Summary of Results for Laypersons

What was the Study Called?

A Phase III, Double-blind, Randomized Study to Evaluate Safety and Efficacy of BAL8557 Versus Voriconazole for Primary Treatment of Invasive Fungal Disease Caused by *Aspergillus* Species or Other Filamentous Fungi. This study is also known as the SECURE study.

Why was this Study Needed?

Isavuconazole (also known as Cresemba® and BAL8557) is a prescription medicine used to treat patients when a fungal infection has spread throughout their body. These types of fungal infections are called invasive fungal infections. These infections can be caused by an overgrowth of a filamentous fungus like *Aspergillus* species. A filamentous fungus is one that looks like thin lines under a microscope. Patients who are immunocompromised (have a weakened immune system) are at risk for these types of fungal infections.

This study was done to find out if isavuconazole was the same or better than voriconazole in treating patients with invasive fungal infections caused by *Aspergillus* species or other filamentous fungi. Voriconazole is a medicine also used to treat these types of infections. It was also important to find out what unwanted effects isavuconazole might cause.

This study for isavuconazole took place at 102 clinics worldwide in Argentina, Australia, Belgium, Brazil, Canada, Chile, China, Egypt, France, Germany, Hungary, India, Israel, Italy, Malaysia, Mexico, The Netherlands, New Zealand, Poland, Russia, South Korea, Spain, Switzerland, Thailand, Turkey and The United States. The study took place from March 2007 to March 2013. 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 a "double-blinded" study. In this study both the doctor and the patient did not know whether the patient was taking isavuconazole or voriconazole. As each patient was enrolled in the study, they were placed equally in 1 of 2 treatment groups:

- Isavuconazole treatment group
- Voriconazole treatment group

Both study medicines were given to the patient in a vein in their arm or orally (by mouth) as a capsule. The patients received the following:

- Isavuconazole treatment group: 200 mg in the vein as a loading dose within 48 hours followed by a maintenance dose from study day 3 continuing for a maximum period of 84 days. The maintenance dose was 200 mg administered in the vein or by mouth once daily.
- Voriconazole treatment group: 6 mg/kg of body weight administered in the vein as a loading dose within 24 hours followed by a maintenance dose from study day 2

continuing for a maximum period of 84 days. The maintenance dose was 4 mg/kg of body weight administered in a vein every 12 hours or 200 mg by mouth every 12 hours.

The patients were seen 4 weeks after the treatment period for a follow-up visit.

Both men and women who were at least 18 years of age took part in this study. They had a proven, probable or possible diagnosis of invasive fungal disease caused by *Aspergillus* species or other filamentous fungi.

A total of 532 patients agreed to be in the study, 527 patients were entered into the study and 516 patients received at least 1 dose of study medicine. Additional information about the 516 patients who received at least 1 dose of study medicine is provided in the table below.

	Number of Patients
Age Group	
Aged less than 45 years	195
Aged older than 45 years and less than 65 years	207
Aged older than 65 years and less than 75 years	97
Aged older than 75 years	17
Men	308
Women	208
EU Countries	210
Outside EU	306

What Were the Study Results?

The results of the study showed that isavuconazole was as good as voriconazole for the treatment of invasive fungal disease caused by *Aspergillus* species and other filamentous fungi. The study also showed that isavuconazole has a better safety profile than voriconazole.

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 received at least 1 dose of study medicine while taking part in this study.

Adverse Reaction	Isavuconazole (out of 257 patients)	Voriconazole (out of 259 patients)
Nausea or the urge to vomit	19	21
Vomiting	13	22
Shortness of breath	8	2
Decreased blood level of potassium	7	5
Increased blood level of a liver enzyme (gamma-glutamyltransferase)	6	14
Headache	6	5
Increased blood level of a liver enzyme (aspartate aminotransferase)	5	11
Increased blood level of a liver or bone enzyme (alkaline phosphatase)	5	11
Rash	5	7
Increased blood level of a liver enzyme (alanine aminotransferase)	4	11
Chills	4	7
High or low blood test results which test for liver function	2	9
Abnormal electrical conduction within the heart	1	8
Seeing or sensing things that aren't there while a person is awake and conscious (such as hearing voices)	1	11
High blood levels of bilirubin	1	6
Vision problems	1	15
Seeing things that aren't there while a person is awake and conscious	0	9

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. Some patients in this study experienced at least 1 serious adverse reaction: 28 patients in the isavuconazole group and 29 patients in the voriconazole group.

A total of 168 patients died during the study (81 patients in the isavuconazole group and 87 in the voriconazole group). Thirteen of the deaths were related to study medicine (7 deaths in the isavuconazole group and 6 deaths in the voriconazole group).

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.

Sponsors contact details:

Astellas Pharma Global Development, Inc.

1 Astellas Way

Northbrook, IL 60062

USA