AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: AZD2811

Study Purpose: This study was done to learn about the safety of AZD2811 in participants with blood and bone marrow cancers

Protocol Number: D6130C00003

Thank you

Thank you for taking part in the clinical study for the study drug AZD2811.

AstraZeneca AB sponsored this study and believes it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you.

If you participated in the study and have questions about the results, please speak with the study doctor or staff at your study site.

Who took part in this study?

The researchers asked for the help of male and female participants with 1 of 2 different types of blood and bone marrow cancer:

- acute myeloid leukemia, also called "AML"
- myelodysplastic syndrome, also called "MDS"

The participants in this study:

- had already tried other treatments for their cancer, but it had come back or was still getting worse, or
- were not eligible to receive other treatments for their cancer.

The participants in this study were 46 to 89 years old when they joined.

The study included 51 participants in Australia and the United States.

Why was the research needed?

Researchers are looking for a better way to treat cancer of the blood and bone marrow. Before a drug can be approved for people to get, researchers do clinical studies to find out how safe it is and how it works.

Cancer is a disease that happens when the body cannot control the growth of some cells. In healthy people, new blood cells grow in the bone marrow, which is the soft part inside of some bones. In blood cancers, the blood cells do not form properly in the bone marrow. These cancer cells then move quickly to the blood.

Acute myeloid leukemia, also called AML, is a blood cancer that affects white blood cells. Myelodysplastic syndrome, also called MDS, is a bone marrow cancer that can affect any type of blood cell.

Existing treatments for cancer do not help every patient. The study drug, AZD2811, was designed to be toxic to cancer cells.

What was the purpose of this study?

In this study, the researchers wanted to find out about the safety of AZD2811 in participants with AML or MDS.

The main questions the researchers wanted to answer in this study were:

- What was the highest dose of AZD2811 that did not cause too many side effects?
- What signs and symptoms did the participants have during the study?
- What medical problems did the participants have during the study?

The answers to these questions are important to know before other studies can be done to find out if AZD2811 helps improve the health of people with blood and bone marrow cancer.

What treatments did the participants get?

The participants got AZD2811 through a needle into a vein, also known as an "IV infusion". Some of the participants also got different types of chemotherapy, depending on what the study doctors thought was best for each participant.

This was an "open-label" study. This means the participants, researchers, study doctors, and other study staff knew what each participant was getting.

This study was also a "dose finding" study. This means that some of the participants started out getting a low dose of AZD2811. The study doctors looked at the results for these participants. Then, the researchers decided whether to change the dose of AZD2811 in the next group of participants.

Each participant stayed in the same dose group throughout the study. The participants got AZD2811 in 4-week periods called "cycles".

The chart below shows the treatments the researchers planned to study. The doses of AZD2811 are measured in milligrams, also called "mg".

	Group 1 **28 participants**	**Group 2** **23 participants**
	• 21 participants with AML • 7 participants with MDS	• 20 participants with AML • 3 participants with MDS
	• Between 100 mg and 800 mg of AZD2811 as an IV infusion by itself	• Between 200 mg and 600 mg of AZD2811 as an IV infusion with chemotherapy
	• Twice every 4 weeks, or • 4 times every 4 weeks	• Twice every 4 weeks, or • 4 times every 4 weeks

Only 50 of the 51 participants who joined the study received AZD2811. There was 1 participant who did not get any doses of AZD2811. This was because this participant's health got worse between signing up for the study and starting the study, so they were too sick to take part.

What happened during this study?

The study started in July 2017 and ended in March 2021. The study was ended early because the study sponsor made a business decision to stop studying AZD2811 in blood and bone marrow cancer.

Before the participants got study treatment, they visited their study site 1 time. This part of the study lasted for up to 28 days. At this visit, the study doctors made sure the participants could join the study. They also:

- did physical exams and asked about the participants' medications and any medical problems they were having
- checked how the participants were able to do their daily activities
- took blood samples
- checked the participants' heart health using an electrocardiogram, also known as an ECG
- took a sample of the participants' bone marrow

The study doctors also did these tests and measurements throughout the study.

While the participants got study treatment, they visited their study site up to 8 times in the first cycle, up to 6 times during the second cycle, and at least 2 times every cycle until they stopped getting study treatment. At these visits, the participants got AZD2811 and the study doctors checked their health. Some of the participants also got chemotherapy.

After the participants stopped getting study treatment, they visited their study site up to 2 times. The last visit could be replaced by a phone call for some participants. This part of the study lasted for up to 1 month. At these visits, the study doctors checked the health of the participants.

What were the results of this study?

This is a summary of the main results from this study overall. The results each participant had might be different and are not in this summary.

Researchers look at the results of many studies to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

The websites listed at the end of this summary may have more information about the study results.

There was 1 participant who did not get any doses of AZD2811. So, the results below are for 50 out of 51 participants.

What was the highest dose of AZD2811 that did not cause too many side effects?

Because the study ended early, the researchers did not collect enough data to answer this question.

What signs and symptoms did the participants have during the study?

To answer this question, the study doctors did tests and measurements before and after the participants got AZD2811. The doctors did physical exams and tested the participants' blood and urine samples to check their overall health. They also did ECGs to check the participants' heart health.

