

Injectable Cellulite Treatment

Michael H. Gold, MD
Gold Skin Care Center
Tennessee Clinical Research Center
Nashville, TN



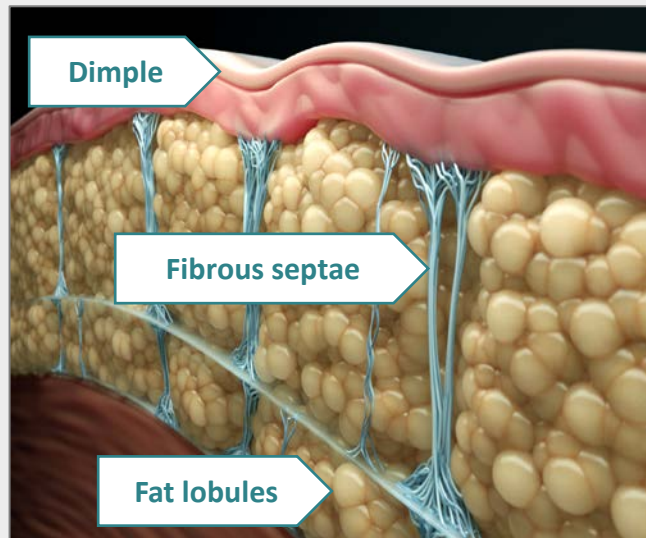
Disclosures

- Consultant to many pharmaceutical, cosmeceutical, and laser- and energy-based device companies
- Consultant, performs research, and speaks on behalf of numerous pharmaceutical and medical device companies
- Related to this presentation, consultant and investigator for Endo Pharmaceuticals Inc.
- Data detailed in this presentation were generated from studies funded by Endo Pharmaceuticals Inc.; medical writing assistance was provided by Synchrony Medical, with funding from Endo Aesthetics LLC

Introduction

Cellulite

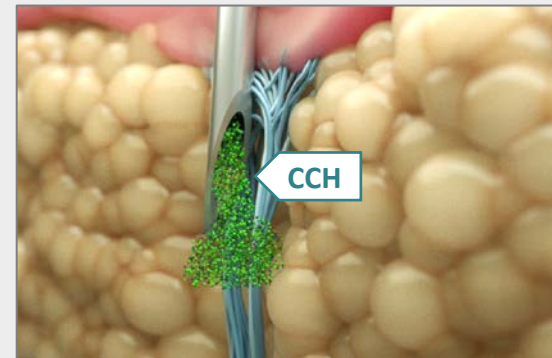
- Thickened and stabilized collagen-rich fibrous septae and associated protrusions of subcutaneous fat play a role in cellulite pathophysiology^{1,2}



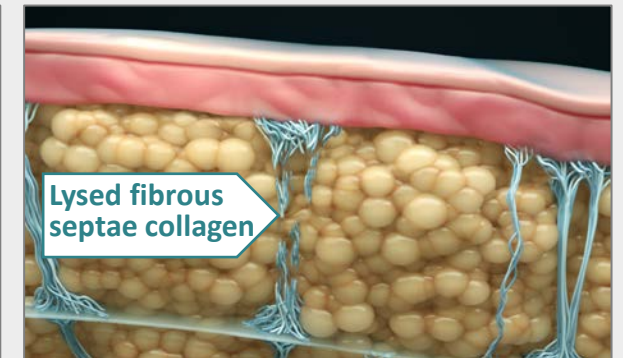
© 2020 Endo Pharmaceuticals Inc. All rights reserved.

Collagenase clostridium histolyticum-aaes (CCH; QWO™)

- Composed of 2 purified collagenases³
 - Enzymatically releases fibrous septae by specifically targeting Type I and Type III collagen
- Approved by the US FDA on July 6, 2020, for the treatment of moderate-to-severe cellulite in the buttocks of adult women⁴



© 2020 Endo Pharmaceuticals Inc. All rights reserved.



© 2020 Endo Pharmaceuticals Inc. All rights reserved.

FDA, Food and Drug Administration.

1. Avram MM. *J Cosmet Laser Ther*. 2004;6(4):181-185. 2. Rudolph C, et al. *Plast Reconstr Surg*. 2019;143(4):1077-1086. 3. French MF, et al. *Biochemistry*. 1987;26:681-687. 4. Qwo™ (collagenase clostridium histolyticum-aaes) for injection [package insert]. Malvern, PA: Endo Aesthetics LLC; 2020.

