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Trial record **1 of 1** for: A Safety and Efficacy Study of Ibrutinib in Pediatric and Young Adult Participants With Relapsed or Refractory Mature B-cell non-Hodgkin Lymphoma

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A Safety and Efficacy Study of Ibrutinib in Pediatric and Young Adult Participants With Relapsed or Refractory Mature B-cell Non-Hodgkin Lymphoma

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal  Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier:
NCT02703272

[Recruitment Status](#)  :

Recruiting

[First Posted](#)  : March 9, 2016

[Last Update Posted](#)  :

January 12, 2018

See [Contacts and Locations](#)

Sponsor:

Janssen Research & Development, LLC

Information provided by (Responsible Party):

Janssen Research & Development, LLC

Study Description

Go to



Brief Summary:

The purpose of this study is to confirm that the pharmacokinetics of ibrutinib in pediatric participants is consistent with that in adults (part 1) and to assess efficacy (event-free survival [EFS]) of ibrutinib in combination with rituximab, ifosfamide, carboplatin, and etoposide (RICE) or rituximab, vincristine, ifosfamide, carboplatin, and idarubicin (RVICI) background therapy compared to RICE or RVICI background therapy alone (part 2).

Condition or disease	Intervention/treatment	Phase
Lymphoma, Non-Hodgkin	Drug: Ibrutinib Drug: Rituximab Drug: Ifosfamide Drug: Carboplatin Drug: Etoposide Drug: Vincristine Drug: Idarubicin Drug: Dexamethasone	Phase 3

Detailed Description:

This is a Phase 3, randomized (study medication assigned to participants by chance), open-label (identity of study drug will be known to participant and study staff), controlled study which consists of two parts: Part 1 and Part 2. The Part 1 is a pharmacokinetic run-in part, which will be conducted before starting the randomized part (Part 2) of the study and Part 2 is a randomized and open-label study. Part 1 and Part 2 of the study will be conducted in 3 phases: a Pretreatment (Screening) Phase (Up to 14 days before administration of study drug), a Treatment Phase, and a Posttreatment Phase. The Treatment Phase will extend from enrollment (in Part 1) or randomization (in Part 2) until 1 of the following: 1) completion of 3 cycles of therapy, 2) transplantation, if clinically indicated, or 3) progressive disease (PD), whichever comes first. The Posttreatment Phase will continue until death, loss to follow up, consent withdrawal, or study end, whichever occurs first. The end of study is defined as when approximately 60 event-free survival (EFS) events have occurred in Part 2 (death, disease progression, or lack of complete response [CR] or partial response [PR] after 3 cycles of treatment based on blinded independent event review), or the sponsor terminates the study, whichever comes first. Participants in Part 1 will be 1 to less than (<) 18 years old. Participants in Part 2 will be 1 to 30 years old. Participants will be primarily evaluated for pharmacokinetics in part 1 and efficacy (EFS) of

ibrutinib in combination with RICE or RVICI background therapy compared to RICE or RVICI background therapy alone in part 2. Participants' safety will be monitored throughout the study.

Study Design

Go to

Study Type ⓘ : Interventional (Clinical Trial)
Estimated Enrollment ⓘ : 96 participants
Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: None (Open Label)
Primary Purpose: Treatment
Official Title: A Randomized, Open-label, Safety and Efficacy Study of Ibrutinib in Pediatric and Young Adult Patients With Relapsed or Refractory Mature B-cell Non-Hodgkin Lymphoma
Actual Study Start Date ⓘ : July 1, 2016
Estimated Primary Completion Date ⓘ : June 29, 2021
Estimated Study Completion Date ⓘ : March 1, 2024

Resource links provided by the National Library of Medicine



[MedlinePlus](#) related topics: [Lymphoma](#)

[Drug Information](#) available for: [Ibrutinib](#)

[Genetic and Rare Diseases Information Center](#) resources: [Lymphosarcoma](#) [B-cell Lymphoma](#)

[U.S. FDA Resources](#)

