British Society for Rheumatology

### Letter to the Editor (Matters arising from published papers)

# Comment on: Benchmarking tocilizumab use for giant cell arteritis

Shalini Janagan<sup>1</sup>, Catherine Guly<sup>2</sup>, Sarah Skeoch<sup>3</sup>, Joanna C. Robson (b) <sup>1,4,\*</sup>

<sup>1</sup>Department of Rheumatology, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK <sup>2</sup>Bristol Eye Hospital, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK <sup>3</sup>Department of Rheumatology, Royal National Hospital for Rheumatic Diseases, Royal United Hospitals, Bath, UK <sup>4</sup>Rheumatology Research, Faculty of Health and Applied Science, University of the West of England, Bristol, UK

\*Correspondence to: Joanna C. Robson, Rheumatology Research, Room 5-054, Rheumatology Research B502, Bristol Royal Infirmary, Bristol BS2 8HW, UK. E-mail: jo.robson@uwe.ac.uk

DEAR EDITOR, It is with great interest that we read the editorial on tocilizumab (TCZ) use in GCA published on 9 May 2022 by Conway *et al.* [1]. We write to share some of our data to add weight to the views expressed, particularly in relationship to use of TCZ beyond 1 year in refractory cases with visual involvement.

In line with NHS England's policy that all cases of refractory or relapsing GCA being considered for TCZ should be discussed regionally, a peer-to-peer Bristol and Bath TCZ multidisciplinary meeting has been held monthly since November 2018, with patients referred from rheumatology and ophthalmology sites across the region. Thirty-eight cases have been discussed between November 2018 and September 2021, with 31 being approved for TCZ use. The mean age of approved cases was 74 years, with three-quarters (74.2%) being female.

Of these, 11 had refractory GCA and 20 had relapsing GCA. Most patients (77.4%) had cranial GCA, with 48.4% having large vessel vasculitis. About 45% (n = 14) had visual involvement, with ~25.8% having visual loss compared with 24% with ocular symptoms reported in a Scottish cohort [2]. All patients had been on glucocorticoids, with the average time to referral being 591 days. Among them, 19.4% had hypertension, cataract progression, weight gain or osteoporosis; 16.1% had diabetes, neuropsychiatric symptoms or sleep disturbances attributed to glucocorticoid use.

On comparing patients with visual involvement vs those without, it was seen that those with visual involvement had presented with headache, jaw pain and scalp tenderness more commonly than large vessel vasculitis-GCA (73.8 vs 52.9%). They were referred to the multidisciplinary meeting earlier (478.2 vs 648.1 days) and were on higher doses of glucocorticoids at the time of referral (71.4 vs 47.1% on  $\geq$ 40 mg).

In December 2021, a follow-up audit revealed that 14 of 31 patients had completed  $\geq$ 12 months of TCZ; 5 of these had had an extension under coronavirus disease 2019 (COVID-19) exceptional guidance (mean duration of

5.2 months). Of the remaining 17, 3 patients had stopped early [1 death, 1 moved away and 1 owing to adverse effects (headache and gastrointestinal side effects)], 4 had not started treatment and 10 had not completed 12 months.

Adverse events in the 14 patients at 12 months included: liver abnormalities (2 of 14; 14.3%), neutropenia (2 of 14; 14.3%), thrombocytopenia (1 of 14; 7.1%), soft tissue infections (3 of 14; 21.4%), urinary tract infections (1 of 14; 7.1%) and lipid derangement (4 of 14 28.6%). One patient was admitted with chest pain but with normal investigations. One case of GCA relapse occurred on TCZ (mild headache and raised inflammatory markers, which settled on increase in prednisolone). After 12 months, the mean prednisolone dose was 3 mg (range 0–15 mg; median 1 mg).

Our data show that patients on TCZ were able to reduce the dose of glucocorticoids and associated side effects significantly and that clinicians and patients chose to continue TCZ beyond 12 months during the COVID-19 pandemic. There was a low incidence of GCA relapse on TCZ, and visual symptoms were not seen as part of any flare. Data from other studies also show similar outcomes [3]. This supports the use of TCZ beyond 12 months; abrupt withdrawal of treatment can precipitate flare-up of GCA, with significant morbidity and mortality from the disease and glucocorticoids [3]. Biologic therapies for other rheumatic diseases are funded under National Institute for Health and Care Excellence guidance until the patient and clinician decide that it is appropriate to stop. Despite this, recent new guidance from NHS England is that the policy of 1 year only (which had been extended on compassionate grounds during the COVID-19 pandemic), has now returned to a strict 1 year only treatment period, with no potential to retreat even if serious visual relapses occur.

We support the stance of EULAR in offering TCZ for patients with relapsing/refractory disease or a high risk of developing complications with glucocorticoids, with the duration of treatment decided on an individual basis [4]. Downloaded from https://academic.oup.com/rheumap/article/6/3/rkac069/6673922 by UWE Bristol user on 21 October 2022

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Continuing TCZ beyond 12 months might prevent GCA relapse and associated morbidity, particularly in those with visual involvement, in whom relapsing disease can cause irreversible blindness and have a significant impact on function and health-related quality of life [5, 6].

#### Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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## A 2nd generation, JAK1 preferential inhibitor for moderate to severe RA<sup>1-6</sup>

While 1st generation JAK inhibitors are relatively non-selective,<sup>2-6</sup> JYSELECA has over 5x greater potency for JAK1 over JAK2/3 and TYK21\*

Balancing sustained efficacy<sup>7-11</sup> with acceptable tolerability<sup>1,12</sup>



( )

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.<sup>1</sup> May be used as monotherapy or in combination with methotrexate.<sup>1</sup>

\*From biochemical assays, the clinical relevance of which is uncertain. JAK, Janus kinase; RA, rheumatoid arthritis; TYK, tyrosine kinase.

Refer to Summary of Product Characteristics (SmPC) before prescribing, and for full prescribing information.

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Refer to Summary of Product Characteristics (SmPC) before prescribing, and for full prescribing information. **JYSELECN** figotinib 100 mg or 200 mg film-coated tablets. **Indication:** 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:** <u>Adults</u>; 200 mg once daily. Taken orally with/without food. It is recommended that tablets are swallowed whole. <u>Laboratory Monitoring:</u> Refer to the SmPC for information regarding laboratory monitoring and dose initiation or interruption. <u>Elderly</u>, 4 starting dose of 100 mg of filgotinib once daily is recommended for patients aged 75 years and older as clinical experience is limited. <u>Renal impairment</u>: 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 estimated and by is recommended for patients. Safety and efficacy not yet 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. <u>Immunosuppression</u>: combination use, with immunosuppressints (AK) inhibitors is not recommended as a risk of additive immunosuppressions infections such as pneumonia and opportunistic infections equipations: thypersensitivity to the active sub excluded. <u>Infections</u>; Infections, including serious infections, Pregnancy. **Warnings/Precautions**: Shave been reported. Risk beneft should be assessed prior to initiating in patients with risk factors for infections (see SmPC). Patients should be closely monitored for the development of the initiation in the advelopment of the development of the development of the material and opportunistic infections equipations have been reported, Kisk benefit should be assessed phore of hitating in patients with risk factors for infections (see SmPC). Yatients should be closely monitored for the development of igns and symptoms of infections during and after fligotinib reatment. 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. <u>Tuberculosis</u>, Patients should be screened for TB before initiating filgotinib, and filgotinib should not be administered to patients with active TE. <u>Viral</u> <u>reactivation</u>: 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. <u>Malignancy</u>: Immunomodulatory medicinal products may increase the risk of malignancies. Malignancies were observed in clinical studies (see SmPC). <u>Ferlility</u>. In animal studies, decreased ferlility, 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. <u>Haematological abnormalities</u>; Do not start therapy, or temporarily stop, if Absolute Neutrophil Count (ANC) 1< 10° (cells/L, ALC - OS + 10° cells/L or chaemoglobin «B g/dL. Temporarily stop therapy if these values are observed during routine patient management. <u>Vaccinations</u>; Use of live vaccines during, or immediately prior to, filgotinib treatment is not recommended. <u>Lipids</u>: Treatment with filgotinib was associated with dose dependent increases in lipid parameters, including total cholesterol, and high-density lipoprotein (LDL) levels, while low density lipoprotein (LDL) levels were slightly increased (see SmPC). <u>Cardiovascular</u> *tisk*; Rheumatoid arthritis patients have an increased insk for cardiovascular disorders. Patients should have risk factors (e.g., hypertension, hyperlipidaemia) managed as part of usual standard of care. <u>Venous thrombobembolism</u>: Events of deep venous thrombosis (OVT) and pulmona of DVT/PE, or patients undergoing surgery, and prolonged

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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. **Side effects:** See SmPC for full information. <u>Common (21/100)</u>: herpes zoster, pneumonia, neutropenia, hypercholesterolasemia infection and dizziness. <u>Uncommon (s1/1000 to 1/100)</u>; herpes zoster, pneumonia, neutropenia, hypercholesterolaemia and 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 authorisation number(5): <u>Great Britain</u> Jyseleca 100mg film-coated tablets PLGB 42147/0002 hypeleca 200mg film-coated tablets PLGB 42147/0002 hypeleca 200mg film-coated tablets PLGB 42147/0002 hypeleca 100mg film-coated tablets EU/1/20/1480/001 EU/1/20/1480/003 EU/1/20/1480/004 **Further information**: Galapagos UK, Belmont House, 148 Belmont Road, Uxbridge (DB8 105, United Kingdom 00800 7387 1345 **medicalinfo@glgg**. <u>com</u> Jyseleca<sup>®</sup> is a trademark. **Date of Preparation**: January 2022 UK-RA-FIL-202201-00019 **W** Additional monitoring required Additional monitoring required

Adverse events should be reported. For Great Britain and Northern Ireland, reporting form and information can be found at <u>yellowcard.mhra.gov.</u> and information can be found at <u>yellowcard.mnra.gov.u</u> or via the Yellow Card app (download from the Apple Ap Store or Google Play Store). Adverse events should also be reported to Galapagos via email to DrugSafety.UK.Ireland@glpg.com or 00800 7878 1345

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