

Real-World Experience With 100 Consecutive Patients Undergoing Neck Contouring With ATX-101 (Deoxycholic Acid): An Updated Report With A 2-Year Analysis

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BACKGROUND Deoxycholic acid (DCA; ATX-101) injection was approved for the treatment of mild-to-moderate convexity associated with submental fat in 2015.

OBJECTIVE To evaluate the experience with DCA injections in a clinical practice setting.

MATERIALS AND METHODS This ongoing, prospective, single-center, single-arm, observational study evaluated 100 consecutive patients treated with subcutaneous DCA (2 mg/cm²) injections (maximum 6 sessions at ≥ 1 -month intervals). Treatment response was assessed using the clinician-reported submental fat rating scale (CR-SMFRS) and confirmed by independent physician review of photographs at 1 and 5 to 7 weeks after treatment.

RESULTS Since the previous published report, 17 patients have undergone additional treatment sessions, with a total of 100 patients having undergone 195 treatment sessions: 41, 36, 14, 6, 2, and 1 patient underwent 1, 2, 3, 4, 5, and 6 sessions, respectively. Overall, 91.7% of patients in the single treatment session group and 100% in the multiple treatment session group had an improvement of ≥ 1 point on the CR-SMFRS. The mean (SD) duration of local edema, numbness, and tenderness after treatment was 7.1 (5.1), 27.9 (11.3), and 3.5 (3.5) days, respectively.

CONCLUSION Deoxycholic acid injections were generally well tolerated, and ≥ 2 treatment sessions were required to achieve the desired aesthetic goal in a private practice setting.

Medical writing support was provided by Cactus Communications and funded by Allergan, Inc. S. M. Shridharani has served as a consultant and has received payment for lectures from Allergan, Galderma, Merz, and Sientra. He is a member of the Facial Aesthetics Advisory Board and the KYBELLA Advisory Board and has received payment for writing assistance from Allergan.

Deoxycholic acid (DCA) is a naturally occurring bile acid that nonselectively causes cell lysis.¹ Deoxycholic acid injection (ATX-101; KYBELLA[®], BELKYRA[®] [Canada and Sweden]; KYTHERA Biopharmaceuticals, Inc., Westlake Village, CA, acquired by Allergan, Inc.) is a proprietary formulation of synthetically derived DCA that is approved for improvement in the appearance of moderate-to-severe convexity/fullness associated with submental fat.²⁻⁵ When injected into adipose tissue, DCA irreversibly disrupts the adipocyte membrane (adipocytolysis), leading to a mild

inflammatory response followed by gradual macrophage-induced phagocytosis of cell debris.⁶⁻⁸

The efficacy and safety of DCA injection was demonstrated in four Phase 3 randomized controlled trials (RCTs).⁹⁻¹³ A previous report describes the initial findings from my early experience with 100 consecutive patients administered DCA injections for treating accumulated submental fat.¹⁴ At the time of the report (data cutoff, February 2016), 100 patients had undergone 152 treatment sessions. Overall, 58 patients had undergone 1

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ISSN: 1076-0512 • Dermatol Surg 2019;45:1285-1293 • DOI: 10.1097/DSS.0000000000001811

treatment session, and 42 had undergone multiple sessions (33, 8, and 1 patient underwent 2, 3, and 4 sessions, respectively), indicating that the treatment sessions were well tolerated. Most (88.0%) patients showed an improvement of ≥ 1 point on the clinician-reported submental fat rating scale (CR-SMFRS), with 46 of these having undergone only 1 session.¹⁴

The author observed similar adverse events (AEs) as reported in RCTs. However, less postinjection bruising/hematoma was observed than in RCTs (20% vs 50%–70% of patients), with no induration/fibrosis (0% vs $\sim 20\%$).^{10–12}

In general, the treatment approach used in this study was conservative as compared to that used in RCTs. The total volume of DCA administered was substantially lower,^{9–13} and the number of treatment sessions was fewer as compared with RCTs, possibly because of the time-delimited nature of the analysis, early patient satisfaction/dissatisfaction, patient willingness for more treatment sessions to reach the ideal aesthetic goal, AEs, and costs.¹⁴

Here, the author provides an update to the previous report of the same 100 patients,¹⁴ accounting for additional treatment sessions during longer-term follow-up.

