A Study to Compare the Efficacy and Safety of Obinutuzumab + GDC-0199 Versus Obinutuzumab + Chlorambucil in Patients With Chronic Lymphocytic Leukemia

This study is currently recruiting participants. (see Contacts and Locations)

Verified February 2016 by Hoffmann-La Roche

Sponsor:
Hoffmann-La Roche

Collaborator:
AbbVie

Information provided by (Responsible Party):
Hoffmann-La Roche

ClinicalTrials.gov Identifier:
NCT02242942

First received: September 16, 2014
Last updated: February 1, 2016
Last verified: February 2016
History of Changes

Purpose

This open-label, multicenter, randomized Phase III study is designed to compare the efficacy and safety of a combined regimen of obinutuzumab and GDC-0199 versus obinutuzumab + chlorambucil (GClb) in patients with chronic lymphocytic leukemia (CLL) and coexisting medical conditions. The anticipated time on study treatment will be approximately one year and the follow-up period will be up to 5 years.

Condition	Intervention	Phase
Lymphocytic Leukemia, Chronic	Drug: Chlorambucil Drug: GDC-0199 Drug: Obinutuzumab	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Resource links provided by NLM:

MedlinePlus related topics: Chronic Lymphocytic Leukemia Leukemia

Drug Information available for: Chlorambucil Obinutuzumab

Genetic and Rare Diseases Information Center resources: Chronic Lymphocytic Leukemia Leukemia, B-cell, Chronic

U.S. FDA Resources

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measures:

- Progression-free survival (PFS), defined as the time from randomization to the first occurrence of progression, relapse or death from any cause as assessed by the investigator using IWCLL criteria [Time Frame: Up to 5 years] [Designated as safety issue: No]

Secondary Outcome Measures:

- PFS based on Institutional Review Committee (IRC)-assessments, defined as the time from randomization to the first occurrence of progression or relapse or death from any cause [Time Frame: Up to 5 years] [Designated as safety issue: No]
- Objective response rate ([ORR] defined as rate of a clinical response of complete response [CR], CR with incomplete bone marrow recovery [CRi] or partial response [PR]) as determined by the investigator, according to the IWCLL criteria [Time Frame: At the completion of treatment assessment, approximately 1 year] [Designated as safety issue: No]
- Minimal residual disease (MRD) response rate, as measured by allele-specific oligonucleotide polymerase chain reaction (ASO-PCR) [Time Frame: At the completion of treatment assessment, approximately 1 year] [Designated as safety issue: No]
- ORR at completion of combination treatment response assessment [Time Frame: Cycle 7 day 1 or 28 days after last IV infusion, approximately 6 months] [Designated as safety issue: No]
- MRD response rate, as measured by ASO-PCR at completion of combination treatment response assessment [Time Frame: Cycle 9 day 1 or 3 months after last IV infusion, approximately 9 months] [Designated as safety issue: No]

- Overall survival [Time Frame: Time betw een the date of randomization and the date of death due to any cause, up to approximately 5 years] [Designated as safety issue: No]
- Duration of objective response [Time Frame: Time from the first occurrence of a documented objective response to the time of progressive disease as determined by the investigator or death from any cause, up to approximately 5 years] [Designated as safety issue: No]
- Best response achieved (CR, CRi, PR, stable disease, or progressive disease) [Time Frame: Up to and including the assessment at completion of treatment assessment, w ithin 3 months of last day of treatment, approximately 1 year] [Designated as safety issue: No]
- Event-free survival [Time Frame: Time betw een date of randomization and the date of disease progression/relapse on the basis of investigator-assessment, death, or start of a new anti-leukemic therapy, up to 5 years] [Designated as safety issue: No]
- Time to next anti-leukemic treatment [Time Frame: Time betw een the date of randomization and the date of first intake of new anti-leukemic therapy, up to 5 years] [Designated as safety issue: No]
- Incidence of adverse events assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0 [Time Frame: 28 days after the last dose of GDC-0199 or after 90 days after last dose of obinutuzumab, w hichever is longer] [Designated as safety issue: No]
- Incidence of severe adverse events [Time Frame: Up to 5 years] [Designated as safety issue: No]
- Incidence of adverse events of special interest [Time Frame: Up to 2 years after last dose of study drug] [Designated as safety issue: No]

