

This presentation discusses an unapproved use for Qwo[®] (collagenase clostridium histolyticum-aaes). It also discusses information that is not provided in the FDA-approved labeling for QWO.

LUXURGERY®

The confluence of luxury and aesthetic surgery

Enzymatic Subcision and Remodeling After Collagenase Clostridium Histolyticum-aaes (CCH-aaes) Subcutaneous Injection: Evidence From Porcine and Human Studies

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S A C H I N M . S H R I D H A R A N I , M D , F A C S

BOARD-CERTIFIED PLASTIC SURGEON

Sachin M. Shridharani, MD, FACS

DISCLOSURES

Dr. Shridharani reports serving as a consultant and advisory board member for Allergan, Endo Pharmaceuticals Inc., Evolus, Galderma, Prolenium, Sientra, and Sinclair Pharma. He reports serving as a clinical investigator for Endo.

Dr. Dalton and Dr. Vijayan are employees of Endo Pharmaceuticals Inc.

Dr. Bhatia reports serving as a consultant to Endo Pharmaceuticals Inc.

Data detailed in this presentation were generated from studies funded by Endo Pharmaceuticals Inc. Medical writing assistance was provided by Synchrony, with funding from Endo Aesthetics LLC.



INTRODUCTION

Cellulite and Collagenase Clostridium Histolyticum-aaes (CCH-aaes)

CELLULITE:

- 85% to 98% of women^{1,2}
- Subcutaneous tissue dimpling: buttocks, thighs, and lower abdomen²
- Multifactorial pathophysiology²⁻⁵
 - ✓ Localized structural changes of skin (shortening of fibrous septae and adipose protrusions in subdermis)
 - ✓ Weakened dermal vascularization
 - ✓ Inflammation

CCH-aaes (Qwo™, Endo Aesthetics LLC, Malvern, PA) is an SC injection approved by the FDA in July 2020 for the treatment of moderate-to-severe cellulite in the buttocks of adult women⁶

Pretreatment



Day 71*



*28 days after final injection; 2-level improvement in both the Clinician Reported Photonumeric Cellulite Severity Scale and Patient Reported Photonumeric Cellulite Severity Scale.

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¹COSMET LASER THER. VOLUME 6, ISSUE 4, 2004, PAGES 181–185. ²J AM ACAD DERMATOL. VOLUME 63, ISSUE 3, 2010, PAGES 361–370. ³SKIN RES TECHNOL, VOLUME 8, ISSUE 2, 2002, PAGES 118–124. ⁴PLAST RECONSTR SURG, VOLUME 143, ISSUE 4, 2019, PAGES 1077–1086.

⁵DERMATOL SURG, VOLUME 35, ISSUE 10, 2009, PAGES 1471–1477. ⁶QWO™ (collagenase clostridium histolyticum-aaes) for injection for subcutaneous use [package insert]. Malvern, PA: Endo Aesthetics LLC; 2020.

CCH-aaes INJECTION-SITE BRUISING



*CCH-aaes treatment can be associated with **INJECTION-SITE BRUISING***

- Two Phase 3 clinical studies: CCH-aaes (84%) vs placebo (21%)

QWO™ (collagenase clostridium histolyticum-aaes) for injection for subcutaneous use [package insert]. Malvern, PA: Endo Aesthetics LLC; 2020.



*Generally **TRANSIENT** and appears to **LESSEN** with subsequent treatment*

SCALE 2020. A Qualitative and Quantitative Characterization of Bruising During Phase 2 Open-Label Studies of Collagenase Clostridium Histolyticum-aaes (CCH-aaes) in the Treatment of Cellulite. July 24–26 (Virtual).

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CCH-aaes, collagenase clostridium histolyticum-aaes.

STUDY RATIONALE/OBJECTIVE

Mechanism of
action?
(efficacy)

QUESTION:

What histological change(s) occur following CCH-aaes injection?

Mode of
action?
(bruising)

OBJECTIVE

*Assess histopathological changes in subcutaneous tissue
and surrounding areas after CCH-aaes injection*

HOW?

Domestic Swine Study

and

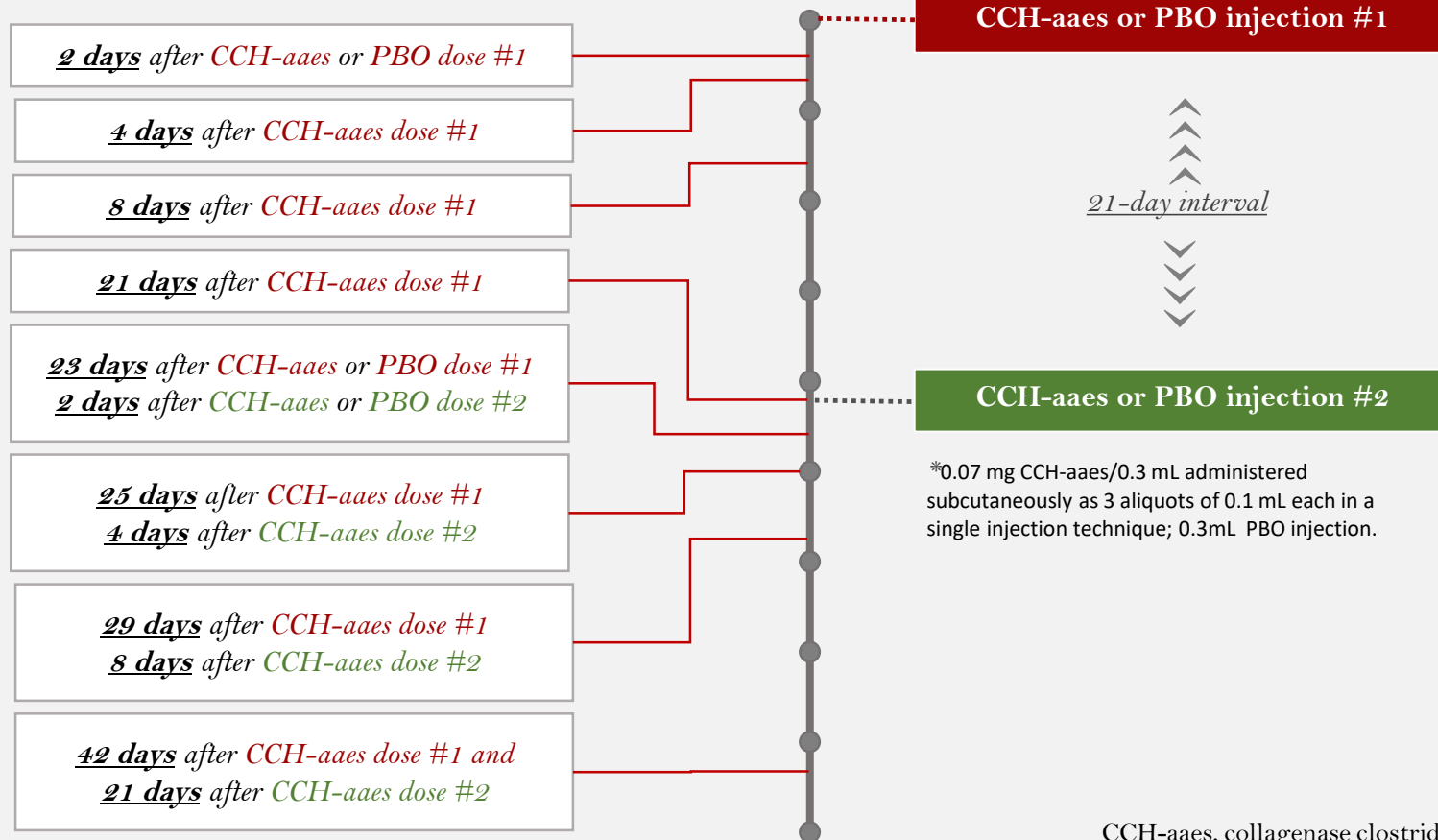
Human
Abdominoplasty Study
(213)

