Three-dimensional imaging for facial vitiligo: Results from a phase 2 randomized controlled trial investigating upadacitinib in patients with vitiligo

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Background: Upadacitinib (UPA), an oral selective Jak inhibitor, showed significantly greater facial repigmentation than placebo as assessed by Facial Vitiligo Area Scoring Index (F-VASI) in a phase 2 clinical trial. A nested substudy explored a 3-dimensional (3D) imaging platform as an objective tool to quantify facial vitiligo repigmentation. **Methods:** Adults with nonsegmental vitiligo received 6, 11, or 22 mg UPA or placebo for 24 weeks (period 1). For weeks 24–52 (period 2), UPA-treated patients continued UPA at assigned doses; patients receiving placebo switched to 11 or 22 mg UPA. In this substudy, efficacy was assessed by the percentage change from baseline in facial vitiligo area with 3D imaging and F-VASI. **Results:** The substudy included 27 patients. Patients receiving UPA showed facial repigmentation at weeks 24 and 52 as assessed by 3D imaging and F-VASI. There was a high correlation between 3D imaging and F-VASI measurements at baseline ($r = 0.85$; $P < .0001$). At week 24, there was a high correlation ($r = 0.71$; $P = .0003$) between the percentage change from baseline in 3D imaging and F-VASI measurements, which diminished by week 52 ($r = 0.01$; $P = .9600$). **Conclusions:** 3D imaging shows potential as an objective tool for evaluating changes in facial vitiligo after UPA treatment.

Keywords: Computer generated, Imaging, Jaks, Nonsegmental vitiligo, Repigmentation

INTRODUCTION

Vitiligo is a chronic autoimmune skin disorder characterized by patchy depigmentation due to selective and progressive loss of melanocytes (Bibeau et al, 2022; Qi et al, 2021). Reports on the global prevalence of vitiligo vary from 0.4 to 2%, with substantial geographic-based variations (Akl et al, 2024; Bibeau et al, 2022). Vitiligo is more prevalent in adults than in children, with males and females affected similarly (Akl et al, 2024). Nonsegmental vitiligo, characterized by bilateral depigmented lesions, progressive onset with multiple flare-ups, and an unpredictable course, is more common than segmental vitiligo (Gandhi et al, 2022). The psychosocial effect of vitiligo (because of the visibility of the skin) is a main concern for patients because it can have a substantial and distressing impact on QOL (Picardo et al, 2022). Therefore, treating and monitoring the lesion progression is an important goal for patients with vitiligo.

The topical Jak inhibitor ruxolitinib is approved for treating vitiligo, but its use is limited by application to ≤10% of body surface area (OPZELURA). Oral Jak inhibitors, such as upadacitinib (UPA) and ritlecitinib, have shown promise for vitiligo treatment (Ezzedine et al, 2023; Passeron et al, 2024). UPA (RINVOQ; AbbVie Inc) is an oral selective Jak inhibitor approved for the treatment of several immune-mediated diseases (AbbVie Inc, 2024; Parmentier et al, 2018). UPA recently demonstrated efficacy in a phase 2 study as the first oral Jak1 inhibitor to induce lesion repigmentation in adults with nonsegmental vitiligo (Passeron et al, 2024).

Clinical investigations exploring treatments for vitiligo often use subjective or semiobjective measures to evaluate the degree of skin depigmentation, such as the Vitiligo Area Scoring Index (VASI) or the Vitiligo Extent Scoring system (Eleftheriadou et al, 2023; Magdaleno-Tapial et al, 2024). Although these measures are generally reliable, the

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Abbreviations: 3D, 3-dimensional; F-VASI, Facial Vitiligo Area Scoring Index; PBO, placebo; UPA, upadacitinib

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subjectivity in the assessments can make it challenging to detect small changes in pigmentation in response to vitiligo treatments for individual patients (Komen et al, 2015). In addition, the potential for subjectivity and inter-rater variability poses difficulties in comparing Facial Vitiligo Area Scoring Index (F-VASI) scores across trials (Ezzedine et al, 2025). Differences in levels of expertise between raters or more heterogenous depigmentation among patients may lead to poor F-VASI inter-rater reliability (Marin Dit Bertoud et al, 2023). More objective assessments, such as the manual tracing of lesions and digital analysis of photographs to calculate surface area, show promise in quantifying target lesions but have limitations, including difficulty in capturing complex patterns on curved surfaces (Marin Dit Bertoud et al, 2023; van Geel et al, 2022). Other technological tools, such as digital imaging, combined with precise area calculations offer the potential for accurate and objective quantification of repigmentation. Researchers recently demonstrated that a method involving standardized UV pictures combined with a specific algorithm showed high reliability and repeatability in measurements on the face of patients with vitiligo (Marin Dit Bertoud et al, 2023). In addition, 3-dimensional (3D) imaging has shown accuracy in estimations of dermatological lesion areas compared with 2-dimensional image analysis (Grochulska et al, 2022; Kohli et al, 2015). A 3D imaging system may show potential for quantifying skin repigmentation when evaluating treatments for vitiligo.

In a prospective, nested substudy of a phase 2, randomized, placebo (PBO)-controlled, UPA trial in patients with nonsegmental vitiligo, we used a proprietary, 3D, high-resolution digital imaging platform (Cherry Imaging LLC) to objectively quantify facial vitiligo lesions. This platform can assess colorimetric, surface, and skin volume changes. The objectives of this nested substudy were to correlate the 3D imaging measurements of facial vitiligo area with F-VASI scores and to assess the ability of the 3D imaging platform to quantitatively measure changes in vitiligo skin pigmentation compared with F-VASI scores after UPA therapy.

RESULTS

Patients

This nested substudy included 27 patients who were enrolled in the primary study (June 16, 2021–June 27, 2022). Baseline characteristics were similar across treatment groups (Table 1). Fitzpatrick skin types ranged from type II to type V. Two patients discontinued the study before week 24, 1 each owing to an adverse event and withdrawal of patient consent; 2 additional patients discontinued the study before week 52, 1 each owing to loss to follow-up and withdrawal of patient consent.

