# *Clinical Study Results*

## 1. Study Name

| | |
|---|---|
| Title of the Study: | A Dose-ranging, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of Tezepelumab Alone or Combined With Topical Corticosteroids in Moderate-to-Severe Atopic Dermatitis |
| Brief Title: | A Dose-ranging, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of Tezepelumab in Atopic Dermatitis |
| Protocol Number: | 20170755 |
| EU Trial Number: | EudraCT Number: 2018-001997-52 |
| Other Identifiers: | NCT03809663 |
| Date of This Summary: | 07 September 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 participants.

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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Thousand Oaks, CA 91320-1799 USA
Phone (United States): +1 805-447-1000
Amgen Inc. is the sponsor of the study and is developing tezepelumab with AstraZeneca as 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 had 2 planned parts, which included the first part of the study evaluating the safety and efficacy of tezepelumab alone (part A) and a study evaluating tezepelumab combined with a topical corticosteroid (part B).
- This study took place in Australia, Canada, Czech Republic, Estonia, Germany, Hungary, Japan, Latvia, Poland, Republic of Korea, Spain, Ukraine, the United Kingdom, and the United States.
- The study began in March 2019 and ended in December 2020.
- The first part of the study (Part A) was stopped earlier than planned because there was no difference in the response of tezepelumab and the response of placebo. The results may be due to chance and not tezepelumab. A placebo does not contain any medicine and helps researchers compare the effects of an investigational medicine to a placebo. Part B of the study was not started.

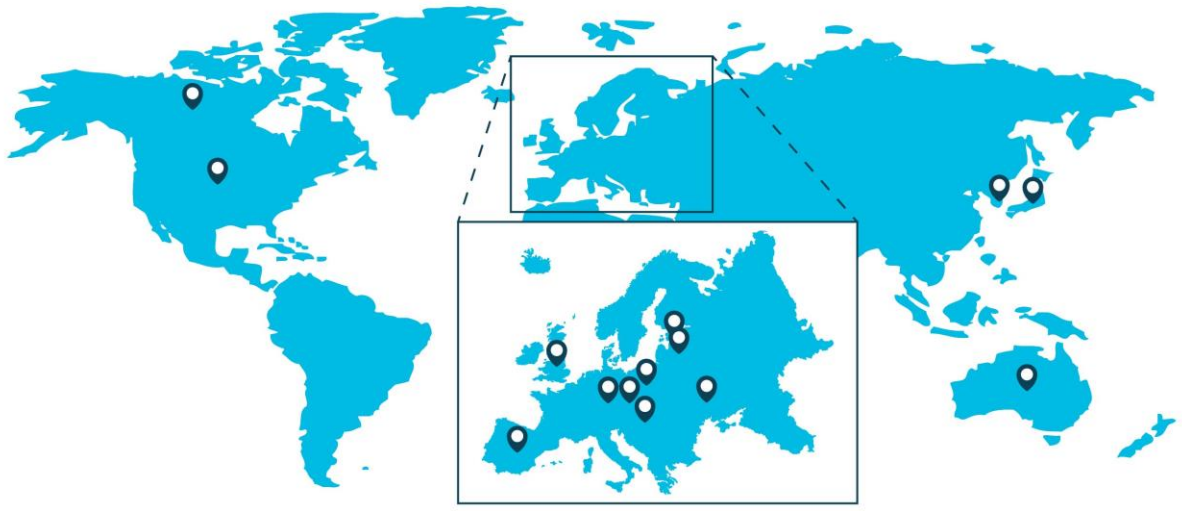
## *Why was the study done?*

- This was a phase 2 study, the second part of the development of medicines for humans. Researchers wanted to learn if this investigational treatment (tezepelumab) could help participants with atopic dermatitis (AD). AD is a condition where the skin is itchy, red, swollen, and cracked. Clear fluid may come from the affected areas. Scratching the affected areas worsens the symptoms and increases the risk of skin infections.
- In this study, researchers wanted to measure the effect of tezepelumab treating AD compared with placebo. The effect of tezepelumab was measured using 2 tools, the Investigator's Global Assessment (IGA) and the Eczema Area and Severity Index (EASI).
    - The IGA was a way for physicians to measure the severity of AD signs of skin rash, redness, and thickness. An IGA score of 0 means clear of AD signs; IGA score of 1 means almost clear; an IGA score of 2 means mild signs; IGA score of 3 means moderate signs; an IGA score of 4 means severe; and an IGA score of 5 means very severe.
    - EASI was scored using the severity of redness, deepness of skin thickening, amount of broken skin from scratching, and thick skin lines. This score was calculated based on the severity of AD symptoms and how much body surface was affected by AD.
- Researchers wanted to find out if participants could achieve an IGA score of 0 (clear) or 1 (almost clear) (IGA 0/1) at week 16, or reduction in the EASI score of at least 75% from the first measurement (EASI 75) at week 16.
- Researchers also wanted to compare the safety of tezepelumab to a placebo.
- A placebo was chosen as the comparator for tezepelumab in this study.

