Request to participate in medical research

Study title: Immunological analysis of lymph node tissue after intralymphatic immunotherapy: A prospective case control study

Dear Madame, dear Sir

We would like to inform you about the above-mentioned study and ask you whether you would like to participate in it. Before a new treatment method can be used by doctors, research must be carried out to find out how this treatment method works.

We call such research a clinical study. In this study we want to find out what effect immunotherapy for hay fever due to grass pollen allergy has on the immune system when administered directly to the lymph nodes. You suffer from grass pollen allergy and are already undergoing treatment for it. Therefore, we are asking you if you would like to participate in this study.

Your participation is voluntary. The following patient information will help you decide. You can ask any questions you have about participating in the study when you talk to the investigator. This is the name given to the doctors who are responsible for a study and who will look after you as part of this study. If you want to participate, please sign the consent form at the end. With your signature you confirm that you have read and understood the patient information. If you do not understand anything, please ask the investigator.

The patient information and consent form consists of four parts:

- Part 1 The most important things in brief
- Part 2 What it's all about in detail: Information about the study
- Part 3 Data protection and insurance coverage
- Part 4 Informed consent

If you read Part 1, you will get an overview of the study. In Part 2 we explain the whole process and background of the study in detail. Part 3 contains information on data protection and insurance coverage. With your signature at the end of the document, part 4, you confirm that you have understood everything and agree to participate.

This study is arranged by the University of Zurich and the University Hospital Zurich. This institution is called the Sponsor. The sponsor is responsible for, manages and finances a study.

Dictionary

FNA = Fine Needle Aspiration; the removal of cells from the lymph node by aspiration with a syringe with a very fine (thin) needle.

ILIT = IntraLymphatic ImmunoTherapy: the injection of therapeutic agent into a lymph node

SCIT = SubCutaneous ImmunoTherapy: the injection of therapeutic agent under the skin.

Rhino-conjunctivitis = Hay fever, allergy concerning the eyes and the nose.

The following person is medically responsible

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Part 1: The most important

1. Why is this study performed?

In case of allergy to grass pollen (hay fever), grass pollen specific immunotherapy (desensitization) is done to desensitize the body against the grass pollen, i.e. to achieve an improvement of the symptoms. There are different methods of administering the medication (grass pollen extract) in grass pollen-specific immunotherapy. Usually it is either injected under the skin (subcutaneous) or administered by means of tablets or a liquid under the tongue (sublingual). Another option, which is still being researched, is to inject the drug directly into a lymph node in the groin (intralymphatic). The grass pollen-specific immunotherapy can be administered either before the pollen season (= pre-seasonal) or throughout the year. Usually, desensitization against pollen lasts 3 - 4 years.

In this study we want to find out which mechanisms of action of the immune response trigger the new intralymphatic immunotherapy (= ILIT) compared to the known subcutaneous immunotherapy (= SCIT).

In chapter 4 you will learn more about the scientific background of the study..

2. What you need to do when you attend?

Participation in this study will last approximately 2 months for you, one month of which is the follow-up observation period. We will invite you for three study visits. All three appointments are study appointments only and are not part of your general treatment. Four short appointments last up to 20 minutes each and one long appointment of about 2 hours, with 1 hour waiting time included. For one third of the patients, the third appointment takes place directly after the second appointment. See the table and figure in Chapter 5 for an overview showing the number of appointments.

Our research project is aimed at grass pollen allergy sufferers who have completed a first SCIT treatment with grass pollen extract before the 2024 pollen season.

If you choose to participate, you will receive an additional grass pollen extract dose 4 weeks after SCIT (5-6 doses total) followed by lymph node tissue sampling.

You will be randomly assigned to one of six experimental groups. You will be told which group you belong to. Depending on the group, you will be injected with the additional grass pollen extract dose either again under your skin or directly into a lymph node in your groin. 2, 6 or 24 hours after the injection of the grass pollen extract, a small amount of lymph node tissue is taken with a fine needle under ultrasound control (a so-called fine needle aspiration of the lymph node). For comparison, a fine needle aspiration of a lymph node in the groin is also performed on the opposite side of the body.

In Chapter 5, you will learn more about the procedure of the study.

3. What benefits and risks are associated with participation?

3.1 Benfits

You may not have a direct benefit from participating in the study. However, it is possible that you will help future patients by participating. The benefit for you may be better desensitization through the additional injection of the grass pollen extract, but for future patients it may be that knowledge can be gained about Intralymphatic Immunotherapy (ILIT) for the treatment of allergies.

