A Phase 3, randomized, double-blind, parallel-group, placebo-controlled, multi-center study to evaluate the efficacy and safety of two doses of GLPG1690 in addition to local standard of care for minimum 52 weeks in subjects with idiopathic pulmonary fibrosis.

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Primary Objective-To evaluate the efficacy of two doses of GLPG1690 in addition to local standard of care compared to placebo in subjects with idiopathic pulmonary fibrosis (IPF) as evaluated by the rate of decline of forced vital capacity (FVC)...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON49396

Source
ToetsingOnline

Brief title
GLPG1690-CL-304

Condition

- Respiratory tract infections

Synonym
Idiopatic pulmonary fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Galapagos NV
Source(s) of monetary or material Support: Pharmaceutische industrie

Intervention

Keyword: idiopathic, placebo-controlled, pulmonary fibrosis, standard of care

Outcome measures

Primary outcome

Primary Endpoint

Rate of decline of FVC (in mL) over a period of 52 weeks

Secondary outcome

Key Secondary Endpoints

- Disease progression defined as the composite endpoint of first

occurrence of *10% absolute decline in percent predicted forced vital

capacity (%FVC) or all-cause mortality at 52 weeks

- Time to first respiratory-related hospitalization until the end of the study

- Change from baseline in the SGRQ total score at 52 weeks

Study description

Background summary

GLPG1690 is a small-molecule autotaxin inhibitor targeting disease-relevant signal transduction pathways, in clinical development for the treatment of subjects with IPF.

Disease-modifying drugs such as pirfenidone and nintedanib have been shown to have a beneficial effect on the rate of decline in lung function (as measured

by FVC over 1 year) and show a trend in favor of a reduction in mortality in patients with mild to moderate IPF. However, the residual decline of FVC over 1 year remains substantial. Therefore, there remains a considerable unmet medical need. In a proof-of-concept Phase 2a study, FVC values remained stable in the majority of subjects after 12 weeks of treatment with GLPG1690 600 mg once daily (q.d.). Moreover, 12 weeks of treatment with GLPG1690 600 mg q.d. was generally well tolerated. The current Phase 3 study is the next step in the clinical development of GLPG1690, evaluating the efficacy and safety of two doses of orally administered GLPG1690 compared to placebo in subjects with IPF in addition to local standard of care.

Study objective

Primary Objective
-To evaluate the efficacy of two doses of GLPG1690 in addition to local standard of care compared to placebo in subjects with idiopathic pulmonary fibrosis (IPF) as evaluated by the rate of decline of forced vital capacity (FVC) over a period of 52 weeks

Secondary Objectives

Key Secondary Objectives
-To evaluate the impact of two doses of GLPG1690 in addition to local standard of care compared to placebo in subjects with IPF on:
-disease progression defined as deterioration of FVC or all-cause mortality at 52 weeks
-respiratory related hospitalization until the end of the study
-changes in quality of life (measured by St. George*s Respiratory Questionnaire [SGRQ] total score) at 52 weeks

Study design

This clinical Phase 3 study is a randomized, double-blind, parallel-group, placebo-controlled multicenter study designed to evaluate the efficacy and safety of two doses of orally administered GLPG1690 in addition to local standard of care for at least 52 weeks in adult subjects with a centrally confirmed diagnosis of IPF. Local standard of care for IPF is defined as receiving either pirfenidone or nintedanib, at a stable dose for at least two months before screening, and during screening; or neither pirfenidone or nintedanib (for any reason). A stable dose is defined as the highest dose tolerated by the subject during those two months. Subjects will have their end of study treatment (EoST) and follow-up visit planned when the last subject has reached his or her Week 52 visit.

Intervention

GLPG1690 or placebo to match will be administered as film-coated tablets for oral use once daily.
Following doses will be tested:
- GLPG1690 Dose A
- GLPG1690 Dose B
- Placebo to match"

Study burden and risks

Risks with GLPG1690
GLPG1690 has been tested in healthy volunteers and IPF subjects. GLPG1690 has been found to be generally safe and well tolerated. The majority of reported side effects from these studies have been mild in intensity. Side effects were very similar as those found in subjects with IPF. Contact the investigator if you develop:
- cough
- headache
- upper and lower respiratory tract infection

Risks and discomfort from procedures
* Blood collection: Collecting blood is normally done as part of routine medical care and may cause some discomfort, bleeding, or bruising where the needle enters the body. A small blood clot may form at this site or there may be swelling in the area. Rarely, fainting or local infection may occur. Care will be taken to prevent these events.
* High-resolution computed tomography (HRCT) if requested by your study doctor. This procedure will expose the patient to a small amount of X-rays in order to get a picture of their lungs. The total exposure will be equivalent to approximately 2 years of natural background radiation in the environment. During the scan, the patient will be asked to lie very still and sometimes you will be asked to hold your breath. The patient should not move until the images are taken (about 15 to 30 minutes). They may feel uncomfortable from this immobilization.
* ECG: For ECGs collected in this study, the patient will have sticky electrodes stuck to your chest, arms, and legs. The adhesive (sticky substance) and gel found in the electrodes and adhesive pads can be irritating to their skin, causing redness or itching. For male subjects, the study staff may also have to shave small areas to make sure the electrodes stick properly to your skin.
* Blood pressure: Although it is very rare, the patient might bruise from having your blood pressure taken. In addition, the blood pressure cuff will be very tight and might pinch a little for a short time.
* Lung function tests (spirometry and DLCO): Lung function tests may cause light headedness, dizziness, tiredness, coughing, or shortness of breath. The patient may experience some general chest discomfort from the deep breaths required to perform these tests.
* 6 Minute Walk Test (6MWT): This test may cause light headedness, dizziness,

tiredness, coughing, or shortness of breath. The patient may experience some general chest discomfort from the increased breathing required to walk for 6 minutes.

