A randomized, controlled, split-face, double-blind comparison of a multimodality pigment-correcting serum containing lotus sprout extract versus hydroquinone for moderate to severe facial hyperpigmentation, including melasma, in a diverse population

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Background: Hyperpigmentation results in uneven skin tone, with darker skin types disproportionately affected.

Objective: Assess efficacy and safety of a novel, hydroquinone (HQ)-free, multimodal pigment-correcting serum (Advanced Brightening Treatment [ABT]) versus 4% HQ in moderate to severe hyperpigmentation, including melasma.

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Funding sources: Allergan Aesthetics, an AbbVie Company, funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. No honoraria or payments were made for authorship. Medical writing support was provided by Lilly Shelomyanov, MS of Peloton Advantage, LLC, an OPEN Health company, and funded by Allergan Aesthetics, an AbbVie Company.

Data from this study have been previously published as a poster presentation (2023 Winter Clinical Hawaii Dermatology Conference; Kohala Coast, HI; January 13-18, 2023): Makino E, Huang P, Acevedo S, Vaughan C, Mehta R. Efficacy of novel multimodality pigment-correcting serum for moderate to severe facial hyperpigmentation, including melasma, in a 12-week, split-face, double-blind, randomized controlled trial. *SKIN: The Journal of Cutaneous Medicine*. 2023;*7*(2):S190.

Patient consent: Consent for the publication of recognizable patient photographs or other identifiable material was obtained by the authors and included at the time of article submission to the journal stating that all patients gave consent with the understanding that this information may be publicly available.

IRB approval status: The study was approved by the institutional review board (Advarra IRB) at the study center, conducted in compliance with all applicable guidelines for the protection of human subjects for research as outlined in 21 CFR 50 and the accepted standards for Good Clinical Practice and International Conference on Harmonization.

Data sharing: AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymized, individual, and trial-level data (analysis data sets), as well as other information (eg, protocols and 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 following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). 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."

Accepted for publication February 20, 2024.

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2666-3287

https://doi.org/10.1016/j.jdin.2024.02.017

Methods: In this split-face study, ABT and 4% HQ were applied topically on randomly assigned facial sides twice daily for 12 weeks. Hyperpigmentation, skin tone evenness, modified Melasma Area and Severity Index (mMASI), Melasma Quality of Life Questionnaire (MelasQoL), self-assessment questionnaires, and tolerability were assessed.

Results: Subjects (n = 113; melasma subgroup, n = 44) were Asian (22%), Black/African American (27%), Hispanic (22%), and White/Caucasian (28%). ABT achieved comparable results to 4% HQ. ABT was well tolerated and resulted in improvement versus baseline at all visits in mean overall hyperpigmentation (−11.7% at week 12; $P \leq .001$), skin tone evenness (−8.8%, $P \leq .005$), and, in the melasma subgroup, mMASI (−50.6%; $P \leq .011$) and MelasQoL scores (33.0 vs 46.6 for week 12 vs baseline, respectively; $P \leq .011$), with similar results across racial subgroups. ABT was preferred over 4% HQ, with high satisfaction rate (≥89%).

Limitations: Quality of life improvements per treatment were not evaluated separately.

Conclusion: Efficacy and safety of ABT is comparable to 4% HQ in individuals with facial hyperpigmentation, including melasma, across multiple racial/ethnic backgrounds. (JAAD Int 2024;15:206-19.)

Key words: brightening; even and correct advanced brightening treatment; lotus sprout extract; melanosis; pigmentation disorders; skin care.

INTRODUCTION

Hyperpigmentation is characterized by uneven skin tone and photoaged appearance due to excess melanin production.[1,2] Facial hyperpigmentation can be aesthetically and psychologically distressing, potentially impacting an individual's quality of life.[3-7] The condition is a frequent reason for seeking dermatological consultations, regardless of age, skin color, and gender.[1,8] Hyperpigmentation and uneven skin tone are signs of skin aging that can be of greater concern in individuals with skin of color.[9,10]

Melasma is an acquired hyperpigmentation disorder that manifests as irregular brown patches on the skin.[8,11,12] It affects up to 6 million people in the United States,[13] is more common in people 20 to 40 years of age, and has a prevalence rate of up to 50% in higher-risk populations, including individuals with darker skin types.[11,14] Melasma occurs primarily on sun-exposed areas of the neck and face[14] and has been associated with genetic influences, UV radiation, pregnancy, and hormonal therapies. Melasma is frequently challenging to treat and often requires long-term therapy.[15] Complete clearance is rare, and relapse is high once treatment is discontinued.[11,15]

CAPSULE SUMMARY

- Our hydroquinone-free, multimodal pigment-correcting topical serum, was effective and well tolerated in treating facial hyperpigmentation, including melasma, across diverse racial and ethnic backgrounds and skin types.
- This cosmeceutical offers a possible treatment option for chronic, challenging-to-treat hyperpigmentation, including melasma, in a broad range of skin types.

Hyperpigmentation is typically treated using a combination approach involving topical agents and in-office cosmetic procedures, including chemical peels, laser/light therapy, microneedling, and microdermabrasion.[8,11] Hydroquinone (HQ) 4% is the prescription-strength mainstay therapy for hyperpigmentation,[16,17] but has tolerability and safety issues that may limit its long-term use,[14,17] including irritation, allergic contact dermatitis, inflammation, xeroderma, stinging, and ochronosis.[17,18] HQ-free cosmeceutical topicals for long-term control of hyperpigmentation, including melasma, are needed that are more effective and tolerable across a range of racial and ethnic backgrounds, including those with darker skin types.[19,20]

Advanced Brightening Treatment (ABT) is a novel, HQ-free, multimodal pigment-correcting serum designed to target cellular pathways that contribute to hyperpigmentation. The multimodal formulation of ABT features a proprietary complex that includes lotus sprout extract, which disrupts melanosome development and function and promotes melanosome degradation; tranexamic acid, which targets melanocyte activation; and niacinamide, an antiinflammatory that impacts

Abbreviations used:

ABT: Advanced Brightening Treatment
FST: Fitzpatrick skin type
HQ: hydroquinone
MelasQoL: Melasma Quality of Life Questionnaire
mMASI: modified Melasma Area and Severity Index

melanocyte activation, melanin distribution, and barrier function.[21] The current study compares the efficacy and tolerability of ABT and 4% HQ in a diverse population with moderate to severe facial hyperpigmentation, including a subgroup of subjects with melasma.

METHODS

Study design

This split-face, double-blind, randomized, controlled, 12-week clinical study was conducted from July 21, 2021 to December 15, 2021. Healthy female subjects (aged 30-65 years) with Fitzpatrick skin types (FSTs) I to VI, with moderate to severe hyperpigmentation on both sides of the face (scores of 4-9 per modified Griffiths scale; 0 = none, 9 = severe), and with ≤1 difference in scores between sides, were enrolled. Enrollment of at least 25 subjects in each of the following ethnic/racial groups was required: Asian, Black/African American, Hispanic, and White/Caucasian. Furthermore, at least 30 subjects with epidermal facial melasma, a score ≥2 on the Melasma Severity Rating Scale, and FST III or higher were required to enroll. Exclusion criteria included a history of skin cancer within the past 5 years, current use of oral or topical prescription medications for acne, and use of over-the-counter retinol-containing antiwrinkle, skin-lightening, or other topical or system products within the previous 4 weeks.

ABT (Even & Correct Advanced Brightening Treatment; SkinMedica, Allergan Aesthetics, an AbbVie Company) was applied topically on a randomly assigned facial side and 4% HQ was applied on the opposite facial side twice (AM/PM) daily for 12 weeks. A basic skincare regimen was also applied (Facial Cleanser [AM/PM], Ultra Sheer Moisturizer [AM/PM], Essential Defense Mineral Shield Broad Spectrum SPF 35 Sunscreen [AM only]; SkinMedica, Allergan Aesthetics, an AbbVie Company). Subjects were instructed to avoid extended periods of sun exposure and to wear protective clothing. Study visits occurred at baseline and weeks 2, 4, 8, and 12 (Fig 1).