3.2 Risks

The study drug Polvac™ Grasses + Rye contains a grass pollen extract as the active ingredient and is already used in Switzerland as grass pollen-specific immunotherapy with subcutaneous injections in grass pollen-allergic patients for desensitization against grass pollen. This is the therapy they are currently receiving or have received, subcutaneous (under the skin) grass pollen-specific immunotherapy. To date, Polvac™ has not been approved for intralymphatic allergen-specific immunotherapy, which is injections directly into the lymph node. The intralymphatic immunotherapy intervention method is new and has not yet been approved as a standard therapy.

You may experience side effects if you are treated with the Intralymphatic Immunotherapy treatment method. We may not yet know all the risks and side effects of the intervention method. So far, the following risks and side effects are known:

- Mild swelling, redness and itching at the injection site in the groin, which will pass over the next day, can be expected in about one-third of participants.
- Moderate allergic symptoms such as urticaria (itchy wheals) and asthmatic symptoms (whistling breathing, coughing, chest tightness, shortness of breath and shortness of breath), can be expected in about 2 out of 100 participants. These complaints can be treated well with the use of anti-allergic medication.
- Severe allergic reactions associated with a drop in blood pressure, urticaria, and/or respiratory distress leading to hospitalization can occur in approximately 2 in 1000 participants.
- One participant in a previous intralymphatic immunotherapy trial was found to have antibodies to the body's own proteins (autoimmune antibodies) after therapy, resulting in hypothyroidism. These antibodies could potentially be related to the intralymphatic treatment.
- Some participants in previous studies have experienced mild fatigue for up to 6 hours after injection.

See Chapter 6 for more information on risks and exposures.

Part 2: This is what it's all about: Information about the study

4. Scientific background of the study

4.1 Background: Why do we conduct this study?

Due to sensitization to grass pollen, many people suffer from allergic rhino-conjunctivitis (= hay fever). Typically, these patients suffer from itching in the nose, eyes or throat and from sneezing, runny nose and swelling of the nasal mucosa.

Allergic hay fever is usually treated with allergen-specific immunotherapy (= desensitization) to desensitize the body to the grass pollen, i.e. to achieve an improvement of the symptoms. There are different methods of administering the medication (grass pollen extract) in allergen-specific immunotherapy. Usually it is either injected under the skin (subcutaneous) or administered by means of tablets or a liquid under the tongue (sublingual). Another option, which is still being researched, is to inject the drug directly into a lymph node in the groin (intralymphatic).

Previous human studies have shown that intralymphatic therapy can provide many benefits to patients. The intralymphatic form requires only 3 injections over 2- 4 months, while the well-known subcutaneous (= under the skin) immunotherapy requires 18 to 24 injections over 3 to 4 years. Furthermore, a smaller amount of the grass pollen extract is used. Thus, the intralymphatic form of administration would be faster, less expensive, more effective, and it reduces the risk of side effects.

In this study, we are investigating how the intralymphatic form of administration of grass pollen extract differs from the known subcutaneous (= under the skin) form of administration in the mechanisms of action of the immune response. This study will help us to better understand the specific immune activations of the intralymphatic (in the lymph nodes) versus the subcutaneous (under the skin) form of administration. Thus, this study may contribute to the introduction of the intralymphatic form of allergy treatment as a new standard treatment.

Only when the efficacy of the intralymphatic form of administration has been scientifically investigated and proven, can it be approved in Switzerland and used against allergic hay fever.

4.2 Structure of the study: How do we proceed?

In our study, participants are randomly assigned to groups. This is important to obtain reliable results of the study. This is called randomization. Each group gets a different treatment. In our study, there are six groups:

Group 1 (ILIT) gets the study drug directly into a lymph node in the groin at one-fifth (20%) of the last dose of your normal immunotherapy. After 2 hours, a fine needle aspiration is done.

Group 2 (ILIT) will get the study drug directly into a lymph node in the groin with one-fifth (20%) of the last dose of your normal immunotherapy. After 6 hrs, a fine needle aspiration will be done.

Group 3 (ILIT) will get the study drug directly into a lymph node in the groin with one-fifth (20%) of the last dose of your normal immunotherapy. After 24 hrs, a fine needle aspiration will be done.

