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COMPOUND NUMBER: PF-05212374 (TRU-015)

PROTOCOL NO.: 3206K2-104-WW (B2051008)

PROTOCOL TITLE: A Phase 1/2 Dose Escalation Study of TRU-015 in Subjects With Relapsed or Refractory B-Cell Non-Hodgkin's Lymphoma

Study Centers: A total of 2 centers in the United States took part in the study and enrolled subjects.

Study Initiation Date and Final Completion Date: 19 November 2007 to 09 April 2008. The study was terminated prematurely due to Sponsor decision.

Phase of Development: Phase 1

Study Objectives:

The primary objectives were to evaluate the safety and to determine the maximum tolerated dose (MTD), if reached, of TRU-015 in subjects with relapsed or refractory B-cell non-Hodgkin lymphoma (NHL).

The secondary objectives of the study were the following:

- To characterize the pharmacokinetics (PK) of TRU-015 in subjects with B-cell NHL.
- To characterize the pharmacodynamic (PD) response after TRU-015 treatment in subjects with B-cell NHL.
- To evaluate the immunogenicity of TRU-015 in subjects with B-cell NHL.
- To evaluate the clinical activity of TRU-015 in an expanded cohort of subjects with relapsed, refractory, or persistent indolent B-cell NHL.

METHODS

Study Design: This was an open-label, dose escalation, phase 1/2 study of TRU-015 administered intravenously (IV) weekly for 4 doses to subjects with relapsed or refractory B-cell NHL. The study was to include dose escalation cohorts as well as MTD confirmation and preliminary efficacy cohorts. In the absence of a dose-limiting toxicity (DLT) that would define the MTD, dose escalation was planned as follows: 400 mg, 700 mg, and 1000 mg. Initially, a minimum of 3 and up to 6 evaluable subjects were to be treated at each

dose level. Escalation to the next dose level was to be permitted after the last subject of the current cohort had been evaluated for the first 28 days after the first dose of TRU-015. If DLT criteria that defined the MTD were observed at the 400-mg dose level, a 200-mg dose level was to be evaluated. The Sponsor selected 1000 mg as the highest allowed dose. Subjects were to participate in the study for up to approximately 100 weeks, including up to 4 weeks for screening, approximately 24 weeks for the treatment phase (test article administration period of 3 weeks and assessment period of 21 weeks), and approximately 72 weeks for the extended follow-up period (the extended follow-up period included subjects in the dose escalation cohorts who exhibited stable disease, partial response, or complete response; subjects in the MTD confirmation cohort; and subjects in the preliminary efficacy cohorts). The study flowchart is presented in Table 1.

Table 1. Study Flowchart

Study Period	Screening[a]	Treatment Phase											Extended Follow-Up Period[c]					
		Test Article Dosing				Assessment Period						Final Visit[b]						
Study Day	**-28 to 0[a]**	**1**	**8**	**15**	**22**	**29**	**43**	**57**	**85**	**113**	**141**	**169**	**253**	**337**	**421**	**505**	**589**	**673**
Study Week	**-4 to 0[a]**	**0**	**1**	**2**	**3**	**4**	**6**	**8**	**12**	**16**	**20**	**24**	**36**	**48**	**60**	**72**	**84**	**96**
Study Visit Window (Days)			**±2**	**±2**	**±2**	**±2**	**+7**	**+7**	**+7**	**+14**	**+14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**
Informed consent[d]	X																	
Medical history/demography	X																	
Cancer history: diagnosis and prior therapies	X																	
CD20 immunophenotyping[e]	X																	
Hepatitis B and C virus testing[f]	X																	
Urinalysis[g]	X											X						
Chest radiograph[h]	X											X						
IgA, IgG, IgM levels[i]	X				X							X						
Enrollment[j]		X																
Pretreatment medications[k]		X	X	X	X													
TRU-015 administration[l]		X	X	X	X													
Vital signs/observation period[m]		X	X	X	X													
Height	X																	
Weight[n]	X											X						
IPI or FLIPI[o]	X																	
ECOG performance status[p]	X	X	X	X	X	X	X		X			X	X	X	X	X	X	X
Physical examination[q]	X	X	X	X	X		X		X			X						
Lymphocyte panel[r]	X											X						
Hematology panel[s]	X	X	X	X	X	X						X						
Blood chemistries[t]	X	X	X	X	X	X						X						
Liver function tests[u]	X	X	X	X	X	X						X						
Pregnancy test[v]	X	X	X	X	X							X						
ECG[w]	X	X	X	X	X							X						
CT scan of chest, abdomen, pelvis, (neck if appropriate); and clinical disease assesments[x]	X						X		X			X	X	X	X	X	X	X
Bone marrow aspirate/biopsy[y]	X											X						
Anti-TRU-015 antibodies[z]		X							X	X		X						
PK		X	X	X	X	X	X	X	X	X	X	X	X	X				

