

# Guidelines for clinical trials of frontal fibrosing alopecia: consensus recommendations from the International FFA Cooperative Group (IFFACG)

E. A. Olsen<sup>1</sup> M. Harries,<sup>2</sup> A. Tosti,<sup>3</sup> W. Bergfeld,<sup>4</sup> U. Blume-Peytavi,<sup>5</sup> V. Callender,<sup>6</sup> V. Chasapi,<sup>7</sup> O. Correia,<sup>8</sup> G. Cotsarelis,<sup>9</sup> R. Dhurat,<sup>10</sup> N. Dlova,<sup>11</sup> I. Doche,<sup>12</sup> N. Enechukwu,<sup>13</sup> R. Grimalt,<sup>14</sup> S. Itami,<sup>15</sup> M. Hordinsky,<sup>16</sup> K. Khobzei,<sup>17</sup> W. -S. Lee,<sup>18</sup> S. Malakar,<sup>19</sup> A. Messenger,<sup>20</sup> A. McMichael,<sup>21</sup> P. Mirmirani,<sup>22</sup> Y. Ovcharenko,<sup>23</sup> S. Papanikou,<sup>7</sup> G. M. Pinto,<sup>3</sup> B. M. Piraccini,<sup>24</sup> R. Pirmez,<sup>25</sup> P. Reygagne,<sup>26</sup> J. Roberts,<sup>27</sup> L. Rudnicka,<sup>28</sup> D. Saceda-Corralo,<sup>29</sup> J. Shapiro,<sup>30</sup> T. Silyuk,<sup>31</sup> R. Sinclair,<sup>32</sup> R. O. Soares,<sup>33</sup> A. Souissi,<sup>34</sup> A. Vogt,<sup>5</sup> K. Washenik,<sup>35</sup> A. Zlotogorski,<sup>36</sup> D. Canfield<sup>37</sup> and S. Vano-Galvan<sup>29</sup>

<sup>1</sup>Duke University Medical Center, Durham, NC, USA

<sup>2</sup>University of Manchester, MAHSC and NIHR Manchester Biomedical Research Centre, Salford Royal NHS Foundation Trust, Salford, UK

<sup>3</sup>University of Miami Miller School of Medicine, Miami, FL, USA

<sup>4</sup>Cleveland Clinic, Cleveland, OH, USA

<sup>5</sup>Charité-Universitätsmedizin, Berlin, Germany

<sup>6</sup>Callender Dermatology & Cosmetic Center and Howard University College of Medicine, Washington, DC, USA

<sup>7</sup>Andreas Sygros Hospital, Athens, Greece

<sup>8</sup>Centro Dermatologia Epidermis, Porto, Portugal

<sup>9</sup>University of Pennsylvania, Philadelphia, PA, USA

<sup>10</sup>LTM Medical College & Hospital Sion, Mumbai, India

<sup>11</sup>University of KwaZulu Natal, Durban, South Africa

<sup>12</sup>University of Sao Paulo Medical School, Sao Paulo, SP, Brazil

<sup>13</sup>Nnamdi Azikiwe University Awka, Anambra State, Nigeria

<sup>14</sup>Universitat Internacional de Catalunya, Barcelona, Spain

<sup>15</sup>Oita University, Oita, Japan

<sup>16</sup>University of Minnesota Medical School, Minneapolis, MN, USA

<sup>17</sup>Kyiv Medical University, Kyiv, Ukraine

<sup>18</sup>Yonsei University, Wonju College of Medicine, Wonju, Gangwon-do, Republic of Korea

<sup>19</sup>Rita Skin Foundation, Kolkata, West Bengal, India

<sup>20</sup>Royal Hallamshire Hospital, Sheffield, UK

<sup>21</sup>Wake Forest School of Medicine, Winston Salem, NC, USA

<sup>22</sup>Kaiser Permanente Northern California, Vallejo, CA, USA

<sup>23</sup>V.N. Karazin Kharkiv National University, Kharkiv, Ukraine

<sup>24</sup>University of Bologna, Bologna, Italy

<sup>25</sup>Instituto de Dermatologia Professor Rubem David Azulay – Santa Casa da Misericórdia do Rio de Janeiro, Rio de Janeiro, RJ, Brazil

<sup>26</sup>Centre Sabouraud, Hôpital Saint Louis, Paris, France

<sup>27</sup>Northwest Dermatology Institute, Portland, OR, USA

<sup>28</sup>Medical University of Warsaw, Warsaw, Poland

<sup>29</sup>Ramón y Cajal Hospital, IRYCIS, University of Alcalá, Madrid, Spain

<sup>30</sup>New York University Grossman School of Medicine, New York, NY, USA

<sup>31</sup>Hair Treatment and Transplantation Center Private Practice, Saint Petersburg, Russia

<sup>32</sup>University of Melbourne and Sinclair Dermatology, Melbourne, VIC, Australia

<sup>33</sup>Cuf Descobertas Hospital, Lisbon, Portugal

<sup>34</sup>Department of Dermatology, University of Tunis El Manar, Tunis, Tunisia

<sup>35</sup>Bosley Medical Group, Beverly Hills, CA and New York University Grossman School of Medicine, New York, NY, USA

<sup>36</sup>Hadassah Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel

<sup>37</sup>Canfield Scientific, Inc, Parsippany, NJ, USA

## Summary

### Correspondence

Elise A. Olsen.

Email: [elise.olsen@dm.duke.edu](mailto:elise.olsen@dm.duke.edu)

Background Frontal fibrosing alopecia (FFA) has become one of the most common causes of cicatricial alopecia worldwide. However, there is a lack of clear

**Accepted for publication**

7 June 2021

**Funding sources**

Duke University Hair Research Fund and the Foundation for the Advancement of Hair Disorders.

**Conflicts of interest**

D.C. is president of Canfield Scientific, Inc.

**Data availability**

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

DOI 10.1111/bjd.20567

aetiology and robust clinical trial evidence for the efficacy and safety of agents currently used for treatment.

**Objectives** To enable data to be collected worldwide on FFA using common criteria and assessment methods.

**Methods** A multicentre, international group of experts in hair loss was convened by email to create consensus recommendations for clinical trials. Consensus was defined at > 90% agreement on each recommended part of these guidelines.

**Results** Standardized diagnostic criteria, severity rating, staging, and investigator and patient assessment of scalp hair loss and other clinical features of FFA were created.

**Conclusions** These guidelines should allow the collection of reliable aggregate data on FFA and advance efforts in both clinical and basic research to close knowledge gaps in this condition.

**What is already known about this topic?**

- Frontal fibrosing alopecia (FFA) is a common psychologically debilitating progressive type of hair loss without a clear aetiology or treatments vetted by well-controlled clinical trials.

**What does this study add?**

- This paper provides methods for collecting meaningful data on FFA in clinical trials, databases and registries across the globe.
- These guidelines will promote clinical and basic research on well-defined populations of patients affected with FFA and provide the means to assess the efficacy and safety of individual treatments.

