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Two Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trials of Collagenase Clostridium Histolyticum (CCH) for the Treatment of Cellulite (Edematous Fibrosclerotic Panniculopathy)

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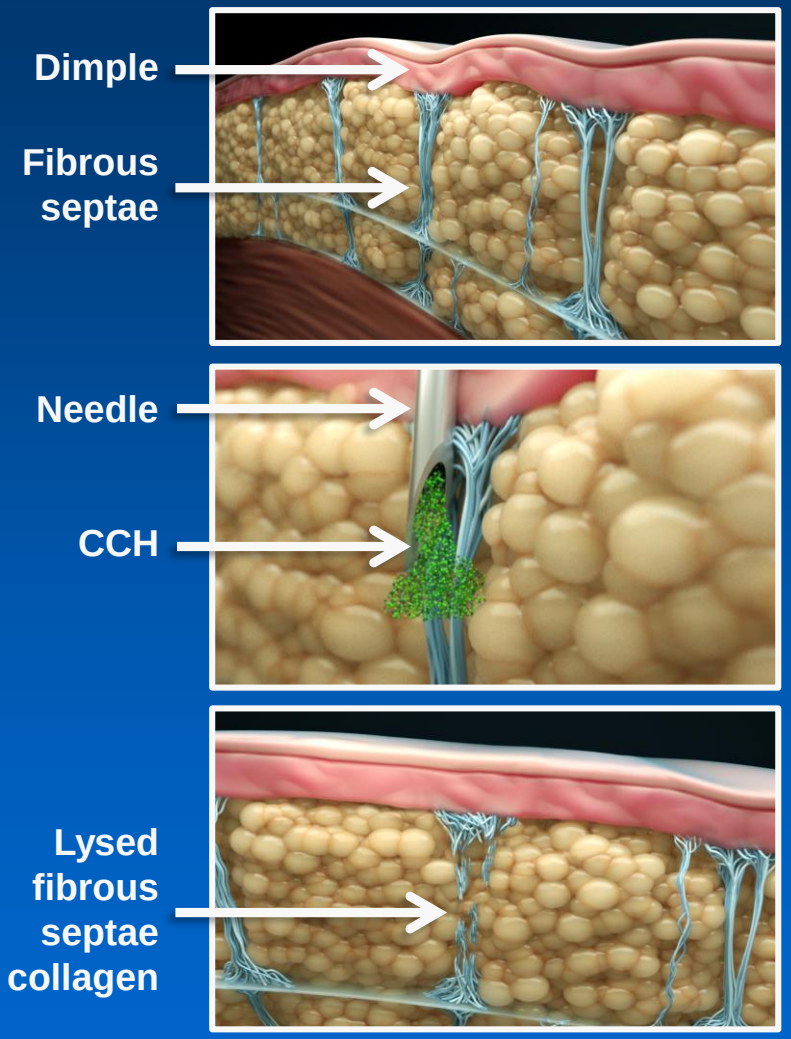
Author Disclosures

- JK and MSK report serving as a clinical investigator and consultant for Endo Pharmaceuticals Inc.
- JHJ reports being a shareholder and serving as a clinical investigator for Endo Pharmaceuticals Inc.
- DH, GL, MPM, and SV are employees of Endo Pharmaceuticals Inc.
- LSB reports being an advisory board participant for Endo Pharmaceuticals Inc. and Merz North America, Inc.; being a clinical investigator for Endo Pharmaceuticals Inc.; and serving as a consultant for Viveve

Introduction and Objective

- Collagen-rich subdermal septae play a role in cellulite[1]
- A novel presentation of collagenase clostridium histolyticum (CCH) is being investigated to correct cellulite-related contour alterations via enzymatic disruption of the septae, creating a skin-smoothing effect[2]
- **Objective:** to evaluate the efficacy and safety of CCH in 2 identically designed, phase 3 RCTs (RELEASE-1 and RELEASE-2)*



*Clinicaltrials.gov identifiers: NCT03446781 and NCT03428750.

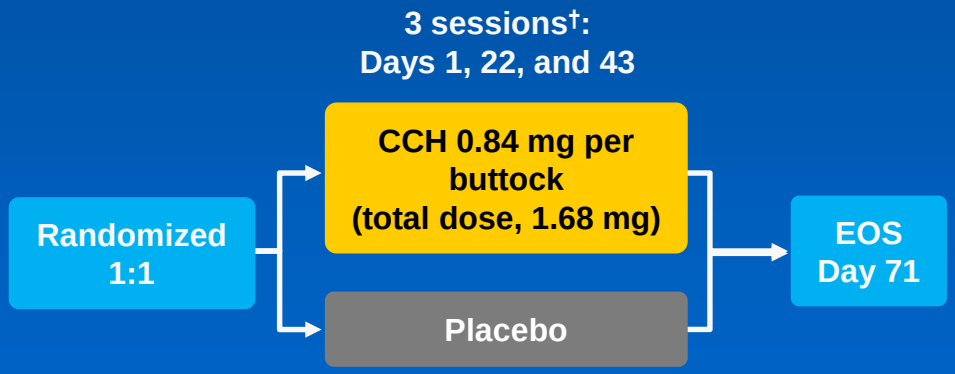
RCT = randomized, controlled trial; RELEASE = randomized evaluation of cellulite reduction by collagenase clostridium histolyticum.