All subjects provided written informed consent prior to study enrollment.

Assessments

Hyperpigmentation and skin tone evenness. Investigator-assessed clinical grading of hyperpigmentation and skin tone evenness was

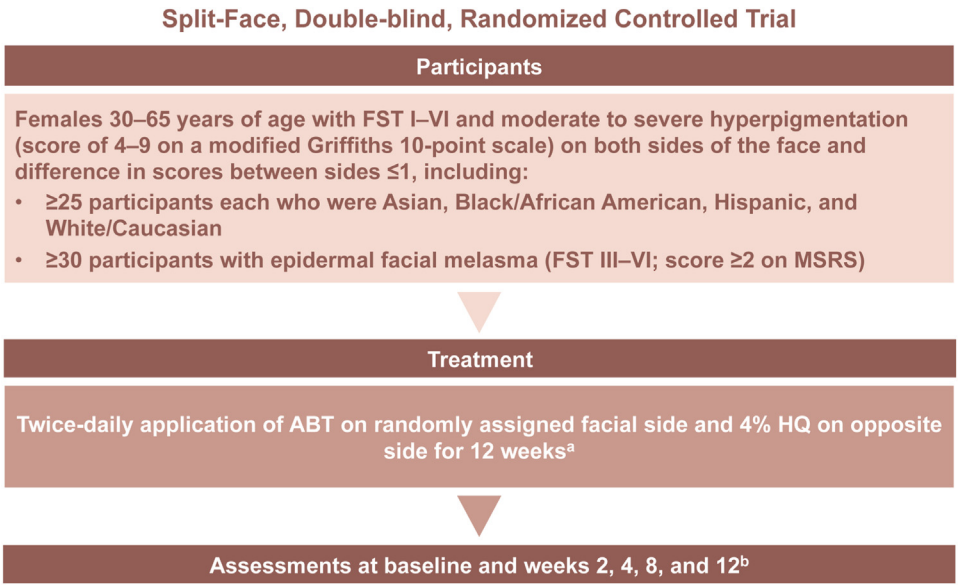

Fig 1. Study design comparing efficacy and tolerability of Advanced Brightening Treatment and 4% hydroquinone. *ABT*, Advanced Brightening Treatment; *FST*, Fitzpatrick skin type; *HQ*, hydroquinone; *MSRS*, Melasma Severity Rating Scale. [a]All subjects were additionally instructed to wash their face twice daily using the SkinMedica Facial Cleanser and apply the SkinMedica Ultra Sheer Moisturizer (AM/PM) and SkinMedica Essential Defense Mineral Shield SPF 35 (AM only) to the entire face. [b]Self-assessment questionnaires completed at weeks 2, 4, 8, and 12.

Table I. Subject disposition and baseline characteristics

Characteristic	All subjects (*N* = 113)	Melasma subgroup (*n* = 44)
Age, y		
Mean (SD)	52.6 (8.0)	49.8 (7.7)
Median (minimum, maximum)	53.0 (31.0, 65.0)	51.0 (31.0, 63.0)
Sex, female, *n* (%)	113 (100)	44 (100)
Race and ethnic subgroup, *n* (%)		
Asian	25 (22.1)	11 (25.0)
Black or African American	31 (27.4)	9 (20.5)
Hispanic	25 (22.1)	12 (27.3)
White or Caucasian	32 (28.3)	12 (27.3)
Fitzpatrick skin type, *n* (%)		
I	1 (0.9)	0
II	11 (9.7)	0
III	48 (42.5)	26 (59.1)
IV	25 (22.1)	11 (25.0)
V	24 (21.2)	6 (13.6)
VI	4 (3.5)	1 (2.3)
Hyperpigmentation score at baseline, mean	ABT side, 4.95 4% HQ side, 4.95	ABT side, 5.16, 4% HQ side, 5.17
mMASI grading at baseline, mean	NA	ABT side, 4.50, 4% HQ, 4.42

ABT, Advanced Brightening Treatment; *HQ*, hydroquinone; *mMASI*, modified Melasma Area and Severity Index.

performed separately on each side of the face at each study visit and scored on a modified Griffiths scale as none (score of 0, best possible condition), mild (1-3), moderate (4-6), and severe (7-9, worst possible condition).

Modified Melasma Area and Severity Index. Melasma severity was assessed using the modified Melasma Area and Severity Index (mMASI)[22] for the melasma subgroup only at each study visit, with left and right sides assessed separately.

Melasma Quality of Life Questionnaire. A validated Melasma Quality of Life (MelasQoL) Questionnaire was used to measure the emotional and psychological impact of melasma in the melasma subgroup at each study visit. Higher scores indicate worse melasma-related health-related quality of life. MelasQoL is validated for full-face melasma[23]; as such, each treatment side was not evaluated separately.

Self-assessment questionnaires. Subjects completed self-assessment questionnaires at weeks 2, 4, 8, and 12 on self-perceived efficacy, test product attributes, overall improvement, overall satisfaction, and face side (ie, test product) preference, all evaluated separately on left and right sides of face.

Standardized photography and image analysis. Subjects were photographed using VISIA CR photo station (Canfield Imaging Systems) with a Canon Mark II digital SLR camera (Canon Incorporated) at each study visit.

Tolerability parameters. Tolerability evaluations, including investigator-assessed objective irritation parameters (erythema, edema, and dryness) and subject-reported subjective irritation parameters (burning, stinging, and itching), were performed at each study visit on a 4-point scale, where 0 = none, 1 = mild, 2 = moderate, and 3 = severe.

Statistical methods

All statistical analyses were conducted on the intent-to-treat population, defined as all subjects who received treatment and participated in at least 1 postbaseline evaluation.

For efficacy parameters, change from baseline was used to compare treatments, and a descriptive statistical summary was developed (eg, mean, SD). The testing hypothesis was that the change from baseline is equal between the 2 treatments, using Wilcoxon's signed rank test for clinical grading of efficacy parameters, mMASI, self-assessment questionnaires, and tolerability evaluations, and paired *t* test for MelasQoL. All statistical tests were 2 sided with significance set at $\alpha = 0.05$ (unless otherwise specified). Statistical analyses were performed using SAS software version 9.4 (SAS Statistical Institute).

RESULTS

Subjects

A total of 113 female subjects, including 44 in the melasma subgroup, were enrolled (Table I), with

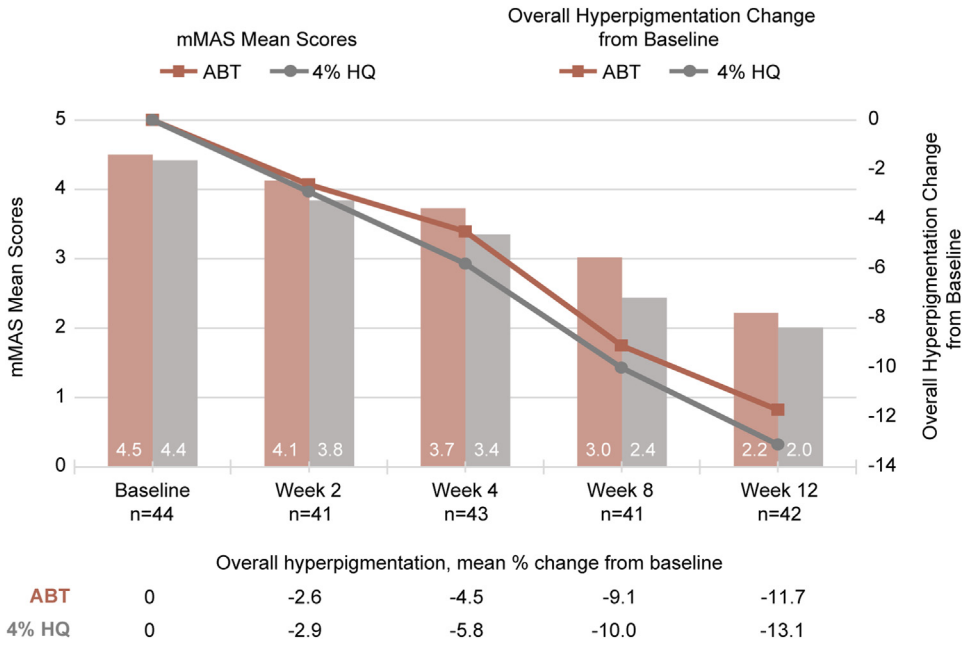

Fig 2. Mean percent change from baseline in overall hyperpigmentation in all subjects (*lines*) and mean scores for modified Melasma Area and Severity Index in melasma subgroup (*bars*) in the Advanced Brightening Treatment and 4% hydroquinone treatment groups. All time points are statistically significant vs baseline (overall hyperpigmentation: $P \leq .001$; modified Melasma Area and Severity Index: $P \leq .011$). No significant differences between treatments. Modified Melasma Area and Severity Index score range = 0 to 12 for split-face (half-face). *ABT*, Advanced Brightening Treatment; *HQ*, hydroquinone; *mMASI*, modified Melasma Area and Severity Index.

