Clinical Trial RESULTS

Allergopharma

ALLERGOPHARMA CLINICAL TRIAL

Research Sponsor:	**ALLERGOPHARMA GmbH & Co. KG**
Drug Studied:	**ALLERGOVIT® Birch and ALLERGOVIT® Grasses**
EudraCT #:	**2013-003095-12**
Protocol #:	**AL1303AV**
Trial Date:	**April 3, 2014 to November 26, 2015**
Short Trial Title:	**A trial to determine whether ALLERGOVIT® Grasses was effective for relieving grass pollen allergy symptoms and ALLERGOVIT® Birch for relieving birch pollen allergy symptoms (specific treatment effect) and to determine any unspecific treatment effects of both medications (effect of ALLERGOVIT® Grasses on birch pollen allergy symptoms and vice versa).**

Thank you for participating in this trial!

As a clinical trial participant, you belong to a large community around the world. You help researchers answer important health questions and help them discover new medical treatments.

Thank you for taking part in the clinical trial for the trial drug ALLERGOVIT® Birch and Grasses. This trial started in April 2014 and ended in November 2015. You and all of the 95 participants helped researchers learn if desensitization with allergen injections provides efficacious relief to people with grass and birch pollen allergy.

ALLERGOPHARMA GmbH & Co. KG, the sponsor (researcher) of this trial, thinks it is important for you to know the results of your trial. We hope it helps you understand and feel proud of your key role in medical research. If you have questions about the results, please speak with the doctor or staff at your trial site.

WHAT´S HAPPENED SINCE MY TRIAL ENDED?

You were in the trial for approximately 10 months, but the entire trial took 21 months to finish. 95 participants at 15 research centers across Germany were included. When the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary thereof.

WHY WAS THE RESEARCH NEEDED?

Hay fever (allergic rhinitis) is caused by an allergy to pollen (mostly birch and grass pollen) and leads to an inflammation of the airways triggering allergy symptoms in the airways. It affects up to 30% of all people worldwide. Many of these people also suffer from asthma (a lung disease). As complete avoidance of pollen is practically not possible during the pollen season, medical treatment is required. There are many medications available that relieve symptoms. However, the only treatment that fights the causes of allergies is desensitization (specific immunotherapy, SIT). With this usually 3 years long treatment, a certain amount of the respective allergen, that normally causes the allergy symptoms, is administered subcutaneously (under the skin, SCIT) or under the tongue (SLIT). Over time and with increasing doses, the body learns to tolerate the allergen without producing symptoms again.

Previous studies showed that the subcutaneous injection of ALLERGOVIT® can resolve allergy symptoms. In this trial, two preparations were used (ALLERGOVIT® Birch and ALLERGOVIT® Grasses) that are already available on the market. Now researchers wanted to know:

1. ***Does ALLERGOVIT® Birch and ALLERGOVIT® Grasses help resolve allergy symptoms?***
2. ***Are the two ALLERGOVIT® medications specific to the birch and grass pollen?***
3. ***Does ALLERGOVIT® change the immune system?***
4. ***Does the trial reveal other interesting findings?***

To answer these questions, researchers asked for the help of men and women like you. All patients were between 18 and 65 years old, all suffered from allergic rhinitis with or without controlled asthma due to dual allergy to birch and grass pollen and had been pre-treated with anti-allergic medications for at least 2 years, but still suffered from relevant allergy symptoms.

WHAT KIND OF TRIAL WAS THIS?

This trial investigated two treatments – ALLERGOVIT® Birch and ALLERGOVIT® Grasses.
At the start of the trial, participants were put into one of the two treatment groups by chance ("randomized") using a computer program. Each patient had the same chance to be selected for either group in the trial.

- ALLERGOVIT® Grasses: 47 patients (on average 34 years old, 53.2% females)
- ALLERGOVIT® Birch: 48 patients (on average 33 years old, 58.3% females)

The treatments had an identical appearance and were packed in a way that neither participants nor researchers knew who had which treatment during the trial (called "double-blind").