1. Hexsel D, et al., eds. Update in Cosmetic Dermatology. Berlin: Springer-Verlag; 2013:21-32.
2. Sadick N, et al. *Dermatologic Surg.* 2019. In press.

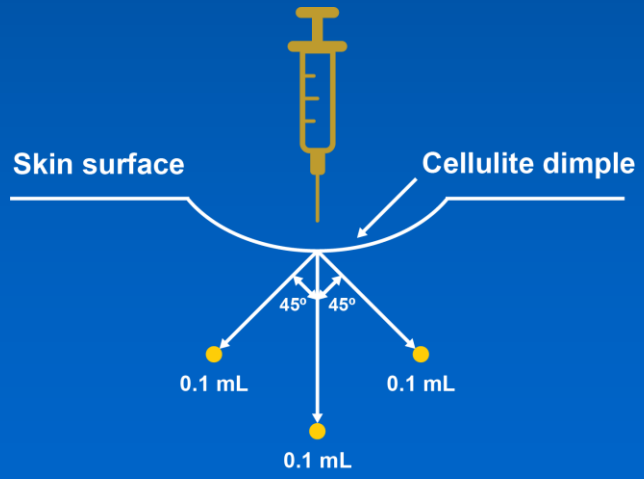
Patients and Study Design

- Women with moderate or severe cellulite* on both buttocks
- 843 women received ≥1 injection (CCH vs placebo: RELEASE-1, n=210 vs n=213; RELEASE-2, n=214 vs n=206)
- The same treatment was administered to both buttocks of each patient (CCH or placebo)
- Patients were well represented in terms of age (range, 18-78 y), BMI (range, 18-67 kg/m^2), and Fitzpatrick category

Double-blind, placebo-controlled



Each injection administered as three 0.1-mL aliquots



*CR-PCSS and PR-PCSS score of 3 or 4.
†12 injections (0.3 mL/injection) per buttock.
BMI = body mass index; CCH = collagenase clostridium histolyticum; CR-PCSS = Clinician Reported Photonumeric Cellulite Severity Scale; EOS = end of study; PR-PCSS = Patient Reported Photonumeric Cellulite Severity Scale.

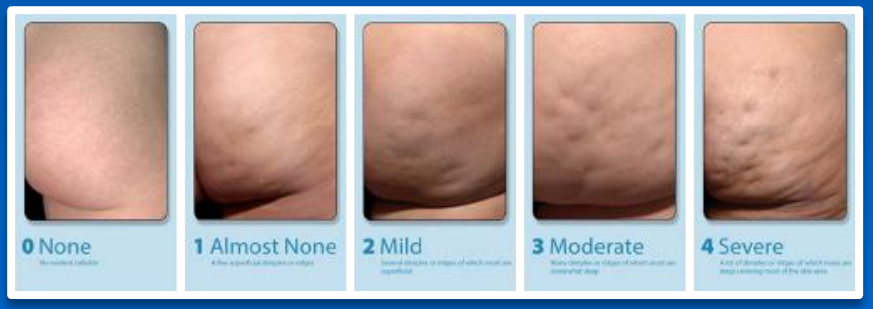
Primary Endpoint

Primary efficacy endpoint:

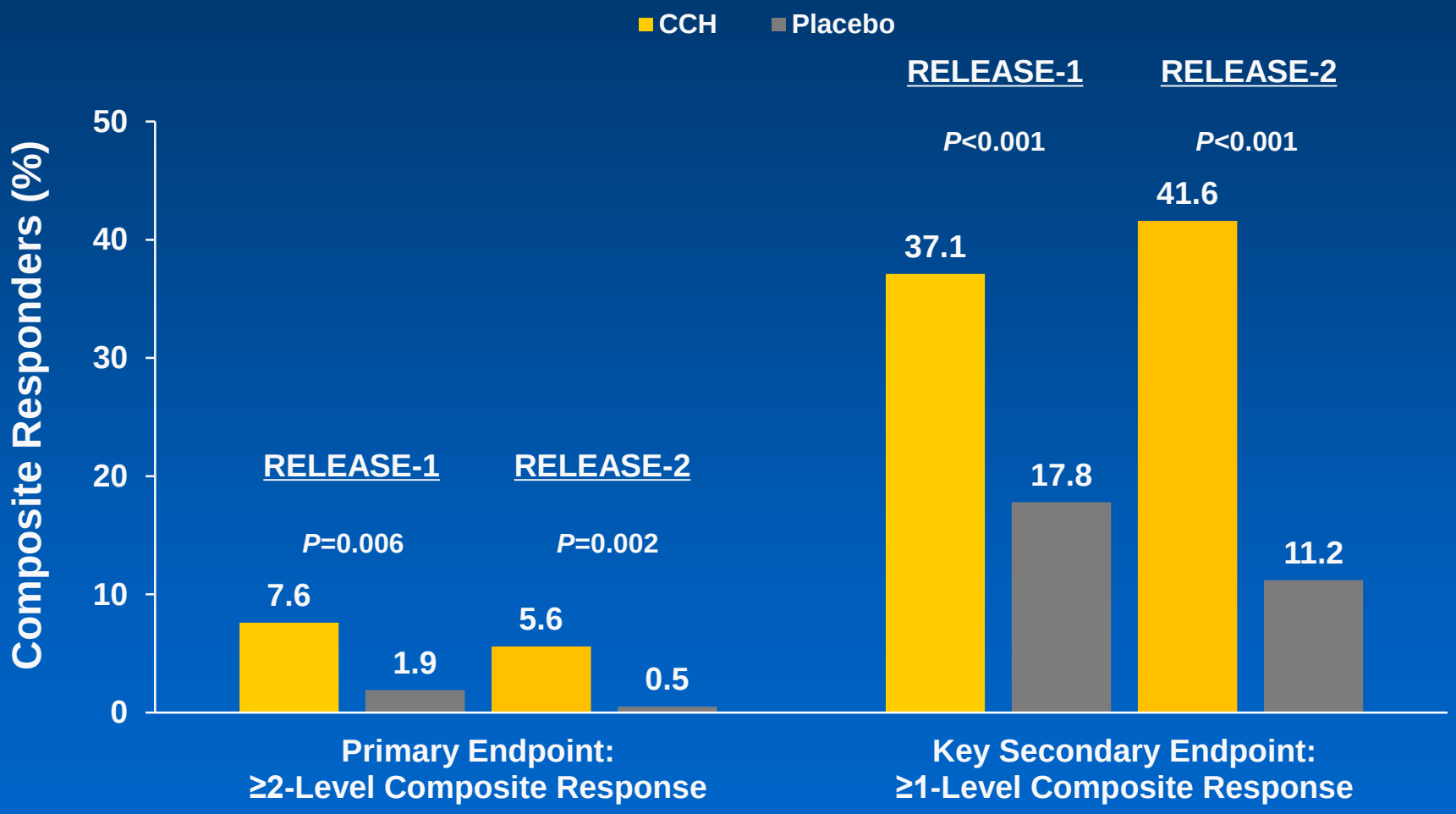
- Percentage of composite responders at Day 71
- Responders defined as ≥2-level improvement from baseline in both PR-PCSS and CR-PCSS for target buttock

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

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

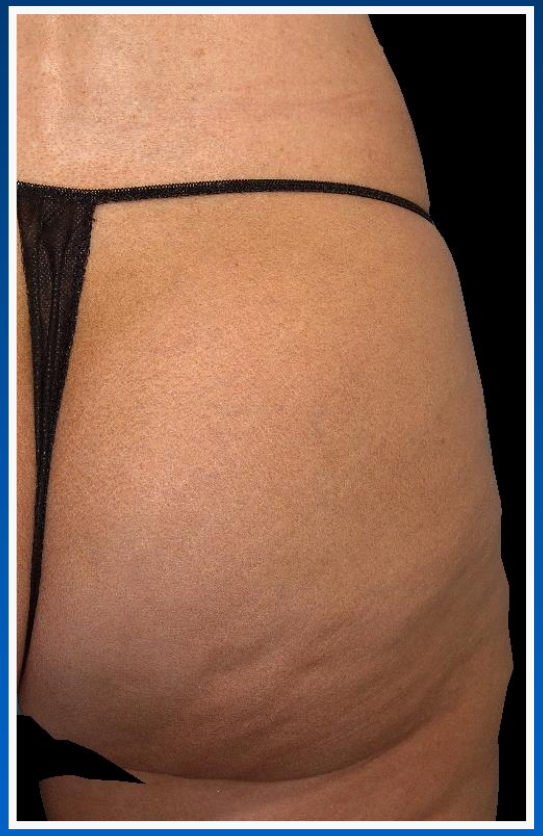


Composite Response* at Day 71

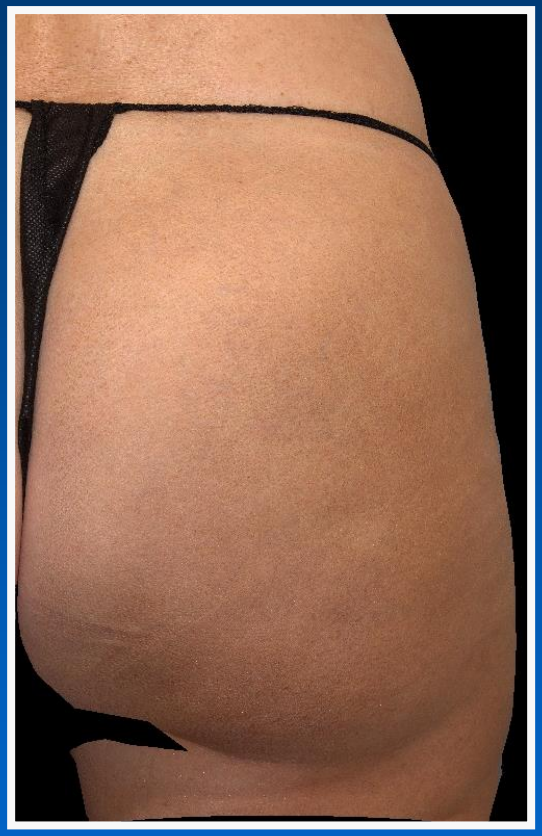


*≥2-level or ≥1-level improvement from baseline in CR-PCSS rating and PR-PCSS rating at Day 71.
CCH = collagenase clostridium histolyticum; CR-PCSS = Clinician Reported Photonumeric Cellulite Severity Scale;
PR-PCSS = Patient Reported Photonumeric Cellulite Severity Scale.