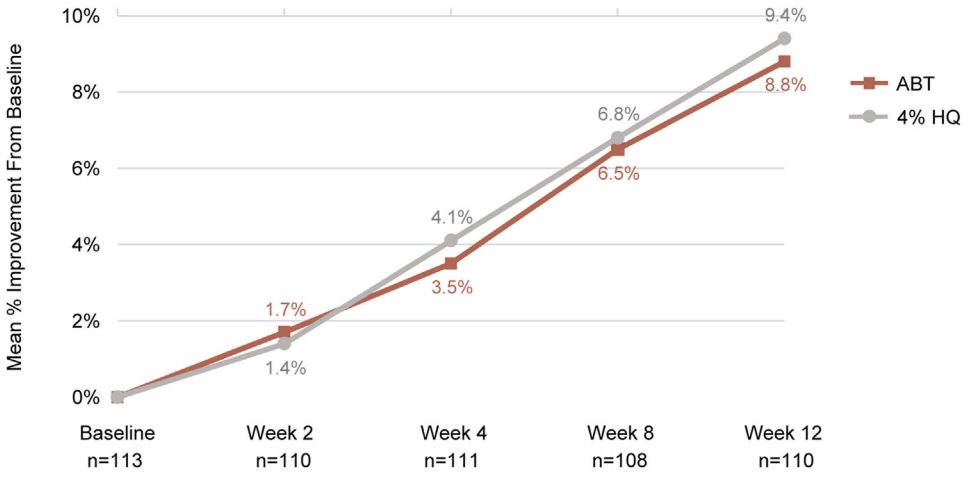

Fig 3. Mean percent change from baseline in skin tone evenness in all subjects in the Advanced Brightening Treatment and 4% hydroquinone treatment groups. All time points are statistically significant vs baseline ($P \leq .005$). No significant differences between treatments. *ABT*, Advanced Brightening Treatment; *HQ*, hydroquinone.

approximately equivalent representation of each race and ethnic subgroup (Asian, Black/African American, Hispanic, White/Caucasian). Nearly half (46.9%) of subjects had FST IV to VI. The melasma subgroup also had approximately equal racial/ethnic representation, and included FST III to VI.

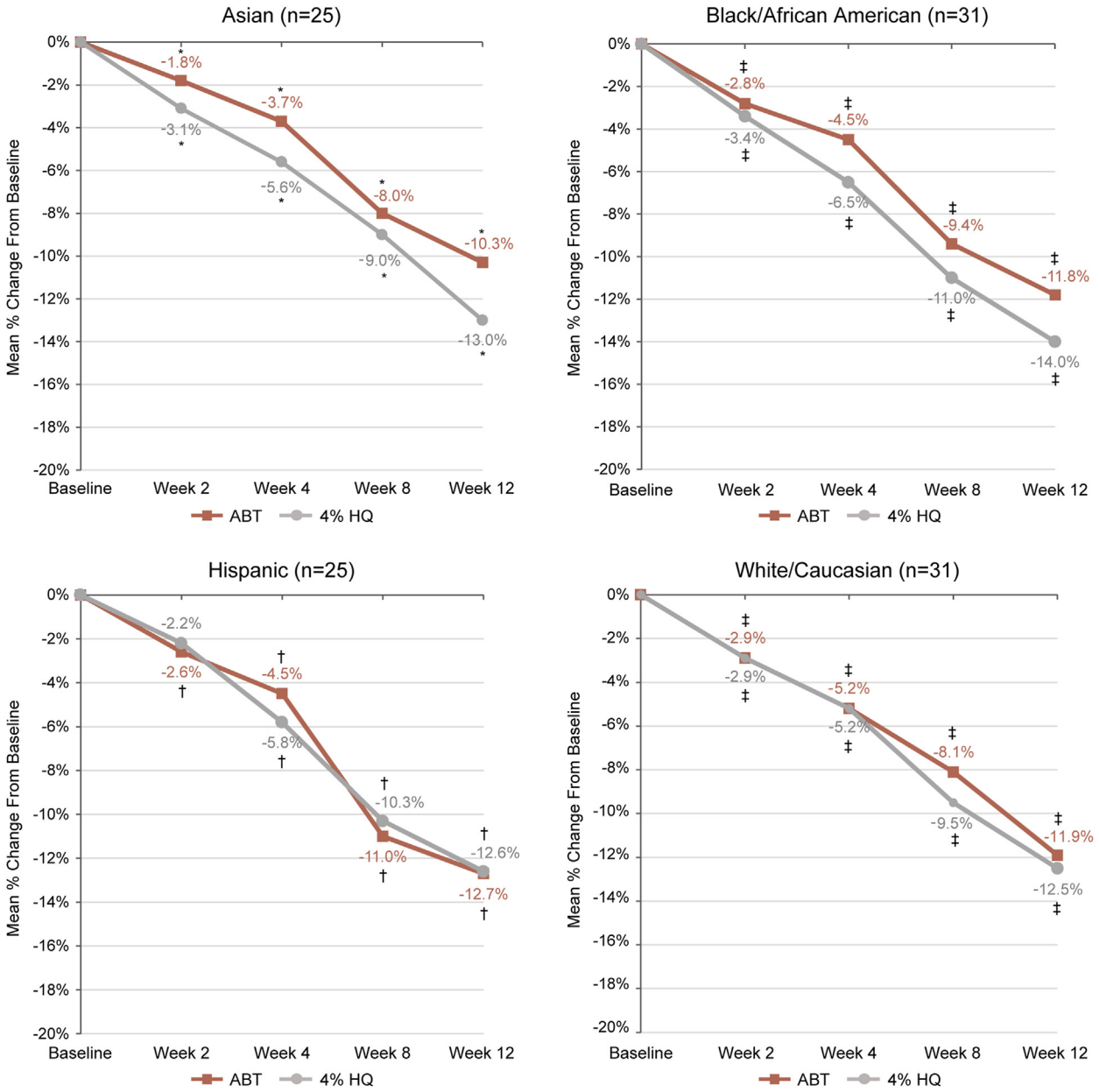

Fig 4. Mean percent change from baseline in overall hyperpigmentation in all subjects by race and ethnic subgroups in the Advanced Brightening Treatment and 4% hydroquinone treatment groups. *ABT*, Advanced Brightening Treatment; *HQ*, hydroquinone. *$P \leq .043$; †$P \leq .031$; ‡$P \leq .001$ vs baseline. No statistical significance between treatments.

Efficacy

Overall hyperpigmentation and skin tone evenness in all subjects. For both ABT and 4% HQ, statistically significant improvements versus baseline were observed as early as week 2 for overall hyperpigmentation (Fig 2) and skin tone evenness (Fig 3), with continuing significant improvements at each follow-up visit through week 12 ($P \leq .005$). Efficacy of ABT was equivalent to that of 4% HQ, with no significant differences between treatments.

