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HEALTH TECHNOLOGY BRIEFING
MAY 2019

Filgotinib for moderate to severe active rheumatoid arthritis

NIHRIO ID	6638	**NICE ID**	10139
Developer/Company	Gilead Sciences Ltd and Galapagos	**UKPS ID**	650818

Licensing and market availability plans	Currently at phase III clinical trials.

SUMMARY

Filgotinib is in development for the treatment of adults with moderate to severe active rheumatoid arthritis (RA) as front-line therapy or for those which previous treatment with a disease-modifying anti-rheumatic drug (DMARD) has not worked or are unable to take it. RA is a long-term, autoimmune disease that causes pain, swelling and stiffness in the joints. The condition occurs in women more often than men. The symptoms usually affect the hands, feet and wrists. There may be periods where symptoms become worse, known as flare-ups. Some people with RA also experience problems in other parts of the body, or more general symptoms such as tiredness and weight loss.

Filgotinib is a new Janus Kinase (JAK) inhibitor. JAK pathways are involved in the inflammatory process in RA. Filgotinib is highly selective for JAK1. By blocking the JAK1 pathway, filgotinib may help ease the RA symptoms. Filgotinib can be taken orally as a tablet once a day and it has shown to be safe. Filgotinib may be taken as monotherapy or in combination with methotrexate or other non-biologic DMARDs. If approved for the treatment of moderate to severe RA, filgotinib will offer an additional front line or a later line treatment option for this population group.

PROPOSED INDICATION

As monotherapy or in combination with methotrexate or non-biologic DMARDs for the treatment of adult patients with moderately to severely active RA - front-line therapy or after inadequate response or intolerance to one or more DMARDs.[a]

TECHNOLOGY

DESCRIPTION

Filgotinib (GLPG0634/GS-6034) is a potent and selective inhibitor of JAK1. JAK inhibitors are low molecular weight, cytoplasmic tyrosine kinases, orally available products that can impact intracellular molecules involved in the signalling of various cytokines, growth factors and hormones, such as pro-inflammatory cytokine interleukin-6.[1,2] JAKs play important roles in the functioning of the immune system, hence JAKs have been targeted for their therapeutic potential in immune-inflammatory disorders.[2] There are four JAKs in humans, JAK1, JAK2, JAK3, and tyrosine kinase 2. A number of JAK inhibitors have been developed over the past decade, with some compounds having greater selectivity for certain JAKs over others.[3] Recent findings suggest that JAK1 dominates JAK1/JAK3/γ_c signalling, suggesting that JAK1 inhibition might be largely responsible for the in vivo efficacy of JAK inhibitors in immune-inflammatory diseases.[2] *In vitro* assays for filgotinib indicated a selective inhibition of JAK1 and JAK2 over JAK3 and TYK2, and specifically in whole blood assays, a selectivity of ~30-fold for JAK1 over JAK2 was revealed.[4]

Filgotinib is currently at phase III development for the treatment of moderate to severely active RA. Filgotinib is proposed to be administered once daily orally as a tablet on a proposed dose of 100 or 200 mg with or without methotrexate or other non-biologic DMARDs.[a]

INNOVATION AND/OR ADVANTAGES

Although treatment with biologic agents results in disease suppression for many patients with RA, only approximately 30% achieve complete remission, and the majority of patients treated with biologics experience disease exacerbation following cessation of treatment.[3] The route of administration is also an important consideration, with the results of two studies suggesting that patients with RA may prefer therapies that can be taken orally over those with other routes of administration.[5,6] Filgotinib orally administered would fulfil that requirement for patient convenience.

There is research that suggests that a selective JAK1 inhibitor could provide an increased therapeutic window allowing for higher dosing and efficacy while avoiding dose-limited pharmacology as observed for the pan-JAK inhibitors.[2] Furthermore, already approved, less selective, JAK inhibitors have shown dose-limiting side effects,[7] initial results from phase III and phase II clinical trials have shown adverse events at phase III being equal amongst the placebo and the 100 mg and 200 mg groups.[8]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Filgotinib does not currently have Marketing Authorisation in the EU/UK for any indication.

