Poster #36

SAFETY, TOLERABILITY AND PHARMACOKINETICS OF A NOVEL CFTR POTENTIATOR GLPG3067 IN HEALTHY VOLUNTEERS

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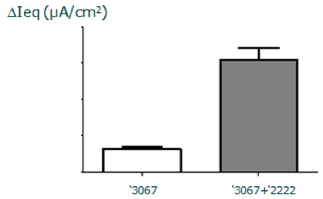
Introduction

GLPG3067 is a novel cystic fibrosis transmembrane conductance regulator (CFTR) potentiator in clinical development for the treatment of cystic fibrosis (CF) and represents one of the components of a future potentiator/corrector combination therapy targeting the F508del CF population.

We report the preliminary results of a Phase 1 study of GLPG3067 in healthy volunteers.



Objectives

- To evaluate the safety and tolerability of single ascending oral doses (SAD) and multiple ascending oral doses (MAD) of GLPG3067 administered to healthy subjects
- To evaluate safety and tolerability of the combination of GLPG3067 and GLPG2222
- To characterize the pharmacokinetics (PK) of GLPG3067 after single and multiple oral administrations alone or in combination with GLPG2222
- To evaluate the relative bioavailability of two formulations of GLPG3067

Methods

Randomized, double-blind, placebo-controlled study:

- SAD: 2 alternating cohorts of 8 subjects received single oral doses ranging from 15 to 1000 mg of GLPG3067 (or placebo)
- MAD: 6 sequential cohorts of 8 subjects received GLPG3067 administered orally at doses starting from 45 mg q.d. for 14 days and received a combination of GLPG3067 and GLPG2222
- Bioavailability: consecutive oral administration of 100 mg GLPG3067 as suspension or tablet after standard breakfast, and tablet under fasted condition

For every cohort, subjects were randomized in a 3:1 ratio (active versus placebo)

Study drug was administered as oral suspension after standard breakfast or as a tablet in the BA part of the study

Safety results

- All TEAEs were rated mild or moderate in intensity
- The study drug was temporarily discontinued in one subject from MAD part of the trial due to elevated liver enzyme values. Study drug was discontinued in onother subject from the combination part due to a TEAE being maculopapular rash.
- No deaths or serious adverse events occurred during the study
- The preliminary blinded data of the trial suggest that the most frequently reported TEAEs were headache, fatigue, back pain and diarrhoea

Pharmacokinetics

SAD

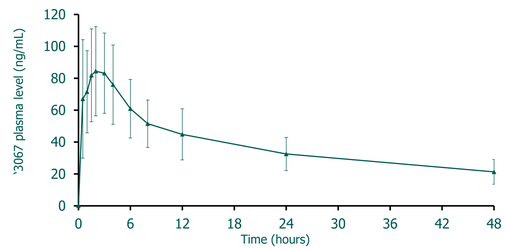


Figure 1: Mean (±SE) GLPG3067 plasma levels after a single oral dose of 15 mg, as oral suspension in fed conditions

Bioavailability

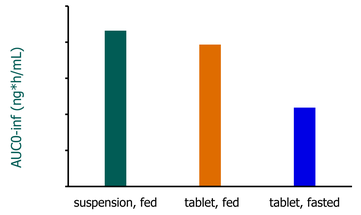


Figure 2: Bar graph GLPG3067 $AUC_{0\text{-}inf}$ after single dose administration of 100 mg of GLPG3067 as suspension (green) and tablet (orange) in fed condition or tablet under fasted condition (blue)

MAD GLPG3067 and Combination GLPG3067 and GLPG2222

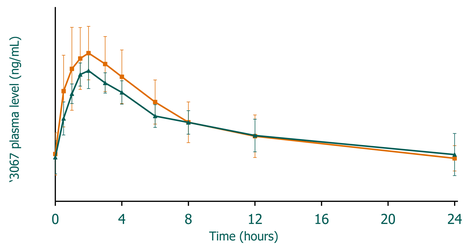


Figure 3: Pharmacokinetics of GLPG3067 when dosed for 14 days as single compound or in combination with GLPG2222. Mean (±SE) GLPG3067 plasma concentration time profiles at D14 after multiple oral doses of: GLPG3067 alone (orange), or GLPG3067 combined with GLPG2222 (green)

* GLPG3067 dosed as suspension and GLPG2222 as tablet

Conclusions

- GLPG3067 was generally well tolerated when dosed up to 1000 mg as single dose and up to 500 mg b.i.d. for 14 days in healthy subjects
- GLPG3067 showed less than dose proportional increases in exposure, at the higher dose range
- GLPG3067 suitable for q.d. and b.i.d. dosing regimen
- Suitable formulation identified for progression of GLPG3067
- GLPG3067 exposure not apparently altered in the presence of GLPG2222, and GLPG2222 exposure similar in the presence of two different doses of GLPG3067

Poster available online at: www.glpg.com