CLINICAL TRIAL RESULTS

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer, Inc.

Medicine(s) Studied: Tanezumab (PF-04383119)

Protocol Number: A4091058

Dates of Trial: 21 July 2015 to 27 February 2019

Title of this Trial: Safety and Pain Relief of Tanezumab in Patients with Osteoarthritis of the Hip or Knee [A Phase 3 Randomized, Double-Blind, Active-Controlled, Multicenter Study of the Long-Term Safety and Efficacy of Subcutaneous Administration of Tanezumab in Subjects With Osteoarthritis of the Hip or Knee]

Date of this Report: 7 January 2020

– 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.

WHY WAS THIS STUDY DONE?

Osteoarthritis is a common joint condition that affects millions of people around the world. Osteoarthritis happens when the "cartilage" in the joint wears down through overuse, injury or patient age. Cartilage is the rubbery material that acts as padding, or a cushion, between the bones in the joint and stops the bones from rubbing together. When the cartilage wears down, the joint can become stiff and painful. Osteoarthritis often affects the knees and hips but can be seen in other joints.

Researchers did this study to compare the long-term pain relief and "joint safety" of non-steroidal anti-inflammatory drugs (also known as NSAIDs) with tanezumab in patients with osteoarthritis of the hips or knees. Joint safety is a measure of how well the bone and joint are doing and whether there are any safety problems. Doctors often prescribe NSAIDs like naproxen, celecoxib, or diclofenac to help patients with their osteoarthritis. Tanezumab is an "investigational drug", which means it is not approved for use in the countries where the patients in this study live. It is a new type of drug that is being studied to see if it may be able to help patients with osteoarthritis pain.

WHAT HAPPENED DURING THE STUDY?

This study compared 3 groups of patients to find out if patients receiving a "subcutaneous injection" or shot of tanezumab that was given under the skin every 8 weeks had the same safety and pain relief compared to patients taking a comparator medicine. In this study, the comparator medicine was tablets or capsules of NSAIDs that were to be taken twice a day. The NSAIDs were naproxen 500 mg, celecoxib 100 mg, or diclofenac ER 75 mg.

The study included patients with osteoarthritis of the hip or knee who were 18 years of age or older and who were taking NSAIDs for their osteoarthritis because acetaminophen (also known as paracetamol) had not provided enough pain relief. The patient also had to be unable to take tramadol or opioids for pain relief or had tried these treatments but found they did not work, or was unwilling to take opioids.

The patients and researchers did not know who took tanezumab and who took the comparator treatment in this study. This is known as a "blinded" study. Studies such

as this will often use a "placebo" to help evaluate drug effects. A placebo does not have any medicine in it, but looks just like the medicine being studied. In this study, placebo treatment was given as either an injection, tablets or capsules so that everyone in the study received an injection (tanezumab or placebo) every 8 weeks and tablets or capsules (placebo or NSAIDs) that they had to take twice a day. Patients were put into 1 of 3 treatment groups by chance alone (see table below). This is known as a "randomized" study. Putting people into groups by chance helps to make the groups more equal and easier to compare.

