Summary of Results for Laypersons

What was the Study Called?

A Phase 1b Multicenter Trial to Determine the Safety, Tolerance and Preliminary Antineoplastic Activity of Gemcitabine Administered in Combination with Escalating Oral Doses of OSI-774 to Patient Cohorts with Recently Diagnosed, Gemcitabine-Naïve, Advanced, Pancreatic Carcinoma or Other Potentially Responsive Malignancies

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.

Treatment with only erlotinib has been evaluated in a number of studies. In those studies the maximum tolerated dose (MTD) was found. The MTD was defined as the highest dose or treatment that does not cause unacceptable side effects. The MTD for erlotinib taken alone is 150 mg daily in patients with advanced cancer. Sometimes a combination of medicines is used to make cancer treatment more effective. In this study a combination treatment of gemcitabine and erlotinib was tried in patients with advanced pancreatic cancer or other cancers that might respond to this type of treatment. Patients entered into this study had not previously been treated with gemcitabine.

The main question this study helped answer was how erlotinib in combination with gemcitabine goes through the body in patients with advanced cancer. Specifically, the study was designed to show if the 2 medicines taken together changed the way that either medicine goes through the body. This study was used to find the MTD of the erlotinib when given along with gemcitabine. Two doses of erlotinib were tested. The 2 doses of erlotinib were 100 mg and 150 mg. This study was also designed to detect unwanted effects which might occur.

This study for erlotinib took place at 3 clinics in the US. The study took place between July 2001 and October 2003. When the study ended, the sponsor (Astellas) reviewed all the study information and created a report of the results. This is a summary of that report.

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

This study was designed to show if the 2 medicines taken together changed the way that either medicine goes through the body. In this study, blood was taken from the patients during the first cycle of treatment in order to assess how the medicines go through the body. This study was also done to determine the MTD for erlotinib when given with gemcitabine.

The patients were given 1 of the following treatments:

- **100 mg erlotinib** orally daily + gemcitabine administered intravenously (in the vein) 1 time during 7 weeks followed by 1 week (this 8-week period was called Cycle 1)
- **150 mg erlotinib** orally daily + gemcitabine in the vein 1 time during 7 weeks followed by 1 week (this 8-week period was called Cycle 1)

All patients received the same dose of gemcitabine which was 1000 mg per square meter of body surface area. If cycle 1 was tolerated the patient could have received more cycles. The additional cycles included the same doses of medicines but the duration was for 4 weeks (3 weeks of treatment followed by 1 week off). In order to determine how the medicines go through the body, blood was taken from the patients at specific times during cycle 1.

Men and women were allowed to volunteer for this study. They were all over 18 years old. They all had advanced cancer that could not be treated with surgery and could possibly be treated with gemcitabine therapy. Patients were required to have adequate blood, kidney and liver function. They could not have serious heart, gastrointestinal, or eye issues nor could they have uncontrolled infections or any life-threatening illness. Also, they were not previously treated with products that target EGFR.

All patients completed the first cycle of treatment which lasted 8 weeks. Additional cycles of treatment were given if the researcher and the medical monitor though that the treatment was helpful. The patient could receive treatment until their cancer got worse or they experienced toxicity.

During the study there were 3 groups of patients received who received treatment:

- 100 mg erlotinib + gemcitabine
    - The first group was recently diagnosed with pancreatic cancer and had not been treated with gemcitabine. Nine patients were enrolled in this group.
    - The second group met the same criteria as the first group and had no or minimal treatment for their cancer. Three patients were enrolled in this group.
- 150 mg erlotinib + gemcitabine
    - This group met the same criteria as the second group but received a higher dose of erlotinib. Fourteen patients were enrolled in this group.

All 26 patients who were enrolled in the study received treatment.

	Number of Patients (out of 26 patients)
Age Group Aged 18 years and older	 26
Women Men	13 13
EU Countries Outside EU	0 26

What Were the Study Results?

Erlotinib does not have an effect on how gemcitabine goes through the body. Gemcitabine does not have an effect on how erlotinib goes through the body. The MTD was determined to be 150 mg daily of erlotinib for use in combination treatment with gemcitabine at 1000 mg per square meter of body surface area.

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. All 26 patients enrolled in the study received at least 1 dose of study medicine.

Adverse Reactions	**100 mg Erlotinib + gemcitabine First Group (out of 9 patients)**	**100 mg Erlotinib + gemcitabine Second Group (out of 3 patients)**	**150 mg Erlotinib + gemcitabine (out of 14 patients)**	**Total (out of 26 patients)**
Rash	5	3	10	18
Diarrhea	4	1	9	14
Fatigue or tiredness	3	1	10	14
Dry skin	4	2	7	13
Increased blood level of a liver enzyme (ALT/SGPT)	4	0	7	11
Nausea or urge to vomit	3	1	7	11
Increase blood level of a liver enzyme (AST/SCOT)	4	0	6	10
Vomiting	2	1	5	8
Lack of enough red blood cells (anemia)	1	1	5	7
Acne	1	0	5	6
Increase blood level of a liver or bone enzyme (alkaline phosphatase)	2	0	4	6

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Adverse Reactions	100 mg Erlotinib + gemcitabine First Group (out of 9 patients)	100 mg Erlotinib + gemcitabine Second Group (out of 3 patients)	150 mg Erlotinib + gemcitabine (out of 14 patients)	Total (out of 26 patients)
Swelling in the extremities (arms and legs)	0	1	4	5
Low levels of a type of white blood cells (neutrophils)	2	0	2	4
Loss of appetite	1	0	3	4
Skin rash caused by dilation of the small blood vessels under the skin	1	2	0	3
Skin rash with the presence of macules (flat discolored areas)	2	1	0	3
Skin rash with the presence of macules (flat discolored areas) and papules (raised bumps)	2	1	0	3
Weakness	1	0	2	3
Increase blood level of a liver enzyme (gamma-glutamyl transferase)	0	0	3	3
Decreased blood level of magnesium	1	0	2	3
Dry eye	0	0	3	3

An adverse reaction is considered “serious” when it is life-threatening, causes lasting problems or needs hospital care. Three patients who received 150 mg erlotinib + gemcitabine treatment experienced serious adverse reactions.

Five patients died within 30 days of their last dose of erlotinib. These patients died because of their cancer.

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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