

**PHASE IIA PROOF-OF-CONCEPT CLINICAL TRIAL FOR THE
INDUCTION TREATMENT OF AUTOIMMUNE HEPATITIS (AIH)
USING INFLIXIMAB (AIH-MAB)**

EUDRACT No.: 2017-003311-19

PATIENT INFORMATION AND INFORMED CONSENT FORM

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ENGLISH TRANSLATION –

FOR MANUSCRIPT SUBMISSION ONLY

Sponsor: University Medical Center Hamburg-Eppendorf

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Introduction

Dear Patient,

We would like to ask whether you are willing to participate in the clinical trial (study) described below.

Clinical trials are essential to gain or expand knowledge about the efficacy and tolerability of medicinal products. Therefore, the German Medicines Act requires that new medicinal products be tested in clinical trials. The clinical trial we present here has, as required by law, been favorably reviewed by the responsible ethics committee and approved by the competent authority. This trial will be conducted at the University Medical Center Hamburg-Eppendorf (UKE), with a total of 12 participants. The study is initiated, organized, and funded by the UKE and the German Research Foundation. Dr. Christina Weiler-Normann will serve as the principal investigator.

Participation in this clinical trial is voluntary. You will only be included if you provide written informed consent. If you choose not to participate or withdraw at a later time, this will not result in any disadvantages and will not affect your future medical care.

You have already been approached about the planned study. This information sheet is meant to explain the objectives and procedure in detail. A study physician will conduct a conversation with you to clarify any questions. Please feel free to ask about anything that remains unclear. You will then be given sufficient time to decide whether to participate. You may also want to discuss the decision with a family member or friend before making your choice.

This patient information document complements the oral explanation by providing detailed information about the investigational product and the clinical trial. It also informs you about the purpose, procedures, and possible risks and benefits of participating. If you decide to take part, you will be asked to sign the consent form at the end. You will receive a copy for your records. You may withdraw your consent at any time, without providing reasons.

Section 1: Why is this study being conducted?

Autoimmune hepatitis is a chronic inflammation of the liver caused by an immune system reaction against the body's own liver tissue. The exact cause remains unknown. Treatment usually involves immunosuppressive medications that weaken the immune response and reduce inflammation. This typically leads to a normalization or significant improvement of liver values, though long-term medication is often required.

Initial treatment usually combines two medications: corticosteroids (or a similar drug) and azathioprine (or a substitute if azathioprine is not tolerated). Corticosteroids quickly suppress liver inflammation (remission induction), while azathioprine is used for long-

term control due to its more favorable side effect profile. However, azathioprine alone is usually insufficient to induce remission.

Due to the rarity of autoimmune hepatitis, few controlled studies exist. This clinical trial aims to evaluate whether infliximab—an alternative immunosuppressive agent—can replace corticosteroids in remission induction. We hope this will lead to better tolerability while maintaining efficacy. Azathioprine will still be required as long-term therapy.

Infliximab is a biologic drug first approved in the U.S. in 1998 and in the EU in 1999 for other immune-mediated conditions such as inflammatory bowel disease, rheumatoid arthritis, and psoriasis. It is not approved for autoimmune hepatitis. It is a monoclonal antibody that targets the messenger TNF-alpha, a key factor in inflammation. Infliximab is administered via intravenous infusion over 1–2 hours, followed by 1–2 hours of monitoring.

Section 2: Will I definitely receive the investigational product?

As part of this clinical trial, the efficacy of infliximab in treating autoimmune hepatitis will be investigated. All patients participating in the study will receive the investigational product.

Section 3: What is the procedure of the study, and what do I need to consider if I participate?

Upon inclusion in the trial, your medical history will be taken, and a comprehensive physical examination will be performed. This includes:

- General physical examination,
- Measurement of blood pressure, pulse, weight, and height,
- Electrocardiogram (ECG),
- Liver stiffness measurement (Fibroscan),
- Blood samples.

The investigator will discuss with you the eligibility criteria, including:

- Diagnosis of autoimmune hepatitis and exclusion of other liver diseases,
- No serious other conditions (e.g., infections, heart, lung, or cancer),
- Body weight between 40 and 90 kg,
- Adequate liver function.

