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Revian LED Cap

Study Title: A Pilot Study of Revian Red All LED cap as a novel treatment for Central Centrifugal Cicatricial Alopecia.

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Sponsor or funding source: None

Background, Rationale and Context

Significance

Central centrifugal cicatricial alopecia (CCCA) is form of scarring hair loss that predominately affects middle-aged women of African descent.[1] The etiology remains unknown; however, inflammatory mediated destruction of the hair follicles is involved in the pathogenesis. Clinically, the natural progression of CCCA starts at the crown as roughly circular scarred patches, which evolve into scarred areas increasing in size circumferentially. Characteristically, the scar is often smooth and shiny, and the hair density in the affected area is frequently decreased. The hair remaining in the scarred areas is more brittle and shorter than the hair in unaffected areas. Since CCCA is a scarring disorder, it can cause permanent hair loss, dyesthesias, and psychological distress which can affect overall quality of life. Affected individuals may complain of pruritus, pain, or tenderness.[2]

The management of CCCA is challenging due to limited current treatments and a lack of randomized controlled trails. Management focuses on behavioral and styling modifications, in addition to symptomatic relief. Any potentially damaging hair care practices such as chemical relaxers, heat application to the scalp, and the use of hardening gels and sprays are discouraged.[3] Many commonly used therapies are anti-inflammatory in nature, including intralesional steroids, topical steroids, oral antibiotics and increased frequency of hair washing with antidandruff shampoos.[4] These treatments not only lead to improvement in pruritus and tenderness, but in some cases result in increased hair density.[5] Since there is limited investigation done to determine the most effective treatment approach for CCCA subjects, it would be of great benefit to determine if there is any advantage in using one particular anti-inflammatory therapy over others and whether one is more efficacious in relieving symptoms or promoting hair regrowth in follicles that have not yet become scarred.

The Revian Red All LED cap is a dual-band LED light therapy wireless “smart” cap. It has been shown to be effective in androgenetic alopecia (used once daily, 10-minute treatment regimen) for both men and women. Though no head-to-head comparisons have been done, cross-study comparisons suggest it may provide greater improvements in hair density than low level red laser devices, topical minoxidil and finasteride.[6] The cap emits two wavelengths of light, 620nm and 660nm, that lead to the production of nitric oxide in the scalp. This increased nitric oxide helps to locally promote blood flow, reduce dihydrotestosterone (DHT), and decrease inflammation.[6] There are also reportedly minimal side effects, unlike with topical minoxidil which can cause pruritus and initial hair shedding in the first few weeks, or finasteride which can cause gynecomastia and loss of libido. In this study we hope to see if the anti-inflammatory capabilities of this cap can improve scalp symptoms, reduce hair loss, and promote maturation of vellus and intermediate hairs in non-scarred areas of the scalp in those affected by CCCA.

Objectives

The purpose of this study is to determine if the Revian Red All LED cap shows potential to be an effective treatment for CCCA by recruiting hair follicles back to anagen growth or by improving inflammation. The

primary outcome is to determine if hair loss regression is halted. Secondary outcomes include hair regrowth and alleviation of signs and symptoms of the disease.

Methods and Measures

Design

23 subjects who are willing to participate in a novel treatment for Revian Red All LED cap will be enrolled in this study. The cap uses two wavelengths of light, 620 nm and 660 nm. A study cap will be provided for each subject. Subjects will use the cap once daily, 10-minute treatment regimen which is the current androgenetic alopecia recommendation. The subjects will use the cap for a total of 6 months. To use the cap, subjects will connect the Revian Red All LED cap to a Smart App on a mobile phone device using Bluetooth. Subjects can use the Smart App to set daily reminders to use the cap, track and log usage, and use the 10 minute timer. No additional information will be stored on the Smart App. Only subjects will have access to the Smart App located on their personal mobile phone device.

Standardized photos and trichoscopic photos before starting treatment and every 2 months for x 6 total months will be taken to assess hairline stabilization and potential for regrowth. A baseline photo and completion photo will also be taken with a visio device. This will help determine pigmentation of the present hairs throughout the study.

Prior to study enrollment, all participants will receive a detailed explanation of the purpose of the study and will undergo written informed consent. Clinical history of hair loss and history of prior treatment will be obtained by administering a standardized questionnaire to all subjects. Subjects will also fill out a questionnaire regarding symptoms of their hair loss at each visit. There will be 4 visits total (1 Pre-treatment visit and 3 Follow up visits). In order to be eligible, subjects must be diagnosed clinically and histologically with CCCA. Diagnosis will be made only by a board-certified dermatologist.

