A human phase 0, microdose pharmacokinetic study of [14C]-Org 201745-0, [14C]-Org 244378-0 and [14C]-Org 245021-0 in post-menopausal female volunteers

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1)To assess the preliminary pharmacokinetics of [14C]-Org 201745, [14C] Org 244378 and [14C] Org 245021 when administered as a sub-therapeutic dose by the oral route to healthy post-menopausal female volunteers.2) To evaluate the safety and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON31864

Source
ToetsingOnline

Brief title
[14C]-Org 201745, [14C]-Org 244378 and [14C]-Org 245021 Microdosing Study

Condition

- Other condition

Synonym
contraception, family planning

Health condition

anticonceptie

Research involving
Human

Sponsors and support

Primary sponsor: Organon Nederland BV
Source(s) of monetary or material Support: 4e geldstroom

Intervention

Keyword: AMS, microdose, progesteron

Outcome measures

Primary outcome

Pharmacokinetics : plasma drug concentrations; pharmacokinetic parameters in

plasma: Cmax, Tmax, AUC0-inf, t1/2; to perform pharmacokinetic analysis of

urine samples will be decided later after analysis of plasma samples

Safety : adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination.

Secondary outcome

none

Study description

Background summary

Currently marketed female contraceptives consist of a steroidal progestagenic compound, either combined with a steroidal estrogenic compound or given as a progesterone only product. Due to their steroidal nature, these compounds, and their metabolites, are often not specific for either the progesterone receptor or the estrogen receptor. It is thought that part of the undesirable side-effects observed with the use of current contraceptives is due to inappropriate agonism or antagonism of the androgenic, mineralocorticoid or glucocorticoid receptors. This results in undesired effects on carbohydrate metabolism, hepatic function, lipid metabolism and thyroid function. In addition, estrogen-related side effects are cardiovascular effects secondary to

hemostatic disturbance.
Org 201745-0, Org 244378-0 and Org 245021-0 are potent, metabolically stable, orally active non-steroidal selective progestagens with high selectivity for the progesterone receptor which are being developed as an estrogen-free female oral contraceptive suitable for once-a-week administration.

Study objective

1)To assess the preliminary pharmacokinetics of [14C]-Org 201745, [14C] Org 244378 and [14C] Org 245021 when administered as a sub-therapeutic dose by the oral route to healthy post-menopausal female volunteers.

2) To evaluate the safety and tolerability of a single oral administration of [14C-Org 201745, [14C] Org 244378 and [14C]-Org 245021 to healthy post-menopausal female volunteers

Study design

a phase 0, open label, single oral dose study in post-menopausal female subjects with the compounds [14C]-Org 201745, [14C] Org 244378 and [14C]-Org 245021; each compound will be administered as a sub-therapeutic dose to 6 female subjects

Intervention

[14C]-Org 201745, [14C]-Org 244378 and [14C]-Org 245021 microdose

Study burden and risks

As ORG 244378-0 en ORG 245021-0 will be administered to man for the first time in this study, adverse effects in man have not been reported up to now. The amount of study drug that is administered in this study is less than 1/100 th of the dose at which an effect is expected in the human body. With this *micro dose* the chance of unfavorable effects on your health may be considered minimal.

The two compounds have not been previously studied in humans. Safety studies conducted in rats demonstrated that the two compounds were well tolerated at a dose 1000-fold higher than the intended human microdose in this study.

In studies conducted in rats with ORG 244378-0 the following changes were observed: increased weight, red blood cell distribution width, total protein, cholesterol and triglycerides in blood.
In studies conducted in rats with ORG 245021-0 the following changes were observed: slight increased weigth and increased level of triglycerides.

ORG 201745-0 has been administered to man recently for the first time in doses from 0.1 to 1 mg. The results from this ongoing study show that ORG 201745-0 can be administered to man safely and is well-tolerated.

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

45-70 years of age
amenorrhoe for 18 months

Exclusion criteria

history of significant disease

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-12-2007
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NAP
Generic name:	NAP

Ethics review

Approved WMO Date:	16-11-2007
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-11-2007
Application type:	First submission
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	EUCTR2007-005740-25-NL
CCMO	NL20522.056.07