Efficacy outcomes

Of the 81 planned 3D facial vitiligo images, 66 were included in the analysis; 6 images were not obtained owing to patient discontinuation before week 24 (2 patients) or week 52 (2 patients), and 9 images were not included in the analysis owing to technical difficulties, extensive facial hair, site error, patients lost to follow-up, or unknown reasons (Figure 1). One patient receiving 6 mg UPA had a 3D imaging value at week 52 notably different from those of other patients. Analyses are presented with and without this patient's data to better understand how the divergent value may have skewed overall results.

Correlation between 3D imaging and F-VASI

At baseline (PBO, n = 4; 6 mg UPA, n = 8; 11 mg UPA, n = 7; 22 mg UPA, n = 7), there was a high correlation between 3D imaging composite facial vitiligo area and F-VASI measurements ($r = 0.85$; $P < .0001$) (Figure 2). There was a high correlation between the percentage change from baseline in 3D imaging facial vitiligo area and F-VASI at week 24 (PBO, n = 3; 6 mg UPA, n = 7; 11 mg UPA, n = 6; 22 mg UPA, n = 5; $r = 0.71$; $P = .0003$). No correlation was observed between the percentage change from baseline in 3D imaging facial vitiligo area and F-VASI at week 52 (PBO/11 mg UPA, n = 1; PBO/22 mg UPA, n = 1; 6 mg UPA, n = 6; 11 mg UPA, n = 5; 22 mg UPA, n = 5; $r = 0.01$; $P = .9600$); notably, this result was substantially affected by the outlier 3D image value (without which, $r = 0.36$; $P = .16$).

Percentage change from baseline in 3D imaging and F-VASI at week 24 and week 52

Representative 3D images from a patient in each of the PBO/22 mg UPA, 6 mg UPA, 11 mg UPA, and 22 mg UPA groups and corresponding percentage change from baseline in 3D imaging composite facial vitiligo area at weeks 24 (6 mg UPA, n = 7; 11 mg UPA, n = 6; 22 mg UPA, n = 5) and 52 (6 mg UPA, n = 6; 11 mg UPA, n = 5; 22 mg UPA, n = 5) are shown in Figure 3. All other patient 3D images can be found in Supplementary Figure S1.

There was a greater reduction from baseline in facial vitiligo area using 3D imaging at week 24 in patients who received any UPA dose (arithmetic mean percentage change from baseline: 6 mg UPA, −15.2%; 11 mg UPA, −35.0%; 22 mg UPA, −29.1%) (Figure 4) than what was observed for patients who received PBO (5.1%; n = 3). The arithmetic mean percentage reduction from baseline in facial vitiligo area, as measured by F-VASI, at week 24 in patients receiving UPA (6 mg UPA, −27.6%; 11 mg UPA, −51.0%; 22 mg UPA, −38.3%) was similar to that observed with 3D imaging; however, the treatment effect of UPA at week 24, as measured by F-VASI, was less pronounced, given that the PBO group showed a greater reduction in the mean percentage change from baseline (−29.4%) than the increase observed with 3D imaging (5.1%). At week 24, the least squares mean difference (95% confidence interval) versus PBO in the percentage change from baseline in facial vitiligo area using 3D imaging was −15.6 (−21.7 to −9.5) for 6 mg UPA, −40.9 (−47.5 to −34.4) for 11 mg UPA, and −36.3 (−46.7 to −25.9) for 22 mg UPA. In comparison, at week 24, the least squares mean difference (95% confidence interval) versus PBO in the percentage change from baseline in facial vitiligo area using F-VASI was −0.8 (−6.5 to 4.8) for 6 mg UPA, −18.7 (−21.5 to −16.0) for 11 mg UPA, and −13.8 (−16.6 to −11.0) for 22 mg UPA.

Patients receiving 11 or 22 mg UPA had reductions from baseline in facial vitiligo area using 3D imaging at week 52 with an arithmetic mean percentage change from baseline of −64.7% for PBO/11 mg UPA (n = 1), −86.2% for PBO/22 mg UPA (n = 1), −46.4% for 11 mg UPA (n = 5), and −44.8% for 22 mg UPA (n = 5). For patients in the 6 mg

Table 1. Baseline Patient Demographics and Characteristics in 3D Imaging Substudy

Characteristic	PBO (n = 4)	6 mg UPA (n = 9)	11 mg UPA (n = 7)	22 mg UPA (n = 7)
Age, y, mean (SD)	50.3 (7.3)	43.7 (13.9)	49.1 (11.4)	39.4 (13.5)
Sex, n (%)				
Female	2 (50.0)	5 (55.6)	5 (71.4)	4 (57.1)
Male	2 (50.0)	4 (44.4)	2 (28.6)	3 (42.9)
Race, n (%)				
American Indian	0	0	0	1 (14.3)
Asian	0	3 (33.3)	1 (14.3)	0
Black or African American	0	0	0	0
Missing	2 (50.0)	1 (11.1)	0	0
Multiple	0	1 (11.1)	0	1 (14.3)
White	2 (50.0)	4 (44.4)	6 (85.7)	5 (71.4)
BMI, kg/m^2, mean (SD)	23.9 (3.5)	24.8 (3.0)	27.3 (5.6)	29.2 (6.1)
Fitzpatrick skin type, n (%)				
Type I	0	0	0	0
Type II	1 (25.0)	3 (33.3)	3 (42.9)	4 (57.1)
Type III	1 (25.0)	2 (22.2)	3 (42.9)	1 (14.3)
Type IV	2 (50.0)	2 (22.2)	1 (14.3)	2 (28.6)
Type V	0	2 (22.2)	0	0
Type VI	0	0	0	0

Abbreviations: 3D, 3-dimensional; BMI, body mass index; PBO, placebo; UPA, upadacitinib.

UPA group (n = 6), there was a mean increase in the 3D image facial vitiligo area of 34.3% due to the outlier 3D image value (mean change in 3D image facial vitiligo area excluding the outlier value was −12.6%). All UPA treatment groups had reductions from baseline in F-VASI at week 52 with an arithmetic mean percentage change from baseline of −95.1% for PBO/11 mg UPA (n = 1), −93.8% for PBO/22 mg UPA (n = 1), −51.7% for 6 mg UPA (n = 6), −82.1% for 11 mg UPA (n = 5), and −50.9 for 22 mg UPA (n = 5).

