The median duration of treatment on maintenance therapy was 20.7 months (range 14 days – 24.8 months).

Forty-seven eligible patients have been assessed for toxicities on maintenance therapy. One patient experienced Grade 4 lymphopenia. An additional seven patients experienced Grade 3 toxicities as maximum degree: one with fatigue and dyspnea, one with sinus infection, one with GGT, one with headache, one with urticaria, one with lymphopenia, and one with neuropathy-sensory.

Of 65 eligible patients assessed for response following induction therapy with R-CHOP-Velcade, 52 patients achieved an objective response to therapy, including 20 (31%) complete responses (CR), 23 (35%) partial responses (PR), and 9 (14%) unconfirmed complete responses (CRu). Nine additional patients (14%) did not have adequate assessments to determine response but were included in the denominator as non-responders. The estimated response rate during induction therapy is 80% (95% CI: 68.2 - 88.9%). Following maintenance therapy, seven partial responders to induction therapy plus one patient with inadequate assessment after induction converted to a CR/CRu, and one patient with stable disease converted to a PR, for an overall best response rate of 83% (57% CR/CRu and 26% PR) (95% CI: 71.7%, 91.2%) during the study. Median duration of response was 27.7 months, and median duration of CR/CRu was 30.3 months.

The median of follow-up among those last known alive is 7 years (range 2.1 - 8.0 years). Fifty-two patients have either progressed or died, with median progression-free survival (PFS) of 2.5 years (95% CI 1.9, 3.0). The Kaplan-Meier estimate of 2-year PFS is 62% (95% CI: 48.6%, 72.1%). There have been 27 deaths, with median overall survival (OS) not yet reached. The Kaplan-Meier estimate of 2-year OS is 85% (95% CI: 73.3%, 91.4%).

## Registration by Institution

| Institutions | Total Reg | Institutions | Total Reg |
|---|---|---|---|
| Rochester, Univ of | 11 | Breslin Cancer Ctr/Henry Ford Hosp | 1 |
| Heartland NCORP | 7 | Cincinnati MC, U of | 1 |
| Southeast COR NCORP | 7 | Hawaii MU-NCORP | 1 |
| Wichita NCORP | 6 | Interlakes Foundatn/Rochester, Univ of | 1 |
| CRC West MI NCORP | 4 | Kansas City NCORP | 1 |
| Dayton NCORP | 4 | Kansas, U of | 1 |
| Montana NCORP | 4 | McKay-Dee Hospital/Intermountain MC | 1 |
| Arizona MC, U of | 3 | Orange Reg Med Ctr/Columbia University | 1 |
| UF Cancer Center/Arkansas, U of | 3 | PCRC NCORP | 1 |
| Columbus NCORP | 2 | St Luke's Mt State/PCRC NCORP | 1 |
| Poudre Valley Hosp/Colorado, U of | 2 | Upstate Carolina | 1 |
| Prov Portland MC/PCRC NCORP | 2 | Utah Valley Reg Med/Intermountain MC | 1 |
| Boston Medical Ctr | 1 | **Total (25 Institutions)** | **68** |

## Registration, Eligibility, and Evaluability

Initial Registration

Data as of August 27, 2015

| | R-CHOP - Velcade |
|---|---|
| NUMBER REGISTERED | 68 |
| INELIGIBLE | 3 |
| Insufficient Documentation | 1 |
| Irreversible | 1 |
| ELIGIBLE | 65 |
| RESPONSE ASSESSMENT | |
| Determinable | 56 |
| Not Determinable | 9 |
| ADVERSE EVENT ASSESSMENT | |
| Evaluable | 65 |

## Patient Characteristics

Initial Registration

Data as of August 27, 2015

| | R-CHOP - Velcade (n=65) | |
|---|---|---|
| AGE | | |
| Median | 61.0 | |
| Minimum | 36.5 | |
| Maximum | 85.1 | |
| SEX | | |
| Males | 52 | 80% |
| Females | 13 | 20% |
| HISPANIC | | |
| Yes | 1 | 2% |
| No | 51 | 78% |
| Unknown | 13 | 20% |
| RACE | | |
| White | 61 | 94% |
| Black | 2 | 3% |
| Asian | 1 | 2% |
| Pacific Islander | 1 | 2% |
| SYMPTOMS | | |
| A | 47 | 72% |
| B | 18 | 28% |

| | R-CHOP - Velcade (n=65) | |
|---|---|---|
| BULKY DISEASE | | |
| N | 55 | 85% |
| Y | 10 | 15% |
| BONE MARROW BIOPSY | | |
| NEG | 15 | 23% |
| POS | 50 | 77% |
| STAGE OF DISEASE | | |
| II | 1 | 2% |
| III | 10 | 15% |
| IV | 54 | 83% |
| PERFORMANCE STATUS | | |
| 0 | 39 | 60% |
| 1 | 24 | 37% |
| 2 | 2 | 3% |

## Treatment Summary

Induction

Data as of August 27, 2015

| | R-CHOP - Velcade |
|---|---|
| NUMBER ON PROTOCOL TREATMENT | 0 |
| NUMBER OFF PROTOCOL TREATMENT | 65 |
| REASON OFF TREATMENT | |
| Treatment completed as planned | 61 |
| Adverse Event or side effects | 3 |
| Refusal unrelated to adverse event | 0 |
| Progression/relapse | 1 |
| Death | 0 |
| Other - not protocol specified | 0 |
| Reason under review | 0 |
| MAJOR PROTOCOL DEVIATIONS | 0 |

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

Induction

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of August 27, 2015

| | R-CHOP - Velcade (n=65) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| ALT | 59 | 5 | 1 | 0 | 0 | 0 |
| AST | 59 | 6 | 0 | 0 | 0 | 0 |
| Acne | 64 | 1 | 0 | 0 | 0 | 0 |
| Alkaline phosphatase | 60 | 5 | 0 | 0 | 0 | 0 |
| Allergic reaction | 60 | 3 | 2 | 0 | 0 | 0 |
| Allergy-other | 64 | 1 | 0 | 0 | 0 | 0 |
| Alopecia | 27 | 11 | 27 | 0 | 0 | 0 |
| Anorexia | 47 | 11 | 6 | 1 | 0 | 0 |
| Bilirubin | 63 | 2 | 0 | 0 | 0 | 0 |
| Blurred vision | 56 | 8 | 1 | 0 | 0 | 0 |
| Bronchospasm | 64 | 0 | 1 | 0 | 0 | 0 |
| Bruising | 63 | 2 | 0 | 0 | 0 | 0 |
| Cardiac Arrhythmia-other | 64 | 0 | 1 | 0 | 0 | 0 |
| Cardiac General-other | 64 | 1 | 0 | 0 | 0 | 0 |
| Cardio. Pain: cardiac/heart | 64 | 1 | 0 | 0 | 0 | 0 |
| Coagulation-other | 64 | 1 | 0 | 0 | 0 | 0 |
| Cognitive disturbance | 64 | 1 | 0 | 0 | 0 | 0 |
| Constipation | 33 | 21 | 10 | 1 | 0 | 0 |
| Constitutional Symptoms-other | 63 | 2 | 0 | 0 | 0 | 0 |
| Cough | 53 | 10 | 2 | 0 | 0 | 0 |
| Creatinine | 58 | 5 | 2 | 0 | 0 | 0 |
| Cystitis | 63 | 0 | 2 | 0 | 0 | 0 |
| Cytokine release syndrome | 63 | 0 | 2 | 0 | 0 | 0 |
| Decubitus | 64 | 0 | 1 | 0 | 0 | 0 |
| Dehydration | 60 | 0 | 4 | 1 | 0 | 0 |
| Dermatology-other | 64 | 0 | 1 | 0 | 0 | 0 |
| Diarrhea | 52 | 8 | 2 | 3 | 0 | 0 |
| Diplopia | 64 | 1 | 0 | 0 | 0 | 0 |
| Distension | 63 | 0 | 2 | 0 | 0 | 0 |
| Dizziness | 57 | 6 | 1 | 1 | 0 | 0 |
| Dry eye | 62 | 2 | 1 | 0 | 0 | 0 |
| Dry mouth | 62 | 3 | 0 | 0 | 0 | 0 |
| Dry skin | 62 | 3 | 0 | 0 | 0 | 0 |
| Dysphagia | 64 | 1 | 0 | 0 | 0 | 0 |
| Dyspnea | 58 | 4 | 2 | 1 | 0 | 0 |
| Ear Inf, 0-2 ANC: ext. ear | 64 | 0 | 0 | 1 | 0 | 0 |
| Ear Inf, 0-2 ANC: mid. ear | 64 | 0 | 1 | 0 | 0 | 0 |
| Ear Pain: external ear | 64 | 1 | 0 | 0 | 0 | 0 |
| Edema-limb | 54 | 9 | 1 | 1 | 0 | 0 |
| Erythema multiforme | 64 | 0 | 1 | 0 | 0 | 0 |
| Fatigue | 14 | 28 | 17 | 4 | 2 | 0 |
| Febrile neutropenia | 53 | 0 | 0 | 11 | 1 | 0 |
| Fever | 60 | 4 | 1 | 0 | 0 | 0 |
| Flashing lights | 64 | 1 | 0 | 0 | 0 | 0 |

