



ORIGINAL RESEARCH

PRESTO 2: An International Survey to Evaluate Patients' Injection Experiences with the Latest Devices/Formulations of Long-Acting Somatostatin Analog Therapies for Neuroendocrine Tumors or Acromegaly

Dermot O'Toole · Pamela L. Kunz · Susan M. Webb ·
Grace Goldstein · Sheila Khawaja · Mark McDonnell ·
Sandra Boiziau · Delphine Gueguen · Aude Houchard ·
Antonio Ribeiro-Oliveira Jr · Ally Prebtani

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ABSTRACT

Introduction: Real-world data evaluating patients' injection experiences using the latest devices/formulations of the long-acting (LA) somatostatin analogs (SSAs) lanreotide Autogel/Depot (LAN; Somatuline®) and octreotide LA release (OCT; Sandostatin®) are limited.

Methods: PRESTO 2 was a 2020/2021 e-survey comparing injection experience of adults with neuroendocrine tumors (NETs) or acromegaly treated with LAN prefilled syringe versus OCT syringe for > 3 months in Canada, Ireland, the UK and the USA (planned sample size, 304). Primary endpoint: the proportion of patients with injection-site pain lasting > 2 days after

D. O'Toole (✉)
Neuro Endocrine Tumours-ENETS Centre of
Excellence, St. Vincent's University Hospital,
Dublin, Ireland
e-mail: OTOOLED1@tcd.ie

P. L. Kunz
Yale School of Medicine and Yale Cancer Center,
New Haven, CT, USA

S. M. Webb
Departamento de Medicina/Endocrinología,
Hospital Sant Pau, IIB-Sant Pau, Universitat
Autònoma de Barcelona, CIBERER U747 Barcelona,
Spain

G. Goldstein
Carcinoid Cancer Foundation, Mount Kisco, NY,
USA

S. Khawaja
World Alliance of Pituitary Organizations, Zeeland,
The Netherlands

M. McDonnell
NET Patient Network Ireland, Dublin, Ireland

S. Boiziau · D. Gueguen · A. Houchard
Ipsen, Boulogne-Billancourt, France

A. Ribeiro-Oliveira Jr
Ipsen, Cambridge, MA, USA

A. Prebtani
Faculty of Health Sciences, McMaster University,
Hamilton, ON, Canada

their most recent injection, analyzed using a multivariate logistic regression model. Secondary endpoints included interference with daily life due to injection-site pain and technical injection problems in patients with current SSA use for ≥ 6 months.

Results: There were 304 respondents (acromegaly, $n = 85$; NETs, $n = 219$; LAN, $n = 168$; OCT, $n = 136$; 69.2% female; mean age, 59.6 years). Fewer patients had injection-site pain lasting > 2 days after the most recent injection with LAN (6.0%) than OCT (22.8%); the odds of pain lasting > 2 days were significantly lower for LAN than OCT, adjusted for disease subgroup and occurrence of injection-site reactions (odds ratio [95% confidence interval]: 0.13 [0.06–0.30]; $p < 0.0001$). Injection-site pain

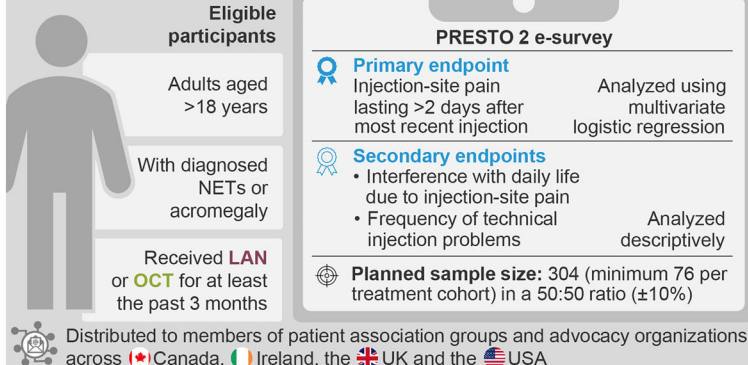
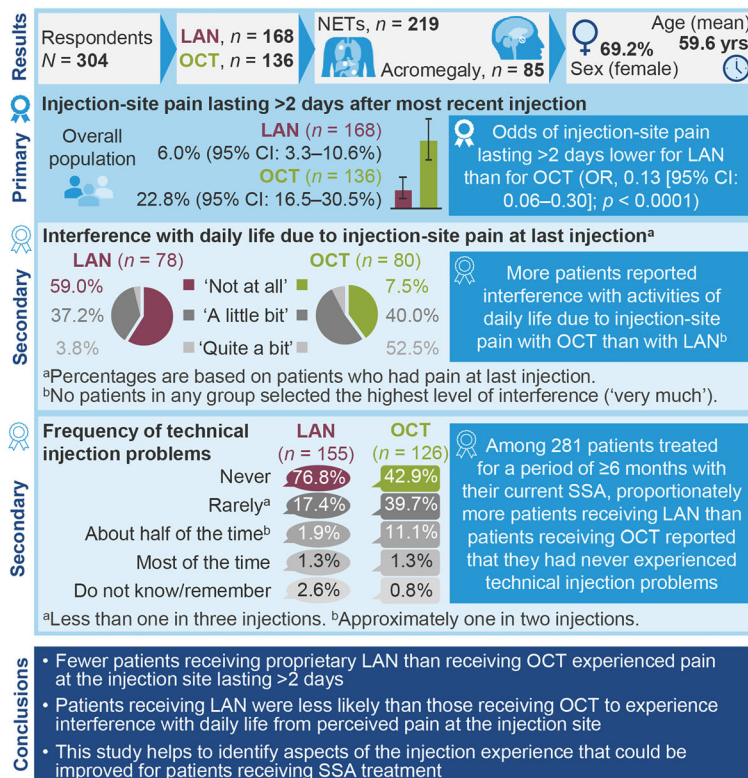
interfered with daily life “a little bit” or “quite a bit” in 37.2% and 3.8% (LAN) versus 52.5% and 7.5% (OCT) of patients, respectively. Among patients with ≥ 6 months’ experience with current SSA (92.4% of patients), technical injection problems never occurred in 76.8% (LAN) and 42.9% (OCT) of patients.

Conclusions: Compared with OCT, significantly fewer patients using LAN had injection-site pain lasting > 2 days after their most recent injection. Also, fewer LAN-treated patients experienced technical problems during injection. These findings demonstrate the importance of injection modality for overall LA SSA injection experience for patients with acromegaly or NETs.

Graphical abstract:

PRESTO 2: an international survey to evaluate patients' injection experiences with the latest devices/formulations of long-acting somatostatin analog therapies

D O'Toole, PL Kunz, SM Webb, G Goldstein, S Khawaja, M McDonnell, S Boiziau, D Gueguen, A Houchard, A Ribeiro-Oliveira Jr, A Prebtani

Objective: To compare and understand the injection experience of patients with acromegaly or NETs receiving treatment with proprietary **lanreotide** or **octreotide****Methods**

CI confidence interval, LAN lanreotide autogel/depot (Somatuline®; Ipsen), NET neuroendocrine tumor, OCT octreotide long-acting release (Sandostatin®; Novartis), OR odds ratio, SSA somatostatin analog

This graphical abstract represents the opinions of the authors. For a full list of declarations including funding and author disclosure statements, please see the full text online.