Table 1. Study Flowchart

Study Period	**Screening**[a]	**Treatment Phase**											**Extended Follow-Up Period**[c]					
		Test Article Dosing				**Assessment Period**						**Final Visit**[b]						
Study Day	**-28 to 0**[a]	**1**	**8**	**15**	**22**	**29**	**43**	**57**	**85**	**113**	**141**	**169**	**253**	**337**	**421**	**505**	**589**	**673**
Study Week	**-4 to 0**[a]	**0**	**1**	**2**	**3**	**4**	**6**	**8**	**12**	**16**	**20**	**24**	**36**	**48**	**60**	**72**	**84**	**96**
Study Visit Window (Days)			**±2**	**±2**	**±2**	**±2**	**+7**	**+7**	**+7**	**+14**	**+14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**
PD		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
PGt[aa]		X																
Survival status													X	X	X	X	X	X
Adverse events[bb]	←Monitored and recorded continuously→																	
Concomitant treatment[bb]	←Monitored and recorded continuously→																	
Other anticancer therapy													X					

Table 1. Study Flowchart

Study Period	Screening[a]	Treatment Phase											Extended Follow-Up Period[c]					
		Test Article Dosing				Assessment Period						Final Visit[b]						
Study Day	**-28 to 0[a]**	**1**	**8**	**15**	**22**	**29**	**43**	**57**	**85**	**113**	**141**	**169**	**253**	**337**	**421**	**505**	**589**	**673**
Study Week	**-4 to 0[a]**	**0**	**1**	**2**	**3**	**4**	**6**	**8**	**12**	**16**	**20**	**24**	**36**	**48**	**60**	**72**	**84**	**96**
Study Visit Window (Days)			**±2**	**±2**	**±2**	**±2**	**+7**	**+7**	**+7**	**+14**	**+14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**

ALT = alanine aminotransferase; Anti-HCV = antibody to hepatitis C virus; ANC = absolute neutrophil count; AST = aspartate aminotransferase; CBC = complete blood count; CT = computed tomography; ECG = electrocardiogram; ECOG = Eastern Cooperative Oncology Group; FLIPI = Follicular Lymphoma International Prognostic Index; HbsAg = hepatitis B surface antigen; IEC = independent ethics committee; Ig = immunoglobulin; IPI = International Prognostic Index; IRB = institutional review board; MTD = maximum tolerated dose; NHL = non-Hodgkin's lymphoma; PD = pharmacodynamic; PG = pharmacogenomic; PGt = pharmacogenetic; PK = pharmacokinetic; QTc = QT interval corrected for heart rate; RBC = red blood cell count; WBC = white blood cell count.

