QWO (COLLAGENASE CLOSTRIDIUM HISTOLYTICUM-AAES) (CCH-AAES) CLINICAL STUDIES

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INDICATION AND IMPORTANT SAFETY INFORMATION FOR QWO™

(COLLAGENASE CLOSTRIDIUM HISTOLYTICUM-AAES)

INDICATION

QWO is indicated for the treatment of moderate to severe cellulite in the buttocks of adult women.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

QWO is contraindicated in patients with a history of hypersensitivity to collagenase or to any of the excipients or the presence of infection at the injection sites.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Serious hypersensitivity reactions including anaphylaxis have been reported with the use of collagenase clostridium histolyticum. If such a reaction occurs, further injection of QWO should be discontinued and appropriate medical therapy immediately instituted. Advise patients to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions.

Injection Site Bruising

In clinical trials, 84% of subjects treated with QWO experienced injection site bruising. Subjects with coagulation disorders or using anticoagulant or antiplatelet medications (except those taking ≤150 mg aspirin daily) were excluded from participating in Trials 1 and 2.

QWO should be used with caution in patients with bleeding abnormalities or who are currently being treated with antiplatelet (except those taking ≤150 mg aspirin daily) or anticoagulant therapy.

Substitution of Collagenase Products

QWO must not be substituted with other injectable collagenase products.

QWO is not intended for the treatment of Peyronie's Disease or Dupuytren's Contracture.

ADVERSE REACTIONS

In clinical trials, the most commonly reported adverse reactions in patients treated with QWO incidence ≥ 10% were at the injection site: bruising, pain, nodule and pruritus.

Please see Full Prescribing Information for QWO at www.qwo.com.

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CLINICAL PHARMACOLOGY STUDIES FOR CCH INDICATE LACK OF SYSTEMIC EXPOSURE WITH FAVORABLE CLEARANCE PROFILE

No systemic exposure detected

No quantifiable exposure attributable to 3.36 mg dose[1]

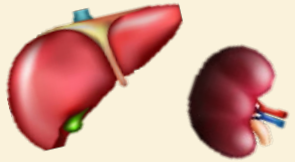
No active metabolites are expected

Given CCH is not a substrate for cytochrome P450 or other drug metabolizing enzyme pathways,[2] no active metabolites are expected

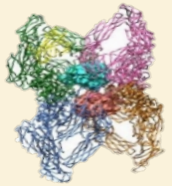
Burden on liver or kidney not expected as hepatic or renal clearance of CCH are unlikely

Route of CCH clearance

Less likely — More likely



Hepatic and renal excretion are unlikely



*a*2-Macroglobulin-mediated clearance[2-4]
Half-life of <30 min may indicate efficient *a*2-macroglobulin (A2M) clearance[5]

CCH = collagenase clostridium histolyticum.

References: 1. QWO [package insert]. Malvern, PA: Endo Aesthetics LLC. **2.** Willingham MC, et al. *J Cell Biol.* 1979;82(3):614-25 **3.** Gliemann J, et al. *Ann N Y Acad Sci.* 1994;737:20-38. **4.** Imber MJ, Pizzo SV. *J Biol Chem.* 1981;256(15):8134-9. **5.** Gabrielson AT, et al. *World J Mens Health*. 2017;35(3):134-45.

KEY EARLY CLINICAL STUDIES FOR CCH-AAES LEADING TO PHASE 3 STUDIES

- Phase 1b – safety study
- Phase 2a – dose ranging study
- Phase 2b – 375 subject study

CCH-aaes = collagenase clostridium histolyticum-aaes.

Sadick NS, et al. *Dermatol Surg*. 2019;45(8):1047-1056.

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RELEASE 1 AND RELEASE 2 PHASE 3 CLINICAL STUDIES

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LARGEST PHASE 3 CLINICAL TRIALS EVER FOR CELLULITE

843 women with moderate or severe cellulite on both buttocks

- *Two identical double blind, placebo-controlled sister clinical trials*, RELEASE-1 (n=210 vs n=213); RELEASE-2 (n=214 vs n=206)
- The same treatment protocol was administered to both buttocks of each patient (CCH-aaes or placebo)
- The diversity of patients was well represented in age (18 to 78 y), BMI (18 to 67 kg/m^2), and Fitzpatrick category (I to VI)

CCH-aaes = collagenase clostridium histolyticum-aaes.

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INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria

- *Women ≥18 years of age* who were not pregnant or lactating
- *Moderate to severe* (3 to 4) on the Clinician Reported Photonumeric Cellulite Severity Scale (CR-PCSS) and Patient Reported Photonumeric Cellulite Severity Scale (PR-PCSS) on both buttocks

Exclusion Criteria

- Severe skin laxity, flaccidity, or sagging skin
- Inflammation or an active infection
- Tattoo(s) located within 2 cm of the areas to be evaluated
- *Current treatment for cellulite* or use, within the previous 12 months, of injectables, laser treatment, liposuction, radiofrequency treatment, implants, cryolipolysis, or surgery for cellulite in the areas to be evaluated
- *Anticoagulant or antiplatelet medication* within 7 days before injection or needed to receive anticoagulant or antiplatelet medication (except aspirin ≤150 mg/day) during the study

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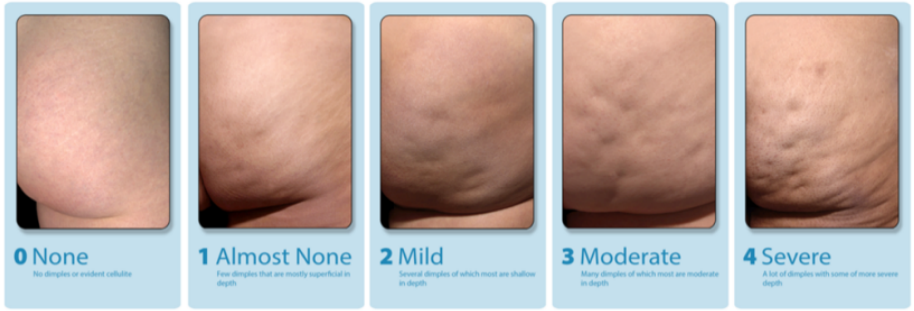
PRIMARY EFFICACY ENDPOINT: 2-LEVEL REDUCTION IN BOTH CELLULITE SEVERITY SCORES

Clinician Reported Photonumeric Cellulite Severity Scale (CR-PCSS)[1]



Patient Reported Photonumeric Cellulite Severity Scale (PR-PCSS)[1]

2-Level Improvement Examples

- severe to mild
- moderate to almost none

2-Level Composite Endpoint

Responders were participants who achieved a >2-level improvement from baseline in both PR-PCSS and CR-PCSS for target buttock[2]

- Physician evaluated the patient live[3]
- Patient rated themselves by evaluating photos[3]

1. Sadick NS, et al. *Dermatol Surg*. 2019;45(8):1047-1056. 2. Qwo [package insert]. Malvern, PA: Endo Aesthetics LLC. 3. Data on File.

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DEMOGRAPHICS

Population and Demographics

Parameter	RELEASE-1		RELEASE-2	
	CCH-aaes (n=210)	Placebo* (n=213)	CCH-aaes (n=214)	Placebo (n=206)
Mean age, y (range)	47.9 (21-70)	45.8 (22-70)	47.7 (20-78)	45.7 (18-72)
Race, %				
White	74.8	75.6	83.6	79.6
Black	22.4	20.2	13.6	15.5
Other	2.8	4.2	2.8	4.9

*Data missing for 1 woman in RELEASE-1 placebo group.

CCH-aaes = collagenase clostridium histolyticum-aaes.

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INCLUSIVE OF ALL FITZPATRICK SKIN TYPES

Population and Demographics

Parameter	RELEASE-1		RELEASE-2	
	CCH-aaes (n=210)	Placebo* (n=213)	CCH-aaes (n=214)	Placebo (n=206)
Fitzpatrick scale category, %				
I/II (pale white/fair)	26.2	24.4	37.4	30.1
III (darker white)	32.9	35.2	23.4	31.1
IV (light brown)	19.0	16.4	24.8	22.8
V (brown)	15.7	12.7	7.0	8.7
VI (dark brown)	6.2	11.3	7.5	7.3

Approximately 40% of patients had a Fitzpatrick score of IV to VI

*Data missing for 1 woman in RELEASE-1 placebo group.

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BMI BY CATEGORY

Population and Demographics

Parameter	RELEASE-1		RELEASE-2	
	CCH-aaes (n=210)	Placebo* (n=213)	CCH-aaes (n=214)	Placebo (n=206)
BMI category, %*				
Underweight/normal (<25 kg/m^2)	20.5	19.3	17.8	20.9
Overweight (25 to <30 kg/m^2)	32.9	29.2	34.6	29.6
Obese (≥30 kg/m^2)	46.7	51.4	47.7	49.5

~80% of participants were overweight or obese

FDA required patients with all BMIs be included in clinical trial.

BMI = body mass index; CCH-aaes = collagenase clostridium histolyticum-aaes.

*Data missing for 1 woman in RELEASE-1 placebo group.

Data on File.

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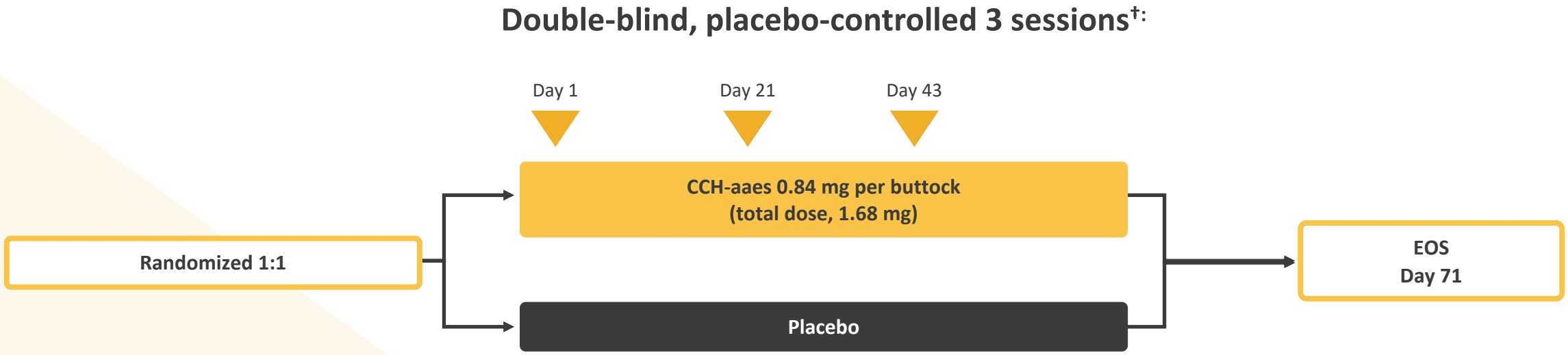
CLINICAL STUDY DESIGN

843 women with moderate or severe cellulite on both buttocks received
12 injections per buttock over 3 treatment sessions



† ±3 days

CCH-aaes = collagenase clostridium histolyticum-aaes; EOS = end of study.