Patient A Treated With CCH: 2-Level Composite Response*



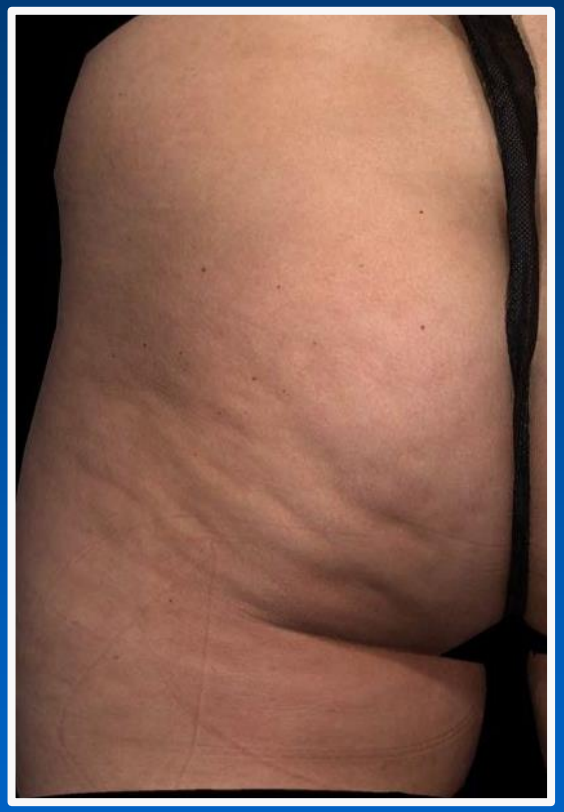
Pre-Treatment



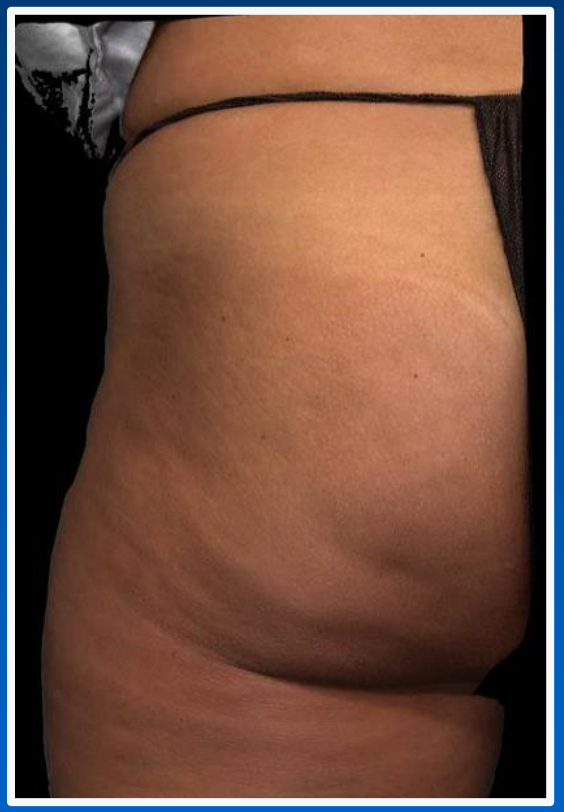
28 Days After Final Injection

*2-level improvement from baseline in CR-PCSS rating and PR-PCSS rating.
CCH = collagenase clostridium histolyticum; CR-PCSS = Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS = Patient Reported Photonumeric Cellulite Severity Scale.

