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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Introduction

Filgotinib (GLPG0634, GS-6034), an oral JAK1 selective inhibitor, has demonstrated safety and efficacy data in two 24-week Phase 2B core studies as add-on to methotrexate (DARWIN 1) or as monotherapy (DARWIN 2) in patients with active rheumatoid arthritis (RA) and inadequate response to methotrexate (MTX)[1,2]. Three daily doses were tested (50 mg, 100 mg or 200 mg) compared with placebo (PBO). Patients who completed the core studies were eligible to enroll in the open-label extension DARWIN 3.

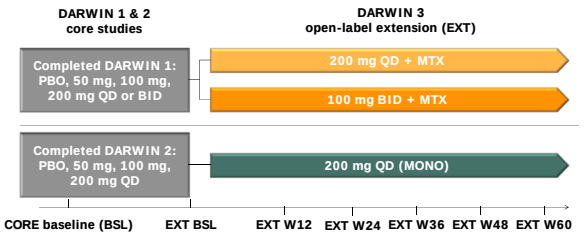
Objectives

The primary objective of the DARWIN 3 interim analysis was to evaluate the long-term safety and tolerability of filgotinib 200 mg once daily (QD) or 100 mg twice daily (BID) for the treatment of RA. Secondary objectives included evaluation of long-term efficacy.

Methods

- The interim analysis data cut-off was when the last patient reached extension Week 60 (EXT W60)
- For the efficacy analysis, all available data up to EXT W60 for the 739 patients who started DARWIN 3 were included. Baseline data were those of the core studies
- For the safety analysis, all available data at the time of cut-off (August 9, 2016) for the 739 subjects who started DARWIN 3 were included, as of the moment they started using filgotinib (in DARWIN 1, 2, or 3). The baseline was filgotinib treatment initiation

Study design



Baseline characteristics

Table 1. Baseline and disease characteristics (start of core studies)

	200 mg + MTX (N=510)	200 mg MONO (N=229)	Overall total (N=739)
Age, mean, years	53.4	51.9	52.9
Female, %	81	83	82
Duration of RA, mean, years	8.8	9.5	9.0
DAS28 (CRP), mean	6.1	6.2	6.1
CRP, mean, mg/L	23.8	27.9	25.1
MTX, mean weekly dose, mg/week	17.0	NA	NA
Previous corticosteroids, %	58	70	62
Previous bDMARDs, %	4	1	3

Early discontinuations

Figure 1. Patient disposition

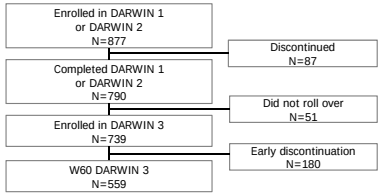


Table 2. Reasons for discontinuation in DARWIN 3

	200 mg + MTX (N=510)	200 mg MONO (N=229)	Overall total (N=739)
Ongoing, n (%)	399 (78)	166 (73)	565 (77)
Discontinued, n (%)	111 (22)	63 (28)	174 (24)
Safety, n (%)	76 (15)	47 (21)	123 (17)
QuantiFERON-TB Gold in tube test, n (%)	39 (8)	25 (11)	64 (9)
AE stopping rule, n (%)	25 (5)	14 (6)	39 (5)
Other AE, n (%)	12 (2)	7 (3)	19 (3)
AE + treatment failure, n (%)	0 (0)	1 (0.4)	1 (0.1)
Efficacy, n (%)	0 (0)	1 (0.4)	1 (0.1)
Other reasons, n (%)	35 (7)	15 (7)	50 (7)

Results: safety – lab

Table 3. Lab parameters of interest, CTCAE grade 3-4 (%), version 3.0

	200 mg + MTX (N=510)		200 mg MONO (N=229)		Overall total (N=739)	
	Grade 3	Grade 4	Grade 3	Grade 4	Grade 3	Grade 4
Hb	0.6	0.0	0.0	0.0	0.4	0.0
Neutrophils	0.4	0.4	0.9	0.4	0.5	0.4
Lymphocytes	1.6	0.4	0.9	0.0	1.4	0.3
Creatinine	0.0	0.0	0.0	0.0	0.0	0.0
ALT	0.4	0.0	0.4	0.0	0.4	0.0

Figure 2. Total cholesterol/HDL over time

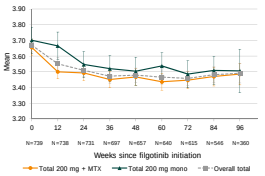


Figure 3. Hemoglobin (g/L) over time

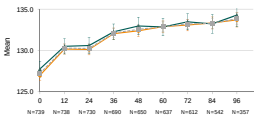


Figure 4. Lymphocytes (giga/L) over time

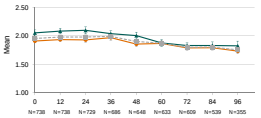


Figure 5. Creatinine (µmol/L) over time

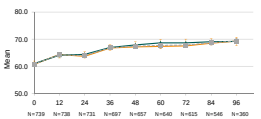
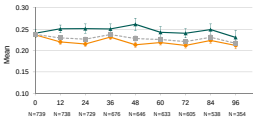


Figure 6. NK cells (giga/L) over time

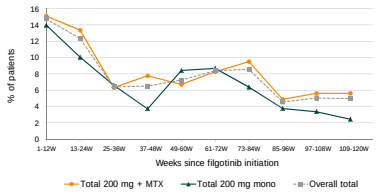


Results: safety

Table 4: Safety overview

Rate per 100 PYE (number of events)	200 mg + MTX (N=510) (929 PYE)	200 mg MONO (N=229) (385 PYE)	Overall total (N=739) (1314 PYE)
TE AE	158.0 (1467)	157.1 (605)	157.7 (2072)
Serious TE AE	4.2 (39)	7.8 (30)	5.3 (69)
Serious infections	1.3 (12)	3.4 (13)	1.9 (25)
SAE leading to death	0.1 (1)	0.5 (2)	0.2 (3)
TE AE leading to stop	9.3 (86)	16.1 (62)	11.2 (148)
AEs of special interest			
Herpes zoster	1.3 (12)	1.0 (4)	1.2 (16)
Active tuberculosis	0 (0)	0 (0)	0 (0)
Malignancies (excl. NMSC)	0.3 (3)	0.8 (3)	0.5 (6)
MACE	0.1 (1)	0 (0)	0.1 (1)

Figure 7: Infections and infestations over time



Conclusions

Filgotinib showed:

- A safety profile consistent with that of previously reported core studies [1,2], with 1314 patient-years exposure
- Sustained improvement in signs and symptoms of active RA, irrespective of dosing regimen (QD/BID) or background treatment (+MTX/MONO), after 60 weeks of treatment in the open-label extension study (EXT W60)

Results: efficacy

Figure 8. ACR20, ACR50 and ACR70, OC

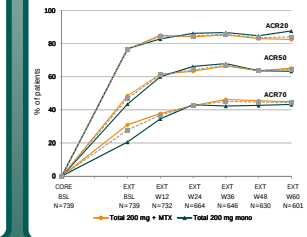
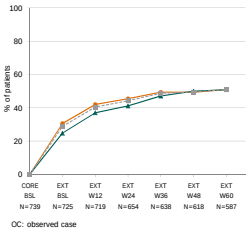


Figure 9. DAS28(CRP) remission, OC



Acknowledgements

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References

[1]Westhovens R, et al. *Ann Rheum Dis* 2017;76:998–1008
[2]Kavanaugh A, et al. *Ann Rheum Dis* 2017;76:1009–1019

Poster available online at: www.glpg.com/filgotinib

Galápagos