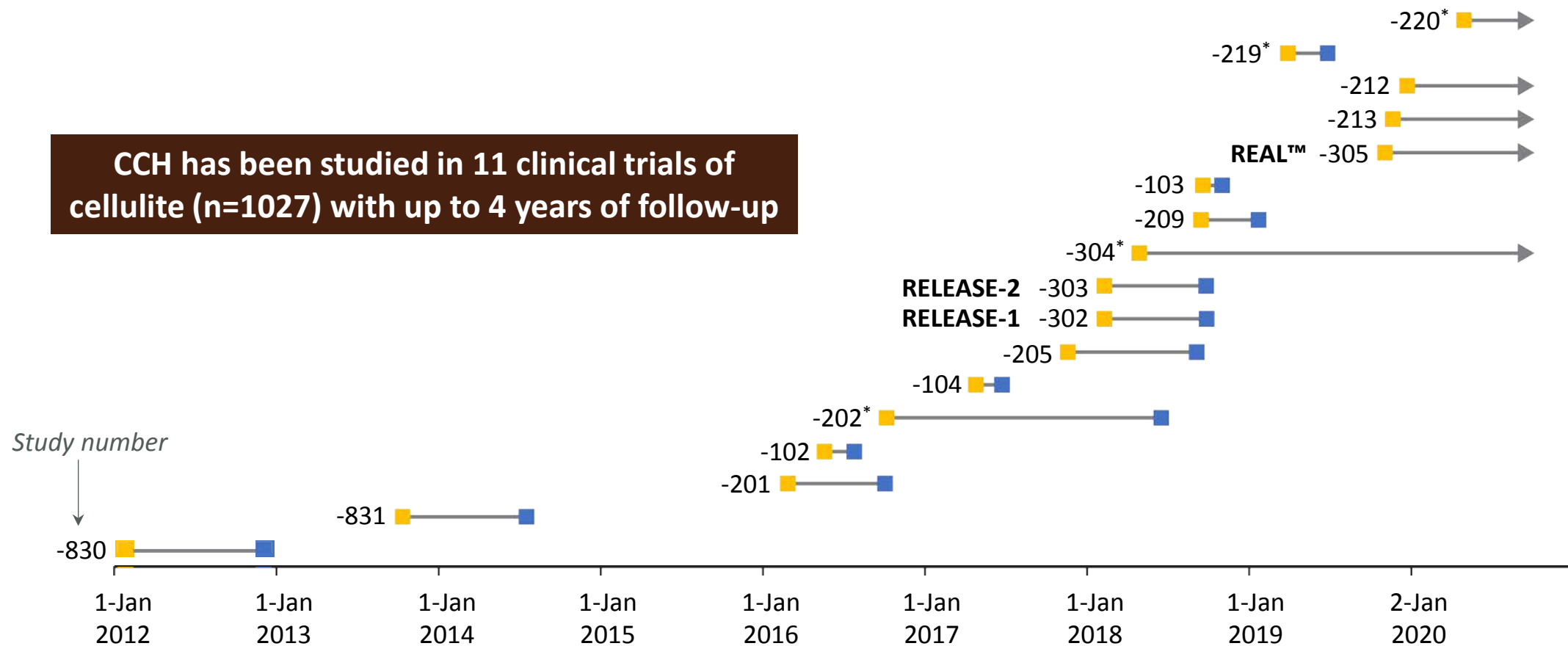
Formulation Differences

| Parameter | Qwo™ | Xiaflex® | Xiaflex® |
|--------------------------|--|--|--|
| Indication | Moderate-to-severe cellulite in the buttocks of adult women ¹ | Adults with Dupuytren contracture with palpable cord affecting MP joints or Peyronie’s disease in adult men with palpable plaque and penile curvature deformity of ≥30° at start of therapy ² | Adults with Dupuytren contracture with palpable cord affecting PIP joints ² |
| Administration | Subcutaneous | Intralesional | Intralesional |
| Reconstituted components | | | |
| Collagenase, mg/mL | 0.23 | 2.3 | 2.9 |
| Mannitol, mg/mL | 9.4 | — | — |
| NaCl, % | 0.6 | 0.9 | 0.9 |

MP, metacarpophalangeal; PIP, proximal interphalangeal.
1. Qwo™ (collagenase clostridium histolyticum-aaes) for injection [package insert]. Malvern, PA: Endo Aesthetics LLC; 2020. 2. Xiaflex® (collagenase clostridium histolyticum) for injection, for intralesional use [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; 2019.

CCH for Cellulite: Robust Clinical Trial Program

CCH has been studied in 11 clinical trials of cellulite (n=1027) with up to 4 years of follow-up



CCH, collagenase clostridium histolyticum-aaes; RELEASE, Randomized Evaluation of Cellulite Reduction by Collagenase Clostridium Histolyticum.

Yellow box: first patient, first visit; blue box: last patient, last visit.