The study doctors also kept track of the "adverse events" that the participants had. An adverse event is any sign or symptom that participants have during a study. Doctors keep track of all the adverse events that happen in studies, even if they do not think the adverse events might be related to the study treatment.

Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to the study treatment. This section is a summary of all the adverse events, whether they might be related to the study treatment or not. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

Adverse events may or may not be caused by the treatments in the study. A lot of research is needed to know whether a treatment causes an adverse event.

	Group 1 (out of 27 participants)	Group 2 (out of 23 participants)
How many participants had adverse events?	96.3% (26)	100.0% (23)
How many participants had serious adverse events?	63.0% (17)	73.9% (17)
How many participants stopped getting study treatment due to adverse events?	14.8% (4)	13.0% (3)

The most common serious adverse events were:

- Low white blood cell counts with fever
- Infection of the lungs
- Blood poisoning
- Streptococcus bacteria, or other types of bacteria, in the blood

The most common adverse events in **Group 1** were:

- Low red blood cell counts
- Low white blood cell counts with or without fever
- Low blood platelet counts, which can lead to bleeding and bruising

The most common adverse events in **Group 2** were:

- Low red blood cell counts
- Low white blood cell counts with or without fever
- Low blood platelet counts, which can lead to bleeding and bruising
- Diarrhea
- Fatigue
- Constipation
- Nausea
- Vomiting
- Cough
- Swelling in the ankles and feet
- Low levels of phosphate in the blood

The study doctors also counted the number of "dose limiting toxicities" the participants had during the study. A dose limiting toxicity is an adverse event that is severe enough to stop the study doctor from increasing the participant's dose of study treatment. A dose limiting toxicity is also known as a "DLT".

Only 23 out of 27 participants in Group 1 and 21 out of 23 participants in Group 2 could be checked for DLTs. This is because only these participants got AZD2811 as planned and completed the follow-up visit or phone call to check their health. Of these participants:

- 21.7% of participants in Group 1 had a DLT. This was 5 out of 23 participants.
- 4.8% of participants in Group 2 had a DLT. This was 1 out of 21 participants.

What medical problems happened during this study?

This section is a summary of the medical problems the participants had during the study that the study doctors thought might be related to the study drug. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study drug. A lot of research is needed to know whether a drug causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for AZD2811.

The websites listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this study.

Did any adverse reactions happen during this study?

	Group 1 (out of 27 participants)	Group 2 (out of 23 participants)
How many participants had adverse reactions?	81.5% (22)	69.6% (16)
How many participants had serious adverse reactions?	37.0% (10)	26.1% (6)
How many participants stopped getting study treatment due to adverse reactions?	11.1% (3)	4.3% (1)

What serious adverse reactions happened during this study?

The only serious adverse reaction that happened in more than 1 participant was low white blood cell counts with fever.

Most common serious adverse reaction

Serious adverse reaction	Group 1 (out of 27 participants)	Group 2 (out of 23 participants)
Low white blood cell counts with fever	25.9% (7)	13.0% (3)

There were 4.0% of participants who died because of serious adverse reactions. This was 2 out of 50 participants.

- There was 1 participant in Group 1 who died because of a serious adverse reaction.
- There was 1 participant in Group 2 who died because of a serious adverse reaction.

What adverse reactions happened during this study?

The most common adverse reaction was low red blood cell counts.

The table below shows the adverse reactions that happened in 4 or more participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	Group 1 (out of 27 participants)	Group 2 (out of 23 participants)
Low red blood cell counts	33.3% (9)	30.4% (7)
Low levels of neutrophils, a type of white blood cell that fights infection	11.1% (3)	34.8% (8)
Diarrhea	14.8% (4)	21.7% (5)
Low white blood cell counts with fever	22.2% (6)	8.7% (2)
Low blood platelet counts, which can lead to bleeding and bruising	11.1% (3)	17.4% (4)
Decreased blood platelet counts	18.5% (5)	8.7% (2)
Fatigue	14.8% (4)	8.7% (2)
Dizziness	7.4% (2)	8.7% (2)
Nausea	0.0% (0)	17.4% (4)
Vomiting	0.0% (0)	17.4% (4)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of AZD2811 in participants with AML or MDS.

Researchers look at the results of many studies to decide which treatments work best and are safest. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Further clinical studies with AZD2811 are not planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If more information about the study results is available, it can also be found here.

- www.clinicaltrials.gov Once you are on the website, type **"NCT03217838"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2018-003857-73"** in the search box and click "Search".
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D6130C00003"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase I/II, Open-Label, Multicentre 2-Part Study to Assess the Safety, Tolerability, Pharmacokinetics, and Efficacy of AZD2811 as Monotherapy or in Combination in Treatment-Naïve or Relapsed/Refractory Acute Myeloid Leukaemia Patients Not Eligible for Intensive Induction Therapy

AstraZeneca AB Protocol Number: D6130C00003

National Clinical Trials Number: NCT03217838

EudraCT Number: 2018-003857-73

AstraZeneca AB sponsored this study and has its headquarters in Södertälje, Sweden.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical studies, nor is it involved in conducting clinical studies.

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