A Study of Idasanutlin in Combination With Obinutuzumab in Relapsed/Refractory (R/R) Follicular Lymphoma (FL) and in Combination With Rituximab in R/R Diffuse Large B-Cell Lymphoma (DLBCL) Participants

This study is currently recruiting participants.

See **Contacts and Locations**

Verified June 2017 by Hoffmann-La Roche

Sponsor:
Hoffmann-La Roche

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

ClinicalTrials.gov Identifier:
NCT02624986

First received: December 1, 2015
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History of Changes

Purpose

This is a open-label, mutlicenter, non-randomized, study to evaluate the safety, efficacy, and pharmacokinetics of idasanutlin in combination with obinutuzumab in participants with R/R FL and rituximab in combination with idasanutlin in R/R DLBCL. The study will include an initial dose-escalation phase followed by an expansion phase. The dose-escalation phase is designed to determine the recommended phase 2 dose (RP2D) for idasanutlin in combination with obinutuzumab for FL and in combination with rituximab for DLBCL. The expansion phase is designed to further assess the safety and efficacy of obinutuzumab in combination with idasanutlin at the RP2D with the selected regimen in participants with R/R FL and of rituximab in combination with idasanutlin at the RP2D in participants with R/R DLBCL.

Condition	Intervention	Phase
Non-Hodgkin's Lymphoma	Drug: Idasanutlin	Phase 1

	Drug: Obinutuzumab Drug: Rituximab	Phase 2

Study Type: Interventional
Study Design: Allocation: Non-Randomized
Intervention Model: Parallel Assignment
Masking: No masking
Primary Purpose: Treatment

Official Title: A Phase Ib/II Study Evaluating the Safety and Efficacy of Obinutuzumab in Combination With Idasanutlin in Patients With Relapsed or Refractory Follicular Lymphoma and Obinutuzumab or Rituximab in Combination With Idasanutlin in Patients With Relapsed or Refractory Diffuse Large B-cell Lymphoma

Resource links provided by NLM:

MedlinePlus related topics: Lymphoma

Drug Information available for: Rituximab Obinutuzumab

Genetic and Rare Diseases Information Center resources: Lymphosarcoma Diffuse Large B-Cell Lymphoma B-cell Lymphoma Follicular Lymphoma

U.S. FDA Resources

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measures:

- Percentage of Participants with Complete Response (CR), Determined by an Independent Review Committee (IRC) on the Basis of Positron Emission Tomography (PET) and Computed Tomography (CT) Scans [Time Frame: Within 6 to 8 weeks after Day 1 of Cycle 6 (up to approximately 28 weeks from Day 1 of Cycle 1) (1 Cycle=28 days)]

Secondary Outcome Measures:

- Percentage of Participants with Dose-Limiting Toxicities (DLTs) [Time Frame: Cycles 1, 2 (1 Cycle=28 days)]
- Recommended Phase 2 Dose (RP2D) for Idasanutlin in Combination with Obinutuzumab [Time Frame: Cycles 1, 2 (1 Cycle=28 days)]
- RP2D of Idasanutlin in Combination with Rituximab [Time Frame: Cycles 1, 2 (1 Cycle=28 days)]
- Percentage of Participants with CR, Determined by the Investigator on the Basis of PET and CT Scans [Time Frame: Within 6 to 8 weeks after Day 1 of Cycle 6 (up to approximately 28 weeks from Day 1 of Cycle 1) (1 Cycle=28 days)]
- Percentage of Participants with CR, Determined by an IRC and the Investigator on the Basis of CT Scans Alone [Time Frame: Within 6 to 8 weeks after Day 1 of Cycle 6 (up to approximately 28 weeks from Day 1 of Cycle 1) (1 Cycle=28 days)]