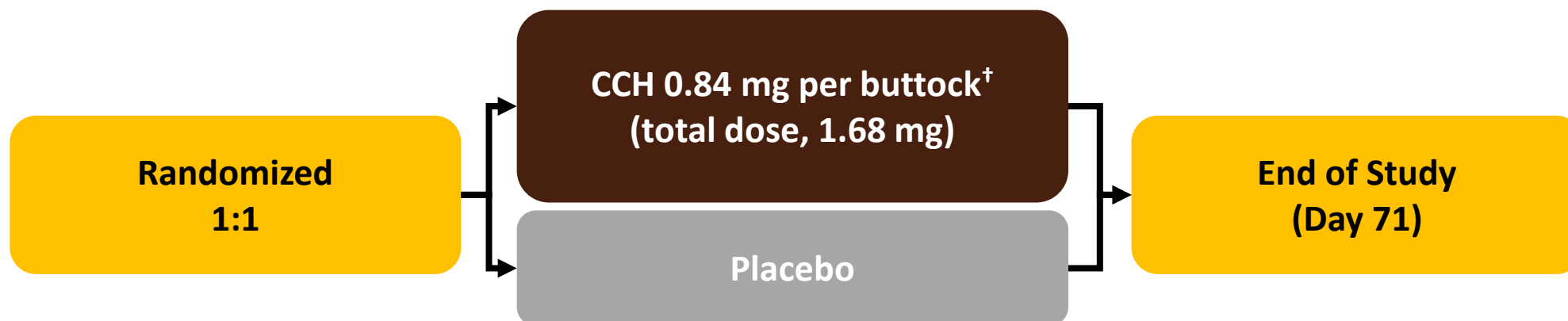
*Open-label extension study.

Pooled Analysis of RELEASE-1/-2: CCH for Buttock Cellulite

Pooled RELEASE-1/-2

- Pooled analysis of 2 identically designed, phase 3 RCTs
- Women with moderate/severe cellulite* on both buttocks received up to 3 treatment sessions of subcutaneous CCH 0.84 mg or placebo per treatment area

3 treatment sessions: Days 1, 22, and 43



CCH, collagenase clostridium histolyticum-aaes; RELEASE, Randomized Evaluation of Cellulite Reduction by Collagenase Clostridium Histolyticum; RCT, randomized, controlled trial.

*Score of 3 or 4 on Patient Reported Photonumeric Cellulite Severity Scale and Clinician Reported Photonumeric Cellulite Severity Scale.

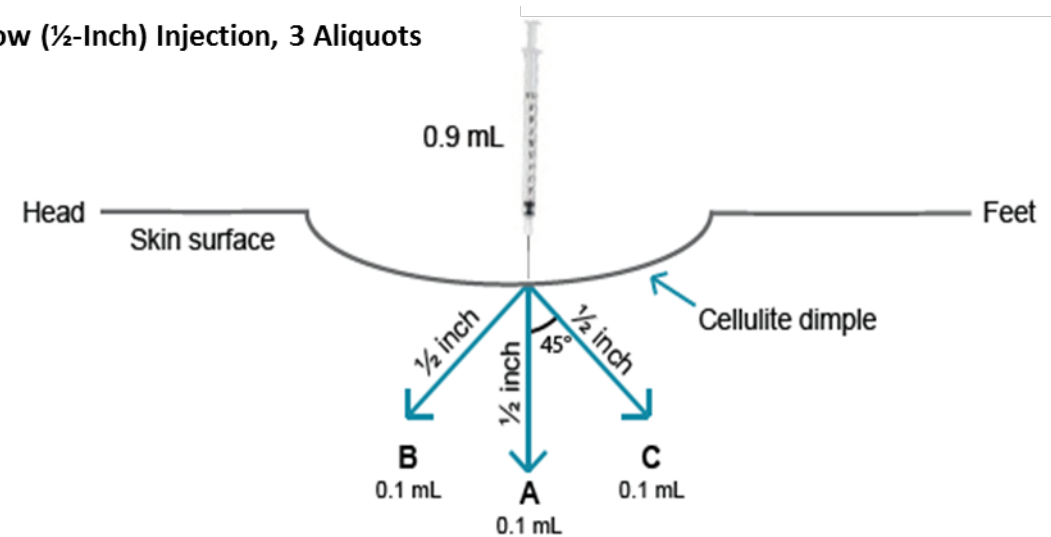
[†]Up to 12 injections (0.3 mL/injection) per buttock.

CCH Injection Technique: Buttock Cellulite

Pooled RELEASE-1/-2



Shallow ($\frac{1}{2}$ -Inch) Injection, 3 Aliquots



©2020 Endo Pharmaceuticals Inc. All rights reserved.

Technique summary: Each of the 12 injections per treatment area was administered as three 0.1-mL aliquots (0.23 mg/mL CCH/injection). The syringe was loaded with 0.9 mL to allow for 3 injections per syringe.

Efficacy Assessments:

Change From Baseline to Day 71

Pooled RELEASE-1/-2

- Primary endpoint: % of patients with ≥ 2 -level improvement in PR-PCSS and CR-PCSS (composite response)
- Key secondary endpoint: % of patients with ≥ 1 -level composite response (PR-PCSS and CR-PCSS)
- S-GAIS*

Patient Reported Photonumeric Cellulite Severity Scale (PR-PCSS) – Buttock



Clinician Reported Photonumeric Cellulite Severity Scale (CR-PCSS) – Buttock



©2017 Auxilium Pharmaceuticals, LLC. All rights reserved.