Results were similar across all ethnicities, with significant improvements versus baseline in overall hyperpigmentation observed at week 2 for both ABT and 4% HQ (week 4 for the Hispanic subgroup) and continuing through week 12 ($P \leq .043$ across all

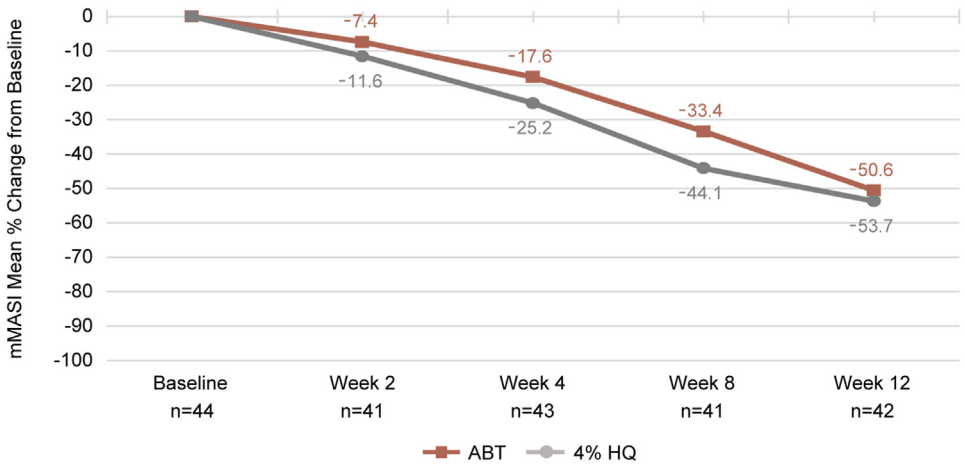

Fig 5. Mean percent improvement from baseline for modified Melasma Area and Severity Index in melasma subgroup in the Advanced Brightening Treatment and 4% hydroquinone treatment groups. No significant difference between treatments. All time points are statistically significant vs baseline ($P \leq .011$). *ABT*, Advanced Brightening Treatment; *HQ*, hydroquinone; *mMASI*, modified Melasma Area and Severity Index.

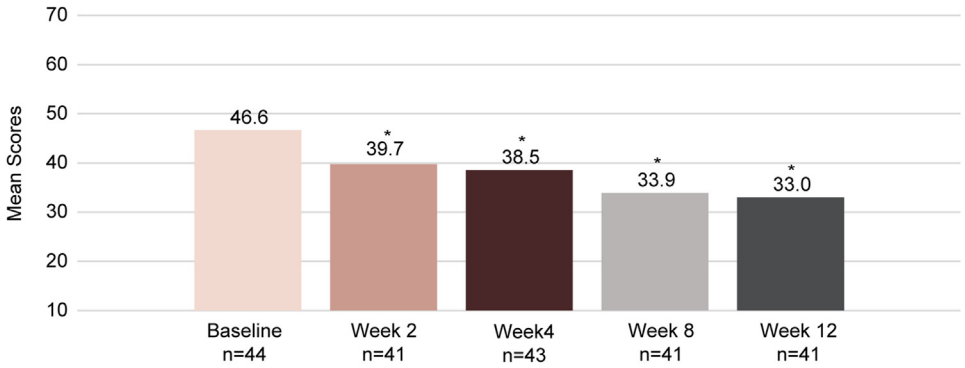

Fig 6. Mean scores for Melasma Quality of Life Questionnaire at week 12 in the melasma subgroup across both sides of the face combined (Advanced Brightening Treatment and 4% hydroquinone treatment groups). No significant difference between treatments. *$P \leq .011$ vs baseline.

ethnicities; Fig 4). Similarly, skin tone evenness was significantly improved with ABT and 4% HQ starting at week 2 in Black/African American subjects and at week 4 in Asian, Hispanic, and White/Caucasian subjects through week 12 ($P \leq .031$ across all ethnicities). ABT achieved comparable results to 4% HQ across all ethnicities, with no significant differences between treatments.

mMASI in melasma subgroup. Compared with baseline, both ABT and 4% HQ significantly improved melasma severity as measured using mMASI at each time point from week 2 through week 12 in the melasma subgroup ($P \leq .011$), with no significant differences between treatments (Figs 2 and 5).

MelasQoL in melasma subgroup. Subject assessment of emotional and psychological effects of melasma using the MelasQoL questionnaire was significantly improved versus baseline in the melasma subgroup at each time point throughout the study ($P \leq .011$ at all time points; Fig 6).

Subject self-assessment questionnaire

Self-assessed overall improvement in skin condition was comparable between treatments across all study visits, with 95% and 94% of subjects reporting at least a ≈25% overall improvement in their skin condition with ABT and 4% HQ, respectively, at week 12 (Fig 7, *A*). Among all subjects, overall satisfaction with results on each facial side was

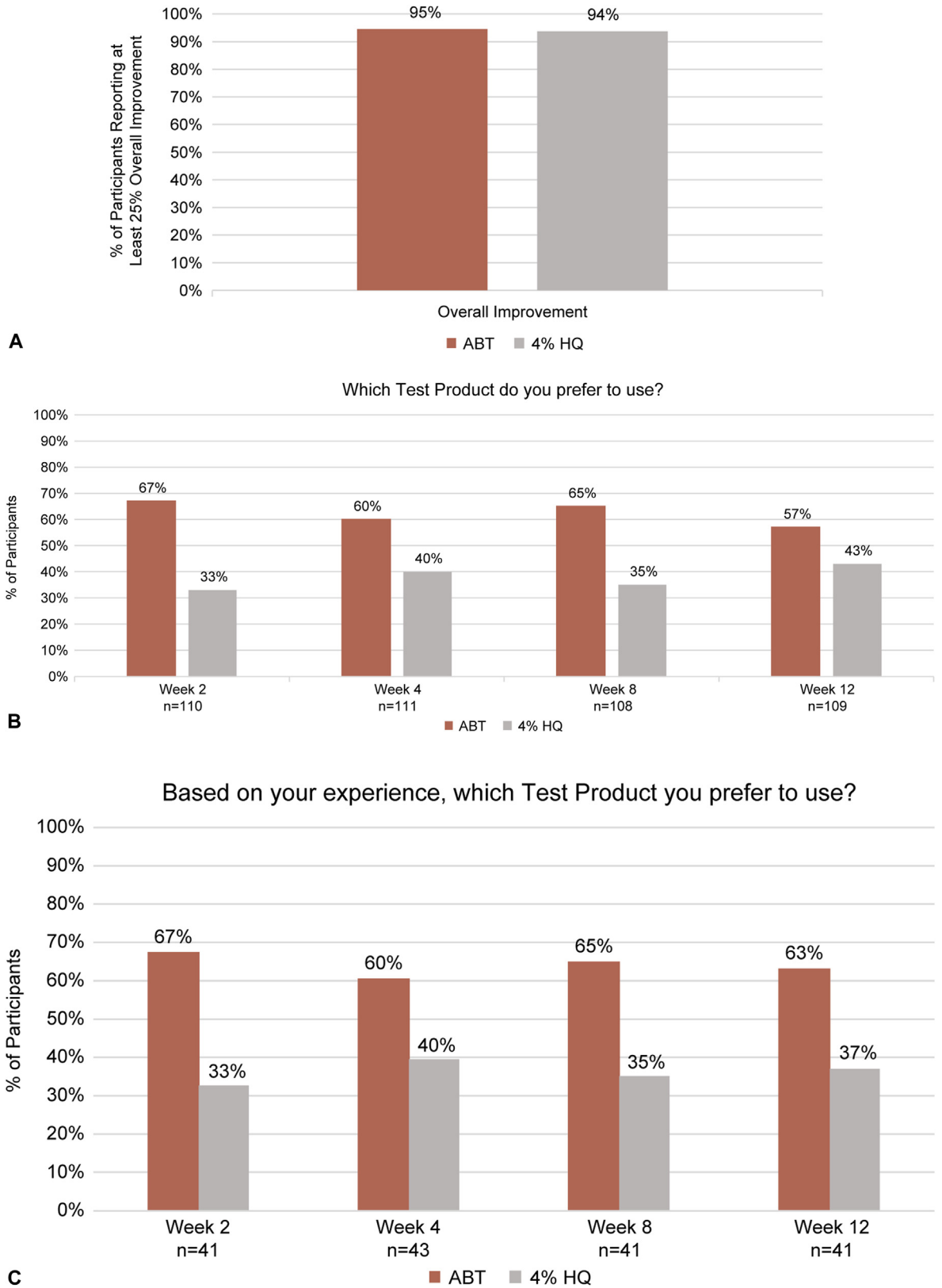

Fig 7. A, Self-perceived overall improvement[a] at week 12 for all subjects. **B,** Product preference for all subjects in the Advanced Brightening Treatment and 4% hydroquinone treatment groups. **C,** Product preference for melasma subgroup 2. [a]Subjects who reported at least a ≈25% overall improvement in their skin condition. *ABT*, Advanced Brightening Treatment; *HQ*, hydroquinone.