Kaufman J, et al. Two Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trials of Collagenase Clostridium Histolyticum (CCH) for the Treatment of Cellulite (Edematous Fibrosclerotic Panniculopathy) Oral presentation at the American Academy of Dermatology Annual Meeting; 11362: March 2, 2019; Washington, DC.

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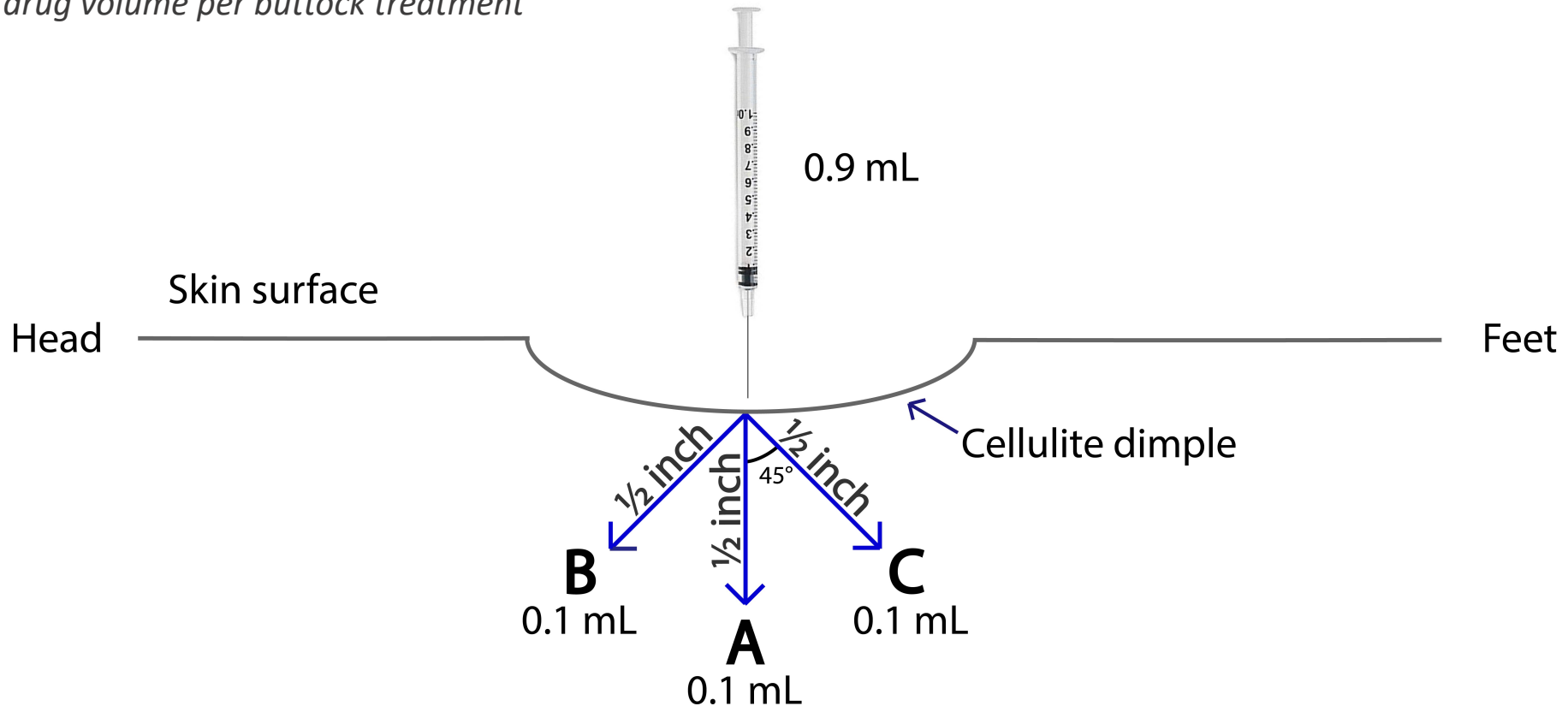
STUDY DRUG ADMINISTRATION

Buttock treatment (3 aliquot injection)

3.6 ml total drug volume per buttock treatment



Qwo [package insert]. Malvern, PA: Endo Aesthetics LLC.

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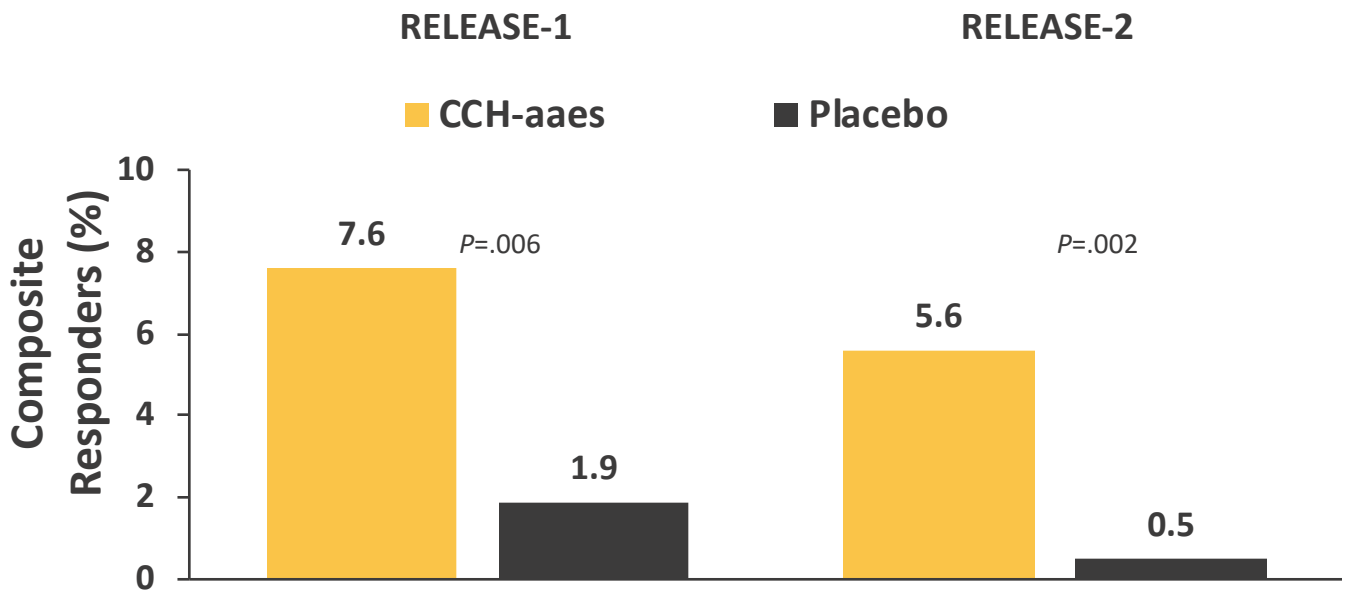
PRIMARY ENDPOINT: ≥2-LEVEL COMPOSITE RESPONSE AT DAY 71



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RESPONDER IMAGES

2-Level Composite Responders

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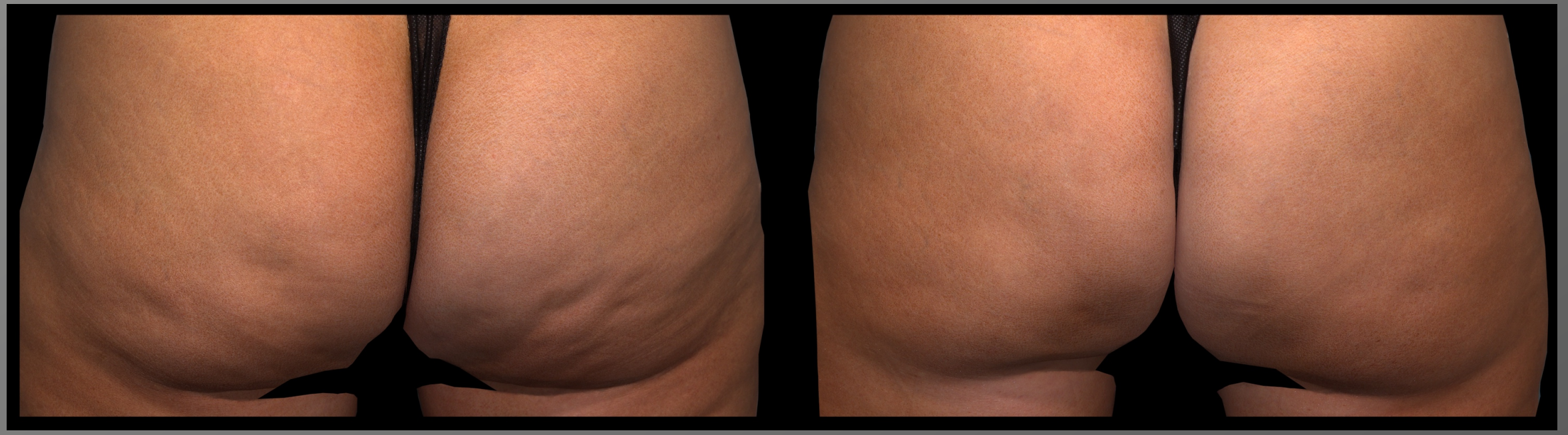
2-LEVEL COMPOSITE RESPONDER* ON BOTH BUTTOCKS



Day 1 Day 71

Patient demographics: Age 52, Fitzpatrick Type II, BMI 23.6
Individual results may vary.

*2-level improvement from baseline in CR-PCSS rating and PR-PCSS rating.

Phase 3 subject images (Data on File). Image presented is from RELEASE I with permission from patient and physician.