CR-PCSS, Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale; S-GAIS, Subject Global Aesthetic Improvement Scale.

*7-level scale scored from +3 “very much improved” to -3 “very much worse.”

Pooled Demographics and Baseline Characteristics

Pooled RELEASE-1/-2

| Parameter | CCH (n=424) | Placebo (n=419) |
|---|--|--|
| Mean age, y (SD) Range | 47.8 (10.5) 20–78 | 45.8 (10.5) 18–72 |
| Race, n (%) White Black Other | 336 (79.2) 76 (17.9) 12 (2.8) | 325 (77.6) 75 (17.9) 19 (4.5) |
| BMI category, n (%) Underweight/normal (<25 kg/m ²) Overweight (25 to <30 kg/m ²) Obese (≥30 kg/m ²) | 81 (19.1) 143 (33.7) 200 (47.2) | n=418* 84 (20.1) 123 (29.4) 211 (50.5) |
| Fitzpatrick scale category, n (%) I/II (pale white/fair) III (darker white) IV (light brown) V (brown) VI (dark brown) | 135 (31.8) 119 (28.1) 93 (21.9) 48 (11.3) 29 (6.8) | 114 (27.2) 139 (33.2) 82 (19.6) 45 (10.7) 39 (9.3) |

BMI, body mass index; CCH, collagenase clostridium histolyticum-aaes; SD, standard deviation.

*Data missing for 1 woman.

Baseline vs Post-CCH Treatment*: 2-Level Responder† (Example 1)

Pooled RELEASE-1/-2

Age: 43 years

Fitzpatrick: Type IV

BMI: 28.9 kg/m²



©2020 Endo Pharmaceuticals Inc. All rights reserved.

Note: Patients' individual right and left buttock images were combined to create the composite bilateral image shown.

CCH, collagenase clostridium histolyticum-aaes; CR-PCSS, Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale.

*Women received up to 3 treatment sessions of CCH 0.84 mg, each separated by ~21 days (up to 12 subcutaneous injections per treatment area on Days 1, 22, and 43).

†2-level improvement from baseline in CR-PCSS and PR-PCSS ratings at Day 71.

Example 1 (cont)

©2020 Endo Pharmaceuticals Inc. All rights reserved.



Day 1



Day 71

Baseline vs Post-CCH Treatment*: 2-Level Responder† (Example 2)

Pooled RELEASE-1/-2

Age: 48 years

Fitzpatrick: Type III

BMI: 17.9 kg/m²



Day 1 (Baseline) Visit



Day 71 Visit

©2020 Endo Pharmaceuticals Inc. All rights reserved.

Note: Patients' individual right and left buttock images were combined to create the composite bilateral image shown.

CCH, collagenase clostridium histolyticum-aaes; CR-PCSS, Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale.

*Women received up to 3 treatment sessions of CCH 0.84 mg, each separated by ~21 days (up to 12 subcutaneous injections per treatment area on Days 1, 22, and 43).

†2-level improvement from baseline in CR-PCSS and PR-PCSS ratings at Day 71.

Example 2 (cont)

©2020 Endo Pharmaceuticals Inc. All rights reserved.



Day 1 (Baseline) Visit



Day 71 Visit

Baseline vs Post-CCH Treatment*: 2-Level Responder† (Example 3)

Pooled RELEASE-1/-2

Age: 52 years

Fitzpatrick: Type II

BMI: 23.6 kg/m²



©2020 Endo Pharmaceuticals Inc. All rights reserved.

CCH, collagenase clostridium histolyticum-aaes; CR-PCSS, Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale.