Filgotinib is currently at phase III development for Crohn's disease and ulcerative colitis.[9]

[a] Information provided by Gilead Sciences Ltd on UK PharmaScan

Filgotinib is at phase II development for ankylosing spondylitis, psoriatic arthritis, fistulizing Crohn's disease, non-infectious uveitis, lupus membranous nephropathy, cutaneous lupus erythematosus and Sjogren's syndrome.[10]

PATIENT GROUP

DISEASE BACKGROUND

Rheumatoid arthritis (RA) is a chronic, inflammatory, multi-system, progressive autoimmune disease affecting the synovial joints, typically the small joints of the hands and feet, which are often affected bilaterally and symmetrically. Clinical features of RA include joint pain (usually worse after periods of rest or inactivity), joint swelling, stiffness and loss of function. On palpation, affected joints are tender, warm and give a 'boggy' feel. Extra-articular presentations may include lymphadenopathy, rheumatoid nodule (occurring over extensor surfaces in 20-30% people with RA), cardiopulmonary disease (e.g. pleurisy, intrapulmonary nodules, diffuse interstitial fibrosis and atherosclerosis), eye disease (including keratoconjunctivitis, dry eyes/sicca, episcleritis and corneal ulcerations) and rheumatoid vasculitis (typically ischaemic mononeuropathy and progressive scleritis).[11] Systemic features include morning stiffness, malaise, fatigue, fever, and weight loss. Symptoms may be insidious, palindromic (waxing and waning) or explosive in onset.[12,13]

Risk factors for RA include a genetic predisposition, which is oligogenic (including the shared epitope on chromosome 6), environmental triggers, including smoking in susceptible individuals and potentially the effect of oestrogen hormone.[12]

The severity of the disease is measured using the composite disease activity score (DAS28), which consists of the assessment of 28 joints for swelling/tenderness, the patient's assessment of health and erythrocyte sedimentation rate or C-reactive protein.[14] A DAS28 greater than 5.1 indicates high disease activity or severe disease, between 3.2 and 5.1 indicates moderate disease activity, and less than 3.2 indicates low disease activity.[15] Additionally the severity of RA can be defined by the stage of disease. As the disease progresses beyond the early stage (stage I), there is a spread of inflammation in synovial tissue, affecting joint cavity space across joint cartilage. This inflammation gradually results in cartilage destruction, accompanied by a narrowing of the joint, and characterises stage II or moderate RA. Severe RA (stage III) is marked by formation of pannus in the synovium and loss of joint cartilage which exposes bone beneath the cartilage. These joint changes and deformities become evident on x-ray. Stage IV is referred to as end stage RA during which the inflammatory process subsides and formation of fibrous tissue and/or deformity of the bone results in ceased joint function. This stage may be associated with formation of subcutaneous nodules.[13]

Without adequate treatment, at 20 years after diagnosis, more than 60% of patients with RA may develop significant functional impairment (stage III), including need of mobility aids, loss of ability for self-caring, and requirement of joint replacement.[16] The overall impact of RA is that it can lead to progressive disability and a decrease in quality of life and functional status, resulting in overall impaired health-related quality of life, and loss of productivity and social functions.[17,18] Approximately one-third of people stop work within two years of onset, and after ten years, 30% of patients are considered severely disabled.[19] People with RA have reduced life expectancy and excess cardiovascular mortality.[20,21]

CLINICAL NEED AND BURDEN OF DISEASE

The prevalence of RA from the NoAR study, the Norfolk Arthritis Register (NoAR), a large primary care inception cohort of patients with inflammatory oligo- and polyarthritis (IP) aged 16 and over, is the first study to estimate the incidence of RA using the 2010 criteria.[22,23] The NoAR study estimated the

overall prevalence of RA in adults of 0.81% (1.16% for women and 0.44% for men, a female: male ratio of 2.7:1).[23-25] This same study estimated the overall incidence rate of 40/100,000 persons; 54/100,000 for women and 25/100,000 for men.[23] Arthritis Research UK reported a prevalence of 0.84% for people aged over 16 in England in 2018 that would approximately equal to 380,000 people.[26] The peak age of incidence in the UK for both men and women is the 70s, but people of all ages can develop the disease.[20]

