CLINICAL TRIAL RESULTS

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer, Inc.

Medicine(s) Studied: Fesoterodine

Protocol Number: A0221047

Dates of Trial: 2 July 2012 to 13 February 2020

Title of this Trial: A Study To Find Out How Fesoterodine Works In Children Aged 6 To 17 Years With Bladder Overactivity Caused By A Neurological Condition

[A 24-Week Randomized, Open-Label, Study to Evaluate the Safety and Efficacy of Fesoterodine in Subjects Aged 6 to17 Years With Symptoms of Detrusor Overactivity Associated With a Neurological Condition (Neurogenic Detrusor Overactivity)]

Date(s) of this Report: 1 October 2020

– Thank You –

Pfizer, the Sponsor, would like to thank you and your child for participating in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your child's study site.

WHY WAS THIS STUDY DONE?

Neurogenic detrusor overactivity, or "NDO", is a bladder condition associated with damage to the nervous system. NDO may be caused by injury or disease to the spinal cord, including certain conditions that are present from birth. People with NDO may not be able to control their bladder and may not be able to hold as much urine in their bladder as other people can, so they may have urine leakage or need to urinate frequently. Additionally, NDO can cause damage to the kidneys and urinary tract if it goes unchecked.

Current treatment options are limited for children and adolescents with NDO, so researchers are looking for new medicines that may help young people with this condition. Fesoterodine was the investigational medicine tested in this study. Fesoterodine has not been approved for use in children or adolescents, outside of research studies like this one.

The main purpose of this study was to learn more about the use and safety of fesoterodine in children and adolescents with NDO. Researchers asked this main question:

- **Did bladder capacity increase following 12 weeks of treatment with fesoterodine?**

To answer this question, the researchers measured each patient's bladder capacity (maximum volume of urine that can be held in the bladder before the patient needs to urinate) 2 times: before the patients started study medicine, and again after the patient had taken study medicine for 12 weeks. They compared each patient's first result to their second result.

WHAT HAPPENED DURING THE STUDY?

This study was done to find out if patients would have increased "bladder capacity" (be able to hold more urine) following 12 weeks of treatment with fesoterodine, compared to before they started taking study medicine. Some of the patients were also compared to patients taking a medicine called oxybutynin XL. Oxybutynin XL

was selected to be the comparator medicine because it is widely used to treat NDO in children and adolescents.

This study included children and adolescents who:

- Were aged 6 to 17 years
- Were diagnosed with NDO
- Had stable nervous system disease, which means that their nervous system disease was not getting worse
- Were checked by the study doctor for other health conditions, and were determined to be appropriate to join the study

The study included 4 parts:

- A "run-in period" before the study started. Patients were screened by the study doctors to make sure they were a good fit to join the study. No study medicines were given during this period.
- An "efficacy phase" for the first 12 weeks of study treatment, when the researchers evaluated how well fesoterodine works, along with its safety.
- A "safety extension phase" for the last 12 weeks of study treatment, when the researchers continued to evaluate the safety of fesoterodine.
- A 2-week "follow-up phase" at the end of the study.

Children and adolescents in this study were divided into 2 groups, based on weight:

- Group 1 (124 patients): Patients weighing more than 25 kilograms (about 55 pounds)
- Group 2 (57 patients): Patients weighing 25 kilograms or less

Patients from Group 1 were assigned to receive 1 of 3 treatments:

- Fesoterodine 4 milligram (mg) tablets (42 patients) for both the efficacy phase and safety extension phase (24 weeks)
- Fesoterodine 8 mg tablets (42 patients) for both the efficacy phase and safety extension phase (24 weeks)

- Oxybutynin XL tablets for the efficacy phase (12 weeks). These patients were then switched to fesoterodine 4 mg or 8 mg tablets for the safety extension phase (12 weeks) (40 patients).

The patients were assigned to receive the treatments by chance alone, which is known as a "randomized" study. This is done to make the groups more similar. Reducing differences between the groups (like age or the number of boys and girls), makes the groups more even to compare.

