Clinical Study Results

1. Study Name

Title of the study:	A Phase 1 Open-label Study Evaluating the Safety, Tolerability, Pharmacokinetics and Efficacy of AMG 397 in Subjects With Selected Relapsed or Refractory Hematological Malignancies
Brief Title:	Safety, Tolerability, Pharmacokinetics and Efficacy of AMG 397 in Subjects With Multiple Myeloma, Myelodysplastic Syndrome, and Acute Myeloid Leukemia
Protocol Number:	20170173
NCT Number:	NCT03465540
Date of This Summary:	11 November 2021

What does this summary cover?

This summary shows the main results from one clinical study. The results are only for this study. Other studies may find different results. Researchers and health authorities look at the results of many studies to decide which medicines work best and are safest for patients.

Amgen has committed to make research results available to the public. This summary has been provided as part of that commitment and should not be used for any other purpose. It should not be considered to make a claim for any product or to guide treatment decisions.

2. Who Sponsored This Study?

Amgen Inc.
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Amgen Inc. is the sponsor of the study who made AMG 397, the medicine being tested in the study. Amgen would like to thank everyone who participated in this study and feels it is important to share the results of this study.

3. General Information About the Clinical Trial

Where and when was the study done?

- This study took place in Australia, France, Greece, and the United States.
- The study began in August 2018 and ended in July 2019.
- The study was stopped earlier than planned because Amgen decided not to continue development of AMG 397. This was due to a business decision and not due to any safety concerns.

Why was the study done?

- This was a phase 1 study conducted in participants with certain cancers of the blood and lymph system, as part of the early process to develop new medicines for humans. Researchers looked at how this medicine that was still being tested works in the body and the effect that it has in the body, including side effects.
- In this study, researchers wanted to learn more about the safety of AMG 397 and determine the optimal dose to test in further studies.

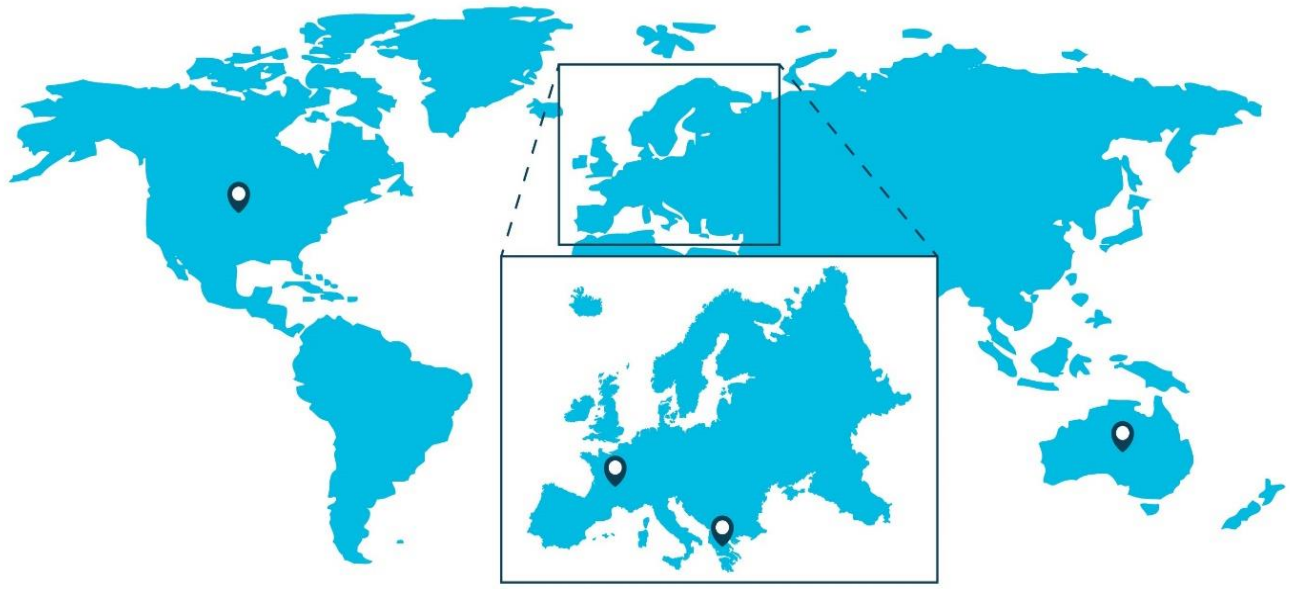
4. Who Was Included in This Study?

