IBD Training Academy

Module 2
Patient case study workshop

Professor Charlie Lees
Professor Ailsa Hart

Filgotinib ▽ Prescribing Information and adverse event reporting information can be found at the end of this presentation

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- Patient case studies are fictional and to be used for educational purposes only

IBD, inflammatory bowel disease.

Introducing the panel

Professor Charlie Lees
University of Edinburgh, UK

Professor Ailsa Hart
St Mark's Hospital and Academic Institute, UK

Disclosures

Professor Charlie Lees

- Funded by a UKRI Future Leaders Fellowship
- Received additional research support from the Chief Scientist's Office, Cure Crohn's Colitis
- Received consultancy fees from Abbvie, Pfizer, Janssen, Gilead, Galapagos, BMS, Celltrion, Boehringer Ingelheim, Dr Falk, Trellus Health, Iterative Scopes and Vifor Pharma
- Received speaking fees and travel support from Abbvie, Pfizer, Janssen, Gilead, Galapagos, Celltion, BMS, Sandoz, Novartis, Dr Falk, Ferring, Fresnius Kabi and Takeda

Professor Ailsa Hart

- I herewith declare the following paid or unpaid consultancies, business interests or sources of honoraria payments since 1 October 2016, and anything else that could potentially be viewed as a conflict of interest: AbbVie, Atlantic, Bristol-Myers Squibb, Celltrion, Falk, Ferring, Janssen, MSD, Napp Pharmaceuticals, Pfizer, Pharmacosmos, Shire and Takeda. Global Steering Committee for Genentech Roche

Agenda

5 mins

Welcome and introduction
Professor Ailsa Hart and Professor Charlie Lees

40 mins

Case study 1
Professor Ailsa Hart

40 mins

Case study 2
Professor Charlie Lees

5 mins

Summary and close
Professor Ailsa Hart and Professor Charlie Lees

Housekeeping

Please **turn your phone to silent** to avoid any disturbances

Please keep your **webcam on** to facilitate participation and discussion

Please include your **full name** on the platform

Please **engage** with your peers and speakers to ensure you gain the most out of this interactive workshop

Please **unmute yourself** or use the **chat** function at any point during the workshop if you have a question

Objectives

- Use patient case studies based on real-life scenarios to aid clinical decision-making
- Consider the impact of IBD on all aspects of a patient's life, and how to approach these different elements
- Understand what is meant by holistic/comprehensive disease control and how this fits into the management of IBD
- Discuss how the multidisciplinary team can best work together and with the patient to achieve optimum care

IBD, inflammatory bowel disease.

Case 1

25 years old, male

Finished university

Just started work

In a relationship

Key points

- Recent diagnosis of total UC
- Treated with mesalazine (good compliance and optimised)
- No bowel symptoms, but ‘feels exhausted’ and ‘everything aches’
- Recent blood tests, faecal calprotectin and colonoscopy are normal

January 2022

- Diagnosed with total UC
- Starts treatment with mesalazine

March 2022

- Reports feelings of exhaustion and muscle aches

May 2022

- Laboratory analysis of blood, faecal calprotectin and colonoscopy are within normal range

Fictitious patient case study.
UC, ulcerative colitis.

Discussion questions

Are goals of therapy being met?

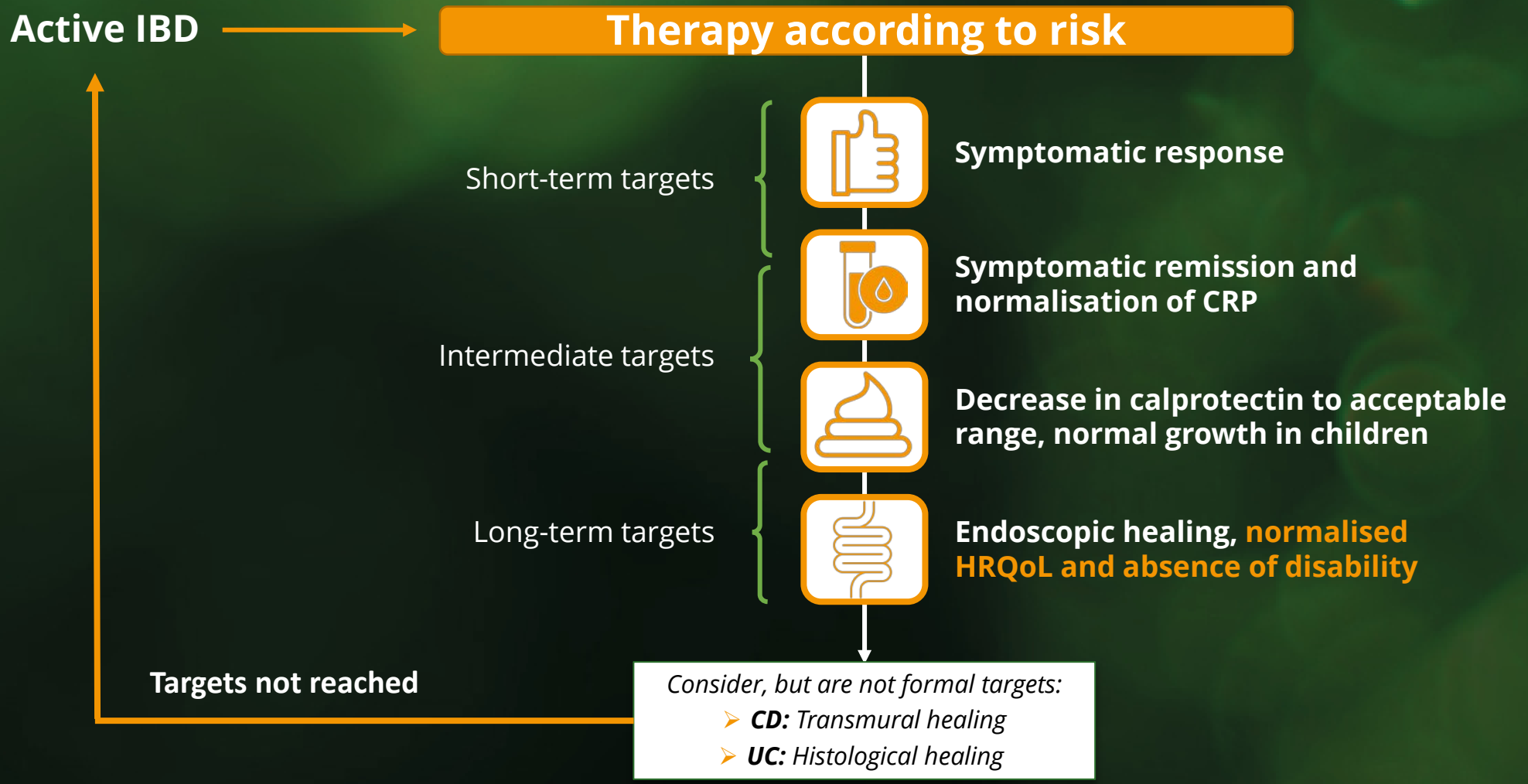
Should we involve other expertise, e.g. GP, other specialists?

How would you approach these symptoms?

