CLINICAL TRIAL RESULTS

Sponsor: Pfizer Inc.

Medicine(s) Studied: Enbrel®/Etanercept

Protocol Number: B1801359

Dates of Trial: 02 April 2015 to 18 June 2016

Title of this Trial: A Study to Collect Information on Etanercept Manufactured Using a New High Capacity Process in Rheumatoid Arthritis Patients

[A Single-Arm, Open-Label Study to Assess the Immunogenicity, Safety, and Efficacy of Etanercept Manufactured Using the High Capacity Process Administered to Subjects With Rheumatoid Arthritis]

Date of this Report: 27 November 2017

– Thank You –

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results please contact the doctor or staff at your study site.

This summary of results represents a single trial only.

WHY WAS THIS STUDY DONE?

Rheumatoid arthritis (also known as "RA") is a disease that causes pain and swelling (inflammation) in or around the joints. The immune system's job is to attack foreign invaders like viruses and other germs. In patients with RA, the immune system mistakenly attacks the joints instead.

If RA inflammation is not treated, it can cause problems for the patient. Joints can become loose or stiff, and even deformed. Medicines that are prescribed for RA work by lowering pain, and/or inflammation, or the activity of the immune system.

Etanercept (Enbrel®) is a medicine that is used to treat RA in adults when other medicines have not worked. Etanercept has received regulatory approval in 118 countries and is approved and available by prescription to treat RA in 110 countries. However, the use of etanercept in this study was investigational. Investigational means that it is being tested in humans. Etanercept was investigational in this study because it was made using a different manufacturing method, a more efficient, high capacity process. It is common for manufacturing changes to be made to drug products as long as the quality of the medicine is maintained. For this study, researchers wanted to answer the following question:

- Does etanercept, made using the new high capacity process, cause any unwanted reactions in patients?

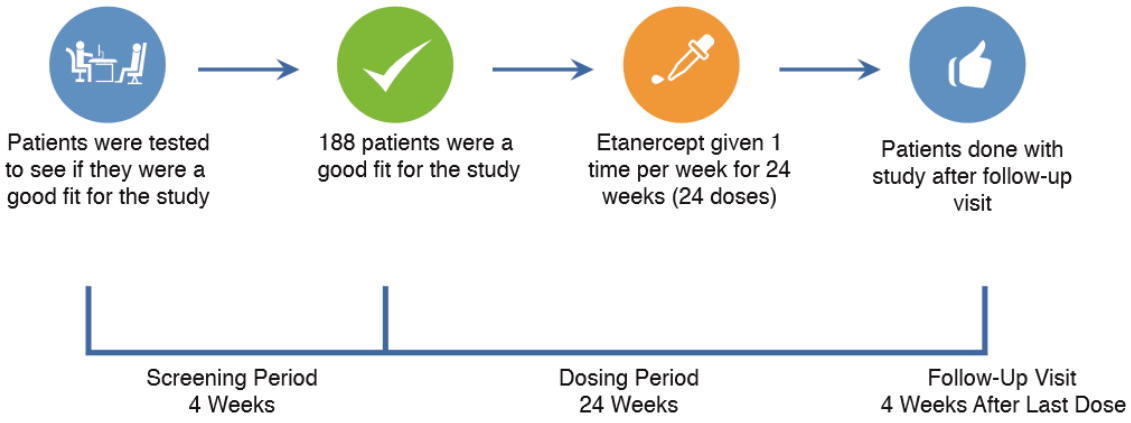
WHAT HAPPENED DURING THE STUDY?

The purpose of this study was to find out whether etanercept, made using the improved high capacity process, caused any unwanted immune response to occur in patients taking etanercept. In this study, an unwanted immune response was when patients' bodies made antibodies (substances produced by the body to protect against foreign material) against etanercept.

The study included patients who had moderate to severe RA and who had not previously been treated with etanercept.

Patients were checked (screened) to make sure they met all the requirements to be in the study up to 4 weeks prior to starting treatment. Next, all patients took the same

treatment for 24 weeks. After taking the study medicines, patients were followed by researchers for 4 weeks (follow-up phase) to see how they did after taking study medicines. See the study plan below.



While each patient was only in the study for 32 weeks (about 8 months), the entire study took about 14 months to complete. Patients joined the study at 1 of 29 locations in 9 countries in Europe and South Africa. The study began 02 April 2015 and ended 18 June 2016. 28 men and 159 women participated. All patients were between the ages of 19 and 79 years.

Patients were supposed to be treated for 24 weeks. Of the 188 patients who started the study, 187 patients took at least 1 dose of the medicine and 163 patients finished the study. 25 patients did not finish the study or left before the study was over by their choice or a doctor decided it was best for a patient to stop the study. The most common reason patients did not finish the study was because of a side effect they were having.

Throughout the study, the Sponsor reviewed the information collected during the study to ensure etanercept made using the new high capacity process was safe for patients. When the study ended in June 2016, the Sponsor created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Does etanercept, made using a high capacity process, cause any unwanted immune response in patients?

To review the immune effects for this study, researchers looked for anti-drug antibodies (ADAs) made by the patients taking etanercept. ADAs can sometimes be made by a patient's body when taking a biologic medicine. A biologic is a medicine made from a natural source which is used to treat or prevent an illness. When patients make ADAs, this is considered an unwanted immune response by the patient taking a medicine because the patient's body thinks of the medicine as an invader in the body. There are 2 types of ADAs: neutralizing and non-neutralizing ADAs. When neutralizing ADAs are formed, they can make the medicine not work, or cause an unwanted medical problem for the patient. Non-neutralizing ADAs have no effect on how the medicine works for the patient.

This study showed that patients taking etanercept, made using the new high capacity process, had a similar amount of antibodies to etanercept as patients taking etanercept made with the currently approved manufacturing process.

Of the 187 patients who took the study medicine, 176 patients had a test done to see if they had made any ADAs against etanercept. 8 out of 176 patients (about 5%) made non-neutralizing ADAs. Because they were non-neutralizing ADAs they did not have any effect on how the medicine worked for the patient. All of the patients who made non-neutralizing ADAs were also taking methotrexate at the same time. Methotrexate is another medicine commonly used to treat RA.

WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the patients had during the study. Patients could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could have been caused by a study treatment, or by another drug the patient was taking.

Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what the side effects of an experimental drug might be.

A total of 14 patients left the study due to medical problems. 85 out of 187 patients in this study had at least 1 non-serious medical problem. The most common are listed below.

Most Common Non-Serious Medical Problems (Reported by More Than 5% of Patients)	
Medical Problem	**Etanercept 50 mg (187 Patients Treated)**
Redness around the injection site	**20 (11%)**
Common cold	**13 (7%)**
Upper respiratory tract infection (infection causing runny nose, sore throat, etc.)	**13 (7%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care.

9 patients (5%, or 9 out of 187 patients) had serious medical problems. One (1) of the 9 patients had a serious medical problem which the researchers thought was due to the study medicine. This patient had a condition called diverticulitis. Diverticulitis is when small bulging pouches in your digestive system form. One (1) other patient died during the study. This patient had sudden onset (acute) heart failure which the researchers considered was not related to the study medicine.

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT02378506**
www.clinicaltrialsregister.eu	Use the study identifier **2013-004569-16**

Findings from this trial will be used to show government regulators, prescribers, and patients that etanercept made using the new high capacity method was as safe as etanercept made using the standard method. This was because etanercept made using the new method did not cause any more ADAs in patients taking it. No further studies are planned.

Please remember that researchers look at the results of many studies to find out which medicines work best and are safest for patients.

Again, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!