The Tea: the latest in injectable trends, indications, and products

Omer Ibrahim, MD

Chicago Cosmetic Surgery and Dermatology, Chicago, IL

Rush University Medical Center, Chicago, IL

Disclosures

- Allergan, consultant
- Galderma, consultant, investigator
- Merz, consultant

Objectives

- Discuss shifts in aesthetic paradigms and treatment goals
- Describe trends and patterns in filler rejuvenation
- Present new fillers/indications on the market
- Review risks and pitfalls of newer trends

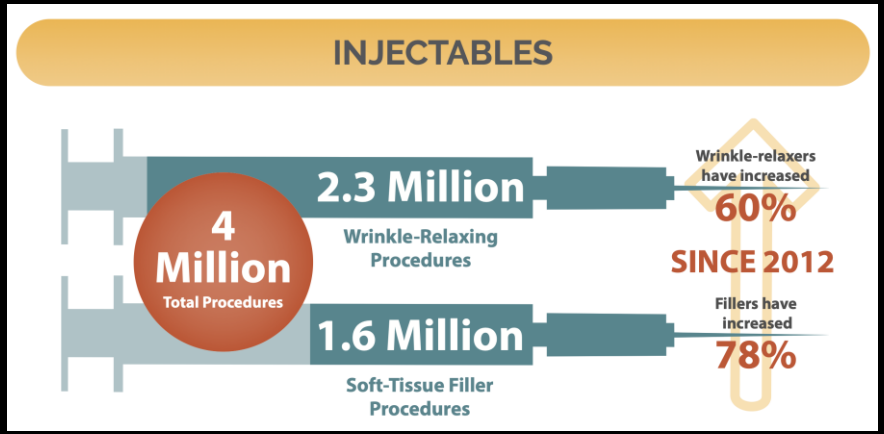
“Let me be very clear. I am extremely happy with who I am and how I look, but sometimes you need a change. There’s nothing wrong with wanting a different look from time to time.”

Female patient, age 36, seen in consultation for jawline enhancement

TikTok

Paradigm Shifts

- In US, 1.6 million soft-tissue filler procedures were performed in 2019, an increase of 78% since 2012
- Increased demand, increased awareness, increased supply of fillers
- Clinician can target deep hollows, moderate furrows, and fine lines
- Clinician = master of anti-aging……
- …… but there is a shift in treatment paradigms



"ASDS Survey on Dermatologic Procedures." *ASDS: American Society for Dermatologic Surgery*, ASDS, 2021, https://www.asds.net/medical-professionals/practice-resources/asds-survey-on-dermatologic-procedures

Paradigm shifts

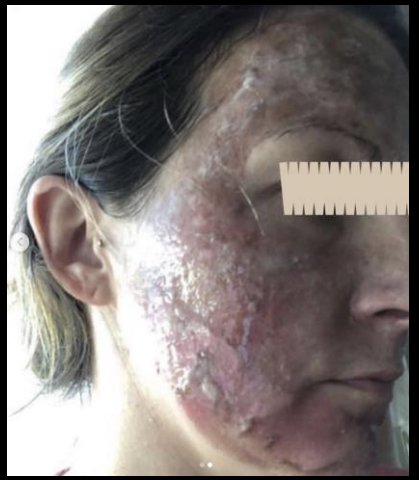
- Popular culture, social media, and increased transparency -> rise in nonsurgical aesthetic treatments
- Instagram, snapchat, and Zoom have changed the way we perceive ourselves
- Younger population: most health-literate, and fastest growing cohort seeking cosmetic consultation
- Patients are requesting treatments for jawlines, chins, cheekbones, lips, etc. for recreative (reconstructive) purposes, rather than rejuvenative
- Google trends analysis showed that post-COVID-19 vaccine era led to increased interest in lower facial procedures (lip lift, lip filler, chin, jawline) -> and industry has responded!!
- The clinician: recreates structures not originally present rather than rejuvenates what was lost with time

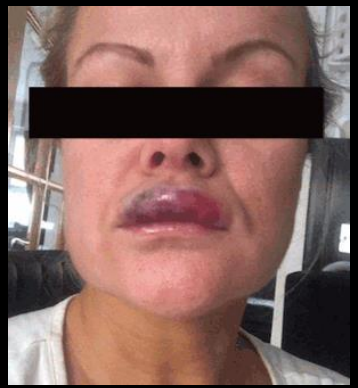
Shift Towards Fluidity…

Gender shifts….

- Men are asking for “chiseled cheekbones”, under eye filler, and body modification, including buttock enhancement
- Women are asking for “stronger jawlines” and “sharper chins”
- Cis, trans, and nonbinary individuals are seeking enhancements in their physical features to reflect how they identify internally

- Change can come with a cost
- The “lipstick effect” = the purchase of less costly luxury goods (many times for DIY purposes) -> incidence has increased with COVID-19
- Unauthorized injectors, at-home medical grade chemical peels, fillers purchased through unauthorized retailers, and even at-home self administered filler injections (cement, motor oil)
- Occlusion, blindness, burns, scarring
- There is an imminent physical danger to patients and consumers, and it is our duty to stand as watchguards and THE authority on safety, science-based evidence, and quality care – so for better or worse, we must keep up with the times.





What are the psychological implications?

- “Snapchat dysmorphia”, “Zoom dysmorphia” – estimated that almost 10% of cosmetic patients have some form of body dysmorphia
- Unrealistic expectations, “quick-fix” attitude – constantly staring at and comparing highly edited and distorted photos on social media
- Undiagnosed anxiety, depression, body dysmorphia
- Increased feelings of self-worthlessness

What are the psychological implications?

- Unprecedented ubiquity of minimally invasive procedures on TVs, tablets, and phones have made the psychological and social impact of the injector even more powerful
- Where is the line between evolving your practice and pandering to impractical beauty ideals?
- “Can I deliver an aesthetically pleasing, genuine result without feeding into unrealistic societal expectations and catering to an underlying dysmorphia?”
- The line is blurry, but the responsibility to uphold ethical standards, while providing patient education and delivering evidence-based treatment ultimately falls upon the clinician

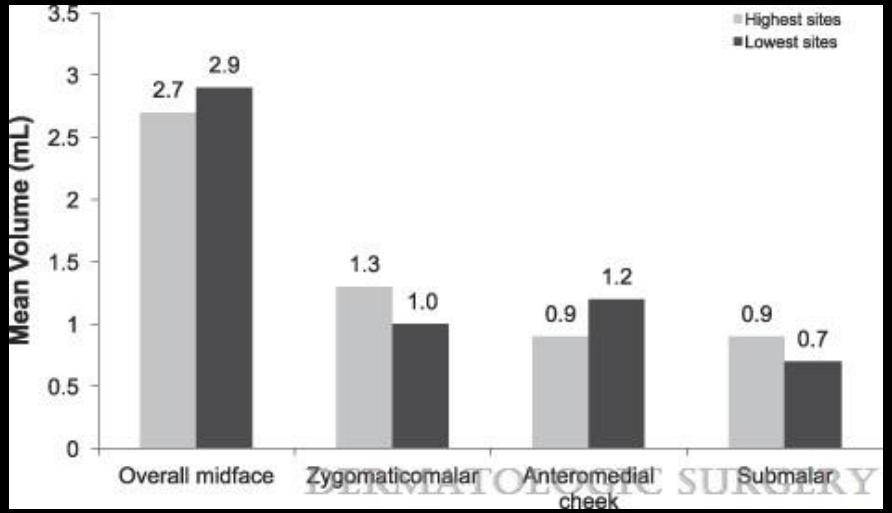
Trends, injectables and indications…

“The higher the cheekbones…”

- … the closer to God.”
- Malar rejuvenation is no longer reserved solely for anti-ageing purposes anymore
- Increased emphasis on “heart-shaped faces”, defined cheekbones, sharp contour
- Can you recreate or enhance with filler what makeup has done for years?

“The higher the cheekbones…”

- The HARMONY study examined the impact of a combination of multiple minimally invasive facial aesthetic treatments



Kaminer MS, Cohen JL, Shamban A, Werschler WP, Shumate GT, Drinkwater A, Gallagher CJ. Maximizing Panfacial Aesthetic Outcomes: Findings and Recommendations From the HARMONY Study. Dermatol Surg. 2020 Jun;46(6):810-817.

“The higher the cheekbones…”

- Despite using less overall volume of VYC-20L (Voluma) in the midface, the highest performing sites were still able to achieve greater improvement

- Placement of greater volumes in the anteromedial cheek region may inhibit expression and movement and may cause a motion-related unnatural fullness at the cheek:tear trough junction, which may result in lower subject satisfaction with the outcome

- “Lateral and less”: use less volume medially, and focus on the zygomaticomalar region

Kaminer MS, Cohen JL, Shamban A, Werschler WP, Shumate GT, Drinkwater A, Gallagher CJ. Maximizing Panfacial Aesthetic Outcomes: Findings and Recommendations From the HARMONY Study. Dermatol Surg. 2020 Jun;46(6):810-817.

“The higher the cheekbones…”

- Results of the HARMONY study validate what patients, especially social media savvy ones, are surmising online and seeking out in the real world

- Although overall patient satisfaction depends on a multipronged treatment approach, appropriate malar correction/augmentation is consistently a key factor in successful facial rejuvenation

Kaminer MS, Cohen JL, Shamban A, Werschler WP, Shumate GT, Drinkwater A, Gallagher CJ. Maximizing Panfacial Aesthetic Outcomes: Findings and Recommendations From the HARMONY Study. Dermatol Surg. 2020 Jun;46(6):810-817.

“The higher the cheekbones…”

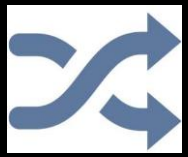
- In turn, the armamentarium of fillers used in the malar area expanded significantly

- Newer fillers used in the malar cheeks include (regardless of official FDA indication):
  - Restylane Defyne
  - Restylane Contour
  - RHA 4
  - Rise in use of Radiesse+

43USV1704 Pivotal Study – Restylane Contour vs. Voluma for Cheek Augmentation and Correction of Midface Contour Deficiencies

Study Design

Purpose:
Evaluate Contour vs. Voluma for cheek augmentation



Randomized, comparator-controlled, multi-center study

15 US CENTERS

DURATION: 48 WEEKS

TREATMENTS

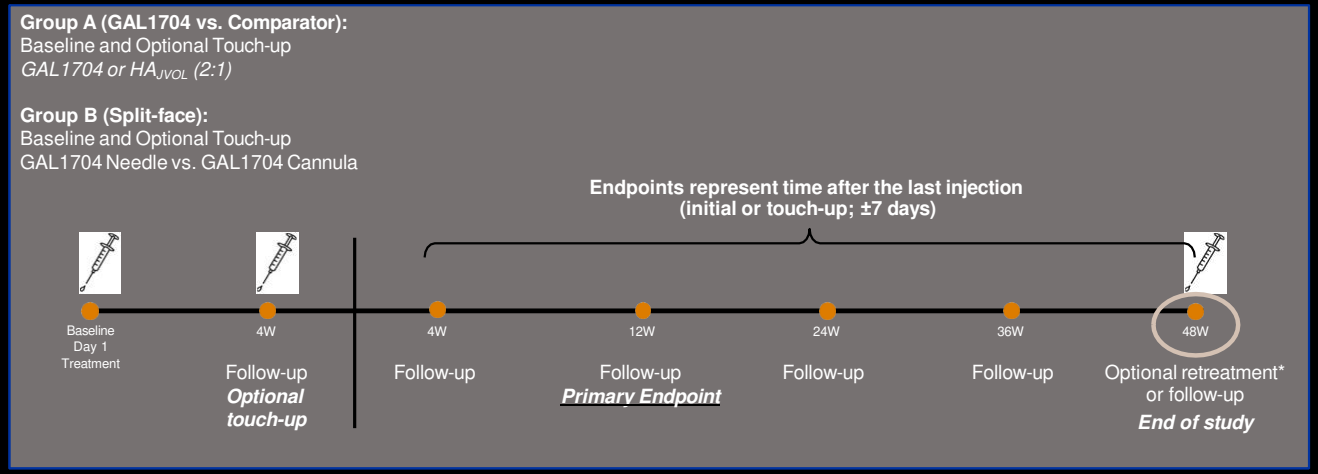
Group A (Randomized 2:1)

Contour (N=142)
Voluma (N=68)

Group B (Split-face)

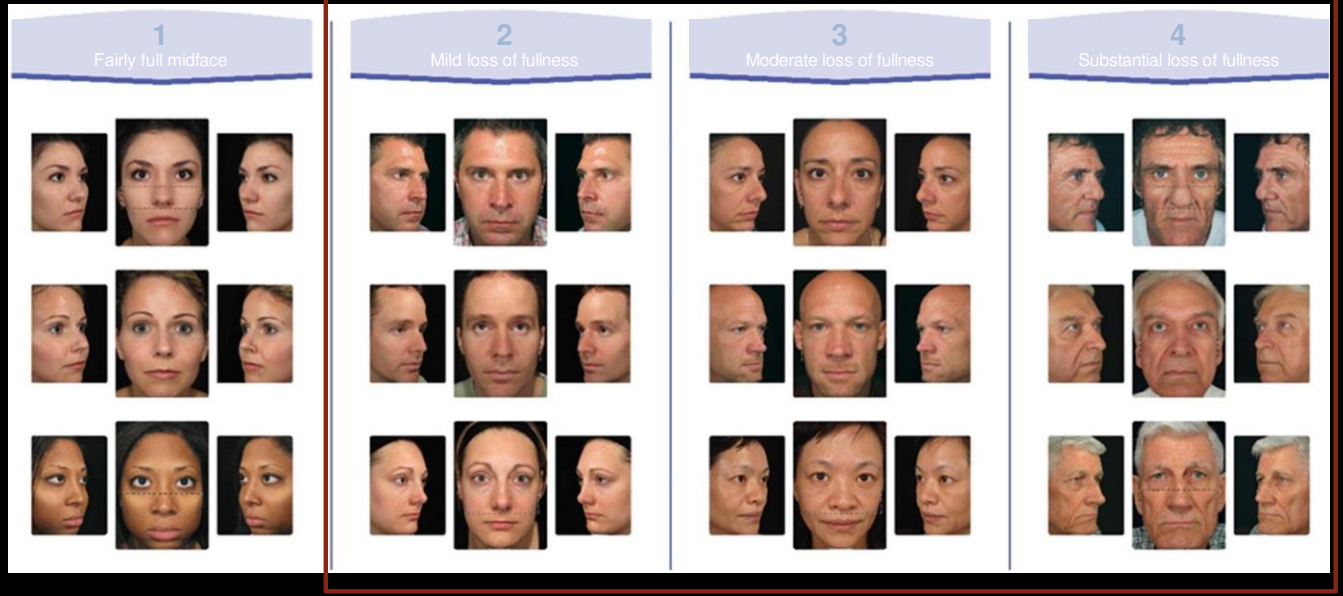
Contour Needle (N=59)
Contour Cannula (N=59)

Study Design



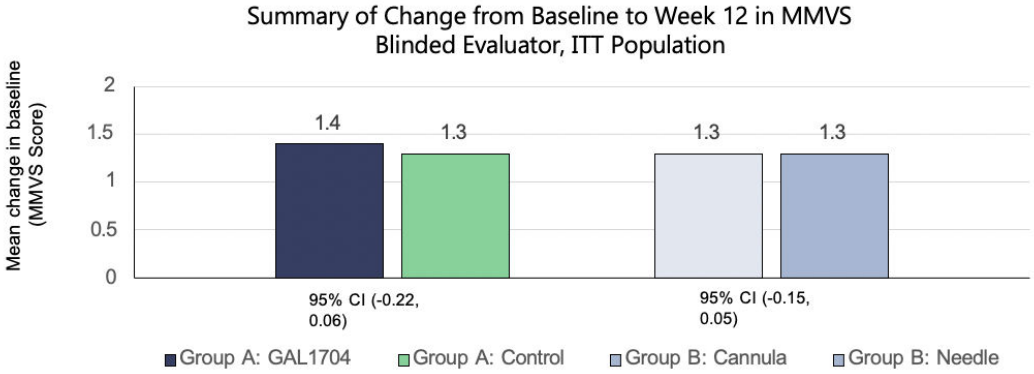
*Retreatment was with product and injection tool received during the initial injection. Subjects were followed-up for safety for an additional 12 weeks.

