Summary of Results for Laypersons

Astellas is grateful to the patients who took part in this clinical study. Thank you.

What was the Study Called?

An Open-label, Phase 1 Dose Escalation Study of Oral ASP8273 in Subjects with Non-small-cell Lung Cancer (NSCLC) Who Have Epidermal Growth Factor Receptor (EGFR) Mutations

Why was this Study Needed?

Non-small cell lung cancer (or NSCLC for short) is the most common type of lung cancer. Some NSCLC cells have a mutation, or change, in the gene for a protein (called EGFR) on the cell surface. The mutated EGFR can cause the cancer cells to grow faster. Erlotinib and gefitinib are prescription medicines taken by mouth that block mutated EGFR. When EGFR is blocked, it can no longer cause cancer cells to grow faster. NSCLC with an EGFR mutation may become resistant to erlotinib and gefitinib, which means that these medicines can no longer stop its growth or keep the cancer stable. Therefore, there was a need to study new treatments for NSCLC with an EGFR mutation. ASP8273 is a new experimental medicine (taken by mouth) that blocks mutated EGFR. That way, ASP8273 may stop or slow down the growth of NSCLC with an EGFR mutation.

This study consisted of 2 parts: part 1 and part 2.

During part 1, patients who had advanced NSCLC with an EGFR mutation took ASP8273 at increasing dose levels. The questions part 1 of this study asked were whether ASP8273 is safe and how well patients tolerate it. And also what is the highest dose of ASP8273 that patients can tolerate. This is called the maximum tolerated dose (MTD) of ASP8273. It was also important to find out what unwanted effects these patients had from ASP8273.

During part 2, patients with advanced NSCLC were included who had some specific EGFR mutations. The main question that Part 2 of the study asked was what would be a safe dose of ASP8273 for future studies. Also, it was important to find out what unwanted effects these patients had from ASP8273.

This study started in April 2014. A few years later, another study of ASP8273 in patients who had NSCLC with an EGFR mutation was going on. In that study, the anticancer effects of ASP8273 did not outweigh its unwanted effects. The sponsor (Astellas) decided to stop the ASP8273 treatment for patients who had other treatment options in July 2017. Astellas continued ASP8273 treatment in this study for 2 patients who had no other treatment options. Astellas decided not to start any new studies of ASP8273.

This study ended in February 2019. When the study ended, the sponsor of this study (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 was an "open-label" study. This means that each patient and the study doctors knew which dose of study medicine a patient took.

Both part 1 and part 2 of the study included women and men aged 18 years or older who had advanced NSCLC with an EGFR mutation. The patients were active or they could perform light daily activities. And they were expected to live at least 3 months.

In part 1, patients who had received prior therapy for their cancer were included.

In part 2, it did not matter if patients had received prior therapy for their cancer or not. In part 2, patients with some specific EGFR mutations were included. One was an EGFR plus T790M resistance mutation. Another was an EGFR mutation with exon 20 insertion.

During the study, the study doctor did a check-up of the patients at several study visits. At the first visit, patients were checked to see if they could be in the study.

In part 1, patients who could be in the study took one of the possible doses of ASP8273. Groups of patients took the dose at the lowest level and other groups took increasing higher doses (doubling the dose). The study doctors looked for intolerable unwanted effects with each dose. If patients had intolerable unwanted effects with medicines in the first dose, they could be moved to a lower dose level. And the next patient could be started at a lower dose level.

Patients took ASP8273 capsules once daily for 21 days (21 day cycle). The dose of ASP8273 was in milligrams (mg) of medicine. The dose levels taken during the study were: **25 mg, 50 mg, 100 mg, 200 mg, 300 mg, 400 mg and 500 mg**.

In part 2, some patients took one of the ASP8273 doses listed above. Patients with the EGFR mutation with exon 20 insertion took a 300 mg dose of ASP8273 for 21 days. Patients who had the EGFR plus T790M resistance mutation took both midazolam and one of the doses of ASP8273 listed above for 21 days.

In both part 1 and part 2, the patients could take study medicine until their cancer got worse, they had unwanted effects they could not tolerate or they asked to stop treatment. Or the study doctors decided that continuing treatment was no longer in the patients' best interest.

This study took place at 10 clinics in the US. 133 patients were in the study. Out of these patients, 130 patients took at least 1 dose of study medicine.

	Number of Patients
Age Group	
Aged less than 65 years	69
Aged 65 years or older	61
Sex	
Men	36
Women	94

What Were the Study Results?

Part 1 of this study asked whether ASP8273 is safe and how well patients tolerate it. And also what is the highest dose of ASP8273 that patients can tolerate (maximum tolerated dose).

The median (a middle value in a sorted list of numbers) number of days that patients took ASP8273 was 127 days. The highest dose of ASP8273 that patients could tolerate (maximum tolerated dose) was 400 mg once daily.

Part 2 of the study asked what would be a safe dose of ASP8273 for future studies.

In this study the recommended dose of ASP8273 was 300 mg once daily.

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 table below shows the most common adverse reactions experienced by patients who took at least 1 dose of study medicine in this study.

Adverse Reaction	**ASP8273 (out of 130 patients)**
Any adverse reaction	111 (85.4%)
Diarrhea	53 (40.8%)
Nausea or the urge to vomit	36 (27.7%)
Fatigue or Tiredness	25 (19.2%)
Decreased blood level of sodium	23 (17.7%)
Increased blood level of enzyme (creatine phosphokinase) from muscle	20 (15.4%)
Decreased appetite	19 (14.6%)
Dry mouth	17 (13.1%)
Inflammation (swelling and redness) or degeneration of the peripheral nerves (those nerves outside of brain and spinal cord) causing numbness, tingling, burning	17 (13.1%)
Vomiting	17 (13.1%)
Commonly known as "pins and needles," where part of the body (typically a foot or hand) begins to tingle and becomes numb, or "falls asleep"	15 (11.5%)
Increased blood level of a liver enzyme (ALT/SGPT)	15 (11.5%)
Increased blood level of a liver enzyme (AST/SGOT)	13 (10.0%)

111 patients (85.4%, or 111 out of 130 patients) experienced an adverse reaction.

An adverse reaction is considered “serious” when it is life-threatening, causes lasting problems or needs hospital care.

14 patients (10.8%, or 14 of 130 patients) experienced a serious adverse reaction in this study when treated with ASP8273.

14 patients died during the study. None of the patients died because of the study medicine.

Where Can I Learn More About This Study?

This document is a short summary of the main results from this study and reflects the information available as of April 2019. You can find this summary and more information about this study 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. This summary only shows the results of this 1 study. Your doctor may help you understand more about the results of this study.

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