a. Screening/Baseline visit (and associated activities) were to occur within 4 weeks before first dose of test article (Week 0; Day 1).
b. In the event of early termination, this visit was to be performed within 30 days after the last dose of test article (inclusive of subjects taken off study because of progressive disease noted before the Week 6 assessment; if disease progression was noted at the Week 6 or Week 12 assessment, the final visit was to be performed within 1 week [±2 days] of the assessment).
c. These follow-up visits were conducted for subjects in the dose escalation cohorts who exhibited stable disease, partial response, or complete response; for subjects in the MTD confirmation cohort; and for subjects in the preliminary efficacy cohorts. These visits occurred approximately every 3 months after the Week 24 assessment for up to approximately 24 months after the first dose of test article, and included disease assessments until disease progression was documented, the subject started another anticancer treatment, the subject withdrew consent, or death, whichever occurred first.
d. Signed and dated informed consent form (IRB/IEC and sponsor-approved) before any study-specific screening procedures were performed.
e. Prior CD20 immunophenotyping of tumors to document B-cell NHL was acceptable. If such prior documentation was not available, then the immunophenotype of the current disease had to be documented by fine-needle aspirate or biopsy, or by circulating CD20-positive NHL cells from peripheral blood before administration of test article.
f. Testing for HbsAg and anti-HCV.
g. Dipstick; in the case of abnormal results, microscopy was to be performed.
h. Chest x-ray was to include posterior-anterior and lateral views.
i. Serum IgA, IgG (including subclasses IgG1, IgG2, IgG3, IgG4), and IgM were measured at Screening, before the final dose of test article, and at the final visit (Week 24). During the study, these were to be measured if clinically indicated.
j. Subject were to be enrolled no more than 3 business days before the first dose of test article.
k. Subjects were to be pretreated with each of the following: oral acetaminophen (eg, 650 to 1000 mg of paracetamol), an oral antihistamine (eg, 25 mg of diphenhydramine), and an intravenous corticosteroid (100 mg of hydrocortisone) to reduce the incidence and severity of anticipated infusion reactions.
l. Subjects received a dose of 400, 700, or 1000 mg during dose escalation studies. Subjects in the preliminary efficacy cohorts received the determined MTD, if reached (or the maximum dose studied if an MTD not reached).

Table 1. Study Flowchart

Study Period	Screening[a]	Treatment Phase											Extended Follow-Up Period[c]					
		Test Article Dosing				Assessment Period						Final Visit[b]						
Study Day	**-28 to 0[a]**	**1**	**8**	**15**	**22**	**29**	**43**	**57**	**85**	**113**	**141**	**169**	**253**	**337**	**421**	**505**	**589**	**673**
Study Week	**-4 to 0[a]**	**0**	**1**	**2**	**3**	**4**	**6**	**8**	**12**	**16**	**20**	**24**	**36**	**48**	**60**	**72**	**84**	**96**
Study Visit Window (Days)			**±2**	**±2**	**±2**	**±2**	**+7**	**+7**	**+7**	**+14**	**+14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**