| | R-CHOP - Velcade (n=65) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Flatulence | 64 | 1 | 0 | 0 | 0 | 0 |
| Flushing | 62 | 2 | 1 | 0 | 0 | 0 |
| GGT | 63 | 1 | 0 | 1 | 0 | 0 |
| GI Inf, 0-2 ANC: gums | 64 | 0 | 0 | 1 | 0 | 0 |
| GI Inf, 3-4 ANC: abdomen, NOS | 64 | 0 | 1 | 0 | 0 | 0 |
| GI Inf, 3-4 ANC: gums | 63 | 0 | 1 | 1 | 0 | 0 |
| GI Pain: abdomen | 58 | 5 | 2 | 0 | 0 | 0 |
| GI Pain: dental | 63 | 2 | 0 | 0 | 0 | 0 |
| GI Pain: oral cavity | 64 | 0 | 1 | 0 | 0 | 0 |
| GI Pain: rectum | 64 | 0 | 1 | 0 | 0 | 0 |
| GI Pain: stomach | 64 | 1 | 0 | 0 | 0 | 0 |
| GI-other | 63 | 1 | 1 | 0 | 0 | 0 |
| GU Inf, 0-2 ANC: UTI | 64 | 0 | 1 | 0 | 0 | 0 |
| Gastritis | 64 | 1 | 0 | 0 | 0 | 0 |
| Heartburn | 55 | 6 | 4 | 0 | 0 | 0 |
| Hemoglobin | 17 | 27 | 18 | 3 | 0 | 0 |
| Hemorrhage-other | 63 | 2 | 0 | 0 | 0 | 0 |
| Hemorrhoids | 62 | 3 | 0 | 0 | 0 | 0 |
| Hiccoughs | 61 | 1 | 3 | 0 | 0 | 0 |
| Hot flashes | 63 | 2 | 0 | 0 | 0 | 0 |
| Hypercalcemia | 64 | 1 | 0 | 0 | 0 | 0 |
| Hyperglycemia | 44 | 15 | 3 | 3 | 0 | 0 |
| Hyperkalemia | 64 | 0 | 1 | 0 | 0 | 0 |
| Hypertension | 63 | 0 | 2 | 0 | 0 | 0 |
| Hyperuricemia | 63 | 1 | 0 | 0 | 1 | 0 |
| Hypoalbuminemia | 57 | 3 | 4 | 1 | 0 | 0 |
| Hypocalcemia | 57 | 5 | 2 | 1 | 0 | 0 |
| Hypoglycemia | 64 | 1 | 0 | 0 | 0 | 0 |
| Hypokalemia | 61 | 2 | 0 | 2 | 0 | 0 |
| Hypomagnesemia | 63 | 2 | 0 | 0 | 0 | 0 |
| Hyponatremia | 58 | 7 | 0 | 0 | 0 | 0 |
| Hypophosphatemia | 64 | 0 | 0 | 1 | 0 | 0 |
| Hypotension | 61 | 0 | 4 | 0 | 0 | 0 |
| Hypoxia | 64 | 0 | 0 | 1 | 0 | 0 |
| Infection-other | 62 | 0 | 2 | 1 | 0 | 0 |
| Insomnia | 50 | 10 | 5 | 0 | 0 | 0 |
| Involuntary movement | 63 | 2 | 0 | 0 | 0 | 0 |
| Leukocytes | 20 | 6 | 13 | 16 | 10 | 0 |
| Lung Hemorrhage: nose | 64 | 1 | 0 | 0 | 0 | 0 |
| Lung Inf, 0-2 ANC: lung | 64 | 0 | 0 | 1 | 0 | 0 |
| Lung Inf, 0-2 ANC: pharynx | 64 | 0 | 1 | 0 | 0 | 0 |
| Lung Inf, 0-2 ANC: sinus | 64 | 0 | 1 | 0 | 0 | 0 |
| Lung Inf, 3-4 ANC: lung | 62 | 0 | 0 | 3 | 0 | 0 |
| Lung Inf, 3-4 ANC: sinus | 63 | 0 | 1 | 1 | 0 | 0 |
| Lung Inf, Unk ANC: up. airway | 64 | 0 | 1 | 0 | 0 | 0 |
| Lung Pain: chest/thorax | 64 | 1 | 0 | 0 | 0 | 0 |
| Lymphopenia | 38 | 2 | 10 | 11 | 4 | 0 |
| Memory impairment | 64 | 0 | 1 | 0 | 0 | 0 |
| Metabolic/Lab-other | 58 | 5 | 2 | 0 | 0 | 0 |
| Mood alteration: agitation | 63 | 2 | 0 | 0 | 0 | 0 |
| Mood alteration: anxiety | 61 | 2 | 2 | 0 | 0 | 0 |

