«Είναι το Filgotinib ο “preferential” JAK1 αναστολέας στη Ρευματοειδή Αρθρίτιδα;»

Παρουσίαση περιπτώσεων ασθενών

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Honorary Consultant, Research & Development Department
The Dudley Group NHS Foundation Trust

ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΑΘΗΝΩΝ
ΙΠΠΟΚΡΑΤΕΙΟ

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Disclosures #1

Τιμητική αμοιβή από τη Sobi για αυτήν την ομιλία

- Honoraria for lectures:
  Genesis Pharma, Abbvie, Novartis, Eli-Lilly, Pfizer, Aenorasis, UCB, GSK, Boehringer, Sobi
- Honoraria for advisory boards:
  Genesis Pharma, Pfizer, Abbvie, Viatris, Aenorasis, Janssen
- Hospitality:
  Eli-Lilly, Novartis, Viatris, UCB, Genesis Pharma, Abbvie, Rafarm
- Research:
  Sub-investigator: Roche, UCB, Eli-Lilly, Novartis, BMS, Pfizer, Genesis Pharma, AMGEN, Merck, Abbvie, Aenorasis

Filgotinib as a preferential JAK1 inhibitor

In biochemical assays, filgotinib has a higher potency for JAK1 vs. other JAKs[1,2]

- A minimum of **5-fold higher potency** was conferred on **JAK1 compared with any other JAK**[1,2]
- Higher and lower fold differences in potency were observed in individual assays[1,2]

Therefore, filgotinib is a JAK1-preferential inhibitor[1]

In cellular assays, filgotinib preferentially inhibited JAK1/JAK3-, JAK1/JAK2- and JAK1/TYK2-mediated signalling[1,3]

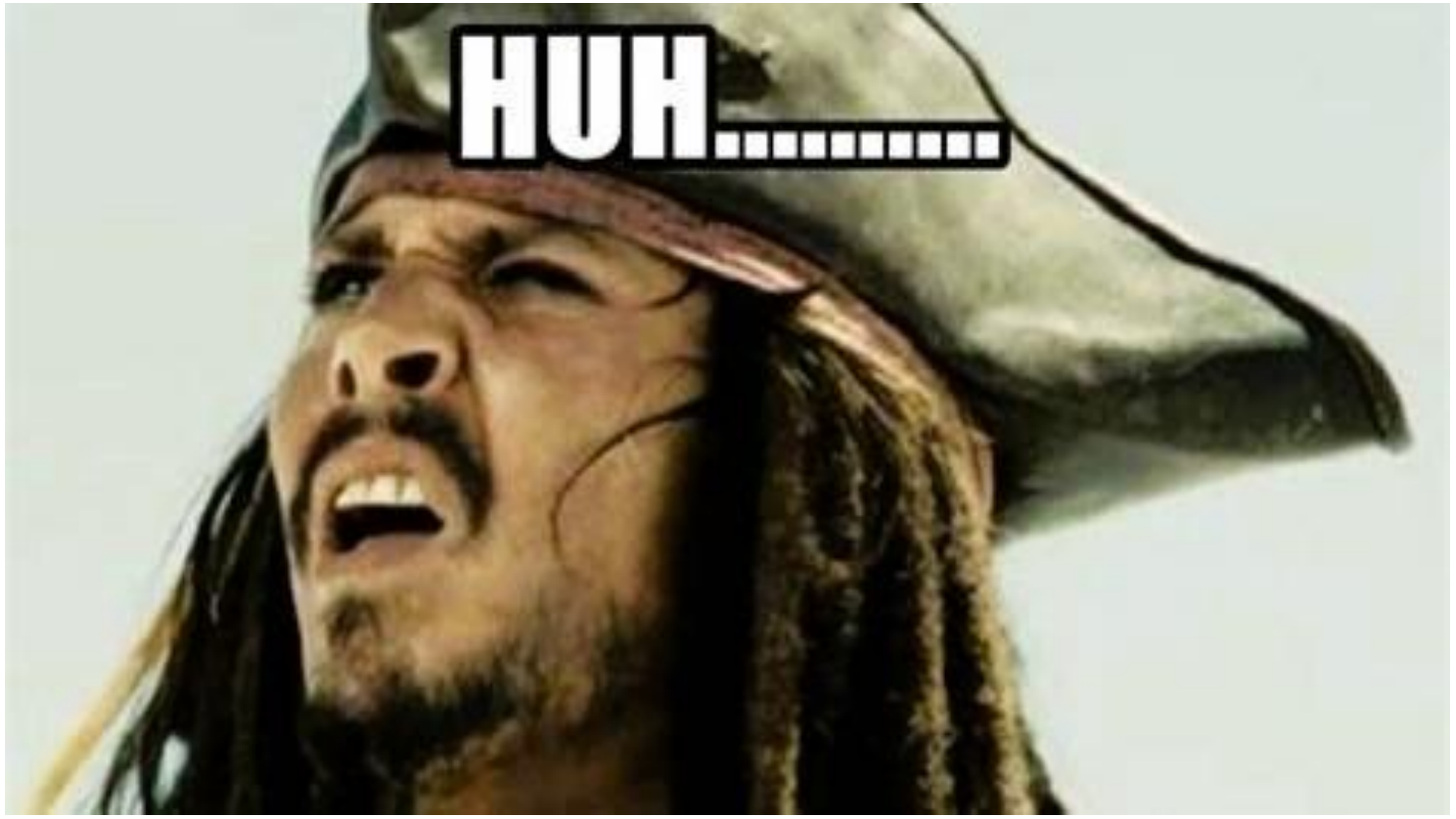
- **Filgotinib preferentially inhibits JAK1/JAK3, JAK1/JAK2** and **JAK1/TYK2** signalling pairs compared with JAK2/JAK2 and JAK2/TYK2[1,3]
- Filgotinib demonstrated **more potent inhibition** of **JAK1/JAK2/TYK2-dependent IL-6 signalling** vs. JAK2/JAK2-dependent GM-CSF signalling[1,4]

Filgotinib is functionally selective for pathways where JAK1 is involved compared with JAK2/JAK2 and JAK2/TYK2[1]

GM-CSF: granulocyte macrophage colony-stimulating factor; IL: interleukin; JAK: janus kinase; TYK: tyrosine kinase

1. Jyseleca EU Summary of Product Characteristics, March 2021. 2. Filgotinib Public Assessment Report 2020. 3. Van Rompaey L, *et al. J Immunol* 2013; 191:3568–3577.
4. Traves P. *et al.* Ann Rheum Dis 2021;0:1-11.

Real world cases for filgotinib



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Disclosures #2

These are not my patients!

NICE guidance on use of filgotinib

NICE National Institute for Health and Care Excellence

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Filgotinib for treating moderate to severe rheumatoid arthritis

Technology appraisal guidance | TA676 | Published: 24 February 2021

Guidance | Tools and resources | Information for the public | Evidence | History

Download guidance (PDF)

Overview

1 Recommendations

2 Information about filgotinib

3 Committee discussion

Overview

Evidence-based recommendations on filgotinib [redacted] for moderate to severe rheumatoid arthritis in adults.

Is this guidance up to date?

Next review: 2024

NICE guidance on use of filgotinib

1 Recommendations

1.1 Filgotinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to intensive therapy with 2 or more conventional disease-modifying antirheumatic drugs (DMARDs), only if:

- disease is moderate or se
- the company provides filg

1.2 Filgotinib, with methotrexate
rheumatoid arthritis in adults
cannot have other DMARDs,

- disease is severe (a DAS2
- they cannot have rituxima
- the company provides filg

1.3 Filgotinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to rituximab and at least 1 biological DMARD, only if:

- disease is severe (a DAS28 of more than 5.1) and
- the company provides filgotinib according to the commercial arrangement.