m. Vital signs (blood pressure, heart rate, respiratory rate, and temperature [oral, axillary, core, temporal, or tympanic]) were taken every 15 minutes for the first hour of test article infusion, then every 30 minutes until the end of infusion, and at 1 hour and 2 hours post infusion.
n. Weight was measured at Screening and at the final visit. During the study, was also to be measured if clinically indicated.
o. IPI or FLIPI score was determined at Screening, as appropriate (ie, according to the subject's primary diagnosis).
p. ECOG performance status on non-dosing visits was to be performed in conjunction with CT scans for overall disease assessment. ECOG assessments were not required for follow-up visits conducted to assess survival only.
q. Physical examination was to include vital signs (blood pressure, heart rate, respiratory rate, and temperature [oral, axillary, core, temporal, or tympanic]), liver and spleen assessments, B-symptom evaluation, and clinical assessment of tumor masses if accessible. When applicable, these examinations had to be completed before test article administration and/or before PK/PD assessments.
r. Blood was collected to measure lymphocyte panel at Screening and at Week 24. The lymphocyte panel = T cells: CD3, CD4, CD8; B cells: CD5, CD19, and CD20; monocytes: CD14. Additional blood collections for B-lymphocyte measurements also occurred for PD analysis.
s. Hematology panel (CBC with 3-part differential [5-part differential, if available], ANC, hemoglobin and hematocrit, and RBC, reticulocyte and platelet counts) was to be done twice a week for the first 2 doses of test article (Weeks 0 and 1); thereafter, the assessment was to be performed predose, when applicable. In the event of Grade 4 hematologic toxicity (or if clinically indicated), it was recommended that the hematology panel be repeated at least every 2 days until ANC $\geq 1.0 \times 10^9$/L (1000/µL), or platelets $\geq 50 \times 10^9$/L (50,000/µL); if WBC was $<0.5 \times 10^9$/L (500/µL), no differential count was needed.
t. Blood chemistries were to include sodium, potassium, chloride, bicarbonate or total carbon dioxide, calcium, phosphorus, glucose, albumin, total protein, serum creatinine, blood urea nitrogen or urea, lactic dehydrogenase, total cholesterol, and uric acid or urate.
u. Liver function test was to include AST, ALT, alkaline phosphatase (fractionated, if needed), total bilirubin, and direct bilirubin.
v. Female subjects of childbearing potential had a qualitative serum pregnancy test performed at Screening and a serum or urine pregnancy test before each administration of test article, at the final visit (Week 24), and whenever clinically indicated.
w. 12-lead ECGs were performed at Screening, before each infusion of test article, immediately before the end of each infusion of test article, approximately 3 hours after completion of the final infusion of test article, and at the final visit (Week 24). Screening ECG was collected to confirm subject eligibility (QTc prolongation >500 msec was an exclusion criterion for this study). During the study, each ECG was collected in triplicate (approximately 2 minutes apart) using digital technology and managed by a central vendor.
x. CT scans and clinical disease assessments were to be performed for all subjects at: Screening, and at 6, 12, and 24 weeks after the first dose of test article (Note: A confirmatory disease assessment with CT scan was to be performed approximately 4 to 6 weeks after first documentation of tumor response [partial or complete response]). Extended follow-up CT scans and clinical disease assessments were only to be performed for: subjects in the dose escalation cohorts who exhibited stable disease, partial response, or complete response; for subjects in the MTD confirmation cohort; and for subjects in the preliminary efficacy cohorts. CT scans and clinical disease assessments occurred approximately every 3 months after the 24 week assessment for up to approximately 24 months after the first dose of test article, until disease progression was documented, the subject started another anticancer treatment, the subject withdrew consent, or death, whichever occurred first. For all subjects enrolled in the preliminary efficacy cohorts, follow-up occurred through the entire follow-up

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Study Visit Window (Days)			**±2**	**±2**	**±2**	**±2**	**+7**	**+7**	**+7**	**+14**	**+14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**	**±14**

period (up to approximately 24 months after the first dose of test article), regardless of the number of doses received, and included: survival, CT scans, and clinical disease assessments for subjects exhibiting stable disease or better who had not begun alternative anticancer treatment; survival only, for subjects with documented, progressive disease or for subjects who had begun treatment with another anticancer therapy.

y. If the bone marrow was involved by lymphoma before treatment, then the bone marrow aspirate/biopsy had to be repeated at the same site in case of complete response. If available during the course of the study, biopsy samples may have been used for PG analyses (gene and/or protein expression profiling).

z. Serum samples for anti-TRU-015 antibody testing were collected before test article infusion on Week 0 (study Day 1), at Week 12, at Week 16, and at the final visit.

aa. A single whole blood sample was collected at Week 0 (study Day 1) for PGt analysis.

bb. Adverse events were monitored and recorded continuously from the date of informed consent signing through 30 days after the last dose of test article. All test article-related adverse events were monitored and recorded continuously from the date of informed consent signing through 21 weeks after the last dose of test article, and followed until resolution/stabilization or until disease progression was documented and the subject started another anticancer treatment regimen, whichever occurred first. All serious adverse events were followed until resolution. Prior non-study treatment (medications or procedures) taken by the subject within 28 days of the first dose of test article (Week 0 [Day 1]) and concomitant treatment (medications or procedures) taken by the subject through 30 days after the last dose of test article were recorded. Collection of concomitant treatment (medications or procedures) may have been extended beyond 30 days after the last dose of test article in the event of test article-related adverse events or in the event of serious adverse events; in these instances, concomitant treatment (medications or procedures) were recorded for the duration that these events were followed (as just described above).

Number of Subjects (Planned and Analyzed): It was planned to enroll approximately 120 to 150 subjects in this study, and 4 subjects were enrolled and entered the study.

Diagnosis and Main Criteria for Inclusion:

- Male and female subjects age 18 years or older.