At secondary care level, the Hospital Episode Statistics for England for the period 2017-18 recorded a total of 77,870 finished consultant episodes (FCEs), 76,669 admissions, of which 59,983 were for women, and 72,356 day cases for rheumatoid arthritis(ICD-10 codes M05.8, M05.9, M06.0, M06.8 and M06.9).[24]

People with RA have a 47% increased risk of death compared to the general population.[26] In England and Wales in 2017 there were a total of 840 deaths recorded due to rheumatoid arthritis and juvenile arthritis (ICD-10 codes M05-M06, M08).[27]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

The aim of treatment is to induce remission or low disease activity, control pain and inflammation, and reduce or prevent joint damage, disability and loss of function, thereby improving quality of life.[19] Adults with RA should have ongoing access to a multidisciplinary team. This should provide the opportunity for periodic assessments of the effect of the disease on their lives (such as pain, fatigue, everyday activities, mobility, ability to work or take part in social or leisure activities, quality of life, mood, impact on sexual relationships) and help to manage the condition.[28] Treatment involves a combination of pharmacological and non-pharmacological interventions. Pharmacological treatment includes various combinations of non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, corticosteroids and DMARDs. DMARDs may be classified as conventional (for example methotrexate, sulfasalazine, leflunomide and hydroxychloroquine) or biological. Biological DMARDs include, but are not limited to, the TNF inhibitors adalimumab, etanercept and infliximab, as well as rituximab and abatacept, plus IL-6 inhibitors tocilizumab and sarilumab. Non-pharmacological interventions include orthopaedic surgery, physiotherapy, psychological interventions, diet and complementary therapies and occupational therapy.[19,29]

CURRENT TREATMENT OPTIONS

In the UK, NICE recommends the following treatment options depending on the stage of the disease:[15]

- For people with newly diagnosed rheumatoid arthritis, NICE clinical guideline 100 recommends a combination of conventional DMARDs (including methotrexate, leflunomide and sulfasalazine) as first-line treatment, ideally beginning within 3 months of the onset of persistent symptoms. Where combination therapies are not appropriate (for example where there are comorbidities or pregnancy) DMARD monotherapy is recommended. Where the disease has not responded to intensive combination therapy with conventional DMARDs, NICE Technology appraisal guidance 375 recommends biological DMARDs (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept) in combination with methotrexate for severe rheumatoid arthritis only. In adults whose disease has responded inadequately to intensive therapy with a combination of conventional DMARDs, NICE Technology appraisal guidance 485 recommends sarilumab with methotrexate.

- For those people with severe rheumatoid arthritis who cannot take methotrexate because it is contraindicated or because of intolerance, the guidance recommends that adalimumab, etanercept, certolizumab pegol, tocilizumab, sarilumab, tofacitinib or baricitinib monotherapy can be used. (NICE Technology appraisal guidance 195, 247, 415, 466, 480, 485) Where the disease has not responded adequately or in the case of intolerance to other DMARDs, including at least one TNF inhibitor (a subgroup of biological DMARDs), rituximab in combination with methotrexate is recommended for severe active disease only (NICE Technology appraisal guidance 195). Where rituximab is contraindicated or withdrawn because of an adverse event, adalimumab, etanercept, infliximab, abatacept, golimumab, tocilizumab and certolizumab pegol each in combination with methotrexate are recommended as options (NICE Technology appraisal guidance 195, 225, 247 and 415). Where rituximab therapy cannot be given because methotrexate is contraindicated or has been withdrawn due to an adverse event, adalimumab, etanercept and certolizumab pegol, sarilumab or tocilizumab, each as a monotherapy, can be used (NICE Technology appraisal guidance 195,415, 485 and 480).

