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Reliability and agreement testing of a new automated measurement method to determine facial vitiligo extent using standardized ultraviolet images and a dedicated algorithm

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Abstract

Background Facial repigmentation is the primary outcome measure for most vitiligo trials. The Facial Vitiligo Area Scoring Index (F-VASI) score is often chosen as the primary outcome measure to assess the efficacy of treatments for facial vitiligo. Although useful, this scoring system remains subjective and has several limitations.

Objectives To assess the agreement and reliability of an algorithmic method to measure the percentage depigmentation of vitiligo on the face.

Methods We developed a dedicated algorithm called Vitil-IA® to assess depigmentation on standardized facial ultraviolet (UV) pictures. We then conducted a cross-sectional study using the framework of the ERASE trial (NCT04843059) in 22 consecutive patients attending a tertiary care centre for vitiligo. Depigmentation was analysed before any treatment and, for 7 of them, after 3 and 6 months of narrowband UVB treatment combined with 16 mg methylprednisolone, both used twice weekly. Interoperator and interacquisition repeatability measures were assessed for the algorithm. The results of the algorithmic measurement were then compared with the F-VASI and the percentage of depigmented skin scores assessed by 13 raters, including 7 experts in the grading of vitiligo lesions.

Results Thirty-one sets of pictures were analysed with the algorithmic method. Internal validation showed excellent reproducibility, with a variation of $<3\%$. The percentage of depigmentation assessed by the system showed high agreement with the percentage of depigmentation assessed by raters [mean error (ME) –11.94 and mean absolute error (MAE) 12.71 for the nonexpert group; ME 0.43 and MAE 5.57 for the expert group]. The intraclass correlation coefficient (ICC) for F-VASI was 0.45 [95% confidence interval (CI) 0.29–0.62] and 0.52 (95% CI 0.37–0.68) for nonexperts and experts, respectively. When the results were analysed separately for homogeneous and heterogeneous depigmentation, the ICC for homogeneous depigmentation was 0.47 (95% CI 0.31–0.77) and 0.85 (95% CI 0.72–0.94) for nonexperts and experts, respectively. When grading heterogeneous depigmentation, the ICC was 0.19 (95% CI 0.05–0.43) and 0.38 (95% CI 0.20–0.62) for nonexperts and experts, respectively.

Conclusions We demonstrated that the Vitil-IA algorithm provides a reliable assessment of facial involvement in vitiligo. The study underlines the limitations of the F-VASI score when performed by nonexperts for homogeneous vitiligo depigmentation, and in all raters when depigmentation is heterogeneous.

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What is already known about this topic?

- The Facial Vitiligo Area Scoring Index (F-VASI) score is the primary outcome measure used to assess the efficacy of treatments for vitiligo on the face.
- Although useful, the F-VASI remains subjective and has several limitations.
- Automatic digital analysis systems that provide an accurate and reliable measurement of facial depigmentation are not yet available.

What does this study add?

- Using standardized ultraviolet pictures of patients with vitiligo, we developed a dedicated algorithm to assess the extent of depigmentation on the face.
- The algorithm showed excellent reproducibility and high agreement with the assessments by raters with expertise in vitiligo management.
- The evaluation of F-VASI by nonexpert raters showed significant variation that may introduce bias into the evaluation of treatments in clinical trials.

What are the clinical implications of this work?

- Significant variations in the evaluation of F-VASI score are shown when performed by nonexperts for homogenous vitiligo depigmentation and in all raters when depigmentation is heterogenous.
- Such variations may induce bias in the evaluation of treatments in clinical trials.
- The use of a dedicated algorithm should be considered in future clinical trials.

Vitiligo is an acquired depigmentation of the skin due to melanocytic loss; it has a prevalence of 0.5–2%.[1,2] Long considered to be a benign condition, there is now clear evidence demonstrating that vitiligo can profoundly affect the quality of life (QoL) of affected individuals and their families.[2–5] Several factors modulate the impact of vitiligo on QoL, including the involvement of visible areas, particularly the face.[6] Furthermore, in a recent study using workshops to assess patient preferences for evaluating treatment success, it has been shown that the face is one of the most important areas to be assessed for this outcome.[7] Several new therapeutic approaches are being developed for vitiligo.[8] The most advanced treatments are Janus kinase (JAK) inhibitors (JAKi), with several phase II studies ongoing with oral JAKi (NCT03715829, NCT04927975 and NCT04818346) and phase III studies of topical ruxolitinib completed.[8] Importantly, many of these trials use repigmentation of the face as the primary endpoint for assessing efficacy of treatment. In a recent international study that reported the results from several workshops in which patients assessed the improvement of target lesion(s), it was recommended that future randomized controlled trials in vitiligo should select patches on visible areas (face, neck or hands) as the main outcome for treatment success.[7] Furthermore, in a study evaluating patient preferences for repigmentation, the face was deemed to be the most important area to repigment.[9]

