Summary of Results for Laypersons

What was the Study Called?

A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 3 Study of Single -agent Tarceva (erlotinib) Following Complete Tumor Resection with or Without Adjuvant Chemotherapy in Patients With Stage IB-IIIA Non-small Cell Lung Carcinoma (NSCLC) Who have EGFR-positive Tumors (OSI-774-302 [5901-CL-0302])

Why was this Study Needed?

Erlotinib (also known as OSI-774 and Tarceva®) is a medicine that blocks a molecule called the epidermal growth factor receptor (EGFR) which is found on the surface of certain cancer cells. This molecule helps cancer cells grow. EGFR is present on solid cancer tumor cells. Since erlotinib is a medicine that blocks EGFR it could be effective in preventing the growth of solid cancer tumor cells.

The standard first-line treatment for patients with stage IB, II and IIIA non-small cell lung cancer (NSCLC) is surgical removal of the tumor with or without chemotherapy. Chemotherapy is a type of cancer treatment that uses medicines to destroy cancer cells. Researchers thought that adding treatment with erlotinib could help patients live longer.

This study enrolled patients with stage IB-IIIA NSCLC. Before entering the study patients had surgery to remove their cancer with or without chemotherapy. All patients had NSCLC that was EGFR-positive.

The main question this study helped answer was if treatment with 150 mg of erlotinib taken once daily resulted in longer disease-free survival (DFS). DFS was defined as the time from the date the patient was placed in the study until:

- The patient's cancer came back, or
- The patient died without the cancer coming back

This study for erlotinib took place at 204 clinics in the US, Argentina, Australia, Austria, Belgium, Canada, Czech Republic, France, Germany, Greece, Hungary, Italy, South Korea, Poland, Romania, Russia, Spain, Taiwan and the United Kingdom/England. The study started in November 2007 and when the study report was written long-term follow-up was still ongoing. The sponsor (Astellas) reviewed all the study information and created a report of the results. The report includes study information from November 2007 to April 2013. This is a summary of that report.

What Kind of Study was This and Who Took Part in it?

This was a "blinded" study. In this study, the patients and the researchers did not know who took which of the treatments (erlotinib or placebo).

A "placebo" is a dummy treatment such as a tablet or capsule that looks like a medicine, but does not have any medicine in it. Using a placebo helps make study results fair and

unbiased, because researchers and patients cannot tell who is taking a placebo, and who is taking the test medicine. In this study the patients received 1 of 2 treatments:

- 150 mg erlotinib orally daily
- 150 mg placebo orally daily

Patients were picked for each treatment by chance alone. Two patients were placed in the erlotinib group for every 1 patient placed in the placebo group. Patients received study medicine once daily for 2 years or until:

- Their cancer got worse
- They died
- They asked to be removed from the study
- The researcher decided to remove the patient from the study
- The patient was not able to tolerate the toxicity of the study medicines

At designated times throughout the study DFS was assessed. The patients were followed until they died, even if it was after the 2 year treatment period.

Men and women were allowed to participate in this study. They were all over 18 years old. All patients had stage IB, II or IIIA NSCLC. They had surgery to remove their cancer with or without chemotherapy. Their cancer was EGFR-positive. Patients had adequate blood, kidney and liver function. They were not in the study if they had:

- A combination of small-cell carcinoma and NSCLC and other specific cancers
- Their cancer was not EGFR-positive
- A history of radiation therapy. Radiation therapy uses beams of intense energy to kill cancer cells.
- Prior cancer except for adequately treated skin cancer or cervical cancer
- Prior treatment with a medicine that blocks EGFR

The study was divided into 2 periods. The treatment period was the 2 year time when the patients received study medicine. After the treatment period there was a long-term follow-up period. During the long-term follow up period, patients were followed for their survival status. For this study, the long-term follow up period was when the patients finished their treatment period.

A total of 973 patients were entered into this study. Nineteen patients did not receive study medicine. A total of 954 patients received at least 1 dose of study medicine. A total of 611 patients were in the erlotinib group and 343 patients were in the placebo group.

	Number of Patients (out of 973 patients)
Age Group Aged 18 years and older	 973
Women Men	398 575
EU Countries Outside EU	413 560

What Were the Study Results?

Although DFS was slightly higher for the patients in the erlotinib group, statistics showed that the difference was not meaningful. Thus, there was no real difference between DFS for the 2 patient groups.

What Adverse Reactions did Patients Have?

A lot of research is needed to know whether a medicine causes a medical problem. So when new medicines are being studied researchers keep track of all medical problems that patients have while they are in the study. These medical problems are called "adverse events" and are recorded whether or not they might be caused by the treatment taken. An "adverse reaction" is any medical problem or "adverse event" that is judged by the study doctor to be possibly caused by a medicine or treatment used in the study.

In this study, twice as many patients were assigned to erlotinib (611 patients) as to placebo (343 patients); therefore, the numbers of adverse events, serious adverse events, and deaths reported below cannot be directly compared between the treatment groups.

The chart below shows the most common adverse reactions experienced by patients while taking part in this study. Information from 954 patients who received at least 1 dose of study medicine is included in the table below.

Adverse Reactions	Erlotinib (out of 611 patients)	Placebo (out of 343 patients)	Total (out of 954 patients)
Rash	352	47	399
Diarrhea	301	39	340
Itchy skin	154	44	198
Dry skin	121	43	164
Acne	110	19	129
Fatigue or tiredness	82	24	106
Nausea or urge to vomit	63	23	86
Hair loss	57	9	66
Loss of appetite	60	8	68
Swelling of the mouth and lips	55	3	58
Infection of the soft tissue around a finger nail	38	2	40
Infection of the eye commonly called pink eye	31	0	31

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. Fifteen patients in the erlotinib group experienced a serious adverse reaction. Five patients in the placebo group experienced a serious adverse reaction.

A total of 15 patients died during the treatment period or within 30 days of their last dose of study medicine. Twelve patients in the erlotinib group died and 3 patients in the placebo group died. None of the deaths were related to the study medicine.

During the long-term follow-up period 179 patients in the erlotinib group died and 93 patients in the placebo group died. None of the deaths were related to the study medicine.

Where Can I Learn More About This Study?

Astellas may perform additional studies to better understand erlotinib.

This summary of the clinical study results is available online at http://www.astellasclinicalstudyresults.com. Please remember that researchers look at the results of many studies to find out how well medicines work and which adverse reactions they might cause. If you have questions about erlotinib, please discuss these with your doctor.

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