A Phase 1 Randomized, Placebo-Controlled, Double-Blind, First- Time-in-Humans, Single-Ascending Dose (SAD) and Multiple- Ascending Dose (MAD) Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of CNM-Au8 in Healthy Male and Female Volunteers

Published: 09-03-2015
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Primary objective:To evaluate the single- and multiple-dose safety and pharmacokinetics of CNM-Au8 upon oral administration of CNM-Au8 to healthy adult male and female subjects.Secondary objective:Exploreing the immune-modulating effects of CNM-Au8...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Demyelinating disorders
Study type	Observational invasive

Summary

ID

NL-OMON42813

Source
ToetsingOnline

Brief title
Safety, tolerability, PK and PD of CNM-Au8

Condition

- Demyelinating disorders

Synonym
nerve disease, Neuromyelitis optica

Research involving
Human

Sponsors and support

Primary sponsor: Clene Nanomedicine
Source(s) of monetary or material Support: Clene Nanomedicine

Intervention

Keyword: First in man, pharmacokinetics&pharmacodynamics, Remyelination, Safety&tolerability

Outcome measures

Primary outcome

Pharmacokinetic endpoints:

SAD Phase: maximum observed plasma concentration (Cmax), time to Cmax (Tmax), the area under the plasma concentration versus time curve from time 0 (predose) to time infinity (AUCinf), AUC from time 0 to time of last measurable plasma concentration (AUClast), the percentage of the AUC that is extrapolated beyond the last measurable concentration (AUCext), the elimination rate constant (*z), the apparent systemic clearance (CL/F), mean residence time (MRT), apparent volume of distribution, terminal phase (Vz/F), and terminal-phase half-life (t*) will be calculated using non-compartmental analyses and PK modeling.

MAD Phase: pharmacokinetic parameters such as the maximum observed plasma concentration (Cmax), time to Cmax (Tmax), Cmin, and the area under the plasma concentration versus time curve from time 0 (predose) to the end of the 24-hour dosing interval (AUC*) will be calculated on Days 1, 7, 14 and 21. The apparent

systemic clearance (CL/F) will be calculated from the steady-state concentration-time profile. Other parameters such as the accumulation ratio (RAcc) elimination rate constant (*z), mean residence time (MRT), apparent volume of distribution, terminal phase (Vz/F), and terminal-phase half-life (t*) will be calculated when appropriate using non-compartmental analyses and PK modeling.

Safety endpoints are as follows:

• Incidence of treatment-emergent Adverse Events (AEs) and Serious Adverse Events
(SAEs) grouped by body system

• Changes from Baseline in clinical laboratory, urinalysis, vital signs, and ECG
parameters to discharge and Follow-Up

• Changes from pre-dose physical exam findings to Follow-Up

Secondary outcome

Pharmacodynamic endpointss

• TLR9-induced cytokines

• Other related cytokines

Study description

Background summary

Gold complexes have been widely used in the treatment of rheumatoid arthritis for over 80 years. The mechanism of action of gold salt compounds is not well understood, but gold appears to accumulate slowly in the body to gradually reduce inflammation and slow the progression of rheumatoid arthritis. Unfortunately, clinical use of traditional gold compounds is compromised by multiple forms of toxicity, commonly including pruritus, dermatitis, stomatitis, diarrhea, and proteinuria, and, less frequently, hematological. The role of gold itself in the pattern of toxicity in gold salts is unclear, but it is hypothesized that at least some complications arise from the related formulations rather than from the gold itself raising the possibility that a cleaner form of gold delivery might incur fewer complications. CNM-Au8 consists of clean-surface gold nanocrystals, and may therefore cause less of the side-effect. Preclinical studies showed gold stimulated remyelination. In the future, CNM-Au8 would possibly be a therapeutic option for diseases like neuromyelitis optica.

Study objective

Primary objective:
To evaluate the single- and multiple-dose safety and pharmacokinetics of CNM-Au8 upon oral administration of CNM-Au8 to healthy adult male and female subjects.

Secondary objective:
Exploreing the immune-modulating effects of CNM-Au8 and qualifying a bioassay for demonstration of CNM-Au8*s anti-inflammatory effects.

Study design

A phase 1 randomized, placebo-controlled, double-blind, first-in-human, single-ascending dose (SAD) and multiple-ascending dose (MAD) Study

Study burden and risks

This is the first time that CNM-Au8 will be administered to human volunteers. Preclinical trials shows that long-term use of the compound could cause a decrease in platelets. Other preclinical data show that gold accumulated a little bit in the kidneys, without interfering with the renal function.
Other compounds with gold (like auranofin) have these side-effects: nausea, diarrhea, decrease in appetite, abdominal cramps, pruritus.

Venapuncture: Inserting a catheter for taking blood for testing may cause pain and discomfort such as bleeding, bruising, dizziness, fainting, inflammation of the vein and infection.

We consider the burden and the risks described above to be minimal. Especially

with the low starting dose and the step-wise dose increase minimize the risk is low.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. An Institutional Review Board (IRB) approved informed consent is signed and dated prior to any study-related activities.
2. Is between the ages of 18 and 45 years, inclusive.
3. Females will be non-pregnant, non-lactating, and either post-menopausal for at least 1 year, surgically sterile (e.g., tubal ligation, hysterectomy) for at least 90 days, or agree, from the time of signing the informed consent or 14 days prior to check-in until 30 90 days after Study Completion/Discharge, to use two forms of contraception.
4. Has a body mass index (BMI) between 18 and 34 kg/m2.

5. All laboratory values at screening fall within normal range or are evaluated as not clinically significant (NCS) by the Investigator if outside normal range.
6. Has no clinically significant abnormal findings during pre-dose physical examination or Screening and Baseline vital signs or ECG.
7. Has not consumed and agrees to abstain from taking any dietary supplements or non-prescription drugs (except as authorized by the Investigator AND Medical Monitor) for 3 days prior to CRU admission through Follow-Up.
8. Has not consumed and agrees to abstain from taking any prescription drugs (except as authorized by the Investigator AND Medical Monitor) during the 14 days prior to CRU admission through Follow-Up.
9. Has not consumed alcohol-containing beverages for starting 3 days prior to CRU admission and agrees not to consume alcohol through Follow-Up.
10. Has not consumed grapefruit or grapefruit juice within the 14 days prior to CRU admission and agrees not to consume grapefruit or grapefruit juice through Follow-Up.
11. Has not used tobacco- and nicotine-containing products within 60 days prior to the CRU admission and agrees to abstain from using tobacco- and nicotine-containing products through Follow-Up.
12. Has the ability to understand the requirements of the study and is willing to comply with all study procedures.

Exclusion criteria

1. Has a history of illicit drug abuse in the past year or current evidence of such abuse in the opinion of the Investigator.
2. Has positive findings on urine drug screen.
3. Is positive for human immunodeficiency virus (HIV), hepatitis B and/or hepatitis C on screening assessments.
4. Is pregnant or lactating.
5. Has clinically significant medical or psychiatric history that, in the Investigator*s judgment, would compromise the subject*s safety or the collection of data.
6. Has donated plasma within 7 days of CRU admission.
7. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening.
8. Participation in a clinical trial within 90 days of screening or more than 4 times in the previous year

Study design

Design

Study type:	Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-04-2015
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CNM-Au8
Generic name:	gold

Ethics review

Approved WMO Date:	09-03-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-04-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-03-2016
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	EUCTR2015-000669-29-NL
CCMO	NL52617.056.15