What questions would you ask?

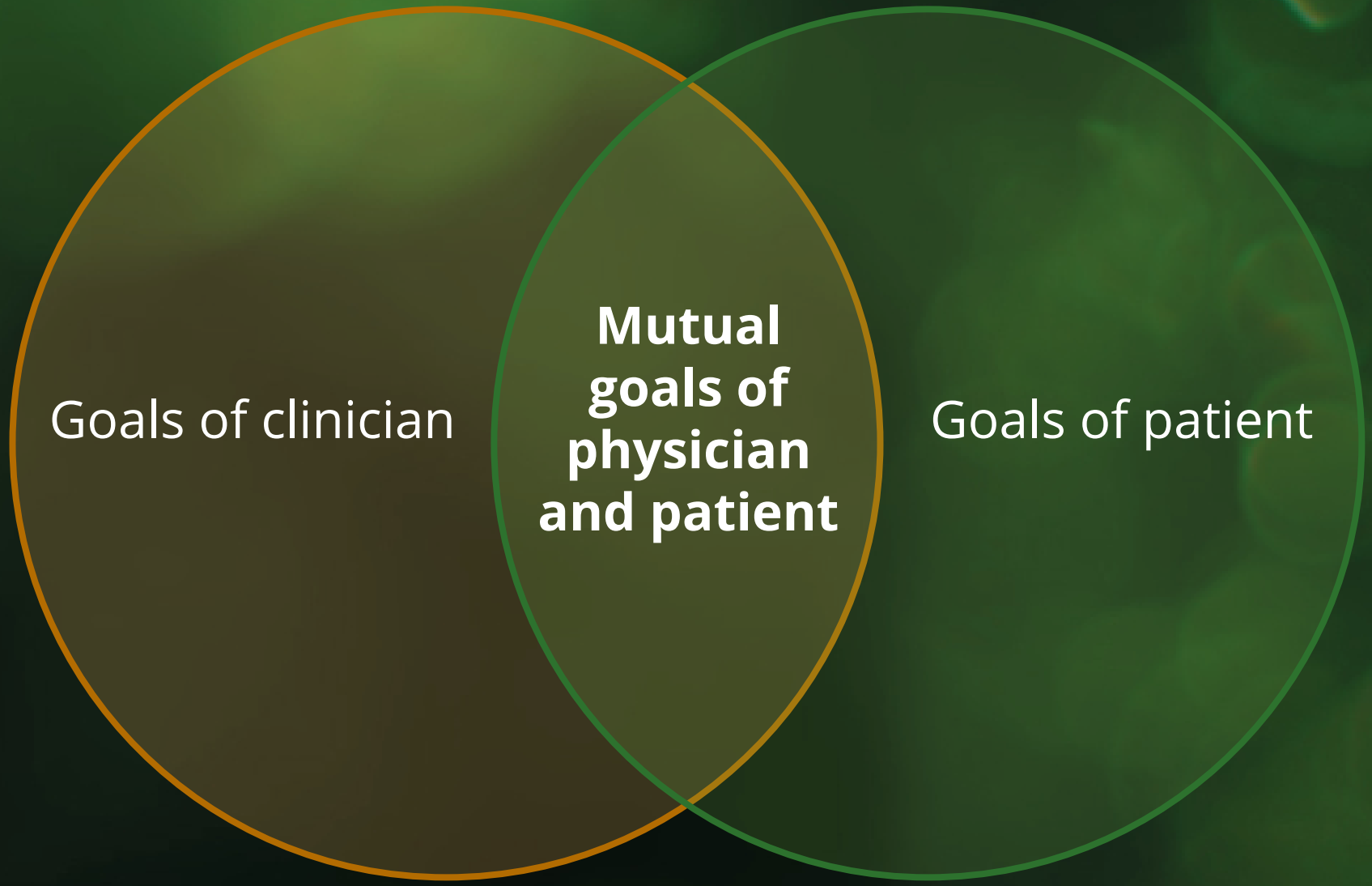
GP, general practioner.

Goals of therapy: STRIDE-II

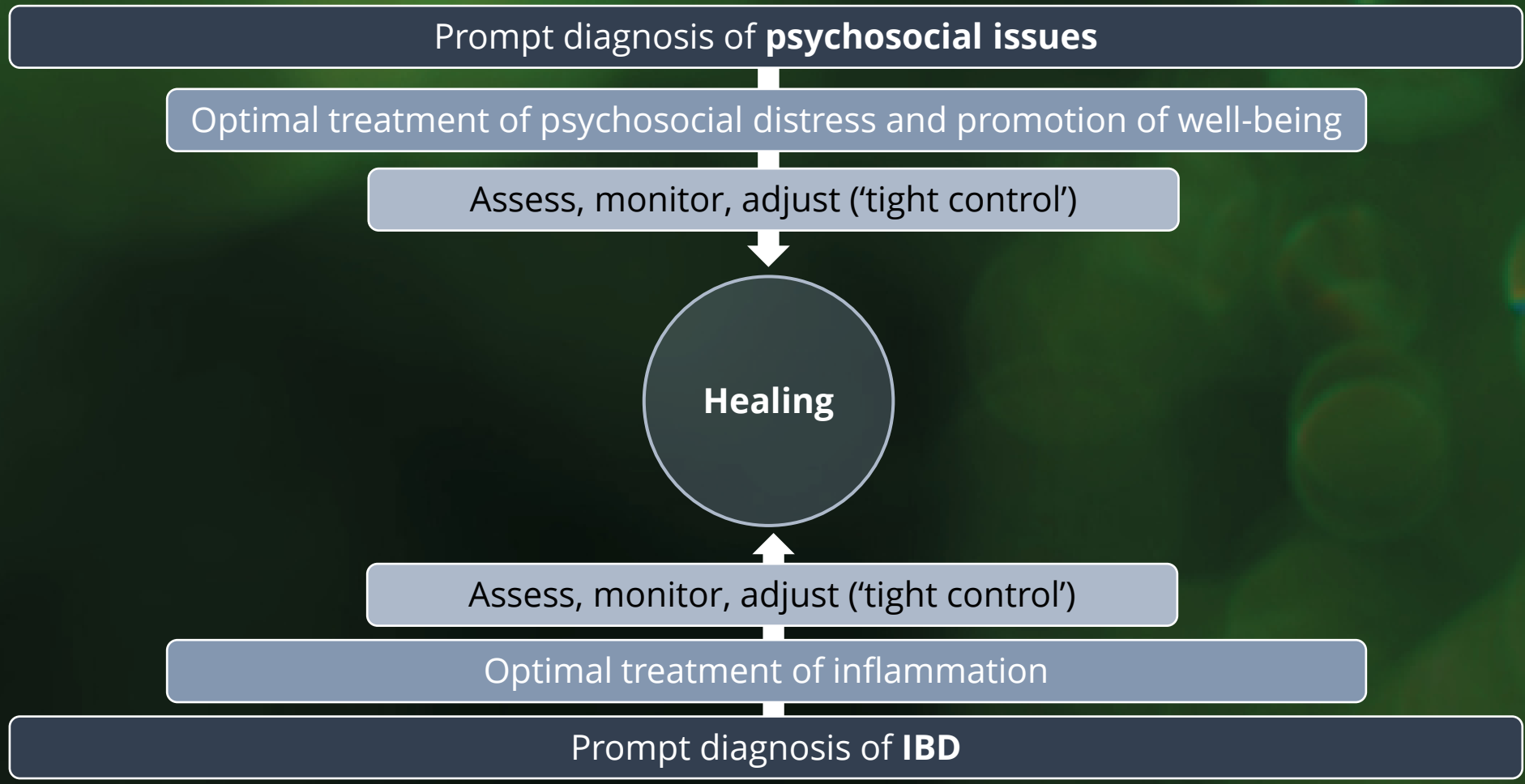


CD, Crohn's disease; CRP, C-reactive protein; HRQoL, health-related quality of life; IBD, inflammatory bowel disease; UC, ulcerative colitis.
Turner D, et al. *Gastroenterology* 2021;160:1570–1583.