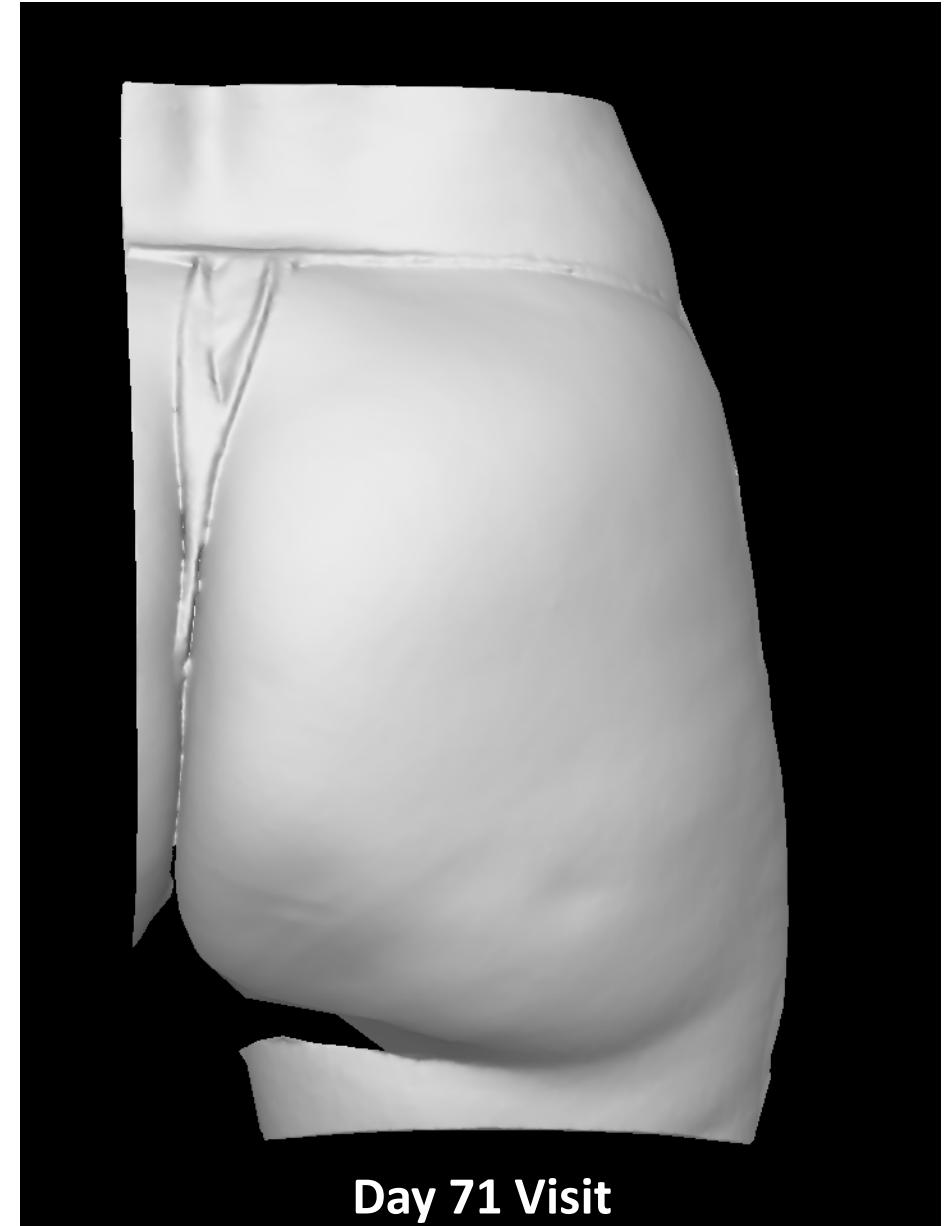
Note: Patients' individual right and left buttock images were combined to create the composite bilateral image shown.

*Women received up to 3 treatment sessions of CCH 0.84 mg, each separated by ~21 days (up to 12 subcutaneous injections per treatment area on Days 1, 22, and 43).

†2-level improvement from baseline in CR-PCSS and PR-PCSS ratings at Day 71.

Example 3 (cont)

©2020 Endo Pharmaceuticals Inc. All rights reserved.



Baseline vs Post-CCH Treatment*: 1-Level Responder†

Pooled RELEASE-1/-2

Age: 47 years

Fitzpatrick: Type IV

BMI: 23.8 kg/m²



©2020 Endo Pharmaceuticals Inc. All rights reserved.

CCH, collagenase clostridium histolyticum-aaes; CR-PCSS, Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale.

*Women received up to 3 treatment sessions of CCH 0.84 mg, each separated by ~21 days (up to 12 subcutaneous injections per treatment area on Days 1, 22, and 43).

†1-level improvement from baseline in PR-PCSS rating and 2-level improvement in CR-PCSS rating at Day 71.

1-Level Responder (cont)

©2020 Endo Pharmaceuticals Inc. All rights reserved.



Baseline vs Post-CCH Treatment*: 1-Level Responder†

Pooled RELEASE-1/-2

Age: 37 years

Fitzpatrick: Type III

BMI: 37.4 kg/m²



Day 1 (Baseline) Visit



Day 71 Visit

©2020 Endo Pharmaceuticals Inc. All rights reserved.

CCH, collagenase clostridium histolyticum-aaes; CR-PCSS, Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale.

*Women received up to 3 treatment sessions of CCH 0.84 mg, each separated by ~21 days (up to 12 subcutaneous injections per treatment area on Days 1, 22, and 43).

†1-level improvement from baseline in CR-PCSS and PR-PCSS ratings at Day 71.

1-Level Responder (cont)

©2020 Endo Pharmaceuticals Inc. All rights reserved.



