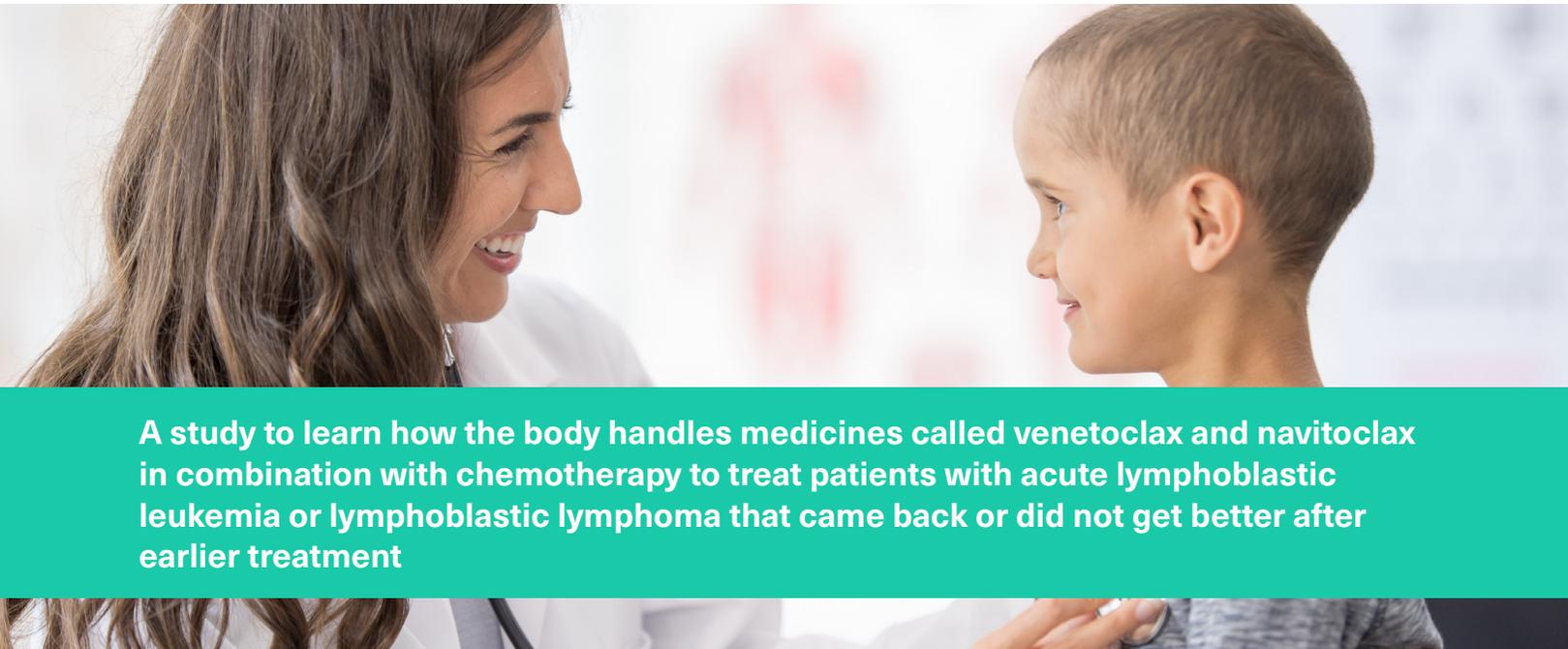


Summary of Clinical Trial Results

For Laypersons



A study to learn how the body handles medicines called venetoclax and navitoclax in combination with chemotherapy to treat patients with acute lymphoblastic leukemia or lymphoblastic lymphoma that came back or did not get better after earlier treatment

Overall Summary

- Researchers are looking for a better way to treat acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LL) that came back or did not get better after earlier treatment.
- In this study, study doctors wanted to know whether two drugs called venetoclax and navitoclax, when taken in combination with chemotherapy, could help treat these types of cancers.
- This study took place from November 2017 to November 2020 in the United States and Australia and included 69 pediatric and adult patients with ALL or LL.
- The main goal of the study was to find out how the body handles venetoclax alone and in combination with navitoclax and chemotherapy.
- The study had 2 parts, dose escalation (Part 1) and safety expansion (Part 2). Dose escalation is when patients are given increasing doses of the study drug. Safety expansion is the part of the study after a dose has been selected during dose escalation.
- In Part 1, patients were given venetoclax and different doses of navitoclax to determine the best dose level. In Part 2, patients were given venetoclax and navitoclax at the dose determined to be the best at the end of Part 1.
- Study doctors learned that the amount of venetoclax and navitoclax in the body's bloodstream was as expected given the doses taken by patients.
- Across the whole study, 79.7% of patients had side effects considered at least possibly related to treatment with venetoclax or navitoclax.
- The most common side effects were nausea, decrease in the number of white blood cells that help fight infection, anemia (low level of red blood cells) and vomiting.
- The results of this study may be used by researchers to further develop these medicines.
- If you participated in this study and have questions about your individual care, contact the doctor or staff at your study site.