PLACE OF TECHNOLOGY

If licensed, filgotinib monotherapy or in combination with methotrexate or other non-biologic DMARDs will offer an additional front line treatment option for adult patients with moderately to severely active RA and a later line treatment option for adult patients with moderately to severely active RA after inadequate response or intolerance to one or more DMARDs (conventional or biologic).

CLINICAL TRIAL INFORMATION

Trial	**FINCH 1, NCT02889796, EudraCT-2016-000568-41, GS-US-417-0301; 18 years and older; filgotinib vs placebo vs adalimumab, all in combination with methotrexate; phase III**
Sponsor	Gilead Sciences and Galapagos NV
Status	Ongoing
Source of Information	Trial registry[30,31]
Location	EU (incl UK), USA, Japan, Australia and Argentina
Design	Randomised; double-blind; placebo and active-controlled
Participants	n= 1,759; aged 18 or over; diagnosis of RA, American College of Rheumatology (ACR) functional class I-III, have >=6 swollen joints (from a swollen joint count based on 66 joints (SJC66)) and >= 6 tender joints (from a tender joint count based on 68 joints (TJC68)) at both screening and Day 1, ongoing treatment with a stable dose of methotrexate (MTX).
Schedule	Randomised to: • Arm A: Filgotinib dose A (200 mg, oral tablet once daily) + placebo to match filgotinib dose B + placebo to match adalimumab (40 mg/ml, subcutaneous, once every two weeks) in addition to a stable dose of MTX; • Arm B: Filgotinib dose B (100 mg, oral tablet once daily) + placebo to match filgotinib dose A + placebo to match adalimumab (40 mg/ml, subcutaneous, once every two weeks) in addition to a stable dose of MTX;

	• Arm C: Placebo to match filgotinib dose A + placebo to match filgotinib dose B + adalimumab in addition to a stable dose of MTX; • Arm D: Placebo to match filgotinib dose A + placebo to match filgotinib dose B + placebo to match adalimumab in addition to a stable dose of MTX.
Follow-up	Active treatment for 52 weeks, overall follow-up not reported.
Primary Outcomes	• Proportion of participants who achieve an ACR 20% improvement (ACR20) response at week 12
Secondary Outcomes	Time frame 12 weeks: • Proportion of participants who achieve disease activity score based on 28 joints (DAS28) (C-reactive protein (CRP)) ≤ 3.2 • Change from baseline in the Health Assessment Questionnaire - Disability Index (HAQ-DI) score Time frame 24 weeks: • Proportion of participants who achieve DAS28 (CRP) < 2.6 • Change from baseline in the modified Total Sharp Score (mTSS) • Change from baseline in Simplified Diagnostic Activity Index (SDAI) at weeks 4, 12, 24, and 52, and over time Time frame weeks 4, 12, 24, and 52: • Proportion of participants who achieve ACR 50% improvement (ACR50) • Proportion of participants who achieve ACR 70% improvement (ACR70) • Proportion of participants who achieve ACR20 Time frame 52 weeks: • Proportion of participants who achieve ACR20 over time • Proportion of participants who achieve ACR50 over time • Proportion of participants who achieve ACR70 over time • Change from baseline in individual components of the ACR response at weeks 4, 12, 24, and 52 and over time • Proportion of participants who achieve change in HAQ-DI of ≥ 0.22 at weeks 4, 12, 24, and 52, and over time • Change from baseline in DAS28 (CRP) at weeks 4, 12, 24, and 52, and over time • Proportion of participants who achieve DAS28 (CRP) ≤ 3.2 at weeks 4, 24, and 52, and over time • Proportion of participants who achieve DAS28 (CRP) < 2.6 at weeks 4, 12, and 52, and over time • American College of Rheumatology N (ACR-N) at weeks 4, 12, 24, and 52, and over time • European League Against Rheumatism (EULAR) response at weeks 4, 12, 24, and 52, and over time • Change from baseline in Clinical Disease Activity Index (CDAI) at weeks 4, 12, 24, and 52, and over time • Change from baseline in the mTSS • Absolute value and change from baseline in Short-form health survey (SF-36) at weeks 4, 12, 24, and 52, and over time • Absolute value and change from baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-Fatigue) at weeks 4, 12, 24, and 52, and over time • Absolute value and change from baseline in the EuroQol 5 Dimensions (EQ-5D) patient-reported outcomes survey at weeks 4, 12, 24, and 52, and over time