Participation depends on these assessments. You will visit the clinic regularly for infusions—at study start, week 2, week 6, and every 4 weeks afterward. Additional blood tests are also planned at weeks 1 and 6. Each blood draw collects approximately 30 ml (about 2 tablespoons) in total, equaling approximately 420ml in total over one year.

Monitoring includes checking blood pressure and pulse during and after infusions (1–2 hours post-infusion). Infliximab will be administered over 6 months, alongside

azathioprine. Continued participation and adherence to appointments are crucial to monitor effectiveness and safety. A 6-month follow-up phase includes additional blood tests and Fibroscan assessments at 3 and 6 months post-treatment.

After the study, long-term monitoring and treatment (typically with azathioprine) will continue. If infliximab is not effective or sufficient, corticosteroids may be needed. As you know, autoimmune hepatitis is a condition that usually requires long-term medication. Even after the study ends, continued care and regular monitoring of blood values will be necessary. Most patients will need to continue taking azathioprine beyond the end of the study. In some cases, azathioprine alone may not be sufficient. It may then be necessary after the study to prescribe an additional corticosteroid medication. If infliximab proves insufficiently effective, a corticosteroid will also be required.

Azathioprine is the standard long-term treatment for autoimmune hepatitis and is approved for maintaining remission. It is not an investigational drug in this context, but part of the standard therapy for this condition. There is over 50 years of clinical experience with azathioprine.

The effect of azathioprine becomes apparent only after a delay of several weeks to a few months. In about 15% of patients, side effects are to be expected. The type, frequency, and severity of adverse reactions may depend on the dose and duration of treatment with azathioprine, the underlying disease, and concurrent medications.

Known side effects include changes in blood counts, especially a reduction in white or red blood cells, and less commonly, platelets. Some patients experience intolerance to azathioprine, usually expressed as skin rash, nausea, vomiting, and diarrhoea, and more rarely as fever or joint pain. In some patients, azathioprine can cause elevated liver enzymes. Rarely, it may lead to pancreatitis, which can sometimes be severe.

Taking azathioprine increases the risk of skin cancer; therefore, consistent UV protection is essential. Regular dermatologic screenings are recommended. There is also a slightly increased risk of lymphoma. Since azathioprine suppresses the immune system, the risk of infections like pneumonia or shingles is also increased.

You will start taking azathioprine from the second week of therapy, in a dosage adjusted to your body weight (usually 1–1.5 mg/kg). It is important that you inform your doctor immediately if you experience any discomfort.

The following table lists the known possible side effects of azathioprine. The frequencies of these side effects are categorized as follows:

- **Very common** ($\geq 1/10$)
- **Common** ($\geq 1/100$ to $< 1/10$)
- **Occasional** ($\geq 1/1,000$ to $< 1/100$)

- **Rare** ($\geq 1/10,000$ to $< 1/1,000$)
 - **Very rare** ($< 1/10,000$)
-

Side Effects of Azathioprine

Infections and parasitic diseases

- **Very common:** Infections (in kidney transplant patients)
- **Common:** Increased susceptibility to infections in patients with inflammatory bowel disease
- **Occasional:** In $< 1\%$ of patients with rheumatoid arthritis (RA)

Benign, malignant, and unspecified tumours (incl. cysts and polyps)

- **Common:** Non-Hodgkin lymphoma, vulvar carcinoma
- **Rare:** Rare form of non-Hodgkin lymphoma in Crohn's disease patients
- **Very rare:** Sarcomas (e.g. Kaposi's sarcoma), in-situ cervical carcinoma

Blood and lymphatic system disorders

- **Very common:** Leukopenia ($> 50\%$ of RH patients, 28% of RA patients, 15% of Crohn's disease patients)
- **Common:** Thrombocytopenia, anaemia; significant leukopenia in 5.3% of RA patients
- **Rare:** Granulocytopenia, pancytopenia, aplastic anaemia, megaloblastic anaemia, erythrocyte hypoplasia