- Percentage of Participants with Objective Response, Determined by an IRC on the Basis of PET and CT Scans [Time Frame: Within 6 to 8 weeks after Day 1 of Cycle 6 (up to approximately 28 weeks from Day 1 of Cycle 1) (1 Cycle=28 days)]
- Percentage of Participants with Objective Response, Determined by the Investigator on the Basis of PET and CT Scans [Time Frame: Within 6 to 8 weeks after Day 1 of Cycle 6 (up to approximately 28 weeks from Day 1 of Cycle 1) (1 Cycle=28 days)]
- Percentage of Participants with Objective Response, Determined by an IRC on the Basis of CT Scans Alone [Time Frame: Within 6 to 8 weeks after Day 1 of Cycle 6 (up to approximately 28 weeks from Day 1 of Cycle 1) (1 Cycle=28 days)]
- Percentage of Participants with Objective Response, Determined by the Investigator on the Basis of CT Scans Alone [Time Frame: Within 6 to 8 weeks after Day 1 of Cycle 6 (up to approximately 28 weeks from Day 1 of Cycle 1) (1 Cycle=28 days)]
- Percentage of Participants with Best Response of CR or Partial Response (PR), Determined by the Investigator on the Basis of CT Scans Alone [Time Frame: Baseline up to disease progression or death whichever occurs first (up to approximately 4 years)]
- Serum Obinutuzumab Concentration [Time Frame: Pre-infusion (0 hours [hr]) up to approximately 4 years (Detailed time frame is available in outcome measure description)]

  Pre-infusion (any time prior to the first dose on that day) (infusion starts at 50 milligrams per hour [mg/hr] then may be increased by 50mg/hr every 30 minutes to maximum of 400mg/hr), 30 minutes (min) after end of infusion on Day 1 Cycle 1; pre-infusion (within 5 hr prior to dose), 30 min after end of obinutuzumab infusion on Day 1 of Cycles 2, 4, 6; pre-obinutuzumab infusion (within 5 hr prior to dose) on Day 1 of months 1, 7, 13, 19; anytime during treatment discontinuation visit, 120 days after the last dose, and 1-2 years after the last dose (1 cycle=28 days) up to approximately 4 years.

- Serum Rituximab Concentration in DLBCL Participants [Time Frame: Pre-infusion (0 hr) up to approximately 4 years (Detailed time frame is available in outcome measure description)]

  Pre-infusion (any time prior to the first dose on that day) (infusion starts at 50 mg/hr then may be increased by 50mg/hr every 30 minutes to maximum of 400mg/hr), 30 min after end of infusion on Day 1 Cycle 1; pre-infusion (within 5 hr prior to dose) on Day 1 of Cycles 2, 4; pre-infusion (within 5 hr prior to dose), 30 min after end of obinutuzumab infusion on Day 1 of Cycle 6 (1 cycle=28 days) up to approximately 4 years.

- Plasma Idasanutlin Concentration in DLBCL Participants [Time Frame: Pre-administration (0 hr) up to end of induction phase of 6 cycles (1 Cycle=28 days) (Detailed time frame is available in outcome measure description)]

  Pre-administration (any time prior the first dose that day), 6 hr post idasanutlin administration on Day 1 of Cycle 1, prior to idasanutlin administration (within 1 hr prior to dose), 2, 4, 6 hrs post-idasanutlin administration on Day 5 of Cycle 1; pre-administration (within 1 hr prior to dose), 6 hr post-idasanutlin administration on Days 1, 5 of Cycles 2, 4 up to end of induction phase of 6 cycles (1 cycle=28 days).

- Plasma Idasanutlin Concentration in FL Participants [Time Frame: Pre-administration (0 hr) up to end of induction phase of 6 cycles (1 Cycle=28 days) (Detailed time frame is available in outcome measure description)]

Pre-administration (any time prior the first dose that day), 6 hr post idasanutlin administration on Day 1 of Cycle 1, prior to idasanutlin administration (within 1 hr prior to dose), 2, 4, 6 hrs post-idasanutlin administration on Day 5 of Cycle 1; pre-administration (within 1 hr prior to dose), 6 hr post-idasanutlin administration on Days 1, 5 of Cycles 2, 4 up to end of induction phase of 6 cycles (1 cycle=28 days).

