# A randomized, double-blind, placebo-controlled, three-period two treatment incomplete-block crossover study to investigate the effects of intravenous GSK3858279 on a battery of evoked pain tests in healthy participants.

Published: 19-09-2019
Last updated: 17-01-2025

To evaluate the effects of IV administration of GSK3858279 in Ultraviolet B (UVB) burn inflammatory, cold pressor test and electrical pain test in the PainCart

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON55004

**Source**
ToetsingOnline

**Brief title**
GSK3858279 vs PBO, Phase 1, Pain Tests, PK and Target Engagement in HV

### Condition

- Other condition

**Synonym**
Chronic pain diseases

**Health condition**

Chronic pain diseases.

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** GlaxoSmithKline
**Source(s) of monetary or material Support:** Pharmaceutical Industry

## Intervention

**Keyword:** Cross over, Intravenous, Pain

## Outcome measures

### Primary outcome

- UVB heat pain detection (oC)

- Cold pressor time to intolerable pain threshold (secs)

- Electrical pain tolerance threshold (mA) - single stimulus

### Secondary outcome

NA

# Study description

### Background summary

GSK3858279 is a high affinity (Kd<1pM), human immunoglobulin G2* (IgG2*) (Fcsilenced), first-in-class monoclonal antibody (mAb), binding specifically to the chemokine CCL17. It functionally inhibits CCL17, which activates the chemokine receptor CCR4, to prevent downstream consequences of CCR4 signalling. At the time of this protocol, GSK3858279 is being developed for treatment of osteoarthritis pain, however non-clinical data suggests an opportunity to treat other chronic pain conditions including neuropathic pain by targeting the aforementioned pathway.

### Study objective

To evaluate the effects of IV administration of GSK3858279 in Ultraviolet B (UVB) burn inflammatory, cold pressor test and electrical pain test in the

PainCart

### Study design

A randomized, double-blind, placebo-controlled, three-period twotreatment incomplete-block crossover study in healthy participants.

### Intervention

GSK3858279, 3 mg/kg. single dose, once per study period or Placebo single dose, once per study period. Participants will receive up to 2 single doses of GSK3858279.

### Study burden and risks

Study participation involves adhering to study lifestyle restrictions for a relative long period (approximately 6 months) and admittance to the clinical unit at given days. A detailed risk assessment related to the study drug is available in section 2.3.1. of the protocol, together with related mitigation strategies.

The healthy study participants included in this study will receive no medical benefit from participation. The risks from taking part in the study will be minimized through the selection of an appropriate dose level, selection of appropriate study participants defined by the inclusion/exclusion criteria, and safety monitoring. The study will be run in a clinical unit with access to hospital facilities for the treatment of medical emergencies. Participants will remain monitored in the clinic for a minimum of 2 hours after completion of dosing in each study period and will only be discharged from the unit if the investigator deems it safe to do so.

## Contacts

**Public**
GlaxoSmithKline

980 Great West Road .
Brentford, Middlesex TW8 9GS
GB
**Scientific**
GlaxoSmithKline

980 Great West Road .
Brentford, Middlesex TW8 9GS

GB

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

1. Participant must be 18 to 50 years of age inclusive, at the time of signing the informed consent.
2. Participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, vital signs and cardiac monitoring.
3. Body weight within 50*100 kg and body mass index (BMI) within the range 18---30 kg/m2 (inclusive).
4. Must be Male:
Participants must agree to the following during the intervention period and for at least 90 days after the last dose of study intervention:
- Refrain from donating sperm.
PLUS, either:
-Be abstinent from heterosexual intercourse as their preferred and usual lifestyle
OR:
- Must agree to use contraception/barrier as detailed below:
- Agree to use a male condom
-And should also be advised of the benefit for a female partner to use a highly effective method of contraception.
5. Capable of giving signed informed consent as described in Appendix 1 of the protocol which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol.

## Exclusion criteria

1. History or presence of/significant history of or current cardiovascular,

respiratory, hepatic, renal, gastrointestinal, endocrine, haematological, or neurological disorders capable of significantly altering the absorption, metabolism, or elimination of drugs; constituting a risk when taking the study intervention or interfering with the interpretation of data
2. Personal or family history of cardiomyopathy.
3. Abnormal blood pressure as determined by the investigator.
4. Symptomatic herpes zoster within 3 months prior to screening.
5. Evidence of active or latent tuberculosis (TB) as documented by medical history andvexamination, and TB testing: a positive (not indeterminate) QuantiFERON-TB Gold test.
6. Significant allergies to humanized monoclonal antibodies.
7. Clinically significant multiple or severe drug allergies, intolerance to topical corticosteroids, or severe post-treatment hypersensitivity reactions (including, but not limited to, erythema multiforme major, linear immunoglobulin A (IgA) dermatosis, toxic epidermal necrolysis, and exfoliative dermatitis)
8. Lymphoma, leukaemia, or any malignancy. Those who are at risk of DNA repair diseases or any family history of DNA repair disease.
9. Alanine transaminase (ALT) >1.5x upper limit of normal (ULN).
10. Bilirubin >1.5xULN (isolated bilirubin >1.5xULN is acceptable if bilirubin is fractionated and direct bilirubin <35%).
11. Current or chronic history of liver disease or known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones).
12. QTc >450 msec
NOTES:
-The QTc is the QT interval corrected for heart rate according to Bazett*s formula (QTcB), Fridericia*s formula (QTcF), and/or another method, machineread or manually over-read.
- The specific formula that will be used to determine eligibility and discontinuation for an individual subject will be QTcF. In other words, several different formulae cannot be used to calculate the QTc for an individual subject and then the lowest QTc value used to include or discontinue the subject from the trial.
-For purposes of data analysis, QTcB, QTcF, another QT correction formula, or a composite of available values of QTc will be used as specified in the Reporting and Analysis Plan (RAP).
13. History of Stevens-Johnson Syndrome.
14. Known immunodeficiency.
15. Participants with an acute, re-current or chronic infection (e.g., osteomyelitis), who have been receiving treatment within three months prior to dosing or individuals with an active infection.
16. Previous or current history of excessive bleeding or coagulation disorders.
17. Previous history of hypertrophic or keloid scarring.
18. Any current, clinically significant, known medical condition in particular any existing conditions that would affect sensitivity to cold (such as atherosclerosis, Raynaud*s disease, urticaria, hypothyroidism) or pain (such as