Benefit
The patient may or may not benefit from taking part in this study. If the patient would benefit, their disease and decrease in lung function may progress more slowly. Participating in clinical research studies like this may also give the patient the opportunity to better understand your own disease and to have more opportunities to talk and clarify any aspect of their disease. By participating in this study, their condition will be closely monitored. In addition, this study may be helpful in developing a new therapy for others with similar illnesses.

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

- Male or female subject aged *40 years on the day of signing the ICF.
- A diagnosis of IPF within 5 years prior to the screening visit, as per applicable ATS/ERS/JRS/ALAT guidelinesat the time of diagnosis.
- Chest HRCT historically performed within 12 months prior to the screening visit and according to the minimum requirements for IPF diagnosis by central review based on subject's HRCT only (if no LB available), or based on both HRCT and LB (with application of the different criteria in either situation). If an evaluable HRCT <12 months prior to screening is not available, an HRCT can be performed at screening to determine eligibility, according to the same requirements as the historical HRCT.
- Subjects receiving local standard of care for the treatment of IPF, defined as either pirfenidone at a stable dose for at least two months before screening, and during screening; or nintedanib, or neither pirfenidone or nintedanib (for any reason). A stable dose is defined as the highest dose tolerated by the subject during those two months.
- The extent of fibrotic changes is greater than the extent of emphysema on the most recent HRCT scan (investigator-determined).
- Meeting all of the following criteria during the screening period: FVC * 45% predicted of normal, Forced expiratory volume in 1 second (FEV1)/FVC *0.7, DLCO corrected for Hb *30% predicted of normal.
- Estimated minimum life expectancy of at least 30 months for non IPF related disease in the opinion of the investigator.
- Male subjects and female subjects of childbearing potential agree to use highly effective contraception/preventive exposure measures from the time of first dose of IMP (for the male subject) or the signing of the ICF (for the female subject), during the study, and until 90 days (male) or 30 days (female) after the last dose of IMP.
- Able to walk at least 150 meters during the 6MWT at screening Visit 1; without having a contraindication to perform the 6MWT (see Appendix 10) or without a condition putting the subject at risk of falling during the test (investigator's discretion). The use of a cane is allowed, the use of a stroller is not allowed at all for any condition. At Visit 2, for the oxygen titration test, resting SpO2 should be *88% with maximum 6 L O2/minute; during the walk, SpO2 should be *83% with 6 L O2/minute or *88% with 0, 2 or 4 L O2/minute.

Exclusion criteria

- History of malignancy within the past 5 years (except for carcinoma in situ of the uterine cervix, basal cell carcinoma of the skin that has been treated with no evidence of recurrence, prostate cancer that has been medically managed through active surveillance or watchful waiting, squamous cell carcinoma of the

skin if fully resected, and Ductal Carcinoma In Situ).
- Clinically significant abnormalities detected on ECG of either rhythm or conduction, a QTcF >450 ms, or a known long QT syndrome. Patients with implantable cardiovascular devices (e.g. pacemaker) affecting the QT interval time may be enrolled in the study based upon investigator judgment following cardiologist consultation if deemed necessary, and only after discussion with the medical monitor
- Acute IPF exacerbation within 6 months prior to screening and/or during the screening period.The definition of an acute IPF exacerbation is as follows: Previous or concurrent diagnosis of IPF; Acute worsening or development of dyspnea typically < 1 month duration; Computed tomography with new bilateral ground-glass opacity and/or consolidation superimposed on a background pattern consistent with usual interstitial pneumonia pattern and deterioration not fully explained by cardiac failure or fluid overload- Lower respiratory tract infection requiring antibiotics within 4 weeks prior to screening and/or during the screening period.
- Lower respiratory tract infection requiring antibiotics within 4 weeks prior to screening and/or during the screening period.
- Interstitial lung disease associated with known primary diseases (e.g. sarcoidosis and amyloidosis), exposures (e.g. radiation, silica, asbestos, and coal dust), or drugs (e.g. amiodarone).
- Diagnosis of severe pulmonary hypertension (investigatordetermined).
- Unstable cardiovascular, pulmonary (other than IPF), or other disease within 6 months prior to screening or during the screening period (e.g. acute coronary disease, heart failure, and stroke).
- Had gastric perforation within 3 months prior to screening or during screening, and/or underwent major surgery within 3 months prior to screening, during screening or have major surgery planned during the study period.
- History of nintedanib-related increase in ALT and/or AST of >5xULN and increased susceptibility to elevated LFT; moderate to severe hepatic impairment (Child-Pugh B or C) and/or abnormal LFT at screening, defined as AST, and/or ALT, and/or total bilirubin *1.5xULN, and/or GGT *3xULN. Retesting is allowed once for abnormal LFT.
- Abnormal renal function defined as estimated creatinine clearance, calculated according to Cockcroft-Gault calculation (CCr) <30 mL/min. Retesting is allowed once.
- Use of any of the following therapies within 4 weeks prior to screening and during the screening period, or planned during the study: warfarin, imatinib, ambrisentan, azathioprine, cyclophosphamide, cyclosporine A, bosentan, methotrexate, sildenafil (except for occasional use), prednisone at steady dose >10 mg/day or equivalent.
- Clinical laboratory test suggestive of cholestasis with total serum bile acid levels >3xULN.

Study design

Design

Study phase:	3
Study type:	Interventional
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):	07-05-2019
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GLPG1690
Generic name:	GLPG1690

Ethics review

Approved WMO Date:	06-12-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-04-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-03-2020

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-04-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2018-001406-29-NL
ClinicalTrials.gov	NCT03733444
CCMO	NL67478.078.18