CCH-aaes, collagenase clostridium histolyticum-aaes.

DOMESTIC SWINE STUDY

Methodology

Timing of Tissue Collection Relative to CCH-aaes or PBO Injection Schedule



*0.07 mg CCH-aaes/0.3 mL administered subcutaneously as 3 aliquots of 0.1 mL each in a single injection technique; 0.3mL PBO injection.

- 4 female Yorkshire pigs with 10 defined dosing sites on ventral-lateral aspect
- 1 or 2 CCH-aaes or PBO injections to dose sites per protocol in advance of tissue sampling (Day 0, sacrifice)

CCH-aaes, collagenase clostridium histolyticum-aaes; PBO, placebo.

DOMESTIC SWINE STUDY

Histology Results

2 days after ***CCH-aaes*** or ***PBO*** dose #1

CCH-aaes/PBO Injection Schedule

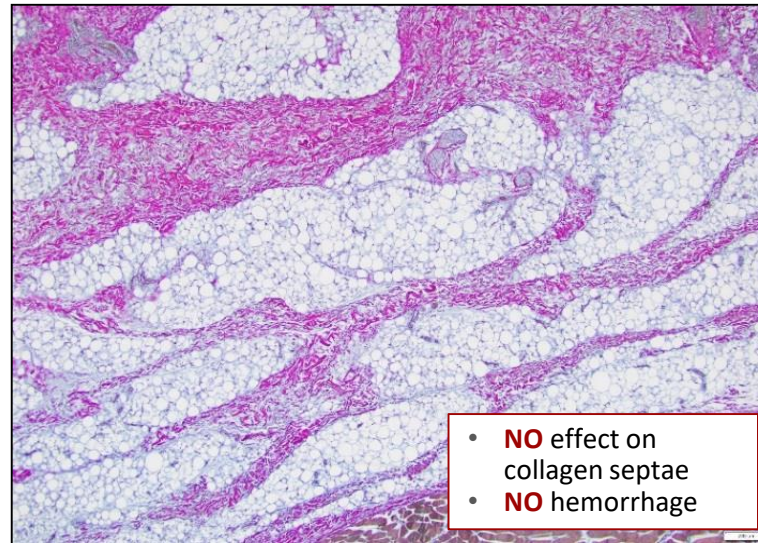
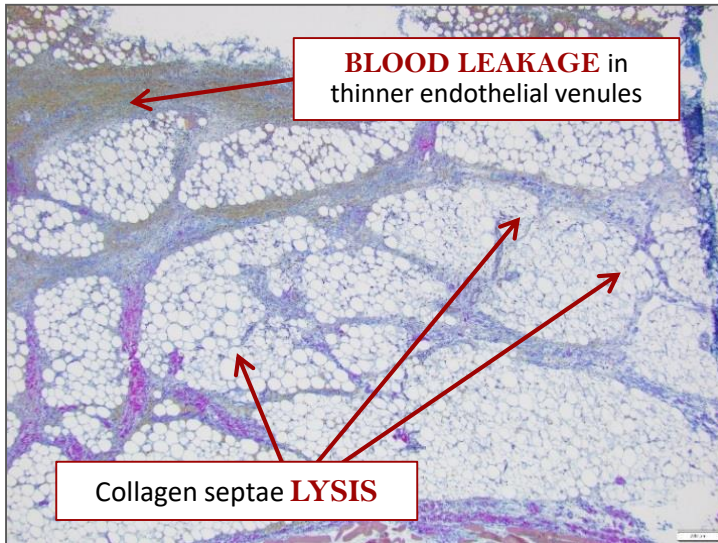
CCH-aaes/ PBO injection #1

