EFFICACY AND SAFETY OF TOPICAL FINASTERIDE 0.5% SOLUTION ONCE DAILY VERSUS TWICE DAILY IN THE TREATMENT OF MALE ANDROGENETIC ALOPECIA

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2024

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CHANTALUCK MUENNARONG

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BY

CHANTALUCK MUENNARONG

HAS BEEN APPROVED BY THE GRADUATE SCHOOL IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE MASTER OF SCIENCE
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Title	EFFICACY AND SAFETY OF TOPICAL FINASTERIDE 0.5% SOLUTION ONCE DAILY VERSUS TWICE DAILY IN THE TREATMENT OF MALE ANDROGENETIC ALOPECIA
Author	CHANTALUCK MUENNARONG
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Androgenetic alopecia (AGA) is the most common form of hair loss in men, resulting from progressive miniaturization of hair follicles. While oral finasteride has demonstrated efficacy, its administration may be associated with systemic adverse events. Topical finasteride has been considered as an alternative with a favorable safety profile; however, the optimal frequency of application remains undefined. This study aimed to evaluate and compare the efficacy and safety of topical finasteride 0.5% solution applied once daily versus twice daily in the treatment of male AGA. A 24-week randomized, investigator-blinded trial was conducted involving 60 male participants aged 22 to 60 years with a clinical diagnosis of mild to moderate androgenetic alopecia (AGA). Participants were randomly assigned to receive either once-daily or twice-daily application of topical finasteride 0.5% solution. Primary outcomes included changes in total hair density, terminal hair density, and non-terminal hair density. Secondary outcomes included changes in hair diameter, global photographic assessment (GPA), patient satisfaction, and the incidence of adverse events. Both regimens resulted in statistically significant improvements in all measured hair parameters compared to baseline (all $p < 0.05$). The twice-daily application demonstrated significantly greater increases in the mean change of total hair density ($p = 0.036$) and non-terminal hair density ($p = 0.044$) compared to the once-daily regimen. Improvements in terminal hair density and hair diameter were observed in both groups, with no significant differences in the mean changes between them. GPA scores were higher in the twice-daily group, indicating a trend toward greater visual improvement. Patient satisfaction was high in both groups, with a slight preference for the twice-daily regimen. No systemic adverse events were reported, and only mild local reactions were observed. Topical finasteride 0.5% solution is effective and well tolerated for the treatment of male androgenetic alopecia (AGA). The twice-daily regimen provides superior improvements in total and non-terminal hair density, thereby enhancing overall treatment outcomes and rendering it appropriate for patients aiming to achieve maximal therapeutic benefit. In contrast, the once-daily application remains a convenient and effective alternative with a comparable safety profile. These findings support the use of topical finasteride as a treatment option with minimal risk of systemic side effects.

Keyword : Topical finasteride, male androgenetic alopecia, videodermoscopy

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CHANTALUCK MUENNARONG

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CHAPTER 1
INTRODUCTION

Androgenetic alopecia is the most common cause of male pattern hair loss. The prevalence and severity of this condition vary across different racial groups and tend to increase with age. Among Caucasian men, the incidence reaches approximately 80% by the age of 70, whereas in Asian men, it is around 50% at the same age. Clinically, male androgenetic alopecia presents as a patterned and progressive form of hair loss, typically beginning with bitemporal recession. As the condition advances, the hair shafts become progressively thinner, and the balding area gradually extends across the scalp. Notably, hair in the lateral and occipital regions is usually preserved.

Male androgenetic alopecia is considered a multifactorial condition, influenced by genetic predisposition, androgenic activity, and environmental factors. These elements contribute to a progressive hair-thinning process known as hair miniaturization, characterized by the gradual transformation of large, long, pigmented terminal hairs into short, fine, and hypopigmented vellus hairs. This change progresses with each hair growth cycle, leading to a shortened anagen phase and, in long-standing cases, eventual follicular dropout [(1)].

Male sex hormones, particularly dihydrotestosterone (DHT), play a central role in the pathogenesis of androgenetic alopecia (AGA) in men. Historical evidence shows that eunuchs who were castrated before puberty do not develop AGA unless they undergo androgen replacement therapy. Similarly, individuals with androgen receptor abnormalities, which prevent the binding of androgens to their receptors, also do not develop AGA. These findings underscore the importance of androgenic activity in the development of the condition. Moreover, the effect of testosterone on hair growth varies by anatomical region. In certain areas, testosterone promotes hair growth, while in others, it must be converted by the enzyme 5α-reductase into the more potent DHT to exert its effect. On balding areas of the scalp, this conversion does not stimulate hair growth but instead induces miniaturization of hair follicles. Studies have demonstrated that balding scalp regions exhibit higher concentrations of DHT and increased

5α-reductase activity compared to non-balding areas. Additionally, individuals with genetic 5α-reductase deficiency do not exhibit signs of hair thinning, further supporting the enzyme's role in AGA. Consequently, pharmacological treatments that inhibit 5α-reductase have proven effective in reducing hair thinning and slowing the progression of AGA [2].

Current management for male androgenetic alopecia, as approved by the U.S. Food and Drug Administration (FDA), include 2% and 5% topical minoxidil, oral finasteride at a daily dose of 1 mg, low-level laser/light therapy, and hair transplantation [3].

Topical minoxidil has been shown to prolong the anagen phase of the hair cycle [4]. In male patients, the 5% formulation is significantly more effective than the 2% formulation in terms of both the extent and the onset of hair regrowth [5]. Reported adverse effects include irritant contact dermatitis, allergic contact dermatitis, and exacerbation of seborrheic dermatitis [6].

Finasteride is a 5α-reductase inhibitor that selectively targets the type II isoenzyme, thereby inhibiting the conversion of testosterone to dihydrotestosterone (DHT). A daily oral dose of 1 mg has been widely used in the treatment of male androgenetic alopecia (AGA), demonstrating favorable efficacy with a low incidence of adverse effects [7]. Reported side effects include hepatic dysfunction, gynecomastia, and sexual dysfunction. Although these adverse events occur in approximately 2% of patients, they have raised ongoing concerns due to their impact on quality of life. Notably, there have been reports of persistent sexual side effects even after discontinuation of the medication, a phenomenon referred to as “post-finasteride syndrome” [8] [9].

Topical finasteride has emerged as a potential alternative to oral administration, aiming to minimize systemic side effects while maintaining therapeutic efficacy. It has been formulated in both solution [10] [11] [12] [13] and gel [14] forms. Recent studies have demonstrated that topical finasteride at concentrations ranging from 0.25% to 1% yields significant improvements in hair density and hair count compared to control groups [11]

[12] [13] [14] In contrast, a concentration of 0.1% did not produce a statistically significant increase in hair density over controls. [10]

Furthermore, topical finasteride in concentrations between 0.25% and 1% has shown comparable efficacy to the standard 1 mg/day oral finasteride regimen[13] [14]. However, the onset of action appears to be faster with oral administration than with topical formulations.

Hajheydari et al. [14] demonstrated that twice-daily application of topical finasteride 1% gel yielded clinical efficacy comparable to that of oral finasteride 1 mg/day over a six-month period. Similarly, Piraccini et al. [13] reported that once-daily application of a 0.25% topical finasteride solution resulted in a comparable mean increase in hair density (20.2 hairs/cm²) to oral finasteride (21.1 hairs/cm²) after six months of treatment. Complementing these efficacy findings, a pharmacokinetic study by Caserini et al. [15] evaluated the effects of once-daily versus twice-daily application of 1 mL of 0.25% finasteride solution over seven days in men with androgenetic alopecia. Once-daily application led to an approximate 70% reduction in scalp DHT, which was significantly greater than the 50% reduction observed with twice-daily use. Both regimens produced similar reductions in serum DHT (~60–70%), with no significant effect on testosterone levels. The authors concluded that low-volume (100–200 µL) once-daily application may optimize scalp DHT suppression while minimizing systemic exposure.

Additionally, an earlier 7-day trial showed that twice-daily 0.25% topical finasteride suppressed plasma DHT levels by approximately 68–75%, comparable to the 62–72% reduction achieved with oral finasteride. These findings collectively support the notion that topical finasteride can replicate the pharmacodynamic effects of oral finasteride while maintaining lower systemic absorption. Notably, a systematic review of available clinical trials concluded that once-daily topical finasteride was more effective than twice-daily application in reducing both scalp and plasma DHT levels.

In summary, current pharmacokinetic and clinical evidence indicates that once-daily application of 0.25% topical finasteride is at least as effective as twice-daily application, and may, in certain studies, demonstrate superior suppression of scalp dihydrotestosterone (DHT) levels. Despite these findings, the optimal dosing frequency and concentration of topical finasteride remain areas of ongoing investigation. Given the inconsistencies in the existing literature, the present study was designed to directly evaluate and compare the clinical efficacy and tolerability of once-daily versus twice-daily application of topical finasteride 0.5% solution in the treatment of mild to moderate androgenetic alopecia in males.

Objectives

Primary Objective

1. To compare the efficacy of topical finasteride 0.5% solution applied once daily versus twice daily, as assessed by changes in hair density using videodermoscopy.

Secondary Objectives

1. To compare the efficacy of topical finasteride 0.5% solution applied once daily versus twice daily in terms of hair diameter, evaluated by videodermoscopy.

2. To assess overall clinical change between the two regimens using global photographic assessment (GPA) evaluated by dermatologists.

3. To evaluate and compare local and systemic adverse events associated with once-daily and twice-daily applications of topical finasteride 0.5%. by standardized evaluation form.

4. To assess patient satisfaction with each treatment regimen using a visual analogue scale (VAS).

Research Questions

Primary Research Question

1. How does the efficacy of topical finasteride 0.5% solution differ between once-daily and twice-daily application in the treatment of male androgenetic alopecia?

Secondary Research Question

1. What are the local and systemic adverse events associated with once-daily versus twice-daily application of topical finasteride 0.5% solution in the treatment of male androgenetic alopecia?

Hypotheses

Primary Hypothesis

1. Once daily application of topical finasteride 0.5% solution is equally effective as twice daily application in the treatment of male androgenetic alopecia, as measured by hair density using videodermoscopy.

Secondary Hypotheses

1. Once daily application of topical finasteride 0.5% solution is equally effective as twice daily application in improving hair diameter, as assessed by videodermoscopy.

2. Once daily application of topical finasteride 0.5% solution is equally effective as twice-daily application in achieving overall clinical improvement, as evaluated by global photographic assessment (GPA) conducted by dermatologists.

Scope of the Research

This study aims to evaluate the efficacy and safety of topical finasteride 0.5% solution applied once daily versus twice daily in the treatment of male androgenetic alopecia (AGA), specifically in patients classified as Hamilton-Norwood scale III vertex, IV, or V, aged 18–60 years. Participants will be recruited from the outpatient department at Srinakharinwirot University Skin Center, Bangkok, Thailand.

A total of 60 eligible male participants will be randomly assigned into two equal groups. Group 1 (n = 30) will apply 1 mL of topical finasteride 0.5% solution once daily

at bedtime, while Group 2 (n = 30) will apply the same concentration and dosage twice daily, once in the morning and once at bedtime, for a duration of 24 weeks.

Treatment efficacy will be evaluated through both objective and subjective measures. Objective assessment includes hair density and hair diameter measured by videodermoscopy (Fotofinder Leviacam®). Subjective evaluation was based on overall clinical improvement assessed through global photographic assessment (GPA) of the frontal and vertex scalp regions, using 90-degree and 45-degree angle views, performed by two dermatologists at baseline and week 24. Additionally, local and systemic adverse events, along with patient satisfaction, will be documented and analyzed throughout the study period.

Benefits and Applications of the Research

1. Direct Benefits for Patients

1.1 Patients participating in this study may benefit from receiving the optimal frequency of topical finasteride 0.5% solution application, providing effective treatment outcomes with minimal cutaneous and systemic adverse effects.

2. Benefits for Clinical Research and the Broader Community

2.1 This study contributes to clinical research by providing evidence on the efficacy of topical finasteride 0.5% solution in the treatment of male androgenetic alopecia, while also identifying the most appropriate frequency of application to minimize adverse events.

2.2 The findings have practical implications for improving patient care. Effective treatment not only enhances physical appearance but may also improve patients' self-esteem and overall quality of life.

Conceptual Framework

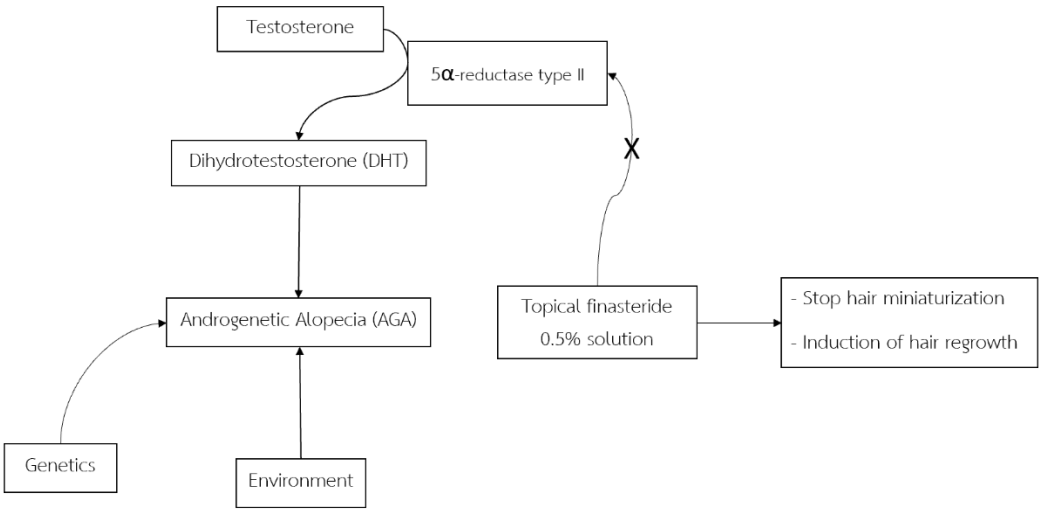

Figure 1.1 Conceptual framework of the protocol

CHAPTER 2
REVIEW OF LITERATURE

1. Male androgenetic alopecia (AGA)

2. Therapy and Level of Evidence in the Treatment of Male Androgenetic Alopecia

3. Minoxidil

4. Systemic finasteride

5. Topical finasteride

6. Outcome Measurements

Male Androgenetic Alopecia (Male AGA)

Male androgenetic alopecia, commonly referred to as male pattern baldness, is the most common cause of hair loss in men and has a significant impact on quality of life. The condition is characterized by progressive hair thinning, in which terminal hairs are gradually miniaturized into vellus hairs following a predictable pattern, ultimately leading to visible scalp hair depletion and baldness. Although androgen-dependent hair loss occurs to some extent in all individuals after puberty, the prevalence of clinically significant alopecia increases with advancing age.

Epidemiology

By the age of 50, approximately 30% to 50% of men are affected by androgenetic alopecia (AGA). Numerous studies, particularly from Western populations, have demonstrated that the incidence and pattern of male AGA vary significantly by race and age.

Caucasian men tend to experience AGA more frequently and with greater severity than men of other ethnic backgrounds. Advanced stages of alopecia are more common and occur at an earlier age in Caucasian populations compared to Asian populations. In contrast, men of African American, Native American, and East Asian descent generally show a tendency to retain their frontal hairlines and experience milder and later-onset forms of hair loss.