1. General information about the study

1.1. What was the main objective of this study?



Researchers are looking for a better way to treat acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LL) that came back or did not get better after earlier treatment.

- **Acute lymphoblastic leukemia** is a cancer of blood and bone marrow (the spongy tissue inside bones) that affects the body's immune system.
- **Lymphoblastic lymphoma** is similar to all but the cancer cells are largely located in the lymph nodes (small structures that help filter harmful substances from the body).

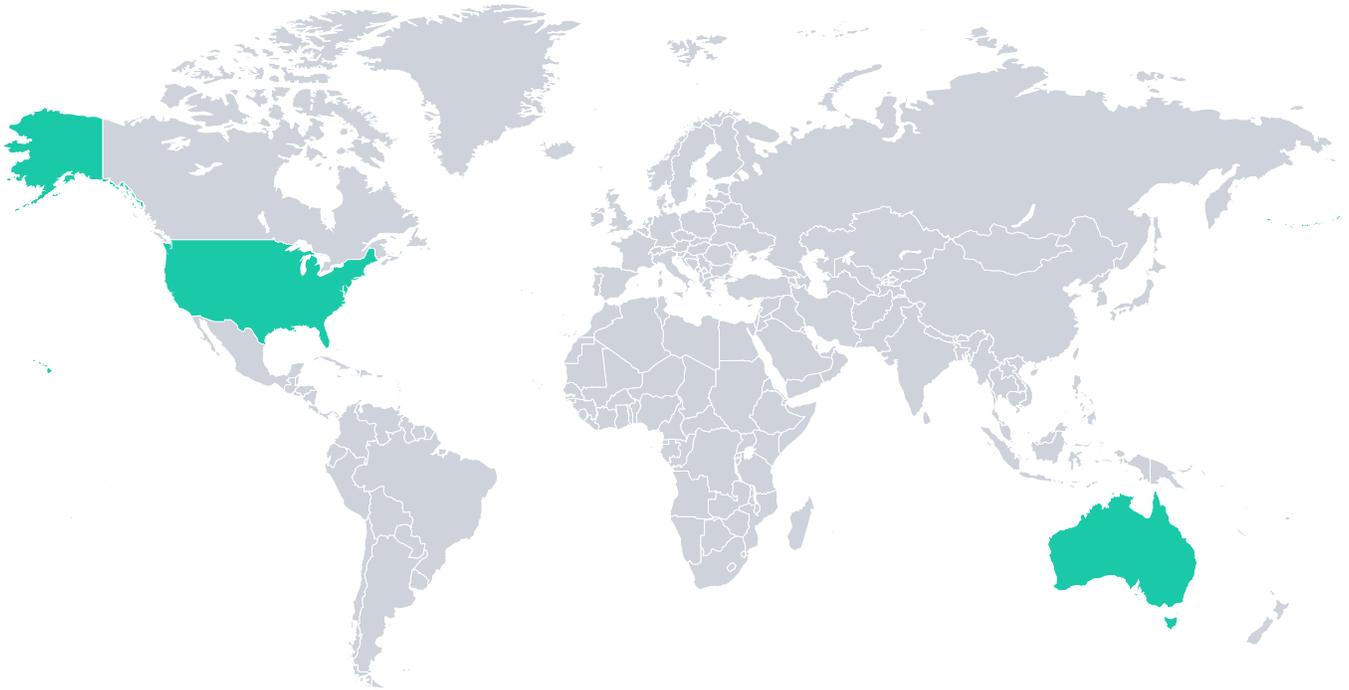
Although some patients' cancers improve with first treatment, they can come back or get worse. Therefore, researchers in this study wanted to know whether drugs called venetoclax and navitoclax taken with chemotherapy could help treat ALL and LL that came back or did not get better after earlier treatment. Venetoclax and navitoclax work by blocking abnormal proteins to prevent cancer cells from repairing themselves, helping make cancer treatments more effective.

The main goal of the study was to find out how the body handles venetoclax alone and in combination with navitoclax and chemotherapy. Researchers planned this study as a Phase 1, open-label study.

- **Phase 1 studies** test potential new treatments in a small number of healthy volunteers or patients. In this Phase 1 study, the study doctors looked for any chemical changes in the body (blood or urine) caused by venetoclax, navitoclax, or chemotherapy. The study doctors also looked for any side effects patients may have had after treatment.
- **Side effects** are medical events considered by the study doctors to be at least possibly related to study treatment.
- The study was **open-label**, which means that both patients and the study doctors knew which treatment and dose was given to patients.