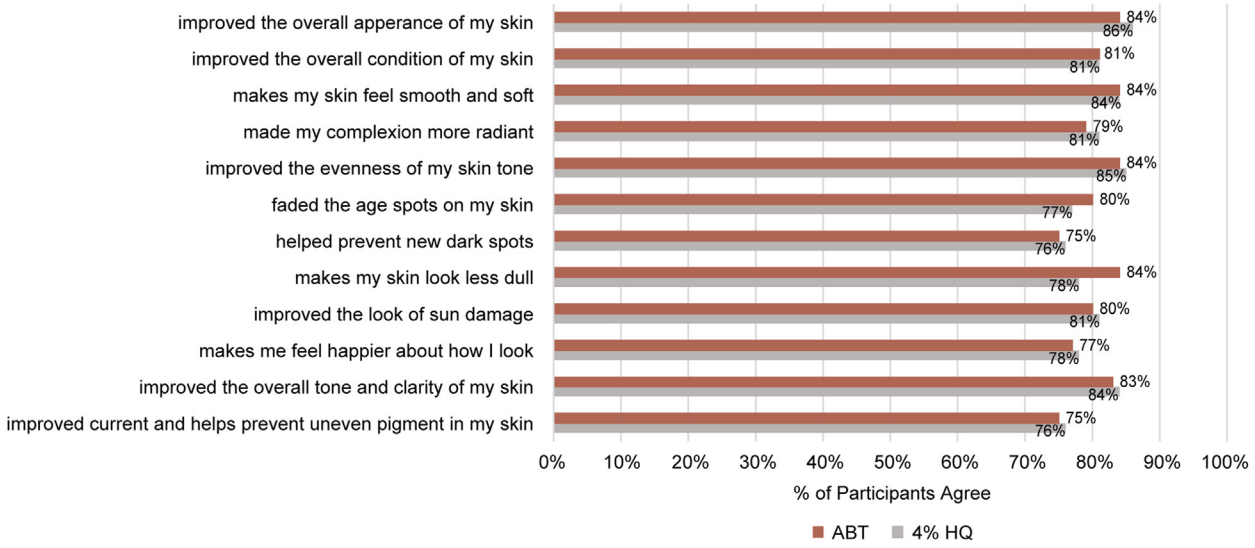

Fig 8. Subject self-assessment questionnaire for product efficacy parameters at week 12 in all subjects in the Advanced Brightening Treatment and 4% hydroquinone treatment groups. *ABT*, Advanced Brightening Treatment; *HQ*, hydroquinone.

comparable between the 2 treatments across all visits. More subjects, both in the overall group (Fig 7, *B*) and the melasma subgroup (Fig 7, *C*), preferred ABT over 4% HQ across all visits from week 2 through week 12. At week 12, self-reported efficacy across a range of parameters was high and comparable between ABT (range, 75%-84%) and 4% HQ (range, 76%-86%; Fig 8).

Photographic evidence

Representative photographs of improvements from baseline in the appearance of melasma and overall hyperpigmentation are presented in Figs 9 to 13.

Safety and tolerability. ABT and 4% HQ were well tolerated in both the overall group (n = 113) and the melasma subgroup (n = 44) at all follow-up visits. Mean scores for all tolerability parameters remained similar to baseline scores (below "mild") at all study visits. No serious treatment-emergent adverse events were reported and no pattern of treatment-emergent adverse events was observed. Treatment-related adverse events were reported by 3 subjects on the ABT-treated side (erythema, pain, dryness, edema, itching, rash, and acne) and by 4 subjects on the 4% HQ-treated side (erythema, dryness, itching, rash, burning, and acne). Two subjects discontinued the study due to adverse events (itching, erythema, pain, dryness, edema, and rash) experienced on both treatment sides. At the end of the study, treatment-related adverse events had resolved in all subjects.

DISCUSSION

In this split-face study, the topical, HQ-free, multimodal pigment-correcting serum ABT was well tolerated and effective in reducing the severity of overall hyperpigmentation and melasma in a broad range of racial/ethnic subgroups and skin types with a high rate of treatment satisfaction.

ABT showed modest but significant improvement from baseline in overall hyperpigmentation comparable to 4% HQ ($P < .001$) and similar subject satisfaction to 4% HQ for both overall hyperpigmentation and melasma. However, ABT was preferred over 4% HQ in the overall population and in the melasma subgroup, suggesting that, when all parameters are considered, subjects tended to favor ABT treatment. ABT demonstrated efficacy earlier in the treatment course in darker skin types versus LYT2 (Lytera 2.0 Pigment Correcting Serum; SkinMedica, Allergan Aesthetics, an AbbVie Company), another multimodal, HQ-free product.[21] In subjects with melasma and FST III to VI, ABT provided significant improvements in the appearance of overall hyperpigmentation and mMASI scores as early as week 2, whereas LYT2 has provided significant improvements in MASI scores in subjects with pregnancy-induced melasma and FST II to IV (n = 34) starting at week 4[24] and at week 8 in 18 subjects with melasma and FST III to VI.[25]

The current study design builds on past studies of multimodal topical hyperpigmentation treatments and includes several key strengths. The split-face,

