Summary of Clinical Study Results for General Audience
Plain Language Summary

1. STUDY NAME

Simple study name: Phase 3 study of SDT-001 in pediatric patients with attention-deficit/hyperactivity disorder

Official study name: Phase 3 study of SDT-001 in pediatric patients with attention-deficit/hyperactivity disorder consisting of randomized, open-label, treatment as usual-control, comparison part and open-label, repetition part

2. WHO SPONSORED THIS STUDY?

This study was sponsored by Shionogi & Co., Ltd.

3. GENERAL INFORMATION ABOUT THIS STUDY

Attention-deficit/hyperactivity disorder (ADHD) is a disease with symptoms such as not being able to pay attention, being restless, and acting impulsively. The cause of this disease is not clear, but one likely cause is problematic functioning of the brain cortex, which controls what you pay attention to and how you behave (executive function).

Symptoms of ADHD generally appear between the ages of around 3 and 6 years, and they become noticed when a child starts interacting with others in a group outside of the family. In fact, ADHD is often diagnosed at ages between around 6 and 12 years, but sometimes it is diagnosed earlier. ADHD often appears in children, but it can occur in adolescents or adults. Sometimes, treatment or adjusting their lifestyle can make symptoms less noticeable, but some patients keep having symptoms even when they are adults. According to research, the prevalence of ADHD in Japan is about 3% to 5% in children and about 2% to 2.5% in adults.

ADHD symptoms can be divided into 2 categories, “attention deficit” and “hyperactivity/impulsivity.” Patients with ADHD are likely to have more difficulty in daily life than other children of the same age range and same sex because of one or both of these symptoms.

The current way of treating ADHD is, firstly, to make environmental adjustment*, and then to give psychosocial treatment* according to the patient’s symptoms and situation, and if these do not have enough effect, drug therapy (Vyvanse, Concerta, Strattera, Intuniv) is used. Psychosocial treatment sometimes takes time to work or may not have enough effect. Drug therapy often starts working after several weeks at the latest, but some patients may have difficulty continuing drug therapy because of side effects.

* Environmental adjustment involves people who relate with the patient, like the patient's guardians and teachers, helps the patient understand the characteristics of the disease and adjust the environment so that it is easy for the patient to do what they need to do to manage the situation around them. An example of psychosocial treatment is social skill training, where the patient learns social manners and rules to maintain good personal relationships, so that the patient can behave appropriately depending on the situation.

SDT-001, which is the medical device used in this study, is a piece of software (an app), and using SDT-001 is expected to improve the function of the brain cortex and improve symptoms relating to attention deficit in pediatric ADHD patients.

A Japanese exploratory study* in pediatric ADHD patients has already been completed. In the study, patients used SDT-001 for 6 weeks, and the strength of their ADHD symptoms after they finished using it were measured. To assess ADHD symptoms, a scale called the ADHD-RS-IV** was used. The results showed an improvement in the ADHD-RS-IV inattentive subscale scores compared to before use. The hyperactivity/impulsivity subscale scores also tended to improve, but not as much as the inattentive subscale scores.

* This is a study to find out whether SDT-001 is effective and safe, and determine how to use SDT-001.

** This is a scale that asks questions to patients or guardians about how the patient is at home or school, and the study doctor assesses the patient's condition on a 4-point scale (0 to 3 points). Three scores were calculated: scores for "inattention" and for "hyperactivity/impulsivity" and the total score. The scores for "inattention" and for "hyperactivity/impulsivity" are each in the range of 0 to 27 points, and the total score is in the range of 0 to 54 points. Higher scores indicate stronger ADHD symptoms.

Following the exploratory study, another study, in which pediatric ADHD patients use SDT-001 to further assess the efficacy and safety, was conducted. This study is called a confirmatory study.

Figure 1 shows a simplified study schedule. This study is made up of 2 parts, a comparison part and a repetition part. In the comparison part, patients were divided into two groups: a group (the SDT-001 group) that uses SDT-001 with the treatment as usual (ie, the treatment such as environmental adjustment and psychosocial treatment) and a group (the treatment as usual group) that continues the treatment as usual (ie, the treatment such as environmental adjustment and psychosocial treatment) without using SDT-001. The efficacy and safety of using SDT-001 for 6 weeks were compared with just continuing treatment as usual.