Several scores have been developed to assess the extent of vitiligo. The two most frequently used are the Vitiligo Area Scoring Index (VASI)[10] and the Vitiligo Extent Score (VES).[11] To assess depigmentation of the face specifically, the facial (F)-VASI score has been developed and is often chosen as the primary outcome measure to assess the efficacy of treatments for vitiligo on the face.[12] Although useful, this scoring system remains subjective and has several limitations, including difficulty in matching the fingertip, finger and hand size of the rater to the patient; difficulty in assessing some areas of the face, such as the medial part of the eyelids; difficulty in measuring very small areas of depigmentation; and evaluation of pigment that is heterogenous in appearance, particularly after treatment. These limitations can lead to inter-rater variation, reducing the reliability of the F-VASI. Automated methods to assess the percentage of depigmented areas on the face have the potential of being more precise, reliable and reproducible, and three approaches have been reported. Tracing vitiligo borders on transparent sheets followed by digital analysis is the most reliable method so far, but it has several limitations: it is time consuming and better suited for the evaluation of target lesions; complex patterns are difficult to capture; curved surfaces are difficult to assess; and the technique still relies on human intervention to trace the borders. More recently, techniques based on two- and three-dimensional images have been reported, but they all lack consistency and require human intervention to define or refine the margins, or adjust the sensitivity of the program to capture vitiligo lesions. A recent systematic review concluded that a validated, fully automatic digital analysis system is not yet available, and underlined many weaknesses in the currently available methods.[13] We hypothesized that a new automated algorithm called Vitil-IA® is a repeatable and reliable method that adjusts to operator and acquisition variations and generates the percentage of depigmentation of the face in agreement with the F-VASI reference method.

The objective of this study was to assess the agreement and reliability of the Vitil-IA algorithm to measure the percentage of depigmentation on the face in patients with vitiligo and to compare them to clinical evaluation using F-VASI and percentage repigmentation performed by trained raters.

Patients and methods

We carried out a cross-sectional study conducted as part of the ERASE trial (NCT04843059). The study used photographs of patients before and after treatment who were attending the Department of Dermatology at CHU Nice, France – a tertiary specialty centre for vitiligo.

Study population and sample

Twenty-two patients in ERASE presenting with facial vitiligo were included in this nested study. Patients received narrowband ultraviolet B (NB-UVB) treatment combined with methylprednisolone 16 mg as part of a twice-weekly regimen. Depigmentation was analysed before any treatment, and for seven patients, after 3 and 6 months of treatment (Table S1; see Supporting Information).

Raters

Depigmentation surface and F-VASI were evaluated with photographs by 13 raters divided into two groups. The first group was composed of six dermatologists considered to be nonexperts in vitiligo. All were trained to assess depigmentation and in using the F-VASI. The second group contained seven international dermatologists, all with expertise in vitiligo. Each photograph was evaluated by every rater independently and in a blinded manner.

Development of the automated measurement method

Full-face photographs were taken at each visit with the ColorFace® acquisition system (Newtone Technologies, Lyon, France), an image-capturing device coupled with an ultraviolet (UV) acquisition modality to assist in capturing lesions in all skin types.

Description of the ColorFace acquisition system

In brief, patients wore identical black hairbands and black capes to cover features that might distract from performing the facial assessments correctly [e.g. scalp hair, chest and clothing; Figure S1 (see Supporting Information)]. Using the ColorFace system, patients' faces were imaged with frontal and side views, with their eyes closed and with a neutral facial expression. The ColorFace has a filter wheel and different light-emitting diodes allowing for the acquisition of standardized images in several modalities, including cross-polarized and UV imaging (Figure 1).

Development of the dedicated algorithm Vitil-IA

To assess depigmentation of facial vitiligo, the face was divided into several subareas. Four areas were evaluated in the frontal images (forehead, periorbital, upper perioral and lower perioral) and three areas in each side image (malar, mandibular and nasal). All areas were defined to avoid overlap between regions. Finally, lips and eyebrows were excluded from the evaluation (Figure S2; see Supporting Information).

The areas were defined on an average face and were applied to images of each patient in an automated manner. The borders of each area were defined using specific morphological points on the face that were automatically detected. Following this we performed a quality-control assessment on the measured areas. In each area, a trained operator defined two areas representative of normal skin and depigmented skin, using a marker to initialize the algorithm. Firstly, a preprocessing software algorithm was applied to highlight vitiligo lesions. Secondly, a classification algorithm using the previously described markers was used to segment most of the vitiligo lesions. Finally, a postprocessing enhancement was applied to improve the final segmentation. This entire process was then carried out on each area independently, to adapt to possible morphological and skin disparities, such as beards, shadow areas or heterogenous areas of vitiligo. A new quality control was then performed to visualize the result of the segmentation and a potential final version was produced (Figure 2). Once the segmentations were done, the surface of vitiligo, defined as the number of pixels in the segmentation, was computed. The percentage of depigmentation was defined as the total surface of vitiligo divided by the total surface of area of analysis, with all views combined. Figure 3 shows an example of segmentation and corresponding percentage of depigmentation over time.

Statistical analysis

Inter-rater reliability was assessed through the calculation of the intraclass correlation coefficient (ICC) within experts and nonexpert groups. The ICC model is a two-way random effects model with an absolute agreement as a type of relationship. The coefficient of correlation between F-VASI score and depigmentation surface was also computed to evaluate the association between the scoring methods. Values >0.90 are considered to be excellent, values between 0.75 and 0.9 are considered good, values between 0.5 and 0.75 are considered moderate and values <0.50 are considered poor.[14] The agreement between visual and algorithmic depigmentation assessment was evaluated through the calculation of mean relative error (visual score – algorithmic score) and mean absolute error (absolute value of the relative error). Bland–Altman plots were also computed to visualize the agreement between the two methods.

Additional information on the methods used is available in Appendix S1 (see Supporting Information).