Arms and Interventions

Go to

Arm ⓘ	Intervention/treatment ⓘ
Experimental: Part 1: Ibrutinib The first 2 participants enrolled in each age group (1-5 years, 6-11 years and 12-17 years) will receive starting dose of Ibrutinib 240 milligram per square meter (mg/m ²) for the first cycle, followed by dose escalation at the start of Cycle 2 as long as all pharmacokinetic assessments are	Drug: Ibrutinib Participants will receive Ibrutinib (dose 240 mg/m ² /329 mg/m ² per day) during part 1 and part 2.

within the expected range and there are no safety concerns. For participants being treated at 240 mg/m² dose level during the first cycle, the maximum dose should not exceed a total of 420 mg/day. All participants will receive rituximab, ifosfamide, carboplatin, etoposide and dexamethasone (RICE) or ituximab, vincristine, ifosfamide, carboplatin, idarubicin and dexamethasone (RVICI) background therapy (investigator's choice), during treatment phase. Participants with PR or better only will receive Ibrutinib for 3 cycles or until PD, unacceptable toxicity or until initiating antilymphoma therapy or a conditioning regimen for stem cell transplantation during post-treatment phase.

Drug: Rituximab

Participants will receive a cumulative dose of rituximab 750 mg/m² as a part of RICE/RVICI regimen in part 1 and part 2 per cycle.

Drug: Ifosfamide

Participants will receive a cumulative dose of Ifosfamide 9 g/m² and 10 g/m² as a part of RICE and RVICI regimen respectively in part 1 and part 2 per cycle.

Drug: Carboplatin

Participants will receive a cumulative dose of carboplatin 635 mg/m² and 800 mg/m² as a part of RICE and RVICI regimen respectively in part 1 and part 2 per cycle.

Drug: Etoposide

Participants will receive a cumulative dose of etoposide 300 mg/m² in part 1 and part 2 as a part of RICE regimen per cycle.

Drug: Vincristine

Participants will receive a cumulative dose of vincristine 1.6 mg/m² in part 1 and part 2 as a part of RVICI regimen per cycle.

Drug: Idarubicin

	<p>Participants will receive a cumulative dose of idarubicin 20 mg/m² in part 1 and part 2 as a part of RVICI regimen per cycle.</p> <p>Drug: Dexamethasone</p> <p>Participants will receive a cumulative dose of dexamethasone 100 mg/m² in part 1 and part 2 as a part of RICE/RVICI regimen per cycle.</p>
<p>Experimental: Part 2: Ibrutinib</p> <p>Participants will either receive ibrutinib and RICE/RVICI background therapy or RICE/RVICI background therapy alone, until 3 cycles are completed or until PD or unacceptable toxicity during the treatment phase. Participants who received ibrutinib and RICE/RVICI background therapy and with PR or better only will receive ibrutinib alone for 3 cycles during post-treatment phase.</p>	<p>Drug: Ibrutinib</p> <p>Participants will receive Ibrutinib (dose 240 mg/m² /329 mg/m² per day) during part 1 and part 2.</p> <p>Drug: Rituximab</p> <p>Participants will receive a cumulative dose of rituximab 750 mg/m² as a part of RICE/RVICI regimen in part 1 and part 2 per cycle.</p> <p>Drug: Ifosfamide</p> <p>Participants will receive a cumulative dose of Ifosfamide 9 g/m² and 10 g/m² as a part of RICE and RVICI regimen respectively in part 1 and part 2 per cycle.</p> <p>Drug: Carboplatin</p> <p>Participants will receive a cumulative dose of carboplatin 635 mg/m²</p>

and 800 mg/m² as a part of RICE and RVICI regimen respectively in part 1 and part 2 per cycle.

Drug: Etoposide

Participants will receive a cumulative dose of etoposide 300 mg/m² in part 1 and part 2 as a part of RICE regimen per cycle.

Drug: Vincristine

Participants will receive a cumulative dose of vincristine 1.6 mg/m² in part 1 and part 2 as a part of RVICI regimen per cycle.

Drug: Idarubicin

Participants will receive a cumulative dose of idarubicin 20 mg/m² in part 1 and part 2 as a part of RVICI regimen per cycle.

Drug: Dexamethasone

Participants will receive a cumulative dose of dexamethasone 100 mg/m² in part 1 and part 2 as a part of RICE/RVICI regimen per cycle.

