Een enkelvoudig geblindeerd, gerandomiseerd onderzoek met meervoudig opklimmende doseringen (deel1) en een onderzoek met 7 periodes naar de biologische beschikbaarheid (deel 2) van LT-NS001 en NAPROXEN met gezonde vrijwilligers

Gepubliceerd: 16-11-2007 Laatst bijgewerkt: 10-05-2024

Primary :To determine the safety and tolerability of multiple doses of LT-NS001 given twice daily as a suspension for 7.5 days in healthy male subjectsSecondary:To determine the plasma pharmacokinetics of LT-NS001 suspension and naproxen tablet (...

Ethische beoordeling	Goedgekeurd WMO
Status	Werving gestopt
Type aandoening	Overige aandoening
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON31529

Bron
ToetsingOnline

Verkorte titel
LT-NS001 MRD en biologische beschikbaarheid onderzoek

Aandoening

- Overige aandoening

Synoniemen aandoening
Chronische pijn

Aandoening

Chronische pijn zoals bij Rheumatische arthritis

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor: Logical Therapeutics, Inc
Overige ondersteuning: Logical Therapeutics Inc

Onderzoeksproduct en/of interventie

Trefwoord: Biologische beschikbaarheid, Enkel-blind, LT-NS001

Uitkomstmaten

Primaire uitkomstmaten

Pharmacokinetics :plasma LT-NS001 and naproxen concentrations, pharmacokinetic

parameters

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

physical examination

Secundaire uitkomstmaten

N.A.

Toelichting onderzoek

Achtergrond van het onderzoek

Part 1: Single-blind, randomized, placebo-controlled, escalating multiple dose (MD) study in 30 healthy male subjects (4 sequential groups, Groups 1-4) who will receive either 500 mg b.i.d. NAPROSYN for 7 days with a final dose in the morning of Day 8 (Group 1, 6 subjects); or 800, 1000 or 1200 mg b.i.d. LT NS001 suspension or placebo for 7 days with a final dose in the morning of Day 8 (Groups 2-4, 8 subjects per group; 6 subjects on active drug and 2 on placebo).

Part 2: open-label, single dose 7-treatment, crossover bioavailability (BA)

study in 3 healthy male subjects and 3 healthy postmenopausal female subjects (one group of subjects, 7 periods, Group 5) involving administration of single doses of 1000 mg LT-NS001 tablet formulation A, B and C, 500 mg NAPROSYN, 1000 mg of LT NS001 suspension, 500 mg EC Naprosyn, 500 mg NAPROSYN and 800 or 1200 mg LT NS001 tablet formulation A, B or C (best option from the first three periods) in a fixed sequence.

Doel van het onderzoek

Primary :
To determine the safety and tolerability of multiple doses of LT-NS001 given twice daily as a suspension for 7.5 days in healthy male subjects

Secondary:
To determine the plasma pharmacokinetics of LT-NS001 suspension and naproxen tablet (NAPROSYN®) when given twice daily for 7.5 days in healthy male subjects
To determine an optimal dose-level range for Phase 2 dosing, i.e. the dose at which AUC and Cpre for b.i.d. LT-NS001 are comparable to 500 mg b.i.d. NAPROSYN
To compare the pharmacokinetics of three different tablet formulations of LT-NS001 with LT-NS001 oral suspension and NAPROSYN tablet given as a single oral dose to healthy subjects

Onderzoeksopzet

Screening and follow-up:Clinical laboratory, height, weight, full physical examination, vital signs (including temperature), and ECG; at eligibility screening: medical and medication history, HBsAg, anti-HCV, anti HIV 1/2, and drug screen; clinical chemistry and drug screen will be repeated upon admission in Part 1; drug screen will be repeated upon each admission in Part 2.

Observation period :
Part 1: in clinic from 17 h prior to first dosing up to 24 h after drug administration on Day 8, with ambulant visits 48 and 72 h after drug administration on Day 8
Part 2: in clinic from 17 h prior to each dosing up to 24 h after drug administration, with ambulant visits 48 and 72 h after each drug administration

Blood sampling :for LT-NS001 and naproxen pharmacokinetics
Part 1: Day 1: pre-dose and 0.25, 0.5, 0.75, 1, 2, 4, 8, 12 (pre-dose), 24 (pre-dose), 48 (predose), and 72 h
(pre-dose); Day 8: pre-dose, and 0.25, 0.5, 0.75, 1, 2, 4, 8, 12, 24, 48 and 72 h after drug administration
Part 2: pre-dose and 0.25, 0.5, 0.75, 1, 2, 4, 8, 12, 16, 24, 48 and 72 h after drug administration

Safety assessments :

Part 1:adverse events and concomitant medication: throughout the study
vital signs: pre-dose and 1, 4, 8 h post-dose on Days 1 and 8
clinical laboratory: predose on Days 1 and 8
ECG: pre-dose, 0.5, 1 and 4 h post dose on Days 1 and 8
Part 2:adverse events and concomitant medication: throughout the study
vital signs: pre-dose and 1, 4, 8 and 24, 48 and 72 h post-dose
ECG: pre-dose, and 0.5, 1 and 4 h post dose

Bioanalysis :Analysis of LT-NS001 and naproxen in human plasma by HPLC by PRA International.