**1. Introduction**

Frontal fibrosing alopecia (FFA), first described in six postmenopausal women by Kossard in 1994, is a type of cicatricial alopecia characterized by hair follicle destruction in a frontal–temporal–parietal distribution.<sup>1,2</sup> It is most commonly seen in postmenopausal women,<sup>3–8</sup> but it has also been observed in premenopausal women<sup>4–7</sup> and men.<sup>5,9,10</sup> While the majority of the reported patients have been of European descent, FFA has also occurred in black<sup>5,8,11,12</sup> and Asian patients<sup>13,14</sup> from various nations. The incidence of FFA is unknown, but the number of women seeking diagnosis and help for this condition has markedly increased in recent years, currently representing the majority of new cases of cicatricial alopecia.<sup>15,16</sup>

The aetiology of FFA is unknown. However, recent work suggests that inflammation-induced hair follicle (HF) stem cell niche damage, epithelial–mesenchymal transition, and immune privilege collapse of the HF bulge region,<sup>17</sup> as well as genetic susceptibility,<sup>18</sup> are important in FFA pathogenesis. Further, given that 5 $\alpha$ -reductase inhibitors appear to help stabilize the condition,<sup>5,8,19–21</sup> and FFA primarily involves portions of the scalp common to pattern hair loss (PHL), a hormonal link is postulated. It is also possible that this condition is triggered by environmental factors. Facial or hair products have been implicated, especially those containing sunscreens, given their now ubiquitous presence in facial moisturizers, foundations and shampoos.<sup>20–25</sup> However, the relationship to FFA has been

particularly difficult to determine due to the changing constituents in these products, various products utilized over time, uncertainty of whether exposure requires a given time period to incite a response, and the unclear mechanisms by which these products contribute to disease development.<sup>26</sup>

The natural history of FFA remains unknown and is quite variable. There have been multiple reports of efficacy of various therapies, but no standardized methodology that will allow comparison of outcomes between treatments or study sites. Internationally accepted guidelines for clinical trials of FFA are needed for future investigator-initiated single or multicentre, collaborative or sponsor-supported studies that address treatment efficacy and potential aetiological factors. To accomplish this, dermatologists with expertise in hair disorders representing 21 countries around the world [the International FFA Cooperative Group (IFFACG)] were convened by email to create standardized measures for clinical trials of FFA. After review of the literature and discussion, consensus (defined as > 90% agreement) was achieved on diagnostic criteria, severity, staging, assessment measures and response criteria for FFA.

**2. Diagnostic criteria**

**2.1. Prior publications and presentations**

Diagnostic criteria for FFA have varied widely in publications or presentations. The US FFA Cooperative Group (USFCG)

used point scoring based on clinical findings and biopsy information for inclusion in their registry.<sup>8</sup> Vañó-Galván *et al.*<sup>5</sup> diagnosed patients by biopsy or recession of the frontotemporal and preauricular hairline, eyebrow loss and characteristic trichoscopic findings. Tolkachjov *et al.*<sup>9</sup> used a diagnostic algorithm that included findings on the scalp and eyebrows, and features common to FFA, but not specific for it, such as non-inflammatory facial papules and preceding or concurrent symptoms of pain or pruritus at areas of involvement.

## 2.2. International FFA Cooperative Group recommendations

In order not to exclude patients with an atypical presentation of FFA, our goal is to create diagnostic criteria for both 'classic FFA', which requires frontal hairline recession, and 'probable FFA', in which this is not necessarily present. Our recommended diagnostic criteria for both include having  $\geq 4$  points from a combination of clinical and pathological findings typical of FFA (Table 1).

## 3. Severity rating

### 3.1. Prior published studies

Two groups have previously published on validated severity ratings for FFA based on point scoring that share some basic premises about FFA but also have some significant differences. While the Frontal Fibrosing Alopecia Severity Index (FFASI)<sup>27</sup> and the Frontal Fibrosing Alopecia Severity Score (FFASS)<sup>28</sup> both weigh recession of the frontal and temporal hairlines as 80% of the total points (80/100 and 20/25 points, respectively) and rate inflammation and eyebrow loss, they diverge significantly from that point forward. FFASI gives points for facial papules, cutaneous lichen planus, oral or genital lichen

planus lesions and nail involvement, but no points for symptoms. FFASI gives no points for nonscalp or noneyebrow involvement but points for pruritus and pain.

### 3.2. Frontal Fibrosing Alopecia Global Staging Score

The IFFACG has created a staging system in which five of the most commonly reported findings each have a range of numbers assigned for a limited severity score. The FFA Global Staging Score is as follows:

- **Scalp hair loss** based on frontal hairline recession as defined in Table 2: 0 = none, 1 = minimal (< 1 cm), 2 = mild (1 to < 3 cm), 3 = moderate (3 to < 5 cm) and 4 = severe ( $\geq 5$  cm).
  - **eyebrow loss**: 0 = none, 1 = partial, 2 = total loss in at least one eyebrow.
  - **Facial papules**: 0 = none 1 = some.
  - **Prominent forehead veins**: 0 = none, 1 = some.
  - **Facial hyperpigmentation**: 0 = none, 1 = some.

Thus, the staging for an individual patient would be shown as  $S_{0-4}E_{0-2}P_{0-1}V_{0-1}H_{0-1}$ .

This very basic staging system facilitates an immediate recognition of certain variables that may be present in a given patient that may have prognostic significance and thus should be considered in inclusion and exclusion criteria and/or separate analysis of treatment cohorts. This staging does not replace more detailed assessment of the severity of each category.

## 4. Assessment measures

### 4.1. Prior published methods

An assessment method termed the Lichen Planopilaris Activity Index (LPPAI) was introduced 10 years ago to allow

**Table 1** International FFA Cooperative Group Criteria for frontal fibrosing alopecia (FFA)

1. Classic FFA
<ul style="list-style-type: none"> <li>• Frontal hairline recession with loss of follicular ostia<sup>a</sup> (2 points); plus</li> <li>• Positive biopsy of a representative section of affected anterior or temporal scalp or eyebrow consistent with FFA<sup>b</sup> (2 points)</li> <li>• At least 50% eyebrow loss (in the absence of alopecia areata)<sup>c</sup> (1 point)</li> <li>• Perifollicular anterior scalp erythema (1 point)</li> <li>• Perifollicular anterior scalp hyperkeratosis or scale (1 point)</li> </ul>
2. Probable FFA
<ul style="list-style-type: none"> <li>• Frontal hairline recession without loss of ostia<sup>a</sup> (1 point)</li> <li>• Positive biopsy of a representative section of affected anterior or temporal scalp or eyebrow consistent with FFA<sup>b</sup> (2 points)</li> <li>• At least 50% eyebrow loss (in the absence of alopecia areata)<sup>c</sup> (1 point)</li> <li>• Perifollicular anterior scalp erythema (1 point)</li> <li>• Perifollicular anterior scalp hyperkeratosis or scale (1 point)</li> <li>• Facial papules (1 point)</li> <li>• Bilateral preauricular hair loss in a patient who previously had hair in this area (1 point)</li> <li>• Documented absence of vellus hairs in affected anterior or temporal hairline (1 point)</li> </ul>

<sup>a</sup>Loss of ostia may be confirmed clinically or by trichoscopy. If no loss of ostia can be confirmed by either method, move to 'probable FFA' criteria, or confirmatory biopsy of FFA from the affected anterior hairline will be necessary as well. <sup>b</sup>Biopsy of a representative section of the affected scalp or eyebrow would be consistent with a diagnosis of FFA if it demonstrates a decreased number of hair follicles and sebaceous glands, concentric perifollicular fibrosis and a lymphocytic infiltrate targeting the isthmus and infundibular regions of the hair follicle. <sup>c</sup>50% eyebrow loss could be 100% loss of only one eyebrow or overall 50% cumulative loss of both eyebrows together.

Table 2 Non-scalp-related clinical signs and symptoms in frontal fibrosing alopecia (FFA)

**I. Hair loss elsewhere**

A. *Eyebrows.* Eyebrow loss is an important diagnostic clue in FFA, occurring in 73–95% of cases,<sup>5–8</sup> including being the initial finding in ~8–40% of cases.<sup>5,6</sup> Eyebrows may also show regrowth with systemic treatment independently of hair loss on the scalp or with local eyebrow-only treatment. Because of this, we wish to specifically have a grading scale that will capture the severity of hair loss if treatment is directed locally at the eyebrows or if using systemic therapy for FFA. We propose that the right and left eyebrows and medial and lateral portions of each eyebrow be assessed individually on a scale of no loss/no interruption in hair growth = 0, partial loss/interruption of hair loss = 1, and complete hair loss = 2

B. *Eyelashes.* While not as common as eyebrow loss, eyelash loss may occur and has been associated with severe FFA.<sup>5,8</sup> We propose a grading system for eyelashes that separately evaluates the right and left and upper and lower lashes, with a scale of no loss/no interruption in hair growth = 0, partial loss/interruption of hair loss = 1, and complete hair loss = 2

C. *Androgen-dependent hair growth or loss.* Facial, axillary and pubic hair have been reported to be negatively affected in FFA. Beard hair loss in men has been reported in several publications, in up to 50% of men in one series.<sup>5,47</sup> Loss of sideburns is also a specifically reported type of facial hair loss.<sup>48,49</sup> Loss of axillary and pubic hair has been reported in > 50% of cases.<sup>6</sup> Hair loss in the beard, moustache, sideburns, and axillary and pubic hair is best assessed by a simple scale of none, partial or total hair loss, recognizing that this assessment relies primarily on patient reporting unless a full physical exam is performed

D. *Body hair.* Loss of hair on the extremities is extremely common,<sup>2,6</sup> but the aetiology is confusing as this may occur normally in postmenopausal women, and the degree of loss is difficult to ascertain without having documentation of the amount of normal hair growth. Although clinically apparent inflammation is not usually seen, biopsies performed in a few cases have shown the same perifollicular lymphocytic infiltrate on hairless extremities as on the scalp.<sup>50,51</sup> We would recommend grading body hair separately on the upper and lower and right and left extremities on a hair loss scale of 0 = no loss, 1 = partial loss, and 2 = total loss

**II. Facial lesions**

A. *Facial papules.* Reports of textural changes in the facial skin by patients are often associated with collections of small (1–2 mm) yellow to flesh-coloured noninflammatory monomorphic papules, most commonly seen in the temporal area, but individual lesions may be distributed in other areas of the face. Facial papules have been reported in 3–22% of cases.<sup>5,52,53</sup> Biopsies of these facial papules have shown either involvement of vellus follicles with perifollicular lichenoid inflammation and/or dilated sebaceous ducts<sup>54,55</sup> or hypertrophic sebaceous glands.<sup>56</sup> To further characterize these papules and to determine their relationship to other clinical features of FFA and response to therapy, the presence or absence of facial papules should be recorded in all patients. If they are present, the following data should be collected: location on the face, size, number and density, shape and colour. Biopsies of isolated lesions may eliminate any alternate aetiologies

B. *Facial veins.* Prominent superficial veins on the forehead are a common occurrence although infrequently noted.<sup>6</sup> The prominent veins are typically seen at the lateral sides of the scalp, although depression of the veins in the centre of the forehead has been reported.<sup>57</sup> We recommend tracking separately right and left lateral and central forehead veins and whether depressed, flat or raised (engorged)

C. *Pigmentation.* At this point, capturing the presence and location of pigmentary changes should suffice to help to determine their incidence and need for further evaluation

a. *Hyperpigmentation.* Acquired dark brown to slate grey macules primarily on the face, neck and flexures may be seen in FFA, more often in dark-skinned individuals than in white patients, and characterized by a lichenoid infiltrate and pigmentary incontinence on biopsy.<sup>58–60</sup>

b. *Hypopigmentation* in the area of frontoparietal hair loss in FFA has also been reported, more easily appreciated with Wood's light<sup>61</sup>

D. *Rosacea-like eruption.* Rosacea was reported in 34% of 103 women with FFA, the majority having the erythematotelangiectatic subtype of mild-to-moderate severity.<sup>62</sup> Whether classic rosacea is more common in FFA or whether this is a particular type of facial erythema specific to FFA will be important to determine

**III. Symptomatology**

Symptoms of pain, pruritus and/or burning have been reported to vary from 3%<sup>7</sup> to 65%.<sup>6</sup> We recommend using a 10-point visual analogue scale to collect data independently on pain/burning and pruritus

comparison of treatments for LPP, but it was also piloted in FFA.<sup>29</sup> The index includes both symptoms (pain, burning and pruritus) and clinical signs of inflammation, a hair pull test, and a score for 'spreading' of the hair loss. The primary issues with this scale include the inexact definition of some signs and the finding that patients may have continued progression of hair loss while the score improves based on only changes in symptomatology or inflammation.<sup>7</sup>

**4.2. International FFA Cooperative Group methods**

The primary assessment measures that our international group suggests for clinical trials of FFA are ones that separate out

and assess progression of hair loss independently from inflammation and symptoms.

**4.2.1. Alopecia Density and Extent frontal fibrosing alopecia score**

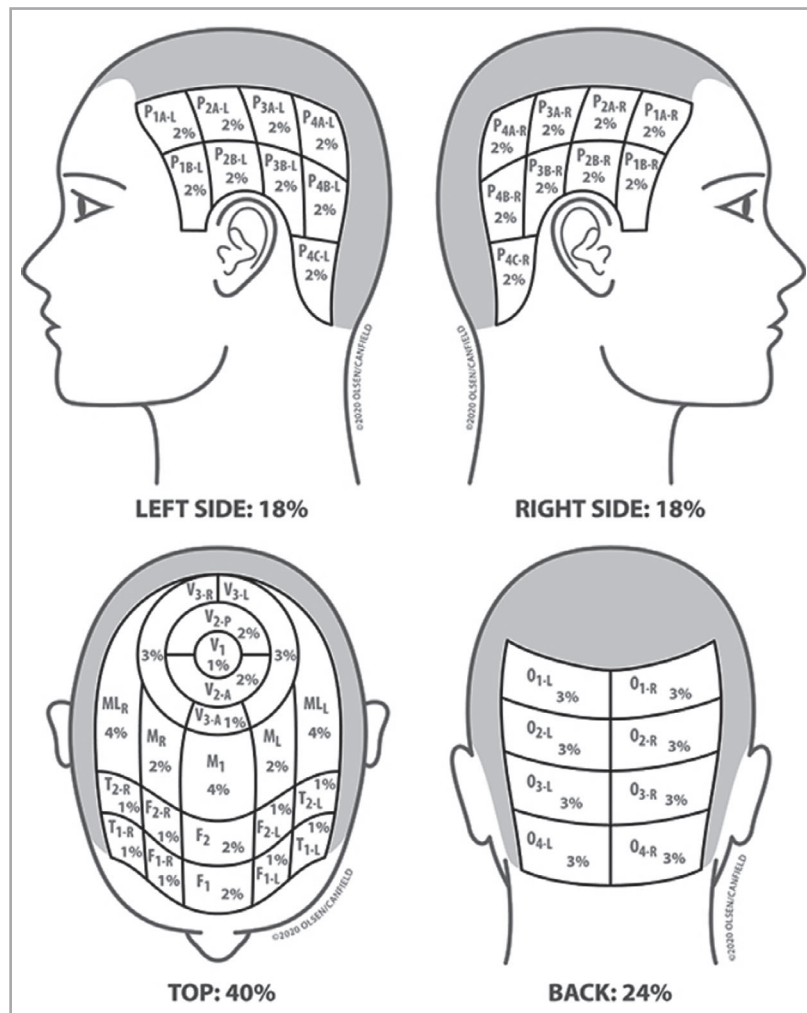
There are two critical components of the hair loss in all forms of FFA: extent of hair loss and changes in hair density of scalp hair loss throughout the scalp. The ALODEX<sub>FFA</sub> score expands on the method of data collection utilized by the USFCG in their original study of FFA<sup>8</sup> and the Alopecia Density and Extent (ALODEX) score, previously published for alopecia areata.<sup>26</sup>

The ALODEX score, first introduced and tested at Duke University in 2016, involves assigning a score of hair density to a figure of the scalp divided into units of 1% scalp surface area (SSA).<sup>30,31</sup> The ALODEX score is determined by summing the hair density rating (which in the original had a maximum of 10 for total hair loss) in each of the 1% areas and dividing by 100 (giving the total percentage SSA).

We have made adjustments to the ALODEX score for FFA in two ways. The first is by consolidating the 1% SSAs into larger areas in the typical distribution pattern of involvement of FFA, PHL and fibrosing alopecia in a pattern distribution,<sup>32</sup> conditions that often occur with FFA [Severity of Alopecia Tool (SALT III); Figure 1]. This change was made in order to simplify the labelling and reporting of key segments and for easy manual computation. Secondly, we have also modified the hair loss density scale from the subjective determination of 10% increments of hair loss noted for the original ALODEX.<sup>30</sup> The ALODEX<sub>FFA</sub> is based on the progressive decrease in normal hair growth and density for a given patient, scored

0 = 0–49%, 1 = 50–74%, 2 = 75–89%, 3 = 90–99% and 4 = 100% hair loss, in close alignment to prior published hair loss scales for alopecia areata<sup>33</sup> and regional hair density in PHL.<sup>34,35</sup> The revision of the prior FFA hair loss density scale is based on (i) the difficulty in clinically identifying 10% degrees of hair loss when this loss is < 50% of normal for an individual patient, (ii) the general consensus that it takes 50% hair loss to first cause notable hair loss<sup>36,37</sup> and (iii) the lower potential for miscalling a minor change in hair loss at the lower end of the hair density scale. The ALODEX<sub>FFA</sub> is calculated by adding together the density assignments in all areas of the scalp and dividing by 100.

The sum of the percentages of scalp areas with a hair loss rating of 1–5 indicates the total percentage SSA involved in FFA at that time. Recording of the density ratings on the SALT III figure with each section of the scalp labelled also allows for tracking hair loss specifically in the frontal, mid scalp, vertex, temporal, parietal and occipital scalp areas separately as desired.



**Figure 1** Severity of Alopecia Tool III (SALT III) figure used for designation of scalp surface area and hair density of typically involved areas of the scalp in frontal fibrosing alopecia and pattern hair loss. For each individual scalp area, the area is labelled and the percentage scalp surface area noted. F, frontal; L, left; M, mid scalp; O, occipital; P, parietal; R, right; T, temporal; V, vertex.

#### 4.2.2. Recession of frontal hairline

The other major component of classic FFA severity is the recession of the frontal hairline, which depends on recognition of both the original frontal and new frontal hairline. Unfortunately, the recession of the frontal hairline in FFA is not always uniform, but usually presents as a density gradient back to what appears to be the new normal hair density, often with 'lonely hairs' out front.<sup>38</sup> Further complicating this assessment is a decrease in hair density that continues for some distance past the middle hairline in women who also have the frontal accentuation or 'Christmas tree' pattern of female pattern hair loss (FPHL).<sup>39</sup> The original frontal hairline can usually be noted by the end of forehead photodamage in white women, but this is not something that can be used in darker-skinned women. The superior edge of wrinkling of the forehead when one raises the eyebrows (where the superior portion of the frontalis muscle inserts on the galea aponeurotica of the scalp)<sup>40</sup> is another way of finding the original hairline, but this is difficult to use in patients who have had botulinum injections in their forehead muscles.

Despite these limitations in identifying the original hairline, we have provided a definition for the degree of recession of the frontal and temporal hairlines (Figure 2) that should allow for reliable measurements. It is recommended that a single observer at a given site defines 'confluent and homogeneous hair growth' for a given patient.

#### 4.2.3. Hair loss in other scalp areas

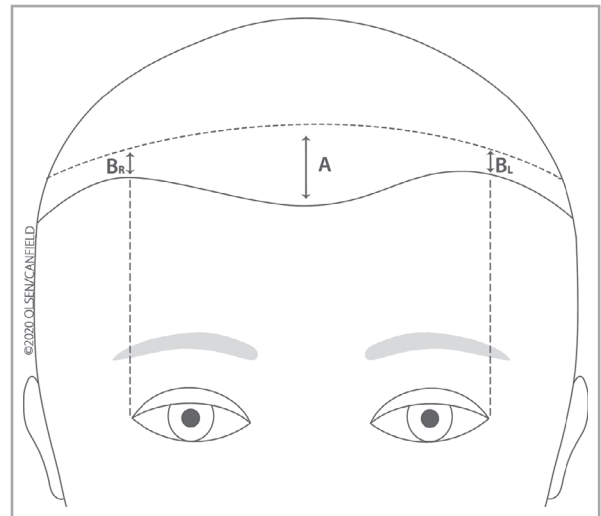
Loss of hair in other scalp areas (e.g. parietal, central scalp, occipital) is best captured with grading of hair density on the SALT III figure.

#### 4.2.4. Inflammation

Perifollicular erythema and/or perifollicular scale is present in the majority of cases and may be associated with progression of disease and/or the severity of the lymphocytic infiltrate on biopsy.<sup>41,42</sup> We propose grading perifollicular erythema or scale separately on the SALT III figure with 0 = none, 1 = mild, 2 = moderate and 3 = severe.

#### 4.2.5. Hair pull

A hair pull is defined as gently pulling a group of hairs from the scalp surface to the ends of the hair and determining by microscopic or dermoscopic examination the type and number of hairs dislodged. Typically, a hair pull is used in telogen effluvium, where the number of telogen hairs dislodged in a given number of pulls at various places in the scalp helps to determine both the diagnosis and the severity of the disorder. However, it can also be used as a diagnostic tool for loose anagen syndrome, where the pulled hairs are loose anagen hairs, or alopecia areata, where the pulled hairs may be telogen or dystrophic anagen hairs. A hair pull showing anagen hairs at the periphery of areas of cicatricial alopecia has been



**Figure 2** Quantitative measurement of frontal and temporal hairline recession. 'A' is the amount or degree of frontal hairline recession, defined as the distance in centimetres out to one decimal point in the middle of the frontal scalp hairline from the superior edge of wrinkling of the forehead when one raises the eyebrows to an area directly behind this where the hair density is most confluent and homogeneous. This number will be used directly, not categorically, in sequential measurements, ensuring that the most reliable information will be collected for this important feature of FFA. For those light-skinned patients who have had botulinum injections or where an additional aid is needed, the end of photodamage would substitute for the superior edge of wrinkling of the forehead when one raises the eyebrows. 'B' is the amount or degree of temporal hairline recession, defined as the distance in centimetres in the middle of each temporal area (defined as the point from the lateral canthus carried superiorly) from the superior edge of wrinkling of the forehead when one raises the eyebrows to an area directly behind this where the hair density is most confluent and homogeneous. For those light-skinned patients who have had botulinum injections or where an additional aid is needed, the end of photodamage would substitute for the superior edge of wrinkling of the forehead when one raises the eyebrows. Measurements of left and right temporal hairline recession should be done separately.

used as a measure of the activity level in these conditions. We propose doing a hair pull in FFA in at least five different scalp areas involved in the balding process as recommended for other hair loss conditions. We propose a recording system for the 'Activity Level' of FFA of 0 = no anagen hairs pulled, 1 = one anagen hair, 2 = two anagen hairs and 3 = more than two anagen hairs in a total of five hair pulls.

#### 4.2.6. Pattern of frontal fibrosing alopecia hairline recession

It has been suggested that the pattern of hairline recession may have prognostic implications<sup>43</sup> and thus the assignment of these patterns at baseline may be important to response assessment. The patterns of hairline recession in FFA currently noted include three classical patterns: (i) linear pattern, (ii) diffuse pattern and (iii) pseudo fringe sign pattern (Figure 3).

For the pseudo fringe sign pattern, the first hairline is likely the original hairline and the posterior one the new one to be measured; it is prudent to track both hairlines. There are other unusual patterns of FFA including male androgenetic alopecia-like pattern (marked and symmetrical recession of frontotemporal hairlines with a peculiar sparing of the paramedian part of the frontal hairline), cockade-like pattern (symmetric oval patches of alopecia with a peculiar thin band of temporal hairline sparing) and ophiasis-like pattern (marginal loss involving from the frontal to the occipital area).<sup>44–46</sup>

## 5. Assessment measures other than scalp hair

Assessment measures for signs or symptoms associated with FFA other than scalp hair are presented in Table 2.<sup>47–62</sup>

## 6. Quality-of-life assessment

In general, for clinical trials, it is recommended that one consider using two quality-of-life assessment methods: (i) a generic assessment of overall health that allows comparison of patients across different specific conditions and (ii) an assessment of the effects of the specific disease or condition.

For a general health quality-of-life tool, we recommend the Short Form-12,<sup>63,64</sup> a comprehensive general health survey questionnaire.

For an FFA disease-specific tool, we recommend the Woman's Androgenetic Alopecia Quality of Life Questionnaire (WAA-QOL)<sup>65,66</sup> (Table 3). The latter was developed by hair experts, pilot tested in women with a wide range of Ludwig stages and Savin Female Density Scale ratings of FPHL, and included in a 1-year, double-blind, placebo-controlled clinical trial of finasteride in postmenopausal women.<sup>67</sup> The pilot study for the WAA-QOL contained pre- and postmenopausal women, the vast majority (87%) white, with over half having moderate-to-severe FPHL, a population not too dissimilar from those with FFA, many of whom also have FPHL. The WAA-QOL has excellent content validity, internal consistency and test–retest reliability. A slightly different version with an additional item was piloted in men and the results correlated with hair counts.<sup>68</sup> Although the concerns noted in the WAA-QOL mirror those in assessing patients with FFA, it, or a similar tool, will need to be further validated in patients with FFA.

## 7. Response criteria and endpoints

### 7.1. Primary endpoint

The primary objective in a scarring hair loss process is to prevent further loss while hoping that there may be some regrowth in certain circumstances. Using the percentage change from baseline of the ALODEX<sub>FFA</sub> score would evaluate the two primary characteristics of hair loss in all types of FFA: extent and hair density. For a clinical trial, the design should address whether a positive response is only a lack of progressive loss from baseline and what



**Figure 3** Classical patterns of hairline recession in frontal fibrosing alopecia (FFA). (a) A 45-year-old woman diagnosed with FFA showing uniform frontal hairline recession in the absence of loss of hair density behind the hairline (pattern I or 'linear pattern'). (b) A 64-year-old woman diagnosed with FFA showing a diffuse bandlike alopecia affecting the frontal hairline with significant loss of hair density behind the hairline (pattern II or 'diffuse pattern'). (c) A 61-year-old woman diagnosed with FFA showing a frontal unaffected primitive hairline forming a 'double line' aspect (pattern III or 'pseudo fringe sign pattern'). The eyebrows are usually spared in this clinical pattern.

**Table 3** The Woman’s Androgenetic Alopecia Quality of Life Questionnaire (WAA-QOL) (modified for use in women or men)

1. In the past WEEK, how self-conscious have you been about people looking at your hair?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
2. In the past WEEK, how jealous/envious have you been of other people who have lots of hair?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
3. In the past WEEK, how much has your hair loss NEGATIVELY affected your self-confidence?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
4. In the past WEEK, how unattractive have you felt because of your hair loss?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
5. In the past WEEK, how much was socializing with people you didn’t know a problem for you because of your hair loss?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
6. In the past WEEK, how much was interacting with the opposite sex (or same sex if lesbian or gay) a problem for you because of your hair loss?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
7. In the past WEEK, how much has your hair loss NEGATIVELY affected your satisfaction with the appearance of your hair?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
8. In the past WEEK, how much has your hair loss NEGATIVELY affected the way you like to style your hair?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
9. In the past WEEK, how powerless (lack of control) have you felt to do anything about your hair loss?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
10. In the past WEEK, how embarrassed have you felt because of the appearance of your hair?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
11. In the past WEEK, how frustrated have you felt because of your hair loss?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
12. In the past WEEK, how concerned have you been about your hair parting and showing your scalp (bare spots)?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
13. In the past WEEK, how concerned have you been that your hair loss will continue?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
14. In the past WEEK, how much time have you spent making your hair look fuller/thicker because of your hair loss?						
Extensive	A whole lot	A lot	A moderate amount	Some	A little bit	None
15. In the past WEEK, how annoyed have you been at having to spend time fixing your hair to cover your scalp (bare spots) because of your hair loss?						
Extremely	Very much	Quite a bit	A good bit	Somewhat	A little bit	Not at all
16. In the past WEEK, how much time have you spent checking your hair in the mirror because of your hair loss?						
Extensive	A whole lot	A lot	A moderate amount	Some	A little bit	None

Reproduced with permission, from Dolte *et al.* *Clin Exp Dermatol* 2000; **25**:637–42.<sup>66</sup>

percentage SD that includes. Certainly, a negative percentage change (the ALODEX score is based on hair loss, not growth) would be considered some degree of hair regrowth.

## 7.2. Secondary endpoints

### 7.2.1. Investigator

For all patients with FFA, especially those with the classic pattern, frontal hairline recession is an important marker, covered somewhat in the ALODEX<sub>FFA</sub> but not specifically. A change from baseline in the frontal hairline recession would be a key finding and specific to the FFA process.

### 7.2.2. Patient and investigator assessment

For patient and investigator assessment of efficacy, we recommend a global assessment comparing hair growth at baseline vs. the timepoint in question. Standardized photographs should be provided with (i) the hair pulled back on the sides and including the ear as a reference point, (ii) the hair pulled

back from the frontal and temporal hairlines with the eyebrows included and (iii) the top of the scalp with the hair parted in the middle. These photographs are key as they corroborate the ALODEX<sub>FFA</sub> grading, allowing patients to see areas of the scalp that they may not otherwise be able to appreciate. If at least baseline photos are provided, this will also eliminate the issue of remembering what the hair loss looked like at the start of a trial for both the patient and investigator. The following scale designating changes in hair growth has been used with success in several pivotal clinical trials of medications approved for PHL and is often referred to as a global response score:

Since the start of the study, how would you describe the patient’s/your growth of hair?

- + 3 = Greatly increased
- + 2 = Moderately increased
- + 1 = Slightly increased
- 0 = No change
- 1 = Slightly decreased
- 2 = Moderately decreased
- 3 = Greatly decreased



### 7.2.3. Other exploratory response measures

Other potential exploratory response measures are noted in Table 4, including a potential patient-reported outcome of satisfaction with treatment. Providing at least a photograph or other visual representation of baseline hair loss to refresh the patient's memory of where they started at the baseline of the study prior to an intervention is recommended and

does not eliminate a static determination of satisfaction at each visit.

## 8. Duration of clinical trial

Each clinical trial should be sufficiently long to address the issue in question. Given that FFA usually progresses only slowly and the primary goal is stability of the current hair loss, a minimum

**Table 4** Exploratory response measures

1. Patient assessment
A. Patient comparative assessment of hair growth using a seven-point scale of $-3$ to $+3$ <sup>69-72</sup>
B. Patient satisfaction assessment of scalp hair <sup>60,61</sup> :
i. Compared with the beginning of the study, which statement best describes your satisfaction with the appearance of the hairline at the front of your head?
Very satisfied = 1
Satisfied = 2
Neutral = 3
Dissatisfied = 4
Very dissatisfied = 5
ii. Compared with the beginning of the study, which statement best describes your satisfaction with the appearance of the hair on top of your head?
Very satisfied = 1
Satisfied = 2
Neutral = 3
Dissatisfied = 4
Very dissatisfied = 5
iii. Compared with the beginning of the study, which statement best describes your satisfaction with the appearance of your hair overall?
Very satisfied = 1
Satisfied = 2
Neutral = 3
Dissatisfied = 4
Very dissatisfied = 5
C. Patient satisfaction assessment of eyebrows (modified from <sup>60,61</sup> ):
i. Compared with the beginning of the study, which statement best describes your satisfaction with the appearance of your eyebrows?
Very satisfied = 1
Satisfied = 2
Neutral = 3
Dissatisfied = 4
Very dissatisfied = 5
ii. Compared with the beginning of the study, which statement best describes your satisfaction with the appearance of your eyebrows?
Very satisfied = 1
Satisfied = 2
Neutral = 3
Dissatisfied = 4
Very dissatisfied = 5
iii. Compared with the beginning of the study, which statement best describes your satisfaction with the appearance of your eyebrows overall?
Very satisfied = 1
Satisfied = 2
Neutral = 3
Dissatisfied = 4
Very dissatisfied = 5
D. Change in symptoms (pruritus, pain/burning): based on visual analogue scales for both
2. Investigator assessment: comparison with baseline
A. Total or percentage change in ALODEX <sub>FFA</sub> score
B. Total or percentage change in extent of hair loss (by scalp surface area)
C. Percentage change in recession hairline
D. Change in inflammation (perifollicular erythema + perifollicular scale score)

study duration of 6 months is recommended for those trials assessing the efficacy of a given treatment in FFA.

## 9. Elimination of effects of prior treatments

Either (i) a washout time of agents currently used for FFA based on their half-lives or typical biological activity or (ii) the stability of current treatment(s) and dose for at least 3 months is suggested to assess the efficacy of the new agent.

## 10. Conclusions

FFA is a common but vexing hair loss disorder in which our understanding of its aetiology or best treatments is limited by the lack of a standardized clinical trial design. We acknowledge that most of what we propose is arbitrary and not yet validated in FFA, but we believe that these guidelines provide a place to begin collection internationally of consistent data on well-defined populations of patients with FFA, something otherwise lacking. The IFFACG hopes that these recommendations for diagnostic criteria, severity rating, staging, assessment methods and response criteria will encourage clinical trials and will allow international aggregate data collection to address knowledge gaps and to determine safe and effective treatments for FFA.

## References

- Kossard S. Postmenopausal frontal fibrosing alopecia. Scarring alopecia in a pattern distribution. *Arch Dermatol* 1994; **130**:770–4.
- Kossard S, Lee MS, Wilkinson B. Postmenopausal frontal fibrosing alopecia: a frontal variant of lichen planopilaris. *J Am Acad Dermatol* 1997; **36**:59–66.
- Vaisse V, Matarid B, Assouly P *et al.* Postmenopausal frontal fibrosing alopecia: 20 cases. *Ann Dermatol Venerol* 2003; **130**:607–10.
- Moreno-Ramirez D, Camacho Martinez F. Frontal fibrosing alopecia: a survey in 16 patients. *J Eur Acad Dermatol Venerol* 2005; **19**:700–5.
- Vañó-Galván S, Molina-Ruiz AM, Serrano-Falcón C *et al.* Frontal fibrosing alopecia: a multicenter review of 355 patients. *J Am Acad Dermatol* 2014; **70**:670–8.
- Banka N, Mubki T, Bunagan MJ *et al.* Frontal fibrosing alopecia: a retrospective clinical review of 62 patients with treatment outcome and long term follow up. *Int J Dermatol* 2014; **53**:1324–30.
- MacDonald A, Clark C, Holmes S. Frontal fibrosing alopecia: a review of 60 cases. *J Am Acad Dermatol* 2012; **67**:955–61.
- Ladizinski B, Bazakas A, Selim MA, Olsen EA. Frontal fibrosing alopecia: a retrospective review of 19 patients seen at Duke University. *J Am Acad Dermatol* 2013; **68**:749–55.
- Tolkachjov SN, Caudhry HM, Camilleri MJ, Torgerson RR. Frontal fibrosing alopecia among men: a clinicopathologic study of 7 cases. *J Am Acad Dermatol* 2017; **77**:683–90.
- Stockmeier M, Kunte C, Sander CA, Wolff H. Kossard frontal fibrosing alopecia in a man. *Hautarzt* 2002; **53**:409–11.
- Dlova NC, Jordaan HF, Skenjane A *et al.* Frontal fibrosing alopecia: a clinical review of 20 black patients from South Africa. *Br J Dermatol* 2013; **169**:939–41.
- Miteva M, Whiting D, Harries M *et al.* Frontal fibrosing alopecia in black patients. *Br J Dermatol* 2012; **167**:208–10.
- Inui S, Nakajima T, Shono F, Itami S. Dermoscopic findings in frontal fibrosing alopecia: report of four cases. *Int J Dermatol* 2008; **47**:796–9.
- Panchaprateep R, Ruxrungtham P, Chancheewa B, Asawanonda P. Clinical characteristics, trichoscopy, histopathology and treatment outcomes of frontal fibrosing alopecia in an Asian population: a retro-prospective cohort study. *J Dermatol* 2020; **47**:1301–11.
- Vañó-Galván S, Saceda-Corralo D, Blume-Peytavi U *et al.* Frequency of the types of alopecia at twenty-two specialist hair clinics: a multicenter study. *Skin Appendage Disord* 2019; **5**:309–15.
- Griffin LL, Griffiths CEM, Michaelides C *et al.* Primary cicatricial alopecias: a UK survey. *Br J Dermatol* 2012; **167**:694–7.
- Harries MJ, Jimenez F, Izeta A *et al.* Lichen planopilaris and frontal fibrosing alopecia as model epithelial stem cell diseases. *Trends Mol Med* 2018; **24**:435–48.
- Tziotzios C, Petridis C, Dand N *et al.* Genome-wide association study in frontal fibrosing alopecia identifies four susceptibility loci including HLA-B\*07:02. *Nat Commun* 2019; **10**:1150.
- Ramos PM, Anzai A, Duque-Estrada B *et al.* Risk factors for frontal fibrosing alopecia: a case-control study in a multiracial population. *J Am Acad Dermatol* 2021; **84**:712–8.
- Moreno-Arrones OM, Saceda-Corralo D, Rodrigues-Barata AR *et al.* Risk factors associated with frontal fibrosing alopecia: a multicenter case-control study. *Clin Exp Dermatol* 2019; **44**:404–10.
- Pindado-Ortega C, Saceda-Corralo D, Moreno-Arrones OM *et al.* Effectiveness of dutasteride in a large series of patients with frontal fibrosing alopecia in real clinical practice. *J Am Acad Dermatol* 2021; **84**:1285–94.
- Debroy-Kidambi A, Dobson K, Holmes S *et al.* Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens. *Br J Dermatol* 2017; **177**:260–1.
- Callander J, Frost J, Stone N. Ultraviolet filters in hair-care products: a possible link with frontal fibrosing alopecia and lichen planopilaris. *Clin Exp Dermatol* 2018; **43**:57–79.
- Aldoori N, Dobson K, Holden CR *et al.* Frontal fibrosing alopecia: possible association with leave-on facial skin care products and sunscreens; a questionnaire study. *Br J Dermatol* 2016; **175**:762–7.
- Cranwell WC, Sinclair R. Sunscreen and facial skin care products in frontal fibrosing alopecia: a case-control study. *Br J Dermatol* 2019; **180**:943–4.
- Felmingham C, Yip L, Tam M, Nixon RL. Allergy to sunscreen and leave-on facial cosmetic products is not a likely causative mechanism in frontal fibrosing alopecia: perspective from contact allergy experts. *Br J Dermatol* 2020; **182**:481–2.
- Holmes S, Ryan T, Young D, Harries M. Frontal Fibrosing Alopecia Severity Index: a validated scoring system for frontal fibrosing alopecia. *Br J Dermatol* 2016; **175**:203–7.
- Saceda-Corralo D, Morena-Arrones OM, Fonda-Pascaual P *et al.* Development and validation of the Frontal Fibrosing Alopecia Severity Score. *J Am Acad Dermatol* 2018; **78**:522–9.
- Samrao A, Chew A-L, Price V. Frontal fibrosing alopecia: a clinical review of 36 patients. *Br J Dermatol* 2010; **163**:1296–300.
- Olsen EA, Roberts J, Sperling L *et al.* Objective outcome measures: collecting meaningful data on alopecia areata. *J Am Acad Dermatol* 2018; **79**:470–8.
- Olsen EA, Canfield D. SALT II: a new take on the Severity of Alopecia Tool (SALT) for determining percentage of scalp hair loss. *J Am Acad Dermatol* 2016; **75**:1268–70.
- Zinkernagel MS, Trueb RM. Fibrosing alopecia in a pattern distribution: patterned lichen planopilaris or androgenetic alopecia with a lichenoid tissue reaction pattern? *Arch Dermatol* 2000; **136**:205–11.
- Olsen EA, Hordinsky MK, Price VH *et al.* Alopecia areata investigational assessment guidelines – part II. *J Am Acad Dermatol* 2004; **51**:440–7.

- 34 Olsen EA, Canfield D, Canfield W, Budris K. A novel method for assessing regional scalp hair density in male pattern hair loss. In: *Hair Science and Technology* (Van Neste D, ed), New York: McGraw-Hill, 2003; 251–4.
- 35 Olsen EA. Current and novel methods for assessing efficacy of hair growth promoters in pattern hair loss. *J Am Acad Dermatol* 2003; **48**:253–62.
- 36 Olsen EA. Clinical tools for assessing hair loss. In: *Disorders of Hair Growth: Diagnosis and Treatment* (Olsen EA, ed), New York: McGraw-Hill, 1994; 59–69.
- 37 Chen A, Setser A, Andakat M *et al.* Grading dermatologic adverse events in cancer patients: the National Cancer Institute's Common Terminology Criteria for Adverse Events Version 4.0. *J Am Acad Dermatol* 2012; **67**:1025–39.
- 38 Tosti A, Miteva M, Torres F. Lonely hair: a clue to the diagnosis of frontal fibrosing alopecia. *Arch Dermatol* 2011; **147**:1240.
- 39 Olsen EA. Female pattern hair loss. *J Am Acad Dermatol* 2001; **45** (3 Suppl.):S70–80.
- 40 Mirmirami P, Zimmerman B. Cocking the eyebrows to find the missing hairline in frontal fibrosing alopecia: a useful clinical maneuver. *J Am Acad Dermatol* 2016; **75**:e63–4.
- 41 Toledo-Pastrana T, Hernandez MJG, Camacho Martinez FM. Perifollicular erythema as a trichoscopy sign of progression in frontal fibrosing alopecia. *Int J Trichol* 2013; **5**:151–3.
- 42 Martinez-Velasco M, Vazquez-Herrera N, Misciali C *et al.* Frontal Fibrosing Alopecia Severity Index: a trichoscopic visual scale that correlates thickness of peripilar casts with severity of inflammatory changes at pathology. *Skin Appendage Disord* 2018; **4**:277–80.
- 43 Moreno-Arrones OM, Saceda-Corralo D, Fonda-Pascual P *et al.* Frontal fibrosing alopecia: clinical and prognostic classification. *J Eur Acad Dermatol Venereol* 2017; **31**:1739–45.
- 44 Pirmez R, Duque-Estrada B, Abraham LS *et al.* It's not all traction: the pseudo 'fringe sign' in frontal fibrosing alopecia. *Br J Dermatol* 2015; **173**:1336–8.
- 45 Rossi A, Grassi S, Fortuna MC *et al.* Unusual patterns of presentation of frontal fibrosing alopecia: a clinical and trichoscopic analysis of 98 patients. *J Am Acad Dermatol* 2017; **77**:172–4.
- 46 Brandi N, Starace M, Alessandrini A *et al.* The doll hairline: a clue for the diagnosis of frontal fibrosing alopecia. *J Am Acad Dermatol* 2017; **77**:e127–8.
- 47 Salido-Vallejo R, Garnacho-Saucedo G, Moreno-Gimenez JC, Camacho-Martinez FM. Beard involvement in a man with frontal fibrosing alopecia. *Indian J Dermatol Venereol Leprol* 2014; **80**:542–4.
- 48 AlGaadi S, Miteva M, Tosti A. Frontal fibrosing alopecia in a male presenting with sideburn loss. *Int J Trichol* 2015; **7**:72–7.
- 49 Ramaswamy P, Mendese G, Goldberg LJ. Scarring alopecia of the sideburns: a unique presentation of frontal fibrosing alopecia in men. *Arch Dermatol* 2012; **148**:1095–6.
- 50 Miteva M, Camacho I, Romanelli P, Tosti A. Acute hair loss on the limbs in frontal fibrosing alopecia: a clinicopathological study of two cases. *Br J Dermatol* 2010; **163**:426–8.
- 51 Armenores P, Shirato K, Reid C, Sidhu S. Frontal fibrosing alopecia associated with generalized hair loss. *Australas J Dermatol* 2010; **51**:183–5.
- 52 Flores-Terry MA, Garcia-Arpa M, Franco-Munoz M, Gonzalez-Ruiz L. Facial papules in frontal fibrosing alopecia: good response to isotretinoin. *Actas Dermosifiliogr* 2018; **109**:831–3.
- 53 Valesky EM, Maier MD, Kippenberger S *et al.* Frontal fibrosing alopecia – review of recent case reports and case series in PubMed. *J Dtsch Dermatol Ges* 2018; **16**:992–9.
- 54 Donati A, Molina L, Doche I *et al.* Facial papules in frontal fibrosing alopecia: evidence of vellus follicle involvement. *Arch Dermatol* 2011; **145**:1424–7.
- 55 Pirmez R, Barreto T, Duque-Estrada B *et al.* Facial papules in frontal fibrosing alopecia: beyond vellus hair follicle involvement. *Skin Appendage Disord* 2018; **4**:145–9.
- 56 Pedrosa AF, Duarte AF, Haneke E, Correia O. Yellow facial papules associated with frontal fibrosing alopecia: a distinct histologic pattern and response to isotretinoin. *J Am Acad Dermatol* 2017; **77**:764–6.
- 57 Vañó-Galván S, Rodrigues-Barata AR, Urech M *et al.* Depression of the frontal veins: a new clinical sign of frontal fibrosing alopecia. *J Am Acad Dermatol* 2015; **72**:1087–8.
- 58 Dlova NC. Familial frontal fibrosing alopecia and lichen planus pigmentosus: is there a link? *Br J Dermatol* 2012; **168**:439–42.
- 59 Robles-Méndez JC, Rizo-Frias P, Herz-Ruelas ME *et al.* Lichen planus pigmentosus and its variants: review and update. *Int J Dermatol* 2018; **57**:505–14.
- 60 Berliner JG, McCalmont TH, Price VH, Berger TG. Frontal fibrosing alopecia and lichen planus pigmentosus. *J Am Acad Dermatol* 2014; **71**:e226–7.
- 61 Lin J, Valdebran M, Bergfeld W *et al.* Hypopigmentation in frontal fibrosing alopecia. *J Am Acad Dermatol* 2017; **76**:1184–6.
- 62 Pindado-Ortega C, Saceda-Corralo D, Buendía-Castaño D *et al.* Frontal fibrosing alopecia and cutaneous comorbidities: a potential relationship with rosacea. *J Am Acad Dermatol* 2018; **78**:596–7.
- 63 Jenkinson C, Wright L, Coulter A. Criterion validity and reliability of the SF-36 in a population sample. *Qual Life Res* 1994; **3**:7–12.
- 64 McHorney CA, Ware JE Jr, Lu JF, Sherborne CD. The MOS-36-item Short Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med Care* 1994; **32**:40–66.
- 65 Girman CJ, Hartmaier S, Roberts J *et al.* Patient-perceived importance of negative effects of androgenetic alopecia in women. *J Womens Health Gen Based Med* 1999; **8**:1091–5.
- 66 Dolte KS, Girman CJ, Hartmaier S *et al.* Development of a health-related quality of life questionnaire for women with androgenetic alopecia. *Clin Exp Dermatol* 2000; **25**:637–42.
- 67 Price VH, Roberts J, Hordinsky M *et al.* Lack of efficacy of finasteride in postmenopausal women with androgenetic alopecia. *J Am Acad Dermatol* 2000; **43**:768–76.
- 68 Barber GL, Kaufman KD, Kozloff RC *et al.* A hair growth questionnaire for use in the evaluation of therapeutic effects in men. *J Dermatol Treat* 1998; **9**:181–6.
- 69 Finasteride Male Pattern Hair Loss Study Group. Long-term (5 year) multinational experience with finasteride 1 mg in the treatment of men with androgenetic alopecia. *Eur J Dermatol* 2002; **12**:38–49.
- 70 Olsen EA, Hordinsky M, Whiting D *et al.* The importance of dual 5 $\alpha$ -reductase inhibition in the treatment of male pattern hair loss: results of a randomized placebo-controlled study of dutasteride versus finasteride. *J Am Acad Dermatol* 2006; **55**:1014–23.
- 71 Olsen EA, Whiting D, Bergfeld W *et al.* A multicenter, randomized, placebo-controlled, double-blind clinical trial of a novel formulation of 5% minoxidil topical foam vs. placebo in the treatment of androgenetic alopecia in men. *J Am Acad Dermatol* 2007; **57**:767–74.
- 72 Kanti V, Hillmann K, Kottner J *et al.* Effect of minoxidil topical foam on frontotemporal and vertex androgenetic alopecia in men: a 104-week open-label clinical trial. *J Eur Acad Dermatol Venereol* 2016; **30**:1183–9.