Patient Preference and Adherence

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ORIGINAL RESEARCH

Usability and Preference Evaluation of the Somapacitan Pen-Injector and Lonapegsomatropin Autoinjector: Results of a US-Based Simulated-Use Study with Adolescent Patients and Caregivers

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Purpose: To compare the preference and ease of use/learning how to use, of the somapacitan (Sogroya®) pen-injector and the lonapegsomatropin (Skytrofa®) autoinjector among adolescents with growth-related disorders (GRDs) and caregivers of individuals with GRDs.

Patients and Methods: This was a randomized, open-label, multicenter, usability-based preference and handling study with a crossover design. Participants recruited were adolescents aged 10–17 years with a GRD, able to self-administer growth hormone (GH) or perform some of substeps required; and caregivers aged ≥18 years and regular care providers for individuals with GRDs. Participants completed a series of simulated injections using both devices and completed a Device Handling and Preference Assessment Questionnaire (DHPAQ). Training time and time to prepare and inject with each device were also evaluated.

Results: Seventy participants were recruited overall; 35 in each of the adolescent and caregiver groups. Most (78.6%) participants preferred the somapacitan device to the lonapegsomatropin device (95% confidence interval [CI] 67.1–87.5). The lonapegsomatropin device was preferred by 14.3% of participants, and 7.1% indicated no preference. Most participants indicated that somapacitan device was easy to use (97.1% [95% CI 90.1–99.7]) and learn how to use (95.7% [95% CI 88.0–99.1]). The same was reported for the lonapegsomatropin device by 57.1% (95% CI 44.8–68.9) and 54.3% (95% CI 41.9–66.3%) of participants, respectively. Average time taken to complete training for the somapacitan device and to prepare and inject was shorter than that for the lonapegsomatropin device (5.9 min vs 24.0 min, and 0.9 vs 10.6 min, respectively).

Conclusion: The somapacitan device was preferred over the lonapegsomatropin device among adolescents with GRDs and caregivers of individuals with GRDs. Individuals receiving GH treatment via the somapacitan device may be more likely to have higher treatment adherence than those using the lonapegsomatropin device.

Plain language summary: Growth hormone (GH) is produced within the body to encourage growth. Children and adolescents with growth-related disorders can receive injections of GH under the skin to improve their chances of reaching an adult height in the expected range. However, administering injections of GH can be a burden and could be difficult for patients and caregivers to maintain.

In this study, we wanted to understand preferences for two different types of GH injection devices: the somapacitan pen-injector and the lonapegsomatropin autoinjector. We asked 35 adolescents (aged 10–17 years) with growth-related disorders and 35 adult caregivers of individuals with growth-related disorders about their preferences between these two devices. After participants were trained and had practiced mock injections with each device, they completed a questionnaire about their experiences.

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Most participants (79%) preferred the somapacitan pen-injector, while 14% preferred the lonapegsomatropin autoinjector. Most participants thought the somapacitan pen-injector was easy to use (97%) and easy to learn how to use (96%). Just over half of the participants thought the lonapegsomatropin autoinjector was easy to use (57%) and easy to learn how to use (54%). Overall, participants learnt how to use the somapacitan pen-injector (6 minutes on average) more quickly than the lonapegsomatropin autoinjector (24 minutes on average).

In our study, participants preferred using the somapacitan pen-injector over the lonapegsomatropin autoinjector. Therefore, using the somapacitan pen-injector could increase regular use of GH treatment, which may help individuals reach their target adult height.

Keywords: adherence to growth hormone, device preference, growth hormone injection device, long-acting growth hormone

Introduction

Growth hormone (GH) is administered for the treatment of a number of growth disorders.[1–4] The aim of administering GH to children and adolescents is to enable them to attain adult height within their genetic potential range.[2–5] However, improvements in height outcomes with GH treatment are directly linked to treatment adherence, which is not always optimal.[6–9]

In an evidence-based systematic review, adherence to GH treatment was assessed in pediatric patients receiving GH for various growth disorders.[1] The review assessed 13 studies designed to investigate adherence using varying methods. Estimates of non-adherence ranged from 5% to 82%, depending on the methods and definitions used. Similar results were found in a real-world study designed to investigate adherence to daily GH in a US-based pediatric population with GH deficiency (GHD).[10] According to a medication possession ratio calculated based on 3,091 patients, non-adherence occurred in 35.9% of patients after 4 years of treatment. The authors of the study concluded that the use of long-acting growth hormones (LAGH) may improve adherence by easing the burden incurred by a daily injection regimen.