Age is also a key factor influencing AGA prevalence. A population-based study conducted in Australia involving 1,390 men aged 40 to 69 years found that the prevalence of vertex or complete baldness increased with age, from 31% in those aged 40–55 to 53% in those aged 65–69, based on the Norwood-Hamilton classification. Additionally, 25% of men aged 40–55 and 31% of those aged 65–69 was reported to have receded frontal hairlines. A separate study in the United States reported that 53% of men aged 40 to 49 exhibited moderate to severe AGA. Similarly, in Korean men, the prevalence of male AGA increases with age, with type III-vertex being the most common pattern observed between the ages of 30 and 70.

Clinical Features and Classifications

According to Hamilton, male pattern hair loss is primarily influenced by hormonal factors, genetic predisposition, and the natural aging process. The Hamilton–Norwood classification remains the gold standard for diagnosing and staging male androgenetic alopecia (AGA). This system categorizes hair loss into seven main types (I–VII), with additional subtypes including IIIa, III vertex, and IV vertex, providing a comprehensive framework for assessing the severity and pattern of hair loss.

Clinically, male AGA typically begins with bitemporal recession of the frontal hairline, followed by progressive thinning over the vertex of the scalp. As the condition advances, hair loss becomes more pronounced in these areas while the parietal and occipital scalp regions are often spared, maintaining a characteristic horseshoe pattern [16] [17].

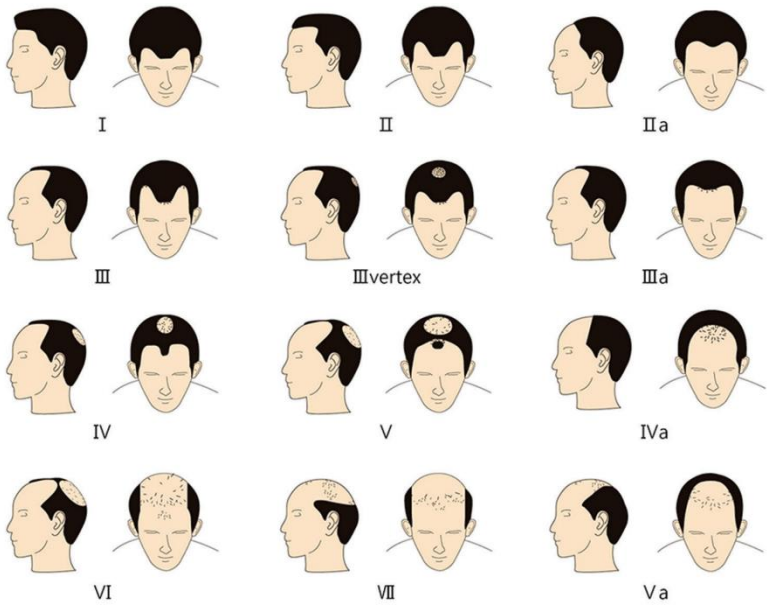

Figure 2.1 Hamilton-Norwood Classification of Male Androgenetic Alopecia [17]

Androgens

Androgens and Hair Follicles

Androgens play a crucial role in regulating a variety of physiological functions across different tissues, including the growth and differentiation of sebaceous glands, enhancement of the epidermal barrier, promotion of wound healing, and stimulation of hair regrowth [18]. However, the effects of androgens vary depending on the anatomical site. For instance, androgens stimulate hair growth in androgen-dependent areas such as the beard, axillae, and pubic region. In contrast, in scalp regions predisposed to androgenetic alopecia (AGA), androgens contribute to the miniaturization of hair follicles, shortening of the anagen phase, and progressive reduction in hair growth [19].

Androgen Metabolism

The rate of androgen synthesis is modulated according to local tissue requirements, resulting in variable responses across different organs, including pilosebaceous units and hair follicles. In male androgenetic alopecia (AGA), elevated levels of testosterone and dihydrotestosterone (DHT) are produced locally within the scalp, despite normal circulating plasma androgen levels. Testosterone, the principal

androgen, is converted by the enzyme 5α-reductase into its more potent form, DHT, which subsequently stimulates sebocytes, sweat glands, and dermal papilla cells.

In addition to testosterone, weaker androgens such as dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA-S), and androstenedione can also be converted into testosterone and DHT. Within the dermal papilla cells—key regulators of hair follicle activity, type II 5α-reductase irreversibly converts testosterone to DHT. These enzymes are predominantly localized in the dermal papilla and are critically involved in the pathogenesis of male AGA by mediating androgen-induced follicular miniaturization.

Androgen Receptors

Androgen receptors are expressed in various skin and hair-related cells, including keratinocytes of the epidermis and hair follicles, sebocytes, sweat gland cells, dermal fibroblasts, endothelial cells, genital melanocytes, and dermal papilla cells. Among these, dermal papilla cells serve as the principal target of androgen activity in hair regulation. Notably, androgen receptor expression is significantly higher in balding scalp regions compared to non-balding areas.

An important protective factor against follicular miniaturization in the occipital region is the higher level of DNA methylation at the promoter region of the androgen receptor gene. This epigenetic modification leads to reduced androgen receptor expression, thereby limiting androgen sensitivity. In contrast, the vertex region exhibits lower methylation levels, making it more susceptible to androgen-mediated miniaturization and thus more prone to hair loss.

Hair Growth Cycle [20] [21]

The normal hair growth cycle consists of four distinct phases: anagen, catagen, telogen, and exogen. The anagen phase, or growth phase, is the longest and most active stage, lasting approximately 2 to 7 years of the scalp hairs. During this phase, long, pigmented terminal hairs are produced. The catagen phase, a brief transitional period lasting about 2 to 3 weeks, is characterized by follicular regression and apoptosis of follicular cells. This is followed by the telogen phase, the resting stage,

which lasts around 12 weeks and culminates in the natural shedding of hairs. Finally, during the exogen phase, old hairs are released from the scalp, allowing new anagen hairs to emerge and begin a new cycle of growth.

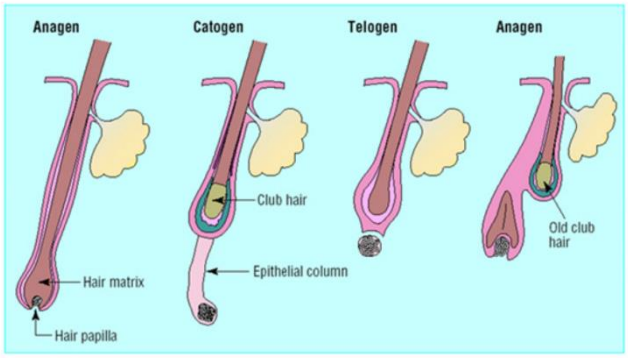

Figure 2.2 Normal hair cycle [22]

Pathogenesis of Male Androgenetic Alopecia

Androgenetic alopecia is characterized by progressive miniaturization of hair follicles and disruption of the normal hair cycle. Specifically, the duration of the anagen (growth) phase is shortened, while the telogen (resting) phase is prolonged. This alteration leads to the production of progressively finer and shorter hairs, a process known as miniaturization.

Dihydrotestosterone (DHT), a more potent derivative of testosterone, plays a central role in this process. DHT is synthesized from testosterone by the enzyme 5α-reductase, which exists in three isoforms: type I, type II, and type III. Elevated levels of 5α-reductase and increased expression of androgen receptors within hair follicles are directly implicated in follicular miniaturization [16].

Studies have shown that reductions in DHT level, both systemically and within the skin, are associated with reversal or stabilization of this miniaturization process. In male androgenetic alopecia, the repeated shortening of the anagen phase and prolongation of the telogen phase ultimately results in thinner, shorter, and less pigmented hair shafts.

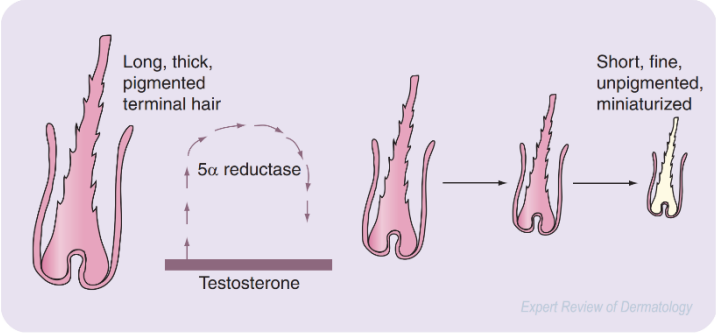

Figure 2.3 Pathogenesis of AGA [20]

Therapy and Level of Evidence in the Treatment of Male Androgenetic Alopecia

Minoxidil 2% solution twice daily is effective to prevent regression of hairlines and improve male AGA (level of evidence 1), whereas minoxidil 5% solution or foam twice daily is more effective than the 2% solution (level of evidence 2). Moreover, taking of finasteride 1 mg daily results in significant increasing in total hair counts compared to placebo in many well-conducted studies (A2, B and C evidence). Two studies conducting finasteride 1 mg/day compared to twice daily with topical minoxidil 2% solution results in superiority for finasteride at 12 months [23].

Table 2.1 Therapy and level of evidence in the treatment of male androgenetic alopecia

Therapy	Level of Evidence	Efficacy to Prevent Progression	Efficacy to Improve	Safety	Practicality (Patient)	Practicality (Physician)
Finasteride 1 mg once daily	1	+++	++	+++	++++	++
Dutasteride 0.5 mg once daily*	1	+++	+++	++	++++	++
Minoxidil 5% twice daily	1	+++	+++	++++	+ / ++	+++
Hair transplantation	2	–	+++	+	+ (intervention) +++ (long-term)	+
LLLT	2	+/–	+/–	++	++	+++
PRP	3	+/–	+/–	+	+/–	++
Global consideration: ⟵ Poor (-) ——— ⟶ Good (++++)						

LLLT, Low-Level Laser Therapy; PRP, Platelet-Rich Plasma. *Off label

Minoxidil

Systemic minoxidil, long-acting, potent vasodilator, was approved by the U.S. Food and Drug Administration in October 1979 for adjuvant therapy of severe hypertension in patients uncontrolled by taking diuretics and β-blockers [24] [25]. Hypertrichosis was noticed as a potential sequelae in patients and it was unacceptable in women while acceptable to the men [26] [27]. Hence, topical minoxidil was formulated for the treatment of male androgenetic alopecia and approved by the USFDA in 1984 [28].

These forms of 2% to 5% solution and 5% foam of topical minoxidil are available in the market [29] [30]. Olsen EA et al. revealed that topical 5% minoxidil was statistically more efficacious than topical 2% minoxidil solution in aspect of non-vellus hair count and global photographic assessment (PGA) by two-independent investigators. Moreover, in the 5% topical minoxidil obviously improved patient's quality of life, especially in psychological status after 48 weeks of the treatment [5]. Nevertheless, the local adverse events of scalp pruritus and dermatitis were more pervasive in the topical 5% (6% of patients) minoxidil group than in the topical 2% minoxidil group (2% of patients) [5].

Systemic Finasteride

There are three isoforms in the 5α-reductase enzyme family—types I, II, and III—each with distinct tissue distributions and physiological roles related to bile acid synthesis, androgens, and estrogen metabolism. Type I 5α-reductase is primarily expressed in the liver, as well as in the sebaceous glands of the adult face and scalp, and has minimal activity in dermal papilla cells and the prostate (Table 2). In contrast, type II 5α-reductase is predominantly localized in male reproductive organs, including the prostate and testes, and plays a more significant role in hair follicle regulation.

Both type I and type II isoenzymes are expressed in the dermal papilla cells of the scalp and beard. In terms of systemic androgen metabolism, type I and type II contribute approximately one-third and two-thirds, respectively, to circulating dihydrotestosterone (DHT) levels. Type III 5α-reductase, although less well

characterized, is primarily expressed in the basal epithelium of the prostate gland and may play a specialized role in prostate function.

Table 2.2 Physiological distribution of 5α-reductase isoenzyme in humans.

Type I 5α-reductase isoenzyme	Type II 5α-reductase isoenzyme	Type III 5α-reductase isoenzyme
Liver	Prostate	Basal epithelium of prostate glands
Sebaceous glands of scalp and face in adults	Testes	
Dermal papilla	Dermal papilla	
Prostate	Liver	

Finasteride is a potent and selective inhibitor of type II 5α-reductase, an enzyme responsible for converting testosterone into its more active form, dihydrotestosterone (DHT) [31]. t was initially approved by the U.S. Food and Drug Administration (FDA) in 1992 for the treatment of benign prostatic hyperplasia (BPH) at a dosage of 5 mg, and subsequently approved in 1997 for the treatment of male androgenetic alopecia (AGA) [32]. The pathogenesis of male AGA is thought to involve increased numbers of DHT receptors in hair follicles, elevated DHT concentrations in the scalp, and heightened activity of 5α-reductase, all of which promote the conversion of testosterone to DHT. These factors contribute to the progressive miniaturization of hair follicles, a hallmark of male AGA [2].

Mechanism of Action

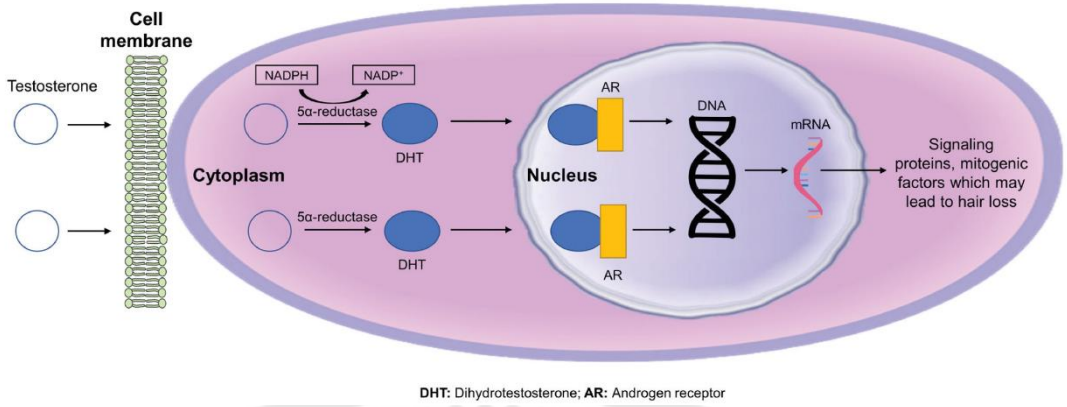

Figure 2.4 Androgens and hair loss [33].

Testosterone is converted into dihydrotestosterone (DHT) by the enzyme 5α-reductase (5AR) (Figure 2.4), a process that contributes to the transformation of terminal hairs into miniaturized hairs, ultimately leading to progressive hair loss [33].

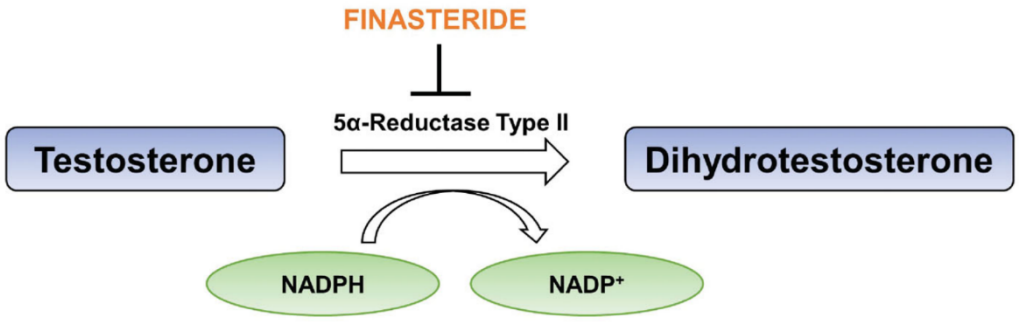

Figure 2.5 Mechanism of action of finasteride.

