ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: C18083/2048 Study to Evaluate the Efficacy and Safety of Treatment With Bendamustine in Combination With Ofatumumab in Previously Untreated Patients With Indolent B-Cell Non-Hodgkin's Lymphoma (NHL) NCT01108341

Protocol Registration and Results Preview

Close

Study to Evaluate the Efficacy and Safety of Treatment With Bendamustine in Combination With Ofatumumab in Previously Untreated Patients With Indolent B-Cell Non-Hodgkin's Lymphoma (NHL)

This study has been completed.

Sponsor:	Cephalon
Collaborators:	
Information provided by (Responsible Party):	Teva Pharmaceutical Industries (Cephalon)
ClinicalTrials.gov Identifier:	NCT01108341

Purpose

The primary objective of the study is to determine the efficacy, as measured by overall response (complete response + partial response) of bendamustine in combination with ofatumumab in previously untreated patients with indolent B-Cell Non-Hodgkin's Lymphoma (NHL).

Condition	Intervention	Phase
Non-Hodgkin's Lymphoma (NHL)	Drug: Bendamustine hydrochloride Drug: Ofatumumab	Phase 2

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, N/A

Official Title: An Open-Label Study to Evaluate the Efficacy and Safety of Treatment With Bendamustine in Combination With Ofatumumab in Previously Untreated Patients With Indolent B-Cell Non-Hodgkin's Lymphoma (NHL)

Further study details as provided by Teva Pharmaceutical Industries (Cephalon):

Primary Outcome Measure:

- Percentage of Participants With a Best Overall Response of Complete Response (CR) or Partial Response (PR), as Determined by the

International Working Group (IWG) Criteria As Assessed by Investigators [Time Frame: up to Week 32] [Designated as safety issue: No]

The IWG criteria (Cheson et al 2007) for a CR is a complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present before therapy. A PR is at least a 50% decrease in sum of the product of the diameters (SPD) of up to 6 of the largest dominant nodes or nodal masses, no increase should be observed in the size of other nodes, liver or spleen, and no new sites of disease should be observed.

Secondary Outcome Measures:

- Percentage of Participants With a Best Overall Response of Complete Response (CR), as Determined by the International Working Group (IWG) Criteria As Assessed by Investigators [Time Frame: up to Week 32] [Designated as safety issue: No]

  The IWG criteria (Cheson et al 2007) for a CR is a complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present before therapy.

Enrollment: 50
Study Start Date: May 2010
Study Completion Date: October 2011
Primary Completion Date: July 2011

Arms	Assigned Interventions
Experimental: Bendamustine and Ofatumumab There are 6 planned and 2 optional 28-day cycles in which participants are administered both bendamustine and ofatumumab in the following doses: Bendamustine administered at 90 mg/m^2 intravenously (iv) on study days 1 and 2. Ofatumumab administered at 300 mg iv on day 1 and 1000 mg iv on day 8 of cycle 1. Ofatumumab administered at 1000 mg iv on day 1 of all additional cycles.	Drug: Bendamustine hydrochloride Bendamustine will be administered at 90 mg/m^2 as a 30-minute intravenous (iv) infusion on days 1 and 2 of each cycle. Other Names: • CEP-18083 • Treanda Drug: Ofatumumab Ofatumumab will be administered at 300 mg as an iv infusion on day 1 and 1000 mg on day 8 of cycle 1 and 1000 mg on day 1 of each subsequent cycle. Other Names: • Arzerra

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Key Inclusion Criteria:

- The patient has histopathologic confirmation of one of the protocol-specific CD20+ B-cell non-Hodgkin's lymphomas. Tissue diagnostic procedures must be performed within 6 months of study entry and with biopsy material available for review.
- The patient meets 1 of the following need-for-treatment criteria:
  a. Presence of at least 1 of the following B-symptoms:
     - fever (>38ºC) of unclear etiology
     - night sweats
     - weight loss of greater than 10% within the prior 6 months
  b. large tumor mass (bulky disease) characterized by lymphomas with a diameter of more than 3 cm in 3 or more regions or by a lymphoma with a diameter of more than 7 cm in 1 region
  c. presence of lymphoma-related complications
  d. hyperviscosity syndrome due to monoclonal gammopathy
- The patient's tumor is verified to be CD20+ positive from current or previous excisional or incisional tissue diagnostic procedures performed within 6 months of study entry.
- The screening phase CT scan (based on local evaluation) shows:
- 2 or more clearly demarcated lesions with a largest diameter ≥1.5 cm, or
- 1 clearly demarcated lesion with a largest diameter ≥2.0 cm
- The patient was not previously treated for indolent lymphoma (with the exception of a single course of local radiation therapy not exceeding 2 adjacent lymph node regions).
- The patient has adequate hematologic and hepatic function.
- The patient has Eastern Cooperative Oncology Group (ECOG) performance status 0, 1, or 2.
- The patient has serum creatinine of 2.0 mg/dL or less or creatinine clearance of 30 mL/min or more, based on the Cockcroft-Gault method, or from a 24-hour urine collection.
- The patient is willing to comply with contraception requirements.

Key Exclusion Criteria:

The patient:

- Has small lymphocytic lymphoma or mantle cell lymphoma.
- Has documented history of central nervous system (CNS) lymphomatous involvement.
- Has or has had an active malignancy, other than NHL, within the past 3 years except for localized prostate cancer without evidence of bone metastases, bladder, cervical, or breast carcinoma in-situ, or non-melanoma skin cancer .

- Has New York Heart Association (NYHC) Class III or IV heart failure, uncontrolled arrythmias or unstable angina, electrocardiographic evidence of active ischemia or active conduction system abnormalities, or myocardial infarction within the last 6 months.
- Has known human immunodeficiency virus (HIV) infection.
- Has acute or chronic hepatitis B or hepatitis C infection.
- Is a pregnant or lactating woman. (Any women becoming pregnant during the study will be withdrawn from the study.)
- Has any serious uncontrolled, medical or psychological disorder that would impair the ability of the subject to receive study drugs.
- Has received another investigational agent within 30 days of study entry.
- Has known hypersensitivity to mannitol.
- Has Ann Arbor stage I disease.

Contacts and Locations

Locations

United States, Alabama

Birmingham Hematology and Oncology Associates, LLC
Birmingham, Alabama, United States, 35235

University of Alabama at Birmingham
Birmingham, Alabama, United States, 35294-3300

United States, California

Tower Cancer Research Foundation
Beverly Hills, California, United States, 90211-1850

United States, Connecticut

Hematology Oncology, P.C.
Stamford, Connecticut, United States, 06902

United States, Florida

University Cancer Institute
Boynton Beach, Florida, United States, 33435

Florida Cancer Institute - New Hope
New Port Richey, Florida, United States, 34655

United States, Georgia

Dublin Hematology Oncology Care P.C.
Dublin, Georgia, United States, 31021

Northwest Georgia Oncology Center
Marietta, Georgia, United States, 30060

Georgia Cancer Specialists
Tucker, Georgia, United States, 30084

United States, Illinois

Cancer Care and Hematology Specialists of Chicagoland
Niles, Illinois, United States, 60714

United States, Iowa

Siouxland Hematology-Oncology Assoc. LLP
Sioux City, Iowa, United States, 51101

United States, Kentucky

Kentucky Cancer Clinic
Hazard, Kentucky, United States, 41701

United States, Maryland

Carroll County Cancer Center
Westminster, Maryland, United States, 21157

United States, Missouri

Columbia Comprehensive Cancer Care Clinic
Jefferson City, Missouri, United States, 65109

United States, Nevada

Nevada Cancer Institute
Las Vegas, Nevada, United States, 89135

United States, New Jersey

Somerset Hematology Oncology Associates
Somerville, New Jersey, United States, 08876

United States, New York

Roswell Park Cancer Institute
Buffalo, New York, United States, 14263

Monter Cancer Center
Lake Success, New York, United States, 11042

United States, North Dakota

Mid Dakota Clinic
Bismarck, North Dakota, United States, 58504

United States, Oregon

Oregon Health Sciences University
Portland, Oregon, United States, 97239

United States, Pennsylvania

University of Pittsburgh Medical Center - Cancer Institute
Pittsburgh, Pennsylvania, United States, 15232