Who took part in the study?

Part 1A of this study included 12 participants with non-Hodgkin's lymphoma (NHL) or multiple myeloma (MM). Four participants (33%, or 33 out of 100) were women and 8 participants (67%, or 67 out of 100) were men. Participants ranged in age from 50 years old to 76 years old.

Part 1B of this study included 12 participants with acute myeloid leukemia (AML). Seven participants (58%, or 58 out of 100) were women and 5 participants (42%, or 42 out of 100) were men. Participants ranged in age from 34 years old to 82 years old.

This study took place at 11 study centers across Australia, France, Greece, and the United States. The numbers of participants in each country are shown below:



AUSTRALIA	FRANCE	GREECE	UNITED STATES
Part 1A: 5 participants	Part 1A: 1 participant	Part 1A: 1 participant	Part 1A: 5 participants
Part 1B: 3 participants	Part 1B: 1 participant	Part 1B: 0 participants	Part 1B: 8 participants

Participants were examined by a study doctor to see if they met specific conditions to be in the study. The major conditions or measures they needed to meet included:

- Diagnosed with certain cancers of the blood or lymph system: multiple myeloma (MM), non-Hodgkin's lymphoma (NHL), acute myeloid leukemia (AML), or myelodysplastic syndrome (MDS; also known as pre-leukemia).
- Cancer was considered relapsed or refractory. Relapsed means participants had disease that recurred. Refractory means participants had disease that did not respond to the first treatment.
- Participants not eligible for other treatments known to help with their cancer or participants cannot take other available treatments known to help with their cancer.

5. Which Medicines Were Studied?

The medicine tested in this study was AMG 397. AMG 397 may block the activity of a protein called Myeloid Cell Leukemia 1 (MCL1). MCL1 causes tumor cells to live and grow. Blocking MCL1 may stop tumor growth. AMG 397 is given as a tablet taken by mouth.

This study was planned for 3 parts. Part 1A and Part 1B were completed. No participants were enrolled in Part 2 or Part 3 because the study ended.

