Clinical Study Results

1. Study Name

Title of the study:	A Randomized, Open-label, Phase 3 Study in Subjects With Relapsed and Refractory Multiple Myeloma Receiving Carfilzomib in Combination With Dexamethasone, Comparing Once-weekly Versus Twice-weekly Carfilzomib Dosing
Brief Title:	Once-weekly Versus Twice-weekly Carfilzomib in Combination With Dexamethasone in Adults With Relapsed and Refractory Multiple Myeloma (A.R.R.O.W.)
Protocol Number:	20140355
EU Trial Number:	2014-005325-12
Other Identifiers:	NCT02412878
Date of This Summary:	17 December 2020

What does this summary cover?

This summary shows the main results from one clinical study, the A.R.R.O.W. 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.

Some information in this summary may be different from the approved labelling for carfilzomib. Your healthcare professional should refer to the full prescribing information for proper use of carfilzomib.

2. Who Sponsored This Study?

Amgen Inc.
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Phone (United States): +1 805-447-1000
Amgen Inc. is the sponsor of the study and also the manufacturer of carfilzomib, the medicine 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, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Italy, Japan, New Zealand, Norway, Poland, Romania, Spain, Sweden, United States, and United Kingdom
- The study began in September 2015 and ended in January 2019
- The study was completed as planned.

Why was the study done?

Multiple myeloma is cancer that begins in the plasma cells, which are a type of white blood cell. Patients can be treated for multiple myeloma. However, multiple myeloma could come back after treatment.

Carfilzomib (Kyprolis®) is a type of treatment known as a proteasome inhibitor. Carfilzomib is currently approved in some countries for the treatment of adults with multiple myeloma that comes back after treatment or that no longer responds to treatment. Carfilzomib may prevent the breakdown of abnormal proteins in cells, causing these cells to die. Cancer cells are more sensitive to these effects than normal cells.

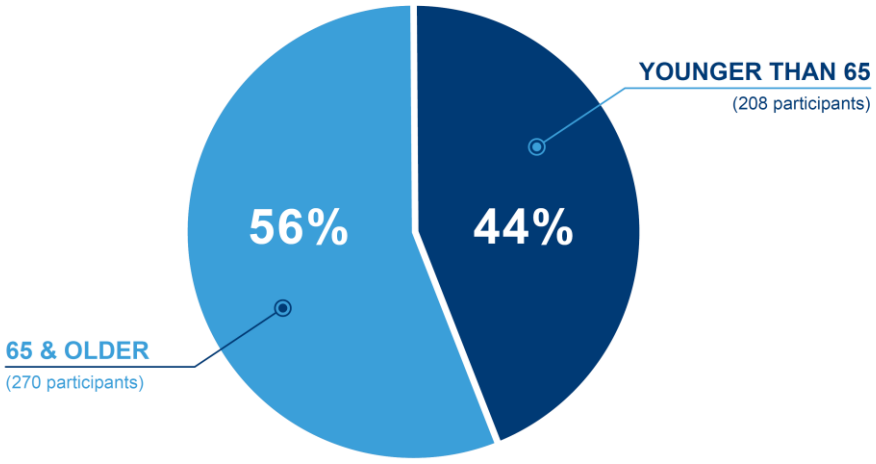
Carfilzomib is given in combination with other medicines that are approved for multiple myeloma, such as dexamethasone (a corticosteroid medicine).

This was a phase 3 study, the late stage of the development process of medicines for humans before they are approved for general use and after the medicines have been tested for safety and effectiveness in earlier phases. The main purpose of this study was to find out whether a once-weekly higher dose of an anti-myeloma medicine, called carfilzomib, works better than a twice-weekly lower dose.

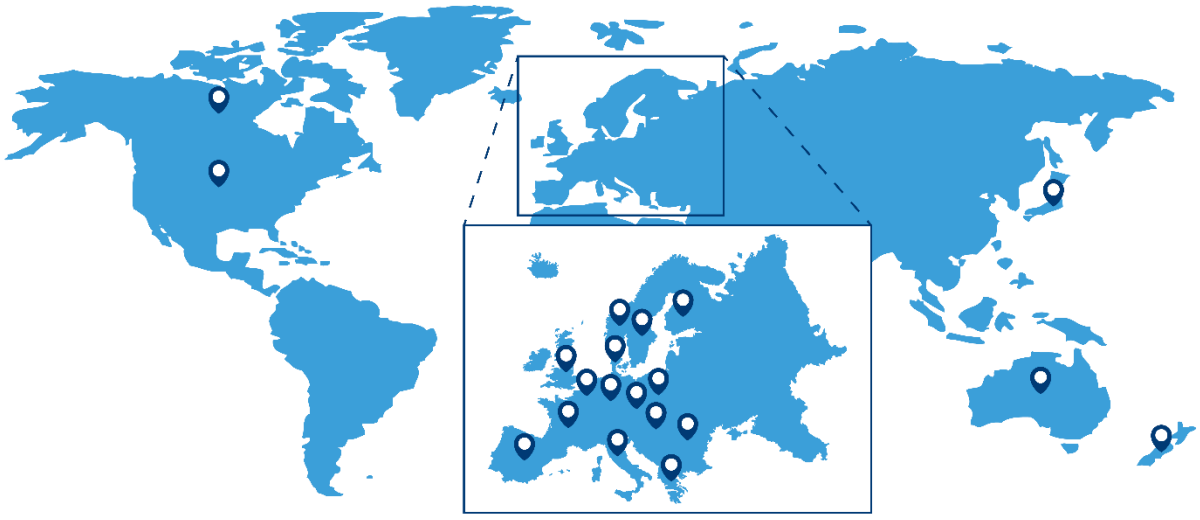
4. Who Was Included in This Study?