Other modifiable factors that influence adherence have also been investigated. In a study that was designed to investigate adherence to GH in 75 deficient children, lack of choice of delivery device was found to be a factor associated with non-adherence ($p<0.005$).[11] In an exploratory analysis employing semi-structured phone interviews with parents or caregivers of 14 children with GHD, device burden was found to be a modifiable factor that can improve adherence.[9] A systematic literature review, conducted to investigate factors associated with adherence, identified device design as a potential barrier to optimal adherence.[12] Furthermore, general guidelines stress the importance of taking into account a patient's preference when deciding on their treatment, which includes their device preference.[1]

Somapacitan (Sogroya®, Novo Nordisk A/S, Bagsvaerd, Denmark) is a LAGH approved for the treatment of GHD in children, adolescents, and adults in a number of countries including the US and the European Union (EU).[13–18] Lonapegsomatropin (Skytrofa®, Ascendis Pharma, Hellerup, Denmark) is a LAGH approved for the treatment of GHD in children and adolescents in the US and the European Union (EU).[19,20]

This US-based study was designed to compare the somapacitan pen-injector and the lonapegsomatropin autoinjector in terms of preference and ease of use/learning how to use for adolescents with growth-related disorders and caregivers of individuals with growth-related disorders. A Device Handling and Preference Assessment Questionnaire (DHPAQ) was used in this study. The DHPAQ was previously deemed to be comprehensive, relevant, and fully comprehendible, and validated for use by adolescents with growth-related disorders and caregivers of individuals with growth-related disorders.[21,22]

Materials and Methods

Study Design

This was a randomized, open-label, multicenter, usability-based preference and handling study. Device preference and ease of use/learning how to use with the somapacitan pen-injector and the lonapegsomatropin autoinjector were compared (Figure 1). A crossover design was used to avoid inter-subject variability between groups. Data were collected between May 2 and June 22, 2024. The study took place in ten locations in the US: Tempe, AZ; Irvine, CA; Los Angeles, CA; Orlando, FL; Fort Lauderdale, FL; Chicago, IL; Houston, TX; Dallas, TX; Saddle Brooke, NJ; and New York, NY.

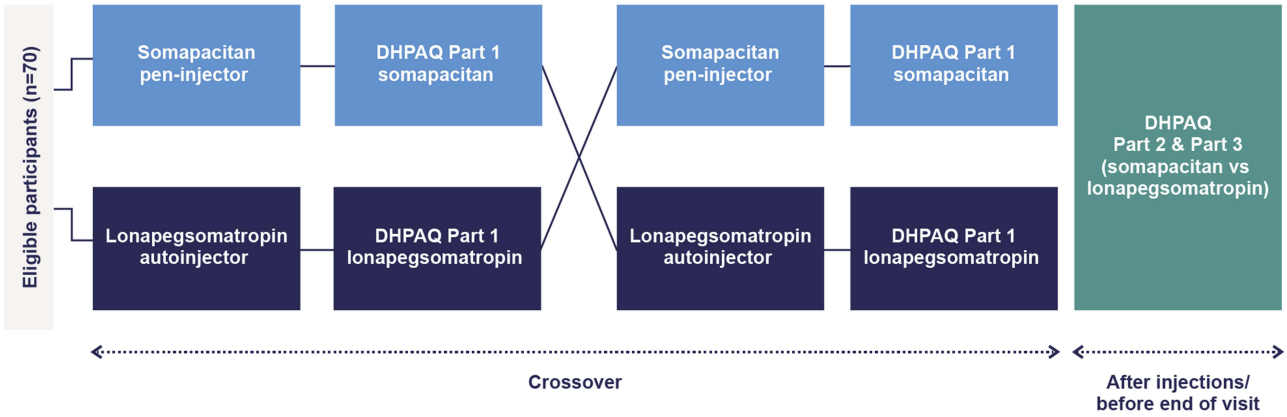

Figure 1 Study design.
Notes: Participants received training prior to the simulated injection for each device. Part 1 of the DHPAQ comprised questions related to ease of use of each device as a single item. Part 2 and Part 3 of the DHPAQ comprised comparative questions related to ease of use/preference of the devices.
Abbreviation: DHPAQ, Device Handling and Preference Assessment Questionnaire.

The facilities involved included a Research Collective usability lab, market research services, and private meeting spaces. Images of the study environments are presented in Supplementary Figure S1.

The test plan for this Human Factors Comparative Preference and Handling study was reviewed and approved by Castle Institutional Review Board (Castle IRB), located in Chesterfield, MO, USA. All participants provided informed written consent prior to the commencement of the study to take part in the study and to allow any data collected to be processed. Adolescent participants were accompanied by a parent or legal guardian who provided the consent on their behalf. This study was conducted in accordance with the Declaration of Helsinki (2013).[23]

Inclusion and Exclusion Criteria

Eligible participants comprised two groups: adolescents and caregivers. Adolescents were aged 10–17 years, with short stature due to GHD or other causes prompting receipt of GH, and were able to self-administer GH injections or perform some of the substeps required. Caregivers were aged ≥18 years and were regular care providers for individuals with short stature due to GHD or other causes prompting receipt of GH. Eligible causes of short stature for both groups (participants in the adolescents group, and individuals supported by participants in the caregiver groups) encompassed GHD, Turner syndrome, Noonan syndrome, idiopathic short stature, and small for gestational age.

