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 patients with post-stroke upper limb spasticity.

Full Scientific Title: A phase III study (a placebo-controlled, randomised, double-blind comparative study and an open-label uncontrolled study) to evaluate the efficacy and safety of GSK1358820 (botulinum toxin type A) in patients with post-stroke upper limb spasticity.

Study Number: 207660

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 2017 and ended in January 2019. All study sites were in Japan.

What was the main reason for this study?

A stroke occurs when the blood (and oxygen) supply to the brain is blocked or reduced. Patients who have had a stroke can experience muscle weakness and/or loss of muscle function, including spasticity. Symptoms of spasticity include: stiffness or tightness in the muscles and/or occasional uncontrolled twitching or movement (spasm).

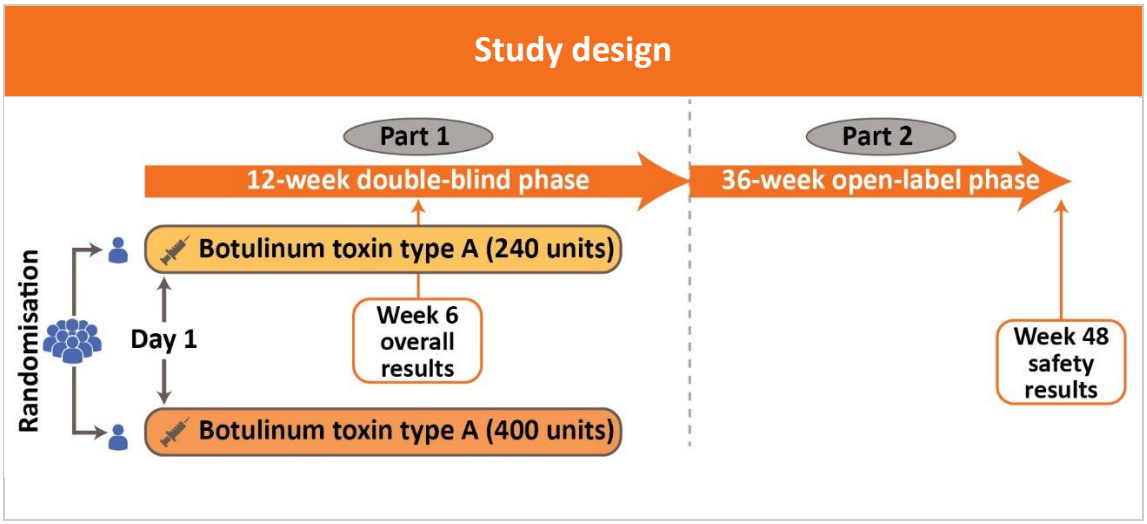
Botulinum toxin type A is a medicine that causes muscle relaxation. Injecting botulinum toxin type A in muscles relaxes them and reduces spasticity.

This study was conducted in Japanese patients with post-stroke upper limb spasticity. In Japan, botulinum toxin type A (240 units) is the approved dose for the treatment of upper limb spasticity. However, a higher dose of botulinum toxin type A may be required in severe cases.

In this study, study doctors wanted to see if a higher dose of botulinum toxin type A (400 units) improved upper limb spasticity compared with the approved dose of botulinum toxin type A (240 units) six weeks after treatment.

Which medicines were studied?

This study took place in two parts. On Day 1, patients received injections of botulinum toxin type A (either 240 units or 400 units) by chance (randomisation), as shown in the figure below.



Botulinum toxin type A (240 units): 240 units were injected into the muscles of the fingers, thumb, and wrist, and placebo (no active medicine) was injected into the muscles of elbow.

Botulinum toxin type A (400 units): 240 units were injected into the muscles of the fingers, thumb, and wrist, and 160 units were injected into the muscles of elbow.

During the first 12 weeks, neither the patients nor the study doctors knew who received which treatment. This is called a double-blind phase.

After 12 weeks, the study doctor decided if a patient could be given up to three more re-treatments with botulinum toxin type A (400 units). All the patients knew that they received botulinum toxin type A (400 units). This is called the open-label phase.

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 upper limb spasticity were included in the study if they:

- Were between 20 and 80 years old.
- Had a stroke at least three months before starting the study.
- Were treated with botulinum toxin type A (240 units) for upper limb spasticity at least 16 weeks before starting the study.
- Had severe symptoms which may benefit from treatment with the higher dose of botulinum toxin type A (400 units).
- Had symptoms of spasticity in the muscles of finger, thumb, wrist, and elbow.
- Had no lung-related problems at the start of the study.

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

- Upper limb spasticity caused by an injury or disease other than stroke.
- Been treated for spasticity in the non-paralysed upper limb.
- Permanent shortening and hardening of any finger, wrist, elbow, or, shoulder muscle.
- Severe swelling and/or pain or slight dislocation in the joints of any finger, wrist, elbow, or, shoulder.
- Any conditions or taken any medicines that could affect the results of the study.

A total of 124 patients received at least one dose of the study medicine. The table below shows the gender and age of these patients.