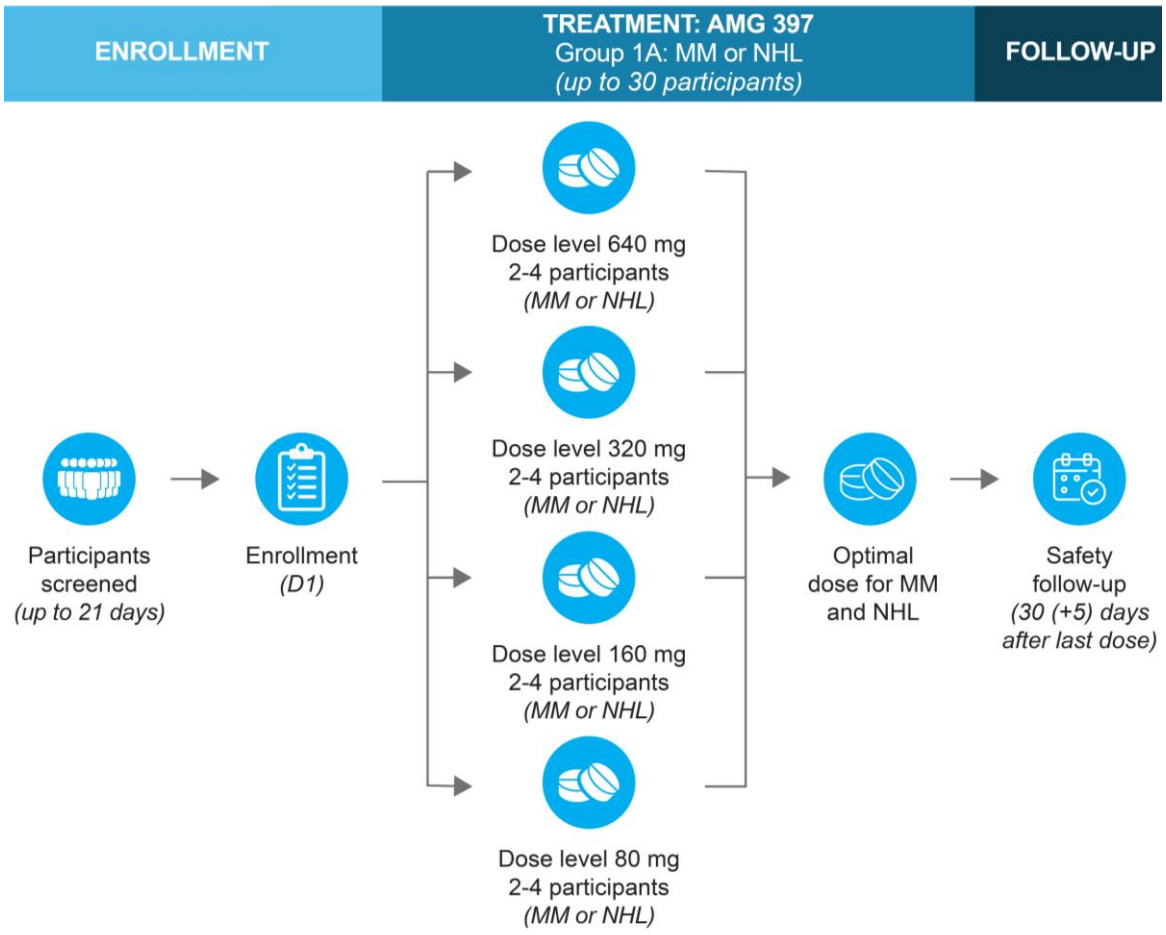
AMG 397 was given in weekly intervals, so participants received treatment once per day for 2 days, followed by a 5-day break. Participants were given different doses of AMG 397. The first group of participants received AMG 397 80 milligrams. The next group of participants could receive a higher dose of AMG 397. Each new group could get a higher dose until participants experienced medical problems that caused them to lower their dose or to stop taking AMG 397; then the dose was not raised any higher.

- In Part 1A, 2 participants received AMG 397 80 mg, 6 participants received AMG 397 160 mg, and 4 participants received AMG 397 320 mg.

- In Part 1B, 4 participants received AMG 397 80 mg, 5 participants received AMG 397 160 mg, and 3 participants received AMG 397 320 mg.

This was an open-label study, which means that the researchers and participants knew which medicine and dose they received. The study included a 3-week screening period, a 6-month treatment period, and a 30-day safety follow-up visit after the last dose of study treatment. Long-term follow-up occurred every 3 months after end of treatment for up to 1 year.