United States, South Carolina

Cancer Centers of the Carolinas
Greenville, South Carolina, United States, 29605

United States, Tennessee

The West Clinic
Memphis, Tennessee, United States, 38138

United States, Texas

Texas Oncology, P.A.
Bedford, Texas, United States, 76022

MD Anderson Cancer Center

Houston, Texas, United States, 77030-4009
Longview Cancer Center
Longview, Texas, United States, 75601
Joe Arrington Cancer Research
Lubbock, Texas, United States, 79410
Texas Oncology, P.A.
McAllen, Texas, United States, 78503
Cancer Care Centers of South Texas
San Antonio, Texas, United States, 78229
Texas Oncology
Waco, Texas, United States, 76712
Texas Oncology, P.A.
Webster, Texas, United States, 77598
US Oncology Research - Texoma Cancer Center
Wichita Falls, Texas, United States, 76310

United States, Virginia

Fairfax/Northern Virginia Hematology/Oncology
Fairfax, Virginia, United States, 22031

United States, Washington

Yakima Valley Memorial Hospital/North Start Lodge
Yakima, Washington, United States, 98902

Belgium

Cephalon Investigational Site
Bruxelles, Belgium, 1000
Cephalon Investigational Site
Bruxelles, Belgium, 1200
Cephalon Investigational Site
Gent, Belgium

Israel

Cephalon Investigational Site
Haifa, Israel, 31096
Cephalon Investigational Site
Nahariya, Israel, 22100

Investigators

Study Director: Sponsor's Medical Expert Cephalon

More Information

Responsible Party: Cephalon
Study ID Numbers: C18083/2048
2009-016725-34 [EudraCT Number]
Health Authority: United States: Food and Drug Administration
Belgium: Federal Agency for Medicinal Products and Health

Products
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Israel: Israeli Health Ministry Pharmaceutical Administration
Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products

Study Results

Participant Flow

Recruitment Details	
Pre-Assignment Details	

Arm/Group Title	Bendamustine and Ofatumumab	Total (Not public)
Arm/Group Description	There are 6 planned and 2 optional 28-day cycles in which participants are administered both bendamustine and ofatumumab in the following doses: Bendamustine administered at 90 mg/m^2 intravenously (iv) on study days 1 and 2. Ofatumumab administered at 300 mg iv on day 1 and 1000 mg iv on day 8 of cycle 1. Ofatumumab administered at 1000 mg iv on day 1 of all additional cycles.	
Period Title: **Overall Study**		
Started	50	50
Safety Set (Enrolled and Treated)	49	49
Completed	45	45
Not Completed	5	5
Reason Not Completed		
Death	2	2
Withdrawal by Subject	1	1
Lost to Follow-up	1	1
not specified	1	1
(Not Public)	Not Completed = 5 Total from all reasons = 5	

Baseline Characteristics

Arm/Group Title	Bendamustine and Ofatumumab
Arm/Group Description	There are 6 planned and 2 optional 28-day cycles in which participants are administered both bendamustine and ofatumumab in the following doses: Bendamustine administered at 90 mg/m^2 intravenously (iv) on study days 1 and 2. Ofatumumab administered at 300 mg iv on day 1 and 1000 mg iv on day 8 of cycle 1. Ofatumumab administered at 1000 mg iv on day 1 of all additional cycles.
Overall Number of Baseline Participants	49
Baseline Analysis Population Description [Not specified]	
Age, Continuous Mean (Standard Deviation) Units: years	59.1 (10.77)
Age, Customized Measure Type: Number Units: participants	
<65 years	31
>=65 years	18
Gender, Male/Female Measure Type: Number Units: participants	
Female	23
Male	26
Ethnicity (NIH/OMB) Measure Type: Number Units: participants	
Hispanic or Latino	3
Not Hispanic or Latino	45
Unknown or Not Reported	1
Race/Ethnicity, Customized Measure Type: Number Units: participants	
American Indian or Alaska Native	1
Asian	2

Pacific Islander	0
Black	2
White	44
Other	0

Outcome Measures

1. Primary Outcome

Title:	Percentage of Participants With a Best Overall Response of Complete Response (CR) or Partial Response (PR), as Determined by the International Working Group (IWG) Criteria As Assessed by Investigators
Description:	The IWG criteria (Cheson et al 2007) for a CR is a complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present before therapy. A PR is at least a 50% decrease in sum of the product of the diameters (SPD) of up to 6 of the largest dominant nodes or nodal masses, no increase should be observed in the size of other nodes, liver or spleen, and no new sites of disease should be observed.
Time Frame:	up to Week 32
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