Outcome Measures

Go to



Primary Outcome Measures ⓘ :

1. Part 1: Area Under The Plasma Concentration-Time Curve (AUC) of Ibrutinib [Time Frame: Predose, at 1, 2, 4, and 6 hours postdose on Day 1, and Day 7 or 8 of cycle 1; predose, 1, 2, 4, and 6 hours postdose on Day 1 of Cycle 2 or Cycle 3 (each cycle of 28 days)]

AUC is the under the plasma concentration-time curve.

2. Part 1: Apparent (oral) Plasma Clearance (CL/F) of Ibrutinib [Time Frame: Predose, at 1, 2, 4, and 6 hours postdose on Day 1, and Day 7 or 8 of Cycle 1; predose, 1, 2, 4, and 6 hours postdose on Day 1 of Cycle 2 or Cycle 3 (each cycle of 28 days)]

CL/F is the apparent (oral) Plasma Clearance.

3. Part 1: Apparent (oral) Volume of Distribution (Vd/F) of Ibrutinib [Time Frame: Predose, at 1, 2, 4, and 6 hours postdose on Day 1, and Day 7 or 8 of cycle 1; predose, 1, 2, 4, and 6 hours postdose on Day 1 of Cycle 2 or Cycle 3 (each cycle of 28 days)]

Vd/F is the apparent (oral) Volume of Distribution.

4. Part 1: Maximum Observed Plasma Concentration (Cmax) [Time Frame: Predose, at 1, 2, 4, and 6 hours postdose on Day 1, and Day 7 or 8 of cycle 1; predose, 1, 2, 4, and 6 hours postdose on Day 1 of Cycle 2 or Cycle 3 (each cycle of 28 days)]

Cmax is the maximum observed plasma concentration.

5. Part 1: Relationship Between Pharmacokinetic Parameters and Age or Measure of Body Size [Time Frame: up to three 28-day cycles]

The impact of age or body size on the pharmacokinetic parameters will also be investigated.

6. Part 2: Event-free Survival [EFS] of Ibrutinib [Time Frame: Randomization to death, disease progression, or lack of CR or PR after 3 cycles of treatment (approximately 4.2 years)]

EFS is the time interval from randomization to death, disease progression, or lack of CR or PR after 3 cycles of treatment, whichever occurs first based on blinded independent event review by the Independent Review Committee (IRC).

Secondary Outcome Measures :

1. Part 1: Number of Participants with Adverse Events [Time Frame: Throughout the study duration (approximately up to 4.2 years)]

2. Part 1: Percentage of Participants Who Achieve Complete Response (CR) and Partial Response (PR) [Time Frame: Approximately up to 4.2 years]

CR: computed tomography (CT) or magnetic resonance imaging (MRI) reveals no residual disease or new lesions; Resected residual mass that is pathologically negative for disease; bone marrow (BM) and cerebrospinal fluid (CSF) morphologically free of disease with no new lesions by imaging examination. PR: 50 percent (%) decrease in sum of the products of the lesion diameters (SPD) on CT or MRI; FDG-PET may be positive (Deauville score of 4 or 5 with reduced lesional uptake compared with baseline); no new or PD; morphologic evidence of disease may be present in BM or CSF if present at diagnosis; however, there should be 50% reduction in percentage of lymphoma cells.

3. Part 1: Disease-specific Biomarkers Assessment [Time Frame: Cycle 1: Days 1, and 7 or 8, Cycle 2: Day 1, and Cycle 3: Day 1 (each cycle of 28 days) and End of treatment visit (30 days after last dose)]

Blood samples will be taken to evaluate the levels of biomarkers such as Phospho-Bruton's tyrosine kinase (BTK), spleen tyrosine kinase (SYK), p-signal transducer, activator of transcription 3 (STAT3), Caspase-3 and B-cell receptor (BCR)/CD79B, CARD11, and MYD Mutations.