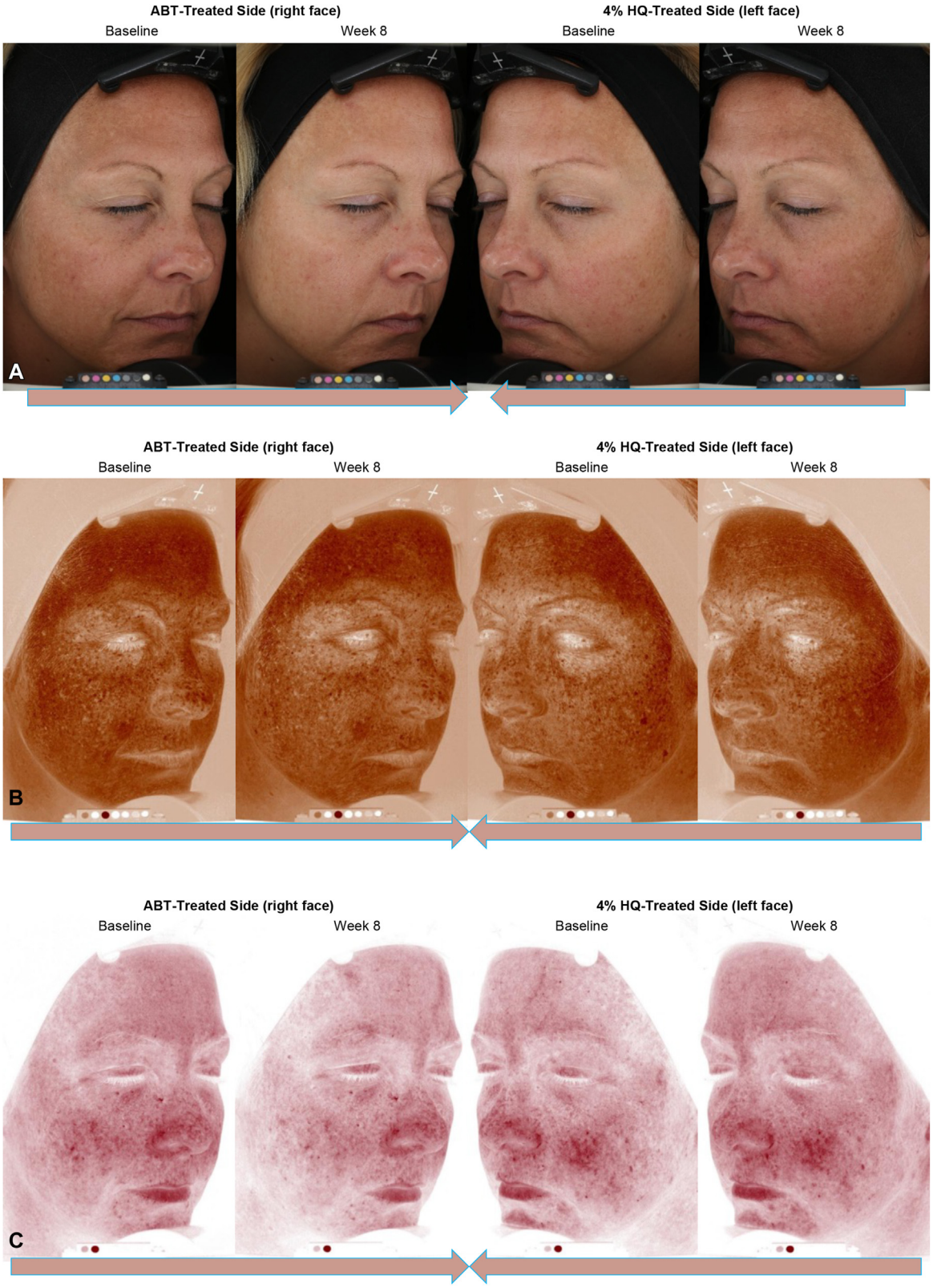

Fig 9. Representative images of a 41-year-old White/Caucasian female with Fitzpatrick skin type III and melasma at baseline and week 8 under (**A**) standard 2 lighting conditions; (**B**) brown channel lighting conditions; and (**C**) red channel lighting conditions. Comparable improvements in skin tone evenness are shown at week 8 in both the Advanced Brightening Treatment–treated side and the 4% hydroquinone–treated side of the face. *Arrows* show direction of improvement. *ABT*, Advanced Brightening Treatment; *HQ*, hydroquinone.

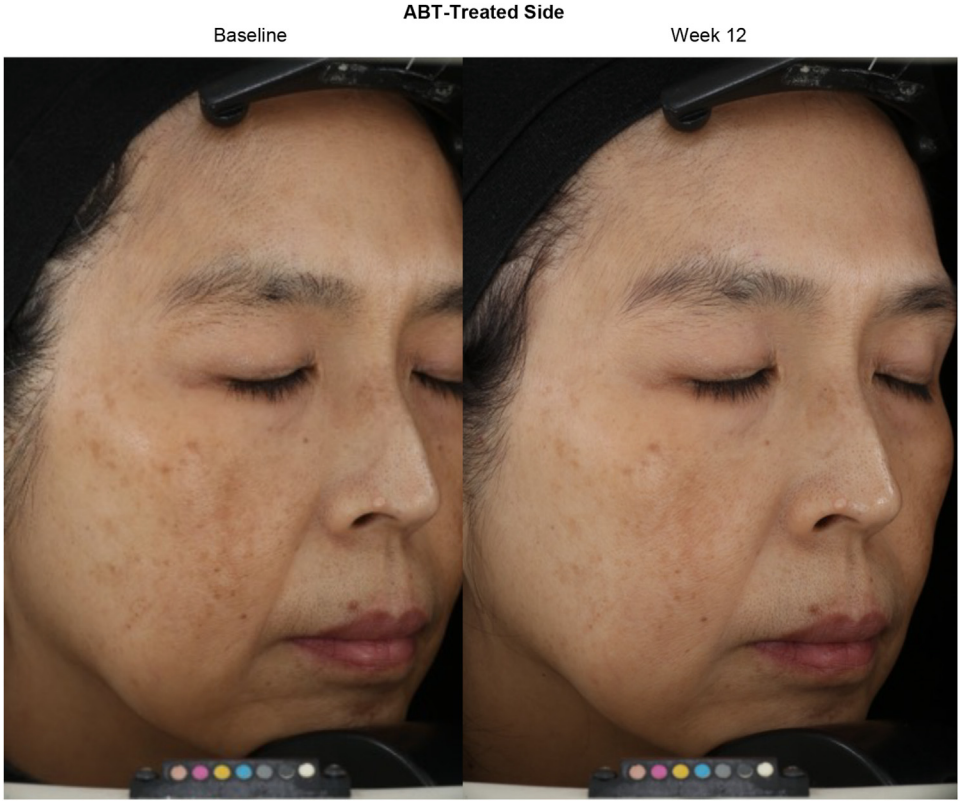

Fig 10. Representative images of a 54-year-old Asian female with Fitzpatrick skin type III and melasma at baseline and week 12 under standard 2 lighting conditions. Reductions in hyperpigmentation and melasma severity are shown on the Advanced Brightening Treatment–treated side of the face. *ABT*, Advanced Brightening Treatment.

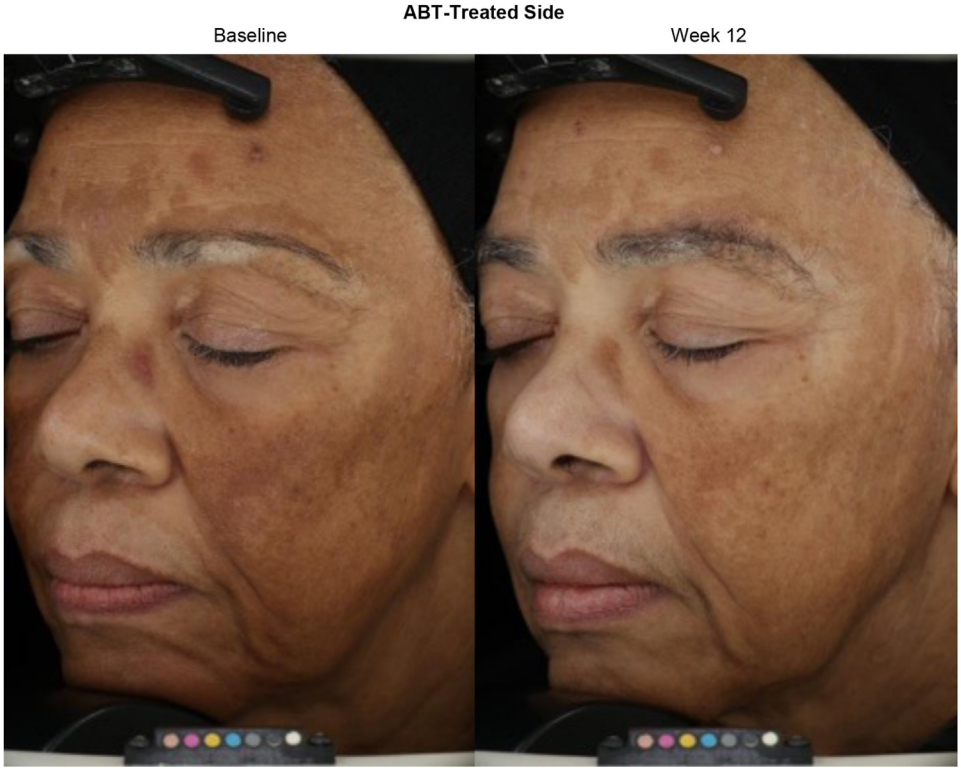

Fig 11. Representative images of a 60-year-old Black/African American female with Fitzpatrick skin type IV and melasma at baseline and week 12 under standard 2 lighting conditions. Improvements in melasma severity and skin tone evenness are shown on the Advanced Brightening Treatment–treated side of the face. *ABT*, Advanced Brightening Treatment.

