Efficacy of filgotinib, a selective JAK1 inhibitor, is independent of prior anti-TNF exposure: subgroup analysis of the Phase 2 FITZROY study in moderate-to-severe Crohn's disease

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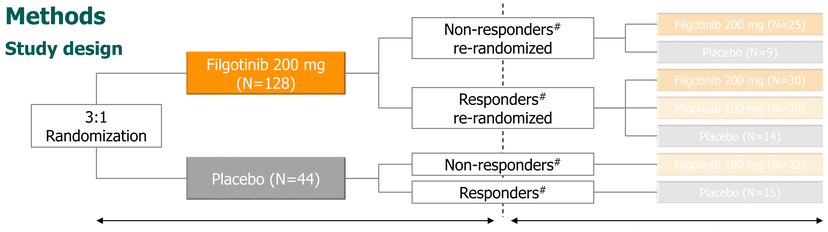
Introduction

- Filgotinib is a once-daily, orally administered, selective Janus kinase 1 (JAK1) inhibitor
- The 20-week, randomized, placebo-controlled, Phase 2 FITZROY study evaluated the efficacy and safety of filgotinib in patients with active Crohn's disease (Vermeire *et al.* 2017)
- The FITZROY study achieved its primary endpoint: significantly more patients achieved clinical remission (CDAI<150) with filgotinib compared with placebo at week 10
- Filgotinib also had an acceptable safety profile

Results at Week 10 of an exploratory subgroup analysis based on prior exposure to anti-tumor necrosis factor (TNF) therapy are presented

Methods

Study design



#Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

Key inclusion criteria

- Ileal, colonic, or ileocolonic Crohn's disease
- CDAI 220–450
- Endoscopic confirmation of active disease with ulceration; scored using central reading based on Simplified Endoscopy Score for Crohn's Disease (SES-CD) scale

Key exclusion criteria

- Indeterminate colitis, ulcerative colitis
- Surgical bowel resection within past 6 months

Concomitant medications

- Allowed: Stable doses of oral steroids, mesalazine, Crohn's disease-related antibiotics, and probiotics
- Not allowed: Anti-TNFs, immunomodulators (azathioprine, methotrexate, 6-mercaptopurine)

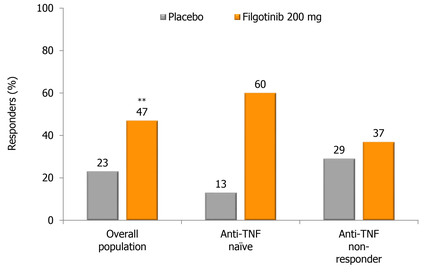
Baseline characteristics*

	Anti-TNF naïve		Anti-TNF non-responder#	
	Placebo (N=16)	200 mg (N=57)	Placebo (N=28)	200 mg (N=73)
Age, mean, years	31.8	38.9	37.0	36.3
Female, %	68.8	50.9	53.6	57.5
Duration of CD, median, years	2.68	4.16	6.55	7.83
CDAI, mean	292.9	279.5	301.9	300.4
IBDQ, mean	125.6	127.7	118.0	119.2
SES-CD, mean	16.9	13.0	15.2	15.1
CRP, median, mg/L	6.95	6.20	10.80	8.80
CRP >10 mg/L, %	25.0	38.6	50.0	43.8
Concomitant oral corticosteroids, %	50.0	49.1	53.6	50.7
Mean daily dose, mg	21.4	19.4	21.3	21.6

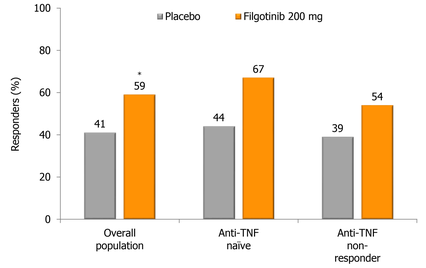
*Safety population; #Primary or secondary non-responder or intolerant to anti-TNF treatment

Results: Efficacy at Week 10

Clinical remission, ITT-NRI (CDAI <150)

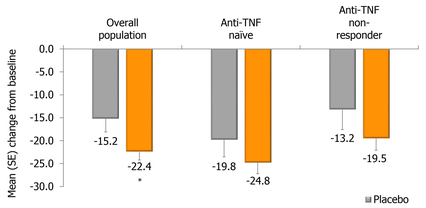


Clinical response, ITT-NRI (≥100-point reduction in CDAI)

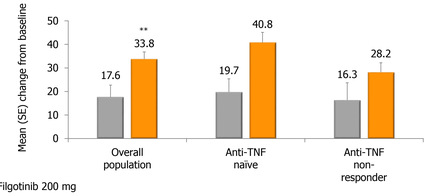


Study was not powered to detect differences in the anti-TNF patient subgroups (no inferential statistics calculated in the subgroups); *p<0.05; **p<0.01