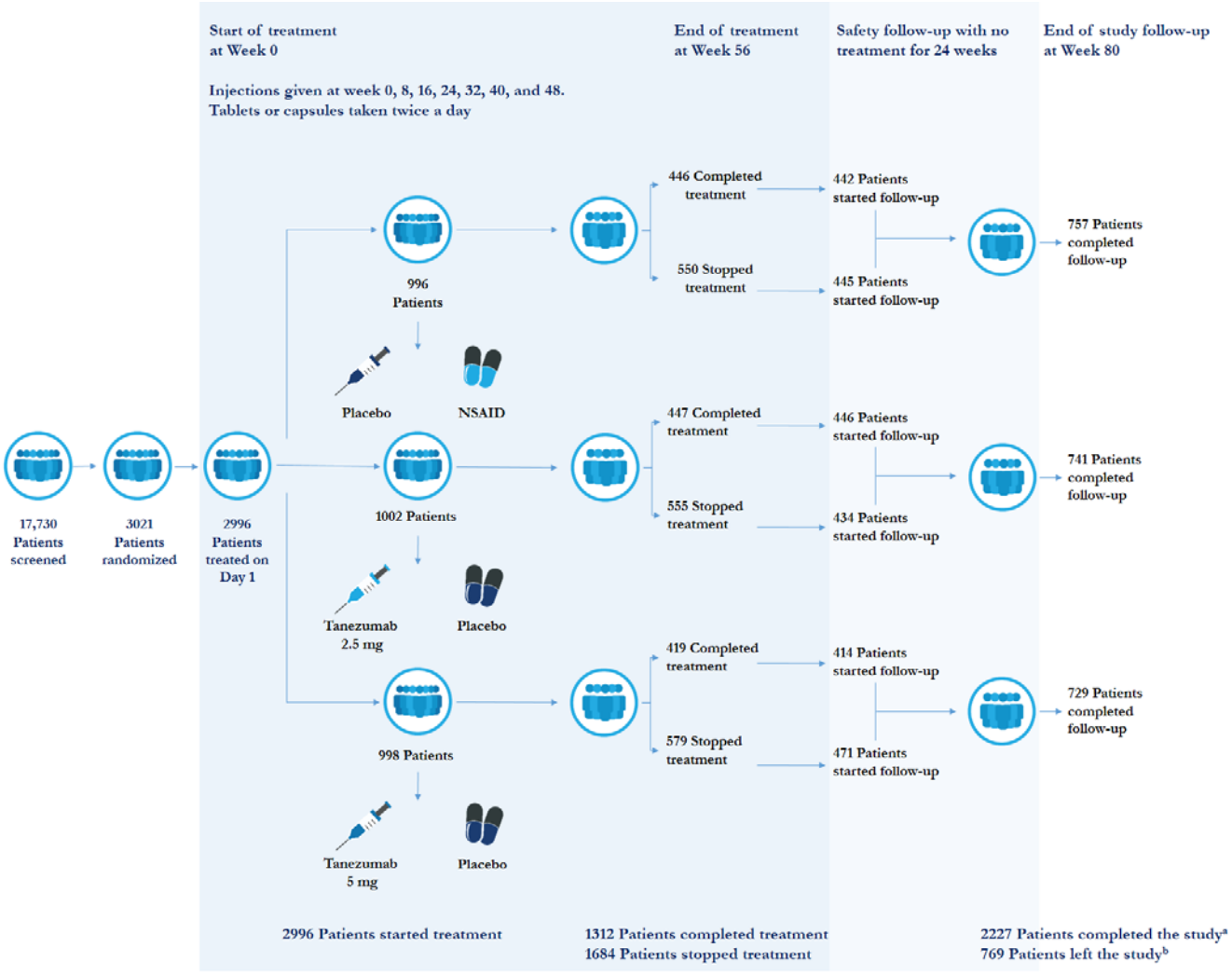
Description of Medicines Given in Each Group

Group	Treatment Given	Number of Patients Treated per Group
1	Tanezumab 2.5 mg injection: Up to 7 injections were given during the study with 1 injection given every 8 weeks Plus Placebo tablets/capsules twice a day	1002
2	Tanezumab 5 mg injection: Up to 7 injections were given during the study with 1 injection given every 8 weeks Plus Placebo tablets/capsules twice a day	998
3	Placebo injection given: Up to 7 injections were given during the study with 1 injection given every 8 weeks Plus NSAIDs (naproxen 500 mg, celecoxib 100 mg, or diclofenac ER 75 mg) tablets/capsules taken twice a day	996

While patients were only in the study for about 21 months (80 weeks), the entire study took over 3 and a half years to complete. The sponsor ran this study at 307 locations in 17 countries in Europe, North and South America, and in the Asia-Pacific area. It began on 21 July 2015 and ended on 27 February 2019. 1043 men and 1953 women participated. All patients were between the ages of 28 and 90 years.