Patient B Treated With CCH: 1-Level Composite Response*



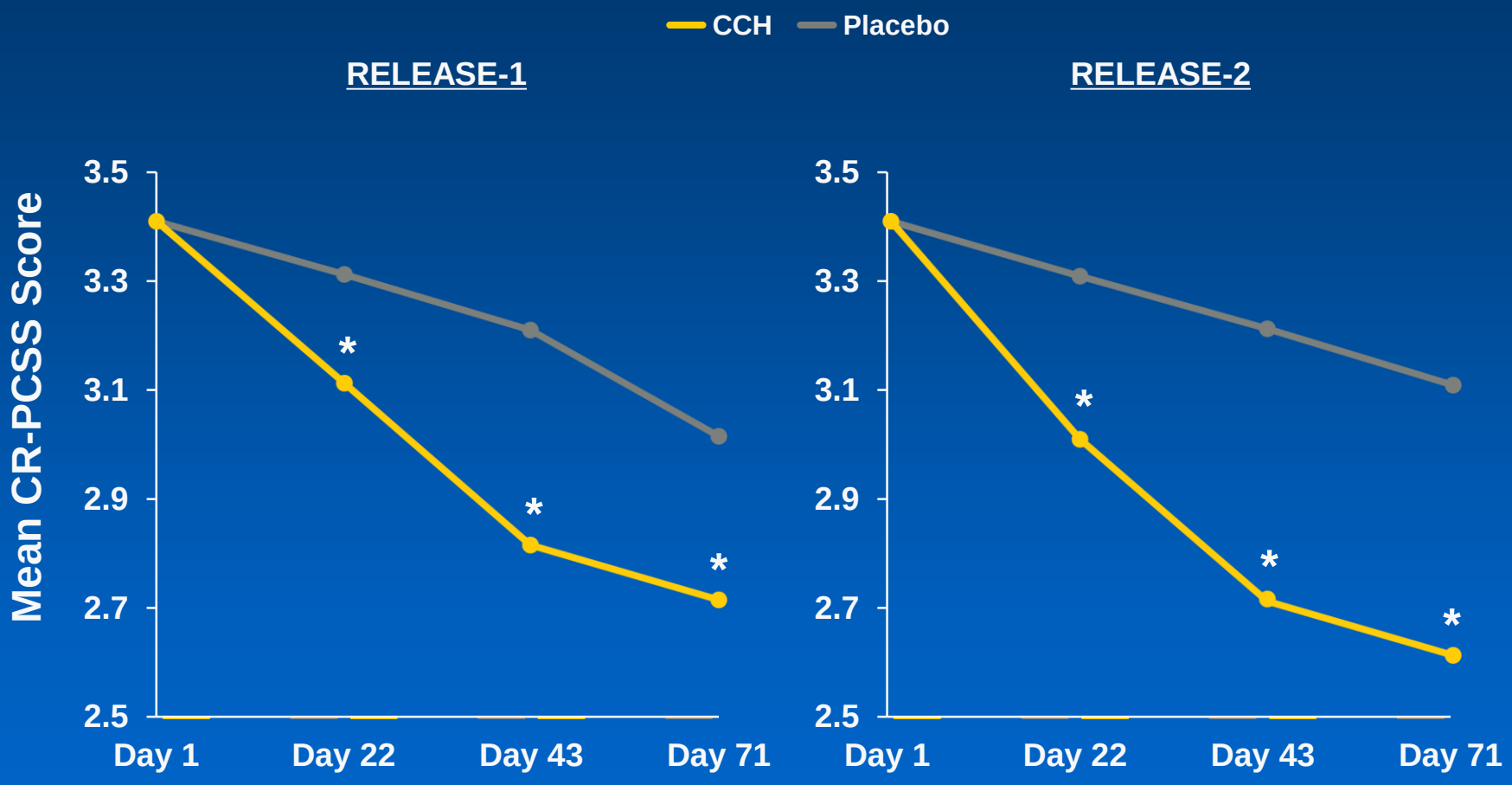
Pre-Treatment



28 Days After Final Injection

*1-level improvement from baseline in CR-PCSS rating and PR-PCSS rating.
CCH = collagenase clostridium histolyticum; CR-PCSS = Clinician Reported Photonumeric Cellulite Severity Scale; PR-PCSS = Patient Reported Photonumeric Cellulite Severity Scale.