Immune system disorders

- **Occasional:** Hypersensitivity reactions including malaise, hypotension, dizziness, leucocytosis, rash, severe nausea and vomiting, diarrhoea, fever, chills, rash, myalgia, arthralgia, vasculitis, kidney dysfunction, elevated liver enzymes
- **Very rare:** Fatal hypersensitivity reactions

Respiratory, thoracic and mediastinal disorders

- **Rare:** Reversible interstitial pneumonia

Gastrointestinal disorders

- **Very common:** Nausea and loss of appetite with occasional vomiting (in 12% of RA patients)
- **Common:** Pancreatitis (0.2–8%), especially in organ transplant and Crohn's disease patients
- **Occasional:** Steatorrhea, diarrhoea, gastroduodenal ulcers, intestinal bleeding, necrosis or perforation, colitis, diverticulitis
- **Rare:** These complications typically occur only after transplantation

Hepatobiliary disorders

- **Common:** Hepatotoxicity (<1% of RA patients)
- **Occasional:** Liver function disturbances
- **Rare:** Life-threatening veno-occlusive liver disease

Skin and subcutaneous tissue disorders

- **Occasional:** Alopecia (hair loss)
- **Very rare:** Stevens-Johnson syndrome, toxic epidermal necrolysis

Additionally, during some of the study visits, you will be asked to complete questionnaires. These questionnaires assess your quality of life as well as other physical and psychological symptoms. Furthermore, a small amount of blood (approximately 7–15 ml) will be collected during the blood draws for scientific analyses. These analyses aim to investigate the effect of infliximab on immune cells. The blood samples taken from you will not be used for genetic testing, DNA analysis, or any purpose other than those described in this patient information without first informing you and obtaining your explicit consent. You have the right to decline any additional testing in accordance with applicable laws and regulations. Using the modern FibroScan procedure, which allows us to examine liver tissue externally, we can assess the success of the therapy and detect the progression of fibrotic changes during the course of liver disease. The FibroScan of the liver, also called elastography, is a painless method that measures liver stiffness, which reflects the extent of fibrotic remodeling. Chronic liver disease—regardless of its cause—can lead to fibrotic remodeling, in which normal liver tissue is replaced by scar and connective tissue. During the examination, you will lie on your back with your right arm placed behind your head. The probe is applied with light pressure. Using this ultrasound-based probe, the liver is observed and measured. The resulting measurements provide us with the desired information on liver stiffness. The ECG (electrocardiogram) is a diagnostic method used to measure and monitor your heart's electrical activity and rhythm. The heartbeat is triggered by an electrical impulse that is generated in the heart and then spreads throughout it. This weak electrical current is

recorded by the ECG through electrodes. To do this, the physician will apply a conductive gel to the electrodes and attach them to your skin. The electrodes are connected by wires to the ECG device, which records your heart's activity. The procedure takes about two minutes. The various phases of the cardiac cycle are displayed as characteristic waveforms on a strip of paper aligned with a timeline. Each peak corresponds to a specific phase of the heartbeat.

A schematic overview of the scheduled visits and the procedures performed can be found below:

Phase	Visit	Assessments/Procedures	
Screening Phase (max. 2 weeks)	Screening 1	Blood sample, ECG, weight, blood pressure, pulse	
	Screening 2	Fibroscan, questionnaire, blood sample	
Treatment Period (24 weeks total)	Study Start	Infusion, blood sample, weight, blood pressure, pulse	
	Week 1	Blood sample	
	Week 2	Infusion, blood sample, questionnaire, weight, start azathioprine	
	Week 4	Blood sample, questionnaire, weight	
	Week 6	Infusion, blood sample, weight, blood pressure, pulse	
	Week 8	Infusion, blood sample, questionnaire, weight	
	Week 12	Infusion, blood sample, questionnaire, weight	
	Week 16	Infusion, blood sample, questionnaire, weight	
	Week 20	Infusion, blood sample, questionnaire, weight	
	Week 24	Infusion, blood sample, questionnaire, weight, Fibroscan	
	Follow-up Period (6 months)	Week 36	Blood sample, questionnaire, weight, Fibroscan

Phase	Visit	Assessments/Procedures
	Week 48	Blood sample, questionnaire, weight, Fibroscan

Additional medications (including over-the-counter drugs) that your study doctor is not yet aware of may only be taken—except in emergencies—after consulting your study doctor. If you are being treated by other physicians, you must inform them that you are participating in this clinical trial. Likewise, your study doctor must be informed about any medical treatment you receive from another doctor during the course of the clinical trial. You will be given a study identification card, which you should carry with you at all times, especially in case of emergency.