Setting

This study will be conducted at the Wake Forest Baptist Health Department of Dermatology, 4618 Country Club Road, Winston-Salem, North Carolina 27104.

Subjects selection criteria

- **Inclusion Criteria**
    - Women who are between the age of eighteen years and sixty-five years with a biopsy-proven diagnosis of CCCA Stage II-IV. They also must be on stable treatment without changes (on doxycycline, topical steroids, minoxidil and/or post 8 rounds of intralesional steroids) for at least 3 months.
    - Subjects will be recruited from outpatient dermatology clinics at the Wake Forest Baptist Health Department of Dermatology.
- **Exclusion Criteria**
    - Subjects with other forms of hair loss that is not CCCA
    - Prior treatment with light source for alopecia
    - Males are excluded from this study since the prevalence of CCCA in males is so significantly low that it is difficult to find cases in a clinical setting
- **Sample Size**

  We anticipate enrolling 23 subjects in order to assess the effect of Revian Red All LED cap.

Interventions and Interactions

Each subject will have a clinical assessment of hair loss by the investigator at the start of the enrollment and every 2 months until the study is completed. Clinical signs and symptoms of CCCA will be documented by administering a standardized questionnaire to all subjects. Subjects will complete the standardized questionnaire regarding symptoms of their hair loss at the start of the enrollment and every 2 months until the study is completed. Standardized camera and dermatoscopic photographs of the scalp will be obtained at the start of the enrollment and every 2 months until the study is completed.

Total Visits (4)
-Visit 1 (Pre-treatment Visit)
-Visit 2 (Follow Up Visit, 2 months after Visit 1)
-Visit 3 (Follow Up Visit, 4 months after Visit 1)
-Visit 4 (Follow Up Visit, 6 months after Visit 1)

Subjects will use the Revian Red All LED cap, once daily for 10 minutes for a total of 6 months. Subjects will also be called every 2 weeks to verbally confirm consistent use of the cap

Outcome Measure(s)

The main outcome measure in this study is hairline stabilization and/or regrowth, as measured by standardized photography, after Revian Red All LED cap treatment. Secondary outcomes include patient assessment of stabilization and hair regrowth and reduction of signs and symptoms, if present.

Analytical Plan

We expect to be able to enroll 23 subjects in this study. Descriptive statistics such as mean, standard deviation, and range for demographics and subject characteristics at baseline will be obtained. Severity and extent of scalp involvement of CCCA will be assessed by two measures. The first measure will be scoring of symptoms obtained from two questionnaires given to subjects (Appendix I and II). One questionnaire will be given before treatment begins, and the second questionnaire will be given at the start of each subsequent follow up visit (visits 2 and 3) and at the follow-up visit (visit 4). Pre and post-treatment photographs will also be assessed to determine if further scalp hairline recession is present and to look for hair regrowth. The estimates obtained from the subjects' and physicians' questionnaires (Appendix III) will help in designing a larger, randomized clinical trial. Given the small number of subjects, this study is not powered to test for statistical significance; the study will provide the estimate of baseline scores as well as an estimate of change in scores from baseline.

Risk and Benefits

Risks

Possible risks could include mild discomfort, skin irritation, or temporary erythema at the site of the scalp where the cap is applied. However, most subjects do not experience any side effects

Benefits

Subjects may or may not receive any direct benefit from their participation. Subjects may have improvement of their hair loss, either by regrowth of hair or by cessation/stabilization of hair loss. Subjects will be contributing to the general scientific knowledge of potential alternative treatments for hair loss with laser therapy, which may be beneficial to the general population in the future.

Human Subjects Protection

This study does not specifically involve subjects who are particularly vulnerable to coercion or undue influence, including pregnant women, prisoners, medical students, and children.

Subject Recruitment Methods

Subjects will be recruited at the Wake Forest Dermatology clinic. We may also use the Translational Data Warehouse or Epic Electronic Health Records in order to identify subjects that may have been seen in the Dermatology Clinic before with FFA for upcoming appointments. Subjects who meet the criteria mentioned above will be told about the study by either their physician or one of the study investigators. They will be asked about their willingness to participate after completion of their regular visit. This process will continue until 5 CCCA subjects have been recruited. Study data will be kept secure on a password-protected network drive.