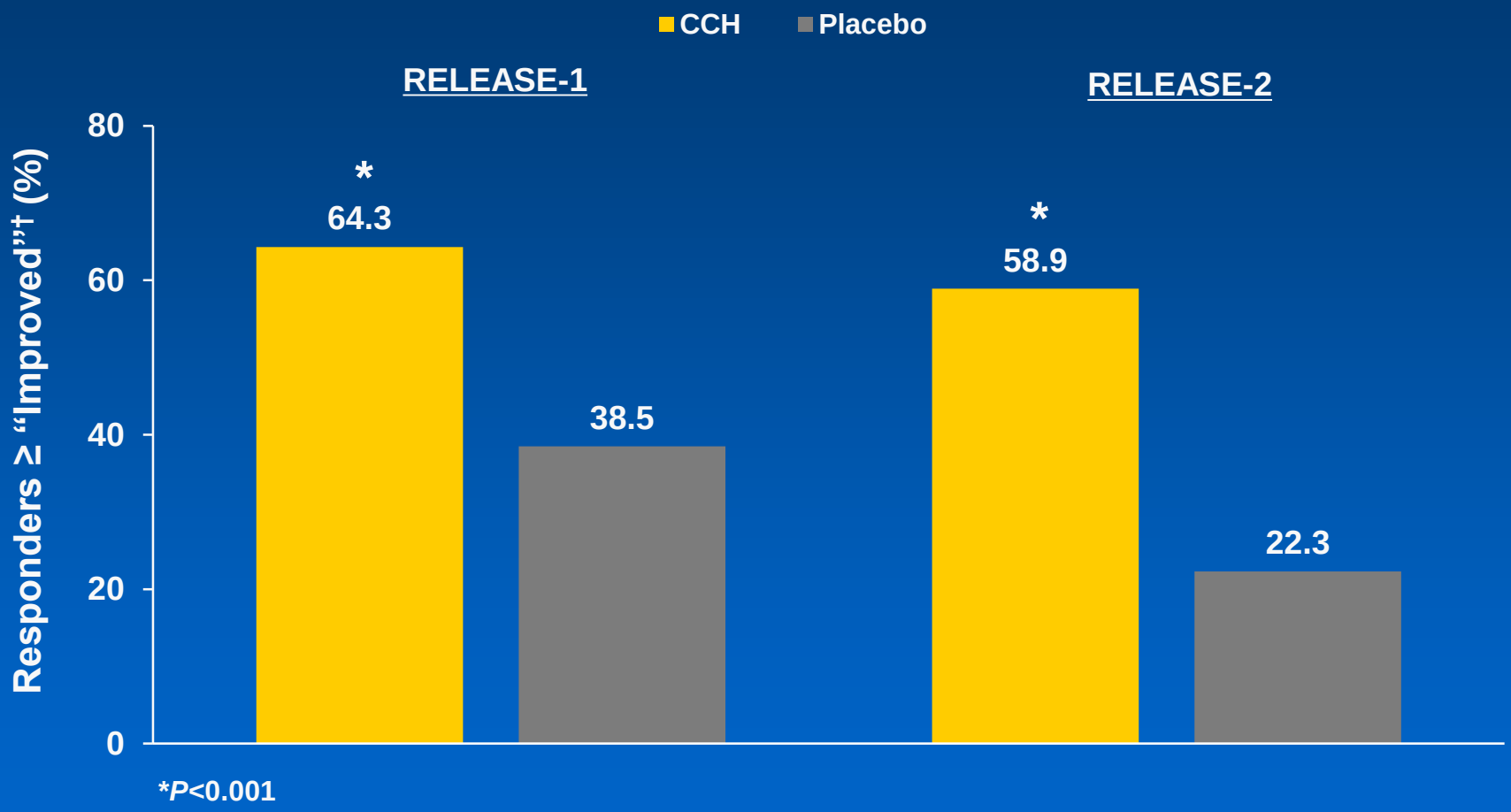
Mean CR-PCSS Scores Over Time



****P*<0.001 vs placebo**

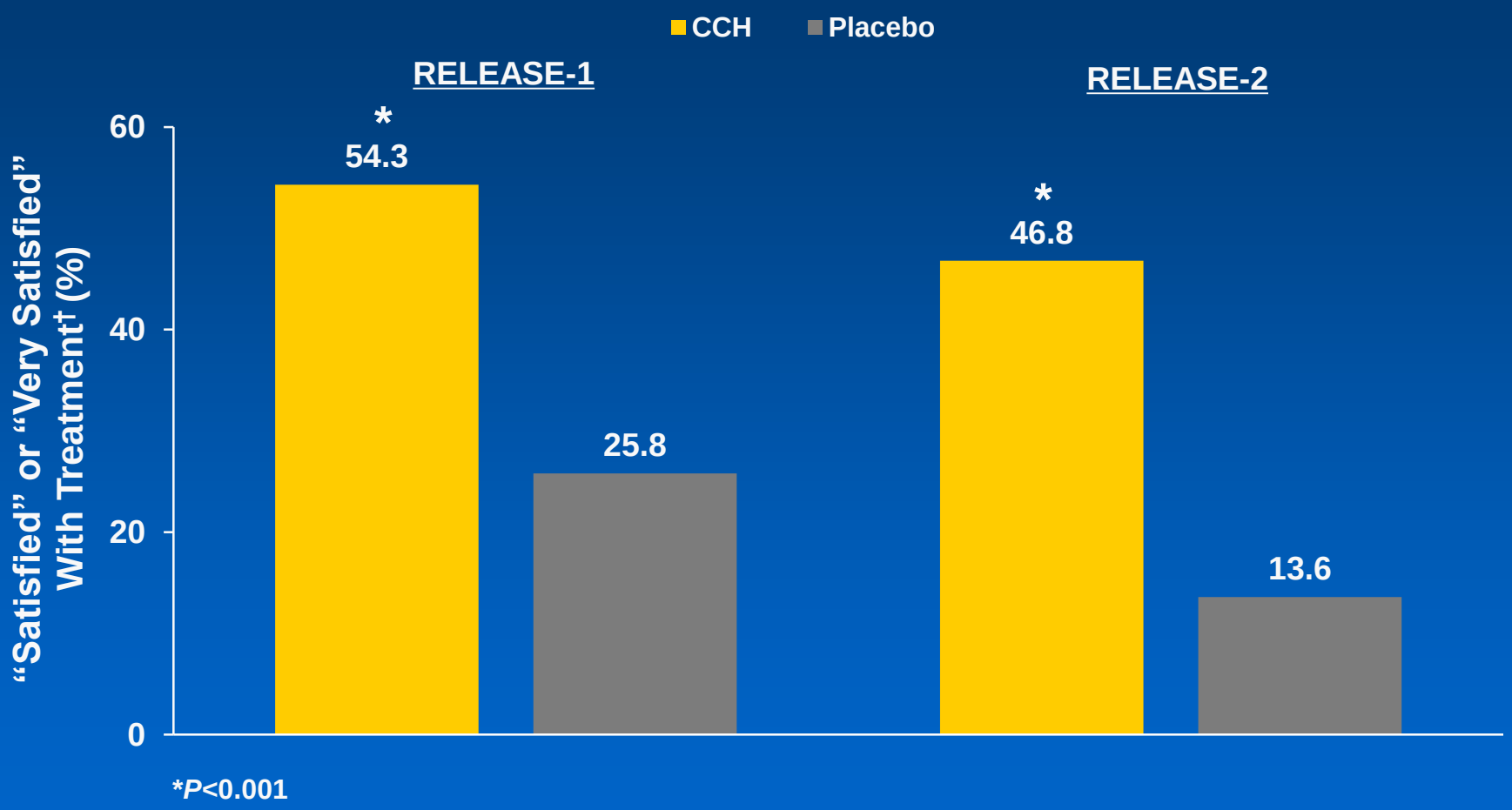
CCH = collagenase clostridium histolyticum; CR-PCSS = Clinician Reported Photonumeric Cellulite Severity Scale.