	• Absolute value and change from baseline in Work Productivity and Activity Impairment - Rheumatoid Arthritis (WPAI-RA) patient-reported outcomes survey at weeks 4, 12, 24, and 52, and over time Time frame 24 and 52 weeks: • Proportion of participants with no radiographic progression from baseline at weeks 24 and 52
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study completion date reported as Apr 2019.

Trial	**FINCH 2,** NCT02873936**,** EudraCT- 2016-000569-21**, GS-US-417-0302; 18 years and older; filgotinib vs placebo both in combination with a stable dose of permitted conventional synthetic DMARD(s); phase III**
Sponsor	Gilead Sciences and Galapagos NV
Status	Completed
Source of Information	Trial registry,[31,32] abstract[33]
Location	EU (incl UK), USA, Japan, Australia and Argentina
Design	Randomised; double-blind; placebo-controlled
Participants	n= 449 (planned); aged 18 or over; diagnosis of RA, ACR functional class I-III, have >=6 swollen joints (from a swollen joint count based on 66 joints (SJC66)) and >= 6 tender joints (from a tender joint count based on 68 joints (TJC68)) at both screening and Day 1, ongoing treatment with a stable dose of MTX, have received at least one biologic DMARD for the treatment of RA to which they have had an inadequate response or intolerance.
Schedule	Randomised to: • Arm A: Filgotinib dose A (200 mg, oral tablet once daily) + placebo to match filgotinib dose B + a stable dose of permitted conventional DMARDs (csDMARDs) (MTX, hydroxychloroquine or chloroquine, sulfasalazine, and/or leflunomide); • Arm B: Filgotinib dose B (100 mg, oral tablet once daily) + placebo to match filgotinib dose A + a stable dose of permitted csDMARD(s) (MTX, hydroxychloroquine or chloroquine, sulfasalazine, and/or leflunomide); • Arm C: Placebo to match filgotinib dose A + placebo to match filgotinib dose B + a stable dose of permitted csDMARD(s) (MTX, hydroxychloroquine or chloroquine, sulfasalazine, and/or leflunomide)
Follow-up	Active treatment for 24 weeks
Primary Outcomes	• Proportion of participants who achieve an ACR 20% improvement (ACR20) response at week 12
Secondary Outcomes	Time frame 12 weeks: • Proportion of Participants who Achieve Disease Activity Score based on 28 joints (DAS28) (C-reactive protein (CRP)) ≤ 3.2 at Week 12 • Change from Baseline in the Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Week 12