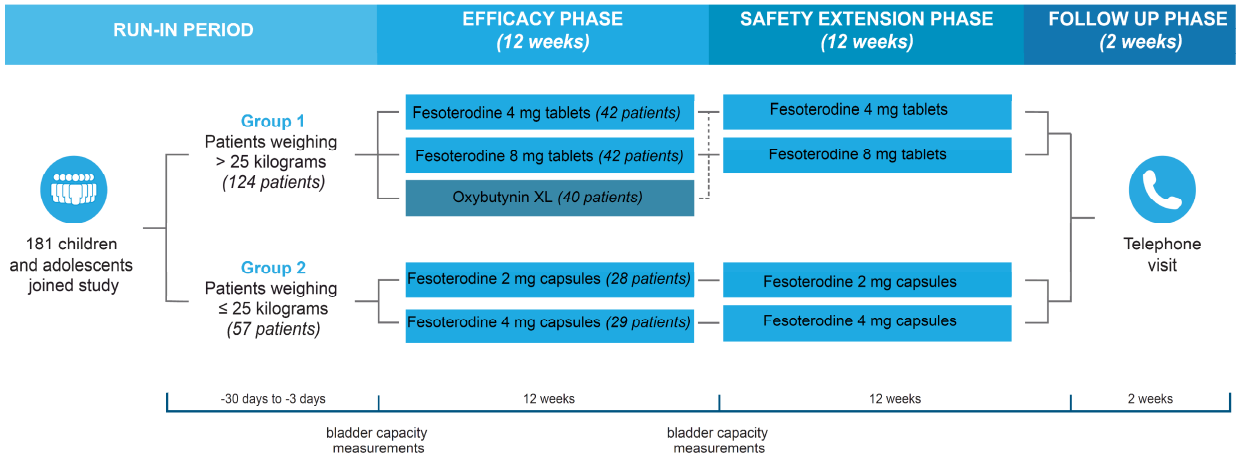
Patients from Group 2 were assigned by chance alone to receive 1 of 2 treatments for both the efficacy phase and safety extension phase (24 weeks):

- Fesoterodine 2 mg capsules (28 patients)
- Fesoterodine 4 mg capsules (29 patients)

This was an "open-label" study, which means that the patients, their families, and the study doctors knew which medicine the patients were taking.

Patients were expected to come to 8 study visits They were checked by study doctors at each visit, to monitor for safety of the study medicines. Bladder capacity was measured before the patients started study medicines, and again after they had been on the study medicines for 12 weeks.

The figure below shows what happened during the study.



Patients were expected to be in this study for about 26 weeks (24 weeks of treatment plus a 2-week follow-up period). The Sponsor ran this study at 102 locations in 28 countries in Africa, Asia, Europe, and North America. The entire study took more

than 7 years to complete. It began 2 July 2012 and ended 13 February 2020. A total of 95 boys (52%) and 86 girls (48%) participated in the study. All patients were between the ages of 6 and 17 years.

Patients were to be treated for 24 weeks. Of the 124 patients in Group 1 who started the study, 101 patients (81%) finished the study. Of the 57 patients in Group 2 who started the study, 48 patients (84%) finished the study. A total of 23 patients from Group 1 (19%) and 9 patients from Group 2 (16%) left before the study was over by their choice or because a doctor decided it was best for a patient to stop being in the study.

When the study ended in February 2020, the Sponsor reviewed the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Did bladder capacity increase following 12 weeks of treatment with fesoterodine?

The researchers measured each patient's bladder capacity (maximum volume of urine that could be held in the bladder) 2 times: before the patient started study medicine, and again after the patient had taken study medicine for 12 weeks. They compared each patient's first result to their second result, to see if bladder capacity increased.

On average, patients from Group 1 who received fesoterodine 4 mg or 8 mg tablets had an increase in bladder capacity at week 12. For the fesoterodine 8 mg tablet group, this increase was comparable to the increase seen in the patients who received oxybutynin XL. Based on these results, the researchers have decided that the results are not likely due to chance. The test medicine may be an option for treating children and adolescents with NDO.

On average, patients from Group 2 who received fesoterodine 2 mg or 4 mg capsules also had an increase in bladder capacity at week 12, but this was smaller than for Group 1, and smaller for the fesoterodine 2 mg capsule group than for the fesoterodine 4 mg capsule group.

This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the patients had during the study. Patients could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the patient was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what the side effects of an experimental drug might be.

During the efficacy phase (first 12 weeks of treatment), a total of 76 out of 124 patients in Group 1 (61%) had at least 1 medical problem. In the fesoterodine 4 mg tablet group, 26 out of 42 patients (62%) had a medical problem. In the fesoterodine 8 mg tablet group, 20 out of 42 patients (48%) had a medical problem. In the oxybutynin XL group, 30 out of 40 patients (75%) had a medical problem. Three out of 42 patients in the fesoterodine 4 mg tablet group (7%) left the study because of medical problems.

A total of 67 patients in Group 1 received fesoterodine during both the efficacy phase and the safety extension phase. 46 of these patients (69%) had at least 1 medical problem. One of these patients (1%) left the study because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems in Group 1 Patients Who Received Fesoterodine During Efficacy Phase and Safety Extension Phase (Reported by 2 or More Patients in Either Group)		
Medical Problem	**Fesoterodine 4 mg Tablets (30 Patients Treated)**	**Fesoterodine 8 mg Tablets (37 Patients Treated)**
Diarrhea	5 (17%)	3 (8%)
Common cold	5 (17%)	3 (8%)
Dry mouth	4 (13%)	4 (11%)
Flu	4 (13%)	1 (3%)
Bed sore	3 (10%)	0 (0%)
Infection of the nose, throat, and upper airways caused by virus	3 (10%)	0 (0%)
Urinary tract infection	3 (10%)	2 (5%)
Trouble seeing objects far away	2 (7%)	1 (3%)
Nausea	2 (7%)	2 (5%)
Fever	2 (7%)	2 (5%)

