A multi-centre, randomized, double-blind (sponsor open), placebocontrolled, repeat-dose, proof of mechanism study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and explore efficacy of GSK2330811 in participants with diffuse cutaneous systemic sclerosis (study 201247)

Published: 09-07-2018
Last updated: 25-03-2025

Primary:To evaluate the safety and tolerability of repeat subcutaneous doses of GSK2330811 in participants with dcSSc.Secondary:PK. PD (serum levels of total and free OSM). Antibodies against GSK2330811.

Ethical review	Approved WMO
Status	Completed
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON49656

Source
ToetsingOnline

Brief title
study 201247

Condition

- Autoimmune disorders

Synonym
systemic sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: cutaneous, GSK2330811, proof of mechanism, systemic sclerosis

Outcome measures

Primary outcome

Adverse events. Effects on laboratory, ECG parameters and vital signs (blood pressure, heart rate, temperature).

Secondary outcome

Plasma concentrations of GSK2330811 and derived PK parameters. Serum levels of total and free OSM. Incidence of anti-GSK2330811 antibodies.

Additional exploratory endpoints are included to explore pharmacology and effect on selected clinical endpoints and biomarkers of fibrosis, inflammation and vasculopathy in blood and skin.

Study description

Background summary

Systemic sclerosis (SSc) is a rare autoimmune disease with high morbidity and mortality. There are no approved disease-modifying therapies and it is an area of high unmet medical need. GSK2330811 is a monoclonal antibody that binds and

neutralises Oncostatin M (OSM). The biological roles of OSM indicate that blocking OSM signalling would be expected to inhibit the key pathologic processes of SSc. This is a proof of mechanism study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of repeat subcutaneous doses of GSK2330811 in participants with diffuse cutaneous SSc (dcSSc).

Study objective

Primary:
To evaluate the safety and tolerability of repeat subcutaneous doses of GSK2330811 in participants with dcSSc.
Secondary:
PK. PD (serum levels of total and free OSM). Antibodies against GSK2330811.

Study design

Double blind (sponsor open) placebo-controlled, parallel group study to evaluate safety and tolerability of subcutaneous GSK2330811.
First study in patients.
Randomization 3:1 to GSK2330811 and placebo (every other week). Co-treatment with e.g. micofenolate and low dose corticosteroids accepted (see question D4A for more details).
Two sequential cohorts. Cohort 1 (performed in other countries) has evaluated the safety and tolerability of a repeat-dose predicted to provide sub-maximal inhibition of OSM (100 mg GSK2330811 per dose), leading to a dose escalation decision. Cohort 2 (multi-country study incl. NL) will now evaluate a repeat-dose predicted to provide maximal inhibition of OSM (300 mg GSK2330811 per dose) to test proof of mechanism.
An internal Data Review Committee has been responsible for determining progression from cohort 1 to cohort 2 and the number of subjects for cohort 2.
Study duration up to 34 weeks. Screening up to 6 weeks, treatment period 12 weeks (6 doses in total of 3 injections per dose for cohort 2), follow-up 16 weeks.
24 to 40 subjects.

Intervention

Treatment with GSK2330811 or placebo.

Study burden and risks

Risk: Adverse events of GSK2330811.
Burden:
11 visits in 34 weeks.
Complete physical examination: all visits.
Blood tests: all visits, 500 mL in total.

Pregnancy test: all visits (urine or blood).
Skin biopsy: 2 visits.
ECG: 4 visits.
Questionnaires (2): 3 visits.
Lung function: 4 visits (hospital), weekly at home (during screening and treatment period).
Optional blood sample (6 mL) for genetic research.

Contacts

Public
GlaxoSmithKline

Van Asch van Wijckstraat 55H
Amersfoort 3811 LP
NL
Scientific
GlaxoSmithKline

Van Asch van Wijckstraat 55H
Amersfoort 3811 LP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Males and females *18 years of age.
* Documented systemic sclerosis with cutaneous involvement and a disease duration of *60 months and an mRSS *10 and *35 at screening.

* Active disease. See protocol section 6.1, item 5 for details.
* An area of uninvolved or mildly thickened skin that would allow subcutaneous injection on abdomen, thigh or upper arm and on the fore arm for skin biopsies. See protocol section 6.1, item 6-7 for details.
* Treatment with mycophenolate mofetil (*3,000 mg/day) or mycophenolate sodium (*1,440 mg/day), oral corticosteroids (*10 mg/day of prednisone or equivalent), phosphodiesterase 5 inhibitors and endothelin receptor antagonists is permitted. See protocol section 6.1, item 8-11 for details.
* Female participants of childbearing potential: see protocol section 6.1, item 12b for details.

Exclusion criteria

* Limited cutaneous SSc subset.
* Rheumatic autoimmune disease other than dcSSc. See protocol section 6.2, item 2 for details.
* FVC *50% of predicted, or a diffusing capacity of the lung for carbon dioxide (DLCO) (corrected for hemoglobin) *40% of predicted.
* Pulmonary arterial hypertension, clinically significant inflammatory myositis.
* SSc renal crisis within 6 months of first dosing of study medication.
* Significant co-morbidities. See protocol section 6.2, item 7-10 for details.
* Active infection or history of infections within 6 months of first dosing. See protocol section 6.2, item 11 for details.
* Prior or concomitant therapy as mentioned in protocol section 6.2, item 17-27.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	29-01-2019
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK2330811
Generic name:	GSK2330811

Ethics review

Approved WMO Date:	09-07-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-09-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-01-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-04-2019

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2016-003417-95-NL
CCMO	NL66668.100.18
Other	www.gsk-clinicalstudyregister.com, registratienummer 201247

Study results

Date completed:	13-04-2020
Results posted:	28-01-2021

First publication
18-01-2021

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File