1.4 Filgotinib can be used as monotherapy when methotrexate is contraindicated or if people cannot tolerate it, when the criteria in sections 1.1, 1.2 or 1.3 are met.

Patient #1

Patient #1

Female 55 yo

RF-/CCP- RA: Dx 2003
Extra-articular: Sjogren's

Comorbidities: none
Non-smoker

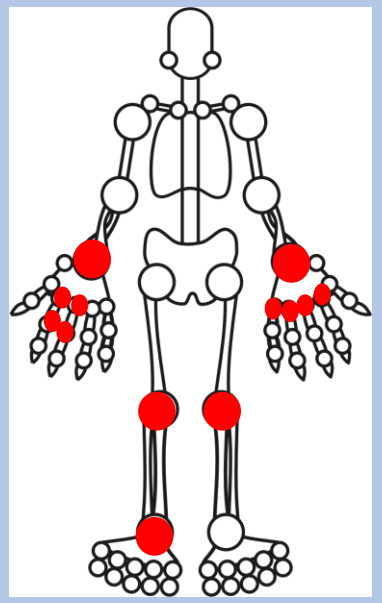
Current meds:
RTX infusions 2009-2022
HCQ 400mg OD

Previous cDMARDs:
MTX: intolerant

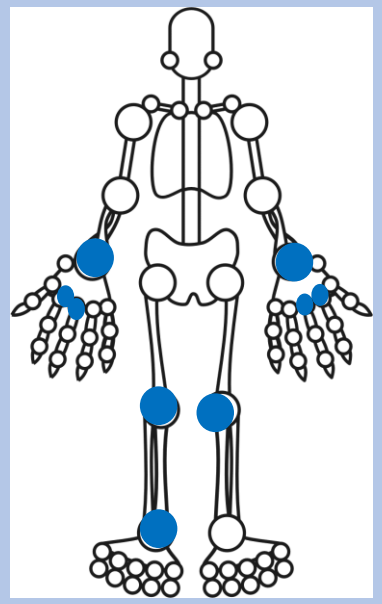
Previous bDMARDs: (-)

July 2022
Clinical examination

TJC



SJC



Metrics

TJC68	12 (+1)
SJC66	8 (+1)
painVAS	8/10
globalVAS	8/10
CRP	**2** mg/dL
DAS28	**5.91**
CDAI	**35**

Patient #1

Female 55 yo

Patient on RTX, initially with good response – but currently

a. Hypogammaglobulinaemia (IgG 415mg/L) and frequent infections (recently severe Covid-19 having received Rx with neutralising Abs)
b. CXR minor upper lobe fibrosis
c. High disease activity, confirmed on MSKUS

July 2022: commenced on **Filgotinib 100mg OD**

Patient #1 – latest FU

Female 55 yo

RF-/CCP- RA: Dx 2003
Extra-articular: secondary SjS

Comorbidities: none
Non-smoker

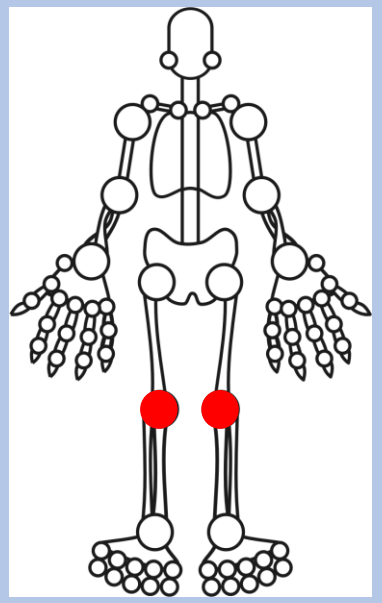
Current meds:
Filgotinib 100mg OD
HCQ 400mg OD

Previous cDMARDs:
MTX: intolerant

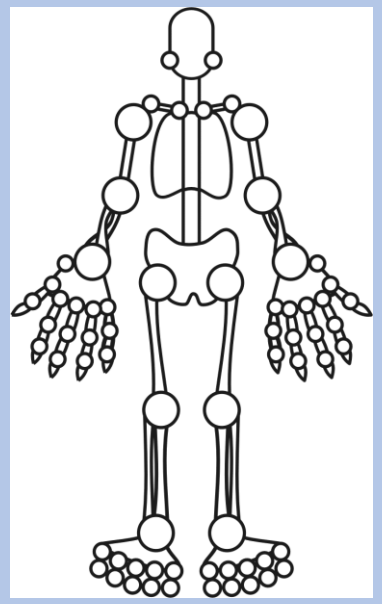
Previous bDMARDs:
RTX (2009-2022)

Feb 2024
Clinical examination

TJC



SJC



Metrics

TJC68	3 (+0)
SJC66	0 (+0)
painVAS	2/10
globalVAS	3/10
CRP	0.3 mg/dL
DAS28	**2.53**
CDAI	**7**

Patient #1: benefits of filgotinib use

Female 55 yo

Excellent response on filgo and no further infections

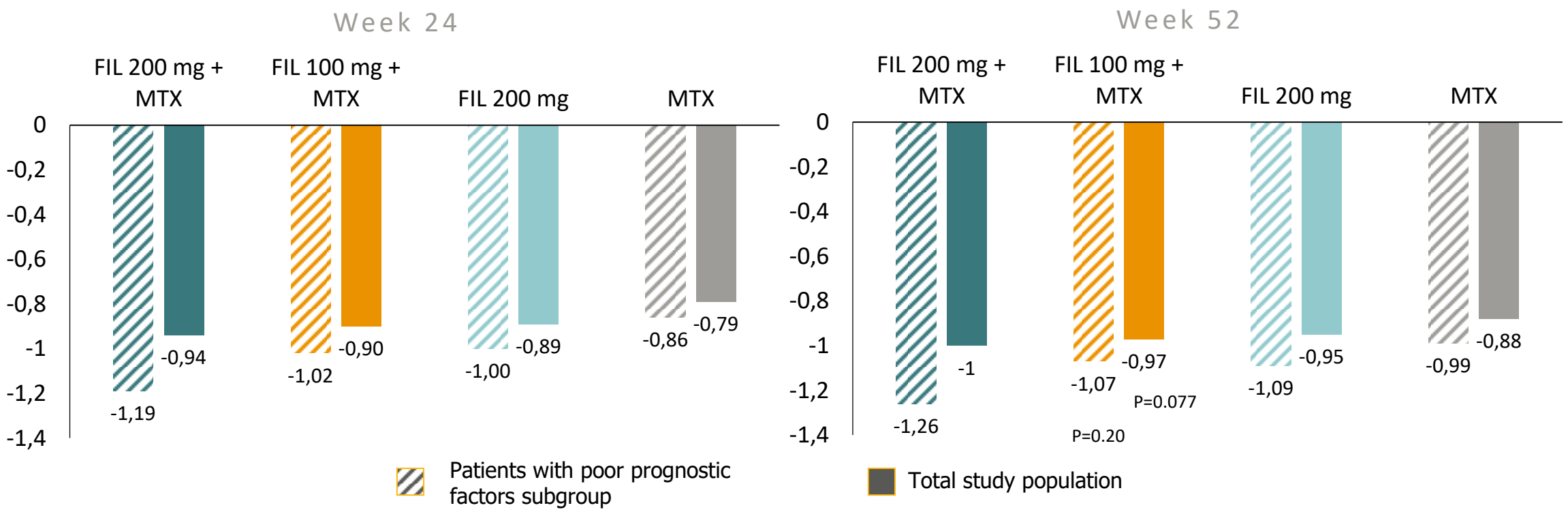
Benefits:

a. Monotherapy

Efficacy of FIL in MTX-naïve patients with poor prognostic factors

FINCH 3

Mean change from baseline in **HAQ-DI score**



In patients with four poor prognostic factors at baseline, improvement in HAQ-DI at Week 24 was greater with all FIL regimens vs. MTX and at Week 52 following treatment with FIL 200 mg + MTX and FIL 200 mg vs. MTX

Filgotinib is not indicated for the treatment of csDMARD-naïve RA patients.

