A multinational, multicenter, open-label, single-assignment extension of the MS-LAQ-301 (ALLEGRO) study, to evaluate the long-term safety, tolerability and effect on disease course of daily oral laquinimod 0.6 mg in subjects with relapsing multiple sclerosis

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To make laquinimod 0.6 mg available for all subjects who completed the placebo-controlled MS-LAQ-301 study according to the protocol and to evaluate the long-term safety, tolerability and effect on disease course of daily oral laquinimod 0.6 mg in...

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

Summary

ID

NL-OMON43625

Source
ToetsingOnline

Brief title
Allegro Extension

Condition

- Demyelinating disorders

Synonym
Multiple Sclerose

Research involving
Human

Sponsors and support

Primary sponsor: TEVA Pharma
Source(s) of monetary or material Support: Teva Pharma

Intervention

Keyword: Allegro, laquinimod, long-term effects, Multiple Sclerose

Outcome measures

Primary outcome

As this study is a single arm study, all statistical analysis will be

descriptive in nature.

Secondary outcome

NA

Study description

Background summary

Laquinimod is a novel synthetic compound with high bioavailability, which is currently being developed as an oral formulation for Relapsing Remitting Multiple Sclerosis and Crohn's Disease.
Laquinimod relates to a predecessor compound, roquinimex (Linomide).Roquinimex demonstrated clinical efficacy in Ms patients in Phase II studies. Serious cardiopulmonary toxicities which occurred during Phase III trials led to early termination of these trials. Extensive research of laquinimod shopws much less clinical symtoms and signs of inflammation/toxicity.

Laquinimod is already been examined in 8 Phase I studies, 3 Phase II/IIb studies in MS, an ongoing longterm open-label extension of the Phase IIb study and 2 ongoing clinical Phase II studies in MS. In addition, a Phase II clinical trial in Crohn's Disease patients has been initiated recently.

Study objective

To make laquinimod 0.6 mg available for all subjects who completed the placebo-controlled MS-LAQ-301 study according to the protocol and to evaluate the long-term safety, tolerability and effect on disease course of daily oral laquinimod 0.6 mg in subjects with relapsing multiple sclerosis.

Study design

This is a multinational, multicenter, open-label, single-assignment extension of the MS-LAQ-301 study, to evaluate the long-term safety, tolerability and effect on disease course of daily oral laquinimod 0.6 mg in subjects with relapsing multiple sclerosis.

Eligible subjects will be treated with laquinimod 0.6 mg capsules once daily. Subjects completing the full-duration of the double-blind MS-LAQ-301 study (completion of Termination visit) according to the MS-LAQ-301 protocol will be offered the opportunity to enter the MS-LAQ-301E study. In this open-label study, the subjects will be treated with laquinimod 0.6 mg (regardless of their initial treatment assignment during the MS-LAQ-301 study) until laquinimod 0.6 mg is commercially available for the treatment of MS patients or until its development for MS is stopped.

Scheduled in-clinic visits will be conducted at Baseline (Month 0E) (the Termination visit of MS-LAQ-301 will serve as the baseline visit of MS-LAQ-301E) and at months 1E, 2E, 3E, 6E and every 6 months thereafter, until Termination/Early discontinuation.
The following assessments will be performed at the specified time points: Vital signs,weight,height, physical- and neurological examinations, bloodwithdrawl and urinetests (including pregnancy test), ECG's. The Sponsor may decide to perform a Magnetic Resonance imaging (MRI) scan at Termination/early discontinuation visit for all subjects.
Starting from Visit Month 6E, all subjects will be regularly contacted by telephone every 3 months between the scheduled visits and asked a general question regarding their well-being. In addition: women of child-bearing potential will be contacted by phone for the monthly home pregnancy urine test call.

For purposes of neurological/medical assessments, the study will be divided into 2 periods:
Period 1: in which all subjects will continue to be evaluated by 2 distinct physicians - a Treating and an Examining Neurologists/ Physician (as in the MS-LAQ-301 study).
Period 2: in which all subjects will be assessed by a single Study Physician/ Neurologist.
The Sponsor will inform the sites when to change from Period 1 to Period 2.

Intervention

All patients receive once daily 0.6 mg Laquinimod.
The allowed treatment for a relapse will be intravenous Methylprednisolone 1 g/day for up to 5 consecutive days.

Study burden and risks

During the first year of the study:physical examination: 3x/ ECG 3x/ bloodwithdrawl and urine test 6x/ home pregnancy test 7x/ neurological tests 3x/ MFIS 3x.
Followed by: every year: physical examination 2x/ ecg 2x/ bloodwithdrawl and urinetest 2x/ home pregnancy test 10x/ neurological examination 2x/ MFIS 2x

Most common reported adverse events as a result of laquinimod: backpain, stomach ache,chestpain, difficulties with falling into sleep or stayng asleep, cystitis, vaginal fungal infections and anxiety.
Laquinimod may cause elevation of liver enzymes, usually within the first few months of treatment. In the majority of cases the abnormality was temporary and resolved on its own without any treatment and without stopping the study drug. In a few other cases laquinimod was stopped and liver enzymes returned to normal.

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

1)Subjects must have completed the Termination visit of MS-LAQ-301 (completion of all Termination visit activities) according to the MS-LAQ-301 protocol.
2)Women of child-bearing potential must practice an acceptable method of birth control during the study and up to 30 days after the last dose of study drug.
3)Subjects must be willing and able to comply with the protocol requirements for the duration of the study.
4)Subjects must be able to comprehend, sign and date a written informed consent prior to entering the MS-LAQ-301 study

Exclusion criteria

1)Premature discontinuation from the MS-LAQ-301 study, for any reason
2)Pregancy [according to urine dipstick β-HCG test perfomed at Baseline (Month 0E) visit] or breastfeeding.
3)Subjects with clinically significant or unstable medical or surgical condition detected or worsened during MS-LAQ-301 study, which preclude safe partcipation and completion of the MS-LAQ-301E study. Acute exacerbation of MS will not exclude participation in the MS-LAQ-301E study.
4)Use of inhibitors of CYP3A4 within 2 weeks prior to baseline visit (V0E, Month 0E)

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-12-2009
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt, nog niet op de markt
Generic name:	laquinimod

Ethics review

Approved WMO Date:	28-07-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-10-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-01-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-01-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-07-2010

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-10-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-01-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	23-12-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-01-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-02-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-03-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-11-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-08-2016
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-10-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
Other	clinicaltrials.gov (nummer nog onbekend)
EudraCT	EUCTR2009-012989-30-NL
CCMO	NL28891.003.09