Group 4 (SCIT) will receive the study drug at a dose of 0.5 ml under the skin (identical to the last normal immunotherapy), but in the groin area and not on the upper arm. After 2 hrs, a fine needle aspiration is done.

Group 5 (SCIT) receives the study drug in a dosage of 0.5 ml under the skin (identical to the last normal immunotherapy), but in the groin area and not on the upper arm. After 6 hrs, a fine needle aspiration is done.

Group 6 (SCIT) receives the study drug in a dosage of 0.5 ml under the skin (identical to the last normal immunotherapy), but in the groin area and not on the upper arm. After 24 hours, a fine needle aspiration is made.

The study is a so-called randomized clinical trial. The study is not blinded, which means that everyone involved in the study knows which group the participants have been assigned to. The participants themselves also know which group they are in. The investigators also know to which group individual participants belong. Randomization allows us to objectively assess how the intervention method intralymphatic immunotherapy really works and whether it is safe.

4.3 Regulations on scientific research with human subjects

We conduct this study in accordance with the laws in Switzerland (Human Research Act, data protection laws). We also comply with all internationally recognized guidelines. The responsible ethics committee and Swissmedic have reviewed and approved the study.

Our study is a national study. This means that there are only participants in Switzerland.

A description of this study can also be found on the website of the Federal Office of Public Health at www.kofam.ch under the SNCTP registration number ..... or the BASEC number 2023-00821.

5. Procedure of the study

5.1 What do you need to do if you participate in the study?

Participation in the study is voluntary and lasts approx. 2 months. You must adhere to the schedule (Chapter 5.2) and also to all specifications made by your investigator.
You must inform your investigator:

- if your state of health changes, e.g. if you get worse or if you have new complaints; this also applies if you stop the study prematurely (Chapters 5.3 and 5.4).
- about concurrent treatment and therapy with other physicians and about taking medications, including medications of complementary and alternative medicine.

- You must effectively prevent the occurrence of pregnancy during participation (Chapter 5.5).

5.2 What happens at the appointments?

The following chapter describes the study-related examinations, the injection of the grass pollen extract and the procedure of visits (appointments). Further below you will find a flow chart summarizing all examinations and procedures.

During the course of your participation, you will visit us five times for a study visit. Each appointment will last approximately 20-30 minutes. The study will take place following your subcutaneous immunotherapy before pollen counts. So the examinations and appointments as part of the study will be an extra expense for you. Through these examinations we will see how well the intervention method Intralymphatic Immunotherapy works and if it is safe.

Search for subjects

If you are willing to participate in this project, you will make an appointment by mail or phone for your first study-related visit, the screening appointment. This will take place in the weeks following fully completed short-term pre-pollen therapy with SCIT. You will already receive this study information at this time, which you should read carefully until your first visit.

Screening appointment (appointment 1)

At your first appointment (screening appointment), you will be informed about the project by the investigator. If you agree, the written consent will be signed by you and the investigator. Afterwards, the prerequisites for participation in the project will be examined in detail. A short physical examination (of heart, lungs, skin) will follow.

Relevant information about your allergic disease and its treatment will be taken from your medical records if necessary. We will ask for your consent that the principal investigator, drug regulatory agency inspectors, relevant foreign health authorities, the sponsor and his/her representative have direct access to relevant health information in the patient record to conduct, monitor and control the study.

Intervention appointment (appointment 2)

This visit includes the injection of the grass pollen extract, a blood draw, a pregnancy test, and a measurement of lung function (peak flow measurement). After the intervention appointment, we will give you four short paper questionnaires to take home, which you can use to record any side effects.

Follow-up appointment (appointment 3)

This visit will take place 2 hours or 6 hours or 24 hours (depending on the allocation to the three subgroups of the study) after the injection of the grass pollen extract. The visit includes two fine-needle aspirations, a blood draw, and a measurement of lung function.

Post-treatment visit (appointment 4)

At this visit, a blood sample is taken 7 days after the grass pollen extract injection.

Post-treatment appointment (visit 5)

At this visit, a blood sample is taken 28 days after the grass pollen extract injection.

Schedule examinations

Table: The schedule shows all dates with the respective examinations.