Primary endpoint – 4-point Medicis Midface Volume Scale (MMVS)



Scores of 2-4 were included in clinical study

Primary Effectiveness Analysis at Week 12: Change in MMVS Scores

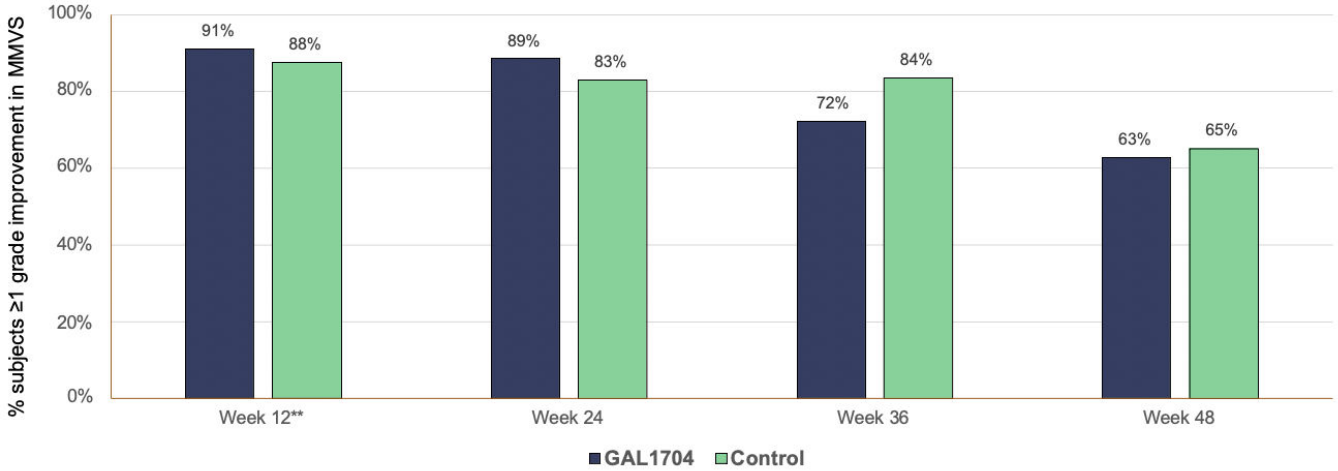


- Non-inferiority established in both treatment groups
- No significant difference between treatments
- ✓ Primary Effectiveness objective met

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, T) 2020

Secondary Efficacy Analysis- MMVS, Group A, Needle

Responder* Rates Measured by the Blinded Evaluator's Assessment of Cheek Fullness (MMVS) at Each Visit; ITT Population, Observed Cases



*Responder defined as a subject with at least 1 point improvement from baseline in MMVS
** Primary endpoint

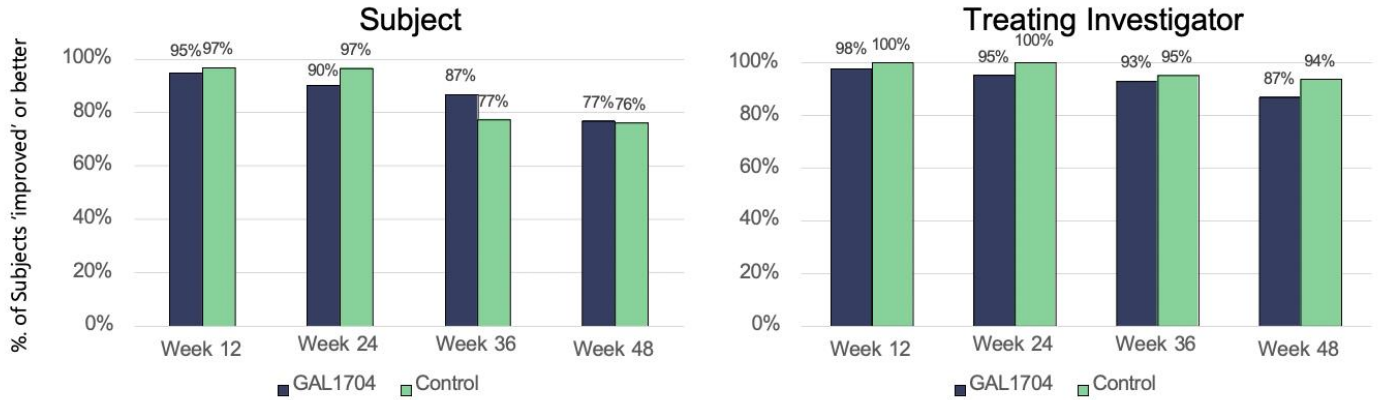
- Midface fullness improvement was comparable with both GAL1704 and Control (no significant differences)
- Responder rate for GAL1704 was 91% at Week 12 and remained ≥63% throughout the remainder of the study

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: 2020

Secondary Effectiveness Analysis – GAIS Aesthetic Improvement, Group A

Percent of GAIS Responders* Assessed by the **Subject** vs **Treating Investigator**

ITT Population



*Responder defined as a subject results that were rated as 'very much improved', 'much improved', or 'improved'

- Aesthetic improvement was comparable with both GAL1704 and Control (no significant differences)

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: , 2020

Safety Results – Related Adverse events, Group A

Preferred Term	Initial + Touch-up Subjects % / Events	
	GAL1704 (N= 141)	Control (N= 68)
Any Related AE (≥2%)	21 (14.9) / 57	13 (19.1) / 79
Implant site nodule	2 (1.4) / 4	2 (2.9) / 3
Implant site induration	0	2 (2.9) / 3
Swelling of eyelid	1 (0.7) / 1	0
Implant site pain	6 (4.3) / 16	9 (13.2) / 36
Implant site bruising	5 (3.5) / 5	1 (1.5) / 1
Implant site edema	3 (2.1) / 6	5 (7.4) / 15
Implant site erythema	2 (1.4) / 6	5 (7.4) / 11
Implant site swelling	3 (2.1) / 4	2 (2.9) / 2
Implant site hemorrhage	1 (0.7) / 2	3 (4.4) / 4

Median time to onset (0 days) and duration (3 days) were comparable in both groups

Moderate events
- GAL1704: Bruising, pain, facial pain
- Control: Pain, edema, erythema

Severe events
- **Control: Implant site swelling**

Late-onset:
- Only 1 event of implant site pain in Control group

Data on file 145USGH1702 Clinical Study Report. Fort Worth, TX: Galderma Laboratories, L.P.; 2021.

Overall Safety Results – Subject Diary Data

- The majority of subjects in Groups A and B reported pre-defined IREs in subject diaries
- There were no remarkable/unexpected IREs
- A smaller proportion of subjects receiving GAL1704 treatment reported pain, tenderness, redness, bruising, swelling, and itching, when compared to Control subjects (not statistically significant)
- Fewer subjects in cannula group experienced ISRs compared to needle

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: , 2020

34 year old female
1.8 mL Initial + 1.3 mL Touch-up

MMVS: 3
(both sides)

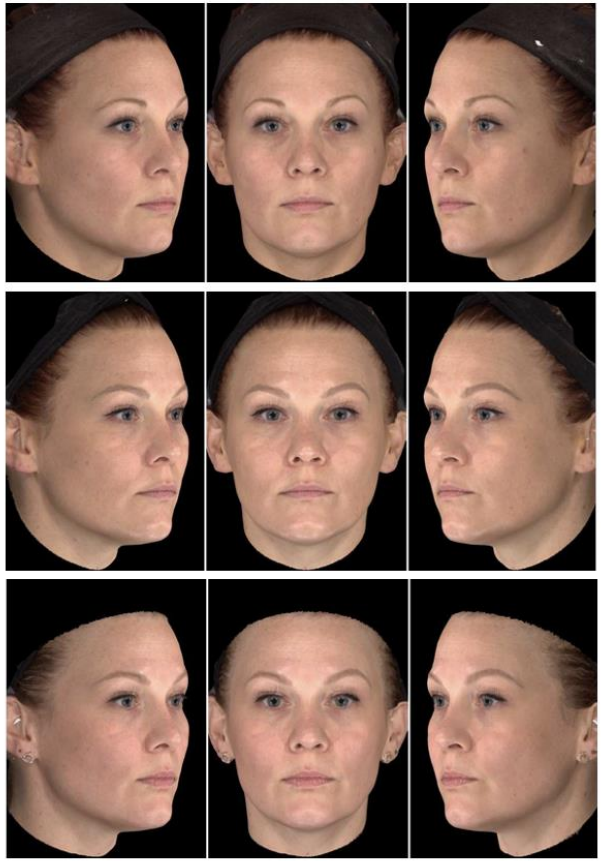
Baseline

MMVS: 1
(both sides)

Week 12

MMVS: 2
(both sides)

Week 48



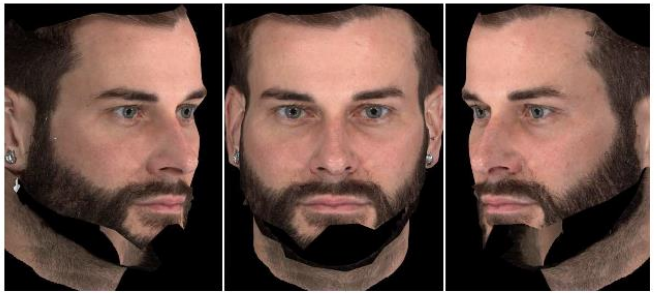
35 year old male
3.4 mL Initial + 1.4 mL Touch-up

MMVS: 3
(both sides)

Baseline

MMVS: 1
(both sides)

Week 12

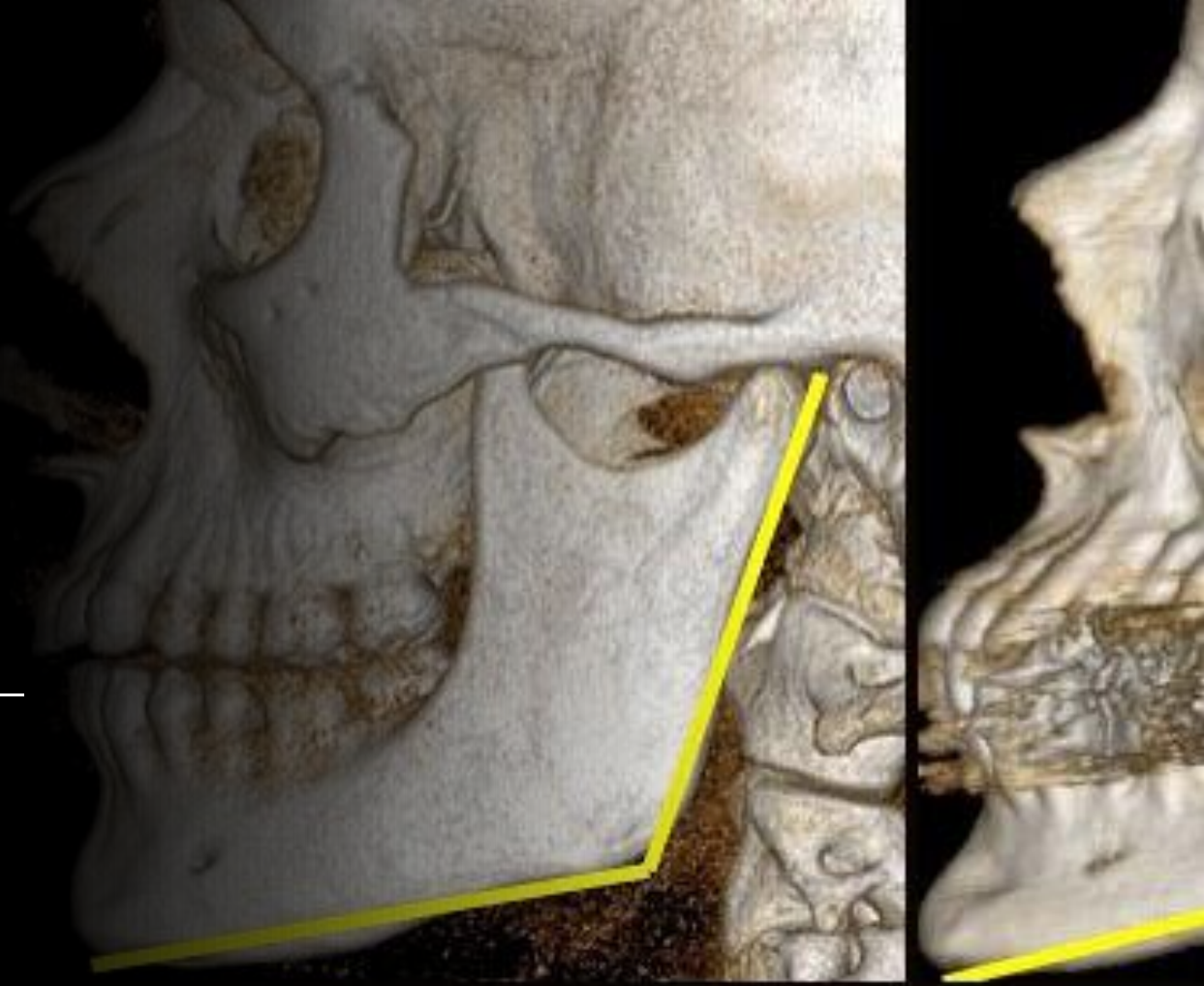


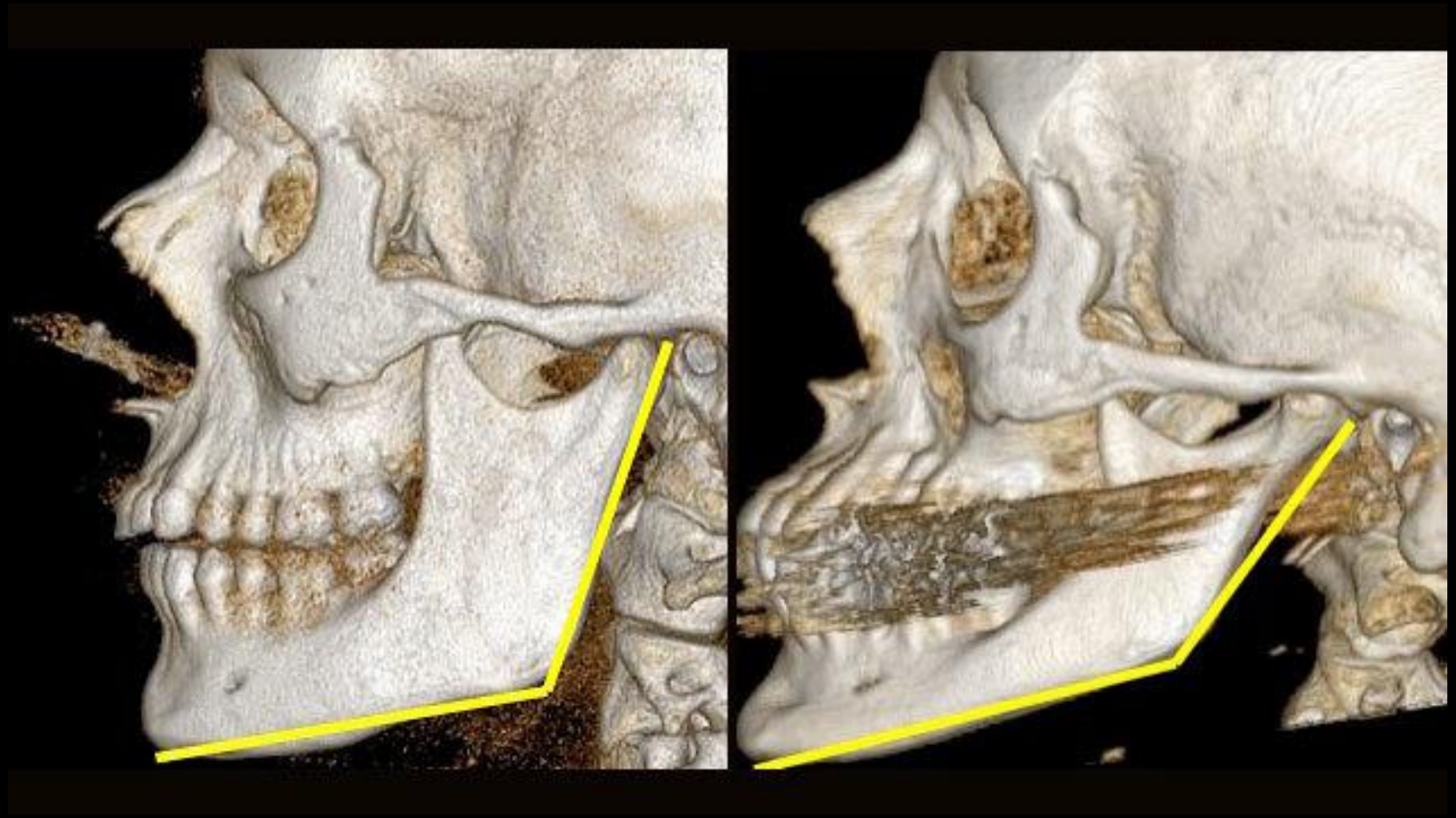
MMVS left: 2

MMVS right: 1

Week 48

Chin and Jawline





Chin and Jawline

- The chin and jawline are integral determinants of not only facial youth and beauty, but of gender identity
- Gender identity is an individual's personal sense of having a particular gender
- May be the same as their assigned sex at birth (cisgender) or not (transgender, among other terms)

Treating the Jawline with Injectables is on the Rise

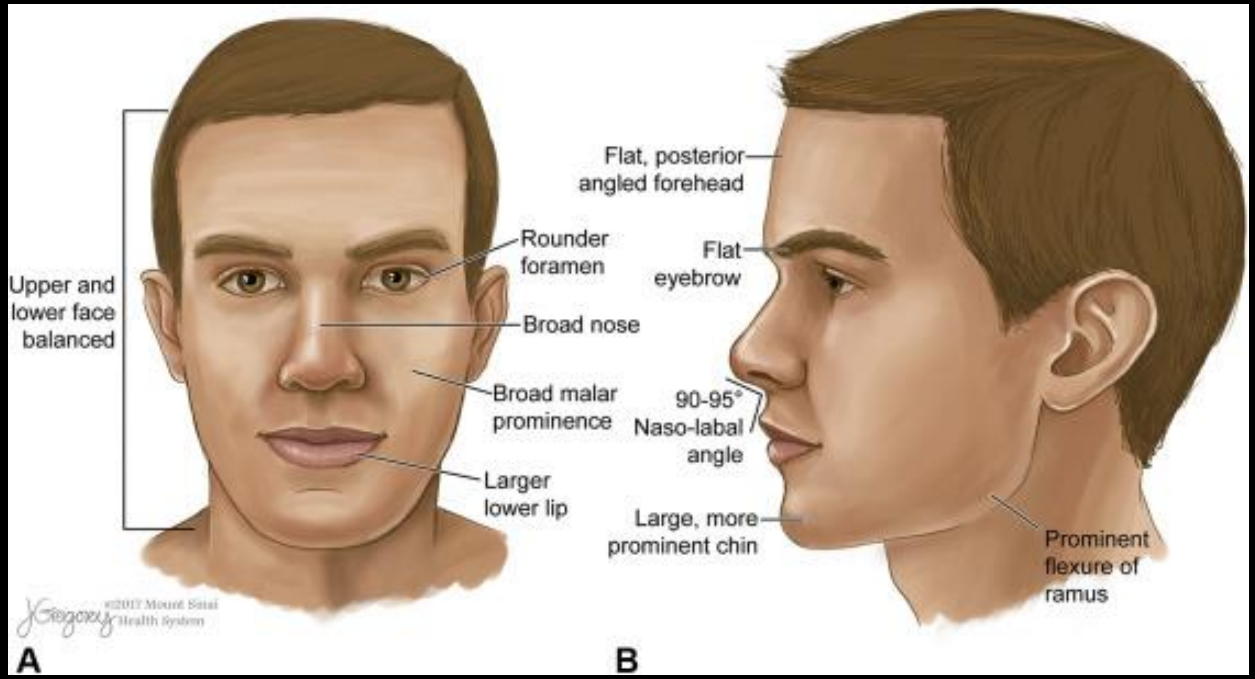
- Rejuvenation of the jawline is now increasingly becoming part of routine aesthetic practice. Both surgical and nonsurgical treatment options are available, with the chosen approach varying based on individual needs and requests.

https://www.gq.com/story/fillers-masculinity

https://www.menshealth.com/grooming/a25843484/jawline-cosmetic-procedures-men/

Chin and Jawline

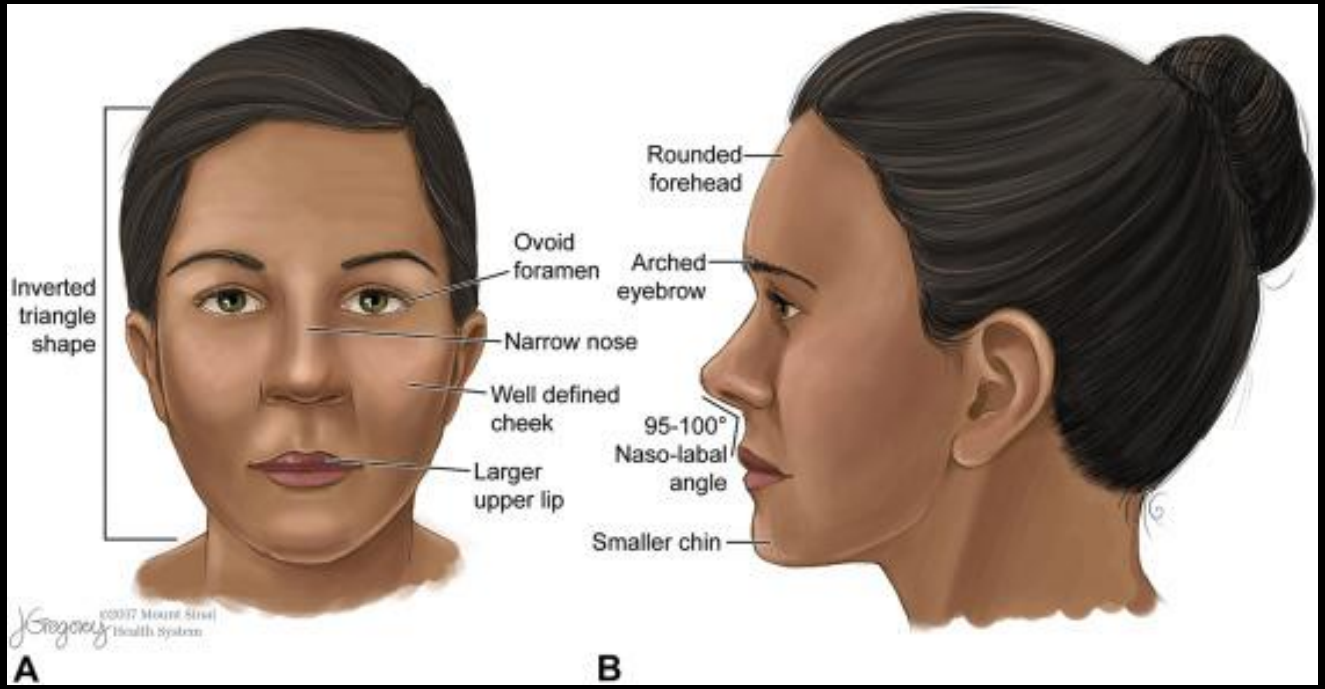
- Masculine features:



Dhingra N, Bonati LM, Wang EB, Chou M, Jagdeo J. Medical and aesthetic procedural dermatology recommendations for transgender patients undergoing transition. J Am Acad Dermatol. 2019 Jun;80(6):1712-21.

Chin and Jawline

- Feminine features:



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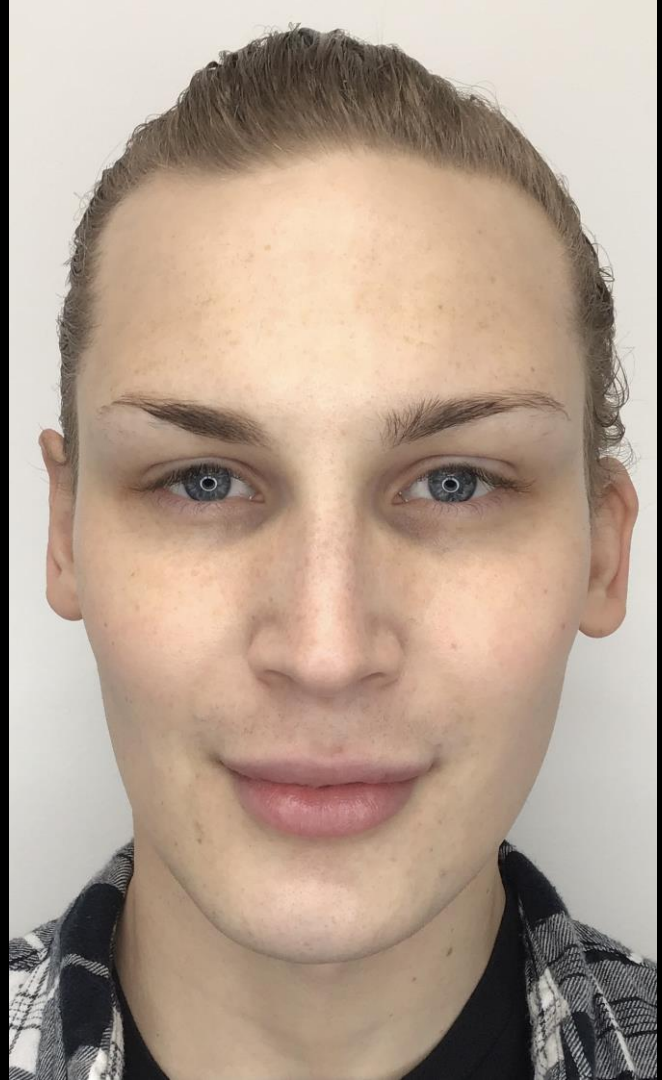
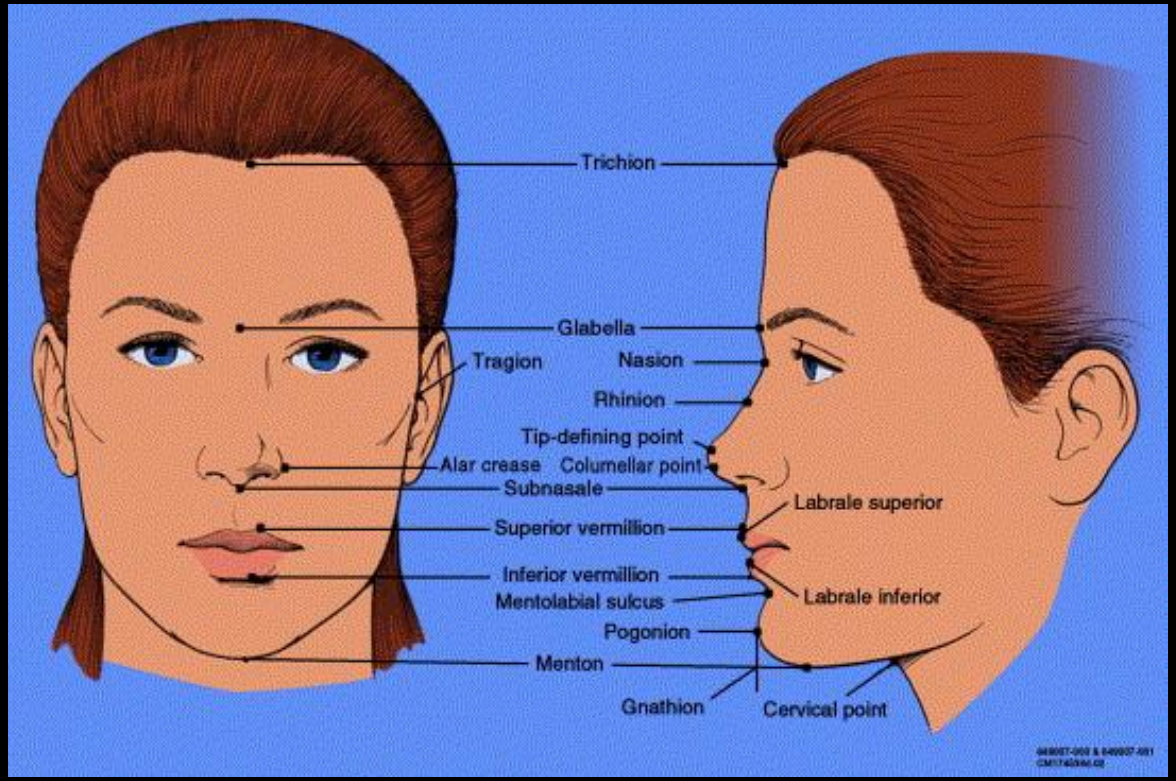


Chin: Anatomy



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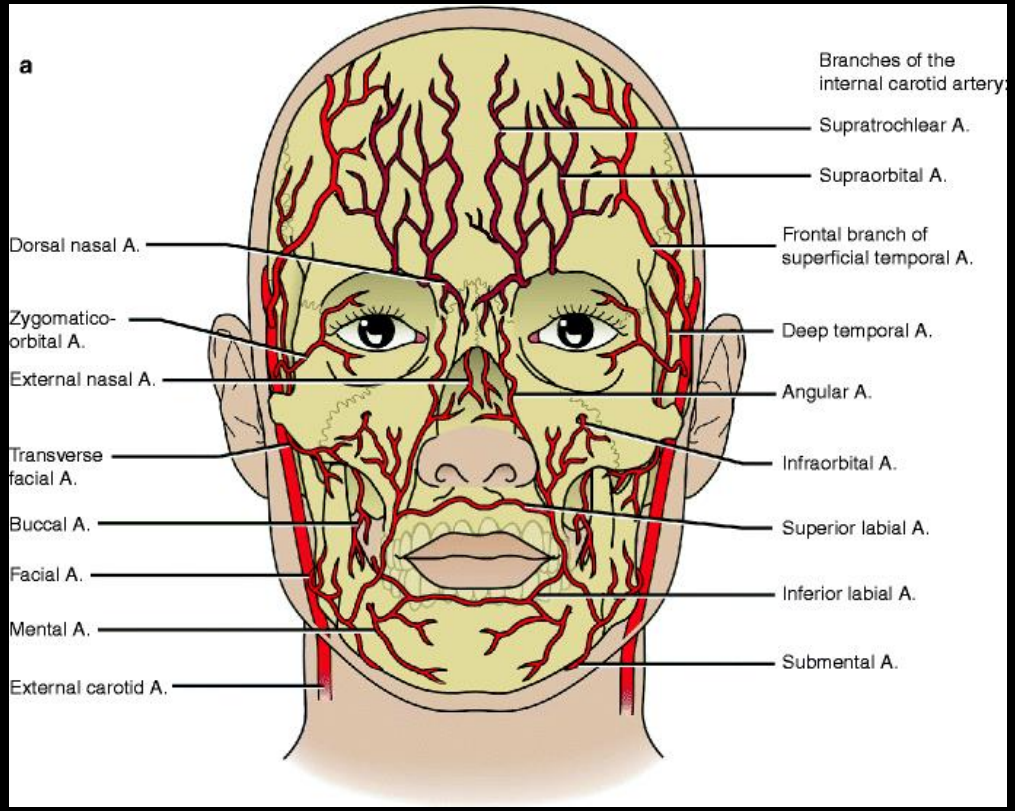
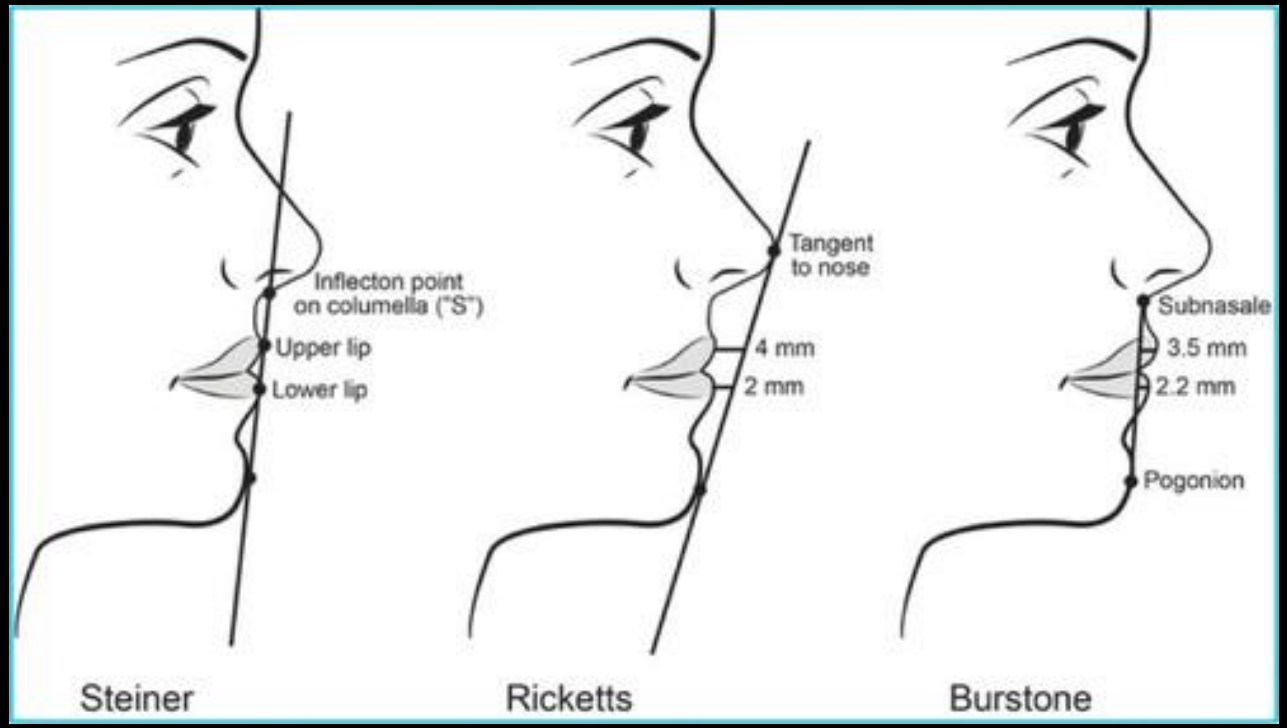
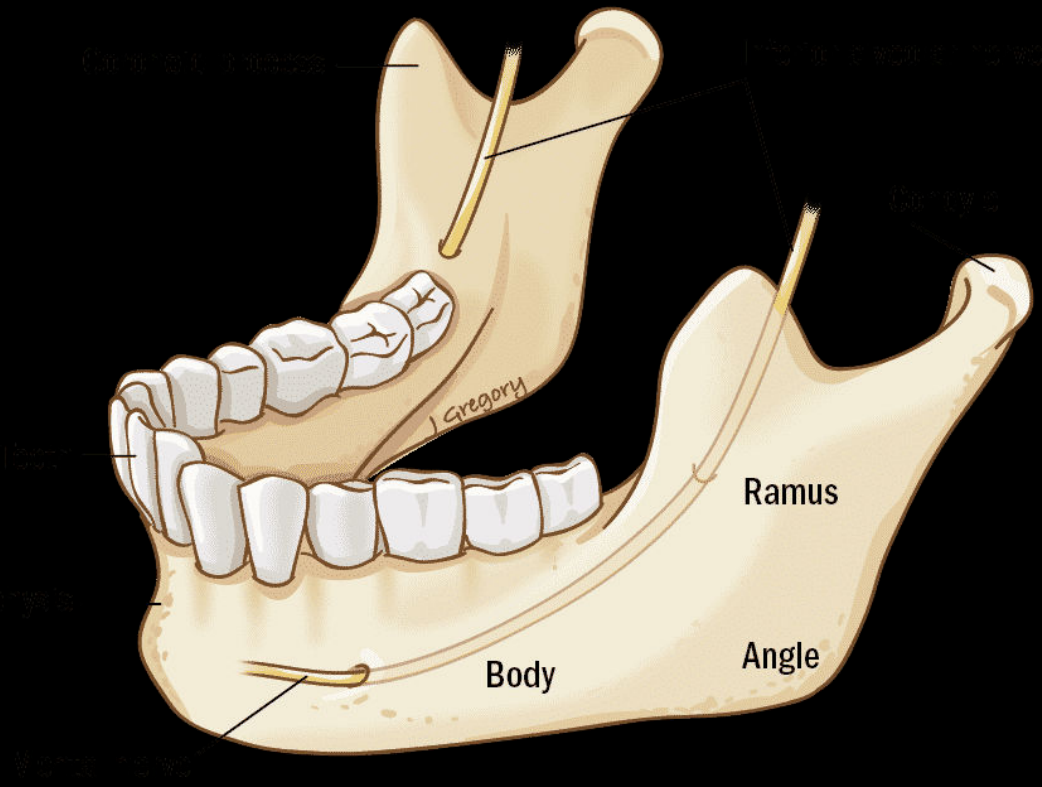


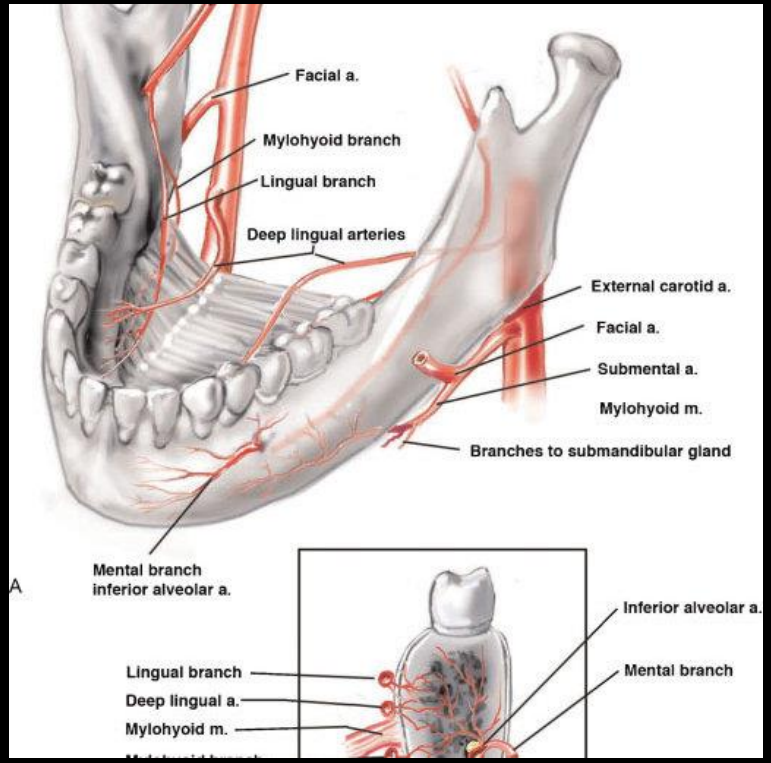
Chin: Proportions



Mandible: Anatomy



Mandible: Anatomy



Chin: Technique

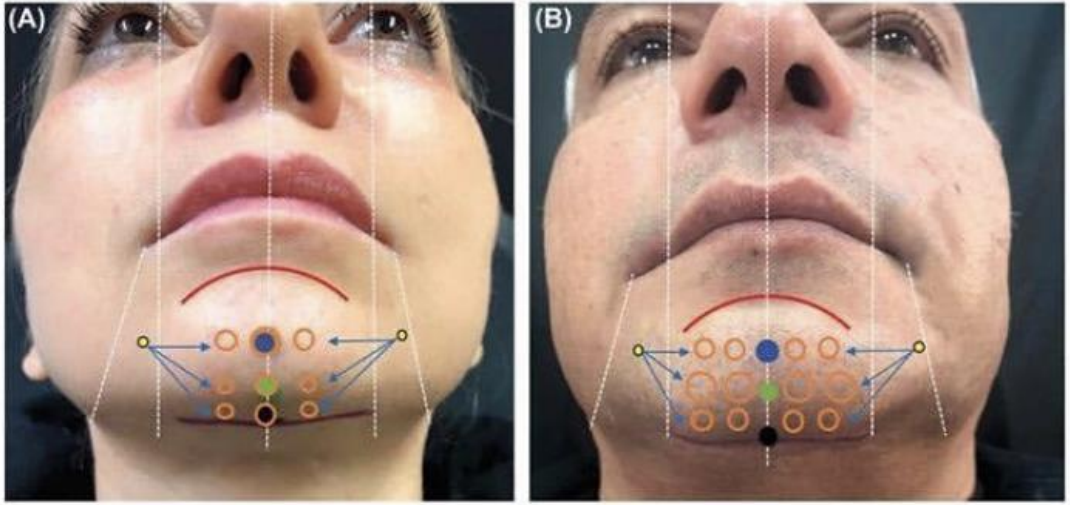
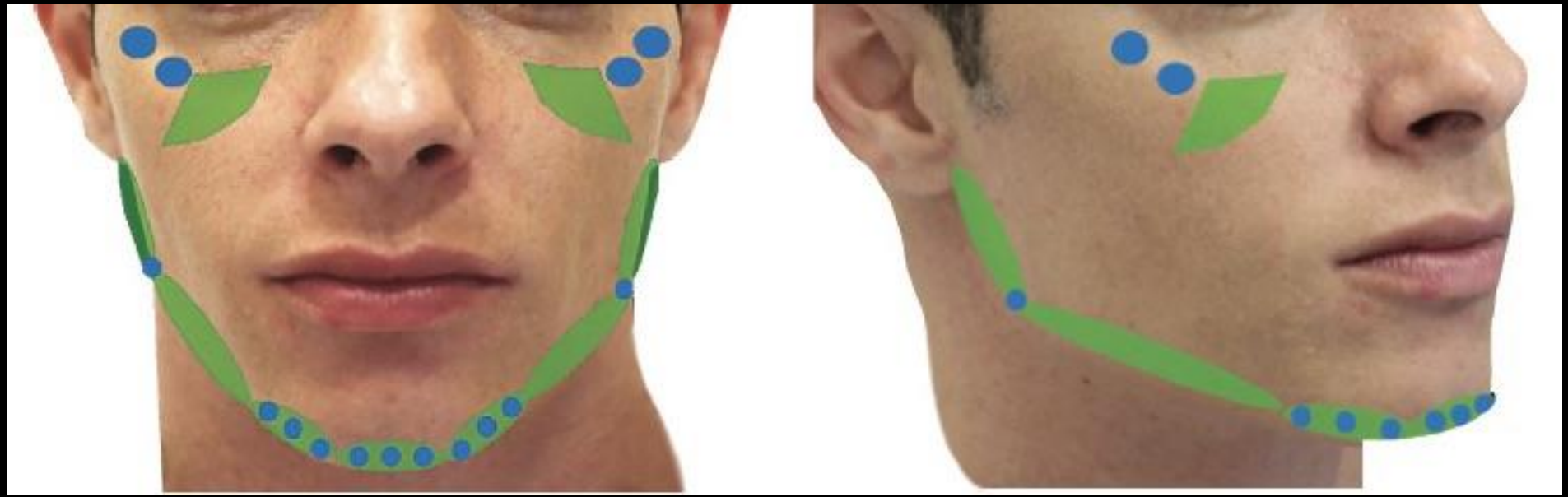


Figure 1. Schematic drawing for determination of injection points in female and male patients. Orange circles indicate the area where each bolus is deposited by the cannula. Larger circles correspond to a larger bolus. (A) In women, a larger bolus is placed in the midline, at the level of the pogonion. (B) In men, equal-sized boluses are placed paramedian, with larger amounts injected at the level of the gnathion. Yellow circle = entry point of the cannula; red line = labiomental sulcus; blue dot = pogonion; light green dot = gnathion; black dot = menton; purple line = submental sulcus.

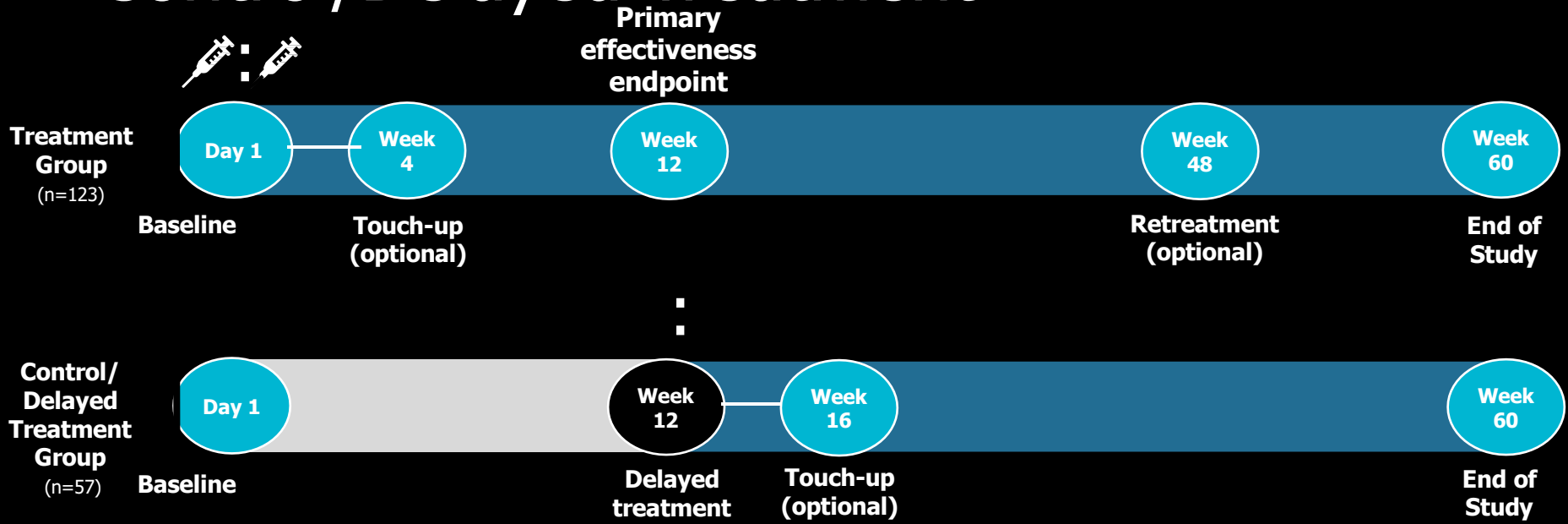
Sakuma TH, Hirano CF, Braz AV. How to Project or Lengthen the Chin With Soft Tissue Fillers Respecting Sexual Dimorphism. Dermatol Surg. 2021 Nov 1;47(11):1524-1525.

Jawline/Mandible: Technique



Efficacy and Safety of Calcium Hydroxylapatite with Lidocaine (Radiesse+) for Improving Jawline Contour

Study Design: Treatment vs Control/Delayed Treatment

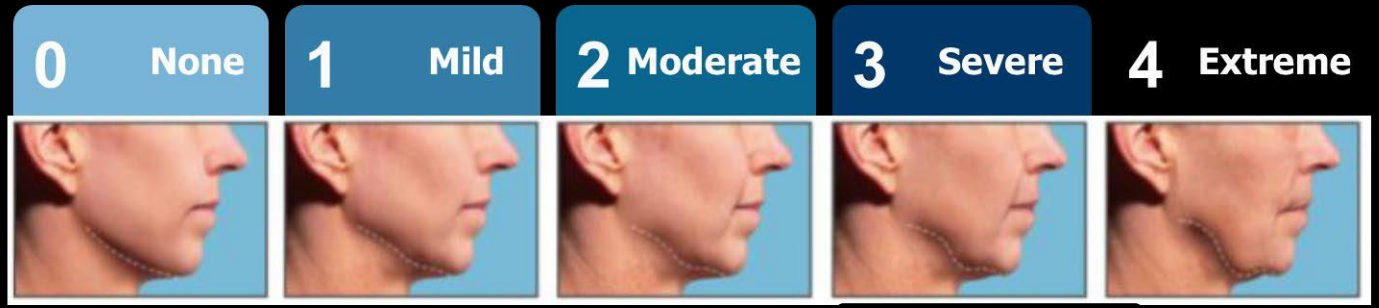


- Randomization 2:1 • Subjects were eligible for touch-ups in both groups • Optional retreatment in treatment group only

Moradi A et al. J Drugs Dermatol. 2021;20(11):1231-1238.

Key Inclusion Criteria

- Patients 22 to 65 years of age
- Right and left jawline ratings of 2 or 3 (moderate or severe) on the Merz Jawline Aesthetic Scale (MJAS) by both blinded evaluator and treating investigator
  - The same MJAS ratings were required for both jawlines
- Patients with select prior facial aesthetic or dental or oral procedures were excluded



Moradi A et al. J Drugs Dermatol. 2021;20(11):1231-1238.

Mean Volume Per Jawline was <2 mL[1-3]

Needle Treatment Group* (N=60)

Mean volume per jawline†
1.82-1.86 mL

Common injection technique was serial puncture (75-76.7%) and linear threading/tunneling (61.7%)

Most common injection depth was subdermal (75%) and supraperiosteal at angle/ramus of the mandible (60-63.3%), subdermal at mid-body (73.3-75%) and subdermal or supraperiosteal at anterior (71.7-75%)

Cannula Treatment Group* (N=62)

Mean volume per jawline†
1.96-1.98 mL

Most common injection technique was linear threading (83.9-85.5%)

Most common (75.8-85.5%) injection depth was subdermal at angle/ramus of the mandible, mid-body and anterior

- No patient was injected with more than 3 mL of CaHA (+) per jawline per treatment session
- For touch-up visits, the median volume injected was 1.10-1.25 mL per jawline

*Includes right and left jawline; †After initial injection

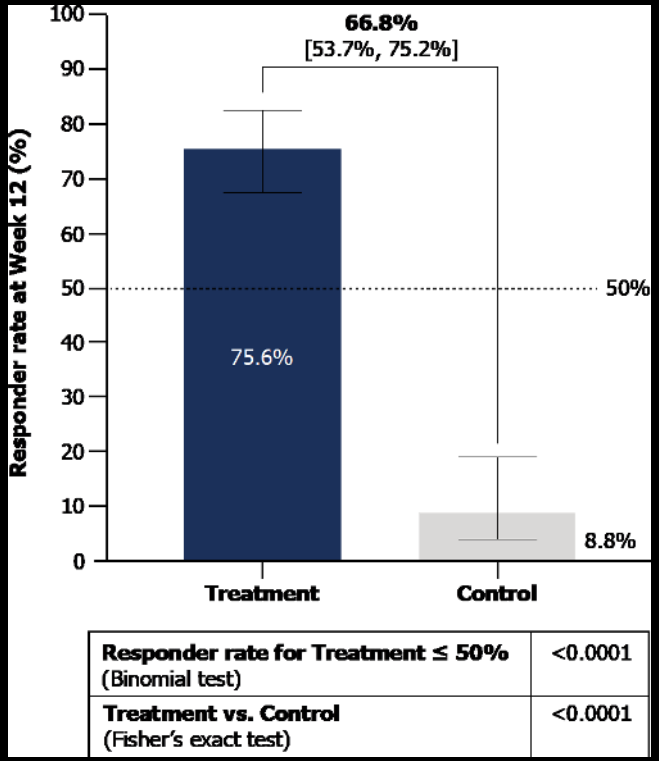
1. Radiesse (+) Instructions for Use, Franksville, Wt. 2021. **2.** Moradi A, Green JB, Cohen JL, et al. J Drugs Dermatol. 2021;20(11):1231-1238. **3.** Data on file. Merz North America, Inc; 2021.

75.6% of the calcium hydroxylapatite with lidocaine treated participants were responders

Responder defined as patient who obtained ≥1-point improvement on MJAS on both jawlines compared to baseline as assessed by blinded evaluator

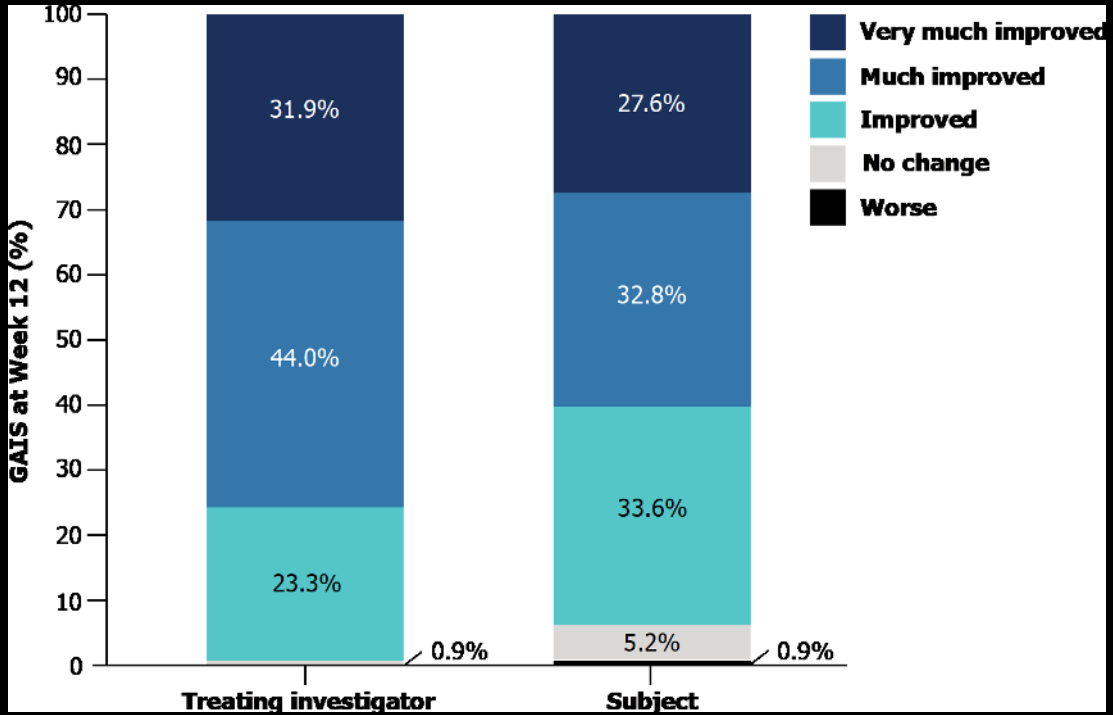
Calcium hydroxylapatite with lidocaine was considered clinically effective if ≥50% of patients in the treatment group were responders

75.6% of the calcium hydroxylapatite with lidocaine-treated subjects achieved at least a 1-point improvement on the MJAS on both jawlines at Week 12, compared to 8.8% in the No Treatment Control.



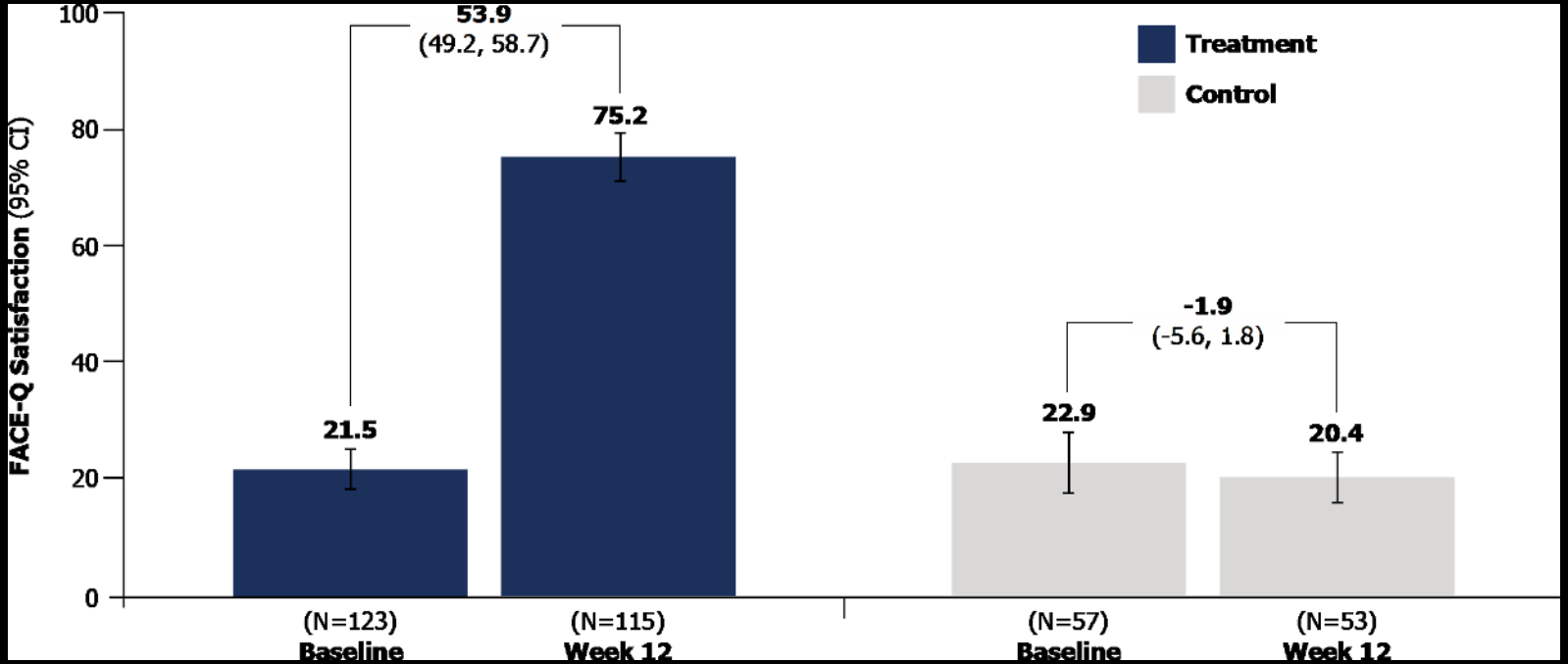
Moradi A et al. J Drugs Dermatol. 2021;20(11):1231-1238.

94% of Participants Rated themselves as Improved to Very Much Improved



Moradi A et al. J Drugs Dermatol. 2021;20(11):1231-1238.

Patients Rated themselves as Significantly More Satisfied after Calcium Hydroxylapatite with Lidocaine Treatment



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The majority of TEAEs were mild and transient

- The safety evaluation set included all treated subjects: 122 (99.2%) subjects in the treatment group and 53 (93.0%) subjects in the control/delayed treatment group
- **The most common TEAEs (>5%) were administration site conditions** (ie, injection site mass, injection site bruising, injection site pain)

Table 15- Subjects with TEAEs with Incidence of >5%

	Total (N=175)	
MedDRA Preferred Term	**n**	**(%)**
Subjects with at least one TEAE	74	(42.3)
Injection site mass	19	(10.9)
Injection site bruising	12	(6.9)
Injection site pain	12	(6.9)

- **The majority of TEAEs were mild, lasting <15 days, and resolved without sequelae[1]**
- No treatment-related serious AEs occurred, and no AEs leading to study discontinuation were reported.

TEAE = A treatment-emergent adverse event with onset date on or after date of initial treatment;
AE = Adverse event

Radiesse (+) IFU, 2021.

Baseline and Week 12 Jawline Contour Results

Right side- Lateral

Right side- 45°

2.25ml of CaHA (+)

Actual patient. Individual results may vary

Baseline and Week 12 Jawline Contour Results

Right side- Lateral

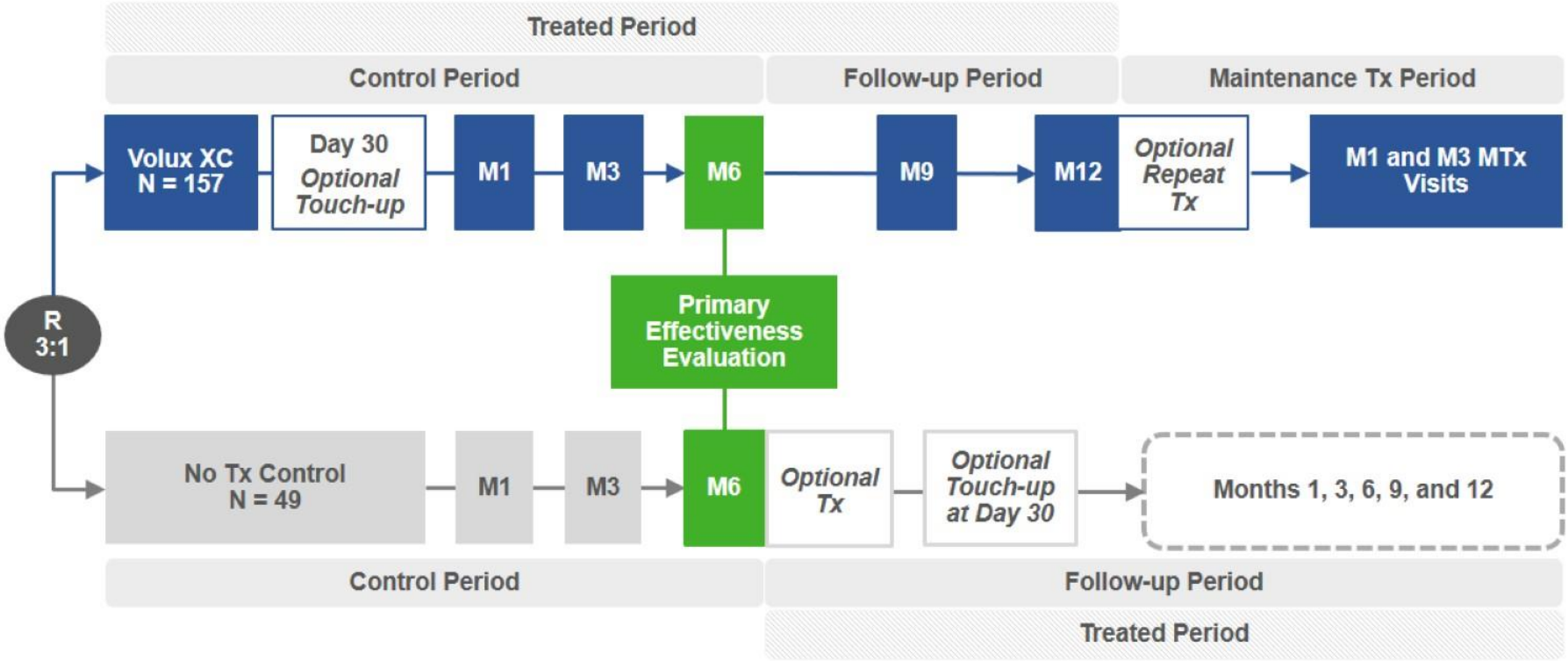
Right side- 45°

1.55ml of CaHA (+)

Actual patient. Individual results may vary

Juvéderm® Volux™ XC for Jawline Definition

Study Design



Study conducted at 19 sites in United States.
R = randomization; M = month; Tx = treatment; MTx = maintenance treatment
JUVÉDERM® VOLUX™ XC [directions for use]. Irvine, CA: 07/2022.

Allergan Loss of Jawline Definition Scale

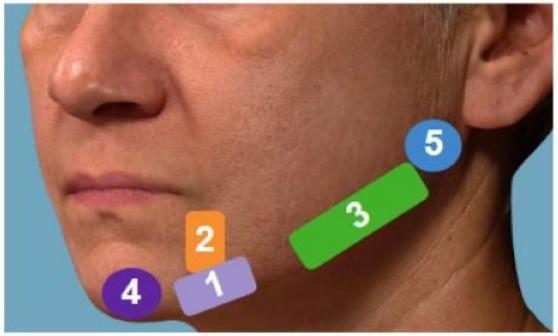
Grade	Term	Description
0	None	Jawline: Straight, well-defined Pre-Jowl Area: No hollowing or pre-jowl sulcus Post-Jowl Area: Do Not Assess
1	Minimal	Jawline: Some loss of jawline definition Pre-Jowl Area: Hollowing only, no jowl formation or pre-jowl sulcus Post-Jowl Area: Do Not Assess
2	Moderate	Jawline: Some blurring of jawline Pre-Jowl Area: Moderate jowl formation and pre-jowl sulcus Post-Jowl Area: No hollowing or post-jowl sulcus
3	Severe	Jawline: Significant blurring of jawline Pre-Jowl Area: Pre-jowl sulcus Post-Jowl Area: Post-jowl hollowing or post-jowl sulcus
4	Extreme	Jawline: Jowl tissue sagging significantly below jawline Pre-Jowl Area: Pre-jowl sulcus Post-Jowl Area: Post-jowl hollowing or post-jowl sulcus

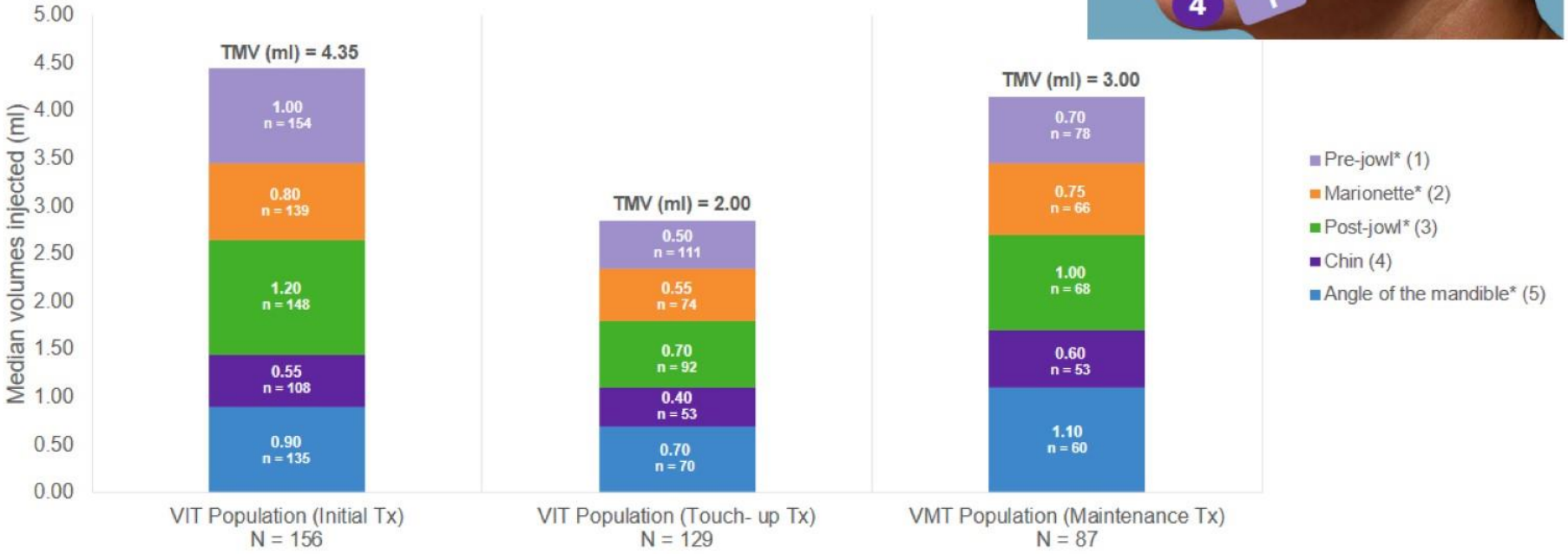
Subjects were required to have bilateral baseline ALJDS scores of 2 (moderate) or 3 (severe) for inclusion in study, but score did not to be the same on both sides.

Data on file,

Treatment Administration[1,2]

Volumes injected





Note: Similar volumes injected in VPC population in initial and touch-up treatment as VIT population.
* Total for right and left sides.
VIT = Volux XC initial treated; VPC = Volux XC post-control treatment; VMT = Volux XC maintenance treatment; Tx = treatment; TMV = total median volume.
1. JUVÉDERM® VOLUX™ XC [directions for use]. Irvine, C s. 07/2022. 2. Data on file,

Primary Effectiveness: ALJDS Responder Rates* at Month 6[1,2]

Subjects with ≥ 1-point improvement on both sides of jaw during control period (mITT population, multiple imputation method for missing data)

	Control (N = 49)	Volux XC (N = 157)
Responder rate, (n/N†), %	18.6/49 (38.0)	108.3/157 (69.0)
95% CI, %	24.25, 51.80	61.53, 76.39
vs. Control		
Rate difference, %		30.9
95% CI, %		15.33, 46.54
P-value		0.0001

ALJDS responder rates through M3 after MTx

Representative subjects

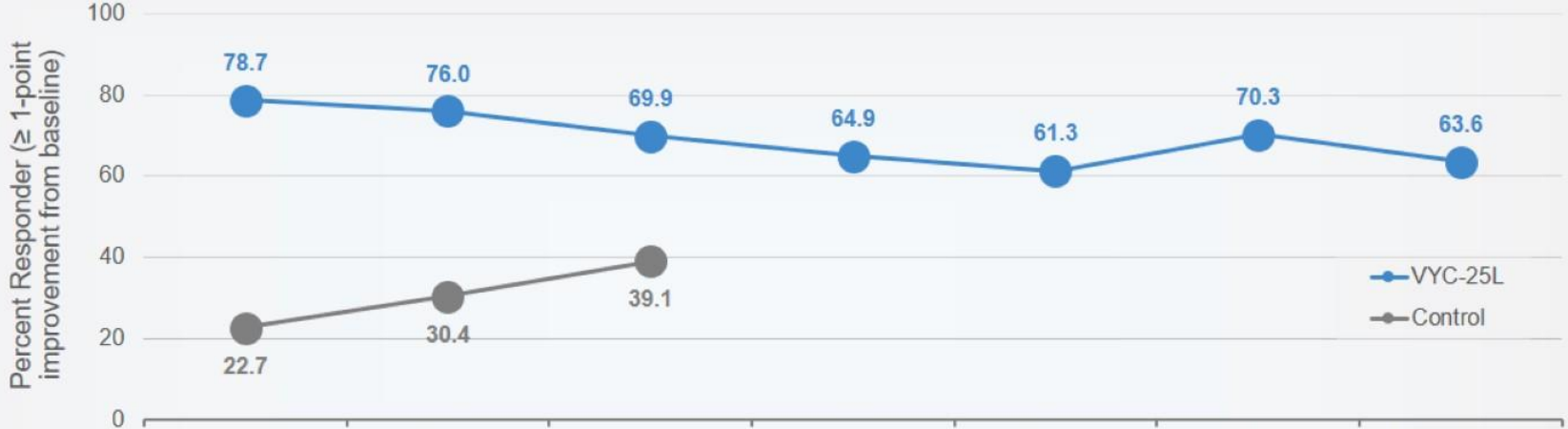
The primary effectiveness endpoint was met:

- **At Month 6 the ALJDS responder rate for the treatment group was statistically superior to the responder rate for the untreated control group in the mITT population (69.0% vs 38.0%, respectively; P = 0.0001)**

* Responder defined as participants with ≥ 1-point improvement from baseline on the ALJDS on both sides of jaw based on EI assessment.
† Responder rate based on multiple imputation model for missing data; observed responder rates in control population and VIT Population were 18/46 (39.1%) and 102/146 (69.9%), respectively.
ALJDS = Allergan Loss of Jawline Definition Scale; CI = confidence interval; VIT = Volux XC initial treated; mITT = modified intent-to-treat, all randomized participants with non-missing baseline assessment the ALJDS scale on both sides of the jaw; M3 = Month 3; MTx = maintenance treatment
1. JUVÉDERM® VOLUX™ XC [directions for use]. Irvine, C[illegible]s. 07/2022. 2. Data on file, [illegible]

ALJDS Responder Rates* at Other Assessment Timepoints

Other analysis, VIT population (observed data in VIT mITT population)[1,2]

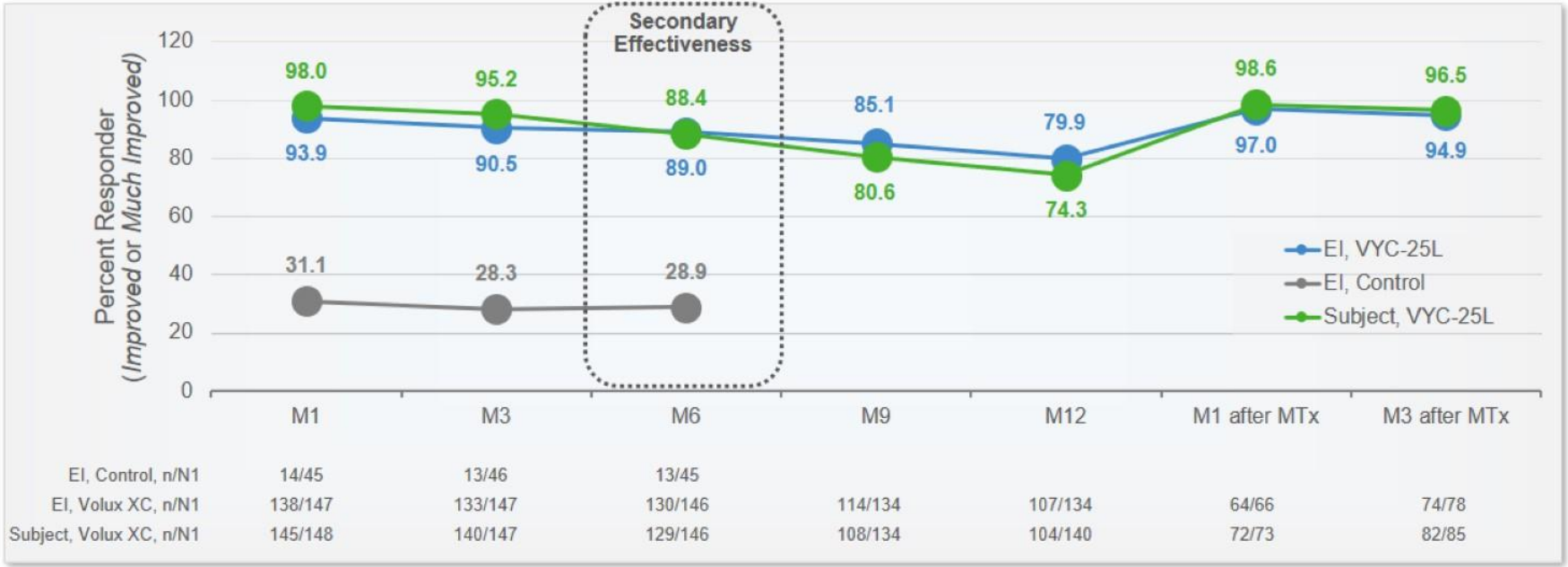


	M1	M3	M6	M9	M12	M1 after MTx	M3 after Mtx
Control, n/N1	10/44	14/46	18/46				
Volux XC, n/N1	118/150	111/146	102/146	87/134	84/137	45/64	49/77

* Responder defined as participants with at least 1-point improvement from baseline on the ALJDS on both sides of jaw based on evaluating investigator assessment.
ALJDS = Allergan Loss of Jawline Definition Scale; N1 = Number of participants with data at baseline and the timepoint; M = month; MTx = maintenance treatment;
VIT = Volux XC initial treated; mITT = modified intent-to-treat, all randomized participants with non-missing baseline assessment the ALJDS scale on both sides of the jaw.
1. JUVÉDERM® VOLUX™ XC [directions for use]. Irvine, CA: 07/2022. 2. Data on file,

GAIS Responder* Rates

Secondary analysis (Month 6) and other analyses (other assessment timepoints), VIT mITT population



	M1	M3	M6	M9	M12	M1 after MTx	M3 after MTx
EI, Control, n/N1	14/45	13/46	13/45				
EI, Volux XC, n/N1	138/147	133/147	130/146	114/134	107/134	64/66	74/78
Subject, Volux XC, n/N1	145/148	140/147	129/146	108/134	104/140	72/73	82/85

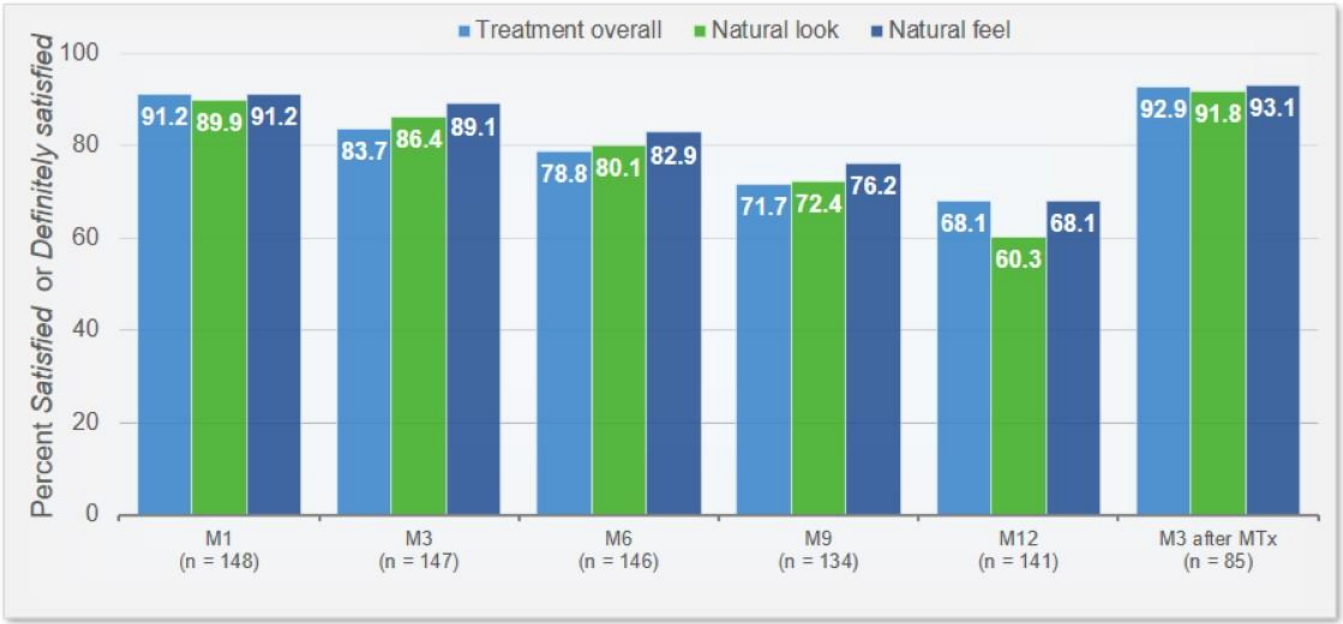
* Responder defined as participant reporting *Improved* or *Much improved* compared with baseline.
GAIS = Global Aesthetic Improvement Scale; EI = evaluating investigator; N1 = Number of participants with data at baseline and the timepoint; M = month; MTx = maintenance treatment; VIT = Volux XC initial treated; mITT = modified intent-to-treat, all randomized participants with non-missing baseline assessment the ALJDS scale on both sides of the jaw.

1. JUVÉDERM® VOLUX™ XC [directions for use]. Irvine, CA: 07/2022. 2. Data on file,

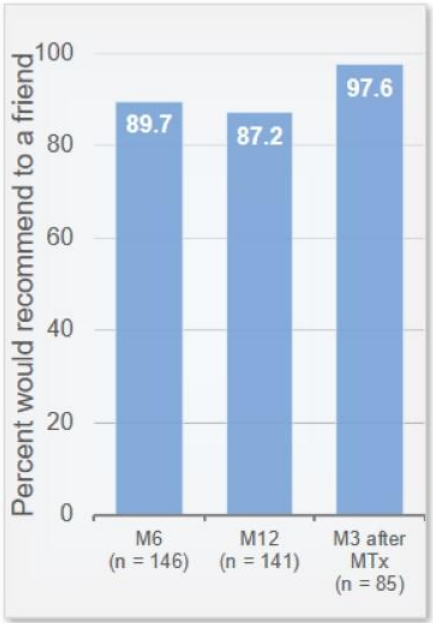
Subject Satisfaction with Treatment

Other analysis, VIT mITT population

'Satisfied' or '*Definitely Satisfied*' with treatment



'Would recommend to a friend'

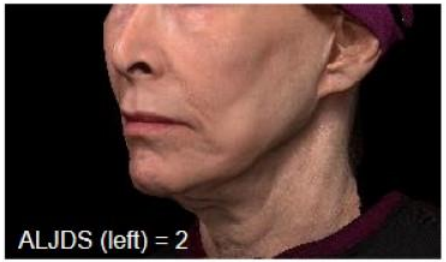


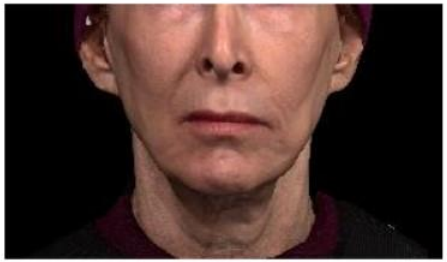
M = month; VIT = Volux XC initial treated; mITT = modified intent-to-treat, all randomized participants with non-missing baseline assessment the ALJDS scale on both sides of the jaw; MTx = maintenance treatment.

1. JUVÉDERM® VOLUX™ XC [directions for use]. Irvine, CA: 07/2022. 2. Data on file,

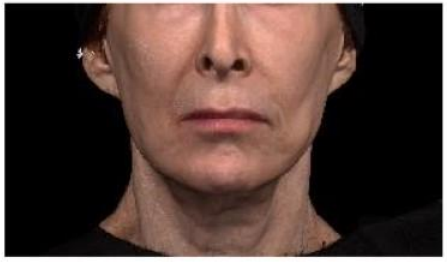
Representative Subject

Baseline





Month 6

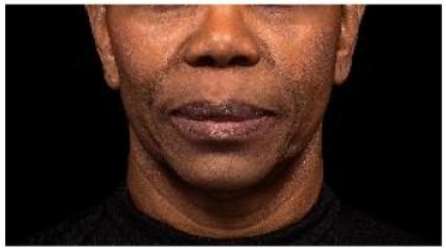


- Female, 71 years of age
- Initial treatment = 4.9 mL (needle)
- Touch-up treatment = 2.9 ml (needle)

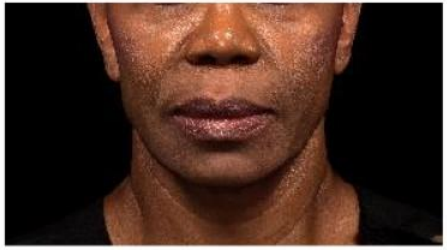
ALJDS = Allergan Loss of Jawline Definition Scale.
Data on file,

Representative Subject

Baseline



Month 6



- Female, 67 years of age
- Initial treatment = 3.7 mL (needle)
- Touch-up treatment = 1.0 ml (needle)

ALJDS = Allergan Loss of Jawline Definition Scale.
Data on file,

Restylane® Defyne (HA_{RD}) for chin augmentation and correction of chin retrusion

Pivotal Study (43USCH1702)

For medical purposes only, not for sales or marketing purposes| DCKacXHA015-21v0

Study Design

Purpose
To evaluate efficacy and safety of HA_{RD} in the chin for augmentation and correction of chin retrusion

Randomized, evaluator-blinded, parallel group, no treatment-controlled, multi-center study

11

US CENTERS
(140 subjects)

DURATION: 48 WEEKS

TREATMENTS
(Randomized 3:1)

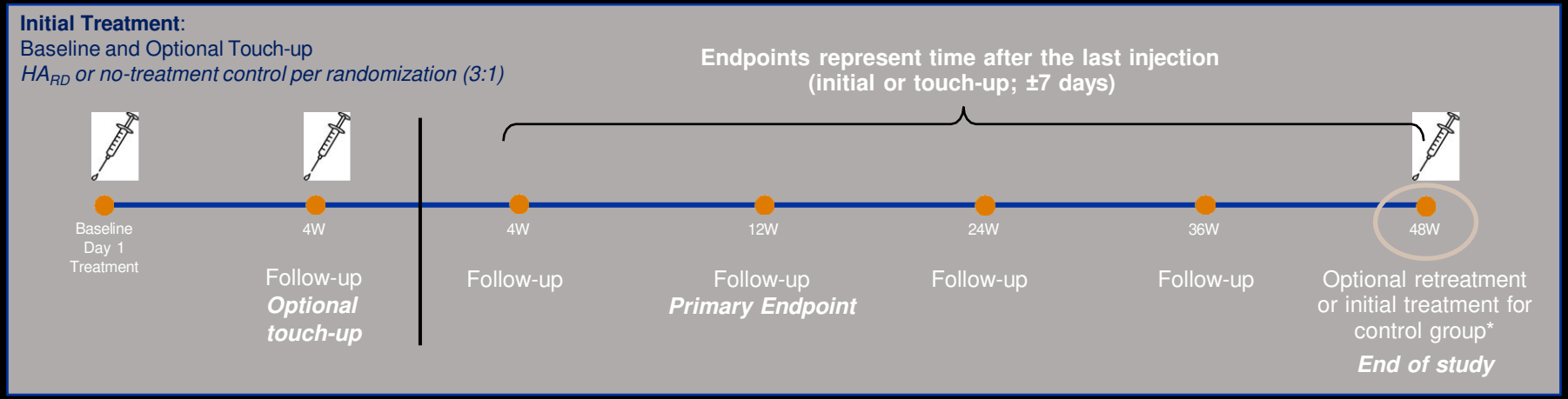
Treatment

Restylane Defyne (N=107)

No treatment control

No treatment (N=33)
Initial treatment at end of study (Week 48)

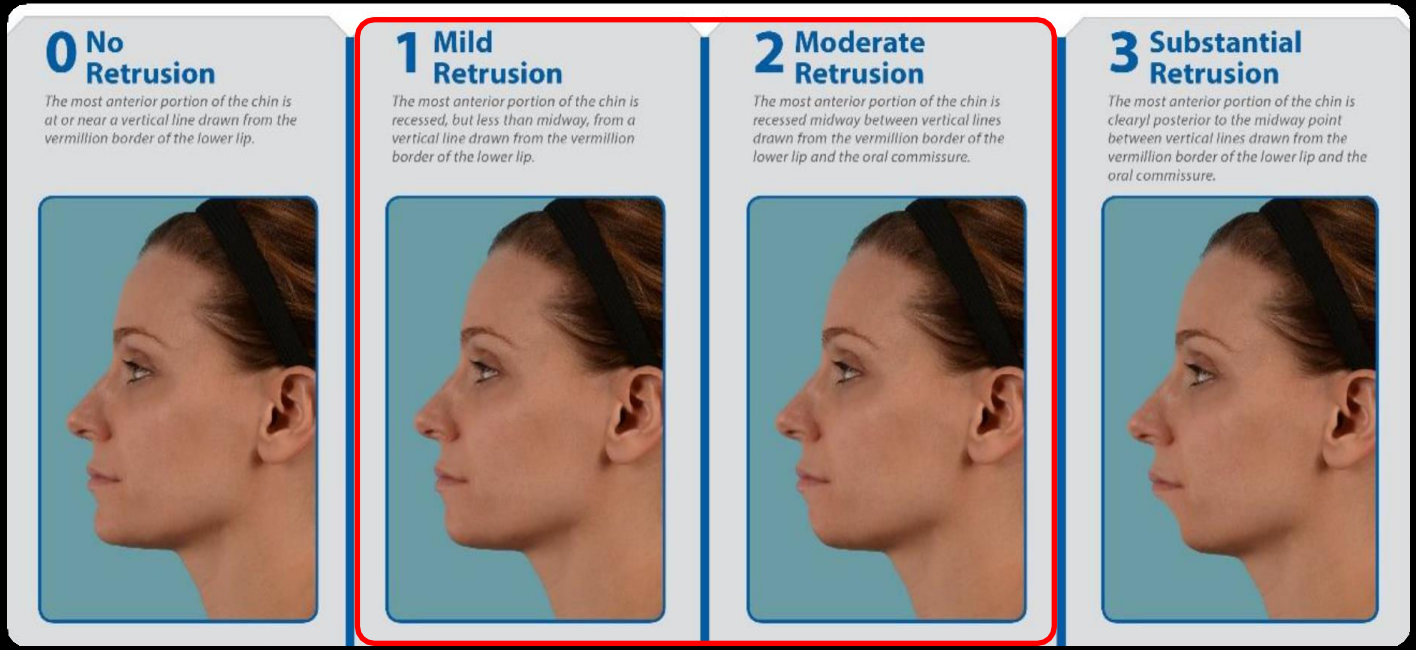
Study Design



*If re-treated or after initial treatment (no treatment group), subjects were followed-up for safety for an additional 12 weeks

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: 2020

Key Eligibility Criteria – Galderma Chin Retrusion Scale (GCRS)



GCRS score of 1 (Mild) or 2 (Moderate) at Screening as assessed by the Blinded Evaluator

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: 2020

Results

Primary Endpoint: GCRS Effectiveness at Week 12

Proportion of Subjects with ≥1 point improvement in GCRS from Baseline Assessed by Blinded Evaluator at Week 12, ITT population, Observed cases

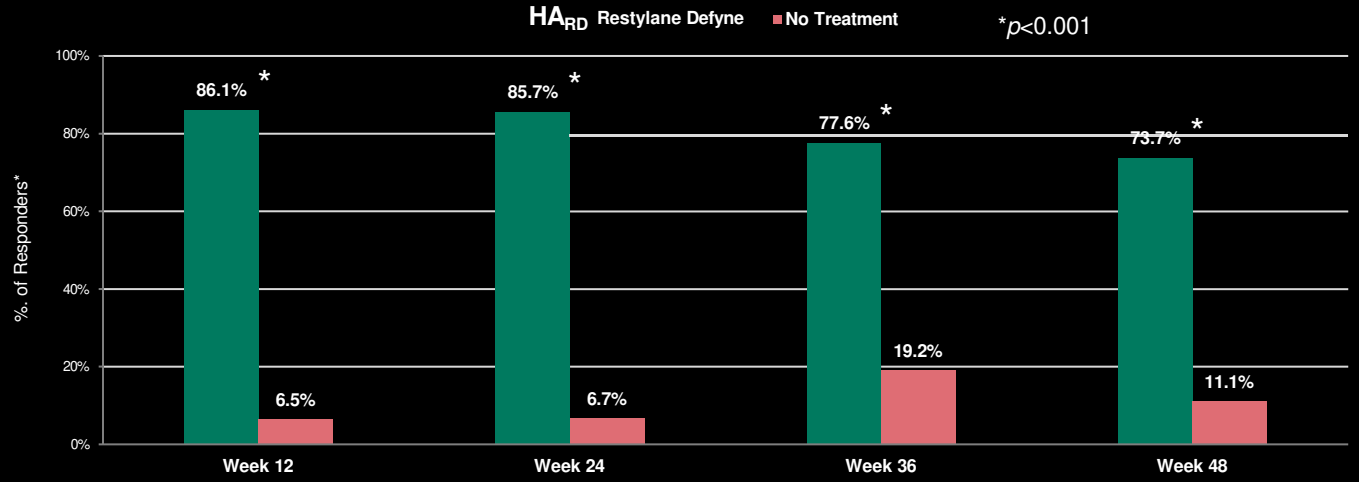
Category	HA_{RD} N=107	No Treatment N=33	Difference	P-Value
At Least 1 Point Improvement	87/101 (86.1%)	2/31 (6.5%)	(79.7%)	<0.001
95% CI	(77.84, 92.21)	(0.79, 21.42)	(66.62, 92.76)	

Difference in responder rates is statistically significant (86.1% of HA_{RD} subjects showing at least 1 point improvement compared to 6.5% of subjects in the no treatment group; $p<0.001$).

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: 2020

Secondary Endpoint: GCRS Effectiveness Over Time

Responder* Rates Measured by the Blinded Evaluator's Assessment of Chin Retrusion (GCRS) at Each Visit; ITT Population, Observed Cases



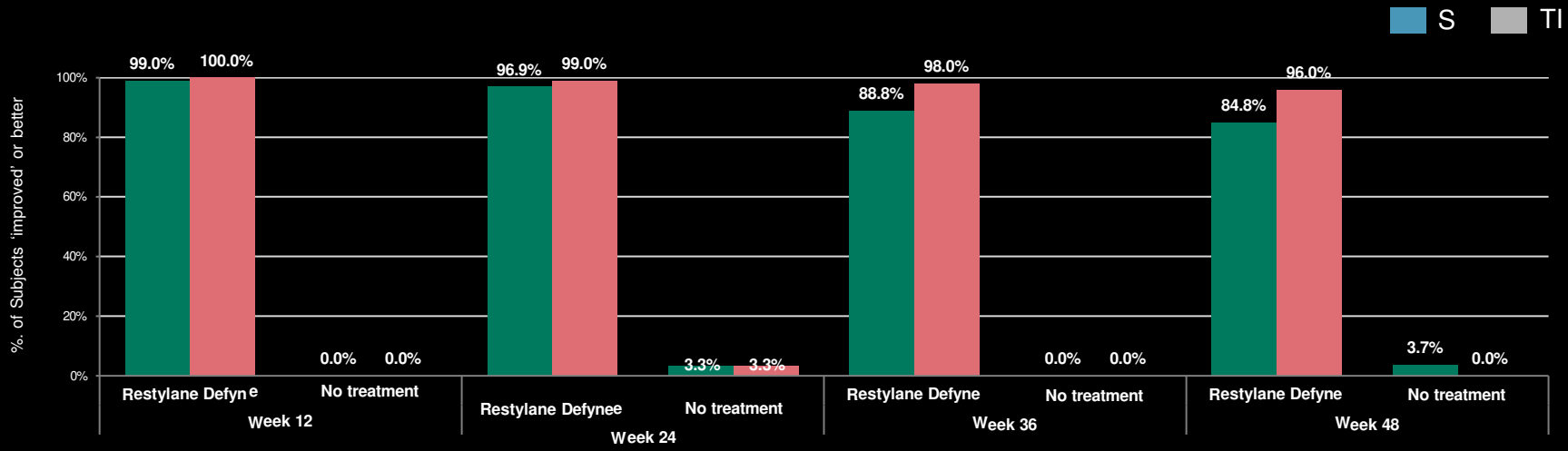
*Responder defined as a subject with at least 1 point improvement from baseline in GCRS

Difference in responder rates at Weeks 12, 24, 36 and 48, are statistically significant ($p<0.001$ at all time points) compared to no treatment control.

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: 2020

Secondary Endpoint: Aesthetic Improvement (GAIS)

Percent of Subjects in GAIS Response Category of “Improved” or Better at Each Visit as Determined by the **Subject (S)** vs **Treating Investigator (TI)**, ITT Population



The proportion of subjects and treating investigator who reported aesthetic improvements in the chin area across all time-points was substantially higher in the Restylane Defyne group compared with the no treatment group

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: 2020

Safety

Safety: Adverse Events (AE's)

- After initial treatment, 14% of subjects experienced a related AE
  - 94% of the subjects with related AEs reported them as Mild.

Characteristic	Statistic	Initial Treatment HA_{RD} (N= 129)	Re-treatment with HA_{RD} (N=58)
Brief summary of AEs: Safety Population	Severity	Subjects (%) / Events	Subjects (%) / Events
AEs related to product and / or injection procedure	Total	18 (14.0%) / 24	1 (1.7%) / 1
	• Mild	17 (94.4%) / 23	1 (1.7%)/1
	• Moderate*	1 (5.9%) / 1*	0
	• Severe	0	0

*Injection site pain

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: [redacted] 2020

Safety: AE's Related to Investigational Product

- All resolved by the end of study
- Duration
  - Mean: 13.1 days Median: 4.0 days
  - Range (2,112)
- Days to onset
  - Mean: 11.5 days
  - Median 0.0 days
  - Range (0,185)

Preferred Term	Initial Treatment with HA_R D (N= 129) Subjects (%) / Events	Re-treatment with HA_{RD} (N=58) Subjects (%) / Events
Any Related AE	18 (14.0%) / 24	1 (1.7%) / 1
Implant site pain	6 (4.7%) / 8	1 (1.7%) / 1
Implant site bruising	3 (2.3%) / 3	0
Implant site swelling	3 (2.3%) / 3	0
Implant site erythema	2 (1.6%) / 2	0
Implant site hemorrhage	2 (1.6%) / 2	0
Implant site nodule	2 (1.6%) / 2	0
Implant site mass	1 (0.8%) / 1	0
Implant site edema	1 (0.8%) / 1	0
Implant site eczema	1 (0.8%) / 1	0
Oral herpes	1 (0.8%) / 1	0

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: 2020

Safety: Adverse Events with Delayed or Late Onset

Subject	Adverse Event with Late Onset	Time to Onset	Intensity	Management	Outcome	Duration
8651-001	Implant site swelling	185 days	Mild	Medication Treatment (Ibuprofen, Acetaminophen, Diphenhydramine)	Recovered	4 days
8649-004	Implant site nodule (6 mm)	53 days	Mild	Medication Treatment (Hylenex)	Recovered	74 days

Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: [redacted] 2020

Safety: Detailed Description of Mass/Nodule AE's

Subject	Adverse Event with Late Onset	Time to Onset	Intensity	Management	Outcome	Duration	Note
8649-004	Implant site nodule (6 mm)	53 days	Mild	Medication Treatment (Hylenex)	Recovered	74 days	(R) lateral chin Secondary to irregular absorption of product; following treatment 2-3 mm in size
8604-003	Implant site nodule	0 days	Mild	None	Recovered	112 days	Persistent filler nodule over the chin. Did not appear inflammatory or infectious. Non-tender to palpation
8650-002	Implant site mass (4 cm)	16 days	Mild	None	Recovered	27 days	Mass formation of 4 cm in center of chin

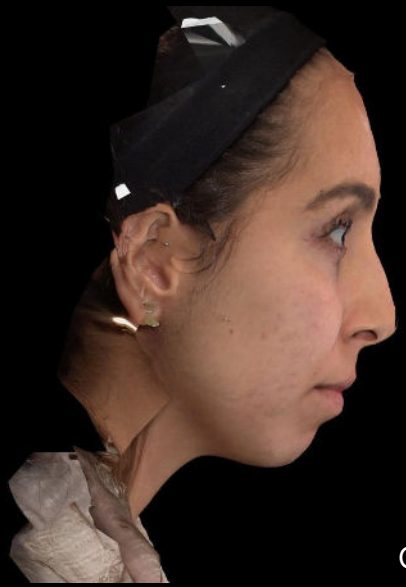
Data on file. 43USCH1702 Clinical Study Report. Fort Worth, TX: [redacted] 2020

B&As

Subject #1

22 year old female, initial treatment volume = 2 mL; touch-up treatment, 2 mL

Total volume = 4 mL

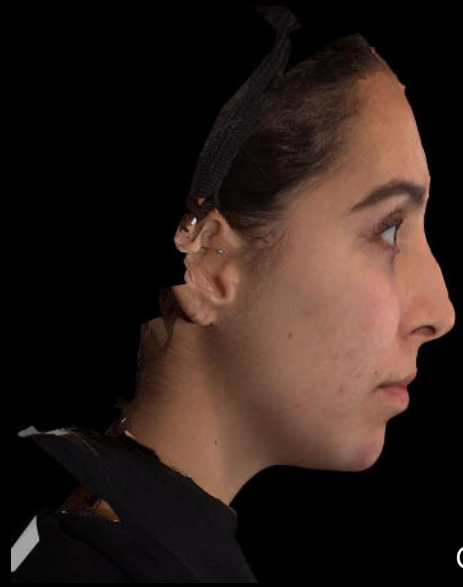


GCRS: 2

Baseline

GCRS: 0

Week 12



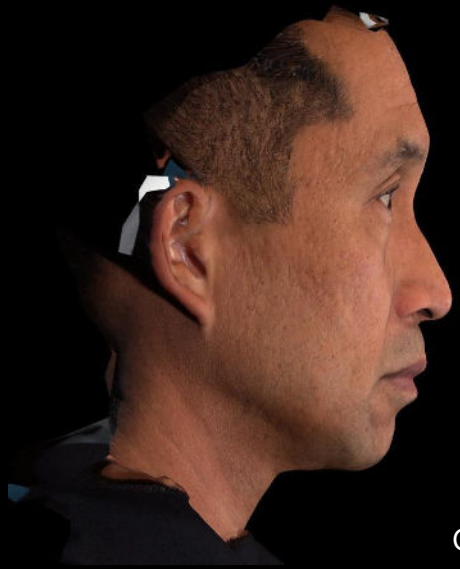
GCRS: 0

Week 48

Subject #2

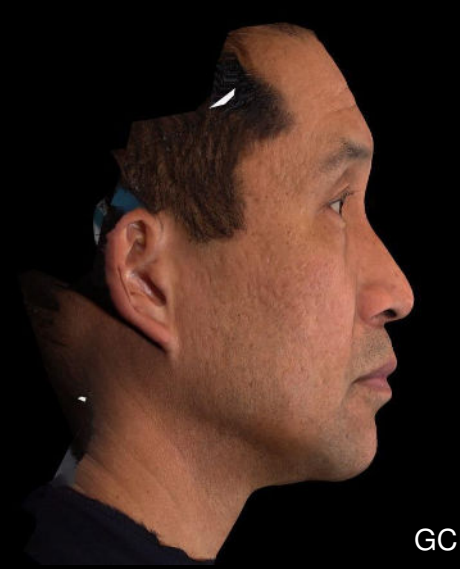
52 year old male, initial treatment volume = 2 mL; touch-up treatment, 2 mL

Total Volume = 4 mL



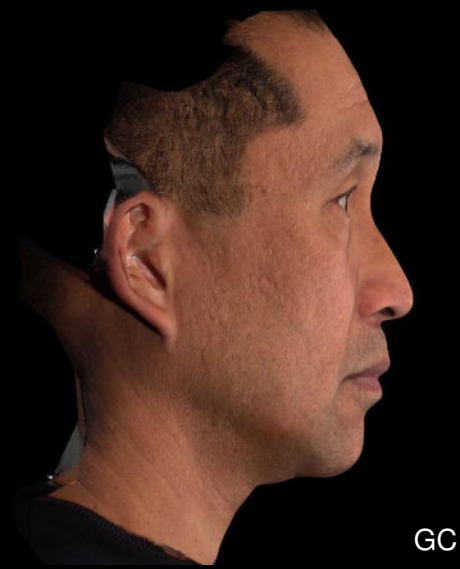
GCRS: 2

Baseline



GCRS: 0

Week 12



GCRS: 1

Week 48

Conclusions

- Evolving patient demographics and beauty trends have challenged injectors to step up to changing tides
- Increased demand, awareness and acceptance of filler procedures has been met with increased supply and new FDA indications
- Although we must face new unique challenges and unexperienced competitors, we still stand as the experts
- Marry evidence-based medicine, psychology, and art to rejuvenate, recreate and reshape

Thank You