References:. Aletaha *RMD Open* 2021;**7:**e001621

PROs with filgotinib monotherapy

Genovese *et al. Arthritis Research & Therapy* (2018) 20:57
https://doi.org/10.1186/s13075-018-1541-z

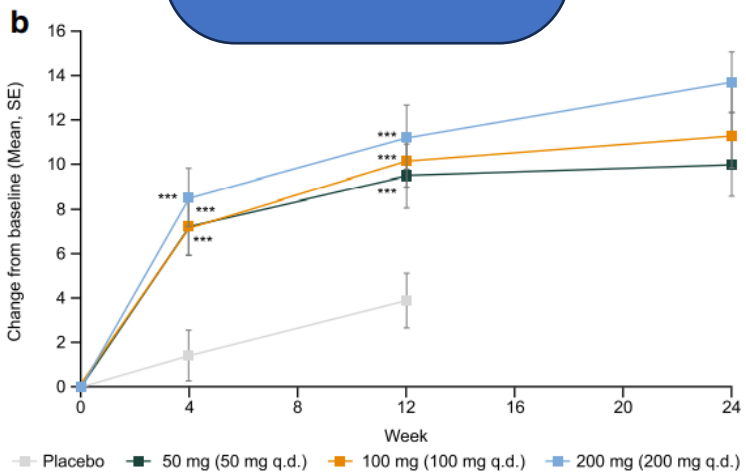
Arthritis Research & Therapy

RESEARCH ARTICLE Open Access

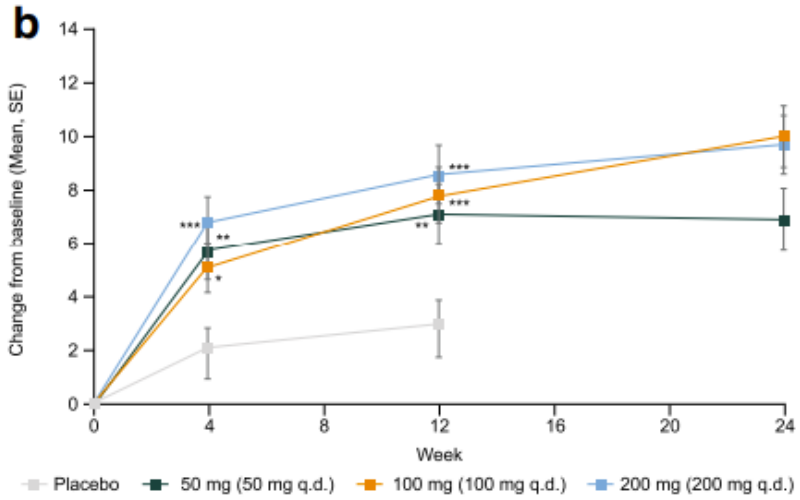
Effect of filgotinib, a selective JAK 1 inhibitor, with and without methotrexate in patients with rheumatoid arthritis: patient-reported outcomes

Mark Genovese[1,5*], Rene Westhovens[2], Luc Meuleners[3], Annegret Van der Aa[3], Pille Harrison[3], Chantal Tasset[3] and Arthur Kavanaugh[4]

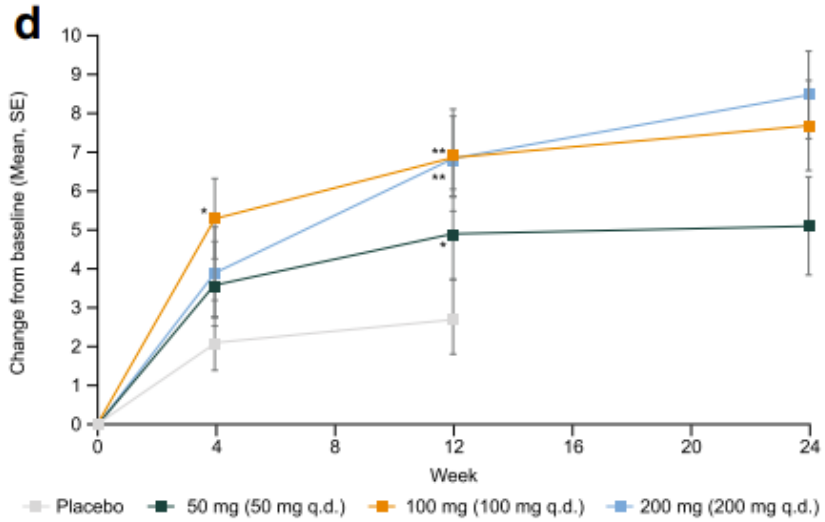
FACIT-F



SF-36 physical component



SF-36 mental component



Genovese et al. Arthritis Research & Therapy (2018) 20:57

Patient #1: benefits of filgotinib use

Female 55 yo

Excellent response on filgo and no further infections

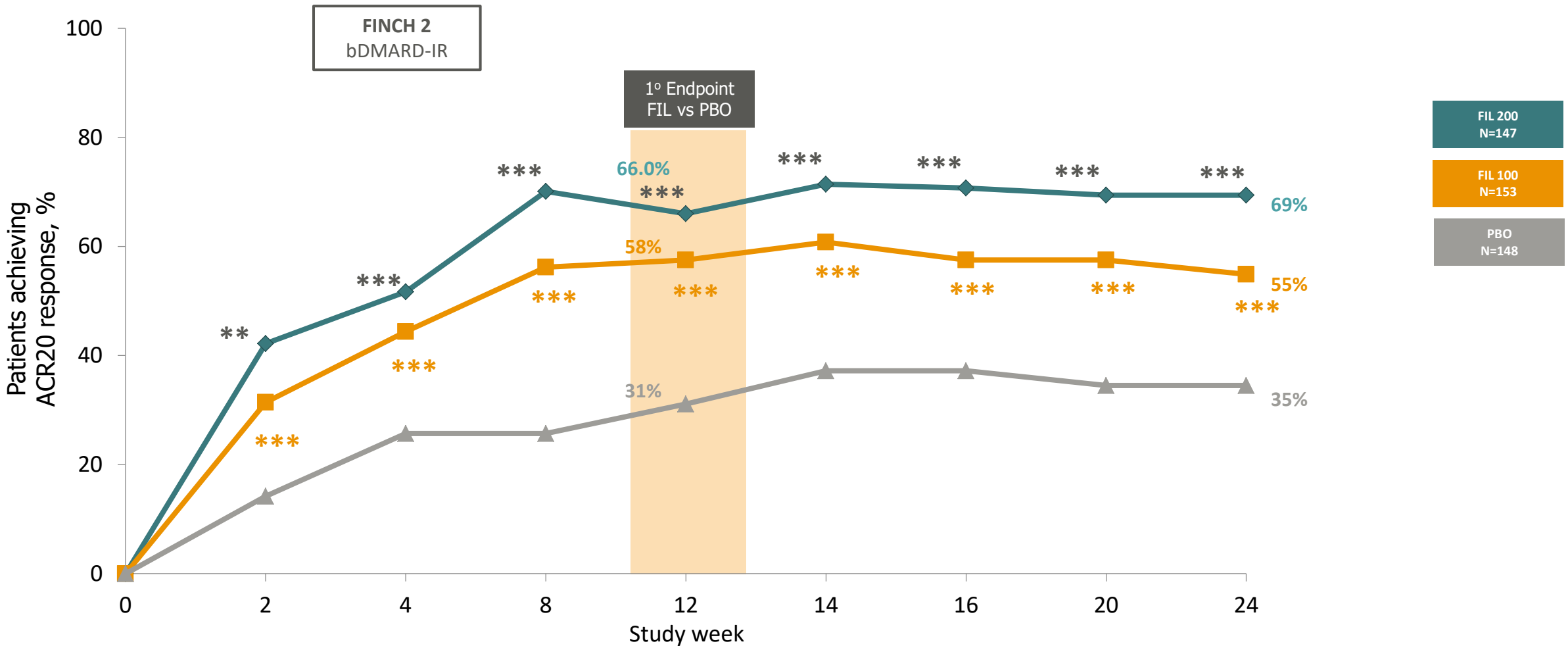
Benefits:

a. Monotherapy

b. Good efficacy on bDMARD – experienced patients

ACR20 responses with FIL as early as week 2 in bDMARD-IR patients

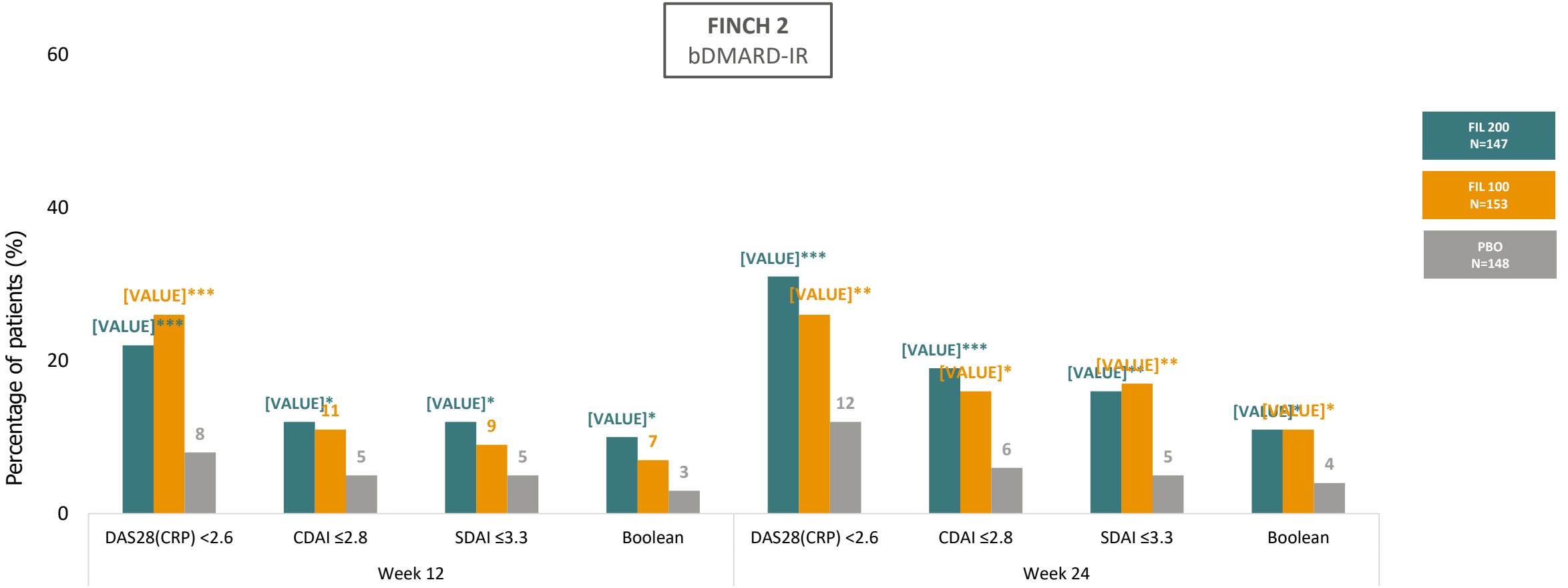
FINCH 2



**p<0.01; ***P<0.001 for FIL vs PBO, Full Analysis Set; NRI
Note: Only the data for the primary endpoint are adjusted for multiplicity; all other significance levels are nominal
References: Genovese. *JAMA.* 2019;322(4):315–325

bDMARD-IR RA patients were more likely to achieve remission on FIL 200mg or FIL 100mg vs PBO

FINCH 2



*p<0.5; **p<0.01; ***P<0.001 for FIL vs PBO, Full Analysis Set; NRI

References: Genovese. *JAMA.* 2019;322(4):315–325. Section 2.5 Clinical Overview Filgotinib 19JUL2019, page 24-25.

Patient #1: benefits of filgotinib use

Female 55 yo

Excellent response on filgo and no further infections

Benefits:

a. Monotherapy

b. Good efficacy on bDMARD – experienced patients

c. No increase in infections

(possibility to start on lower dose and then increase in patients with difficult comorbidities)

Patient #2

Patient #2

Female 66 yo

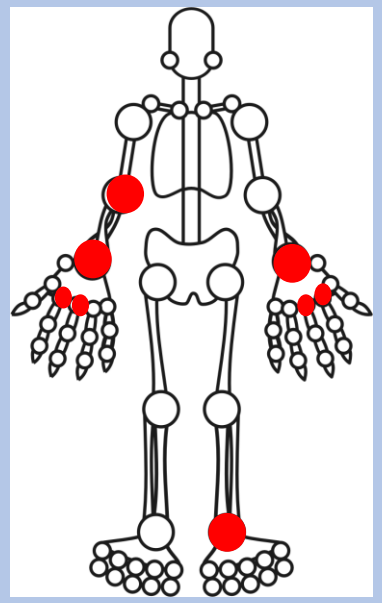
RF-/CCP+ RA: Dx 2020
Extra-articular: interstitial changes on HRCT, but normal PFTs
Comorbidities: Depression, irritable bowel syndrome, frequent LRTIs
Non-smoker

Current meds:
Prednisolone 5mg OD
HCQ 400mg OD

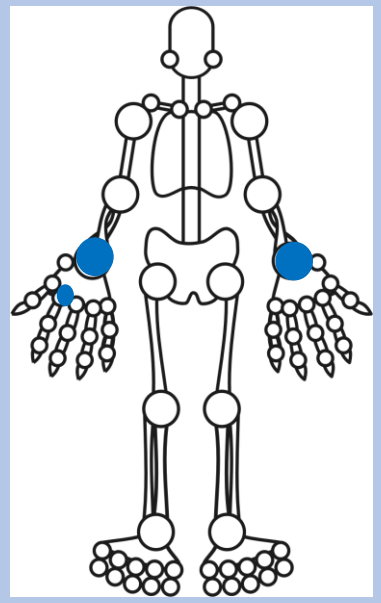
Previous cDMARDs:
MTX: intolerant
SSZ: intolerant

March 2024
Clinical examination

TJC



SJC



Metrics

TJC68	7 (+1)
SJC66	3 (+1)
painVAS	6/10
globalVAS	6/10
CRP	**1.1** mg/dL
DAS28	**4.68**
CDAI	**22.5**