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PLAIN LANGUAGE SUMMARY

Patients with neuroendocrine tumors or acromegaly often receive long-term monthly treatment with somatostatin analogs. These injectable drugs stop the body from making an excess of certain hormones. Understanding patients' experiences of these injections helps to provide better care. The PRESTO 2 online study surveyed 304 patients in Canada, Ireland, the UK and the USA with neuroendocrine tumors or acromegaly who were being treated with a somatostatin analog, either lanreotide Autogel/Depot (LAN) or octreotide long-acting release (OCT). The survey asked about injection experience, including injection-site pain lasting > 2 days and how it affected patients' lives, anxiety before injections and technical problems during injections (like syringe blockages). The survey showed fewer patients receiving LAN than OCT had injection-site pain that lasted > 2 days, and fewer said that the pain interfered with their daily lives. There were fewer technical injection problems with LAN than with OCT. However, more patients receiving LAN than OCT felt anxious before their injection. In some countries (including Canada, Ireland and the UK, but not the USA), the patient (or family member/friend) can inject LAN if they are on a stable dose, their doctor agrees, and they received training. A nurse/doctor must inject OCT. In PRESTO 2, about 40% of non-US patients who were eligible injected themselves (or were helped by a family member/friend). This may explain why more patients reported anxiety in the LAN group. PRESTO 2 provides important insights into patients' experiences of receiving somatostatin analogs and helps identify areas for improving patient care.

Keywords: Acromegaly; Injection; Neuroendocrine tumors; Pain; Patient experience; Somatostatin analog

Key Summary Points

Why carry out this study?

Understanding patients' experience of treatment is important in delivering the best care possible

The PRESTO 2 survey asked patients with acromegaly or neuroendocrine tumors (NETs) about their experience of long-acting somatostatin analogues (LA SSA: lanreotide [LAN] or octreotide [OCT]) injections), using questions including their evaluation of pain at the injection site lasting > 2 days, the effects on their daily lives, their anxiety before injections and any technical problems that occurred during injections

What was learned from the study?

Compared with those patients receiving OCT injections, significantly fewer patients receiving LAN had injection-site pain lasting > 2 days after their most recent injection

Fewer technical problems were reported with the injections received by LAN-treated patients than by those receiving OCT

The findings of the PRESTO 2 survey demonstrate the importance of injection modality in the treatment experience of patients receiving LA SSAs for acromegaly or NETs

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract, to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.21333102>.

INTRODUCTION

Injectable long-acting (LA) somatostatin analogs (SSAs) are often used long term to treat acromegaly and advanced, unresectable, moderately-to-well-differentiated neuroendocrine tumors (NETs) [1, 2]. Acromegaly is usually caused by excess production of growth hormone as a result of a benign tumor (adenoma) in the pituitary gland [3–5]. NETs are a heterogeneous group of slow-growing neoplasms that occur in diffuse neuroendocrine cells and that are accompanied, in some patients, by carcinoid syndrome [6, 7]. There are currently two proprietary (branded) injectable LA SSAs available for first-line treatment of NETs and acromegaly: Somatuline® (lanreotide) Autogel/Depot (Ipsen)—herein referred to as LAN—and Sandostatin® (octreotide) Long-Acting Release (Novartis)—herein referred to as OCT. LAN is provided as a ready-to-use prefilled syringe for administration by deep subcutaneous injection once every 28 days [8, 9]. OCT is provided in single-use kits with a vial containing octreotide powder and a syringe containing the diluent; after reconstitution, it is administered by intramuscular injection once every 28 days [10–12]. Nonproprietary (generic) LA SSAs are now available in some markets, although generic lanreotide was not available at the time of this study.

Evaluation of treatment success has traditionally focused on clinician assessments of efficacy or effectiveness and safety, but there is a growing recognition of the key role that patient experience has in overall treatment outcomes [13, 14]. Positive patient perspectives and acceptance of treatment can contribute to patient empowerment, helping patients to self-manage their condition, increase treatment adherence and persistence, and improve treatment outcomes [14]. In the case of chronic conditions requiring long-term injectable drugs, the injection experience is an important part of the overall patient reality. To maximize treatment adherence, patients should ideally have access to effective, tolerable treatments that are easy and efficient to deliver.

In 2019, Cella et al. conducted a systematic literature review to investigate which characteristics, beyond therapeutic efficacy, influenced the patient and healthcare professional (HCP) experience of LAN and OCT for the treatment of NETs or acromegaly. The review included 18 studies that reported patients' perspectives of LAN and of OCT treatment and concluded that factors underlying the patient treatment experience included injection-associated pain, time and convenience, technical problems and emotional aspects/anxiety. Most of these studies compared LAN with OCT, and results generally favored LAN [15], but the LAN syringe has since been redesigned and the diluent for OCT has been reformulated, limiting the generalizability of these findings to current treatment options.

The LAN syringe was redesigned (v3.0) in collaboration with patients, caregivers and HCPs [16] to make the device more user-friendly and to improve its overall ergonomics. The redesigned syringe has been approved in many countries and has largely replaced the former LAN syringe. For OCT, the diluent used in the syringe was reformulated to facilitate its preparation and administration, resulting in fewer administration problems than with the previous formulation, improved ease of use and overall increased nurse satisfaction [17]. The PRESTO simulated-use study, conducted in 2019, found that nurses preferred the redesigned LAN syringe to the OCT syringe with the reformulated diluent, particularly in terms of the faster speed of administration and greater confidence that the LAN syringe will not become clogged [18]. However, no studies have explored the real-world preference or opinions of patients using the latest proprietary LAN and OCT devices and formulations.

PRESTO 2 was an online, international patient survey conducted to compare the injection experiences of patients receiving SSA therapy via the current LAN device versus the new OCT formulation for the management of NETs or acromegaly.

METHODS

Study Design

PRESTO 2 was an online, English-language, patient-experience survey conducted in Canada, Ireland, the UK and the USA in adults with NETs or acromegaly who had received treatment with LAN or OCT. The survey was launched on 5 August 2020, put on hold between 31 August 2020 and 8 July 2021 on the Sponsor's decision, to assess and review the internal processes applicable to this type of project and ended on 1 September 2021.

The survey design was based on concepts identified from the previous preference studies [18–20] and a gap analysis of the published literature, as well as input from an advisory board consisting of an expert on patient-reported outcomes (PROs), physicians and nurses. Before the survey was launched, validity of the questionnaire was tested through a cognitive debriefing with patients with NETs ($n = 3$) and acromegaly ($n = 2$).

Participants

Participants were adults (aged ≥ 18 years) who had been receiving LA SSA treatment with either LAN or OCT for NETs or acromegaly for at least the previous 3 months. Those who had received both were asked to complete the survey based on the SSA currently being used. Participants treated with LAN were included irrespective of the mode of injection (administered by an HCP or independently [self-injection or by a caregiver] in countries where independent injection was approved). Self-injection is not indicated in the label for patients receiving LAN in the USA, or for those receiving OCT in any country; these participants were therefore not asked any of the questions on independent injection.

Recruitment

Participants were recruited electronically in collaboration with patient association groups and advocacy organizations from selected

English-speaking countries (Acromegaly Canada, Acromegaly Community, the Canadian Neuroendocrine Tumour Society, the Carcinoid Cancer Foundation, NET Patient Network, the Neuroendocrine Tumor Research Foundation, the Pituitary Network Alliance and the World Alliance of Pituitary Organizations) and Carenity (a social network for people living with chronic conditions), which shared a link to the online survey with their members. Respondents were asked to enter their initials, date of birth and the name of their treating center (so that quality and plausibility checks could be made). Data were pseudo-anonymized before analysis to protect participants' confidentiality.