Section 4: What personal benefits can I expect from participating?

If you participate, it may be possible to achieve remission in autoimmune hepatitis without corticosteroids. Corticosteroids can have significant side effects affecting metabolism and mental health. Infliximab may reduce the need for steroids, but since its effectiveness in autoimmune hepatitis is unproven, personal benefit cannot be guaranteed. The findings may, however, benefit future patients.

Section 5: What are the risks of participating in the study?

Risks and Side Effects Associated with Infliximab Treatment

Treatment with infliximab may lead to adverse effects or symptoms. Since infliximab has been regularly used for over 15 years, many of its side effects are well known and well documented. Most of the side effects listed in the package insert are rare, usually mild to moderate in severity, and generally manageable.

Infliximab is a protein that can cause allergic reactions—even after repeated use. Depending on the severity, such a reaction may require immediate treatment. In some cases, allergic reactions may be delayed, which is why monitoring during and after the infusion is necessary. Symptoms may include circulatory problems, skin reactions, itching, shortness of breath, visual disturbances, cardiac issues, or swelling.

The signalling molecule TNF-alpha, which is neutralized by infliximab, also plays a role in immune defence. Therefore, treatment with infliximab may lead to severe infections such as pneumonia, shingles, herpes, and others.

Since you will also be receiving azathioprine, which also suppresses the immune system, it is especially important that you inform your doctor immediately of any signs of illness (especially cough, fever, malaise, slow-healing wounds, dental issues, or burning sensation while urinating)—even if you're unsure.

There may also be an increased risk of lymphoma and non-melanoma skin cancer. This risk is also increased by azathioprine. Therefore, regular skin check-ups are important over the long term.

Rarely, other autoimmune diseases may newly appear during infliximab therapy, such as multiple sclerosis, autoimmune skin conditions, intestinal diseases, and others. Rare symptoms resembling lupus erythematosus (inflammation of the skin and joints) may occur, but typically resolve after stopping treatment.

Side Effects – Tabular Overview

The following table categorizes side effects by frequency:

- **Very common:** $\geq 1/10$
- **Common:** $\geq 1/100$ to $< 1/10$
- **Occasional:** $\geq 1/1,000$ to $< 1/100$
- **Rare:** $\geq 1/10,000$ to $< 1/1,000$
- **Very rare:** $< 1/10,000$
- **Unknown:** Frequency cannot be estimated due to insufficient data

Infections and Parasitic Diseases

- **Common:** Viral infections (e.g., influenza, herpes), bacterial infections (e.g., sepsis, cellulitis, abscesses)
- **Occasional:** Tuberculosis, fungal infections (e.g., candidiasis)
- **Rare:** Meningitis, opportunistic infections

Tumours (Benign, Malignant, and Unspecified)

- **Rare:** Lymphoma, Non-Hodgkin lymphoma, Hodgkin's disease, leukaemia, melanoma, cervical cancer
- **Unknown:** Hepatosplenic T-cell lymphoma, Merkel cell carcinoma

Blood and Lymphatic Disorders

- **Common:** Neutropenia, leukopenia, anaemia, lymph node swelling
- **Occasional:** Thrombocytopenia, lymphopenia, lymphocytosis
- **Rare:** Agranulocytosis, thrombotic thrombocytopenic purpura, pancytopenia, haemolytic anaemia, idiopathic thrombocytopenic purpura

Immune System Disorders

- **Occasional:** Allergic respiratory reactions, anaphylaxis, lupus-like syndrome, serum sickness
- **Rare:** Anaphylactic shock, vasculitis, sarcoid-like reactions

Psychiatric Disorders

- **Common:** Depression, insomnia
- **Occasional:** Amnesia, agitation, confusion, drowsiness, nervousness
- **Rare:** Apathy