Participants were excluded if, at the time of their enrollment into this study, they were using either of the two devices being investigated (somapacitan or lonapegsomatropin), or if they were currently receiving any medications administered using PDS290 pen-injectors (eg, somatropin [Norditropin® FlexPro®], Novo Nordisk A/S, Bagsvaerd, Denmark). Prior use of the devices investigated in this study, or similar ones (PDS290 pen-injectors), was permitted. Participants in the caregiver group were excluded if they were clinicians.

Objectives and Endpoints

The primary objective of this study was to demonstrate patient preference for the somapacitan pen-injector versus the lonapegsomatropin autoinjector in adolescents with growth-related disorders and caregivers of individuals with growth-related disorders. The secondary objective was to evaluate ease of use and ease of learning how to use of the somapacitan pen-injector compared with the lonapegsomatropin autoinjector.

The DHPAQ was used to evaluate the primary objective. The secondary objective was evaluated using patient-reported outcomes from the DHPAQ, training time with each device, and time to prepare and inject with each device.

The DHPAQ had been validated for use in a study with a similar design.[21] There were two types of questions in the DHPAQ: preference questions that compared the two devices, and rating questions that measured the ease of use/learning how to use of each device.

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Devices

The devices used in this study were the somapacitan 15 mg/1.5 mL (at a dose of 4.8 mg) pen-injector (Figure 2A) and the lonapegsomatropin 7.6 mg autoinjector (Figure 2B). The somapacitan pen-injector is prefilled, available in multiple doses (5 mg/1.5 mL, 10 mg/1.5 mL, and 15 mg/1.5 mL), and can be disposed of after final use. The lonapegsomatropin electronic autoinjector includes a powder and a solvent within a dual-chamber cartridge available in multiple doses (3.0–13.3 mg of powder plus the solvent), and requires reconstitution prior to immediate use.

Visit Procedures

Participants were randomized in a crossover fashion to receive training in the use of a single device followed by the other device, with the training administered by a registered nurse using the instructions for use of each device. The registered nurse commenced the training session by introducing themselves to the participant and providing an overview of the device, before showing the participant how to perform a complete simulated injection using an injection pad. Participants performed practice injections using an injection pad until they had successfully completed an injection with each one of the devices according to the randomization order. Throughout the training sessions, participants had opportunities to ask the registered nurse any questions.

Participants were then asked to perform one complete simulated injection for the device on which they had been trained. For a successful complete injection with the somapacitan pen-injector, the steps that had to be completed were to attach the needle, remove the outer and inner needle caps, set the dose, and inject the dose. For an injection to be considered complete with the lonapegsomatropin autoinjector, the steps were to attach the needle to the cartridge; turn on the autoinjector; set up the cartridge in the autoinjector; run the automatic mixing step; perform the manual mixing step; remove the needle cover; and inject the medication.

For any unsuccessful or incomplete simulated injection attempts, the participant was informed in a debrief interview of the steps that were not completed or that were completed incorrectly. Following the debrief interview, participants commenced training with the other device. If no debrief interview was required, participants commenced training with the other device following the successful simulated injection of the first device on which they had been trained.

The order of training and simulated injections of each device was randomized between participants (eg, participant 1 was initially trained on the somapacitan pen-injector, followed by the lonapegsomatropin autoinjector, and participant 2

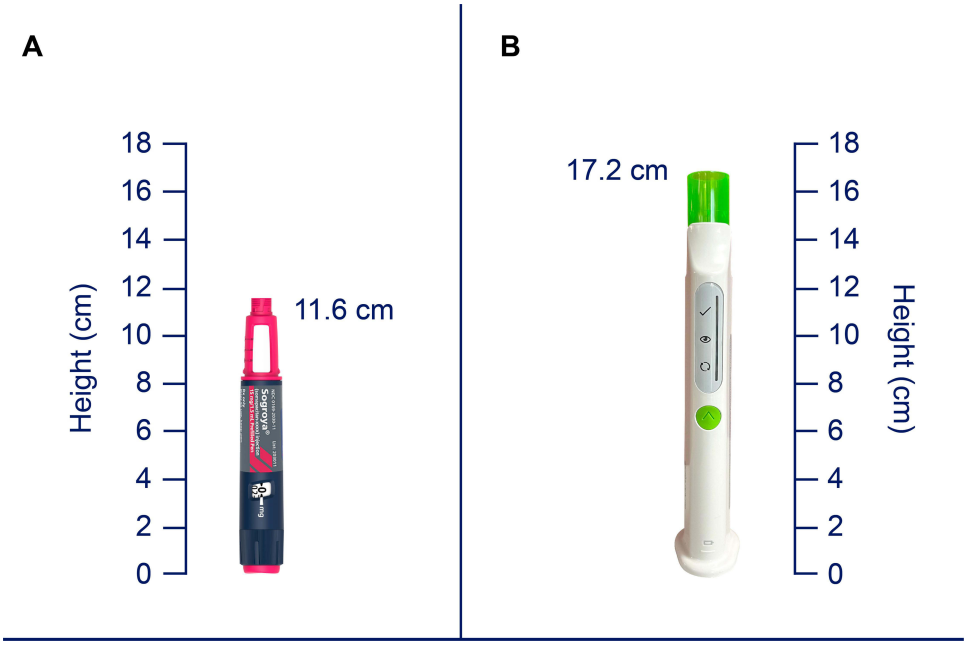

Figure 2 Photographs of the devices used in this study: (**A**) somapacitan pen-injector and (**B**) lonapegsomatropin autoinjector.

was initially trained on the lonapegsomatropin autoinjector, followed by the somapacitan pen-injector). The time needed to train was calculated for each session either in real time or upon video review.