Finasteride was first approved by the U.S. Food and Drug Administration (FDA) in 1992 for the treatment of benign prostatic hyperplasia (BPH). Subsequently, in 1997, oral finasteride received FDA approval for the treatment of androgenetic alopecia (AGA), also known as pattern hair loss (PHL). Various clinical studies have investigated a range of dosages—from 0.2 mg to 5 mg daily—for the treatment of male AGA [34].

Based on efficacy and safety profiles, a daily dose of 1 mg oral finasteride was established as the optimal therapeutic dose for this indication.

Systemic finasteride selectively inhibits the type II isoenzyme of 5α-reductase with approximately 100-fold greater potency than the type I isoenzyme. This inhibition prevents the conversion of testosterone to dihydrotestosterone (DHT) within the dermal papilla cells. As a result, DHT concentrations are significantly reduced both in the scalp and systemic circulation. Evidence has shown that a single 1 mg dose of finasteride can reduce DHT levels by approximately 70% in both the serum and the scalp [34].

Metabolism of Finasteride

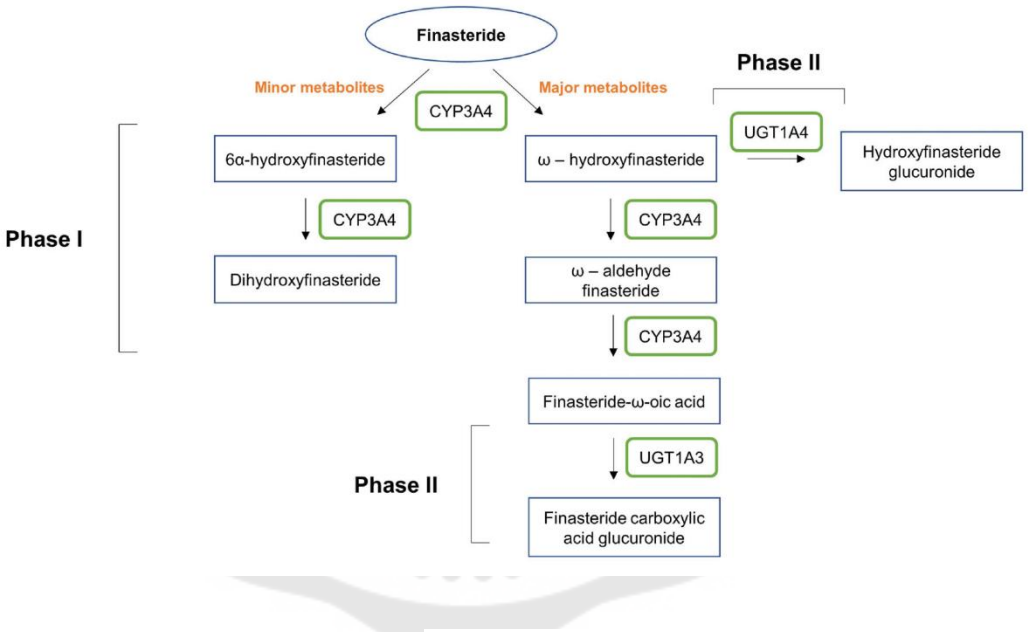

Figure 2.6 Metabolism of finasteride

Finasteride is primarily metabolized in the liver by the cytochrome P450 3A4 (CYP3A4) enzyme. Its metabolism proceeds through two major pathways: Phase I and Phase II (Figure 2.6). In Phase I, finasteride undergoes hydroxylation at the *tert*-butyl group, producing ω-hydroxyfinasteride, which represents the principal biotransformation product.

In Phase II metabolism, also known as glucuronidation, the Phase I metabolites are further conjugated to form hydroxyfinasteride glucuronide and

finasteride carboxylic acid glucuronide. These final metabolites are hydrophilic and retain approximately 20% of finasteride's original 5α-reductase inhibitory activity. It is also possible that additional metabolic pathways exist, as suggested by in vitro studies documenting various minor metabolites and the complexity of both Phase I and Phase II transformations.

Bioavailability of Finasteride [33]

Several studies conducted in healthy young male volunteers have reported the oral bioavailability of finasteride to range between 63% and 80% (15, 16). One study specifically demonstrated that the average bioavailability of a 1 mg dose of systemic finasteride was approximately 65%, with a wide range from 26% to 170% among 15 healthy participants. The mean elimination half-life of finasteride is approximately 5 to 6 hours in men aged 18–60 years, and extends to around 8 hours in men over 70 years of age. Following oral administration, the peak plasma concentration of finasteride reaches 9.2 ng/mL, with steady-state levels achieved within 2 hours. The drug and its metabolites are subsequently excreted, with approximately 39% eliminated via urine and 57% via feces.

Efficacy of Systemic Finasteride

Kaufman KD et al. (1998) [35] conducted two parallel 1-year randomized controlled trials involving 1,553 men aged 18–41 years with androgenetic alopecia classified as Hamilton-Norwood type II vertex to V. Participants received either 1 mg of oral finasteride daily or a placebo. Hair counts were measured within a 1-inch diameter target area and showed improvement as early as month 6, with continued increases at month 12.

At 12 months, the finasteride group demonstrated a mean increase of 86 ± 3.4 hairs, whereas the placebo group showed a mean decrease of 21 ± 3.4 hairs, resulting in a statistically significant difference between groups ($P < 0.001$). Global photographic assessment (GPA) conducted by investigators revealed clinical improvement in 48% of participants in the finasteride group, compared to only 7% in the placebo group. Across all time points, the GPA scores in the finasteride group were significantly higher than those in the placebo group ($P < 0.001$).

Regarding safety, 4.2% of participants in the finasteride group and 2.2% in the placebo group reported sexual dysfunction during the first year of treatment, a statistically significant difference ($P < 0.05$). Treatment discontinuation due to this adverse effect occurred in 1.4% of finasteride-treated subjects and 1.0% of placebo recipients. In all cases, symptoms resolved following discontinuation of the medication.

Roberts JL et al. (1999) [29] conducted a randomized, double-blind study involving 227 men aged 18 to 36 years with androgenetic alopecia classified as Hamilton-Norwood type III vertex to IV. Participants were assigned to receive oral finasteride at doses of 5 mg, 1 mg, 0.2 mg, or 0.01 mg daily, or placebo, over a 12-month period. By the end of the study, hair counts within a 1-inch diameter target area had significantly increased in the 5 mg, 1 mg, and 0.2 mg finasteride groups by 93 ± 10, 85 ± 11, and 63 ± 13 hairs, respectively, from baseline—each significantly superior to both the 0.01 mg group and placebo ($P < 0.001$).

All finasteride-treated groups demonstrated significant reductions in circulating dihydrotestosterone (DHT) levels by month 6, with decreases of −67.6% ± 3.1%, −68.5% ± 1.4%, −61.2% ± 1.7%, and −10.8% ± 4.2% for the 5 mg, 1 mg, 0.2 mg, and 0.01 mg groups, respectively, compared to placebo ($P < 0.01$).

At month 6, the incidence of finasteride-related adverse events was reported as 3.6%, 4.3%, 6.1%, 1.7%, and 3.4% for the 5 mg, 1 mg, 0.2 mg, 0.01 mg, and placebo groups, respectively.

David A et al. (1999) [36] conducted a study comparing the efficacy of oral finasteride 1 mg/day to placebo in 26 men aged 18–41 years with androgenetic alopecia (AGA). After 12 months, the finasteride group showed a statistically significant mean increase of 4.9 terminal anagen hairs, whereas the placebo group exhibited a mean decrease of 0.2 hairs. The difference between groups at the end of the study was statistically significant.

Neste DV et al. (2000) [37] administered oral finasteride 1 mg/day or placebo to 212 men aged 18–40 years with AGA classified as Hamilton-Norwood type II vertex to V. After 48 weeks, both total hair count and anagen hair count within a 1-inch

diameter target area were significantly higher in the finasteride group compared to placebo. The increases were 17.3 ± 2.5 hairs (8.3% ± 1.4%) for total hair count and 27.0 ± 2.9 hairs (26% ± 3.1%) for anagen hair count ($P < 0.001$).

Regarding safety, two participants (1.9%) in the finasteride group and one participant (0.9%) in the placebo group reported sexual side effects. In the finasteride group, one case resolved spontaneously during treatment, while the other resolved within two weeks after study completion.

Hajheydari Z et al. (2009) [14] randomized 45 men with AGA (mean age 22.8 ± 3.3 years) to receive either oral finasteride 1 mg/day or topical finasteride 1% gel for 6 months. Both groups showed a significant increase in hair count and the number of terminal hairs from baseline; however, no statistically significant difference was observed between the two treatment groups. One participant (5.26%) in the oral finasteride group reported a decrease in libido.

In terms of efficacy, multiple studies have confirmed that finasteride acts as a selective type II 5α-reductase inhibitor, reducing the conversion of testosterone to dihydrotestosterone (DHT) [38], a key androgen involved in the miniaturization of hair follicles in androgenetic alopecia. Approximately two-thirds of men with AGA who were treated with 1 mg of finasteride daily demonstrated significant improvements, including increased total and anagen hair counts, accompanied by hair regrowth and reduced hair shaft miniaturization.

Finasteride at a daily dose of 1 mg has shown the greatest efficacy in patients with Hamilton-Norwood classification type III vertex to type IV. Clinical benefits typically become evident after at least 6 to 12 months of treatment. Furthermore, this regimen has been associated with a reduction in dihydrotestosterone levels by approximately 64% in the scalp and 68% in the serum. [39].

Sexual adverse effects associated with finasteride have been reported in approximately 1.5% to 2% of patients. These include decreased libido, erectile dysfunction, and reduced ejaculatory volume. In addition to sexual side effects, psychological disturbances such as depression and suicidal ideation have also been

documented, although these are less common and require further investigation to establish causality.

Safety and Post-finasteride Syndrome (PFS)

Finasteride is generally considered safe and well-tolerated for the treatment of benign prostatic hyperplasia (BPH), for reducing the risk of prostate cancer, and for improving hair count in patients with androgenetic alopecia (AGA). However, a higher incidence of adverse effects has been reported in patients receiving the 5 mg daily dose typically used for BPH, compared to the 1 mg daily dose used for AGA. Nevertheless, even at the lower 1 mg dose, some patients have experienced adverse events, including sexual dysfunction and psychiatric symptoms.

Sexual Effects

Evidence from clinical studies indicates that sexual adverse events associated with systemic finasteride in the treatment of male androgenetic alopecia occur in approximately 2.1% to 3.8% of patients [(34)]. The most commonly reported side effect is erectile dysfunction, followed by decreased ejaculatory volume and reduced libido.

Neuropsychiatric Action

Endogenous neurosteroids are synthesized within glial cells of the central nervous system (CNS) as well as in peripheral endocrine organs such as the adrenal glands and gonads. (11) Key neurosteroids—including progesterone, pregnenolone (PREG), dehydroepiandrosterone (DHEA), 17β-estradiol, and testosterone—play critical roles in modulating sexual behavior and neuropsychological functions. These neurosteroids interact with various cerebral neurotransmitter systems, such as gamma-aminobutyric acid (GABA), serotonin, nicotine, and N-methyl-D-aspartate (NMDA), and are involved in regulating numerous physiological processes, including anticonvulsant activity, stress reduction, mood stabilization, sedation, memory, concentration, attention, and cognitive recognition.

Within the CNS, neurosteroids are metabolized by several enzymes, including 5α-reductase, 3β-hydroxysteroid dehydrogenase, and 17β-hydroxysteroid dehydrogenase. Specifically, 5α-reductase enzymatically converts progesterone to

dihydroprogesterone (DHP) and testosterone to dihydrotestosterone (DHT), which are subsequently metabolized into neuroactive derivatives such as 17β-diol and 5α-androstane-3α, molecules known to exert modulatory effects on androgen, estrogen, progestogen, and GABA-A receptors.

Systemic finasteride can cross the blood-brain barrier, which leads to interference with 5-reductase. Consequently, brain function and activity are affected (11). Finasteride directly dominates hormonal instability, especially the metabolism of cerebral corticosteroids such as progesterone and testosterone, resulting in gamma-aminobutyric acid (GABA) imbalance (12). However, these disproportions of GABA mainly become the cause of finasteride adverse events, which include sexual dysfunction, depression, suicidal ideation, anxiety, etc. (13). In the case of some patients, the mentioned side effects persist despite discontinuation of systemic finasteride (PFS) (14).

Ali AK, et al. (2015) [40] reported that there were 11.8% of persistent sexual dysfunction and 7.9% of suicidal idea among former young men treated with low dose finasteride (1 mg) daily for male AGA. In addition, 87% of these patients suffered from suicidal idea was concomitant with sexual dysfunction. Moreover, the average age of male patients who receive 1 mg of oral finasteride experienced sexual dysfunction alone and sexual dysfunction coexisting with suicidal idea were 31.6 years, and 32.2 years, respectively. The mean duration of low-dose systemic finasteride treatment among the patients who suffered from sexual dysfunction was 2.2 years, and among those who were affected by sexual dysfunction with suicidal idea was 1.3 years.

Infertility

Another point 5-reductase inhibitors affect male fertility. Only 0.6% and 0.9% of the males in Samplaski et al.'s two investigations of populations of men who treated at infertility clinics (from a total of 4400 and 4287 persons, respectively) reported using finasteride.

Metabolic and Cardiovascular Events

According to the altered corticosteroid metabolism (20) and the reduced glucocorticoid and mineralocorticoid clearance (21) caused by 5-reductase inhibitors, there is a higher propensity for type 2 diabetes, changes in body fat distribution, hepatic steatosis, metabolic syndrome, and cardiovascular diseases. The clinical investigations were not conclusive in terms of cardiovascular risk.

Post Finasteride Syndrome (PFS) [41] [42]

Post-finasteride syndrome (PFS) is a condition characterized by the persistence of clinical symptoms despite discontinuation of finasteride. According to various studies, PFS may last from several months to several years—typically ranging from 3 months to 4 years—and includes a constellation of symptoms such as sexual dysfunction and psychiatric disturbances. These symptoms have been reported in patients who have used 5α-reductase inhibitors, including finasteride and dutasteride, and can significantly impair quality of life. Of particular concern is the observation that some sexual side effects may not be fully reversible, highlighting the need for continued investigation and clinical awareness.

Topical Finasteride [43]

In response to the increasing reports of adverse events associated with systemic finasteride, particularly sexual dysfunction and neuropsychiatric disorders, topical finasteride was developed to target hair follicles directly while minimizing systemic absorption and associated risks. [44] However, topical finasteride is currently being investigated as an alternative therapeutic approach.

Mazzarela F, et al. (1997) [45] conducted a single-blind, placebo-controlled, 16-month trial carried out in 52 patients with 28 male androgenetic alopecia (AGA) Hamilton-Norwood scale I-III and 24 female pattern hair loss (FPHL) Ludwig scores I-II participants aged 18-38 years applying a 1.0 ml finasteride 0.005% solution versus topical placebo twice daily. Hair regrowth and balding areas reduction were clinically improved evaluated by six-point scale score and progressive reduction of hair count after wash test was from 49.8±5.9 to 45.2±7.4 at 6th month, and 36.8±8.1 at 16th month,

respectively. Investigators noticed a significant diminish of hair loss rate in topical finasteride group compared to the placebo group without changes in total testosterone, free testosterone, and plasma dihydrotestosterone (DHT) level at sixth month.

