Summary of Results for Laypersons

What was the Study Called?

Randomized, Open Label, Non-inferiority Study of Micafungin Versus Standard Care for the Prevention of Invasive Fungal Disease in High Risk Liver Transplant Recipients. This was also called the TENPIN study.

Why was this Study Needed?

Micafungin (also known as FK463 and Mycamine®) is a prescription medicine used to treat patients when a fungal infection has spread throughout their body (called an "invasive" infection). Invasive fungal infections can be caused by a yeast called *Candida* (invasive candidiasis) or a mold called *Aspergillus* (invasive aspergillosis). Yeast infections can be grouped into *Candida albicans* infections and non-*albicans Candida* species infections. Patients who have had an organ transplant are at risk for these types of fungal infections.

This study was done to find out if the study medicine called micafungin was as effective as the standard of care treatment that is given to liver transplant recipients for the prevention of invasive fungal diseases. "Standard of care treatment" refers to prescription medicines commonly given to patients for the prevention of invasive fungal infections. In this study the standard of care medicines included fluconazole, liposomal amphotericin B, and caspofungin. Also, it was important to find out what unwanted effects micafungin might cause.

This study for micafungin enrolled patients at 34 clinics in Europe (Austria, Germany, Belgium, Hungary, France, Italy, Portugal, Spain, Ireland, the United Kingdom, Romania and Sweden) and Russia. The study took place from December 2009 to May 2012. 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. All patients knew the name of the study medicine that they were receiving. Patients satisfying all selection criteria entered the study at admission to the hospital for liver transplantation. Only patients identified at "high-risk" for developing an invasive fungal infection were eligible for the study.

Patients were randomly assigned (like flipping a coin) to one of two treatment groups: 1) micafungin 100 mg administered intravenously (in the vein) or 2) "Standard of Care" medicines (fluconazole 200 to 400 mg; liposomal amphotericin B 1 mg to 3 mg/kg; or caspofungin, one 70 mg dose followed by a 50 mg dose. All study medicines were administered in the vein once daily for 21 days or until hospital discharge, whichever came first. The end of the study was 3 months after the start of treatment; however, patients were followed for an additional 6 months for survival status (i.e., to see if they were still living).

Both men and women aged 18 years or older who were having liver transplant surgery took part in the study.

A total of 347 patients were enrolled in the study and 345 patients received at least 1 dose of study medicine. Additional information on the 345 patients are listed in the table below.

	Number of Patients
Age Group	
Aged less than 45 years	80
Aged 45 to 65 years	243
Aged 66 to75 years	22
Men	233
Women	112
EU Countries	335
Outside EU	10

What Were the Study Results?

Micafungin was found to be as effective as "standard of care" medicines for prevention of invasive fungal diseases in liver transplant patients considered at high-risk for getting a fungal infection. All medicines were well tolerated and improved the quality of life for patients. "Quality of life" refers to the patient's mobility, self care, and ability to perform usual activities, pain/discomfort, and anxiety/depression.

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 in more than 1% of patients in the standard of care or micafungin treatment groups.

Adverse Reactions	**Fluconazole (out of 78 patients)**	**Liposomal Amphotericin B (out of 71 patients)**	**Caspofungin (out of 23 patients)**	**Standard of Care (out of 172 patients)**	**Micafungin (out of 173 patients)**
Increase blood level of a liver enzyme (called gamma-glutamyl transferase)	0	0	0	0	2
Nausea or the urge to vomit	0	0	0	0	2
Table continued on next page					

Adverse Reactions	Fluconazole (out of 78 patients)	Liposomal Amphotericin B (out of 71 patients)	Caspofungin (out of 23 patients)	Standard of Care (out of 172 patients)	Micafungin (out of 173 patients)
Drug toxicity (when the amount of medicine in the blood is too high)	0	0	0	0	2
An infection caused by use of a catheter (a flexible tube inserted through a narrow opening into a body cavity such as the bladder)	0	2	0	2	0
Decreased number of platelets (platelets are blood cells that help blood clot)	1	1	0	2	0
Back pain	0	8	0	8	0
Kidney failure	1	3	0	4	0
Kidneys not working well	0	2	0	2	0

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care. A total of 17 patients experienced at least 1 serious adverse reaction: 7 patients who received "Standard of Care" medicines and 10 patients who received micafungin.

At the time of this report, despite the medical advances and the availability of several antifungal medicines, fungal infections in liver transplant recipients are still associated with poor outcome with the rate of deaths ranging from 30% to 50% for invasive candidiasis and 65% to 90% for invasive aspergillosis.

In this study, 52 patients died. Two of the deaths were judged by the investigator to be related to study medicine (1 death in the micafungin group and 1 death in the "standard of care" group).

Where Can I Learn More About This Study?

Astellas may perform additional studies to better understand micafungin.

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 micafungin, please discuss these with your doctor.

Sponsor contact details:

Astellas Pharma Europe, Ltd

2000 Hillswood Drive

Chertsey

Surrey KT16 0RS

United Kingdom