Summary of Results for Laypersons

What was the Study Called?

Open-label Study of Isavuconazole in the Treatment of Patients with Aspergillosis and Renal Impairment or of Patients with Invasive Fungal Disease Caused by Rare Molds, Yeasts or Dimorphic Fungi. This study is also known as the VITAL study.

Why was this Study Needed?

Isavuconazole (also known as Cresemba® and BAL8557) is a prescription medicine used to treat patients with a fungal infection that has spread throughout their body. These types of fungal infections are called invasive fungal infections. Invasive mucormycosis, also known as zygomycosis, is a very aggressive invasive fungal infection.

In developed countries, this disease is seen mostly in patients with diabetes, blood cancers who undergo chemotherapy and in patients who have undergone a blood stem cell transplant. Chemotherapy is a type of cancer treatment that uses drugs to destroy cancer cells. Invasive mucormycosis is the third most common type of invasive fungal infection after candidiasis and invasive aspergillosis. Candidiasis is an infection caused by yeast and invasive aspergillosis is caused by a filamentous fungus called *Aspergillus* species. In the developing countries, invasive mucormycosis occurs in patients with uncontrolled diabetes or trauma.

Isavuconazole can be used to treat an invasive fungal infection caused by filamentous fungi such as *Aspergillus* species. Filamentous fungi look like thin lines under a microscope. Patients can also be infected with less common molds, yeasts or other fungi.

This study was done to see if isavuconazole was effective in treating invasive aspergillosis in patients with kidney dysfunction or in patients with invasive fungal disease. The patient's invasive fungal infection could have been caused by rare molds, yeasts or other fungi. It was also important to find out what unwanted effects isavuconazole might cause.

This study took place at 34 clinics worldwide including clinics in Belgium, Brazil, Germany, India, Israel, Lebanon, Mexico, Russia, South Korea, Thailand and the United States between April 2008 and January 2014. 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 was an "open-label" study. In this study, all patients knew they were given isavuconazole. Patients were given isavuconazole 200 mg in a vein in their arm or oral capsules 3 times daily on study days 1 and 2. Starting on day 3, isavuconazole 200 mg was given once daily for a period of up to 180 days.

Both men and women who were at least 18 years of age took part in this study. Patients could be enrolled in the study if they had:

- Proven or probable invasive aspergillosis with kidney dysfunction

- Proven or probable invasive fungal disease caused by rare molds, yeasts or other fungi
- Proven or probable zygomycosis
- Proven or probable diagnosis of invasive fungal disease caused by *Aspergillus* species or other filamentous fungi with or without kidney dysfunction

A total of 149 patients were enrolled into the study and 146 patients received at least 1 dose of study medicine during the study.

Additional information regarding the 146 patients who received at least 1 dose of study medicine is provided in the table below.

	Number of Patients
Age Group	
Aged 18 to 92 years	146
Men	100
Women	46
EU Countries	17
Outside EU	129

What Were the Study Results?

Isavuconazole was well tolerated and effective for the treatment of mucormycosis and invasive aspergillosis in patients with kidney dysfunction. Isavuconazole was also effective for the treatment of other types of fungal infections. The safety profile for the patients was similar to that seen in another large study conducted during the same time period (9766-CL-0104/SECURE Study).

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 while taking part in this study.

Adverse Reaction	Total (out of 146 patients)
Nausea or the urge to vomit	11
Vomiting	9
Increased blood level of a liver enzyme (gamma-glutamyl transferase)	7
Diarrhea	7
Inflammation (swelling or redness) of a vein	4
Increased blood level of a liver or bone enzyme (alkaline phosphatase)	4
Hair loss	3
Decreased appetite	3
Sleepiness, the state of feeling drowsy, ready to fall asleep	3

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. A total of 13 patients had serious adverse reactions.

A total of 44 patients died during the study. One of the deaths was judged by the study doctor to be related to study medicine.

Where Can I Learn More About This Study?

After evaluating the results of this clinical study Astellas may perform additional studies to better understand isavuconazole.

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 isavuconazole, please discuss these with your doctor.

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