1.2. When and where was the study done?

This study took place from November 2017 to November 2020 in Australia and the United States.

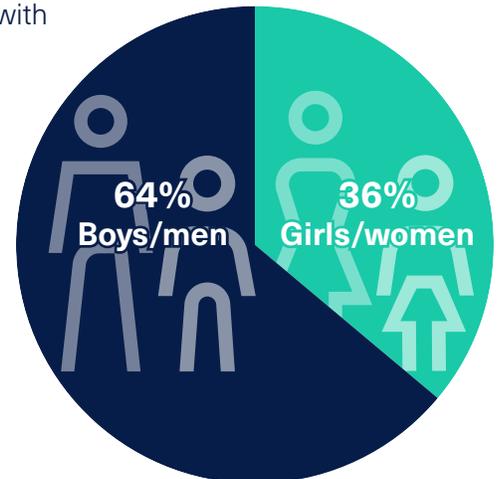


2. What patients were included in this study?

A total of 69 patients joined the study. All patients were diagnosed with either ALL (63 patients) or LL (6 patients) that came back or did not get better with other chemotherapy treatments.

All patients left by the end of the study, mostly due to worsening of the disease (disease progression).

There were more boys/men (64%) than girls/women (36%) in the study. Patient ages ranged from 6 to 72 years of age with an average age of 31 years.



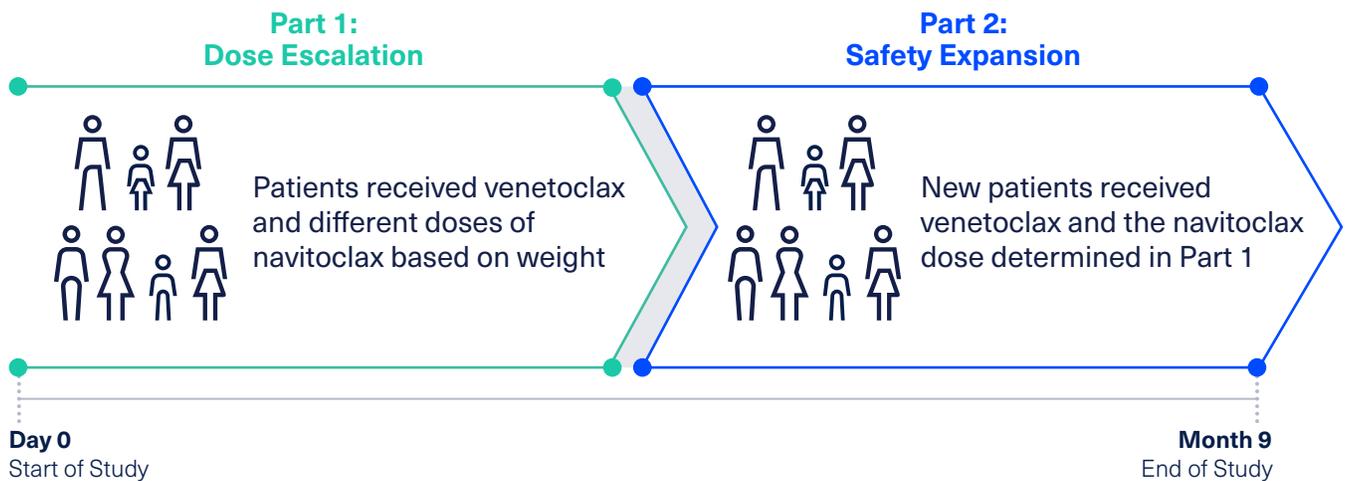
3. Which medicines were studied?

The medicines in this study were called venetoclax and navitoclax. Both medicines were taken by mouth daily. Patients could also receive chemotherapy as recommended by their doctor but chemotherapy was not required by the study and not given to all patients.

Study doctors tested different doses of venetoclax and navitoclax in this study. The study was split into 2 parts, Part 1 (Dose Escalation) and Part 2 (Safety Expansion).

- In Part 1, patients received venetoclax and different doses of navitoclax based on weight.
- In Part 2, patients received venetoclax and 50 mg navitoclax.

The diagram below shows how the study was organized.



4. What were the side effects?

Side effects are unwanted medical events that were considered by the study doctor to be at least possibly related to the study drugs.

A side effect is serious if it leads to death, is life-threatening, puts a patient in the hospital, keeps a patient in the hospital for a long time, or causes a disability that lasts a long time.

- 39.1% of patients (27 patients) had serious side effects during the study.
- 10.1% of patients (7 patients) stopped taking the study drug because of side effects during the study.
- 2 patients died from the serious side effects that were considered at least possibly related to venetoclax, navitoclax, or chemotherapy. 1 patient died of intestinal ischemia (blood flow through major artery that supplies blood to the intestines is slowed or stopped) and 1 patient died of multiple organ dysfunction syndrome (full-body immune response to illness or injury that causes one or more organs to stop working properly).