	Visit				
	1	2	3	4	5
Wann	After SCIT*	Day 0	Day 0-1	Day 7	Day 28
Dauer	20 min	2 h (incl. waiting)	20 min	10 min	20 min
Informed consent	X				
Inclusion/Exclusion criteria	X				
History of disease	X				
Clinical investigations	X				
Blood collections		X		X	X
Pregnancy test		X			
Immunotherapy (ILIT/SCIT)		X			
Fine needle aspiration (FNA) (2x)			X		
Lung function tests (before and after immunotherapy)		X			
1 h observations at the allergy unit after immunotherapy		X			
Questions on adverse effects		X			X

* The first visit takes place 0-6 weeks after your treatment visit in the clinic

Lung function test: A short examination of the lungs (peak flow measurement) is performed before and 40 minutes after grass pollen extract administration. For an un-examination, they must exhale strongly into a mouthpiece three times.

Blood collection: A blood draw is scheduled at two visits. A total of three blood draws are planned of an average of 15 milliliters (ml) each, which is a total of about 45 ml (0.045 liter) of blood or about 7 tablespoons spread over a month. To give you a better idea, a person of 70 kg body weight has about 5 liters of blood and a blood donation is about 450 ml (0.45 liters) and can be done 3 (women) to 4 (men) times a year. In the laboratory, the blood is tested for antibodies and other immune reactions directed against grass pollen. Thus, it can be examined how your immune system reacts to the treatment.

Pregnancy test: Before the injection, a pregnancy test is performed for women of childbearing age. A urine sample is needed for this.

Intervention (the injection of grass pollen extract under the skin or into the lymph node): 4 weeks after completing a full short-term cycle of subcutaneous (under the skin) immunotherapy before pollen season, you will receive additional treatment as part of this study. Depending on the group assigned, you will receive immunotherapy with the study drug (Polvac™ grasses and rye) again either under the skin or into a lymph node in the groin at the second appointment of the study.

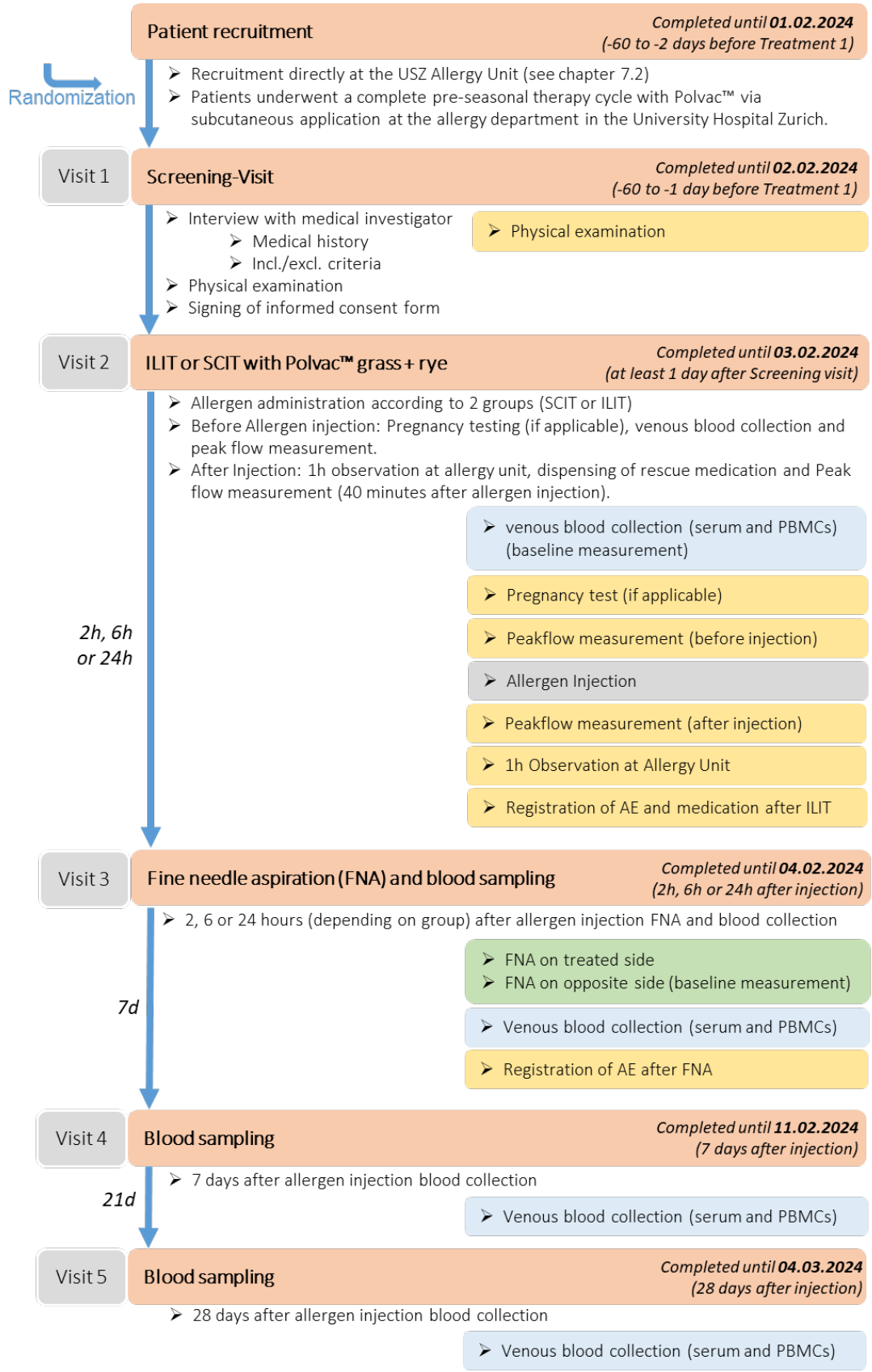
The **injection under the skin** will be in the groin area. You are already familiar with this delivery method from SCIT, only the site of injection is in the groin rather than the upper arm. The treatment is performed under ultrasound control to document the position of the needle.