Patients were to be treated for up to 56 weeks and this was then followed by a 24-week safety follow-up period when the patients were observed and no treatment was given (total of 80 weeks). Of the 2996 patients who started the study and received at least 1 injection in the study, 1312 patients finished the treatment period and 1684 patients did not finish the treatment period. A total of 2227 patients completed the safety follow-up part of the study, whether or not they completed the treatment period. A total of 769 patients left before the study was over by their choice or a doctor decided it was best for a patient to stop the study.

When the study ended in February 2019, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.



[a] The 2227 patients who completed the study included 1222 patients who completed treatment and 1005 who stopped treatment
[b] The 769 patients who left the study included 90 who completed treatment and 679 who stopped treatment

WHAT WERE THE RESULTS OF THE STUDY?

Did the tanezumab injections help with osteoarthritis pain?

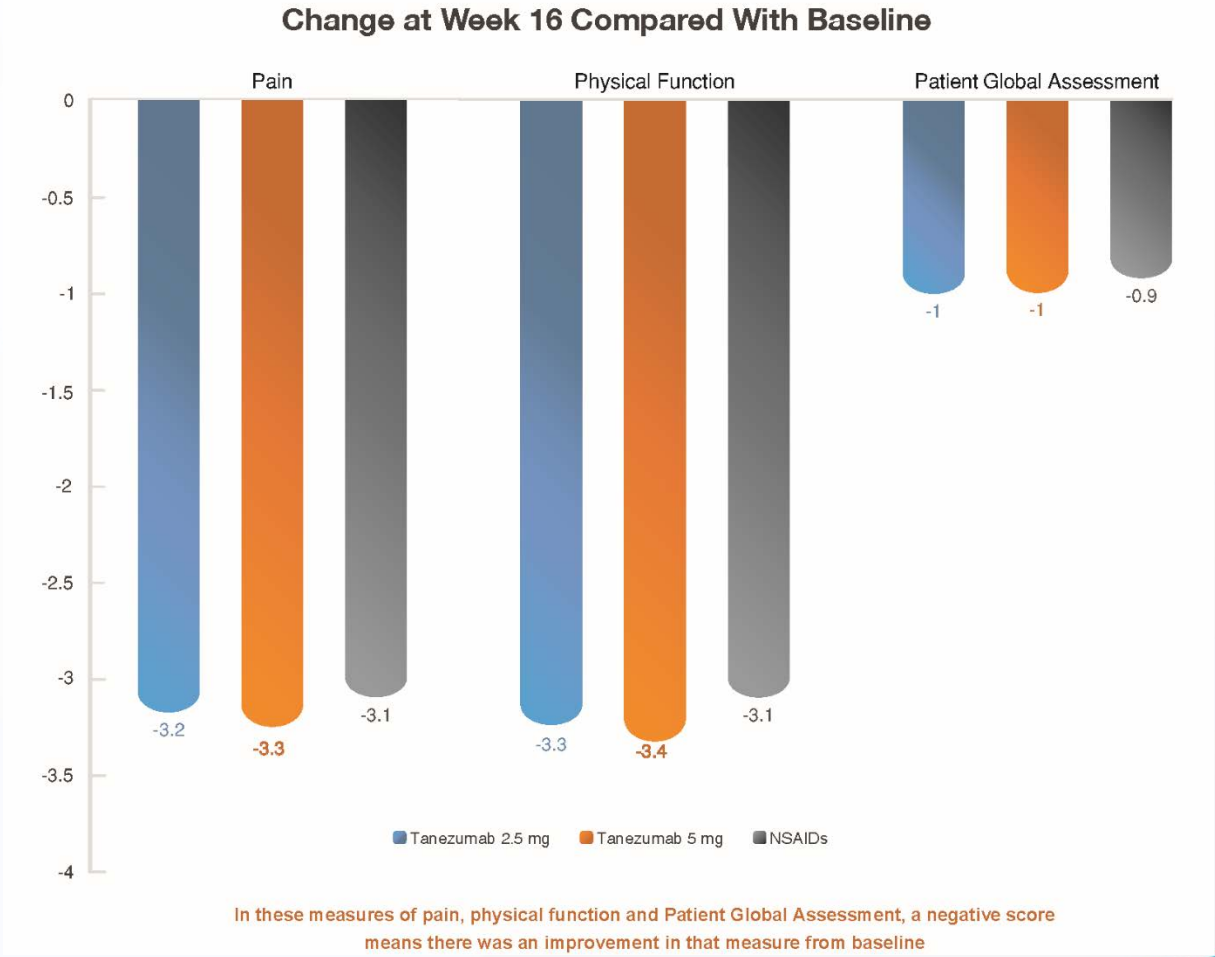
When patients came into the clinic at Week 16, they were asked to think about the osteoarthritis pain they had felt in the previous 2 days. The patient's answers to questions about this pain were used to work out a score that went from 0 to 10, with 0 being the least pain and 10 being the most pain (see figure). On average, pain in patients given the tanezumab 5 mg injection was improved at Week 16 compared with the pain in patients who were given NSAIDs. The researchers determined that the results were not likely a result of chance. On average, pain in patients given the tanezumab 2.5 mg injection was slightly improved at Week 16 compared with the pain in patients who were given NSAIDs. The researchers could not rule out that the observed difference between the tanezumab 2.5 mg and NSAID groups was simply due to chance.

