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

samumed

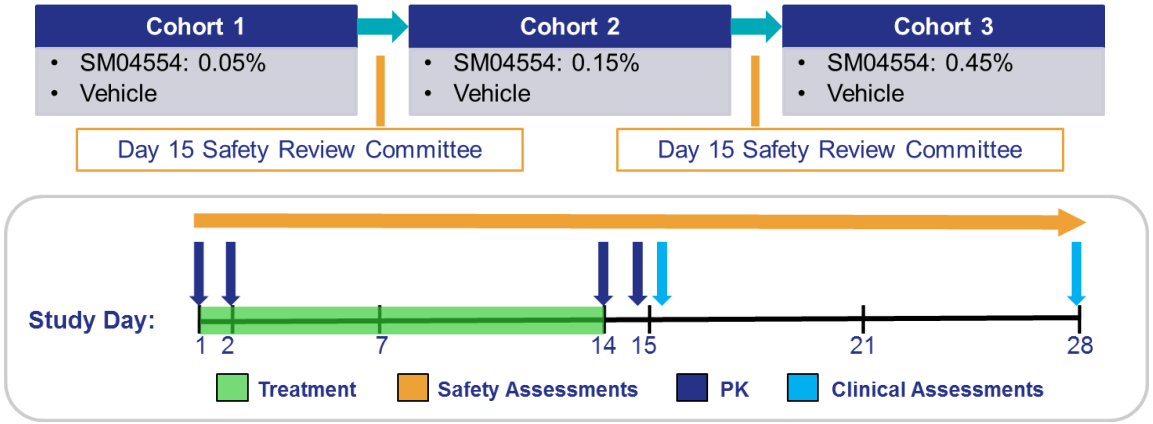
Yusuf Yazici, MD[1], Stacy R. Smith, MD[2], Christopher J. Swearingen, PhD[1], Ismail Simsek, MD[1], Anita DiFrancesco[1], John D. Hood, PhD[1]
[1]Samumed LLC, San Diego, CA, USA, [2]California Dermatology & Clinical Research Institute, Encinitas, CA, USA

Poster #3299

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.[1]
- Alternative treatment options for AGA that have improved efficacy and safety profiles are needed.
- 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 topical small molecule shown to activate the Wnt pathway.

Figure 1. SM04554-01 Study Schematic



Methods

- Male subjects [N=29] between 18 and 60 years of age (inclusive) 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 to the scalp once daily for 14 days) in an 8:2 (SM04554:vehicle) ratio per dose cohort (Figure 1).
- After daily treatment visits on Days 1-14, subjects participated in safety and exploratory clinical assessment visits on Days 15 and 28 (Figure 1).
- Safety assessments included:
  - Investigator Scalp Assessment, which included scoring “Dermal response” on a scale of 0-7 and “Other effects” on a scale of A-H
  - Medical history, vital signs, ECGs, clinical laboratory sampling
  - Collection of adverse events (AEs) and concomitant medications
- Blood samples for pharmacokinetics (PK) analysis were collected at baseline prior to study medication application and on Treatment Visit Days 1, 2, and 14, and on Day 15. The range of quantitation for this study was 0.10 – 150 ng/mL.
- Exploratory efficacy outcomes were collected at Day 15 and Day 28. Assessments included:
  - Investigator Hair Growth Assessment, scored on 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.

samumed

Table 1. 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%)**

Results

Safety – Investigator Scalp Assessment

- 1 (13%) "(A) Slight glazed appearance" at Day 9 in the 0.15% cohort, resolved by Day 10
- 1 (13%) "(A) Slight glazed appearance" at Day 14 in the 0.15% cohort, resolved by Day 15
- 1 (17%) "(1) Minimal erythema" at Day 10 in the vehicle group, resolved by Day 13

Safety – Assessments and Serious Adverse Events

- ECGs, labs and vital signs were unremarkable with no clinically significant changes from baseline reported in any subject.
- No serious adverse events (SAEs) were reported during the study.
- A dose limiting toxicity (DLT) was defined as a serious, severe, or life-threatening AE determined by the investigator to be possibly or probably related to study medication. No DLTs were reported during the study.

