Clinical Study Results

1. Study Name

Title of the Study:	A phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of apremilast (CC-10004) in Japanese subjects with palmoplantar pustulosis
Brief Title:	Efficacy and safety phase 2 study of apremilast in Japanese subjects with palmoplantar pustulosis
Protocol Number:	CC-10004-PPP-001 (20200055)
EU Trial Number:	Not applicable
Other Identifiers:	NCT04057937
Date of This Summary:	14 April 2022

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.

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

2. Who Sponsored This Study?

Amgen Inc.
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Thousand Oaks, CA 91320-1799 USA
Phone (United States): +1 805-447-1000
Amgen Inc. is the sponsor of the study who made apremilast, 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 Study

Where and when was the study done?

- This study took place in Japan.
- The study began in October 2019 and ended in June 2021.
- The study was completed as planned.

Why was the study done?

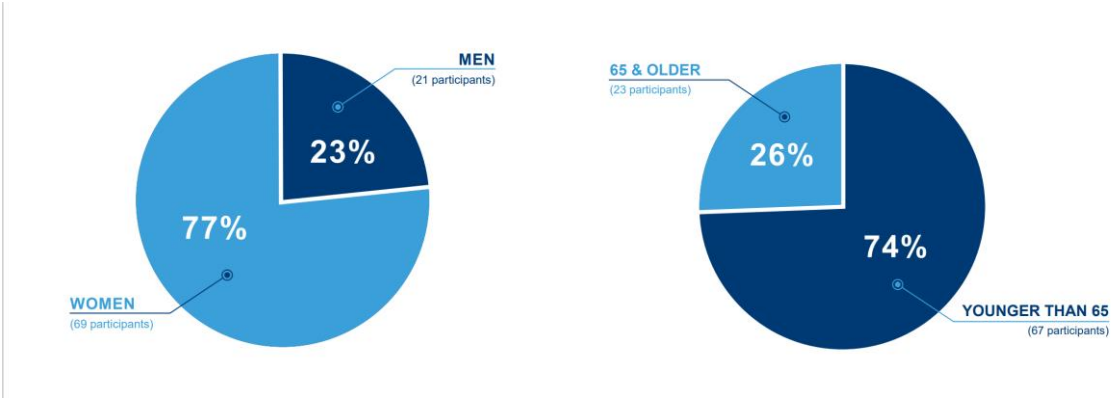
- Palmopustular pustulosois (PPP) is a disease in which developing small blisters, pustules, and redness, along with peeling of the upper layers of skin appear on the palms of the hands and soles of the feet. In the pustules, there are no disease-causing microbes such as bacteria and viruses, and these are called sterile pustules. When the pustules first appear there may be itching, and after a while the pustules dry out and become a brownish scab or crust and peel off. The skin around this area is inflamed and reddened. Pustules often come out one after the other and in some cases repeat becoming better or worse.

- Participants in this study had PPP and had previously been treated with topical (medicine applied to the skin) steroids and/or vitamin D3 preparations with an unsatisfactory response.
- Apremilast works by blocking an enzyme in the body called phosphodiesterase 4 (PDE4) that is usually increased in medical conditions involving inflammation, such as at skin. Apremilast is in the form of tablets and is taken by mouth.
- This was a phase 2 study, the second part of the development of medicines for humans. Researchers wanted to learn if this new study medicine could help participants with PPP. Researchers compared the study medicine, apremilast, to a placebo. A placebo does not contain any medicine and helps researchers compare the effects of a study medicine to taking no medicine. The main purpose of this study was to find out if participants who took apremilast saw an improvement in their PPP compared to participants who took placebo.

4. Who Was Included in This Study?

Who took part in the study?

This study included 90 participants with PPP. 69 participants (77% or about 77 out of 100) were women and 21 participants (23% or about 23 out of 100) were men. They ranged in age from 28 to 81 years. 67 participants (74% or about 74 out of 100) were younger than 65 years old, and 23 participants (26% or about 26 out of 100) were 65 years old or older.



This study took place in 22 study centers in Japan.