Results

We first assessed interoperator repeatability and found that, regardless of the difficulty in identifying vitiligo lesions, the maximum difference observed with the algorithm was 3.6% (Table S2; see Supporting Information).

We further evaluated interacquisition repeatability and found that, regardless of a slight variation in patient positioning, the maximum difference observed with the algorithm was $<2\%$ (Table S3; see Supporting Information).

As described in the 'Patients and methods' section, vitiligo is sometimes oversegmented and a manual adjustment is made by a technician. In this study, 195 segmentations

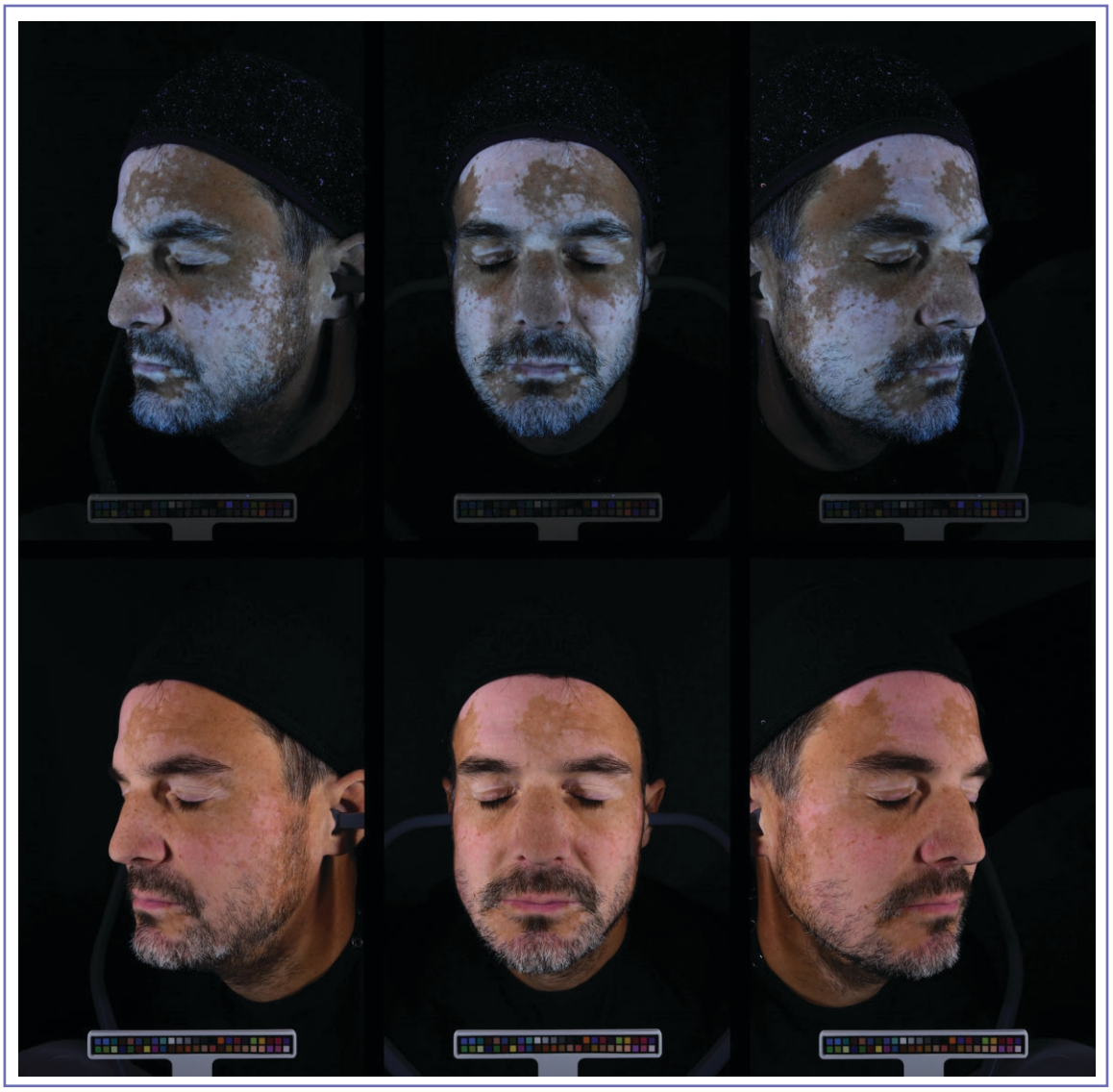

Figure 1 ColorFace® images in the ultraviolet polarized modality (first row) and cross polarized modality (second row). Newtone® has provided permission to use the images generated by the ColorFace acquisition system.

were done, 100 with front-view pictures and 95 in profile. Of 195 segmentations analysed with quality control, 29 manual adjustments were necessary (7 frontal views and 22 profile views). The percentage of segmentations requiring manual adjustment was 14.9%, indicating that the algorithm can successfully detect vitiligo lesions without any intervention in 85.1% of segmentations. Furthermore, the mean difference between the calculation of depigmented areas with and without manual adjustments was only 3.7% (Figure S3; see Supporting Information).

All results presented hereafter are based on analyses performed in each group independently. The values of the correlation coefficients between F-VASI and depigmentation surface assessment for the six nonexpert and seven expert raters are presented in Table S4 (see Supporting Information). The correlation for nonexperts ranged from 0.89 to 0.98, and the correlation coefficients for the seven expert raters ranged between 0.91 and 0.99.