Filgotinib for moderate to severe RA

PharmacoEconomics (2021) 39:1397–1410
https://doi.org/10.1007/s40273-021-01080-z

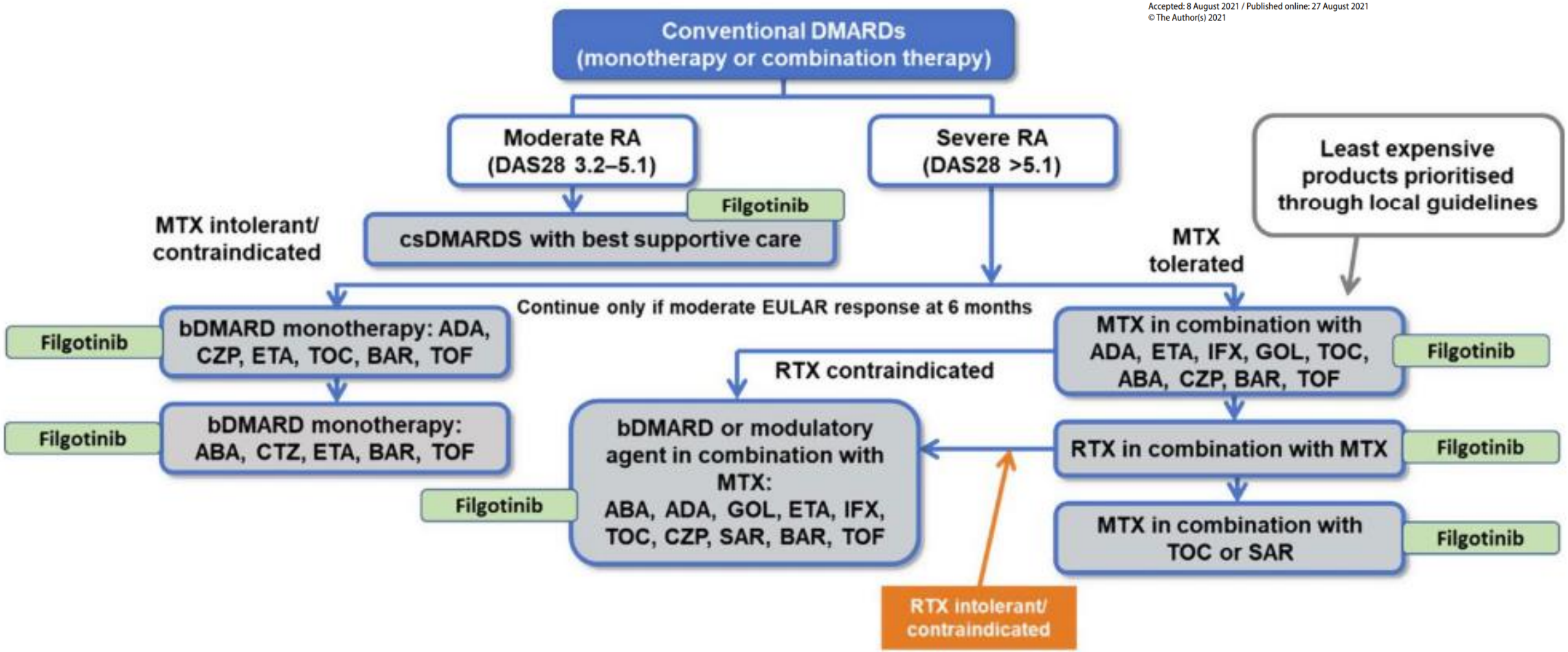
REVIEW ARTICLE

Check for updates

Filgotinib for Moderate to Severe Rheumatoid Arthritis: An Evidence Review Group Perspective of a NICE Single Technology Appraisal

Sabine E. Grimm[1] · Ben Wijnen[1] · Rob Riemsma[2] · Debra Fayter[2] · Nigel Armstrong[2] · Charlotte Ahmadu[2] · Lloyd Brandts[1] · Kate Misso[2] · John R. Kirwan[3] · Jos Kleijnen[2,4] · Manuela A. Joore[1,4]

Accepted: 8 August 2021 / Published online: 27 August 2021



Grimm et al Pharmacoeconomics 2021 Dec;39(12):1397-1410

Patient #2

Female 66 yo

Patient with moderate disease activity (in the UK unable to start bDMARD otherwise)

First biologic choice

a. Non-smoker
b. No history of ASCVD
c. History of Lower Respiratory Tract Infection and potential ILD (but satisfactory PFTs)

March 2024: commenced on **Filgotinib 200mg OD**

Patient #2 – latest nurse led FU

Female 66 yo

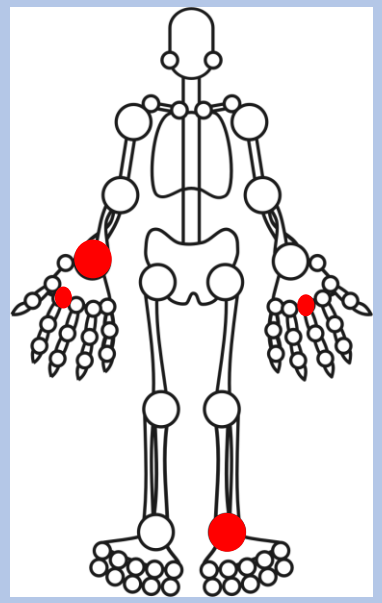
RF-/CCP+ RA: Dx 2020
Extra-articular: interstitial changes on HRCT, but normal PFTs
Comorbidities: Depression, irritable bowel syndrome, frequent LRTIs
Non-smoker

Current meds:
Prednisolone 5mg OD
HCQ 400mg OD

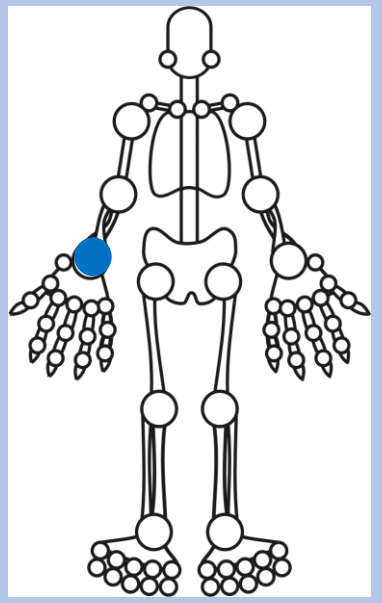
Previous cDMARDs:
MTX: intolerant
SSZ: intolerant

Sep 2024
Clinical examination

TJC



SJC



Metrics

TJC68	3 (+1)
SJC66	1 (+0)
painVAS	2/10
globalVAS	3/10
CRP	**0.2** mg/dL
DAS28	**2.89**
CDAI	**8.5**

TEAEs of special interest were generally balanced amongst treatment arms

n (%) in RA patients with inadequate response to MTX	Placebo-controlled period (Week 0 to 24)				Week 24 to 52					
	FIL 200 mg (n=475)	FIL 100 mg (n=480)	ADA (n=325)	PBO (n=475)	FIL 200 mg (n=475)	FIL 100 mg (n=480)	ADA (n=325)	PBO to FIL 200 mg (n=190)	PBO to FIL 100 mg (n=191)	On PBO period (N=475)
Infectious AEs	133 (28.0)	128 (26.7)	88 (27.1)	105 (22.1)	206 (23.4)	194 (40.4)	129 (39.7)	45 (23.7)	39 (20.4)	106 (22.3)
Serious infectious AEs	8 (1.7)	8 (1.7)	8 (2.5)	4 (0.8)	13 (2.7)	13 (2.7)	10 (3.1)	1 (0.5)	2 (1.0)	4 (0.8)
Herpes zoster	2 (0.4)	2 (0.4)	2 (0.6)	2 (0.4)	6 (1.3)	4 (0.8)	2 (0.6)	2 (1.1)	1 (0.5)	2 (0.4)
Hepatitis B or C	0	0	1 (0.3)	0	1 (0.2)	1 (0.2)	1 (0.3)	1 (0.5)	1 (0.5)	0
Opportunistic infections	0	0	1 (0.3)	0	0	0	2 (0.6)	0	0	0
Active tuberculosis	0	0	0	0	0	0	1 (0.3)	0	0	0
MACE[a]	0	1 (0.2)	1 (0.3)	2 (0.4)	0	2 (0.4)	1 (0.3)	1 (0.5)	1 (0.5)	2 (0.4)
Malignancy										
Excluding NMSC	0	1 (0.2)	1 (0.3)	3 (0.6)	2 (0.4)	2 (0.4)	2 (0.6)	0	0	3 (0.6)
NMSC	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
VTE[a]	1 (0.2)	0	0	2 (0.4)	1 (0.2)	0	1 (0.3)	1 (0.5)	0	2 (0.4)
GI perforation	0	0	0	0	1 (0.2)	0	0	0	0	0

[a] Positively adjudicated

ADA: adalimumab; AE: adverse event; FIL: filgotinib; GI: gastrointestinal; MACE: major adverse cardiac event; MTX, methotrexate; NMSC: nonmelanoma skin cancer; PBO: placebo; RA, rheumatoid arthritis; TEAE: treatment-emergent adverse event; VTE: venous thromboembolism

Combe B, et al. *Ann Rheum Dis*. 2021 Jul;80(7):848-858.