Day 1 (Baseline) Visit

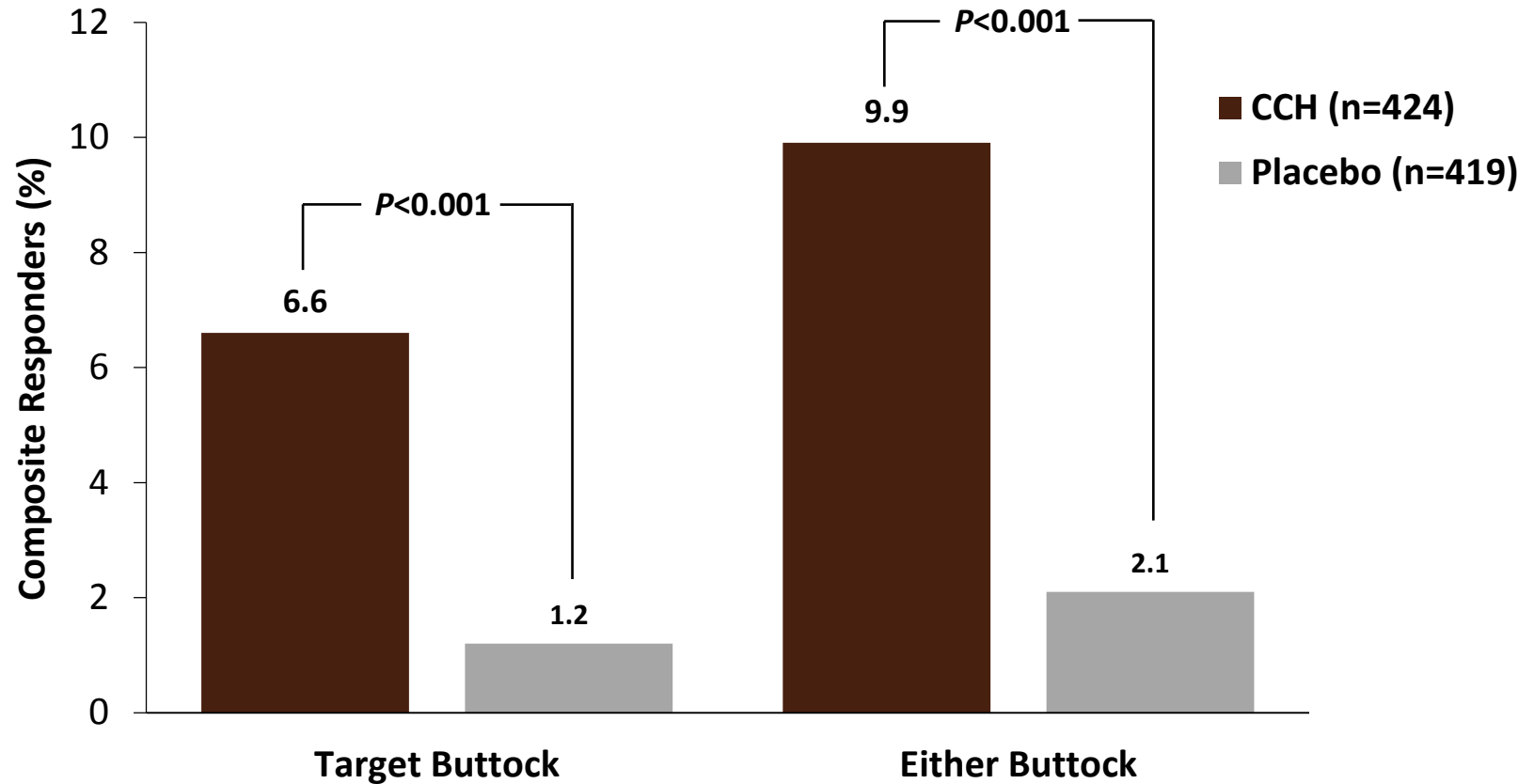


Day 71 Visit

Primary Endpoint: ≥2-Level Composite Responders at Day 71*

Pooled RELEASE-1/-2

CCH-treated women were
5.9 times more likely to be a
2-level composite responder
(OR, 5.9; 95% CI, 2.2–15.4; $P<0.001$)†