Mutual goals of clinician and patient



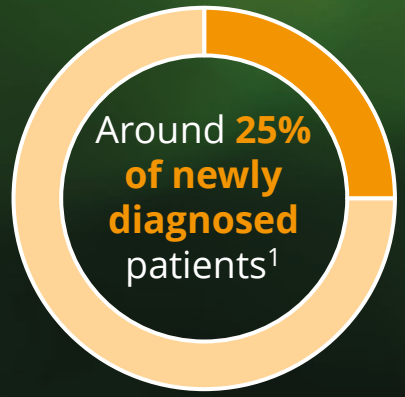
Treat to ALL targets in IBD

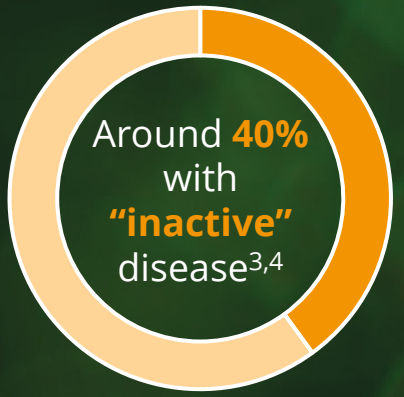


IBD, inflammatory bowel disease.
Figure adapted from Keefer L, et al. *Gastroenterology* 2022;162:1439–1451.

Fatigue in IBD

Fatigue is a frequently experienced symptom in patients with IBD[1–5]





- Patients report fatigue as one of the **most debilitating** symptoms[4]
- Patients find it **difficult to talk about** fatigue[6]
- Patients report that fatigue is **not addressed** in clinics[6]

IBD, inflammatory bowel disease.

1. Cohen BL, et al. *Aliment Pharmacol Ther* 2014;39:811–822; 2. Crohn's and Colitis UK. Tackling Challenges in IBD Fatigue Report 2014. Available at: http://www.fatigueinibd.co.uk/wp-content/uploads/2017/11/Tackling-Challenges-in-IBD-Fatigue-2014-report.pdf (Last accessed: May 2022); 3. Minderhoud IM, et al. *Am J Gastroenterol* 2003;98:1088–1093; 4. Romberg-Camps MJ, et al. *Inflamm Bowel Dis* 2010;16:2137–2147; 5. Keefer L, et al. *Gastroenterology* 2022;162:1439–1451; 6. Czuber-Dochan W, et al. *J Crohns Colitis* 2014;8:835–844.

Pain in IBD

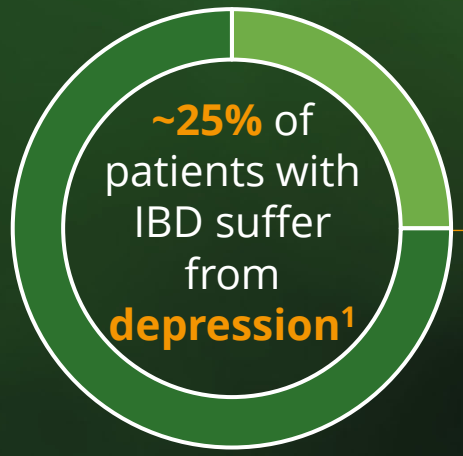
Chronic pain is reported by up to **60%** of patients with IBD

There is often a **dissociation** between pain and indices of inflammation, and the issue of fear of symptoms (visceral anxiety) and pain

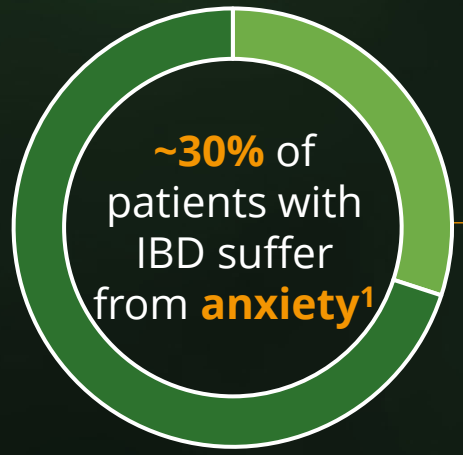
"...unless I'm in a flare up, no one asks me about pain...healthcare professionals dismiss my symptoms as they don't know what to say, as they don't understand pain in IBD and feel as powerless as I do."

IBD, inflammatory bowel disease.
Keefer L, et al. *Gastroenterology* 2022;162:1439–1451.

Depression and anxiety in IBD



- Common within the **first year** of diagnosis
- Assessed using **PHQ-9**
- Familiarise with dosing and side effects of **tricyclic anti-depressants** and **SSRIs/SNRIs**



- **Symptom-specific** anxiety, **generalised** anxiety and **post-traumatic stress** (surgery and in-patient admissions are a risk factor)
- Assessed using **GAD-7**
- Treatment options include **brain–gut psychotherapies**, such as CBT and gut hypnotherapy

A recent study in patients with CD (n=33) receiving **bupropion*** in addition to BBT exhibited significant improvements in sleep, fatigue, daytime sleepiness, anxiety and depressive severity vs. previous BBT alone[2]

*Bupropion is not approved for the management of fatigue in patients with IBD. Galapagos does not have an approved product for use in CD.
BBT, brief behavioural therapy; CBT, cognitive behavioural therapy; CD, Crohn's disease; GAD-7, generalised anxiety disorder-7; IBD, inflammatory bowel disease; PHQ-9, patient health questionannaire-9; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

1. Keefer L, et al. *Gastroenterology* 2022;162:1439–1451; 2. Hashash JG, et al. *Clin Gastroenterol Hepatol* 2022;20:96–104.

Case 2

37 years old, female

Non-smoker

Nurse

Single

Key points

- Diagnosed with left-sided UC with partial response to 5-ASA
- Good response to prednisolone but becomes steroid dependent with side effects and increased stool frequency, blood and urgency when dose is lowered
- Non-response to a TNF inhibitor and poor response to an anti-integrin treatment
- Is frustrated and feels she has been unwell for several years

2017

- Diagnosed with left-sided UC
- Partial response to treatment with top and tail 5-ASA
  - BO: 3–4x /day
  - Blood: <50%
  - Urgency: +
  - No nocturnal disturbance
  - CRP: 8 mg/l
  - fCAL: 466 mcg/g

How do you approach this patient at diagnosis?