Did the tanezumab injections help with the functioning of the joint affected by osteoarthritis?

When patients came into the clinic at Week 16, they were asked about how their osteoarthritis affected them and their difficulties in moving around and doing the things that they normally wanted or needed to do in the previous 2 days. The patient's answers to these questions were used to work out a score that went from 0 to 10, with 0 being no reduction/difficulty with physical function and 10 being the worst reduction/most difficulty with physical function possible (see figure). On average, functioning of the joint affected by osteoarthritis in patients given the tanezumab 5 mg injection was improved at Week 16 compared with the functioning of the joint affected by osteoarthritis in patients who were given NSAIDs. The researchers determined that the results were not likely a result of chance. On average, the functioning of the joint affected by osteoarthritis in patients given the tanezumab 2.5 mg injection was slightly improved at Week 16 compared with the functioning of the joint affected by osteoarthritis in patients who were given NSAIDs. The researchers could not rule out that the observed difference between the tanezumab 2.5 mg and NSAID groups was simply due to chance.

How did patients feel about their osteoarthritis during tanezumab treatment?

When the patients attended the clinic at Week 16, they were asked how they were doing after considering all the ways that their osteoarthritis affected them (see figure). This is the "patient's global assessment of osteoarthritis". The patient's response ranged from 1 (= they had no symptoms of osteoarthritis and were able to do all of their normal activities) to 5 (= the symptoms were very bad and they could not do what they would normally want to do). There was no difference between the patients given the tanezumab 5 mg injection and patients who were given NSAIDs in how they felt about their osteoarthritis in this patient's global assessment of osteoarthritis. There was also no difference between how patients in the tanezumab 2.5 mg and the NSAID groups felt about their osteoarthritis in this patient's global assessment of osteoarthritis.



How did tanezumab treatment affect joint health?

The researchers looked at joints (mainly the shoulders, hips and knees) to see if the patient's osteoarthritis was worsening more rapidly than usual, if the bone tissue had died, and/or if there were any fractures of the bones in the joint. These conditions were seen in 39 out of 1002 patients (4%) in the tanezumab 2.5 mg group, in 71 out of 998 patients (7%) in the tanezumab 5 mg group, and in 15 out of 996 patients (2%) in the NSAIDs group. There was also a greater risk or chance of the osteoarthritis worsening more rapidly than expected, the bone tissue dying, or a fracture developing in the tanezumab groups compared with the NSAIDs group. The chance of this happening was higher in the tanezumab 2.5 mg and 5 mg groups than in the NSAIDs group. The researchers determined that these results were not likely a result of chance.

This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the participants had during the study. Participants 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 also have been caused by a study treatment, or by another medicine the participant 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 1900 out of the 2996 patients (63%) treated in this study had at least 1 medical problem during the treatment period of the study. A total of 50 patients left the study during the treatment period because of medical problems. The most common medical problems are listed in the following table.