Onderzoeksproduct en/of interventie

Active substance :LT-NS001 Activity : prodrug of naproxen, non-selective COX inhibitor Indication : acute, sub-acute and chronic musculoskeletal inflammatory diseases Strength : see Dosage Forms Dosage form :Part 1, Groups 2-4; Part 2, Group 5: 800, 1000 or 1200 mg LT-NS001 / 50 mL, mixed with corn starch, in oral suspension Part 2, Group 5: 3 different tbd-mg LT-NS001 tablet formulations (A, B and C) Reference medication Name : NAPROSYN® Active substance :naproxen free acid Activity : non-selective COX inhibitor Indication : acute, sub-acute and chronic musculoskeletal inflammatory diseases Strength : 500 mg (free acid) Dosage form :Part 1, Group 1 and Part 2, Group 5: 500 mg NAPROSYN EU equivalent dosage form Reference medication Name : NAPROSYN® EC Active substance :naproxen free acid Activity : non-selective COX inhibitor Indication : acute, sub-acute and chronic musculoskeletal inflammatory diseases Strength : 500 mg (free acid) Dosage form : Part 2, Group 5: 500 mg NAPROSYN EC Placebo Oral suspension visually matching LT-NS001 oral suspension

Inschatting van belasting en risico

LT-NS001 was previously administered to 47 healthy male volunteers at doses, ranging from 30 to 600 mg per day. In this earlier study, a number of Adverse Events (AEs; adverse side effects) were noted among subjects treated with either LT-NS001 or an inactive placebo., In the single rising dose part of the study, there was no relationship observed between dose level and number AEs or number of subjects reporting AEs.
All AEs were of mild intensity. In the multiple risng dose part of the study, AEs increased slightly with increasing doses All AEs were of mild intensity except for elevated liver enzymes, which were of moderate intensity and were reported by 3 subjects. One subject reported pain of moderate intensity at a venipuncture site pain. Overall, the most frequently reported AEs were upper abdominal discomfort and distension, abnormal liver function tests and change in urinary frequency. These most frequently reported AEs were mainly reported by subjects of the multiple dose group. There were no deaths or serious AEs. Except for elevated liver function test values reported by subjects receiving multiple doses of LT-NS001, no clinically relevant abnormalities in laboratory measurements were observed. None of the increases in liver function tests

exceeded 3-times the upper limit of the normal range for the test. All of the increases in liver function tests resolved spontaneously before or after cessation of the study medication. According to the package inserts for marketed forms of NAPROSYN, as many as 15% of subjects taking this drug report mild increases in liver function tests similar in magnitude to those observed in the prior study of LT-NS001
The doses of LT-NS001 to evaluate in this study are not anticipated to cause any serious adverse effects. However, there is a possibility that any of the above-mentioned side effects or other adverse effects may occur.

Contactpersonen

Publiek

Logical Therapeutics, Inc

255 Bear Hill Rd, 4th Floor
Waltham, MA 02451
USA

Wetenschappelijk

Logical Therapeutics, Inc

255 Bear Hill Rd, 4th Floor
Waltham, MA 02451
USA

Locaties

Landen waar het onderzoek wordt uitgevoerd

Netherlands

Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Gezonde vrijwilligers
Mannen, 18-70 jaar oud, inclusief (Deel 1)
Mannen/Vrouwen, 45-70 jaar oud, inclusief (Deel 2), vrouwen dienen post menopauzaal te zijn

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Lijdend aan: ernstige aandoening zoals bijvoorbeeld hepatitis B, kanker of HIV/AIDS. Indien gedurende de 90 dagen voorafgaand aan de start van dit onderzoek aan een ander geneesmiddelenonderzoek is deelgenomen.
Indien gedurende de 60 dagen voor start van dit onderzoek bloed gegeven of plotseling bloedverlies gehad van een gelijkwaardige hoeveelheid bloed.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Placebo
Doel:	Behandeling / therapie

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	21-11-2008
Aantal proefpersonen:	36
Type:	Werkelijke startdatum

In onderzoek gebruikte producten en hulpmiddelen

Soort:	Geneesmiddel
Merknaam:	nvt
Generieke naam:	LT-NS001

Ethische beoordeling

Goedgekeurd WMO Datum:	16-11-2007
Soort:	Eerste indiening
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	21-11-2007
Soort:	Eerste indiening
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	28-02-2008
Soort:	Amendement
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	06-03-2008
Soort:	Amendement
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Goedgekeurd WMO Datum:	15-04-2008
Soort:	Amendement
Toetsingscommissie:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
EudraCT	EUCTR2007-006163-71-NL
CCMO	NL20480.056.07