Fictitious patient case study.
BO, bowel open; CRP, C-reactive protein; fCAL, faecal calprotectin; 5-ASA, 5-aminosalicylic acid; TNF, tumour necrosis factor; UC, ulcerative colitis.

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2017–2022

- No response after 2 weeks of treatment with budesonide
- Good response after switching to treatment with prednisolone

The patient has become steroid dependent

What do you do?
How do you discuss next steps with the patient?

BO, bowel open; CRP, C-reactive protein; fCAL, faecal calprotectin; 5-ASA, 5-aminosalicylic acid; TNF, tumour necrosis factor; UC, ulcerative colitis.

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2017–2022

- No response after 2 weeks of treatment with budesonide
- Good response after switching to treatment with prednisolone
- Treatment with azathioprine and mercaptopurine poorly tolerated (nausea)
- Treatment with prednisolone 10 mg daily due to steroid dependency. When dose reduced:
  - BO: 4–5x /day with blood
  - Marked urgency
- Primary non-response to treatment with adalimumab

How do you approach a conversation about reducing steroid use due to unfavourable side effects?

BO, bowel open; CRP, C-reactive protein; fCAL, faecal calprotectin; 5-ASA, 5-aminosalicylic acid; TNF, tumour necrosis factor; UC, ulcerative colitis.

Case 2

37 years old, female

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  - BO: 4–5x /day with blood
  - Marked urgency
- Primary non-response to treatment with adalimumab
- Patient starts vedolizumab and after 18 weeks, comes off steroids for 3 months
  - BO: 3–4x /day
  - Occasional blood
  - Urgency persists
  - CRP: 6 mg/l
  - fCAL: 310 mcg/g

The patient responds poorly to biologic dose escalation

What do you do?

BO, bowel open; CRP, C-reactive protein; fCAL, faecal calprotectin; 5-ASA, 5-aminosalicylic acid; TNF, tumour necrosis factor; UC, ulcerative colitis.

Case 2

37 years old, female

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Today

- No response after increasing vedolizumab to q4w
  - Symptoms unchanged
  - CRP: 9 mg/l
  - fCAL: 984 mcg/g
- Patient restarts steroids but has gained weight from long-term use and feels depressed

BO, bowel open; CRP, C-reactive protein; fCAL, faecal calprotectin; 5-ASA, 5-aminosalicylic acid; q4w, every 4 weeks; TNF, tumour necrosis factor; UC, ulcerative colitis.

Case 2

Key points to consider:

- **How do you approach the high QoL burden?**
- **Do you involve any colleagues?**
- **How do you discuss a new treatment strategy with the patient that balances QoL with treatment efficacy?**

2017

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BO, bowel open; CRP, C-reactive protein; fCAL, faecal calprotectin; 5-ASA, 5-aminosalicylic acid; q4w, every 4 weeks; TNF, tumour necrosis factor; UC, ulcerative colitis.

Need for steroid-free remission

Prolonged use of corticosteroids is associated with risks that outweigh the benefits[1,2]

Osteopenia
Osteoporosis
Avascular necrosis

Adrenal insufficiency

Infections
Delayed wound healing

Weight gain

Insomnia
Mood changes
Delirium
Skin changes

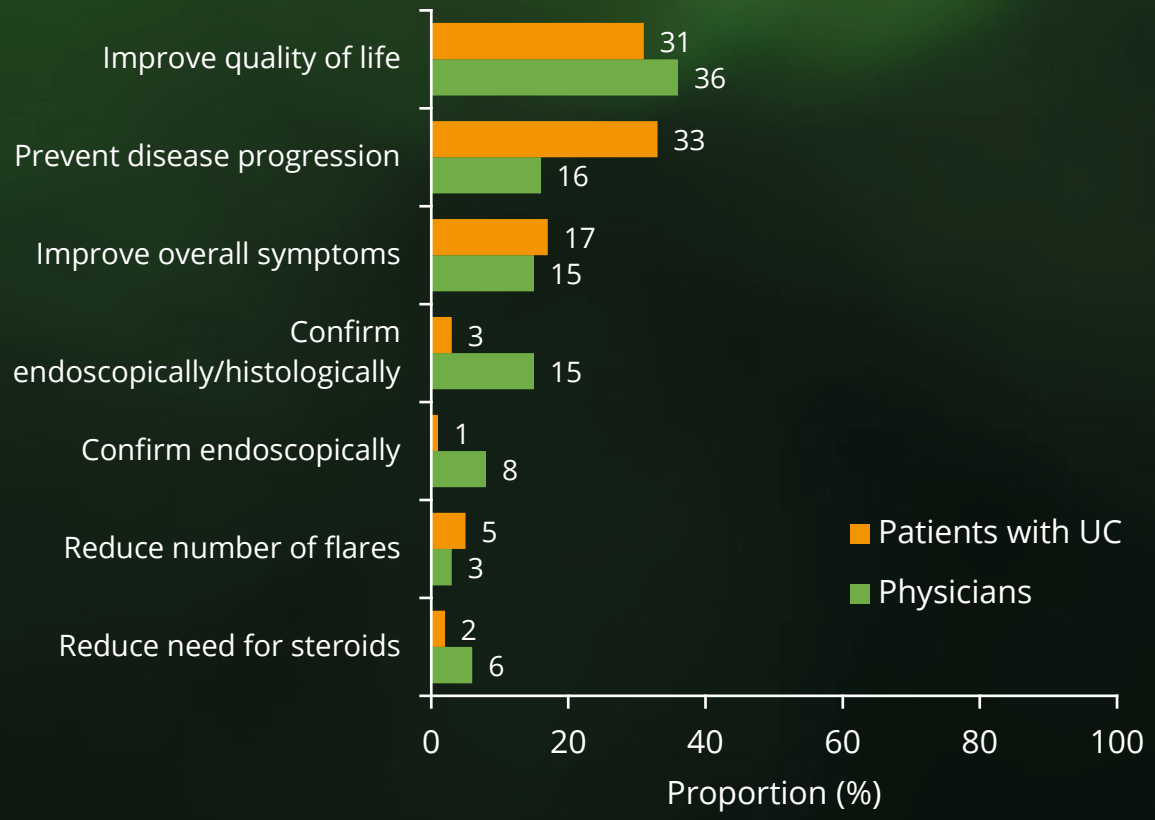
Cataracts
Glaucoma

An increasing body of data shows that steroid-free remission is an achievable treatment target with advanced therapies[3–7]