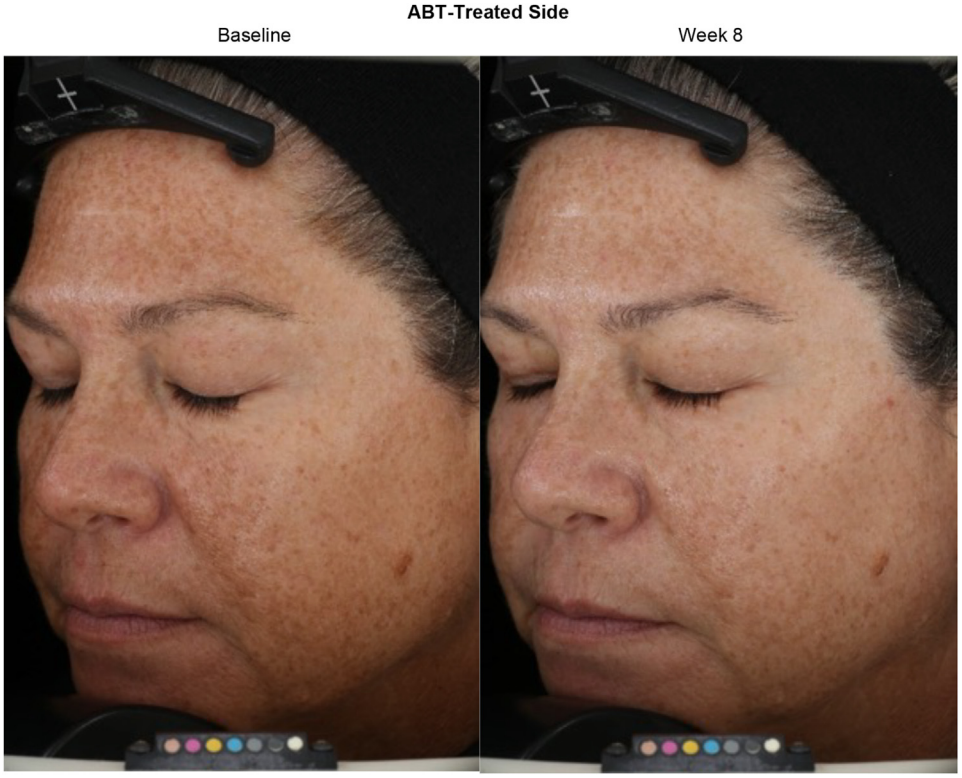

Fig 12. Standardized images of a 51-year-old Hispanic female with Fitzpatrick skin type III with overall hyperpigmentation at baseline and week 12 under standard 2 lighting conditions. Reduction in hyperpigmentation and greater skin tone evenness are shown on the Advanced Brightening Treatment—treated side of the face. *ABT*, Advanced Brightening Treatment.

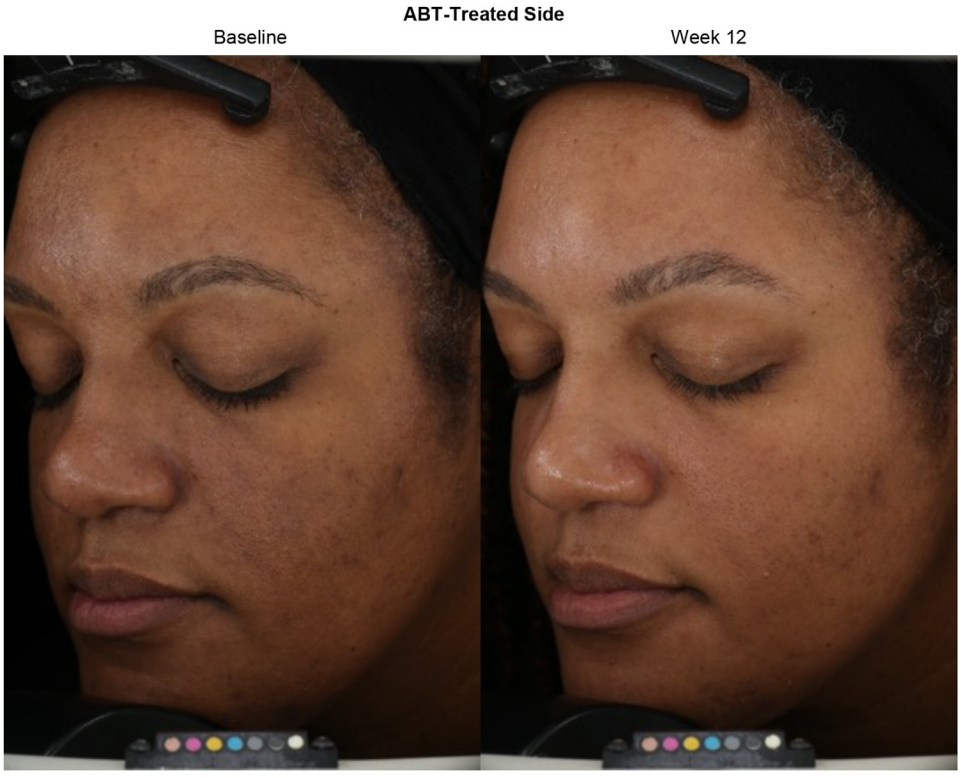

Fig 13. Representative images of a 43-year-old Black/African American female with Fitzpatrick skin type V and overall hyperpigmentation under standard 2 lighting conditions. Reductions in hyperpigmentation and improved skin tone evenness are shown on the Advanced Brightening Treatment—treated side of the face. *ABT*, Advanced Brightening Treatment.

double-blind, randomized, controlled design of this study is similar to 2 past smaller studies comparing the efficacy and tolerability of other multimodal pigment-correcting serums versus 4% HQ.[21,26] Because the multifactorial etiology of hyperpigmentation can potentially confound study results, the split-face design ensured that any factors that could influence outcome (eg, sun exposure, lifestyle, hormonal changes) would apply to both treatments.[1,2] In addition, because pigment biology differs between ethnicities and hyperpigmentation is often more challenging to treat in skin of color, this study imposed minimum enrollment targets for different skin types to facilitate evaluation of ABT in an ethnically diverse population so as to better assess its suitability for treating hyperpigmentation in individuals with darker skin types.[9] As a result, there was near equal representation across race/ethnicity categories (ie, Asian, Black/African American, Hispanic, and White/Caucasian), and 47% of study subjects had darker skin types (FST IV-VI). This study also assessed a subgroup of patients with melasma and FST III to VI, one of the most challenging-to-treat forms of hyperpigmentation, especially in darker skin types,[1,27] which are often underrepresented in cosmeceutical studies. Lastly, to fully assess the effects of ABT, a comprehensive set of efficacy endpoints was applied at all study visits, encompassing clinical grading, validated severity measures, instrumentation analysis, and quality of life assessments. These outcomes were comparable to those in the 2 similarly designed prior studies.[21,26]

Aging predisposes all individuals to hyperpigmentation, but certain skin types are especially vulnerable, including Asian, Black/African American, and Hispanic populations.[9,10] Pigmentary changes are often the first signs of aging in skin of color, and the risk of hyperpigmentation is increased in these populations. Therefore, treating hyperpigmentation should be considered as part of the antiaging or skin rejuvenation strategy because of the vulnerable nature of darker skin types to pigmentary changes.[9,10] In addition, the type and distribution of melanin in darker skin types (FST IV-VI) make hyperpigmentation disorders, especially melasma, more refractory to treatment.[9,16]

The negative impact of hyperpigmentation on quality of life is also a particular concern in individuals with skin of color, in large part due to predominance of pigmentary changes in this population, compounded by increased difficulty in achieving significant improvements in darker skin types.[16,20,28] In addition, cultural perceptions and impact on socioeconomic status, productivity, and perception by self and others further affect quality of life in this population.[6,7,20,29] As such, products like ABT help to fill the treatment gap for hyperpigmentation and melasma, especially in difficult-to-treat darker skin types.[15]

Treatment strategies that employ combinations of topical agents in conjunction with procedural therapies for hyperpigmentation are an effective treatment approach for skin of color.[20,28,30-32] The efficacy reported in this study for ABT in individuals from a range of racial/ethnic backgrounds, and including all FSTs, suggests that ABT might be considered for use as part of combination treatment for hyperpigmentation in all individuals regardless of background and skin type.

