A large European collaborative project.

**INTRODUCTION**
Rheumatoid arthritis is a chronic inflammatory disease that affects a person’s joints, causing pain and disability. It can also affect internal organs. It is more common in older people, but there is also a high prevalence in young adults, adolescents and even children and affects both men and women. People with rheumatoid arthritis naturally have an increased risk of developing some types of cancer due to their underlying disease, as well as some of the medicines that are used to treat it. Melanoma is a type of cancer that starts in the cells that produce a pigment called melanin. Melanin is what gives us colour in our skin, hair and eyes. Melanoma most often affects the skin, but it may also develop on mucous membranes or in the eyes. Melanomas often start as a dark spot like a mole. They can usually be cured with surgical removal, as long as they have not spread.

Tumour necrosis factor inhibitors (often shortened to TNF inhibitors or TNFi) are a type of medicine known as biologic disease-modifying antirheumatic drugs (also called bDMARDS or biologics). Examples include adalimumab (brand name Humira), etanercept (brand name Enbrel) and infliximab (brand name Remicade). They work by blocking the action of certain molecules involved in the development of inflammation in the body. Some studies have suggested that biologic medicines may increase the risk of developing some types of cancer as they can also alter the biology of tumours.

**WHAT DID THE AUTHORS HOPE TO FIND?**
Previous studies in Sweden, Denmark and the US have raised concerns that people with rheumatoid arthritis who are treated with TNF inhibitors have a higher risk of getting melanoma. The authors hoped to find out whether this is the case.

**WHO WAS STUDIED?**
The study looked at 130,315 people aged 18 and above with rheumatoid arthritis from nine countries across Europe. People could not be included if they had any previous history of invasive melanoma.

**HOW WAS THE STUDY CONDUCTED?**
This study included people who were already enrolled in 11 registries. A registry is a database that collects information about people with a particular disease or who are receiving a particular treatment. Registries are important as they include very large numbers of people, which means they are able to detect rare events.

In this study, each registry grouped people according to what medicines they had taken for their rheumatoid arthritis. Three registries in the study received reports of melanoma from their national cancer registry. The other eight registries received reports of melanoma directly from each person’s rheumatologist. Then the researchers calculated how many people had invasive melanomas in each group and compared it to the expected incidence in the general population of the corresponding country.

**WHAT WERE THE MAIN FINDINGS?**
In total, 287 people developed a first melanoma. Overall, there was no increased risk of developing melanoma in people with rheumatoid arthritis who were treated with TNF inhibitors. There was also no significant overall difference based on people’s age or gender.

The risk of developing an invasive melanoma was a little bit higher for people with rheumatoid arthritis than people without the disease, but there were no differences that could be attributed to the medicines.

**ARE THESE FINDINGS NEW?**
These findings are new, and are different to previous results in smaller groups of people.

**ARE THERE ANY LIMITATIONS?**
There are some limitations. Firstly, the number of melanomas observed in most of the participating registries was small. Also, the reliability of the overall findings depends on the accuracy of the data in each individual
registry. For these reasons the authors do not think it is possible to completely rule out a risk of there being a link between TNF inhibitors and melanoma.

**WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?**

The authors have started another collaborative project to investigate whether TNF inhibitors have an impact on lymphoma, another type of cancer.

**WHAT DOES THIS MEAN FOR ME?**

It is important to understand that medicines to treat diseases can have side effects. In the past, if you were prescribed a TNF inhibitor for your rheumatoid arthritis, your doctor might have talked to you about the increased risk of melanoma. In future, this may not be the case.

If you have rheumatoid arthritis, you may be at increased risk of developing melanoma. You should see your doctor if you have any suspicious or odd-looking moles, for example, if you notice a change in colour or shape. If you have any concerns about the medicine you are taking, speak to your doctor.

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