OPEN

PRS GLOBAL OPEN

ORIGINAL ARTICLE
Cosmetic

CONTOUR Australia: Condition of Submental Fullness and Treatment Outcomes with Belkyra Registry

Sarah G. Boxley, MBBS, FRACGP, FACAM*
Frank Lin, MBBS, FRACS†
Neville Lee See, MBBS‡
Suzanne St. Rose, PhD, MBA§
Simona Battucci, MD¶
Susan Simonyi, BScN, RN‖

Background: Submental fat (SMF) contributes to an aged or overweight appearance that may negatively impact an individual's psychological well-being. Deoxycholic acid (ATX-101) is an injectable formulation of deoxycholic acid approved to treat SMF. The Condition of Submental Fullness and Treatment Outcomes Registry (CONTOUR) Australia study was designed to understand treatment patterns and outcomes with ATX-101 in Australia.

Methods: CONTOUR Australia was a phase 4, prospective, observational, multicenter registry that enrolled adults considering treatment for SMF reduction.

Results: The registry enrolled 86 patients from six sites. Significant changes from baseline through the end of treatment indicated improvement in mild to moderate fullness associated with SMF on the Clinician-Reported SMF Rating Scale and the Patient-Reported SMF Rating Scale, improvement in SMF-associated psychological impact after treatment on the Patient-Reported SMF Impact Scale, no overall worsening in skin laxity based on Submental Skin Laxity Grade, and increased patient satisfaction with the face/chin on the Subject Self-Rating Scale after receiving treatment. Adverse events were all mild and mostly related to the injection site (ie, bruising and swelling).

Conclusion: CONTOUR Australia observed clinically meaningful and significant outcomes and further supports ATX-101 as a well-tolerated and effective treatment for SMF reduction. *(Plast Reconstr Surg Glob Open 2023; 11:e5123; doi: 10.1097/GOX.0000000000005123; Published online 18 July 2023.)*

INTRODUCTION

Genetics or lifestyle factors can result in fat accumulation in the preplatysmal submental area, also known as submental fat (SMF).[1,2] During aging, excess SMF and weakening of the mandible septum, which holds fat compartments in place, obscure jawline contour/definition, thus contributing to an aged or overweight appearance, which may negatively impact an individual's psychological well-being.[1,3,4] Minimally invasive techniques for SMF reduction have become increasingly popular because they require less recovery time and can be used as part of a multimodal approach to create customizable treatment plans.[5]

ATX-101 [Belkyra in Australia, Canada, Europe, and South Korea, and Kybella in the United States; Kythera Biopharmaceuticals, Inc. (an affiliate of Allergan)] is an injectable formulation of deoxycholic acid, a secondary bile acid involved in dietary fat emulsification.[2,6] ATX-101 causes adipocyte lysis when injected into subcutaneous fat tissue.[2,6] Clinical trials have demonstrated the safety and efficacy of ATX-101 for reducing SMF and for improving patient satisfaction with the chin/jawline.[7–11] Real-world clinical practice setting data from the Condition of Submental Fullness and Treatment Outcomes Registry

*From *SkinBox Clinics, Perth, WA, Australia; †Eastern Plastic Surgery, Box Hill North, VIC, Australia; ‡Kiora Medical Spa, Hawthorn, VIC, Australia; §Global Epidemiology Pharmacovigilance and Patient Safety, AbbVie, Marlow, United Kingdom; ¶Pharmacovigilance and Patient Safety, AbbVie, Rome, Italy; and ‖Clinical Program Development, AbbVie, Singapore.*

Received for publication June 16, 2022; accepted June 1, 2023.

DOI: 10.1097/GOX.0000000000005123

Disclosure statements are at the end of this article, following the correspondence information.

Related Digital Media are available in the full-text version of the article on www.PRSGlobalOpen.com.

(CONTOUR) study North America provided insights on the types of patients who seek SMF reduction, patient and physician treatment goals, and posttreatment perspectives.[12,13]

After the approval of ATX-101 in Australia in July 2016 for the treatment of submental fullness due to SMF,[14] we conducted the current registry study (CONTOUR Australia) to develop a comprehensive understanding of how ATX-101 is utilized in clinical practice in Australia and assess the risks and benefits associated with its treatment.

Takeaways

Question: What are the treatment patterns and clinical outcomes of the injectable form of deoxycholic acid in Australia?

Findings: The Condition of Submental Fullness and Treatment Outcomes Registry (CONTOUR) Australia study (a phase 4, prospective, observational, multicenter registry) showed improvement in mild to moderate fullness associated with submental fat and increased patient satisfaction with face/chin on clinician- and patient-assessed rating scales after treatment with deoxycholic acid, with no overall worsening in skin laxity. Adverse events were mild and mostly related to the injection site.

Meaning: CONTOUR Australia demonstrated clinically meaningful outcomes that further support deoxycholic acid as a well-tolerated and effective treatment for submental fat reduction.

METHODS

Patients

Eligible patients were adults aged 18 years or older presenting with submental fullness due to accumulation of unwanted SMF and considered by their treating physician to be a candidate for SMF reduction. Key exclusion criteria included severe skin laxity, any other cause of fullness in the submental region (eg, thyroid enlargement, thyromegaly, cervical adenopathy, cervical lymphadenopathy, pronounced submandibular glands, lymph nodes, and muscles), and current or previous participation in an interventional clinical study involving ATX-101.

Study Design

CONTOUR Australia was a phase 4, prospective, observational, multicenter registry for patients with SMF treated with ATX-101 to help understand treatment patterns and outcomes in Australia. Study approval was obtained from each center's independent ethics committee, and all patients provided written informed consent. No treatment assignment was performed in the study. Physicians and patients must have agreed on ATX-101 treatment before study enrollment. Patients who elected treatment were followed up until their SMF reduction treatment was completed or discontinued. Enrolled patients were assessed regularly by their treating physician according to usual clinical practice. Data collection was anticipated to continue for approximately 15 months after enrollment. The duration of individual patient participation (treatment and retreatment) varied depending on treatment characteristics, individual requirements, and the discretion of the treating physician.

