



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: Crizotinib (XALKORI®)

Protocol Number: A8081029

Dates of Trial: 29 September 2012 to 08 January 2020

Title of this Trial: A Study Of Crizotinib Versus Chemotherapy In Previously Untreated ALK Positive East Asian Non-Small Cell Lung Cancer Patients

[Phase 3, Randomized, Open-Label Study of the Efficacy and Safety of Crizotinib Versus Pemetrexed/Cisplatin or Pemetrexed/Carboplatin in Previously Untreated East Asian Patients With Non-Squamous Carcinoma of the Lung Harboring a Translocation or Inversion Event Involving the Anaplastic Lymphoma Kinase (ALK) Gene Locus]

Date(s) of this Report: 12 January 2021

— *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?

Non-small-cell lung cancer (NSCLC) is the most common type of lung cancer. In some patients with NSCLC, their cancer cells have changes in their DNA (genes) where 2 genes combine to create a new gene. When this happens with the gene that makes the protein “ALK”, the new gene is called an “ALK gene fusion”. This ALK gene fusion can cause tumors to form or can help existing cancer cells grow faster. Researchers are looking for better treatments for patients with NSCLC whose cancer cells have an ALK gene fusion.

Crizotinib (also known as XALKORI[®]) is a drug that is now approved for use in many countries including East Asian countries to treat NSCLC with ALK gene fusions. Crizotinib works by blocking the activity of ALK, which is thought to slow or stop the growth of cancer cells with an ALK gene fusion. This study compared crizotinib treatment to “platinum-based chemotherapy”, which is a medicine combination that was used as a first-line treatment for patients with NSCLC. Platinum-based chemotherapy is made up of the combination of the drug pemetrexed with either cisplatin or carboplatin.

The main purpose of this study was to see whether crizotinib treatment would keep patients’ cancer from growing for a longer period of time compared to patients treated with platinum-based chemotherapy. To do this the researchers asked,

- **Do patients treated with crizotinib have more time before their cancer begins to grow, or before they pass away from any cause, compared to patients treated with platinum-based chemotherapy?**

The researchers measured the “progression-free survival time” which was defined as the time between starting the study and the patients’ NSCLC getting worse, or the patient passing away from any cause (such as from disease or an accident). The researchers then calculated the “median” progression-free survival time, which was the time point where half (50%) of the patients in a study group had their NSCLC start to grow, or had passed away from any cause.

Researchers were also interested in learning more about the safety of crizotinib. They

monitored the patients for any medical problems that happened while they were taking crizotinib or after they stopped taking crizotinib.

WHAT HAPPENED DURING THE STUDY?

This study compared 2 groups of patients to find out if patients treated with crizotinib would have more time before their cancer began to grow, or before they passed away from any cause, compared to patients treated with platinum-based chemotherapy.

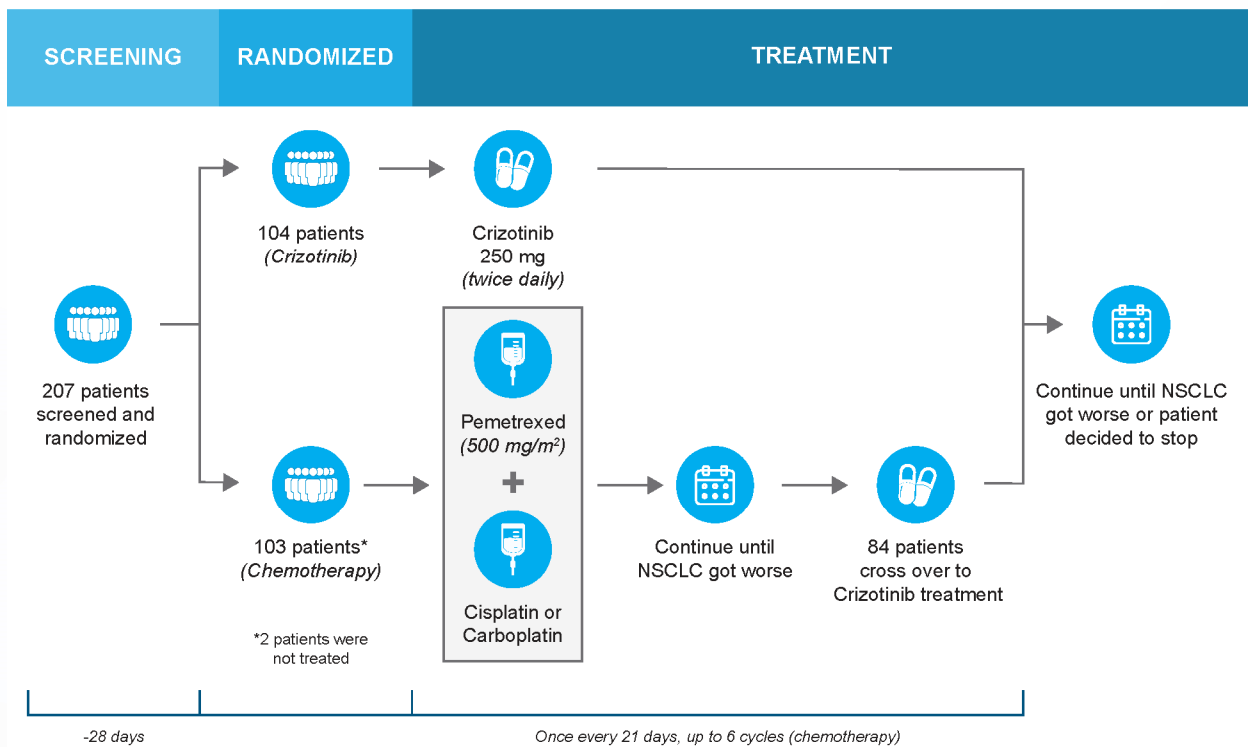
The study included men and women who were 18 to 70 years of age who met the following criteria:

- Diagnosed with NSCLC that also had the following:
 - Positive test for ALK fusion gene;
 - Locally advanced NSCLC and not suitable for local treatment, OR
 - Metastatic NSCLC (cancer had spread outside of the lungs);
- Had not been treated for their NSCLC before using “systemic” medicines (taken by mouth or intravenously);
- Had not been treated before with medicines that block ALK activity;
- Had any major surgeries completed at least 4 weeks before entering the study;
- Had any radiation procedures completed at least 2 weeks before entering the study, and had mostly recovered from radiation side effects;
- Were able to at least walk around and care for themselves, and were out of bed at least 50% of the day.

The patients were assigned to either take 250 mg of crizotinib twice daily by mouth, or to receive platinum-based chemotherapy. If the patient was assigned to receive platinum-based chemotherapy, they received standard doses of pemetrexed and either cisplatin or carboplatin, with the patient’s doctor deciding whether cisplatin or carboplatin was best for the patient. The patients were assigned to either group by chance alone. This is known as a “randomized” study. This is done to reduce the differences between groups (like age or the number of men and women), which makes the groups more even to compare. Patients who were assigned to receive

platinum-based chemotherapy and had their NSCLC get worse were allowed to switch, or 'cross over', into the crizotinib treatment group.

The diagram below shows what happened during the study.



While patients taking crizotinib were treated for an average of 106 weeks, the entire study took over 7 years to complete. The Sponsor ran this study at 35 locations in 5 countries in East Asia. It began 29 September 2012 and ended 08 January 2020. A total of 114 women and 93 men participated. All patients were between the ages of 23 and 69.

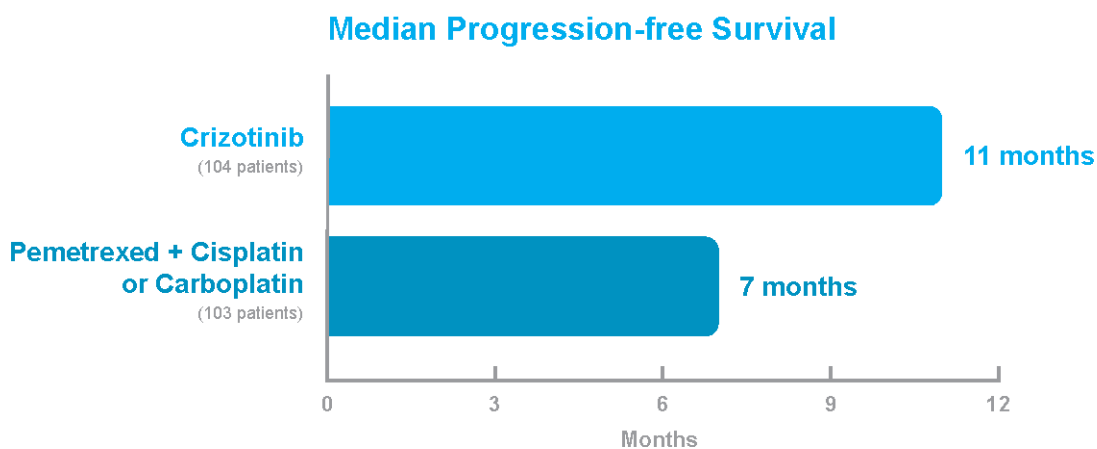
Patients were to be treated until their NSCLC got worse, they had too many medical problems or couldn't tolerate the medicines, their overall health declined, or they passed away. Of the 205 patients who started treatment in the study, 55 finished the study. A total of 123 patients passed away before the study was completed, and 3 patients did not finish the study because of other reasons. Twenty one (21) patients left before the study was over by their choice or a doctor decided it was best for a patient to stop being in the study. In addition, 3 patients were lost to follow-up.