## 4. Who Was Included in This Study?

### *Who took part in the study?*

This study included 251 participants with moderate-to-severe AD. 109 participants (43%, or about 43 out of 100) were women and 142 participants (57%, or about 57 out of 100) were men. They ranged in age from 18 years old to 71 years old.
125 participants (50%, or 50 out of 100) were age 35 years old or younger and 50% were older than 36 years old.
This study took place at 78 study centers across Australia, Canada, Czech Republic, Estonia, Germany, Hungary, Japan, Latvia, Poland, Republic of Korea, Spain, Ukraine, the United Kingdom, and the United States.



**ASIA: 49 *(20%)***
Japan: 35 *(14%)*
Republic of Korea: 14 *(6%)*

**EASTERN EUROPE: 101 *(40%)***
Czech Republic: 16 *(6%)*
Estonia: 10 *(4%)*
Hungary: 4 *(2%)*
Latvia: 12 *(5%)*
Poland: 41 *(16%)*
Ukraine: 18 *(7%)*

**NORTH AMERICA: 59 *(24%)***
Canada: 23 *(9%)*
United States: 36 *(14%)*

**WESTERN EUROPE AND AUSTRALIA: 42 *(17%)***
Australia: 10 *(4%)*
Germany: 7 *(3%)*
Spain: 16 *(6%)*
United Kingdom: 9 *(4%)*

The numbers of participants in each country are listed below:

| Countries Where Participants were From | Number of Participants (% of Total) (251 participants) |
|---|---|
| ASIA | 49 (20%) |
| Japan | 35 (14%) |
| Republic of Korea | 14 (6%) |
| EASTERN EUROPE | 101 (40%) |
| Czech Republic | 16 (6%) |
| Estonia | 10 (4%) |
| Hungary | 4 (2%) |
| Latvia | 12 (5%) |
| Poland | 41 (16%) |
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| Australia | 10 (4%) |
| Germany | 7 (3%) |
| Spain | 16 (6%) |
| United Kingdom | 9 (4%) |

Participants were examined by a study doctor and chosen to be in the study if they: were adults aged 18 years old to 75 years old; have a diagnosis of chronic AD for greater than or equal to 2 years prior to screening, had an inadequate response to topical treatments (lotions, ointments); had AD involved with greater than or equal to 10% body; an IGA score of ≥ 3; and an EASI score of greater than or equal to 16.

## 5. Which Medicines Were Studied?

The medication in this study was tezepelumab. Tezepelumab is a type of antibody. That means it is a copy of a protein produced by white blood cells that helps fight disease or infection. Tezepelumab was developed in a lab. It was previously studied in patients with AD and showed improvements in patients with AD. Tezepelumab has shown in previous studies that it blocks a protein called thymic stromal lymphopoeitin (TSLP). TSLP causes skin itching and inflammation and is increased in AD.

Participants were given one of the following study medications:

- Tezepelumab 420 mg subcutaneous (SC; under the skin) every 2 weeks (Q2W)
- Tezepelumab 280 mg SC Q2W
- Tezepelumab 210 mg SC every 4 weeks (Q4W)
- Placebo SC Q2W