A comparison between the grading of each rater using the F-VASI and facial depigmentation surface score was performed. The ICC was calculated for each group. In the nonexpert group, the ICC was only 0.49 [95% confidence interval (CI) 0.33–0.66] for the facial surface depigmentation score and 0.45 (95% CI 0.29–0.62) for the F-VASI. For the expert group, the ICC was 0.60 (95% CI 0.45–0.75) for the facial surface depigmentation score and 0.52 (95% CI 0.37–0.68) for the F-VASI. We then divided the patients into two groups: group 1 contained patients whose lesions were well demarcated and homogeneous; group 2 contained patients with heterogeneously distributed lesions and/or the presence of punctate repigmentation. The ICC was significantly higher when lesions had homogeneous compared with heterogenous depigmentation (Table 1). In all cases, the ICC of vitiligo experts remained much higher than that of nonexperts. This was associated with a wide variation in the grading of vitiligo among the raters. For nonexpert raters, some evaluations differed by up to 84%. Although better than nonexperts, the maximum discrepancy between expert raters was also high, with two expert raters differing by 55% in the evaluation of one patient.

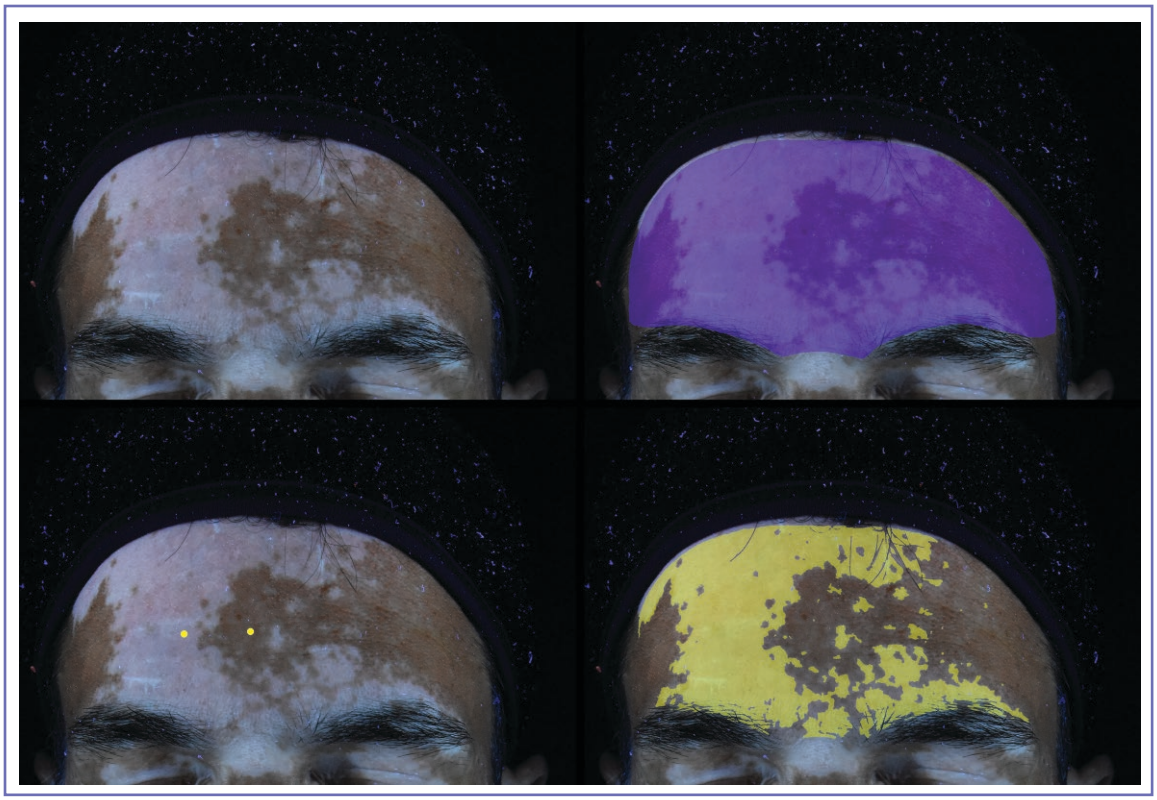

Figure 2 From left to right and top to bottom: initial image, forehead region of interest, vitiligo and normal skin tone markers and final segmentation. Newtone® has provided permission to use the images generated by the ColorFace® acquisition system.

Finally, the raters and algorithm scores were compared. The results of the algorithm were compared with the scores of each rater independently and with the median score of each group. Mean absolute and relative errors are presented in Table 2. The reference for the relative error was the algorithm score, with a positive value indicating that the facial depigmentation surface score was higher for the rater than calculated by the algorithm. The maximum mean relative and absolute errors were –24.46 and 24.99, respectively. The errors were lower for expert raters, with a maximum mean relative and absolute error of –11.01 and 11.80, respectively. When considering median score, errors were globally lower than the scores of single raters. Errors toward the median score remained high for the nonexpert group (mean relative error –11.94, mean absolute error 12.71), but they were low for the expert group (mean relative error 0.43, mean absolute error 5.57). The agreement for each group of raters and their 95% limits of agreement can also be seen in Figure S4 (see Supporting Information). We found higher limits of agreement for the nonexpert group (almost ±44) than for the expert group (almost ±20), as expected.