Primary and Secondary Endpoints

The endpoints were chosen based on those identified as most relevant to patients' injection experiences with SSAs in the systematic literature review by Cella et al. [15]. The primary endpoint of PRESTO 2 was the proportion of participants with injection-site pain lasting > 2 days after their most recent injection of LAN or OCT in the Survey population (which included all participants who started the survey with no data quality concerns; this was irrespective of whether they had NETs or acromegaly). Secondary endpoints related to participants' most recent injection experience were as follows: perceived pain during injection, duration of perceived pain at the injection site, extent of interference with daily life from pain at the injection site, pre-injection anxiety and occurrence of reactions (i.e., nodules, bruising or swelling) at the injection site. Secondary endpoints related to participants' overall injection experience were as follows: frequency, details and consequences of technical injection problems, frequency of pain at the injection site and most burdensome injection-related issues. An additional secondary endpoint was the most important benefits of independent injection (non-US participants in the LAN group only). It was also planned to evaluate patient preference for LAN or OCT based on the overall injection experience and comparative experience of their current SSA with their previous SSA. However,

because of the small sample size (and imbalances in sample sizes between groups), as well as the potential for recall bias, patient preference data are not presented. Safety was not in the scope of this study. Because this survey collected retrospective data on participants' general experience regarding very well known, non-serious, listed adverse drug reactions (ADRs) for LAN, i.e., pain and local reactions at the injection site, the collection and reporting of adverse events, special situations and/or product complaints followed regulations related to spontaneous cases. In case of ADRs, special situations and/or product complaints, participants were advised to report these to National Health Authorities or their local Ipsen contact as mentioned in the informed consent form.

Statistics and Prespecified Analyses

It was assumed that the proportions of participants with pain lasting > 2 days would be approximately 25% for LAN and 40% for OCT. This assumption was based on the results of a previous study in patients with acromegaly ($N = 195$) in which the odds ratio (OR) of no pain days after LAN or OCT injection was 2 (74% and 57% of patients receiving LAN and OCT respectively, had no pain) [21]. Using a chi-squared test with a 5% two-sided significance level and 80% power, it was estimated that 152 participants should be enrolled in each treatment group. Based on this sample size calculation, the target sample size was 304 participants. A minimum of 76 participants in each disease cohort was to be recruited.

For the primary endpoint, the proportions of participants, and the 95% Wilson score confidence intervals (CIs) were estimated for the Survey population. The relationships between the primary endpoint and potentially relevant participant or treatment characteristics were investigated by univariate logistic regression. The potential factors investigated (country, disease [acromegaly versus NET], treatment [LAN versus OCT], age, sex [male, female], BMI, time since initiation of treatment [3–6 months vs. > 6 months to < 1 year vs. > 1 year to < 3 years vs. ≥ 3 years] and occurrence of

reaction at injection side [yes vs. no]) were selected because they were perceived by the study team to have the potential to influence injection experience. Variables that were significant at a 20% level in the univariate analysis were assessed to identify potential collinearity using the Spearman's correlation coefficient, Fisher's exact test and Wilcoxon-Mann-Whitney tests, as appropriate. Noncollinear factors with a p value < 20% in the univariate context were included in a multivariate logistic regression model, with treatment (LAN/OCT) and disease (NETs/acromegaly) parameters forced into the model. ORs and 95% CIs were provided for all parameters included in the final model.

Secondary endpoints were evaluated for the Survey population and by treatment (LAN/OCT) and disease (NETs/acromegaly) subgroups. Endpoints relating to overall injection experience (rather than the most recent injection) were evaluated only in participants with at least 6 months' experience with their current SSA treatment (the Overall experience population). All secondary endpoint analyses were descriptive; no formal statistical tests were performed.

Post hoc Analyses

Details of post hoc analyses are given in the supplementary materials. Briefly, analyses were conducted to evaluate injection-site pain according to disease type, the extent to which certain factors were associated with anxiety before injection, and pre-injection anxiety in those whose injections were administered by HCPs versus those whose injections were administered independently (non-US LAN group only).

Ethics

The survey was reviewed and approved by the Western Instructional Review Board (IRB protocol number 20202117). Ethical committee review was not required in Ireland or the UK. The survey was conducted in compliance with relevant regulations pertaining to the ethical conduct of patient surveys, including with the Declaration of Helsinki [22] and with the

International Ethical Guidelines for Epidemiological Studies published by the Council for International Organizations of Medical Sciences [23]. All participants had to provide consent in an electronic format before starting the survey. The study was initiated and sponsored by Ipsen.

RESULTS

Participant Disposition

Of 538 patients screened, 304 completed the survey with no data quality concerns (Survey population, Fig. 1); 168 (55.3%) were receiving LAN and 136 (44.7%) were receiving OCT (four patients were receiving generic OCT); 219

(72.0%) had NETs and 85 (28.0%) had acromegaly. Most participants ($n = 281$; 92.4%) had at least 6 months' experience with their current SSA treatment (Overall experience population); 51.3% had been receiving their current SSA for at least 3 years. Forty-nine participants (29.2%) in the LAN group had previously received OCT, and 18 in the OCT group (13.2%) had previously received LAN. Of the 102 non-US participants in the LAN group, 40 (39.2%) had their most recent injection administered independently (i.e., by the patient or a partner/relative) (Independent injection population).

In the Survey population, mean age was 59.6 years and most participants (209/302; 69.2%) were female (Table 1A). Participants in the acromegaly subgroup were younger than

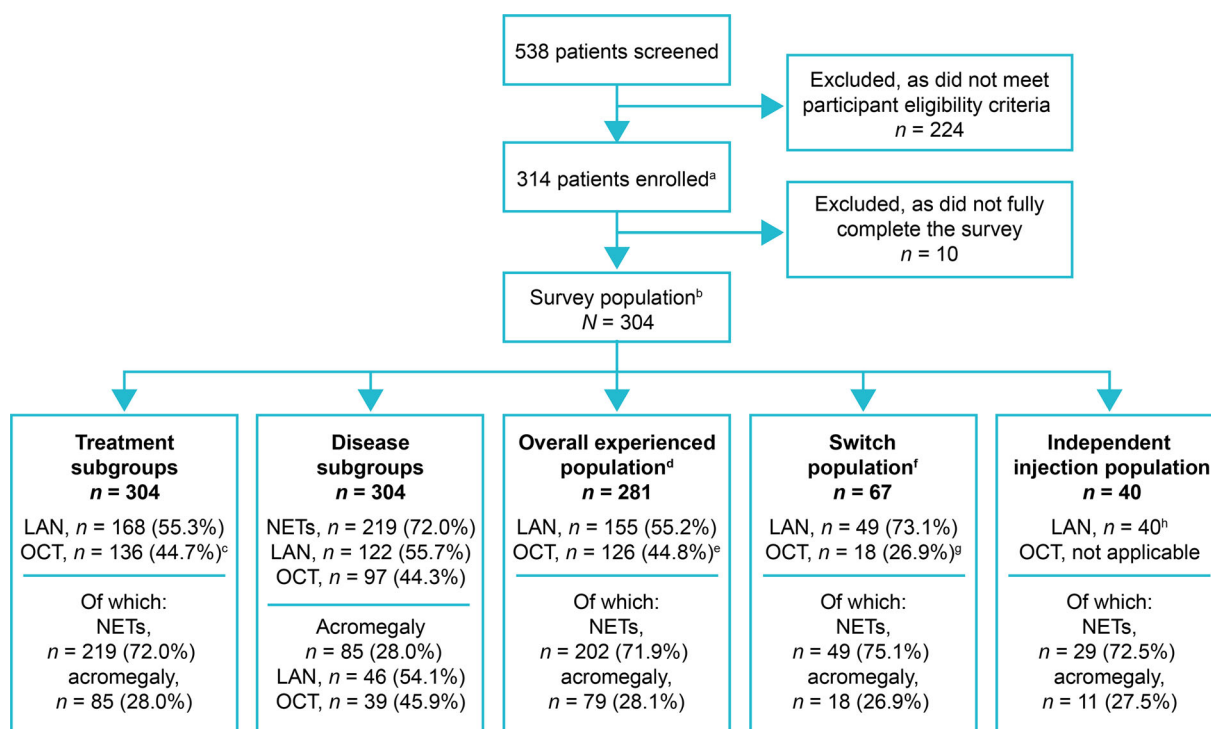


Fig. 1 Patient disposition. ^aAll participants from the screened population who met the inclusion/exclusion criteria and started to complete the survey. ^bAll enrolled participants who completed the survey with no data quality concerns and irrespective of whether they had NETs or acromegaly; ^c132 patients (97.1%) had received the branded formulation, and 4 patients (2.9%) had received the generic formulation. ^dParticipants with at least 6 months' experience of their current SSA treatment; ^e122

