A study in healthy volunteers to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple doses of BN201, an investigational compound for the treatment of acute optic neuritis.

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Ocular neuromuscular disorders
Study type	Interventional

Summary

ID

NL-OMON42731

Source
ToetsingOnline

Brief title
BN201 SAD MAD study

Condition

- Ocular neuromuscular disorders

Synonym
inflammation of the optic nerve.

Research involving
Human

Sponsors and support

Primary sponsor: Bionure Pharma S.L. Barcelona
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: BN201 SAD MAD

Outcome measures

Primary outcome

Safety : In both study parts: adverse events (AEs; including infusion site reactions), clinical laboratory, vital signs, 12 lead electrocardiogram (ECG), telemetry and physical examination

In Part A only: Holter monitoring and electroencephalogram (EEG)

In Part B only: Columbia-Suicide Severity Rating Scale (C-SSRS) questionnaire, quantitative sensory testing (QST) for mechano-sensitivity, and visual analog scale (VAS) for spontaneous pain

PK : Plasma BN201 concentrations

Plasma PK parameters estimated using noncompartmental analysis, as appropriate: Cmax, tmax, kel, t1/2, AUC0-t, AUC0-24, AUC0-inf, %AUCextra, CL, Vz and dose linearity (Parts A and B), and Ctrough and Rac (Part B only)

PD : Translocation of Foxo3 from nucleus to cytoplasm in peripheral blood mononuclear cells (PBMCs)

Secondary outcome

n/a

Study description

Background summary

BN201 is a new investigational compound that may eventually be used for the treatment of acute optic neuritis. Optic neuritis is an inflammation of the optic nerve, the bundle of nerve fibers that transmits visual information from your eye to your brain. BN201 is a compound that activates the enzyme called *serum glucocorticoid kinase-2* (SGK2) which promotes the survival of cells by changing the cellular localization of the forkhead transcription factor Foxo-3, thus inhibiting cell death.

Study objective

The study will be performed in 2 parts, Parts A and B. The purpose of the study is to investigate to what extent BN201 is tolerated. It will also be investigated how quickly and to what extent BN201 is absorbed and eliminated from the body (this is called pharmacokinetics). In addition, the effect of the compound on the location of the protein Foxo-3 in white blood cells will be investigated (this is called pharmacodynamics).

This study will be performed in 32 healthy male and female volunteers, divided over 4 groups.

For each group, the study will consist of 2 periods. In each period you will receive a single dose of BN201 or a single dose of placebo. A placebo is the same formulation without the active ingredient. BN201 and placebo will be given in the form of an intravenous (iv) infusion. The duration of the iv infusion will be approximately 1 hour. There will be at least 14 days between each time you will receive the research compound.

Study design

Part 1:
The actual study will consist of 2 periods during which the volunteer will stay in the clinical research center in Groningen for
3 days (2 nights). There will be a resting period of at least 14 days between each period. In each period, the volunteer will
receive the study compound on Day 1 and will leave the clinical research center on Day 2.

Part 2:
The actual study will consist of 1 period. The volunteer will stay in the clinical research center in Groningen for 7 days (6 nights). The volunteer will receive the study compound 5 days (once a day) and will leave the clinical

research center on Day 6.

Intervention

Part 1:
During the study you will receive BN201 or placebo after an overnight fast (at least 10 hours no eating and drinking) as an iv infusion. The duration of the iv infusion will be approximately 1 hour.

Part 2:
During the study you will receive BN201 or placebo after an overnight fast (at least 10 hours no eating and drinking) as an iv infusion. The duration of the iv infusion will be approximately 1 hour.

For all groups it is applicable that fasting will continue until 2 hours after the start of the iv infusion. Then you will receive breakfast. During fasting and after intake of the study compound, you are allowed to drink water with the exception of 2 hours prior to until 1 hour after drug administration.

Study burden and risks

As BN201 will be administered to humans for the first time in this study, adverse effects of BN201 in humans have not been reported to date. However, BN201 has been studied in animals. BN201 was welltolerated in rats (at a dose level of 50 mg per kg body weight per day) and dogs (at dose levels up to 18 mg per kg body weight per day), when administered once-daily as an iv infusion for 14 consecutive days. In dogs, the most frequently observed adverse effects after once-daily administration of BN201 (36 mg per kg body weight per day) for 14 consecutive days were: incoordination, body tremors and/or shaking, decreased activity, convulsions, and increase in heart rate. All observed adverse effects were of short duration and generally resolved within 1 day after administration of the study compound.

In each group and in each period, initially 2 volunteers will be dosed (1 volunteer will receive BN201 and 1 volunteer will receive placebo). After dosing, the safety and tolerability of BN201 in these 2 volunteers will be closely monitored for 24 hours. If there are no unacceptable adverse reactions and both PRA and the Sponsor agree on the safety and tolerability of the study compound in the first 2 volunteers, the remaining 6 volunteers of the group will be dosed.

Contacts

Public

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- healthy male or female
- 18-55 years old inclusive
- BMI between 18.0 - 32 kg/m2
- smokes less than 6 cigarettes per day (or 1 cigar or pipe)

Exclusion criteria

strenuous activity (e.g. sports) is not allowed from 96 hours (4 days) prior to entry into the clinical research center and during your stay in the clinical research center. you are not allowed to eat or drink (fast) from 4 hours prior to the pre-study screening, from 4 hours prior to entry into the clinical research center and from 4 hours prior to the poststudy screening .you are not allowed to consume any methylxanthine-containing beverages or food (coffee, tea, cola, chocolate, *powerdrinks*) or alcohol, from 48 hours (2 days) prior to entry into the clinical research center and during your stay in the clinical research center. you are not allowed to consume any foods containing poppy seeds from 48 hours (2 days) prior to the

prestudy screening and entry into the clinical research center as this could cause a false-positive drug screen result. you are not allowed to use any prescribed medication during 30 days prior to entry into the clinical research center until the poststudy screening .you are not allowed to use any over-the-counter medication, vitamin preparations and other food supplements, or herbal medications (e.g. St. John*s Wort), from 14 days prior to entry into the clinical research center until the poststudy screening. you are not allowed to have had a serious infection (e.g., pneumonia) within 2 months before the pre-study screening. you are not allowed to have had an active bacterial or viral infection and fever (body temperature >38°C) within 48 hours (2 days) prior to the first administration of the study compound.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	32
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	BN201
Generic name:	BN201

Ethics review

Approved WMO

Date:	05-08-2015

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-08-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-11-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-07-2016
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	EUCTR2015-002722-39-NL
CCMO	NL54253.056.15