Estimated Enrollment: 432
Study Start Date: December 2014
Estimated Study Completion Date: January 2020
Estimated Primary Completion Date: November 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Safety run-in phase Non-randomized phase	Drug: GDC-0199 GDC-0199, oral tablet: 20 mg daily during Cycle 1, Day 22-28; 50 mg daily during Cycle 2, Day 1-7; 100 mg daily during Cycle 2, Day 8-14; 200 mg daily during Cycle 2, Day 15-21; 400 mg daily during Cycle 2, Day 22-28 and on Day 1-28 for all subsequent cycles until the end of Cycle 12 Other Name: ABT-0199 Drug: Obinutuzumab Obinutuzumab, intravenous (IV) infusion: 100 mg or 1000 mg, depending on splitting rules, at Cycle 1, Day 1 (if 100 mg w as received on Day 1, 900 mg w ill be administered on Cycle 1, Day 2); 1000 mg at Cycle 1, Day 8 and Day 15; 1000 mg at Day 1 for all subsequent cycles until the end of Cycle 6 Other Name: GA-101; gazyva
Experimental: Treatment A Randomized phase	Drug: GDC-0199 GDC-0199, oral tablet: 20 mg daily during Cycle 1, Day 22-28; 50 mg daily during Cycle 2, Day 1-7; 100 mg daily during Cycle 2, Day 8-14; 200 mg daily during Cycle 2, Day 15-21; 400 mg daily during Cycle 2, Day 22-28 and on Day 1-28 for all subsequent cycles until the end of Cycle 12 Other Name: ABT-0199 Drug: Obinutuzumab Obinutuzumab, intravenous (IV) infusion: 100 mg or 1000 mg, depending on splitting rules, at Cycle 1, Day 1 (if 100 mg w as received on Day 1, 900 mg w ill be administered on Cycle 1, Day 2); 1000 mg at Cycle 1, Day 8 and Day 15; 1000 mg at Day 1 for all subsequent cycles until the end of Cycle 6 Other Name: GA-101; gazyva
Experimental: Treatment B Randomized phase	Drug: Chlorambucil Chlorambucil, administered orally: 0.5 mg/kg at Day 1 and Day 15 for Cycle 1-12 Drug: Obinutuzumab Obinutuzumab, intravenous (IV) infusion: 100 mg or 1000 mg, depending on splitting rules, at Cycle 1, Day 1 (if 100 mg w as received on Day 1, 900 mg w ill be administered on Cycle 1, Day 2); 1000 mg at Cycle 1, Day 8 and Day 15; 1000 mg at Day 1 for all subsequent cycles until the end of Cycle 6 Other Name: GA-101; gazyva

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Documented previously untreated CLL according to the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria
- CLL requiring treatment according to IWCLL criteria
- Total Cumulative Illness Rating Scale (CIRS score) > 6
- Adequate marrow function independent of grow th factor or transfusion support w ithin 2 w eeks of screening as per protocol, unless cytopenia is due to marrow involvement of CLL
- Adequate liver function
- Life expectancy > 6 months
- Agreement to use highly effective contraceptive methods per protocol

Exclusion Criteria:

- Transformation of CLL to aggressive Non-Hodgkin's lymphoma (Richter's transformation or pro-lymphocytic leukemia)
- Know n central nervous system involvement
- Patients w ith a history of confirmed progressive multifocal leukoencephalopathy (PML)
- An individual organ/ system impairment score of 4 as assessed by the CIRS definition limiting the ability to receive the treatment regimen of this trial w ith the exception of eyes, ears, nose, throat organ system
- Patients w ith uncontrolled autoimmune hemolytic anemia or immune thrombocytopenia
- Inadequate renal function
- History of prior malignancy, except for conditions as listed in the protocol if patients have recovered from the acute side effects incurred as a result of previous therapy
- Use of investigational agents or concurrent anti-cancer treatment w ithin the last 4 w eeks of registration
- Patients w ith active bacterial, viral, or fungal infection requiring systemic treatment w ithin the last tw o months prior to registration
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies or know n sensitivity or allergy to murine products
- Hypersensitivity to chlorambucil, obinutuzumab, or GDC-0199 or to any of the excipients
- Pregnant w omen and nursing mothers
- Positive test results for chronic HBV infection (defined as positive HBsAg serology) or positive test result for hepatitis C (hepatitis C virus [HCV] antibody serology testing)
- Patients w ith know n infection w ith human immunodeficiency virus (HIV) or human T-cell leukemia virus-1 (HTLV-1)
- Requires the use of w arfarin, marcumar, or phenprocoumon
- Received agents know n to be strong CYP3A4 inhibitors or inducers w ithin 7 days prior to the first dose of study drug

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk w ith your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02242942

Contacts

Contact: Reference Study ID Number: **BO25323** w w w .roche.com/about_roche/roche_w orldw ide.htm 888-662-6728 (U.S. Only) global.rochegenentechtrials@roche.cc

Show 196 Study Locations

Sponsors and Collaborators

Hoffmann-La Roche

AbbVie

Investigators

Study Director: Clinical Trials Hoffmann-La Roche

More Information

No publications provided

Responsible Party:	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT02242942 History of Changes
Other Study ID Numbers:	**BO25323** 2014-001810-24
Study First Received:	September 16, 2014
Last Updated:	February 1, 2016
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Leukemia, Lymphocytic, Chronic, B-Cell	Neoplasms by Histologic Type
Leukemia, Lymphoid	Chlorambucil
Immune System Diseases	Obinutuzumab
Immunoproliferative Disorders	Alkylating Agents
Leukemia	Antineoplastic Agents
Leukemia, B-Cell	Antineoplastic Agents, Alkylating
Lymphatic Diseases	Molecular Mechanisms of Pharmacological Action
Lymphoproliferative Disorders	Pharmacologic Actions
Neoplasms	Therapeutic Uses

ClinicalTrials.gov processed this record on February 03, 2016