participants (96.8%) had received the branded formulation, and 4 participants had received (3.2%) the generic formulation. ^fParticipants who had been treated with both LAN and OCT. ^gAll participants received the branded formulation. ^hExcluded participants from the USA as independent injection of lanreotide autogel is not approved in the USA. LAN lanreotide autogel/depot, NET neuroendocrine tumor, OCT octreotide long-acting release

Table 1 Patient and treatment characteristics in (A) Survey population^a and (B) disease subgroups stratified by treatment

(A) Characteristic	Survey population, <i>N</i> = 304			
	LAN (<i>n</i> = 168)	OCT (<i>n</i> = 136)	All (<i>N</i> = 304)	
Country of residence, <i>n</i> (%)				
Canada	44 (26.2)	39 (28.7)	83 (27.3)	
Ireland	28 (16.7)	13 (9.6)	41 (13.5)	
UK	30 (17.9)	10 (7.4)	40 (13.2)	
USA	66 (39.3)	74 (54.4)	140 (46.1)	
Sex, <i>n</i> (%)				
Male	40 (23.8)	51 (38.1)	91 (30.1)	
Female	128 (76.2)	81 (60.4)	209 (69.2)	
Nonbinary	0	2 (1.5)	2 (0.7)	
Missing	0	2 (1.5)	2 (0.7)	
Age, mean (SD), years	59.4 (10.7)	59.9 (11.5)	59.6 (11.1)	
BMI category, <i>n</i> (%)				
Underweight (< 18.5 kg/m ²)	4 (2.5)	2 (1.5)	6 (2.1)	
Normal weight (18.5 to < 25.0 kg/m ²)	40 (25.3)	29 (22.1)	69 (23.9)	
Overweight (25 to < 30 kg/m ²)	52 (32.9)	40 (30.5)	92 (31.8)	
Obese (≥ 30 kg/m ²)	62 (39.2)	60 (45.8)	122 (42.2)	
Missing	10	5	15	
Duration of treatment with LAN or OCT, <i>n</i> (%)				
3 to 6 months	13 (7.7)	10 (7.4)	23 (7.6)	
> 6 months to < 1 year	23 (13.7)	10 (7.4)	33 (10.9)	
≥ 1 to < 3 years	59 (35.1)	33 (24.3)	92 (30.3)	
≥ 3 years	73 (43.5)	83 (61.0)	156 (51.3)	
(B) Characteristic	Population with NETs, <i>n</i> = 219		Population with acromegaly, <i>n</i> = 85	
	LAN (<i>n</i> = 122)	OCT (<i>n</i> = 97)	LAN (<i>n</i> = 46)	OCT (<i>n</i> = 39)
Country of residence, <i>n</i> (%)				
Canada	35 (28.7)	28 (28.9)	9 (19.6)	11 (28.2)
Ireland	25 (20.5)	10 (10.3)	3 (6.5)	3 (7.7)

Table 1 continued

(B) Characteristic	Population with NETs, <i>n</i> = 219		Population with acromegaly, <i>n</i> = 85	
	LAN (<i>n</i> = 122)	OCT (<i>n</i> = 97)	LAN (<i>n</i> = 46)	OCT (<i>n</i> = 39)
UK	15 (12.3)	2 (2.1)	15 (32.6)	8 (20.5)
USA	47 (38.5)	57 (58.8)	19 (41.3)	17 (43.6)
Sex, <i>n</i> (%)				
Male	38 (31.1)	40 (41.7)	2 (4.3)	11 (28.9)
Female	84 (68.9)	55 (57.3)	44 (95.7)	26 (68.4)
Nonbinary	0	1 (1.0)	0	1 (2.6)
Missing	0	1 (1.0)	0	1 (2.6)
Age, mean (SD), years	61.9 (9.5)	63.2 (9.2)	52.9 (11.2)	51.8 (12.8)
BMI category, <i>n</i> (%)				
Underweight (< 18.5 kg/m ²)	4 (3.5)	2 (2.1)	0	0
Normal weight (18.5 to < 25.0 kg/m ²)	34 (29.8)	26 (27.4)	6 (13.6)	3 (8.3)
Overweight (25 to < 30 kg/m ²)	35 (30.7)	27 (28.4)	17 (38.6)	13 (36.1)
Obese (≥ 30 kg/m ²)	41 (36.0)	40 (42.1)	21 (47.7)	20 (55.6)
Missing	8 (6.6)	2 (2.1)	2 (4.3)	3 (8.3)
Work status, <i>n</i> (%)				
In full or part-time work	36 (29.8)	32 (33.3)	26 (56.5)	23 (59.0)
Retired from work	55 (45.5)	48 (50.0)	6 (13.0)	8 (20.5)
Unable to work due to my disease	25 (20.7)	15 (15.6)	5 (10.9)	7 (17.9)
Not working (other reasons)	4 (3.3)	1 (1.0)	7 (15.2)	0
Other	1 (0.8)	0	2 (4.3)	1 (2.6)
Missing	1	1	0	0
Duration of treatment with LAN or OCT, <i>n</i> (%)				
3 to 6 months	11 (9.0)	6 (6.2)	2 (4.3)	4 (10.3)
> 6 months to < 1 year	16 (13.1)	7 (7.2)	7 (15.2)	3 (7.7)

Table 1 continued

(B) Characteristic	Population with NETs, <i>n</i> = 219		Population with acromegaly, <i>n</i> = 85	
	LAN (<i>n</i> = 122)	OCT (<i>n</i> = 97)	LAN (<i>n</i> = 46)	OCT (<i>n</i> = 39)
≥ 1 to < 3 years	49 (40.2)	23 (23.7)	10 (21.7)	10 (25.6)
≥ 3 years	46 (37.7)	61 (62.9)	27 (58.7)	22 (56.4)

BMI body mass index, *LAN* lanreotide autogel/depot, *NET* neuroendocrine tumor, *OCT* octreotide long-acting release, *SD* standard deviation

^aAll participants who completed the survey with no data quality concerns and irrespective of whether they had NETs or acromegaly