Discussion

There are currently > 20 interventional studies registered on ClinicalTrials.gov that aim to repigment patients with vitiligo. A better understanding of the mechanisms involved in the pathogenesis of vitiligo has allowed the development of new therapeutic approaches.[8] The therapeutic need remains high and new treatments are much welcome. However, a standardized, automated and reliable measurement of the efficacy of those new approaches is needed to assess their efficacy and compare one study with another.[13] We report here the validation of a dedicated system with a specific algorithm named Vitil-IA. We have shown that the Vitil-IA algorithm provides highly reliable measurements of depigmentation on the face of patients with vitiligo. Excellent repeatability of the algorithm was shown by a mean difference of < 2% from positioning and a maximum of 3.6% in operators' variability. Importantly, we not only assessed patients with well-demarcated and homogenous vitiligo, but also included patients with very fair skin, ill-defined borders and heterogeneous depigmentation. We also calculated the evolution of the depigmented area under treatment, which allowed us to assess the reliability of this outcome measure, show its ability to assess the repigmentation process and test it on lesions where small macules of repigmentation are scattered within depigmented areas.

In addition to its reliability, this system has the main advantage of having very limited human intervention. Only the position of the marker on nondepigmented and depigmented skin, and – when needed – some manual adjustments are performed centrally by a technician. Importantly, we showed that these limited human interventions do not affect the final score by > 4%. In all cases, the operator caring for the patient never has to manipulate any threshold, delimit an area or perform any kind of intervention that could introduce bias to the final calculation of the depigmented areas.

We concomitantly asked nonexpert raters trained to score vitiligo and international experts in vitiligo to assess the same images assessed by the algorithm. Recently, a

Figure 3 Assessment over time by Vitil-IA® of the percentage of depigmentation of the face. (Top row) Baseline (week 0): depigmentation of 45.5%; (middle row) week 12: depigmentation of 20.9%; (bottom row) week 24: depigmentation of 1.1%. Newtone® has provided permission to use the images generated by the ColorFace® acquisition system.

Table 1 Intraclass correlation coefficients (ICCs) according to lesion heterogeneity

	Surface depigmentation: nonexperts (95% CI)	Surface depigmentation: experts (95% CI)	F-VASI: nonexperts (95% CI)	F-VASI: nonexperts (95% CI)
ICC global	0.49 (0.33–0.66)	0.60 (0.45–0.75)	0.45 (0.29–0.62	0.52 (0.37–0.68)
ICC group 1 – homogeneous	0.48 (0.25–0.73)	0.82 (0.60–0.93)	0.47 (0.31–0.77)	0.85 (0.72–0.94)
ICC group 2 – homogeneous	0.17 (0.04–0.42)	0.62 (0.42–0.81)	0.19 (0.05–0.43)	0.38 (0.20–0.62)

CI, confidence interval; F-VASI, Facial Vitiligo Area Scoring Index.

study showed that the evaluation of the F-VASI could be performed on standardized images.[15] The median score of expert raters showed good agreement with a mean relative error close to 0, indicating there was no bias, and a mean absolute error of 5.57, which was almost equal to the lowest value among all raters individually. However, we observed poor reliability between the raters, with an ICC < 0.55 for experts and nonexperts when assessing the F-VASI. This is much less than an ICC of 0.77 in the F-VASI evaluation performed by experts in the study by Merhi *et al*. or in the initial validation study of the F-VASI.[12,15] This poorer correlation could be explained by the fact that we could not include the palmar aspect of the hand or thumb in the image of the face to help calculate the F-VASI. We performed a subanalysis to compare the assessment of homogenous and well-defined lesions to heterogeneous depigmentation, or those with small repigmenting spots. When the grading was done on homogenous pictures, the ICC of the expert group was good (0.85), but it was poor when assessing heterogeneous pictures (0.38). Despite proper training, the ICC for nonexpert raters remained poor for homogeneous depigmentation (0.47) and very poor when it was heterogeneous (0.19). Thus, some evaluations of depigmentation surface differed by up to 55% in the expert group and up to 84% in the nonexpert group. This discrepancy could be a concern given the fact that grading by raters of depigmented areas is the gold standard for assessing the efficacy of treatments in clinical trials. Indeed, in phase II – and particularly phase III studies – the requirement for a large number of patients will lead to the inclusion of centres with nonexpert raters. Our results have shown that, despite training in F-VASI scoring, the ICC is poor for nonexpert raters and becomes very poor when the depigmentation is heterogeneous. We observed large variations in the assessment of the same patient by some experts in the field. Such a discrepancy is problematic when considering the fact that optimal repigmentation of vitiligo usually requires 12–24 months of treatment and that the primary endpoint of clinical trials is usually assessed at 6 months, when the difference between the active drug and placebo is still relatively low. For example, in the phase III study of ruxolitinib cream, the main endpoint ($\geq$ 75% improvement in F-VASI at 6 months) was reached by 29.8% of patients in the ruxolitinib group and 7.4% in the placebo group,[16] which is well within the variability rate we observed between our raters. Although variation in the assessment of disease severity is normal in clinical research and does not affect the relevance of the results as long as allocation is randomized, the potential variability between raters could become an issue in early stages of the development for pharmaceutical companies that might decide to abandon a treatment that was actually effective, or to pursue to a long and costly phase III study when the results with the phase II study were actually poor. This difficulty in assessing efficacy is also critical for regulatory agencies that must assess the results of trials for approval.