Subject Global Aesthetic Improvement Scale (S-GAIS) Response at Day 71



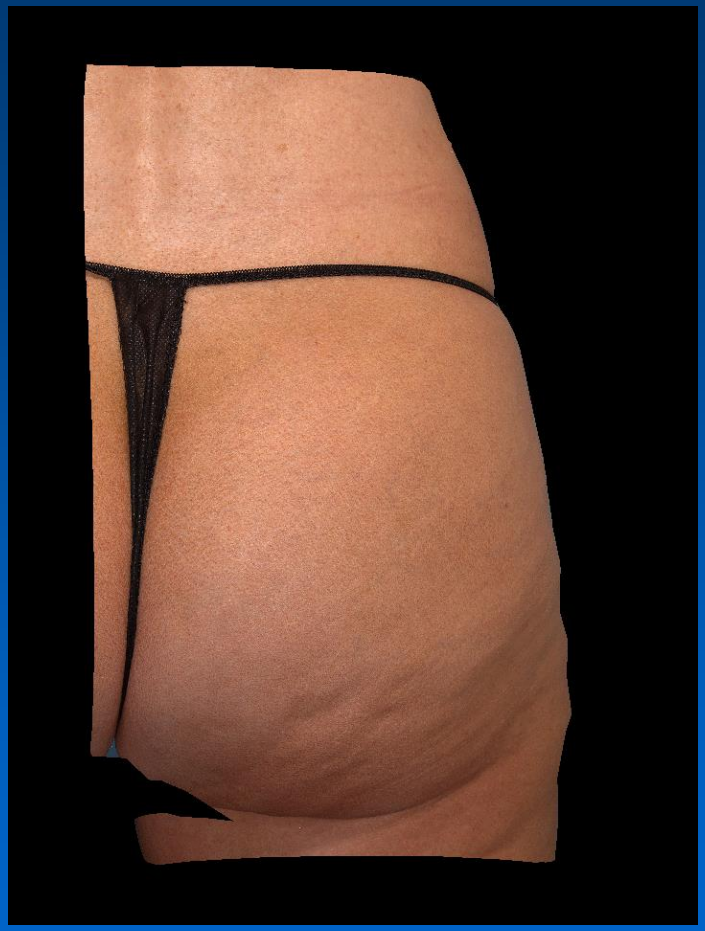
†S-GAIS responders included patients who were "Improved", "Much Improved" or "Very Much Improved" following treatment.
CCH = collagenase clostridium histolyticum.