A limitation of the current study was the inability to assess improvement in quality of life with each treatment, as MelasQoL is validated for the full face, and this was a split-face study. There are also limitations inherent to the split-face design; for example, subjects may attempt off-protocol use of the test products (ie, use of only 1 product, or both products, on both sides of the face). However, to verify usage compliance, the test materials of each subject were visually inspected and weighed at each visit.

CONCLUSION

This study demonstrates that ABT is effective, safe, and preferred over 4% HQ in individuals with moderate to severe facial hyperpigmentation, including melasma, across multiple races and ethnicities and all FSTs (I-VI). These results suggest that ABT is a suitable option for long-term treatment of chronic, challenging-to-treat facial hyperpigmentation, including melasma.

The authors thank the participants, study sites, and investigators who participated in this clinical trial, as well as Cheryl H. Vaughan, PhD of SGS Inc for her support as study sub-investigator. Dr Vaughan is an employee of SGS Inc.

Conflicts of interest

Author Huang, Author Makino, and Dr Cheng are full-time employees of AbbVie and may hold AbbVie stock. Dr Acevedo is an employee of SGS Inc. Dr Mehta is a former full-time employee of AbbVie and may hold AbbVie stock.

REFERENCES

1. Huerth KA, Hassan S, Callender VD. Therapeutic insights in melasma and hyperpigmentation management. *J Drugs Dermatol*. 2019;18:718-729.
2. Markiewicz E, Karaman-Jurukovska N, Mammone T, Idowu OC. Post-inflammatory hyperpigmentation in dark skin: molecular mechanism and skincare implications. *Clin Cosmet Investig Dermatol*. 2022;15:2555-2565.

3. Jiang J, Akinseye O, Tovar-Garza A, Pandya AG. The effect of melasma on self-esteem: a pilot study. *Int J Womens Dermatol*. 2018;4:38-42.
4. Maymone MBC, Neamah HH, Wirya SA, et al. The impact of skin hyperpigmentation and hyperchromia on quality of life: a cross-sectional study. *J Am Acad Dermatol*. 2017;77:775-778.
5. Searle T, Al-Niaimi F, Ali FR. The top 10 cosmeceuticals for facial hyperpigmentation. *Dermatol Ther*. 2020;33:e14095.
6. Zhu Y, Zeng X, Ying J, Cai Y, Qiu Y, Xiang W. Evaluating the quality of life among melasma patients using the MELASQoL scale: a systematic review and meta-analysis. *PLoS One*. 2022; 17:e0262833.
7. Darji K, Varade R, West D, Armbrecht ES, Guo MA. Psychosocial impact of postinflammatory hyperpigmentation in patients with acne vulgaris. *J Clin Aesthet Dermatol*. 2017;10:18-23.
8. Spierings NMK. Melasma: a critical analysis of clinical trials investigating treatment modalities published in the past 10 years. *J Cosmet Dermatol*. 2020;19:1284-1289.
9. Venkatesh S, Maymone MBC, Vashi NA. Aging in skin of color. *Clin Dermatol*. 2019;37:351-357.
10. Alexis AF, Obioha JO. Ethnicity and aging skin. *J Drugs Dermatol*. 2017;16:s77-s80.
11. Ogbechie-Godec OA, Elbuluk N. Melasma: an up-to-date comprehensive review. *Dermatol Ther (Heidelb)*. 2017;7:305-318.
12. Grimes PE, Ijaz S, Nashawati R, Kwak D. New oral and topical approaches for the treatment of melasma. *Int J Womens Dermatol*. 2019;5:30-36.
13. Kim C, Cline A, Safai B. Melasma cost and factors influencing patient satisfaction [abstract 18821]. *J Am Acad Dermatol*. 2020;83(6 suppl):AB222.
14. Piętowska Z, Nowicka D, Szepietowski JC. Understanding melasma—how can pharmacology and cosmetology procedures and prevention help to achieve optimal treatment results? A narrative review. *Int J Environ Res Public Health*. 2022;19:12084.
15. Morgado-Carrasco D, Piquero-Casals J, Granger C, Trullàs C, Passeron T. Melasma: the need for tailored photoprotection to improve clinical outcomes. *Photodermatol Photoimmunol Photomed*. 2022;38:515-521.
16. Yoo J. Differential diagnosis and management of hyperpigmentation. *Clin Exp Dermatol*. 2022;47:251-258.
17. Schwartz C, Jan A, Zito PM. Hydroquinone. *StatPearls*. StatPearls Publishing; 2022.
18. González-Molina V, Martí-Pineda A, González N. Topical treatments for melasma and their mechanism of action. *J Clin Aesthet Dermatol*. 2022;15:19-28.
19. Moolla S, Miller-Monthrope Y. Dermatology: how to manage facial hyperpigmentation in skin of colour. *Drugs Context*. 2022;11:2021-11-2.
20. Vashi NA, Wirya SA, Inyang M, Kundu RV. Facial hyperpigmentation in skin of color: special considerations and treatment. *Am J Clin Dermatol*. 2017;18:215-230.
21. Makino ET, Kadoya K, Sigler ML, Hino PD, Mehta RC. Development and clinical assessment of a comprehensive product for pigmentation control in multiple ethnic populations. *J Drugs Dermatol*. 2016;15:1562-1570.
22. Pandya AG, Hynan LS, Bhore R, et al. Reliability assessment and validation of the Melasma Area and Severity Index (MASI) and a new modified MASI scoring method. *J Am Acad Dermatol*. 2011;64:78-83, 83.e71-72.
23. Balkrishnan R, McMichael AJ, Camacho FT, et al. Development and validation of a health-related quality of life instrument for women with melasma. *Br J Dermatol*. 2003;149:572-577.
24. Makino ET, Jiang LI, Stephens TJ, Mikati M, Mehta RC. Pigmentation control in pregnancy-induced melasma: clinical assessment of a non-hydroquinone, non-retinol pigment-correcting serum. *J Cosmet Dermatol*. 2022;21:5739-5746.
25. Kaufman BP, Alexis AF. Randomized, double-blinded, split-face study comparing the efficacy and tolerability of two topical products for melasma. *J Drugs Dermatol*. 2020;19:822-827.
26. Makino ET, Mehta RC, Garruto J, Gotz V, Sigler ML, Herndon JH. Clinical efficacy and safety of a multimodality skin brightener composition compared with 4% hydroquinone. *J Drugs Dermatol*. 2013;12:s21-s26.
27. Sheth VM, Pandya AG. Melasma: a comprehensive update: part I. *J Am Acad Dermatol*. 2011;65:689-697.
28. Desai S, Manry S, Makino E, Mehta R. Assessment of circadian-based antioxidants plus a comprehensive brightener in skin of color patients with hyperpigmentation. *J Drugs Dermatol*. 2022;21:376-380.
29. Ortonne JP, Arellano I, Berneburg M, et al. A global survey of the role of ultraviolet radiation and hormonal influences in the development of melasma. *J Eur Acad Dermatol Venereol*. 2009; 23:1254-1262.
30. Downie J, Schneider K, Goberdhan L, Makino ET, Mehta RC. Combination of in-office chemical peels with a topical comprehensive pigmentation control product in skin of color subjects with facial hyperpigmentation. *J Drugs Dermatol*. 2017;16:301-306.
31. Cestari T, Arellano I, Hexsel D, Ortonne JP. Melasma in Latin America: options for therapy and treatment algorithm. *J Eur Acad Dermatol Venereol*. 2009;23:760-772.
32. Shah S, Manry S, Makino ET, Mehta RC. Clinical assessment of a circadian-based antioxidant system combined with a comprehensive brightening serum in diverse subjects with moderate-to-severe facial hyperpigmentation. *J Cosmet Dermatol*. 2022; 21:2082-2088.