Summary of Results for Laypersons

What was the Study Called?

A Phase 2, Double-Masked, Randomized, Active Controlled Study to Evaluate the Efficacy and Safety of ASP8232 in Reducing Central Retinal Thickness in Subjects with Diabetic Macular Edema. This is also known as the VIDI study.

Why was this Study Needed?

The retina is a multilayered sensory tissue that lines the back of the eye responsible for sight. The macula is the part of the retina that gives you sharp vision (needed for reading, driving and seeing faces). Diabetic macular edema (or DME for short) is swelling of the macula in 1 or both eyes that may occur in patients with diabetes. (Diabetes is a disease in which the blood sugar level is too high.) The swelling of the macula leads to vision problems such as reduced or blurred vision. Ranibizumab (also known as Lucentis®) is a medicine that is injected into the eye to slow the progress of DME. It blocks the growth of abnormal blood vessels in the eye. Ranibizumab may not work well in some patients. And it would be easier for patients to take a medicine by mouth than to have the medicine injected into the eye. Therefore, there was a need to study new treatments for DME.

ASP8232 is an experimental medicine taken by mouth. It works by blocking a protein (vascular adhesion protein-1) in the body, including blood vessels in the eye. Blocking that protein may reduce the swelling in the eyes and improve vision.

This study was conducted in patients with DME. Patients took ASP8232 together with sham injections into the eye (ASP8232/sham injections); ASP8232 together with ranibizumab injections into the eye (ASP8232/ranibizumab injections); or placebo capsules together with ranibizumab injections into the eye (placebo/ranibizumab injections). (The section below describes what sham injections and placebo capsules are.) The main question this study helped answer was if the thickness of the back of the eye changed 12 weeks after the start of treatment with ASP8232/sham injections. It was also important to find out what unwanted effects the patients had from the study medicines.

The study started in January 2015 and ended in August 2016. When this 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 was a “double-masked” study. That means that the patients and the researchers did not know who took which of the study medicines (ASP8232/ranibizumab, ASP8232/sham injections or placebo/ranibizumab). A sham injection is where the hub of the syringe (without a needle) touches the eye and nothing is injected into the eye. 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 sham injection or a placebo helps make study results fair and

unbiased, because researchers and patients cannot tell who is taking a sham injection or a placebo, and who is taking the test medicine.

Clinical studies have a list of requirements for patients who can be in a study ("inclusion" criteria) and patients who cannot take part in a study ("exclusion" criteria). The requirements for this study are listed below.

During the study, 1 of the patient's 2 eyes ("study eye") was treated with ranibizumab or sham injections. The other eye was not treated with injections. Several of the requirements for this study applied to the study eye.

Men and women aged between 18 and 85 years could take part in the study if:

- A doctor had confirmed that they had diabetes (type 1 or 2).
- Their average level of blood sugar over the past 3 months ("HbA1C level") was 12.0% or less.
- The back of their study eye had grown thicker because of their DME. This was determined during a doctor's examination and an eye test. This eye test was done with a very thin, nonharmful, light beam that created a picture of the tissues in the back of the eye.
- There was a buildup of fluid within the study eye that had resulted in increased thickness of the back of the study eye. And at study start and treatment assignment, the thickness of the back of the study eye was at least 375 μm in the eye test with the light beam. (μm or micrometer is a unit that measures thickness. The usual thickness of the back of the eye is maximally 320 μm for patients with diabetes.)
- At study visit 1, the vision of their study eye was between 24 and 73 on a test where patients read a series of different sized letters shown to them on an eye chart.

Patients could not take part in this study if:

- The cause of the macular edema in their study eye was not DME.
- The cause of the worsening vision of their study eye was not DME.
- An eye test showed that the retina of their study eye had a substantial number of blocked blood vessels. For this eye test, a patient received an injection of a fluorescent dye in an arm blood vessel. The dye traveled through the bloodstream. A special camera took several pictures as the dye moved through the blood vessels in the retina at the back of the patient's eye.
- Their study eye had an eye disease (different from DME) that could have caused substantial worsening of vision.

During the study, the study doctor did a check-up of the patients at periodic study visits. At visit 1, patients were checked to see if they could be in the study. Patients who could be in the study were checked at visit 2 to determine which eye was going to be treated with a ranibizumab or sham injection ("the study eye"). Next, patients were picked for 1 of 3 treatments by chance alone:

- ASP8232/sham injections: Patients took 1 ASP8232 capsule (40 mg) by mouth once a day for 84 days. At visit 2 and at visits that were 4 and 8 weeks later, the study doctor

anesthetized the patients' study eye. The patients then received a sham injection (nothing was injected into the study eye).

- ASP8232/ranibizumab injections: Patients took 1 ASP8232 capsule (40 mg) by mouth once a day for 84 days. At visit 2 and at visits that were 4 and 8 weeks later, the study doctor anesthetized the patients' study eye. The patients then received an injection of ranibizumab (0.3 mg) into that eye.
- Placebo/ranibizumab injections: Patients took 1 placebo capsule by mouth once a day for 84 days. At visit 2 and at visits that were 4 and 8 weeks later, the study doctor anesthetized the patients' study eye. The patients then received an injection of ranibizumab (0.3 mg) into that eye.

This study took place at 21 clinics in the United States. 96 patients were in the study and took at least 1 dose of study medicines.

	Number of Patients (out of 96 Patients)
Age Group	
Aged 64 years or younger	58
Aged 65 years or older	38
Sex	
Men	48
Women	48
Clinic Location	
United States	96

What Were the Study Results?

This study in patients with DME looked at the change in thickness of the back of the study eye 12 weeks after the start of treatment with ASP8232/sham injections.

After 12 weeks of treatment, the thickness of the back of the study eye had on average not decreased in the ASP8232/sham injections group. The thickness after 12 weeks of treatment was approximately 11% (11.4%) greater than that at treatment start. Statistical testing showed that this difference was likely to be due to chance.

The study showed that the treatment with ASP8232/sham injections did not change the thickness of the back of the study eye.

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 adverse reactions experienced by patients who took at least 1 dose of study medicines in this study.

Adverse Reaction	ASP8232 + Sham Injections (out of 32 patients)	ASP8232 + Ranibizumab Injections (out of 33 patients)	Placebo + Ranibizumab Injections (out of 31 patients)
Any adverse reaction	2 (6.3%)	3 (9.1%)	3 (9.7%)
Abnormal electrical conduction within the heart	1 (3.1%)	0	0
Acne	1 (3.1%)	0	0
Feeling jittery	1 (3.1%)	0	0
Increased blood level of a liver enzyme (alanine aminotransferase)	1 (3.1%)	0	0
Increased blood level of a liver enzyme (aspartate aminotransferase)	1 (3.1%)	0	0
Problem that affects the retina (a multilayered sensory tissue that lines the back of the eye responsible for sight)	1 (3.1%)	1 (3.0%)	0
Distorted vision in which objects appear warped	0	0	1 (3.2%)
Dizziness (or sensation of lightheadedness, unsteadiness or giddiness)	0	0	1 (3.2%)
Fear of light	0	0	1 (3.2%)
Feeling of confusion as to time, place or identity	0	1 (3.0%)	0
Headache or head pain	0	1 (3.0%)	0

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

None of the patients experienced serious adverse reactions.

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 2017. 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.

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