The registry included four phases: enrollment visit, baseline visit, follow-up visit, and end-of-treatment (EOT) visit. The EOT visit occurred either at the last scheduled follow-up visit after completion of ATX-101 treatment, within 3 months of the last treatment session, when a patient elected to discontinue treatment, or before study closure.

Study Procedures

ATX-101 was injected into the subcutaneous fat tissue in the submental area using an area-adjusted dose of 2 mg per cm^2. A single treatment consisted of up to 50 injections, 0.2 mL per injection supplied in single-use vials (up to a total of 10 mL), spaced 1 cm apart. Up to six single treatments could be administered at intervals no less than 1 month apart.

Assessments and End Points

The primary effectiveness end points have been used in previous clinical studies[15,16] and in the CONTOUR North America study.[12,13] SMF severity was assessed using the validated Clinician-Reported Submental Fat Rating Scale (CR-SMFRS; 0 = absent, 1 = mild, 2 = moderate, 3 = severe, and 4 = extreme) and validated Patient-Reported Submental Fat Rating Scale (PR-SMFRS; 0 = no chin fat, 1 = slight amount, 2 = moderate amount, 3 = large amount, 4 = very large amount); lower values indicate improvement/less SMF.[15,17] The psychological impact of SMF was evaluated using the validated Patient-Reported Submental Fat Impact Scale (PR-SMFIS), with scores ranging from 0 (no impact) to 10 (greatest negative impact).[15,17] Skin laxity was assessed using the Submental Skin Laxity Grade (SMSLG; 1 = none, 2 = mild, 3 = moderate, 4 = severe).[15] Patient satisfaction with the appearance of the face and chin was evaluated using the seven-point Subject Self-Rating Scale (SSRS), ranging from 0 (extremely dissatisfied) to 6 (extremely satisfied).[15] The patient's self-perception of age (SPA),[18] which assesses whether the patient perceives oneself to look younger or older than actual age, was also evaluated. With the exception of the SPA scale, which was assessed during enrollment and at the EOT visit only, these end points were assessed at enrollment, follow-up visits, and the EOT visit.

Other effectiveness end points collected during the EOT were the patient global questions (PGQ), as well as patient EOT and physician EOT questionnaires, which have also been used in previous clinical studies[7,8] and the CONTOUR North America study.[13] The PGQ included patients' ratings of the fat under the chin, definition between the chin and neck, and satisfaction with treatment. Pain scores based on the pain numeric rating scale were collected at each treatment session, follow-up visit, and EOT and were categorized into four severity categories: none (0), mild (1–3), moderate (4–6), and severe (7–10). The worst category of pain experienced at patient level throughout the study was reported.

Additional assessments included the Physician Practice Setting Questionnaire and the Patient and Physician Treatment Goals questionnaires. Exposure to study treatment was also assessed. Treatment details and treatment procedures questionnaires were completed by the physician at the enrollment visit, each treatment session, and all follow-up visits. (**See document, Supplemental Digital Content 1**, which describes these questionnaires in more detail. **http://links.lww.com/PRSGO/C659**.) The incidence, severity, and duration of adverse events (AEs) were assessed throughout the study in the safety population, which included all patients who received at least 1 ATX-101 injection.

Statistical Analyses

Effectiveness analyses were performed on the evaluable population, which consisted of all enrolled patients who received at least one ATX-101 injection, as well as at least one effectiveness assessment at the enrollment visit (baseline) and at least one effectiveness assessment at the follow-up or EOT visit.

SMF assessments were summarized using descriptive statistics. For the follow-up and EOT visits, the mean change from baseline for each SMF assessment was analyzed using a paired *t* test. The number and proportion [and its associated 95% Clopper-Pearson confidence interval (CI)] of patients with at least a one-grade improvement in the assessment were reported for CR-SMFRS, PR-SMFRS, SMSLG, and SSRS. SPA assessments were summarized as frequency counts. For the categorical responses in the PGQ, the 95% CIs for the proportion of the response categories of interest were reported. Data from the Physician Practice Setting Questionnaire, the Patient and Physician Treatment Goals Questionnaires, exposure to study treatment, as well as treatment procedures and details questionnaires were summarized using descriptive statistics. AEs were summarized using descriptive statistics. Statistical analyses were performed using SAS software, version 9.3 (SAS Institute, Cary, N.C.).

RESULTS

Site and Physician Characteristics

A total of six Australian sites/practices were involved in the study. The mean percentage of practices that focused on facial aesthetics was 72.5%. The sites provided aesthetic treatments for a mean of 13.2 years and had a median number of two physicians per site who focused on aesthetics. All six sites used injectable treatments. The mean percentage of patients presenting to the practices in the past week who had submental fullness due to SMF was 31.5%; only 0.8% of patients were referred by other physicians for treatment. The most frequently reported treatment options by sites were energy devices (laser- and radiofrequency-specified) and injectables (ATX-101), which were reported in five sites each (83.3%).

Patients

Of the 86 patients enrolled in the registry study, 79 (91.9%) were in the safety population, whereas 77 patients comprised the evaluable population. The majority of patients (75/86, 87.2%) completed the study. Among the 11 patients who did not complete the study, seven (8.1%) patients were lost to follow-up, three (3.5%) decided to discontinue, and one (1.2%) did not complete for other reasons (pregnancy).