Table 2 Mean relative and absolute error of depigmentation surface and correlation of vitiligo with the Vitil-IA® algorithm

	Depigmentation surface (mean relative error)	Depigmentation surface (mean absolute error)
Rater 1	–6.54	11.05
Rater 2	13.49	14.56
Rater 3	–24.46	24.99
Rater 4	–1.98	6.74
Rater 5	–18.01	20.10
Rater 6	–15.22	19.97
Median	–11.94	12.71
Rater expert 1	1.84	5.28
Rater expert 2	–1.84	9.85
Rater expert 3	–11.01	11.80
Rater expert 4	0.11	7.12
Rater expert 5	7.59	9.58
Rater expert 6	3.96	7.28
Rater expert 7	–2.63	9.48
Median	0.43	5.57

One of the main limitations of our study was the absence of patients with skin types V or VI. Although vitiligo lesions are more easily distinguished in darker skin types and scoring is potentially easier, larger studies including all skin types are warranted to confirm these results. As discussed above, another limitation is the absence of patients' thumbs or hands in the evaluation, which might have decreased the reliability of the F-VASI scoring. Finally, the ColorFace acquisition system and the Vitil-IA algorithm were used for the first time in assessing vitiligo. Additional studies are warranted to confirm these encouraging results.

In conclusion, we developed and validated a standardized, automated and reliable image-based system using standardized UV pictures combined with a dedicated algorithm that provides an reliable assessment of the depigmented lesions on the face of patients with vitiligo. The results obtained were highly reproducible compared with evaluations performed by raters. Such a reliable assessment tool should be considered for future clinical trials.

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ultraviolet modality in the ColorFace® acquisition system, and the team in charge of image preparation and processing.

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Conflicts of interest

Q.M.D.B., M.C., A.C.M. and M.-A.S. are employees of Newtone; J.-M.D. is the founder of Newtone. K.E. is a consultant for AbbVie, Incyte, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi and Viela Bio. A.G.P. has served as an investigator for Immune Tolerance Network, Incyte and Pfizer; is a consultant for AbbVie, Arcutis, Avita Medical, Immune Tolerance Network, Incyte, Pfizer, Trifecta, TWi, Viela Bio, Vyne and Villaris; and holds stock options for Tara Medical and Zerigo Health. J.M.B. has acted as a consultant for Pfizer, AbbVie, LaserOptek, Illoco, Cutech Korea and Ilooda. D.R. has received honoraria as a consultant for AbbVie, Abcuro, AltruBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, Dermavant Sciences, Dermira, Incyte, Janssen, Kyowa Kirin, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Revolo Biotherapeutics, Sanofi, Sun Pharmaceuticals, UCB and Viela Bio; has received research support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Dermira, Galderma, Incyte, Janssen, Lilly, Merck, Novartis, Pfizer and Regeneron Pharmaceuticals; and has served as a paid speaker for AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals and Sanofi. A.W. has received research grants from AVITA Medical, Lumenis and Merz; is a consultant for AVITA Medical, Lumenis, Novartis, Almirall, Janssen, AbbVie and InCyte; and has received equipment from Humeca and PerfAction. M. Böhm is a consultant for Incyte, Pfizer, AbbVie, Jansen and LEO Pharma; and has received honoraria from Incyte, Isispharma, Pfizer, AbbVie, Jansen and LEO Pharma. P.B. has received grants or honoraria from LEO Pharma, Pierre Fabre, BMS and Eli Lilly. P.-M.D. has received grants or honoraria from Almirall, Eli Lilly, Sanofi and UCB. T.P. has received grants and/or honoraria from AbbVie, ACM Pharma, Amgen, Almirall, Boehringer Ingelheim, Bristol-Myers Squibb, Calypso, Celgene, Galderma, Genzyme/Sanofi, GlaxoSmithKline, Incyte, Janssen, LEO Pharma, Eli Lilly, Novartis, Pfizer, Roivant, Sun Pharmaceuticals, UCB and Vyne therapeutics; is the co-founder of YUKIN Therapeutics; and has patent rights on the use of CXCR3B, WNT agonists and GSK3b in the treatment of vitiligo. C.B., M.A., D.P., M. Blaise and V.P. declare no conflicts of interest.

Data availability

Anonymized data are available for scientific purposes upon reasonable request to passeron@unice.fr

Ethics statement

All patients gave written informed consent to participate in this study and written approval for the use and publication of their images (Institutional Review Board approval number 2021-A00012-39; NCT04843059).