Most Common Medical Problems (Reported by 2% or More Patients in the 56-Week Treatment Period)			
Medical Problem	Tanezumab 2.5 mg (1002 Patients Treated)	Tanezumab 5 mg (998 Patients Treated)	NSAIDs (996 Patients Treated)
Pain in the joints	133 (13%)	165 (17%)	117 (12%)
Common cold	57 (6%)	67 (7%)	40 (4%)
Pain in the back	34 (3%)	55 (6%)	35 (4%)
Osteoarthritis	39 (4%)	54 (5%)	23 (2%)
Fall	65 (7%)	53 (5%)	46 (5%)
Swollen joints	43 (4%)	48 (5%)	10 (1%)
Headache	56 (6%)	45 (5%)	25 (3%)
Chest infection	57 (6%)	45 (5%)	59 (6%)
Swelling in the legs and arms	19 (2%)	43 (4%)	17 (2%)
Pain in the muscles and joints	43 (4%)	41 (4%)	37 (4%)
Rapidly worsening osteoarthritis	18 (2%)	41 (4%)	4 (<1%)
Pain in fingers and toes	31 (3%)	37 (4%)	28 (3%)
Tingling, numbness, pricking and/or burning in fingers or toes	18 (2%)	30 (3%)	13 (1%)
Bronchitis	22 (2%)	28 (3%)	13 (1%)
Reduced sense of touch	27 (3%)	28 (3%)	18 (2%)
Carpal tunnel syndrome	16 (2%)	27 (3%)	6 (1%)
Cough	13 (1%)	26 (3%)	7 (1%)

Medical Problem	Tanezumab 2.5 mg (1002 Patients Treated)	Tanezumab 5 mg (998 Patients Treated)	NSAIDs (996 Patients Treated)
Influenza	20 (2%)	21 (2%)	26 (3%)
Swelling in the joints	8 (1%)	21 (2%)	5 (1%)
Muscle spasms	15 (2%)	20 (2%)	19 (2%)
Urinary tract infection	12 (1%)	20 (2%)	15 (2%)
High blood pressure	16 (2%)	11 (1%)	25 (3%)
Upset stomach	14 (1%)	11 (1%)	21 (2%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

A total of 177 patients (6%, or 177 out of 2996 patients) had serious medical problems during the treatment period. This included 51 patients in the tanezumab 2.5 mg group (5%), 80 patients (8%) in the tanezumab 5 mg group, and 46 patients (5%) in the NSAID group. The serious medical problems of osteoarthritis, rapidly worsening osteoarthritis, and pain in the joints were seen more often in the tanezumab 5 mg group than in the tanezumab 2.5 mg group or the NSAID group. Serious medical problems that occurred in more than 2 patients in any treatment group are shown in the following table. All other serious medical problems occurred in 1 or 2 patients in each treatment group.

There were 10 patients who died during the study. This included 5 patients who died during the treatment period, 3 patients who died during the safety follow-up period and 2 patients who died after they had left the study. The doctors did not think any of these deaths were linked to the treatments given in this study.

Most Common Serious Medical Problems (Reported by More Than 2 Patients in Any Group in the 56-Week Treatment Period)			
Serious Medical Problem	**Tanezumab 2.5 mg (1002 Patients Treated)**	**Tanezumab 5 mg (998 Patients Treated)**	**NSAIDs (996 Patients Treated)**
Osteoarthritis	**9 (1%)**	**17 (2%)**	**4 (<1)**
Rapidly worsening osteoarthritis	**3 (<1%)**	**11 (1%)**	**0**
Pain in the joints	**4 (<1%)**	**9 (1%)**	**0**
Stress fracture	**1 (<1%)**	**4 (<1%)**	**2 (<1%)**
Torn cartilage (meniscus injury)	**1 (<1%)**	**3 (<1%)**	**1 (<1%)**
Heart attack	**1 (<1%)**	**1 (<1%)**	**3 (<1%)**

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

If you have questions about the results of your study, please speak with the doctor. For more details on this study protocol, please visit:

www.clinicaltrials.gov	Use the study identifier **NCT02528188**
www.clinicaltrialsregister.eu	Use the study identifier **2012-003721-22**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe 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!