WHAT HAPPENED DURING THE TRIAL?

Before the start of the trial, doctors tested participants to see if they could participate. Only participants who showed sufficient symptoms after allergen contact in a pollen room (at the Fraunhofer Institute in Hannover) could take part. Participants like you were treated with ALLERGOVIT® Birch OR ALLERGOVIT® Grasses for about 10 months. The treatment started with a low strength of allergen, which was then cautiously increased in 7 steps at intervals of 7 days ("dose-escalation phase" lasting for 6 weeks).

After the maximum foreseen dose or the maximum individually tolerated dose had been reached, this dose was administered again after 2 weeks. Afterwards, the injection interval was prolonged to 4 weeks and finally 6 to 8 weeks. These intervals were then kept. This "maintenance" phase of the trial lasted for about 8-10 months. Overall, you received up to 13 injections.

To evaluate the treatment effects, your allergic reactions were tested before and after the treatment phase. This was done by recording your allergic symptoms:

- nasal congestion
- rhinorrhea
- nasal itching
- sneezing

Each symptom rated on a 4-point scale from 0 (no symptoms) to 3 (most severe) during the pollen room visit. This pollen room visit lasted for 120 minutes during which you were exposed to birch pollen and, after 5 days, again to grass pollen atmosphere. The symptom scores obtained at the two time-points and under the different pollen atmospheres were then compared by the researchers.

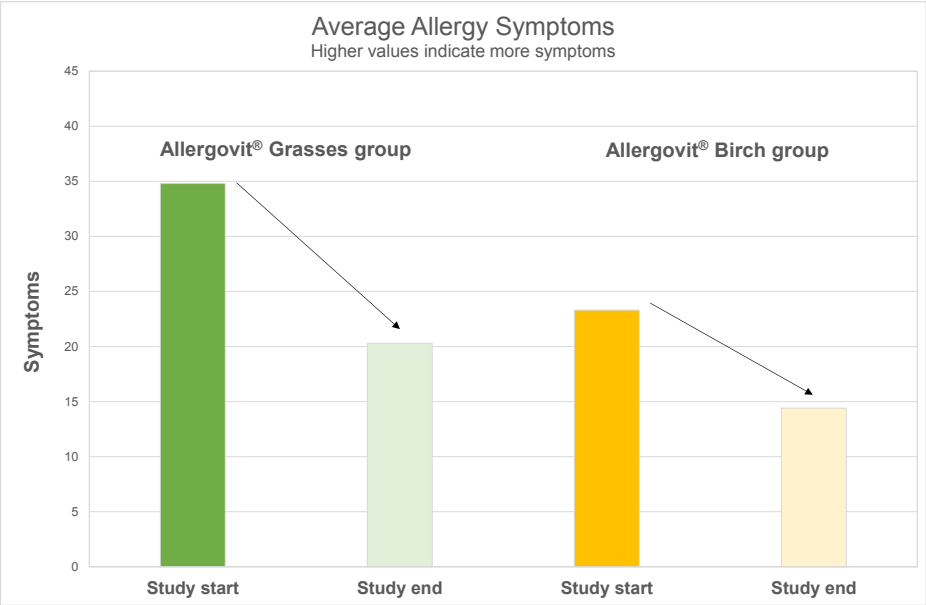
Trial staff checked your health each time you visited your trial site, including blood pressure, heart rate and how fast you were breathing. You also had blood and urine tests done and a lung function test at the beginning of the trial. After stopping getting your trial treatment you went to the final visit and your health was checked again.

Initially, 269 patients were screened. Of these, 95 participants continued in the trial and were treated with one of the ALLERGOVIT® injections. Eight patients discontinued the trial before the planned trial end. Overall, participants saw their trial doctor at least 19 times during the trial.

