Rationale, Design and Objectives of Two Phase III, Randomized, Placebo-Controlled Studies of GLPG1690, a Novel Autotaxin Inhibitor, in Idiopathic Pulmonary Fibrosis (ISABELA 1 and 2)


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Introduction and rationale

IPF is a rare disease with an estimated prevalence in Europe and North America of 3–9 cases per 100,000.1 IPF is associated with progressive loss of lung function and median survival without therapy is 2–3 years.2,3

Current SOC with the antifibrotic agents pirfenidone and nintedanib slows disease progression, but prognosis remains poor.

The first-in-class autotaxin inhibitor GLPG1690 has demonstrated encouraging results in early clinical trials, including the phase IIa FLORA study, warranting further evaluation as a once-daily oral therapy for IPF.

ISABELA 1 and 2 (NCT03711162 and NCT03733444) are two identically designed, phase III studies with the primary objective of evaluating the efficacy of GLPG1690 compared with placebo, each given on top of SOC (i.e. pirfenidone or nintedanib), in subjects with IPF diagnosis by central review.

Study design

In each study, ~750 subjects will be randomized 1:1:1 across three arms: randomization will be stratified by local SOC (i.e. pirfenidone or nintedanib) and by geographical area. Treatment will be given for 152 weeks; studies will continue until the last subject reaches 52 weeks in the study.

Day –28 to Day 1

Day 1

FLORA study

Day 0

ISABELA 1

ISABELA 2

FLORA study

FLORA study

MAY 2017

NOV 2018

NOV 2018

May 2017

Nov 2018

Nov 2018

Endpoints

Primary

Rate of decline in FVC over 52 weeks

Secondary

Disease progression: time to first respiratory-related hospitalization; SGRQ change from baseline

Other secondary

Additional efficacy measures (e.g. GW64, tough OAS cough, urge to cough, LDDQ, mortality, biomarkers; PK and PD; QoL (EQ-5D, K-BILD); safety

Conclusions

The study design is innovative and ambitious

For the first time, a registrational study will assess a novel IPF treatment not only as monotherapy, but also in combination with pirfenidone or nintedanib

Key milestones

Phase IIa FLORA study initiated

May 2017

May 2017

ISABELA 1 recruitment initiated

NOV 2018

ISABELA 2 recruitment initiated

NOV 2018

Participating countries

APAC

Australia

China

India

Japan

Korea

New Zealand

South Africa

SS

Thailand

Vietnam

LA

Brazil

Canada

South Africa

EMEA

APAC, Asia-Pacific; EMEA, Europe, the Middle East and Africa; LA, Latin America; NA, North America

Key eligibility criteria

Inclusion

IPF diagnosis (last 5 years)

IPF diagnosis, by central review, based on HRCT

Progression of IPF (worsening of any IPF severity measures over 12 months)

Recruiting local SOC (i.e. pirfenidone or nintedanib), neither discontinued nor interrupted

Visit 1: able to walk ≥150 m during 6MW

Pronounced non-dependent lung volume reduction (transplant)

LRTI requiring antibiotics

Interstitial lung disease associated with known primary diseases, malignancies or drugs

Clinically significant ECG abnormalities; QTcF > 450 ms

Medications: substrates metabolized by CYP2C8; strong inducers/inhibitors of CYP3A4 do not allowed

Unstable CV, pulmonary hypertension > extent of emphysema

FVC ≥35% predicted of normal

FEV1 ≥88% with max 6 L O2

SpO2 ≥88% with max 6 L O2

Hb level ≥10 g/dL

Other secondary

Additional efficacy measures (e.g. GW64, tough OAS cough, urge to cough, LDDQ, mortality, biomarkers; PK and PD; QoL (EQ-5D, K-BILD); safety

Exclusion

Acute IPF exacerbation

Severe pulmonary hypertension

Lung volume reduction surgery/transplant

LRTI requiring antibiotics

Interstitial lung disease associated with known primary diseases, malignancies or drugs

Clinically significant ECG abnormalities; QTcF > 450 ms

Medications: substrates metabolized by CYP2C8; strong inducers/inhibitors of CYP3A4 do not allowed

Unstable CV, pulmonary hypertension > extent of emphysema

FVC ≥35% predicted of normal

FEV1 ≥88% with max 6 L O2

SpO2 ≥88% with max 6 L O2

Hb level <10 g/dL

References


Disclosures

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