Methods

Study Design

This prospective, observational study was conducted at the LUXURGERY clinic (New York, NY) between June 2015 and June 2017. Experience through February 2016 has been published previously.¹⁴ This study was conducted in accordance with the Declaration of Helsinki and the International Conference on Harmonisation Tripartite Guidelines for Good Clinical Practice. Written informed consent was obtained from each patient.

Patients and Treatment

The first 100 consecutive patients aged between 18 and 80 years who were seeking improvement in convexity/fullness associated with submental fat were

enrolled. Exclusion criteria and details of the treatment procedure have been published previously.¹⁴

Effectiveness Assessments

Treatment response was defined as an improvement of ≥ 1 point on the CR-SMFRS (0 = absent; 1 = mild; 2 = moderate; 3 = severe; and 4 = extreme), which was applied before treatment (baseline) and at 1 week and between 5 and 7 weeks after treatment. Photographs were taken at each follow-up visit, and the overall treatment response was confirmed by a blinded, retrospective, independent review of the photographs by 2 practicing board-certified plastic surgeons.

Safety Assessments

Adverse events, including injection-site AEs, were monitored at each follow-up visit. Patient-reported AEs were also included.

Statistical Analyses

Categorical variables were summarized as counts and percentages and continuous variables as valid data count, missing data count, mean (SD), and median (interquartile range and minimum and maximum). Patients were categorized into single treatment session (STS) and multiple treatment session (MTS) groups. A post hoc analysis was performed for all relevant parameters categorized by increasing number of treatment sessions. Comparisons were performed using the Mann–Whitney *U* test because of high dispersion of continuous variables. Categorical variables were compared using the chi-square/Fisher exact/Kruskal–Wallis test (IBM SPSS Statistics version 21.0).

Results

Patient Demographics and Baseline Characteristics

Overall, 61 of the 100 patients were women. As of February 2016, 58 patients had undergone an STS. During the subsequent year (up to June 2017), 17 of these patients underwent 1 or ≥ 2 additional treatment sessions. Therefore, the STS group comprised 41 patients, and the MTS group comprised 59 patients.

No statistical differences were observed between the 2 groups, except with regard to the Fitzpatrick score and sex. The mean (SD; min, max) age of the patients was 45.4 (12.2; 23, 76) years; 43 patients had undergone a previous plastic surgery procedure, most commonly (16.3% [7/43]) neck liposuction. Body mass index (BMI; mean: 26.1 [4.4; 17.3, 44.8] kg/m²)

was ≥ 25 kg/m² in 57 patients, and 17 patients had a Fitzpatrick score >3 (Table 1). A higher proportion of patients in the STS group had lower BMI (26.8% [11/41] ≤ 22 kg/m² and 51.2% [21/41] < 25 kg/m²) versus the MTS group (10.2% [6/59] ≤ 22 kg/m² and 37.3% [22/59] < 25 kg/m²). Significantly, more men versus women underwent MTS (men: 1 session, 11 vs ≥ 2 sessions, 28; women: 1 session, 30 vs ≥ 2 sessions, 31; $p = .038$). A total of 11 and 19 patients in the STS and MTS groups, respectively, underwent other cosmetic procedures with their ongoing DCA treatment for neck contouring.

Procedural Outcomes

As of June 2017, 100 patients underwent 195 (41 single and 59 multiple [total, 154]) treatment sessions. In the MTS group, most (36/59 [61.0%]) patients had 2 sessions; 14 (23.7%) had 3 sessions, 6 (10.2%) had 4 sessions, 2 (3.4%) had 5 sessions, and 1 (1.7%) had 6 sessions. The duration between treatment sessions varied considerably, ranging from 24 to 614 days. Among MTS patients, the mean (SD) time between the first and second, second and third, third and fourth, fourth and fifth, and fifth and sixth sessions was 145.8 (157.7), 149.1 (120.5), 292.7 (109.4), 161.0 (178.2), and 75.0 days, respectively.