- Subjects with CD20-positive, B cell NHL who, after at least 2 prior therapies of probable clinical benefit, had relapsed or refractory disease. The following histologies could have been included: lymphoplasmacytic lymphoma (formerly known as lymphoplasmacytoid lymphoma), splenic marginal zone B cell lymphoma, extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue, nodal marginal zone B-cell lymphoma, follicular lymphoma, mantle cell lymphoma, diffuse large-cell B-cell lymphoma, and mediastinal large B-cell lymphoma. Small lymphocytic lymphoma could be included if it was a primary diagnosis and if the lymphoma cells were $<5.0 \times 10^9$/L ($5000/mm^3$) in the peripheral blood. Subjects enrolled in the preliminary efficacy cohorts had to have relapsed, refractory, or persistent follicular lymphoma (persistent disease defined as computed tomography [CT] positive for 3 months after last treatment), and must not have received anti-CD20 targeted therapy within 3 months of receiving the first dose of test article. Subjects may have been considered eligible after a single therapy of probable clinical benefit, if no further standard effective treatment was available in the opinion of the Investigator. Prior CD20 immunophenotyping of tumors to document B-cell NHL was acceptable. If such prior documentation was not available, then the immunophenotype of the current disease must have been documented by fine-needle aspirate or biopsy, or by circulating CD20-positive NHL cells from peripheral blood before administration of test article.

- At least 1 measurable lesion that was 1.5 cm in at least 1 dimension by CT or magnetic resonance imaging (MRI), in an area of no prior radiation therapy, or documented progression in an area that was previously irradiated.

- Recovery to baseline or Grade 1 [according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), version 3.0] from all acute adverse effects of prior therapies (excluding alopecia).

Main Exclusion Criteria:

- Candidate for potentially curative therapy that was available to the subject, in the clinical opinion of the Investigator.

- Diagnosis of chronic lymphocytic leukemia, Burkitt's lymphoma, primary effusion lymphoma, and/or precursor B-cell lymphoblastic lymphoma.

- Prior treatments: radioimmunotherapy; allogeneic hematopoietic stem cell transplant (within 6 months of first dose of study drug); chemotherapy, cancer immunosuppressive therapy, growth factors (except erythropoietin), or investigational

agents (within 4 weeks of first dose of study drug); major surgery not related to debulking surgical procedures (within 4 weeks of first dose of study drug).

Study Treatment: Test article was supplied in vials containing 200 mg of TRU-015 as lyophilized powder that was reconstituted with 4 mL of sterile water for injection and diluted with 500 mL of normal saline prior to IV infusion. Four (4) doses of TRU-015 were administered IV on a weekly schedule: 1 dose on Days 1, 8, 15, and 22 (Weeks 0, 1, 2, and 3, respectively). In the absence of a DLT that defined the MTD, dose escalation was planned as follows: 400 mg, 700 mg, and 1000 mg.

Efficacy and Safety Endpoints:

Primary and Secondary Safety Endpoints:

Because this was a dose ascending trial, the primary and secondary safety endpoints were combined as 1 endpoint. Primary and secondary safety endpoints were the incidence and severity of adverse events (AEs) and DLTs at each dose level and for all subjects combined, as applicable, and changes in laboratory test results over time.

Secondary Efficacy Endpoints:

To obtain preliminary information on the antitumor activity of TRU-015, enrolled subjects had tumor and clinical disease assessments. Antitumor activity was to be measured by objective response rate (ORR), progression-free survival (PFS), and overall survival (OS).

The focus for antitumor activity was on the ORR. PFS and OS were to provide supportive data.

In addition to evaluating and assessing the best response by using the International Response Criteria for Non-Hodgkin's Lymphomas, duration of response, duration of stable disease, and time to tumor progression, as applicable, may have been analyzed.

Safety Evaluations: Safety was assessed by physical examination findings, vital sign measurements, and clinical laboratory evaluations. Safety assessments included monitoring of AEs, safety evaluations (including chest radiographs and electrocardiogram findings), and laboratory determinations.

Statistical Methods:

The following population sets were analyzed:

Efficacy Population: The efficacy population was defined as subjects who received at least 1 dose of TRU-015 and who underwent at least 1 tumor assessment after starting treatment.