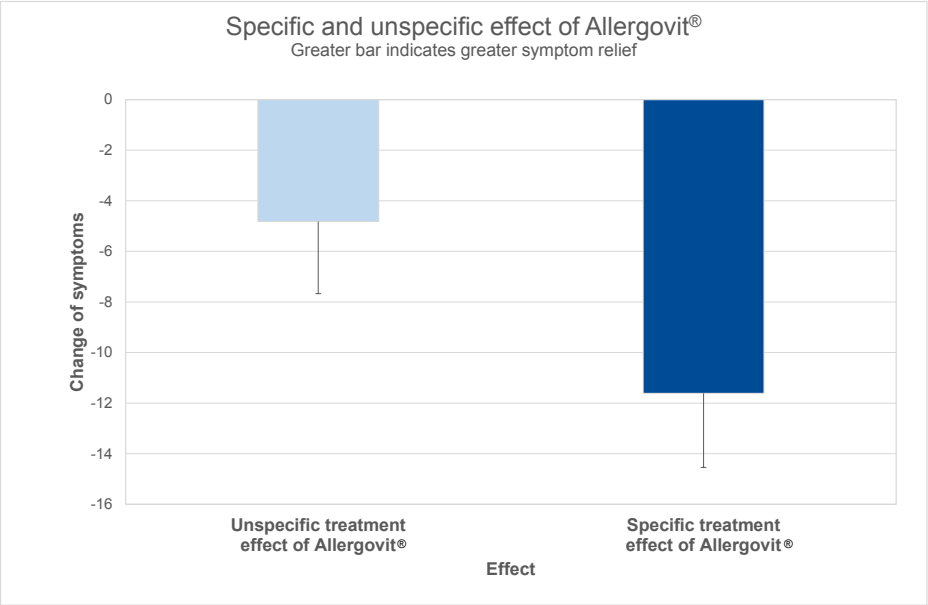
WHAT WERE THE TRIAL RESULTS?

Below is a summary of the medical questions that were asked in this trial, and the trial results:

1. ***Did ALLERGOVIT® Birch and ALLERGOVIT® Grasses help resolve allergy symptoms?***
   Yes. After 10 months of treatment with about 13 injections, both groups of participants had allergy symptoms, but less than before treatment.



2. ***Were the two ALLERGOVIT® medications specific to the birch and grass pollen?***
   Yes. At the end of the trial, participants in the ALLERGOVIT® Birch group had less birch allergy symptoms. When they were exposed to grass pollen there was no remarkable reaction. Accordingly, participants in the ALLERGOVIT® Grasses group had less grass pollen symptoms but still suffered from birch pollen symptoms. Taken both treatments groups together, the specific effect of ALLERGOVIT® was greater than the unspecific effect.



3. ***Did ALLERGOVIT® change the immune system?***
   Yes. Treatment with ALLERGOVIT® induced a specific immune response to immunotherapy. This means that participants in the ALLERGOVIT® Birch group had more birch specific IgG4 and participants in the ALLERGOVIT® Grasses group more grass specific IgG4 in their blood. These immunological results are in line with the clinical results on symptom relief that ALLERGOVIT® was allergen specific. ALLERGOVIT® treatment could induce a specific change of the immune system response.

4. ***Did the trial reveal other interesting findings?***
   Yes. This trial demonstrated that one treatment can be used as control group, which is helpful for the researchers to design future studies on allergies. Further, no dose reductions during the pollen season were needed, which makes treatment easier.

WHAT SIDE EFFECTS DID PARTICIPANTS HAVE?

A side effect is any medical problem caused by a drug or treatment. When drugs are being studied, researchers keep track of all medical problems that patients have. These medical problems are called “adverse events”, and may or may not be caused by the trial drugs.

How many participants had side effects during or after treatment with Allergovit?

Many participants had side effects. Most side effects were not serious but some were. Most of the side effects that were related to the treatment were local, non-serious reactions of the skin (e.g. swelling, redness, itching). The table below shows how many participants had side effects during the trial.