A mean (SD) of 6.7 (2.3) mL of DCA was administered per treatment session, with significantly more DCA administered to the MTS group than the STS group (6.8 [2.3] vs 6.1 [2.2] mL/session; $p = .049$). A significantly higher mean (SD) dose of DCA was administered with increasing number of treatment sessions (first, 6.2 [2.2] mL; second, 7.0 [2.2] mL; third, 7.3 [2.6] mL; fourth, 6.7 [2.6] mL; fifth, 8.0 [2.0] mL; and sixth, 10 mL; $p < .001$). Significantly higher doses of DCA were administered during the second and third treatment sessions versus the first session ($p = .016$ and $p = .033$, respectively). The mean (SD) volume of total DCA injected during all treatment sessions in men (16.8 [9.4] mL) was significantly higher than that injected in women

(10.5 [8.9] mL; $p = .0012$). The mean (SD) volume of DCA injected in men was also significantly higher than that injected in women for the first (men, 7.3 [2.3] mL; women, 5.6 [1.8] mL; $p < .0001$) and second (men, 8.1 [2.2] mL; women, 6 [1.8] mL; $p < .0001$) treatment sessions.

The use of preinjection oral analgesia was significantly higher in the STS group than the MTS group (100% [41/41] vs 89.0% [137/154]; $p = .026$). However, volume of local anesthetic (overall mean [SD]: 5.7 [2.1] mL/session; STS: 5.3 [1.4] mL/session; MTS: 5.8 [2.2] mL/session; $p = .159$) and use of ice packs (STS: 100% [41/41]; MTS: 94.8% [146/154]; $p = .586$) did not differ significantly between groups. In addition, the mean (SD) dose of local anesthetic did not change significantly with increasing number of treatment sessions (first, 5.5 [1.7] mL; second, 6.0 [2.2] mL; third, 6.3 [2.9] mL; fourth, 5.1 [2.1] mL; fifth, 5.3 [0.6] mL; and sixth, 6.0 mL; $p = .185$).

Treatment Response

As published previously, the CR-SMFRS score improved by ≥ 1 point from baseline in 88 (88%) patients; of these, 46, 33, 8, and 1 patient had undergone 1, 2, 3, and 4 treatment sessions, respectively. Based on the CR-SMFRS results, 12/58 patients did not respond to a single treatment; however, 46 patients had an improvement of ≥ 1 point (45 [45%] by 1 point and 1 [1%] by 2 points). By contrast, all 42 patients who underwent MTS responded to treatment (31 [31%] by 1 point and 11 [11%] by 2 points). At the additional follow-up, 33 of 36 (91.7%) patients in the STS group and all 59 (100%) in the MTS group had an improvement of ≥ 1 point on the CR-SMFRS (i.e., treatment response); data were missing for 2 patients in the STS group Figures 1–3.

Safety Outcomes

Vomiting and headache were reported in 1 patient each in the STS group, and nausea was reported in 1 patient in the MTS group (Table 2). Local edema, numbness, and tenderness were reported for a mean (SD) of 7.1 (5.1), 27.9 (11.3), and 3.5 (3.5) days, respectively. Data on edema were missing after 17 treatment sessions. Among patients with edema ($n = 178$ treatment sessions), the mean (SD) number of days with edema was significantly

TABLE 1. Patient Demographics and Baseline Characteristics

	1 Treatment Session	≥2 Treatment Sessions	Total	p (Chi-Square)
Patients, <i>n</i>	41	59	100	
Treatment sessions				
2		36	36	
3		14	14	
4		6	6	
5		2	2	
6		1	1	
Age, mean (SD), yr	47.3 (12.4)	44.1 (11.9)	45.4 (12.2)	.192*
Sex, <i>n</i> (%)				
Male	11 (26.8)	28 (47.5)	39 (39)	.038
Female	30 (73.2)	31 (52.5)	61 (61)	
Body mass index, mean (SD), kg/m ²	25.1 (3.9)	26.8 (4.5)	26.1 (4.4)	.094†
<25 kg/m ²	21 (51.2)	22 (37.3)	43 (43.0)	.166
≥25 kg/m ²	20 (48.8)	37 (62.7)	57 (57.0)	
Fitzpatrick score:				
≤3	52 (89.7)	31 (73.8)	83 (83.0)	.037
>3	6 (10.3)	11 (26.2)	17 (17.0)	
Previous plastic surgery procedure, <i>n</i> (%)				
No	23 (56.1)	34 (57.6)	57 (57.0)	.879
Yes	18 (43.9)	25 (42.4)	43 (43.0)‡	
Postprocedure treatment				
Blepharoplasty	0	1	1	
Breast augmentation	0	1	1	
Coolsculpt [®] , injectables	1	0	1	
Injectable	9	6	15	
Injectables, platelet-rich plasma, hair transplant	0	1	1	
Liposuction	0	4	4	
Liposuction, breast augmentation	0	1	1	
Liposuction, injectables	0	3	3	
Neck lift	1	0	1	
Rhinoplasty	0	2	2	

*The Student's *t*-test.†The Mann-Whitney *U* test.