Informed Consent

Signed informed consent will be obtained from each subject by one of the physicians in the Wake Forest Dermatology Clinic or by one of the study investigators. Subjects will be recruited from regular clinic visits. Consent will be obtained after their regular clinic visit is complete.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected subject identifying information corresponding to the unique study identifier will be maintained on a linkage file, stored separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed via shredding 6 years after study closure, consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

References

1. Sperling L, Sau P: The follicular degeneration syndrome in black patients: “hot comb alopecia” revisited and revised. *Arch Dermatol* 1992;128:68-74.
2. Bin Saif GA, Ericson ME, Yosipovitch G. The itchy scalp – scratching for an explanation. Exp Dermatol. 2011;20:959–68.

3. Ogunleye TA, McMichael A, Olsen EA. Central centrifugal cicatricial alopecia: what has been achieved, current clues for future research. Dermatol Clin. 2014 Apr;32(2):173-81
4. Madu P, Kundu RV. Follicular and scarring disorders in skin of color: presentation and management.Am J Clin Dermatol. 2014 Aug;15(4):307-21
5. Eginli A, Dothard E, Bagayoko CW, Huang K, Daniel A, McMichael AJ. A Retrospective Review of Treatment Results for Patients With Central Centrifugal Cicatrical Alopecia. J Drugs Dermatol. 2017 Apr 1;16(4):317-320. PMID: 28403264.
6. REVIAN RED All LED Red Light Therapy For Hair Loss - 10 Minutes Per Day. 2020. *Clinical Results - REVIAN RED All LED Red Light Therapy For Hair Loss - 10 Minutes Per Day*. [online] Available at: <https://revian.com/clinical-results/> [Accessed 27 September 2020].

Appendix I: Pre-Treatment Questionnaire for subjects

Subject Study Number: _____(will be 1-5 in the order of enrollment)

1. **What is your data of birth? _____(mm/dd/yyyy)**

2. Which one choice best describes your race? (Please choose only one answer)

   ____ Black or African American

   If Black or African American is checked, is your ethnic background:

   ____ African

   ____ Caribbean

   ____ Other Black or African descent

   ____ Mixed race (Black or African American + Other)

3. **What is your ethnicity**? (PLEASE CHECK ONLY ONE)

   ☐ Hispanic or Latin origin
   ☐ Non-Hispanic or Non-Latin origin
   ☐ Unknown

Hair Loss History

4. **When did you first notice your hair loss**? _____/_____(month/year)

5. **How many dermatologists did you consult for the hair loss on the crown of scalp before a diagnosis of central centrifugal cicatricial alopecia (CCCA) was made? _____**

6. **Have you been given any type of medical treatment for your vertex hairline recession? Yes ☐ No ☐**

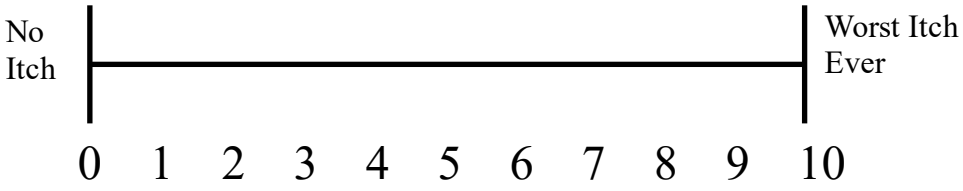
If yes, please check all medications that you used for a time period of AT LEAST 3 MONTHS and indicate the effect of each treatment on your hair loss by placing an X in the appropriate box.

Treatment Used	Response			
	Regrowth	**Prevented further loss**	**Did not stop loss**	**Do not know**
□ Oral Steroid (e.g. Prednisone)				
□ Intralesional (injection into the scalp) steroids				
□ Topical steroids (clobetasol, halobetasol, fluocinolone, betamethasone diproprionate, triamcinolone, fluocinonide, mometasone)				
□ Hydroxychloroquine (Plaquenil®)				