Charuwichitrana, et al. (2003) [43] randomly assigned 12 men with AGA Hamilton-Norwood scale III-VI with topical 0.1% finasteride solution (mean aged 39.3 years) twice daily versus topical placebo (mean aged 46.2 years) twice daily for 12 months. At the end of the study, all finasteride-treated patients (100%) and 40% of placebo group were improved. Hair count increased 28.6% and 20% in finasteride group and placebo-treated group, respectively. Additionally, folliculitis in placebo group were reported.

Sitticharoenchai P. (2006) [46] determined the efficacy and safety of topical finasteride 0.5% solution versus topical placebo twice daily in 50 men aged 18-60 years with androgenetic alopecia Hamilton-Norwood scale III-V for 6 months. At the end of the study, hair count in the finasteride group significantly increased 81 hairs per 1 inch diameter compared to placebo group which was -7 hairs (p<0.01). Moreover, the global photographic assessment (GPA) by dermatologists in the finasteride group revealed 46.2% improvement and 53.8% remained unchanged. In the placebo group, 83.3% of patients remained unchanged while 16.7% of the subjects diminished in GPA. There was no sexual dysfunction reported and the drug level in plasma was minimal.

Hajheydari Z et al. (2009) [14] compared the topical 1% finasteride gel and oral finasteride 1 mg daily in 45 male patients with androgenetic alopecia aged 22.8±3.3 years for 6 months. Hair count and number of terminal hairs of both groups at sixth month similarly showed a significant increase from the baseline. Both clinical outcomes were no statistically different between two groups. Furthermore, the size of the alopecic area was no significant difference between two groups. One patient who applied topical finasteride gel had erythema and the symptom immediately disappeared after discontinuation and one patient who took oral finasteride experienced loss of libido.

Caserini et al. (2016) [15] conducted randomized controlled trial evaluated a novel 0.25% finasteride topical solution (P-3074) for its effects on scalp and serum

dihydrotestosterone (DHT) in men with androgenetic alopecia. Two parallel one-week studies were conducted: Study I (n=18) compared 1 mL (2.275 mg) P-3074 applied once daily (o.d.) or twice daily (b.i.d.) to a 1 mg oral finasteride tablet once daily, while Study II (n=32) compared daily scalp application of 100, 200, 300, or 400 μL of P-3074 versus vehicle. Scalp and serum DHT (plus serum testosterone) were measured at baseline and treatment end. In Study I, one week of 1 mL P-3074 o.d. reduced scalp DHT by ~70%, whereas twice-daily P-3074 and 1 mg oral finasteride each achieved ~50% scalp DHT reduction. In that same comparison, serum DHT fell by roughly 60–70% with both the topical and the oral regimens. In the dose-ranging Study II, 100 and 200 μL (0.2275–0.455 mg) P-3074 once daily produced ~47–52% inhibition of scalp DHT, comparable to the 37–54% reduction seen with 300–400 μL applications. Vehicle treatment yielded only a negligible scalp DHT reduction (~5.6%). Systemic DHT suppression was markedly dose-dependent: 100–200 μL P-3074 reduced serum DHT by only ~24–26%, versus ~44–48% with 300–400 μL. No significant changes in serum testosterone were observed for any regimen. The authors concluded that once-daily topical finasteride at 100–200 μL provides adequate scalp DHT inhibition while minimizing systemic DHT reduction and thus potentially reducing the risk of the sexual side effects associated with systemic 5α-reductase inhibition.

Suchonwanit P, et al. (2018) [11] compared the efficacy and safety of topical finasteride 0.25% admixed with minoxidil 3% solution versus 3% minoxidil solution in forty men with androgenetic alopecia. The study revealed the improvement of hair density, hair diameter and global photographic assessment were significantly efficacious in combination group compared to minoxidil alone group (all $P < 0.05$). There were neither serious adverse events nor sexual dysfunctions reported in both groups.

Rai PB, et al. (2018) [47] randomly assigned 50 men aged 18-45 years with androgenetic alopecia stage III and IV of Hamilton-Norwood classification into two groups. Group A received oral finasteride 1 mg daily with topical minoxidil 5% solution while group B was assigned to apply topical finasteride 0.1% with minoxidil 5% solution

for 12 months. There were 65% in group A experienced significantly good hair density improvement (p<0.05). Also, 83% of patients in group B revealed statistically good hair density assessed by global photography at the end of the study compared to baseline (p<0.05). In aspect of side effects, group A who received an oral finasteride mainly suffered from systemic side effects such as erectile dysfunction 8%, ejaculatory dysfunction 8%, decreased libido 12%, facial oedema 12%, mood changes 8%, and anxiety or depression 16%. Meanwhile, group B who applying topical combination reported only local adverse events which were scalp itching 20%, and erythema over scalp 16%.

Piraccini, et al. (2022) [13] randomly allocated 458 patients with male androgenetic alopecia Hamilton-Norwood scale III vertex-V in a 2 : 2 : 1 ratio to receive one of the three treatments: topical finasteride 0.25% spray once daily and oral placebo, topical placebo once daily and oral placebo, or topical placebo once daily and oral finasteride 1 mg for 24 weeks. At the end of the study, the mean changed of total hair count was significantly superior to with topical finasteride 0.25% spray than with placebo (20.2 vs. 6.7 hairs; P<0.001) and was similar to oral finasteride 1 mg once daily (21.1 hairs; P<0.001). In topical finasteride once-daily application, placebo, and oral finasteride group reported: pruritus (2.2%, 0.6%, and 1.2%), erythema (2.2%, 0%, and 0%), and decrease libido (0.6%, 2.8%, and 4.8%), respectively.

In conclusion, further research is warranted to establish the optimal drug delivery method, dosage, and frequency of administration. However, the safety profile of topical finasteride has already been well-documented in existing literature. Accordingly, the primary objective of this study is to determine the most effective frequency of application that maximizes therapeutic efficacy while minimizing adverse events.

Table 2.3 Clinical studies of topical finasteride in the treatment of male androgenetic alopecia (AGA)

Authors	Study Design	N	Population	Duration of Treatment	Regimen	Results	Adverse Events
Mazzarela et al., 1997 [45]	Retrospective	52	28 male androgenetic alopecia (AGA) Hamilton-Norwood scale I-III and 24 female pattern hair loss (FPHL) Ludwig scores I-II participants aged 18-38 years	16 months	Topical finasteride 0.005% solution versus topical placebo twice daily	Progressive reduction of hair count after wash test was from 49.8±5.9 to 45.2±7.4 at 6th month, and 36.8±8.1 at 16th month. Hair regrowth and balding areas reduction were clinically improved evaluated by six-point scale score.	None
Charuwichitrana et al., 2003 [43]	RCT	12	Men with AGA Hamilton-Norwood scale III-VI, mean aged 39.3 and 46.2 years in finasteride and placebo group respectively	12 months	Topical finasteride 0.1% solution versus topical placebo twice daily	All finasteride-treated patients (100%) and 40% of placebo group were improved. Hair count increased by 28.6% and 20% in the finasteride group and placebo-treated group, respectively.	Folliculitis in the placebo group

Table 2.3 (continued)

Authors	Study Design	N	Population	Duration of Treatment	Regimen	Results	Adverse Events
Sitticharoenchai, 2006 [46]	RCT	50	Men aged 18-60 years with AGA Hamilton-Norwood scale III-V	6 months	Topical finasteride 0.5% solution versus topical placebo twice daily	Hair count at the 6th month in the finasteride group significantly increased by 81 hairs/inch diameter cycle (12.56 hairs/circular 1 cm^2) compared to the placebo group which was -7 hairs (p<0.01). GPA by dermatologists in the finasteride group revealed a 46.2% improvement and 53.8% remained unchanged In the placebo group, 83.3% of patients remained unchanged while 16.7% of the subjects diminished in GPA.	None

Table 2.3 (continued)

Authors	Study Design	N	Population	Duration of Treatment	Regimen	Results	Adverse Events
Hajheydari et al., 2009 [14]	RCT	45	Men aged 22.8±3.3 years with AGA	6 months	Topical finasteride 1% gel twice daily versus oral finasteride 1 mg daily	Hair count and number of terminal hairs in the sixth month similarly showed a significant increase from the baseline in both groups. In addition, both clinical outcomes were no statistically different between two groups. The size of the alopecic area was no significant difference between two groups.	Finasteride gel had erythema (one patient)
Suchonwanit et al., 2018 [11]	RCT	40	Men 18 - 60 years of age with AGA type III vertex, IV and V by the Norwood-Hamilton classification	24 weeks (6 months)	Topical finasteride 0.25% admixed with 3% minoxidil versus 3% minoxidil solution	The study at week 24 revealed the improvement of hair density (61.84 vs 34.88 hairs/cm^2), hair diameter and global	None

Table 2.3 (continued)

Authors	Study Design	N	Population	Duration of Treatment	Regimen	Results	Adverse Events
					twice daily	photographic assessment were significantly efficacious in combination group compared to minoxidil alone group (all P < 0.05)	
Rai et al., 2018 [47]	RCT	50	Men aged 18-45 years with AGA stage III and IV of the Hamilton-Norwood classification	12 months	Topical finasteride 0.1% admixed with 5% minoxidil solution twice daily (group A) versus oral finasteride 1 mg daily with 5% minoxidil solution twice daily (group B)	There were 65% in group A experienced significantly good hair density improvement (p<0.05). Also, 83% of patients in group B revealed statistically good hair density assessed by GPA compared to baseline (p<0.05).	The topical group reported scalp itching 20%, and erythema 16%.

Table 2.3 (continued)

Authors	Study Design	N	Population	Duration of Treatment	Regimen	Results	Adverse Events
Piraccini et al., 2022 [13]	RCT	458	Men aged 18-40 years with AGA stage III vertex to V of the Hamilton-Norwood classification	6 months	Topical finasteride 0.25% spray once daily versus oral finasteride 1 mg daily versus placebo	The mean change of total hair count was significantly superior to with topical finasteride 0.25% spray than with placebo (20.2 vs. 6.7 hairs; *P*<0.001) and was similar to oral finasteride 1 mg once daily (21.1 hairs; *P*<0.001).	In topical finasteride group reported pruritus at 2.2%, and erythema at 2.2%.

Outcome Measurements

Dermoscopy and Videodermoscopy [48]

Dermoscopy and videodermoscopy are valuable diagnostic tools commonly used to evaluate scalp and hair disorders, as well as to collect objective data for clinical research. These handheld instruments enable image acquisition at magnifications ranging from 20× to 70×, enhancing visualization of the scalp and hair shafts. Videodermoscopy, an advanced electronic imaging device, offers high-resolution capabilities with magnification levels of up to 1,000×. It allows for consistent imaging of a fixed 1 cm^2 circular area on the vertex of the scalp, typically marked by a semi-permanent tattoo to ensure accurate follow-up assessments. Captured images are digitally stored for subsequent analysis.

Hair density is determined by counting the number of hairs within the 1 cm^2 area, while hair shaft diameter is measured in micrometers using integrated videodermoscopy software. These parameters are widely utilized in clinical trials and research studies as reliable and reproducible indicators of treatment efficacy in hair-related conditions.

Global photography assessment (GPA) and 7-point rating scale [49]

Global Photographic Assessment (GPA) is a valuable tool for the objective evaluation of treatment outcomes related to hair growth, hair volume, and hair density. It is widely employed in clinical research and long-term follow-up in clinical practice. Standardized photographs are captured using a fixed stereotactic device in combination with a digital camera to ensure consistent positioning. Four standard views—vertex, midline, frontal, and temporal—are obtained by placing the subject's head in a stereotactic holder.

GPA involves a paired comparison of clinical images taken before and after treatment. The degree of improvement is assessed using a 7-point rating scale, evaluated independently by blinded dermatologists. This method provides a standardized and semi-quantitative measure of clinical response.

-3 greatly decreased

-2 moderately decreased

-1 slightly decreased

0 unchanged

1. slightly increased

2. moderately increased

3. greatly increased

One of the key advantages of Global Photographic Assessment (GPA), particularly when combined with the 7-point rating scale, is its ability to provide a more precise and standardized evaluation of hair regrowth following treatment, compared to subjective assessments by investigators or patients alone. In this study, GPA will be conducted at each follow-up visit using the 7-point scale, as evaluated by two blinded

dermatologists. This approach is expected to enhance the accuracy and reliability of treatment outcome assessments.

Visual analogue scale (VAS) [50]

The Visual Analogue Scale (VAS) is a widely used subjective tool for assessing patients' perceptions of hair loss severity and treatment outcomes. Its simplicity and adaptability make it suitable for diverse populations and clinical settings. VAS can be presented in various formats, including numerical rating scales, curvilinear scales, box scales, and Likert-type scales. The most commonly used version ranges from 0 to 10, where 0 represents complete dissatisfaction and 10 represents complete satisfaction.

CHAPTER 3
RESEARCH METHODOLOGY

Research Design

A randomized, investigator-blinded, controlled trial

Target Population

Male patients aged 18–60 years with androgenetic alopecia classified as Hamilton-Norwood stage III vertex, IV, or V.

Sample Size Calculation

The sample size was calculated based on the primary outcome, which was the change in hair density from baseline to week 24, as assessed by videodermoscopy, in order to detect a difference between the means of two independent groups. According to a randomized controlled trial conducted by Sitticharoenchai P. [46] reported that the mean change in terminal hair count from baseline to week 24 in subjects treated with twice-daily application of topical finasteride 0.5% solution was 16.72 ± 9.8 hairs/cm². Based on the outcome of terminal hair count, which exhibited a higher standard deviation, the sample size was calculated to detect a between-group difference of more than 8 hairs/cm², with a significance level of 0.05 and a statistical power of 80%. The calculation was performed using the PS (Power and Sample Size Calculation) software. A minimum of 25 subjects per group was required. Accounting for an estimated 20% dropout rate, the final target sample size was set at 60 participants, with 30 subjects in each group.