When the study ended in January 2020, the Sponsor reviewed the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Did patients treated with crizotinib have more time before their cancer began to grow, or before they passed away from any cause, compared to patients treated with platinum-based chemotherapy?

This study found that patients treated with crizotinib had more time before their cancer began to grow, or before they passed away from any cause, compared to patients treated with platinum-based chemotherapy. The patients treated with crizotinib had a median time of 11 months before their NSCLC began to grow or they passed away from any cause. In comparison, the patients treated with platinum-based chemotherapy had a median time of 7 months before their NSCLC began to grow or they passed away from any cause.



Based on these results, the researchers have decided that the results are not likely the result of chance. Crizotinib may be an option for treating patients with NSCLC whose cancer cells have an ALK gene fusion. 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 PARTICIPANTS 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.

All but 1 patient in each treatment group in this study had at least 1 medical problem. A total of 32 patients left the study because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems (Reported by 5% or More of Patients, with 10% or More Difference Between Treatment Groups)		
Medical Problem	Crizotinib (104 Patients Treated)	Platinum-based Chemotherapy (101 Patients Treated)
Increased liver enzymes in blood	73 (70%)	48 (48%)
Diarrhea	63 (61%)	9 (9%)
Problems with eyesight	61 (59%)	11 (11%)
Vomiting	61 (59%)	46 (46%)
Low white blood cells	49 (47%)	67 (66%)

(neutrophils)		
Low white blood cells (leukocytes)	47 (45%)	70 (69%)
Constipation	37 (36%)	27 (27%)
Fluid buildup in tissues	37 (36%)	8 (8%)
Cough	36 (35%)	27 (27%)
Infection of nose, sinuses, or throat	35 (34%)	15 (15%)
Headache	29 (28%)	9 (9%)
Dizziness	28 (27%)	11 (11%)
Low appetite	27 (26%)	33 (33%)
Blood protein levels decreased (albumin)	26 (25%)	16 (16%)
Low red blood cells	23 (22%)	67 (66%)
Leg pain	22 (21%)	6 (6%)
Stomach pain	21 (20%)	8 (8%)
Too little blood protein (albumin)	19 (18%)	8 (8%)
Pain, numbness, or tingling due to nerve damage	19 (18%)	6 (6%)
Slow heartbeat	17 (16%)	0
Increased blood enzymes (LDH)	15 (14%)	1 (1%)
NSCLC got worse	15 (14%)	1 (1%)
Increased blood enzymes (CPK)	14 (14%)	0
Blood protein levels	14 (14%)	3 (3%)

decreased (total)		
Low blood calcium	13 (13%)	4 (4%)
Feeling tired	9 (9%)	17 (17%)
Low blood platelets	8 (8%)	32 (32%)
Low blood sodium	6 (6%)	16 (16%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

Forty six (46, or 44%) patients taking crizotinib and 13 patients (13%) treated with platinum-based chemotherapy had serious medical problems.

At the end of the study, 62 patients assigned to take crizotinib and 61 patients assigned to platinum-based chemotherapy had passed away. Most deaths were due to the patient’s NSCLC getting worse. Two (2) patients taking crizotinib passed away from medical problems that their doctor thought might have been caused by taking crizotinib. Serious medical problems are summarized in the table on the next page.

Serious Medical Problems (Reported by 2 or More Patients in Either Treatment Group)

Serious Medical Problem	Crizotinib (104 Patients Treated)	Platinum-based Chemotherapy (101 Patients Treated)
NSCLC got worse	15 (15%)	1 (1%)
Pneumonia	5 (5%)	1 (1%)
Blood clot in lung	3 (3%)	0
Death	2 (2%)	1 (1%)
Difficulty swallowing	2 (2%)	0
Increased liver enzymes in blood	2 (2%)	1 (1%)
Scarring of lung tissue	2 (2%)	0
Buildup of fluid around lungs	2 (2%)	1 (1%)
Collapsed lung	2 (2%)	0
Spitting blood	1 (1%)	2 (2%)
Low blood platelets	0	2 (2%)

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 **NCT01639001**

www.pfizer.com/research/research-clinical-trials/trial-results

Use the protocol number **A8081029**

Other clinical trials with crizotinib are ongoing.

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!