The repetition part was conducted as follows. Patients in the SDT-001 group started using second cycle of SDT-001 in the repetition part after the comparison part in which they used SDT-001 for 6 weeks and received follow-up for 4 weeks. Patients in the treatment as usual group started using SDT-001 in the repetition part just after the comparison part in which they received treatment as usual for 6 weeks. In other words, in the treatment period of the repetition part, all patients in both groups used SDT-001. In the repetition part, the efficacy and safety were investigated after additional 1 cycle

(1 period of 6 weeks) in patients who were in the SDT-001 group in the comparison part (2 cycles in total through the study) and after 1 cycle (1 period of 6 weeks) in patients who were in the treatment as usual group in the comparison part (1 cycle through the study).

Figure 1 Simplified Study Schedule

SDT-001 group

Comparison part		Repetition part		
Treatment period (6 weeks)	Follow-up period (4 weeks)	Treatment period (6 weeks)	Follow-up period (12 weeks)	Questionnaire (up to 24 weeks)
<SDT-001 used>	<SDT-001 not used>	<SDT-001 used>	<SDT-001 not used>	<SDT-001 not used>
<----------Treatment such as environmental adjustment and psychosocial treatment---------->				

Treatment as usual group

Comparison part	Repetition part		
Treatment period (6 weeks)	Treatment period (6 weeks)	Follow-up period (12 weeks)	Questionnaire (up to 24 weeks)
<SDT-001 not used>	<SDT-001 used>	<SDT-001 not used>	<SDT-001 not used>
<---------Treatment such as environmental adjustment and psychosocial treatment--------->			

The efficacy of SDT-001 was assessed mainly using the change in ADHD-RS-IV inattentive subscale score in the comparison part from before the start of the study to after SDT-001 was used for 6 weeks. In the comparison part, the changes in the ADHD-RS-IV hyperactivity/impulsivity subscale score and the total score were also assessed. In the repetition part, the changes in each ADHD-RS-IV score from the start of the comparison part and repeated part were assessed after SDT-001 was used for additional 1 cycle (ie, 2 cycles in total through the study, 2 periods of 6 weeks) or 1 cycle (ie, 1 cycle in total through the study, 1 period of 6 weeks).

This study was done in Japan. It started in May 2022 and ended in December 2023.

4. WHAT PATIENTS WERE INCLUDED IN THIS STUDY?

Pediatric ADHD patients took part in this study. This was an “open-label” study. This means that all participants and study doctors knew whether or not participants were using SDT-001.

In the comparison part, 164 pediatric ADHD patients participated. Of these, the efficacy was assessed in 163 patients; 109 patients were in the SDT-001 group and 54 patients were in the treatment as usual group. Seven patients (SDT-001 group, 5 patients; treatment as usual group, 2 patients) had stopped their participation to the study during the comparison part. The primary reason for stopping participation to the study was the request of the patient.

Of the patients who completed the comparison part, 126 patients took part in the repetition part. Of these, 75 patients were in the SDT-001 group in the comparison part (SDT-001/SDT-001 group) and 51 patients were in the treatment as usual group in the

comparison part (treatment as usual/SDT-001 group). Nine patients (SDT-001/SDT-001 group, 7 patients; treatment as usual/SDT-001 group, 2 patients) had stopped their participation to the study during the repetition part. The primary reason for stopping participation to the study was the request of the patient.

5. WHICH MEDICAL DEVICES WERE STUDIED?

The medical device used in this study was SDT-001. SDT-001 is a piece of software (an app), and a version installed on a tablet computer (iPad mini) was used. SDT-001 was used once (for about 25 minutes) per day for 6 weeks per 1 cycle.

6. WHAT WERE THE OVERALL RESULTS OF THIS STUDY?

Main results in this study are shown as follows.

The results of ADHD-RS-IV assessment in the comparison part are shown in Table 1. The changes in ADHD-RS-IV inattentive subscale score from before the start of the study to after 6 weeks of use were −4.44 points in the SDT-001 group and −1.47 points in the treatment as usual group, and there was a large improvement in the SDT-001 group compared to the treatment as usual group (p<0.0001). For the total ADHD-RS-IV score and hyperactivity/impulsivity subscale score, there was a large improvement in the SDT-001 group compared to the treatment as usual group (total score, p<0.0001; hyperactivity/impulsivity subscale score, p=0.0056).