Safety population of participants who were treated

Arm/Group Title	Bendamustine and Ofatumumab
▼ Arm/Group Description:	There are 6 planned and 2 optional 28-day cycles in which participants are administered both bendamustine and ofatumumab in the following doses: Bendamustine administered at 90 mg/m^2 intravenously (iv) on study days 1 and 2. Ofatumumab administered at 300 mg iv on day 1 and 1000 mg iv on day 8 of cycle 1. Ofatumumab administered at 1000 mg iv on day 1 of all additional cycles.
Number of Participants Analyzed	49
Number (95% Confidence Interval) Units: percentage of participants	90 (77.8 to 96.6)

2. Secondary Outcome

Title:	Percentage of Participants With a Best Overall Response of Complete Response (CR), as Determined by the International Working Group (IWG) Criteria As Assessed by Investigators
▼ Description:	The IWG criteria (Cheson et al 2007) for a CR is a complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present before therapy.
Time Frame:	up to Week 32
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description
Safety population of participants who were treated

Arm/Group Title	Bendamustine and Ofatumumab
▼ Arm/Group Description:	There are 6 planned and 2 optional 28-day cycles in which participants are administered both bendamustine and ofatumumab in the following doses: Bendamustine administered at 90 mg/m^2 intravenously (iv) on study days 1 and 2. Ofatumumab administered at 300 mg iv on day 1 and 1000 mg iv on day 8 of cycle 1. Ofatumumab administered at 1000 mg iv on day 1 of all additional cycles.

Number of Participants Analyzed	49
Number (95% Confidence Interval) Units: percentage of participants	67 (52.6 to 80.1)

Adverse Events

Time Frame	up to 39 weeks
Additional Description	
Source Vocabulary Name	MedDRA (13.0)
Assessment Type	Systematic Assessment

Arm/Group Title	Bendamustine and Ofatumumab
Arm/Group Description	There are 6 planned and 2 optional 28-day cycles in which participants are administered both bendamustine and ofatumumab in the following doses: Bendamustine administered at 90 mg/m^2 intravenously (iv) on study days 1 and 2. Ofatumumab administered at 300 mg iv on day 1 and 1000 mg iv on day 8 of cycle 1. Ofatumumab administered at 1000 mg iv on day 1 of all additional cycles.

Serious Adverse Events

	Bendamustine and Ofatumumab
	Affected / at Risk (%)
Total	14/49 (28.57%)
Blood and lymphatic system disorders	
Febrile neutropenia †A	2/49 (4.08%)
Eye disorders	
Diplopia †A	1/49 (2.04%)
Gastrointestinal disorders	
Ascites †A	1/49 (2.04%)
Colitis †A	1/49 (2.04%)
Diarrhoea †A	1/49 (2.04%)

Faeces discoloured †A	1/49 (2.04%)
Nausea †A	1/49 (2.04%)
General disorders	
Asthenia †A	1/49 (2.04%)
Device dislocation †A	1/49 (2.04%)
Fatigue †A	1/49 (2.04%)
Infusion related reaction †A	2/49 (4.08%)
Pyrexia †A	2/49 (4.08%)
Hepatobiliary disorders	
Portal vein thrombosis †A	1/49 (2.04%)
Infections and infestations	
Bacterial sepsis †A	1/49 (2.04%)
Device related sepsis †A	1/49 (2.04%)
Gastroenteritis †A	1/49 (2.04%)
Pneumonia †A	1/49 (2.04%)
Sepsis †A	1/49 (2.04%)
Tooth abscess †A	1/49 (2.04%)
Investigations	
Oxygen saturation decreased †A	1/49 (2.04%)
Metabolism and nutrition disorders	
Dehydration †A	1/49 (2.04%)
Failure to thrive †A	1/49 (2.04%)
Hypercalcaemia †A	1/49 (2.04%)
Hyperkalaemia †A	1/49 (2.04%)
Hypophagia †A	1/49 (2.04%)
Musculoskeletal and connective tissue disorders	
Muscular weakness †A	1/49 (2.04%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Non-small cell lung cancer †A	1/49 (2.04%)
Nervous system disorders	
Depressed level of consciousness †A	1/49 (2.04%)
Renal and urinary disorders	
Renal failure acute †A	1/49 (2.04%)
Respiratory, thoracic and mediastinal disorders	
Bronchospasm †A	1/49 (2.04%)
Sinus congestion †A	1/49 (2.04%)
Skin and subcutaneous tissue disorders	
Hyperhidrosis †A	1/49 (2.04%)