‡Documented previous plastic surgery procedure data available in 42 patients.

higher in the STS group (7.8 [3.8] days) versus the MTS group (6.9 [5.4] days; $p < .001$).

There was a significant decrease in mean (SD) duration of postinjection edema with each subsequent treatment session (first: 8.8 [5.4] days, 97 sessions; second: 5.7 [4.6] days, 54 sessions; third: 4.2 [1.3] days, 20 sessions; fourth: 3.7 [1.4] days, 6 sessions; fifth: 3 [not applicable (NA)] days, 1 session; and sixth: 3 [NA] days, 1 session; $p < .001$). Duration of edema was

significantly shorter for all treatment sessions versus the first session ($p < .001$).

However, no significant difference was observed between treatment groups in duration of numbness (27.4 [11.0] vs 29.9 [12.4] days; $p = .243$, respectively) or tenderness at injection sites (3.1 [3.2] vs 3.5 [3.7] days; $p = .481$, respectively). The duration of numbness (mean [SD]) did not change significantly with increasing number of treatment sessions (first, 29.2

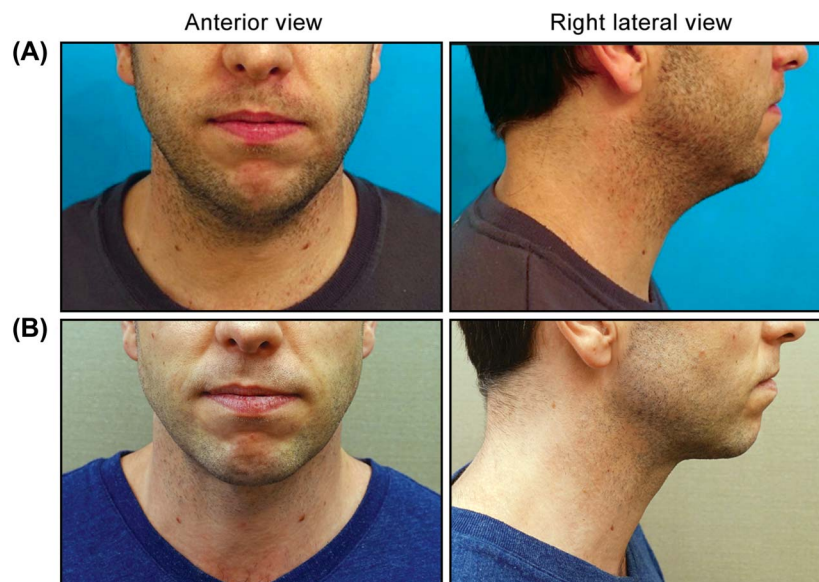


Figure 1. Photographs showing response in a 38-year-old male patient who underwent 3 treatment sessions (8-mL DCA first session, 6-mL DCA second session, and 4-mL DCA third session; 10 weeks between treatment 1 and treatment 2, 24 weeks between treatment 2 and treatment 3): (A) before treatment and (B) 24 weeks after the third session. DCA, deoxycholic acid.

[11.1] days; second, 27.7 [11.3] days; third, 24.6 [11.5] days; fourth, 15 [11.0] days; fifth, 30 [0.0; missing, 2] days; and sixth, missing; $p = .141$). Similarly, the duration of tenderness (mean [SD]) did not change significantly with increasing number of treatment sessions (first, 3.8 [3.9] days; second, 2.7 [2.5] days; third, 2.3 [1.8] days; fourth, 1.0 [0.9] days; fifth, 3.5 [3.5] days; and sixth, 1 day; $p = .071$).