Table 1. Baseline Demographic Parameters

Parameter	Enrolled Population (N = 86)
Mean (SD; range) age, y	43.2 (10.2; 24–66)
Women, n (%)	82 (95.3)
Mean (SD) weight, kg	67.9 (10.8)
Mean (SD; range) BMI, kg/m^2	25.2 (3.7; 16.6–34.8)
Race, n (%)	
White	62 (72.1)
Asian (Chinese)	23 (26.7)
Not reported	1 (1.2)
Lifestyle and medical history, n (%)	
Smoker	6 (7.0)
Diabetes	1 (1.2)
Hypertension	2 (2.3)
Other	1 (1.2)

The majority of enrolled patients were women (95.3%) and White (72.1%), with a mean age of 43.2 years, a mean weight of 67.9 kg, and a mean body mass index of 25.2 kg per m^2. Most patients were nonsmokers (Table 1). At the end of treatment, the change from baseline (mean [SD]) in weight (n = 56) and body mass index (n = 55) was 0.1 (3.55) kg and –0.0 (1.4) kg/m^2, respectively.

Patient and Physician Treatment Goals Questionnaires

According to physicians, the top two goals for patients were to achieve a more defined jawline (34/86 patients, 39.5%) and to achieve an ideal submental contour (31/86 patients, 36.0%). The top four treatment goals endorsed by patients were to achieve a more defined jawline (40/86, 46.5%), to look younger (18/86, 20.9%), to look thinner (12/86, 14.0%), and to feel more confident (6/86, 7.0%). The mean amount of time patients had concerns about their double chin was 65.0 months. The majority of patients (76/86, 88.4%) did not receive previous SMF treatment, and most patients (61/86, 70.9%) did not report weight change in the past 12 months. A total of 37 patients (43.0%) reported being lightly active (1–3 days/week), 31 (36.0%) reported being moderately active (3–5 days/week), and 16 (18.6%) reported being sedentary.

Treatment Procedures and Details

A summary of treatment procedures and details for the baseline and first follow-up visits are presented in Table 2. Similar results were observed for follow-up visits two to four. The majority of patients did not receive other treatments in combination with ATX-101. However, for patients who received concomitant aesthetic treatments, the most frequently coadministered treatments were injectables, specifically botulinum toxin.

Extent of Exposure

Table 3 summarizes the extent of exposure. The average treatment duration was 104.5 days with an average number of 1.6 treatment sessions, an average interval

Table 2. Treatment Procedures and Details (Safety Population)

Parameter	Baseline	Follow-up Visit 1
Skin marking grid used		
n/N (%)	54/79 (68.4)	31/33 (93.9)
Mean application time, min	2.8	5.2
Pretreatment comfort regimen used		
n/N (%)	68/79 (86.1)	29/33 (87.9)
Effectiveness, n/N (%)	63/68 (92.6)	29/29 (100.0)
Patients who received other treatments, n/N (%)	10/79 (12.7)	3/33 (9.1)
Mean number of other treatments given	1.5	1.5
Other treatment categories		
Energy-based devices (eg, laser, ultrasound), n/N (%)	3/79 (3.8)	0/33 (0.0)
Injectables (eg, botulinum toxin, dermal fillers)	8/79 (10.1)	3/33 (9.1)
Other (eg, skin booster)	1/79 (1.3)	0/33 (0.0)
Mean time spent for patient consultation, min	20.3	
Mean time to administer treatment, min	10.0	
Mean time to posttreatment, min	12.1	

Table 3. Exposure to Treatment over the Study Period (Safety Population)

Parameter	Result
Treatment duration, d* (N = 79)	
Mean (SD)	104.5 (120.6)
Median (range)	58.0 (1.0–372.0)
Number of sessions (N = 79)	
Mean (SD)	1.6 (0.9)
Median (range)	1.0 (1.0–6.0)
Total volume of injection, mL	
Mean (SD)	3.6 (1.5)
Median (range)	4.0 (2.0–8.0)
Volume of treatment per injection site, mL (N = 78)	
Mean (SD)	0.2 (0.1)
Median (range)	0.2 (0.1–0.5)
Interval between treatments, days† (N = 33)	
Mean (SD)	73.4 (39.5)
Median (range)	65.0 (24.0–220.0)
Injection instrument used	
Needle, n/N (%)	78/79 (98.7)
Cannula, n/N (%)	1/79 (1.3)
Off-label use, n/N (%)‡	7/79 (8.9)
Total volume injected outside of submentum (mL)	
Mean (SD)	1.6 (1.3)
Median (range)	0.8 (0.4–3.6)

*Treatment duration in days was calculated as date of last treatment session – (date of index treatment + 1).
†Patients who had only one treatment session were excluded. The interval between treatments was calculated as treatment duration in days/(number of treatment sessions during the treatment period – 1).
‡"Off-label use" refers to the use of ATX-101 outside the approved submental area.

between sessions of 73.4 days, and an average volume of ATX-101 administered per injection site of 0.2 mL (Table 3). The mean (SD) injection volume across all treatment sessions was 3.6 (1.5) mL. The total volume of ATX-101 administered per treatment decreased from a mean (SD) of 3.7 (1.4) mL at treatment 1 (n = 79) to 2.7 (1.2) mL at treatment 4 (n = 3).

Primary Effectiveness End Points

Mean CR-SMFRS, PR-SMFRS, PR-SMFIS, and SMSLG scores decreased from baseline through the EOT (Figs. 1 and 2). Mean SSRS scores increased from baseline through the EOT (Fig. 2). Compared with baseline, the mean changes from baseline in CR-SMFRS, PR-SMFRS, PR-SMFIS, SMSLG, and SSRS scores were significantly different across follow-up visits one to three and EOT. By the EOT visit, the majority of patients had a 1-grade or more improvement in CR-SMFRS (Fig. 1), PR-SMFRS, and SSRS scores, whereas 41.7% (30/72) of patients had a 1-grade or more improvement in SMSLG scores (Table 4). The mean (SD) number of treatment sessions for patients with a 1-grade or more improvement in CR-SMFRS and PR-SMFRS scores was 1.6 (1.02) and 1.7 (0.98) sessions, respectively. In the SPA assessment, 27.3% (21/77) of patients at the EOT visit thought that they looked younger than their actual age (median number of years younger, 4; range, 2–10) compared with 14.3% (11/77) of patients at baseline (Fig. 3). Similarly, the number of patients who thought that they looked older than their actual age decreased from 28.6% to 1.3%. Representative patient photographs taken before and after treatment are shown in Figures 4 and 5.