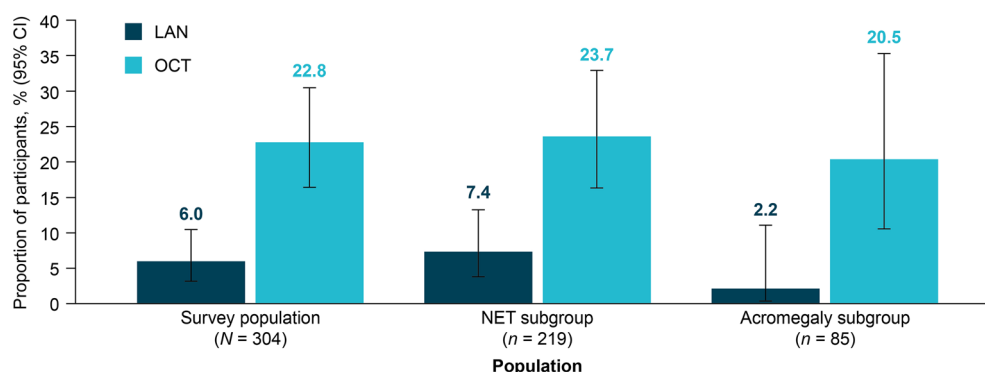


Fig. 2 Proportion of patients with pain at injection site lasting > 2 days after most recent injection (Survey population^a). ^aAll participants who completed the survey with no data quality concerns and irrespective of whether they

had NETs or acromegaly. *CI* confidence interval, *LAN* lanreotide autogel/depot, *NET* neuroendocrine tumor, *OCT* octreotide long-acting release

those with NETs: mean age was 52.4 years in the acromegaly group and 64.2 years in the NETs group (Table 1B). In both disease subgroups, there were more female participants in the LAN group than in the OCT group (Table 1B). Among those with NETs, a high proportion had carcinoid syndrome (62.3% in the LAN group and 72.2% in the OCT group). Disease characteristics are summarized in Supplementary Table S1, stratified by treatment.

Primary Endpoint: Injection-Site Pain Lasting More Than 2 Days

Fewer patients receiving LAN than OCT had injection-site pain lasting > 2 days after the most recent injection (6.0% [95% CI 3.3–10.6%]

vs. 22.8% [95% CI 16.5–30.5%]) (Fig. 2; Table 2). In the multivariate analysis, the odds of experiencing injection-site pain lasting > 2 days were significantly lower for LAN than for OCT when controlled for disease group and occurrence of injection-site reactions (OR [95% CI] 0.13 [0.06–0.30]; $p < 0.0001$ [country of residence, age, sex, body mass index and duration of treatment were not significant in the univariate analysis]). The odds of injection-site reactions were significantly higher in participants who experienced injection-site pain lasting > 2 days than in those who did not (OR [95% CI] 9.09 [4.00–20.65]; $p < 0.0001$) (Table 2).

In post hoc subgroup analyses, the proportion of participants with injection-site pain

Table 2 Primary endpoint analysis (Survey population)^a

	Survey population, <i>N</i> = 304		
	LAN (<i>n</i> = 168)	OCT (<i>n</i> = 136)	All (<i>n</i> = 304)
Participants with perceived pain at injection site with a duration of > 2 days, <i>n</i> (%) [95% CI]			
Yes	10 (6.0) [3.3–10.6]	31 (22.8) [16.5–30.5]	41 (13.5) [10.1–17.8]
No	158 (94.0) [89.4–96.7]	105 (77.2) [69.5–83.5]	263 (86.5) [82.2–89.9]
Multivariate logistic regression^b of influential participant characteristics, OR (95% CI) [<i>p</i> value]			
LAN vs. OCT	0.13 (0.06–0.30) [< 0.0001]		
Acromegaly vs. NETs	0.77 (0.32–1.83) [0.5518]		
Injection-site reaction occurrence vs. none	9.09 (4.00–20.65) [< 0.0001]		

BMI body mass index, *CI* confidence interval, *LAN* lanreotide autogel/depot, *NET* neuroendocrine tumor, *OCT* octreotide long-acting release, *OR* odds ratio

^aAll participants who completed the survey with no data quality concerns and irrespective of whether they had NETs or acromegaly

^bCharacteristics included in the univariate analysis were country of residence (Canada, Ireland, UK, USA); disease (NETs, acromegaly); treatment (LAN, OCT); age (continuous—rather than patient age being categorized according to specific age brackets [e.g., 45–55 years], i.e., a categorical variable—all patient ages were included in the model); sex (male, female); BMI (< 18.5, 18.5 to < 25, 25 to < 30, ≥ 30 kg/m²); time since treatment initiation (3–6 months, > 6 months to < 1 year, 1 year to < 3 years, ≥ 3 years); occurrence of injection-site reactions (yes, no)

lasting > 2 days after their most recent injection was lower with LAN than with OCT for both NETs and acromegaly subgroups (Fig. 2).

Secondary Endpoints

Pain, Interference with Daily Living, Local Site Reactions and Anxiety Associated with Patients' Most Recent Injection Experience

In the Survey population, 46.4% of patients receiving LAN had injection-site pain of any duration after their most recent injection versus 58.8% with OCT (Table 3). Among those who experienced injection-site pain, 33.3% of

patients receiving LAN had pain only during the injection vs. 7.5% receiving OCT.

Among participants who experienced pain, median (95% CI) pain intensity (on a scale of 0 to 10, where higher scores represent greater intensity) was similar with LAN and OCT: 4.00 (3.00–5.00) and 4.00 (4.00–5.00), respectively. Nevertheless, a higher proportion of patients receiving LAN than OCT reported no interference with their daily life resulting from injection-site pain from their latest injection (59.0% vs. 40.0%) (Table 3). By contrast, more patients receiving LAN than OCT reported injection-site reactions (45.2% vs. 33.1%) (Table 3). Similar results on occurrence of injection-site pain, interference with daily life and injection-site

Table 3 Secondary endpoints relating to most recent injection experience (Survey population)^a

Endpoint	Survey population, <i>N</i> = 304		
	LAN (<i>n</i> = 168)	OCT (<i>n</i> = 136)	All (<i>n</i> = 304)
Occurrence of injection-site pain, <i>n</i> (%) [95% CI]	78 (46.4) [39.1–54.0]	80 (58.8) [50.4–66.7]	158 (52.0) [46.4–57.5]
Perceived pain intensity during injection, median (95% CI)^b	4.0 (3.0–5.0)	4.0 (4.0–5.0)	4.0 (4.0–5.0)
Duration of perceived pain at injection site,^b <i>n</i> (%) [95% CI]			
Only during the injection	26 (33.3) [23.9–44.4]	6 (7.5) [3.5–15.4]	32 (20.3) [14.7–27.2]
< 1 day	26 (33.3) [23.9–44.4]	17 (21.3) [13.7–31.4]	43 (27.2) [20.9–34.6]
1–2 days	16 (20.5) [13.0–30.8]	26 (32.5) [23.2–43.4]	42 (26.6) [20.3–34.0]
> 2 days	10 (12.8) [7.1–22.0]	31 (38.8) [28.8–49.7]	41 (25.9) [19.7–33.3]
Extent of interference with daily life from perceived pain at injection site,^b <i>n</i> (%) [95% CI]			
Not at all	46 (59.0) [47.9–69.2]	32 (40.0) [30.0–51.0]	78 (49.4) [41.7–57.1]
A little bit	29 (37.2) [27.3–48.3]	42 (52.5) [41.7–63.1]	71 (44.9) [37.4–52.7]
Quite a bit	3 (3.8) [1.3–10.7]	6 (7.5) [3.5–15.4]	9 (5.7) [3.0–10.5]
Very much	0 (0) [0.0–0.0]	0 (0) [0.0–0.0]	0 (0) [0.0–0.0]
Occurrence of reactions at injection site,^c <i>n</i> (%) [95% CI]	76 (45.2) [37.9–52.8]	45 (33.1) [25.7–41.4]	121 (39.8) [34.5–45.4]
Occurrence of pre-injection anxiety, <i>n</i> (%)^d	100 (59.5)	59 (43.7)	159 (52.5)

