Safety and Efficacy of Entospletinib With Vincristine and Dexamethasone in Adults With Relapsed or Refractory Acute Lymphoid Leukemia (ALL)

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

Verified August 2016 by Gilead Sciences

Sponsor:
Gilead Sciences

Information provided by (Responsible Party):
Gilead Sciences

ClinicalTrials.gov Identifier:
NCT02404220

First received: March 2, 2015
Last updated: August 16, 2016
Last verified: August 2016
History of Changes

Purpose

This study will evaluate the safety, efficacy, tolerability, and pharmacokinetics of entospletinib (GS-9973) in combination with vincristine (VCR), and dexamethasone in adults with previously treated relapsed or refractory B-cell lineage acute lymphoid leukemia (ALL).

This study consists of two parts: Dose Escalation and Dose Expansion. After 2 induction cycles during either parts of the study, participants may be put on maintenance for up to 36 cycles if they have obtained clinical benefit from the treatment.

Condition	Intervention	Phase
Acute Lymphoid Leukemia	Drug: Entospletinib Drug: VCR Drug: Dexamethasone Drug: CNS Prophylaxis	Phase 1

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Phase 1b, Open-Label, Dose Escalation and Expansion Study Evaluating the Safety and Efficacy of Entospletinib (GS-9973) With Vincristine and Dexamethasone in Adult Subjects With Relapsed or Refractory Acute Lymphoid Leukemia (ALL)

Resource links provided by NLM:

MedlinePlus related topics: Chronic Lymphocytic Leukemia Leukemia

Drug Information available for: Dexamethasone Vincristine sulfate Dexamethasone sodium phosphate Dexamethasone acetate

Genetic and Rare Diseases Information Center resources: Acute Lymphoblastic Leukemia Lymphosarcoma

U.S. FDA Resources

Further study details as provided by Gilead Sciences:

Primary Outcome Measures:

- Occurrence of adverse events and laboratory abnormalities defined as dose limiting toxicities (DLTs) [Time Frame: Up to 2 years] [Designated as safety issue: No]

  This composite endpoint will measure the safety profile of entospletinib.

Secondary Outcome Measures:

- Overall remission (CR or CRi) rate at end of induction [Time Frame: Up to 2 years] [Designated as safety issue: No]

  Overall remission rate is defined as the proportion of participants who achieve a complete remission (CR) or complete remission with incomplete hematologic recovery (CRi) at end of induction.

- Complete remission (CR) rate at end of induction [Time Frame: Up to 2 years] [Designated as safety issue: No]

  Complete remission (CR) rate is defined as proportion of participants who achieve a complete remission.

- Number and proportion of participants who receive post-treatment hematopoietic stem cell transplant (HSCT) [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Number and proportion of participants who receive other post-treatment leukemia therapy [Time Frame: Up to 2 years] [Designated as safety issue: No]
- Partial response (PR) rate at end of induction [Time Frame: Up to 2 years] [Designated as safety issue: No]
  - Partial response (PR) rate is defined as the proportion of participants who achieve a partial response of marrow or by imaging criteria for patients with extramedullary disease.
  - Imaging will not be performed for participants at sites in Germany.

- Overall response (CR, CRi, or PR) rate at end of induction [Time Frame: Up to 2 years] [Designated as safety issue: No]

  Overall response (CR, CRi, or PR) rate is defined as the proportion of participants who achieve a complete remission (CR), complete remission with incomplete hematologic recovery (CRi) or partial response (PR) at end of induction.

Estimated Enrollment:	35
Study Start Date:	May 2015
Estimated Study Completion Date:	September 2021
Estimated Primary Completion Date:	September 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Entospletinib Dose Escalation: Lead-in (7 day): Entospletinib up to 400 mg twice daily Cycle 1 and 2 (28 days each): Entospletinib up to 400 mg twice daily+ VCR up to 2 mg once weekly + CNS prophylaxis on Day 28 + dexamethasone 20 mg twice daily on days 8-11 and 22-25 (Cycle 1) and Days 1- 4 and 15-18 (Cycle 2) Cycle 3 (up to 36 maintenance cycles): Entospletinib up to 400 mg twice daily + VCR up to 2 mg on Day 1+ dexamethasone 20 mg once daily on Days 1- 4 and 15-28 of each 28 day cycle Dose Expansion: Cycle 1 and 2 (28 days each): Entospletinib at the maximum tolerated dose (MTD) or recommended dose twice daily+ VCR up to 2 mg once weekly+ CNS prophylaxis on Day 28 +dexamethasone 20 mg on Days 8-11 and 22-25 (Cycle 1) and Days 1-4 and 15-18 (Cycle 2) Cycle 3 (up to 36 maintenance cycles): Entospletinib at the MTD or recommended dose twice daily + VCR up to 2 mg on Day 1+ dexamethasone 20 mg once daily on Days 1- 4 and 15-18 of each 28-day cycle	Drug: Entospletinib Entospletinib tablet(s) administered orally Other Name: GS-9973 Drug: VCR Vincristine (VCR) administered intravenously Drug: Dexamethasone Dexamethasone tablet(s) administered orally Drug: CNS Prophylaxis CNS prophylaxis per institutional standard