Additional End Points

Based on PGQ responses at the EOT, more than 70% of patients rated the fat under their chin and the definition between chin and neck as moderately or a great deal better, and more than 75% of patients were moderately or extremely satisfied with their treatment (Table 4).

At baseline, the mean (SD) pain numeric rating scale score was 4.1 (2.5), which decreased to 3.1 (2.2) at post-baseline treatment visit 1 and 2.6 (2.6) at the EOT visit. An equal number of patients reported worst pain experienced as mild and moderate (28/77, 36.4% for each category), whereas 26.0% (20/77) of patients reported the worst pain experienced as severe.

On the patient EOT questionnaire, 49 of 77 patients (63.6%) reported that they achieved their treatment goals, 17 (22.1%) indicated that they partially achieved their treatment goals, and only seven patients (9.1%) reported that they did not achieve their treatment goals. The most frequently reported reason for patients ending SMF reduction treatment was meeting their treatment goal (38/77, 49.4%), followed by treatment being too expensive (11/77, 14.3%). More than half of patients (53.2%) reported that meeting their treatment goal was the main reason for ending treatment. Additionally, 77.9% of patients indicated that after ending treatment they would undergo treatment again.

Responses to the physician EOT questionnaire (**See table, Supplemental Digital Content 2,** which shows the physician end-of-treatment questionnaire. **http://links.lww.com/PRSGO/C660**) showed that physicians achieved

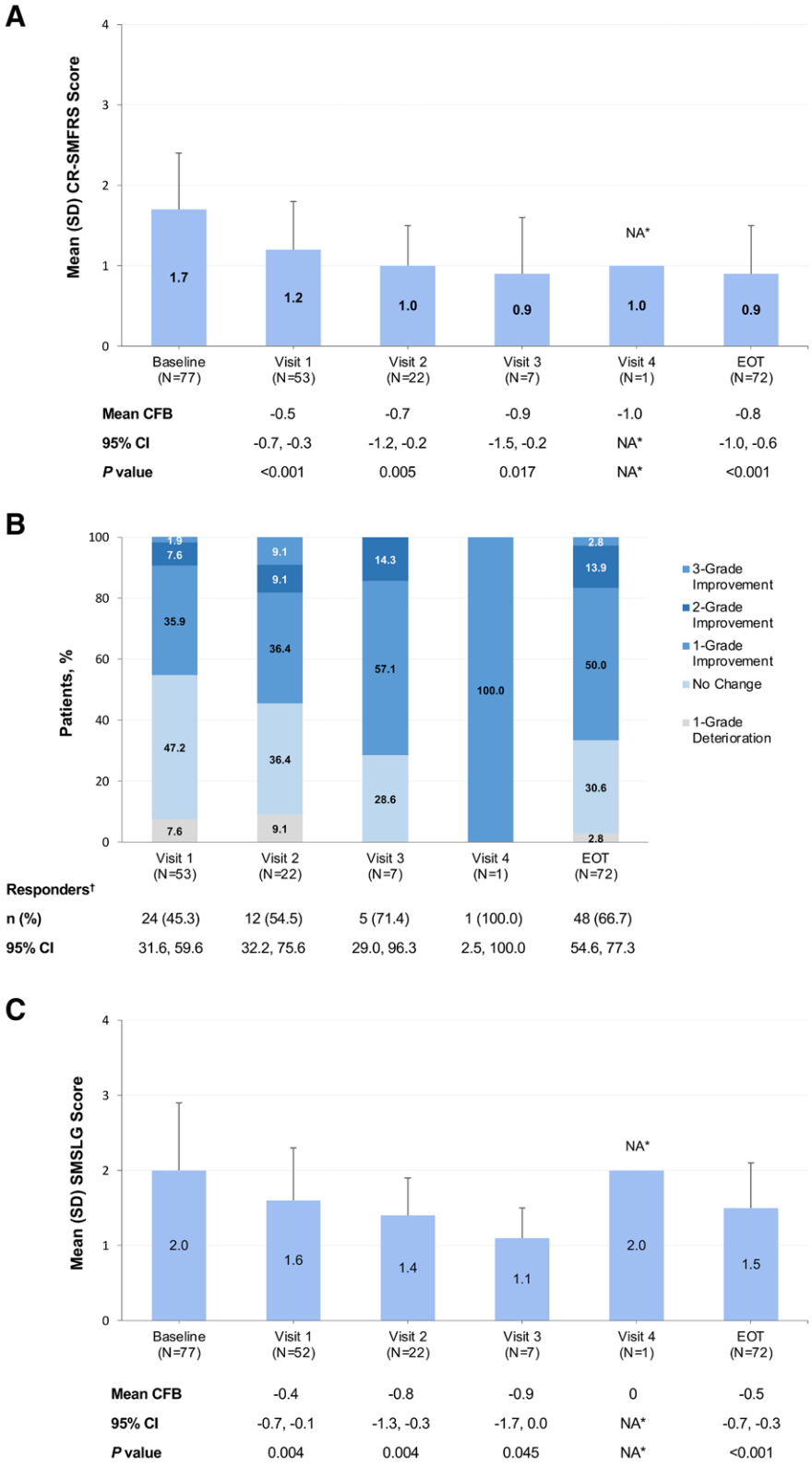

Fig. 1. Clinician-reported end points. A, Mean CR-SMFRS score by visit. B, Percentage of patients showing no. 1-, 2-, or 3-grade improvements, or a 1-grade deterioration, in CR-SMFRS by visit. C, Mean SMSLG score by visit. CFB, change from baseline; NA, not available. *No statistics available because n = 1. †CR-SMFRS 1-grade or more improvement.