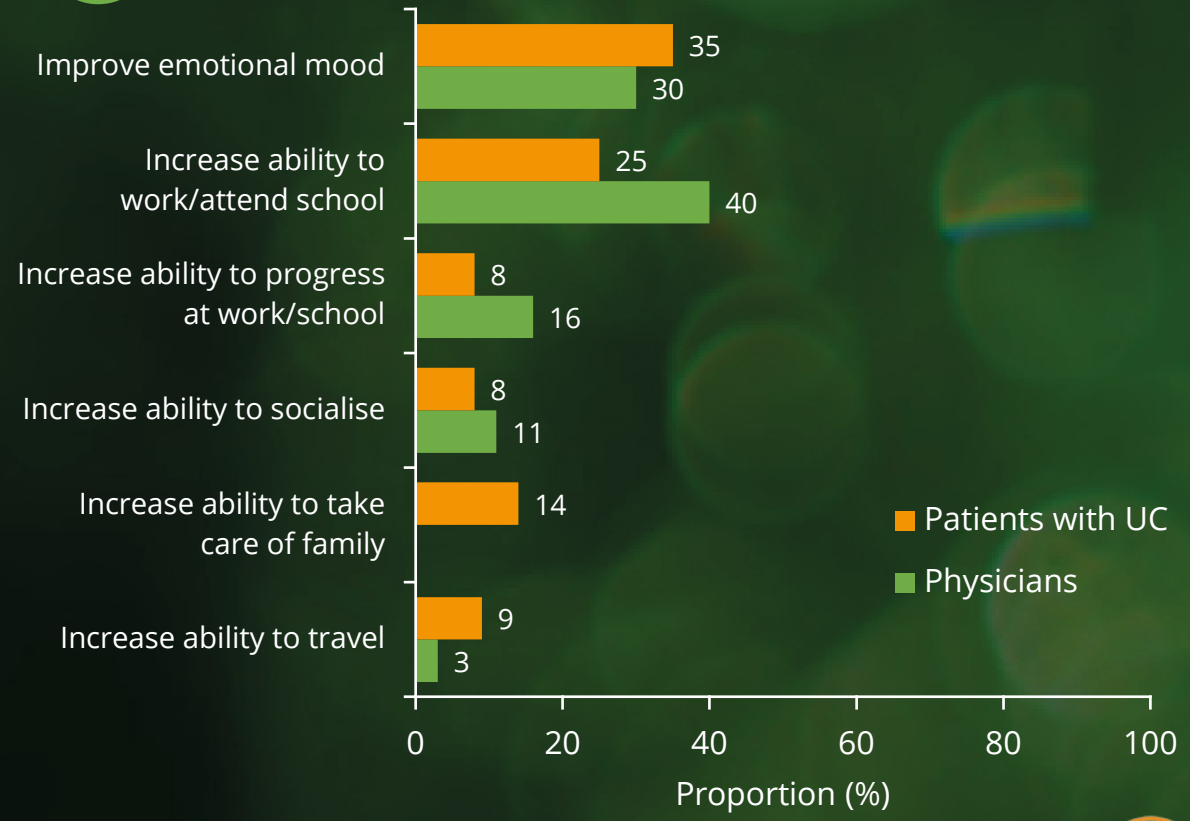
1. Danese S, et al. *Dig Dis* 2019;37:266–283; 2. Feuerstein JD, et al. *Mayo Clin Proc* 2019;94:1357–1373; 3. Sands BE, et al. *N Engl J Med* 2019;381:1201–1214;
4. Vavricka SR, et al. ECCO 2021. DOP85; 5. Feagan BG, et al. *Lancet* 2021;397:2372–2384; 6. Scherl EJ, et al. ECCO 2021. DOP86;
7. Loftus Jr, et al. ECCO 2021. DOP82.

Do patients and physicians share the same UC treatment goals?

Disease-related goals of UC treatment



Quality of life-related goals of UC treatment



Figures adapted from Rubin DT, et al. 2021.
UC, ulcerative colitis.
Rubin DT, et al. *Inflamm Bowel Dis* 2021;27:1942–1953.

Top 10 treatment attributes most relevant to patients when making IBD treatment choices

Domain	Attribute: defined through literature search, focus group and structured voting*
Efficacy	Abdominal pain
	Other disease-related pain (anal pain, joint pain/stiffness or eye pain, etc.)
	Bowel urgency
	Fatigue
Complications/risk	Risk of cancer and serious infections within 10 years (excluding non-melanoma skin cancer)
	Risk of mild-to-moderate complications†
	Aesthetic complications related to treatment
HRQoL	Emotional status
	Sexual life
	Social life and relationships (interpersonal interactions)

Table adapted from Louis E, et al. 2020.
*A literature review followed by a patient and physician focus group led to the identification of attributes. List of attributes were grouped in redefined domains agreed on in a focus group meeting and by patient ranking; †Nausea, vomiting, headache, non-serious infections, lab abnormalities, skin reactions and infusion reactions. HRQoL, health-related quality of life; IBD, inflammatory bowel disease.
Louis E, et al. *Patient* 2020;13:317–325.

Novel treatment options will further increase the opportunity to meet patient needs[1]

Treatment options on the horizon in IBD

Small molecule drugs[2,3]

- JAK1-selective JAK inhibitors
- Gut-selective JAK inhibitors
- S1PR modulators (lymphocyte trapping)

Biologics[2]

- Gut-selective oral anti-TNFs
- Specific IL-23 inhibitors
- Integrin and MadCAM-1 inhibitors

Several differences between small molecule therapeutics and biologics[4–6]

Novel treatment mechanisms of action aim to improve efficacy and safety outcomes[1]

- Elimination half-life

Patient-friendly monitoring and administration[4,5]

IL, interleukin; JAK, Janus kinase; MadCAM-1, mucosal addressin cell adhesion molecule-1; S1PR, sphingosine-1-phosphate receptor; TDM, therapeutic drug monitoring; TNF, tumour necrosis factor.

1. Troncone E, et al. *Clin Exp Gastroenterol* 2020;13:131–139; 2. Misselwitz B, et al. *Digestion* 2020;101(Suppl 1):69–82; 3. D'Amico F, et al. *J Crohns Colitis* 2020;14:1185–1187; 4. Gilardi D, et al. *Expert Rev Gastroenterol Hepatol* 2020;14:797–806; 5. Lee S, et al. *J Clin Gastroenterol* 2021;55:195–206; 6. Lucaciu LA, et al. *Eur J Gastroenterol Hepatol* 2020;32:669–677.

Need for rapid and sustained symptom relief

Speed of onset is the 3rd most important driver of treatment choice after efficacy and tolerability[1]*

Corticosteroids[2,3]	Conventional therapies[4]	Biologics[4–6]	Small molecules[4,7]
• Achieve responses in **days** • Significant side effects prevent long-term use	• **Several months** to achieve maximal effect	• Can show clinical responses within **2 weeks** • Immunogenicity	• Can achieve responses within **1 week**

Patients require sustained symptom relief in addition to rapid responses[8]

*Based on the results of the IBD Global Assessment of Patient and Physician Unmet Need Surveys of 2398 patients with IBD and 654 physicians.
IBD, inflammatory bowel disease.