Pharmacokinetics Population: The PK population was defined as all subjects who provided serum samples for PK assessments.

Safety Population: The safety population was defined as all subjects who received at least 1 dose of study drug.

Evaluation of the data consisted primarily of summary displays (descriptive statistics). All subjects who received at least 1 dose of TRU-015 were considered for safety analysis. AE incidence rates were described by dose level with and without regard to causality. The frequency of occurrence of overall toxicity, categorized by NCI CTCAE, version 3.0, Grades 1 through 5, was also summarized.

RESULTS

Subject Disposition and Demography: A total of 4 subjects (1 woman and 3 men) with relapsed or refractory B-cell NHL were enrolled in the study and received TRU-015. All 4 subjects were assigned to receive 400 mg of IV TRU-015, once weekly for 4 weeks. All 4 subjects were withdrawn from the study. Three (3) subjects were withdrawn from the treatment phase of the study because of disease progression and 1 was withdrawn from the treatment phase and from the study simultaneously by the Investigator after being notified of the Sponsor's plans to terminate the study. All 3 subjects with disease progression were withdrawn from the study within 10 days of withdrawal from the treatment phase; 1 was withdrawn from the study by the Investigator, 1 was withdrawn from the study because of subject request, and 1 was withdrawn from the study because the subject had progressive disease and went on to other therapy.

Of the 4 subjects, 1 (25%) was African American and 3 (75%) were White. The subjects were aged 45 to 64 years with a median age of 54 years. Subject demographic characteristics are presented in Table 2.

Table 2. Subject Demographic Characteristics

Characteristic	Treatment	
	TRU-015 400 mg (N=4)	Total (N=4)
Age (years)		
n	4	4
Mean	54.25	54.25
Standard deviation	10.69	10.69
Minimum	45.00	45.00
Maximum	64.00	64.00
Median	54.00	54.00
Age range		
18≤age<65	4 (100)	4 (100)
Sex		
Female	1 (25.00)	1 (25.00)
Male	3 (75.00)	3 (75.00)

N = total number of subjects; n = number of subjects in a subgroup.

Efficacy Results:

Analyses of clinical activity, PK and PD were not performed because development of TRU-015 for treatment of NHL was discontinued.

Safety Results:

Adverse Events: All 4 (100%) subjects had at least 1 AE during the study. All AEs with the exception of decreased hemoglobin were treatment-emergent. The most commonly reported treatment-emergent adverse events (TEAEs) were neutropenia, fatigue, pyrexia, decreased white blood cell (WBC) count, and myalgia (2, 50% each). TEAEs considered by the Investigator to be at least possibly related to TRU-015 were reported in 3 (75%) subjects. The most commonly reported drug-related TEAEs were neutropenia, decreased WBC count, and myalgia (2, 50% each).

TEAEs of Grade 3 toxicity were reported in 3 (75%) subjects. There were no reports of Grade 4 toxicities. TEAEs of Grade 3 toxicity included neutropenia (2, 50%) and hypoxia (1, 25%); per Investigator judgment, the cases of neutropenia were related to the test article, while hypoxia was not related to the test article.

The number (%) of subjects reporting TEAEs is presented in Table 3.