21-day interval

CCH -aaes/ PBO injection #2

CCH-aaes

PBO



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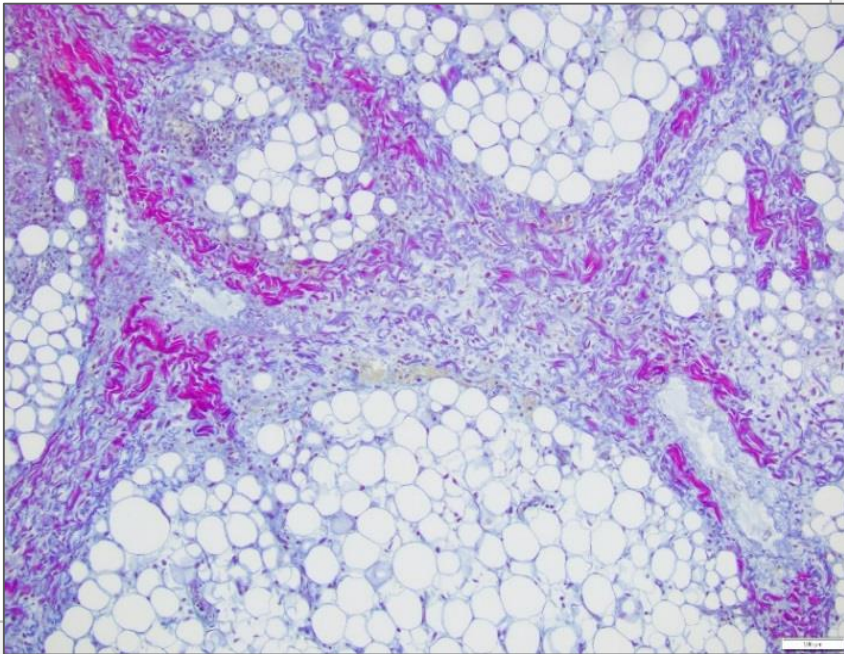
Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

CCH-aaes, collagenase clostridium histolyticum-aaes; PBO, placebo.

DOMESTIC SWINE STUDY

Histology Results

4 days after ***CCH-aaes*** dose #1



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Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

PATHOLOGY FINDINGS:

- New, immature collagen fibers
- Fragmented mature collagen
- Hemorrhage

CCH-aaes Injection Schedule

CCH-aaes injection #1

21-day interval

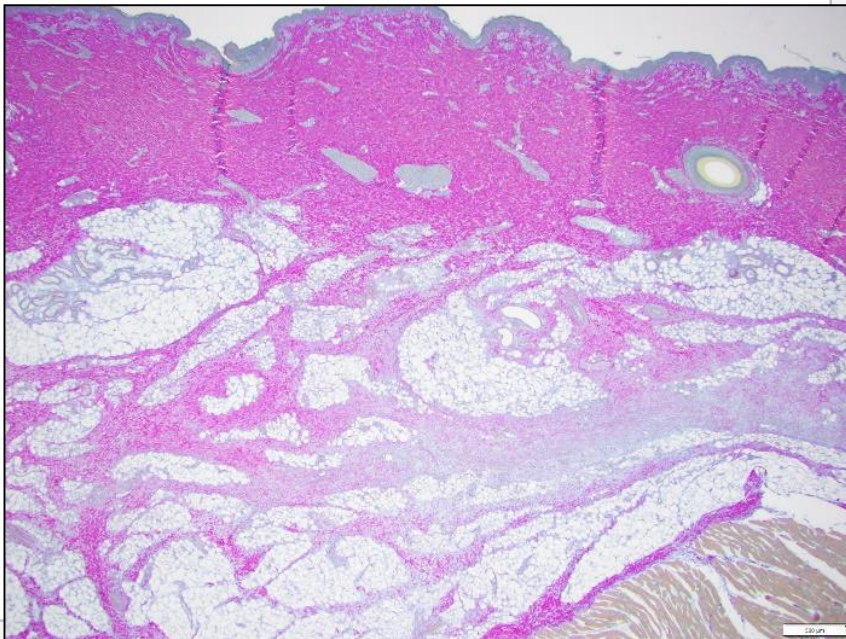
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

DOMESTIC SWINE STUDY

Histology Results

21 days after *CCH-aaes* dose #1



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Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

PATHOLOGY FINDINGS:

- Signs of significant collagen neogenesis (ie, remodeling)
- Reorganization of subcutaneous adipose tissue; fat lobules smaller and more homogeneous

CCH-aaes Injection Schedule

CCH-aaes injection #1



21-day interval



CCH-aaes injection #2

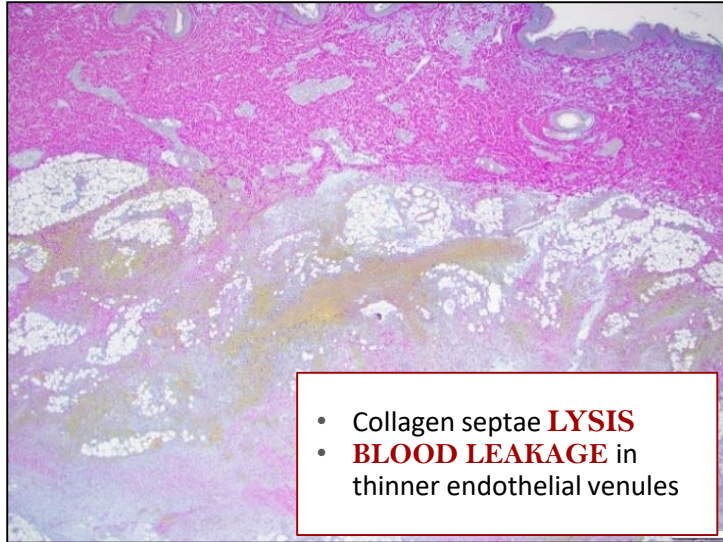
CCH-aaes, collagenase clostridium histolyticum-aaes.

DOMESTIC SWINE STUDY

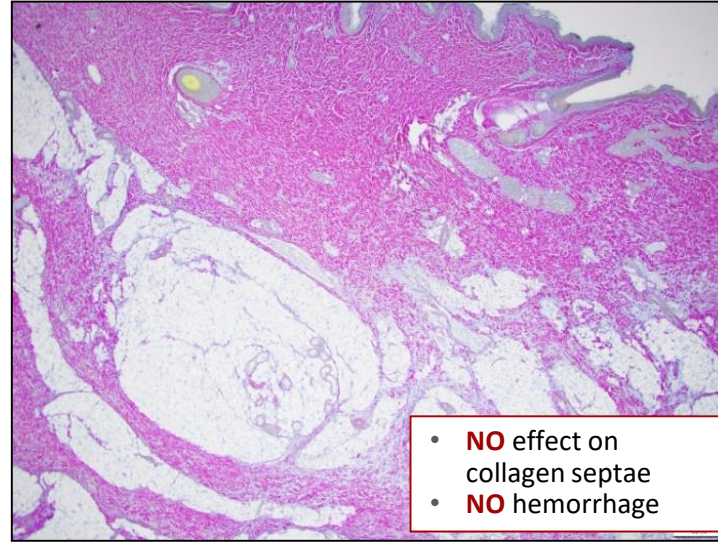
Histology Results

23 days after CCH-aaes or PBO dose #1 and
2 days after CCH-aaes or PBO dose #2

CCH-aaes



PBO



CCH-aaes/PBO Injection Schedule

CCH-aaes/ PBO injection #1



21-day interval



CCH-aaes / PBO injection #2

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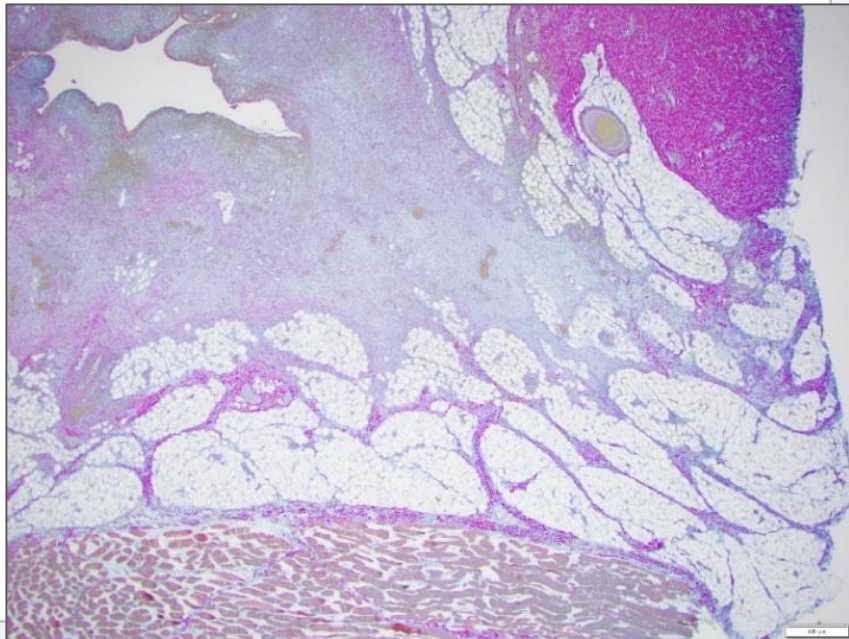
Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

CCH-aaes, collagenase clostridium histolyticum-aaes; PBO, placebo.

DOMESTIC SWINE STUDY

Histology Results

25 days after ***CCH-aaes dose #1*** and
4 days after ***CCH-aaes dose #2***



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Herovici stain: **Mature Collagen**, **Immature Collagen**, **Hemorrhage**

PATHOLOGY FINDINGS:

- Mixture of immature collagen fibers and delicate mature collagen fragments
- Preserved septal architecture at periphery of injection site but with more immature collagen fibers
- Hemorrhage

CCH-aaes Injection Schedule

CCH-aaes injection #1



21-day interval



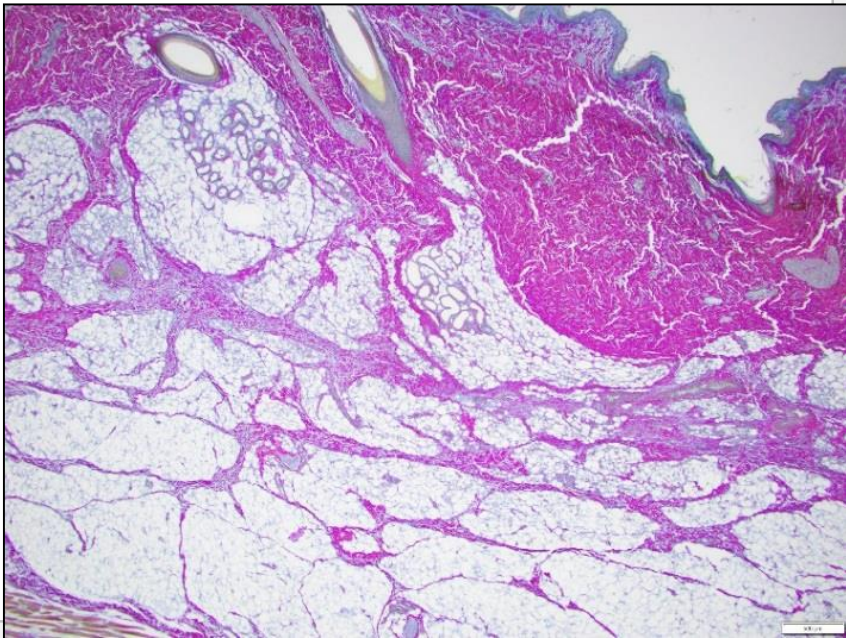
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

DOMESTIC SWINE STUDY

Histology Results

42 days after ***CCH-aaes dose #1*** and
21 days after ***CCH-aaes dose #2***



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Herovici stain: **Mature Collagen**, **Immature Collagen**, **Hemorrhage**

PATHOLOGY FINDINGS:

- Signs of significant collagen neogenesis (ie, remodeling)
- Reorganization of subcutaneous adipose tissue; fat lobules smaller and more homogeneous

CCH-aaes Injection Schedule

CCH-aaes injection #1



21-day interval

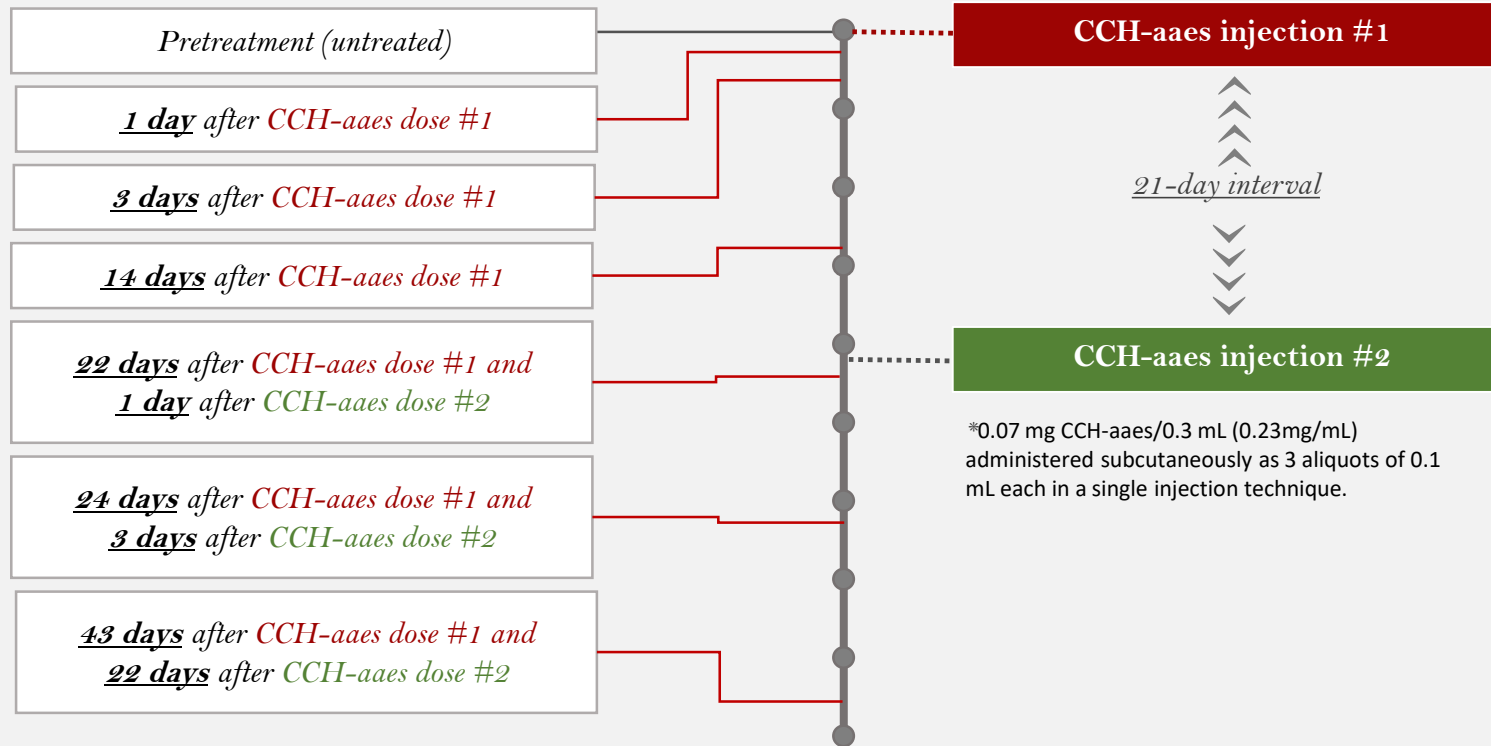


CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY *Methodology*

Timing of Tissue Collection Relative to CCH-aaes Injection Schedule



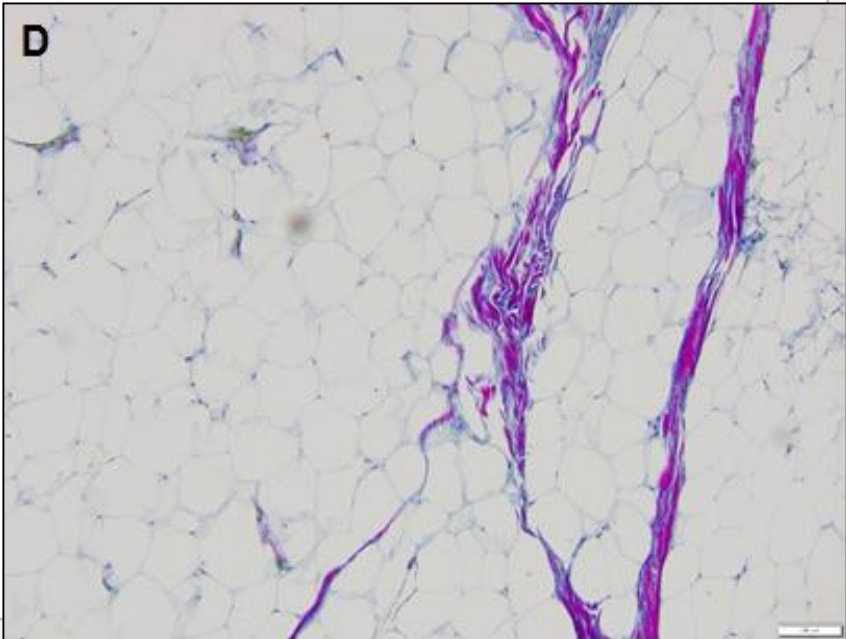
- Open-label, exploratory Phase 2b
- 4 women undergoing abdominoplasty
- Administered 1 or 2 CCH-aaes injections per protocol prior to tissue sampling – Day 0 (abdominoplasty)
- Histopathology and immunohistochemistry – Blinded review by pathologist

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY

Histology Results

Pretreatment (untreated)



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Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

PATHOLOGY FINDINGS:

- Predominantly older, mature collagen fibers
- Fat lobules of heterogeneous size

CCH-aaes Injection Schedule

CCH-aaes injection #1



21-day interval



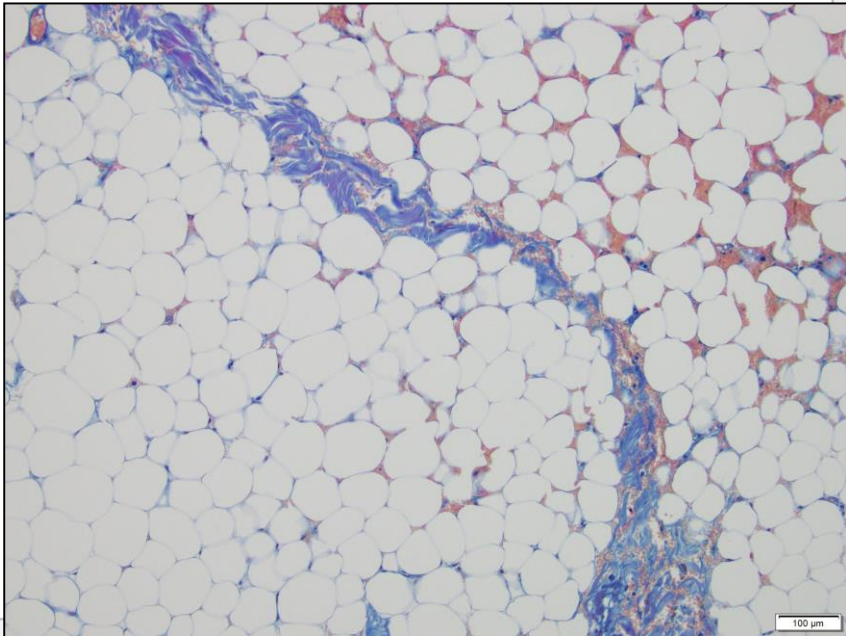
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY

Histology Results

1 day after CCH-aaes dose #1



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Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

PATHOLOGY FINDINGS:

- New, immature collagen fibers
- Fragmented mature collagen fibers

CCH-aaes Injection Schedule

CCH-aaes injection #1

21-day interval

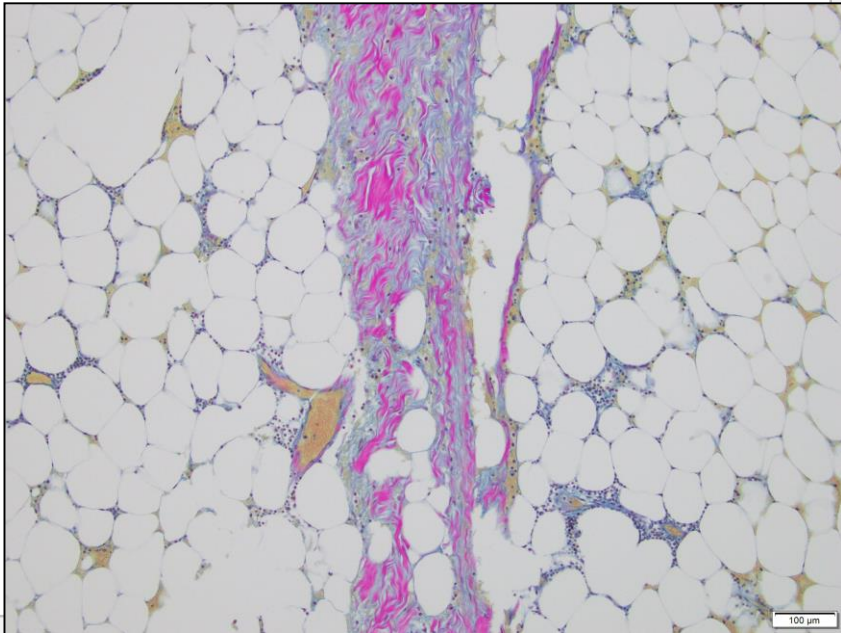
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY

Histology Results

3 days after CCH-aaes dose #1



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Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

PATHOLOGY FINDINGS:

- New, immature collagen fibers
- Fragmented mature collagen fibers
- Hemorrhage

CCH-aaes Injection Schedule

CCH-aaes injection #1

21-day interval

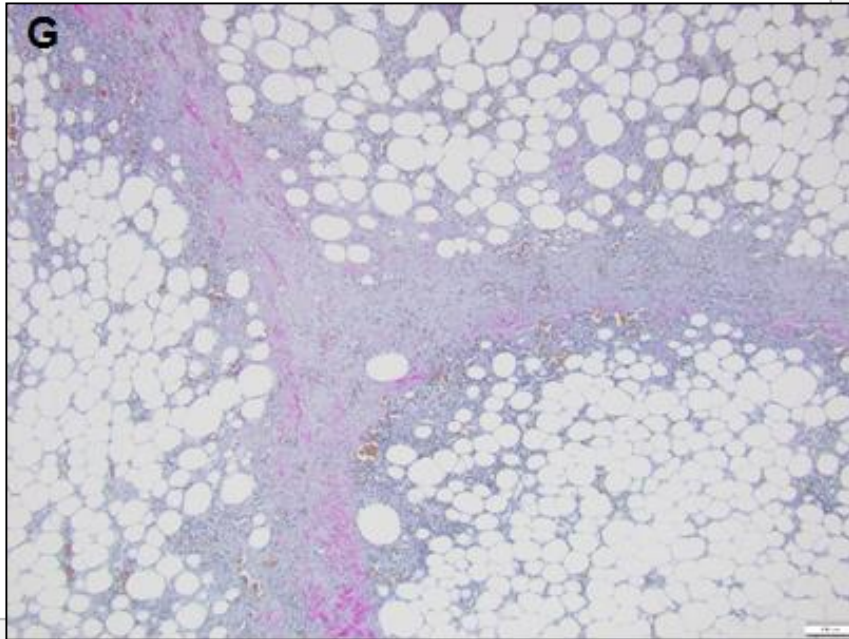
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY

Histology Results

14 days after *CCH-aaes* dose #1



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Herovici stain: **Mature Collagen**, **Immature Collagen**, **Hemorrhage**

PATHOLOGY FINDINGS:

- Expansion of septae (immature collagen fibers)
- Fragmented mature collagen fibers
- More immature vs mature collagen fibers
- Homogenous distribution of smaller fat lobules
- Minimal hemorrhage

CCH-aaes Injection Schedule

CCH-aaes injection #1



21-day interval



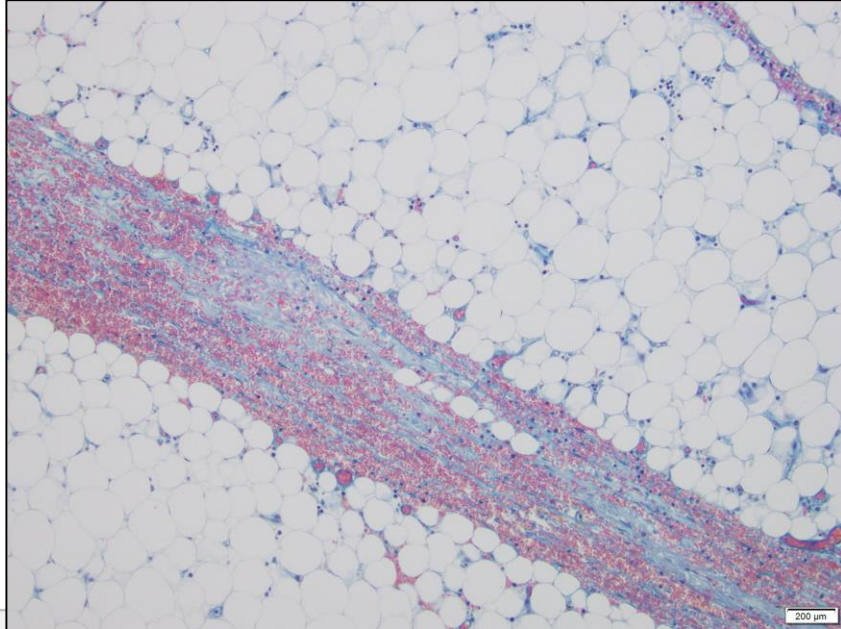
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY

Histology Results

22 days after *CCH-aaes dose #1* and
1 day after *CCH-aaes dose #2*



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Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

PATHOLOGY FINDINGS:

- Predominantly immature collagen fibers
- Homogenous distribution of smaller fat lobules

CCH-aaes Injection Schedule

CCH-aaes injection #1



21-day interval



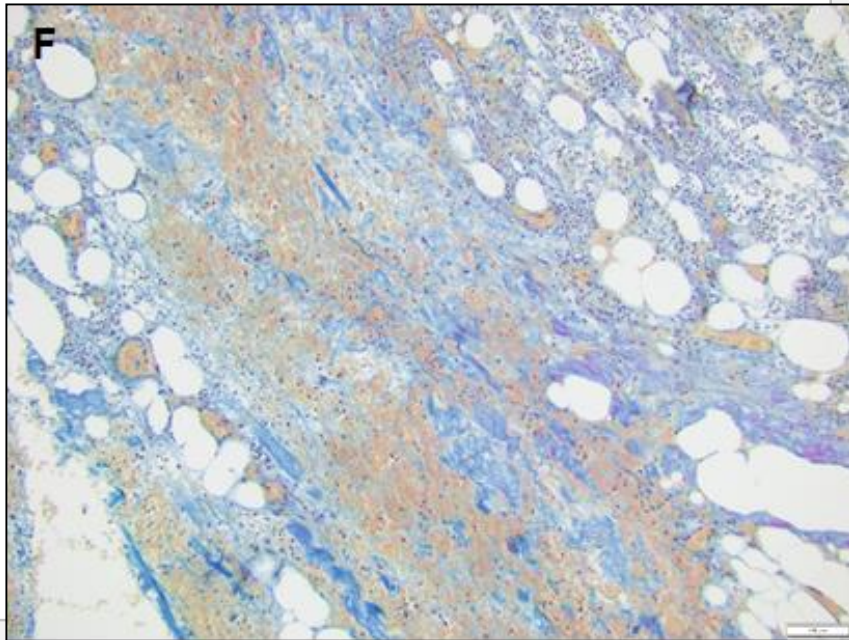
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY

Histology Results

24 days after CCH-aaes dose #1 and
3 days after CCH-aaes dose #2



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Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

PATHOLOGY FINDINGS:

- Predominantly immature collagen fibers
- Hemorrhage (less than observed with Day -3 tissue sample)
- Homogenous distribution of smaller fat lobules

CCH-aaes Injection Schedule

CCH-aaes injection #1



21-day interval



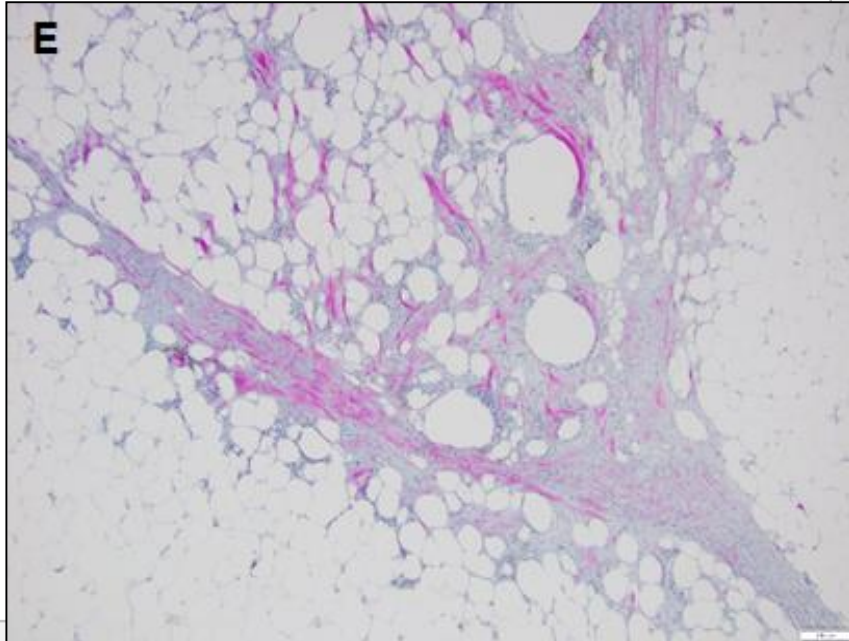
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY

Histology Results

43 days after **CCH-aaes dose #1** and
22 days after **CCH-aaes dose #2**



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Herovici stain: Mature Collagen, Immature Collagen, Hemorrhage

PATHOLOGY FINDINGS:

- Predominantly immature collagen fibers
- Fragmented mature collagen fibers
- Homogenous distribution of smaller fat lobules

CCH-aaes Injection Schedule

CCH-aaes injection #1



21-day interval



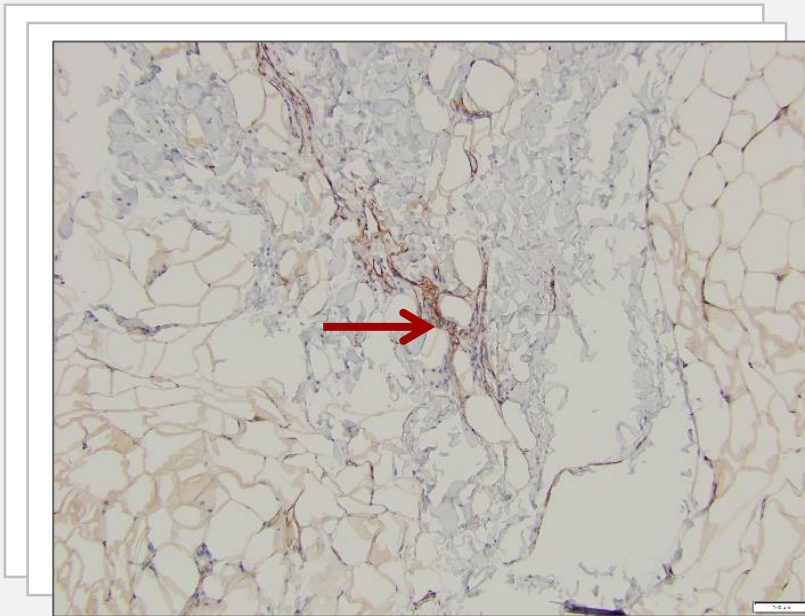
CCH-aaes injection #2

CCH-aaes, collagenase clostridium histolyticum-aaes.

HUMAN (213) STUDY

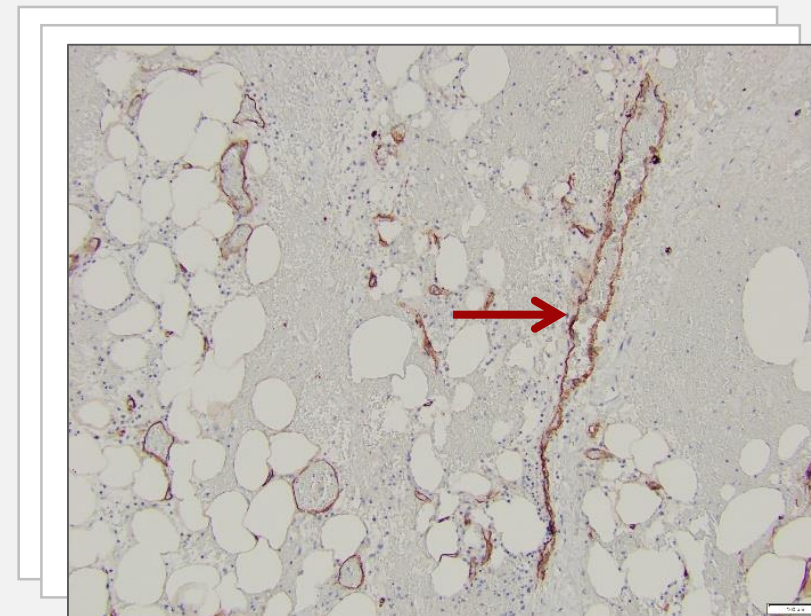
Does CCH-aaes affect Type IV collagen in Blood Vessels?

Untreated



Collagen Type IV immunohistochemical stain.

*24 days after CCH-aaes dose #1 and
3 days after CCH-aaes dose #2*



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CCH-aaes has no effect on Type IV collagen present in
the basement membrane of blood vessels

CCH-aaes, collagenase clostridium histolyticum-aaes.

SUMMARY

- CCH-aaes injection associated with **ENZYMATIC SUBCISION AND REMODELING™**
 - **Lysis** of mature, collagen-rich septa
 - Stimulation of **neocollagenesis** and **fat lobule re-organization**
 - **Rapid onset** of neocollagenesis
- CCH-aaes injection → blood leakage of thinner endothelial venules
BUT... does not affect Type IV collagen
- Basement membranes of blood vessels not affected
- No necrosis seen at any time

CCH-aaes, collagenase clostridium histolyticum-aaes.

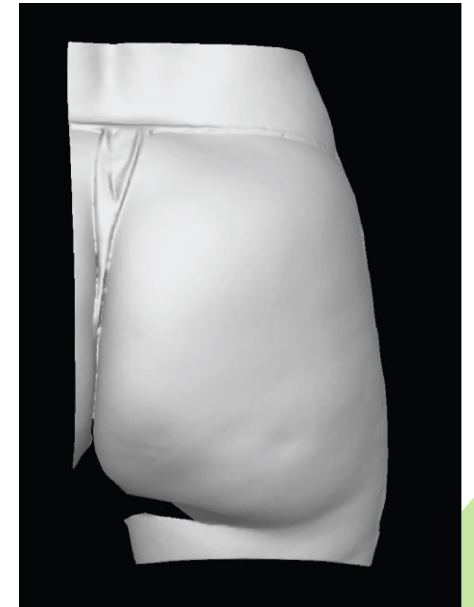
CLINICAL RELEVANCE

- **CCH-aaes injection** is a new treatment for cellulite, associated with **transient** injection-site bruising and **lessens** with subsequent treatment
- CCH-aaes is believed to initiate **ESR[™]**, which is composed of lysis of fibrous septae, fat remodeling, and neocollagenesis

Pretreatment



Day 71*



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*28 days after final injection; 2-level improvement in both the Clinician Reported Photonumeric Cellulite Severity Scale and Patient Reported Photonumeric Cellulite Severity Scale.

CCH-aaes, collagenase clostridium histolyticum-aaes; ESR, Enzymatic Subcision and Remodeling.

Thank You

Sachin M. Shridharani, MD, FACS

New York, NY



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