Side Effects in this Trial

	ALLERGOVIT® Grasses (Out of 47 participants)	ALLERGOVIT® Birch (Out of 48 participants)
How many participants had side effects?	37 participants (78.7%)	33 participants (68.8%)
In how many participants were the side effects (probably) caused by the treatment?	21 participants (44.7%)	15 participants (31.3%)
How many participants stopped treatment because of side effects?	1 participant	1 participant

WHAT SERIOUS SIDE EFFECTS DID PARTICIPANTS HAVE?

A side effect is considered serious e.g. when it is life-threatening, it causes lasting problems or the patient needs hospital care.

Overall 7 serious adverse events occurred in the trial. However, none of these serious adverse events were rated by the treating doctors as being caused by the trial drugs. Two of the participants stopped the treatment earlier because of their serious adverse events.

WHAT WERE THE MOST COMMON SIDE EFFECTS?

The table below shows the most common of 230 side effects found in this trial – both serious and not serious. Less common side effects are not in the table.

Most Common Side Effects in this Trial

	ALLERGOVIT® Grasses (Out of 47 participants)	ALLERGOVIT® Birch (Out of 48 participants)
Nasopharyngitis (Common cold)	12 participants (25.5%)	16 participants (33.3%)
Injection site swelling	11 participants (23.4%)	5 participants (10.4%)
Injection site redness	8 participants (17.0%)	8 participants (16.7%)
Injection site itching	8 participants (17.0%)	6 participants (12.5%)
Headache	4 participants (8.5%)	4 participants (8.3%)

Full list can be found on the European Union Clinical Trial Register website at www.clinicaltrialsregister.eu/2013-003095-12

The most common side effects were viral infection of the airways (nasopharyngitis) and local skin reactions at the injection site such as swelling, redness and itching. These side effects are common in patients treated with SCIT. The local skin reactions occurred predominately during the dose escalation phase and were of mild intensity in most participants. These local reactions disappeared later in the trial.

An anaphylactic reaction has a quick onset and can include various symptoms at different organ systems (heart beating quickly, tingling sensations, vomiting etc.). Three patients experienced anaphylactic reactions with the following symptoms: sneezing, shortness of breath, swelling under the skin of the left ear (angioedema).

OVERALL RESULTS OF THE TRIAL

Researchers found that treatment with ALLERGOVIT® was efficacious in relieving allergy symptoms. Both ALLERGOVIT® Grasses and ALLERGOVIT® Birch treatments were specific to the respective grass and birch pollen allergens. ALLERGOVIT® treatment could induce a change of the immune system response. In general, the side effects with ALLERGOVIT® Grasses and ALLERGOVT® Birch were similar, non-serious and of mild and temporary nature. A dose reduction of treatment during the pollen season was not necessary. Researchers did not see any new side effects in this trial.

This report describes the trial findings for the combined trial participants. This means, the results of this trial may not reflect individual results. At this time, we don't believe that any of the findings from this trial would impact your care. Findings from this trial will be used in future studies to compare this drug with other treatments for patients with pollen allergies.

WHERE CAN I LEARN MORE ABOUT THIS TRIAL?

This research was important. Thank you for helping us to understand more about allergies and desensitization. You can find more information about this trial online at www.clinicaltrialsregister.eu/2013-003095-12. A full report of the study results has not yet been published. Short summaries of the results were presented at the European Academy of Allergy & Clinical and German Allergy Congresses 2015 and 2016. If you have questions about the results, please speak with the doctor or staff at your research center.

The official trial title is *Double-blind phase IV multicenter clinical trial to evaluate and compare specific and non-specific effects of SCIT by use of an Environmental Challenge Chamber after treatment with Allergovit® grasses or Allergovit® birch in patients with grass and birch pollen allergy (AL1303AV)*.

ALLERGOPHARMA GmbH & Co. KG, the sponsor of this trial, has it's headquarter at Hermann-Koerner-Strasse 52, 21465 Reinbek, Germany.

This document was developed and approved by ALLERGOPHARMA GmbH & Co. KG on 27 September 2016, and the links to information may not remain active or accurate over time.

Thank you

Thanks again for being part of this trial.

We continuously do research to try to find the best ways to help patients, and you helped us to do that. Please continue to do so.