A first-in-human, randomized, subject-blinded, placebocontrolled, single ascending dose study to investigate the safety, tolerability and pharmacokinetics of MHS552 in healthy volunteers

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

To assess the safety and tolerability of MHS552 of single i.v./s.c. doses. Cohort 1-5 will be i.v. and cohort 6-8 will be s.c. In addition, in each of the 5 first cohorts, a sentinel group is included.

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

Summary

ID

NL-OMON49201

Source
ToetsingOnline

Brief title
A FIH study to investigate the safety, tolerability and PK of MHS552

Condition

- Autoimmune disorders

Synonym
Teff-driven autoimmune and inflammatory diseases

Research involving
Human

Sponsors and support

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

Intervention

Keyword: healthy volunteers, pharmacokinetics, Safety, Tolerability

Outcome measures

Primary outcome

All safety endpoints (including physical examination findings, vital signs, ECG

parameters, safety laboratory, adverse events)

Secondary outcome

PK parameters of MHS552 after i.v. and s.c. single doses such as Cmax, Tmax,

AUClast, AUCinf, T1/2, Vz, CL and other PK parameters as appropriate

Study description

Background summary

The investigational compound MHS552 consists of (IL-2) molecules harboring a single point mutation (D49A) into the heavy chain complement determining region1 (CDR1). This therapeutic Ab has been designed to selectively expand T regulatory cells (Tregs) and thus restore Treg-mediated immune regulation of T effector (Teff) responses. MHS552 is in early clinical development for the treatment of Teff-driven autoimmune and inflammatory diseases, such as graft-versus-host disease (GvHD), type 1 diabetes (T1D) and vitiligo. The purpose of this FIH study is to assess the safety and tolerability, PK, immunogenicity (IG) and PD of single ascending doses (SAD) of MHS552 given by i.v. infusion and s.c. injection in healthy subjects. The results are intended to support further clinical development of MHS552 by guiding the dosing regimens for the assessment of safety, tolerability, PK and PD in future studies.

Study objective

To assess the safety and tolerability of MHS552 of single i.v./s.c. doses.

Cohort 1-5 will be i.v. and cohort 6-8 will be s.c. In addition, in each of the 5 first cohorts, a sentinel group is included.

Study design

This is a randomized, placebo-controlled, subject-blinded FIH study in healthy subjects.

Intervention

MHS552, 2 different routes of administration; i.v. and s.c.

Study burden and risks

MHS552 has not yet been administered to human subjects, the in vitro and in vivo pharmacology of MHS552 has been carefully characterized in primary human cells and murine models of T1D and GvHD. The toxicology and pharmacokinetics were also extensively studied in the rat and cynomolgus monkeys, cross reactive species. Given the limited clinical data on the administration of Treg selective IL-2 muteins with half-life extension to humans (AMG592 and RO7049665), the potential risks associated with human use of MHS552 are inferred from biological understanding of the IL-2 pathway, relevant non-clinical findings, the general risks associated with therapeutic Ab administration and, extensive historical clinical experience with the high and low dose Proleukin® treatment regimens. Based on the data acquired in non-clinical toxicology studies, potential toxicities to be considered for MHS552 include reversible hematological effects, skin rashes and lymphocytic or mixed cellular infiltrates.There is no benefit expected for healthy subjects participating in this study. The risk to subjects in this trial will be minimized by adherence to the eligibility criteria, sentinel dosing, close clinical monitoring, frequent follow-up, minimal duration of the study (single dose) and prespecified
study stopping rules. The absence, in these healthy subjects, of co-morbid disease and concomitant immunosuppressive treatment allows for an unbiased assessment of the safety and tolerability of MHS552 . Based on the clinical experience with low-dose Proleukin® and from SAD FIH trials of the long-lived IL-2 muteins AMG592 and RO7049665 in healthy subjects where no class-specific risks were reported, the risk with single low doses of MHS552 is considered to be acceptable for healthy subjects.

Contacts

Public
Novartis

Lichtstrasse 35
Basel 4056
CH
Scientific
Novartis

Lichtstrasse 35
Basel 4056
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy female and male subjects 18 to 45 years of age included, and in good health as determined by past medical history, physical examination, vital signs, electrocardiogram, and laboratory tests at screening and/or baseline.

Exclusion criteria

- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant
- A history of ongoing, chronic or recurrent infectious disease, or evidence of tuberculosis infection
- Receipt of live/attenuated vaccine within a 3-month period before first dose
- Active, known, or suspected autoimmune disease or documented history of autoimmune disease

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	08-10-2019
Enrollment:	64
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MHS552
Generic name:	NA

Ethics review

Approved WMO Date:	09-09-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	16-09-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-05-2021
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	EUCTR2018-004233-33-NL
CCMO	NL71107.056.19

Study results

Date completed: 19-07-2021

Results posted: 18-05-2022

Summary results
Trial ended prematurely

First publication
18-03-2022