- Percentage of Participants with Adverse Events [Time Frame: Baseline up to approximately 4 years]

Estimated Enrollment:	120
Actual Study Start Date:	December 23, 2015
Estimated Study Completion Date:	May 15, 2022
Estimated Primary Completion Date:	May 15, 2022 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Dose-Escalation Cohort (DLBCL Participants) Participants will receive 'Regimen A', which includes escalating doses of idasanutlin in combination with a fixed dose of obinutuzumab (1000 milligrams [mg]) for 6 cycles (1 Cycle=28 days) until maximum tolerated dose (MTD) is achieved. Regimen A will be followed by treatment which includes idasanutlin in combination with fixed dose of rituximab (375 milligrams per square meter [mg/m^2]) for 6 cycles (1 Cycle=28 days) to determine the RP2D for this treatment.	Drug: Idasanutlin Participants will receive idasanutlin film-coated tablets at a starting dose of 100 mg daily on Days 1 to 5 of each 28-day cycle. Escalation will occur in at least 50-mg increments, and daily dosages greater than or equal to (>/=) 400 mg will be split into twice daily dosing. Other Name: RO5503781 Drug: Obinutuzumab Participants will receive a fixed dose of obinutuzumab, 1000 mg intravenous (IV) infusion to be given on Days 1, 8 and 15 of Cycle 1 and on Day 1 of Cycles 2 to 6 (1 Cycle=28 days). For eligible participants with FL, post-induction treatment may be given at a dose of 1000 mg via IV infusion on Day 1 of every other month for a maximum of up to 24 months. Other Name: RO5072759 Drug: Rituximab Participants will receive a fixed dose of rituximab, 375 mg/m^2 IV infusion on Day 1 of Cycles 1-6. Post-induction treatment for eligible participants may be given at a dose of 375 mg/m^2 IV infusion on Day 1 of every other month for up to 6 months, until disease progression or unacceptable toxicity. Other Name: RO0452294

Experimental: Dose-Escalation Cohort (FL Participants) Participants will receive 'Regimen A', which includes escalating doses of idasanutlin in combination with a fixed dose of obinutuzumab (1000 mg) for 6 cycles (1 Cycle=28 days) until MTD is achieved. Regimen A will be followed by Regimen B which includes obinutuzumab given alone in Cycle 1 and idasanutlin and obinutuzumab combination from Cycles 2-6 (1 Cycle=28 days) to determine the RP2D for this regimen.	Drug: Idasanutlin Participants will receive idasanutlin film-coated tablets at a starting dose of 100 mg daily on Days 1 to 5 of each 28-day cycle. Escalation will occur in at least 50-mg increments, and daily dosages greater than or equal to (>/=) 400 mg will be split into twice daily dosing. Other Name: RO5503781 Drug: Obinutuzumab Participants will receive a fixed dose of obinutuzumab, 1000 mg intravenous (IV) infusion to be given on Days 1, 8 and 15 of Cycle 1 and on Day 1 of Cycles 2 to 6 (1 Cycle=28 days). For eligible participants with FL, post-induction treatment may be given at a dose of 1000 mg via IV infusion on Day 1 of every other month for a maximum of up to 24 months. Other Name: RO5072759
Experimental: Expansion Cohort: DLBCL Participants Participants with DLBCL will receive 6 cycles (1 Cycle=28 days) of induction treatment with idasanutlin at the RP2D identified during the dose-escalation phase, in combination with rituximab. Induction treatment will be followed by post-induction consolidation treatment with rituximab and idasanutlin for 6 months.	Drug: Idasanutlin Participants will receive idasanutlin film-coated tablets at a starting dose of 100 mg daily on Days 1 to 5 of each 28-day cycle. Escalation will occur in at least 50-mg increments, and daily dosages greater than or equal to (>/=) 400 mg will be split into twice daily dosing. Other Name: RO5503781 Drug: Rituximab Participants will receive a fixed dose of rituximab, 375 mg/m^2 IV infusion on Day 1 of Cycles 1-6. Post-induction treatment for eligible participants may be given at a dose of 375 mg/m^2 IV infusion on Day 1 of every other month for up to 6 months, until disease progression or unacceptable toxicity. Other Name: RO0452294
Experimental: Expansion Cohort: FL Participants Participants will receive 6 cycles (1 Cycle=28 days) of induction treatment with idasanutlin at the RP2D identified during the dose-escalation phase, in combination with obinutuzumab. Participants will receive either 'Regimen A' or 'Regimen B' which will be determined at the end of the dose-escalation	Drug: Idasanutlin Participants will receive idasanutlin film-coated tablets at a starting dose of 100 mg daily on Days 1 to 5 of each 28-day cycle. Escalation will occur in at least 50-mg increments, and daily dosages greater than