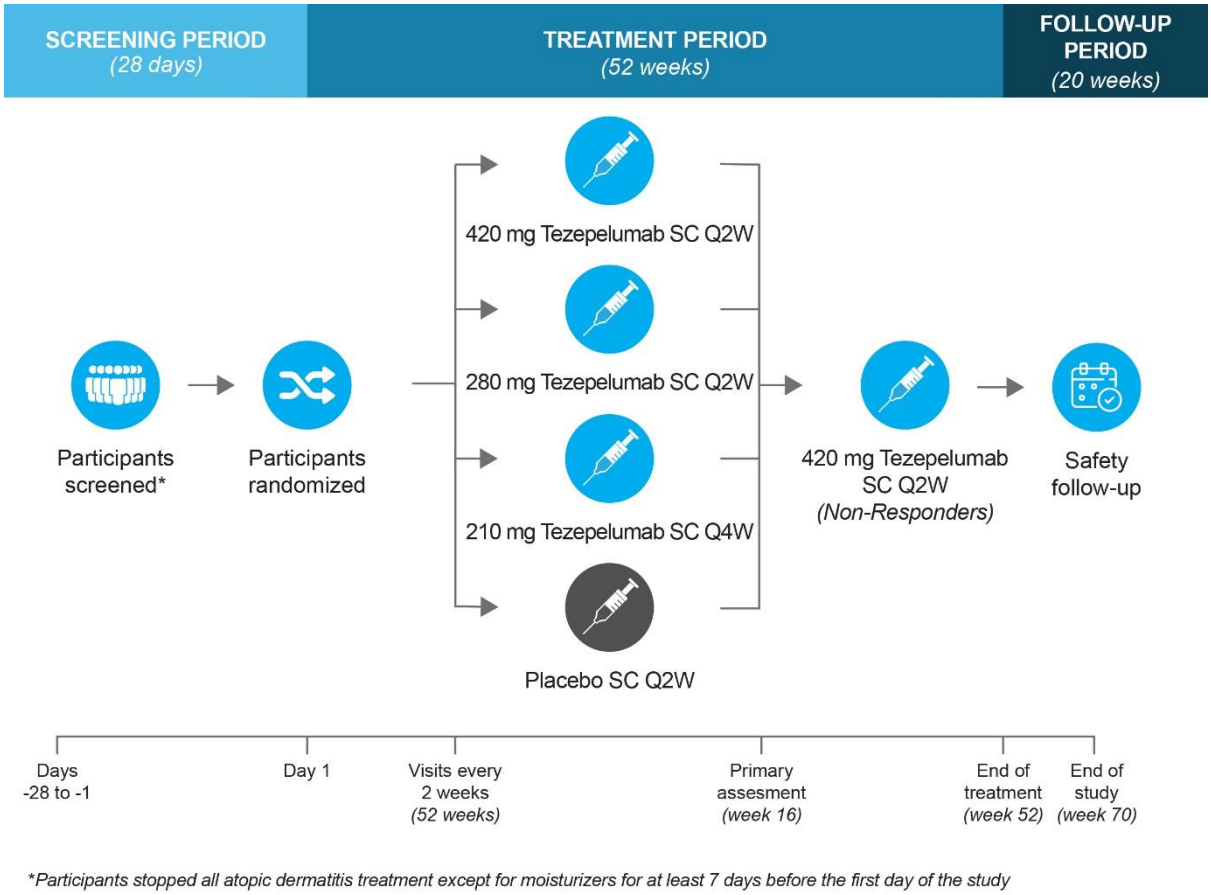
In Part A, some participants did not respond to tezepelumab and were referred to as non-responders. Non-responders did not achieve at least a 50% improvement in the EASI score at week 16 compared to baseline (day 1). Non-responders then received study drug tezepelumab 420 mg SC Q2W for the remainder of the study, beginning with the week 18 dose.

**Study Design**

Neither the participants nor the study doctor could choose the treatment the participants received. Participants agreed to be put into a treatment group by chance (randomized). This is like flipping a coin or drawing numbers out of a hat. Neither the participants nor the doctors knew which treatment each participant was given (double-blinded) until after the study was over. This was done to make sure the study results were not influenced in any way.

Part A of the study consisted of:

- 28-day screening period; participants stopped all AD treatment except for moisturizers or lotions for at least 7 days before the first day of the study
- 52-week treatment period; all participants received a 420 mg SC dose (tezepelumab or placebo) as the first dose and then received their assigned dose starting at the week 2 visit
- 20-week safety follow-up period




*Participants stopped all atopic dermatitis treatment except for moisturizers for at least 7 days before the first day of the study

## 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?*

When reporting side effects in this study, the study doctor did not know which treatment a participant was receiving.

The table below shows how many participants had side effects during the 16 weeks of the study.

**Table 1. Side Effects During the First 16 Weeks of the Study**

| | Tezepelumab 210 mg Q4W (59 participants) | Tezepelumab 280 mg Q2W (58 participants) | Tezepelumab 420 mg Q2W (70 participants) | Placebo Q2W (63 participants) |
|---|---|---|---|---|
| **How many participants had serious side effects?** | 2 participants (3%) | 0 participants (0%) | 1 participant (1%) | 0 participants (0%) |
| **How many participants had non-serious side effects?** | 34 participants (58%) | 40 participants (69%) | 39 participants (56%) | 35 participants (56%) |
| **How many participants died from side effects?** | 0 participants (0%) | 0 participants (0%) | 0 participants (0%) | 0 participants (0%) |
| **How many participants stopped taking the study medicine because of side effects?** | 1 participant (2%) | 0 participants (0%) | 4 participants (6%) | 0 participants (0%) |

If a participant had to stay in the hospital 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 effects.