DHPAQ Questionnaire

The DHPAQ questionnaire was developed based on the Haemophilia Device Handling and Preference Assessment Questionnaire and has been validated for use in adolescents with growth-related disorders and caregivers of individuals with growth-related disorders.[21,24] The questionnaire comprises preference questions that compare devices and rating questions to measure ease of use and training. After participants received training for the first device, performed the simulated injection, and completed the debrief interview, they were asked to complete part 1 of the DHPAQ for the relevant device. They then received training with the other device, performed the simulated injection, and completed the debrief interview. After this, they completed the first part of the DHPAQ for the other device. After completing both simulated injections and the first part of the DHPAQ for both devices, the participants were shown both devices and completed the comparison and preference sections of the questionnaire.

Statistical Analyses

The total sample size was determined by simulation based on Prescott's test with a 5% level of significance. Prescott's test takes into account the choice of "no preference" between the two devices, as well as the order of device use. If 10% of the participants reported "no preference", 63% reported preference for the somapacitan device, and 27% reported a preference for the lonapegsomatropin device, then 70 participants would be needed to detect a true preference with ≥90% power. Preference data were analyzed using Prescott's test of equality. When more than one answer category was favorable for a device, these categories were pooled to allow calculation of the test.

Demographic data and clinical characteristics were managed in Microsoft Excel to generate tables of basic descriptive statistics (count, percent, mean and median). Endpoints were summarized using descriptive statistics. Statistical analyses (Prescott's test) were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Sensitivity Analysis

A sensitivity analysis only including participants who never used either of the injection devices being tested in this study (including PDS290 family devices) prior to enrollment was conducted. The device preferences of this subgroup are reported.

Results

Participant Demographics and Clinical Characteristics

There were 70 participants recruited overall and included in the main analyses: 35 participants in the adolescents group and 35 in the caregivers group. Participant demographics and clinical characteristics are presented in Table 1. A total of 42 participants (20 in the adolescents group and 22 in the caregivers group) were included in the sensitivity analyses.

Five participants in the adolescents group reported the use of glasses or contact lenses. In the caregivers group, 28 participants reported the use of glasses or contact lenses, one participant reported deafness in one ear, one participant reported minor hearing loss, and one participant indicated good hearing 'sometimes'. All other participants in both groups reported good eyesight, hearing, and dexterity.

Following the crossover design used in this study, 17 participants in the adolescents group used the somapacitan device first followed by the lonapegsomatropin device. In the same group, 18 participants used the lonapegsomatropin device first followed by the somapacitan device. In the caregivers group, 18 participants used the somapacitan device first followed by the lonapegsomatropin device and 17 participants used the lonapegsomatropin device first followed by the somapacitan device.

Device Preference

Overall device preference for the somapacitan device versus the lonapegsomatropin device was 78.6% (95% confidence interval [CI] 67.1–87.5), taking into consideration all elements and for all participants. Preference for the lonapegsomatropin device was indicated by 14.3% of participants, and 7.1% indicated no preference for either device. Within the

Table 1 Participant Demographics and Clinical Characteristics

Characteristic	Adolescents (n=35)	Caregivers (n=35)
Mean age, years	13.7	46.3
Gender, n (%)		
Female	14 (40)	29 (83)
Male	21 (60)	6 (17)
Condition[a], n (%)		
Growth hormone deficiency	25 (71.4)	23 (65.7)
Turner syndrome	5 (14.3)	5 (14.3)
Idiopathic short stature	5 (14.3)	5 (14.3)
Noonan syndrome	1 (2.9)	1 (2.9)
Short for gestational age	1 (2.9)	2 (5.7)
Current device type, n (%)		
Pen-injector	26 (74.3)	26 (74.3)
Not applicable	6 (17.1)	7 (20)
Prefilled syringe	2 (5.7)	1 (2.9)
Vial and syringe	1 (2.9)	1 (2.9)
Current treatment frequency, n (%)		
Daily	23 (65.7)	22 (62.9)
Weekly	6 (17.1)	6 (17.1)
Not applicable	6 (17.1)	7 (20)

Notes: [a]Some individuals were recorded with more than one condition. All patient demographics and clinical characteristics were self-reported.
Abbreviation: n, number of participants.

adolescents and caregivers groups, 71.4% (95% CI 53.7–85.4) and 85.7% (95% CI 69.7–95.2), respectively, preferred the somapacitan device. Prescott's test provided evidence that the difference in preference between the somapacitan and the lonapegsomatropin devices was statistically significant for adolescents ($p=0.0025$) and caregivers ($p<0.0001$). The p-value based on data from all participants was ($p<0.0001$).

