



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 (PF-02341066)

Protocol Number: A8081063

Dates of Trial: 25 September 2013 to 22 January 2020

Title of this Trial: Efficacy Study of Crizotinib in East Asian Patients With ROS1-Positive, ALK-Negative Advanced NSCLC [Phase-2, Open-Label, Single-Arm Study of the Efficacy and Safety of Crizotinib in East Asian Patients with Advanced ALK-Negative Non-Small Cell Lung Cancer (NSCLC) Harboring a Translocation or Inversion Involving the C-ROS Oncogene (ROS1) Locus]

Date of this Report: 19 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?

Lung cancer is the name for cancer that starts in the lungs. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. Some patients have NSCLC that is referred to as “anaplastic lymphoma kinase (ALK)-negative” or “c-ros oncogene 1 (ROS1)-positive”. These patients have changes in their genes that can cause cancer cells to grow.

The Sponsor is developing an anti-cancer medication called crizotinib to treat ALK-negative and ROS1-positive lung cancers. ALK and ROS1 belong to a certain group of proteins called “kinases”. These proteins can help cancer cells to grow. As they grow, the cancer cells can form into a tumor and spread to other parts of the body. Crizotinib may be able to block kinases, potentially reducing tumor size and stopping ALK-negative and ROS1-positive lung cancers from being able to grow and spread. Crizotinib is known as an “ALK-inhibitor and ROS1-inhibitor” medication.

Xalkori[®] (crizotinib) is approved in the United States (US), Europe, and countries in East Asia including South Korea, Taiwan, Japan, and China, for treatment of locally advanced (cancer has not spread to distant regions of the body but has spread to nearby organs) or metastatic (cancer has spread outside lungs) NSCLC that are ALK-positive. Crizotinib is also approved in the US and Europe for advanced (metastatic) NSCLC whose tumors have an ROS1 gene alteration, resulting in ROS1-positive NSCLC. Crizotinib is given in a capsule and is taken by mouth twice daily at around the same time every morning and every evening.

The main purpose of this study was to see if treatment with crizotinib is useful in patients in East-Asia, including South Korea, Taiwan, Japan, and China, with ROS1-positive and ALK-negative NSCLC. To do this, researchers asked:

- **How well did crizotinib treatment work to keep ROS1-positive and ALK-negative NSCLC from growing?**

The researchers also wanted to know if any of the patients’ cancer got smaller during the study. To do this, they measured many things, including the “Objective Response

Rate”. This is the percentage of patients whose cancer disappeared or got smaller during treatment.

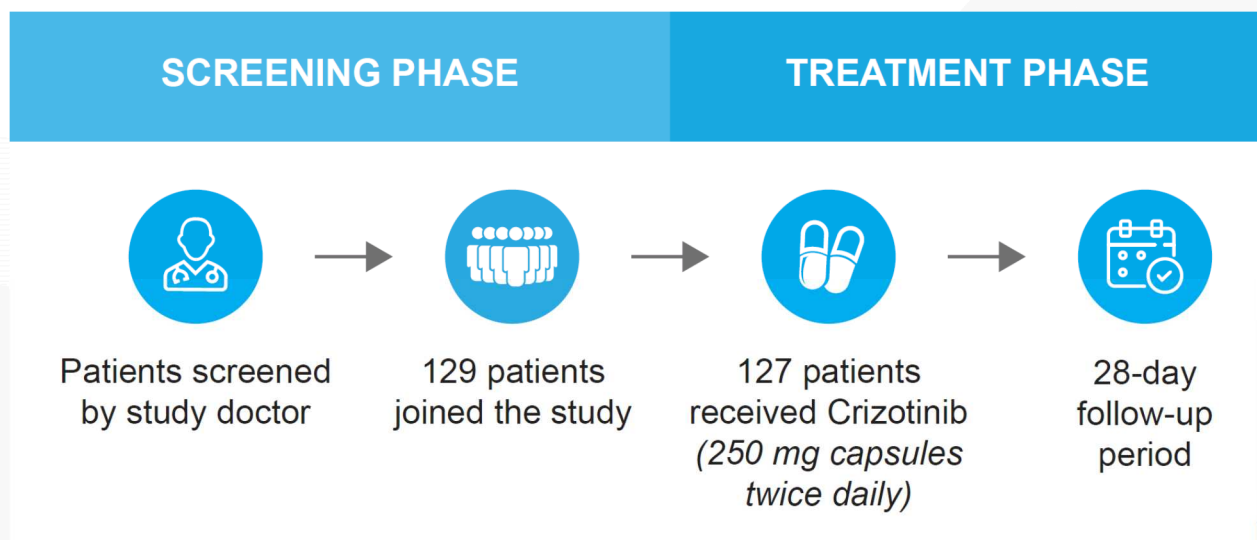
Researchers were also interested in learning more about the safety of crizotinib. They monitored the patients for any medical problems that happened while they were taking crizotinib or after they stopped taking crizotinib.