Safety data from the primary study have been previously published (Passeron et al, 2024), and no new safety concerns were identified in this substudy.

DISCUSSION

The Cherry 3D Imaging platform enabled objective measurements of facial vitiligo area and detected changes in pigmentation over time in this nested substudy of adults with nonsegmental vitiligo. There were high correlations between 3D imaging composite facial vitiligo area score and F-VASI at baseline and week 24. After UPA treatment, divergences between the 3D imaging facial vitiligo area and F-VASI increased over time, and at week 52, there was a lack of correlation in percentage change from baseline between 3D imaging and F-VASI.

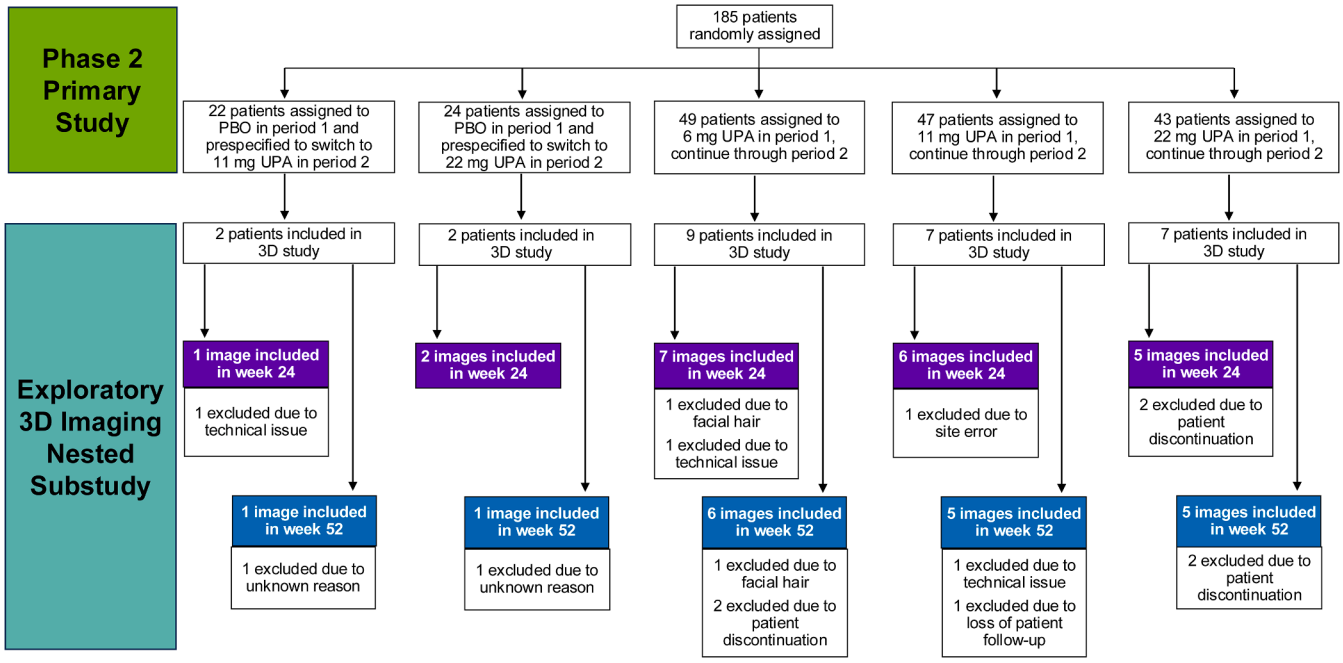

Figure 1. Flow diagram of patients and images included in study at each time point. 3D, 3-dimensional; PBO, placebo; UPA, upadacitinib.

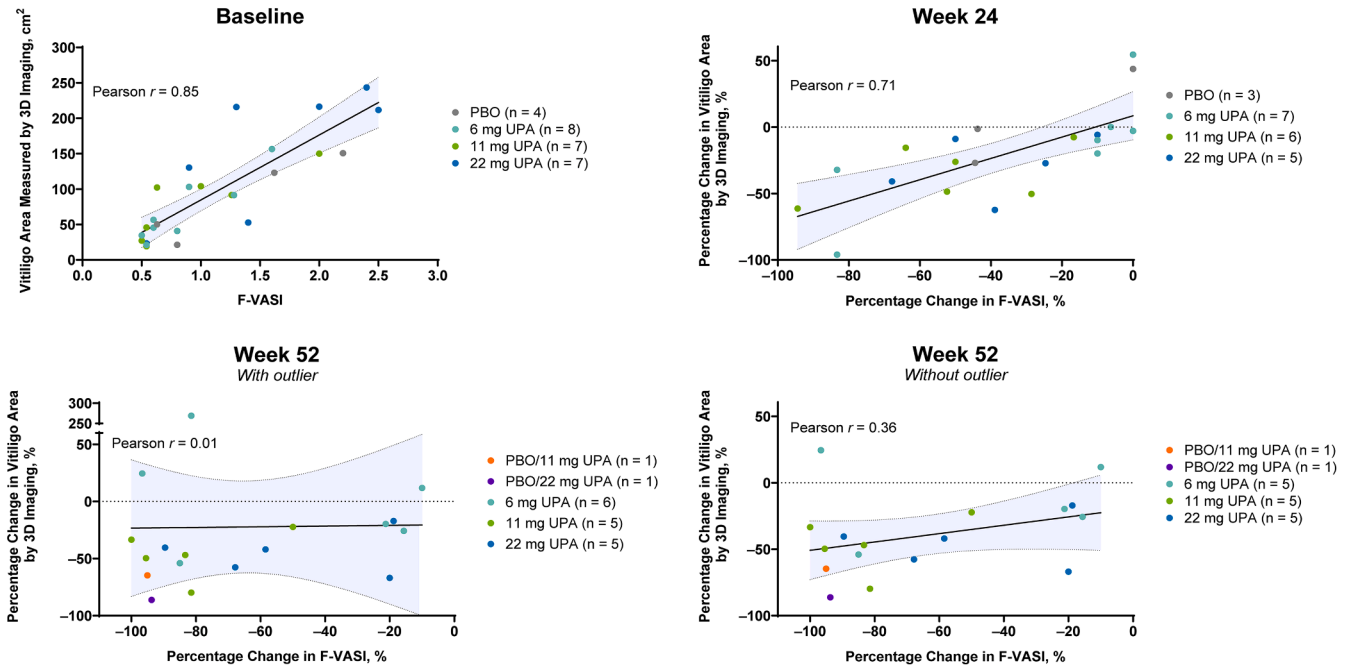

Figure 2. Correlation between 3D imaging and F-VASI. The correlation in facial vitiligo area between 3D imaging and F-VASI at baseline and the correlation between 3D imaging and F-VASI in measuring the percentage change from baseline in facial vitiligo area at 24 and 52 weeks. 3D, 3-dimensional; F-VASI, Facial Vitiligo Scoring Index; PBO, placebo; UPA, upadacitinib.

Reflecting what was reported for the primary study population (Passeron et al, 2024), we observed vitiligo lesion repigmentation on the basis of F-VASI at week 24 and week 52 in this nested substudy for all UPA treatment groups. We also observed repigmentation on the basis of 3D imaging at week 24 and week 52 among patients randomized at baseline to receive 11 mg UPA or 22 mg UPA. A greater change in pigmentation from baseline was recorded in the PBO-treated group with F-VASI (−29.4%) than with 3D imaging (5.1%) at week 24, indicating that 3D imaging may be a more objective tool to differentiate clinical response than F-VASI. Because patients initially randomized to PBO switched to UPA after week 24, it is unknown whether divergences in the percentage change from baseline between F-VASI and 3D imaging in the PBO-treated group would have been observed at later time points.

Vitiligo pathogenesis and response to treatment can be a slow process, often taking months, making it difficult for healthcare providers to accurately assess small differences in skin pigmentation using subjective measurements (Nugroho et al, 2007). Two recent studies also reported the use of new technologies in the effort to objectively quantify changes in facial vitiligo. One study used an automated algorithm to quantify the percentage of facial vitiligo lesions from standardized UV photographs (Marin Dit Bertoud et al, 2023). The other study used an artificial intelligence machine learning model to assess depigmentation in facial vitiligo, utilizing standardized UV photographs (Hillmer et al, 2024). Although both studies showed promising results toward objective quantification of facial vitiligo, they were limited by either manual intervention by a technician or image quality (Eleftheriadou and Seneschal, 2023). In addition, both of these methods used 2-dimensional photographs, which may have lacked facial structural information captured with the use of a 3D model.

A study using a different 3D imaging technique to quantify vitiligo lesions across the total body surface area also found 3D imaging to provide accurate, objective measurements with the precise documentation of a lesion's location, extent, and pattern over time, allowing for quantification of pigment changes with treatment without the variability present in subjective measures (Kohli et al, 2015). The Cherry 3D Imaging platform was used successfully in a small study (n = 30) investigating acute facial skin changes due to long-term mask use (Elsanadi et al, 2022) and has demonstrated repeatability, accuracy, and reliability for imaging scars in a split intra and interindividual study design (Hendel et al, 2021). Because scar imaging involves complex color and texture differentiation (Hendel et al, 2021), it is likely that 3D imaging for vitiligo will also show repeatability and reliability across investigators. Indeed, in a clinical study, the Cherry 3D Imaging platform showed high reliability in determining facial vitiligo area and high accuracy and sensitivity in detecting changes in vitiligo area in different skin types over time (He et al, 2025[1]). It also demonstrated high inter- and intrarater and scanner reliability (He et al, 2025[1]). Objective 3D imaging techniques may allow a more accurate assessment of vitiligo lesion changes over time and could complement physician-rated indices, particularly for subtle perilesional repigmentation that is difficult to detect visually.

[1] He T, Wollach S, Goss SL, Loyman M, Bastero R, Schlosser BJ, et al. Novel three-dimensional imaging platform for digital facial vitiligo area assessment. medRxiv 2025.

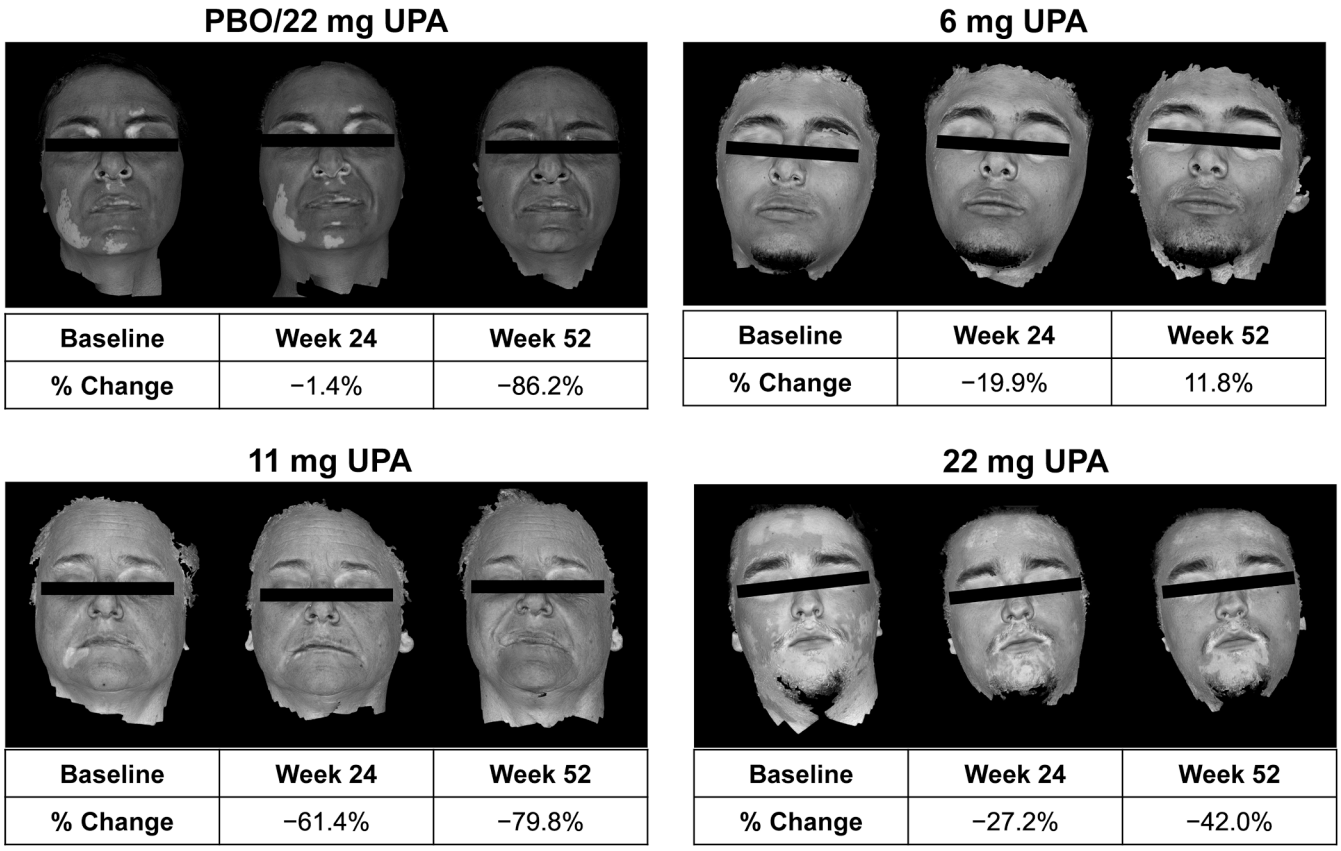

Figure 3. Representative 3D images of patients receiving UPA. The 3D images and percentage change from baseline of 1 patient each from the PBO/22 mg UPA, 6 mg UPA, 11 mg UPA, and 22 mg UPA groups at baseline, week 24, and week 52. All patients provided written informed consent for publication of images. % Change denotes percentage change from baseline. 3D, 3-dimensional; PBO, placebo; UPA, upadacitinib.

Limitations

The 3D Imaging system shows promise in evaluating vitiligo lesions; however, definitive interpretation of these results is hampered by several limitations. The observed lack of correlation at week 52 is possibly due to decreased sample size over time, individual patient discrepancies, a difference in inherent measurement precision, or other variables. Furthermore, there was an image at week 52 in the 6-mg UPA–treated group that appeared to be an outlier to the rest of the dataset. Because this analysis was limited by a small sample size, an outlier may have substantially affected the results. In addition, overestimating the UPA treatment effect and the cumulative skill and familiarity of investigators with the device may have also contributed to the divergence between 3D imaging facial vitiligo area and F-VASI over time. Finally, the loss of correlation at week 52 may partially reflect progressive melanization that may shift lesion contrast beyond the baseline-defined intensity thresholds, suggesting

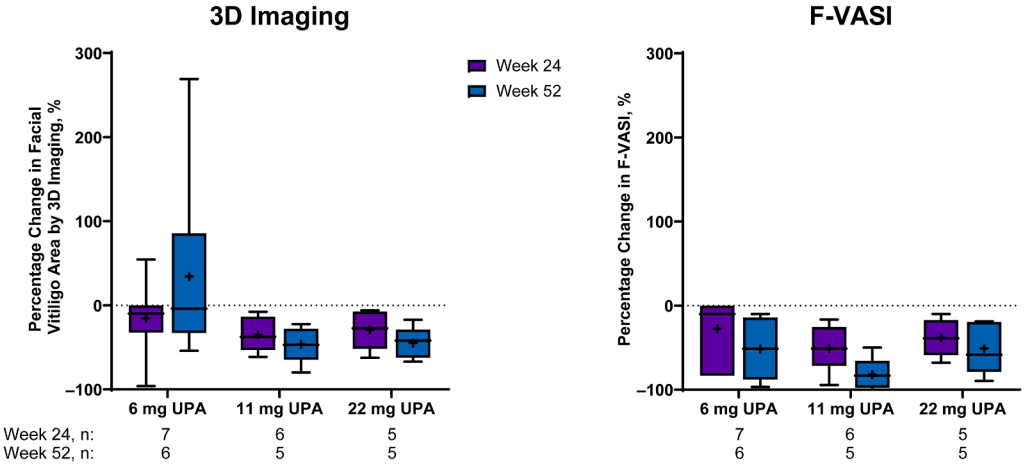

Figure 4. Percentage change from baseline at weeks 24 and 52 in 3D imaging measurements and F-VASI score in UPA treatment groups. Error bars represent the minimum to the maximum data point, and the upper and lower edges of the boxes denote the upper and lower quartiles. The line represents the median, and the plus sign designates the mean of each dataset. 3D, 3-dimensional; F-VASI, Facial Vitiligo Area Scoring Index; UPA, upadacitinib.

a need for dynamic calibration in future imaging algorithms. Additional research with more patients, consistent training, and real-time quality control is needed to fully characterize the observed lack of correlation between 3D imaging and F-VASI at week 52.

This study did not investigate the correlation between 3D imaging for the total body and Total VASI, nor did it evaluate vitiligo response to treatment for the total body. Other limitations included a small study population and limited Fitzpatrick skin type and racial representation. Technical difficulties during the 3D imaging procedure resulted in the exclusion of several images from the analysis, thus reducing the sample size at later time points, which constrains any conclusions. Internet connectivity for sites posed challenges, and 1 patient was excluded from the analysis owing to unshaved facial hair. The 3D imaging system does not acquire images under UV exposure, limiting accuracy in fair-skin patients, and the multiple flashes of intense light during imaging may be bothersome for some patients and operators. The 3D imaging has a sensitivity advantage because it is based on pixel measurement. Yet, the presence of vitiligo skin is binary (yes or no) and is determined by the investigator's subjective naked-eye assessment. In the future, there may be an opportunity to use 3D imaging without the need for human threshold setting. Assessments across Fitzpatrick skin types would be required to train an algorithm to detect areas of vitiligo.

Owing to the steep learning curve and possible subjectivity introduced by investigators manually setting vitiligo threshold intensities, variability could be introduced in a study with a small sample size. Although the sample size in this study was small, this was a pioneer study using a recently developed objective digital 3D imaging technology within a clinical study to determine how it compares with a more subjective measure, such as F-VASI. A larger phase 3 study with more patients will aid in clarifying the relationship between 3D imaging measurements and F-VASI over time and is necessary to demonstrate functionality, reliability, validity, and potential advantages of the platform's objectivity. An ongoing phase 3 UPA study in adults and adolescents with nonsegmental vitiligo (Viti-Up; NCT06118411) is using the Cherry 3D imaging system in a larger patient population as a secondary endpoint. To our knowledge, this study was the first time investigators and technicians used the 3D imaging platform, which resulted in a learning curve in acquiring optimal scans; additional site staff (technicians and investigators) training will be performed before initiation of the next study to streamline the process, prepare for technical difficulties, and reduce variability across groups for more conclusive results. The phase 3 study will also include quality control of images in real time, whereas this study only included a centralized quality-control process twice (when approximately half the patients had completed and at study completion).

The 3D imaging platform enabled the objective measurement of facial vitiligo area, detected pigmentation changes with UPA treatment over time, and provided visual confirmation of those changes. We observed high correlations between the 3D imaging measurements and F-VASI scores at baseline and week 24. Although limited by a small sample size and model constraints, our results support further investigation of this objective technology in evaluating treatments for nonsegmental vitiligo. The ongoing phase 3 UPA study in adults and adolescents with nonsegmental vitiligo (Viti-Up) will further characterize how 3D imaging may be a valuable objective measure for investigating treatment effects. If validated, 3D imaging may serve as a standardized digital endpoint, enabling multicenter comparability in vitiligo trials.

MATERIALS AND METHODS

Patients

Patients aged 18−65 years with nonsegmental vitiligo and an F-VASI ≥0.5 were enrolled in the primary study. The full inclusion and exclusion criteria for the primary study population have been previously published (Passeron et al, 2024). Patients were recruited for this nested substudy from 6 demographically diverse investigational sites in France, Canada, and the United States; all patients at the selected imaging sites were enrolled with the aim of fully representing the Fitzpatrick Skin type phototype spectrum. In the phase 2 study, patients self-identified their race and ethnicity; this information was then documented by authorized and trained site staff. These data were collected because of the United States Food and Drug Administration filing requirements. Patients who were known to experience epileptic episodes, severe headaches, or migraines were excluded.

Study design and treatment

This was a prospective, nested substudy of a randomized, double-blind, PBO-controlled phase 2 trial (NCT04927975) (Passeron et al, 2024). The primary study included a 24-week double-blind treatment period (period 1) followed by a 28-week blinded long-term extension period (period 2). Patients were randomized (2:2:2:1:1) to receive once-daily orally administered 6 mg UPA, 11 mg UPA, 22 mg UPA, or PBO (2 groups; prespecified to switch to blinded 11 mg UPA [PBO/11 mg UPA] or 22 mg UPA [PBO/22 mg UPA] at 24 weeks) throughout the 52-week study (Supplementary Figure S2).

The independent ethics committee or institutional review board at each study site approved the study protocol, informed consent forms, and recruitment materials before patient enrollment. The studies were conducted in accordance with the International Conference for Harmonisation guidelines, applicable regulations, and the Declaration of Helsinki. All patients provided written informed consent for participation in this study and publication of results and images.

Assessments

The 3D imaging and F-VASI were performed for each patient during the baseline visit and at weeks 4, 12, 24, 36, and 52. Investigators independently assessed F-VASI for each patient at every study visit. Because the primary endpoint of the main study occurred at week 24, and the study continued for 52 weeks, week 24 and 52 time points were chosen for analysis in this 3D imaging nested substudy. The primary goal of the substudy was to compare the reliability of the 3D image−based facial vitiligo area measurements with F-VASI scores from the same time point.

The 3D imaging

The Cherry 3D Imaging platform consists of a handheld stereoscopic optical scanner and proprietary imaging software (Trace) that

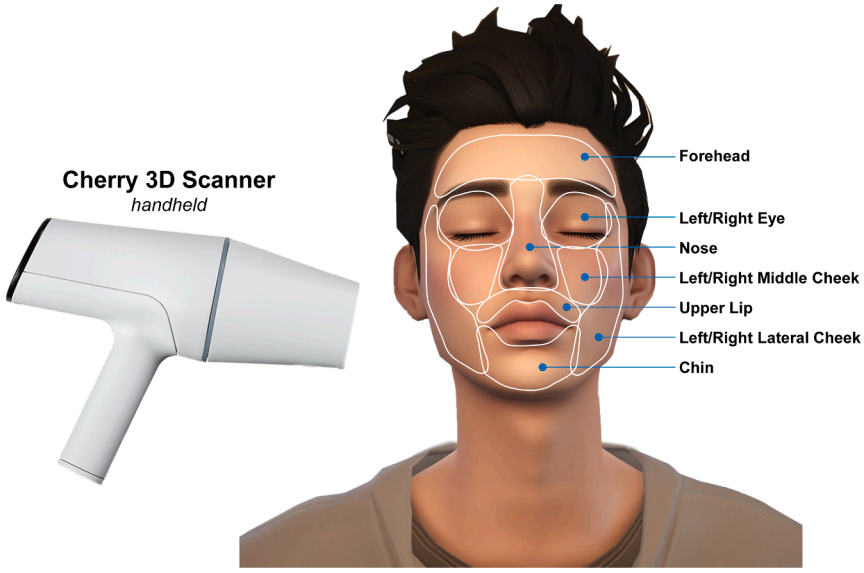

Figure 5. The Cherry 3D scanner and representative patient with 10 predefined facial anatomic regions illustrated. The Cherry imaging platform consists of a handheld stereoscopic optical scanner, a computer, and proprietary imaging software (Trace). The difference in pigmentation between vitiligo and nonvitiligo skin was assessed in 10 predefined facial anatomic regions (and any other regions of interest, as determined by the investigator), and the area measurements were summed to determine the composite facial vitiligo area (cm^2). 3D, 3-dimensional.

captures thousands of images under a range of color illuminations per scan to build a 3D model of the entire face, highlighting skin pigmentation (Figure 5). Each investigator was individually trained in person or virtually by Cherry Imaging personnel; investigators received a certificate on completion. Training occurred before setting thresholds for the first time and enrollment of the first patient. Throughout the study, investigators had access to reference manuals, as needed. First, an imaging technician used the Cherry 3D scanner to scan the patient's face while the scanner simultaneously transferred the raw 3D color image data to the computer. The Cherry Imaging software (Trace) converted the color images into a real-time, gray-scaled, low-resolution 3D model until the scan was complete. Then, a high-resolution color 3D model was constructed. This high-resolution color model was uploaded to the cloud, and the investigator, while examining the patient in person, manually selected the intensity threshold that most accurately captured the areas of vitiligo for each region on the face. This selection allowed the detected vitiligo area to be measured and reported. Investigators were blinded throughout the study. At baseline, an investigator independently determined and manually set 3D vitiligo intensity thresholds to distinguish vitiligo from nonvitiligo skin for 10 predefined facial anatomic regions (forehead, right and left eye, nose, right and left lateral cheeks, right and left middle cheeks, upper lip, and chin) and any other regions of interest, as determined by the investigator. To ensure the accuracy of the 3D model, the investigator was recommended to use Wood's lamp when examining patients while setting the vitiligo intensity threshold. A composite score of total vitiligo area (cm^2) on the face was calculated by summing the automatic vitiligo areas for all regions into a composite score, and the regions and thresholds defined at baseline for each patient were automatically applied for all subsequent postbaseline scans. Images were excluded from data analysis if the original image had noise (hair, makeup, scars, glasses, etc) that significantly impacted the vitiligo area calculation, if there was no corresponding F-VASI result, if the size variability of the automatically generated whole facial region among visits was >10% (indicating incorrect scanning), or if a visual review of the image showed that the facial vitiligo area on the image was impacted because the size variability of the automatically generated whole facial region among visits was 5−10%. The time required for scanning and threshold setting varied on the basis of the experience of the investigator, but generally, facial scanning took approximately 5−10 minutes. Threshold setting took approximately 30 minutes and was dependent on the number of areas with vitiligo, the complexity of the lesions within each area, and the quality of the scan. There was a central quality-control check of the images twice during the study, when approximately half of patients had completed the substudy and at study completion.

Statistical analysis

All analyses were conducted after all patients had completed period 1 and period 2 or prematurely discontinued the study, and the database was locked. All data were reported as observed with no special handling for missing data. The Pearson correlations between the 3D facial vitiligo area and F-VASI at baseline and the percentage change from baseline at week 24 and week 52 were calculated in GraphPad Prism 10 (GraphPad Software). The degree of correlation was prespecified in the protocol to be defined with the following correlation coefficients: very high, >0.9; high, 0.7−0.9; moderate, 0.5−0.7; low, 0.3−0.5; and very low, <0.3. The percentage change from baseline at week 24 and week 52 and the PBO-adjusted treatment effect (the difference between the PBO and UPA groups) at week 24 for the 3D imaging facial vitiligo area and F-VASI were also reported.

ETHICS STATEMENT

The independent ethics committee or institutional review board at each study site approved the study protocol, informed consent forms, and recruitment materials before patient enrollment. The studies were conducted in accordance with the International Conference for Harmonisation guidelines, applicable regulations, and the Declaration of Helsinki. All patients provided written informed consent for participation in this study and publication of results and images.

DATA AVAILABILITY STATEMENT

AbbVie is committed to responsible data sharing regarding the clinical trials that they sponsor. This includes access to anonymized, individual, and trial-level data (analysis datasets) as well as other information (eg, protocols, clinical study reports, or analysis plans) as long as the trials are not part of an

ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications.

These clinical trial data can be requested by any qualified researchers who engage in rigorous, independent, scientific research and will be provided after review and approval of a research proposal, Statistical Analysis Plan, and execution of a Data Sharing Agreement. Data requests can be submitted at any time after approval in the United States and Europe and after acceptance of this manuscript for publication. The data will be accessible for 12 months, with possible extensions considered. For more information on the process or to submit a request, visit the following link: https://vivli.org/ourmember/abbvie/ then select "Home."

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CONFLICT OF INTEREST

AKG is/has been a consultant for AbbVie, Avita Medical, and Viela Bio. KE is a consultant for AbbVie, Incyte, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. SH has been a consultant, speaker, and/or investigator for AbbVie, Acelyrin, Akros, Altius Healthcare, Amgen, Aralez, Arcutis, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Biopharma, Caliway, Celgene, Coherus, Concert Pharma, Cutanea, Dermira, Galapagos, Galderma, Glenmark, Incyte, Janssen, LEO Pharma, Lilly, Novartis, Pedia-Pharm, Pfizer, Regeneron, Reistone, Sandoz, Sanofi, Sun Pharma, UCB, and Vichy. MR has been a consultant, speaker, and/or investigator for AbbVie, Abeona Therapeutics, Biogen, Dermavant, Incyte, Johnson & Johnson, LEO Pharma, Medicxi, Pfizer, Related Sciences, Sanofi, Target RWE, and VisualDx. JS has received grants and/or honoraria from AbbVie, Bristol Myers Squibb, Calypso Biotech, Incyte, LEO Pharma, Lilly, Novartis, Pfizer, Pierre Fabre, Sanofi, Sun Pharmaceuticals, and Viela Bio. He has a patent on matrix metalloproteinase-9 inhibitors and their uses in the prevention or treatment of a depigmenting disorder and 3-dimensional model of depigmenting disorder. SLG, BJS, XH, TH, MC, and HSC are full-time employees of AbbVie and may hold AbbVie stock and/or stock options. TP has received grants and/or honoraria from AbbVie, ACM Pharma, Almirall, Amgen, Astellas, Bristol Myers Squibb, Celgene, Calypso, Galderma, Genzyme/Sanofi, GlaxoSmithKline, Incyte, Janssen, LEO Pharma, Lilly, Novartis, Pfizer, Sun Pharmaceuticals, Takeda, UCB, Vimela, and Vyne Therapeutics. He is the cofounder of NIKAIA Pharmaceuticals. He has registered patents on WNT agonists or GSK3b antagonist for repigmentation of vitiligo and on the use of CXCR3B blockers in vitiligo.

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AUTHOR CONTRIBUTIONS

Conceptualization: SLG, BJS, XH, TH, MC, HSC, TP; Data Curation: SLG, BJS, TH, MC, HSC; Formal Analysis: SLG, BJS, XH, TH, MC, HSC; Funding Acquisition: HSC; Investigation: AKG, KE, SH, MR, JS, SLG, BJS, TH, HSC, TP; Methodology: SLG, BJS, XH, TH, MC, HSC; Project Administration: SLG, BJS, XH, TH, MC, HSC; Resources: AKG, KE, SH, MR, JS, SLG, BJS, TH, TP; Software: SLG, BJS, TH; Supervision: AKG, KE, SH, MR, JS, SLG, BJS, TH, HSC, TP; Validation: SLG, BJS, TH; Visualization: SLG, BJS, XH, TH, MC, HSC; Writing – Review and Editing: AKG, KE, SH, MR, JS, SLG, BJS, XH, MC, HSC, TP; Writing – Original Draft Preparation: AKG, KE, SH, MR, JS, SLG, BJS, XH, TH, MC, HSC, TP

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at 10.1016/j.jid.2025.12.036.

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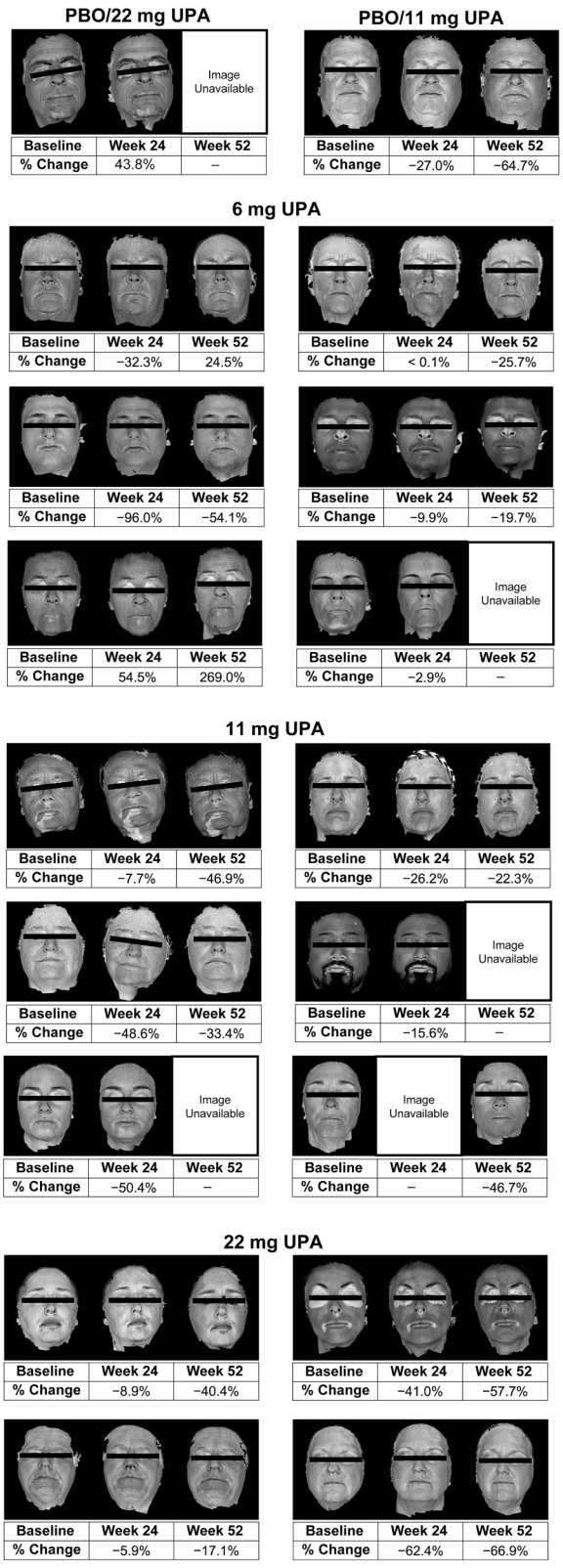
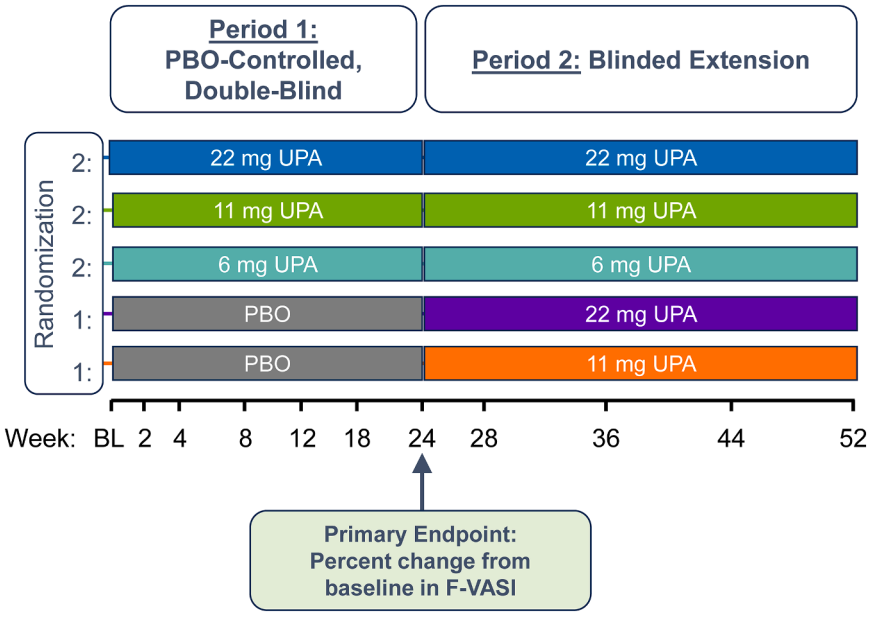


Supplementary Figure S1. The 3D scanned images of patients at baseline, week 24, and week 52. All patients provided written informed consent for publication of images. % Change denotes the percentage change from baseline. 3D, 3-dimentional; PBO, placebo; UPA, upadacitinib.



Supplementary Figure S2. Study design. Patients were randomized into groups at BL. At week 24, patients receiving PBO switched to either 11 or 22 mg UPA. BL, baseline; F-VASI, Facial Vitiligo Area Scoring Index; PBO, placebo; UPA, upadacitinib.