Of all participants who preferred the somapacitan device, 96.4% (95% CI 87.5–99.6) indicated that their preference was fairly strong or very strong. By participant group, this was 100% (95% CI 86.3–100) for the adolescents and 93.3% (95% CI 77.9–99.2) for the caregivers. Of participants who preferred the lonapegsomatropin device, 80.0% indicated that their preference was fairly strong or very strong by both participants in the adolescents and caregivers groups.

In terms of confidence in using the device correctly, the majority of participants (61.5%) indicated that they were more, or much more, confident in using the somapacitan device correctly than the lonapegsomatropin device, while 17.1% indicated the same for the lonapegsomatropin device ($p<0.001$).

DHPAQ direct comparison questions and participants' responses of preference between the two devices are presented in Table 2.

Device preferences were also analyzed for the subgroup of participants who had never used either injection device investigated in this study, or PDS290 family pen-injectors, (n=42). These results showed that 70.0% (14 out of 20) of adolescents and 86.4% (19 out of 22) of caregivers indicated an overall preference for the somapacitan device ($p=0.03$ and $p<0.0001$, respectively). These findings are consistent with the preferences indicated by all participants, which were 71.4% for adolescents and 85.7% for caregivers.

Ease of Use/Learning How to Use

When asked for their thoughts on the overall ease of use of each device, 97.1% (95% CI 90.1–99.7) of all participants indicated that the somapacitan device was easy or very easy to use, while 57.1% (95% CI 44.8–68.9) indicated the same for the lonapegsomatropin device.

Table 2 Questions and Responses on Preference Between the Two Devices in the DHPAQ

	Response, %					
Question: Comparing the somapacitan device to the lonapegsomatropin device, which one is easier to…						
	Somapacitan device much easier	**Somapacitan device easier**	**No difference**	**Lonapegsomatropin device easier**	**Lonapegsomatropin device much easier**	**P-value (*post hoc analysis*)**
Learn how to use the device?	21.4	15.7	57.1	4.3	1.4	p<0.0001
Prepare the device for injection?	64.3	21.4	4.3	5.7	4.3	p<0.0001
Inject the dose?	18.6	11.4	31.4	24.3	14.3	p=0.4699
Hold the device while injecting the dose?	12.9	14.3	40.0	18.6	14.3	p=0.6461
Bring the device with you when you are out (eg, travel or vacation)?	31.4	38.6	18.6	5.7	5.7	p<0.0001
Use the device when you are outside your home?	28.6	37.1	22.9	4.3	7.1	p<0.0001
Overall, which device is easier to use?	45.7	35.7	7.1	7.1	4.3	p<0.0001
Question: Comparing the somapacitan device to the lonapegsomatropin device, with which one are you more confident that…						
	Much more confident with the somapacitan device	**More confident with the somapacitan device**	**No difference**	**More confident with the lonapegsomatropin device**	**Much more confident with the lonapegsomatropin device**	**P-value (*post hoc analysis*)[a]**
You can use the device correctly?	28.6	32.9	21.4	10.0	7.1	p<0.0001
The device has delivered the correct full dose?	14.3	15.7	45.7	14.3	10.0	p=0.6294

Question: Comparing the somapacitan device with the lonapegsomatropin device, which one is faster to prepare and inject the medication?					
Much faster with the somapacitan device	**Faster with the somapacitan device**	**No difference**	**Faster with the lonapegsomatropin device**	**Much faster with the lonapegsomatropin device**	**P-value (*post hoc analysis*)[a]**
87.1	4.3	1.4	1.4	5.7	p<0.0001

Question: All things considered, which device do you prefer?			
Somapacitan device	**No preference**	**Lonapegsomatropin device**	**P-value (*post hoc analysis*)[a]**
78.57	7.14	14.29	p<0.0001

Note: The number of patients who completed each section of the DHPAQ was 70.
Abbreviation: DHPAQ, Device Handling and Preference Assessment Questionnaire.

When comparing the somapacitan device with the lonapegsomatropin device, 37.1% indicated that the somapacitan device was easier or much easier to learn how to use, while 5.7% indicated the same for the lonapegsomatropin device. This difference was statistically significant (p<0.0001).

Within direct comparisons, almost all participants (98.5%) indicated that the somapacitan device was easy or very easy to prepare for injection while about half (55.7%) indicated the same for the lonapegsomatropin device.

With regards to learning how to use the device, 95.7% (95% CI 88.0–99.1) of participants indicated that the somapacitan device was easy or very easy to learn how to use while 54.3% (95% CI 41.9–66.3%) indicated the same for the lonapegsomatropin device. The majority of participants indicated that the somapacitan device was fast or very fast to prepare and inject (90%), while few indicated the same for the lonapegsomatropin device (1.4%).

DHPAQ questions and participants' responses on the ease of use/learning how to use each device are presented in Table 3.