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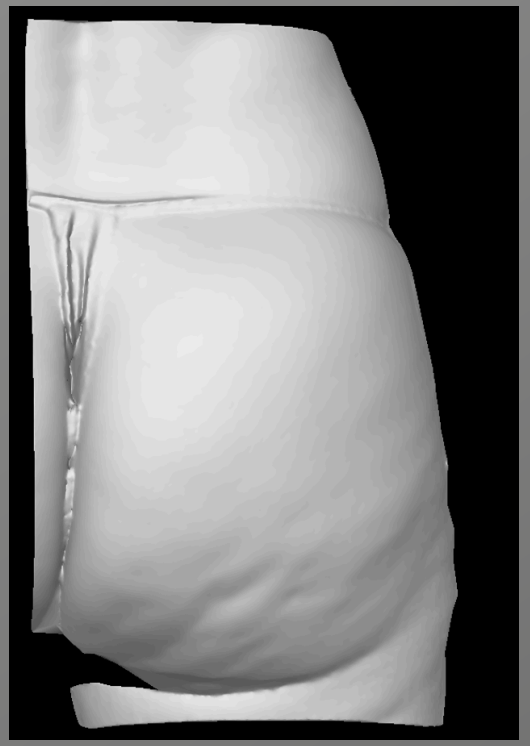
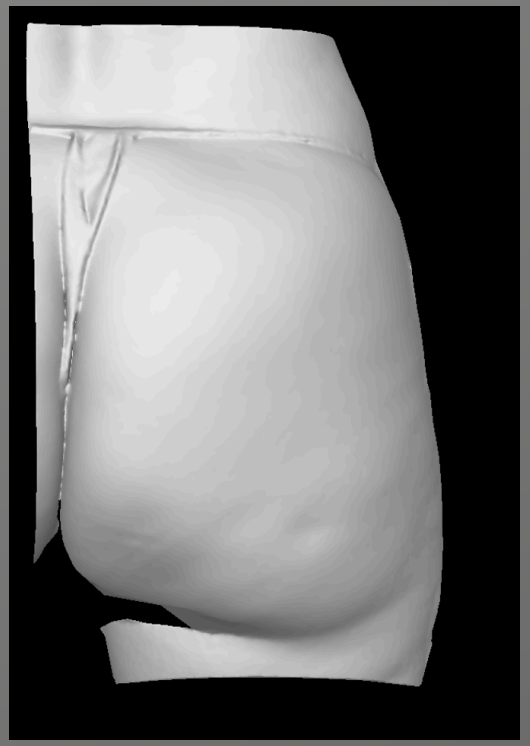
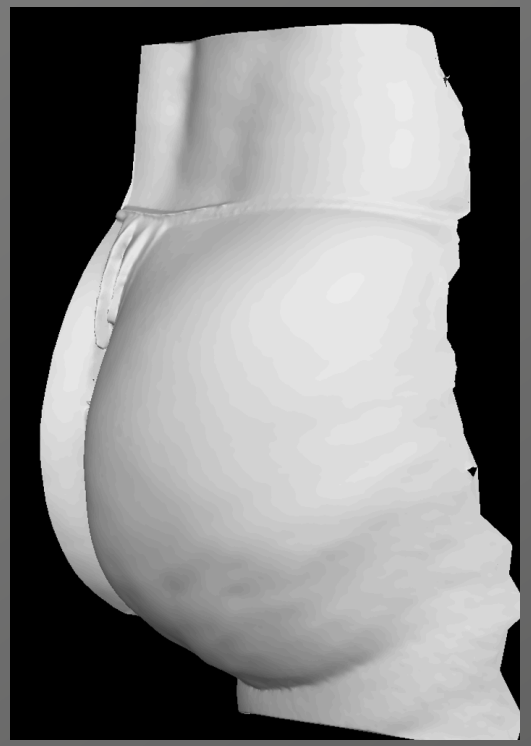
2-LEVEL COMPOSITE RESPONDER* – 3D GREY SCALE IMAGING



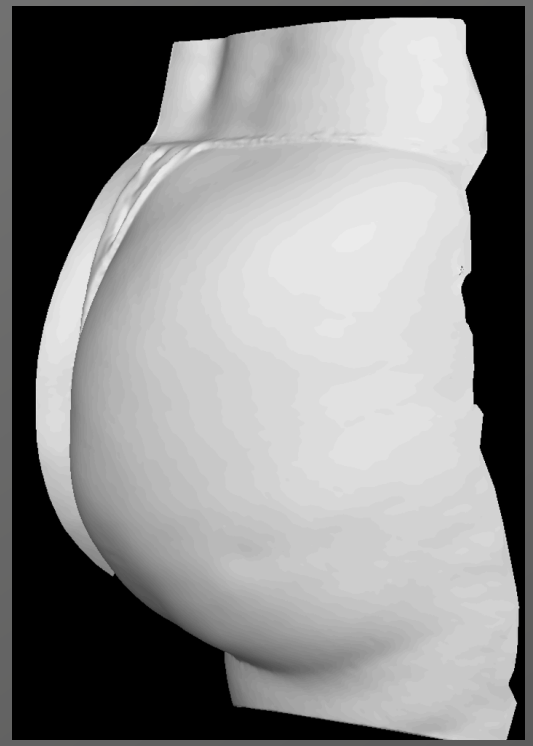
Pre-Treatment
(Back)



Day 71 - After 3 Treatments
(Back)



Pre-Treatment
(Right Side)



Day 71 - After 3 Treatments
(Right Side)

Individual results may vary.

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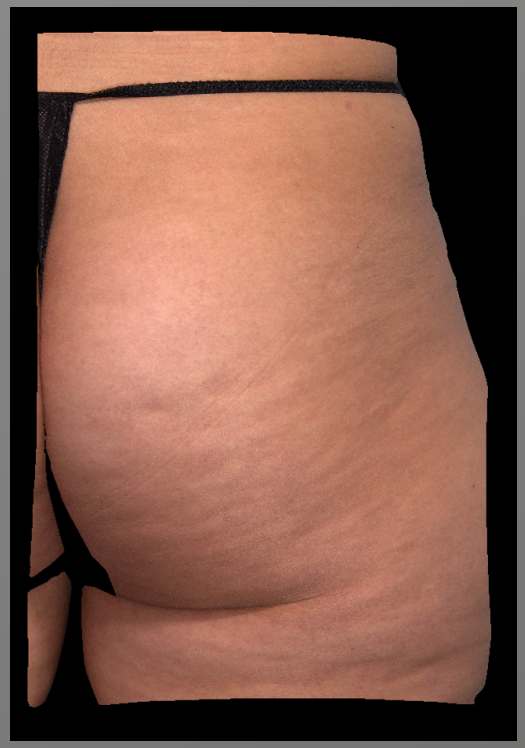
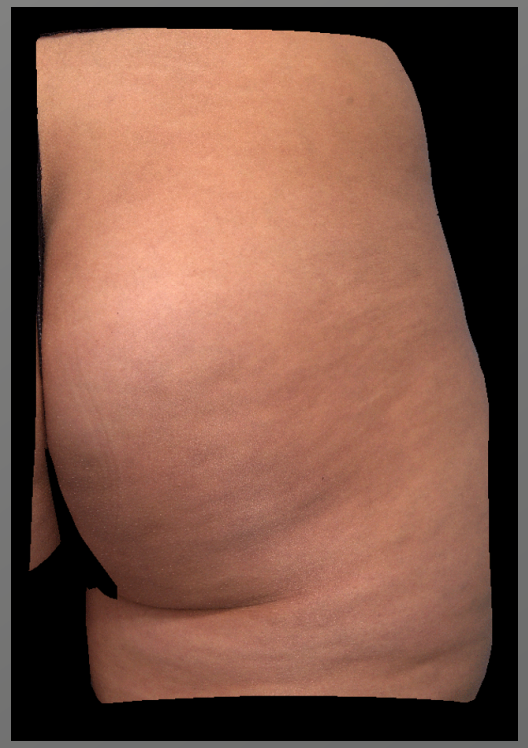
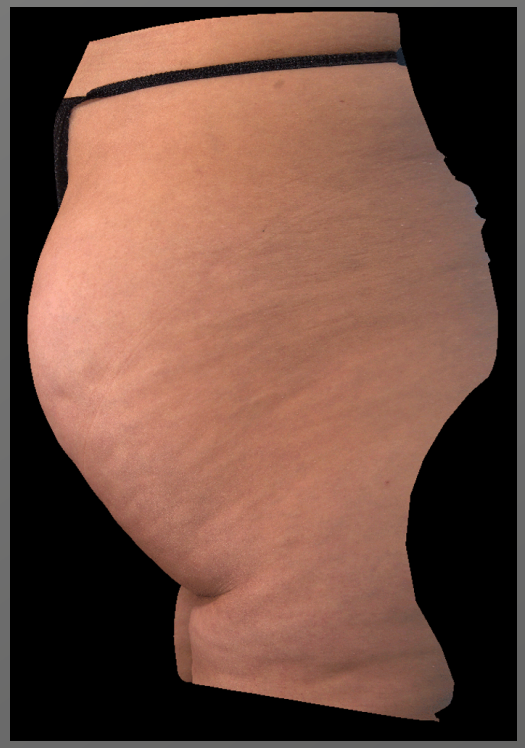
2-LEVEL COMPOSITE RESPONDER – 3D IMAGING



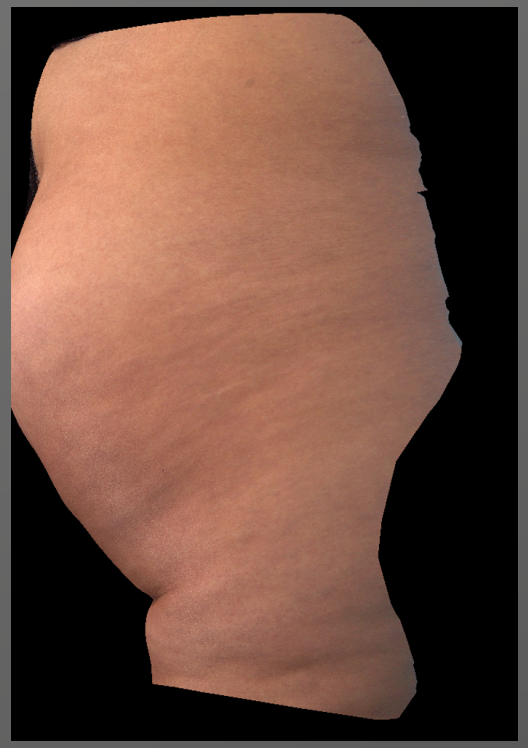
Pre-Treatment
(Back)



Day 71
(Back)



Pre-Treatment
(Right Side)



Day 71
(Right Side)