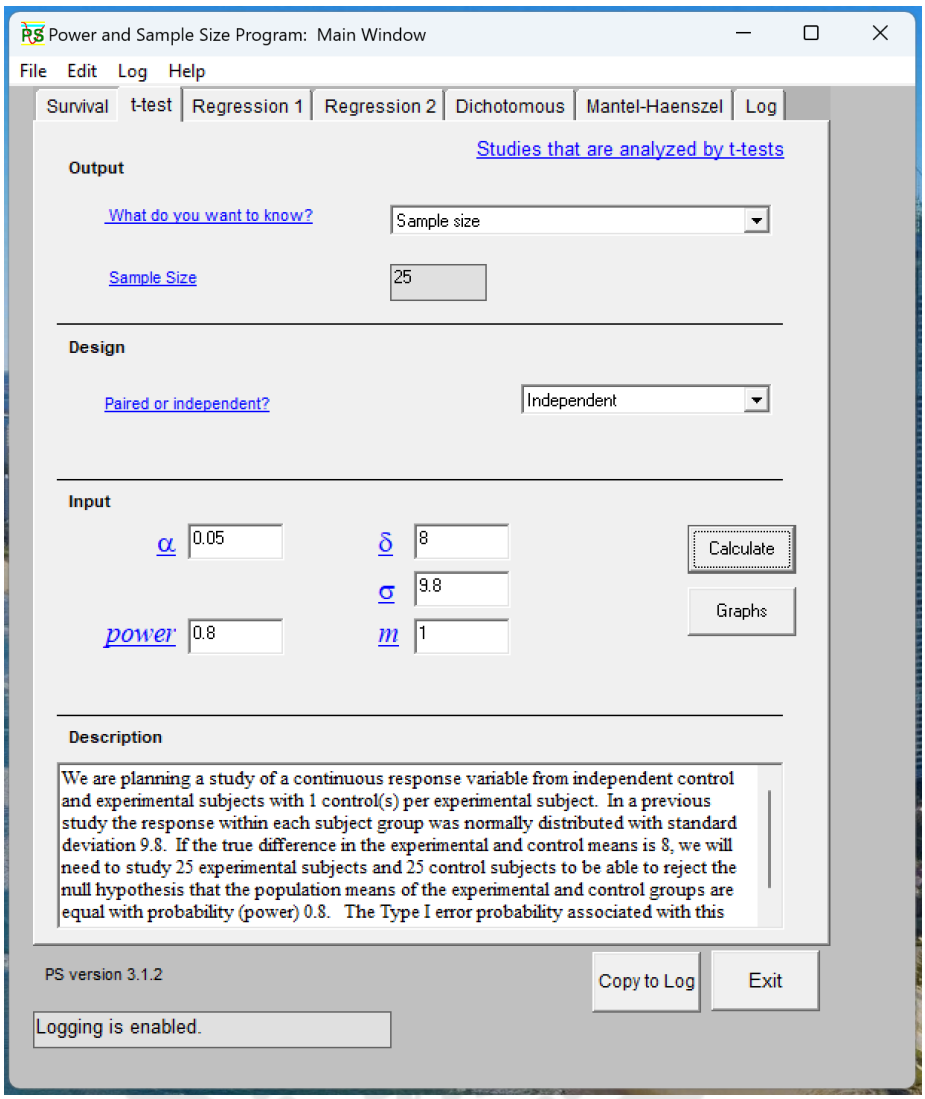

Figure 3.1 Sample size calculation by power and sample size programme

Sampling Population

Eligible participants will be male patients aged 18–60 years with androgenetic alopecia (AGA) classified as Hamilton-Norwood stage III vertex, IV, or V, attending the outpatient department at Srinakharinwirot University Skin Center, Bangkok, Thailand. Recruitment will be conducted through consecutive sampling. Potential subjects will be invited to participate in the study through physician referrals, printed materials, and announcements on social media platforms.

Randomization and Allocation Concealment

Sixty eligible participants will be randomly allocated into two groups in a 1:1 ratio using a computer-generated randomization list with variable block sizes of 2, 4, and 6 to ensure balanced group assignment. The randomization process will be carried out through a computerized system, managed by an independent study coordinator who is not involved in participant enrollment or outcome assessment.

Allocation concealment will be maintained through a computer-based system, which automatically assigns participants to their respective groups after baseline data entry is completed. Investigators and outcome assessors will remain blinded to group allocation throughout the study period until all data collection is completed.

Inclusion Criteria

1. Male participants aged 18–60 years with a clinical diagnosis of androgenetic alopecia (AGA).

2. Classified as Hamilton-Norwood stage III vertex, IV, or V.

3. Willing and able to comply with the requirements of the study protocol, as documented by written informed consent.

Exclusion Criteria

1. Known hypersensitivity to finasteride, ethanol, or butylene glycol.

2. Personal or first-degree family history of breast cancer or prostate cancer.

3. History of chronic kidney disease (CKD), liver disease, or congestive heart failure (CHF).

4. History of sexual dysfunction, depression, psychiatric illness, or suicidal ideation.

5. Presence of medical conditions known to affect hair growth, including anemia, hypothyroidism, hyperthyroidism, systemic lupus erythematosus (SLE), chronic alcoholism, or nutritional deficiencies.

6. History of psychological disorders associated with hair loss, such as trichotillomania (TTM).

7. Presence of scalp abnormalities including infections, psoriasis, or significant abrasions/ulcers.

8. History of hair transplantation or hair weaving.

9. Use of topical hair growth products (e.g., minoxidil or topical finasteride) within 6 months prior to study enrollment.

10. Use of systemic medications with hair-promoting or anti-androgenic effects—such as minoxidil, finasteride, dutasteride, cimetidine, diazoxide, cyclosporine, ketoconazole, corticosteroids, anticonvulsants, or vasodilators, within 6 months prior to the study.

11. Use of other hair regrowth therapies, including low-level laser/light therapy or platelet-rich plasma, within 3 months prior to study enrollment.

12. Use of medications known to induce hair loss, including chemotherapeutic agents, within 6 months prior to the study.

13. Current use of medications known to interact with finasteride, such as rifampicin, carbamazepine, fluconazole, itraconazole, or voriconazole.

Discontinuation Criteria

1. Occurrence of serious adverse reactions or anaphylaxis.

2. Onset of depressive symptoms during the study.

3. Non-compliance with the study protocol.

4. Voluntary withdrawal of consent during the course of the study.

Materials and Instruments

1. Videodermoscope (FotoFinder Leviacam®; FotoFinder Systems, Inc., Columbia, USA) with TrichoLAB Space® software

2. Digital camera DSLR Canon 500D 1.5 million pixels

3. Stereotactic instrument

4. Semi-permanent tattoo makeup device kit (Cherman II®)

5. Finasteride powder

6. Butylene glycol

7. Ethanol 95%
8. Sterile water
9. Solution containers

Research Tools

1. Paper documents and electronic case record forms
2. Patient information sheet
3. Informed consent form
4. Treatment protocol and subject's daily diary for compliance

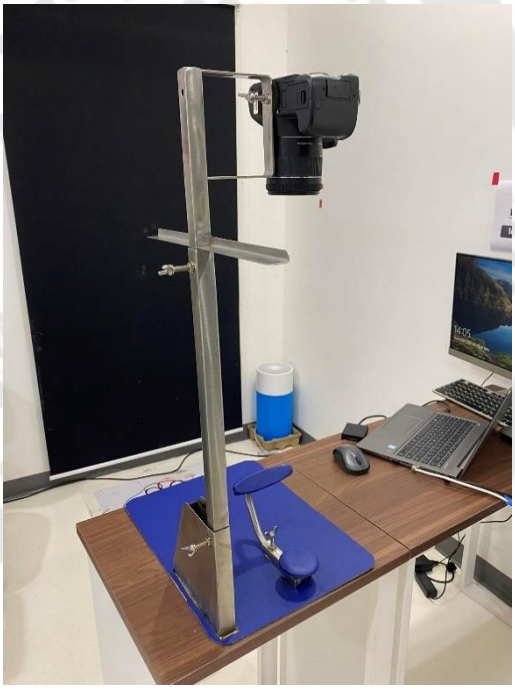

Figure 3.2 Stereotaxic instrument photographed from a 90-degree angle with an attached digital camera.

Figure 3.3 Stereotaxic instrument photographed from a 45-degree angle with an attached digital camera.

Protocol Flow Chart

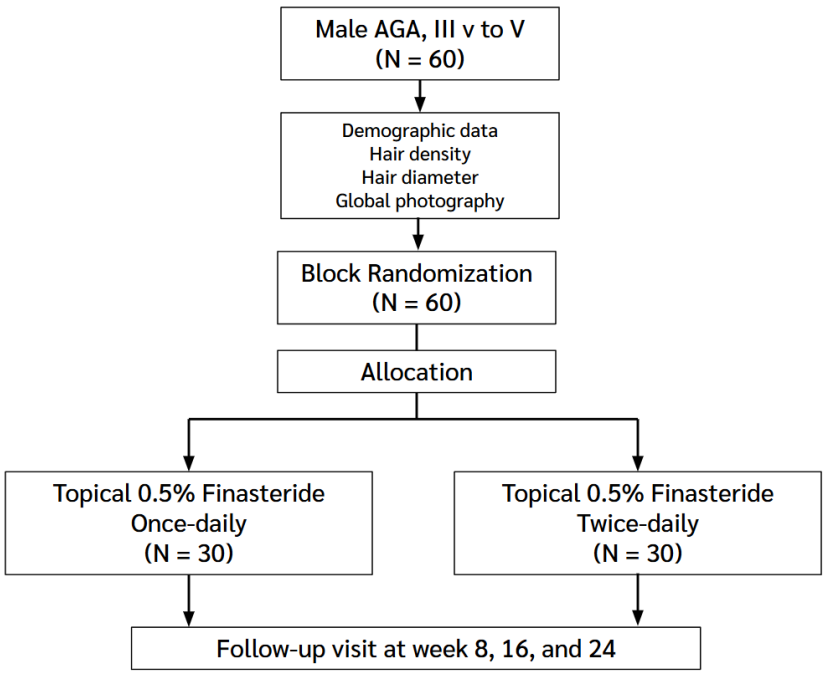

Figure 3.4 Protocol flow chart

Study Procedures

1. Screening and Enrollment

1.1 Study participants will be recruited through social media platforms and direct invitations at the outpatient department (OPD).

1.2 Eligible candidates will undergo clinical evaluation, and the severity of androgenetic alopecia will be classified according to the Hamilton-Norwood classification system.

1.3 All candidates will receive comprehensive information regarding the study protocol, including the intervention, potential risks and benefits, and possible adverse drug reactions.

1.4 Participants who meet the inclusion and exclusion criteria will be formally enrolled in the study.

1.5 Baseline demographic data, along with relevant clinical information, including personal and family history of androgenetic alopecia, past medical history, prior treatments, and any previous adverse drug reactions will be collected at the screening visit (week 0).

2. Randomization, Allocation, and Concealment

2.1 Randomization will be conducted using variable block sizes of 2, 4, and 6 to ensure balanced group assignment.

2.2 Eligible participants will be randomly allocated into two groups in a 1:1 ratio using a computer-generated randomization list.

2.3 The investigators will remain blinded to the treatment allocation throughout the study to maintain allocation concealment and reduce bias.

3. Baseline Characteristics Measurement

3.1 Objective Assessment

3.1.1 Videodermoscopy for Hair Density and Hair Diameter Measurement

Hair density and hair diameter will be assessed using a videodermoscope (Fotofinder Leviacam®) to capture high-resolution images of the vertex scalp area. To ensure consistency across follow-up visits, the target

measurement site will be marked with a small semi-permanent tattoo. Hair density is defined as the number of total hairs (including both terminal and non-terminal hairs) per 1 cm^2 and will be analyzed using TrichoLAB Space® software in conjunction with investigator evaluation, utilizing images magnified at 50×. Hair diameter, incorporating both terminal and non-terminal hairs, will also be measured in micrometers using the same software and magnification. All data will be recorded by the investigator in the case record form.

3.2 Subjective Assessment

3.2.1 Global Photographic Assessment (GPA) for Overall Clinical Evaluation

Global photographic images will be obtained using a Canon EOS 500D DSLR camera with a resolution of 15 megapixels, mounted on a stereotactic device to ensure standardized image acquisition. Photographs will include a 45-degree view to assess the frontal scalp and a 90-degree view to assess the vertex. Consistent camera-to-scalp distance, lighting conditions, and patient positioning will be maintained throughout the study to ensure reliable comparisons across time points.

4. Treatment and Intervention

4.1 On Day 1, participants are randomly allocated into two treatment groups

4.2 Subjects in the first group are instructed to apply topical finasteride 0.5% solution once daily, before bedtime. Subjects in the second group are instructed to apply the same concentration of the solution twice daily—once in the morning and once before bedtime—for a duration of 24 weeks. Follow-up assessments are scheduled at weeks 8, 16, and 24.

4.3 The solution should be applied to the affected (balding) scalp area and left in place for a minimum of 6 hours to ensure adequate absorption.

4.4 Efficacy and safety assessments will be conducted at each follow-up visit (weeks 8, 16, and 24).

4.5 Treatment adherence will be monitored through subject-maintained daily diaries and by evaluating the returned containers of the study medication.

5. Follow-up Visits

All participants will undergo clinical evaluation and adverse event monitoring during follow-up visits at the Srinakharinwirot University Skin Center at week 8, 16, and 24. These assessments include the following components:

5.1 Efficacy Assessment

5.1.1 Objective Assessment

5.1.1.1 Hair Density (hairs/cm²)

Hair density will be assessed using a videodermoscope by quantifying the total number of hairs (including both terminal and non-terminal hairs) within a predefined 1 cm^2 target area. The analysis will be performed using specialized software, in conjunction with the investigator's evaluation.

5.1.1.2 Hair Diameter (micrometers)

Average hair shaft diameter will be measured using a videotrichoscope in the same target area. The software calculates the mean diameter of all hairs (terminal and non-terminal), supported by the investigator's assessment. Terminal hairs are defined as those with a diameter of $\geq$ 0.06 mm, while non-terminal hairs are < 0.06 mm.

5.1.2 Subjective Assessment

5.1.2.1 Global Photographic Assessment (GPA)

Overall clinical improvement will be evaluated using GPA, based on standardized images taken with a Canon EOS 500D DSLR camera (15 megapixels), mounted on a stereotactic device. Two standardized views will be used: a 45-degree angle for the frontal view and a 90-degree angle for the vertex view. Imaging conditions—including distance, illumination, and head positioning, will be strictly controlled across all follow-up visits.

Each subject's global photographs will be independently assessed by two blinded dermatologists using a 7-point rating scale:

—3 = greatly decreased

—2 = moderately decreased

—1 = slightly decreased

0 = no change

+1 = slightly increased

+2 = moderately increased

+3 = greatly increased

5.2 Safety Assessment

Both local and systemic adverse events will be assessed at each follow-up visit (weeks 8, 16, and 24) using a standardized evaluation form completed confidentially. Local adverse effects may include scalp pruritus and irritation, while systemic adverse events may include sexual dysfunction, depression, testicular pain or swelling, gynecomastia, breast tenderness, and dizziness.

5.3 Satisfaction Assessment

Patient satisfaction with the treatment will be evaluated at week 24 using a 10-point Visual Analogue Scale (VAS), where 0 represents complete dissatisfaction and 10 represents complete satisfaction.

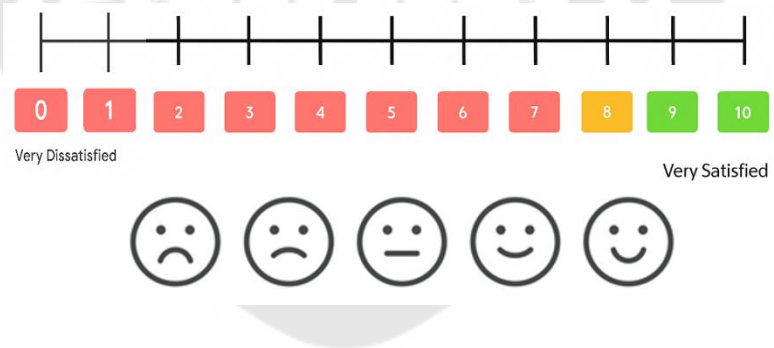

Figure 3.5 Satisfaction level assessment

5.4 Compliance Assessment

Treatment compliance will be assessed using two complementary methods: (1) review of participants' self-reported daily diaries documenting each application, and (2) evaluation of returned study medication containers to verify actual usage. These procedures are intended to ensure adherence to the treatment protocol throughout the study period.