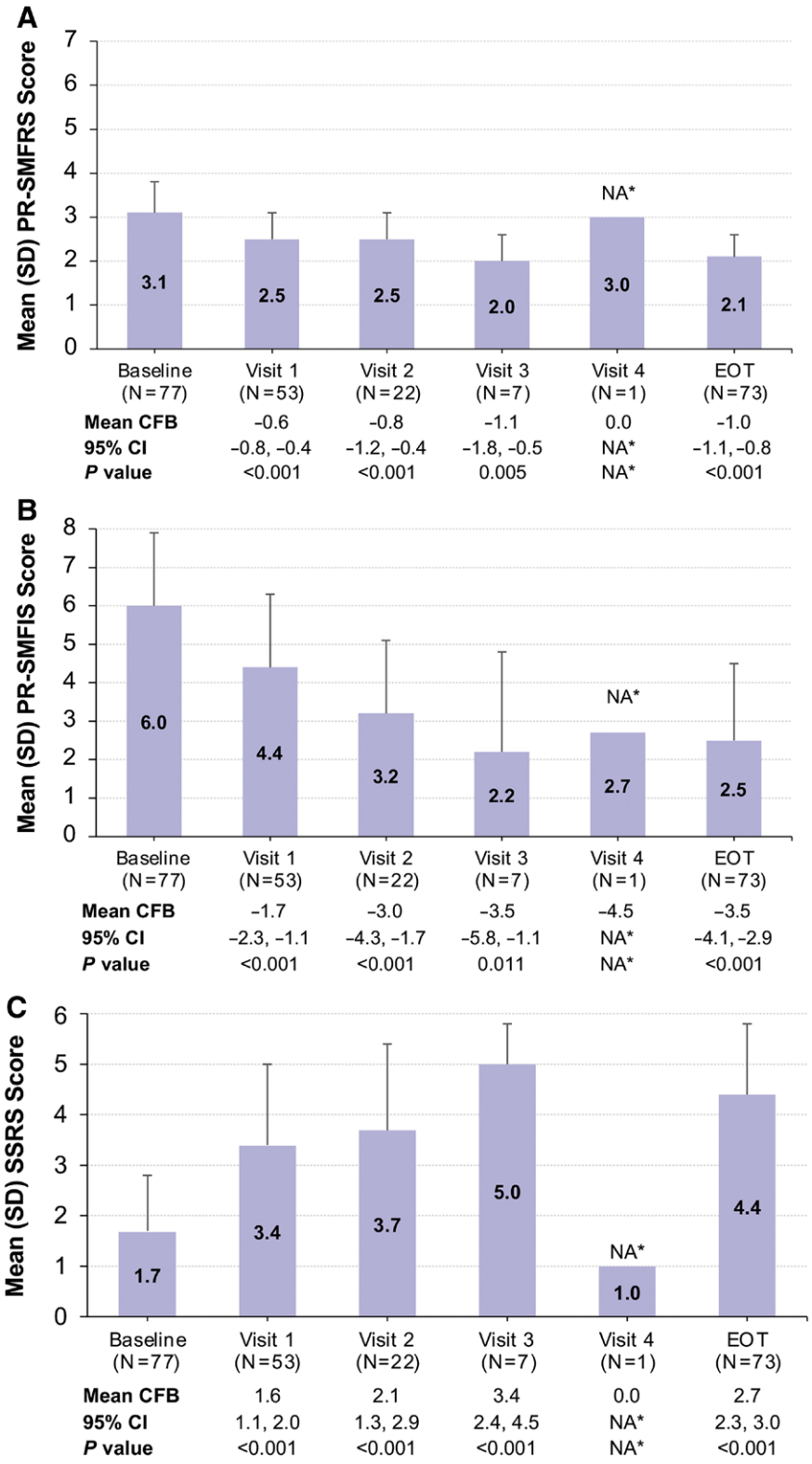

Fig. 2. Patient-reported end points. A, Mean PR-SMFRS score by visit. B, Mean PR-SMFIS score by visit. C, Mean SSRS score by visit. CFB, change from baseline; NA, not available. *No statistics available because n = 1.

Table 4. Responder Rates for Primary Effectiveness End Points (Evaluable Population)

End Point	Visit	Result	95% CI
PR-SMFRS ≥1-grade improvement, n/N (%)	1	27/53 (50.9)	36.8, 64.9
	2	14/22 (63.6)	40.7, 82.8
	3	6/7 (85.7)	42.1, 99.6
	4	0/1 (0.0)	NA*
	EOT	54/72 (75.0)	63.4, 85.4
SMSLG ≥1-grade improvement, n/N (%)	1	17/52 (32.7)	20.3, 47.1
	2	11/22 (50.0)	28.2, 71.8
	3	4/7 (57.1)	18.4, 90.1
	4	0/1 (0.0)	NA*
	EOT	30/72 (41.7)	30.2, 53.9
SSRS ≥1-grade improvement, n/N (%)	1	37/53 (69.8)	55.7, 81.7
	2	18/22 (81.8)	59.7, 94.8
	3	7/7 (100.0)	59.0, 100.0
	4	0/1 (0.0)	NA*
	EOT	64/73 (87.7)	77.9, 94.2
PGQ responder rate for fat under chin, n/N (%)	EOT		
A great deal better		27/77 (35.1)	
Moderately better		28/77 (36.4)	
PGQ responder rate for definition between chin and neck, n/N (%)	EOT		
A great deal better		25/77 (32.5)	
Moderately better		29/77 (37.7)	
PGQ responder rate for satisfaction with treatment, n/N (%)	EOT		
Extremely satisfied		35/77 (45.5)	
Moderately satisfied		23/77 (29.9)	

*No CIs available because n/N = 0/1.

