Summary of Results for Laypersons

What was the Study Called?

A Randomized Placebo Controlled Study of OSI-774 (Tarceva™) Plus Gemcitabine in Patients With Locally Advanced, Unresectable or Metastatic Pancreatic Cancer

Why was this Study Needed?

Erlotinib (also called 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. Metastatic means that the cancer has spread from the place where it first started to another place in the body.

Erlotinib has been tested alone and with some common chemotherapy treatments in a number of studies. Chemotherapy is a type of cancer treatment that uses medicines to destroy cancer cells. These studies show that the chemotherapy medicine gemcitabine and erlotinib can be given together.

This study enrolled patients with advanced pancreatic cancer that could not be removed by surgery. This study also enrolled patients with metastatic pancreatic cancer that had spread throughout their body. The standard treatment for patients with advanced pancreatic cancer or metastatic pancreatic cancer is the chemotherapy medicine gemcitabine. Gemcitabine offers some improvement in patient survival and some of the cancer symptoms become better. EGFR is found in pancreatic cancer at a relatively high rate. A few studies have shown shorter survival for patients who have advanced or metastatic pancreatic cancer with EGFR.

The main question this study helped answer was if treatment with erlotinib and gemcitabine was more effective than treatment with gemcitabine and placebo in increasing overall survival (OS). OS was defined as the time from the date the patient was placed in the study until death due to any cause.

This study for erlotinib took place at 176 clinics in 18 countries across North and South America, Europe, Asia, New Zealand and Australia. Of the 176 clinics, 140 clinics enrolled patients in the study. The study started in November 2001 and when the report was written the study 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 2001 to January 2004. 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). All patients received gemcitabine.

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 were randomized to 1 of 2 treatments:

- **100 mg erlotinib** orally daily and gemcitabine in the vein 7 times during 8 weeks called Cycle 1.
- **100 mg placebo** orally daily and gemcitabine in the vein 7 times during 8 weeks called Cycle 1.

Both patient groups received the same dose of gemcitabine which was 1000 mg per square meter of body surface area. If the patient tolerated the treatment, Cycle 1 could have been followed by 1 or more 4-week cycles. Each of the later cycles included the same dose of erlotinib or placebo and 3 doses of gemcitabine over the 4-week cycle.

After the start of the study, the information collected was periodically reviewed for patient safety. After 3 safety reviews a decision was made to increase the dose of erlotinib and placebo to 150 mg orally daily for a limited number of patients.

All patients continued to receive study medication until their cancer got worse or they experienced toxicity that they could not tolerate. At set times throughout the study OS and quality of life were assessed. The patient's safety was evaluated every month. The patients were followed until they died, even if they left the study.

Men and women were allowed to volunteer for this study. They were all over 18 years old. All patients had advanced pancreatic cancer that could not be removed by surgery. They could have received only certain types of chemotherapy and radiation therapy before entering the study. Radiation therapy uses beams of intense energy to kill cancer cells. Patients had adequate blood, kidney and liver function. They did not have any previous treatment with a medicine to lower EGFR.

A total of 569 patients entered this study: 7 patients did not receive study medication and 562 patients received at least 1 dose of study medication. Additional information on the 569 patients who entered the study is provided in the table below.

	Number of Patients (out of 569 patients)
Age Group Aged 18 years and older	 569
Women Men	271 298
EU Countries Outside EU	91 478

What Were the Study Results?

Treating patients with advanced or metastatic pancreatic cancer with erlotinib and gemcitabine resulted in an increase in OS compared to placebo and gemcitabine. Additionally, it took longer for the cancer to get worse when patients were treated with

erlotinib and gemcitabine. Treatment with 100 mg erlotinib and gemcitabine is justified for patients with metastatic pancreatic cancer because the benefits outweigh the risks.

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.

The chart below shows the most common adverse reactions experienced by patients while taking part in this study. A total of 562 patients received at least 1 dose of study medication and are included in the table below.

Adverse Reactions	100 mg Erlotinib and Gemcitabine (out of 259 patients)	100 mg Placebo and Gemcitabine (out of 256 patients)	150 mg Erlotinib and Gemcitabine (out of 23 patients)	150 mg Placebo and Gemcitabine (out of 24 patients)
Vomiting	58	46	4	8
Fatigue or tiredness	104	96	13	11
Rash	169	66	18	3
Diarrhea	83	51	13	6
Loss of hair	18	12	3	1
Swelling	19	18	3	2
Dry skin	17	1	6	2
Nausea or urge to vomit	92	86	10	7
Fever	18	21	2	5
Constipation	15	18	2	0
Swelling of the mouth and lips	33	12	4	2
Loss of appetite	60	49	6	7
Weight loss	26	17		
Headache or head pain	14	14	4	4
Dry eye syndrome	17	12	4	3
Dry mouth	12	11	3	2
Flu-like illness	2	1	3	0
Nose bleed	4	1	4	1
Cough	6	4	2	0
Itchy skin	17	15	1	1
Belly pain	14	15	1	3
Muscle pain	10	9	4	1
Shortness of breath	9	10	2	3
Infection	13	11	2	3

An adverse reaction is considered “serious” when it is life-threatening, causes lasting problems, or needs hospital care. At least 1 serious adverse reaction was experienced by the following:

- 42 of 259 patients who received 100 mg erlotinib and gemcitabine
- 25 of 256 patients who received 100 mg placebo and gemcitabine
- 3 of 23 patients who received 150 mg erlotinib and gemcitabine
- 4 of 24 patients who received 150 mg placebo and gemcitabine

A total of 157 patients died during treatment or within 30 days of their last treatment. See the summary below.

- 80 patients who received 100 mg of erlotinib and gemcitabine
- 69 patients who received 100 mg placebo and gemcitabine
- 3 patients who received 150 mg of erlotinib and gemcitabine
- 5 patients who received 150 mg placebo and gemcitabine

Most of these patients died because their cancer got worse. Of the 157 patients who died, 131 patients died because their pancreatic cancer got worse.

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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