Table 3 Questions and Responses Relating to Ease of Use of Each Device in the DHPAQ

Question	**Device**	**Response, %**				
How difficult or easy is it to…		**Very difficult**	**Difficult**	**Neither difficult nor easy**	**Easy**	**Very easy**
Learn how to use the device?	Somapacitan	0.0	0.0	4.3	24.3	71.4
	Lonapegsomatropin	0.0	17.1	28.6	37.1	17.1
Prepare the device for injection?	Somapacitan	0.0	0.0	1.4	21.4	77.1
	Lonapegsomatropin	2.9	18.6	22.9	41.4	14.3
Inject the dose?	Somapacitan	0.0	0.0	4.3	17.1	78.6
	Lonapegsomatropin	0.0	4.3	5.7	38.9	57.1
Hold the device while injecting the dose?	Somapacitan	0.0	1.4	11.4	27.1	60.0
	Lonapegsomatropin	0.0	4.3	11.4	27.1	57.1
Bring the device with you when you are out?	Somapacitan	0.0	8.6	18.6	25.7	47.1
	Lonapegsomatropin	0.0	20	22.9	40.0	17.1
Use the device when you are outside your home?	Somapacitan	0.0	5.7	10.0	35.7	48.6
	Lonapegsomatropin	2.9	21.4	27.1	24.3	24.3
Overall, how difficult or easy is it to use the device?	Somapacitan	0.0	0.0	2.9	28.6	68.6
	Lonapegsomatropin	0.0	15.7	27.1	37.1	20.0
How confident are you that…	**Device**	**Not at all confident**	**A little confident**	**Somewhat confident**	**Very confident**	**Extremely confident**
You can use the device correctly?	Somapacitan	0.0	0.0	5.7	25.7	68.6
	Lonapegsomatropin	0.0	1.4	20.0	47.1	31.4
The device has delivered the correct full dose?	Somapacitan	0.0	0.0	4.3	30.0	65.7
	Lonapegsomatropin	0.0	2.9	18.6	38.6	40.0
Overall, how slow or fast is it to prepare and inject the medication with the device?	**Device**	**Very slow**	**Slow**	**Neither slow nor fast**	**Fast**	**Very fast**
	Somapacitan	0.0	1.4	8.6	31.4	58.6
	Lonapegsomatropin	48.6	42.9	7.1	1.4	0.0

Note: The number of patients who completed each section of the DHPAQ was 70.
Abbreviation: DHPAQ, Device Handling and Preference Assessment Questionnaire.

Training Time and Injection Time

Across all participants, the average time taken to complete the training for the handling tasks of the somapacitan device was shorter than that for the lonapegsomatropin device (5.9 min vs 24.0 min, respectively; Figure 3A). By participant group, adolescents took an average of 6.0 min for the somapacitan device and 24.2 min for the lonapegsomatropin device, while caregivers took an average of 5.8 min and 23.8 min for respective devices.

Across all participants, the average time taken to complete an injection with the somapacitan device was also shorter compared with the lonapegsomatropin device (0.9 vs 10.6 min, respectively; Figure 3B). To complete an injection with the somapacitan device, adolescents took an average of 1 min, while caregivers took an average of 0.8 min. For the lonapegsomatropin device, adolescents took an average of 10.8 min and caregivers took an average of 10.5 min.