| | R-CHOP - Velcade (n=65) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Mood alteration: depression | 61 | 3 | 1 | 0 | 0 | 0 |
| Mucositis, clin: oral cavity | 61 | 2 | 2 | 0 | 0 | 0 |
| Mucositis, clin: pharynx | 64 | 1 | 0 | 0 | 0 | 0 |
| Mucositis, funct: oral cav. | 55 | 5 | 4 | 1 | 0 | 0 |
| Muscle weakness: low. extrem. | 63 | 1 | 1 | 0 | 0 | 0 |
| Muscle weakness: whole body | 60 | 3 | 1 | 1 | 0 | 0 |
| Musculo. Pain: back | 62 | 2 | 1 | 0 | 0 | 0 |
| Musculo. Pain: bone | 63 | 1 | 1 | 0 | 0 | 0 |
| Musculo. Pain: joint | 53 | 10 | 2 | 0 | 0 | 0 |
| Musculo. Pain: limb | 64 | 1 | 0 | 0 | 0 | 0 |
| Musculo. Pain: muscle | 52 | 12 | 1 | 0 | 0 | 0 |
| Musculo. Pain: neck | 64 | 1 | 0 | 0 | 0 | 0 |
| Musculoskeletal-other | 64 | 0 | 1 | 0 | 0 | 0 |
| Nail changes | 64 | 1 | 0 | 0 | 0 | 0 |
| Nausea | 29 | 26 | 7 | 3 | 0 | 0 |
| Neuro Inf, 0-2 ANC: periph nrv | 64 | 0 | 0 | 1 | 0 | 0 |
| Neuro Pain: head/headache | 60 | 4 | 1 | 0 | 0 | 0 |
| Neurology-other | 64 | 1 | 0 | 0 | 0 | 0 |
| Neurop: mot-jaw; sens-facial | 64 | 0 | 0 | 1 | 0 | 0 |
| Neuropathy-motor | 61 | 0 | 2 | 2 | 0 | 0 |
| Neuropathy-sensory | 26 | 31 | 6 | 2 | 0 | 0 |
| Neutrophils | 24 | 2 | 5 | 9 | 25 | 0 |
| Ocular-other | 63 | 2 | 0 | 0 | 0 | 0 |
| Pain-other | 64 | 0 | 1 | 0 | 0 | 0 |
| Pain: NOS | 64 | 1 | 0 | 0 | 0 | 0 |
| Palpitations | 63 | 2 | 0 | 0 | 0 | 0 |
| Pericardial effusion | 64 | 1 | 0 | 0 | 0 | 0 |
| Phlebitis | 64 | 0 | 1 | 0 | 0 | 0 |
| Photophobia | 64 | 1 | 0 | 0 | 0 | 0 |
| Platelets | 38 | 11 | 5 | 5 | 6 | 0 |
| Pleural effusion | 64 | 0 | 1 | 0 | 0 | 0 |
| Pneumonitis | 64 | 0 | 0 | 1 | 0 | 0 |
| Pruritus | 63 | 1 | 0 | 1 | 0 | 0 |
| Pulmonary-other | 64 | 1 | 0 | 0 | 0 | 0 |
| Rash | 60 | 3 | 2 | 0 | 0 | 0 |
| Renal failure | 64 | 0 | 0 | 1 | 0 | 0 |
| Rhinitis | 59 | 4 | 2 | 0 | 0 | 0 |
| Rigors/chills | 54 | 6 | 5 | 0 | 0 | 0 |
| Salivary gland changes | 64 | 1 | 0 | 0 | 0 | 0 |
| Skin Inf, 0-2 ANC: lip/perior | 64 | 0 | 1 | 0 | 0 | 0 |
| Skin Inf, 3-4 ANC: lip/perior. | 64 | 0 | 1 | 0 | 0 | 0 |
| Skin Inf, 3-4 ANC: skin | 63 | 0 | 2 | 0 | 0 | 0 |
| Skin Pain: scalp | 64 | 0 | 1 | 0 | 0 | 0 |
| Sudden death | 64 | 0 | 0 | 0 | 0 | 1 |
| Supra Arrhyth: Sinus Tachy. | 64 | 1 | 0 | 0 | 0 | 0 |
| Sweating | 60 | 3 | 2 | 0 | 0 | 0 |
| Syncope | 63 | 0 | 0 | 2 | 0 | 0 |
| Taste alteration | 51 | 10 | 4 | 0 | 0 | 0 |
| Thrombosis/embolism | 63 | 0 | 1 | 1 | 0 | 0 |
| Thrombosis/embolism (vasc acc) | 64 | 0 | 0 | 1 | 0 | 0 |
| Tremor | 64 | 1 | 0 | 0 | 0 | 0 |

| | R-CHOP - Velcade (n=65) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Urinary frequency | 59 | 6 | 0 | 0 | 0 | 0 |
| Urticaria | 62 | 0 | 3 | 0 | 0 | 0 |
| Vascular-other | 64 | 0 | 1 | 0 | 0 | 0 |
| Voice changes | 63 | 2 | 0 | 0 | 0 | 0 |
| Vomiting | 51 | 10 | 3 | 1 | 0 | 0 |
| Watery eye | 59 | 3 | 3 | 0 | 0 | 0 |
| Weight Loss | 57 | 3 | 5 | 0 | 0 | 0 |
| Weight gain | 63 | 2 | 0 | 0 | 0 | 0 |
| **MAX. GRADE ANY ADVERSE EVENT** | 2 | 2 | 11 | 18 | 31 | 1 |

## Response

Induction

Data as of August 27, 2015

| | R-CHOP -Velcade | |
|---|---|---|
| | **N** | **%** |
| Complete Response | 20 | 31 |
| Partial Response | 23 | 35 |
| Unconfirmed Complete Response | 9 | 14 |
| Unconfirmed Partial Response | 0 | 0 |
| Stable/No Response | 3 | 5 |
| Increasing Disease | 1 | 2 |
| Assessment Inadequate | 9 | 14 |
| **Total** | 65 | 100 |

## Registration, Eligibility, and Evaluability

Maintenance

Data as of August 27, 2015

| | Velcade Maintenance (VM) |
|---|---|
| NUMBER REGISTERED | 50 |
| INELIGIBLE | 3 |
| Insufficient Documentation | 1 |
| Irreversible | 1 |
| ELIGIBLE | 47 |
| RESPONSE ASSESSMENT | |
| Determinable | 46 |
| Not Determinable | 1 |
| ADVERSE EVENT ASSESSMENT | |
| Evaluable | 47 |

## Treatment Summary

Maintenance

Data as of August 27, 2015

| | Velcade Maintenance (VM) |
|---|---|
| NUMBER ON PROTOCOL TREATMENT | 0 |
| NUMBER OFF PROTOCOL TREATMENT | 47 |
| REASON OFF TREATMENT | |
| Treatment completed as planned | 27 |
| Adverse Event or side effects | 1 |
| Refusal unrelated to adverse event | 1 |
| Progression/relapse | 18 |
| Death | 0 |
| Other - not protocol specified | 0 |
| Reason under review | 0 |
| MAJOR PROTOCOL DEVIATIONS | 0 |

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

Maintenance

Adverse Events Unlikely or Not Related to Treatment Excluded

Data as of August 27, 2015

| | Velcade Maintenance (VM) (n=47) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| ALT | 46 | 1 | 0 | 0 | 0 | 0 |
| AST | 46 | 1 | 0 | 0 | 0 | 0 |
| Acne | 45 | 0 | 2 | 0 | 0 | 0 |
| Alkaline phosphatase | 45 | 2 | 0 | 0 | 0 | 0 |
| Alopecia | 45 | 2 | 0 | 0 | 0 | 0 |
| Anorexia | 43 | 3 | 1 | 0 | 0 | 0 |
| Arthritis | 46 | 0 | 1 | 0 | 0 | 0 |
| Ataxia | 46 | 1 | 0 | 0 | 0 | 0 |
| Auditory/Ear-other | 45 | 1 | 1 | 0 | 0 | 0 |
| Bilirubin | 42 | 5 | 0 | 0 | 0 | 0 |
| Bruising | 46 | 1 | 0 | 0 | 0 | 0 |
| CPK | 46 | 1 | 0 | 0 | 0 | 0 |
| Constipation | 40 | 5 | 2 | 0 | 0 | 0 |
| Cough | 42 | 4 | 1 | 0 | 0 | 0 |
| Creatinine | 42 | 4 | 1 | 0 | 0 | 0 |
| Cytokine release syndrome | 46 | 1 | 0 | 0 | 0 | 0 |
| Diarrhea | 42 | 4 | 1 | 0 | 0 | 0 |
| Distension | 46 | 0 | 1 | 0 | 0 | 0 |
| Dizziness | 45 | 2 | 0 | 0 | 0 | 0 |
| Dry mouth | 46 | 1 | 0 | 0 | 0 | 0 |
| Dry skin | 43 | 3 | 1 | 0 | 0 | 0 |
| Dyspnea | 43 | 1 | 2 | 1 | 0 | 0 |