No significant difference in duration of local edema or tenderness at injection sites was observed between men and women (6.7 [4.4] vs 7.5 [5.5] days; $p = .183$ and 3.0 [3.0] vs 3.3 [3.5] days; $p = .691$, respectively). However, men experienced numbness (mean [SD]: 31.2 [13.1] days) for a significantly longer duration than women (25.5 [9.2] days; $p = .002$). Two patients had marginal mandibular nerve (MMN) paresis lasting for 17 and 22 days in the STS group.¹⁴ No new cases occurred since the previous report. Postinjection bruising was reported after 26 of 192 sessions, with no significant difference between the STS and MTS groups (20% [8/40] and 11.8% [18/152], respectively; $p = .180$); data for 3 (STS, 1; MTS, 2) patients were missing. No significant difference was observed in occurrence of bruising between the first (17/99 [17.2%]) and subsequent treatment sessions (second: 7/59 [11.9%], $p = .064$; third: 1/22 [4.5%],

$p = .227$; fourth: 0/8 [0%]; fifth: 1/3 [33.3%]; and sixth: no bruising, $p = .256$).

Transient alopecia at injection site lasting for 6 weeks to 12 months was noted in 9 of 39 male patients (STS, 1/11 [9.1%]; MTS, 8/28 [28.6%]; $p = .136$).

Discussion

Longer-term follow-up after administration of DCA injections for treating accumulated submental fat showed that although submental convexity improves with an STS, patients will likely require ≥ 2 sessions to achieve the desired aesthetic goal. Both STS and MTS were generally well tolerated.

Of the 58 patients who underwent an STS during the first analysis period (June to February 2016),¹⁴ 17 returned for further sessions during the follow-up period. It is likely that many of the remaining 41 patients required an STS (STS group) and were satisfied with their treatment. This could be attributed to the higher proportion of patients with lower BMI who received early treatment for mild submental convexity in the STS group versus the MTS group. Of note, this subgroup of patients would not have been eligible for enrolment in the clinical trial



Figure 2. Photographs showing response in a 27-year-old female patient who underwent 2 treatment sessions (6-mL DCA first session and 6-mL DCA second session; 152 days between treatment 1 and treatment 2): (A) before treatment and (B) 24 weeks after the second session. DCA, deoxycholic acid.

in a real-world setting. Patient satisfaction and their continued interest in cosmetic procedures were reflected by the fact that 30 patients (18 women and 12 men) underwent other cosmetic procedures alongside DCA treatment for neck contouring. In comparison with the previous report, the increase in proportion of procedure-naïve men who returned for additional cosmetic procedures was higher (19% [5/26]–27% [7/26]) compared with women (12.9% [4/31]–16.1% [5/31]). Moreover, when additional treatment sessions were considered, significantly more men than women ultimately underwent MTS. However, other factors influencing the number of treatment sessions such as patient dissatisfaction, AEs, willingness to undergo MTS, cost of treatment, and lack of patient enthusiasm to pursue the ideal aesthetic goal cannot be ruled out.

Regarding safety and tolerability, male patients experienced numbness significantly longer than

female patients; duration of other injection-site AEs was not significantly different between men and women. However, a higher volume of DCA was injected in men versus women, which could be attributed to the fact that this treatment is predicated on surface area, which, in men, tends to be larger due to a larger body frame in general. Furthermore, an additional male patient experienced transient alopecia after undergoing further treatment sessions; therefore, a total of 9 of the 39 male patients—8 in the MTS group and 1 in the STS group—experienced this AE. As mentioned, in contrast to a single case report in the published literature, which mentions DCA-induced submental patchy alopecia that was persistent and refractory to treatment with topical bimatoprost after 11 months, the alopecia observed in this study was transient (6 weeks–12 months) and did not require treatment.¹⁵ In the case report, a 37-year-old man underwent an STS comprising 21 discrete DCA



Figure 3. Photographs showing response in a 37-year-old female patient who underwent 3 treatment sessions (6-mL DCA first session, 6-mL DCA second session, and 6-mL DCA third session; 45 days between treatment 1 and treatment 2 and 35 days between treatment 2 and treatment 3): (A) before treatment and (B) 24 weeks after the third session. DCA, deoxycholic acid.

injections (2 mg/injection) into the submental subcutaneous fat (SMFRS Grade 2). Injections were administered 1 cm² apart using a 30-gauge, half-inch needle at two-third-needle depth.¹⁵ The only difference versus this procedure was the use of a 32-gauge needle in this study. The author of the case study proposed a need for postmarketing surveillance data to enable a more comprehensive description of AEs associated with DCA treatment.¹⁵

In the RCTs, most patients required 2 to 4 treatment sessions to achieve a clinically meaningful treatment response with DCA (52% achieved a ≥ 1 -grade improvement in CR-SMFRS after the second session, and 72% achieved this improvement after the fourth session).¹⁶ In this study, 33 of 36 (91.7%) patients in the STS group and all 59 (100%) in the MTS group had an improvement of ≥ 1 point on the CR-SMFRS.