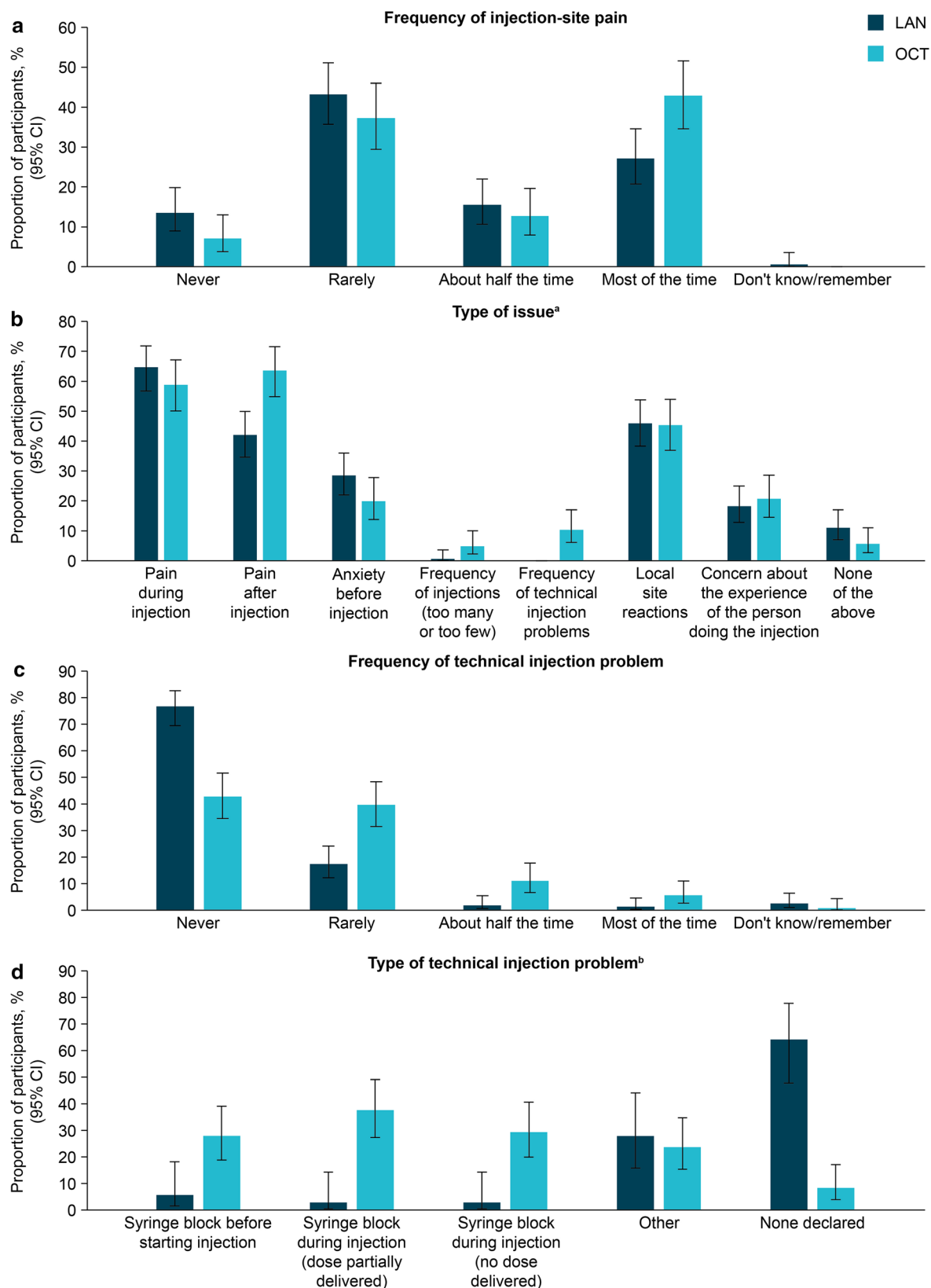
CI confidence interval, LAN lanreotide autogel/depot, NET neuroendocrine tumor, OCT octreotide long-acting release

^aAll participants who completed the survey with no data quality concerns and irrespective of whether they had NETs or acromegaly

^bIn participants who declared injection-site pain with intensity > 0 (pain intensity was rated on a scale of 0 to 10, where higher scores represent greater pain intensity)

^cNodules, bruising or swelling

^dPercentages based on number of patients with data available (168 in the LAN group and 135 in the OCT group)



◀**Fig. 3** Injection-site pain (a), injection-related issues (b) and technical injection problems (c, d) associated with LA SSA injection (Overall experience population^a). ^aParticipants with at least 6 months' experience with their current SSA treatment. ^bParticipants were asked which symptoms/problems they had experienced—data are for those who experienced at least one issue (note that participants could choose more than one issue). ^cIn participants who experienced technical problems (36 participants in the LAN group and 72 in the OCT group). *CI* confidence interval, *LA* long-acting, *LAN* lanreotide autogel/depot, *OCT* octreotide long-acting release, *SSA* somatostatin analog

reactions were observed in the NET and acromegaly subgroups (Supplementary Table S2).

Anxiety before their most recent injection was reported by 59.5% of patients receiving LAN and 43.7% receiving OCT (Table 3). Corresponding values for pre-injection anxiety in the population with NETs were 54.9% (LAN) and 38.5% (OCT) and in the population with acromegaly were 71.7% (LAN) and 56.4% (OCT) (Supplementary Table S2).

In the post hoc multivariate analysis, the odds of pre-injection anxiety were higher for LAN than for OCT (OR [95% CI] 2.40 [1.40–4.11]; $p = 0.0014$). Older age decreased the odds of pre-injection anxiety (OR [95% CI]: 0.97 [0.95–1.00]; $p = 0.0462$), while mild and severe (vs. no) injection-site pain increased the odds (OR [95% CI] 2.19 [1.23–3.90]; $p = 0.0074$ and 9.47 [3.74–23.98]; $p < 0.0001$, respectively).

In the post hoc analysis of data from the LAN group, the proportion of participants reporting anxiety before their most recent injection was higher among those receiving injections by independent administration (72.5%) than among those receiving the injection from an HCP (55.5%).

Pain Associated with Injections Based on Participants' Overall Injection Experience

Participants with at least 6 months' experience with their current SSA treatment (the Overall experience population) also answered questions about their overall experience with SSA injections.

In the Overall experience population, 21 patients (13.5%) in the LAN group and 9 patients (7.1%) in the OCT group had never experienced injection-site pain. Overall, 42 patients (27.1%) in the LAN group and 54 patients (42.9%) in the OCT group reported injection-site pain most of the time (Fig. 3A and Supplementary Table S3).

Issues Associated with Injections Based on Participants' Overall Injection Experience

Among all participants who reported experiencing at least one issue with their injections (89.0% in the LAN group and 94.4% in the OCT group), the most common (with multiple selections allowed) was pain during injection (61.9%), followed by pain after injection (51.6%). Pain after injection was more frequent with OCT than with LAN (Fig. 3B). Other issues (see Fig. 3B) were selected by similar proportions of patients in both treatment groups, though with a tendency for higher percentages for pain during injection and anxiety before injection with LAN than with OCT (pain, 64.5% vs. 58.7%; anxiety, 28.4% vs. 19.8%). The higher frequency of anxiety before injection with LAN (than with OCT) was driven by the participants with acromegaly, among whom 43.2% receiving LAN reported anxiety compared with 22.9% receiving OCT. Within the NETs treatment group, rates of anxiety were similar for the LAN and OCT groups (22.5% and 18.7%, respectively) (Supplementary Table S3).

