

Safety and Efficacy of a Topical Treatment (SM04554) for Androgenetic Alopecia (AGA): Results from a Phase 1 Trial

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Poster# P238

Background

- Androgenetic Alopecia (AGA), which is also known as male pattern baldness, is a common form of hair loss in both men and women.
- In the U.S., it is estimated that approximately 35 million men are affected by AGA.
- Only two products have been approved in the U.S. in the past 15 years for the treatment of AGA: (1) minoxidil (Rogaine®, Upjohn Co.) and (2) finasteride (Propecia®, Merck).
 - While minoxidil is considered safe for use as an OTC product, its efficacy to promote hair growth is considered variable, with cosmetically acceptable results reported in only a subset of patients.¹
 - In April 2012, the FDA expanded the warning label of finasteride, a prescription medication, to include libido disorders, ejaculation disorders, and orgasm disorders that persisted after discontinuation of treatment.
- There is a need for alternative treatment options for AGA that have improved efficacy and safety profiles.
- Wnt signaling helps support hair growth:
 - Wnt signaling initiates and maintains the anagen phase of the hair cycle.²
 - Wnt pathway activation induces endogenous dermal progenitor cells to differentiate into a hair bulge, leading to the formation of new hair follicles.²
 - Reduction of Wnt pathway signaling is associated with hair loss in AGA.³
- Samumed is developing SM04554 for the treatment of AGA. SM04554 is a novel small molecule shown to activate the Wnt pathway.

Purpose

Samumed has performed a Phase 1 trial to evaluate the safety, tolerability, and efficacy of topical SM04554 solution applied to the scalp of male subjects with AGA.

Methods

- Male subjects [N=29] with AGA (Norwood-Hamilton Classification score of 4, 5, 6, or 7) were randomized to receive either topical SM04554 solution 0.05%, 0.15%, 0.45% or vehicle (applied once daily for 14 days) in an 8:2 (SM04554: vehicle) ratio per dose cohort. After treatment visits on Days 1 to 14, subjects participated in safety follow-up visits on Days 15 and 28.
- Safety assessments were collected at baseline prior to study medication application and during the 28-day treatment and follow-up period. Assessments included:
 - Medical history, vital signs, ECGs, clinical laboratory sampling
 - Collection of adverse events (AEs) and concomitant medications
 - Investigator Scalp Assessment, which included scoring a dermal response and "Other effects" with the scoring system below:

Dermal Response	
0 = No evidence of irritation	
1 = Minimal erythema, barely perceptible	
2 = Definite erythema, readily visible, minimal edema or minimal papular response	
3 = Erythema and papules	
4 = Definite edema	
5 = Erythema, edema and papules	
6 = Vesicular eruption	
7 = Strong reaction spreading beyond test site	

Other effects	
A = Slight glazed appearance	
B = Marked glazing	
C = Glazing with peeling and cracking	
F = Glazing with fissures	
G = Film of dried serous exudate covering all or part of the patch site	
H = Small petechial erosions and/or scabs	

- Blood samples for pharmacokinetics (PK) analysis were collected at baseline prior to study medication application and on Treatment Visit Days 1, 2, 14 and 15. The quantitation range for this study was between 0.10 – 150 ng/mL.
- Efficacy outcomes were collected after final study medication application and at end of study. Assessments included:
 - Investigator Hair Growth Assessment, a 7 point Likert scale from -3 (greatly decreased) to +3 (greatly increased)
 - Subject self-assessment using the Men's Hair Growth Questionnaire® (MHGQ)⁴, consisting of 5 questions
- Exploratory efficacy analysis was performed using both the Intention-to-Treat (ITT) and the Per-Protocol (PP) populations.

Author Disclosures: Y. Yazici: Salary, Contractual Services; Samumed, LLC. S.R. Smith: Consultant; Samumed, LLC. C.J. Swearingen: Salary, Contractual Services; Samumed, LLC. I. Simsek: Salary, Contractual Services; Samumed, LLC. A. DiFrancesco: Salary, Contractual Services; Samumed, LLC. J.D. Hood: Salary, Contractual Services; Samumed, LLC.

Results

SM04554-01 Demographics

	0.05%	0.15%	0.45%	Vehicle
N	7	8	8	6
Age at Consent (Years) [Mean (SD)]	48.4 (5.0)	41.5 (4.4)	44.0 (11.1)	44.6 (7.9)
White [N(%)]	7 (100%)	8 (100%)	7 (88%)	5 (83%)
Norwood-Hamilton [N(%)]				
4	4 (57.1%)	2 (25.0%)	2 (25.0%)	2 (33.3%)
5	3 (42.9%)	5 (62.5%)	3 (37.5%)	2 (33.3%)
6	0 (0%)	0 (0%)	3 (37.5%)	1 (16.7%)
7	0 (0%)	1 (12.5%)	0 (0%)	1 (16.7%)

Safety – Adverse Events

- 15 adverse events (AEs) were reported by 11 (38%) subjects:
 - 4 (67%) subjects in the vehicle group
 - 1 (14%) subject in the 0.05% cohort
 - 4 (50%) subjects in the 0.15% cohort
 - 2 (25%) subjects in the 0.45% cohort
- Only 1 AE (eye irritation, 0.45% cohort) was considered related to study medication by the reporting investigator.
- ECGs, labs and vital signs were unremarkable with no clinically significant changes from baseline reported in any subject.
- No serious adverse events (SAEs) or dose limiting toxicities (DLTs) were reported during the study.

