This document provides a short summary of this study for a general audience. You can find more information in the scientific summary of the study. A link to this summary is provided at the end of this document.

Study names

Short Title: A study to assess how well GSK1358820 works and how safe it is in patients with overactive bladder.

Full Scientific Title: A phase III study to evaluate the efficacy and safety of GSK1358820 (botulinum toxin type A) in patients with overactive bladder.

Study Number: 204947

Who sponsored this study?

GlaxoSmithKline (GSK)
GSK Clinical Support Help Desk
Website: clinicalsupporthd.gsk.com/contact.html
Email: GSKClinicalSupportHD@gsk.com

General information about the clinical study

When and where was this study done?

The study started in August 2016 and ended in November 2018. All study sites were in Japan.

What was the main reason for this study?

Patients with overactive bladder (OAB) may have the following symptoms related to the bladder's abnormal storage of urine:

- Sudden urge to urinate (urinary urgency).
- Urinate more often than normal - usually more than eight times a day (urinary frequency).
- Waking to urinate more than once at night (nocturia).
- Uncontrolled leaking of urine (urinary incontinence).

GSK1358820 is a medicine containing a protein (botulinum toxin type A). It causes muscle relaxation. Injecting GSK1358820 into the bladder wall may relax the bladder muscles and reduce urinary urgency.

This study was conducted in Japanese patients with OAB. Study doctors wanted to see if GSK1358820 reduced the number of urinary incontinence episodes compared with placebo (containing no active medicine) 12 weeks after treatment.

Which medicines were studied?

During the study, patients were placed in one of the following two treatment groups by chance (randomisation):

- Placebo
- GSK1358820 (containing 100 units of botulinum toxin type A)

On Day 1, patients received 10 millilitres [mL] of placebo or GSK1358820 in the form of 20 (0.5 mL) injections. The injections were given evenly across the muscles of the bladder wall. Neither the patients nor the study doctors knew who was receiving which treatment. This is called a double-blind phase.

After Week 12, a patient could request re-treatment. If the study doctor agreed, the patient could be given up to two more re-treatments with GSK1358820. All the patients knew that they received GSK1358820 during the re-treatment. This is called the open-label phase.

For details on the results reported after Week 12 until the end of the study, see the scientific results summary (link provided at the end of this document).

Which patients were included in this study?

Studies have a list of requirements for patients who can enrol (inclusion criteria) and those who can't (exclusion criteria). For this study, the main inclusion and exclusion criteria are listed below.

Main Inclusion Criteria

Men and women were included in the study if they:

- Were at least 20 years old.
- Had OAB that was not well controlled on their current OAB medicine(s).
- Had three or more episodes of urgent urinary incontinence and experienced urinary frequency before starting the study treatment.
- Agreed to have a thin, plastic tube inserted into the bladder (catheterisation) to empty the urine, if needed.

Main Exclusion Criteria

Men and women were excluded from the study if they:

- Had OAB caused by an injury or disease (e.g. Alzheimer's or Parkinson's disease).
- Had urinary incontinence when pressure within the abdomen increased suddenly (e.g. due to coughing or jumping).
- Had bladder surgery or any disease that could affect the bladder function.
- Had more than 100 mL of urine left in the bladder after urination at the start of the study.
- Had taken any medicine(s) to treat OAB symptoms in the week before starting the study.
- Had received botulinum toxin for the treatment of any disease of the urinary system.

A total of 248 patients received the study medicine. The table below shows the gender and age of these patients.

Patients who received the study medicines		
	Placebo 124 patients	**GSK1358820 124 patients**
Gender		
Female	94 (76%)	92 (74%)
Male	30 (24%)	32 (26%)
Age - in years		
Range	34 to 89	21 to 86
Average	66	66

For more detailed information about the patients included in this study, see the scientific results summary (link provided at the end of this document).

What were the overall results of the study?