The **injection into the lymph node** is also done under ultrasound control and in the groin region to find the lymph node exactly. For the treatment, a thin needle is used, which is inserted about 1-2.5 cm deep to the lymph node, where the drug is administered. The treatments are performed only by specially trained personnel and are very safe. The procedure takes about 15 minutes.

After the treatment, whether subcutaneous or intralymphatic, you will need to stay in the allergy ward for one hour for **monitoring**. For the time afterwards, you will be given an allergy emergency kit consisting of 4 tablets for safety. You will receive explanations on how to use them, if necessary.

Fine needle aspiration of lymph node tissue: 2, 6 or 24 hours after the grass pollen extract injection, a fine needle aspiration of the lymph node is performed. For this purpose, a small amount of lymph node tissue is aspirated with a fine needle under ultrasound control on the side where the injection was performed. A second fine-needle aspiration of a lymph node in the groin is performed on the opposite half of the body to serve as a basis for comparison.

Flow chart of study



Flowchart showing the process of the study. The study for you lasts a total of approx. 1-2 months and includes 3 appointments. The study ends no later than the end of March 2024 after the last appointment (appointment 3).

We arrange the appointments together with you. You will receive an exact overview of the appointments. The appointments cannot simply be postponed. We ask you to inform us quickly if you nevertheless have to postpone an appointment for important reasons.

5.3 When does the study end?

For you, participation lasts approx. 2 months and ends after the third appointment. You can also terminate your participation earlier at any time (□ Chapter 5.4). You do not have to explain why you no longer wish to participate. If you yourself would like to end your participation earlier, please talk to your investigator.

Even if you end your participation early, we will continue to treat and care for you medically as well as possible according to current standards (□ Chapter 5.4 for alternative treatment options). In this case, we will perform a final examination for your safety. Please then return all remaining study medications to us.

If you stop the study early, we ask that you continue to inform your investigator if your health changes, for example, if you get worse or if you have new medical conditions. If your participation ends early, we will still evaluate the data and samples collected up to that point (e.g., blood counts, fine needle aspirates) for the study.

We may also have to ask you to end the study early. This is the case, for example, if you have to take medication that could influence our study results (e.g. cortisone preparations, further immunotherapies, vaccination) or you cannot receive any further injections or treatments for other reasons.

5.4 What happens if you do not want to participate?

Even if you do not participate in this study, we will treat and care for you medically in the best possible way according to current standards. The study will take place at a later date independently of your subcutaneous immunotherapy before pollen flight and therefore has no effect on it.

5.5 Pregnancy

The intervention method Intralymphatic Immunotherapy is not approved yet. It may be dangerous and harmful to an unborn child.

Therefore, you must not have children during the month of your participation in the study. This applies only to women who are participating in this study. You will discuss these issues with your investigator.

There is no evidence from studies that immunotherapy solutions can cause malformations in unborn children. Although the possibility of harm to the fetus from specific immunotherapy is unlikely per se, treatment is not recommended during pregnancy. Nonetheless, the reactivity of the immune system during pregnancy is unpredictable and an exuberant allergic reaction requiring treatment is possible at any time during immunotherapy. There is no evidence on whether Polvac Grasses+Rye passes into breast milk.