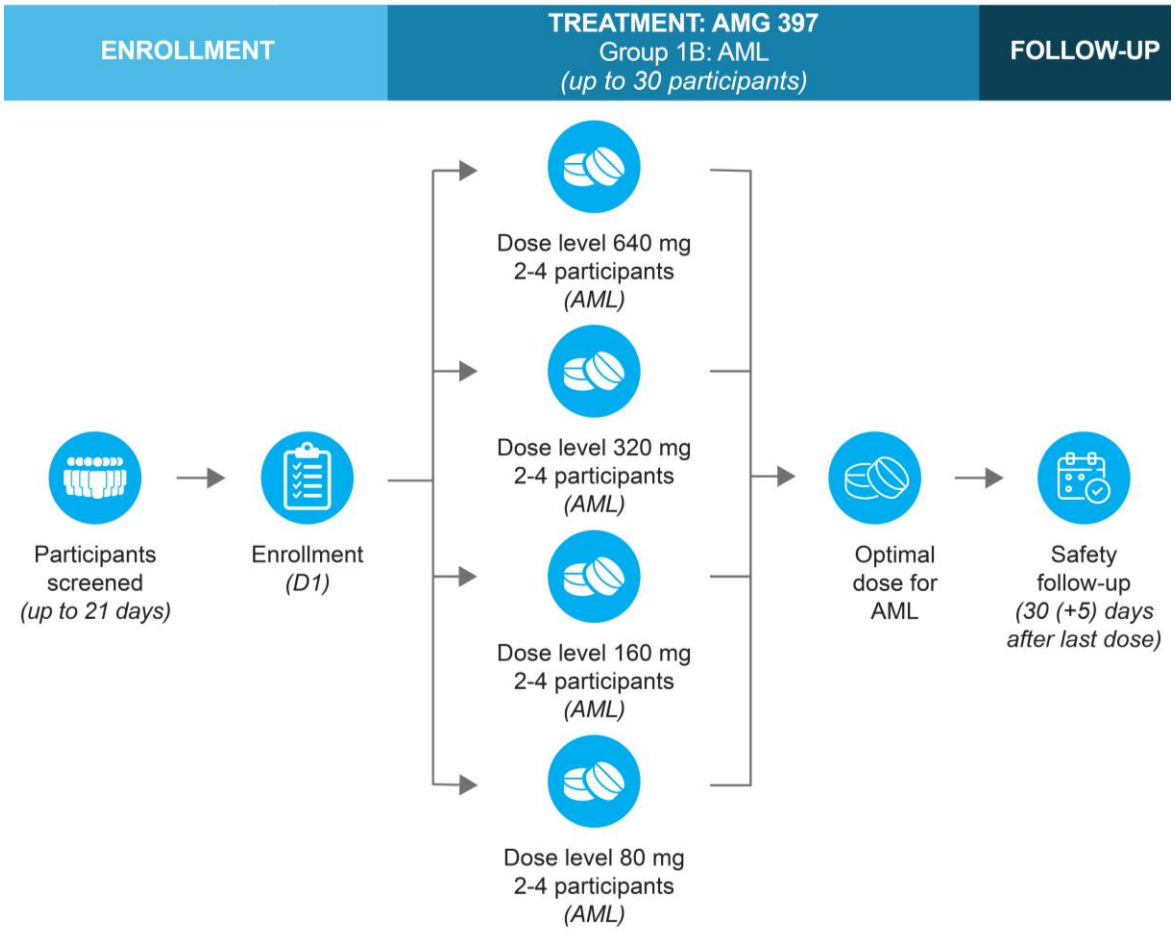
PART 1A STUDY DESIGN



**Part 1A: AMG 397 was given weekly by mouth once-daily for 2 days in a row. This was followed by a break from treatment for 5 days.*

MM= multiple myeloma; NHL= non-Hodgkin's lymphoma; D= day

PART 1B STUDY DESIGN



**Part 1B: AMG 397 was given weekly by mouth once-daily for 2 days in a row. This was followed by a break from treatment for 5 days.*
AML= acute myeloid leukemia; D= day

6. What Were the Side Effects?

What is a side effect?

All medicines can cause side effects, or unwanted medical problems that may happen when you take a medicine. In this study, doctors reported all the medical problems participants had. Side effects that doctors believed could have been caused by the study treatment(s) are listed below.

What side effects were seen?

The table below shows how many participants had side effects.

Side Effects During the Study

	Part 1A (12 participants)	**Part 1B (12 participants)**
How many participants had serious side effects?	3 participants (25%)	2 participants (17%)
How many participants had non-serious side effects?	12 participants (100%)	9 participants (75%)
How many participants died from side effects?	0 participants (0%)	0 participants (0%)
How many participants stopped taking the study medicine because of side effects?	2 participants (17%)	1 participants (8%)

If a participant had to stay in the hospital or died because of a side effect, the doctor reported that the side effect was serious. In Part 1A of this study, 2 participants died from RR MM, and researchers did not think the deaths were related to AMG 397. In Part 1B of this study, 4 participants died from AML, and researchers did not think the deaths were related to AMG 397. No participants died due to a side effect.

The table below lists the serious side effects that occurred in the participants.