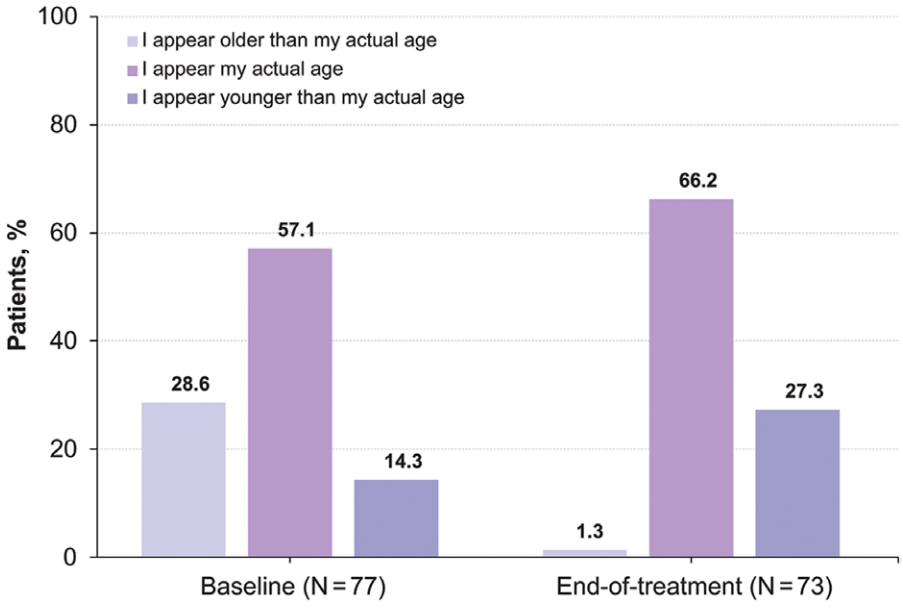

Fig. 3. Summary of patient SPA by visit.

treatment goals and were satisfied with the SMF outcome in the majority of patients (65/77, 84.4% for both responses). More than 90% of physicians believed that the injection training adequately prepared them to administer treatment and for patient side effects. Physicians reported that the decision to end SMF treatment was the patients in 51.9% of cases.

Safety

Of the 79 patients in the safety population, 18 (22.8%) reported 31 treatment-emergent AEs, all of which were mild in severity, were considered related to treatment, and resolved by the end of the study. Seventeen patients (21.5%) reported AEs during the first treatment session. Of the 31 reported AEs, 20 (64.5%) were reported

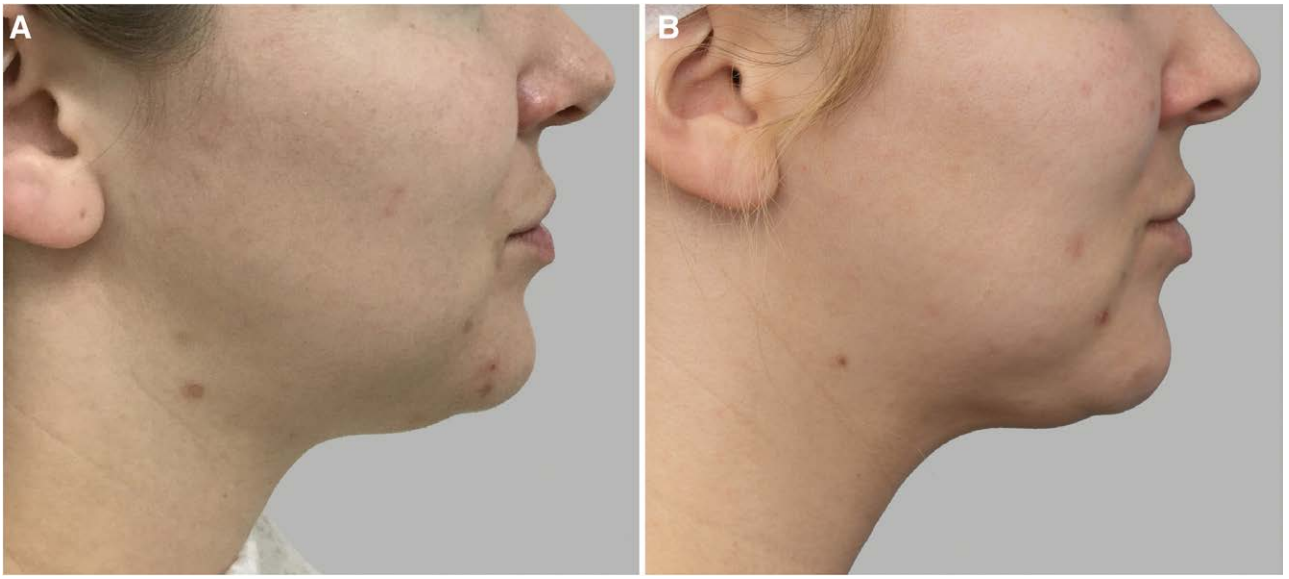

Fig. 4. Representative patient photographs. Before (A) and after treatment (B) photographs of a 31-year-old, nonsmoking White female patient who underwent two treatment sessions with ATX-101 (total of four ATX-101 vials) and achieved a 1-grade improvement in the CR-SMFRS, with slight worsening of skin laxity as measured by SMSLG scale 4 months after the last treatment session.