WHAT HAPPENED DURING THE STUDY?

The study included patients who had NSCLC (referred to as “disease” in this summary) that was advanced or has spread to other parts of the body during or after earlier treatment and was caused by a defect in a gene called receptor tyrosine kinase (C-ROS1).

A total of 129 patients with ALK-negative and ROS1-positive NSCLC joined this study and 127 patients were treated with crizotinib.

This was an open-label study, which means that both the patients and researchers knew which study drug and dose they received. The figure below shows what happened during this study.



Patients in this study took crizotinib 2 times per day in “cycles” that lasted 28 days. They began with a dose of 250 mg. The patients were watched closely for any medical problems.

While patients were only in the study for an average of 102 weeks, the entire study took almost 7 years to complete. The Sponsor ran this study at 40 locations in 4 countries in East Asia (Japan, China, South Korea, and Taiwan). It began 25 September 2013 and ended 22 January 2020. Fifty-four (54) men and seventy-three (73) women participated. All patients were between the ages of 23 and 80.

Patients were to be treated until their cancer stopped responding or got worse, until they developed unacceptable medical problems, or until they chose to stop treatment. Of the 127 patients who started the study, all patients stopped the study; 65 patients (51%) died. A total of 18 patients (14%) had stopped the study by their choice or a doctor decided it was best for a patient to stop the study. Forty-four (44) patients (35%) were still ongoing in the study when the study was closed and, if they were still on treatment, they were moved to either commercial treatment available in their country or they enrolled into another study (Study A8081067).

When the study ended in January 2020, the Sponsor began reviewing 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?

What percentage of patients in the study had their NSCLC get better when taking crizotinib?

Seventeen (17) patients (13%) had a 'Complete Response', which means that their NSCLC completely disappeared. Seventy-four (74) patients (58%) achieved a 'Partial Response', which means that their NSCLC got smaller, but did not disappear. The Objective Response Rate (Complete Response + Partial Response) for all patients, was therefore 72%. Nine (9) (7%) of patients' NSCLC worsened.

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.

One-hundred and twenty-seven (127) out of 127 patients in this study had at least 1 medical problem. A total of 11 patients (9%) stopped treatment because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems (Reported by More Than 30% of Patients)

Medical Problem	Crizotinib (127 Patients Treated)
Elevated liver enzymes, which may indicate liver damage (elevated transaminase)	89 (70%)
Vision problem	66 (52%)
Diarrhea	62 (49%)
Nausea	58 (46%)
Vomiting	50 (39%)
Constipation	49 (39%)

Abnormally low count of a type of white blood cell called neutrophils (Neutropenia)	45 (35%)
Edema (when body fluids build up too much)	45 (35%)
Nose and throat infection	44 (35%)

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) patients (36%) had serious medical problems. There were 11 (9%) patients with serious medical problems that researchers believe was related to crizotinib. Sixty-five (65) patients (51%) died during the study, 1 patient (1%) died within 30 days after receiving crizotinib. Most of the patients who died during the study, was because their condition worsened.

Serious Medical Problems (Reported by More Than 3% of Patients)

Serious Medical Problem	Crizotinib (127 Patients Treated)
Infection of the lung	10 (8%)
Disease progression (worsening of the patient's NSCLC)	7 (6%)
Failure of respiratory system (lungs are unable to get enough oxygen to the blood)	5 (4%)
Elevated liver enzymes, which may indicate liver damage (elevated transaminase)	4 (3%)

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 **NCT01945021**

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