For women who can become pregnant

You must not become pregnant during your participation in the study. You must inform your partner(s) that you are participating in this study. On appointment 2 before administration of the grass pollen extract, you will take a urine pregnancy test. If you are breastfeeding, you may not participate.

While participating in the study, you must use a simple method of contraception:

- a preparation that suppresses ovulation either as a tablet ("pill" / "mini-pill"), injection, stick under the skin, patch, or vaginal ring; or
- Copper or hormonal IUD.

You do not need to use these birth control methods after the study ends. If you still become pregnant during the study, you must tell your investigator right away. She/he will then talk to you and your partner about what to do next.

6. Risks, burdens and side effects

6.1 What risks and burdens can occur?

There are risks and burdens in participating in this study, as with any medical treatment. Some risks we already know, others are still unknown. This uncertainty is not unusual in the study environment. You will find a list of the most common and serious risks in Chapter 6.2. Many side effects are medically treatable. We will inform you of any new findings on risks and side effects during the study.

With a new intervention method, it is possible that there are risks that we do not yet know. These risks and side effects can be serious or even life-threatening.

The intervention method Intralymphatic Immunotherapy has been received by very few people.

In addition, there are risks with the medical exams we do in this study. You will already be familiar with some of the examinations. You will find a list of these risks of the examinations in Chapter 6.3.

6.2 The most common and serious risks posed by the study drug and route of administration

You can find information about the most common and serious side effects that we already know about.

We use the following descriptions for this:

- Very common: We find the side effect in more than 10 people out of 100 (> 10%).
- Frequently: We find the side effect in 1 to 10 people out of 100 (1%-10%).
- Occasionally: We find the side effect in 1 to 10 people out of 1,000 (0.1%-1%).
- Rarely: We find the side effect in 1 to 10 people out of 10,000 (0.01%-0.1%).
- Very rarely: We find the side effect in less than 1 person out of 10,000 (< 0.01%).

Very common side effects are:

- Mild swelling, redness, and itching at the injection site that pass over the next day are expected in about one-third of participants (mild side effect, grade 1)

Common side effects include:

- Allergic symptoms, such as urticaria and asthmatic symptoms, can be expected in about 2 out of 100 participants. These symptoms can be treated well with anti-allergic medication (moderate side effect, grade 2).

Occasional but dangerous side effects are:

- More severe allergic reactions associated with a drop in blood pressure, urticaria, and/or respiratory distress leading to hospitalization can occur in approximately 2 out of 1000 participants (severe side effect, grade 3).

6.3 Risiken und Belastungen durch Untersuchungen in der Studie

We do several medical examinations for this study (□ chapter 5.2). These examinations are proven procedures. Nevertheless, they can have risks and burdens, that is, they can be unpleasant or have undesirable side effects. In this study, there are the following risks and burdens:

- Blood collection: bruising, bleeding or swelling at the injection site may occur. Rarely, infection may occur at the puncture site.
- Fine needle aspiration: Fine needle aspiration (FNA) exposes you to only minor risks comparable to those of blood sampling. FNA is a minimally invasive medical procedure associated with risk of the following complications in the region of the puncture site: tenderness, local pain, bruising, and/or infection.

7. Funding and compensation

The study is fully paid by the University Hospital Zurich. The study drug is provided free of charge by the manufacturer Bencard AG.

The participating researchers have no direct financial benefit from conducting this study.

If you participate in this study, you will not receive any money or other compensation.

There will be no additional costs to you or to your health insurance company as a result of your participation in the study. We will reimburse you for travel expenses incurred as a result of your participation.

The results of this study may contribute to the later sale of a drug. You will not be involved in this if you participate in this study.

8. Study results

There are results that concern you yourself. These results will be communicated to you by your investigator. There are also incidental findings. Incidental findings are "accompanying results" that are not intended. These can be, for example, results from the blood test or the fine needle puncture. We will inform you if these incidental findings are relevant to your health.

For example, we will inform you if we accidentally discover a disease that you do not yet know about and that we can treat. If you do not want to be informed, please discuss this with your investigator.

There are also overall study results that come from data from all participants. This includes, for example, knowing more about the mechanism of action of immunotherapy (Chapter 4.1). These results do not directly affect you or your health. However, your investigator will be happy to give you a summary of the overall results of the study at the end of the study if you wish

Part 3: Data protection and insurance coverage

9. Protection of data and samples

We protect your data (e.g. information such as blood pressure and pulse from your medical history) and your samples (e.g. your blood samples). There are strict legal regulations in Switzerland for the protection of data and samples.