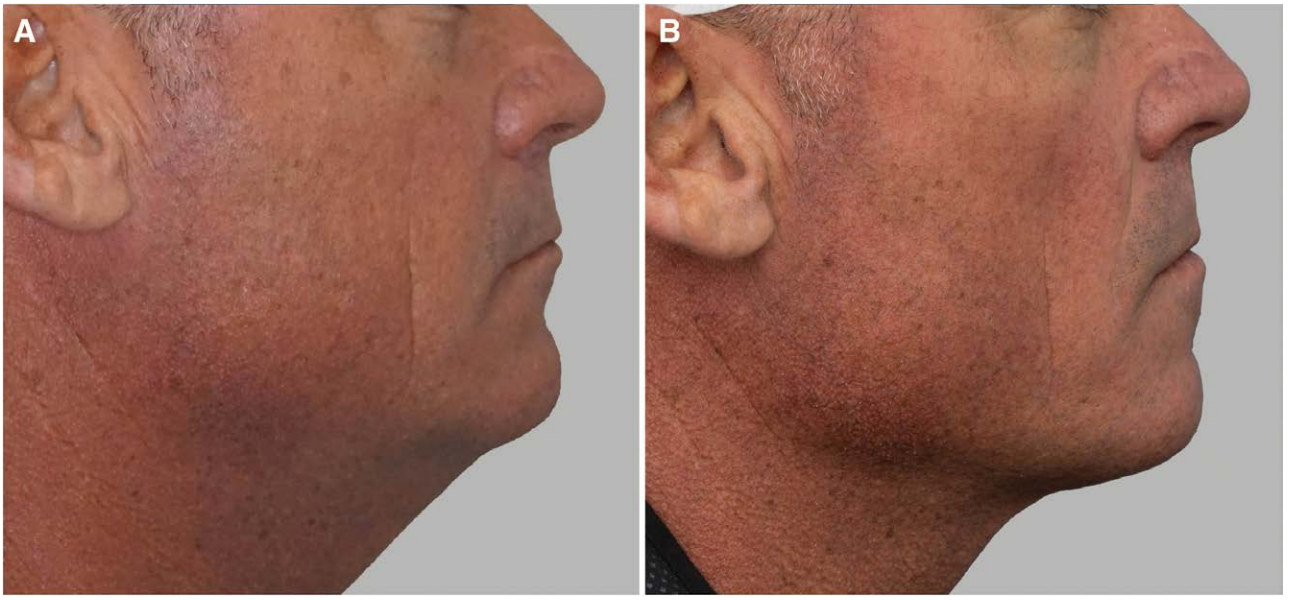

Fig. 5. Representative patient photographs. Before (A) and after treatment (B) photographs of a 50-year-old, nonsmoking White male patient who underwent four treatment sessions with ATX-101 (total of 11 ATX-101 vials) and achieved a 1-grade or more improvement in the CR-SMFRS and no change in skin laxity as measured by the SMSLG scale 2 months after the last treatment session.

during the first treatment session. Most AEs were related to the injection site (eg, bruising and swelling). A summary of AEs with corresponding average durations is reported in Table 5.

One patient experienced an AE of special interest, and a vascular injury at or near the injection site. In this patient, injury to a small-caliber vessel may have occurred during injection of her left jowl area (not SMF). Postinjection, immediate blanching (diameter: ≈10 mm) was observed in an area away from but adjacent to the injection site; no hematoma was observed. The blanched skin led to a superficial skin ulcer (diameter: 2 mm) that healed spontaneously with no sequelae. The AE of vascular injury was mild in severity. No treatment of the AE was undertaken, and the patient continued in the study. The AE was assessed as being treatment related. Another patient experienced lethargy and a decreased heart rate that were considered related to treatment. Although both AEs were mild in severity and no medications were administered, the patient discontinued from treatment.

Table 5. Summary of AEs*

	Safety Population (N = 79)
Summary of AEs	
Patients with at least 1 AE, n (%)	18 (22.8)
Total number of AEs†	31
Patients discontinued from treatment due to AE, n (%)	1 (1.3)
Total number of AEs resulting in discontinuation from treatment†	2
Classification of AEs, n (%)	
Injection site	17 (21.5)
Bruising	3 (3.8)
Swelling	17 (21.5)
Arterial injury	1 (1.3)
Heart rate decreased	1 (1.3)
Lethargy	1 (1.3)

*All AEs were mild in severity and resolved by the end of the study.
†The count is at event level (ie, if a patient has multiple AEs, all of his/her AEs are counted).

DISCUSSION

The primary effectiveness end points demonstrated significant changes from baseline through the EOT visit, which indicate an improvement in mild to moderate fullness associated with SMF (CR-SMFRS and PR-SMFRS), improvement in SMF-associated psychological impact (PR-SMFIS), no overall worsening in skin laxity (SMSLG), and increased patient satisfaction with face/chin (SSRS). All 31 AEs reported in 18 patients were mild in severity and resolved by the end of the study. The safety profile of ATX-101 in this study was consistent with the known safety profile of this treatment, and no new safety findings were reported. Nearly 80% of patients indicated that, after ending treatment with ATX-101, they would undergo treatment again, highlighting the satisfaction with and acceptable tolerability profile of this treatment modality.

Improvements in SMF reduction, patient satisfaction, and psychological impact observed in the current study were comparable to those reported in the REFINE-1 and REFINE-2 clinical trials,[7,8,15] as well as in the CONTOUR North America study.[12,13] As with the current study, these studies also reported a lack of overall worsening of skin laxity despite reductions in SMF.[13,15] Lower overall rates of AEs were observed in the registry studies compared with the clinical studies (13.0% and 22.8% of patients reporting AEs in the CONTOUR North America and Australia studies, respectively, versus 97.3% in the pooled data from REFINE-1 and 2).[12,13,15] This finding may be a result of patients undergoing fewer treatments with lower total ATX-101 volumes used in clinical practice compared with the clinical trials, wherein investigators apply the dose as per protocol.[12] Similar to previous studies, most AEs were related to the injection site (eg, swelling and bruising).[12,13,15] Unlike previous studies,[13,15] there were no reports of mandibular nerve injury/paresis, alopecia, or dysphagia in the current study. One patient experienced an arterial injury at or close to the injection site, and another patient experienced both decreased heart rate and lethargy; these three AEs were assessed as treatment related.

This prospective, observational registry study provides valuable insights on the use of ATX-101 to treat SMF in a real-world setting. In general, patient registries not only collect postmarketing surveillance data for approved drugs, but they also characterize the experiences of patients and physicians.[19] Data from patient registries can be used to improve clinical care guidelines and prompt deeper engagement among the healthcare community. CONTOUR North America has helped guide clinical practice patterns, such as understanding the importance of patient selection and adequate treatment volumes and intervals, the use of combination therapies (eg, cryolipolysis or liposuction for severe SMF, injectables for lower face rejuvenation), and the need to educate patients on treatment course and expected AEs.[12,13]

A key limitation of the observational study design is the potential loss of data attributed to patients being lost to follow-up or having irregular follow-up visits. Additionally, compared with CONTOUR North America and the phase 3 REFINE trials,[13,15,16] CONTOUR Australia enrolled considerably fewer patients, creating challenges in drawing parallels between these studies. Due to the limited sample size and patient demographic (the majority were women and White), the data may not represent the full population of Australian clinics that treat submental fullness due to SMF and also may not reflect the different perspectives of other populations toward SMF. The current study design did not quantify changes in SMF volume; future studies can use photographic imaging analysis to quantify these and other changes, such as changes in the submental angle.