Rash †A	1/49 (2.04%)
Vascular disorders	
Hot flush †A	1/49 (2.04%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (13.0)

▼ Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%
	Bendamustine and Ofatumumab
	Affected / at Risk (%)
Total	49/49 (100%)
Blood and lymphatic system disorders	
Anaemia †A	5/49 (10.2%)
Leukopenia †A	7/49 (14.29%)
Lymphopenia †A	3/49 (6.12%)
Neutropenia †A	10/49 (20.41%)
Thrombocytopenia †A	4/49 (8.16%)
Cardiac disorders	
Palpitations †A	3/49 (6.12%)
Tachycardia †A	5/49 (10.2%)
Eye disorders	
Eye irritation †A	4/49 (8.16%)
Gastrointestinal disorders	
Abdominal pain †A	5/49 (10.2%)
Constipation †A	17/49 (34.69%)
Diarrhoea †A	12/49 (24.49%)
Dyspepsia †A	3/49 (6.12%)
Gastrooesophageal reflux disease †A	4/49 (8.16%)
Nausea †A	29/49 (59.18%)
Stomatitis †A	4/49 (8.16%)
Vomiting †A	12/49 (24.49%)
General disorders	
Asthenia †A	4/49 (8.16%)
Chills †A	6/49 (12.24%)
Fatigue †A	26/49 (53.06%)
Infusion related reaction †A	20/49 (40.82%)
Oedema peripheral †A	10/49 (20.41%)
Pyrexia †A	6/49 (12.24%)

Immune system disorders	
Drug hypersensitivity †A	5/49 (10.2%)
Infections and infestations	
Sinusitis †A	4/49 (8.16%)
Upper respiratory tract infection †A	4/49 (8.16%)
Investigations	
Haemoglobin decreased †A	3/49 (6.12%)
Neutrophil count decreased †A	11/49 (22.45%)
Platelet count decreased †A	7/49 (14.29%)
Weight decreased †A	4/49 (8.16%)
White blood cell count decreased †A	13/49 (26.53%)
Metabolism and nutrition disorders	
Decreased appetite †A	7/49 (14.29%)
Hypokalaemia †A	3/49 (6.12%)
Hypomagnesaemia †A	3/49 (6.12%)
Musculoskeletal and connective tissue disorders	
Back pain †A	6/49 (12.24%)
Myalgia †A	7/49 (14.29%)
Pain in extremity †A	3/49 (6.12%)
Nervous system disorders	
Dizziness †A	10/49 (20.41%)
Dysgeusia †A	4/49 (8.16%)
Headache †A	12/49 (24.49%)
Psychiatric disorders	
Anxiety †A	4/49 (8.16%)
Insomnia †A	7/49 (14.29%)
Respiratory, thoracic and mediastinal disorders	
Cough †A	8/49 (16.33%)
Dyspnoea †A	13/49 (26.53%)
Nasal congestion †A	4/49 (8.16%)
Rhinitis allergic †A	3/49 (6.12%)
Skin and subcutaneous tissue disorders	
Periorbital oedema †A	3/49 (6.12%)
Pruritus †A	8/49 (16.33%)
Rash †A	9/49 (18.37%)
Urticaria †A	8/49 (16.33%)
Vascular disorders	
Hypertension †A	5/49 (10.2%)
Hypotension †A	3/49 (6.12%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (13.0)

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Sponsor has the right 60 days before submission for publication to review/provide comments. If the Sponsor's review shows that potentially patentable subject matter would be disclosed, publication or public disclosure shall be delayed for up to 90 additional days in order for the Sponsor, or Sponsor's designees, to file the necessary patent applications. In multicenter trials, each PI will postpone single center publications until after disclosure or publication of multicenter data.

Results Point of Contact

Name/Official Title: Director, Clinical Research
Organization: Teva Branded Pharmaceutical Products, R&D Inc.
Phone: 215-591-3000
Email: ustevatrials@tevapharm.com

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