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LONG TERM SAFETY AND EFFICACY OF FILGOTINIB IN A PHASE 2B OPEN LABEL EXTENSION STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS UP TO 144 WEEKS

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Background: Filgotinib (GLPG0634, GS-6034) is an oral JAK1 selective inhibitor with a favorable safety and efficacy profile in two 24-week Phase 2b studies as add-on to methotrexate (DARWIN 1) or as monotherapy (DARWIN 2) in patients with active rheumatoid arthritis (RA). Three daily doses were tested (50mg, 100mg or 200mg) in comparison to placebo.

Objectives: To assess long term safety and efficacy of filgotinib 200mg daily in patients from the DARWIN 3 Phase 2 open-label extension study.

Methods: Patients who completed DARWIN 1 or 2 and enrolled in DARWIN 3 received filgotinib 200mg once daily or 100mg twice daily, depending on prior treatment assignment. The DARWIN 3 data cut off was when the last patient reached extension Week 60. For safety, all data from the first intake of filgotinib in DARWIN 1/2/3 were analysed (up to 144 weeks).

Results: 877 patients participated in DARWIN 1 or 2, 790 completed and 739 entered DARWIN 3 from 22 countries (82% females, mean age 53y). 559 patients (75.6%) completed Week 60, 9.3% discontinued due to positive Quantiferon, 7.8% due to other adverse events, 6.8% for other reasons and 0.3% due to insufficient response. Overall exposure to filgotinib was 1314 patient-years (PYE).

Treatment-emergent adverse events (157.7/100PYE), serious adverse events (5.3/100PYE) and serious infections (1.9/100PYE) occurred at similar rates compared to the core studies, however infections decreased on a percentage basis from 15% (109/739, W0-12) to 5% (25/549, W85-96). 16 cases of Herpes zoster

were reported (1.2/100PYE), 6 cases of malignancy (excl. NMSC) (0.5/100PYE) and 1 case of MACE (0.1/100PYE). There was no active case of tuberculosis. Three fatalities were reported (0.2/100PYE). Mean change from baseline (CFB) at Week 96 and CTCAE toxicity grading in lab parameters of special interest are shown in table 1.

Table 1: Mean CFB at Week 96 and CTCAE toxicity grading of selected lab parameters

	Mean CFB	CTCAE Grade 3-4 (%)
Hb	+6.5 g/L	0.4
Neutrophils	-1.73 giga/L	1
Lymphocytes	-0.19 giga/L	2
Creatinine	+8.2 µmol/L	0
ALT	+6.1 U/L	0.4
LDL	+13%	-
HDL	+23%	-
Tot chol/HDL	-4%	-
NK cells	-0.02 giga/L	-

Based on an observed case analysis 84% (505/601), 65% (389/601), 44% (267/601) and 51% (299/587) of patients reached ACR20, ACR50, ACR70 and DAS28(CRP) remission at Week 60 respectively.

Conclusions: With 1314 patient-years of exposure, the safety profile of filgotinib appears consistent with that of previously reported double-blind studies and the clinical response appears durable.

References: 1Westhovens R et al. Ann Rheum Dis 2016;0:1-11.

2Kavanaugh A et al. Ann Rheum Dis 2016;0:1-11

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