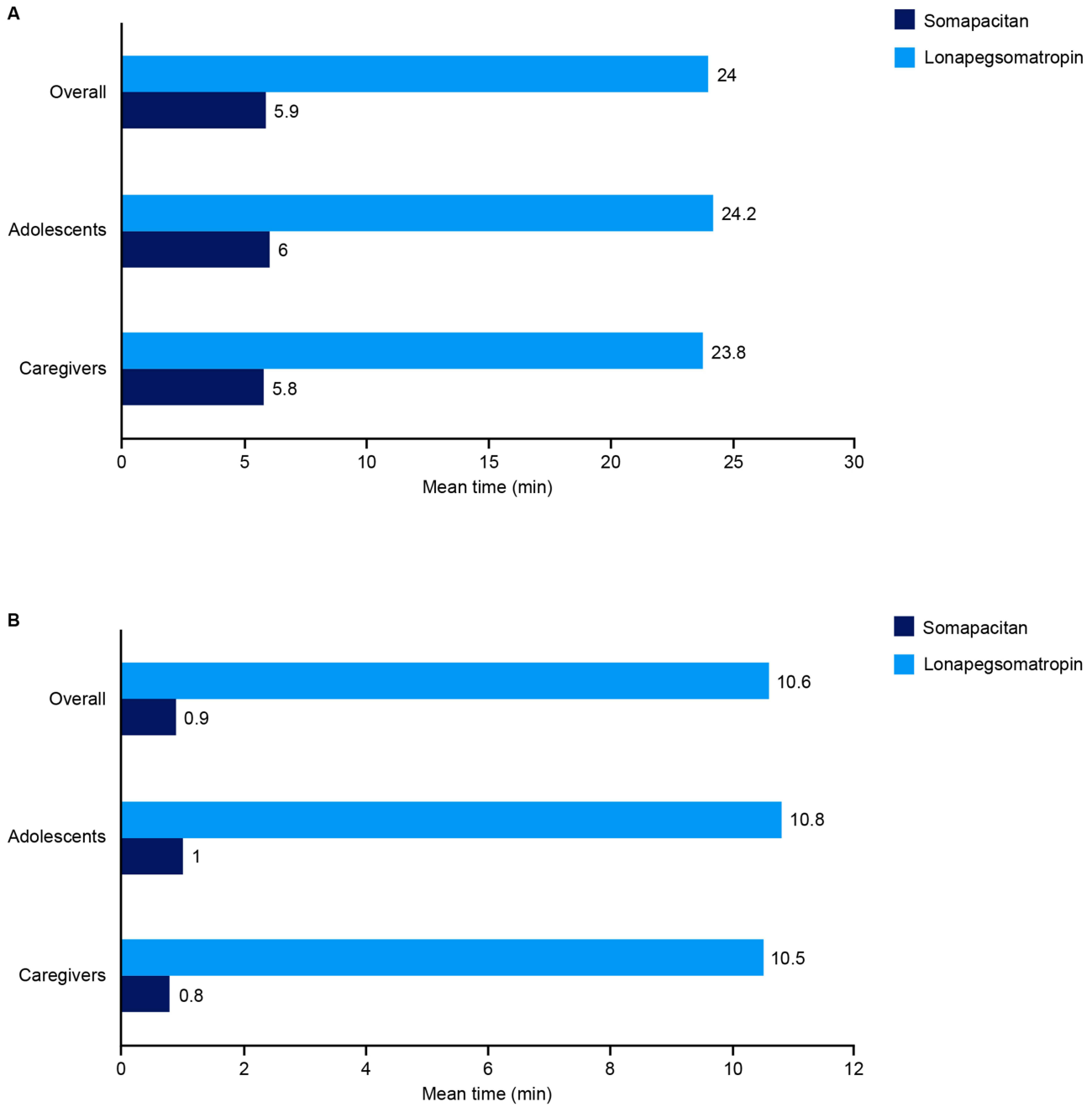

Figure 3 Average (**A**) training time and (**B**) time to prepare and inject for the somapacitan and lonapegsomatropin devices.

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Based on the results of the DHPAQ, 90% of participants indicated that the somapacitan device was fast or very fast to prepare and inject, while only 1.4% indicated the same for the lonapegsomatropin device (Table 3). Additionally, 91.4% ($p<0.001$) of participants indicated that the somapacitan device was faster or much faster than the lonapegsomatropin device to prepare and inject (Table 2).

Complete Injections

For the somapacitan device, 98.6% of participants completed the simulated injection successfully. One participant in the adolescents group did not count to six after administering the injection, which led to the injection being deemed incomplete.

For the lonapegsomatropin device, 95.7% of participants completed the simulated injection successfully. One participant in the adolescents group did not turn on the autoinjector, and two participants (one from each group) did not perform the manual mixing step. For these cases of incomplete injections, the moderator had to step in to provide assistance.

Device Portability

When asked about the portability of the device, 70% ($p<0.0001$) of participants found the somapacitan device easier or much easier to bring with them when they were out (eg, when traveling or on vacation) compared with the lonapegsomatropin device (Table 2). Furthermore, 65.7% ($p<0.0001$) found the somapacitan device easier or much easier to use outside the home.

Protocol Amendments

During the recruitment process, few suitable participants aged <10 years were identified. Providing the opportunity for these participants to take part in the study was deemed beneficial to increase the pool of participants from this rare patient population. One 9-year-old participant was recruited based on their cognitive and behavioral capabilities, which had no impact on the results of the study. One 9-year-old participant was dismissed due to inability to complete the study steps and an adolescent participant was enrolled instead.

Discussion

This study was designed to compare preference and ease of use/learning how to use of the somapacitan and lonapegsomatropin devices in adolescents with growth-related disorders and caregivers of individuals with growth-related disorders. The primary objective was to demonstrate patient preference for the somapacitan pen-injector versus the lonapegsomatropin autoinjector. There was a statistically significant preference from the majority of participants, 78.6% (95% CI 67.1–87.5), for the somapacitan pen-injector over the lonapegsomatropin autoinjector. Few participants preferred the lonapegsomatropin device (14.3%), and some participants indicated no preference for either device (7.1%). The results of the sensitivity analysis, where only participants with no prior experience with either device (or similar devices) were included, were consistent with the full cohort tested where a preference for the somapacitan device over the lonapegsomatropin device was indicated. Thus, prior use of either device (including PDS290 family devices) at any point in time, regardless of duration, did not seem to bias the participants' preferences for the devices during the study.