Nervous System Disorders

- **Very common:** Headache
- **Common:** Dizziness, numbness, tingling
- **Occasional:** Seizures, neuropathy
- **Rare:** Transverse myelitis, central and peripheral demyelinating disorders

Eye Disorders

- **Common:** Conjunctivitis
- **Occasional:** Keratitis, swelling around the eyes, stye
- **Rare:** Endophthalmitis
- **Unknown:** Temporary vision loss during or shortly after infusion

Heart Disorders

- **Common:** Tachycardia, palpitations
- **Occasional:** Cyanosis, pericardial effusion
- **Rare:** Myocardial ischemia/heart attack

Vascular Disorders

- **Common:** New or worsening heart failure, arrhythmia, syncope, bradycardia
- **Occasional:** Low/high blood pressure, bruising, hot flashes, flushing
- **Rare:** Peripheral ischemia, thrombophlebitis, hematoma, circulatory collapse, petechiae, vascular spasms

Respiratory Disorders

- **Very common:** Upper respiratory tract infections, sinusitis
- **Common:** Lower respiratory infections (e.g., bronchitis, pneumonia), shortness of breath, nosebleeds
- **Occasional:** Pulmonary oedema, bronchospasm, pleurisy, pleural effusion
- **Rare:** Interstitial lung disease

Gastrointestinal Disorders

- **Very common:** Abdominal pain, nausea
- **Common:** Gastrointestinal bleeding, diarrhoea, dyspepsia, acid reflux, constipation
- **Occasional:** Intestinal perforation, stenosis, diverticulitis, pancreatitis, cheilitis

Liver and Biliary Disorders

- **Common:** Liver dysfunction, elevated transaminases
- **Occasional:** Hepatitis, liver cell damage, cholecystitis
- **Rare:** Autoimmune hepatitis, jaundice
- **Unknown:** Liver failure

Skin and Subcutaneous Tissue Disorders

- **Common:** New or worsening psoriasis, hives, rash, itching, excessive sweating, dry skin, fungal infections, eczema, hair loss
- **Occasional:** Blisters, nail fungus, seborrhoea, rosacea, skin papilloma, thickened skin, pigmentation disorders
- **Rare:** Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, boils
- **Unknown:** Worsening symptoms of dermatomyositis

Musculoskeletal and Connective Tissue Disorders

- **Common:** Joint pain, muscle pain, back pain

Kidney and Urinary Disorders

- **Common:** Urinary tract infection

- **Occasional:** Kidney infection (pyelonephritis)

Reproductive System and Breast Disorders

- **Occasional:** Vaginitis

General Disorders and Administration Site Conditions

- **Very common:** Infusion-related reactions, pain
- **Common:** Chest pain, fatigue, fever, injection site reaction, chills, swelling
- **Occasional:** Delayed wound healing
- **Rare:** Granulomatous lesions

Investigations

- **Occasional:** Detection of autoantibodies
 - **Rare:** Complement system disorders
-

Other Risks from Study Procedures

Procedures such as infusions and blood draws may cause bruising, pain, and—rarely—nerve injury (numbness or paralysis). Liver elastography (FibroScan) may be noticeable during the procedure but is not known to cause harm.

Blood sampling for check-ups may temporarily reduce blood volume, but this is quickly replenished by the body. No harmful effects from blood loss are expected. Needle insertion for blood draws may cause bruising, local irritation, or—very rarely—infection, nerve injury, vein inflammation, or thrombosis.

Please report any symptoms, illnesses, or injuries that occur during the clinical trial to the study staff—regardless of whether they are already described here or not. If they are serious, please inform the study site immediately, possibly by phone.

Section 6: What other treatment options are available outside the study?

Alternative treatment options include standard therapy with prednisone or budesonide in combination with azathioprine. Prednisone is typically started at a dose of 1 mg/kg body weight and then tapered weekly. After two weeks, azathioprine is introduced. Alternatively, budesonide can be used, starting at 3x3 mg per day.