□ Methotrexate				
□ Mycophenolate (Cellcept®)				
□ Cyclosporin (Neoral®, Sandimmune®)				
□ Topical imiquimod (Aldara®)				
□ Spironolactone (Aldactone®)				
□ Finasteride (Propecia®, Proscar®)				
□ Dutasteride (Avodart®)				
□ Tetracycline antibiotic class (e.g. Tetracycline®, Doxycycline®, Minocycline® etc.)				
□ Topical tacrolimus (Protopic®)				
□ Pioglitazone (Actos®)				
□ Azathioprine (Imuran®)				
□ Topical minoxidil (Rogaine®)				
□ Hair transplants in area of hair loss				
□ Other: _____				

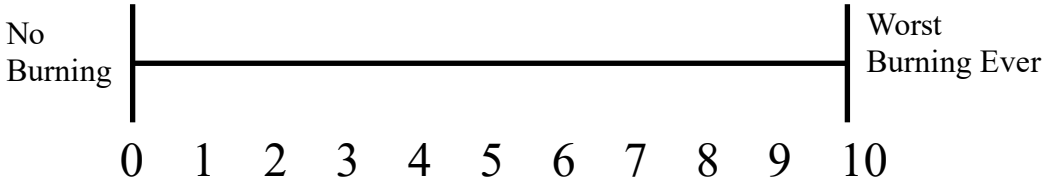
Symptoms

9. Please indicate your current level of scalp itch from 0-10 by <u>marking the line</u> on the scale below

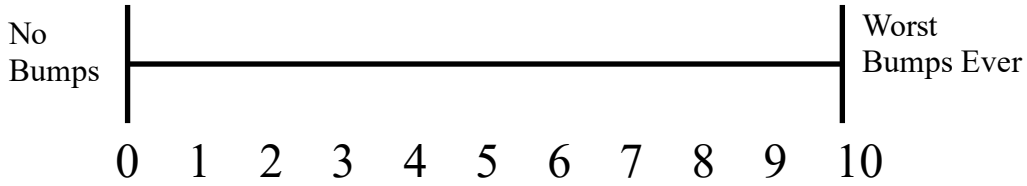


10. Please indicate your current level of scalp pain from 0-10 by <u>marking the line</u> on the scale below

12. **Please indicate your current level of scalp burning from 0-10 by marking the line on the scale below.**



13. **Please indicate your current level of scalp bumps from 0-10 by marking the line on the scale below.**



14. **Would you like to add any other comments?**

_____
_____
_____

Date of Questionnaire completion: _____(mm/dd/yyyy)

Thank you for your time.

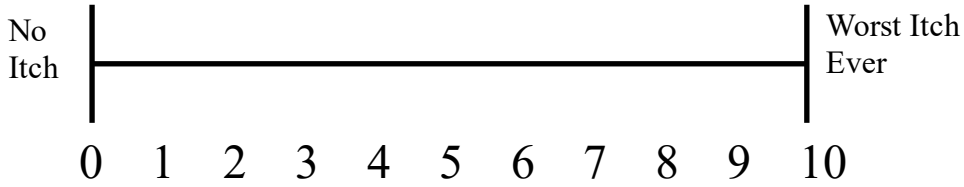
Appendix II: Treatment and Follow-Up Questionnaire for Subjects

Subject Study Number: _____(will be 1-5 in the order of enrollment)

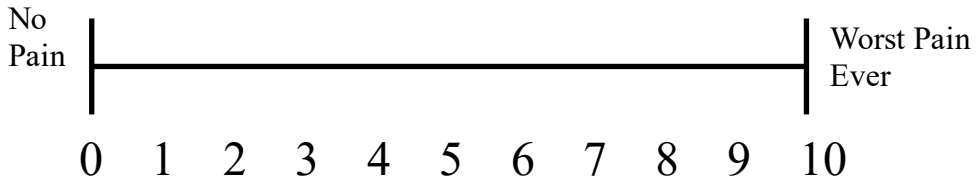
15. **Please indicate the effect Revian Red All LED cap treatment had on your hair loss**:

Regrowth ☐ Prevented Further Loss ☐ Did Not Stop Loss ☐ Do Not Know ☐

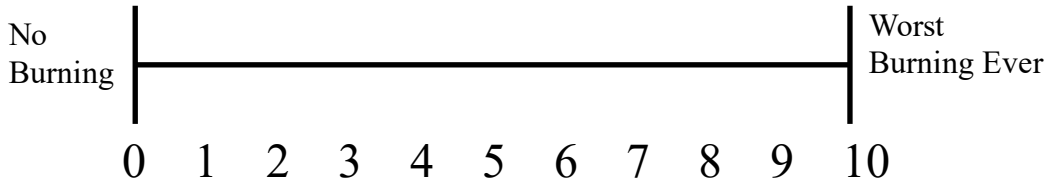
16. **Please indicate your current level of scalp itch from 0-10 by marking the line on the scale below**