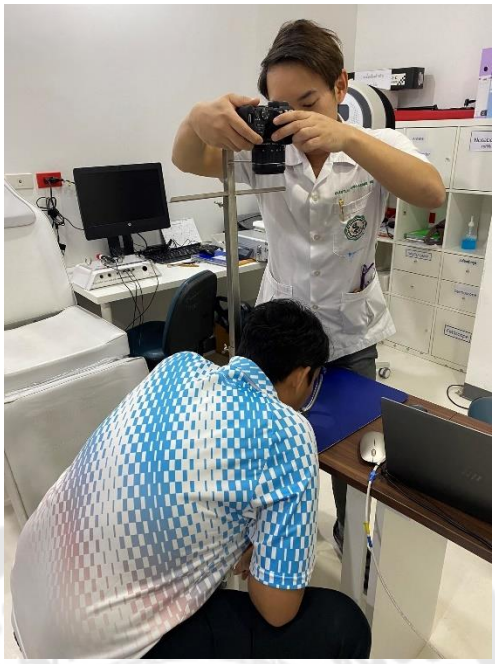

Figure 3.6 Global photography from a 90-degree angle to evaluate the vertex region.

Study Outcome

Primary Outcome

1. Change in hair density from baseline to week 24, as measured by videodermoscopy.

Secondary Outcomes

1. Change in hair diameter from baseline to week 24, as measured by videodermoscopy.

2. Overall clinical change from baseline to week 24, evaluated through Global Photographic Assessment (GPA) by blinded dermatologists.

3. Patient satisfaction with the treatment, assessed at week 24 using a 10-point Visual Analogue Scale (VAS).

4. Incidence and nature of clinical adverse events observed throughout the study period.

Outcome Measurement

1. Efficacy Assessment

1.1 Objective Measurement using videodermoscope

1.1.1 Hair Density (hairs/1 cm2 area)

Hair density, defined as the number of total hairs (including both terminal and non-terminal hairs) per 1 cm^2, is objectively assessed using a videodermoscopy (FotoFinder Leviacam®) with TrichoLAB Space® software in conjunction with investigator evaluation. The analysis is based on standardized images captured at 20× magnification. Mean changes in hair density will be compared across all follow-up visits, specifically at weeks 8, 16, and 24.

1.1.2 Hair Diameter (average μm in diameter)

At each follow-up visit (weeks 8, 16, and 24), the average hair diameter of all hairs within the same predefined scalp location, marked with a small semi-permanent tattoo, is measured in micrometers using videodermoscopy software at 20× magnification. Terminal hairs are defined as having a diameter of 0.06 mm (60 μm) or greater, whereas non-terminal hairs have a diameter of less than 0.06 mm.

1.2 Subjective Measurement using global photography and assessment form

1.2.1 Global Photography Assessment (7-point rating scale) by Dermatologists

Two independent dermatologists will be assigned to evaluate overall clinical improvement by reviewing standardized global photographs. Assessments will be based on two photographic angles: a 45-degree view for the frontal scalp and a 90-degree view for the vertex. Evaluations will be conducted at all follow-up visits, including weeks 8, 16, and 24. Clinical changes will be rated using a 7-point scale as follows:

-3 greatly decreased

-2 moderately decreased

-1 slightly decreased

0 unchanged

1 slightly increased

2 moderately increased

3 greatly increased

1.2.2 Patient Satisfaction (10-point visual analogue scale)

Patient satisfaction will be assessed at each follow-up visit, including at week 24, using a 10-point Visual Analogue Scale (VAS), where 0 indicates complete dissatisfaction and 10 indicates complete satisfaction.

2. Safety Assessment

Localized and systemic adverse events will be assessed confidentially at all follow-up visits (week 8 , 1 6 , and 2 4) using a standardized evaluation form. Localized side effects may include scalp pruritus and irritation, while potential systemic adverse events include sexual dysfunction, depressive symptoms, testicular pain or swelling, gynecomastia or breast tenderness, and dizziness.

Table 3.1 Outcome measurement and follow-up timeline

No.	Measurement \ Visit	Week 0	Week 8	Week 16	Week 24
1	Hair density videodermoscopy (FotoFinder Leviacam®)	✓	✓	✓	✓
2	Hair diameter videodermoscopy (FotoFinder Leviacam®)	✓	✓	✓	✓
3	Overall clinical change (Global Photography Assessment by dermatologists)	✓	-	-	✓
4	Localized and systemic adverse events (standardized evaluation form)	-	✓	✓	✓
5	Patient satisfaction (VAS)	-	-	-	✓

Data Collection and Management

All participant data, including textual records and imaging files will be collected using both paper-based documentation and electronic case record forms (eCRFs). Data will be securely stored and managed in compliance with confidentiality and data protection standards.

Statistical Analysis

All statistical analyses will be performed using STATA version 16 for Windows. A *p*-value $<$ 0.05 will be considered statistically significant.

Descriptive Statistics

1. Categorical variables will be presented as frequencies and percentages.

2. Continuous variables will be assessed for normality. Normally distributed data will be expressed as mean ± standard deviation, while non-normally distributed data will be reported as median and interquartile range (IQR).

Interferential Statistics

1. The chi-square test will be used to compare categorical variables between groups.

2. A linear mixed-effects model will be used to evaluate differences in mean values between treatment groups over time, while independent t-tests will assess Global Photographic Assessment (GPA) scores, as rated by both dermatologists and patients, at each follow-up visit compared to baseline.

3. Data will be tested for normality prior to within-group analysis. For normally distributed data, the paired t-test will be used; for non-normally distributed data, the Wilcoxon Signed-Rank test will be applied.

4. All primary efficacy analyses will be conducted based on the intention-to-treat (ITT) population.

Ethical Consideration

This study is conducted in accordance with Good Clinical Practice (GCP) guidelines. The study protocol, patient information sheet, and informed consent form were reviewed and approved by the Ethics Committee of Srinakharinwirot University (Approval No. SWUCE-671003). Written informed consent was gathered from all participants prior to enrollment. All study procedures are carried out with strict adherence to patient confidentiality and data protection standards.

Duration of the Study

Table 3.2 Duration of the study

No.	Information \ Month	1	2	3	4	5	6	7	8	9	10	11	12	Percent of Product	Product
1	Review of literature	✓												20	Hypothesis
2	Research protocol development	✓												15	Research protocol
3	Applying for ethical approval	✓	✓	✓										5	Ethical approval
4	Data collection				✓	✓	✓	✓	✓	✓	✓	✓		50	Research data
5	Data analysis											✓		2	Research outcome
6	Discussion and conclusion												✓	3	Research discussion and conclusion
7	Manuscript												✓	5	International publication

Research Budget

Table 3.3 Research budget

Information	Budget (baht)
Research fellow compensation	15,000
Participant compensation (60 subjects × 150 Baht × 4 visits)	36,000
Topical finasteride 0.5% solution (36,000 cc)	
- Finasteride powder 225 grams (8,400 Baht/25 gm)	75,600
- Butylene glycol 10 liters (2,500 Baht/5 L)	5,000
- Ethanol 95% 20 liters (600 Baht/5 L)	2,400
- Sterile water 20 liters (50 Baht/1 L)	1,000
Documentation charges 60 subjects x 4 visits x 20 baht	5,000
Telephone charges 60 subjects x 4 visits x 20 baht	5,000
Reimbursement for potential clinical complications	5,000
One hundred and fifty thousand Baht	**150,000**

CHAPTER 4
RESULTS

This study, titled 'Efficacy and Safety of Topical Finasteride 0.5% Solution Once Daily Versus Twice Daily in the Treatment of Male Androgenetic Alopecia,' was approved by the Human Research Ethics Committee of Srinakharinwirot University (Approval No. SWUCE-671003). Data analysis was carried out in four main phases, as detailed below.

1. Baseline Characteristics

General demographic information and baseline hair characteristics of all participants were collected and analyzed prior to the initiation of treatment.

2. Changes in Hair Parameters Following Treatment

Changes in hair density and hair diameter were evaluated over the study period to assess treatment efficacy. Additionally, a global photographic assessment was conducted to provide a visual evaluation of clinical improvement.

3. Patient Satisfaction

Patient satisfaction with treatment outcomes was assessed using a standardized evaluation form to capture their perceptions and overall improvement.

4. Adverse Events

All adverse events reported during the study period were documented and analyzed to ensure the safety of the treatment regimens.

Baseline Characteristics

General demographic information

The calculated sample size for this study was 50 participants, with 25 participants allocated to each treatment group. However, a total of 60 participants were recruited to compensate for potential dropouts and to ensure an adequate final sample size for analysis.

Of the 60 enrolled participants, 48 completed the study. Thirty participants were randomized to receive topical finasteride 0.5% solution once daily, applied before

bedtime, while the remaining thirty were assigned to apply the solution twice daily, once in the morning and once before bedtime.

A total of 12 participants withdrew from the study.

- Once-daily group: Five participants withdrew—two due to relocation for work in rural areas and three due to loss to follow-up as they could not be contacted despite repeated attempts.
- Twice-daily group: Seven participants withdrew—one due to a major accident resulting in both lower legs with fractures, three due to relocation to another province, and three owing to difficulty adhering to scheduled follow-up visits.

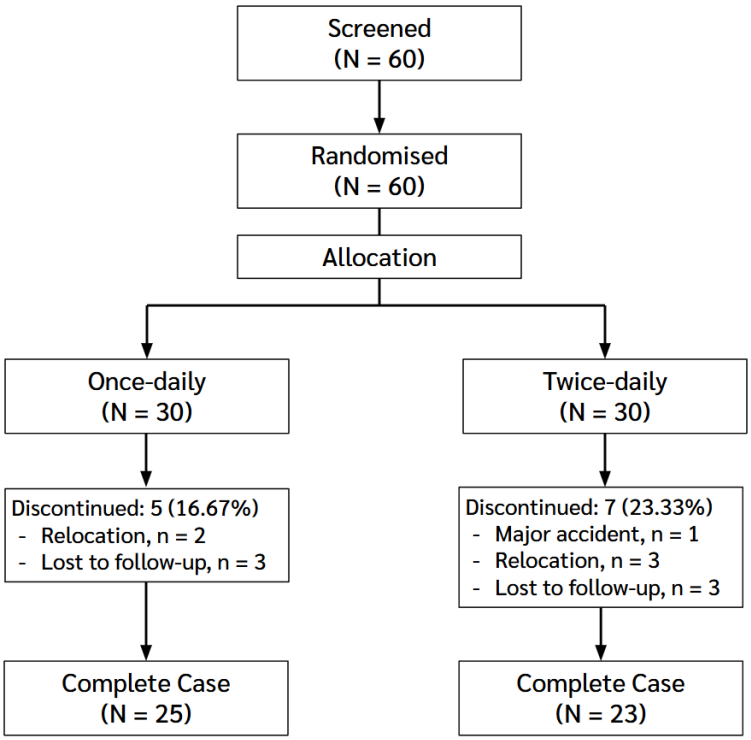

Figure 4.1 Patient disposition.

A total of 48 male participants with androgenetic alopecia completed the study. The distribution between the treatment groups was relatively balanced, with 25 participants in the once-daily group and 23 in the twice-daily group. The mean age of the participants was 40.69 ± 9.45 years.

In terms of hair loss severity, based on the Hamilton-Norwood classification, 30 participants (50%) were categorized as stage III vertex, 19 participants (31.67%) as stage IV, and 11 participants (18.33%) as stage V (Table 4.1).

Table 4.1 Number and percentage of participants' baseline demographic characteristics by treatment group

Baseline Characteristics	Once Daily Group (N = 30)	Twice Daily Group (N = 30)	*p*-value
Age (years)			
Mean ± SD	40.50 ± 10.79	41.27 ± 8.64	0.76
Minimun-maximum	22 - 60	23 - 58	
Duration of hair thinning (years)			
Mean ± SD	9.13 ± 7.18	7.73 ± 6.34	0.42
Minimun-maximum	0.5 - 30	1 – 20.5	
Underlying disease, n (%)			
No	22 (73.33)	22 (73.33)	> 0.99
Yes	8 (26.67)	8 (26.67)	
Smoking, n (%)			
No	30 (100)	30 (100)	> 0.99
Yes	0 (0)	0 (0)	
Family history of AGA, n (%)			
No	0 (0)	0 (0)	> 0.99
Yes	30 (100)	30 (100)	
Previous treatment, n (%)			
No	20 (66.67)	17 (56.67)	0.43
Yes	10 (33.33)	13 (43.33)	
Form of previous treatment, n (%)			
No	20 (66.67)	17 (56.67)	0.40
Topical	3 (10.00)	4 (13.33)	
Oral	5 (16.67)	5 (16.67)	
Others	2 (6.67)	4 (13.33)	

Table 4.1 (continued)

Baseline Characteristics	Once Daily Group (N = 30)	Twice Daily Group (N = 30)	*p*-value
Hamilton-Norwood Classification, n (%)			
III vertex	13 (43.33)	17 (56.67)	
IV	13 (43.33)	6 (20.00)	0.87
V	4 (13.33)	7 (23.33)	

The mean age was comparable between the two groups, with the once-daily group having a mean age of 40.50 ± 10.79 years and the twice-daily group 41.27 ± 8.64 years (p = 0.76). The mean duration of hair thinning was 9.13 ± 7.18 years in the once-daily group and 7.73 ± 6.34 years in the twice-daily group, showing no significant difference (p = 0.42).

The proportion of participants with underlying diseases was identical between groups (26.67% in both), as was the smoking status, with all participants in both groups reporting no history of smoking. All participants had a family history of AGA.

Regarding prior treatment history, 33.33% of participants in the once-daily group and 43.33% in the twice-daily group reported previous AGA treatments. The types of prior treatments used (topical, oral, or other) were similar between groups, with no statistically significant difference (p = 0.40).

In terms of AGA severity, based on the Hamilton-Norwood classification, both groups were relatively balanced. In the once-daily group, 43.33% were classified as stage III vertex, 43.33% as stage IV, and 13.33% as stage V. In comparison, the twice-daily group included 56.67% at stage III vertex, 20.00% at stage IV, and 23.33% at stage V (p = 0.87) (Table 4.1).

There were no statistically significant differences in any of the baseline characteristics between the two treatment groups, indicating that the randomization process successfully achieved balanced groups for comparative analysis.

Baseline Hair Characteristics

The baseline hair characteristics of participants in the once-daily and twice-daily treatment groups are summarized in tables 4.2 and 4.3, corresponding to the intention-to-treat (ITT) and complete case analyses, respectively.

Table 4.2 Baseline hair characteristics of all participants included in the intention-to-treat (ITT) analysis.