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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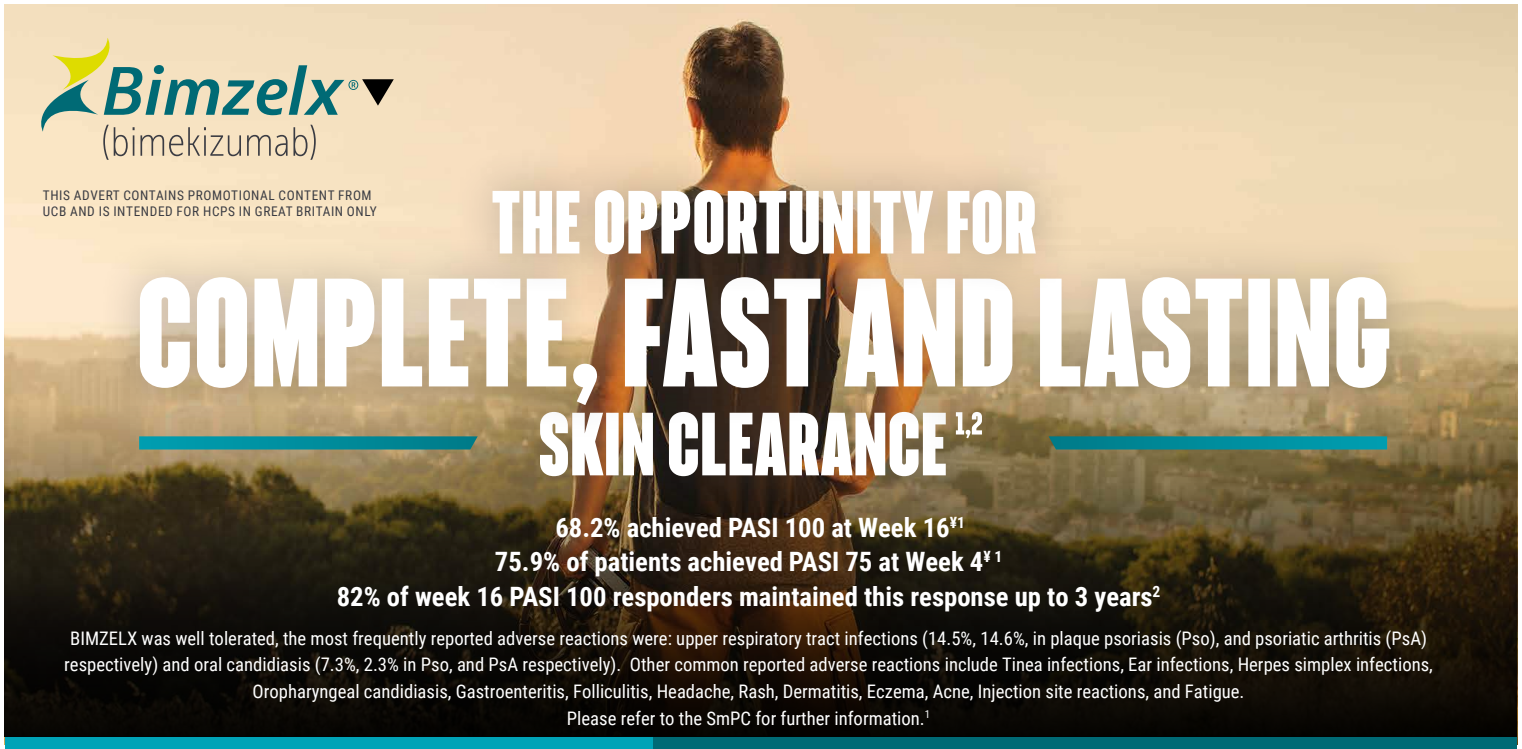
Bimzelx® ▼
(bimekizumab)

THIS ADVERT CONTAINS PROMOTIONAL CONTENT FROM UCB AND IS INTENDED FOR HCPS IN GREAT BRITAIN ONLY



THE OPPORTUNITY FOR COMPLETE, FAST AND LASTING SKIN CLEARANCE[1,2]

68.2% achieved PASI 100 at Week 16[¥1]
75.9% of patients achieved PASI 75 at Week 4[¥1]
82% of week 16 PASI 100 responders maintained this response up to 3 years[2]

BIMZELX was well tolerated, the most frequently reported adverse reactions were: upper respiratory tract infections (14.5%, 14.6%, in plaque psoriasis (Pso), and psoriatic arthritis (PsA) respectively) and oral candidiasis (7.3%, 2.3% in Pso, and PsA respectively). Other common reported adverse reactions include Tinea infections, Ear infections, Herpes simplex infections, Oropharyngeal candidiasis, Gastroenteritis, Folliculitis, Headache, Rash, Dermatitis, Eczema, Acne, Injection site reactions, and Fatigue.
Please refer to the SmPC for further information.[1]

Challenge expectations in plaque psoriasis[1,2]

Visit **Bimzelx.co.uk** to discover more.

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Footnotes: ¥co-primary endpoints PASI 90 and IGA 0/1 at Week 16

Pso - Plaque Psoriais; PsA - Psoriatic Athritis

BIMZELX® (Bimekizumab) is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. Bimzelx, alone or in combination with methotrexate, is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). Please refer to the SmPC for further information.[1]

PRESCRIBING INFORMATION FOR HCP'S IN GREAT BRITAIN

BIMZELX® ▼ (Bimekizumab) is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy; and for active psoriasis arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs), alone or in combination with methotrexate.[1] (Please consult the Summary of Product Characteristics (SmPC) before prescribing).