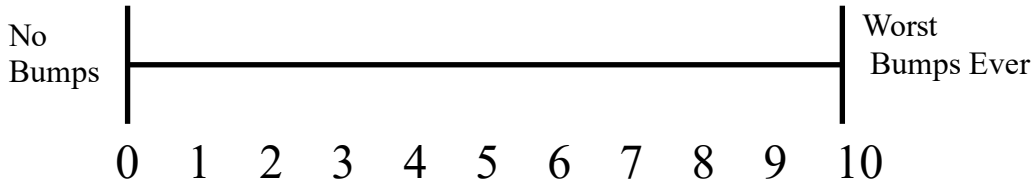
17. **Please indicate your current level of scalp pain from 0-10 by marking the line on the scale below.**



18. **Please indicate your current level of scalp burning from 0-10 by marking the line on the scale below.**



19. **Please indicate your current level of scalp bumps from 0-10 by marking the line on the scale below.**



20. **Would you like to add any other comments?**

_____
_____
_____

Date of Questionnaire completion: _____(mm/dd/yyyy)
Thank you for your time.

Appendix III: Clinician evaluation of signs.

SIGNS	CLINICIAN EVALUATION (Mild/Moderate/Severe)*
Perifollicular scale	
Hyperpigmentation	
Breakage	
Interfollicular scale	

Erythema	
Loss of follicular openings	
Vellus/Intermediate/Terminal hair shafts[a]	

*Mild – affecting <10% of scalp. Moderate – affecting 10-30% of scalp. Severe – affecting >30% of scalp.

For all signs other than Vellus/Intermediate/Terminal hair shafts (see below).

a. Percentage of types of hair shafts

Appendix IV: Study Flow Chart

Perception DLQI

DERMATOLOGY LIFE QUALITY INDEX

DLQI

Score:

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick ☑ one box for each question.

1. Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?
Very much ❒
A lot ❒
A little ❒
Not at all ❒

2. Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?
Very much ❒
A lot ❒
A little ❒
Not at all ❒

3. Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?
Very much ❒
A lot ❒
A little ❒
Not at all ❒ Not relevant ❒

4. Over the last week, how much has your skin influenced the **clothes** you wear?
Very much ❒
A lot ❒
A little ❒
Not at all ❒ Not relevant ❒

5. Over the last week, how much has your skin affected any **social** or **leisure** activities?
Very much ❒
A lot ❒
A little ❒
Not at all ❒ Not relevant ❒

6. Over the last week, how much has your skin made it difficult for you to do any **sport**?

Very much ❒
A lot ❒
A little ❒
Not at all ❒
Not relevant ❒

7. Over the last week, has your skin prevented you from **working** or **studying**?

Yes ❒
No ❒
Not relevant ❒

If "No", over the last week how much has your skin been a problem at **work** or **studying**?

A lot ❒
A little ❒
Not at all ❒

8. Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?

Very much ❒
A lot ❒
A little ❒
Not at all ❒
Not relevant ❒

9. Over the last week, how much has your skin caused any **sexual difficulties**?

Very much ❒
A lot ❒
A little ❒
Not at all ❒
Not relevant ❒

10. Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?

Very much ❒
A lot ❒
A little ❒
Not at all ❒
Not relevant ❒

Please check you have answered EVERY question. Thank you.

Appendix V: Study Flow Chart

SCHEDULE OF STUDY PROCEDURES	BASELINE VISIT 1	VISIT 2	VISIT 3	VISIT 4 Post-treatment Follow-up
Informed Consent, HIPPA	X			
Medical History/Demographic information	X			
Inclusion/Exclusion criteria	X			
Subject Initial Questionnaire	X			
Standard Scalp Digital Photography	X	X	X	X

DLQI	**X**			**X**
Scalp and hair exam and assessment with completion of grader survey	**X**	**X**	**X**	**X**
Dermoscopic photography	**X**	**X**	**X**	**X**
Subject Post-Treatment Questionnaire		**X**	**X**	**X**