# Randomized, double-blind, placebo-controlled study to characterize the immune response after repeated KLH immunizations in healthy volunteers

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Primary To characterize systemic and local KLH-specific B and T cell responses by repeated KLH immunizationsSecondaryTo characterize the molecular basis of the KLH-driven skin response (acute versus delayed response, Th1 versus Th2 response)To...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Immune disorders NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON50194

**Source**
ToetsingOnline

**Brief title**
Repeated KLH immunization in healthy volunteers

### Condition

- Immune disorders NEC

**Synonym**
Immune System disorders /Immune Diseases

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Centre for Human Drug Research

**Source(s) of monetary or material Support:** Clinical Research Organization (investigator initiated)

## Intervention

**Keyword:** Healthy volunteers, Intradermal, KHL immunization

## Outcome measures

### Primary outcome

* KLH-specific B cell responses

* KLH-specific T cell responses

* KLH-driven skin response after intradermal KLH challenge

### Secondary outcome

* KLH-specific immune response (T and B cells)

* KLH-driven skin response after intradermal KLH challenge (LSCI / Multispectral)

* Treatment-emergent (serious) adverse events ((S)AEs)

* Concomitant medication

* Toxicity Grading Scale

# Study description

### Background summary

In previous studies (CHDR1825, CHDR1829 and CHDR1701, CHDR1647), healthy volunteers were immunized once with intramuscular KLH after which they were challenged with KLH intradermally. Although this model has been proven to be valuable so far, there is room for further refinement and more thorough mechanistic profiling. The current study will evaluate the effect of repeated immunizations. Compared to a single immunization, this regimen is expected to enhance the humoral and cellular response to KLH, thereby potentially enhancing the local skin response upon intradermal rechallenge. This approach should enlarge the DTH response window, and overall reduce the variability of the

response. In addition, the current study will evaluate the skin response to injected KLH over a time course of 48 hours, rather than a single assessment at 48 hours, and include in-depth molecular and cellular evaluations of blister exudate and skin biopsies. This approach will increase our understanding of the physiological mechanisms involved in the KLH response, and as such guide the application of the model for future clinical pharmacology trials.

## Study objective

Primary
To characterize systemic and local KLH-specific B and T cell responses by repeated KLH immunizations

Secondary
To characterize the molecular basis of the KLH-driven skin response (acute versus delayed response, Th1 versus Th2 response)
To explore the correlation between antibody, T cell, and skin responses

## Study design

This is a randomized, double-blind, placebo-controlled study investigating the effects of repeated immunizations with 100 µg KLH, adsorbed to 900 µg aluminium hydroxide, and multiple doses of intradermal KLH administrations administered to healthy volunteers.

## Intervention

Immucothel® (Biosyn), the 400 kDa subunit of keyhole limpet hemocyanin (KLH). Placebo will consist of 0.9% NaCl.

## Study burden and risks

Immunization with KLH is not expected to yield any benefit for the participating subjects. In terms of risks, all drugs that are used in the present study are widely used in the Netherlands, and, apart from temporary side effects associated with the administration of the drugs, it is unlikely to expect that the subjects will be at risk of unforeseen events. This is also illustrated by the studies listed in Table 2 of the protocol. Furthermore, all study drug administrations will be done in the clinic under medical supervision, and the subjects remain in the clinic for at least 30 minutes to closely monitor any adverse signs. Therefore, the risks associated with study participation are considered minimal.

KLH is a registered drug in the Netherlands. After the injections you may experience redness, a small swelling in the area and itching symptoms before the injections into the skin. A slight increase in temperature has also been

reported at <1/100 administrations. It is not expected that the investigational drug will increase the risk of infection with the coronavirus or the symptoms after infection.

Biopsies: Possible adverse effects include persistent bleeding or infection. A small scar may remain at the site of the skin biopsy. People with a dark skin type are more at risk of developing a scar and are therefore not allowed to participate. Blisters: The entire procedure is safe and generally not perceived as disruptive. Possible complications include infection. The blister has healed within about a week, after which a visible skin discoloration can remain for a few months to longer than a year. People with a dark skin type are more at risk of this.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)

## Inclusion criteria

1. Signed informed consent prior to any study-mandated procedure;
2. Healthy male subjects, 18 to 45 years of age (inclusive). Health status is defined by absence or evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead ECG, haematology, blood chemistry, blood serology and urinalysis. In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects;
3. Body mass index (BMI) between 18 and 30 kg/m2, inclusive, and with a minimum bodyweight of 50 kg;*
4. Fitzpatrick skin type I-III.
5. Has the ability to communicate well with the Investigator in the Dutch language and willing and able to comply with the study restrictions.

## Exclusion criteria

1. Evidence of any active or chronic disease or condition that could interfere with, or for which the treatment of might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and 12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance;
2. Clinically significant abnormalities, as judged by the Investigator, in laboratory test results (including haematology panel, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects;
3. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening;
4. Any disease associated with immune system impairment, including immune mediated diseases, transplantation patients and any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug or multiple drug allergies (non-active hay fever is acceptable);
5. Use of any medications (prescription or over-the-counter [OTC]), within 21 days prior to initial KLH immunization, or less than 5 half-lives (whichever is longer). An exception is made for paracetamol (up to 4 g/day). Other exceptions will only be made if the rationale is clearly documented by the Investigator;
6. Use of immunosuppressive or immunomodulatory medication within 30 days prior to initial KLH immunization or planned to use during the course of the study;
7. Any vaccination within 30 days prior to initial KLH immunization or planned

during the course of the study with exception of vaccination for SARS-CoV-2;
8. Vaccination for SARS-CoV-2 within 14 days prior to initial KLH immunization, or planned during the course of the study;
9. Use of antibiotic therapy within 90 days prior to initial KLH immunization or planned to use during the course of the study;
10. Alcohol will not be allowed from at least 24 hours before screening and each scheduled visit. At other times during the course of the study no more than 2 units of alcohol per day will be allowed;
11. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 14 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent;
12. Positive test for drugs of abuse or alcohol breath test at screening;
13. Smoker of more than 5 cigarettes per day prior to screening or who use tobacco products equivalent to more than 5 cigarettes per day and unable to abstain from smoking whilst in the unit.
14. Previous known exposure to Immucothel® or KLH;
15. History of Schistosomiasis (infection with Schistosoma parasite);
16. Participation in an investigational drug or device study (last dosing of previous study was within 90 days prior to initial KLH immunization of this study and participation more than 4 times a year);
17. Loss or donation of blood over 500 mL within 90 days prior to screening or intention to donate blood or blood products during the study;
18. Have any current and / or recurrent clinically significant skin condition at the treatment area (i.e. atopic dermatitis); including tattoos;
19. Any known factor, condition, or disease that might interfere with treatment compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 17-09-2021 |
| Enrollment: | 12 |
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Immucothel |

## Ethics review

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| Approved WMO Date: | 24-08-2021 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 06-09-2021 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

ID: 24998
Source: Nationaal Trial Register
Title:

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2021-004136-28-NL |
| CCMO | NL78698.056.21 |
| OMON | NL-OMON24998 |