| | Velcade Maintenance (VM) (n=47) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Ear Inf, Unk ANC: ext. ear | 46 | 0 | 1 | 0 | 0 | 0 |
| Edema-limb | 44 | 3 | 0 | 0 | 0 | 0 |
| Eye Pain: eye | 46 | 1 | 0 | 0 | 0 | 0 |
| Fatigue | 24 | 18 | 4 | 1 | 0 | 0 |
| GGT | 46 | 0 | 0 | 1 | 0 | 0 |
| GI Hemorrhage: upper GI | 46 | 1 | 0 | 0 | 0 | 0 |
| GI Pain: abdomen | 44 | 2 | 1 | 0 | 0 | 0 |
| GI-other | 45 | 2 | 0 | 0 | 0 | 0 |
| Gastritis | 46 | 0 | 1 | 0 | 0 | 0 |
| Heartburn | 45 | 1 | 1 | 0 | 0 | 0 |
| Hemoglobin | 33 | 13 | 1 | 0 | 0 | 0 |
| Hyperglycemia | 35 | 11 | 1 | 0 | 0 | 0 |
| Hyperkalemia | 46 | 1 | 0 | 0 | 0 | 0 |
| Hypermagnesemia | 46 | 1 | 0 | 0 | 0 | 0 |
| Hypertension | 46 | 1 | 0 | 0 | 0 | 0 |
| Hyperuricemia | 46 | 1 | 0 | 0 | 0 | 0 |
| Hypoalbuminemia | 45 | 2 | 0 | 0 | 0 | 0 |
| Hypophosphatemia | 46 | 1 | 0 | 0 | 0 | 0 |
| Infection-other | 46 | 1 | 0 | 0 | 0 | 0 |
| Insomnia | 44 | 3 | 0 | 0 | 0 | 0 |
| Leukocytes | 34 | 9 | 4 | 0 | 0 | 0 |
| Lung Inf, 0-2 ANC: bronch. | 46 | 0 | 1 | 0 | 0 | 0 |
| Lung Inf, 0-2 ANC: nose | 46 | 0 | 1 | 0 | 0 | 0 |
| Lung Inf, 0-2 ANC: sinus | 45 | 0 | 1 | 1 | 0 | 0 |
| Lung Inf, 0-2 ANC: up. airway | 43 | 0 | 4 | 0 | 0 | 0 |
| Lymphopenia | 36 | 3 | 6 | 1 | 1 | 0 |
| Metabolic/Lab-other | 46 | 1 | 0 | 0 | 0 | 0 |
| Mood alteration: depression | 46 | 1 | 0 | 0 | 0 | 0 |
| Mucositis, funct: oral cav. | 46 | 0 | 1 | 0 | 0 | 0 |
| Muscle weakness: low. extrem. | 46 | 0 | 1 | 0 | 0 | 0 |
| Musculo. Pain: back | 46 | 0 | 1 | 0 | 0 | 0 |
| Musculo. Pain: joint | 42 | 4 | 1 | 0 | 0 | 0 |
| Musculo. Pain: muscle | 42 | 5 | 0 | 0 | 0 | 0 |
| Nail changes | 45 | 1 | 1 | 0 | 0 | 0 |
| Nausea | 41 | 4 | 2 | 0 | 0 | 0 |
| Neuro Pain: head/headache | 41 | 4 | 1 | 1 | 0 | 0 |
| Neuropathy-motor | 45 | 2 | 0 | 0 | 0 | 0 |
| Neuropathy-sensory | 13 | 17 | 16 | 1 | 0 | 0 |
| Neutrophils | 44 | 0 | 3 | 0 | 0 | 0 |
| Ocular-other | 46 | 1 | 0 | 0 | 0 | 0 |
| Pain-other | 46 | 1 | 0 | 0 | 0 | 0 |
| Petechiae | 46 | 1 | 0 | 0 | 0 | 0 |
| Platelets | 29 | 16 | 2 | 0 | 0 | 0 |
| Pruritus | 44 | 3 | 0 | 0 | 0 | 0 |
| Pulmonary hypertension | 46 | 1 | 0 | 0 | 0 | 0 |
| Rash | 42 | 2 | 3 | 0 | 0 | 0 |
| Rhinitis | 45 | 1 | 1 | 0 | 0 | 0 |
| Rigors/chills | 44 | 2 | 1 | 0 | 0 | 0 |
| Skin Inf, 0-2 ANC: skin | 46 | 0 | 1 | 0 | 0 | 0 |
| Skin Pain: skin | 46 | 1 | 0 | 0 | 0 | 0 |
| Sweating | 45 | 2 | 0 | 0 | 0 | 0 |

| | Velcade Maintenance (VM) (n=47) Grade | | | | | |
|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** |
| Taste alteration | 44 | 3 | 0 | 0 | 0 | 0 |
| Teeth | 46 | 0 | 1 | 0 | 0 | 0 |
| Urinary frequency | 46 | 1 | 0 | 0 | 0 | 0 |
| Urinary retention | 46 | 1 | 0 | 0 | 0 | 0 |
| Urticaria | 45 | 0 | 1 | 1 | 0 | 0 |
| Watery eye | 46 | 1 | 0 | 0 | 0 | 0 |
| Weight Loss | 46 | 1 | 0 | 0 | 0 | 0 |
| Weight gain | 45 | 2 | 0 | 0 | 0 | 0 |
| **MAX. GRADE ANY ADVERSE EVENT** | 4 | 11 | 24 | 7 | 1 | 0 |

## Overall Best Response

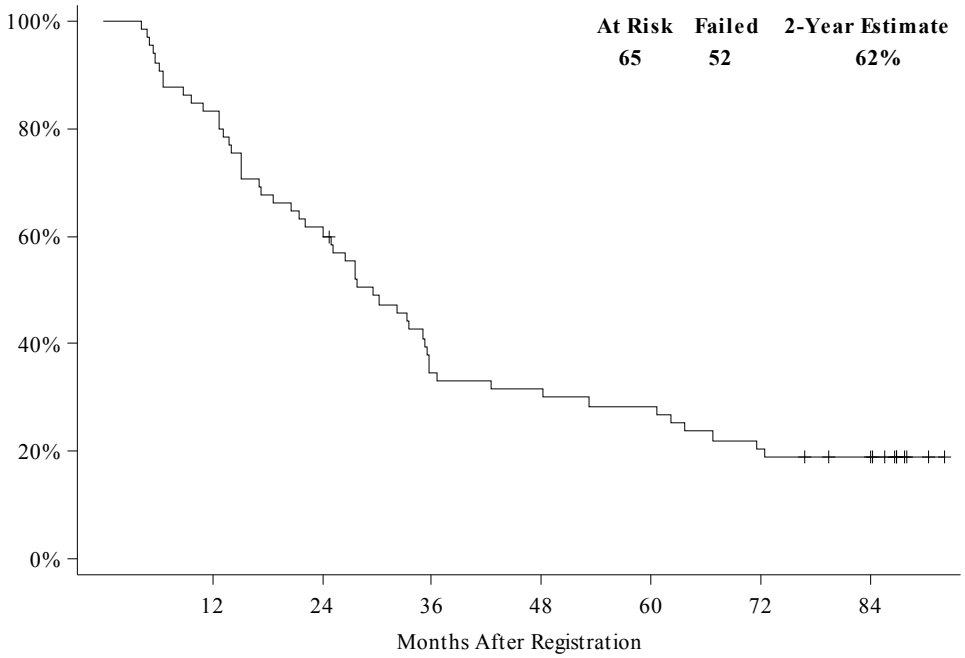
Induction followed by Maintenance

Data as of August 27, 2015

| | VelcadeMaintenance(VM) | |
|---|---|---|
| | **N** | **%** |
| Complete Response | 26 | 40 |
| Partial Response | 17 | 26 |
| Unconfirmed Complete Response | 11 | 17 |
| Unconfirmed Partial Response | 0 | 0 |
| Stable/No Response | 3 | 5 |
| Increasing Disease | 1 | 2 |
| Assessment Inadequate | 7 | 11 |
| **Total** | 65 | 100 |