Table 1 Results of ADHD-RS-IV Assessment in the Comparison Part

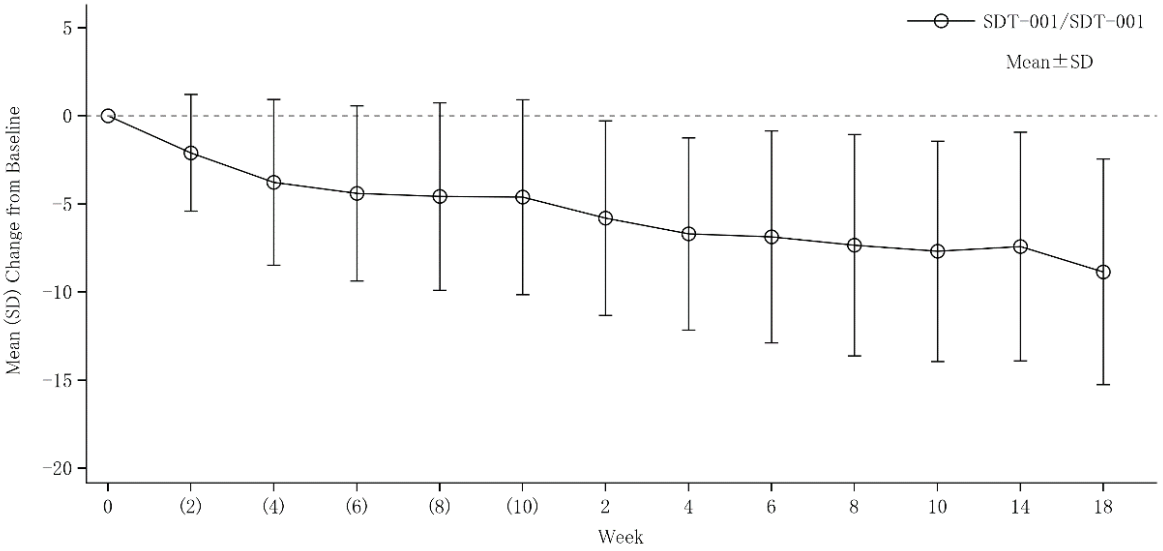
	SDT-001 group			Treatment as usual group		
ADHD-RS-IV score	Inattentive subscale	Hyperactivity/ impulsivity subscale	Total	Inattentive subscale	Hyperactivity/ impulsivity subscale	Total
Change from before the start of the study to after 6 weeks of use*	−4.44 points	−2.57 points	−7.02 points	−1.47 points	−1.02 points	−2.46 points
Difference from the treatment as usual group	−2.97 points	−1.55 points	−4.56 points	---	---	---
p value	<0.0001	0.0056	<0.0001			

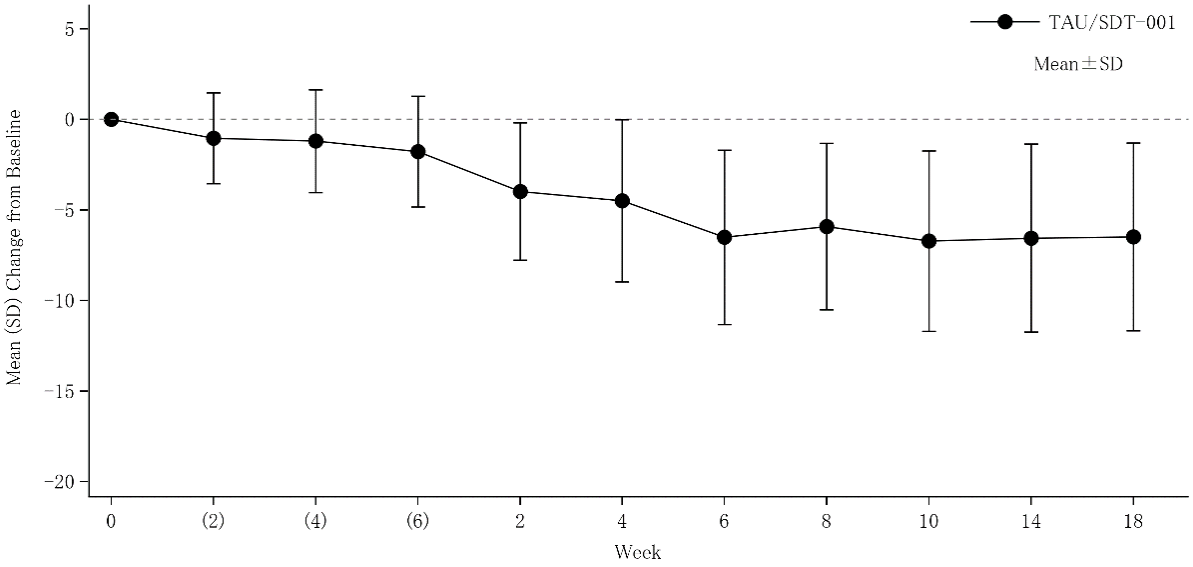
* Larger negative numbers show a larger improvement in symptoms.