At the start of the study, each patient was given a diary to write down their bladder symptoms, including urinary incontinence. The patients were asked to bring the diary to each clinic visit.

The study doctor noted the number of urinary incontinence episodes for each patient over any three consecutive days before visiting the clinic. The number of episodes were averaged for each patient at Day 1 (baseline) and Week 12. This is called a **daily average number of urinary incontinence episodes**.

The results from all patients within each treatment group were combined and averaged to get the baseline and Week 12 values for each treatment group. The difference between these two values of the daily average number of urinary incontinence episodes is called the **change from baseline**.

Two patients from each treatment group did not have values for the daily average number of urinary incontinence episodes at both baseline and Week 12, so they were not included in the results. Results are shown for 244 patients in the table below.

Change from baseline in daily average number of urinary incontinence episodes at Week 12		
	Placebo 122 patients	**GSK1358820 122 patients**
Change from baseline in daily average number of urinary incontinence episodes at Week 12	1.25 lower	3.42 lower
Difference between GSK1358820 group and placebo group	2.16	

At Week 12, patients taking GSK1358820 had fewer urinary incontinence episodes than patients taking placebo.

More information about the study results is available in the scientific results summary (see the link at the end of this document).

What were the side effects?

Unwanted medical events (adverse events) can happen to people when they receive a medicine. Study doctors record these events. A summary of all these events can be found in the scientific results summary (see the link at the end of this document).

If the study doctor thinks that the event was caused by the study treatment (study medicine and/or the injections), they record this as a possible side effect (adverse reaction).

In this summary, “side effects” refer to those events that the study doctor thinks may have been caused by the study treatment. The side effects in this summary may be different to those in the Informed Consent or other documents related to the study treatment.

Two patients from the GSK1358820 group had serious side effects up to Week 12. Both patients had the serious side effects on Day 1. One patient had a study medicine-related serious side effect of difficulty in speaking and another patient had an injection-

related serious side effect of bladder bleeding. No patients from the placebo group had serious side effects up to Week 12.

The table below shows the non-serious side effects reported by at least three percent of the patients in any treatment group up to Week 12.

Non-serious side effects reported by at least three percent of patients in any treatment group up to Week 12		
	Placebo 124 patients	**GSK1358820 124 patients**
Study medicine-related non-serious side effect		
Painful urination*	3 (2%)	6 (5%)
Inability to empty the bladder completely	2 (2%)	6 (5%)
Increase in the amount of urine left in the bladder after urination	0	6 (5%)
Urinary tract infection	1 (less than 1%)	5 (4%)
Injection-related non-serious side effect		
Painful urination*	3 (2%)	5 (4%)
Blood in the urine	4 (3%)	3 (2%)

*Some patients had painful urination related to both the study medicine and injections.

How has this study helped patients and researchers?

This was a Phase III study. Phase III studies collect information about how well new medicines work and how safe they are. This study showed that GSK1358820 was better than placebo in reducing the number of urinary incontinence episodes. Compared to the placebo group, more patients in the GSK1358820 group reported side effects. Results from this study will help regulators make decisions about whether to approve GSK1358820 for the treatment of OAB in Japanese patients.

Are there plans for further studies?

No further studies are planned at this time.

Where can I find more information about this study?

Clinical studies have unique study numbers that are included in publications and other information about the study. The unique study number associated with this study is shown below with an internet link to the scientific summary and other information.

The scientific summary includes more details about the requirements for study enrolment, the study visit schedule, results from other endpoints and more detailed information about side effects.

Organisation	Website	Study Number
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02820844[1]

Your doctor can help you understand more about this study and the results. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

We would like to thank the patients who contributed to this study. The results of this study will help answer scientific questions about treating patients with OAB.

The content for this document was finalised by GSK on the of 3rd of July 2019. The information in this summary does not include additional information available after this date.

[1] https://clinicaltrials.gov/ct2/show/NCT02820844