Participants were examined by a study doctor and chosen to be in the study if they met certain study requirements

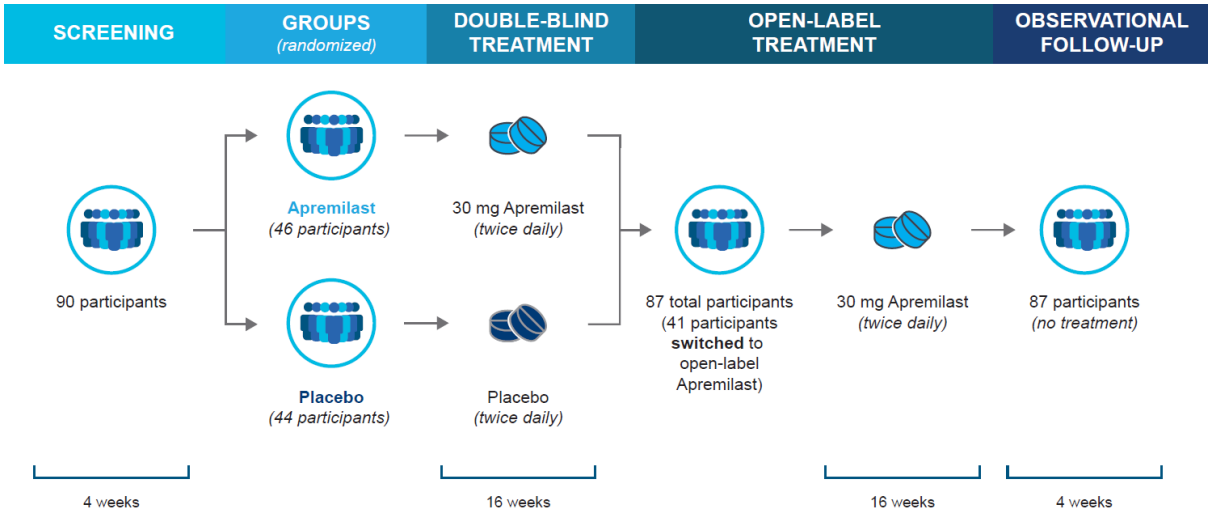
- Were 20 years or older
- Were diagnosed with PPP at least 5 and a half months before starting the study
- Had moderate or severe pustules on palms or soles as measured by the study doctor
- Had not had success in treating their PPP with topical steroid and/or Vitamin D3 preparations.

5. Which Medicines Were Studied?

In this study, apremilast was compared to a placebo. Participants had an equal chance of receiving either apremilast or a placebo. This study had 4 parts: a 4-week screening part, 16-week double-blind placebo-controlled part, a 16-week open-label part and a 4-week follow-up part where no medicine was taken by the participants.
In the double-blind part of the study, neither the participants nor the study doctor could choose the medicine the participants received. Participants agreed to be put into a medicine group by chance ("randomized"). This is like flipping a coin or drawing numbers out of a hat.
During the double-blind part of the study, neither the participants nor the doctors knew which medicine each participant was given until after the study was over. This was done to make sure the study results were not influenced in any way. This was known as the double-blind part of the study. Each participant took either 30 mg apremilast or placebo twice a day for 16 weeks.
At the end of 16 weeks, the participants had their PPP evaluated by their doctors. Participants then continued the study with open-label 30 mg apremilast twice a day for another 16 weeks as shown in the graphic below.

- Open-label means that both the participants and the study doctors knew what medicine the participants received.

The information collected from all subjects at the end of the 16 weeks gave the researchers the information needed to decide if the main aim of the study was met. At the end of the open-label part of the study all participants then had a 4-week follow-up period where no one took any medicine.



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 medicine(s). These possible side effects are listed below.

What side effects were seen?

When reporting side effects in this study, the study doctor did not know which study medicine a participant was receiving for the double-blind part of the study.

The table below shows how many participants had side effects.

Side Effects During the Double-blind Part of the Study

	Placebo (44 participants)	Apremilast 30 mg twice a day (46 participants)
How many participants had serious side effects?	0 participants (0%)	0 participants (0%)
How many participants had non-serious side effects?	8 participants (18%)	27 participants (59%)
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 (5%)	0 participants (0%)

Side Effects During the Open-label Part of the Study

	Apremilast 30 mg twice a day (87 participants)
How many participants had serious side effects?	1 participant (1%)
How many participants had non-serious side effects?	44 participants (51%)
How many participants died from side effects?	0 participants (0%)
How many participants stopped taking the study medicine because of side effects?	0 participants (0%)

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. No participant died due to a side effect.

The table below shows the serious side effects.

Serious Side Effects During the Open-label Part of the Study	
Serious side effect	**Apremilast 30 mg twice a day (87 participants)**
Peritonitis (inflammation of the membrane which forms the lining of the belly cavity)	1 participant (1%)

There were no serious side effects in the double-blind part of the study.

The table below shows the non-serious side effects that occurred in at least 5% of participants (or about 5 out of 100).