Baseline Hair Characteristics	Once Daily Group (N = 30)	Twice Daily Group (N = 30)	*p*-value
Hair density (hairs/cm^2), mean ± SD			
Total hair	165.13 ± 29.78	169.37 ± 29.53	0.58
Terminal hair	51.00 ± 26.18	56.93 ± 31.51	0.43
Non-terminal hair	114.20 ± 39.94	112.37 ± 41.95	0.86
Hair diameter (μm), mean ± SD	49.43 ± 7.99	51.07 ± 9.40	0.47

Table 4.3 Baseline hair characteristics of all participants included in the complete case analysis

Baseline Hair Characteristics	Once Daily Group (N = 25)	Twice Daily Group (N = 23)	*p*-value
Hair density (hairs/cm^2), mean ± SD			
Total hair	163.72 ± 30.42	170.61 ± 30.85	0.44
Terminal hair	51.6 ± 27.54	52.26 ± 30.47	0.94
Non-terminal hair	112.20 ± 40.80	118.39 ± 40.71	0.60
Hair diameter (μm), mean ± SD	49.84 ± 8.24	49.65 ± 9.17	0.94

Intention-to-Treat Analysis

The baseline hair characteristics of participants included in the intention-to-treat (ITT) analysis are presented in table 4.2. The mean total hair density was 165.13 ± 29.78 hairs/cm² in the once-daily group and 169.37 ± 29.53 hairs/cm² in the twice-daily group, with no statistically significant difference observed (p = 0.58). Terminal hair density was slightly higher in the twice-daily group (56.93 ± 31.51 hairs/cm²) compared to the once-daily group (51.00 ± 26.18 hairs/cm²), although the difference was not statistically significant (p = 0.43). Non-terminal hair density was comparable between the groups, with values of 114.20 ± 39.94 and 112.37 ± 41.95 hairs/cm², respectively (p = 0.86). Likewise, mean hair diameter did not differ significantly between the once-daily (49.43 ± 7.99 μm) and twice-daily (51.07 ± 9.40 μm) groups (p = 0.47). These findings indicate that baseline hair parameters differed slightly but were comparable between the two treatment groups in the ITT population. Statistical testing revealed that the differences were not significant.

Complete Case Analysis

Baseline hair characteristics of participants included in the complete case analysis are presented in table 4.3. The mean total hair density was 163.72 ± 30.42 hairs/cm² in the once-daily group and 170.61 ± 30.85 hairs/cm² in the twice-daily group, with no statistically significant difference between groups (p = 0.44). Terminal hair density was also comparable, with values of 51.6 ± 27.54 hairs/cm² in the once-daily group and 52.26 ± 30.47 hairs/cm² in the twice-daily group (p = 0.94). Similarly, non-terminal hair density did not differ significantly between groups (112.20 ± 40.80 vs. 118.39 ± 40.71 hairs/cm²; p = 0.60). The mean hair diameter was nearly identical between the once-daily (49.84 ± 8.24 μm) and twice-daily (49.65 ± 9.17 μm) groups (p = 0.94). These findings confirm that both groups were slightly different but comparable at baseline, with no statistically significant differences, thereby supporting the validity of subsequent treatment comparisons within the complete case population.

Participant Compliance

The mean compliance rates of participants during the study period are presented in table 4.4. The once-daily group exhibited a mean compliance of 98.30% ± 2.41%, while the twice-daily group demonstrated a comparable mean compliance of 97.82% ± 3.12%. The difference between groups was not statistically significant (p = 0.52). These results indicate a high level of adherence to the treatment protocol in both groups, thereby reinforcing the reliability of subsequent efficacy and safety assessments.

Table 4.4 Participant compliance during the study period.

Compliance	Once Daily Group (N = 30)	Twice Daily Group (N = 30)	*p*-value
Compliance, % (mean ± SD)	98.30 ± 2.41	97.82 ± 3.12	0.52

Changes in Hair Parameters Following Treatment

The treatment period lasted a total of 24 weeks, during which participants in both treatment groups were evaluated at baseline (week 0), week 8, week 16, and week 24. The primary outcome measure was hair density. Changes in hair parameters were assessed both within each group over time and between groups at each time point. Analyses were conducted using both the intention-to-treat (ITT) and complete case approaches to ensure the robustness of the findings.

Data Analysis by Intention-to-Treat (ITT) Approach

The statistical analysis was conducted based on the intention-to-treat (ITT) principle. To handle missing data, the last observation carried forward (LOCF) method was employed. The results are summarized in Table 4.5 and Table 4.6.

Table 4.5 Hair density and hair diameter at each follow-up visit during the study based on the intention-to-treat (ITT) analysis

Hair Density and Diameter	Once Daily Group (N = 30)				Twice Daily Group (N = 30)			
	Week 0	Week 8	Week 16	Week 24	Week 0	Week 8	Week 16	Week 24
Hair density (hairs/cm^2), mean ± SD								
Total hair	165.13 ± 29.78	175.10 ± 31.57	180.62 ± 35.21	186.03 ± 33.40	169.37 ± 29.53	181.03 ± 29.54	188.73 ± 28.55	198.93 ± 30.55
Terminal hair	51.00 ± 26.18	57.69 ± 28	64.93 ± 32.38	69.97 ± 34.16	56.93 ± 31.51	63.27 ± 33.25	70.5 ± 34.39	76.57 ± 36.23
Non-terminal hair	114.20 ± 39.94	117.59 ± 39.94	115.72 ± 42.85	116.20 ± 43.17	112.37 ± 41.95	117.83 ± 44.19	118.3 ± 42.90	122.67 ± 45.16
Hair diameter (μm), mean ± SD	49.43 ± 7.99	49.86 ± 8.28	52.28 ± 8.04	51.93 ± 7.91	51.07 ± 9.40	50.97 ± 9.03	52.83 ± 8.99	53.07 ± 9.10

Table 4.6 Comparison of hair density and hair diameter between baseline (week 0) and week 24, based on the intention-to-treat (ITT) analysis

Hair Density and Diameter	Once Daily Group (N = 30)		Twice Daily Group (N = 30)		*p*-value*
	Week 0	Week 24	Week 0	Week 24	
Hair density (hairs/cm^2), mean ± SD					
Total hair	165.13 ± 29.78	186.03 ± 33.40	169.37 ± 29.53	198.93 ± 30.55	0.006
Terminal hair	51.00 ± 26.18	69.97 ± 34.16	56.93 ± 31.51	76.57 ± 36.23	0.918
Non-terminal hair	114.20 ± 39.94	116.20 ± 43.17	112.37 ± 41.95	122.67 ± 45.16	0.016
Hair diameter (μm), mean ± SD	49.43 ± 7.99	51.93 ± 7.91	51.07 ± 9.40	53.07 ± 9.10	0.427

* Baseline adjustment

Total Hair Density

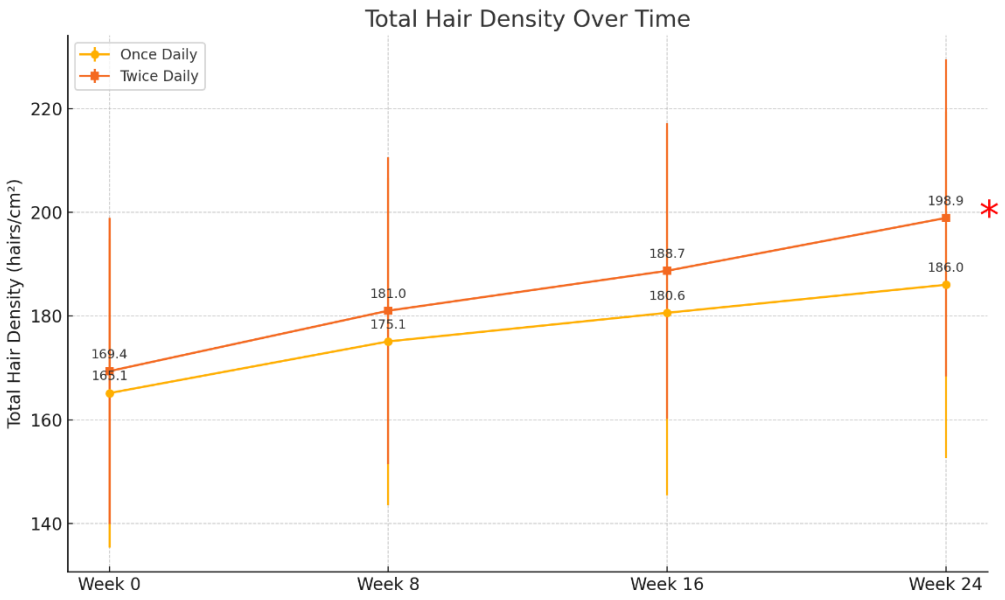

Figure 4.2 Line graph illustrating total hair density over time based on intention-to-treat analysis; **P*=0.006.

The analysis revealed statistically significant increases in total hair density at each follow-up time point compared to baseline. The estimated mean (± SD) total hair densities were 167.25 ± 29.78 at baseline, 178.32 ± 31.57 at week 8, 184.95 ± 35.21 at week 16, and 192.79 ± 33.40 at week 24 ($p < 0.001$ for all time points). The corresponding mean changes from baseline were +11.07 (week 8), +17.70 (week 16), and +25.54 hairs/cm² (week 24), all statistically significant ($p < 0.001$).

In the once-daily group, total hair density increased from 165.13 ± 29.78 at baseline to 186.03 ± 33.40 at week 24, representing a mean change of +20.90 hairs/cm². In the twice-daily group, the density rose from 169.37 ± 29.53 to 198.93 ± 30.55, indicating a greater mean change of +29.56 hairs/cm².

A linear mixed-effects model was employed to assess the interaction between treatment group and time, adjusting for baseline values. A statistically significant interaction was observed at week 24 (95% CI: 2.35 to 13.97, $p = 0.006$),

indicating a greater increase in total hair density in the twice-daily group compared to the once-daily group at the end of the study. No significant differences between groups were detected at week 8 (p = 0.688) or week 16 (p = 0.255).

These findings suggest that although both treatment regimens resulted in progressive improvement in total hair density over time, the twice-daily application demonstrated a significantly greater effect by week 24.

Terminal Hair Density

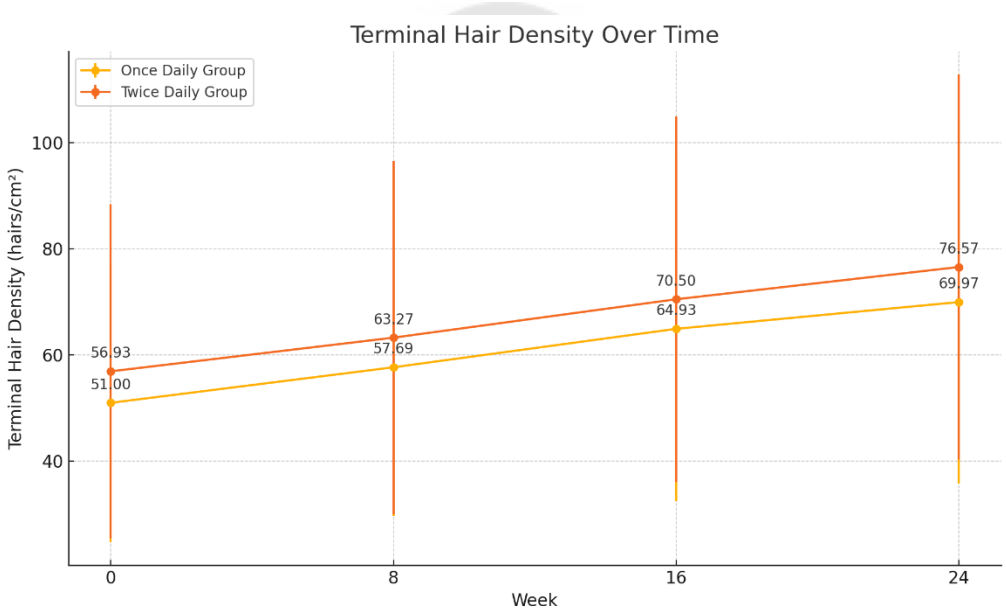

Figure 4.3 Line graph showing terminal hair density over time based on intention-to-treat analysis.

Terminal hair density significantly increased from baseline across all follow-up time points. The mean increases from baseline were +6.71 hairs/cm² at week 8 (95% CI: 4.46 to 8.95, p < 0.001), +13.94 at week 16 (95% CI: 11.70 to 16.19, p < 0.001), and +19.50 hairs/cm² at week 24 (95% CI: 17.26 to 21.75, p < 0.001). These findings indicate a consistent and statistically significant improvement in terminal hair density over the 24-week treatment period.

In the once-daily group, terminal hair density increased from 51.00 ± 26.18 at baseline to 69.97 ± 34.16 at week 24, yielding a mean change of +18.97 hairs/cm².

In the twice-daily group, the density rose from 56.93 ± 31.51 to 76.57 ± 36.23, representing a mean change of +19.64 hairs/cm².

When adjusted for baseline terminal hair density, no significant differences were observed between the treatment groups at any follow-up time point (week 8: p = 0.729; week 16: p = 0.727; week 24: p = 0.918), suggesting that both once-daily and twice-daily applications produced comparable efficacy throughout the study duration.

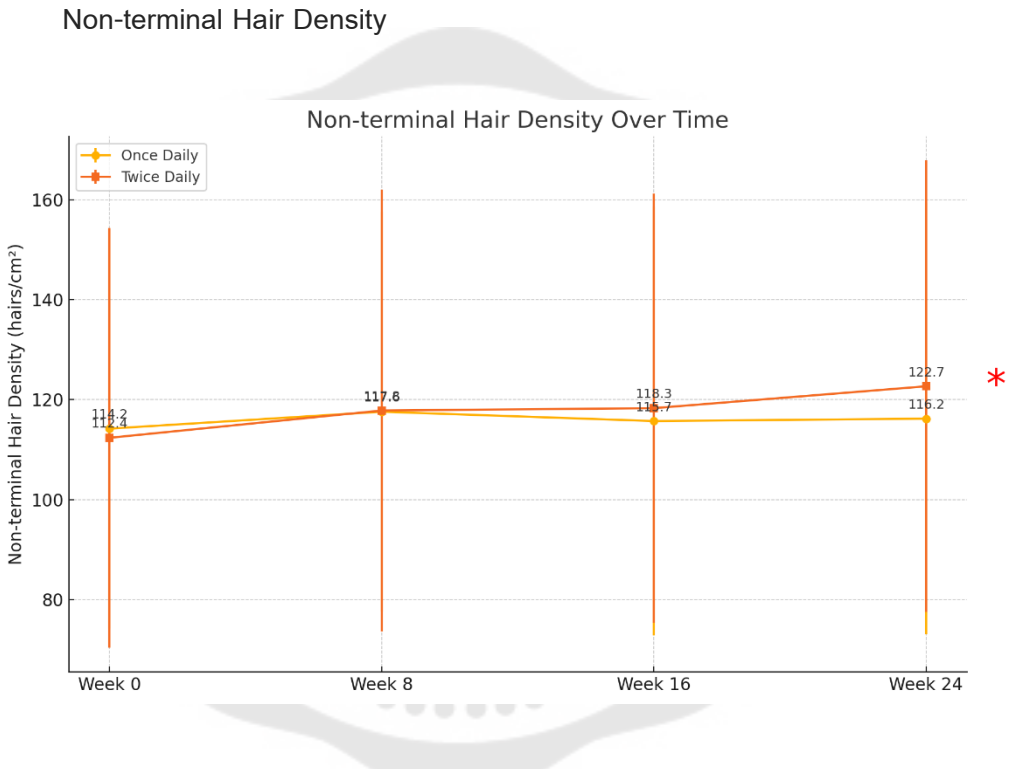

Figure 4.4 Line graph illustrating non-terminal hair density over time based on intention-to-treat analysis; *P=0.016.

In once-daily application, the mean non-terminal hair density increased modestly from baseline to each follow-up point, but none of the changes reached statistical significance. Specifically, the mean differences at week 8, 16, and 24 were 3.48 hairs/cm² (p = 0.1184), 1.62 hairs/cm² (p = 0.4713), and 2.10 hairs/cm² (p = 0.4246), respectively.