The advantage of corticosteroid-based treatment is that it is taken orally, without the need for infusions. However, regular blood monitoring (at least every 2 weeks) is necessary to assess effectiveness and side effects. Corticosteroids suppress the

immune system and may increase susceptibility to infections and impact metabolism (e.g., blood sugar elevation, increased appetite, water retention). Rare psychological effects like depression or mania may occur. This standard therapy achieves normalization of liver values and immunoglobulin G levels in 40–75% of cases within 6 months. Currently, no other officially approved treatment options exist in Germany, although other substances have shown effectiveness in case reports.

Section 7: Who is not allowed to participate in this clinical trial?

You may not participate if

- You are involved in another clinical trial or have participated in one in the past 6 months
- You are pregnant or planning pregnancy within the next 12 months.
- You are breastfeeding.

At the beginning of the clinical trial, all women must therefore undergo a pregnancy test. Exempt from this requirement are women who have reached menopause or have undergone surgical sterilization.

However, a pregnancy test can only reliably detect a pregnancy a few days after conception. Therefore, if you choose to participate in this clinical trial, you must use reliable contraceptive measures. These include the use of two effective methods of contraception, such as:

- Condom or diaphragm plus spermicide,
- Hormonal contraception (e.g., the pill, contraceptive patch, 3-month injection, or Implanon),
- Intrauterine device (IUD),
- Surgical sterilization of the male partner (performed more than 6 months prior).

The reason for these requirements is that the use of infliximab during pregnancy may cause a (temporary) suppression of the unborn child's immune system. If you become pregnant or suspect you may be pregnant during the course of the clinical trial, you must inform the study doctor immediately. Breastfeeding women are also not permitted to participate in this clinical trial, as infliximab can pass into breast milk and may harm the child.

Section 8: Will I incur any costs or receive compensation?

There are no additional costs for participating in the study. All study-related procedures, visits, and the investigational drug are provided free of charge. Compensation for your time or travel expenses is not mentioned in this section.

Section 9: Am I insured during the clinical trial?

All participants in a clinical trial involving a medicinal product are insured in accordance with the German Medicines Act (Arzneimittelgesetz). If you become ill or suffer an injury during the course of this trial, and the illness or injury is directly related to your participation, you will receive medical treatment and monitoring free of charge. In the event that participation in the clinical trial results in harm to your health, insurance coverage is provided under the terms of the clinical trial insurance policy. The scope of this coverage is detailed in the insurance documents provided to you. This insurance has been arranged as a legal requirement, and not because we expect such harm to occur.

To ensure that your insurance coverage remains valid, the following rules must be observed:

- Follow exactly the instructions given by the staff at the study site.
- Do not undergo any other medical treatment during the clinical trial without consulting one of the study doctors. This does not apply in emergencies, but in such cases, you must inform the study physician as soon as possible.
- Report any suspected health damage resulting from the clinical trial immediately to the insurer (see contact details below). You may do this directly or with the help of your study doctor.

Please note that under the terms of the policy, health damage caused by wilful violation of explicit instructions from study staff is explicitly excluded from insurance coverage. If you intentionally or with gross negligence violate any obligations required under the insurance contract, this may result in the loss of insurance coverage. A copy of the insurance policy is available for review from the investigator. If you suspect that participation in the clinical trial has harmed your health or worsened a pre-existing condition, you must report this immediately and directly to the insurer listed below—possibly with the support of your study doctor—to avoid jeopardizing your insurance coverage. If your study doctor assists you in submitting the report, you will receive a copy of the notification. If you contact the insurer directly, please also inform your study doctor. You are required to cooperate in clarifying the cause and extent of any damage, and to take all reasonable measures to prevent or minimize further harm. In the event that your health is impaired due to the investigational product, the insurance policy provides coverage for damages of up to €5,000,000 per study and €500,000 per insured individual, subject to the terms and conditions of the policy.

Insurance Provider and Accident Coverage

Clinical Trial Insurance

Provider: HDI Global SE

Administered by: Ecclesia Mildenerger Hospital GmbH

Address: Klingenbergstr. 4, 32758 Detmold, Germany

Phone: +49 5231 603-6426

Fax: +49 5231 603-606426
Policy Number: 1969059103073

You will receive a copy of the insurance certificate, including the full insurance terms and conditions.