Serious Side Effects During the Study		
Serious side effect	**Part 1A (12 participants)**	**Part 1B (12 participants)**
Increase in enzyme found in heart and muscles, which could indicate damage to muscle tissues	1 participant (8%)	0 participants (0%)
Side effects that affect the digestive tract like nausea, vomiting, and diarrhea	1 participant (8%)	0 participants (0%)
Nausea	1 participant (8%)	0 participants (0%)
Low number of white blood cells that fight infection	1 participant (8%)	0 participants (0%)
Feeling faint or light-headed	1 participant (8%)	0 participant (0%)
Increase in enzyme found in heart and muscles, which could indicate heart injury	1 participant (8%)	1 participant (8%)
Feeling weak	0 participants (0%)	1 participant (8%)

The table below shows the non-serious side effects that occurred in more than 2 participants.

Non-serious Side Effects During the Study

Non-serious side effect	Part 1A (12 participants)	Part 1B (12 participants)
Nausea	8 participants (67%)	3 participants (25%)
Low number of white blood cells that fight infection	8 participants (67%)	0 participants (0%)
Diarrhea	7 participants (58%)	5 participants (42%)
Vomiting	7 participants (58%)	3 participants (25%)
Low appetite	2 participants (17%)	3 participants (25%)

Additional safety results for this study include:

- All participants in Part 1A (100%) had a medical problem during the study (treatment-related or not treatment-related).
- All participants in Part 1B (100%) had a medical problem during the study (treatment-related or not treatment-related).
- No participants had treatment-related changes in physical exam findings or vital signs that were considered to be clinically significant. 2 participants had changes in electrocardiograms (heart tracings) that were considered to be clinically significant.
- Changes in lab results that were considered to be treatment-related and severe are listed below:

Grade 3 or Higher Lab Changes During the Study		
Grade 3 or higher lab changes	**Part 1A (12 participants)**	**Part 1B (12 participants)**
Very low number of white blood cells that fight infection	8 participants (67%)	0 participants (0%)
Increase in an enzyme found in the heart, brain, and muscles, which could indicate damage to muscle tissues	1 participant (8%)	0 participants (0%)
Low potassium in blood	0 participants (0%)	1 participant (8%)
Increased liver enzyme, which may indicate liver damage	0 participants (0%)	1 participant (8%)
Low number of white blood cells that fight infection	1 participant (8%)	0 participants (0%)
Increase in enzyme found in heart and muscles, which could indicate heart injury	1 participant (8%)	1 participant (8%)

No single clinical study can give a complete picture of the benefits and risks of a medicine. Information about other side effects may be available at the websites listed at the end of this summary.

7. What Were the Overall Results of the Study?

How many study participants had "dose-limiting toxicities"?

In this study, researchers wanted to determine the optimal dose of AMG 397 to test in future studies. One way to determine this optimal dose is for researchers to look at the number of participants who had "dose-limiting toxicities" (DLTs) at each different dose level that was tested in the study. A DLT is a side effect that is related to the treatment and that causes the participant to lower their dose or to stop taking the medicine altogether.

- In Part 1A, 1 participant had 2 DLTs (increase in enzyme found in muscles and heart that could indicate muscle damage, and increase in enzyme found in muscles and heart that could indicate heart injury). This participant received AMG 397 320 mg. No participants had DLTs at the other dose levels.

- In Part 1B, 2 participants had a DLT. One participant had an increased liver enzyme that could indicate liver damage, and one participant had an increase in enzyme found in muscles and heart that could indicate heart injury. These participants received AMG 397 320 mg. No participants had DLTs at the other dose levels.

More results may be available at the website listed at the end of this summary.

8. How Has This Study Helped Participants and Researchers?

What else is important to know about these results?

These results are only for this clinical study, which looked at a sample of 24 people with relapsed or refractory MM, NHL, AML, or MDS. These results add to the understanding of the study drug. Not all participants in each part of the study had the same results. The results for any single participant could have been better or worse than the results for their group. Other studies may find different results. These results do not explain how a treatment may work in a single person. Many studies are needed to show the benefits and risks of a medicine. This research may help future participants and families by helping doctors understand more about the treatment being studied.

9. Are There Plans for Further Studies?

If more clinical studies are done, they may be listed on public websites, such as those below. Search for the study medicine name AMG 397 on the website below.

10. Where Can I Find More Information About This Study?

To find out more about this study, check these websites:

- www.clinicaltrials.gov. Use the study identifier NCT03465540

If you participated in the study and have questions about the study results, the doctor or staff at your study site may be able to answer them.