9.1 Encryption of data and samples

Each study generates data from the examinations (e.g. blood values, lung values, fine needle puncture). These data are documented. This is usually done electronically in large tables, the so-called "data collection sheets". All data are documented in encrypted form. "Encrypted" means that personal information is kept separate from the examination results. For this purpose, there is a list that identifies each person with a unique code. For example, your name, date of birth or place of residence do not appear directly on the data collection form. This list stays at the hospital for a period of 10 years. No one else gets this list.

At the end of the study, your data will be completely anonymized, at the earliest at the end of the legally prescribed retention period. This means that it will no longer be possible to identify you without disproportionate effort. Various measures are used for anonymization, including the destruction of the code and the list.

When we pass on data - to specialists who do further investigations - the data is always encrypted and your personal data is protected. This also applies if the data is passed on abroad.

All samples (e.g. blood samples) are also always encrypted in this way. Your personal data is therefore protected when we send samples to be examined in the laboratory. Because even in the laboratory, the data and samples always remain encrypted.

9.2 Safe handling of data and samples during the study

The sponsor Professor Pål Johansen is responsible for the safe handling of your data and samples from this study. He is responsible for ensuring that applicable laws, e.g. data protection laws, are complied with. This also applies if (encrypted) data or samples for studies are sent to countries where data protection laws are less good. This is how the sponsor of this study protects your data:

In this study, your data are collected and transmitted electronically. The data is stored on a server in Switzerland. Nevertheless, there is always a certain residual risk that strangers access your personal data (e.g. risk of "hacking").

It is often important that your family doctor shares data of your medical history with the investigator. This also applies to other physicians who treat you. By giving your consent at the end of the document, you allow this.

9.3 Safe handling of data and samples after the study

The sponsor remains responsible for the safe handling of your data and samples after the end of the study. The law requires that all study documents, e.g. data collection forms, are kept for at least 10 years. If there are leftovers from the samples after the end of the study, we collect these leftovers and store them encrypted in a safe place for at least 10 years. This way they can be used later for further studies (chapter 9.4). Such a collection of encrypted samples is called a "biobank". There are strict rules for biobanks so that the information from your samples is well protected.

After a study is completed, the results are usually published in scientific journals. For this purpose, the results are reviewed by other experts. Your encrypted data must be forwarded to these experts. However, the data may not be used for new research purposes. Your separate consent would be required for this (see 9.4).

9.4 Further use of your data and samples in other, future studies

Your data and samples from this study are very important for future research. Data and samples that have not already been completely consumed for this study may be reused for other studies. We need your separate consent to reuse your samples. This is voluntary. Please read the additional consent form at the end of the document carefully. Please sign the consent form if you wish to use your data and samples to support further research in the future. Even if you do not consent, you can still participate in the study.

9.5 Inspection rights

The conduct of this study may be subject to review. The review is carried out by authorities such as the responsible ethics committee or the regulatory authority Swissmedic or also by foreign regulatory authorities. The sponsor must also make such checks to ensure the quality of this study and the results.

For this purpose, a small number of specially trained persons are given access to your personal data and medical history. So for this review, the data is not encrypted. The persons who see your unencrypted data are subject to confidentiality.

10. Insurance

You are insured if you suffer harm as a result of the study - i.e. the study drug Polvac Gräser+Roggen or the intervention method intralymphatic immunotherapy. The procedure is regulated by law. The sponsor has taken out insurance for this purpose (*Zurich Versicherungs-Gesellschaft AG* (policy number 14.970.888). If you believe that you have suffered damage as a result of the study, please contact your investigator or the insurance company directly.

In the case of damage caused by an approved drug / medical device used according to medical standards or which would also have occurred during the use of a usual therapy, the same liability regulations apply as for treatment outside of a study. In such a case, the hospital's liability insurance will cover the costs / compensation.

Part 4: Informed consent

This consent consists of two independent consent forms:

- Informed consent for participation in this study "Investigation of innate and adaptive immune responses after intralymphatic allergen immunotherapy (ILIT): a clinical trial".
- Informed consent for the further use of data and samples from this study in encrypted form.

Please read this form carefully. Please ask us if there is anything you do not understand or if there is anything else you would like to know. Your written consent is required for participation.

