# A multicenter, open-label, non-randomized, Phase 1b/2 study to evaluate the safety, pharmacokinetics, and efficacy of subcutaneous isatuximab in adults with warm autoimmune hemolytic anemia

Published: 03-02-2021
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Primary:• Part A: To evaluate the safety and tolerability of subcutaneous injections of isatuximab in adults with wAIHA.• Part B: To evaluate the efficacy of the selected dose in adults with wAIHA.Secondary:• Part A (Cohorts 2 and 3 only)-To...

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Autoimmune disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON51964

**Source**
ToetsingOnline

**Brief title**
ACT16832

### Condition

- Autoimmune disorders

**Synonym**
autoimmune anemia, warm AIHA

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Genzyme Europe BV
**Source(s) of monetary or material Support:** Genzyme Europe BV

## Intervention

**Keyword:** isatuximab, Phase 1b/2, warm autoimmune hemolytic anemia

## Outcome measures

### Primary outcome

Part A:

- To assess safety and tolerability

Part B:

- To evaluate overall response rate (R) or complete response (CR) at Day 85

### Secondary outcome

Part A (Cohorts 2 and 3 Only):

- To evaluate overall response rate (R) or complete response (CR) at Day 85

- Proportion of participants with durable hemoglobin response by Day 169

- Overall response rate at Day 169, median time to R or CR, median time to loss of R or CR, proportion of participants requiring rescue therapy (any wAIHA-directed therapy other than prednisone or transfusion) or splenectomy

- FACIT-fatigue scale score

Part B

- To assess safety and tolerability

- Proportion of participants with durable hemoglobin response by Day 169

- Overall response rate at Day 169, median time to PR or CR, median time to

loss of PR or CR, proportion of participants requiring rescue therapy (any

wAIHA-directed therapy other than prednisone or transfusion) or splenectomy

- FACIT-fatigue scale score

Part A (All cohorts) and B

- Change from baseline in LDH, haptoglobin, reticulocytes, and total bilirubin

- PK parameters after subcutaneous administrations

- Incidence and titer (if relevant) of anti-isatuximab antibodies

# Study description

**Background summary**

The purpose of the study is to evaluate the safety of isatuximab injected subcutaneously, how well tolerated it is, and to see if it can increase hemoglobin levels and reduce the need for blood transfusions and other medications for anemia in adults who have warm autoimmune hemolytic anemia. Additional purposes of the study are to see how treatment with isatuximab may help fatigue, to measure how isatuximab is distributed and removed from the body, and to determine if the body develops antibodies against isatuximab.

**Study objective**

Primary:
• Part A: To evaluate the safety and tolerability of subcutaneous injections of isatuximab in adults with wAIHA.
• Part B: To evaluate the efficacy of the selected dose in adults with wAIHA.

Secondary:
• Part A (Cohorts 2 and 3 only)
-To evaluate the efficacy of isatuximab in adults with wAIHA
-To evaluate the durability of response to isatuximab and time to response

-To evaluate the impact of isatuximab treatment on fatigue
• Part B
-To evaluate the safety and tolerability of isatuximab in adults with wAIHA
-To evaluate the durability of response to isatuximab and time to response
-To evaluate the impact of isatuximab treatment on fatigue
• Parts A (all Cohorts) and B
-To evaluate the effect of isatuximab on markers of hemolysis
-To characterize the pharmacokinetic profile of isatuximab in adults with wAIHA
-To evaluate the immunogenicity of isatuximab

### Study design

Multicenter, open-label, non-randomized, Phase 1b/2 study.

### Intervention

Part A, Cohort 1: 140 mg every 2 weeks x 2
Part A, Cohort 2: 70 mg, or 140 mg, or 280 mg every 2 weeks x 6
Part A, Cohort 3, and Part B: every 2 weeks x 6; dose level to be determined based on results from prior Cohorts; the dose will not exceed 560 mg

### Study burden and risks

Risks and burdens related to blood collection, study procedures and possible adverse events.