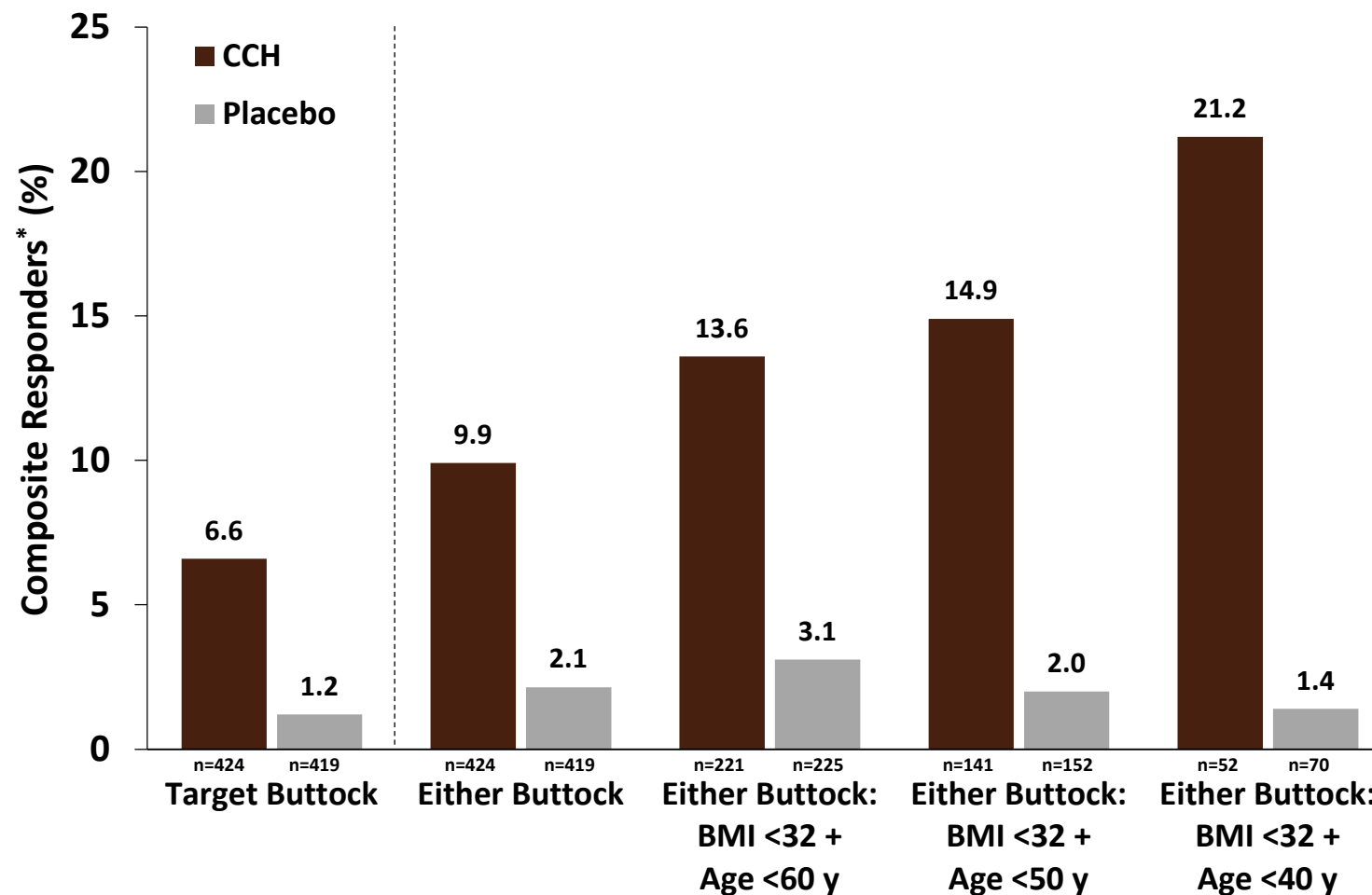
CCH, collagenase clostridium histolyticum-aaes; CI, confidence interval; CR-PCSS, Clinician Reported Photonumeric Cellulite Severity Scale; OR, odds ratio; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale.

*≥2-level improvement from baseline in CR-PCSS rating and PR-PCSS rating at Day 71. †Target buttock.

Post Hoc Subgroup Analyses

As with all aesthetic treatments, patient selection is important

Preliminary subgroup analyses suggests higher response rates with decreased age and lower BMI



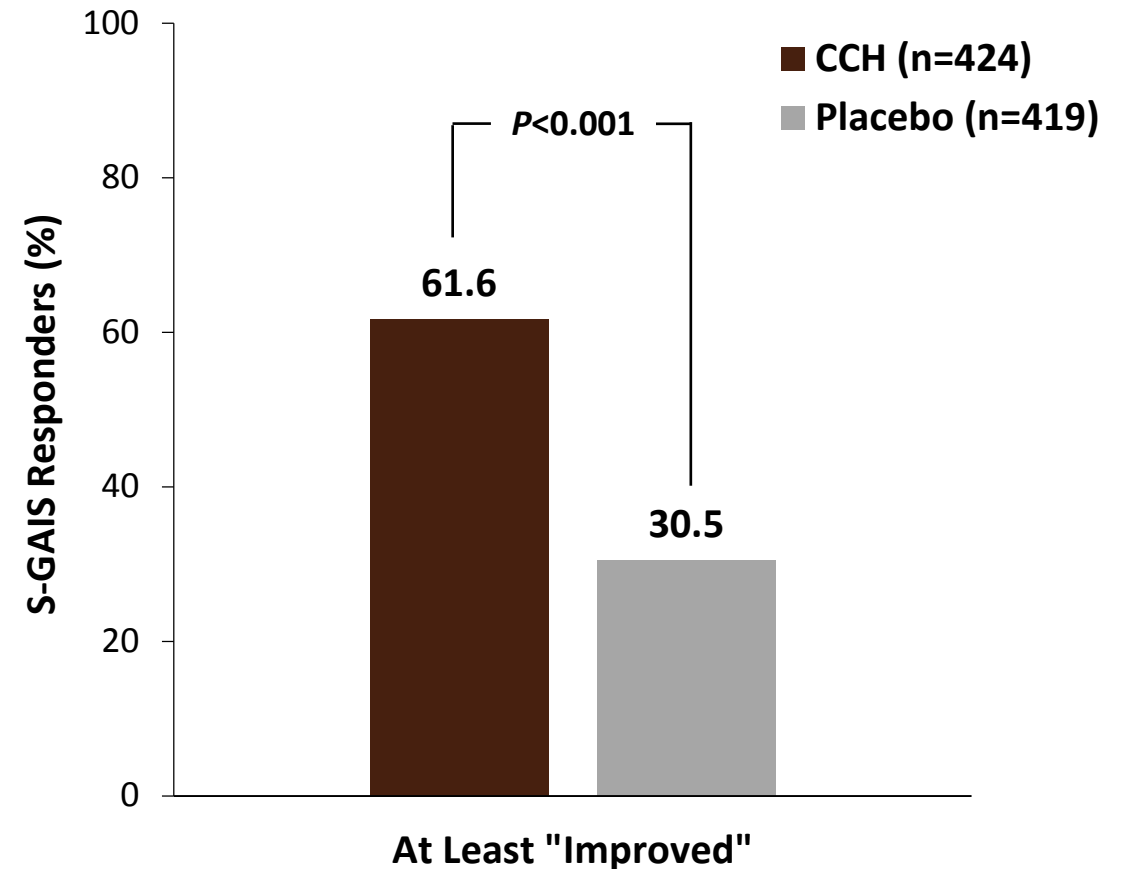
CCH, collagenase clostridium histolyticum-aes; CR-PCSS, Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale.