We particularly draw your attention to § 3 – Exclusions from coverage, § 6 – Scope of benefits, § 14 II – Your obligations as the insured person.

Accident Insurance (Coverage for Travel to/from the Study Site)

Provider: **SV Sparkassen Versicherung**
Address: P.O. Box 3120, 65021 Wiesbaden, Germany
Phone: +49 (0)611 178 100
Fax: +49 (0)611 178 109
Policy Number: 50070642022

You will also receive a certificate of accident insurance coverage and the respective terms and conditions for your records. Please note: This insurance coverage applies to direct travel to and from the study site, as well as during your stay at the study centre. However, coverage does not apply if the normal duration of travel is extended or the route is interrupted for purely private reasons.

Section 10: Will I be informed of new findings during the trial?

Yes. Any new information relevant to your continued participation will be shared with you. Based on this, you can decide whether to continue participation or withdraw your consent.

Section 11: Who decides if I leave the trial?

Your participation is voluntary. You may withdraw at any time without consequences for your medical care. The investigator or sponsor may also end your participation for medical reasons or if the entire study is discontinued. If you withdraw or are withdrawn, a final safety examination is recommended. If new information becomes available, you will be asked to sign an updated consent form, or your participation may be ended for safety.

Under certain circumstances, your study doctor or the sponsor may decide to end your participation in the clinical trial prematurely, without your influence on the decision. Reasons for this may include, for example:

- Your continued participation in the clinical trial is no longer medically justifiable
- The entire clinical trial is discontinued.

If you choose to withdraw from the clinical trial before its scheduled end, or if your participation is terminated early for one of the reasons mentioned above, it is important for your own safety that you undergo a recommended final follow-up examination. Sometimes, new information becomes available during a research project about the

treatment or medicinal product being investigated. If this happens, your study doctor will inform you and discuss with you whether you still wish to continue participating in the clinical trial. If you decide to withdraw, your study doctor will make arrangements for your continued medical care. If you decide to continue participating, you will be asked to sign an updated consent form. It is also possible that your study doctor may determine—based on new information—that continued participation in the clinical trial is not in your best interest. In such a case, they will explain the reasons to you and ensure appropriate continuation of your medical treatment.

Section 12: What happens with my data?

During the clinical trial, medical findings and personal information about you will be collected and recorded at the study site, either in your personal medical file or in electronic form. The data relevant to the clinical trial will also be stored, analysed, and potentially shared in pseudonymized form. Pseudonymized means that no names or initials are used—instead, a numeric and/or letter code is assigned, possibly along with your year of birth. These data are protected against unauthorized access. Decoding (i.e., re-identification) may only take place under the conditions prescribed by law. The German Medicines Act sets out specific legal requirements regarding the necessary scope of consent for data collection and usage. For full details—particularly regarding your right to withdraw consent—please refer to the informed consent form, which follows this patient information document.

Section 13: What happens to my blood samples?

After completion of the clinical trial, the collected blood samples will be used as follows: Any remaining blood samples will be stored in pseudonymized form and subjected to immunological analyses within one year after the end of the study. These analyses will address scientific questions aimed at understanding the mechanisms of infliximab treatment. If you decide to withdraw your consent to participate in the clinical trial, any blood samples collected up to that point will still be analyzed as part of the study. Further use of your blood samples for other scientific purposes outside the scope of this study is not planned.

Section 15: Who can I contact with further questions?

You can always contact the study doctor mentioned on page 1 or another investigator for further consultation. You may also contact the federal authority responsible for clinical trials:

Paul-Ehrlich-Institut

Clinical Trials Department Paul-Ehrlich-Str. 51-59, 63225 Langen, Germany

Phone: +49 6103 77-1810; Fax: +49 6103 77-1277; Email: klinpruefung@pei.de

INFORMED CONSENT FORM

Phase IIA Proof-of-Principle Study on the Efficacy of Infliximab in the Induction Therapy of Autoimmune Hepatitis (AIH-MAB)

Patient's Name (in block letters):

Date of Birth:

Subject ID:

I have been thoroughly and clearly informed by the study physician

Name of the physician:

Investigator ID:

in a personal consultation about the investigational drug and the additional required therapy, as well as about the nature, purpose, risks, and scope of the clinical trial.