Declaration of consent to participate in the study

BASEC number	2023 - 00821
Study title	Immunological analysis of lymph node tissue after intralymphatic immunotherapy: A prospective case control study
Lay study title	Immunotherapy in grass pollen-allergic patients - comparison of immune response when injected into a lymph node and injected under the skin
Responsible institution (Sponsor with address	Professor Pål Johansen, PhD, Dept. Dermatology University Hospital Zurich Raemistrasse 100 8091 Zürich, Switzerland Mail: pal.johansen@usz.ch Tel. +41 44 78 609 35 36
Place of study implementation	University Hospital Zurich, Airport, The Circle
Study doctors	Pract. med. Emma Widmer (study doctor) Dr. med. Lara Šošić (study doctor)
Study participant: Name und first name in block letters: Date of birth:	

- I have received oral and written information about the study from the investigator signing below.
- I am participating in the study voluntarily.

- The investigator has explained to me what possible standard treatments are available outside the study.
- I have had sufficient time to make this decision. I will keep the written information and receive a copy of my written informed consent.
- I can stop participating at any time. I do not have to explain why. Even if I stop participating, I will continue to receive my medical treatment. The data and samples collected up to that point will remain on file and will be analyzed as part of the study.
- If it is better for my health, the investigator can exclude me from the study at any time.
- I understand that my data and samples will only be shared or sent abroad in encrypted form. The sponsor will ensure that data protection is maintained according to Swiss standards.
- In case of results and/or incidental findings that directly affect my health, I will be informed. If I do not wish to be informed, I will discuss this with my investigator.
- My primary care physician must know that I am participating in the study. My primary care physician may share data from my medical history that is important for the study with the investigator. This also applies to other physicians who treat me.
- The responsible experts of the sponsor, the ethics committee and the medicines authority Swissmedic may view my unencrypted data for control purposes. All these persons are bound to secrecy.
- I know that the sponsor Professor Pål Johansen has taken out an insurance policy with Zurich, *Versicherungs-Gesellschaft AG*. This insurance pays if I suffer damage - but only if the damage is directly related to the study. The liability insurance of the hospital (University Hospital Zurich) covers possible damages.
- The remaining tissue of my lymph node may be used for research purposes within the framework of this study. I understand that this residual tissue can then no longer be used to do further research on my disease.

Place, date	Name und first name in block letters Signature of study participant

Confirmation by the investigator: I hereby confirm that I have explained the nature, significance and scope of the study to this participant. I assure that I will fulfil all obligations related to this

study according to Swiss law. If, in the course of the study, I learn of aspects that could influence the participant's willingness to take part in the study, I will inform him/her immediately.

Place, date	Name und first name (in block letters) of study doctor Signature of study doctor

Declaration of consent for further use of data and samples in encrypted form

This consent does not concern you in the sense of personal participation in a study. "Further use" means that data and samples may be stored beyond the time of your participation in the study and used in encrypted form for further research. This can mean, for example, that a blood sample and corresponding laboratory values from you are statistically evaluated together with a large number of other values or that new investigations are carried out on them.

BASEC number:	2023-00821
Study title	Immunological analysis of lymph node tissue after intralymphatic immunotherapy: A prospective case control study
Lay study title	Immunotherapy in grass pollen-allergic patients - comparison of immune response when injected into a lymph node and injected under the skin
Study participant: Name und first name in block letters: Date of birth:	

- I give permission for my encrypted data and samples from this study to be reused for medical research. The samples will be stored in a biobank. They will then be available for future, further research projects indefinitely.
- I understand that the samples are encrypted and the key will be stored securely.
- The data can be analyzed at home or abroad and stored in a database here or abroad. The samples can be analyzed here or abroad and stored in a biobank. Research institutions abroad must comply with the same data protection standards as those in Switzerland.
- I decide voluntarily and can withdraw this decision at any time. If I withdraw, all my data will be anonymized. I only inform my investigator and do not have to justify this decision.
- Normally, all data and samples are evaluated together. If by chance a result is found that is very important for my health, I will be contacted. If I do not wish to be contacted, I will inform my investigator accordingly.

Place, date	Name und first name (in block letters) of study participant Signature of study participant

Confirmation by the investigator: I confirm that I have explained to the participant the nature, significance and implications of the further use of samples and/or genetic data.

Place, data	Name und first name (in block letters) of study doctor Signature of study doctor