Results (continued)

Safety – Adverse Events

- Only 1 AE (eye irritation, 0.45% cohort) was considered related to study medication by the reporting investigator.
- A total of 15 adverse events (AEs) were reported by 11 (38%) subjects. All AEs were a single event reported by one subject unless otherwise noted below.
  - 6 AEs reported by 4 (67%) subjects in the vehicle group:
    - Fatigue, Seasonal allergy, Sunburn, Headache (2 AEs by 2 subjects), Acne
  - 1 AE reported by 1 (14%) subject in the 0.05% cohort:
    - Back pain
  - 5 AEs reported by 4 (50%) subjects in the 0.15% cohort:
    - Eye irritation, Ocular hyperaemia, Back pain, Papule, Phlebitis
  - 3 AEs reported by 2 (25%) subjects in the 0.45% cohort:
    - Eye irritation, Dry mouth, Joint dislocation

Pharmacokinetics (PK)

- All pre-dose samples on Day 1 were below the limit of quantitation, confirming the drug-naïve state of the subjects.
- At the end of daily exposure on Day 14, PK was dose-dependent (Table 2).

Table 2. Blood Plasma Concentrations on Day 15

	0.05%	0.15%	0.45%
Systemic Exposure [N]	**0**	**3**	**7**
Average AUC [ng*h/ml (SE)]	**-**	**1.02 (0.57)**	**2.14 (0.52)**
Cmax [ng/ml]	**-**	**0.202**	**0.188**
Tmax [hours]	**-**	**9**	**12**

samumed

Results (continued)

Efficacy – Investigator Hair Growth Assessment

Investigators did not rate any subject as changing hair growth (increased versus decreased).

Efficacy – Men's Hair Growth Questionnaire© (MHGQ)

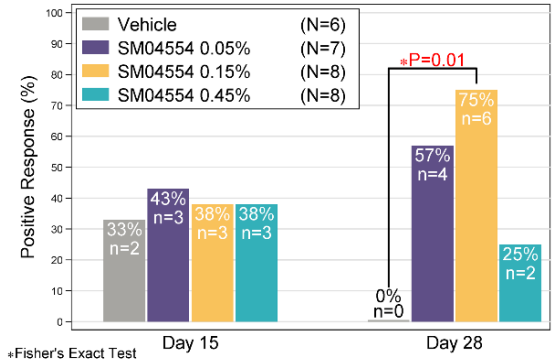
- The length of this Phase 1 study was short and the sample size was small.
- Nevertheless, a significant difference in positive responses was observed between subjects in the 0.15% cohort and vehicle on Day 28 in MHGQ question 4 (Figure 2).

Figure 2. MHGQ Q4 Positive Responders

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).

Negative responders are not displayed.



Discussion

- SM04554 appears to be safe, well-tolerated, and potentially efficacious.
  - At the end of Day 14, estimated pharmacokinetics were dose-dependent (Table 2).
  - 18 of 29 (62%) exposed subjects reported no AEs. There was no evidence of dose-dependent increases in AEs, and no SAEs were reported in the study.
  - The majority of AEs were reported once, were mild in intensity, and 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 a trend toward slowing of hair loss in treated subjects (MHGQ Q4; Figure 2):
  - 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.
- Subjects in the 0.15% cohort reported more effective/somewhat effective slowing down of hair loss than subjects in the vehicle cohort 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

1. Gupta AK, Charrette A. *Skinmed. 2015 May-Jun;13(3):185-9.*
2. Kishimoto J, et al. *Genes & Dev*. 2000;14(10):1181-1185.
3. Beaudoin GM, 3rd, et al. *PNAS*. 2005;102(41):14653-14658.
4. Barber BL, et al. *J Dermatol Treat*. 1998;9:181–6.

To obtain a PDF of this poster, scan the QR code or visit www.samumed.com/publications/

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.

samumed

9381 Judicial Drive • San Diego, CA 92121 • Email: info@samumed.com