Subject Satisfaction at Day 71

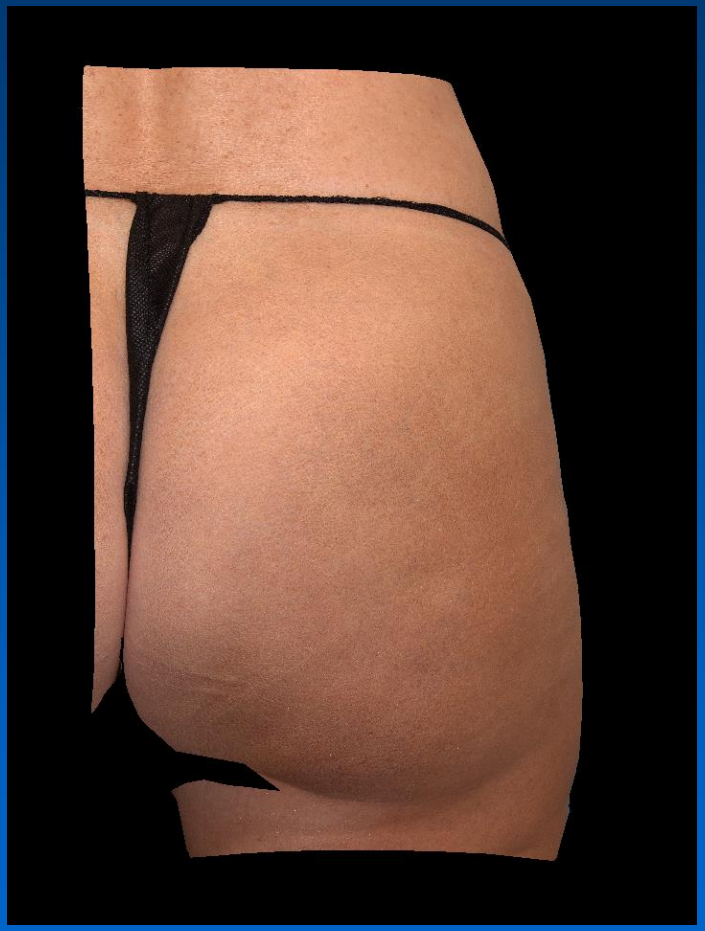


†Subject satisfaction with cellulite treatment assessment: 5-level scale ranging from 2 (very satisfied) to −2 (very dissatisfied).
CCH = collagenase clostridium histolyticum.

Patient A: Skin Surface Texture After CCH Treatment



Pre-Treatment

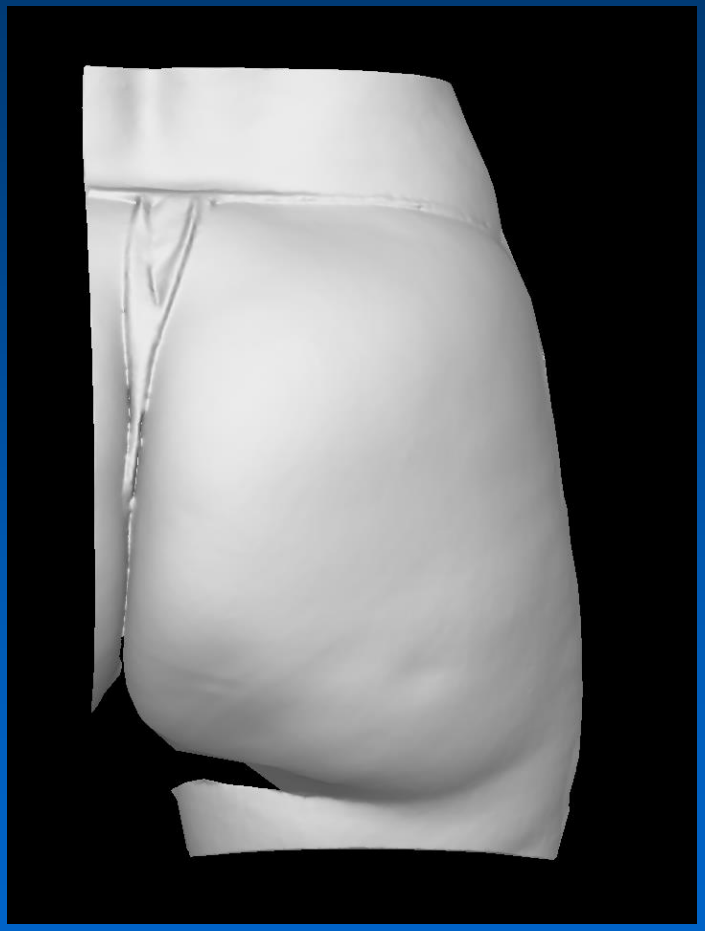


28 Days After Final Injection

CCH = collagenase clostridium histolyticum.

Patient A: Skin Surface Texture After CCH Treatment

Pre-Treatment



28 Days After Final Injection

CCH = collagenase clostridium histolyticum.

Adverse Event Profile

Women With an AE, %	RELEASE-1		RELEASE-2	
	CCH (n=210)	Placebo (n=213)	CCH (n=214)	Placebo (n=206)
≥1 AE	81.0	38.0	95.3	42.7
AE leading to discontinuation	4.3	0.5	3.7	1.0
Most common AEs (≥7.0% of women in any CCH group)*				
Injection-site bruising	65.2	19.7	90.2	20.4
Injection-site pain	36.2	5.2	59.3	12.6
Injection-site nodule	18.1	0	32.7	1.0
Injection-site pruritus	13.8	0.5	15.9	1.5
Injection-site erythema	3.8	1.9	13.1	8.3
Injection-site discoloration	5.7	0	9.8	1.0
Injection-site mass	8.6	0.5	7.0	0
Injection-site hemorrhage†	11.9	2.3	2.8	0.5
Injection-site swelling	7.1	0	4.2	0.5

*Ordered in table by most common AE in pooled CCH group for the 2 studies.
†Preferred for the verbatim term “injection-site ecchymosis.”
AE = adverse event; CCH = collagenase clostridium histolyticum.

Conclusions

- CCH significantly improved cellulite severity and appearance in women with moderate to severe cellulite on the buttocks, using both clinician- and patient-report outcome measures
- Administration of CCH for cellulite was generally well tolerated
- A phase 3, open-label, 5-year study is currently ongoing to assess the durability of response of CCH for the treatment of cellulite in women (Clinicaltrials.gov identifier: NCT03526549)

CCH = collagenase clostridium histolyticum.