Non-serious Side Effects During the Double-blind Part of the Study		
Non-serious side effect	**Placebo (44 participants)**	**Apremilast 30 mg twice a day (46 participants)**
Diarrhoea	3 participants (7%)	12 participants (26%)
Abdominal discomfort (belly pain)	1 participant (2%)	7 participants (15%)
Nausea	1 participant (2%)	6 participants (13%)
Faeces soft (soft stools)	2 participants (5%)	5 participants (11%)
Headache	0 participants (0%)	5 participants (11%)
Decreased appetite	0 participants (0%)	3 participants (7%)

Non-serious Side Effects During the Open-label Part of the Study	
Non-serious side effect	**Apremilast 30 mg twice a day (87 participants)**
Diarrhoea	17 participants (20%)
Abdominal discomfort (belly pain)	12 participants (14%)
Nausea	9 participants (10%)
Faeces soft (soft stools)	8 participants (9%)
Headache	6 participants (7%)
Decreased appetite	4 participants (5%)

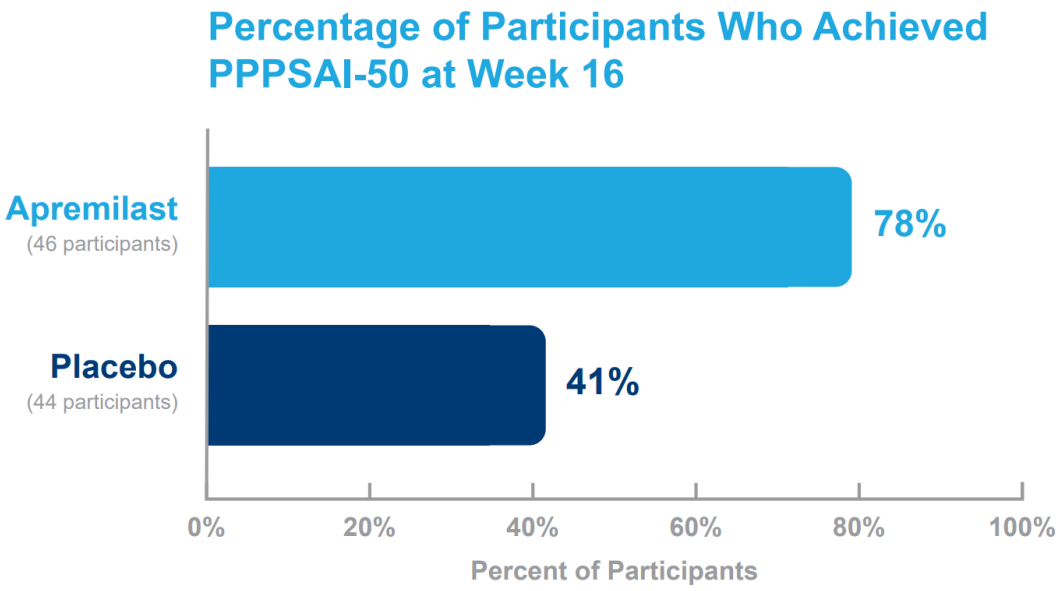
This section only shows the most often reported side effects considered by the study doctor as related to study medicine. No single clinical study can give a complete picture of the benefits and risks of a medicine. Information about other side effects may be available at the websites listed at the end of this summary.

7. What Were the Overall Results of the Study?

Did participants who took apremilast see their PPP improve, compared to participants who took placebo?

- To answer this question, the researchers measured the improvement of PPP using the Palmoplantar Pustulosis Area and Severity Index (PPPASI) total score to find out how many participants achieved PPPASI-50 response which is 50% or greater improvement of PPPASI score from starting the study.
    - The PPPASI is a system used for assessing and grading the severity and area of PPP lesions and their response to therapy. Each of the palms and soles are assessed separately for both the area involved and severity of the lesions and given a number value. A calculation is then used to get a total score.

- In this study, 78% of participants in the apremilast group and 41% of participants in the placebo group saw an improvement in their PPP as measured by PPPASI-50 response by the end of the double-blind part of the study, as shown in the graph below.
- These results are based on information that was collected until the researchers had finished gathering the information needed to achieve the main aim of the study.
- 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?

These results are only for this clinical study, which looked at a sample of 90 people with PPP. 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 study

medicine may work in a single person. Many studies are needed to show the benefits and risks of a medicine that is still being tested. This research may help future participants and families by helping doctors understand more about the study medicine being studied.

9. Are There Plans for Further Studies?

If more clinical studies are done, they may be listed on public websites, such as the one below. Search for study medicine name apremilast (Otezla®) on the website below.

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

To find out more about this study, check this website:

- www.clinicaltrials.gov. Use the study identifier NCT04057937

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