Patients who received at least one dose of the study medicine		
	Botulinum toxin type A (240 units) 63 patients	**Botulinum toxin type A (400 units) 61 patients**
Gender		
Female	10 (16%)	15 (25%)
Male	53 (84%)	46 (75%)
Age - in years		
Range	21 to 79	29 to 73
Average	57	57

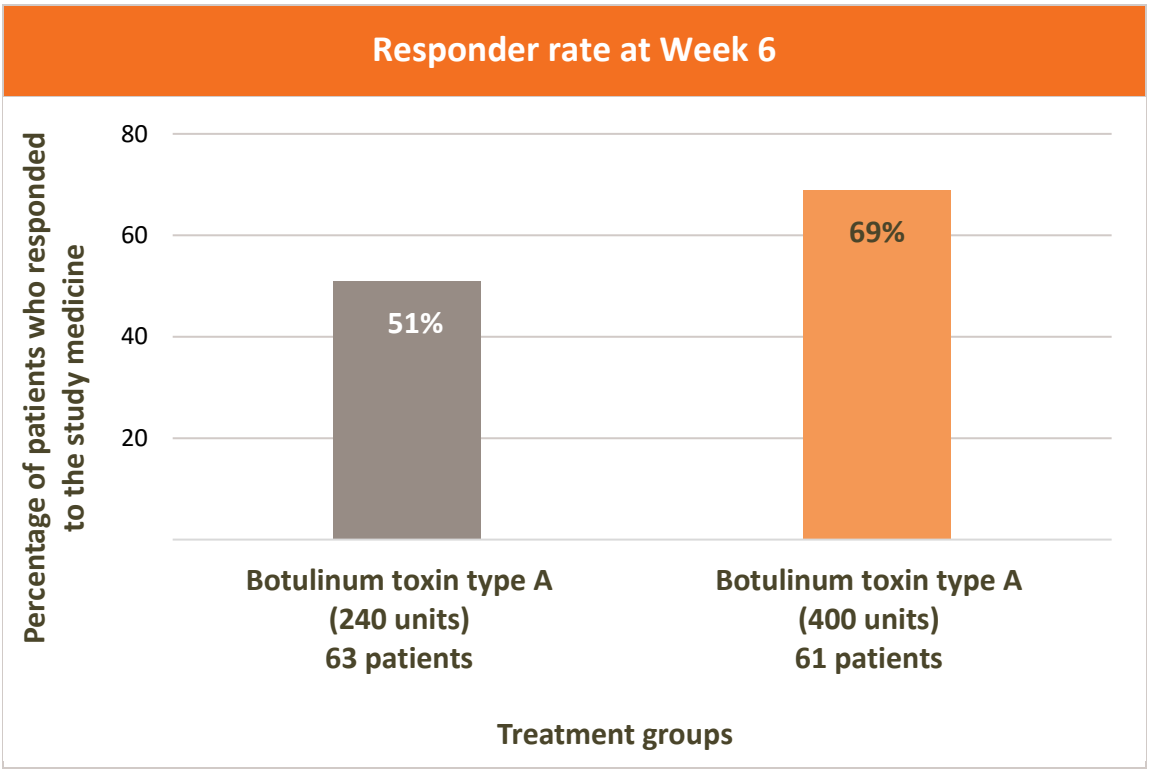
For more detailed information about the patients included in this study, see the scientific results summary (a link to the summary is provided at the end of this document).

What were the overall results of the study?

The main objective of this study focused on the movement of elbow muscles. Study doctors used the Modified Ashworth Scale (MAS) to measure the difficulty (resistance) seen while bending a patient's elbow. This scale ranges from zero to four, where a lower score means there is less resistance while bending the elbow.

Study doctors scored the elbow movements at the start of the study (baseline) and at Weeks 2, 4, and 6. A reduced MAS score indicates an improvement in elbow muscle movement. Patients were considered to have responded to the study medicine if their Week 6 MAS score decreased by at least one point from baseline.

At Week 6, the percentage of patients who responded to the study medicine (responder rate) was calculated. Results are shown in the figure below.



The responder rate at Week 6 was 18% higher in the botulinum toxin type A (400 units) group compared with the botulinum toxin type A (240 units) group. This means patients who received 400 units of botulinum toxin type A showed more improvement in the movement of elbow muscles compared with patients receiving 240 units of botulinum toxin type A.

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 (see the link at the end of this document).

If the study doctor thinks that the event was caused by the study medicine, 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. The side effects in this summary may be

different to those in the Informed Consent or other documents related to the study medicine.

No serious side effects were reported by any patients in any treatment group in this study.

During the first 12 weeks, no patients from the botulinum toxin type A (240 units) group and one patient from the botulinum toxin type A (400 units) group reported a non-serious side effect of muscle weakness. After Week 12, one patient originally randomised to the botulinum toxin type A (240 units) reported a non-serious side effect of swelling where the injection(s) was given and no patients from the botulinum toxin type A (400 units) reported a non-serious side effect.

For the details on all the side effects reported in this study, see the scientific results summary (a link to the summary is provided at the end of this document).

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 giving botulinum toxin type A (400 units) was more effective in treating patients with post-stroke upper limb spasticity. The side effects reported in this study were similar between the treatment groups. The results from this study will help government regulators make decisions about the approval of botulinum toxin type A (400 units) in Japan.

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	NCT03261167[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 post-stroke upper limb spasticity.

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/NCT03261167?term=207660&rank=1