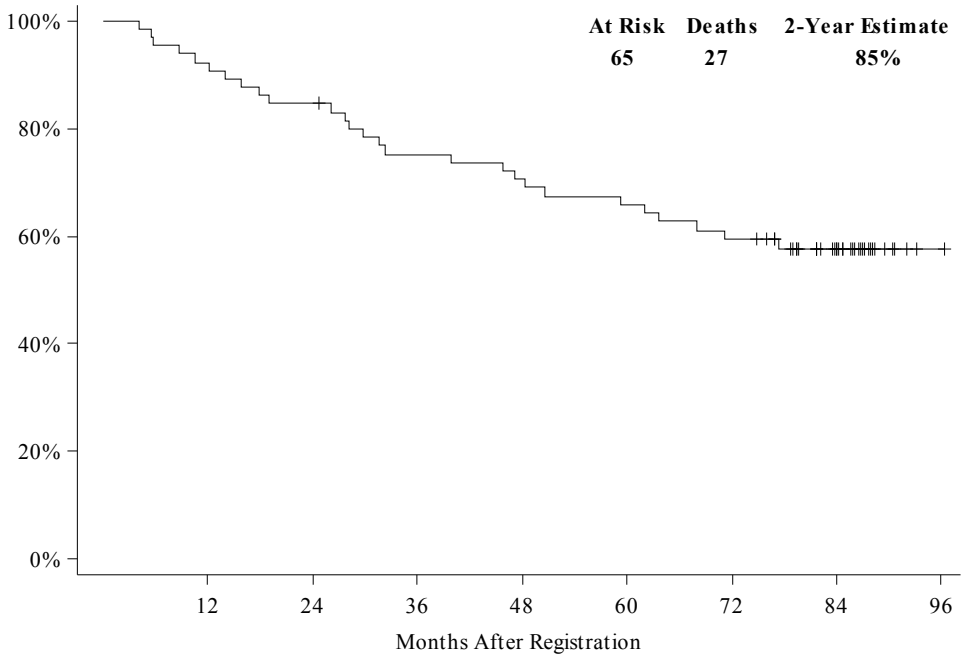
## Progression-Free Survival

Data as of August 27, 2015



## Overall Survival

Data as of August 27, 2015



# 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, T Miller, S Park (Alliance), L Swinnen (ECOG-ACRIN)

**Statisticians:**
M LeBlanc, H Li

**Data Coordinator:**
J Jardine

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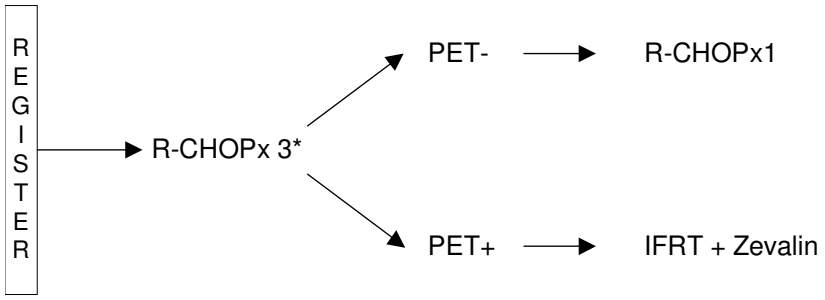
## SCHEMA




*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 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 June 30, 2015, 125 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 incorrect histology and one due to no required baseline specimens submitted for pathology review.

One hundred fifteen 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 19 patients experienced Grade 4 hematologic toxicities, two of whom also experienced Grade 4 non-hematologic toxicities: febrile neutropenia and hyponatremia (1 each).

One hundred nine patients have been registered to PET-directed therapy, 98 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 89 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. Eight additional patients on this arm experienced treatment-related Grade 4 hematologic toxicities, one of whom also experienced Grade 4 secondary leukemia. One of the 11 patients assessed for toxicities on the IFRT + Zevalin arm experienced Grade 4 thrombocytopenia.

## Registration by Institution

Initial Registration

Registrations ending June 30, 2015

| Institutions | Total Reg | Institutions | Total Reg |
|---|---|---|---|
| Alliance | 29 | Loyola University | 3 |
| Rochester, Univ of | 25 | St Luke's Mt State/PCRC NCORP | 2 |
| ECOG-ACRIN | 17 | Virginia Mason MC/Northwest NCORP | 2 |
| Michigan CRC NCORP | 8 | City of Hope Med Ctr | 1 |
| Upstate Carolina | 7 | Fred Hutchinson CRC | 1 |
| Arizona MC, U of | 6 | Greenville NCORP | 1 |
| Yale University | 5 | Montana NCORP | 1 |
| Kansas City NCORP | 4 | Northwest NCORP | 1 |
| Wichita NCORP | 4 | NRG | 1 |
| Hawaii MU-NCORP | 3 | Southeast COR NCORP | 1 |
| Kentucky, U of | 3 | **Total (21 Institutions)** | **125** |

## Registration, Eligibility, and Evaluability

Initial Registration

Registrations ending June 30, 2015; Data as of July 27, 2015

| | TOTAL | R-CHOP x 3 | R-CHOP x 6 |
|---|---|---|---|
| NUMBER REGISTERED | 125 | 124 | 1 |
| INELIGIBLE | 2 | 2 | 0 |
| Insufficient Documentation | 1 | 1 | 0 |
| Irreversible | 1 | 1 | 0 |
| ELIGIBLE | 123 | 122 | 1 |
| Analyzable, Pend. Elig. | 116 | 115 | 1 |
| RESPONSE ASSESSMENT | | | |
| Determinable | 97 | 96 | 1 |
| Not Determinable | 2 | 2 | 0 |
| Too Early | 24 | 24 | 0 |
| ADVERSE EVENT ASSESSMENT | | | |
| Evaluable | 115 | 114 | 1 |
| Too Early | 8 | 8 | 0 |

## Patient Characteristics

Initial Registration

Registrations ending June 30, 2015; Data as of July 27, 2015

| | R-CHOP x 3 (n=122) | | R-CHOP x 6 (n=1) | |
|---|---|---|---|---|
| AGE | | | | |
| Median | 61.8 | | 74.3 | |
| Minimum | 18.5 | | 74.3 | |
| Maximum | 85.5 | | 74.3 | |
| SEX | | | | |
| Males | 64 | 52% | 0 | 0% |
| Females | 58 | 48% | 1 | 100% |
| HISPANIC | | | | |
| Yes | 5 | 4% | 0 | 0% |
| No | 112 | 92% | 1 | 100% |
| Unknown | 5 | 4% | 0 | 0% |
| RACE | | | | |
| White | 106 | 87% | 1 | 100% |
| Black | 6 | 5% | 0 | 0% |
| Asian | 8 | 7% | 0 | 0% |
| Native American | 1 | 1% | 0 | 0% |
| Unknown | 1 | 1% | 0 | 0% |
| PET UPSTAGED | | | | |
| Yes | 0 | 0% | 1 | 100% |
| No | 122 | 100% | 0 | 0% |

## Treatment Summary

Initial Registration

Registrations ending June 30, 2015; Data as of July 27, 2015

| | TOTAL | R-CHOP x 3 | R-CHOP x 6 |
|---|---|---|---|
| NUMBER ON PROTOCOL TREATMENT | 17 | 17 | 0 |
| NUMBER OFF PROTOCOL TREATMENT | 106 | 105 | 1 |
| REASON OFF TREATMENT | | | |
| Treatment completed as planned | 103 | 102 | 1 |
| Adverse Event or side effects | 1 | 1 | 0 |
| Refusal unrelated to adverse event | 0 | 0 | 0 |
| Other - not protocol specified | 1 | 1 | 0 |
| Reason under review | 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 June 30, 2015; Data as of July 27, 2015

| | R-CHOP x 3 (n=114) Grade | | | | | | R-CHOP x 6 (n=1) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| ALT increased | 100 | 12 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| AST increased | 106 | 8 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Abdominal pain | 112 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Agitation | 112 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Alkaline phosphatase increased | 109 | 4 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Allergic reaction | 108 | 1 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Alopecia | 67 | 16 | 31 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Anal hemorrhage | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Anemia | 59 | 41 | 10 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Anorexia | 99 | 11 | 4 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Anxiety | 109 | 1 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Arthralgia | 108 | 5 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Back pain | 110 | 3 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Bloating | 112 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Blood bilirubin increased | 112 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Blurred vision | 112 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Bone pain | 105 | 5 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| CD4 lymphocytes decreased | 111 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Chills | 108 | 5 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Concentration impairment | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Confusion | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Constipation | 71 | 34 | 9 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Cough | 108 | 4 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Creatinine increased | 111 | 3 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dehydration | 108 | 1 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Depression | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Diarrhea | 101 | 9 | 1 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dizziness | 108 | 6 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dry mouth | 107 | 7 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dry skin | 114 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Dysgeusia | 102 | 7 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dyspepsia | 102 | 6 | 6 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Dyspnea | 103 | 8 | 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Edema face | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Edema limbs | 106 | 6 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Endocrine disorders-Other | 113 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Epistaxis | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Eye disorders - Other, specify | 112 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Eye pain | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Fatigue | 35 | 62 | 15 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Febrile neutropenia | 103 | 0 | 0 | 9 | 2 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Fever | 103 | 9 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Flatulence | 112 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Flu like symptoms | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |

| | R-CHOP x 3 (n=114) Grade | | | | | | R-CHOP x 6 (n=1) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| GERD | 109 | 3 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| GI disorders-Other, specify | 112 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Gastritis | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Generalized muscle weakness | 106 | 6 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Headache | 106 | 8 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hematuria | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hemoglobin increased | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hemorrhoids | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hiccups | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hoarseness | 113 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Hot flashes | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hyperglycemia | 98 | 9 | 4 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hyperhidrosis | 112 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hyperkalemia | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypernatremia | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypertension | 109 | 2 | 0 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypoalbuminemia | 103 | 5 | 6 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Hypocalcemia | 104 | 7 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypokalemia | 108 | 4 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypomagnesemia | 110 | 4 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hyponatremia | 109 | 4 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypophosphatemia | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Hypotension | 110 | 2 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Infusion related reaction | 101 | 2 | 11 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Injection site reaction | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Insomnia | 99 | 9 | 6 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Localized edema | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lower GI hemorrhage | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lung infection | 113 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lymphocyte count decreased | 68 | 18 | 14 | 12 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Memory impairment | 112 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Mucositis oral | 96 | 13 | 4 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Myalgia | 109 | 5 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Nasal congestion | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Nausea | 60 | 40 | 13 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Neck pain | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Neutrophil count decreased | 74 | 4 | 7 | 9 | 20 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Oral pain | 113 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Pain | 110 | 0 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Paresthesia | 112 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Peripheral motor neuropathy | 111 | 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Peripheral nerve infection | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Peripheral sensory neuropathy | 92 | 18 | 3 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Phlebitis | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Platelet count decreased | 96 | 12 | 3 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Proteinuria | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Pruritus | 111 | 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Rash acneiform | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Rash maculo-papular | 108 | 5 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Renal/urinary disorders-Other | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Repro system/breast ds-Oth | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |

| | R-CHOP x 3 (n=114) Grade | | | | | | R-CHOP x 6 (n=1) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| Resp/thoracic/mediastinal ds | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Scalp pain | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sepsis | 113 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sinus tachycardia | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sinusitis | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Skin infection | 111 | 2 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Skin/subq tissue ds-Other | 111 | 3 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Sore throat | 109 | 4 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Stomach pain | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Superficial thrombophlebitis | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Thromboembolic event | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Upper respiratory infection | 108 | 0 | 6 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urinary frequency | 106 | 7 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urinary incontinence | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urinary tract infection | 105 | 0 | 6 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Urine discoloration | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Vaginal infection | 113 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Voice alteration | 112 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Vomiting | 103 | 7 | 4 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Watering eyes | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Weight gain | 112 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Weight loss | 108 | 5 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Wheezing | 113 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| White blood cell decreased | 72 | 13 | 8 | 10 | 11 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| **MAX. GRADE ANY ADVERSE EVENT** | 2 | 20 | 44 | 28 | 19 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |

## Registration, Eligibility, and Evaluability

PET-Directed Therapy

Registrations ending June 30, 2015; Data as of July 27, 2015

| | TOTAL | Continued R -CHOP | IFRT + Zevalin |
|---|---|---|---|
| NUMBER REGISTERED | 109 | 98 | 11 |
| INELIGIBLE | 1 | 1 | 0 |
| Insufficient Documentation | 1 | 1 | 0 |
| Irreversible | 1 | 1 | 0 |
| ELIGIBLE | 108 | 97 | 11 |
| Analyzable, Pend. Elig. | 103 | 92 | 11 |
| RESPONSE ASSESSMENT | | | |
| Determinable | 82 | 77 | 5 |
| Too Early | 26 | 20 | 6 |
| ADVERSE EVENT ASSESSMENT | | | |
| Evaluable | 100 | 89 | 11 |
| Too Early | 8 | 8 | 0 |

## Treatment Summary

PET-Directed Therapy

Registrations ending June 30, 2015; Data as of July 27, 2015

| | TOTAL | Continued R -CHOP | IFRT + Zevalin |
|---|---|---|---|
| NUMBER ON PROTOCOL TREATMENT | 11 | 11 | 0 |
| NUMBER OFF PROTOCOL TREATMENT | 97 | 86 | 11 |
| REASON OFF TREATMENT | | | |
| Treatment completed as planned | 97 | 86 | 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 | 0 | 0 | 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 June 30, 2015; Data as of July 27, 2015

| | Continued R-CHOP (n=89) Grade | | | | | | IFRT + Zevalin (n=11) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| ALT increased | 84 | 5 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| AST increased | 87 | 2 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Abdominal pain | 88 | 0 | 0 | 1 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Allergic rhinitis | 88 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Alopecia | 74 | 6 | 9 | 0 | 0 | 0 | 9 | 0 | 2 | 0 | 0 | 0 |
| Anemia | 55 | 23 | 9 | 2 | 0 | 0 | 7 | 2 | 1 | 1 | 0 | 0 |
| Anorexia | 87 | 0 | 1 | 1 | 0 | 0 | 9 | 1 | 1 | 0 | 0 | 0 |
| Anxiety | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Arthralgia | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Arthritis | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Blurred vision | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Bone pain | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Chills | 88 | 1 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Constipation | 85 | 4 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Cough | 85 | 3 | 1 | 0 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| Creatinine increased | 86 | 2 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Dehydration | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Depression | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Dermatitis radiation | 89 | 0 | 0 | 0 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| Diarrhea | 87 | 2 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Dizziness | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Dry mouth | 87 | 2 | 0 | 0 | 0 | 0 | 9 | 0 | 2 | 0 | 0 | 0 |

| | Continued R-CHOP (n=89) Grade | | | | | | IFRT + Zevalin (n=11) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| Dysgeusia | 85 | 2 | 2 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Dyspepsia | 87 | 2 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Dysphagia | 89 | 0 | 0 | 0 | 0 | 0 | 9 | 1 | 1 | 0 | 0 | 0 |
| Dyspnea | 86 | 2 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Ear pain | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Edema limbs | 86 | 3 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Ejection fraction decreased | 88 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Esophagitis | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Eye disorders - Other, specify | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Eye pain | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Fall | 88 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Fatigue | 58 | 27 | 3 | 1 | 0 | 0 | 5 | 5 | 1 | 0 | 0 | 0 |
| Febrile neutropenia | 87 | 0 | 0 | 2 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Fever | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Flu like symptoms | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| GERD | 86 | 3 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Gastritis | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Generalized muscle weakness | 86 | 1 | 2 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Gum infection | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hearing impaired | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hot flashes | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypercalcemia | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hyperglycemia | 83 | 3 | 2 | 1 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Hyperhidrosis | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Hyperkalemia | 87 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypertension | 85 | 3 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hyperuricemia | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypoalbuminemia | 87 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypocalcemia | 87 | 1 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypoglycemia | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypokalemia | 86 | 1 | 1 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypomagnesemia | 88 | 1 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Hypotension | 88 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Hypoxia | 88 | 0 | 0 | 0 | 0 | 1 | 11 | 0 | 0 | 0 | 0 | 0 |
| Insomnia | 89 | 0 | 0 | 0 | 0 | 0 | 9 | 0 | 2 | 0 | 0 | 0 |
| Laryngeal edema | 89 | 0 | 0 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Leukocytosis | 88 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Lymphedema | 88 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Lymphocyte count decreased | 54 | 15 | 14 | 6 | 0 | 0 | 7 | 2 | 0 | 2 | 0 | 0 |
| Malaise | 88 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Memory impairment | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Mucositis oral | 85 | 3 | 1 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Muscle weakness lower limb | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Muscle weakness upper limb | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Myalgia | 88 | 1 | 0 | 0 | 0 | 0 | 9 | 1 | 1 | 0 | 0 | 0 |
| Nail discoloration | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nail loss | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nail ridging | 87 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nasal congestion | 87 | 0 | 2 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Nausea | 83 | 6 | 0 | 0 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| Nervous sys disorders-Other | 88 | 0 | 0 | 1 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |

| | Continued R-CHOP (n=89) Grade | | | | | | IFRT + Zevalin (n=11) Grade | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ADVERSE EVENTS** | **0** | **1** | **2** | **3** | **4** | **5** | **0** | **1** | **2** | **3** | **4** | **5** |
| Neutrophil count decreased | 76 | 2 | 2 | 2 | 7 | 0 | 6 | 1 | 3 | 1 | 0 | 0 |
| Oral pain | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Pain | 87 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Pain in extremity | 87 | 1 | 1 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Paresthesia | 87 | 2 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Peripheral motor neuropathy | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Peripheral sensory neuropathy | 76 | 11 | 1 | 1 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| Pharyngitis | 88 | 0 | 1 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Phlebitis | 88 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Platelet count decreased | 78 | 9 | 0 | 1 | 1 | 0 | 8 | 0 | 1 | 1 | 1 | 0 |
| Productive cough | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Resp/thoracic/mediastinal ds | 87 | 1 | 0 | 0 | 1 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Secondary Leukemia | 88 | 0 | 0 | 0 | 1 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Sinus tachycardia | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Skin infection | 87 | 1 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Skin/subq tissue ds-Other | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Small intestine infection | 88 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Sore throat | 88 | 0 | 1 | 0 | 0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 |
| Telangiectasia | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Thromboembolic event | 88 | 0 | 0 | 1 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Upper respiratory infection | 86 | 0 | 3 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Urinary tract infection | 87 | 0 | 2 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 | 0 |
| Urine discoloration | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Voice alteration | 88 | 0 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Vomiting | 88 | 1 | 0 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Weight gain | 86 | 2 | 1 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 0 | 0 |
| Weight loss | 87 | 0 | 1 | 1 | 0 | 0 | 9 | 2 | 0 | 0 | 0 | 0 |
| White blood cell decreased | 63 | 15 | 3 | 5 | 3 | 0 | 7 | 1 | 1 | 2 | 0 | 0 |
| **MAX. GRADE ANY ADVERSE EVENT** | 7 | 25 | 34 | 14 | 8 | 1 | 1 | 4 | 3 | 2 | 1 | 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, R Loomba, R Chugh, D Hershman, J Hwang

**Statisticians:**
J Unger, K Arnold

**Data Coordinator:**
M Yee

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

## Objectives

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

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

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

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

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

Create a biorepository of stored serum for future translational medicine studies that may include identifying genomic and viral factors that increase the risk of serious adverse effects among participants infected with HIV, HBV, and/or HCV being treated for invasive cancers.

## Patient Population

Patients must be presenting for evaluation or treatment for the first diagnosis of a new solid or hematologic cancer malignancy. Confirmed diagnosis date must be within 120 days prior to first clinic visit as a newly diagnosed cancer patient at the registering clinic. Patients presenting for "second opinions" of confirmed malignancies are eligible, including those who have started cancer treatment at other facilities. Patients must be registered within 90 days after their first clinic visit. Patients must not have been diagnosed with a malignancy other than the current malignancy within the past five years, with the exception of basal cell or squamous cell skin cancer, in situ cervical cancer, or in situ breast cancer. Patients must have no evidence of disease for a prior malignancy for at least five years prior to randomization except as noted above.

Patients must be 18 years of age or older. Patients must have had their blood drawn for viral status testing for HIV, HBV and HCV or provide acceptable viral status documentation prior to registration, as defined in the protocol. Note that patients must have blood drawn for testing prior to registration for any of the three viruses not covered by the documentation. Patients are allowed to participate in other clinical trials.

## Accrual Goals

A total of 3,000 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)

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**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 127 patients as of June 30, 2015, including 18 SWOG registrations.

## Registration by Institution

Registrations ending June 30, 2015

| 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)

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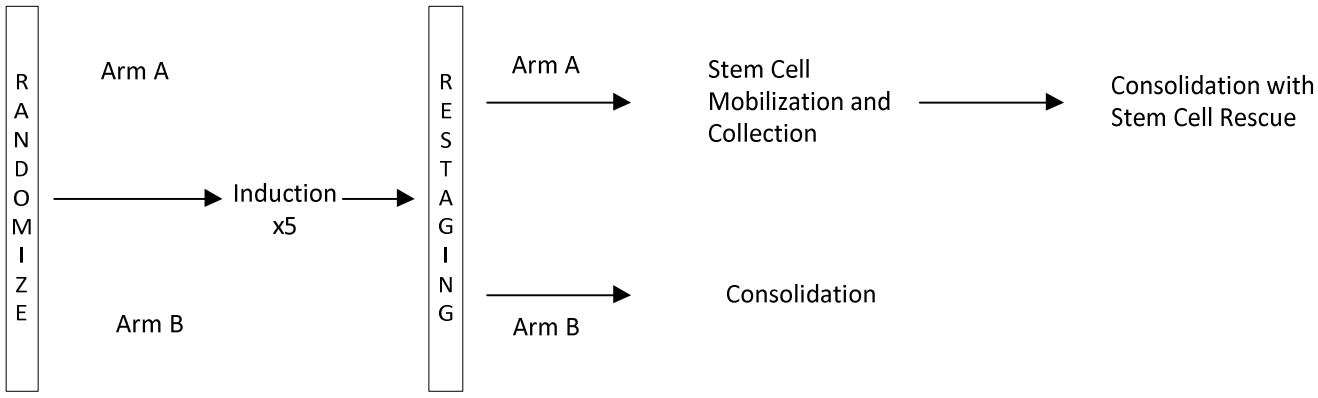
## SCHEMA




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

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

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

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

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

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

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

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

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

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

**Patient Population**

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

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

Patients must be between 18 to 75 years old and have Karnofsky Performance Scale (KPS) ≥ 30 (≥ 50 for patients ages 60-70). Patients must have adequate cardiac, pulmonary, hematologic, renal, and hepatic function. Patients must be HIV negative and HCV negative (unless HBsAb positive patients has 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 ≥ 51 years and KPS ≥ 70 vs age ≥ 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 49 patients as of June 30, 2015, including five SWOG registrations, one from University of California Davis, two from Fred Hutchinson Cancer Research Center, and two from 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)

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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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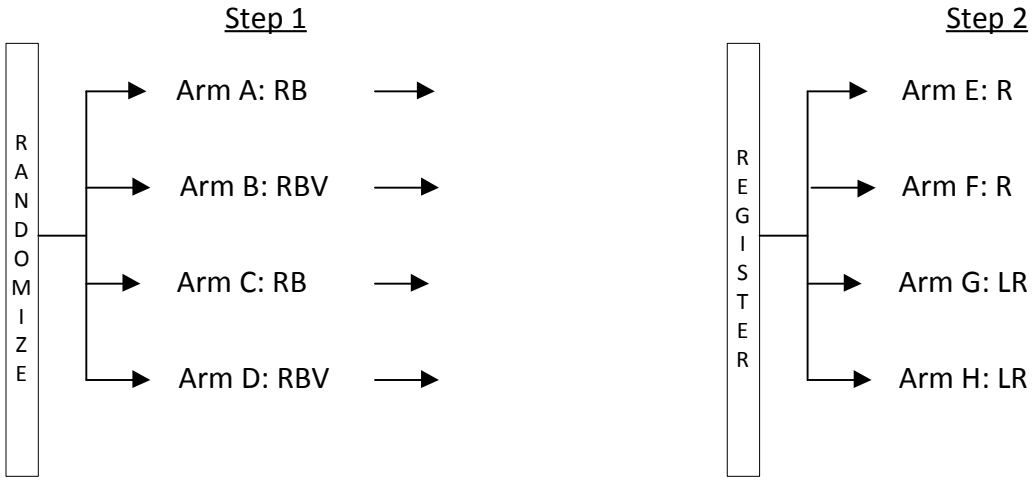
## SCHEMA




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 > 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 two 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.

**Accrual Goals**

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

**Summary Statement**

ECOG-ACRIN reported a total accrual of 233 patients as of June 30, 2015, including 55 SWOG registrations. The complete Spring 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

# Registration by Institution

Registrations ending June 30, 2015

| Institutions | Total Reg | Institutions | Total Reg |
|---|---|---|---|
| Rochester, Univ of | 15 | KaiserPermanenteCOL/Kaiser Vallejo NCORP | 2 |
| Kaiser Vallejo NCORP | 7 | Kansas City NCORP | 2 |
| Cleveland Clinic OH | 6 | Poudre Valley Hosp/Colorado, U of | 2 |
| CRC West MI NCORP | 3 | Southeast COR NCORP | 1 |
| Fred Hutchinson CRC | 3 | UF Cancer Center/Arkansas, U of | 1 |
| Hawaii MU-NCORP | 3 | Upstate Carolina | 1 |
| Montana NCORP | 3 | Wayne State Univ | 1 |
| Prov Portland MC/PCRC NCORP | 3 | **Total (16 Institutions)** | **55** |
| Dayton NCORP | 2 | | |

# 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

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

**Date Activated:**
01/22/2014

**Date Closed*:**
05/22/2015

*Temporary closure

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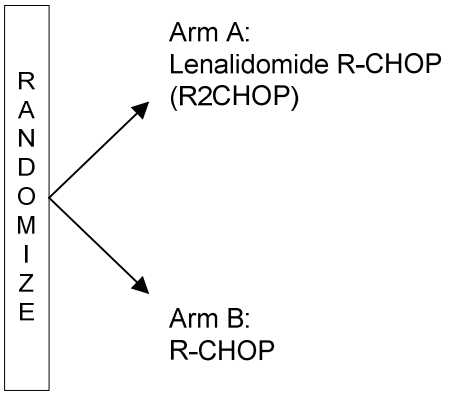
## SCHEMA




**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).

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**

This study was temporarily closed to accrual on May 22, 2015, to evaluate the accrual of ABC subtype as outlined in Section 9.1 of the protocol.

ECOG-ACRIN reported a total accrual of 219 patients as of May 22, 2015, including 26 SWOG registrations. The complete Spring 2015 summary of this study from ECOG-ACRIN is available on the SWOG web site.

## Registration by Institution

Registrations ending May 22, 2015

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

# EAY131 Master Protocol / Phase II

## Coordinating Group: ECOG-ACRIN

## NCI-MATCH: Molecular Analysis for Therapy Choice

---

**Participants:**
ECOG-ACRIN, CTSU

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

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

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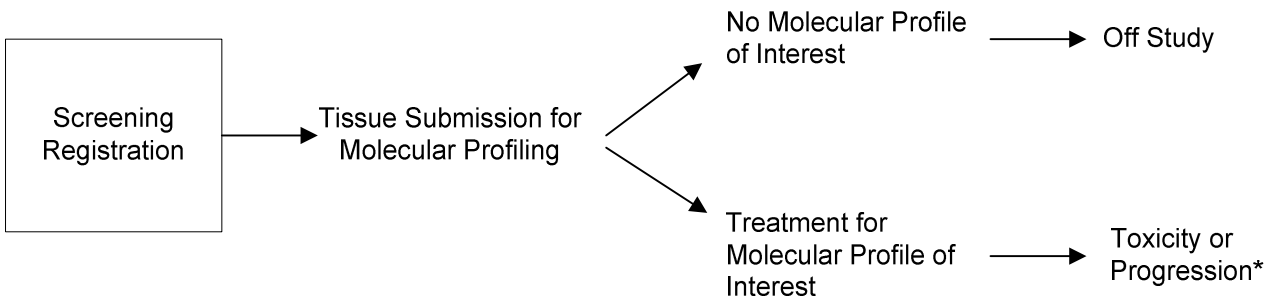
## SCHEMA




*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.

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

To evaluate the time until death or disease progression.

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

**Patient Population**

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

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

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

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

**Accrual Goals**

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

**Summary Statement**

This study activated on August 12, 2015, with ten subprotocols included in the activation. Only sites utilizing the CIRB as their IRB of record will be able to participate in the trial.