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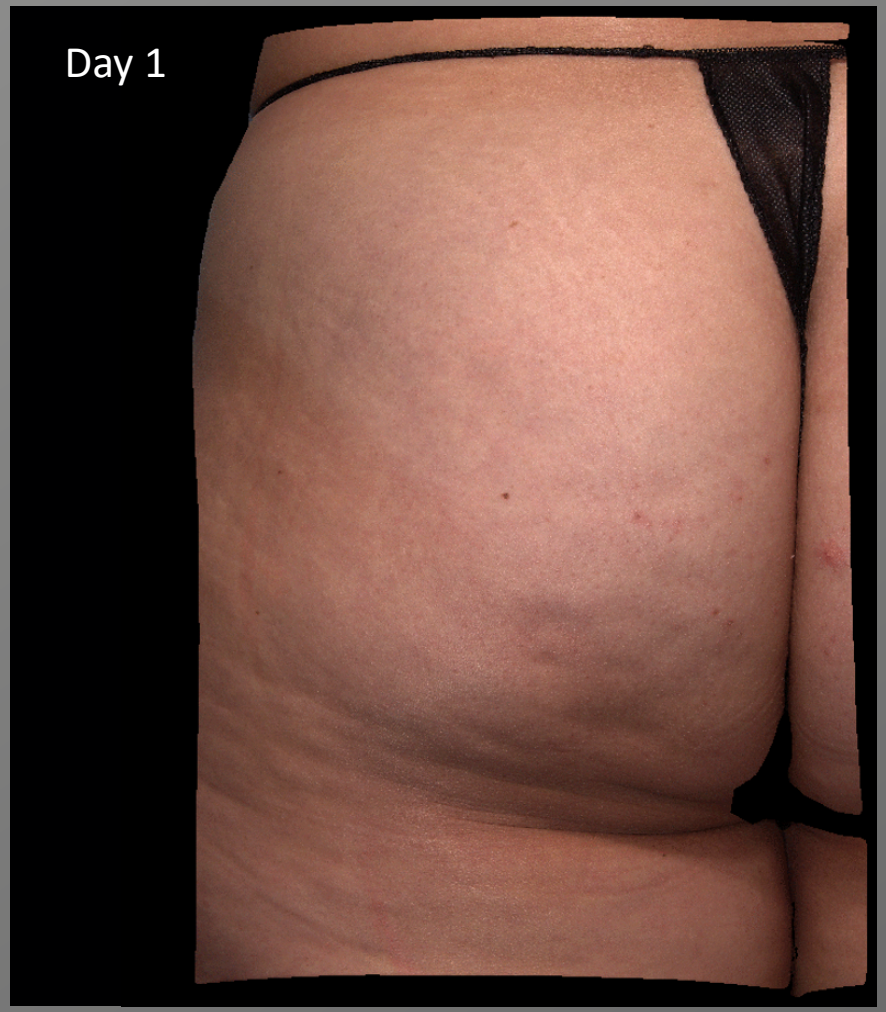
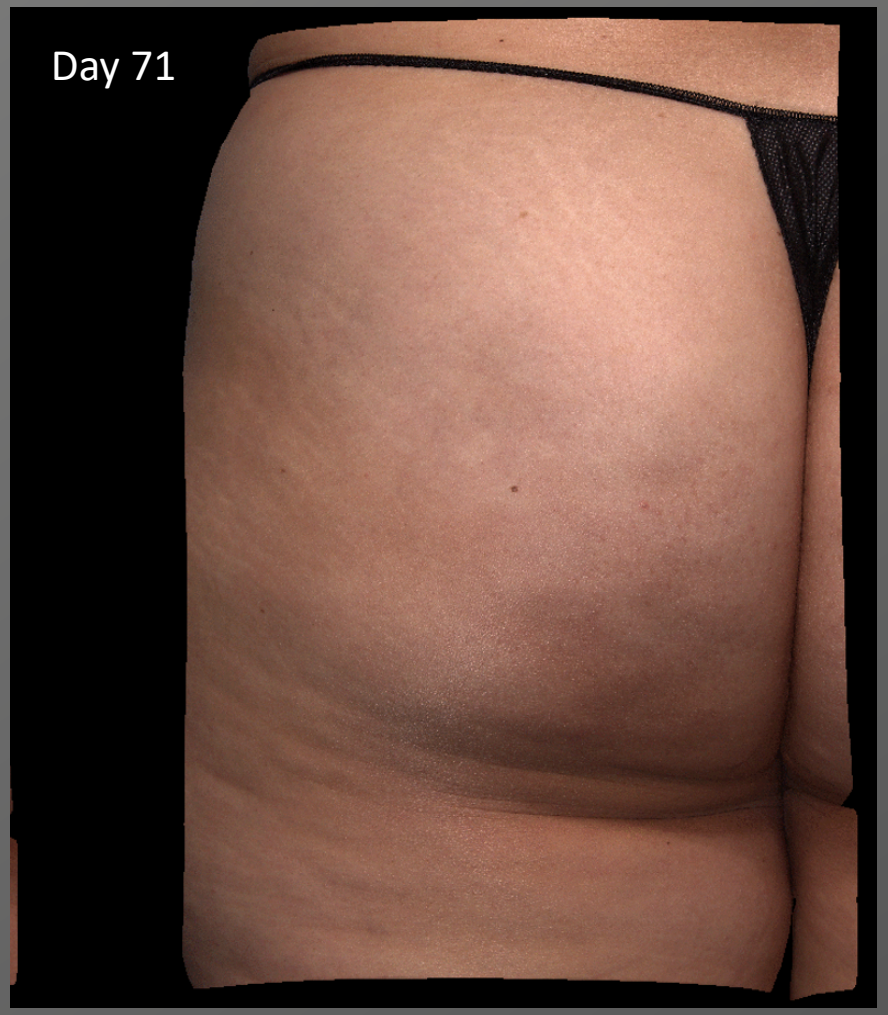
2-LEVEL COMPOSITE RESPONDER



Patient demographics:
Age 41
Fitzpatrick Type IV
BMI 29.8
Individual results may vary.



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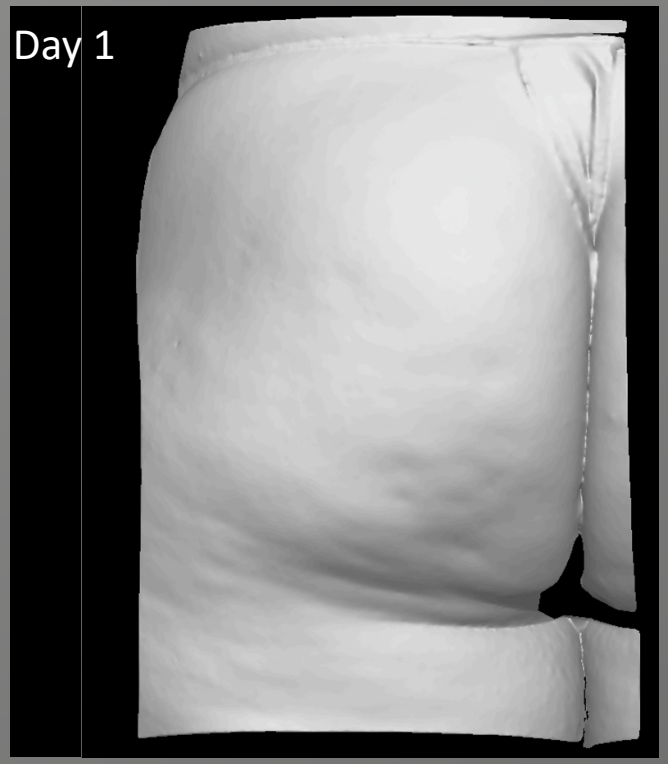
2-LEVEL COMPOSITE RESPONDER – GREY SCALE



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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

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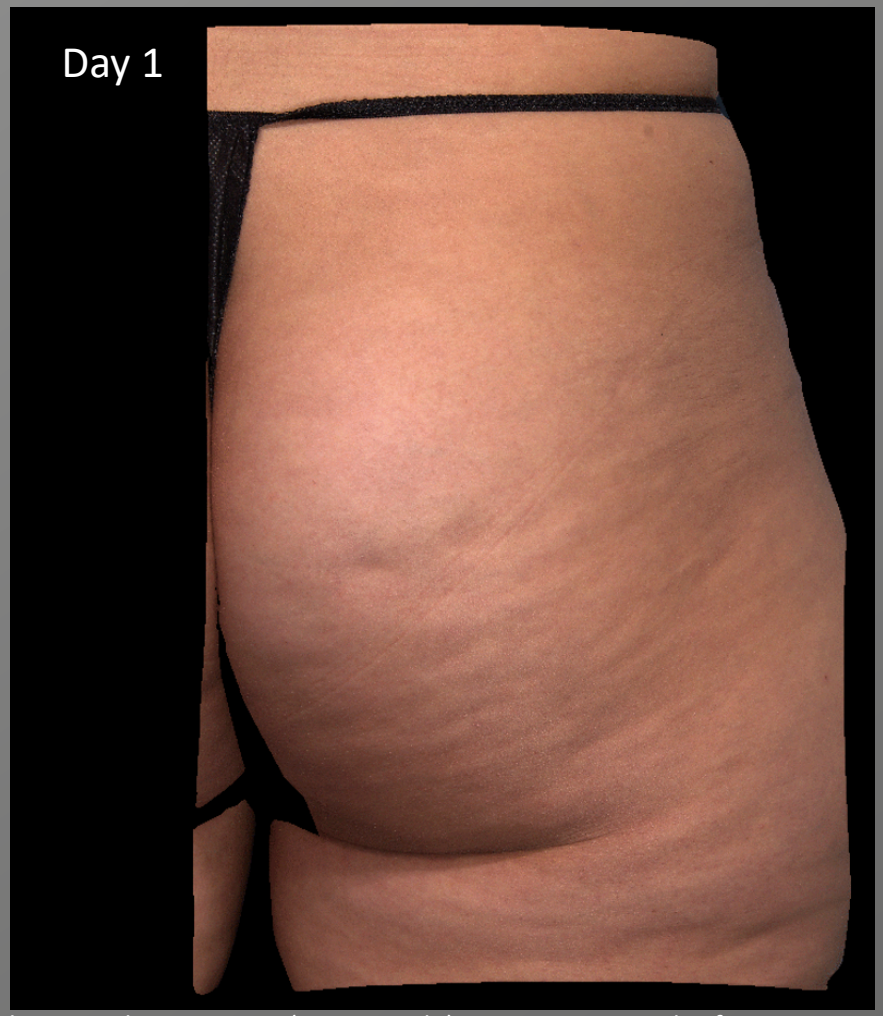
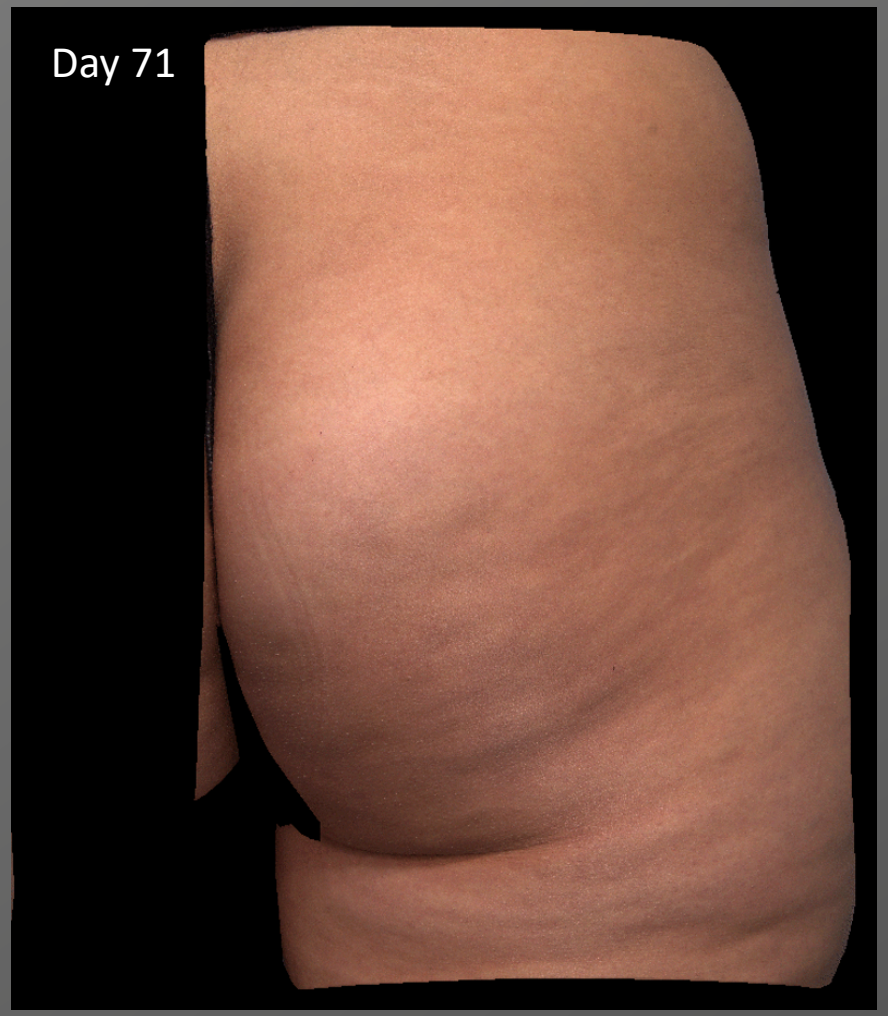
2-LEVEL COMPOSITE RESPONDER



Patient demographics:
Age 22
Fitzpatrick Type V
BMI 24.1
Individual results may vary.