Who took part in the study?

This study included 478 participants with multiple myeloma. 260 participants (54%, or about 54 out of 100) were men and 218 participants (46%, or about 46 out of 100) were women. They ranged in age from 35 to 85 years. 208 participants (44%, or about 44 out of 100) were younger than 65 years old, and 270 participants (56%, or about 56 out 100) were 65 and older.



This study took place at 118 study centers in 20 countries. The number of participants in each country are shown below:



ASIA

Japan: 40

AUSTRALIA

Australia: 8
New Zealand: 1

NORTH AMERICA

Canada: 31
United States: 3

EUROPE

Belgium: 19
Czech Republic: 48
Denmark: 11
Finland: 4
France: 35
Germany: 11
Greece: 46
Hungary: 36
Italy: 65
Norway: 2
Poland: 40
Romania: 14
Spain: 27
Sweden: 6
United Kingdom: 31

Participants were examined by a study doctor and chosen to be in the study if they met certain study requirements. Some of the key requirements included that they:

- were 18 years of age or older
- were diagnosed with multiple myeloma that came back after treatment or that no longer responded to treatment
- had received 2 or 3 treatments for multiple myeloma before entering the study, including a type of medicine that may work on the immune system to slow the growth of cancer cells (immunomodulatory agent), and a type of medicine that may prevent the breakdown of abnormal proteins in cancer cells, causing these cells to die (proteasome inhibitor)
- had multiple myeloma that could be accurately measured by the study doctor

5. Which Medicines Were Studied?

Participants in this study had an equal chance of receiving either once-weekly or twice-weekly treatment. Neither the participants nor the study doctors could choose which treatment participants were given. Participants agreed to be put into a treatment group by chance ("randomized") using an automated computer system. This is like flipping a coin or drawing numbers out of a hat.

Participants in both groups received carfilzomib and dexamethasone. Each dosing cycle was 28 days (4 weeks).

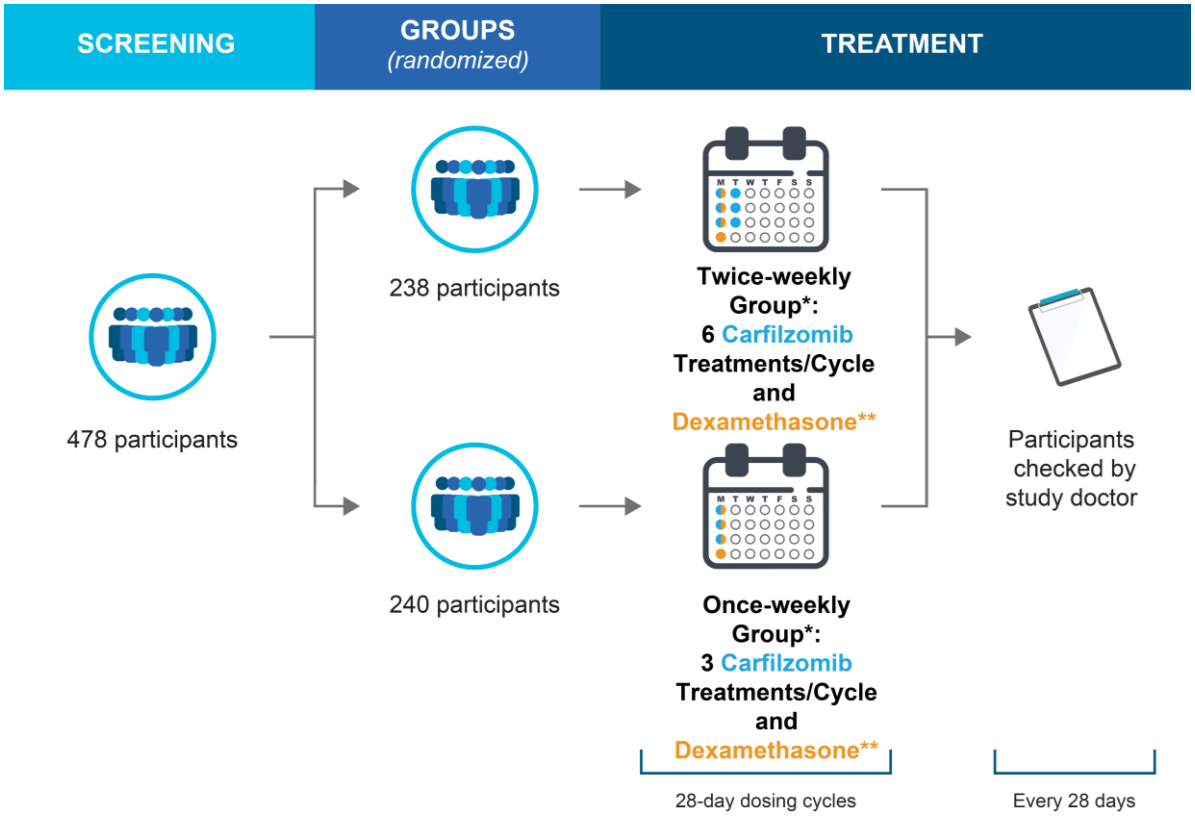
In the once-weekly dosing group, participants received high-dose carfilzomib (70 mg/m2) once per week for 3 out of the 4 weeks of each cycle, at the clinic. Participants also received dexamethasone once per week (40 mg) for the 4-week cycle for Cycles 1 through 9, then for 3 out of 4 weeks of each cycle.

