SAFETY AND EFFICACY OF GLPG0634, A SELECTIVE JAK1 INHIBITOR, IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF A 4-WEEK PHASE IIA MULTI-CENTER, DOSE RANGING STUDY

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Study design

This Phase IIA study was a 4-week, double-blind, placebo-controlled dose-ranging study in 91 patients with active RA, with insufficient response to methotrexate (MTX), and who had not received biological therapies. Patients continued their stable background therapy of MTX.

In this multinational study, the safety and efficacy of GLPG0634 were evaluated at doses of 30, 75, 150 and 300 mg or placebo (pbo), as once daily (QD) oral treatment. The study was not powered to show statistical significance.

Results

Demographics (Table 1)

- an unexpected imbalance in baseline patient characteristics favored the placebo group (short duration of disease)

Efficacy (Figures 1 and 2)

- dose dependent improvements in CRP, DAS28, ACR20, TJC68, SJC66, and HAQ-DI

Safety (Tables 2 and 3)

- statistically significant improvements were found for CRP, DAS28, ACR50, and HAQ-DI

- no SAEs or AEs leading to treatment interruption

- no hypercholesterolemia and no LFTs >1.5 x ULN

- no neutropenia

Discussion and conclusions

- Selective inhibition of JAK1 by once-daily GLPG0634 from 75 – 300 mg was well tolerated and efficacious in this 4 week study.

- The encouraging short term efficacy and favourable safety profile in this study supports the potential of selective inhibition of JAK1 as a future RA treatment option, and confirms data from a previous Proof of Concept study at a 200 mg daily dose.

- A dose trend for improvement in RA disease parameters was found: 30 mg QD was sub-optimal, while doses of 75, 150 and 300 mg showed promising efficacy, with similar response rates in CRP, TJC, SJC and DAS28.

- An imbalance in baseline patient characteristics may have influenced the study outcome:
  - a relatively high placebo response correlating with a short history of RA
  - the most severely diseased 150 mg group showed a robust response in CRP, TJC, SJC and DAS28.

- A dose trend for improvement in RA disease parameters was found: 30 mg QD was sub-optimal, while doses of 75, 150 and 300 mg showed promising efficacy, with similar response rates in CRP, TJC, SJC and DAS28.

- Overall drug-related TEAEs reported in ≥1 patient

Table 1: Baseline patient characteristics

Table 2: Changes in lab parameters of particular interest

Table 3: TEAEs at least possibly related to study medication

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