Qwo® (collagenase clostridium histolyticum-aaes)

PREPARATION, CELLULITE MARKING, AND INJECTION TECHNIQUE

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

endo aesthetics™
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on Slides 27-28.

QWO PACKAGING: 4-ML AND 8-ML VIALS

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

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

PREPARATION OF QWO FOR TREATMENT

Preparation[1]:

- **The QWO vial and diluent vial – This was studied as a 3-treatment protocol**
  - Single treatment area **(12 injections)**: 0.92-mg vial of lyophilized powder and 4-mL vial of sterile diluent
  - Two treatment areas **(24 injections)**: 1.84-mg vial of lyophilized powder and 8-mL vial of sterile diluent
- Appropriate size syringes and needle for reconstitution (eg: 5mL/10mL, 22-gauge or larger)
- 1.0-mL syringes with no needle attached (4 syringes/8 syringes)
- 30-gauge, ½-inch needles

Reconstitution[1]:

- Before reconstitution, remove the vials from refrigerator and let stand at room temperature for 15 minutes
- Inspect the vials containing QWO. The cake of lyophilized powder should be white in color and intact, showing no signs of erosion. The diluent should be a colorless solution, free of particulate matter
- Using aseptic technique, swab rubber stoppers with alcohol and withdraw 4 mL diluent from the vial for 1 treatment area or 8 mL diluent for 2 treatment areas and inject into the CCH vial
- Inject the diluent slowly into the sides of the vial containing the lyophilized powder of QWO. Do not invert the vial or shake the solution. Swirl to reconstitute the CCH lyophilized powder
- **Use only supplied diluent for reconstitution**
- Diluent for QWO is a sterile, preservative-free, colorless solution in a single-dose vial containing either 4 mL or 8 mL of 0.03% calcium chloride dehydrate in 0.6% sodium chloride, and water for injection, USP
- Calcium is a co-factor that is needed to allow binding of QWO to collagen and enhancement of enzymatic activity[2,3]
- The formulation is also nearly isotonic

Sources: 1. QWO [package insert]. Malvern, PA: Endo Aesthetics LLC. **2.** Eckhard U, Schönauer E, Brandstetter H. Structural basis for activity regulation and substrate preference of clostridial collagenases G, H, and T. *J Biol Chem.* 2013;288(28):20184-20194. **3.** Wilson JJ, Matsushita O, Okabe A, Sakon J. A bacterial collagen-binding domain with novel calcium-binding motif controls domain orientation. *EMBO J.* 2003;22(8):1743-1752.

Please see Important Safety Information on slides 27-28.

PREPARATION OF QWO FOR TREATMENT

After reconstitution:

- The solution can be kept at room temperature for up to 8 hours in the provided drug vial
- If more time is needed prior to injection, refrigerate the reconstituted drug for up to 72 hours in the provided drug vial
- After you draw up the reconstituted drug in the 1-mL syringes, they need to be used immediately and not stored in the refrigerator

Contraindications:

- History of hypersensitivity to any collagenase or to any of the components of the formulation
- Infection at the injection site

Warnings and precautions:

- Serious hypersensitivity reactions including anaphylaxis have been reported with the use of collagenase clostridium histolyticum
- 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. Use 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

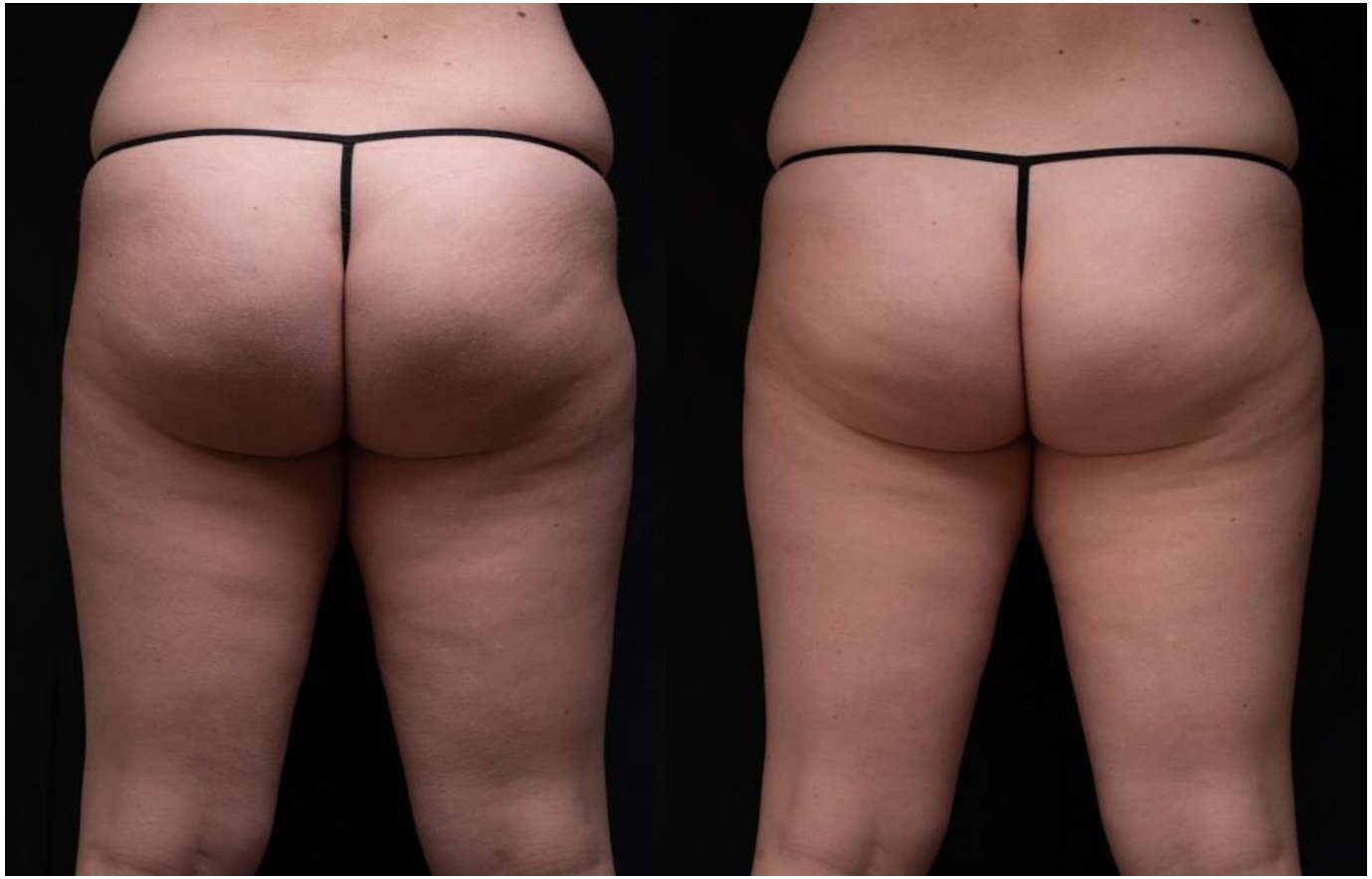
Source: QWO [package insert]. Malvern, PA: Endo Aesthetics LLC.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

PHOTOGRAPHY: WITH 3D VECTRA OR DSLR CAMERA

- All photos taken in same room
- Artificial light only; lighting is critical
- Matte black background
- If using DSLR camera – vertical position set to AF/A and white balance set to “auto”
- Ask patient to cross arms at chest and to stand at a relaxed position
- Have the patient take a deep breath and clench and then relax the buttocks while releasing breath
- Take the posterior photo after breath
- Quickly review the photo for accuracy and no clenching. If approved, then repeat process at a 22° right and 22° left views
- Photos to be posterior, 22° L and R views
- Comfortable loose clothing worn to office so imprints not seen
- Timing – at each Tx visit before and after dimple markings, and 28 days after the 3rd and final treatment at Day 71



Sub-optimal lighting

Preferred lighting choice

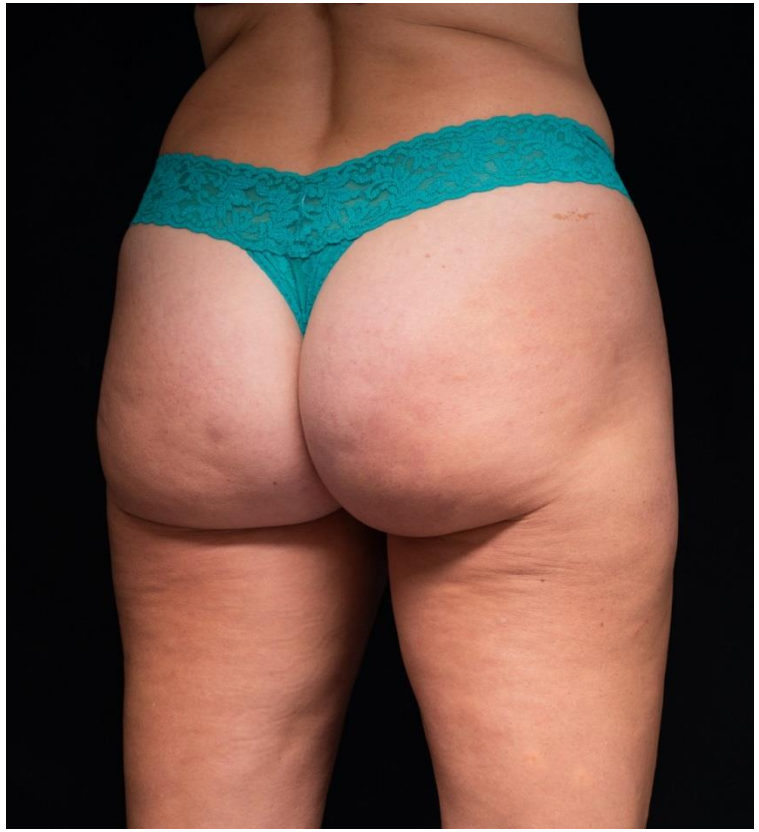
Source: Study 305: Photography and Imaging Experimental study (PIXELS) protocol.

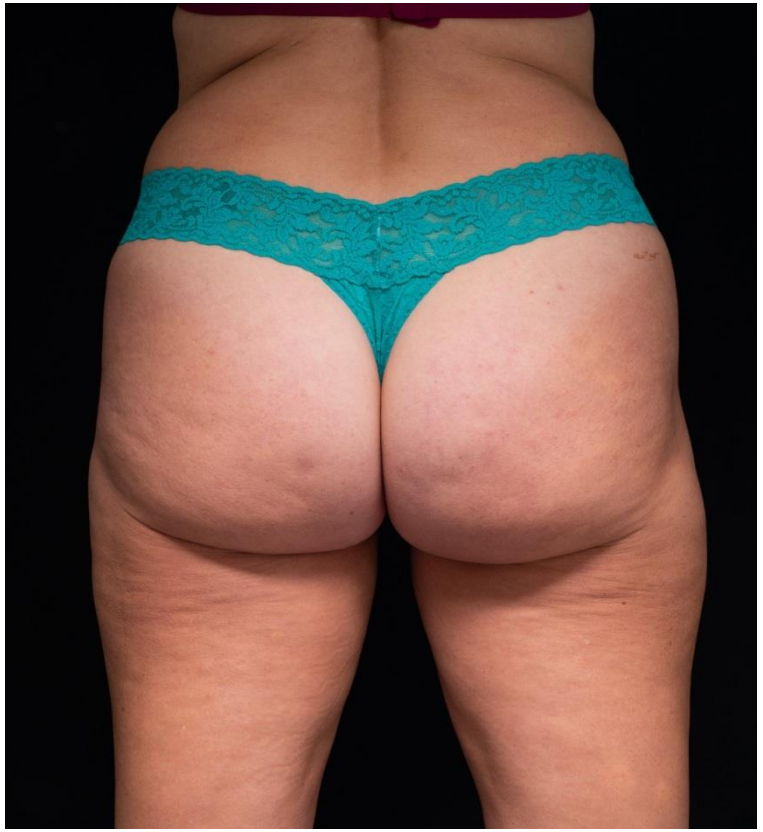
endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

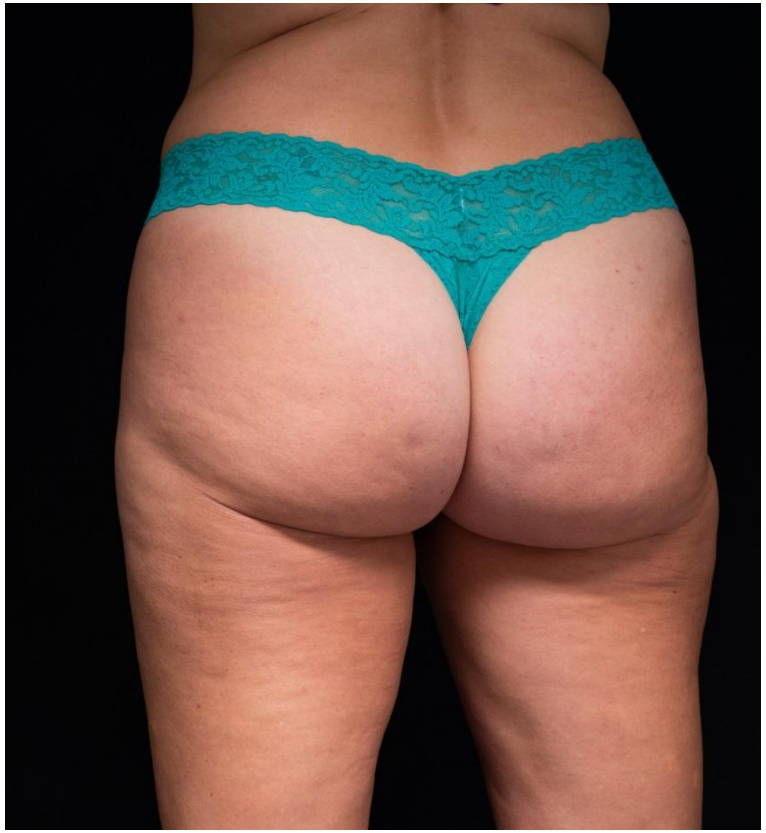
Please see Important Safety Information on slides 27-28.

EXAMPLE PRE-MARKING PHOTOGRAPHY DAY 1

Example of posterior and 22° angles







Source: Endo Aesthetics Patient Selection training materials.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

PHOTOGRAPHY: 22° ANGLE RIGHT AND LEFT

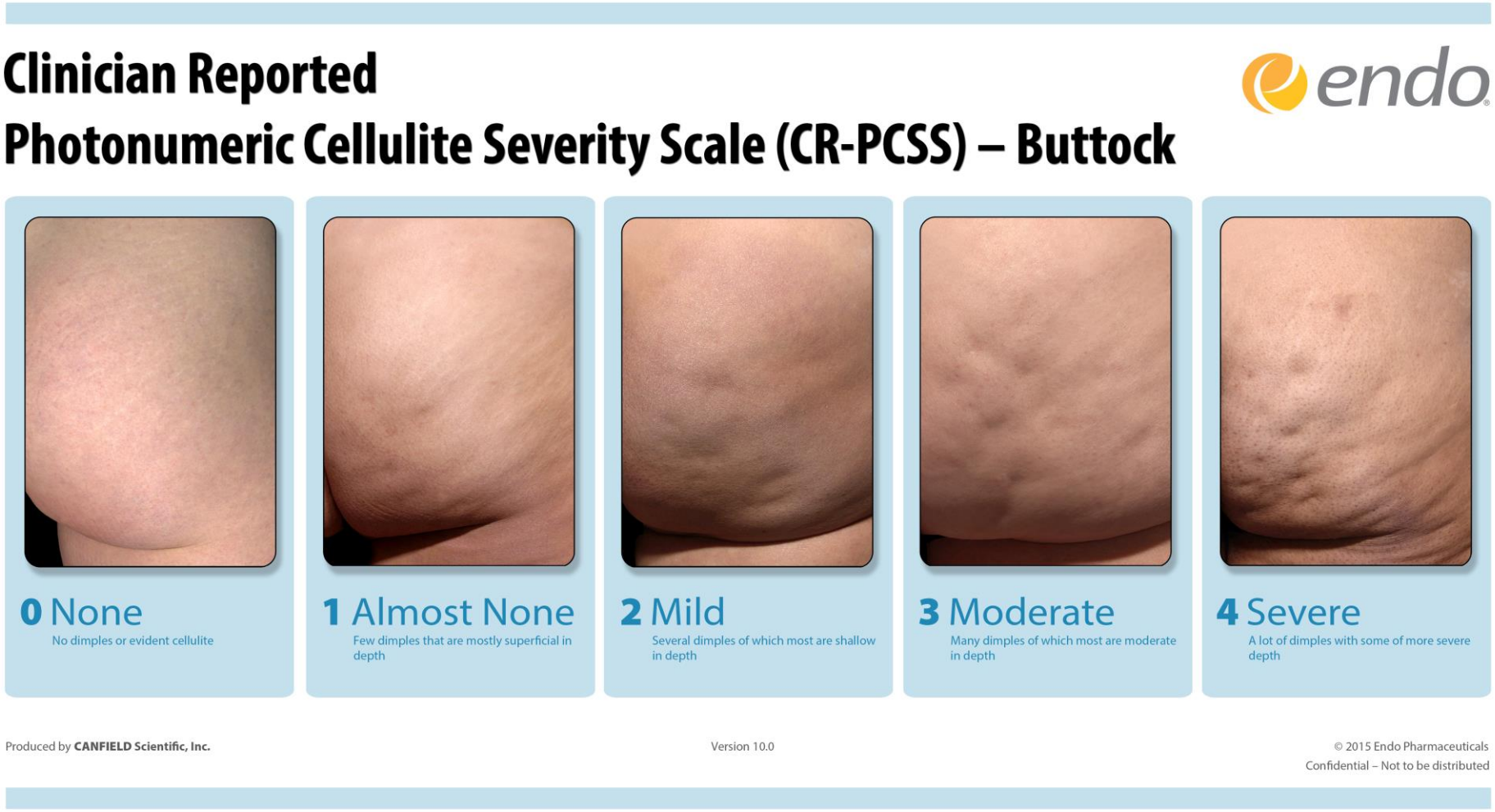
Example of a standing mat for posterior and 22° angles

Source: Study 305: Photography and Imaging Experimental study (PIXELS) protocol.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

DIMPLE SELECTION AND MARKING



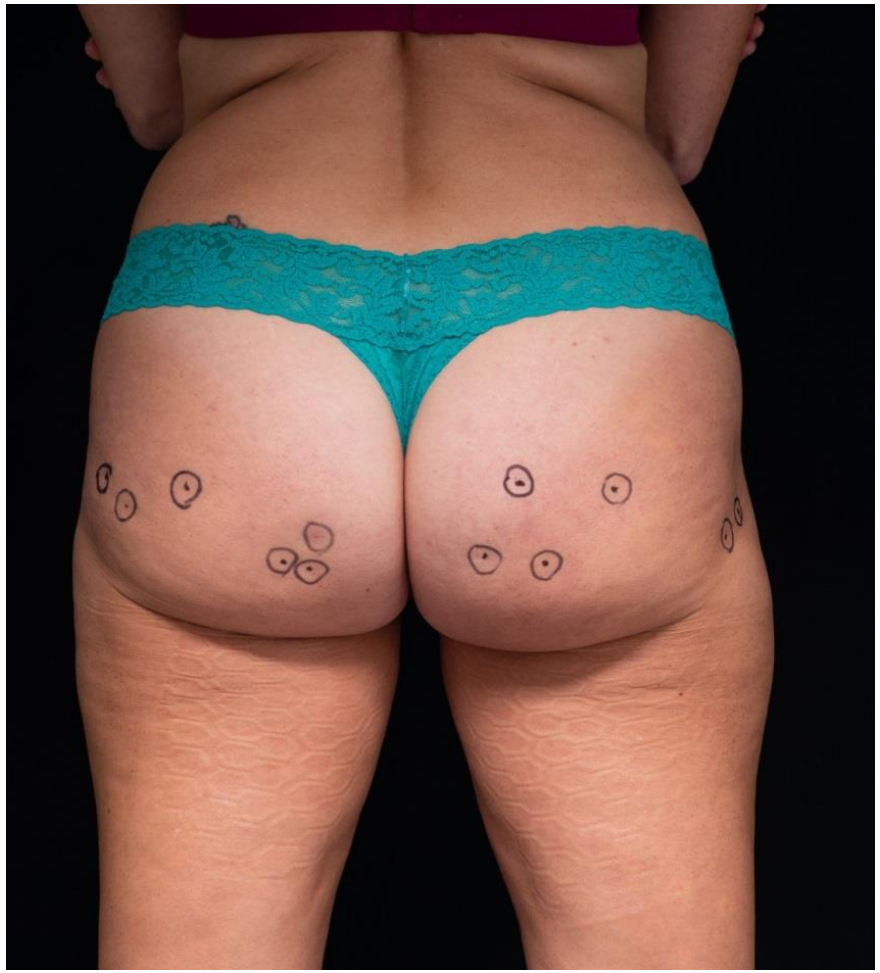
Source: Sadick NS, Goldman MP, Liu G, et al. Collagenase clostridium histolyticum for the treatment of edematous fibrosclerotic panniculopathy (cellulite): a randomized trial. *Derm Surg.* 2019;45:1047-1056.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

DIMPLE SELECTION AND MARKING

- Dimples should be well-defined and evident when subject is standing in a position with relaxed gluteus muscles
- A dot should be placed immediately superior to where the injection site will be (where the dimple is tethered)
- Dimples should then be circled
- For elongated dimples, space injection marks about 2 cm apart if they require more than one injection (where dimples are tethered)
- Circles should not overlap
- Do not place markings within 2 cm of the gluteal fold
- Buttocks should be photographed before and after marking



Source: EN3835-302 and 303 study protocol section 12.2.

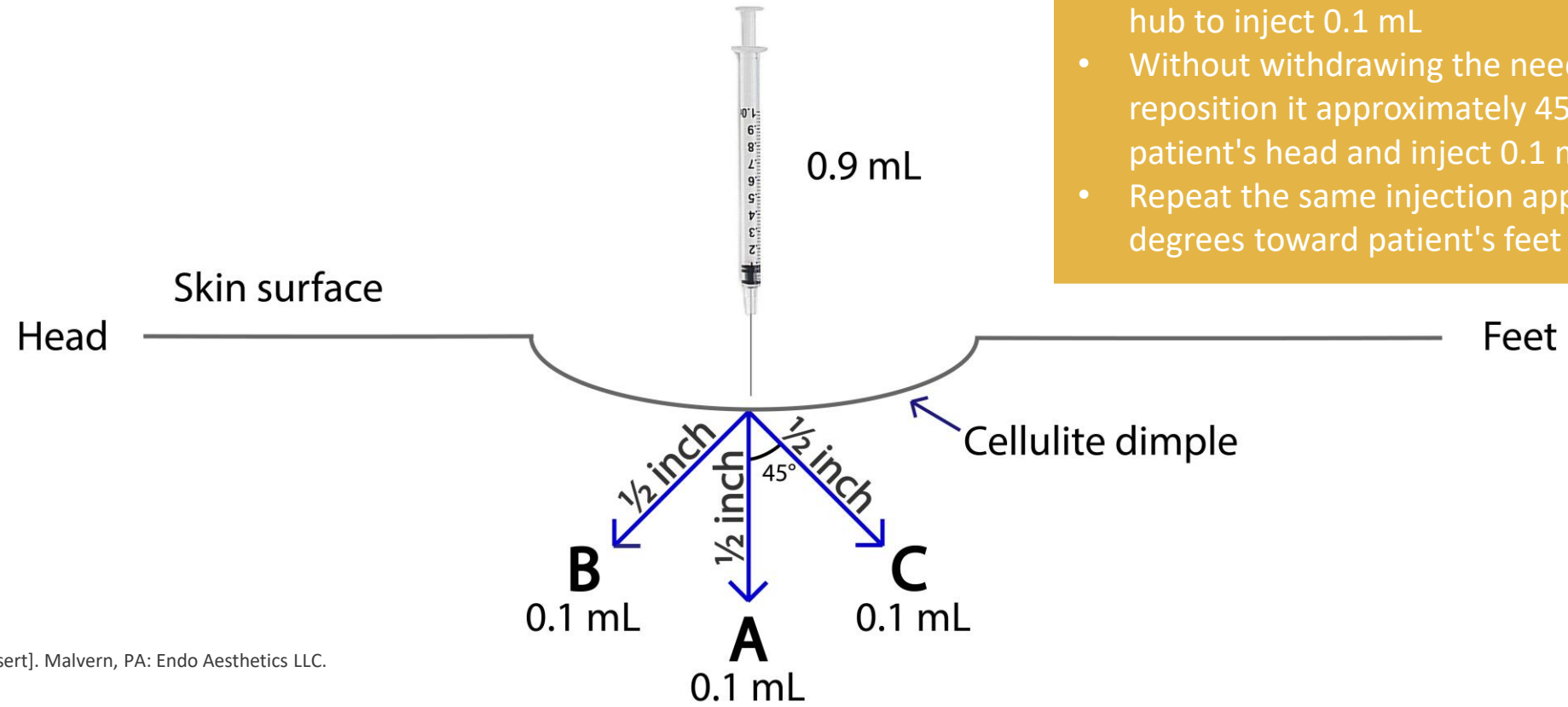
endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

QWO ADMINISTRATION

UP TO 3.6 ML TOTAL DRUG VOLUME PER BUTTOCK TREATMENT

Buttock treatment (3-aliquot injection): Injected with a 1-mL syringe and 30 g x ½" needle, which is enough for 3 separate dimple injections.



- Starting with position A, insert needle up to the hub to inject 0.1 mL
- Without withdrawing the needle completely, reposition it approximately 45 degrees toward patient's head and inject 0.1 mL at position B
- Repeat the same injection approximately 45 degrees toward patient's feet at position C

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

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

INJECTION TECHNIQUE

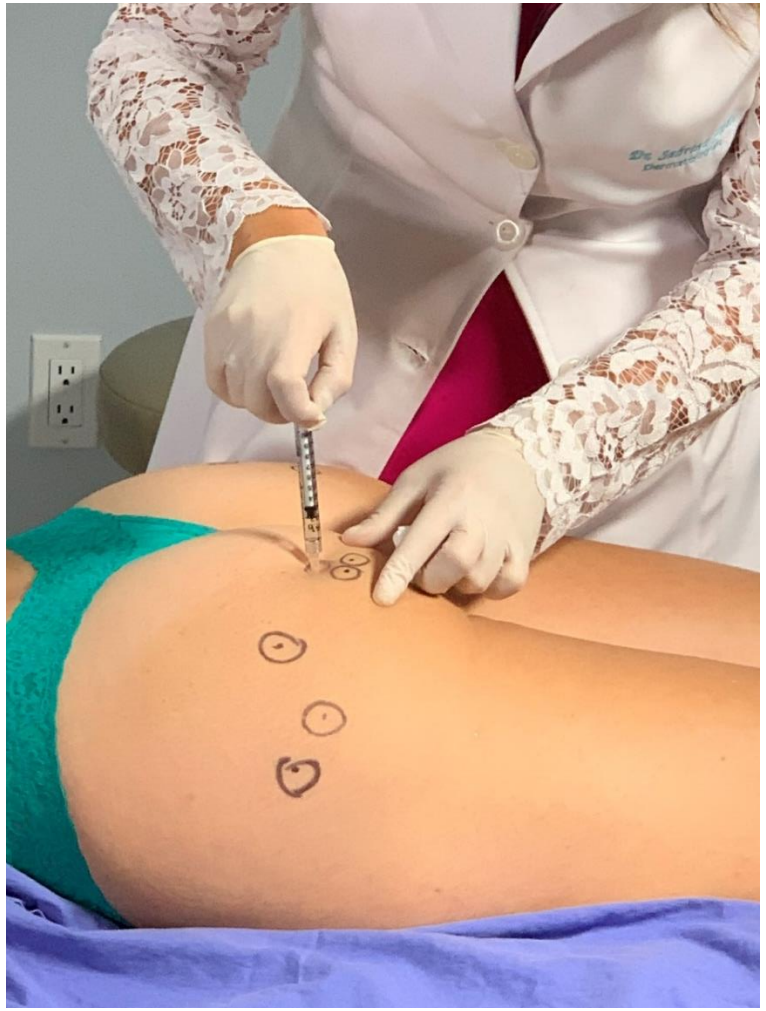
- **Withdraw needle from first injection site and move to the next injection site**
- Complete a total of three 0.3-mL injections (each administered as three 0.1-mL aliquots) and discard the syringe appropriately
- Use additional syringes to complete dosing in each buttock (three 0.3-mL injections per syringe, each injection administered as three 0.1-mL aliquots)
- Patient should remain in the prone position for at least 5 minutes after administration of last injection
- Each buttock can receive up to 12 injections

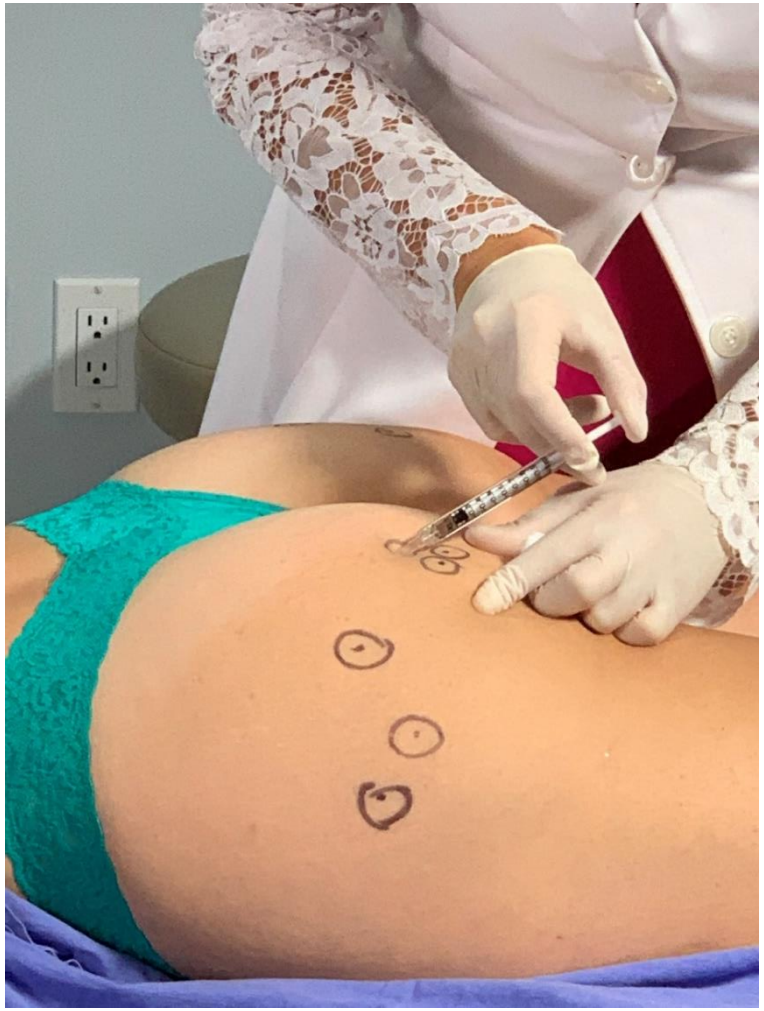
Source: QWO [package insert]. Malvern, PA: Endo Aesthetics LLC.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

EXAMPLE ADMINISTRATION





Source: Endo Aesthetics Patient Selection training materials.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

ADVERSE EVENTS IN THE CLINICAL STUDIES

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

ADVERSE EVENTS OCCURRING IN ≥1% OF SUBJECTS IN RELEASE-1 AND RELEASE-2 TRIALS

Adverse Reactions at Injection Site	Combined RELEASE-1 and RELEASE-2	
	QWO (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

Generally, adverse reactions had a duration of less than 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.

Pooled terms: Bruising, injection site bruising, injection site hematoma, and injection site hemorrhage (refers to verbatim term injection site ecchymosis); Pain, injection site pain, injection site discomfort, and injection site dysesthesia; Swelling, injection site swelling, injection site edema, injection site induration; Discoloration, injection site discoloration; Nodule, injection site mass and injection site nodule.

Information on this slide presented previously by Gold at VCS meeting 2020.

Source: Data on file. Endo Aesthetics LLC.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

INJECTION SITE HYPERPIGMENTATION – RELEASE-1 AND RELEASE-2

	CCH N=424	Placebo N=419
Number of Subjects with Discoloration	33 (8%)	2 (0.5%)
Number of Subjects with Hyperpigmentation	29 (7%)	1 (0.2%)
Number of Subjects with Ongoing Hyperpigmentation	14 (3%)	0 (0%)
Number of Subjects with Hyperpigmentation with:		
Fitzpatrick skin rating I	0 (0%)	0 (0%)
Fitzpatrick skin rating II	8 (2%)	0 (0%)
Fitzpatrick skin rating III	II (3%)	0 (0%)
Fitzpatrick skin rating IV	8 (2%)	0 (0%)
Fitzpatrick skin rating V	2 (0.5%)	0 (0%)
Fitzpatrick skin rating VI	0 (0%)	1 (0.2%)

Source: Data on file. Endo Aesthetics LLC.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

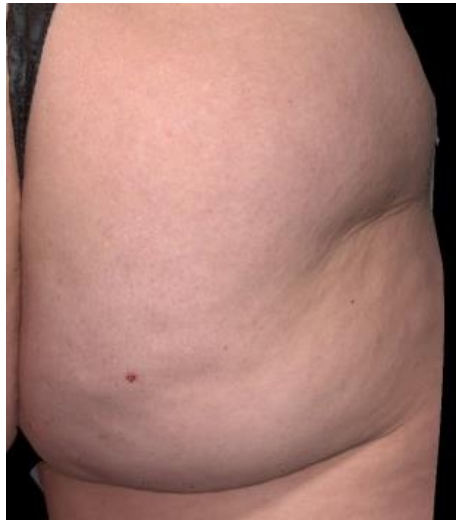
BRUISING DURING PHASE 2 OPEN-LABEL STUDIES OF QWO IN THE TREATMENT OF CELLULITE

Source: Information on this slide previously presented by Fabi, et al at SCALE meeting; 2020.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

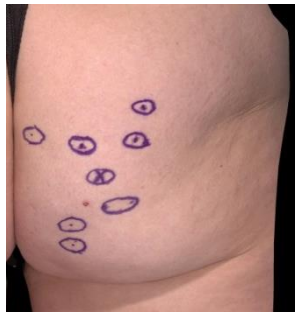
Please see Important Safety Information on slides 27-28.

BRUISING DURING PHASE 2A STUDY OF CCH IN THE TREATMENT OF CELLULITE

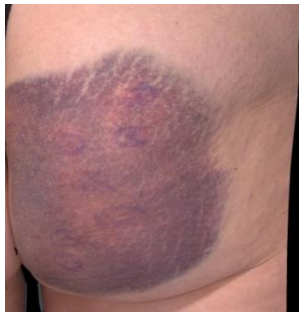


Day 1 (Pre-Injection)

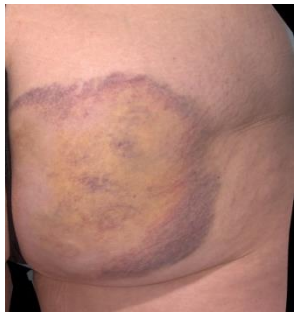
Tx 1



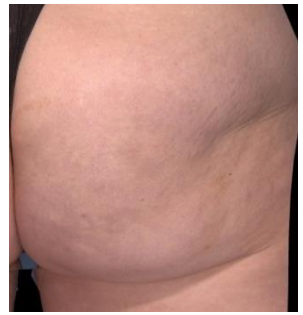
Day 1



Day 2

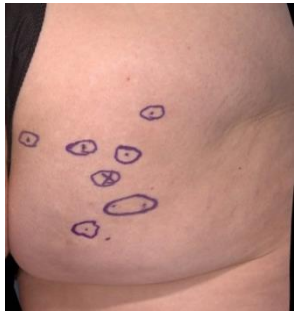


Day 8

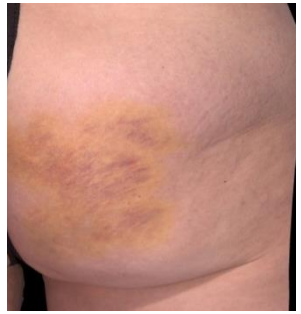


Day 15

Tx 2

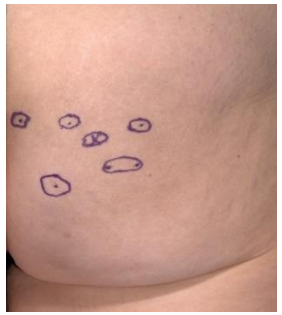


Day 22

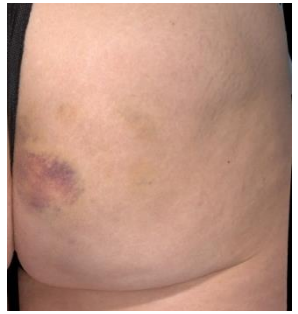


Day 23

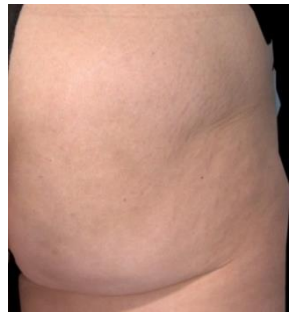
Tx 3



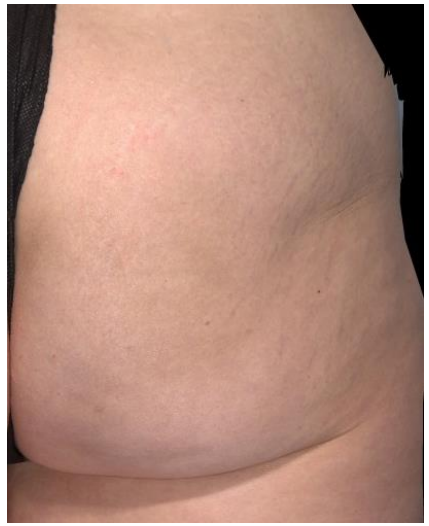
Day 43



Day 44



Day 50



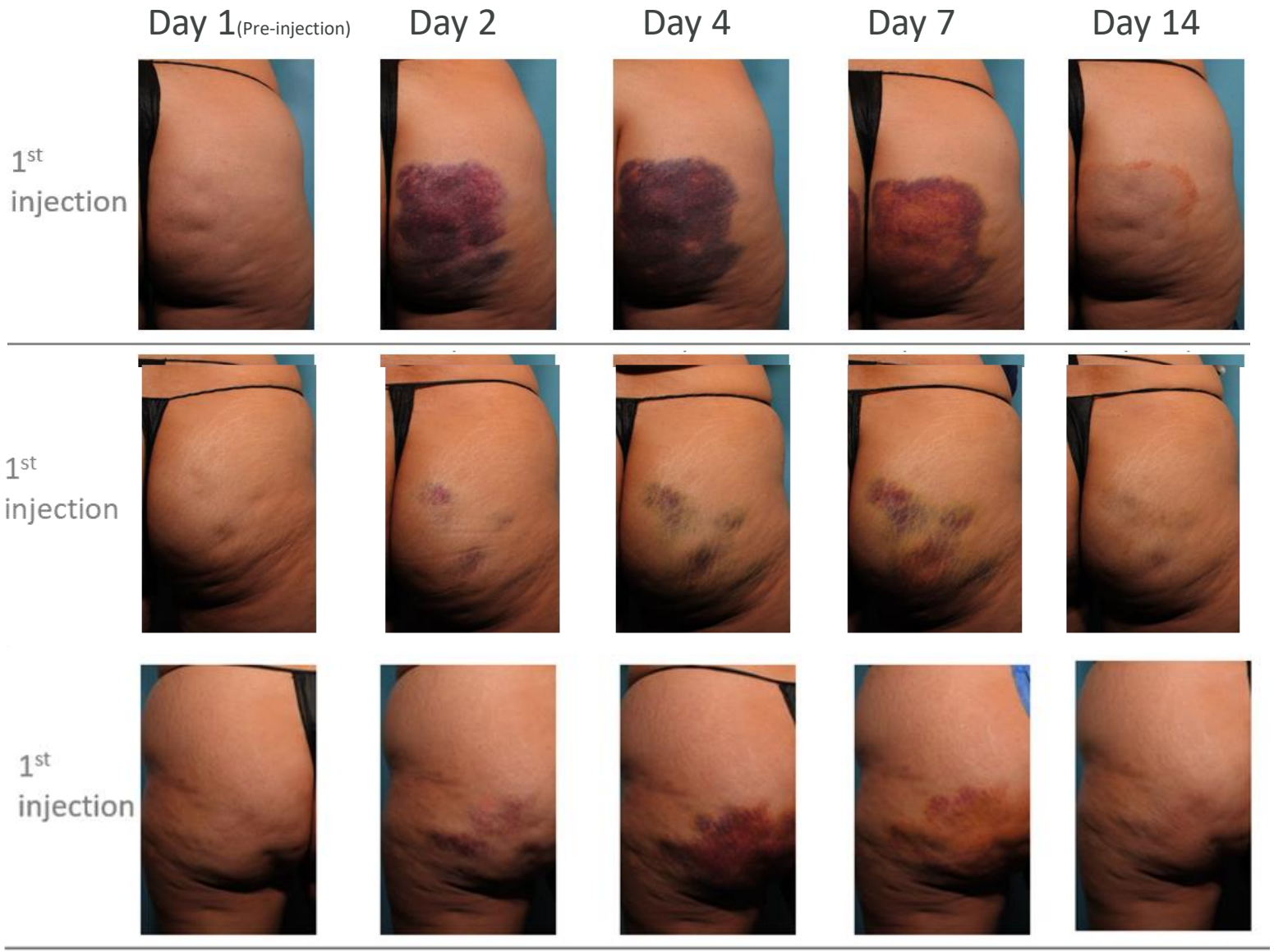
Day 73

Source: Subject images from study 831.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

BRUISING AFTER 1ST INJECTION OF QWO INJECTION IN PHASE 2 OPEN-LABEL STUDIES

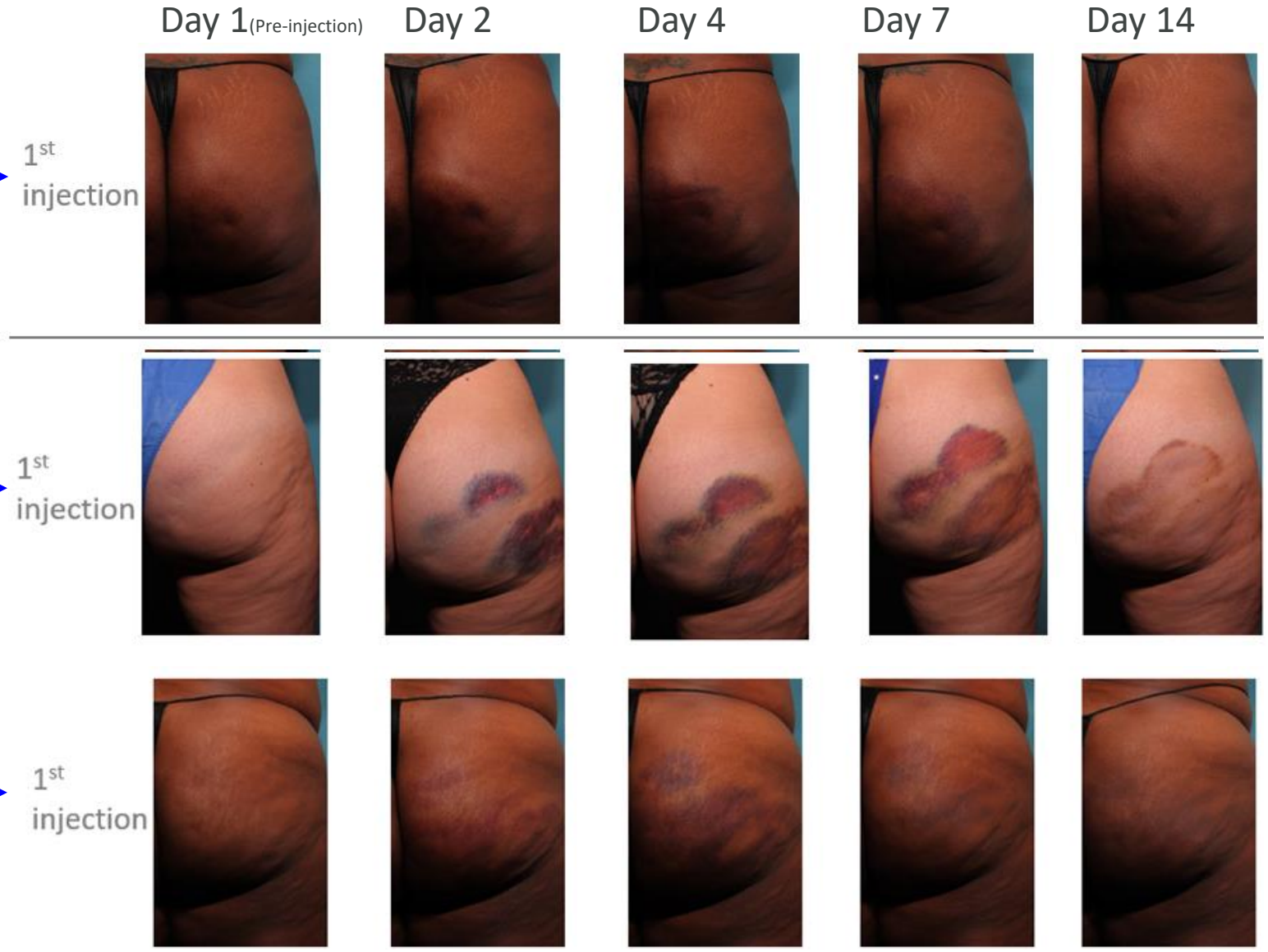


Source: Subject images from studies 205.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

BRUISING AFTER 1ST INJECTION OF QWO INJECTION IN PHASE 2 OPEN-LABEL STUDIES



Source: Subject images from studies 205.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

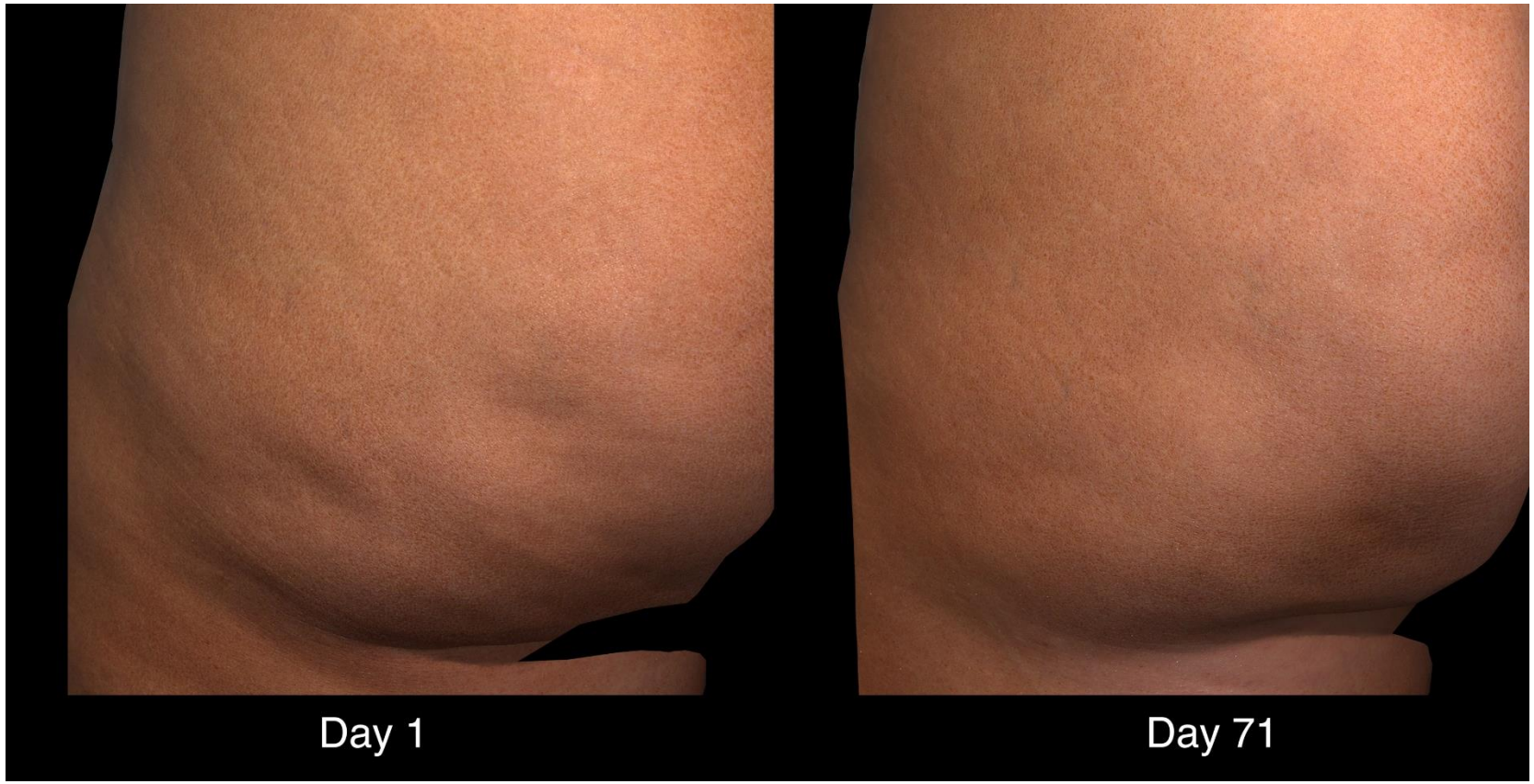
BEFORE AND AFTER

endo aesthetics™
REDEFINING SCIENTIFIC ARTISTRY

2-LEVEL COMPOSITE RESPONDER*

Patient Information

Age: 52 years
Fitzpatrick: Type II
BMI: 23.6 kg/m^2



*From baseline in CR-PCSS rating and PR-PCSS rating.

Image presented from RELEASE-1 with permission from patient and physician.

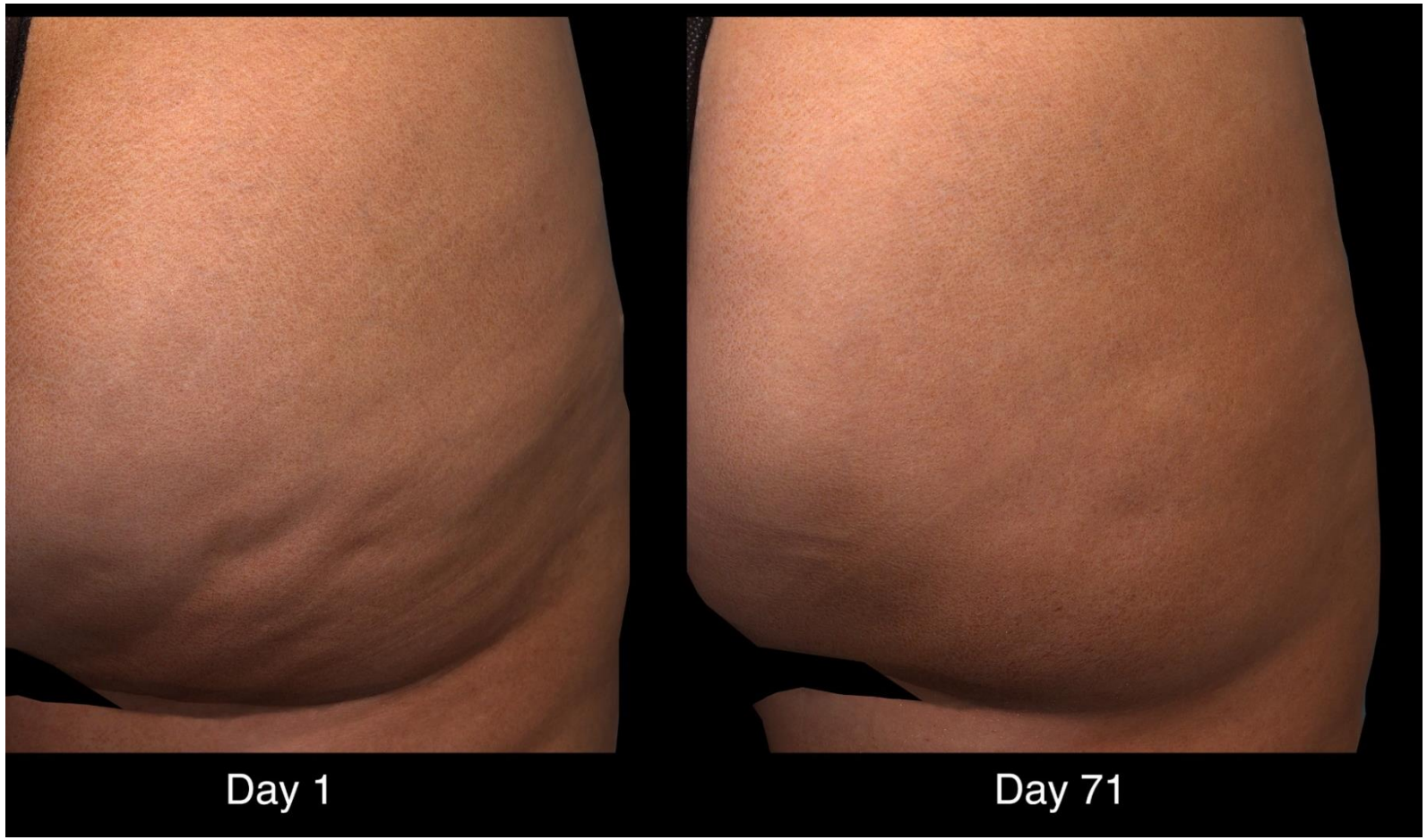
endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

2-LEVEL COMPOSITE RESPONDER*

Patient Information

Age: 52 years
Fitzpatrick: Type II
BMI: 23.6 kg/m^2



*From baseline in CR-PCSS rating and PR-PCSS rating.

Image presented from RELEASE-1 with permission from patient and physician.

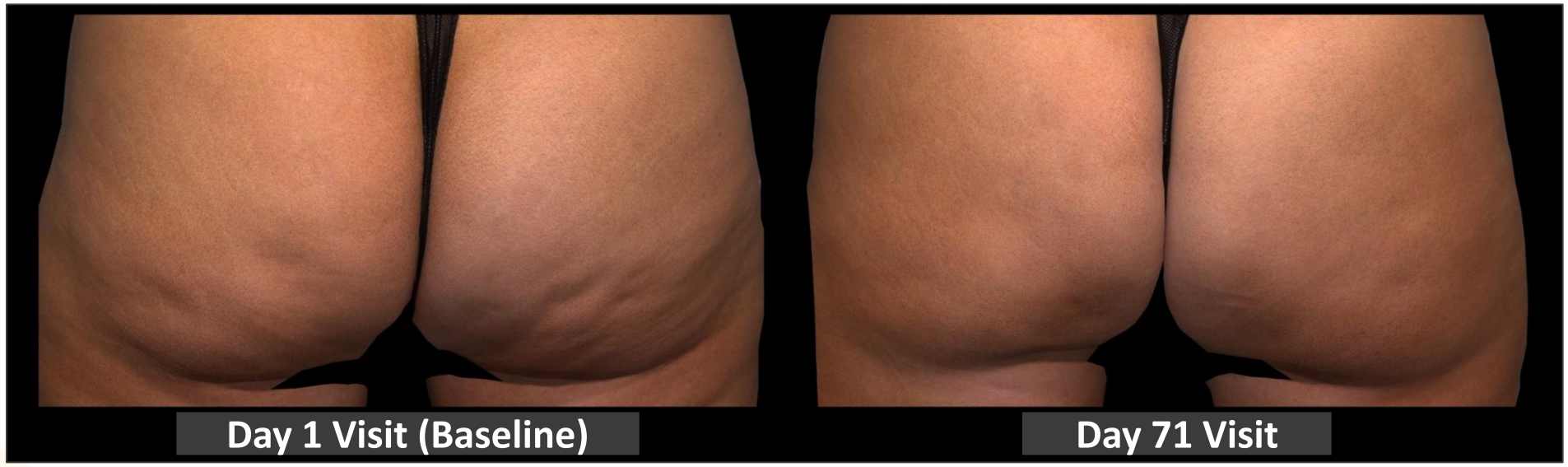
endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

2-LEVEL COMPOSITE RESPONDER*, BOTH BUTTOCKS

Patient Information

Age: 52 years
Fitzpatrick: Type II
BMI: 23.6 kg/m^2



*From baseline in CR-PCSS rating and PR-PCSS rating.

Image presented from RELEASE-1 with permission from patient and physician.

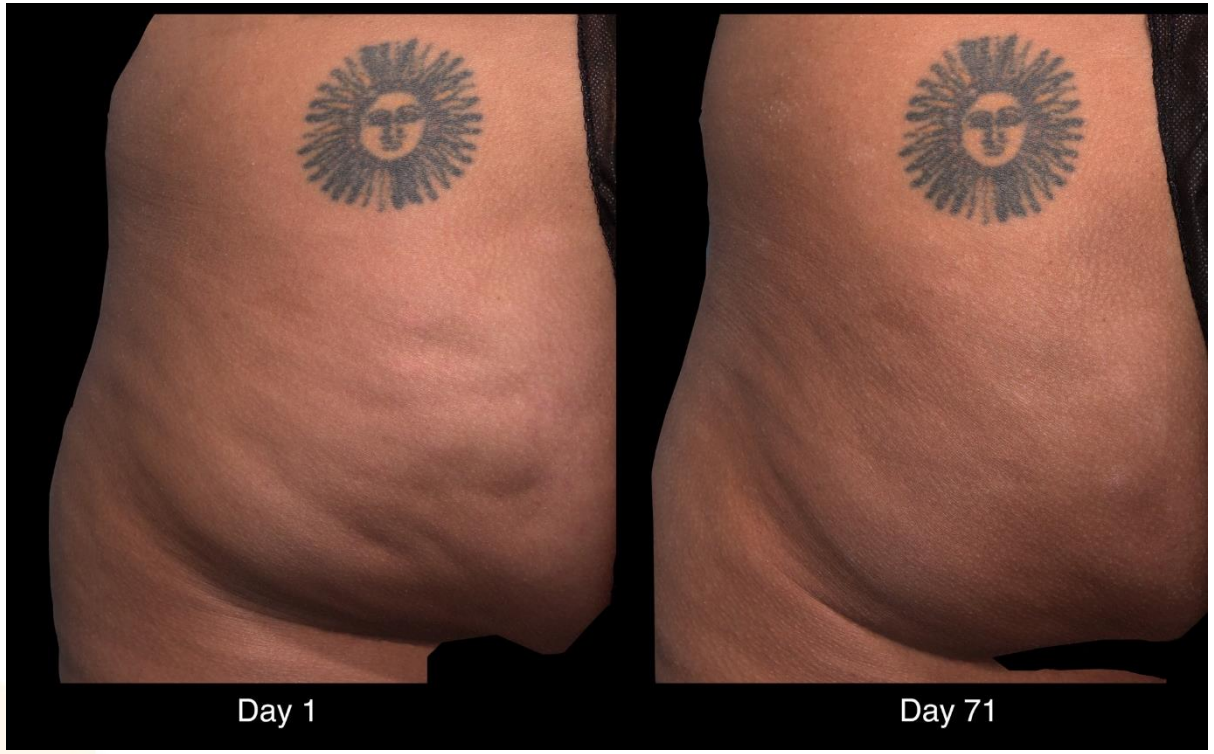
endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

2-LEVEL COMPOSITE RESPONDER*

Patient Information

Age: 43
Fitzpatrick: Type IV
BMI: 28.9 kg/m^2



*From baseline in CR-PCSS rating and PR-PCSS rating.

Image presented from RELEASE-1 with permission from patient and physician.

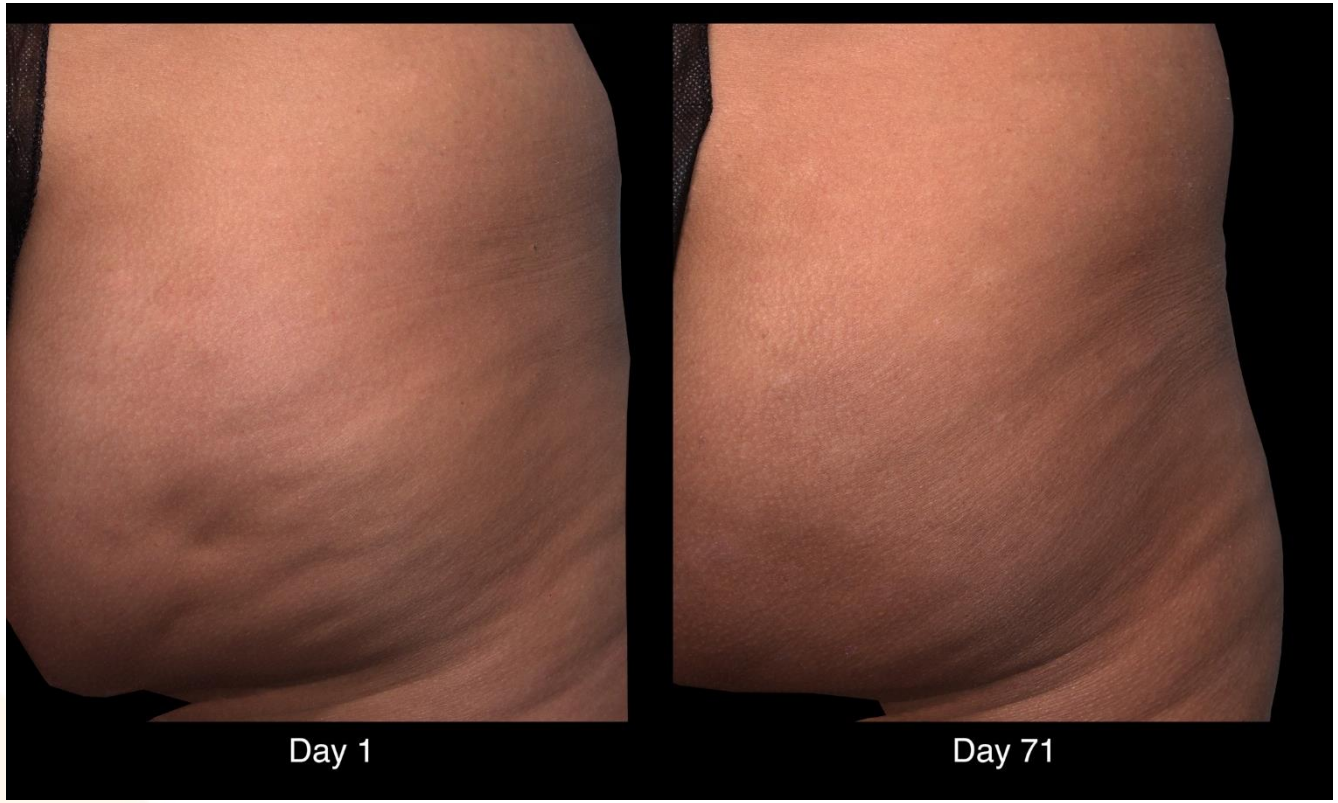
endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

2-LEVEL COMPOSITE RESPONDER*

Patient Information

Age: 43
Fitzpatrick: Type IV
BMI: 28.9 kg/m^2



*From baseline in CR-PCSS rating and PR-PCSS rating.

Image presented from RELEASE-1 with permission from patient and physician.

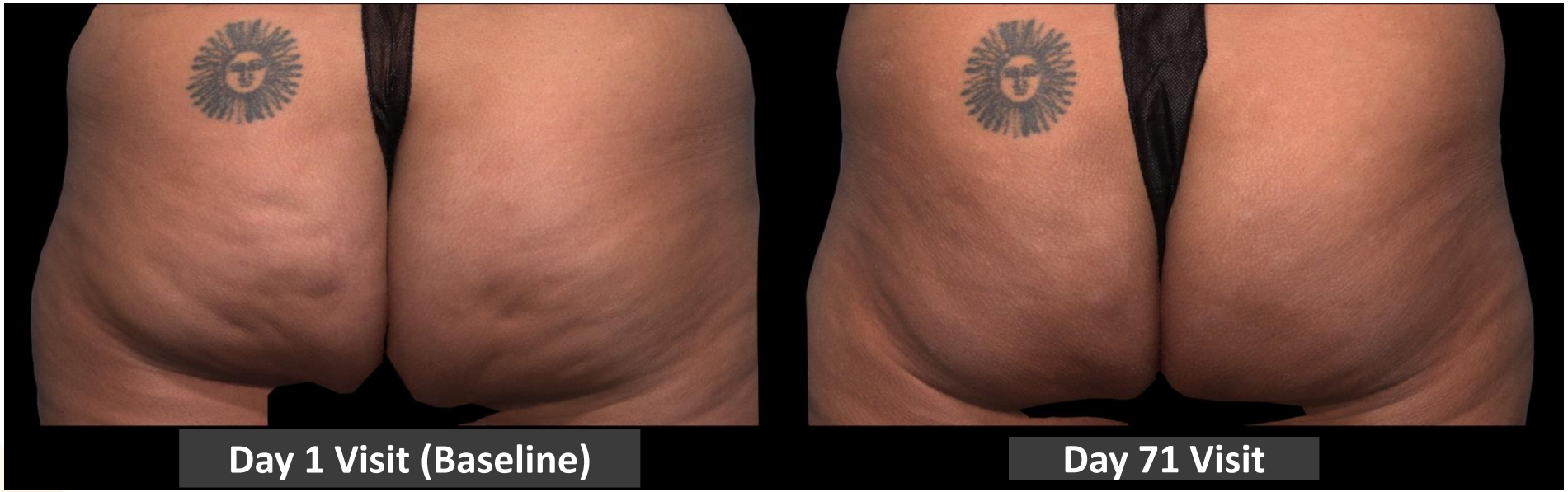
endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

2-LEVEL COMPOSITE RESPONDER*

Patient Information

Age: 43
Fitzpatrick: Type IV
BMI: 28.9 kg/m^2



*From baseline in CR-PCSS rating and PR-PCSS rating.

Image presented from RELEASE-1 with permission from patient and physician.

endo aesthetics
REDEFINING SCIENTIFIC ARTISTRY

Please see Important Safety Information on slides 27-28.

IMPORTANT SAFETY INFORMATION FOR QWO

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.

IMPORTANT SAFETY INFORMATION FOR QWO (cont)

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 with an incidence ≥ 10% were at the injection site: bruising, pain, nodule and pruritus.

Please see Full Prescribing Information for QWO, available at this presentation.

QUESTIONS?

endo aesthetics™
REDEFINING SCIENTIFIC ARTISTRY