Headache	**2 (7%)**	**6 (16%)**
Constipation	**1 (3%)**	**3 (8%)**
Throat pain	**1 (3%)**	**2 (5%)**
Infection of the nose, throat, and upper airways	**1 (3%)**	**2 (5%)**
Stomach flu	**1 (3%)**	**3 (8%)**
Cough	**0 (0%)**	**2 (5%)**
Trouble controlling bladder	**0 (0%)**	**2 (5%)**

During the efficacy phase (first 12 weeks of treatment), a total of 37 out of 57 patients in Group 2 (65%) had at least 1 medical problem. In the fesoterodine 2 mg capsule group, 19 out of 28 patients (68%) had a medical problem. In the fesoterodine 4 mg capsule group, 18 out of 29 patients (62%) had a medical problem. Three out of 28 patients in the fesoterodine 2 mg capsule group (11%) left the study because of medical problems.

A total of 57 patients in Group 2 received fesoterodine during either the efficacy phase or the safety extension phase. 44 of these patients (77%) had at least 1 medical problem. Three of these patients (5%) left the study because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems in Group 2 Patients Who Received Fesoterodine During Efficacy Phase or Safety Extension Phase (Reported by 2 or More Patients in Either Group)		
Medical Problem	**Fesoterodine 2 mg Capsules (28 Patients Treated)**	**Fesoterodine 4 mg Capsules (29 Patients Treated)**
Bacteria in urine	6 (21%)	2 (7%)
Common cold	4 (14%)	4 (14%)
Urinary tract infection	3 (11%)	7 (24%)
Diarrhea	2 (7%)	1 (3%)
Fever	2 (7%)	3 (10%)
Stomach flu	2 (7%)	0 (0%)
Abnormal urine odor	2 (7%)	1 (3%)
Overactive bladder	2 (7%)	0 (0%)
Feeling dizzy	2 (7%)	0 (0%)
Infection of the nose, throat, and upper airways	1 (4%)	3 (10%)
Sore throat	1 (4%)	2 (7%)

Trouble seeing objects far away	**0 (0%)**	**2 (7%)**
Headache	**0 (0%)**	**3 (10%)**
Constipation	**0 (0%)**	**2 (7%)**
Nosebleed	**0 (0%)**	**2 (7%)**
Trouble controlling bladder	**0 (0%)**	**2 (7%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

During the efficacy phase (first 12 weeks of treatment), a total of 6 out of 124 patients in Group 1 (5%) had serious medical problems. In the fesoterodine 4 mg tablet group, 3 out of 42 patients (7%) had serious medical problems. In the fesoterodine 8 mg tablet group, 2 out of 42 patients (5%) had serious medical problems. In the oxybutynin XL group, 1 out of 40 patients (3%) had serious medical problems. Urinary tract infection was the most common serious medical problem and occurred in 2 out of 124 patients (2%), including 1 out of 42 patients (2%) who received fesoterodine 4 mg tablets and 1 out of 40 patients (3%) who received oxybutynin XL. None of the serious medical problems were considered to be related to study medicines. No patients (0%) passed away during this phase of the study.

A total of 5 out of 67 patients from Group 1 (7%) who received fesoterodine during both the efficacy phase and the safety extension phase had serious medical problems, including 1 out of 30 patients (3%) who received fesoterodine 4 mg tablets and 4 out of 37 patients (11%) who received fesoterodine 8 mg tablets. No serious medical problem occurred in more than 1 patient, and none of the serious medical problems

were considered to be related to fesoterodine. No patients passed away during this study.

A total of 5 out of 57 patients from Group 2 (9%) who received fesoterodine during the efficacy phase or the safety extension phase had serious medical problems, including 2 out of 28 patients (7%) who received fesoterodine 2 mg capsules and 3 out of 29 patients (10%) who received fesoterodine 4 mg capsules. Urinary tract infection was the most common serious medical problem and occurred in 2 out of 57 patients (4%), including 1 out of 28 patients (4%) who received fesoterodine 2 mg capsules and 1 out of 29 patients (3%) who received fesoterodine 4 mg capsules. None of the serious medical problems were considered to be related to fesoterodine. No patients (0%) passed away during this study.

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

If you have questions about the results of your child's study, please speak with the doctor or staff at your child's study site.

For more details on your child's study protocol, please visit:

www.clinicaltrials.gov	Use the study identifier **NCT01557244**
www.clinicaltrialsregister.eu	Use the study identifier **2010-022475-55**

No further trials with fesoterodine in children or adolescents are planned.

Again, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you and your child helped us to do that!