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Lymphoma risk in RA is more dependent on the underlying disease than use of bDMARD treatments

There is no evidence that using bDMARDS to treat rheumatoid arthritis has an effect on the type of lymphoma that people might get

INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease that affects a person's joints, causing pain and disability. It can also affect internal organs. Rheumatoid arthritis affects women more frequently than men.

Lymphoma is the name for a group of cancers that affect lymphocytes, a type of white blood cells, and occurs primarily in lymph nodes. It is one of the ten most common cancers in the general population. Age and gender can have an impact. For most subtypes, men have more lymphomas than women, and tend to be diagnosed at a younger age. People with rheumatoid arthritis are twice as likely to have a lymphoma compared to people without the disease. This is thought to be because of the underlying long-standing activation of the immune system in the course of the inflammation involved in rheumatoid arthritis. Some drugs used to treat rheumatoid arthritis may also increase the risk of developing lymphoma.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to find out whether certain treatments for rheumatoid arthritis affect the development of specific types of lymphoma. In particular, they wanted to find out if there was a difference in the number and types of lymphoma that developed in people who had never taken biologic disease-modifying anti-rheumatic drugs (often called biologics, or bDMARDs), and people who had been treated with one or more of these drugs.

WHO WAS STUDIED?

The study included over 120,000 people with rheumatoid arthritis from 9 European countries. Most were women, and the average age was 59. There were 71,088 people who had never taken a bDMARD, 47,864 who had taken a tumour necrosis factor inhibitor (a class of drug often shortened to TNFi or anti-TNF, and including different medicines such as etanercept, adalimumab and infliximab that all work in a similar way), 9.094 who had taken rituximab, 2,029 who had taken tocilizumab, and 1,708 who had taken abatacept. Of these, 533 developed lymphoma.

HOW WAS THE STUDY CONDUCTED?

The study used information collected from twelve registry databases to identify people with rheumatoid arthritis who had developed lymphoma. The people were divided into two groups. The first group was people who had not taken a biologic at any point before being diagnosed with lymphoma. The second group was people who had taken a biologic drug before they were diagnosed with lymphoma. This second group was then divided into four smaller groups depending on which particular bDMARD they had received most recently before the development of the lymphoma: TNFi, rituximab, tocilizumab, or abatacept. These results were then compared with information about lymphomas in the general population from a database called HAEMACARE.

WHAT WERE THE MAIN FINDINGS OF THE STUDY?

The most common type of lymphoma in people was rheumatoid arthritis was Diffuse Large B-cell lymphoma, followed by follicular lymphoma and chronic lymphocytic leukaemia. There were more cases of Diffuse Large B-cell lymphoma and less cases of chronic lymphocytic leukemia in people with rheumatoid arthritis compared to what was seen in the general population.

The most important finding was that there was no difference between people treated with bDMARDs compared with those not having received bDMARDs in occurrence of lymphoma in general or regarding the subtypes. This is important because the different types of lymphoma have very different survival rates. For example, 80% of people who have Hodgkin lymphoma will survive for 5 years, but only 40% of people with some T-cell types of lymphoma would survive for the same time.

This study found that using bDMARDS to treat rheumatoid arthritis does not change the subtype distribution of lymphomas and that there is no increased risk in people treated with anti-TNFs. This means that the arthritis itself is responsible for the higher lymphoma risk, and not the treatment. The numbers of people treated with other drugs was too small to draw conclusions.

ARE THESE FINDINGS NEW?

The evidence that bDMARDs do not increase the risk of lymphoma was growing before this publication.

These new findings were therefore not really surprising; however, the authors were pleased that so many registries across Europe worked together for this large analysis. This meant that this study looked at the largest sample of lymphoma in rheumatoid arthritis that has ever been collected. This very large analysis provides reassurance that drugs to treat rheumatoid arthritis deliver more benefits than risks.

WHAT ARE THE LIMITATIONS OF THE STUDY?

Everyone in the study was categorised into a treatment group according to the bDMARD that they had received most recently before the lymphoma diagnosis. A limitation is that it is not possible to exclude an influence of bDMARDs that the person might have used before this. Furthermore, it was not possible to work out the potential influence of additional drugs that might have been taken, such as methotrexate or other conventional synthetic DMARDs.

Because of the small numbers, it was also not possible to work out a separate subtype distribution for other treatments than TNFi. For example, only three lymphomas occurred in people treated with abatacept, and only six each in people treated with rituximab or tocilizumab, and the overall numbers of patients treated with these drugs were much smaller than of those treated with anti-TNFs.

Another limitation is the fact that the people who had never taken bDMARDs before they developed lymphoma were older than the bDMARD group (average ages of 61 and 55 years). Since age is an important contributing factor in the development of lymphoma, the comparison between the treatment groups might be affected by this difference.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

The registry databases are continuing to collect information about people with rheumatoid arthritis, and it is hoped that future collaborative analyses on rare events will be possible.

WHAT DOES THIS MEAN FOR ME?

If you have rheumatoid arthritis, you are twice as likely to develop lymphoma as someone without the disease. However, controlling your arthritis with appropriate drug treatments that help to lower or halt inflammation may reduce your risk of developing complications such as lymphoma or cardiovascular problems. The drugs used to treat rheumatoid arthritis deliver more benefits than risks.

If you have concerns about your medicine, it is very important that you do not stop taking it without talking to your doctor first. If you think you have symptoms of lymphoma such as swollen lymph nodes, you should make an appointment to see your doctor.

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