Cancers are rare in JAKi-treated patients across inflammatory diseases

JAKi associated with a higher malignancy compared with TNFi but not placebo or methotrexate; cancers were rare events in all comparisons.

INTRODUCTION
Janus kinase inhibitors (shortened to JAKi) are a group of medicines that are prescribed for autoimmune inflammatory conditions such as rheumatoid arthritis, psoriasis, and inflammatory bowel disease. They have also been studied in psoriatic arthritis, axial spondyloarthritis, and atopic dermatitis. JAKi licensed for use in at least one of these conditions include tofacitinib, baricitinib, upadacitinib, filgotinib, and peficitinib. Tumour necrosis factor inhibitors (TNFi) are another group of medicines that are also commonly used in these same diseases. TNFi include adalimumab, etanercept, infliximab, and golimumab. Both classes of drug work by targeting specific molecules that cause inflammation. By doing so, they decrease pain and disease worsening.

In 2022, a large trial called ORAL Surveillance reported an increased risk of cancer in specific groups of people with rheumatoid arthritis who had been treated with a JAKi compared with those treated with a TNFi.

WHAT DID THE AUTHORS HOPE TO FIND?
The authors wanted to bring together all the available trial evidence on JAKi across multiple diseases. They intended to compare the risk of cancer between JAKi, TNFi, another drug called methotrexate, and placebo (a dummy drug with no active ingredient).

WHO WAS STUDIED?
This study looked at over 50,000 people. Everyone had been included in a trial of a JAKi. They had either rheumatoid arthritis, psoriasis, psoriatic arthritis, inflammatory bowel disease, or atopic dermatitis.

HOW WAS THE STUDY CONDUCTED?
This was a systematic review, which aimed to identify all the published evidence on a particular topic and draw it together into one summary. The authors used major electronic databases and clinical trial registries to search for trials and studies of JAKi in people with inflammatory autoimmune diseases. The authors included information from 78 clinical trials.

This paper also included a meta-analysis. This is a statistical method that allows results to be pooled across the different studies. This enabled comparison of the risk of cancer between the four different treatment groups: JAKi, TNFi, methotrexate, and placebo.

WHAT WERE THE MAIN FINDINGS?
The meta-analysis found that JAKi were associated with a higher rate of cancer compared with TNFi, but not when compared with placebo or methotrexate. Importantly, cancers were rare events in all comparisons.

ARE THESE FINDINGS NEW?
This is the largest study until now to have analysed the risk of cancer with JAKi across multiple autoimmune diseases. The findings support those of the ORAL Surveillance trial, which showed a higher risk of cancer with JAKi than TNFi, but the present study shows that JAKi do not appear to increase the risk of cancer relative to methotrexate or placebo.

WHAT ARE THE LIMITATIONS?
One limitation is that the finding of a higher rate of cancer with JAKi compared with TNFi was primarily due to the results of one large study (ORAL Surveillance). When the results of this study were excluded from the analyses, there was no longer a statistically significantly increased risk of cancer with JAKi compared with TNFi.
Another limitation is that cancers often take several years to develop. People entering clinical trials are screened, and those with symptoms suggestive of malignancy are unlikely to be included. This could mean that trials will see a lower rate of malignancy early on, with rates increasing over time. The authors acknowledge the imbalance in size and follow-up duration for different study arms – JAKi had large amounts of follow-up data, whereas placebo had much less follow-up time available. This can potentially lead to the introduction of bias, although they say that they tried to account for this as much as possible in the analyses.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?
Real-world data from outside trial settings is needed to further investigate the risk of cancer with JAKi compared with other treatments. The authors’ research group is planning to investigate this using some large real-world datasets that are available in the UK.

WHAT DOES THIS MEAN FOR ME?
If you have an inflammatory autoimmune condition, these findings highlight the importance of discussing the risks and benefits of different treatment options with your medical team. The results might influence the choice of treatment where the decision is between a JAKi or TNFi, particularly if you have an increased risk of malignancy for some reason.

The authors stress that the risk of side effects should be weighed against the potential benefits of controlling inflammation and preventing disease complications – and these will vary from person to person.

If you have any concerns about your disease or its treatment, you should speak to your doctor.

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