Title	A Post Market Clinical Follow Up (PMCF) Study to Assess the Safety and Efficacy of Use of Perfectha Subskin Lidocaine in the Treatment of Significant Loss of Volume in the Cheeks, Jawline and/or Chin
Protocol number	CS-22-05
Name of medical device and classification (MDR)	Perfectha Subskin Lidocaine: cross-linked hyaluronic acid (HA) (20mg/mL) + 0.3% lidocaine hydrochloride + phosphate buffer saline (q.s. 1mL) Class III
Intended use	Treatment of significant loss of volume in the cheeks, jawline and/or chin
Sponsor	Sinclair Pharmaceuticals Ltd Eden House, Lakeside Chester Business Park Chester CH4 9QT, United Kingdom
Study design	Prospective open label, post-market follow-up study
Study population (ICD)	Male or female subjects between the ages of 25 and 65 years of age inclusively across a range of Fitzpatrick skin types who presented with significant loss of volume in the cheeks, jawline and/or chin (ICD10: R23.4, changes in skin texture).
Planned number of participants	In total, at a dropout rate of 15%, 69 subjects were planned, with a minimum of 25 subjects per site, assigned equally (n=23) to one of three primary treatment groups. 60 subjects were planned to complete the study. The subjects received injections in the primary treatment area (as determined by the investigator) and had the option to receive injections in up to two other treatment areas if they met the inclusion criteria. Therefore, data for more than one treatment indication could be generated from one subject.
Actual number of participants	69 participants across two sites
Number of study sites	Two specialist aesthetic specialists at two sites located in the United Kingdom (UK).
Inclusion criteria	1. Male or female subjects between the ages of 25 and 65 years of age 2. Subject seeking aesthetic improvement of of volume loss in his/her cheeks, jawline and/or chin with a hyaluronic acid dermal filler. 3. Subjects who present significant loss of volume in the cheeks, jawline and/or chin as assessed by a suitable recognised photographic scale: Mild to significant volume deficit in the mid-face (score of 2-4 on the designated photographic assessment scale) or Mild to moderate jawline ptosis (score of 1-2 on the designated photographic assessment scale) or Minimal to severe chin retrusion (score of 1-3 on the designated photographic assessment scale) 4. Subjects who are willing to provide written informed consent, including approval for facial photographs to be taken 5. Subjects willing to commit to having no further facial aesthetic treatments, that could affect the appearance of the facial treatment area, for the duration of the study period, including follow-up

<table>
<tr><td></td><td>6. Subjects must be willing and able to comply with protocol requirements, instructions, and protocol-stated restrictions and be likely to complete the study as planned.
7. Women of childbearing potential should be using a medically accepted contraceptive regimen for at least 12 weeks prior to study entry and over the entire study duration.</td></tr>
<tr><td>Exclusion criteria</td><td>1. Subjects who, in the twelve months prior to their enrolment assessment had undergone:
- cosmetic facial plastic surgery (other than rhinoplasty),
- tissue grafting (e.g., fat injections),
- tissue lifting implants (e.g., threads, barbs) or other implants,
- augmentation with any semi-permanent filler (e.g., silicone, PMMA, PLLA) or temporary filler (e.g., HA, CaHA, PCL)
- neuromodulator injections,
- mesotherapy,
- resurfacing (e.g., laser, radio frequency, dermabrasion, or chemical peel)
in the facial region to be treated.
2. Subjects who have received permanent filler in the facial region to be treated.
3. Subjects who have received any other facial aesthetic procedures that will affect the appearance in the region of the face to be treated, at any time during the study period (see table below)
<table>
<tr><th>Subject treatment area</th><th>No further aesthetic treatments are allowed in the region of:</th><th>Reason</th></tr>
<tr><td>Mid-face</td><td>Nasolabial folds
Nose

Tear troughs
Prejowl sulcus
Nasojugal folds</td><td>Adjacent to treatment area
Effect on facial appearance is too significant
Area assessed within mid-face scale
Area assessed within mid-face scale
Area assessed within mid-face scale</td></tr>
<tr><td>Jawline/Jowls</td><td>Nose

Pre-jowl sulcus
Marionette lines</td><td>Effect on facial appearance is too significant
Adjacent to treatment area
Adjacent to treatment area</td></tr>
<tr><td>Chin</td><td>Nose

Platysma
Pre-jowl sulcus
Lips</td><td>Effect on facial appearance is too significant
Adjacent to treatment area
Adjacent to treatment area
Lips are reference points for chin scoring scale</td></tr>
</table>
4. Subject is in institutional care
5. Subject who had been deprived of their freedom by administrative or legal decision or who is under guardianship.
6. Subject is an employee of the aesthetic surgery department on the investigational site, the Clinical Research Organisation (CRO) or study sponsor.
7. Pregnant or nursing woman or a woman planning a pregnancy during the study.
8. Subject who is not using or has changed or started their medically accepted contraceptive regimen or any other hormonal treatment during the 12 weeks prior to study entry.
9. Subjects who, in the opinion of the investigator, are unsuitable to take part in the study for scientific or medical reasons.
10. Subject suspected to be non-compliant according to the investigator’s judgment.
11. Subjects currently enrolled in other clinical trials.
12. Subjects with scar(s), mole(s), tattoo(s), semipermanent makeup or facial hair in the region to be treated as this could interfere with study evaluations.</td></tr>
</table>

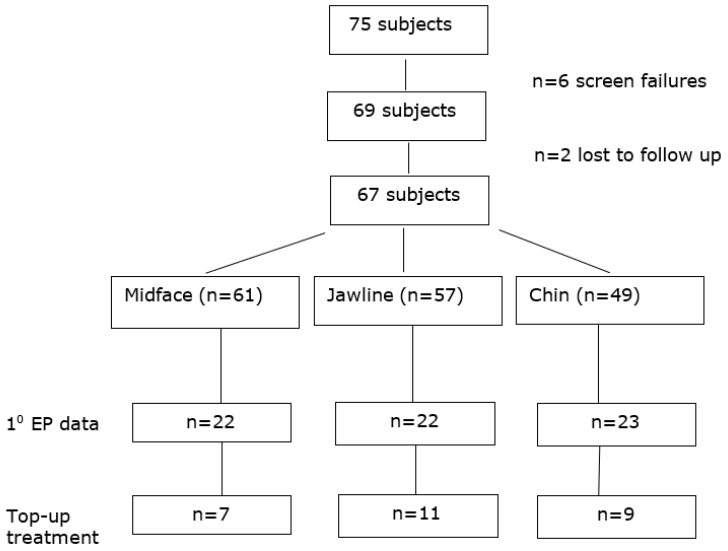
	13. Subject using medication such as aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), antiplatelet agents, thrombolytics or anticoagulants within one week prior to injection visit and 1 month after treatment. 14. Subject with known bleeding disorder or is receiving medication that will likely increase the risk of bleeding during treatment. 15. Subjects with a tendency to form keloids, hypertrophic scars or any other healing disorders. 16. Subject receiving medical treatment that reduces or inhibits liver metabolism (cimetidine, beta blockers) 17. Subject with epilepsy not controlled by treatment. 18. Subject with known history of streptococcal disease (recurrent throat infections, acute rheumatic fever with or without cardiac involvement). 19. Subject suffering from active disease/symptoms such as inflammation, infection, tumours, psoriasis, allergic oedema, inflammatory and/or infectious cutaneous disorders (e.g., herpes, acne, rosacea) on the face within 6 months of the study entry. 20. Subjects with a history of any disease which may have resulted in changes to facial contour or oedema during the study period (e.g., facial psoriasis, herpes zoster). 21. Subject with known history of precancerous lesions/skin malignancies 22. Any medication which may interfere, in the interpretation of the investigator, with the study objectives in terms of efficacy and safety. 23. Subject suffering from a severe or progressive disease or any other pathology that may interfere with the evaluation of the study result and/or subject safety. 24. Subject with major dental problems or subject who received oral surgery (e.g., tooth extraction, orthodontia, or implantation) within 6 weeks prior to study entry 25. Subjects with known hypersensitivities to hyaluronic acid, lidocaine, amide local anesthetics or other components of the treatment including avian proteins, feathers and egg products (hyaluronic acid). 26. Subjects with a history of severe allergy or anaphylactic shock. 27. Subjects with active (or a history of) autoimmune disease and immune deficiency. 28. Subjects with porphyria. 29.Subjects having received or receiving Coronavirus disease (COVID)-19 vaccination for the 14 days before and following injection.
Primary objective	Improved aesthetics and correction of volume loss in the treated area(s) of the face at three months (category clinical performance in PMCF guidance); safety objective (category safety in PMCF guidance)
Secondary objectives	Improved aesthetics and correction of volume loss of the treated area(s) of the face at earlier and later timepoints and satisfaction (category effectiveness in PMCF guidance)
Exploratory objectives	Quantitative assessments of the aesthetic treatment successes in cheeks, jawline and the chin
Primary endpoint	The primary effectiveness endpoint is the proportion of subjects with an improvement (score of 3 and above) at 3 months in Global Aesthetic Improvement Scale (GAIS) assessments of Perfectha Subskin Lidocaine as a treatment for significant loss of volume in the cheeks, jawline or chin, as rated by an on-site live independent evaluator. In cases where more than one area was treated, the improvement

	relates to the primary treatment area.
Secondary endpoints	• The proportion of subjects (%) with an improvement (score of 3 and above) at 3 months in Global Aesthetic Improvement Scale (GAIS) assessments of the non-primary treatment area(s) in cases where more than one area is treated. • The proportion of subjects (%) with an improvement (score of 3 and above) in Global Aesthetic Improvement Scale (GAIS) assessments of the i) cheeks, (ii) jawline and/or iii) chin area at 1, 6, 9, 12, and 18 months post treatment by an on-site live independent evaluator. • The proportion of subjects (%) with an improvement (score of 3 and above) in Global Aesthetic Improvement Scale (GAIS) assessments of the i) cheeks, (ii) jawline and/or iii) chin area at 1, 3, 6, 9, 12, and 18 months post treatment by the subject. • The proportion of subjects (%) exhibiting an improvement of ≥ 1 point from baseline on the mid-face volume deficit scale at 1, 3, 6, 9, 12, and 18 months post treatment as rated by a blinded remote independent evaluator. • The proportion of subjects (%) exhibiting an improvement of ≥ 1 point from baseline on the scale for the assessment of loss of volume at the jawline sagging at 1, 3, 6, 9, 12, and 18 months post treatment as rated by a blinded remote independent evaluator. • The proportion of subjects (%) exhibiting an improvement of ≥ 1 point from baseline on loss of volume on the chin retrusion assessment scale at 1, 3, 6, 9, 12, and 18 months post treatment as rated by a blinded remote independent evaluator • Patient self-assessment of their overall satisfaction with the results of the treatment at 1, 3, 6, 9, 12, and 18 months post treatment. • The use of the medical device through an investigator satisfaction questionnaire.
Exploratory endpoints	• To evaluate that the proportion of subjects achieving a GAIS score of 3 or above at 3 months is significantly greater than 66%. • To evaluate whether there is a significant difference in the proportion of subjects achieving improvement (score of 3 and above) according to the GAIS assessments of the i) cheeks, (ii) jawline and/or iii) chin area at 1, 6-, 9-, 12-, and 18-months post treatment by an on-site live independent evaluator. • To evaluate whether there is a significant difference in the proportion of subjects achieving improvement (score of 3 and above) according to the GAIS assessments of the i) cheeks, (ii) jawline and/or iii) chin area at 1, 3, 6-, 9-, 12-, and 18-months post treatment by the subject. • To evaluate whether there is a significant difference in the proportion of subjects (%) exhibiting an improvement of ≥ 1 point from baseline on the mid-face volume deficit scale at 1, 3, 6-, 9-, 12, and 18-months post treatment as rated by a blinded remote independent evaluator. • To evaluate whether there is a significant difference in the proportion of subjects (%) exhibiting an improvement of ≥ 1 point from baseline baseline on the scale for the assessment of loss of volume at the jawline sagging at 1, 3, 6-, 9-, 12-, and 18-months post treatment as rated by a blinded remote independent evaluator. • To evaluate whether there is a significant difference in the

	proportion of subjects (%) exhibiting an improvement of ≥ 1 point from baseline on loss of volume on the chin retrusion assessment scale at 1, 3, 6-, 9-, 12-, and 18-months post treatment as rated by a blinded remote independent evaluator. • To evaluate whether there is a significant difference in patient self-assessment of overall satisfaction with the results of the treatment at 1, 3, 6-, 9-, 12-, and 18-months post.
Safety endpoint	The safety endpoint of the study will be to record all Adverse Events (AEs), inclusive of Serious Adverse Events (SAEs), Unanticipated Problems (UPs), and Unanticipated Adverse Device Effects (UADEs), experienced in the post-treatment follow-up period. ISRs reported by the investigator and by the subjects were analysed.
Timeline	First patient in: 20 Feb 2023 Last Subject Month 3 Visit: 09 Oct 2023 (site 1) / 03 Oct 2023 (site 2) Last patient out: 19 Dec 2024 (site 1) / 13 Dec 2024 (site 2)
Study registration	ISRCTN63865080
Duration of participation	The total duration of the study per patient was 18 months.
Screening	Potential participants were screened according to the prespecified inclusion and exclusion criteria after informed consent. The proposed treatment areas were assessed using the Photometric Midface Volume Deficit Scale, the Aesthetics scale for Jawline and the Chin Retrusion Scale.
Assessments	The study consisted of 6 on-site visits to assess efficacy and safety at month 1, month 3, month 6, month 9, month 12, and month 18. At week 2, a phone call was made between the investigator and subject to discuss whether any (Serious) Adverse Events ((S)AEs) that had occurred in the two weeks following treatment. If the subject received the optional touch-up treatment at month 1, there was an additional follow-up phone call at 6 weeks to assess safety only.
Implantation procedure	As per the Instructions for Use (IFU): The injection was administered slowly into the deep subcutaneous fat tissue and/or into the supraperiostic zone in the appropriate area of the face by a well-trained physician. The injection volume of Perfectha Subskin Lidocaine varied, depending on the required area of treatment and level of correction. However, the injection volume shall not exceed 3 mL per area (consider left and right as separate areas). If required, an optional touch-up treatment was administered at month 1. The subject had a primary treatment area and that was the treatment group they were assigned to. However, if the subject met the inclusion criteria, they had the option to receive injections in more treatment areas and generate data for more than one treatment indication.
Follow Up	As part of the investigation, participants were followed up for 18 months after primary treatment.
Statistics	An interim analysis was conducted at three months as planned to obtain preliminary efficacy and safety results. The final analysis was conducted at the end of study, following SAP v02 (24 Oct 2024).
Results	The recruitment target was reached across the two sites. 69 subjects were enrolled (safety set). 67 subjects provided an evaluable data set (FAS): 3 male, 64 female, 46 ± 9.99 years. 31 subjects had no

major protocol deviations (PP set).

Disposition:



Primary endpoint:

Proportion of subjects with GAIS score improvement at month 3, primary treatment areas, independent evaluator assessed:

	Analysis set	improvement at 3 months (GAIS); 95%CI
midface	FAS (n=22)	100%; 95% CI 100 – 100%
	PP (n=9)	100%; 95% CI 100 – 100%
jawline	FAS (n=22)	95.5%; 95% CI 86.8 - 100%
	PP (n=4)	75.0%; 95% CI 32.6 – 100%
chin	FAS (n=23)	91.3%; 95% CI 79.8 - 100%
	PP (n=18)	88.9%; 95% CI 74.4 - 100%
Total	FAS (n=67)	95.5%; 95% CI 90.6 – 100%
	PP (n=31)	90.3%; 95% CI 79.9 – 100%

Secondary endpoints:

In subjects in whom more than one area was treated, the proportions of achieving an improvement at 3 months using GAIS were 94.9% for midface treatment, 94.3% for jawline treatment and 100% for chin treatment (FAS).

Proportion of subjects with GAIS score improvement at month 3, total (subject evaluation)

	Analysis set	improvement at 3 months (GAIS); 95% CI
total	FAS (n=67)	95.5%; 95% CI 90.6 – 100.0%
	PP (n=31)	96.8%; 95% CI 90.6 – 100.0%

For the FAS and PP, a statistically significant change was observed across the evaluation periods in all subjects based on self-assessment (midface: p=0.004; jawline: p<0.001; chin: p<0.001).

Independent site-evaluators´ assessments using GAIS: Improvement at the 18-month timepoint for PP was found in 76.9% for midface treatments, in 59.3% for the treated jawlines, and in 57.7% for treated chins.

Self-assessment by treatment areas using GAIS: Improvement at the 18-month timepoint for PP was found in 69.2% for midface treatments, in 59.3% for the treated jawlines, and in 65.4% for treated chins.

Subject satisfaction with treatment was very good overall.

Using treatment indication specific photonumeric scales in

	independent assessment, the changes from baseline (FAS) were significant at the twelve-month timepoint after treatment of the chin ($p<0.05$), and at the one-month and three-month timepoints after treatment of the jawlines ($p<0.005$ and $p<0.05$, respectively). Statistical analysis of the changes from baseline showed significance for the one-month timepoint after treatment of the jawline for the PP set ($p<0.05$). Subjects recorded mild pain at injection and investigators were satisfied with the performance of device. There were no device deficiencies. ISRs were generally mild and transitory but 14 were graded as adverse events.