Importantly, RCTs underscore the importance of tailoring DCA treatment for each individual. As the submental fat reduces with each subsequent treatment session, a lower amount of DCA requirement is anticipated.¹⁶ The results of this study were contrary to this understanding, as a significant increase was observed in the DCA dose administered with an increase in the number of treatment sessions. This finding is primarily attributed to my apprehensions, which reflect in the initial conservative approach for this cosmetic procedure in the real-world setting. For pain management, all patients were administered a local anesthetic during all the treatment sessions. Previously, it was reported that more local anesthetic per session was administered to patients in the MTS group than the STS group¹⁴; however, the volume per session did not differ significantly in this longer-term analysis. The dose of local anesthetic did not change

TABLE 2. Adverse Events

	1 Treatment Session	≥2 Treatment Sessions	Total	p (The Fisher Exact Test)
Patients, <i>n</i>	41	59	100	
Treatment sessions, <i>n</i>	41	154	195	
Nausea	0	1	1	1.000
Vomiting	1	0	1	1.000
Headache	1	0	1	.410
Alopecia	1	8	9	.136
Local edema (days after session), mean (SD)	7.8 (3.8)§	6.9 (5.4)	7.1 (5.1)	.004*
Local numbness (days after session), mean (SD)	29.9 (12.4)¶	27.4 (11.0)#	27.9 (11.3)	.243†
Local tenderness (days after session), mean (SD)	3.5 (3.7)**	3.1 (3.2)††	3.5 (3.5)	.481*
Paresis, <i>n</i> (days after session for resolution)	2 (17, 22)	0	2	.226*
Bruising, <i>n</i>	8	18	26	.180‡

*The Mann–Whitney *U* test.
†The Student's *t*-test.
‡Chi-square test.
§*n* = 38.
||*n* = 140.
¶*n* = 37.
#*n* = 130.
***n* = 39.
††*n* = 148.

significantly with increasing number of treatment sessions. An ice pack was used in 100% and 94.8% of patients in the STS and MTS groups, respectively. Also, in contrast to the previous report, analgesia was used significantly ($p = .026$) more often in the STS group than the MTS group in the longer-term analysis period.

A double-blind, parallel-group, exploratory Phase 3b study evaluated 4 patient experience management paradigms (paradigm 1, icepacks; paradigm 2, icepacks + topical/local lidocaine with epinephrine; paradigm 3, paradigm 2 + loratadine and ibuprofen; and paradigm 4, paradigm 3 + chin strap) targeting the injection-site AEs with DCA injections for submental fat reduction. Compared with paradigm 1, paradigm 2 reduced median peak pain by 17%; paradigm 3 showed a total reduction in pain by 40%. Swelling/edema was not substantially mitigated by any of the treatment paradigms, while bruising remained confined to the treatment area and was modestly reduced by injectable lidocaine with epi-

nephrine.¹⁷ Furthermore, the incidence of pain, swelling, edema, and bruising in previous Phase 3 trials was 70%, 87%, and 72%, respectively; however, in practice, pain and swelling occur 100% of the time with considerable interpatient variability. Repeated treatment leads to a reduction in both pain and swelling over time, because of lower target tissue volume, persistent numbness, thickened fibrous septae formation, and lower doses.¹⁸ Although data were missing for 17 treatment sessions, postinjection edema was reported after all sessions, with a significant decrease in the duration of edema with each subsequent session. However, the occurrence of bruising and duration of numbness and tenderness did not change significantly with increasing number of treatment sessions. Also, the duration of local edema and tenderness at injection sites did not vary with sex. Although the duration of most injection-site AEs was similar to that reported in the REFINE 2 study (median duration ranging from 3.0 to 15.5 days), no AEs of nodule formation or induration were observed in this study.¹⁹

Limitations of this study are reported in the previous publication.¹⁴

Conclusion

In real-world settings, DCA injections are safe and well tolerated for permanent submental fat reduction, and patients are likely to require >1 session to achieve the desired aesthetic goal from a clinician's perspective. There was an increase in the DCA dose and decrease in injection-site edema with increasing number of treatment sessions.

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