The results of ADHD-RS-IV inattentive subscale score assessment in the repetition part are shown in Figure 2. A consistent decreasing trend in the ADHD-RS-IV inattentive subscale score was observed throughout the treatment period both in patients who use SDT-001 for 1 cycle after proceeding to the repetition part (treatment

as usual/SDT-001 group) and who use SDT-001 for 2 cycles in total through the study (SDT-001/SDT-001 group). The same trend was found in the ADHD-RS-IV total and hyperactivity/impulsivity subscale scores. In patients who use SDT-001 for 1 cycle in the repetition period (treatment as usual/SDT-001 group), each ADHD-RS-IV score improved by about the same amount as in the patients who used SDT-001 in the comparison part (the SDT-001 group). In the patients who used SDT-001 for a total of 2 cycles in the comparison part and the repetition part (the SDT-001/SDT-001 group), ADHD-RS-IV scores inattentive subscale score showed a tendfency to decreace over time from the start of the comparison part to the end of the repetition part, and showed improved further after 2 cycles compared to after 1 cycle (Figure 2). The same trend was found in the ADHD-RS-IV total and hyperactivity/impulsivity subscale scores.

Figure 2 **Change in ADHD-RS-IV Inattentive Subscale Score Assessment by the End of the Repetition Part (Horizontal Axis: Number With Bracket, Week in Comparison Part; Number Without Bracket, Week in Repetition Part)**





SD = standard deviation; TAU = treatment as usual

Investigation of how long the effect lasted after the end of each cycle showed that the effect after use in cycle 1 and after use in cycle 2 lasted for at least 12 weeks.

7. WHAT WERE THE SIDE EFFECTS AND MEDICAL DEVICE DEFICIENCY?

A lot of research of study information, especially that on side effects, is needed to know whether a medical device causes medical problems. Also, information on medical device deficiency is collected and assessed in a study with a medical device.

- A “side effect” (undesirable effect) is a medical problem that happens in a patient in a clinical study for which a causal relationship with the medical device used in the study cannot be ruled out.
- A “serious side effect” means a device-related adverse event possibly caused by a medical device that is considered “serious” when it results in death, is life-threatening, causes lasting problems, needs hospital care, causes birth problems or is other important state.
- A “medical device deficiency” is an undesirable event that occurs in a medical device.

No patients died or experienced serious side effect during the study. One patient in the comparison part (109 patients [0.9%] in the SDT-001 group) stopped using SDT-001 due to a side effect (frustration tolerance decreased*).

* This is a state of reduced tolerance to frustration, when someone becomes unable or less able to endure situations in daily life.

Medical device deficiencies (such as malfunction after login) were reported; 6 cases in 6 patients out of 109 patients (5.5%) in the SDT-001 group in the comparison part and 9 cases in 9 patients out of 126 patients (7.1%) in the repetition part. It was judged that none of these led to serious adverse events.

Table 2 shows the side effects experienced by patients while taking part in this study.

Throughout the study, there were no major safety problems with SDT-001.

Table 2 Side Effects Experienced by Patients While Taking Part in the Study

Side effects	Number of patients with side effects	
Comparison part	SDT-001 (out of 109)	Treatment as usual (out of 55)
Frustration tolerance decreased	1 patient (0.9%)	0 patients (0%)
Headache	1 patient (0.9%)	0 patients (0%)
Nausea	1 patient (0.9%)	0 patients (0%)
Repetition part	SDT-001/SDT-001 (out of 75)	Treatment as usual/SDT-001 (out of 51)
Vomiting	0 patients (0%)	1 patient (2.0%)

8. HOW HAS THIS STUDY HELPED OR WILL HELP PATIENTS AND RESEARCHERS?

The information from this research helps future patients and families by helping researchers understand more about each medical device being studied. The study results are limited to the study patients and cannot be assumed to be true for everybody. This document reports the results of this study only. New information on or different results about the medical device may become or have become available from other studies.

9. ARE THERE PLANS FOR FURTHER STUDIES?

At present, no other studies of SDT-001 in patients with ADHD are ongoing or planned.

10. WHERE CAN I FIND MORE INFORMATION ABOUT THIS STUDY?

You may find more information about this study at the following website:

Website	URL	Identifier
jRCT	Japanese: https://jrct.mhlw.go.jp/latest-detail/jRCT2042220012	number of clinical trial plan: jRCT2042220012

Contact information for the company that conducted this study:

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