Safety – Investigator Scalp Assessment

- 1 (13%) "slight glazed appearance" reported at Day 9 in the 0.15% cohort, which resolved by Day 10
- 1 (13%) "slight glazed appearance" reported at Day 14 in the 0.15% cohort, which resolved by Day 15
- 1 (17%) "minimal erythema" reported at Day 10 in the vehicle group, which resolved by Day 13

Pharmacokinetics (PK)

- All pre-dose samples on Day 1 were below the limit of quantitation, confirming the drug-naïve state of the subjects.
- Day 14 PK was dose-dependent:
 - No subjects had a detectable SM04554 concentration in the 0.05% cohort.
 - 3 (38%) subjects had systemic exposure in the 0.15% cohort (Tmax=9hrs).
 - 7 (88%) subjects had systemic exposure in the 0.45% cohort (Tmax=15hrs).

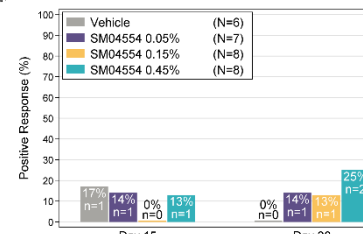
Efficacy – Investigator Hair Growth Assessment

Investigators did not rate any subject as changing hair growth in either direction (increased vs. decreased).

Efficacy – Men's Hair Growth Questionnaire®

Positive Responders

Negative responders are not displayed.

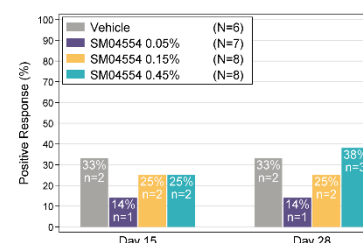


Q1: Since start of study, I can see my bald spot getting smaller.

Response is defined as Strongly agree/Agree (positive response) versus No opinion/Disagree/Strongly disagree (negative response).

Q2: Because of the treatment I have received since the start of the study, the appearance of my hair is:

Response is defined as Better/Little better (positive response) versus Same/Little worse/Worse (negative response).



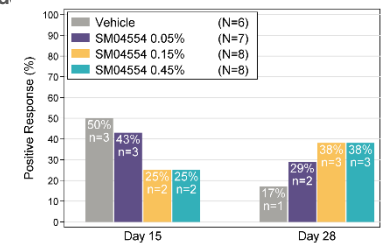
Efficacy – Men's Hair Growth Questionnaire® (continued)

Positive Responders

Negative responders are not displayed.

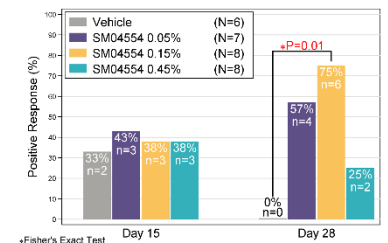
Q3: Since start of study, how would you describe the growth of your hair?

Response is defined as Greatly Increased/Moderately Increased/Slightly Increased (positive response) versus No Change/Slightly Decreased/Moderately Decreased/Greatly Decreased (negative response).



Q4: Since start of study, how effective do you think this treatment has been in slowing down your hair loss?

Response is defined as Effective/Somewhat effective (positive response) versus Not very effective/Not effective at all (negative response).



Q5: Compared to the beginning of the study, which statement best describes your satisfaction with the appearance of the hair on top of your head?

Response is defined as Very satisfied/Satisfied (positive response) versus Neutral/Dissatisfied/Very dissatisfied (negative response).



Discussion

- SM04554 appears to be safe, well-tolerated, and potentially efficacious.
 - At the end of Day 14, estimated pharmacokinetics was dose-dependent.
 - 18 of 29 (62%) exposed subjects reported no AEs. There was no evidence of a dose-dependent increase in AEs, and no SAEs were reported in the study.
 - The majority of AEs were reported only once, were mild in intensity, and were not related to study medication. Only one AE (eye irritation) was considered related to study medication by the reporting investigator.
- Subject self-assessments at Day 28 demonstrated:
 - Trend toward new hair growth in treated subjects (Q3)
 - 2/7 (29%) subjects in the 0.05% cohort had a positive response.
 - 3/8 (38%) subjects enrolled in both the 0.15% and 0.45% cohorts reported a positive response.
 - Trend toward slowing of hair loss in treated subjects (Q4)
 - 4/7 (57%) subjects in the 0.05% cohort had a positive response.
 - 6/8 (75%) subjects in the 0.15% cohort had a positive response.
 - 2/8 (25%) subjects in the 0.45% cohort had a positive response.
- This phase 1 study was not powered to see any statistically significant differences between treatment groups and vehicle. Nevertheless, the 0.15% cohort subjects reported significantly more effective slowing of hair loss than compared to vehicle on Day 28 (unadjusted P = 0.01).
- Efficacy trends observed for hair growth and decreased hair loss will be investigated in further clinical studies.
- These study results supported the development of phase 2 AGA trials using SM04554 (NCT02275351 and NCT02503137).

References

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Author Biography



Dr. Yazici is the Chief Medical Officer of Samumed, LLC. Additionally, Dr. Yazici is an Assistant Professor at New York University School of Medicine Department of Rheumatology, where he serves as Director of the Seligman Center for Advanced Therapeutics and Director of the Behcet's Syndrome Center, the largest U.S. center for Behcet's Disease. Recognized nationally and internationally, Dr. Yazici has more than 250 publications. After receiving his medical degree from Istanbul University, his Rheumatology Fellowship was completed at the Weill Medical College Hospital for Special Surgery of Cornell University and his Internal Medicine Residency at Creighton University in Nebraska.

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