4. Part 1: Bruton's tyrosine kinase (BTK) Percent Occupancy [Time Frame: Predose and 4 hours postdose on Day 1, Day 7 or 8 of Cycle 1, predose on Cycle 2 Day 1 or Cycle 3 Day 1 (each cycle of 28 days), and the End-of-Treatment visit (30 days after last dose)]

The pharmacodynamic activity of ibrutinib in the presence of chemoimmunotherapy (CIT) (RICE or RVICl) will be assessed by determining the percentage of probe occupancy of the BTK receptor. Blood samples will be obtained for pharmacodynamic assessments (BTK occupancy).

5. Part 1: Visual analog Scale Score for Palatability [Time Frame: Cycle 1 Day 1 and Cycle 3 Day 1 (each cycle of 28 days)]

Palatability will be measured using a visual analog scale. The scale is a 5-point visual analog scale incorporating a facial hedonic scale designed to span pediatric ages and levels of participant comprehension.

6. Part 2: Number of Participants with Adverse Events [Time Frame: Throughout the study duration (approximately up to 4.2 years)]

7. Part 2: Percentage of Participants Who Achieve Complete Response (CR) and Partial Response (PR) [Time Frame: Approximately up to 4.2 years]

CR: CT or MRI reveals no residual disease or new lesions; Resected residual mass that is pathologically negative for disease; BM and CSF morphologically free of disease with no new lesions by imaging examination. PR: 50% decrease in SPD on CT or MRI; FDG-PET may be positive Deauville score or 4 or 5 with reduced lesional uptake compared with baseline); no new or PD; morphologic evidence of disease may be present in BM or CSF if present at diagnosis; however, there should be 50% reduction in percentage of lymphoma cells.

8. Part 2: Tumor Volume Reduction [Time Frame: Day 14]

Tumor volume reduction will be measured by decrease in the sum of the products of the lesion diameters.

9. Part 2: Percentage of Participants who Proceed to Stem Cell Transplantation [Time Frame: Cycle 2 (Day 28)]

Percentage of participants who proceeded to stem cell transplantation will be calculated.

10. Part 2: Time to Response [Time Frame: Up to 4.2 years]

The time interval from the first dose of ibrutinib to the first documented response for those participants who respond.

11. Part 2: Duration of Response [Time Frame: Up to 4.2 years]

Duration calculated from the date of initial documentation of a response (CR or PR) to the date of first documented evidence of PD or death.

12. Part 2: Percentage of Participants with Long-term Survival [Time Frame: 2, 3 years]

Participants with event-free survival (EFS) at 2 and 3 years will be assessed.

13. Part 2: Overall Survival [Time Frame: Randomization to the date of death (maximum up to 4.2 years)]

Duration from the date of randomization to the date of the subject's death.

14. Part 2: Disease-specific Biomarkers Assessment [Time Frame: Cycle 1: Days 1 and 14, Cycle 2: Day 1, Cycle 3: Day 1 (each cycle of 28 days) and End of treatment visit (30 days after last dose)]

Blood samples will be taken to evaluate the levels of biomarkers such as Phospho-Bruton's tyrosine kinase (BTK), spleen tyrosine kinase (SYK), p-signal transducer, activator of transcription 3 (STAT3), Caspase-3 and B-cell receptor (BCR)/CD79B, CARD11, and MYD Mutations.

15. Part 2: Bruton's tyrosine kinase (BTK) Percent Occupancy [Time Frame: Predose and 4 hours postdose on Cycle 1 Day 1, predose and 4 hours post dose on Cycle 1 Day 14 or Cycle 2 Day 1, predose on Cycle 3 Day 1 (each cycle of 28 days), and End-of-Treatment visit (30 days after last dose)]

The pharmacodynamic activity of ibrutinib will be assessed by determining the percentage of probe occupancy of the BTK receptor. Blood samples will be obtained for pharmacodynamic assessments (BTK occupancy).

16. Part 2: Visual analog Scale Score for Palatability [Time Frame: Cycle 1 Day 1 and Cycle 3 Day 1 (each cycle of 28 days)]

Palatability will be measured using a visual analog scale. The scale is a 5-point visual analog scale incorporating a facial hedonic scale designed to span pediatric ages and levels of participant comprehension.