Table 3. Number (%) of Subjects Reporting Treatment-Emergent Adverse Events

System Organ Class[a] Preferred Term	Treatment	
	TRU-015 400 mg (N=4)	Total (N=4)
Any adverse event	4 (100)	4 (100)
Blood and lymphatic system disorders	2 (50.0)	2 (50.0)
Neutropenia	2 (50.0)	2 (50.0)
Cardiac disorders	1 (25.0)	1 (25.0)
Sinus bradycardia	1 (25.0)	1 (25.0)
Gastrointestinal disorders	1 (25.0)	1 (25.0)
Abdominal pain	1 (25.0)	1 (25.0)
Nausea	1 (25.0)	1 (25.0)
Vomiting	1 (25.0)	1 (25.0)
General disorders and administration site conditions	4 (100)	4 (100)
Chest pain	1 (25.0)	1 (25.0)
Chills	1 (25.0)	1 (25.0)
Fatigue	2 (50.0)	2 (50.0)
Pyrexia	2 (50.0)	2 (50.0)
Hepatobiliary disorders	1 (25.0)	1 (25.0)
Hepatomegaly	1 (25.0)	1 (25.0)
Liver tenderness	1 (25.0)	1 (25.0)
Injury, poisoning and procedural complications	1 (25.0)	1 (25.0)
Medical device pain	1 (25.0)	1 (25.0)
Investigations	2 (50.0)	2 (50.0)
White blood cell count decreased	2 (50.0)	2 (50.0)
Metabolism and nutrition disorders	1 (25.0)	1 (25.0)
Anorexia	1 (25.0)	1 (25.0)
Musculoskeletal and connective tissue disorders	3 (75.0)	3 (75.0)
Arthralgia	1 (25.0)	1 (25.0)
Myalgia	2 (50.0)	2 (50.0)
Nervous system disorders	1 (25.0)	1 (25.0)
Headache	1 (25.0)	1 (25.0)
Renal and urinary disorders	1 (25.0)	1 (25.0)
Chromaturia	1 (25.0)	1 (25.0)
Respiratory, thoracic and mediastinal disorders	3 (75.0)	3 (75.0)
Dysphonia	1 (25.0)	1 (25.0)
Dyspnoea	1 (25.0)	1 (25.0)
Hypoxia	1 (25.0)	1 (25.0)
Pharyngolaryngeal pain	1 (25.0)	1 (25.0)
Skin and subcutaneous tissue disorders	2 (50.0)	2 (50.0)
Alopecia	1 (25.0)	1 (25.0)
Dry skin	1 (25.0)	1 (25.0)
Erythema	1 (25.0)	1 (25.0)
Night sweats	1 (25.0)	1 (25.0)
Rash	1 (25.0)	1 (25.0)
Skin exfoliation	1 (25.0)	1 (25.0)
Skin plaque	1 (25.0)	1 (25.0)

Classifications of adverse events are based on the MedDRA.
MedDRA = Medical Dictionary for Regulatory Activities; N = total number of subjects.
a. Totals at a higher level are not necessarily the sum of those at the lower levels since a subject may report ≥2 different adverse events within the higher level category.

The number (%) of subjects reporting drug-related AEs is presented in Table 4.

Table 4. Number (%) of Subjects Reporting Drug-Related Adverse Events

System Organ Class[a] Preferred Term	Treatment	
	TRU-015 400 mg (N=4)	Total (N=4)
Any adverse event	3 (75.0)	3 (75.0)
Blood and lymphatic system disorders	2 (50.0)	2 (50.0)
Neutropenia	2 (50.0)	2 (50.0)
General disorders and administration site conditions	2 (50.0)	2 (50.0)
Chills	1 (25.0)	1 (25.0)
Fatigue	1 (25.0)	1 (25.0)
Pyrexia	1 (25.0)	1 (25.0)
Investigations	2 (50.0)	2 (50.0)
White blood cell count decreased	2 (50.0)	2 (50.0)
Musculoskeletal and connective tissue disorders	2 (50.0)	2 (50.0)
Myalgia	2 (50.0)	2 (50.0)

Classifications of adverse events are based on the MedDRA.
MedDRA = Medical Dictionary for Regulatory Activities; N = total number of subjects.
a. Totals at a higher level are not necessarily the sum of those at the lower levels since a subject may report ≥2 different adverse events within the higher level category.

There were no serious AEs, deaths, or AEs leading to treatment discontinuation in the study.

CONCLUSIONS: In this study, 4 subjects with NHL received 4 weekly infusions of TRU-015 at the initial dose of 400 mg. The Sponsor made a business decision to discontinue development of TRU-015 for oncology indications and hence the study was terminated in March 2008 before the MTD was reached.

All 4 (100%) subjects had at least 1 TEAE during the study and 3 (75%) subjects had TEAEs considered by the Investigator to be related to treatment. TEAEs of Grade 3 toxicity were reported in 3 (75%) subjects. There were no reports of Grade 4 toxicities. There were no SAEs, deaths, or safety-related discontinuations in the study.