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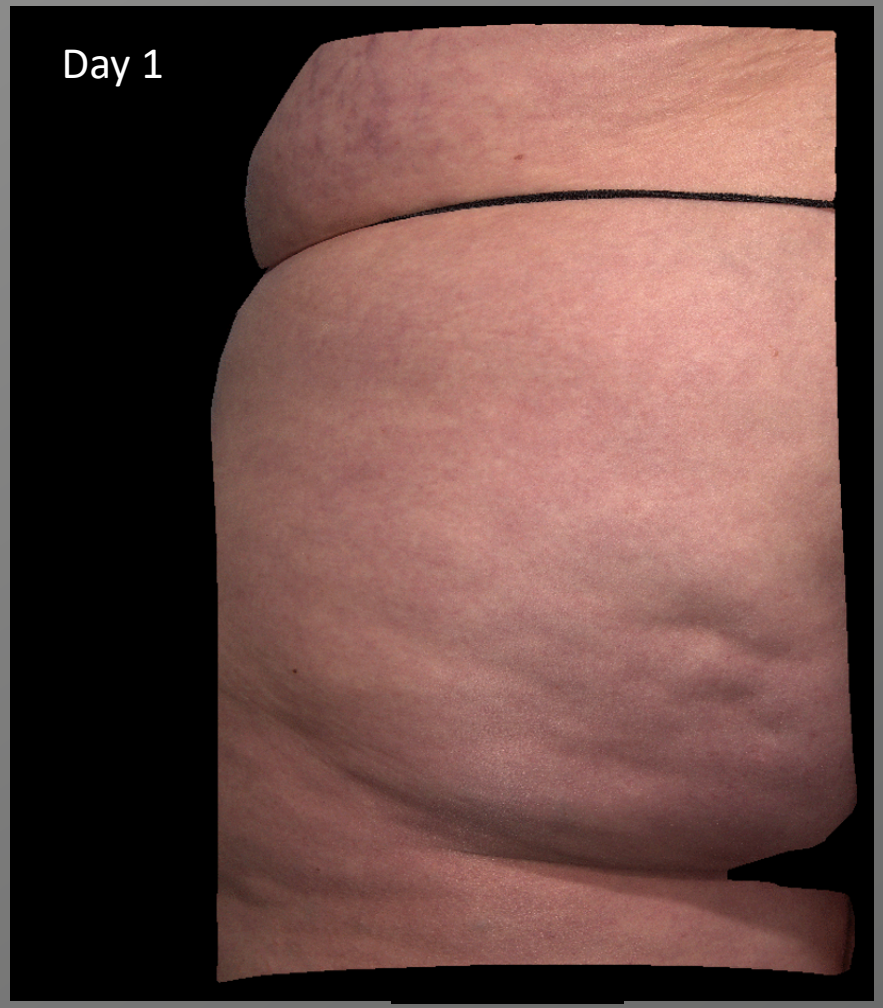
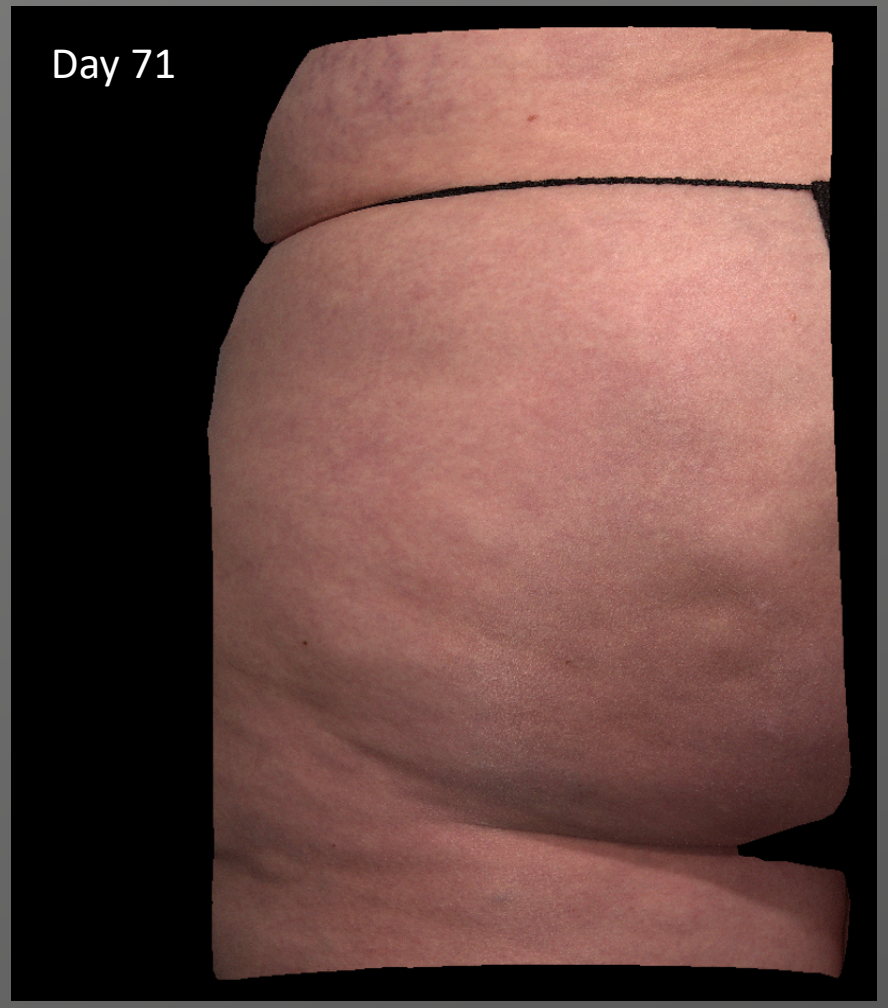
2-LEVEL COMPOSITE RESPONDER



Patient demographics:
Age 37
Fitzpatrick Type III
BMI 37.4
Individual results may vary.



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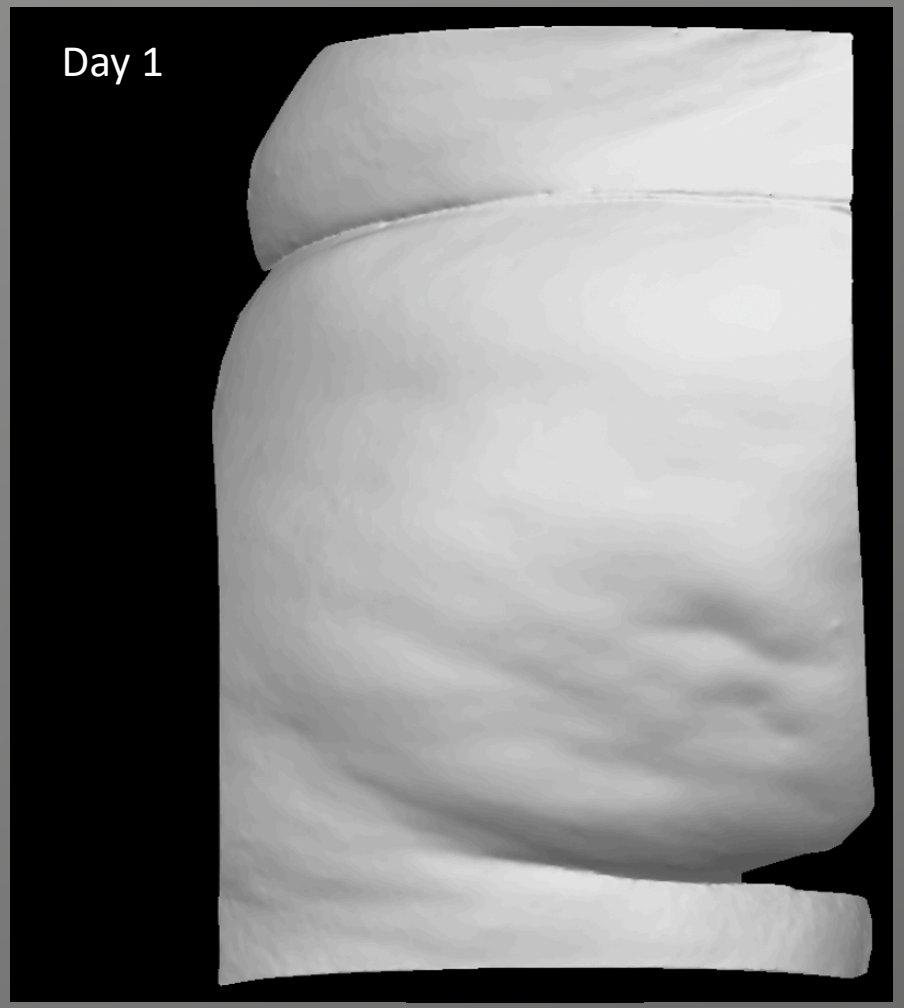
2-LEVEL COMPOSITE RESPONDER – GREY SCALE



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OTHER SECONDARY ENDPOINTS (DAY 71 VS DAY 1)

6 of 8 secondary endpoints in each study were subject response endpoints and 2 were composite response (subject + investigator) endpoints. Proportion of –

- ≥2-level PR-PCSS responders of target buttock
- ≥1-level PR-PCSS responders of target buttock
- ≥1-level composite responders of target buttock
- ≥2-level composite responders of non-target buttock
- ≥1-level improvement in Subject Self-Rating Scale (SSRS)
- Change from baseline of Patient Reported Cellulite Impact Scale (PR-CIS) total score
- ≥2-level Subject Global Aesthetic Improvement Scale (S-GAIS) responders of target buttock
- ≥1-level S-GAIS responders of target buttock

RELEASE-1
8 of 8 key secondary endpoints

RELEASE-2
7 of 8 key secondary endpoints

Statistically significant vs placebo.

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RESPONDER IMAGES

1-Level Composite Responders

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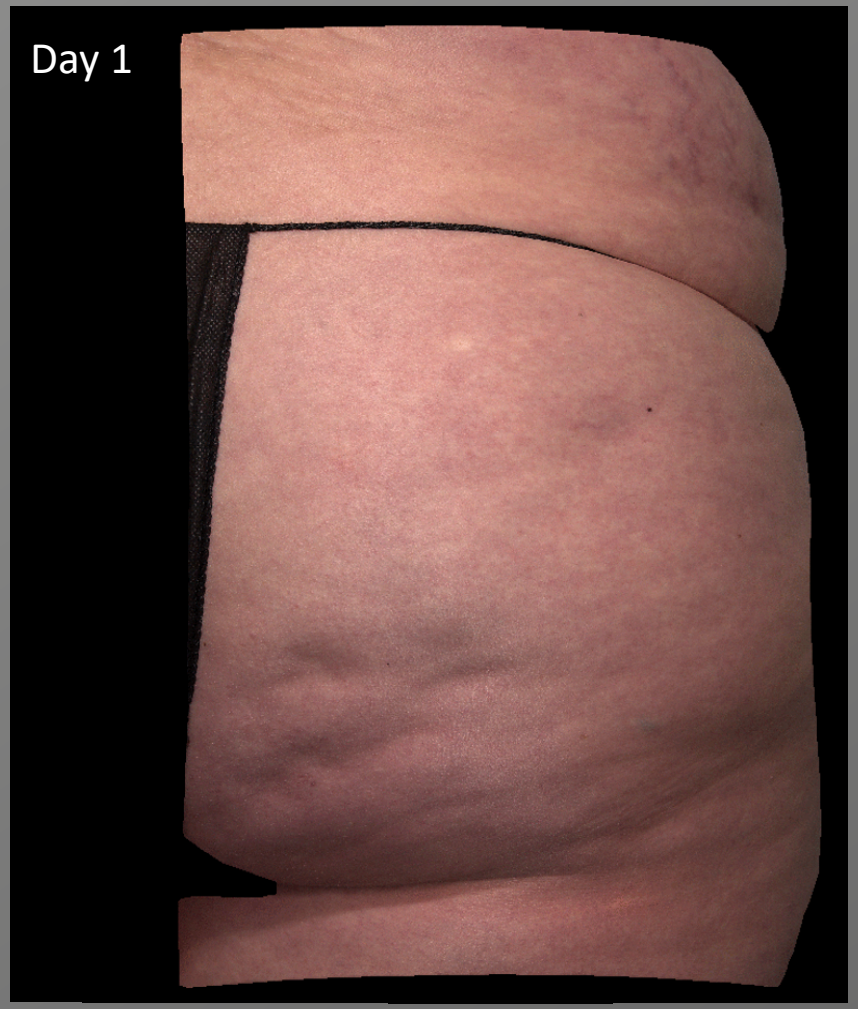
1-LEVEL COMPOSITE RESPONDER



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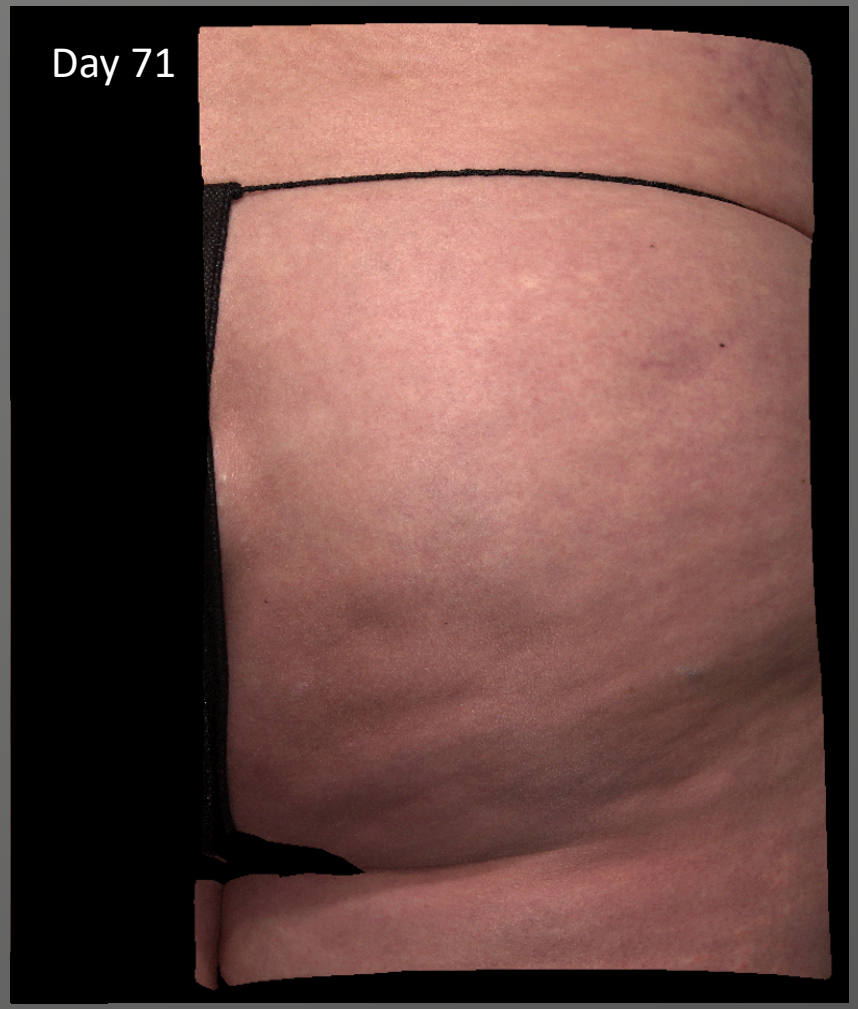

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1-LEVEL COMPOSITE RESPONDER – GREY SCALE

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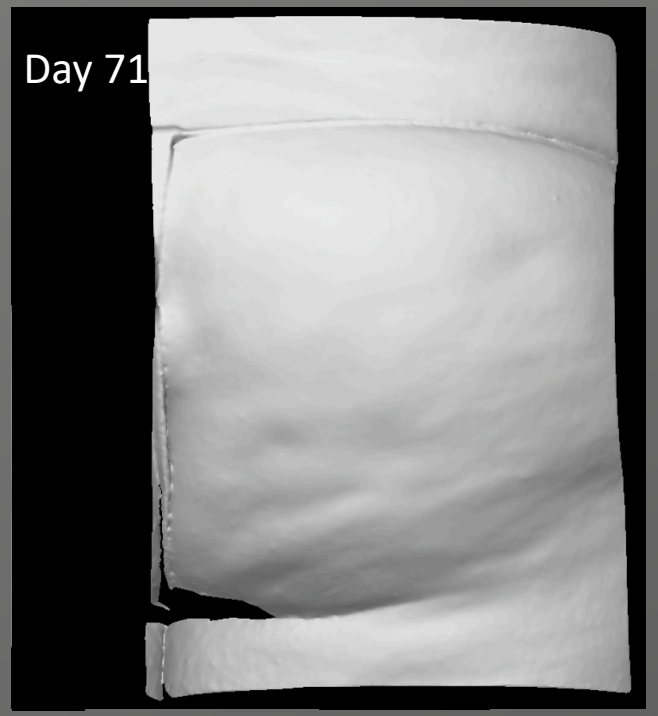

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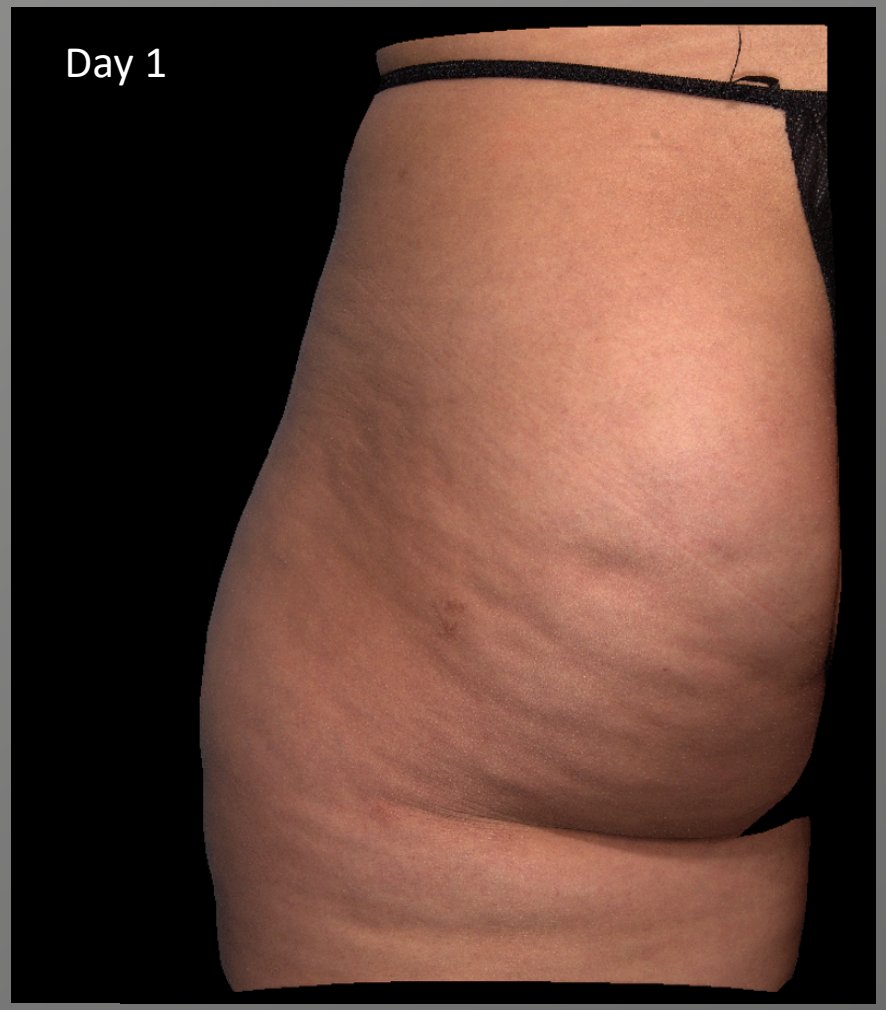
1-LEVEL COMPOSITE RESPONDER



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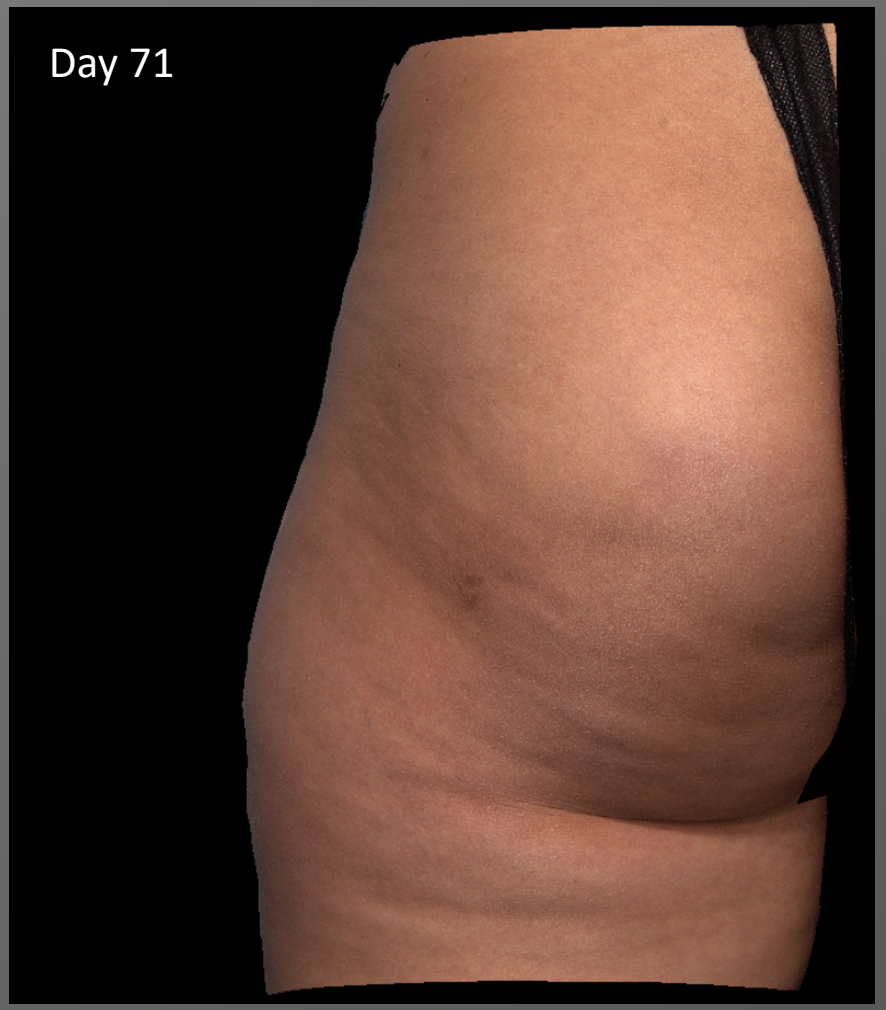
BMI 24.1
Individual results may vary.