Risk of Serious Infections with filgotinib

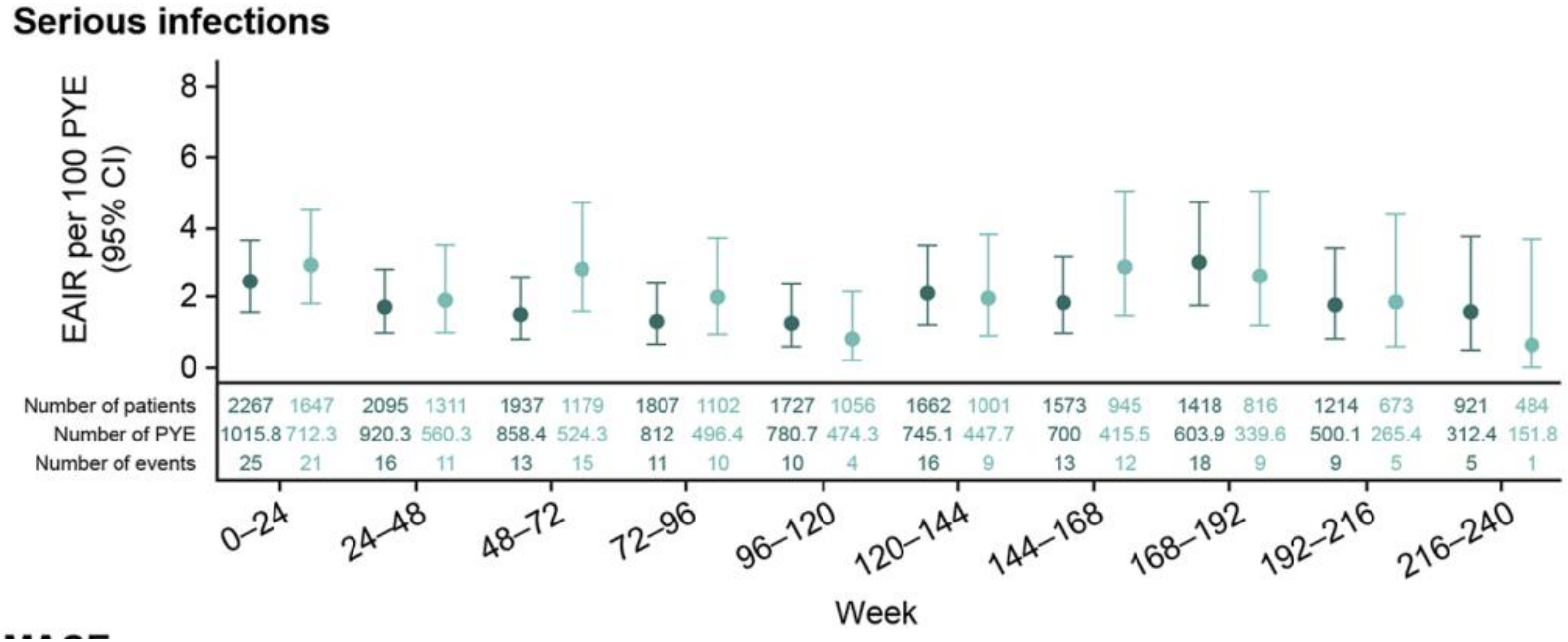
Rheumatoid arthritis

OPEN ACCESS

CLINICAL SCIENCE

Integrated safety analysis of filgotinib in patients with moderate-to-severe rheumatoid arthritis over a treatment duration of up to 8.3 years

Gerd R Burmester [1], Jacques-Eric Gottenberg [2], Roberto Caporali [3], Kevin L Winthrop [4], Yoshiya Tanaka [5], Edmund V Ekoka Omoruyi [6], Vijay Rajendran,[6] Paul Van Hoek [6], Katrien Van Beneden [6], Tsutomu Takeuchi [7,8], René Westhovens [9], Daniel Aletaha [10]



	Filgotinib 200 mg QD (PYE=8008.6) (N=2267)	Filgotinib 100 mg QD (PYE=4532.4) (N=1647)	Pooled filgotinib (PYE=12541.0) (N=3691)
	n (%), EAIR per 100 PYE (95% CI)		
Infections			
Serious infections	149 (6.6), 1.9 (1.6 to 2.2)	97 (5.9), 2.2 (1.8 to 2.7)	246 (6.7) 2.0 (1.7 to 2.2)
Herpes zoster	114 (5.0), 1.5 (1.2 to 1.8)	49 (3.0), 1.1 (0.8 to 1.5)	163 (4.4) 1.3 (1.1 to 1.6)
COVID-19	249 (11.0), 3.2 (2.8 to 3.6)	147 (8.9), 3.3 (2.8 to 3.9)	396 (10.7), 3.2 (2.9 to 3.6)
Cardiovascular events			

Burmester GR, et al. Ann Rheum Dis 2024;83:1110–1117.

Which real-life patients take filgotinib?

Originalien

Z Rheumatol
https://doi.org/10.1007/s00393-024-01506-x
Accepted: 21 March 2024

Redaktion
Ulf Müller-Ladner, Bad Nauheim
Uwe Lange, Bad Nauheim

Real-world experience with filgotinib for rheumatoid arthritis in Germany

A retrospective chart review

Olaf Schultz[1] · Christoph Fiehn[2] · Christian Kneitz[3] · Nils Picker[4] · Daniel Kromer[5] · Monia Zignani[6] · Francesco De Leonardis[6] · Hans-Dieter Orzechowski[7] · Margot Gurrath[7] · Klaus Krüger[8]

[1] ACURA Kliniken Baden-Baden/Rheumazentrum, Baden-Baden, Germany
[2] Praxis for Rheumatology and Clinical Immunology, Medical Center Baden-Baden, Baden-Baden, Germany
[3] Rheumatologische Schwerpunktpraxis Schwerin, Schwerin, Germany
[4] Ingress-Health HWM GmbH—A Cytel Company, Wismar, Germany
[5] Ingress-Health HWM GmbH—A Cytel Company, Berlin, Germany
[6] Galapagos GmbH, Basel, Switzerland
[7] Galapagos Biopharma Germany GmbH, Munich, Germany
[8] Rheumatologisches Praxiszentrum St. Bonifatius, Munich, Germany

Table 2 Baseline comorbidities

	Total ($N = 301$), *n* (%)
CV disease	
Any CV risk factor[a]	140 (46.5)
Arterial hypertension	103 (34.2)
Dyslipidemia	39 (13.0)
Diabetes mellitus	32 (10.6)
Cardiac arrhythmias	16 (5.3)
Coronary heart disease	13 (4.3)
Condition following myocardial or cerebral infarction	9 (3.0)
Condition following deep vein thrombosis or pulmonary embolism	8 (2.7)
Heart failure	7 (2.3)
Metabolic syndrome	
Obesity (body mass index ≥ 30 kg/m²)	35 (11.6)
Cancers	
Other cancers	9 (3.0)
Nonmelanoma skin cancer	3 (1.0)
Gastroenterological diseases	
Liver disease	11 (3.7)
Gastroesophageal reflux disease	8 (2.7)
Inflammatory bowel disease	6 (2.0)