disease that causes pain, hypesthesia, hyperalgesia, allodynia, paraesthesia, neuropathy).
19. Participants indicating pain tests intolerable at screening. Participants achieving tolerance at >80% of maximum input intensity for cold pressor and electrical pain tests are to be excluded. If pressure pain test tolerance is >80% of maximum input intensity they may be enrolled as per PI judgement.
20. History or presence of post-inflammatory hyperpigmentation. Applicable for the participants in the UVB-MITT population only.
21. Participants with Fitzpatrick skin type IV, V or VI. Applicable for the participants in the UVB-MITT population only.
22. Any of the following on the proposed test area on the back: widespread acne, freckles, tattoos, birthmarks or scarring (investigator discretion may be used to determine if small areas may be avoided in the testing area on the back). Applicable for the participants in the UVB-MITT population only.
23. A minimal erythema dose (MED) higher than 355 mJ/cm2 at screening. Applicable for the participants in the UVB-MITT population only.
24. Past or intended use of over-the-counter or prescription medication including herbal medications within 7 days prior to dosing until after follow-up visit.
25. Live vaccine(s) within 1 month prior to dosing or plans to receive such vaccines during the study.
26. Treatment with biologic agents (such as monoclonal antibodies including marketed drugs) or immunosuppressants within 3 months or 5 half-lives (whichever is longer) prior to dosing.
27. Treatment with anti-platelet or anti-coagulant agents within 7 days of dosing.
28. Major surgery (as per investigator*s judgement) within 3 months prior to dosing.
29. Participant has made a blood or plasma donation or has had a comparable blood loss
(>450mL) within the last 3 months prior to the Screening Visit. Blood donation during the study is not permitted.
30. Exposure to more than 4 new chemical entities within 12 months prior to the first dosing day.
31. Current enrolment or past participation in any other clinical study involving an investigational study intervention within the last 3 months, 5-half-lives or twice the
duration of the biological product before dosing in this current study.
32. Presence of Hepatitis B surface antigen (HBsAg) at screening or within 3 months prior to first dose of study intervention.
33. Presence of Hepatitis B core antibody (HbcAb) at screening or within 3 months prior to first dose of study intervention.
34. Positive Hepatitis C antibody test result at screening or within 3 months prior to first dose of study intervention.
NOTE: Subjects with positive Hepatitis C antibody due to prior resolved disease can be enrolled, only if a confirmatory negative Hepatitis C RNA test is obtained

35. Positive Hepatitis C RNA test result at screening or within 3 months prior to first dose of study intervention. NOTE: Test is optional and subjects with negative Hepatitis C antibody test are not required to also undergo Hepatitis C RNA testing
36. Abnormal clinically significant echocardiogram at screening, as assessed by the investigator.
37. Cardiac troponin T or NT-proBNP levels out of normal range at screening.
38. Positive pre-study drug/alcohol screen.
39. Positive human immunodeficiency virus (HIV) antibody test.
40. Regular use of known drugs of abuse.
41. Estimated glomerular filtration rate (eGFR) of <90 mL/min/1.73 m2 or serum creatinine >1.5xULN or urine albumin:creatinine ratio of >300mg/g at screening.
42. Positive SARS-CoV-2 PCR test at screening. Participants may be re-screened once they present a negative SARS-CoV-2 PCR.
43. Subjects with known COVID-19 positive contacts in the past 14 days
44. Regular alcohol consumption within 6 months prior to the study defined as:
-an average weekly intake of >21 units for males. One unit is equivalent to 8 g of alcohol: a half-pint (~240 mL) of beer, 1 glass (125 mL) of wine or 1 (25 mL) measure of spirits.
45. Smoker, smoking history or use of tobacco- or nicotine-containing products (e.g. nicotine patches or vaporizing devices) within 6 months prior to screening.
46. Sensitivity to heparin or heparin-induced thrombocytopenia.
47. Sensitivity to any of the study interventions, or components thereof, or drug or other allergy that, in the opinion of the investigator or medical monitor, contraindicates
participation in the study.

# Study design

## Design

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

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 15-10-2019 |
| Enrollment: | 30 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | GSK3858279 |
| Generic name: | NA |

# Ethics review

| | |
|---|---|
| Approved WMO Date: | 19-09-2019 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 30-09-2019 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 19-08-2020 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 25-08-2020 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 29-09-2020 |

| | |
|---|---|
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 18-03-2021 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 04-06-2021 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 10-06-2021 |
| Application type: | Amendment |
| 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

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2019-002609-23-NL |
| CCMO | NL71013.056.19 |

# Study results

| | |
|---|---|
| Date completed: | 16-09-2021 |
| Results posted: | 06-07-2022 |

**Summary results**
Trial ended prematurely

**First publication**
06-06-2022