## Contacts

**Public**
Genzyme Europe BV

Paasheuvelweg 25
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**Scientific**
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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Participant must be >=18 to years of age, inclusive, at the time of signing the informed consent.
- Males and females with a confirmed diagnosis of primary w AIHA or systemic lupus erythematosus (SLE)-associated wAIHA (without other SLE-related manifestations apart from cutaneous and musculoskeletal manifestations) who meet the following criteria:
a) Hemoglobin level <10 g/dL at screening.
b) Hemolysis (haptoglobin <=40 mg/dL and total or indirect/unconjugated bilirubin above the upper limit of normal).
c) Positive direct antiglobulin test (DAT) (IgG or IgG + complement C3d pattern or IgM warm autoantibodies (positive dual DAT)).
- Participants who have previously failed to maintain a sustained response after treatment with corticosteroids (corticosteroid-refractory or corticosteroid-dependent primary wAIHA).
- Part A only: Participants who have previously failed to maintain a sustained response after treatment with rituximab (or other anti-CD20 monoclonal antibodies). The last dose of the anti-CD20 antibody must have been administered at least 12 weeks before enrollment.
- Part B: Participants who have had an insufficient response to at least 1 prior therapy in addition to corticosteroids (splenectomy is regarded as a prior therapy).
- Contraceptive use by men and women.

## Exclusion criteria

Participants are excluded from the study if any of the following criteria apply:
- Clinically significant medical history or ongoing chronic illness that would

jeopardize the safety of the participant or compromise the quality of the data derived from his or her participation in the study as determined by the Investigator.
- Serious infection that required hospitalization within 3 months prior to enrollment.
- Secondary wAIHA from any cause including drugs, lymphoproliferative disorders, infectious or autoimmune disease (SLE without other SLE-related manifestations apart from cutaneous and musculoskeletal manifestations is allowed), or active hematologic malignancies. Participants with positive antinuclear antibodies but without a definitive diagnosis of an autoimmune disease are allowed.
- History of coagulation or bleeding disorders (Evans Syndrome is allowed).
- Uncontrolled or active HBV or HCV infection.
- HIV infection.
- Serum gammaglobulin levels <3 g/L.
- Females who are pregnant, lactating, or considered unreliable with respect to contraceptive practice.
- Concurrent treatment with corticosteroids, unless the participant has been on a stable daily dose for >= 15 days prior to enrollment.
- Treatment with cyclophosphamide within 4 weeks prior to enrollment.
- Treatment with cytotoxic drugs (other than cyclophosphamide) within 12 weeks prior to enrollment.
- Treatment with non-cytotoxic, immunomodulatory drugs (including but not limited to Cyclosporine, Sirolimus, Tacrolimus, Idelalisib, Ibrutinib), excluding biologic agents, within 4 weeks prior to enrollment.
- Treatment with any biologic agent within 12 weeks prior to enrollment.

# Study design

## Design

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|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL
Recruitment status: Recruitment stopped

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|---|---|
| Start date (anticipated): | 25-10-2022 |
| Enrollment: | 2 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | nvt |
| Generic name: | isatuximab |
| Registration: | Yes - NL outside intended use |

## Ethics review

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|---|---|
| Approved WMO Date: | 03-02-2021 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 09-06-2021 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 30-06-2021 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 19-07-2021 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

Approved WMO
Date: 26-10-2021

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 30-12-2021

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 06-01-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 02-02-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 26-04-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 23-06-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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|---|---|
| Approved WMO Date: | 18-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 02-08-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 26-11-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

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|---|---|
| Approved WMO Date: | 16-12-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden) |
| | metc-ldd@lumc.nl |

# Study registrations

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

No registrations found.

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

No registrations found.

## In other registers

| Register | ID |
| --- | --- |
| Other | 2020‑003880‑24 |
| EudraCT | EUCTR2020‑003880‑24-NL |
| CCMO | NL75800.058.21 |