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 the summary is provided at the end of this document.

Study names

Short Title: A study to assess how well botulinum toxin type A works and how safe it is in Japanese patients with urinary incontinence due to neurogenic detrusor overactivity.

Full Scientific Title: A phase III study to evaluate the efficacy and safety of GSK1358820 (botulinum toxin type A) in patients with urinary incontinence due to neurogenic detrusor overactivity.

Study Number: 204948

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 October 2016 and ended in December 2018. All study sites were in Japan.

What was the main reason for this study?

Neurogenic detrusor overactivity (NDO) is often observed in patients following a spinal cord injury or in patients with certain diseases of the nervous system in which the nerves controlling the detrusor muscle in the bladder wall are damaged. This can cause irregular contractions of these muscles and lead to leakage of urine (urinary incontinence).

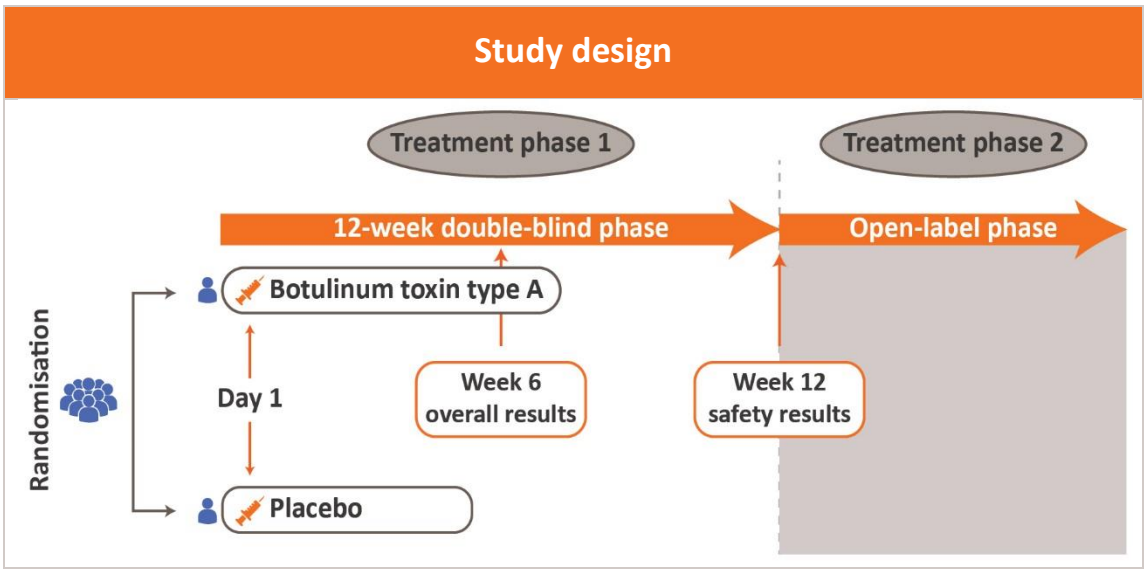
Botulinum toxin type A is a medicine that causes muscle relaxation. Injecting botulinum toxin type A in the bladder's detrusor muscle may relax them, thus reducing the contractions. This reduction in the contraction of the muscles may help reduce the number of episodes of urinary incontinence due to NDO.

This study was conducted in Japanese patients with urinary incontinence due to NDO, whose symptoms were not well controlled with their regular medicine(s). Study doctors wanted to see if addition of botulinum toxin type A to patients' regular medicine(s) reduced the number of urinary incontinence episodes. They also assessed the safety of botulinum toxin type A.

Which medicines were studied?

On Day 1, patients were placed in one of the two treatment groups by chance (randomisation), as shown in the figure below:

- Botulinum toxin type A (200 units)
- Placebo (no active study medicine)



This study took place in two parts (phases). On Day 1, patients received 30 millilitres (mL) of botulinum toxin type A or placebo in the form of 30 (1 mL) injections. The injections were given evenly across the detrusor muscle. Neither patients nor 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 botulinum toxin type A. All

patients knew that they received botulinum toxin type A. 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 (a link to the summary is 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.

Men and women with urinary incontinence due to NDO were included in the study if they:

- Were at least 20 years old.
- Had symptoms due to spinal cord injury or multiple sclerosis (a condition that affects brain and spinal cord), for at least three months before starting the study.
- Had symptoms that were not well controlled with their regular medicine(s).
- Had frequent urinary incontinence episodes before starting the treatment.
- Were using or agreed to have a thin, plastic tube inserted through the urethra (catheterisation) to empty the bladder of urine, if needed.

Men and women were excluded from the study if they had:

- Urinary incontinence caused by any other condition (e.g. bladder stones or bladder surgery).
- More than 200 mL of urine left in the bladder after urination (before starting the treatment).
- A urinary tract infection.
- Received botulinum toxin.
- Received medicines directly into the bladder through a catheter.

A total of 21 patients received the study medicine. The table below shows the gender and age of these patients.

Patients who received the study medicine		
	Placebo **10 patients**	**Botulinum toxin type A** **11 patients**
Gender – number of patients (percent)		
Female	1 (10%)	3 (27%)
Male	9 (90%)	8 (73%)
Age - in years		
Range	21 to 81	21 to 63
Average	47	51

For more detailed information about the patients included in this study, see the scientific results summary (a link to the summary is 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. Patients were asked to bring the diary to each 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 at Week 6. This is called the 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 6 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.

Results are shown in the table below.

Change from baseline in daily average number of urinary incontinence episodes at Week 6		
	Placebo 10 patients	**Botulinum toxin type A 11 patients**
Change from baseline in daily average number of urinary incontinence episodes at Week 6	0.18 lower	3.20 lower
Difference between botulinum toxin type A group and placebo group	3.02	

At Week 6, patients taking botulinum toxin type A had fewer urinary incontinence episodes than patients taking placebo.

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

If the study doctor thinks that the event was caused by the 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 medicine and/or the injections. The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicine.

In blinded studies, the doctor does not know which study medicine the patient is taking. In some cases, side effects will be assigned to placebo.

No serious side effects were reported by patients up to Week 12.

The table below shows the number of patients (percent) reporting non-serious side effects in any treatment group up to Week 12.

Number of patients (percent) reporting non-serious side effects up to Week 12		
	Placebo 10 patients	**Botulinum toxin type A 11 patients**
Study medicine-related non-serious side effect		
Inability to empty the bladder completely	0	1 (9%)
Injection-related non-serious side effect		
Abnormal high blood pressure caused by overactivity of the body's involuntary nervous system	0	1 (9%)
Blood in the urine	1 (10%)	1 (9%)

How has this study helped patients and researchers?

This was a Phase III study. Phase III studies collect information about how well a new medicine works and how safe it is. The study showed that the addition of botulinum toxin type A to Japanese patients' regular medicine(s) for NDO reduced the number of urinary incontinence episodes compared with placebo. Side effects were limited and

non-serious. Results from this study will help regulators make decisions about whether to approve botulinum toxin type A for the treatment of urinary incontinence due to NDO 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 adverse events.

Organisation	Website	Study Number
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02849418[1]

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. 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 urinary incontinence due to NDO.

The content for this document was finalised by GSK on the 14th of October 2019. The information in this summary does not include additional information available after this date.

[1] https://clinicaltrials.gov/ct2/show/study/NCT02849418