**Table 2. Serious Side Effects During the First 16 Weeks of the Study**

| Serious side effect | Tezepelumab 210 mg Q4W (59 participants) | Tezepelumab 280 mg Q2W (58 participants) | Tezepelumab 420 mg Q2W (70 participants) | Placebo Q2W (63 participants) |
|---|---|---|---|---|
| **Inflammation of the tubes going to the lungs** | 1 participant (2%) | 0 participants (0%) | 0 participants (0%) | 0 participants (0%) |
| **Inflammation of the skin with red, itchy patches** | 1 participant (2%) | 0 participants (0%) | 0 participants (0%) | 0 participants (0%) |
| **Inflammation of the skin with itchiness and blisters** | 1 participant (2%) | 0 participants (0%) | 0 participants (0%) | 0 participants (0%) |
| **High blood pressure** | 0 participants (0%) | 0 participants (0%) | 1 participant (1%) | 0 participants (0%) |

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

**Table 3. Non-Serious Side Effects During the First 16 Weeks of the Study**

| Non-serious side effect | Tezepelumab 210 mg Q4W (59 participants) | Tezepelumab 280 mg Q2W (58 participants) | Tezepelumab 420 mg Q2W (70 participants) | Placebo Q2W (63 participants) |
|---|---|---|---|---|
| **Atopic dermatitis** | 10 participants (17%) | 13 participants (22%) | 13 participants (19%) | 12 participants (19%) |
| **Nose/throat inflammation** | 5 participants (9%) | 10 participants (17%) | 6 participants (9%) | 6 participants (10%) |
| **Upper respiratory tract infection** | 3 participants (5%) | 2 participants (3%) | 1 participant (1%) | 4 participants (6%) |
| **Headache** | 1 participant (2%) | 1 participant (2%) | 4 participants (6%) | 3 participants (5%) |
| **High blood pressure** | 0 participants (0%) | 3 participants (5%) | 2 participants (3%) | 1 participant (2%) |
| **Itching** | 0 participants (0%) | 3 participants (5%) | 0 participants (0%) | 2 participants (3%) |

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?

**Did participants achieve an IGA score of 0 (clear) or 1 (almost clear; IGA 0/1) at week 16, or a 75% reduction in EASI (EASI 75) at week 16?**

- There were no statistically significant differences in IGA 0/1 or EASI 75 in participants at week 16 for any tezepelumab treatment group compared with placebo. That means that the differences seen could have been due to chance and not tezepelumab.

- The first part of the study (Part A) was stopped earlier than planned because there was no difference between the response in participants in the tezepelumab groups and placebo group.
- Part B, the part of the study studying tezepelumab combined with a topical corticosteroid regimen, was not started.
- Plans were made to manage the study during the coronavirus disease in 2019 (COVID-19) pandemic. These plans were started on April 6, 2020 and included other visits (phone calls, video conferences, and alternative sites when subjects could not enter the hospital), temporary stopping of investigational drug for subjects showing COVID-19 symptoms, and use of other laboratories or data processing.

## How long were participants in the study before the study ended?

Participants were treated in the study for about one year.

## Did tezepelumab relieve signs of AD more than placebo?

There were no statistically significant differences in IGA 0/1 or EASI 75 in participants at Week 16 for any tezepelumab treatment group compared with placebo. The differences seen may be due to chance. The table below shows the number and percentage (%) of participants who reached an IGA score of 0 (clear) or 1 (almost clear) and EASI 75 (at least a 75% reduction in the EASI score from the beginning of the study).

**Table 4. IGA and EASI 75 Scores by Treatment and Placebo**

| Participants achieving response<br>Number (%) | Tezepelumab 210 mg Q4W<br>(62 participants) | Tezepelumab 280 mg Q2W<br>(63 participants) | Tezepelumab 420 mg Q2W<br>(63 participants) | Placebo Q2W<br>(63 participants) |
|---|---|---|---|---|
| **IGA 0/1 (%)** | 4 (7%) | 2 (3%) | 5 (8%) | 2 (3%) |
| **EASI 75 (%)** | 9 (15%) | 10 (16%) | 7 (11%) | 8 (13%) |

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

## 8. How Has This Study Helped Participants and Researchers?

- This study contributed to the relevant area of research and potential next steps to build on that knowledge.
- These results are the outcome of one study – and other studies may show something different (either already done or future studies).

**What else is important to know about these results?**

These results are only for this clinical study, which looked at a sample of 251 participants with moderate-to-severe atopic dermatitis. 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 that is still being tested. 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 study medicine name tezepelumab 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 NCT03809663
- www.clinicaltrialsregister.eu. Use the study identifier EUDRA CT: 2018-001997-52

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.