I have also read and understood the patient information text as well as the data Protection statement printed below. I had the opportunity to speak with the study physician about the course of the clinical trial. All my questions were answered satisfactorily.

Optional documentation of further questions or discussion points raised by the patient:

.....

I had sufficient time to make my decision. I understand that participating in this clinical trial may not provide me with any direct medical benefit, and that I may withdraw my consent to participate in the trial at any time (verbally or in writing), without giving reasons and without affecting the medical care I receive. I am aware that it is extremely important to strictly follow all instructions given to me by the study staff. I confirm that the information I have provided about my medical history is complete and correct. I further confirm that I am not currently undergoing medical treatment, that I have not participated in any other clinical trial in the past six months, and that I will not participate in any other clinical trial until the end of this study. Should it become medically necessary for me to take any medication during the study, I will inform the treating physician that I am currently enrolled in a clinical drug trial, and—if at all possible—notify a responsible study physician before starting the medication or as soon as possible thereafter. I am aware that I will be immediately excluded from the trial if it is discovered during clinical assessments that I provided false information or withheld important facts regarding the points mentioned above or my medical history.

I understand that national and state data protection regulations are fully observed. I have been informed about the use of my personal data and have read and understood the following data protection statement. In case the results of the trial are published, the

confidentiality of my personal data will be preserved. I have been informed about the existence of subject insurance and the conditions under which this insurance coverage applies. I have received a copy of the insurance terms and conditions. This informed consent may be withdrawn by me at any time. I have read and understood the subject information sheet

Version

dated

and I accept the conditions of the study. All my questions have been answered to my satisfaction.

DATA PROTECTION

I understand that this clinical trial involves the collection, storage, and analysis of personal data, particularly medical findings about me. Data processing will be conducted in accordance with legal regulations and requires the following voluntary consent prior to participation in the trial. Without this consent, I cannot participate in the study.

1. I agree that personal data, particularly concerning my health and ethnic background, may be collected during this clinical trial and recorded at the University Medical Centre Hamburg-Eppendorf both in paper form and electronically.
2. Where necessary, this data may be pseudonymized (coded) and shared:
 - a) with a third party commissioned by the University Medical Centre Hamburg-Eppendorf for scientific analysis,
 - b) in case of adverse events: with the responsible ethics committee and the competent federal authority (Paul-Ehrlich-Institute in Langen), and from there to the European database.
3. I also consent to authorized and confidentiality-bound representatives of the sponsor, as well as competent regulatory authorities, being granted access to my personal data (especially medical data) kept by the study physician, as far as necessary to verify the proper conduct of the study. I release the study physician from medical confidentiality for this purpose.
4. I have been informed that I may withdraw from the clinical trial at any time. However, the consent to collect and process my personal data—especially data concerning my health—is irrevocable.
5. I understand that if I withdraw from the trial, the data collected up to that point may still be used to:

- a) assess the effects of the investigational drug,
 - b) ensure that my legitimate interests are not compromised,
 - c) fulfil legal obligations to submit complete documentation for regulatory approval.
6. I agree that my data will be retained for at least ten years after the study ends or is terminated, as required by clinical trial regulations. After this period, the data will be deleted, unless other legal retention requirements apply.
7. I am aware of the following legal requirement: If I withdraw my consent to participate in the study, all parties that have stored my personal data—especially health data—must immediately review whether continued storage of the data is still necessary for the purposes listed in 5 (a) to (c). Data no longer required must be deleted without delay.
8. I consent to the collection of health data from other treating physicians / from the following physicians: **Name(s):** insofar as this is necessary for the proper conduct and monitoring of the study. I release these physicians from their duty of confidentiality (Please strike this sentence if not desired).
9. I consent to my general practitioner **Name:** being informed about my participation in the clinical trial (Please strike this sentence if not desired).

I hereby voluntarily consent to participate in the above-mentioned clinical trial.
 I have received a copy of the patient information and informed consent form, as well as the insurance terms. One copy remains at the study centre.

Patient's Name (in block letters):

Date:

Patient's Signature: