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ORIGINAL ARTICLE

Visualizing Severity of Alopecia Tool (SALT) scores in the clinical setting using patient images from a clinical trial

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Abstract

Background: The Severity of Alopecia Tool (SALT) is a standardized method for quantifying scalp hair loss in alopecia areata (AA). SALT scores can be used to guide treatment decisions and are widely used as eligibility criteria and endpoints for clinical trials in AA. However, clinicians may be unfamiliar with assessing and envisioning SALT scores in practice.

Objectives: To aid clinicians in the determination and application of SALT scores in a clinical setting, this manuscript seeks to contextualize SALT scores using patient images from a clinical trial of adults with severe AA.

Methods: Images from 722 patients enrolled in BRAVE-AA1, a phase 2/3 study of baricitinib in adults with severe AA (SALT score ≥50; ≥50% scalp hair loss), were obtained at baseline and Weeks 12, 36, and 52 and compiled into a repository. Photographs were selected to represent SALT scores across the full range of disease (SALT scores 0–100) and to demonstrate the progression of SALT scores during the course of treatment.

Results: Images of six patients depict the range of SALT scores (0–100). Photographs are of male and female patients of different ages (21–69) and races (Asian, Black, White) with varying extent, density, and patterns of hair loss. Images of two additional patients demonstrate the use of SALT to monitor treatment progress, showing distinct patterns and timing of clinical response over 52 weeks of therapy.

Conclusions: The SALT is widely used in clinical trials for AA, but clinicians may lack familiarity. Presented patient images show SALT scores commonly used as eligibility criteria and endpoints in clinical trials, which may be useful in identifying patients eligible for systemic treatment and in visualizing therapeutic response.

KEYWORDS
alopecia areata, baricitinib, hair loss, JAK inhibitor, SALT, Severity of Alopecia Tool

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INTRODUCTION

Alopecia areata (AA) is chronic autoimmune disease marked by non-scarring hair loss that can affect any hair-bearing site.[1] Scalp hair loss is frequently reported by patients as the most bothersome symptom of AA,[2] and the extent of scalp hair loss is often the basis of treatment decisions.[3]

The Severity of Alopecia Tool (SALT) was developed as a standardized method for quantifying scalp hair loss.[4] The SALT is commonly used in clinical trials to assess disease severity and treatment progress.[5] Achieving a SALT score ≤20 has been identified as a successful target treatment outcome for patients with severe AA (≥50% scalp hair loss/SALT score ≥50)[3] and is used as the primary endpoint in clinical trials of drug therapies for AA. For example, baricitinib, an oral selective Janus kinase (JAK) inhibitor approved in the United States and elsewhere for the treatment of adult patients with severe AA, demonstrated efficacy in hair regrowth based on a SALT score ≤20 in phase 3 trials.[6]

The SALT may be a useful measure for guiding treatment decisions and monitoring disease progression.[7] While often reported in clinical trials, clinicians may be unfamiliar with assessing SALT scores in practice. Thus, this paper aims to contextualize SALT scores using images of patients with severe AA from BRAVE-AA1.

MATERIALS AND METHODS

Trial design and SALT assessments

BRAVE-AA1 (NCT03570749) is an adaptive, randomized, double-blind, parallel-group, placebo-controlled phase 2/3 study evaluating the efficacy and safety of baricitinib for AA. Trial details have been reported previously.[6] Briefly, adult patients with ≥50% scalp hair loss, as measured by a SALT score ≥50, were randomized 2:2:3 to receive once-daily oral placebo, baricitinib 2 mg, or baricitinib 4 mg. Investigators determined SALT scores at each clinic visit. The primary outcome was a SALT score ≤20 at Week 36. Patients randomized to baricitinib at baseline retained their treatment allocation through Week 52 regardless of clinical response at Week 36. The trial was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines and approved by individual institutional review boards at each participating study center.

The SALT uses a visual aid to divide the hair-bearing areas of the scalp into four quadrants, with the top, left,

Quadrant	Hair Loss	Area of Scalp	Quadrant Score
Top	12%	× 0.40	= 4.8
Left	95%	× 0.18	= 17.1
Right	85%	× 0.18	= 15.3
Back	50%	× 0.24	= 12
SALT Score			= 49

FIGURE 1 Calculation of a Severity of Alopecia Tool (SALT) score. SSA, scalp surface area. The SALT score is calculated by (1) multiplying the percentage of hair loss in each quadrant by the surface area of that quadrant and (2) summing the products. Scores range from 0 to 100, reflecting 0%–100% scalp hair loss.

right, and back of the head constituting 40%, 18%, 18%, and 24% of the scalp's surface area (SSA), respectively.[4,8] Based on the methodology proposed by Olsen et al., the SALT score is a weighted sum of the percentage of hair loss in each quadrant.[4] Scores range from 0 to 100, reflecting 0%–100% scalp hair loss. Only terminal hair is included in the SALT; vellus or intermediate hairs are not considered in the SALT scoring process.[4,8] The calculation of a SALT score is demonstrated using patient images in Figure 1.

Photography and image selection

All patients provided written informed consent for photographs at baseline and Weeks 12, 36, and 52. Site personnel obtained photographs of the scalp, including the top, left, right, and back of the head with sponsor-provided camera equipment. Photographs were taken under similar lighting conditions and magnifications, and according to instructions as outlined in a study-specific photographic procedure manual. Images of patients were compiled into a repository.

Images for inclusion in this manuscript were selected from the repository to demonstrate SALT scores across the full range of disease (SALT scores 0–100). The SALT scores of the selected images were verified by the authors. Selected photographs included male and female patients randomized to any treatment group, taken at any clinic visit through Week 52. To demonstrate examples of scalp hair growth over the course of treatment, a separate set of images was selected to represent SALT scores across the spectrum of disease severity at baseline (SALT score ≥50) and after achieving clinical response (SALT score ≤20). Images were selected to represent various patterns of hair loss in patients of different ages and races. All photographs were deidentified.

RESULTS

Photographs of 722 patients were compiled into an image repository. Mean age of patients was 37.5 years, 60.2% were female, and approximately half (49.4%) were White (Table 1). Mean and median SALT scores at baseline were 85.5 and 96.5, and 53.7% had very severe scalp hair loss (SALT score 95-100).

Figure 2 depicts representative photographs of SALT scores ranging from 1 (1% scalp hair loss) to 100 (100% scalp hair loss). The images include six male and female patients of different ages (21–69 years) and races (Asian, Black, White) with varying patterns of hair loss. Each set of photographs includes the four quadrants of the scalp used to determine a SALT score. The first row in each set features a "tilted down" view to better visualize the top quadrant, which comprises 40% of the SSA. The second and third rows show the left and right quadrant views, which each comprise 18% of the SSA. The fourth row shows the posterior quadrant, which comprises 24% of the SSA. The hair loss percentage in each quadrant of the scalp and associated quadrant score are listed in the top left corner of each image. The quadrant scores sum to the patient's rounded SALT score, reflecting the total amount of scalp hair loss.

Figure 3a,b exemplifies the progression of SALT scores over 52 weeks of treatment with baricitinib in two patients with different extent, density, and patterns of hair loss. Both patients had severe AA (SALT score ≥50) at baseline and achieved clinical response (SALT score ≤20) after 36 weeks of treatment. However, the patients showed distinct patterns of improvement over the course of treatment. Figure 3a shows a 49-year-old White female who presented with SALT score 59 at baseline, with the lateral quadrants most affected by AA. The patient improved to a score of 1 at Week 36; she achieved

TABLE 1 Baseline demographics and disease characteristics of patients included in the BRAVE-AA1 image repository.

Characteristics	Patients ($N = 722$)
Age in years, mean (SD)	37.5 (13.1)
Female, *n* (%)	435 (60.2)
Race, *n* (%)	
White	355 (49.4)
Asian	274 (38.2)
Black or African American	57 (7.9)
American Indian or Alaska Native	22 (3.1)
Other	10 (1.4)
SALT score at baseline, mean (SD)	85.5 (18.1)
SALT score at baseline, median	96.5
SALT severity at baseline, *n* (%)	
Severe (SALT score 50–94)	334 (46.3)
Very severe (SALT score 95–100)	388 (53.7)
Duration since AA onset in years, mean (SD)	12.4 (10.9)
Duration of current AA episode in years, mean (SD)	3.7 (4.0)
Alopecia universalis, *n* (%)	318 (44.0)
Alopecia totalis, *n* (%)	284 (39.3)

Note: All patients included in the repository provided photographic informed consent and had photographs taken at study baseline.

FIGURE 2 Representative photographs of SALT scores in patients with severe alopecia areata. SALT, Severity of Alopecia Tool. Percentages and numbers on each image indicate quadrant-specific hair loss and SALT scores, respectively. Copyright © 2023. Eli Lilly and Company. All rights reserved. Permission for any use should be sought from Eli Lilly and Company.

complete scalp hair coverage (SALT score 0) at Week 52. Figure 3b presents a 56-year-old Asian female who had a SALT score 66 at baseline, with all four quadrants similarly affected by AA. The patient reached a SALT score 27 by Week 12 and achieved clinical response at Week 36 (SALT score 9), which was sustained at Week 52 (SALT score 12).

DISCUSSION

To aid clinicians in the application of SALT scores in a clinical setting, images from the BRAVE-AA1 clinical trial were used to show representative examples of SALT scores in adults with AA. The photographs include a diverse set of patients across demographic and clinical characteristics, reflecting the heterogeneity of disease and illustrating the spectrum of hair loss and regrowth in individuals with AA. Photographs were also used to illustrate SALT scores in two patients before and after treatment with baricitinib, demonstrating the utility of the SALT score to monitor treatment response. The images represent SALT scores commonly used as eligibility criteria and endpoints in clinical trials, which may help clinicians identify patients eligible for systemic treatment and visualize therapeutic response.

As observed in the example photographs in Figure 3a,b, AA can vary widely in presentation and clinical response.[9] As a standardized tool for objective measurement of scalp hair loss, the SALT score is accepted by regulators as a primary outcome for registration trials and is a key component of assessing outcomes across clinical trials for AA.[10] Clinicians who are not familiar with the SALT may approximate the percentage of scalp hair loss. However, more widespread use of SALT scores can better enable comparison of

treatment outcomes and help establish best treatment practices for AA.[10] As therapeutic advances continue to occur in AA, it will be increasingly important for clinicians to understand treatment outcomes as measured by SALT in a clinical setting.

The extent of scalp hair loss is an important prognostic factor in AA, and the determination of a SALT score is fundamental to developing a treatment plan for patients and monitoring treatment progress.[7,11] However, other key factors in clinical decision-making