CONCLUSIONS

The primary effectiveness end points used in the current study suggest that in an Australian population, ATX-101 treatment reduced SMF severity and increased patient satisfaction in the appearance of the chin. Overall, the study reports clinically meaningful and significant outcomes and further supports ATX-101 as a well-tolerated and effective treatment for SMF reduction.

Sarah G. Boxley, MBBS, FRACGP, FACAM
SkinBox Clinics
4/6 Short Street
Fremantle, WA 6160
Australia
E-mail: sboxley@me.com

DISCLOSURES

Simona Battucci is an employee of AbbVie. Sarah G. Boxley is paid consultant and advisory board member for Allergan Aesthetics, an AbbVie Company. Neville Lee See is investigator for Allergan Aesthetics, an AbbVie Company. Susan Simonyi is an employee of AbbVie. Suzanne St. Rose is employee of AbbVie at the time the study was conducted. Frank Lin has no financial interest to declare in relation to the content of this article. This study was supported by Allergan (before its acquisition by AbbVie). Writing and editorial assistance was provided to the authors by Adrienne Drinkwater, PhD, and Maria Lim, PhD, of Peloton Advantage, LLC, an OPEN Health company, and was

funded by AbbVie. Neither honoraria nor other form of payment were made for authorship.

ACKNOWLEDGMENT

Study approval was obtained from each center's independent ethics committee, and all patients provided written informed consent.

REFERENCES

1. Baumann L, Shridharani SM, Humphrey S, et al. Personal (self) perceptions of submental fat among adults in the United States. *Dermatol Surg*. 2019;45:124–130.
2. Ascher B, Fellmann J, Monheit G. ATX-101 (deoxycholic acid injection) for reduction of submental fat. *Expert Rev Clin Pharmacol*. 2016;9:1131–1143.
3. Goodman GJ, Subramanian M, Sutch S, et al. Beauty from the neck up: introduction to the special issue. *Dermatol Surg*. 2016;42:S260–S262.
4. Swift A, Liew S, Weinkle S, et al. The facial aging process from the "inside out." *Aesthet Surg J*. 2021;41:1107–1119.
5. Shamban AT. Noninvasive submental fat compartment treatment. *Plast Reconstr Surg Glob Open*. 2016;4:e1155.
6. Walker PS, Lee DR, Toth BA, et al. Histological analysis of the effect of ATX-101 (deoxycholic acid injection) on subcutaneous fat: results from a phase 1 open-label study. *Dermatol Surg*. 2020;46:70–77.
7. Humphrey S, Sykes J, Kantor J, et al. ATX-101 for reduction of submental fat: a phase III randomized controlled trial. *J Am Acad Dermatol*. 2016;75:788–797.e7.
8. Jones DH, Carruthers J, Joseph JH, et al. REFINE-1, a multicenter, randomized, double-blind, placebo-controlled, phase 3 trial with ATX-101, an injectable drug for submental fat reduction. *Dermatol Surg*. 2016;42:38–49.
9. Rzany B, Griffiths T, Walker P, et al. Reduction of unwanted submental fat with ATX-101 (deoxycholic acid), an adipocytolytic injectable treatment: results from a phase III, randomized, placebo-controlled study. *Br J Dermatol*. 2014;170:445–453.
10. Ascher B, Hoffmann K, Walker P, et al. Efficacy, patient-reported outcomes and safety profile of ATX-101 (deoxycholic acid), an injectable drug for the reduction of unwanted submental fat: results from a phase III, randomized, placebo-controlled study. *J Eur Acad Dermatol Venereol*. 2014;28:1707–1715.
11. Dover JS, Kenkel JM, Carruthers A, et al. Management of patient experience with ATX-101 (deoxycholic acid injection) for reduction of submental fat. *Dermatol Surg*. 2016;42:S288–S299.
12. Behr K, Kavali CM, Munavalli G, et al. ATX-101 (deoxycholic acid injection) leads to clinically meaningful improvement in submental fat: final data from CONTOUR. *Dermatol Surg*. 2020;46:639–645.
13. Palm MD, Schlessinger J, Callender VD, et al. Final data from the Condition of Submental Fullness and Treatment Outcomes Registry (CONTOUR). *J Drugs Dermatol*. 2019;18:40–48.
14. Australian Public Assessment Report for Deoxycholic Acid. Woden, ACT, Australia: Australian Government Department of Health Therapeutic Good Administration; 2017.
15. Dayan SH, Schlessinger J, Beer K, et al. Efficacy and safety of ATX-101 by treatment session: pooled analysis of data from the phase 3 REFINE trials. *Aesthet Surg J*. 2018;38:998–1010.
16. McDiarmid J, Ruiz JB, Lee D, et al. Results from a pooled analysis of two European, randomized, placebo-controlled, phase 3 studies of ATX-101 for the pharmacologic reduction of excess submental fat. *Aesthetic Plast Surg*. 2014;38:849–860.
17. Lupo M, Dover JS, Baradaran S, et al. Development and validation of the patient-reported submental fat rating scale and the patient-reported submental fat impact scale. *Dermatol Surg*. 2021;47:522–525.
18. Carruthers J, Carruthers A. Botulinum toxin type a treatment of multiple upper facial sites: patient-reported outcomes. *Dermatol Surg*. 2007;33:S10–S17.
19. de Souza MP, Rangel Miller V. Significance of patient registries for dermatological disorders. *J Invest Dermatol*. 2012;132:1749–1752.