PRO2 score, ITT-LOCF

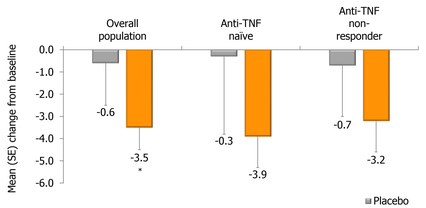


Total IBDQ score, ITT-LOCF

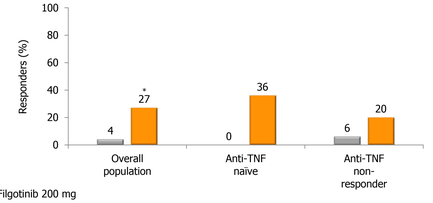


PRO2: a composite score based on daily stool frequency and self-reported abdominal pain, calculated as "7 × (mean daily number of liquid or very soft stools) + 7 × (mean daily self-reported abdominal pain)"; IBDQ = International Bowel Disease Questionnaire: a quality of life index; study was not powered to detect differences in the anti-TNF patient subgroups (no inferential statistics calculated in the subgroups); *p<0.05; **p<0.01

Total D'Haens histopathology score, ITT-LOCF



Combined clinical remission-biological response#, ITT-NRI



#Combined clinical remission/biological response: CDAI-score <150 points and CRP decrease >50% and/or fecal calprotectin decrease >50% from baseline; study was not powered to detect differences in the anti-TNF patient subgroups (no inferential statistics calculated in the subgroups); ITT subpopulation: baseline CRP>7.9mg/L or baseline fecal calprotectin >250mg/kg; *p<0.05

Conclusions

- **Filgotinib showed efficacy in patients with active Crohn's disease independently of prior anti-TNF exposure across all endpoints**
- **Filgotinib was well tolerated, with a similar safety profile in both anti-TNF subgroups**
- **The data suggest a favorable risk/benefit profile for filgotinib in both anti-TNF naïve and anti-TNF non-responder patients**

Results: Safety at Week 10

n (%)	Anti-TNF naïve		Anti-TNF non-responder	
	Placebo (N=16)	200 mg (N=57)	Placebo (N=28)	200 mg (N=73)
TE AE	5 (31)	33 (58)	21 (75)	53 (73)
Infections and infestations	1 (6)	12 (21)	8 (29)	20 (27)
Gastrointestinal disorders	1 (6)	9 (16)	9 (32)	23 (32)
Nervous system disorders	2 (13)	7 (12)	6 (21)	14 (19)
Serious TE AE	0 (0)	2 (4)	3 (11)	4 (5)
Serious TE infections	0 (0)	0 (0)	0 (0)	1 (1)
SAE leading to death	0 (0)	0 (0)	0 (0)	0 (0)
TE AE leading to discontinuation	1 (6)	6 (11)	4 (14)	9 (12)

AE = adverse event; SAE = serious adverse event; TE = treatment emergent

- Filgotinib was safe and well tolerated in both anti-TNF subgroups
- There was a similar incidence of SAEs, treatment-emergent adverse events (TE AEs) leading to discontinuation, and infections in both anti-TNF subgroups
- The incidence of TE AEs was somewhat higher in anti-TNF non-responders

Disclosures

GDH has received lecture fees from Abbvie, Ferring, Johnson and Johnson, MSD, Mundipharma, Norgine, Pfizer, Shire, Millenium/Takeda, Tillotts and Vifor; and consultancy fees from Abbvie, Ablynx, Amakem, AM Pharma, Avaxia, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Celltrion, Cosmo, Covidien, Ferring, Dr FALK Pharma, Engene, Galapagos, Gilead, GlaxoSmithKline, Hospira, Immunic, Johnson and Johnson, Lycera, Medimetrics, Millenium/Takeda, Mitsubishi Pharma, MSD, Mundipharma, Novo Nordisk, Pfizer, Prometheus laboratories/Nestle, Protagonist, Receptos, Robarts Clinical Trials, Salix, Sandoz, Setpoint, Shire, Teva, Tigenix, Tillotts, Topivert, Versant and Vifor. **SS** has received research funding from Galapagos; consultancy fees from Abbvie, Galapagos and Pfizer; and speaker fees from Abbvie. **RP** has received research funding from Galapagos. **TK** has received research funding from Galapagos; speaker fees from Abbvie, Almirall, Arena, Dr Falk Pharma, Ferring, MSD, Mundipharma and Takeda; consultancy fees from Arena, MSD, Mundipharma, Stellic and Takeda. **XH** has received research funding from Galapagos; consultancy fees from Abbvie, Fresenius Kabi, Nutricia, MSD, Takeda, Vifor and Galapagos; and has served on an advisory board for Janssen. **XR** has received research funding from Galapagos; speaker fees from Abbie, Janssen, MSD and Takeda; consultancy fees from Abbie, Janssen, MSD and Takeda; and support to attend congresses from Abbie, Janssen, MSD and Takeda. **MK** has received research funding from Galapagos; speaker fees from Abbvie, Alvogen, Ferring and Takeda; and support to attend congresses from Abbie, Alvogen and Ferring. **AG, HW1, AB,** and **RS** have received research funding from Galapagos. **KS** has received fees for medical monitoring and data cleaning from Galapagos. **LM, CTT, AVdA** and **PH** are employees of Galapagos and receive warrants (i.e. rights to subscribe to new shares at a predetermined price) from the company. **SV** has received research funding from Abbvie, Galapagos, MSD and Takeda; speaker fees from Abbie, MSD, Takeda, Ferring, Falk Pharma, Hospira and Tillotts; and consultancy fees from Abbvie, MSD, Takeda, Ferring, Genentech/Roche, Shire, Pfizer, Galapagos, Mundipharma, Hospira, Celgene, Second Genome and Janssen.

Reference

Vermeire S *et al. Lancet* 2017;389:266—275

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