17. Part 2: Area under the plasma concentration-time curve (AUC) [Time Frame: Predose, 1, 2, and 4 hours postdose, either on Cycle 1 Day 14 or Cycle 2 Day 1 (each cycle of 28 days)]

AUC is the area under the plasma concentration-time curve.

Eligibility Criteria

Go to



Information from the National Library of Medicine



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, [Learn About Clinical Studies](#).

Ages Eligible for Study: 1 Year to 30 Years (Child, Adult)
Sexes Eligible for Study: All
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Participants with 1 to less than (<) 18 years of age (Part 1 only), or 1 to 30 years of age, inclusive, if initial diagnosis of mature B-cell non-Hodgkin lymphoma (NHL) occurred at <18 years of age (Part 2 only)
- Participants must be in first or later recurrence or have disease that is primarily refractory to conventional therapy
- Participants must have at least 1 of the following: 1 site of measurable disease greater than (>) 1 centimeter (cm) in the longest diameter and >1 cm in the shortest diameter by radiological imaging; bone marrow involvement; cerebrospinal fluid with blasts present
- Participants with lansky-Karnofsky score of greater than or equal to (>=) 50
- Adolescent women/young women of childbearing potential must have a negative highly sensitive serum or urine beta-human chorionic gonadotropin (beta-hCG) pregnancy test at Screening before enrollment/randomization. Adolescent/young women who are pregnant or breastfeeding are ineligible for this study

Exclusion Criteria:

- Participants with ongoing anticoagulation treatment with warfarin or equivalent vitamin K antagonists (example phenprocoumon), or ongoing treatment with agents known to be strong CYP3A4/5 inhibitors, or has taken any disallowed therapies as noted in Section 8.2, Prohibited Medications, before the planned first dose of study drug
- Participants with inherited or acquired bleeding disorders
- Participants with clinically significant arrhythmias, complex congenital heart disease, or left ventricular ejection fraction (LVEF) <50 percent (%) or shortening fraction (SF) <=28%
- Participants with known history of human immunodeficiency virus (HIV) or active Hepatitis B or C virus
- Participants with any condition that could interfere with the absorption or metabolism of ibrutinib including malabsorption syndrome, disease significantly affecting gastrointestinal function, or resection of the stomach or small bowel
- Participants with known allergies, hypersensitivity, or intolerance to ibrutinib or its excipients (refer to Investigator's Brochure)
- A diagnosis of post-transplant lymphoproliferative disease (PTLD)
- Participants who are within 6 months of an allogeneic bone marrow transplant

Information from the National Library of Medicine



To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): **NCT02703272**

Contacts

Contact: Use link at the bottom of the page to see if you qualify for an enrolling site (see list). If



[+ Show 99 Study Locations](#)

Sponsors and Collaborators

Janssen Research & Development, LLC

Investigators

Study Director: Janssen Research & Development, LLC Clinical Trial Janssen Research & D



More Information

Additional Information:

[To learn how to participate in this trial please click here.](#)

Responsible Party:	Janssen Research & Development, LLC
ClinicalTrials.gov Identifier:	NCT02703272 History of Changes
Other Study ID Numbers:	CR108134 54179060LYM3003 (Other Identifier: Janssen Research & Development, LLC) 2016-000259-28 (EudraCT Number)
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Lymphoma, Non-Hodgkin

Ibrutinib

JNJ-54179060

Additional relevant MeSH terms:

Lymphoma

Lymphoma, Non-Hodgkin

Lymphoma, B-Cell

Neoplasms by Histologic Type

Neoplasms

Lymphoproliferative Disorders

Lymphatic Diseases

Immunoproliferative Disorders

Immune System Diseases

Dexamethasone acetate

Dexamethasone

Etoposide phosphate

Isophosphamide mustard

Carboplatin

Rituximab

Etoposide

Vincristine

Ifosfamide

Idarubicin

BB 1101

Anti-Inflammatory Agents

Antiemetics

Autonomic Agents

Peripheral Nervous System Agents

Physiological Effects of Drugs

Gastrointestinal Agents

Glucocorticoids

Hormones

Hormones, Hormone Substitutes, and

Hormone Antagonists

Antineoplastic Agents, Hormonal