Eligibility

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

Criteria

Inclusion Criteria:

- Adults with ALL in need of treatment

Exclusion Criteria:

- Diagnosis of Burkitt's Leukemia, or lymphoid blast crisis of chronic myelogenous leukemia (CML)
- History of myelodysplastic syndrome or solid organ transplantation
- Prior allogeneic bone marrow progenitor cell transplant within 100 days or on active immunosuppression for graft versus host disease (GVHD) treatment or prophylaxis within 28 days prior to enrollment

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: NCT02404220

Contacts

Contact: Gilead Study Team GS9973alerts@gilead.com

Locations

United States, California

City of Hope Duarte, California, United States	**Recruiting**
UCLA Los Angeles, California, United States	**Not yet recruiting**
Stanford Cancer Institute Palo Alto, California, United States	**Recruiting**
University of California San Diego (UCSD) San Diego, California, United States	**Recruiting**

United States, Illinois

University of Chicago Chicago, Illinois, United States	**Recruiting**

United States, Indiana

Indiana University Bloomington, Indiana, United States	**Recruiting**

United States, Massachusetts

Dana Farber Cancer Institute Boston, Massachusetts, United States	**Withdrawn**

United States, Michigan

Henry Ford health systems Detroit, Michigan, United States	**Recruiting**

United States, Minnesota

Mayo Clinic Rochester, Minnesota, United States	**Withdrawn**

United States, New Jersey

Hackensack University Medical Center Hackensack, New Jersey, United States	**Recruiting**

United States, New York

Long Island Jewish Medical Center New York, New York, United States	**Withdrawn**
Memorial Sloan-Kettering New York, New York, United States	**Recruiting**

United States, Ohio

The Cleveland Clinic Foundation Cleveland, Ohio, United States	**Not yet recruiting**
The Ohio State University Columbus, Ohio, United States	**Recruiting**

United States, South Carolina

Bon Secour St. Francis Hospital Greenville, South Carolina, United States	**Recruiting**

United States, Texas

Houston Methodist Hospital Houston, Texas, United States	**Withdrawn**
MD Anderson Cancer Center Houston, Texas, United States	**Not yet recruiting**

United States, Washington

University of WA Seattle, Washington, United States	**Recruiting**

Canada, Ontario

Princess Margaret Toronto, Ontario, Canada	**Recruiting**

Canada, Quebec

Jewish General Hospital Montreal, Quebec, Canada	**Recruiting**

Sponsors and Collaborators

Gilead Sciences

Investigators

Study Director: Patrick Chun, MD Gilead Sciences

More Information

Responsible Party:	Gilead Sciences
ClinicalTrials.gov Identifier:	NCT02404220 History of Changes
Other Study ID Numbers:	**GS-US-339-1560** 2015-002768-18
Study First Received:	March 2, 2015
Last Updated:	August 16, 2016
Health Authority:	United States: Food and Drug Administration Canada: Health Canada Germany: Ministry of Health

Keywords provided by Gilead Sciences:
Syk inhibitor
Blood malignancy
Leukemia

Additional relevant MeSH terms:

Leukemia	Antiemetics
Leukemia, Lymphoid	Autonomic Agents
Precursor Cell Lymphoblastic Leukemia-Lymphoma	Peripheral Nervous System Agents
Neoplasms by Histologic Type	Physiological Effects of Drugs
Neoplasms	Gastrointestinal Agents
Lymphoproliferative Disorders	Glucocorticoids
Lymphatic Diseases	Hormones
Immunoproliferative Disorders	Hormones, Hormone Substitutes, and Hormone Antagonists
Immune System Diseases	Antineoplastic Agents, Hormonal
Dexamethasone acetate	Antineoplastic Agents
Dexamethasone	Protease Inhibitors
Dexamethasone 21-phosphate	Enzyme Inhibitors
Vincristine	Molecular Mechanisms of Pharmacological Action
BB 1101	Antineoplastic Agents, Phytogenic
Anti-Inflammatory Agents	Tubulin Modulators

ClinicalTrials.gov processed this record on August 18, 2016