The secondary objective of this study was to evaluate ease of use and ease of learning how to use the somapacitan pen-injector versus the lonapegsomatropin autoinjector. The majority of participants indicated that the somapacitan device was easy or very easy to use (97.1%), or easier or much easier to use (81.4%), compared with the lonapegsomatropin device (57.1% and 11.4%, respectively). Just over a third of participants indicated that the somapacitan device was easier or much easier to learn how to use (37.1%) compared with the lonapegsomatropin device (5.7%). The somapacitan device required considerably less time to train (6 min vs 24 min) and complete an injection (0.9 min vs 10.6 min) and was deemed fast or very fast to prepare and inject (90%) compared with the lonapegsomatropin device (1.4%). Lastly, 61.5% of participants were more or much more confident using the somapacitan device correctly compared with the lonapegsomatropin device. One of the reasons for these results being in favor of the somapacitan device could be the differing administration techniques that the two devices utilize. The somapacitan device utilizes a prefilled, ready-to-use pen, while the lonapegsomatropin autoinjector device requires reconstitution prior to use.[13,14,19] Incomplete injections

occurred with one participant with the somapacitan device at the counting step and two participants with the lonapegsomatropin device at the manual mixing step. However, a statistical difference could not be established due to the low number of incomplete injections.

The results of this study indicated that the somapacitan device was preferred by the majority of study participants over the lonapegsomatropin device. This may be related to ease of use/learning how to use of the somapacitan device versus the lonapegsomatropin device. Other reports conducted on adherence to GH in similar patient populations showed similar findings. In a discrete choice questionnaire study, 47 Japanese children with GHD, or their caregivers, were asked to evaluate the device attributes that are most important to them.[25] Children with GHD indicated a higher preference for a ready-to-use injection device rather than a device that requires reconstitution.[25] In the REAL 4 trial, the safety and efficacy of somapacitan versus daily GH, along with patient-reported outcomes, were investigated in 200 children with GHD.[2] The majority of patients indicated that the somapacitan device was easy or very easy to use (96%) and easy or very easy to learn how to use (>90%). Lastly, in an analysis designed to compare the somapacitan pen-injector with the somatrogon pen-injector, similar methods to our study were utilized and 70 participants were recruited. The results showed that the somapacitan device was preferred to the somatrogon device by 84.3% of participants (95% CI 74–92). Additionally, research has shown that device features linked to usability, design, and preference are important to ensure optimal adherence.[1,9,11,12] This suggests that a more convenient injection pen in the areas of usage learning, preparation, and injection process may lead to improved adherence.[26,27]

There were some limitations that could have influenced the results of this analysis. The use of a test environment could have influenced the participants' preferences as it was not a true reflection of the natural environment where they would administer GH injections. In addition, the study was only conducted in the US and therefore may not be globally representative. Due to recruitment difficulties when conducting a study in a population with growth-related disorders in a single country, some participants may not have been naïve to the devices (or similar devices) being investigated in this study, and, although current use of tested devices or PDS290 family devices, like FlexPro®, was an exclusion criterion, prior exposure may have affected some participants' perceptions with regard to device ease of use. Prescott's test is calculated based on the assumption that data points are independent, which may be questionable for the pooled data as it mostly consists of pairs of adolescents and caregivers.

Furthermore, this study was not designed to include children aged <10 years, who may present a different perspective based on specific-age characteristics, such as hand size or expectancy on duration of the process, which differ from the experiences of adults or adolescents. Lastly, conclusions drawn regarding adherence with each device are only theoretical, as adherence was not measured directly.

The strengths of this study included the use of crossover design where inter-subject variability between comparison groups was avoided, allowing for a direct comparison. Participants diagnosed with or caring for children with GHD and other growth-related disorders were recruited. Furthermore, the DHPAQ questionnaire that was used in this study was previously validated to be comprehensive, relevant, and fully comprehended by respondents.

Conclusion

In this randomized, multicenter, crossover study, the somapacitan device was preferred over the lonapegsomatropin device following simulated injections among adolescents with growth-related disorders and caregivers of individuals with growth-related disorders. The somapacitan pen-injector required considerably less time to train and less time to prepare and inject the medication. Additionally, it was deemed significantly easier to use compared with the lonapegsomatropin autoinjector. The results of this study suggest that adolescents receiving GH treatment via the somapacitan device may be more likely to have higher treatment adherence than those receiving GH treatment via the lonapegsomatropin device.

Abbreviations

CI, confidence interval; DHPAQ, Device Handling and Preference Assessment Questionnaire; EU, European Union; GH, growth hormone; GHD, growth hormone deficiency; IRB, Institutional Review Board; LAGH, long-acting growth hormone; n, number of participants; US, United States.

Data Sharing Statement

Participant-level data used for the analysis of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

The test plan for this Human Factors Comparative Preference and Handling study was reviewed and approved by Castle Institutional Review Board (Castle IRB), located in Chesterfield, MO, USA.

All participants provided informed written consent prior to the commencement of the study to take part in the study and to allow any data collected to be processed. All adolescent participants were accompanied by a parent or legal guardian who provided the consent on their behalf.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Johan Medina, Gitte Ter-Borch, and Shahid Akhtar are full-time employees and shareholders of Novo Nordisk A/S. Nicky Kelepouris and Sophie Hamilton are full-time employees and shareholders of Novo Nordisk Inc. Maya Gonczi is an employee of Research Collective and has received funding from Novo Nordisk A/S for research carried out in this work. Jørgen Vinsløv Hansen is a full-time employee of Novo Nordisk A/S. The authors report no other conflicts of interest in this work.

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