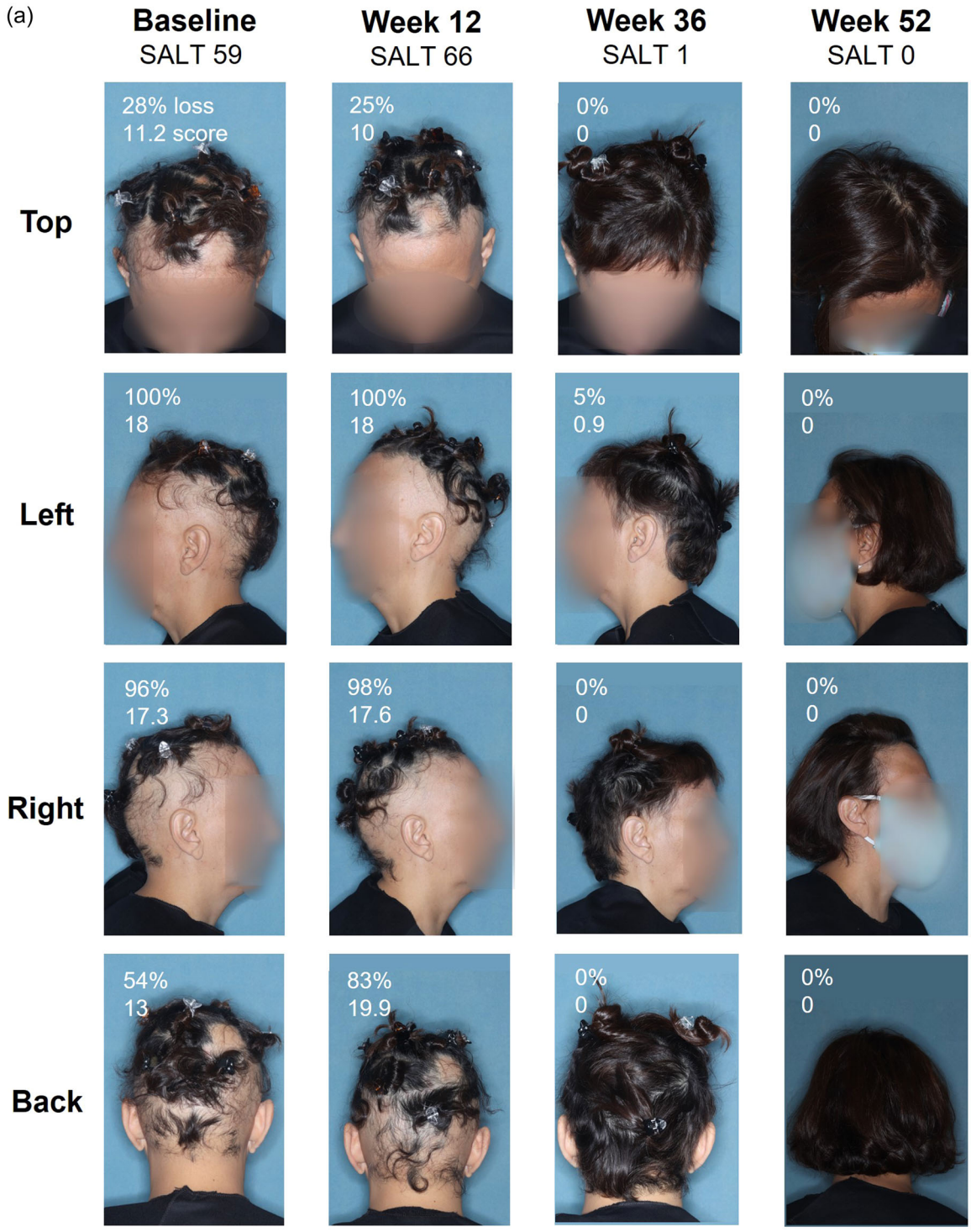

FIGURE 3 Photographs of a range of SALT scores demonstrating clinical response to therapy for severe alopecia over 52 weeks in (a) a 49-year-old White female treated with baricitinib 4 mg and (b) a 56-year-old Asian female treated with baricitinib 2 mg. SALT, Severity of Alopecia Tool. Percentages and numbers on each image indicate quadrant-specific hair loss and SALT scores, respectively. Copyright © 2023. Eli Lilly and Company. All rights reserved. Permission for any use should be sought from Eli Lilly and Company.