The most burdensome issues included local site reactions (LAN, 20.2%; OCT, 29.6%), pain during injection (LAN, 34.0%; OCT, 12.3%), pain after injection (LAN, 13.8%; OCT, 33.3%) and anxiety before injection (LAN, 18.1%; OCT, 3.7%) (Supplementary Table S3; results were generally consistent in the disease subgroups). Anxiety was more commonly reported as the most burdensome issue in those treated with LAN by patients with acromegaly (LAN, 25.0%; OCT, 4.8%) than by those with NETs (LAN, 14.5%; OCT; 3.3%).

Technical Injection Problems Based on Participants' Overall Injection Experience

Participants with at least 6 months' experience with their current SSA treatment reported that technical injection problems occurred less frequently with LAN than with OCT (Fig. 3C, D, and Supplementary Table S3). The syringe became blocked either before (20 participants) or during (27 participants) injections in participants in the OCT group compared with two before injection and one during injection in the LAN group. The most frequent consequence of the technical injection problems was needle replacement (meaning that the person performing the injection had to replace the needle on the syringe before the dose could be given), which occurred with 36 participants in the OCT group, but no participants in the LAN group. The whole syringe had to be replaced before the dose could be administered for 17 participants receiving OCT versus two receiving LAN. The patient's appointment had to be rescheduled because of technical injection problems for four participants receiving OCT group and one receiving LAN.

Most Important Benefits of Independent Injection

Among the 102 non-US participants (i.e., those potentially eligible for independent injection), 40 had their most recent LAN injection administered by independent injection (NETs, $n = 29$; acromegaly, $n = 11$). The most common reasons for choosing independent injection were 'It gave me flexibility' (80.0%), 'It saved time' (70.0%), 'The injection is easy to do' (60.0%) and 'It helped me feel more independent' (45.0%). Results were similar in the NET and acromegaly subgroups, except for 'The injection is easy to do' (NETs, 69.0%; acromegaly, 36.4%). However, due to the small number of participants in the acromegaly subgroup, it is not possible to determine whether this difference is meaningful; further research is needed.

DISCUSSION

Patients' experiences of their disease management have a critical role in their adherence to

treatment, and in their overall outcomes, particularly in chronic conditions [13, 14]. PRESTO 2 is the first international online patient survey comparing the latest LAN and OCT devices/formulations in patients with NETs or acromegaly. In the primary analysis, the likelihood of patients experiencing pain lasting > 2 days was significantly lower with LAN than with OCT when controlled for disease group and occurrence of injection-site reactions. These results were supported by the secondary analyses, which showed that fewer patients treated with LAN than with OCT experienced injection-site pain of any duration and fewer LAN-treated patients reported that pain after injection was one of the most burdensome issues. Also, fewer patients receiving LAN than OCT reported pain "most of the time."

Patients reported that the injection-related issues associated with the greatest burden were pain after injection and local injection-site reactions (both more common with OCT than with LAN) as well as pain during injection and pre-injection anxiety (the latter more common with LAN than with OCT). Importantly, from the patient's perspective, fewer participants receiving LAN than OCT reported that injection-site pain interfered with their daily living, possibly because of the smaller proportion of patients with injection-site pain lasting > 2 days in the LAN (vs. OCT) group, and relatively few patients in either treatment group reported substantial interference with daily living as a result of injection-site pain.

Pre-injection anxiety was assessed via several secondary endpoints, and the results suggested that more patients receiving LAN than OCT experienced pre-injection anxiety. These results contrast with those of a previous study in patients with NETs that reported lower rates of pre-injection anxiety with LAN than with OCT [24]. The subgroup and post hoc analyses of PRESTO 2 provide some insight into the potential drivers of anxiety: pre-injection anxiety was more common in the acromegaly (vs. NETs) disease group and in patients receiving LAN via independent (vs. HCP-administered) injections. LAN, but not OCT, is approved for independent administration, which may in part

explain why pre-injection anxiety was higher in the LAN group. Greater training and education of patients/caregivers conducting independent LAN injections may help to mitigate these issues.

Compared with the LAN group, more than twice as many participants receiving OCT reported technical injection problems. These results are clinically relevant and may indicate that further improvements in the devices are warranted or that improved education around the injection process is required. As well as affecting patients, technical problems may have a negative impact on healthcare costs if they lead to syringe/device replacement and rescheduling of appointments. In the PRESTO simulated-use study, 97.8% of nurses preferred the LAN syringe to the OCT syringe, and one of the attributes most frequently rated as being the most important was confidence that the syringe would not become clogged [18].

Almost 40% of eligible (i.e., non-US) participants received independent LAN injection. The most common reasons participants gave for choosing independent injection were that it gave them flexibility, saved time, was easy to do and helped them feel more independent. These findings indicate that independent injection is a valuable treatment option for a substantial number of patients. However, the findings also indicate a potential need to increase patients' confidence and level of training on non-HCP injection to reduce or avoid pre-injection anxiety and/or pain during injection. Fewer participants with acromegaly than with NETs specified that the reason for choosing independent injection was because the injection was easy to do; this finding may reflect the physical difficulties associated with acromegaly (i.e., larger fingers and hands, making it more difficult to hold the syringe).

Strengths and Limitations

PRESTO 2 is the first international, English-language, online survey in patients receiving current LA SSA therapies and captures direct insights from many patients in Ireland, North America and the UK. Several earlier studies have

compared patients' experiences of LAN and OCT treatment for NETs and/or acromegaly [15]; however, none of these older studies were in patients treated with the current LAN syringe. A more recent study (a prospective, single-blind, single-center "crossover" study in 51 patients with NETs) found that mean pain scores over the first three injections were similar for LAN and OCT but, unlike PRESTO 2, pain was only assessed immediately after the injection—delayed pain was not measured [25]. PRESTO 2 assessed factors identified as being important to the patient's experiences of LAN and OCT treatment, i.e., injection pain, injection time and convenience, technical problems and emotional aspects/anxiety [15]. Furthermore, an expert in PROs tested the validity of the questionnaire through a cognitive debriefing with a small group of patients ($n = 5$), ensuring its robustness before use in the survey.

Another strength of PRESTO 2 was the use of patient groups and networks to help ensure the enrollment of relevant individuals. The survey also included data capture fields to validate participants as genuine recipients of SSA therapy; as such, the characteristics of the study population were generally consistent with those expected for patient populations with NETs or acromegaly. One exception is the overrepresentation of female participants, though this is typical of surveys [26]; also, sex did not have a significant effect on the primary endpoint in the logistic regression modeling, suggesting that the overrepresentation of women is not likely to have affected the findings. Finally, a minority of patients recorded 'do not know' answers, which implies a high-quality survey design and supports the value of including cognitive debriefings with patients with NETs or acromegaly as part of the design process.

Limitations include possible selection bias in view of recruitment of participants via patient organizations and potential recall bias, particularly related to overall injection experience. The use of an online survey may also be a source of bias in the form of variation in participation due to demographic differences (sex, age) and/or level of education. Also, the study was conducted in a small number of English-speaking countries and in English language only,

limiting the ethnic diversity of the participants. The small size of the acromegaly subgroup limits the ability to draw strong disease-specific conclusions. Also, the impact (on patients' responses/experiences) of conducting the survey during the COVID-19 pandemic is unknown. Results for LAN are specific to the current syringe design and cannot be extrapolated to earlier versions of the syringe or to generic products. Likewise, the vast majority of patients in the OCT group were being treated with proprietary OCT. In patients with NETs, there were some differences in baseline characteristics between the LAN and OCT groups, but these differences were not unexpected given the variations in the licensed indications for LAN and OCT and the dates of product approval.