Phase 3 subject images (Data on File). Image presented is from RELEASE II with permission from patient and physician.

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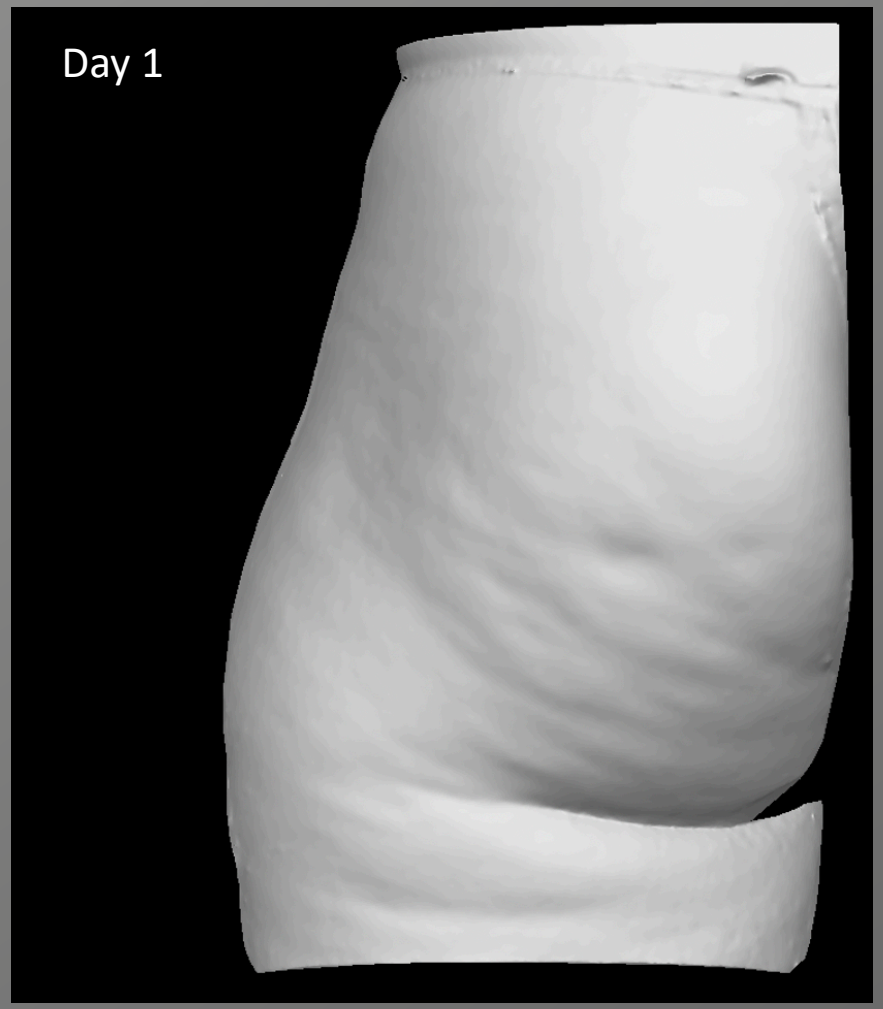
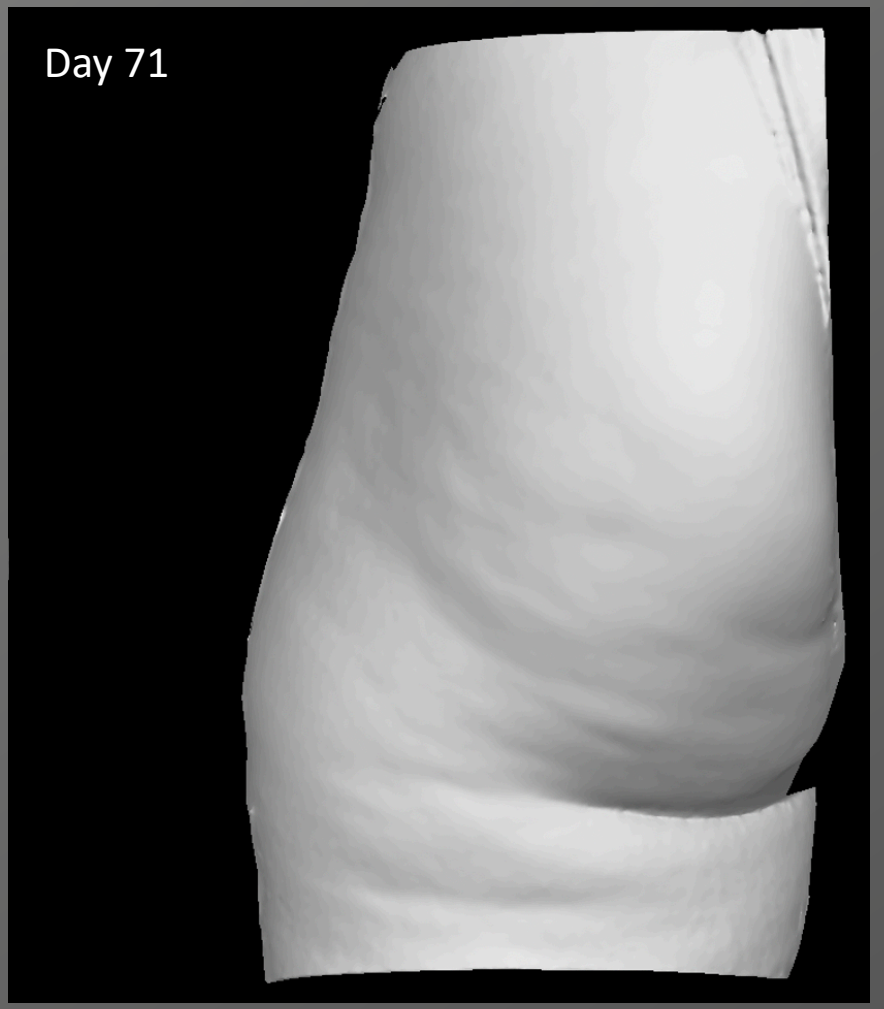
1-LEVEL COMPOSITE RESPONDER – GREY SCALE



Patient demographics:
Age 22
Fitzpatrick Type V
BMI 24.1
Individual results may vary.



Phase 3 subject images (Data on File). Image presented is from RELEASE II with permission from patient and physician.

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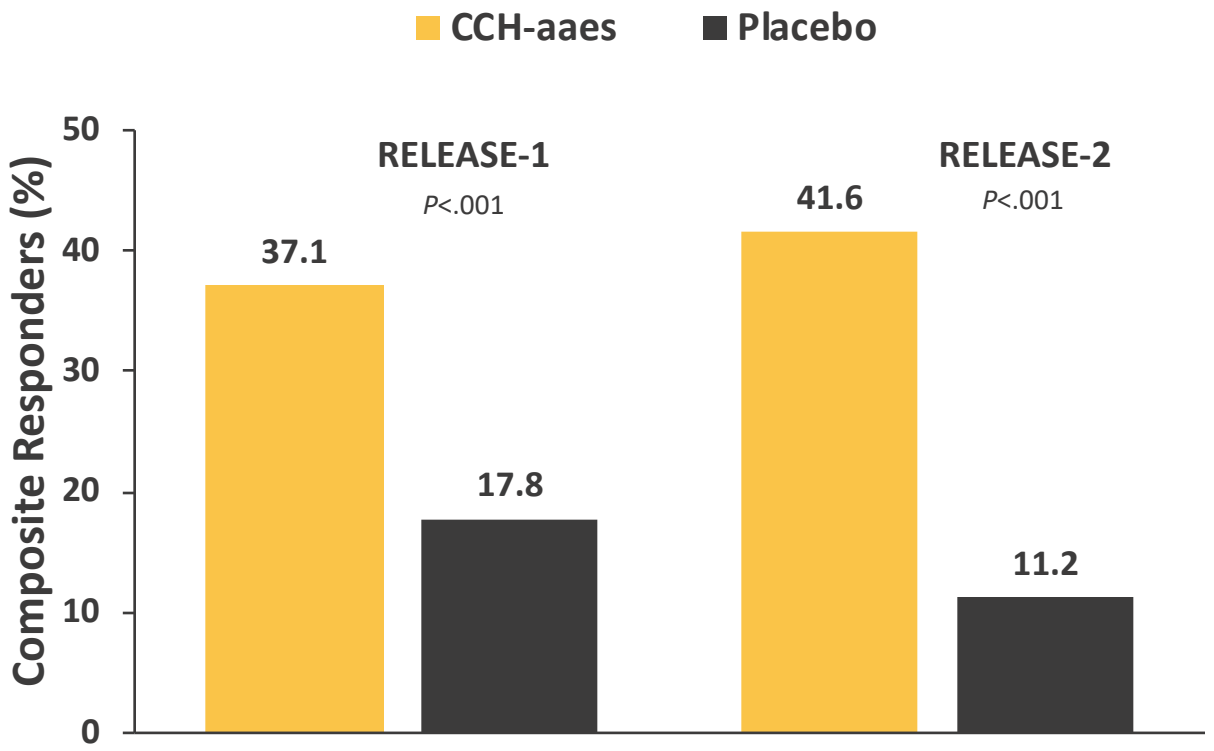
KEY SECONDARY ENDPOINTS: >1-LEVEL COMPOSITE RESPONSE* AT DAY 71



*One level or more improvement from baseline in CR-PCSS rating and PR-PCSS rating at Day 71.

CCH-aaes = collagenase clostridium histolyticum-aaes.