phase. Induction treatment will be followed by post-induction maintenance treatment with obinutuzumab and idasanutlin for a maximum of up to 24 months.	or equal to (>/=) 400 mg will be split into twice daily dosing. Other Name: RO5503781 Drug: Obinutuzumab Participants will receive a fixed dose of obinutuzumab, 1000 mg intravenous (IV) infusion to be given on Days 1, 8 and 15 of Cycle 1 and on Day 1 of Cycles 2 to 6 (1 Cycle=28 days). For eligible participants with FL, post-induction treatment may be given at a dose of 1000 mg via IV infusion on Day 1 of every other month for a maximum of up to 24 months. Other Name: RO5072759

Eligibility

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2
- Histologically documented cluster of differentiation (CD) 20-positive B-cell lymphoma classified as relapsed or refractory FL or DLBCL after treatment with at least two prior chemoimmunotherapy regimens that included an anti-CD20 monoclonal antibody (mAb) and for which no other more appropriate treatment option exists
- At least one bidimensionally measurable lesion
- Agreement to remain abstinent or use adequate contraception, among women or men of childbearing potential

Exclusion Criteria:

- Known CD20-negative status at relapse or progression
- Prior allogeneic stem cell transplantation (SCT), or autologous SCT within 100 days prior to Day 1 of Cycle 1
- Current use of systemic corticosteroids greater than (>) 20 mg prednisone per day (or equivalent), or prior anti-cancer therapy to include: radioimmunoconjugate within 12 weeks; mAb or antibody-drug conjugate within 4 weeks; or radiotherapy/chemotherapy/hormone therapy/targeted small-molecule therapy within 2 weeks prior to Day 1 of Cycle 1
- Requirement for chronic anticoagulation
- Central nervous system (CNS) disease
- Active infection
- Positive for human immunodeficiency virus (HIV) or hepatitis B or C
- Receipt of a live virus vaccine within 28 days prior to Day 1 of Cycle 1

- Poor hematologic, renal, or hepatic function
- Pregnant or lactating women
- History of progressive multifocal leukoencephalopathy (PML)

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with 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: NCT02624986

Contacts

Contact: Reference Study ID Number: **BH29812** www.roche.com/about_roche/roche_worldwide.htm

Show 26 Study Locations

Sponsors and Collaborators

Hoffmann-La Roche

Investigators

Study Director: Sai Li, M.D., Ph.D. Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT02624986 History of Changes
Other Study ID Numbers:	**BH29812** 2015-002100-83 (EudraCT Number)
Study First Received:	December 1, 2015
Last Updated:	June 29, 2017

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Additional relevant MeSH terms:

Lymphoma	Immunoproliferative Disorders
Lymphoma, Follicular	Immune System Diseases
Lymphoma, Non-Hodgkin	Obinutuzumab
Lymphoma, B-Cell	Rituximab
Lymphoma, Large B-Cell, Diffuse	Antineoplastic Agents
Neoplasms by Histologic Type	Immunologic Factors
Neoplasms	Physiological Effects of Drugs
Lymphoproliferative Disorders	Antirheumatic Agents
Lymphatic Diseases	

ClinicalTrials.gov processed this record on July 21, 2017