CONCLUSIONS

In this survey, LAN was associated with advantages relative to OCT in terms of less prolonged pain at the injection site, less interference of injection-site pain with everyday life and fewer occurrences of technical problems. More patients receiving LAN than OCT reported anxiety before injection, although these findings may reflect the fact that LAN, but not OCT, can be administered by independent injection. Overall, the results demonstrate the importance of mode of injection and device for the injection experience of patients with acromegaly or NETs using LA SSAs. The results also highlight the impact of SSA therapy on patients' everyday lives and the need to consider and improve this aspect of patient management.

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speaker for, and conducts research on behalf of, Ipsen.

Compliance with Ethics Guidelines. The survey was reviewed and approved by the Western Instructional Review Board (IRB protocol number 20202117). Ethical committee review was not required in Ireland or the UK. The survey was conducted in compliance with relevant regulations pertaining to the ethical conduct of patient surveys, including with the Declaration of Helsinki [22] and with the International Ethical Guidelines for Epidemiological Studies published by the Council for International Organizations of Medical Sciences [23]. All participants had to provide consent in an electronic format before starting the survey.

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Data Availability. Qualified researchers may request access to patient-level study data that underlie the results reported in this publication. Additional relevant study documents, including the clinical study report, study protocol with any amendments, annotated case report form, statistical analysis plan and dataset specifications may also be made available. Patient level data will be anonymized, and study documents will be redacted to protect the privacy of study participants. Where applicable, data from eligible studies are available 6 months after the studied medicine and indication have been approved in the US and EU or after the primary manuscript describing the results has been accepted for publication, whichever is later. Further details on Ipsen's sharing criteria, eligible studies and process for sharing are available here (<https://vivli.org/members/ourmembers/>). Any requests should be

submitted to www.vivli.org for assessment by an independent scientific review board.

REFERENCES

1. Caplin ME, Pavel M, Ćwikła JB, Phan AT, Raderer M, Sedláčková E, et al. Lanreotide in metastatic enteropancreatic neuroendocrine tumors. *N Engl J Med*. 2014;371(3):224–33.
2. Strosberg J, Kvols L. Antiproliferative effect of somatostatin analogs in gastroenteropancreatic neuroendocrine tumors. *World J Gastroenterol*. 2010;16(24):2963–70.
3. Melmed S. Medical progress: acromegaly. *N Engl J Med*. 2006;355(24):2558–73.
4. Melmed S, Bronstein MD, Chanson P, Klubanski A, Casanueva FF, Wass JAH, et al. A consensus statement on acromegaly therapeutic outcomes. *Nat Rev Endocrinol*. 2018;14(9):552–61.
5. Vilar L, Vilar CF, Lyra R, Lyra R, Naves LA. Acromegaly: clinical features at diagnosis. *Pituitary*. 2017;20(1):22–32.
6. Grozinsky-Glasberg S, Davar J, Hofland J, Dobson R, Prasad V, Pascher A, et al. European neuroendocrine tumor society (ENETS) 2022 guidance paper for carcinoid syndrome and carcinoid heart disease. *J Neuroendocrinol*. 2022;2:e13146.
7. Shah MH, Goldner WS, Benson AB, Bergsland E, Blaszkowsky LS, Brock P, et al. Neuroendocrine and Adrenal Tumors, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network : JNCCN*. 2021;19(7):839–68.
8. Ipsen Ltd. Summary of product characteristics, Somatuline Autogel 60 mg, 90 mg, 120 mg, solution for injection in a prefilled syringe. European Medicines Compendium 2021 [Available from: <https://www.medicines.org.uk/emc/product/4808/smpc>].
9. Ipsen Pharma. Prescribing Information, Somatuline® Depot (lanreotide) injection for subcutaneous use 04/2019 [Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022074s0241bl.pdf].
10. Novartis Pharmaceuticals Corporation e. Prescribing information, Sandostatin LAR® Depot (octreotide acetate for injectable suspension) 03/2021 [Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021008s0411bl.pdf].

11. Novartis Pharmaceuticals UK Ltd. Prescribing information, Sandostatin LAR 10 mg powder and solvent for suspension for injection. European Medicines Agency 2018 [Available from: <https://www.medicines.org.uk/emc/product/1038/smpc>.
12. Teva UK Limited. Prescribing information, Olatuton 30 mg Powder and Solvent for Prolonged-release Suspension for Injection. European Medicines Agency 2018 [Available from: <https://www.medicines.org.uk/emc/product/10841/smpc>.
13. Forestier B, Anthoine E, Reguiat Z, Fohrer C, Blanchin M. A systematic review of dimensions evaluating patient experience in chronic illness. *Health Qual Life Outcomes*. 2019;17(1):19.
14. Glasgow RE, Wagner EH, Schaefer J, Mahoney LD, Reid RJ, Greene SM. Development and validation of the patient assessment of chronic illness care (PACIC). *Med Care*. 2005;43(5):436–44.
15. Cella D, Evans J, Feuilly M, Neggers S, Van Genechten D, Herman J, et al. Patient and healthcare provider perspectives of first-generation somatostatin analogs in the management of neuroendocrine tumors and acromegaly: a systematic literature review. *Adv Ther*. 2021;38(2):969–93.
16. Adelman DT, Van Genechten D, Megret CM, Truong Thanh XT, Hand P, Martin WA. Co-creation of a lanreotide autogel/depot syringe for the treatment of acromegaly and neuroendocrine tumours through collaborative human factor studies. *Adv Ther*. 2019;36(12):3409–23.
17. Delemer B, Nguyen-Tan-Hon T, Coriat R, Smith D, Schillo F, Raingeard I, et al. Evaluation of nurses' and patients' overall satisfaction with new and previous formulations of octreotide long-acting release (sandostatin LAR®): a French observational study. *Adv Ther*. 2020;37(9):3901–15.
18. Adelman D, Truong Thanh XM, Feuilly M, Houchard A, Cella D. Evaluation of nurse preferences between the lanreotide autogel new syringe and the octreotide long-acting release syringe: an international simulated-use study (PRESTO). *Adv Ther*. 2020;37(4):1608–19.
19. Adelman DT, Burgess A, Davies PR. Evaluation of long-acting somatostatin analog injection devices by nurses: a quantitative study. *Medical devices (Auckland, NZ)*. 2012;5:103–9.
20. Ryan P, Phan AT, Adelman DT, Iwasaki M. Neuroendocrine tumors and lanreotide depot: clinical considerations and nurse and patient preferences. *Clin J Oncol Nurs*. 2016;20(6):E139–46.
21. Strasburger CJ, Karavitaki N, Störmann S, Trainer PJ, Kreitschmann-Andermahr I, Droste M, et al. Patient-reported outcomes of parenteral somatostatin analogue injections in 195 patients with acromegaly. *Eur J Endocrinol*. 2016;174(3):355–62.
22. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191–4.
23. Council for International Organizations of Medical Sciences. International ethical guidelines for epidemiological studies. Available from: <https://cioms.ch> (Accessed 20 December 2021) 2009.
24. Ström T, Kozlovacki G, Myrenfors P, Almquist M. Patient and nurse experience of using somatostatin analogues to treat gastroenteropancreatic neuroendocrine tumors: results of the somatostatin treatment experience trial (STREET). *Patient Preference Adherence*. 2019;13:1799–807.
25. Raj N, Cruz E, O'Shaughnessy S, Calderon C, Chou JF, Capanu M, et al. A randomized trial evaluating patient experience and preference between octreotide long-acting release and lanreotide for treatment of well-differentiated neuroendocrine tumors. *JCO Oncol Pract*. 2022;2:200055.
26. Smith G. Does gender influence online survey participation?: A record-linkage analysis of university faculty online survey response behavior. ERIC Document Reproduction Service No. ED 501717 2008.

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