*≥2-level improvement from baseline in CR-PCSS rating and PR-PCSS rating at Day 71.

S-GAIS Responders* at Day 71

Pooled RELEASE-1/-2

- Anchor-based analyses indicated PR-PCSS score change ≥ 1 in PR-PCSS was clinically meaningful[†]
- Based on 1-level improvement in S-GAIS, PR-PCSS meaningful change threshold was 0.94 points (~1-level PR-PCSS rating change)
 - Effect size was statistically large at –1.89



ANOVA, analysis of variance; CCH, collagenase clostridium histolyticum-aaes; PR-PCSS, Patient Reported Photonumeric Cellulite Severity Scale; S-GAIS, Subject Global Aesthetic Improvement Scale.

*1-level responder ("very much improved," "much improved," or "improved") from baseline (7-level scale scored from +3 "very much improved" to -3 "very much worse"). [†]Anchor-based analysis to determine clinically meaningful threshold for PR-PCSS using 1-way ANOVA model with S-GAIS group (independent variable) and change in PR-PCSS score (dependent variable).

Summary of Adverse Events

Pooled RELEASE-1/-2

| Women With an AE , %* | CCH (n=424) | Placebo (n=419) |
|--------------------------------------|-------------|-----------------|
| Injection-site bruising [†] | 84 | 21 |
| Injection-site pain [‡] | 48 | 10 |
| Injection-site nodule [§] | 33 | 1 |
| Injection-site pruritus | 15 | 1 |
| Injection-site erythema | 9 | 5 |
| Injection-site discoloration | 8 | 1 |
| Injection-site swelling [¶] | 8 | 1 |
| Injection-site warmth | 3 | 0 |

AE, adverse event; CCH, collagenase clostridium histolyticum-aaes.

*Treatment-emergent AEs occurring in ≥1.0% of women in any group and ordered by frequency in CCH group.

[†]Injection-site bruising, injection-site hematoma, and injection-site hemorrhage (hemorrhage MedDRA term refers to verbatim term injection-site ecchymosis).

[‡]Injection-site pain, injection-site discomfort, and injection-site dysesthesia.

[§]Injection-site mass and injection-site nodule.

[¶]Injection-site swelling, injection-site edema, injection-site induration.

Example of CCH Injection-Site Bruising¹



Bruising was generally transient and appeared to lessen with subsequent treatment



Mechanism of bruising is being investigated in ongoing research²

© 2020 Endo Pharmaceuticals Inc. All rights reserved.

Note: Images are from a phase 2, open-label study (Study 205 photography substudy; Clinicaltrials.gov identifier: NCT03329989). Study did not employ a pre- or post-treatment protocol to potentially mitigate injection-site bruising.

CCH, collagenase clostridium histolyticum-aes. **1.** Fabi SG, et al. Presented at SCALE (Symposium for Cosmetic Advances & Laser Education) 2020; July 24-26, 2020; Virtual Meeting.

2. Shridharani S. Presented at Vegas Cosmetic Surgery & Aesthetic Dermatology; September 24-27, 2020; Virtual Meeting.

Conclusions

- CCH treatment provided statistically significant improvement in the appearance of moderate-to-severe cellulite on the buttocks of adult women
- CCH was generally well tolerated
 - Injection-site reactions were generally transient and self-limiting

Thank You



If you do not have a QR code reader on your phone, please download the Quick Scan (iPhone) or QR Droid (Androids) free app from your mobile app store.