Active Ingredient: Bimekizumab – solution for injection in pre-filled syringe or pre-filled pen: *160 mg of bimekizumab in 1 mL of solution (160mg/mL).* **Indications:** Moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. Alone or in combination with methotrexate, for active psoriatic arthritis in adults who have had an inadequate response or intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). Adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) who have responded inadequately or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs). Adults with active ankylosing spondylitis who have responded inadequately or are intolerant to conventional therapy. **Dosage and Administration:** Should be initiated and supervised by a physician experienced in the diagnosis and treatment of conditions for which Bimzelx is indicated. **Recommended dose:** Plaque Psoriasis: 320 mg (given as two subcutaneous injections of 160 mg each) at week 0, 4, 8, 12, 16 and every 8 weeks thereafter. Psoriatic arthritis: 160 mg (given as 1 subcutaneous injection of 160 mg) every 4 weeks. For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, the recommended dose is the same as for plaque psoriasis. After 16 weeks, regular assessment of efficacy is recommended and if a sufficient clinical response in joints cannot be maintained, a switch to 160 mg every 4 weeks can be considered. Axial spondyloarthritis (nr-axSpA and AS): 160 mg (given as 1 subcutaneous injection) every 4 weeks. For patients with plaque psoriasis (including psoriatic arthritis with coexistent moderate to severe psoriasis) and a body weight ≥ 120 kg who did not achieve complete skin clearance at week 16, 320 mg every 4 weeks after week 16 may further improve treatment response. Consider discontinuing if no improvement by 16 weeks of treatment. Renal or hepatic impairment: No dose adjustment needed. Elderly: No dose adjustment needed. Administer by subcutaneous injection to thigh, abdomen or upper arm. Rotate injection sites and do not inject into psoriatic plaques or skin that is tender, bruised, erythematous or indurated. Do not shake pre-filled syringe or pre-filled pen. Patients may be trained to self-inject. **Contraindications:** Hypersensitivity to bimekizumab or any excipient; Clinically important active infections (e.g. active tuberculosis). **Warnings and Precautions:** Record name and batch number of administered product. *Infection:* Bimekizumab may increase the risk of infections e.g. upper respiratory tract infections, oral candidiasis. Caution when considering use in patients with a chronic infection or a history of recurrent infection. Must not be initiated if any clinically important active infection until infection resolves or is adequately treated. Advise patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops an infection, the patient should be carefully monitored. If the infection becomes serious or is not responding to standard therapy do not administer bimekizumab until infection resolves. *TB:* Evaluate for TB infection prior to initiating bimekizumab – do not give if active TB. While on bimekizumab, monitor for signs and symptoms of active TB. Consider anti-TB therapy prior to bimekizumab initiation if past history of latent or active TB in whom adequate treatment course cannot be confirmed. *Inflammatory bowel disease:* Bimekizumab is not recommended in patients with inflammatory bowel disease. Cases of new or exacerbations of inflammatory bowel disease have been reported. If inflammatory bowel disease signs/symptoms develop or patient experiences exacerbation of pre-existing inflammatory bowel disease, discontinue bimekizumab and initiate medical management. *Hypersensitivity:* Serious hypersensitivity reactions including anaphylactic reactions have been observed with IL-17 inhibitors. If a serious hypersensitivity reaction occurs, discontinue immediately and treat. *Vaccinations:* Complete all age appropriate immunisations prior to bimekizumab initiation. Do not give live vaccines to bimekizumab patients. Patients may receive inactivated or non-live vaccinations. **Interactions:** A clinically relevant effect on CYP450 substrates with a narrow therapeutic index in which the dose is individually adjusted e.g. warfarin, cannot be excluded. Therapeutic monitoring should be considered. **Fertility, pregnancy and lactation:** Women of child-bearing potential should use an effective method of contraception during treatment and for at least 17 weeks after treatment. Avoid use of bimekizumab during pregnancy. It is unknown whether bimekizumab is excreted in human milk, hence a risk to the newborn/infant cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Bimzelx therapy. No data available on human fertility. **Driving and use of machines:** No or negligible influence on ability to drive and use machines. **Adverse Effects:** Refer to SmPC for full information. Very Common *(≥ 1/10):* upper respiratory tract infection; Common *(≥ 1/100 to < 1/10):* oral candidiasis, tinea infections, ear infections, herpes simplex infections, oropharyngeal candidiasis, gastroenteritis, folliculitis; headache, rash, dermatitis and eczema, acne, injection site reactions, fatigue; Uncommon *(≥ 1/1,000 to < 1/100):* mucosal and cutaneous candidiasis (including oesophageal candidiasis), conjunctivitis, neutropenia, inflammatory bowel disease. Storage precautions: Store in a refrigerator (2°C – 8°C), do not freeze. Keep in outer carton to protect from light. Bimzelx can be kept at up to 25°C for a single period of maximum 25 days with protection from light. Product should be discarded after this period or by the expiry date, whichever occurs first.

Legal Category: POM

Marketing Authorisation Numbers: PLGB 00039/0802 (Pre-filled Syringe), PLGB 00039/0803 (Pre-filled Pen).

UK NHS Costs: £2,443 per pack of 2 pre-filled syringes or pens of 160 mg each.

Marketing Authorisation Holder: UCB Pharma Ltd, 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom.

Further information is available from: UCB Pharma Ltd, 208 Bath Road, Slough, Berkshire, SL1 3WE. Tel: 0800 2793177 Email: ucbcares.uk@ucb.com

Date of Revision: August 2023 (GB-P-BK-AS-2300047)

Bimzelx is a registered trademark.

Adverse events should be reported. Reporting forms and information can be found at http://www.mhra.gov.uk/yellowcard. Adverse events should also be reported to UCB Pharma Ltd at ucbcares.uk@ucb.com or 0800 2793177.

References: 1. BIMZELX (bimekizumab) SmPC. Available at: https://www.medicines.org.uk/emc/product/12834/smpc. Accessed September 2023 **2.** Strober et al. [BE BRIGHT open label extension] Br J Dermatol. 2023. 188(6): 749-759.

GB-BK-2300081 Date of preparation: September 2023.

Inspired by patients. Driven by science.

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