Z Rheumatol https://doi.org/10.1007/s00393-024-01506-x Accepted: 21 March 202

Patient #3

Patient #3

Female 49 yo

RF+/CCP+ RA: Dx 2010
Extra-articular: (-)
Comorbidities: Latent TB treated 2013, depression, firomyalgia
Current smoker

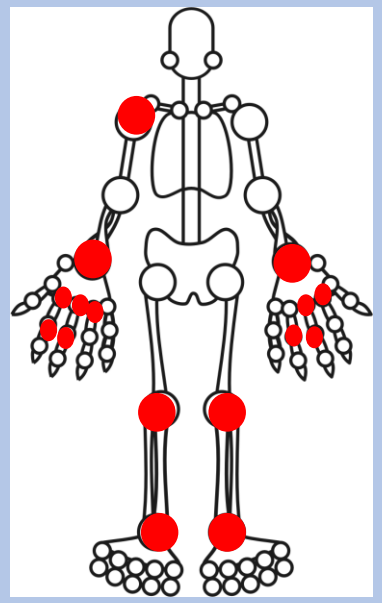
Current meds:
Prednisolone 10mg OD
RTX 2023-2024

Previous cDMARDs:
MTX and LEF: intolerant

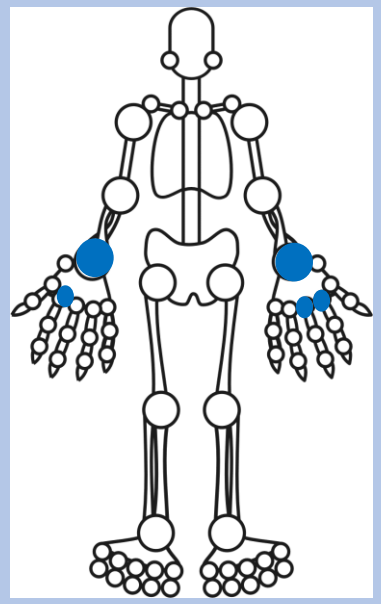
Previous bDMARDs:
Etanercept, abatacept, rituximab, sarilumab

August 2024
Clinical examination

TJC



SJC



Metrics

TJC68	14 (+2)
SJC66	5 (+0)
painVAS	9/10
globalVAS	9/10
CRP	**0.4** mg/dL
DAS28	**5.44**
CDAI	**36**

Patient #3:

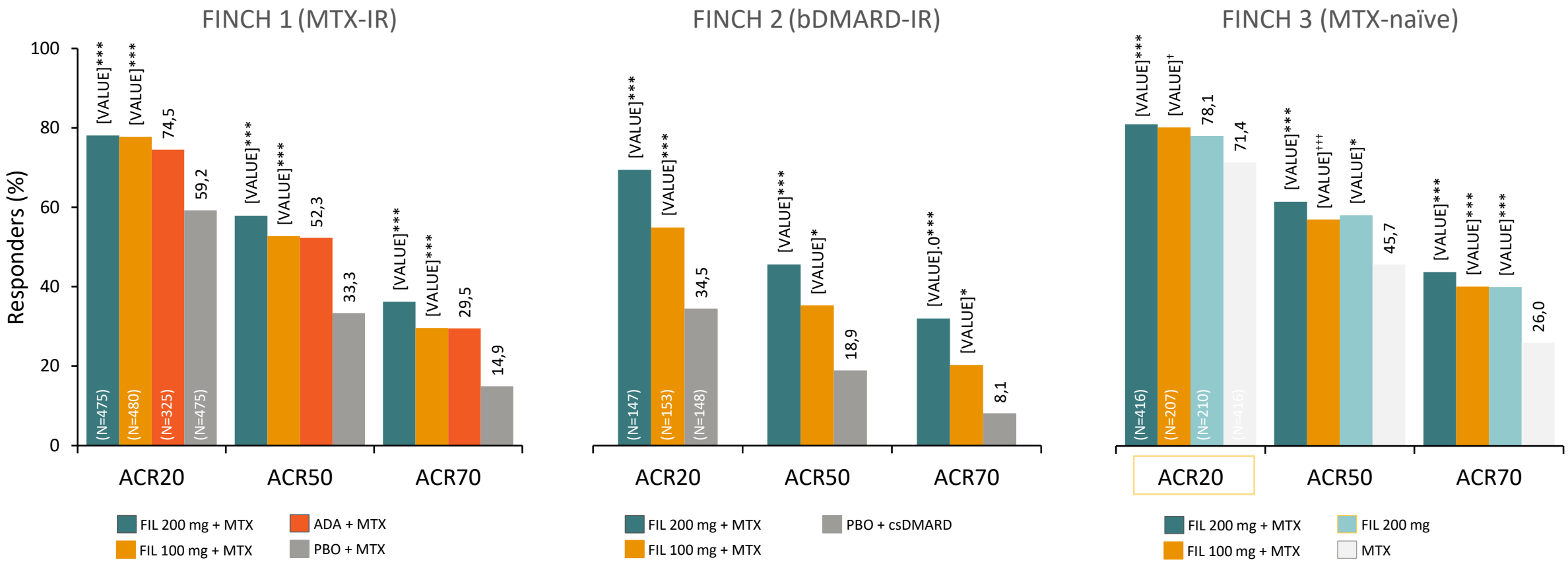
Female 49 yo

Patient with

a. High disease activity on high dose prednisolone
b. Pain augmentation / FMS
c. History of multiple bDMARD failures