	Time Frame: Weeks 4, 12, and 24 : • Proportion of Participants who Achieve ACR 50% Improvement (ACR50) at Weeks 4, 12, and 24 • Proportion of Participants who Achieve ACR 70% Improvement (ACR70) at Weeks 4, 12, and 24 Time Frame: Weeks 4 and 24: • Proportion of Participants who Achieve ACR20 at Weeks 4 and 24 Time Frame: Up to 24 weeks: • Proportion of Participants who Achieve ACR20 Over Time from Day 1 through Week 24 • Proportion of Participants who Achieve ACR50 Over Time from Day 1 through Week 24 • Proportion of Participants who Achieve ACR70 Over Time from Day 1 through Week 24 • Proportion of Participants who Achieve Change in HAQ-DI of ≥ 0.22 at Weeks 4, 12, and 24, and Over Time from Day 1 through Week 24 • Change from Baseline in Individual Components of the ACR Response at Weeks 4, 12, and 24 and Over Time from Day 1 through Week 24 [Time Frame: Baseline and up to 24 weeks] • Proportion of Participants who Achieve DAS28 (CRP) ≤ 3.2 at Weeks 4, and 24, and Over Time from Day 1 through Week 24 • Proportion of Participants who Achieve DAS28 (CRP) < 2.6 at Weeks 4, and 24, and Over Time from Day 1 through Week 24 • American College of Rheumatology N (ACR-N) at Weeks 4, 12, and 24, and Over Time from Day 1 through Week 24 • European League Against Rheumatism (EULAR) Response at Weeks 4, 12, and 24, and Over Time from Day 1 through Week 24 Time Frame: Baseline and up to 24 weeks: • Change from Baseline in DAS28 (CRP) at Weeks 4, 12, and 24, and Over Time from Day 1 through Week 24 • Change from Baseline in Clinical Diagnostic Activity Index (CDAI) at Weeks 4, 12, and 24, and Over Time from Day 1 through Week 24 • Change from Baseline in Simplified Diagnostic Activity Index (SDAI) at Weeks 4, 12, and 24, and over time from Day 1 through Week 24 • Absolute Value and Change from Baseline in Short-form Health Survey (SF-36) at Weeks 4, 12 and 24, and Over Time from Day 1 through Week 24 • Absolute Value and Change from Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-Fatigue) at Weeks 4, 12 and 24, and Over Time from Day 1 through Week 24 • Absolute Value and Change from Baseline in the EuroQol 5 Dimensions (EQ-5D) Patient-Reported Outcomes Survey at Weeks 4, 12 and 24, and Over Time from Day 1 through Week 24 • Absolute Value and Change from Baseline in Work Productivity and Activity Impairment- Rheumatoid Arthritis (WPAI-RA) at Weeks 4, 12, 24, and Over Time from Day 1 through Week 24
Key Results	Patients with highly active RA and prior inadequate response/intolerance to biologic DMARDS (bDMARDs), treatment with FIL over a 24-week period was associated with significant improvement in the signs and symptoms of RA, with a safety profile consistent with Phase 2 data. FIL may provide a novel treatment option for pts who continue to have active RA despite prior biologic therapies.

Adverse effects (AEs)	Filgotinib was generally well-tolerated in the FINCH 2 trial, with no new safety signals compared to those reported in previous trials of filgotinib. Adverse event (AE) rates were similar for FIL 200 mg, FIL 100 mg and PBO groups (69.4%and 63.4% vs 67.6%, respectively) as were rates of serious AEs (4.1%, 5.2% and 3.4%, respectively). There were 4 cases of uncomplicated herpes zoster (2 in each FIL group). There was one non-serious AE of retinal vein occlusion in the FIL 200 mg group; no other venous thrombotic events were reported. Two adjudicated Major Adverse Cardiac Events were reported: subarachnoid haemorrhage in the PBO group and myocardial ischemia in the FIL 100 mg group. There were no cases of opportunistic infection/active TB, malignancy, gastrointestinal perforation or death.
Expected reporting date	-

Trial	**FINCH 3,** NCT02886728**,** EudraCT- 2016-000570-37**, GS-US-417-0303; 18 years and older; filgotinib vs placebo, both in combination with methotrexate; phase III**
Sponsor	Gilead Sciences and Galapagos NV
Status	Ongoing
Source of Information	Trial registry,[34] manufacturer[35]
Location	EU (incl UK), USA, Canada and other countries
Design	Randomised; double-blind; placebo- and active-controlled
Participants	n= 1,252; aged 18 or over; diagnosis of RA, ACR functional class I-III, have >=6 swollen joints (from a swollen joint count based on 66 joints (SJC66)) and >= 6 tender joints (from a tender joint count based on 68 joints (TJC68)) at both screening and day 1, limited or no prior treatment with MTX.
Schedule	Randomised to: • Arm A: Filgotinib dose A (200 mg, oral tablet once daily) + placebo to match filgotinib dose B + MTX (2.5 mg, oral capsule once weekly), • Arm B: Filgotinib dose B (100 mg, oral tablet once daily) + placebo to match filgotinib dose A + MTX (2.5 mg, oral capsule once weekly), • Arm C: Filgotinib dose A (200 mg, oral tablet once daily) + placebo to match filgotinib dose B + placebo to match MTX, • Arm D: Placebo to match filgotinib dose A + placebo to match filgotinib dose B + MTX (2.5 mg, oral capsule once weekly).
Follow-up	Active treatment for 52 weeks
Primary Outcomes	• Proportion of participants who achieve an ACR 20% improvement (ACR20) response at week 24
Secondary Outcomes	Time Frame: Week 24: • Change from Baseline in the Health Assessment Questionnaire - Disability Index (HAQ-DI) Score at Week 24 • Proportion of Participants who Achieve Disease Activity Score based on 28 joints (DAS28) (C-reactive protein (CRP)) < 2.6 at Week 24 Time Frame: Baseline; Weeks 24 and 52: • Change from Baseline in the Modified Total Sharp Score (mTSS) at Weeks 24 and 52