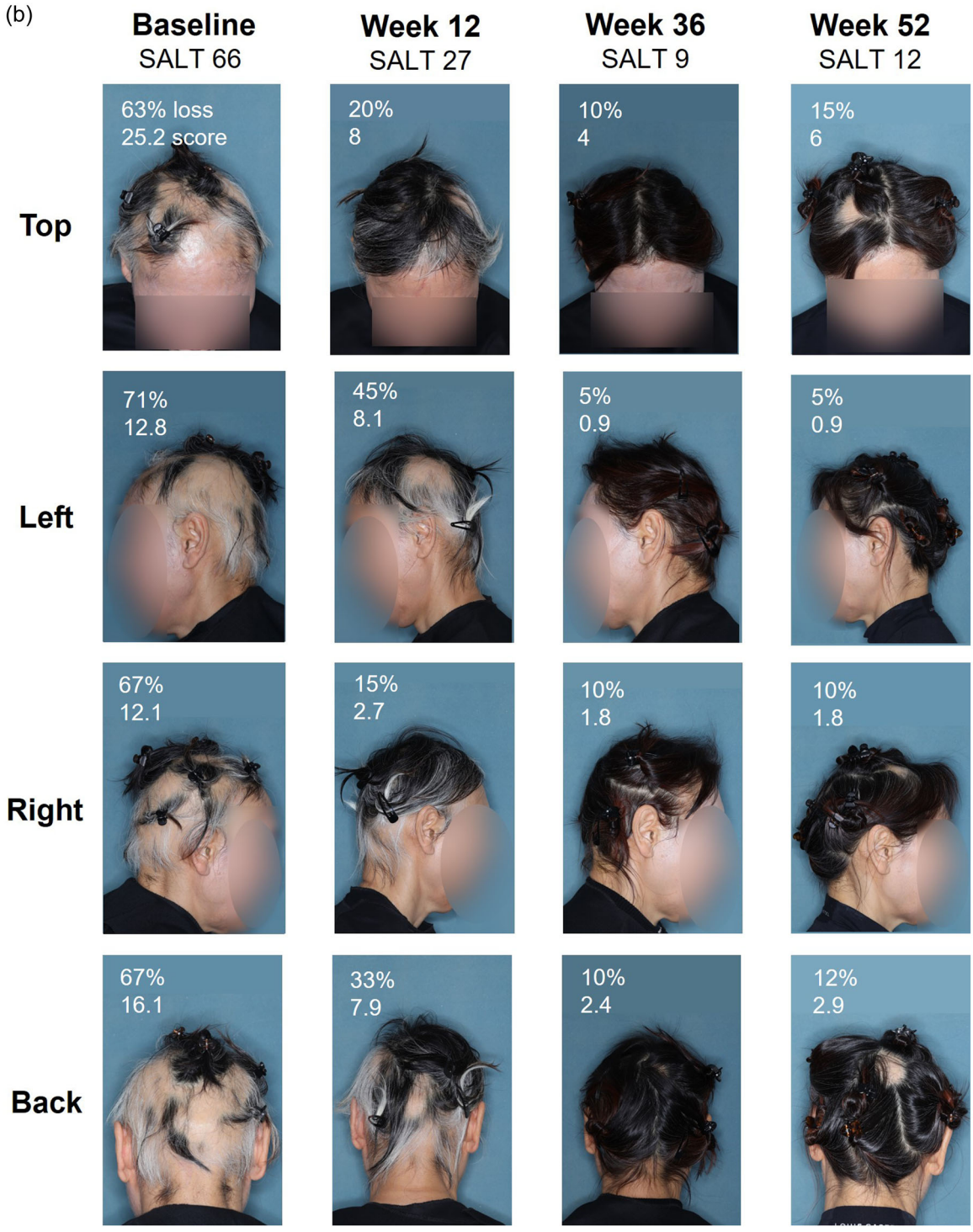

FIGURE 3 (Continued)

include the location, pattern, and duration of hair loss and the impact on patient's quality of life.[9] It is important that clinicians consider the SALT in context with other factors when making treatment decisions.[9]

Several limitations should be noted. The images presented here are intended to provide visual examples of SALT scores and to reinforce their calculation using the methodology proposed by Olsen et al.[4] The images are not intended to represent the full spectrum of possible presentations and responses to treatment for patients with severe AA. The full extent of an individual's hair loss may not be completely represented in photographs, in particular because changes in hair density are difficult to visualize in an image. The SALT does not

account for active shedding that may better be assessed with a hair pull test. There may be inter-rater variability in SALT scores, but with training and repeated SALT score assessment, this is usually not clinically meaningful in clinical trials or practice. The photographs from this trial were used to provide visual evidence of clinical response but should not be interpreted as representative of treatment efficacy in all patients.

CONCLUSION

Patient images from a clinical trial demonstrate a range of SALT scores in adult patients across the spectrum of AA, before and during treatment. The photographs include a diverse set of patients, demonstrating unique patterns of hair loss and regrowth in individuals with AA. The images represent SALT scores commonly used as both eligibility criteria and primary endpoints in clinical trials, which serve as a useful component in identifying patients eligible for systemic treatment and monitoring therapeutic response.

AUTHOR CONTRIBUTIONS

Each author has met the authorship criteria established by the International Committee of Medical Journal Editors.

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CONFLICT OF INTEREST STATEMENT

Natasha Atanaskova Mesinkovska serves on the Board of the American Hair Research Association, was a Chief Scientific Officer for the National Alopecia Areata Foundation (2022), and has received honoraria for advisory boards for Arena Pharmaceuticals, Concert Pharmaceuticals, Eli Lilly and Company, Nutrafol, and Pfizer. Brett A. King has served on advisory boards and/or is a consultant and/or is a clinical trial investigator for Abbvie, AltruBio Inc., Almirall, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol-Meyers Squibb, Concert Pharmaceuticals Inc., Horizon Therapeutics, Eli Lilly and Company, Incyte Corp., LEO Pharma, Otsuka/Visterra Inc., Pfizer Inc., Regeneron, Sanofi Genzyme, TWi Biotechnology Inc., and Viela Bio. He is on speaker bureaus for Abbvie, Incyte, Eli Lilly, Pfizer, Regeneron, and Sanofi Genzyme. Sergio Vañó-Galván received advisory funding from Eli Lilly and Company and Pfizer. Yutaka Shimomura receives advisory fees from Eli Lilly Japan K.K. and Maruho Co. Yutaka Shimomura also receives research grants for studies not related to this work from Eli Lilly Japan K.K., Maruho Co., and Sun Pharma Japan Ltd. Rodney Sinclair is a member of the Eli Lilly advisory board and was principal investigator in the Eli Lilly sponsored BRAVE clinical trials. Jakub Jedynak, Evangeline Pierce, and Amy K. Ellinwood are employees and shareholders of Eli Lilly and Company. Jill McCollam was an employee of Eli Lilly and Company at the time of manuscript development.

DATA AVAILABILITY STATEMENT

Patient images © Eli Lilly and Company. Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

The trial was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines and approved by individual institutional review boards at each participating study center. All patients in this manuscript have given written informed consent for participation in the study and the use of their deidentified, anonymized, aggregated data and their case details (including photographs) for publication.

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