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?

A Phase III, Randomized, Double-blind, Double-dummy, Multi-center Clinical Study to Observe the Efficacy and Safety of Febuxostat Compared with Allopurinol in Subjects with Hyperuricemia (Including Gout).

Why was this Study Needed?

Uric acid is a waste material from food digestion. Most uric acid dissolves in blood and travels to the kidneys. From there, it passes out in urine. If your body produces too much uric acid or does not remove enough if it, you can get sick. An increased level of uric acid in the blood is called hyperuricemia. This may worsen kidney function, cause joint pain (gout) and cause kidney stones. There are prescription medicines available to treat increased uric acid. One of these medicines is allopurinol. However, this medicine may not be appropriate for some patients with kidney problems. Therefore, there was a need to study new treatments for increased uric acid. This study was conducted in China where there was an increase in people with hyperuricemia. After this study had ended, febuxostat provided by Astellas was approved in China. It is now approved in countries all over the world.

This study was conducted in patients who had increased uric acid level in blood (with or without gout). Patients took either allopurinol or febuxostat (low or high dose). The main question this study helped answer was if low dose febuxostat was not worse than allopurinol in decreasing uric acid level. The study looked at how many patients' uric acid levels were decreased at the last visit, compared to start of the study. It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in April 2013 and ended in January 2015. 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 a "double-blinded" study. That means that the patients and the study doctors did not know who took which of the study medicines (febuxostat and placebo or allopurinol and placebo). A "placebo" is a dummy treatment such as a tablet that looks like a medicine, but does not have any medicine in it. Using a placebo helps make study results fair and unbiased, because the study doctors and patients could not tell who was taking febuxostat, and who was taking allopurinol.

This study included Chinese men and women aged 18 to 85 years of age. They had increased uric acid level in the blood, with or without gout. Their uric acid level was 7.0 mg/dL or greater before the study.

During the study, the study doctor did a check-up of the patients at several study visits. If a patient was taking other medicines that might interfere with the study medicine they stopped them for at least 2 weeks before entering the study. At the first visit, patients were checked to see if they could be in the study. Patients who could be in the study were picked for a treatment (low or high dose febuxostat or allopurinol), by chance alone. Both study medicines needed to start with a low dose and slowly increase the dose over time. Patients took the study medicines for a total of 24 weeks.

- Febuxostat 40 mg (low dose): Patients took an initial dose of 20 mg febuxostat a day. This was gradually increased to 40 mg a day after 4 weeks. Patients also took placebo tablets each day.
- Febuxostat 80 mg (high dose): Patients took an initial dose of 20 mg febuxostat a day. This was gradually increased to 40 mg a day after 4 weeks, 60 mg a day after 8 weeks and 80 mg a day after 16 weeks. Patients also took placebo tablets each day.
- Allopurinol 300 mg: Patients took an initial dose of 100 mg allopurinol once a day. This was gradually increased to 200 mg a day after 2 weeks and then to 300 mg a day after 4 weeks. Patients also took placebo tablets each day.

This study took place at 14 clinics in China. 763 Chinese males and females aged from 18 to 85 years old were in the study. Out of these, 590 patients took at least 1 dose of study medicine.

What Were the Study Results?

This study was conducted in patients who had increased uric acid level in blood (with or without gout). The main question this study helped answer was if 40 mg febuxostat was not worse than allopurinol.

The table below summarizes patients who had reduced uric acid (6.0 mg/dL or less) at the end of treatment, compared to study start. The results for 40 mg febuxostat were similar to 300 mg allopurinol but there was not enough of a difference to prove it was not worse than allopurinol at reducing uric acid.

Patients with reduced uric acid of 6.0 mg/dL or less			
40 mg Febuxostat At week 24 150 patients	60 mg Febuxostat At week 16 160 patients	80 mg Febuxostat At week 24 160 patients	300 mg Allopurinol At week 24 162 patients
45% (67 out of 150)	66% (106 out of 160)	70% (112 out of 160)	50% (81 out of 162)

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	Febuxostat 40 mg (out of 193 patients)	Febuxostat 80 mg (out of 200 patients)	Allopurinol 300 mg (out of 197 patients)
Any adverse reaction	130 (67.4%)	138 (69.0%)	133 (67.5%)
Gout (joint pain)	92 (47.7%)	100 (50.0%)	95 (48.2%)
Increased blood level of a liver enzyme (ALT/SGPT)	11 (5.7%)	11 (5.5%)	14 (7.1%)
C-reactive protein increased	7 (3.6%)	9 (4.5%)	7 (3.6%)
Liver function abnormal	2 (1.0%)	7 (3.5%)	1 (0.5%)
Increased blood level of a liver enzyme (AST/SGOT)	3 (1.6%)	5 (2.5%)	5 (2.5%)
Blood triglycerides increased	4 (2.1%)	5 (2.5%)	2 (1.0%)
Blood creatine phosphokinase increased	3 (1.6%)	5 (2.5%)	0 (0.0%)

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

The table below shows the number of patients with serious adverse reactions.

Serious Adverse Reactions		
Febuxostat 40 mg	**Febuxostat 80 mg**	**Allopurinol 300 mg**
5 patients (2.6%, or 5 out of 193)	5 patients (2.5%, or 5 out of 200)	3 patients (1.5%, or 3 out of 197)

One patient who took 40 mg febuxostat died during the study. The doctor in charge of the study did not think the patient died due to febuxostat.

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 August 2015. 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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