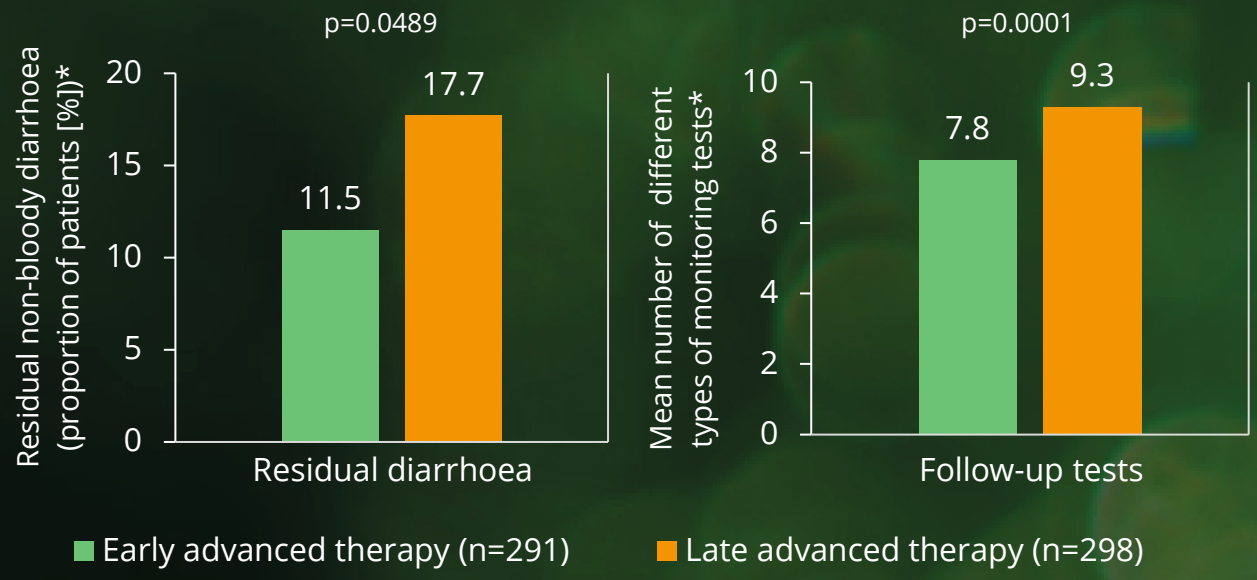
1. Rubin DT, et al. *Inflamm Bowel Dis* 2021;27:1942–1953; 2. Lichtenstein GR, et al. *Gastroenterol* 2006;130:940–987; 3. Mowat C, et al. *Gut* 2011;60:571–607;
4. Hanauer S, et al. *Clin Gastroenterol Hepatol* 2019;17:139–147; 5. Schreiber SW, et al. ECCO 2021. OP26; 6. Vermeire S, et al. *Ther Adv Gastroenterol* 2018;11:1–13;
7. Danese S, et al. ECCO 2021. OP37; 8. Danese S, et al. *Dig Dis* 2019;37:266–283.

Role of early advanced therapy in reducing cumulative disease burden

Compared with later use of advanced therapy early implementation could:

- Reduce residual symptoms
- Reduce the need for follow-up monitoring
- Improve HRQoL

Fewer patients with residual diarrhoea and lower need for follow-up tests with early (≤1.5 years after diagnosis) vs. late advanced therapy (>1.5 years after diagnosis)



Early advanced therapy provides greater improvement in disease vs. late advanced therapy

*Adjusted for patient demographic and clinical characteristics.
HRQoL, health-related quality of life.
Armuzzi A, et al. UEGW 2021. P0412.

Thank you for your participation!

ABBREVIATED SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions**.**

Jyseleca 100 / 200 mg film coated tablets. Composition: Each film coated tablet contains filgotinib maleate equivalent to 100 or 200 mg of filgotinib. Each 100 mg film coated tablet contains 76 mg of lactose (as monohydrate). Each 200 mg film coated tablet contains 152 mg of lactose (as monohydrate). For the full list of excipients, see section 6.1 of the Summary of Product Characteristics (SmPC). **Pharmaceutical form:** Film coated tablet. *Jyseleca 100 mg film coated tablets:* Beige 12 × 7 mm, capsule shaped, film coated tablet debossed with "GSI" on one side and "100" on the other side. *Jyseleca 200 mg film coated tablets:* Beige 17 × 8 mm, capsule shaped, film coated tablet debossed with "GSI" on one side and "200" on the other side. **Therapeutic indications:** *Rheumatoid arthritis* Jyseleca is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti rheumatic drugs (DMARDs). Jyseleca may be used as monotherapy or in combination with methotrexate (MTX). *Ulcerative colitis* Jyseleca is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic agent. **Posology and method of administration:** Treatment with filgotinib should be initiated by a physician experienced in the treatment of rheumatoid arthritis or ulcerative colitis. *Posology Rheumatoid arthritis* The recommended dose of filgotinib for adult patients is 200 mg once daily. *Ulcerative colitis* The recommended dose for induction and maintenance treatment is 200 mg once daily. For patients with ulcerative colitis who do not show an adequate therapeutic benefit during the initial 10 weeks of treatment, 12 additional weeks of induction treatment with filgotinib 200 mg once daily may provide additional relief of symptoms (see section 5.1 of the SmPC). Patients who have not shown any therapeutic benefit after 22 weeks of treatment should discontinue filgotinib. *Laboratory monitoring, and dose initiation or interruption* Guidance for laboratory monitoring, and dose initiation or interruption is provided in Table 1. Treatment should be interrupted if a patient develops a serious infection until the infection is controlled (see section 4.4 of the SmPC).

Table 1: Laboratory measures and monitoring guidance

Laboratory measure	Action	Monitoring guidance
Absolute neutrophil count (ANC)	Treatment should not be initiated, or should be interrupted, if ANC is < 1×10^9 cells/L. Treatment may be restarted once ANC returns above this value	Before treatment initiation and thereafter according to routine patient management
Absolute lymphocyte count (ALC)	Treatment should not be initiated, or should be interrupted, if ALC is < 0.5×10^9 cells/L. Treatment may be restarted once ALC returns above this value	
Haemoglobin (Hb)	Treatment should not be initiated, or should be interrupted, if Hb is < 8 g/dL. Treatment may be restarted once Hb returns above this value	
Lipid parameters	Patients should be managed according to international clinical guidelines for hyperlipidaemia	12 weeks after initiation of treatment and thereafter according to international clinical guidelines for hyperlipidaemia