	Time Frame: Weeks 4, 12, 24, and 52: • Proportion of Participants who Achieve ACR 50% Improvement (ACR50) at Weeks 4, 12, 24, and 52 • Proportion of Participants who Achieve ACR 70% Improvement (ACR70) at Weeks 4, 12, 24, and 52 Time Frame: Weeks 4, 12, and 52: • Proportion of Participants who Achieve ACR20 at Weeks 4, 12, and 52 Time Frame: Up to 52 weeks: • Proportion of Participants who Achieve ACR20 Over Time from Day 1 through Week 52 • Proportion of Participants who Achieve ACR50 Over Time from Day 1 through Week 52 • Proportion of Participants who Achieve ACR70 Over Time from Day 1 through Week 52 • Proportion of Participants who Achieve Change in HAQ-DI of ≥ 0.22 at Weeks 4, 12, 24, and 52, and Over Time from Day 1 through Week 52 • Proportion of Participants who Achieve DAS28 (CRP) ≤ 3.2 at Weeks 4, 12, 24, and 52, and Over Time from Day 1 through Week 52 • Proportion of Participants who Achieve DAS28 (CRP) < 2.6 at Weeks 4, 12, and 52, and Over Time from Day 1 through Week 52 • American College of Rheumatology N (ACR-N) at Weeks 4, 12, 24, and 52, and Over Time from Day 1 through Week 52 • European League Against Rheumatism (EULAR) Response at Weeks 4, 12, 24, and 52, and Over Time from Day 1 through Week 52 Time Frame: Baseline and up to 52 weeks: • Change from Baseline in Individual Components of the ACR Response at Weeks 4, 12, 24, and 52 and Over Time from Day 1 through Week 52 • Change from Baseline in DAS28 (CRP) at Weeks 4, 12, 24, and 52, and Over Time from Day 1 through Week 52 • Change from Baseline in Clinical Disease Activity Index (CDAI) at Weeks 4, 12, 24, and 52, and Over Time from Day 1 through Week 52 • Change from Baseline in Simplified Diagnostic Activity Index (SDAI) at Weeks 4, 12, 24, and 52, and Over Time from Day 1 through Week 52 • Absolute Value and Change from Baseline in Short-form Health Survey (SF-36) at Weeks 4, 12, 24 and 52, and Over Time from Day 1 through Week 52 • Absolute Value and Change from Baseline in the Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-Fatigue) at Weeks 4, 12, 24 and 52, and Over Time from Day 1 through Week 52 • Absolute Value and Change from Baseline in the EuroQol 5 Dimensions (EQ-5D) Patient-Reported Outcomes Survey at Weeks 4, 12, 24 and 52, and Over Time from Day 1 through Week 52] • Absolute Value and Change from Baseline in Work Productivity and Activity Impairment - Rheumatoid Arthritis (WPAI-RA) Patient-Reported Outcomes Survey at Weeks 4, 12, 24, and 52, and Over Time from Day 1 through Week 52 Time Frame: Baseline; Weeks 24 and 52: • Proportion of Participants with no Radiographic Progression from Baseline at Week 24 and 52
Key Results	Top-line FINCH 3 efficacy[†] data are summarized in the table below:

		Filgotinib 200 mg + MTX (n=416)[&]	Filgotinib 100 mg + MTX (n=207)[&]	Filgotinib 200 mg monotherapy (n=210)[&]	MTX (n=416)[&]
	ACR20 (%)	81.0***	80.2*	78.1	71.4
	ACR50 (%)	61.5***	57.0**	58.1**[#]	45.7
	ACR70 (%)	43.8***	40.1***	40.0***[#]	26.0
	DAS28(CRP) < 2.6 (Clinical remission) (%)	54.1***	42.5***	42.4***[#]	29.1
	HAQ-DI change	-0.94***	-0.90**	-0.89*[#]	-0.79
	mTSS change	0.20	0.22	-0.04**[#]	0.52
	[†]Efficacy assessed at Week 24 for all endpoints [&]Number of patients randomized to each treatment group and who received at least one dose of study drug ACR20/50/70 represents American College of Rheumatology 20%/50%/70% improvements. *** p <0.001, compared with MTX * p < 0.05, compared with MTX ** p <0.01, compared with MTX [#] Comparison not adjusted for multiplicity				
Adverse effects (AEs)	The safety profile of filgotinib in FINCH 3 is consistent with prior studies up to Week 24. Serious adverse events occurred in 4.1 percent, 2.4 percent, 4.8 percent, and 2.9 percent of patients receiving filgotinib 200 mg plus MTX, filgotinib 100 mg plus MTX, filgotinib 200 mg monotherapy and MTX alone, respectively. There was one venous thrombotic event (in the MTX group), five cases of adjudicated major adverse cardiovascular events (two in the filgotinib 200 mg plus MTX group, one in the filgotinib 200 mg group and two in the MTX group) and one malignancy (in the MTX group). There was one death, reported in the filgotinib 200 mg plus MTX group. Serious infections occurred in 1.0 percent, 1.0 percent, 1.4 percent and 1.0 percent of the patients in the filgotinib 200 mg plus MTX, filgotinib 100 mg plus MTX, filgotinib 200 mg monotherapy and MTX groups, respectively. The proportion of patients reporting herpes zoster was 0.5 percent in each of the treatment groups.				
Expected reporting date	Study completion date reported as May 2019				

ESTIMATED COST

The cost of filgotinib not yet known.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal in development (GID-TA10389). Upadacitinib for treating moderate to severe rheumatoid arthritis. Expected publication date TBC.

- NICE technology appraisal guidance (TA485). Sarilumab for moderate to severe rheumatoid arthritis. November 2017
- NICE technology appraisal guidance (TA480). Tofacitinib for moderate to severe rheumatoid arthritis. October 2017
- NICE technology appraisal guidance (TA466). Baricitinib for moderate to severe rheumatoid arthritis. August 2017
- NICE technology appraisal guidance (TA225). Golimumab for the treatment of rheumatoid arthritis after the failure of previous disease-modifying anti-rheumatic drugs. June 2011
- NICE technology appraisal guidance (TA195). Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor. August 2010.
- NICE clinical guideline (NG100). Rheumatoid arthritis in adults: management. July 2018
- NICE quality standard (QS33). Rheumatoid arthritis in over 16s. Updated July 2018.
- NICE diagnostic guidance in development (GID-DG10022). Therapeutic monitoring of TNF-alpha inhibitors in rheumatoid arthritis. Expected publication date July 2019.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Specialised Rheumatology Services (Adult). A13/S/a.

OTHER GUIDANCE

- Greater Manchester Clinical Standards Board (GMMMG). High Cost Drugs Pathway for Rheumatoid Arthritis. July 2017.[36]
- European League Against Rheumatism (EULAR). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update.[16]
- Scottish Intercollegiate Guidelines Network. Management of early rheumatoid arthritis: A national clinical guideline. February 2011.[37]

ADDITIONAL INFORMATION

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