Kaufman J, et al. Two Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trials of Collagenase Clostridium Histolyticum (CCH) for the Treatment of Cellulite (Edematous Fibrosclerotic Panniculopathy) Oral presentation at the American Academy of Dermatology Annual Meeting; 11362: March 2, 2019; Washington, DC.

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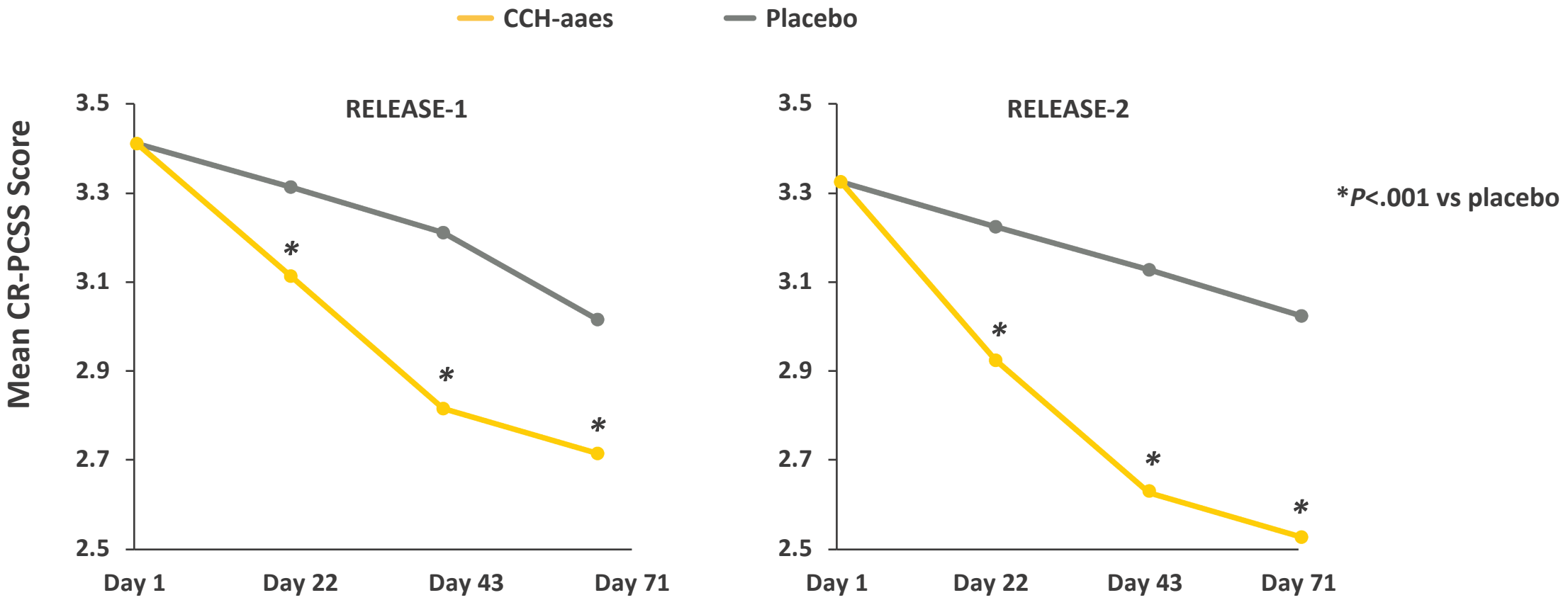
REDUCTION IN CELLULITE SEVERITY OVER TIME



CCH-aaes = collagenase clostridium histolyticum-aaes.

Kaufman J, et al. Two Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trials of Collagenase Clostridium Histolyticum (CCH) for the Treatment of Cellulite (Edematous Fibrosclerotic Panniculopathy) Oral presentation at the American Academy of Dermatology Annual Meeting; 11362: March 2, 2019; Washington, DC.

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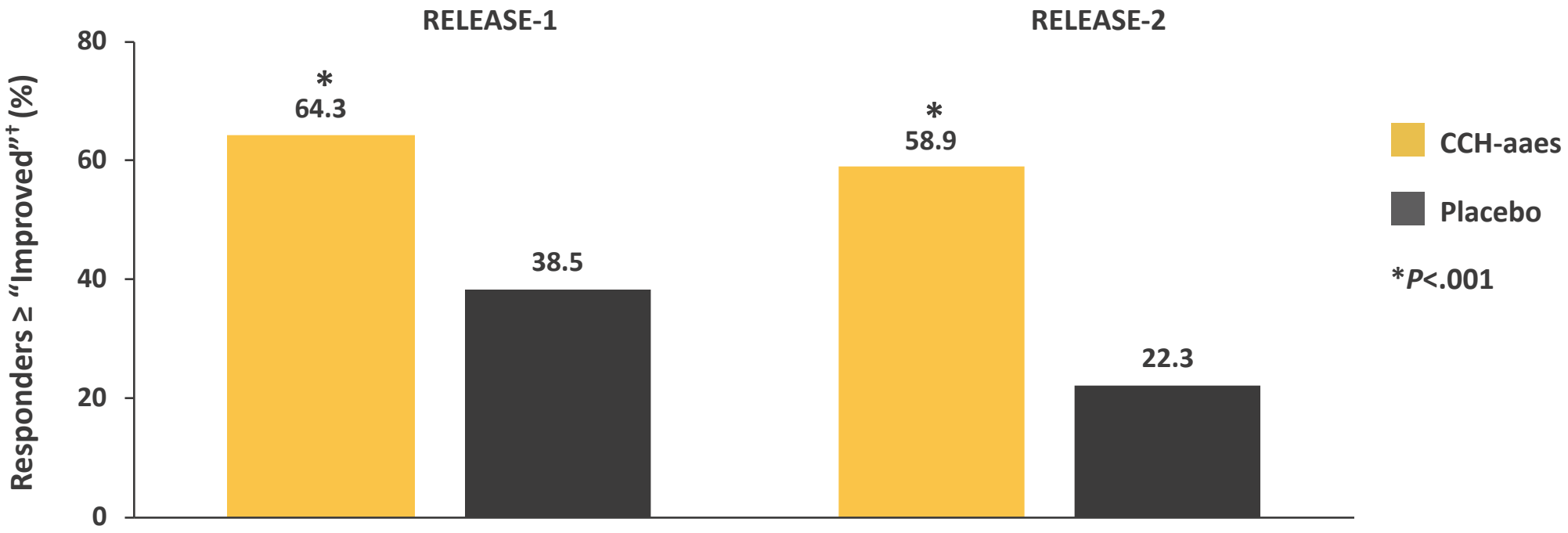
S-GAIS† RESPONSE AT DAY 71

Majority of patients were improved or very much improved



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

Kaufman J, et al. Two Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trials of Collagenase Clostridium Histolyticum (CCH) for the Treatment of Cellulite (Edematous Fibrosclerotic Panniculopathy) Oral presentation at the American Academy of Dermatology Annual Meeting; 11362: March 2, 2019; Washington, DC.

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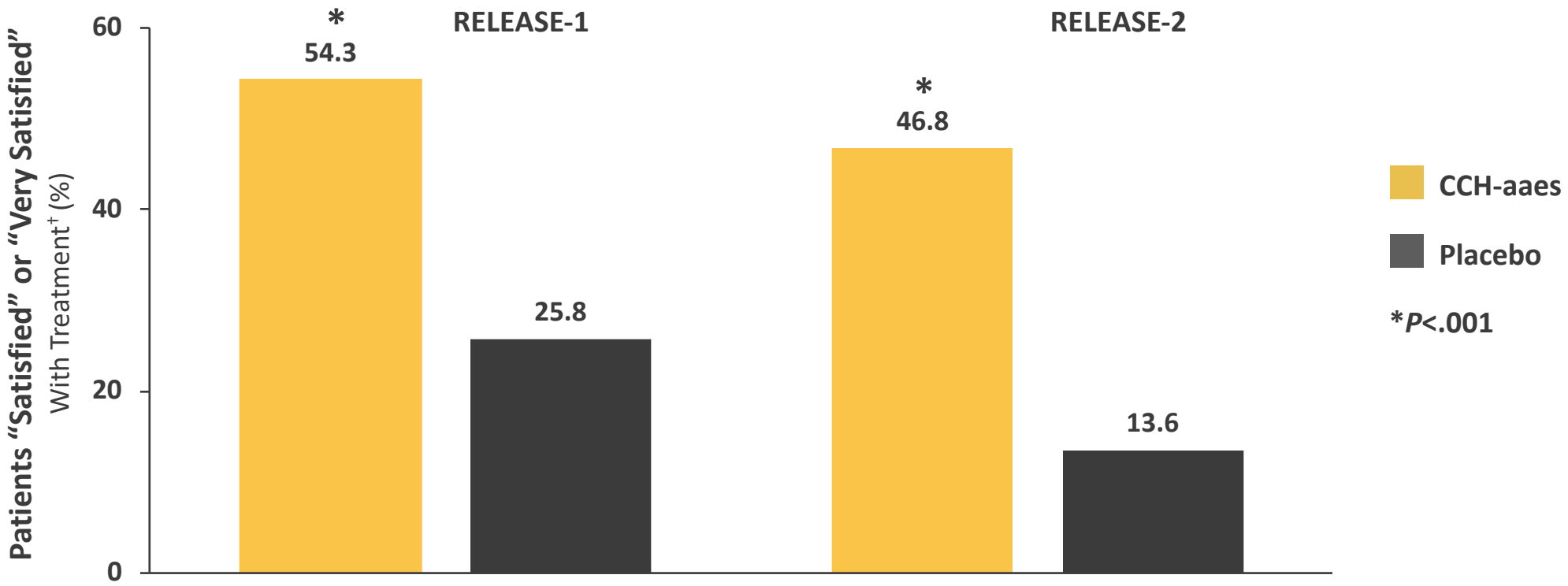
PHASE 3 SUBJECT SATISFACTION AT DAY 71



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

Kaufman J, et al. Two Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trials of Collagenase Clostridium Histolyticum (CCH) for the Treatment of Cellulite (Edematous Fibrosclerotic Panniculopathy) Oral presentation at the American Academy of Dermatology Annual Meeting; 11362: March 2, 2019; Washington, DC.

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ADVERSE EVENTS REPORTED IN RELEASE 1 AND RELEASE 2

In ≥1% of Subjects in Trials 1 and 2 Through Day 71

	CCH-aaes, n = 424 %	Placebo, n = 419 %
Bruising*	84	21
Pain	48	10
Nodule	33	1
Pruritus	15	1
Erythema	9	5
Discoloration	8	1
Swelling	8	1
Warmth	3	0

*Ordered in table by most common AE in pooled CCH-aaes group for the 2 studies.

†Preferred for the verbatim term “injection-site ecchymosis.”

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

Qwo [package insert]. Malvern, PA: Endo Aesthetics LLC.

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DURATION OF ADVERSE EVENTS IN RELEASE 1 AND RELEASE 2

- The majority of treatment-related AEs were self-limiting and resolved within 21 days
- The majority of injection site bruising resolved within 14 days and injection site pain resolved within 7 days
- The incidence, duration, and severity of treatment-related AEs decreased with each subsequent treatment session

Data on File.

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