Special populations Elderly *Rheumatoid arthritis* A starting dose of 100 mg once daily is recommended for patients with rheumatoid arthritis aged 75 years and older as clinical experience is limited. *Ulcerative colitis* No dose adjustment is recommended for patients with ulcerative colitis up to 75 years of age. Filgotinib is not recommended in patients aged 75 years and older as there is no data in this population. Renal impairment No dose adjustment is required in patients with mild renal impairment (creatinine clearance [CrCl] ≥ 60 mL/min). A dose of 100 mg of filgotinib once daily is recommended for patients with moderate or severe renal impairment (CrCl 15 to < 60 mL/min). Filgotinib has not been studied in patients with end stage renal disease (CrCl < 15 mL/min) and is therefore not recommended for use in these patients (see section 5.2 of the SmPC). Hepatic impairment No dose adjustment is required in patients with mild or moderate hepatic impairment (Child Pugh A or B). Filgotinib has not been studied in patients with severe hepatic impairment (Child Pugh C) and is therefore not recommended for use in these patients (see section 5.2 of the SmPC). Paediatric population The safety and efficacy of filgotinib in children under the age of 18 years have not yet been established. No data are available. *Method of administration* Oral use. Jyseleca can be taken with or without food (see section 5.2 of the SmPC). It has not been studied if tablets can be split, crushed, or chewed, and it is recommended that tablets are swallowed whole. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SmPC. Active tuberculosis (TB) or active serious infections (see section 4.4 of the SmPC). Pregnancy (see section 4.6 of the SmPC). **Undesirable effects:** *Summary of the safety profile Rheumatoid arthritis* The most frequently reported adverse reactions are nausea (3.5%), upper respiratory tract infection (URTI, 3.3%), urinary tract infection (UTI, 1.7%) and dizziness (1.2%). *Ulcerative colitis* In general, the overall safety profile observed in filgotinib-treated patients with ulcerative colitis was generally consistent with the safety profile observed in patients with rheumatoid arthritis. *Tabulated list of adverse reactions* The following adverse reactions are based on clinical studies (Table 2). The adverse reactions are listed below by system organ class and frequency. Frequencies are defined as follows: common (≥ 1/100 to < 1/10) and uncommon (≥ 1/1,000 to < 1/100).

Table 2: Adverse reactions

Frequency[a]	Adverse reaction
Infections and infestations	
Common	Urinary tract infection (UTI) Upper respiratory tract infection (URTI)
Uncommon	Herpes zoster Pneumonia
Blood and lymphatic system disorders	
Uncommon	Neutropenia
Metabolism and nutrition disorders	
Uncommon	Hypercholesterolaemia
Nervous system disorders	
Common	Dizziness
Gastrointestinal disorders	
Common	Nausea
Investigations	
Uncommon	Blood creatine phosphokinase increased

a Frequency based on placebo controlled pre rescue period (week 12) pooled across FINCH 1 and 2, and DARWIN 1 and 2, for patients with rheumatoid arthritis who received filgotinib 200 mg. Frequencies reported in the SELECTION study in patients with ulcerative colitis who received filgotinib 200 mg were generally consistent with those reported in the rheumatoid arthritis studies.

Laboratory changes Creatinine An increase in serum creatinine occurred with filgotinib treatment. At week 24 in the Phase 3 studies (FINCH 1, 2, and 3), the mean (SD) increase from baseline in serum creatinine was 0.07 (0.12) and 0.04 (0.11) mg/dL for filgotinib 200 mg and 100 mg, respectively. Mean creatinine values remained within the normal range. Lipids Treatment with filgotinib was associated with dose dependent increases in total cholesterol and HDL levels, while LDL levels were slightly increased. LDL/HDL ratios were generally unchanged. Lipid changes were observed within the first 12 weeks of filgotinib treatment and remained stable thereafter. Description of selected adverse reactions Infections *Rheumatoid arthritis* In placebo controlled studies with background DMARDs (FINCH 1, FINCH 2, DARWIN 1, and DARWIN 2), the frequency of infection over 12 weeks in the filgotinib 200 mg group was 18.1% compared to 13.3% in the placebo group. In the MTX controlled study FINCH 3, the frequency of infection over 24 weeks in the filgotinib 200 mg monotherapy and filgotinib 200 mg plus MTX groups was 25.2% and 23.1%, respectively, compared to 24.5% in the MTX group. The overall exposure adjusted incidence rate (EAIR) of infections for the filgotinib 200 mg group across all seven Phase 2 and 3 clinical studies (2,267 patients) was 26.5 per 100 patient years of exposure (PYE). In placebo controlled studies with background DMARDs, the frequency of serious infection over 12 weeks in the filgotinib 200 mg group was 1.0% compared to 0.6% in the placebo group. In the MTX controlled study FINCH 3, the frequency of serious infection over 24 weeks in the filgotinib 200 mg monotherapy and filgotinib 200 mg plus MTX groups was 1.4% and 1.0%, respectively, compared to 1.0% in the MTX group. The overall EAIR of serious infections for the filgotinib 200 mg group across all seven Phase 2 and 3 clinical studies (2,267 patients) was 1.7 per 100 PYE. The most common serious infection was pneumonia. The EAIR of serious infections remained stable with long term exposure. In rheumatoid arthritis clinical studies, there was a higher incidence of serious infections in patients aged 75 years and older, although data are limited. In placebo controlled studies with background DMARDs, the frequencies of infectious ADRs over 12 weeks for filgotinib 200 mg compared to placebo were: URTI (3.3% versus 1.8%), UTI (1.7% versus 0.9%), pneumonia (0.6% versus 0.4%), and herpes zoster (0.1% versus 0.3%). Most of the herpes zoster events involved a single dermatome and were non serious. *Ulcerative colitis* The types of serious infections in the ulcerative colitis clinical studies were generally similar to those reported in the rheumatoid arthritis clinical studies with filgotinib monotherapy treatment groups. Across the two placebo-controlled induction studies, the frequency of serious infections was 0.6% in the filgotinib 200 mg group, 1.1% in the filgotinib 100 mg group, and 1.1% in the placebo group. In the placebo-controlled maintenance study, the frequency of serious infections in the filgotinib 200 mg group was 1%, compared to 0% in the respective placebo group. In the maintenance study filgotinib 100 mg group, the frequency of serious infections was 1.7%, compared with 2.2% in the respective placebo group. *Opportunistic infections (excluding TB)* In rheumatoid arthritis placebo controlled studies with background DMARDs, there were no opportunistic infections over 12 weeks in the filgotinib 200 mg group or the placebo group. In the MTX controlled study FINCH 3, the frequency of opportunistic infections over 24 weeks was 0, 0.2%, and 0 in the filgotinib 200 mg monotherapy, filgotinib 200 mg plus MTX, and MTX groups, respectively. The overall EAIR of opportunistic infections for the filgotinib 200 mg group across all seven Phase 2 and 3 rheumatoid arthritis clinical studies (2,267 patients) was 0.1 per 100 PYE. Nausea Nausea was generally transient and reported during the first 24 weeks of filgotinib treatment. *Creatine phosphokinase* Dose dependent increases in creatine phosphokinase (CPK) occurred within the first 12 weeks of filgotinib treatment and remained stable thereafter. At week 24 in the Phase 3 studies (FINCH 1, 2, and 3), the mean (SD) increase from baseline in CPK was 16 (449), 61 (260), and 33 (80) U/L for placebo, filgotinib 200 mg and 100 mg, respectively. In placebo controlled Phase 3 studies with background DMARDs (FINCH 1 and FINCH 2) through 12 weeks, CPK elevations > 5 × upper limit of normal (ULN) were reported in 0.5%, 0.3%, and 0.3% of patients in the placebo, filgotinib 200 mg, and filgotinib 100 mg groups, respectively. Most elevations > 5 × ULN did not require treatment discontinuation. *Experience from long term extension studies Rheumatoid arthritis* In the long term extension study DARWIN 3, among patients enrolled from DARWIN 1 (N = 497), 238 patients received filgotinib 200 mg once a day for a median duration of 4.4 years; among patients enrolled from DARWIN 2 (N = 242), 234 patients received filgotinib 200 mg once a day for a median duration of 4.4 years. The safety profile of filgotinib was similar to that in the Phase 2 and Phase 3 studies. *Ulcerative colitis* In the long-term extension study (SELECTION LTE) in patients who participated in the SELECTION study, patients received filgotinib 200 mg (N = 871), filgotinib 100 mg (N = 157), or placebo (N = 133) for median durations of 55, 36, and 32 weeks, respectively. The safety profile of filgotinib was similar to that in the SELECTION induction and maintenance studies. *Reporting of suspected adverse reactions* Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting systems. **Marketing Authorisation Holder (MAH):** Galapagos NV, Generaal De Wittelaan L11 A3, 2800 Mechelen, Belgium **Marketing Authorisation numbers:** EU/1/20/1480/001-002-003-004. **Delivery status:** On medical prescription. **Date of revision of the text:** 12/2021. For any safety reporting to the MAH, please email to **DrugSafety.Benelux@glpg.com**.

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

PRESCRIBING INFORMATION
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JYSELECA® ▼ filgotinib 100 mg or 200 mg film-coated tablets.

Indications: Jyseleca is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with lost response to, or were intolerant to either conventional therapy or a biologic agent. Jyseleca is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti rheumatic drugs (DMARDs). Jyseleca may be used as monotherapy or in combination with methotrexate (MTX). **Dosage:** Adults: 200 mg once daily. Taken orally with/without food. It is recommended that tablets are swallowed whole. *Ulcerative colitis* In patients who do not show an adequate therapeutic benefit during the initial 10 weeks of treatment, 12 additional weeks of induction treatment with filgotinib 200 mg once daily may provide additional relief of symptoms (see SmPC). Patients who have not shown any therapeutic benefit after 22 weeks of treatment should discontinue filgotinib. Laboratory Monitoring: Refer to the SmPC for information regarding laboratory monitoring and dose initiation or interruption. Elderly: *Ulcerative colitis* No dose adjustment is recommended for patients with ulcerative colitis up to 75 years of age. Filgotinib is not recommended in patients aged 75 years and older as there is no data in this population. Elderly: Rheumatoid Arthritis A starting dose of 100 mg once daily is recommended for patients aged 75 years and older as clinical experience is limited. Renal impairment: No dose adjustment required in patients with estimated creatinine clearance (CrCl) ≥ 60 mL/min. A dose of 100 mg of filgotinib once daily is recommended for patients with moderate or severe renal impairment (CrCl 15 to < 60 mL/min). Not recommended in patients with CrCl < 15mL/min. Hepatic impairment: Mild/moderate hepatic impairment: No dose adjustment required. Severe hepatic impairment not recommended. Children (<18 years) Safety and efficacy not yet been established. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Active tuberculosis (TB) or active serious infections. Pregnancy. **Warnings/Precautions:** See SmPC for full information. Immunosuppression: Combination use, with immunosuppressants e.g., ciclosporin, tacrolimus, biologics or other Janus kinase (JAK) inhibitors is not recommended as a risk of additive immunosuppression cannot be excluded. Infections: Infections, including serious infections such as pneumonia and opportunistic infections e.g. tuberculosis (TB), oesophageal candidiasis, and cryptococcosis have been reported. Risk benefit should be applied prior to initiating in patients with infection risk factors (see SmPC). Patients should be closely monitored for the development of signs and symptoms of infections during and after filgotinib treatment. Treatment should be interrupted if the patient is not responding to antimicrobial therapy, until infection is controlled. There is a higher incidence of serious infections in the elderly aged 75 years and older, caution should be used when treating this population. Tuberculosis: Patients should be screened for TB before initiating filgotinib, and filgotinib should not be administered to patients with active TB. Viral reactivation: Cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical studies (see SmPC). If a patient develops herpes zoster, filgotinib treatment should be temporarily interrupted until the episode resolves. Screening for viral hepatitis and monitoring for reactivation should be performed. Malignancy: Immunomodulatory medicinal products may increase the risk of malignancies. Malignancies were observed in clinical studies (see SmPC). Fertility: In animal studies, decreased fertility, impaired spermatogenesis, and histopathological effects on male reproductive organs were observed (see SmPC). The potential effect of filgotinib on sperm production and male fertility in humans is currently unknown. Haematological abnormalities: Do not start therapy, or temporarily stop, if Absolute Neutrophil Count (ANC) <1 × 10^9 cells/L, ALC <0.5 × 10^9 cells/L or haemoglobin <8 g/dL Temporarily stop therapy if these values are observed during routine patient management. Vaccinations: Use of live vaccines during, or immediately prior to, filgotinib treatment is not recommended. Lipids: Treatment with filgotinib was associated with dose dependent increases in lipid parameters, including total cholesterol, and high-density lipoprotein (HDL) levels, while low density lipoprotein (LDL) levels were slightly increased (see SmPC). Cardiovascular risk: Rheumatoid arthritis and ulcerative colitis patients have an increased risk for cardiovascular disorders. Patients should have risk factors (e.g., hypertension, hyperlipidaemia) managed as part of usual standard of care. Venous thromboembolism: Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving JAK inhibitors including filgotinib. Caution should be used in patients with risk factors for DVT/PE, such as older age, obesity, a medical history of DVT/PE, or patients undergoing surgery, and prolonged immobilisation. Lactose content: Contains lactose; patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take filgotinib. Pregnancy/Lactation: Filgotinib is contraindicated in pregnancy. Filgotinib should not be used during breast-feeding. Women of childbearing potential must use effective contraception during and for at least 1 week after cessation of treatment. **Driving/ Using machinery:** No or negligible influence, however dizziness has been reported, during treatment with Jyseleca (SmPC for full information) **Side effects:** See SmPC for full information. Common (≥1/100 to <1/10): nausea, upper respiratory tract infection, urinary tract infection and dizziness. Uncommon (≥1/1000 to <1/100): herpes zoster, pneumonia, neutropenia hypercholesterolaemia, blood creatine phosphokinase increase, **Serious side effects:** See SmPC for full information
Legal category: POM
Pack: 30 film-coated tablets/ bottle
Price: UK Basic NHS cost: £863.10
Marketing authorisationnumber(s):
Jyseleca 100mg film-coated tablets PLGB 42147/0001
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Further information:
Galapagos UK, Belmont House, 148 Belmont Road, Uxbridge UB8 1QS, United Kingdom
00800 78781345
medicalinfo@glpg.com.
Jyseleca® is a trademark.

Date of Preparation: January 2022 UK-FIL-202112-00003

▼ **Additionalmonitoring required**

Adverse events should be reported.
For Great Britain, reporting forms and information can be found at yellowcard.mhra.gov.uk or via the Yellow Card app (download from the Apple App Store or Google Play Store).
Adverse events should also be reported to Galapagos via email to DrugSafety.UK.Ireland@glpg.com or 008007878 1345

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Further information:
Galapagos UK, Belmont House, 148 Belmont Road, Uxbridge UB8 1QS, United Kingdom
00800 7878 1345 medicalinfo@glpg.com.
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