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Filgotinib is effective in people with insufficient response to methotrexate

Filgotinib improved signs and symptoms of rheumatoid arthritis over 24 weeks and was associated with fast onset of action.

INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease that affects a person's joints, causing pain and disability. Filgotinib belongs to a new group of medicines called targeted synthetic disease modifying antirheumatic drugs (sometimes also called tsDMARDs). Filgotinib is also known as a JAK (janus kinase) inhibitor. These molecules bind to intracellular JAK molecules, not to cell receptors and block signaling pathways involved in inflammation, amongst others. As a result, both pain and inflammation in the joints are decreased. Filgotinib and other JAK inhibitors are taken orally as a pill.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors hoped to confirm the initial results from the first two small and short studies that showed that filgotinib is effective in treating the signs and symptoms in people with active rheumatoid arthritis who are receiving stable background treatment with methotrexate. They also wanted to see how well filgotinib works at different doses when added to methotrexate compared to placebo, and whether it makes a difference if the dose is given once or twice a day. Finally, they hoped to gain better understanding of the safety of filgotinib in people with rheumatoid arthritis.

WHO WAS STUDIED?

The study looked at 594 people from 21 countries. Everyone was over the age of 18 and had moderate-to-severe active rheumatoid arthritis, diagnosed for at least 6 months. Everyone had to be on a stable dose of methotrexate for at least 4 weeks before the study started. Certain other medicines were not allowed, for example biologic DMARDs.

HOW WAS THE STUDY CONDUCTED?

This was randomised, double-blind, placebo-controlled study over 24 weeks. People were assigned by chance to one of seven treatment groups to receive filgotinib 50 mg, 100 mg or 200 mg as once or twice daily treatment, or placebo (dummy drug). Everyone stayed on their stable dose of methotrexate. Using chance in this way means that the groups of patients allocated to the different doses of filgotinib or to placebo are comparable and that the treatment groups can be compared objectively. During the treatment neither patients nor their doctors knew which group they were in.

During the study everyone went back to the clinic regularly for a general health check and to look for side effects and effects on signs and symptoms of the disease. Everyone also reported back on their quality of life and levels of fatigue. After 12 weeks of treatment, people in the 50 mg or placebo groups were swapped to 100 mg if they did not show at least a 20% improvement in their signs and symptoms number of tender and swollen joints. After completing the study, people could take part in a long-term, open-label extension study where they all receive filgotinib at the 200mg dose daily.

WHAT WERE THE MAIN FINDINGS?

The main finding was that significantly more people achieved a 20% improvement with filgotinib 100 mg once daily and 200 mg once or twice daily as add-on to methotrexate compared to people taking placebo plus methotrexate. There was no significant difference between once- or twice-daily administration. Filgotinib improved all signs and symptoms studied, and people taking filgotinib had a fast onset of response, with effects seen as early as 1 week of treatment, which were maintained over the 24 week treatment period. Beneficial effects on patient-reported outcomes such as pain, fatigue and quality of life were also reported as of the first evaluation. Filgotinib was well tolerated at all tested doses and the side effects were similar between people receiving filgotinib and those receiving placebo.

ARE THESE FINDINGS NEW?

Yes, this is the first study of filgotinib in a global setting with patients treated for a period of 24 weeks. It confirms the findings of the two initial 4-week studies (we perform two studies before the Phase 2B study).

ARE THERE ANY LIMITATIONS?

The main limitation of the study was that it took place over a relatively short period (24 weeks). This means it is not possible to draw conclusions about the long term maintenance of efficacy and possible side effects. Also, there was no radiographic (X-ray) assessment included, so there is no information on how filgotinib affects the structure of bones and joints.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

Most of the people who took part in this study are now in the ongoing long-term, open-label extension study where they are all receiving a daily dose of 200mg. Furthermore, based on the results of this study, doses of 100 mg and 200 mg filgotinib are also being investigated in other larger studies in people who have not responded to previous treatment either with methotrexate or biologic drugs, as well as in people recently diagnosed with early rheumatoid arthritis.

WHAT DOES THIS MEAN FOR ME?

If you have rheumatoid arthritis, there might be new treatment options for you in the future. If you are interested in being in a clinical trial you should speak to your doctor.

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Summary based on research article published on: 19 December 2016

From: Westhovens, R. *et al*. Filgotinib (GLPG0634/GS-6034), an oral JAK1 selective inhibitor, is effective in combination with methotrexate (MTX) in patients with active rheumatoid arthritis and insufficient response to MTX: results from a randomised, dose-finding study (DARWIN 1). *Ann Rheum Dis* 2017;76:998–1008. doi:10.1136/annrheumdis-2016-210104