Serious side effects experienced by more than one patient included febrile neutropenia (fever while body has decreased white blood cells that help fight infection), neutropenic sepsis (a severe response to infection while the body has decreased white blood cells that help fight infections), pneumonia (infection in one or both lungs), sepsis (severe response to infection causing a serious condition can lead to organ damage), septic shock (dangerously low blood pressure after an infection), upper respiratory tract infection (infection of the nose, throat, and upper airways), and vascular device infection (infection caused by equipment implanted into the skin to help deliver certain medications).

The table below shows information about the serious side effects in more than one patient, as well as side effects patients had that led to the patient stopping study drug, and side effects leading to death.

Venetoclax + Navitoclax (69 Patients)	
Number of patients with serious side effects	27 (39.1% of patients)
• Febrile neutropenia	12 (17.4%)
• Neutropenic sepsis	3 (4.3%)
• Pneumonia	3 (4.3%)
• Sepsis	3 (4.3%)
• Septic shock	2 (2.9%)
• Upper respiratory tract infection	2 (2.9%)
• Vascular device infection	2 (2.9%)
Number of patients who stopped taking study drug because of side effects	7 (10.1%)
Reasons for stopping	Blood bilirubin increased (may be a sign of liver damage or disease), febrile neutropenia, intestinal ischemia (blood flow through major artery that supplies blood to the intestines is slowed or stopped), klebsiella sepsis (severe response to bacterial infection and can lead to organ damage), lymphocyte count increased (which may show that your body is fighting an infection), sepsis, septic shock
Number of side effects leading to death	2 (2.9%)

About 79.7% of patients (55 patients) had side effects during the study. The table below shows information about the common side effects (in at least 10 or more patients) in this study. The most common side effects were nausea, decrease in the number of white blood cells that help fight infection, and vomiting.

Venetoclax + Navitoclax (69 Patients)	
Number of patients with at least one side effect	55 (79.7% of patients)
Common side effects (occurring in at least 10 patients)	
• Decrease in the number of white blood cells that help fight infection	28 (40.6%)
• Nausea	26 (37.7%)
• Vomiting	18 (26.1%)
• Anemia (low number of red blood cells)	17 (25.6%)
• Diarrhea	16 (23.2%)
• Febrile neutropenia	16 (23.2%)
• Thrombocytopenia (low number of a type of blood cell that helps stop bleeding)	11 (15.9%)
• Tiredness	10 (14.5%)

5. What were the overall results of the study?

The study was completed as planned. The study doctors tested several things to see how safely the body handles venetoclax and navitoclax in patients with ALL and LL that came back or did not get better with earlier treatment.

The amount of venetoclax and navitoclax in the body's bloodstream was as expected given the doses taken by patients.

In Part 1 of the study, 8 patients had dose-limiting toxicities (DLTs) which are medical events that happen during treatment that are serious enough to stop the patient from receiving additional doses of the medication. These medical events may or may not be related to treatment with venetoclax or navitoclax.

Based on the DLTs in Part 1, study doctors selected a dose of 25 mg navitoclax for patients under 45 kg (approximately 99 pounds) and 50 mg of navitoclax for patients over 45 kg and a venetoclax dose of 400 mg for adults (and adjusted by weight for children) for Part 2 of the study.

6. How has the study helped patients and researchers?

This study found a dose of navitoclax and venetoclax in combination with chemotherapy that could be studied further in patients with ALL or LL. Findings from this study may be used in other studies to learn whether patients are helped by venetoclax and navitoclax.

This summary only shows the results from this study, which may be different from the results of other studies.



7. Are there any plans for future studies?

Multiple studies of venetoclax and navitoclax are ongoing in patients with a wide range of conditions.

8. Who sponsored this study?

This study was sponsored by AbbVie. This summary was reviewed for readability by a patient advocacy group.

9. Where can I find out more information about this study?

Title of Study	A Phase 1 Dose Escalation, Open-Label Study of Venetoclax in Combination with Navitoclax and Chemotherapy in Subjects with Relapsed/Refractory Acute Lymphoblastic Leukemia or Relapsed/Refractory Lymphoblastic Lymphoma
Protocol Number	M16-106
Clinicaltrials.gov	NCT03181126 https://clinicaltrials.gov/ct2/show/NCT03181126?term=M16-106&draw=2&rank=1
EudraCT	2017-001541-26 https://www.clinicaltrialsregister.eu/ctr-search/search?query=2017-001541-26
Study Sponsor	AbbVie, Inc. Phone: +1 800-633-9110 Email: abbvieclinicaltrials@abbvie.com

Thank You

AbbVie wants to thank all the participants for their time and effort that went into making this study possible.

Clinical study participants help advance science!