August 2024: commenced on **Filgotinib 200mg OD**

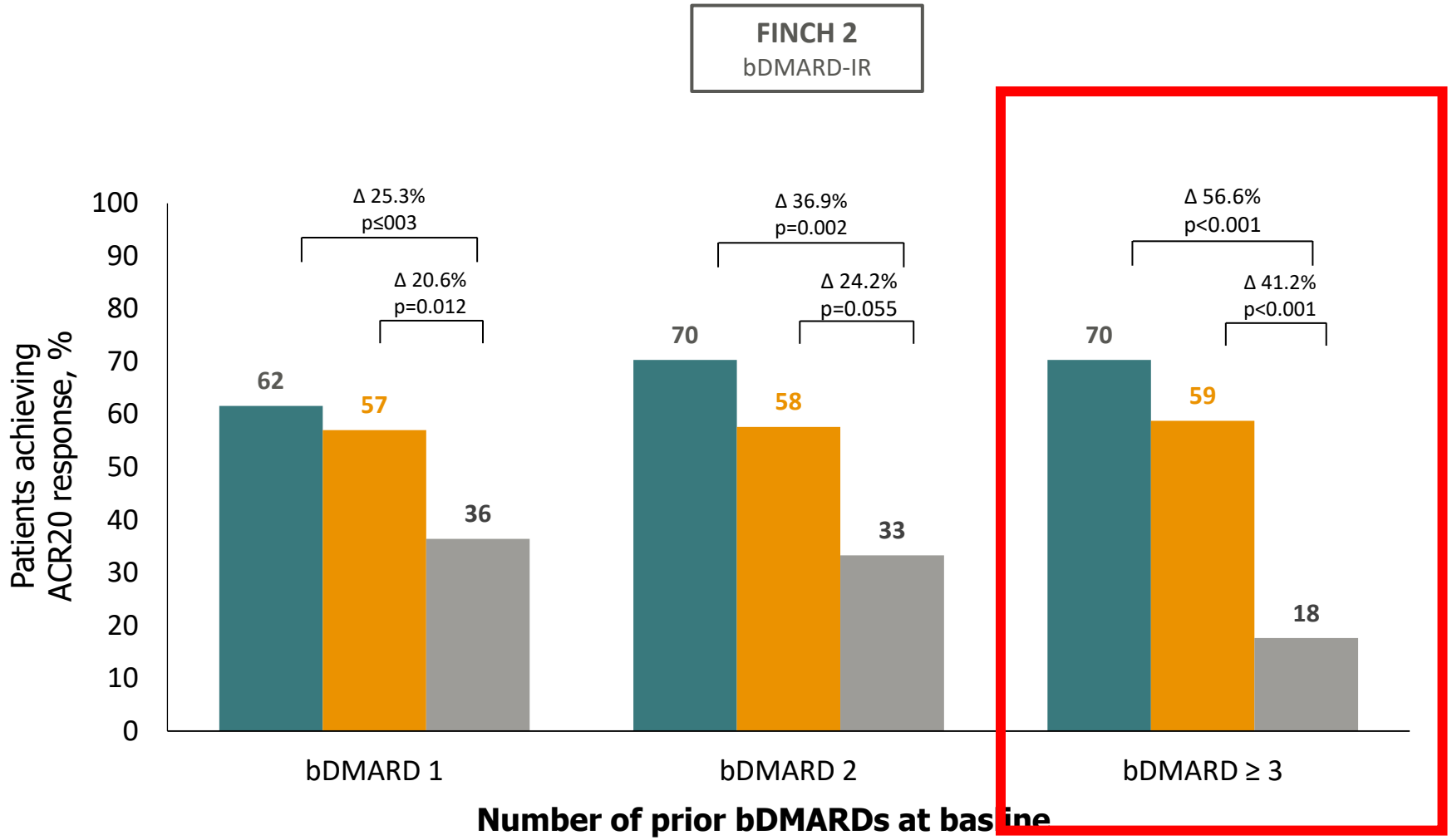
Efficacy in different stages of RA



Filgotinib is not indicated for the treatment of csDMARD-naïve RA patients.
***P<0.001; **P=0.001 *P<0.005; $^{\dagger\dagger\dagger}P$<0.01; $^{\dagger\dagger}P$=0.01; $^{\dagger}P$<0.05 vs PBO + MTX (FINCH 1); PBO + csDMARDs (FINCH 2); or MTX (FINCH 3). Endpoints boxed indicate primary endpoint for the study.

References: : Combe B. Ann Rheum Dis 2021;80:848–858. Genovese. J*AMA.* 2019;322(4):315–325. Westhovens. Ann Rheum Dis 2021;80:727-738

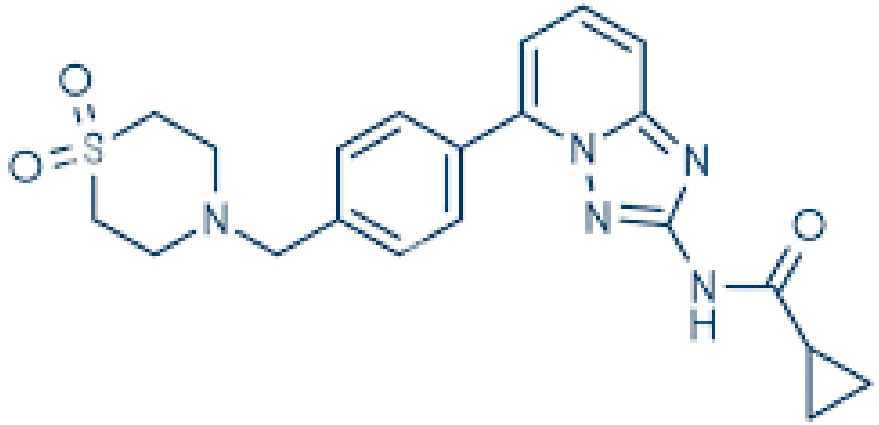
Efficacy in “difficult” RA patients



Even when patients failed ≥ 3 prior bDMARDs, high ACR20 responses were achieved at week 12

References: Genovese. J*AMA.* 2019;322(4):315–325

Why should I think about filgotinib for my next RA patient (when available?)



filgotinib

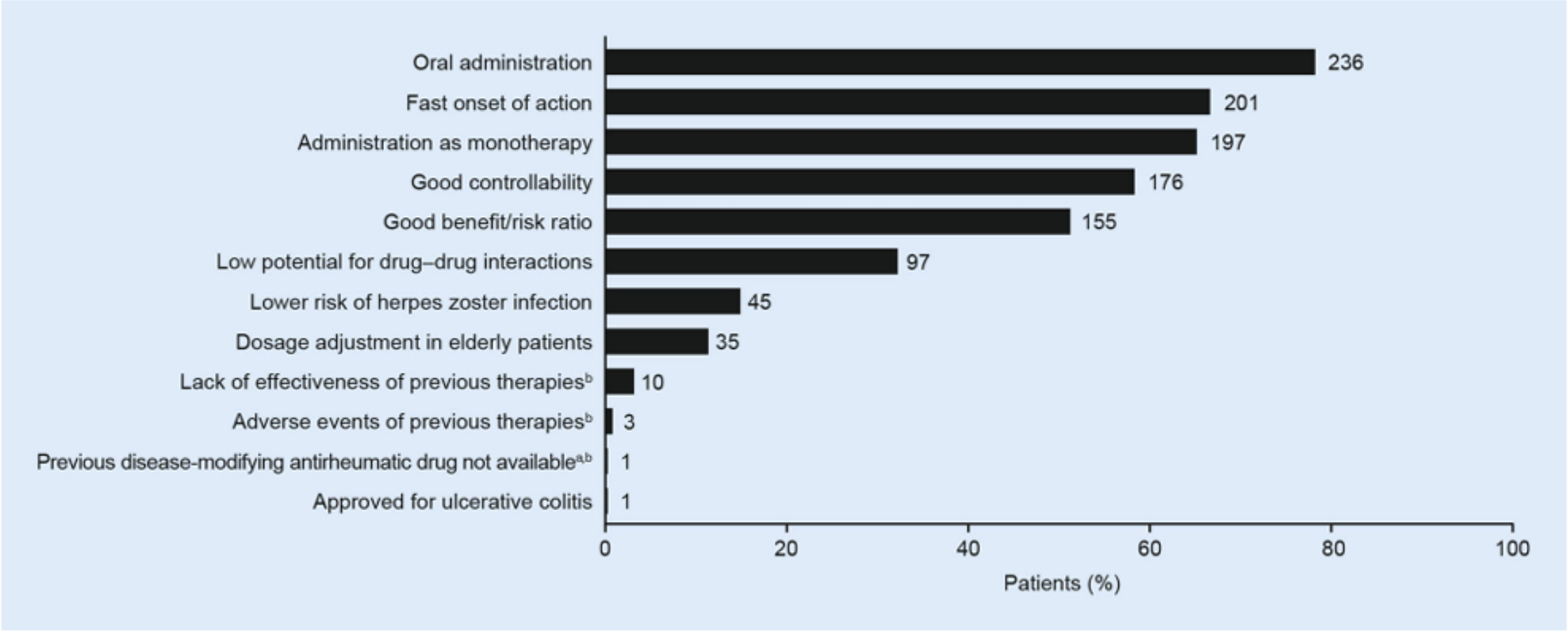
Why do people choose filgotinib?

Originalien

Z Rheumatol
https://doi.org/10.1007/s00393-024-01506-x
Accepted: 21 March 2024

Redaktion
Ulf Müller-Ladner, Bad Nauheim
Uwe Lange, Bad Nauheim

Real-world experience with filgotinib for rheumatoid arthritis in Germany



Z Rheumatol https://doi.org/10.1007/s00393-024-01506-x Accepted: 21 March 202

Filgotinib in real life practice (With a little help from my friends)

The previous cases have shown that filgotinib represents a good bDMARD choice in patients with

1. Need for efficacious and fast-acting treatment
2. Even with moderate disease activity
3. Increased risk of infection
4. Where quick “wash-out” is important
5. Previous multiple bDMARD failures

Huge thanks to Dr Karen MJ Douglas for providing the patient cases


THANK
YOU
FOR
YOUR
ATTENTION