In the twice-weekly dosing group, participants received low-dose carfilzomib (27 mg/m2) twice per week for 3 out of the 4 weeks each cycle, at the clinic.

Participants also received dexamethasone once per week for the 4-week (40mg) cycle for Cycles 1 through 9, then for 3 out of 4 weeks each cycle.

Carfilzomib was given as intravenous (in the vein) infusions. This was an open-label study, which means that both the participants and the study doctors knew which treatment regimen the participants received.

Participants were checked by the study doctor every 28 days, to see if multiple myeloma was getting better or worse, or staying the same. Participants could continue receiving study treatment until multiple myeloma worsened, they died, or they started receiving a different treatment for multiple myeloma.



*The carfilzomib dose for each administration was 27 mg/m2 for the twice-weekly group and 70 mg/m2 for the once-weekly group
Dexamethasone was given on the fourth week for the ***first 9 cycles only*

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. Doctors believed some of the problems could have been caused by the study treatment(s). These possible side effects are listed below.

What side effects were seen?

The table below shows how many participants had side effects within 30 days after their last dose of study treatment.

Side Effects During the Study

	Twice Weekly Group (235 participants)	Once Weekly Group (238 participants)
How many participants had serious side effects?	31 participants (13%)	57 participants (24%)
How many participants had non-serious side effects?	173 participants (74%)	170 participants (71%)
How many participants died from side effects?	20 participants (9%)	21 participants (9%)
How many participants stopped taking carfilzomib because of side effects?	29 participants (12%)	35 participants (15%)
How many participants stopped taking dexamethasone because of side effects?	31 participants (13%)	40 participants (17%)

If a participant had to stay in the hospital, had a life-threatening side effect, or died because of a side effect that the doctor believed could have been caused by the study treatment(s), the doctor reported that the side effect was serious.

The table below shows the serious side effects that that occurred in at least 2% of participants (or about 2 out of 100) in either group.

Serious Side Effects During the Study

Serious side effect	Twice Weekly Group (235 participants)	Once Weekly Group (238 participants)
Lung infection (pneumonia)	10 participants (4%)	8 participants (3%)
Serious complication that can happen when many cancer cells are destroyed, and release their contents into bloodstream	1 participant (less than 1%)	4 participants (2%)
Sudden loss of kidney function	0 participants (0%)	4 participants (2%)

The table below shows the non-serious side effects that occurred in at least 10% of participants (or about 10 out of 100) in either group.

Non-serious Side Effects During the Study

Non-serious side effect	Twice Weekly Group (235 participants)	Once Weekly Group (238 participants)
Trouble sleeping	42 participants (18%)	32 participants (13%)
High blood pressure	32 participants (14%)	39 participants (16%)
Low number of red blood cells	25 participants (11%)	26 participants (11%)
Feeling tired	23 participants (10%)	26 participants (11%)
Nausea	17 participants (7%)	26 participants (11%)

This section only shows the most often reported side effects considered by the study doctor as related to treatment. 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 long did participants who received once-weekly carfilzomib plus dexamethasone survive without multiple myeloma getting worse, compared to participants who received twice-weekly carfilzomib plus dexamethasone?

- To answer this question, the researchers looked at progression-free survival. The median progression free survival is estimated as the length of time that half of the participants are expected to survive without their multiple myeloma getting worse.
- In the once-weekly carfilzomib plus dexamethasone group, median progression-free survival was 11.2 months.
- In the twice-weekly carfilzomib plus dexamethasone group, median progression-free survival was 7.6 months.
- These results were not likely due to chance.
- This study was completed as planned.
- More results may be available at the websites 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?

Amgen would like to thank everyone who participated in this study. These results are only for this clinical study, which looked at a sample of 478 people with multiple myeloma. Not all participants in 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. This research may help future participants

and families by helping doctors understand more about how a once-weekly higher dose of carfilzomib may work in patients with multiple myeloma.

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 study medicine name carfilzomib (Kyprolis®) on the websites 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 NCT02412878
- www.clinicaltrialsregister.eu. Use the study identifier 2014-005325-12

  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.