In contrast, twice-daily application demonstrated statistically significant increases in non-terminal hair density at all timepoints compared to baseline. The mean changes were 5.47 hairs/cm² at week 8 (p = 0.0478), 5.93 hairs/cm² at week 16 (p = 0.0205), and 10.30 hairs/cm² at week 24 (p = 0.0018). These findings suggest a greater and more consistent improvement in non-terminal hair density in the twice-daily group over the 24-week period.

After adjusting for baseline, a statistically significant group-by-time interaction was detected at week 24 (95% CI: 1.52 to 14.87, p = 0.016), indicating a significantly greater increase in non-terminal hair density in the twice-daily group compared to the once-daily group. No significant differences between groups were observed at week 8 (p = 0.560) or week 16 (p = 0.205), suggesting that the superior efficacy of the twice-daily regimen became more apparent during the later phase of the study.

Hair Diameter

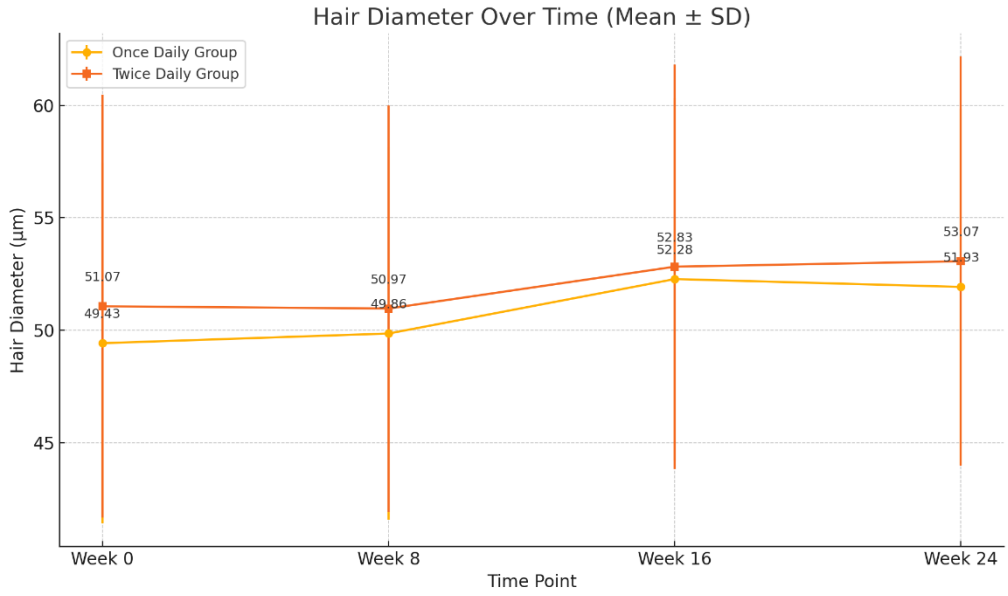

Figure 4.5 Line graph showing hair diameter over time based on intention-to-treat analysis.

There was no statistically significant change in hair diameter at week 8 compared to baseline ($p = 0.606$). However, significant increases were observed at week 16 and week 24. The mean changes from baseline were +2.31 μm at week 16 (95% CI: 1.66 to 2.95, $p < 0.001$) and +2.25 μm at week 24 (95% CI: 1.61 to 2.90, $p < 0.001$). These findings suggest that the treatment was associated with a delayed but statistically significant increase in hair shaft thickness over time.

In the once-daily group, the mean hair diameter increased from 49.43 ± 7.99 μm at baseline to 51.93 ± 7.91 μm at week 24, yielding a mean change of +2.50 μm. Similarly, the twice-daily group showed an increase from 51.07 ± 9.40 μm to 53.07 ± 9.10 μm, representing a mean change of +2.00 μm.

Following adjustment for baseline hair diameter, no statistically significant differences were observed between the once-daily and twice-daily groups at any time point (week 8: $p = 0.400$; week 16: $p = 0.093$; week 24: $p = 0.427$). While both regimens led to a progressive increase in hair diameter, the lack of significant between-group differences suggests that once-daily and twice-daily applications exerted comparable effects on average hair diameter.

Complete Case Analysis

The results were analyzed using a complete case approach (Table 4.7 and 4.8).

Table 4.7 Hair density and hair diameter at each follow-up visit during the study based on the complete case analysis

Hair Density and Diameter	Once Daily Group (N = 25)				Twice Daily Group (N = 23)			
	Week 0	Week 8	Week 16	Week 24	Week 0	Week 8	Week 16	Week 24
Hair density (hairs/cm^2), mean ± SD								
Total hair	163.72 ± 30.42	173 ± 30.07	177.52 ± 32.78	183.80 ± 31.06	170.61 ± 30.85	183.39 ± 29.09	191.61 ± 28.11	204.91 ± 28.68
Terminal hair	51.60 ± 27.54	57.60 ± 29.21	64.44 ± 32.31	70.28 ± 34.40	52.26 ± 30.47	58.26 ± 31.16	66.34 ± 33.56	74.26 ± 36.76
Non-terminal hair	112.20 ± 40.80	115.56 ± 39.86	113.08 ± 42.12	113.64 ± 42.54	118.39 ± 40.71	125.22 ± 38.20	125.13 ± 38.93	130.83 ± 41.09
Hair diameter (μm), mean ± SD	49.84 ± 8.24	50.08 ± 8.44	52.40 ± 8.18	52 ± 8.03	49.65 ± 9.17	49.52 ± 8.38	51.48 ± 8.33	51.78 ± 8.55

Table 4.8 Comparison of hair density and hair diameter between baseline (week 0) and week 24, based on the complete case analysis

Hair Density and Diameter	Once Daily Group (N = 25)		Twice Daily Group (N = 23)		*p*-value*
	Week 0	Week 24	Week 0	Week 24	
Hair density (hairs/cm^2), mean ± SD					
Total hair	163.72 ± 30.42	183.80 ± 31.06	170.61 ± 30.85	204.91 ± 28.68	< 0.001
Terminal hair	51.60 ± 27.54	70.28 ± 34.40	52.26 ± 30.47	74.26 ± 36.76	0.149
Non-terminal hair	112.20 ± 40.80	113.64 ± 42.54	118.39 ± 40.71	130.83 ± 41.09	0.004
Hair diameter (μm), mean ± SD	49.84 ± 8.24	52 ± 8.03	49.65 ± 9.17	51.78 ± 8.55	0.968

* Baseline adjustment.

Total Hair Density

In the complete case analysis, which was consistent with the intention-to-treat findings, both treatment groups demonstrated a progressive and statistically significant increase in total hair density over the 24-week period after adjusting for baseline. In the once-daily group, total hair density increased from 163.72 ± 30.42 hairs/cm² at baseline to 183.80 ± 31.06 hairs/cm² at week 24 (mean change = 20.08 hairs/cm²). In the twice-daily group, the increase was from 170.61 ± 30.85 to 204.91 ± 28.68 hairs/cm² (mean change = 34.30 hairs/cm²). Linear mixed-effects modeling confirmed significant within-group improvements from baseline at week 8, week 16, and week 24 (all $p < 0.001$). Notably, the between-group comparison at week 24 revealed a significantly greater increase in the twice-daily group compared to the once-daily group ($p < 0.001$), indicating superior efficacy of the twice-daily regimen in enhancing total hair density by the end of the study.

Terminal Hair Density

In the complete case analysis, which was consistent with the findings from the intention-to-treat analysis, both treatment groups demonstrated a statistically significant increase in terminal hair density over time after adjusting for baseline values. In the once-daily group, terminal hair density increased from 51.60 ± 27.54 hairs/cm² at baseline to 70.28 ± 34.40 hairs/cm² at week 24, representing a mean change of +18.68 hairs/cm² ($p < 0.001$). Similarly, the twice-daily group showed an increase from 52.26 ± 30.47 to 74.26 ± 36.76 hairs/cm², corresponding to a mean change of +22.00 hairs/cm² ($p < 0.001$). Mixed-effects regression analysis further confirmed significant improvements from baseline at each follow-up visit: week 8 ($p < 0.001$), week 16 ($p < 0.001$), and week 24 ($p < 0.001$). However, no statistically significant differences were observed between the two groups at any time point ($p = 0.149$ at week 24), indicating that both once- and twice-daily applications were similarly effective in promoting terminal hair growth.

Non-terminal Hair Density

Both groups exhibited mild increases in non-terminal hair density over time after adjusting for baseline values. In the once-daily group, the mean density increased from 115.38 ± 42.15 to 116.20 ± 43.17 hairs/cm² at week 24, reflecting a modest mean change of +0.82 hairs/cm² ($p = 0.001$), with only marginal and inconsistent changes observed at earlier timepoints. In contrast, the twice-daily group demonstrated a more pronounced increase, from 112.84 ± 40.70 to 122.67 ± 45.16 hairs/cm², corresponding to a mean change of +9.83 hairs/cm² ($p = 0.001$). Linear mixed-effects analysis with baseline adjustment revealed a statistically significant interaction between treatment and time at week 24 (coefficient = 10.90, 95% CI: 3.45–18.32, $p = 0.004$), indicating a significantly greater increase in the twice-daily group. No significant between-group differences were found at week 8 ($p = 0.367$) or week 16 ($p = 0.128$). These findings suggest a modest but statistically significant advantage of the twice-daily regimen by the end of the study, based on the complete case analysis, which was consistent with the results of the intention-to-treat analysis.

Hair Diameter

In the complete case analysis, which was concordant with the intention-to-treat findings and adjusted for baseline, both once-daily and twice-daily regimens led to a statistically significant increase in hair diameter over time. In the once-daily group, diameter increased from 48.94 ± 8.06 μm at baseline to 52.28 ± 8.04 μm at week 16 and remained stable at 51.93 ± 7.91 μm at week 24 ($p < 0.001$). The twice-daily group showed a similar pattern, rising from 50.81 ± 9.16 μm to 52.83 ± 8.99 μm at week 16 and reaching 53.07 ± 9.10 μm at week 24 ($p < 0.001$). Linear mixed-effects analysis confirmed that the increase became statistically significant from week 16 onward in both groups. However, no significant between-group differences were observed at any time point (week 24: $p = 0.968$), indicating that increasing the application frequency did not enhance the effect on average hair diameter.

Comparison of Mean Change from Baseline Between Two Groups Using Intention-to-Treat (ITT) Analysis

Table 4.9 Mean change from baseline in hair density and hair diameter at each follow-up visit, based on the intention-to-treat (ITT) analysis

Mean Change	Hair density (hairs/cm^2), mean ± SD						Hair diameter (μm), mean ± SD	
	Total hair		Terminal hair		Non-terminal hair			
	Once Daily (N = 30)	Twice Daily (N = 30)	Once Daily (N = 30)	Twice Daily (N = 30)	Once Daily (N = 30)	Twice Daily (N = 30)	Once Daily (N = 30)	Twice Daily (N = 30)
Week 8	10.48 ± 11.04	11.67 ± 11.61	7.10 ± 5.57	6.33 ± 7.04	3.48 ± 11.64	5.47 ± 14.49	0.45 ± 2.52	-0.10 ± 2.37
p-value	0.690		0.644		0.565		0.392	
Week 16	16.00 ± 13.54	19.37 ± 12.39	14.34 ± 11.20	13.57 ± 8.08	1.62 ± 11.95	5.93 ± 13.26	2.86 ± 2.63	1.77 ± 2.80
p-value	0.323		0.760		0.195		0.127	
Week 24	21.41 ± 12.27	29.57 ± 16.54	19.38 ± 11.99	19.63 ± 10.46	2.10 ± 13.98	10.30 ± 16.38	2.52 ± 2.59	2.00 ± 2.60
p-value	0.036		0.931		0.044		0.447	

Total Hair Density

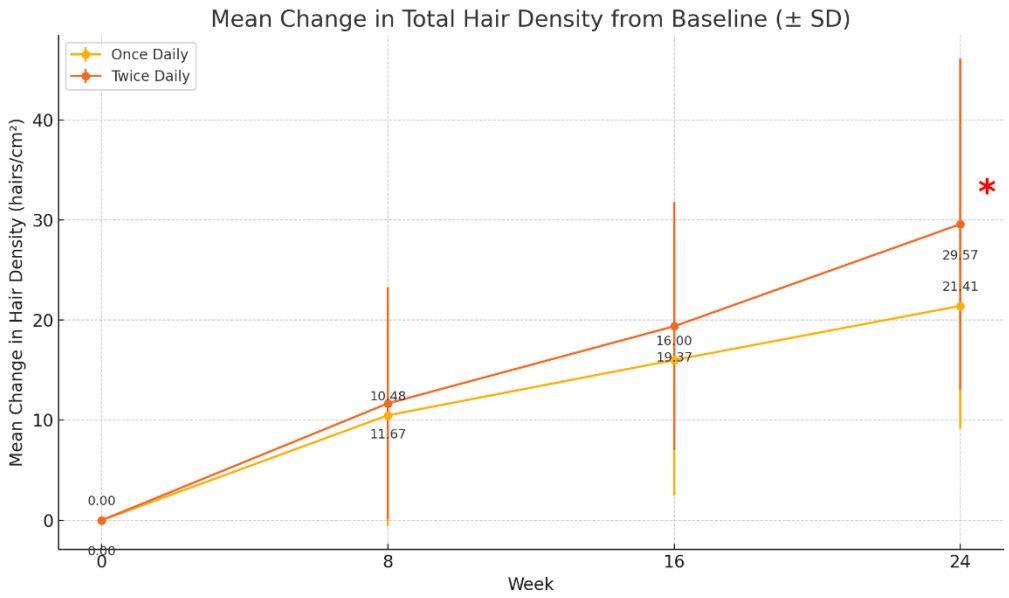

Figure 4.6 Line graph illustrating the mean change in total hair density over time based on intention-to-treat (ITT) analysis; *P=0.036.

At week 8, the mean increase in total hair density from baseline was 10.48 hairs/cm² (SD = 11.04) in the once-daily group and 11.67 hairs/cm² (SD = 11.61) in the twice-daily group. The between-group difference of 1.18 hairs/cm² (95% CI: –7.09 to 4.73; p = 0.690) was not statistically significant, indicating comparable efficacy of the two regimens at this early stage.

By week 16, the once-daily group showed a mean increase of 16.00 hairs/cm² (SD = 13.54), while the twice-daily group exhibited a slightly greater gain of 19.37 hairs/cm² (SD = 12.39). The mean difference of 3.37 hairs/cm² (95% CI: –10.13 to 3.40; p = 0.323) remained statistically non-significant, suggesting no clear advantage of increased application frequency at the midpoint of the study.

At the end of the 24-week treatment period, the mean increase in total hair density reached 21.41 hairs/cm² (SD = 12.27) in the once-daily group and 29.57 hairs/cm² (SD = 16.54) in the twice-daily group. The between-group difference of 8.15

hairs/cm² (95% CI: –15.77 to –0.54; p = 0.036) was statistically significant, favoring the twice-daily regimen.

In conclusion, while both once-daily and twice-daily applications of topical finasteride significantly improved total hair density over time, only the twice-daily regimen demonstrated a statistically superior outcome by the end of the 24-week study period. This suggests that increased frequency of application may enhance long-term treatment efficacy for total hair density.

Terminal Hair Density

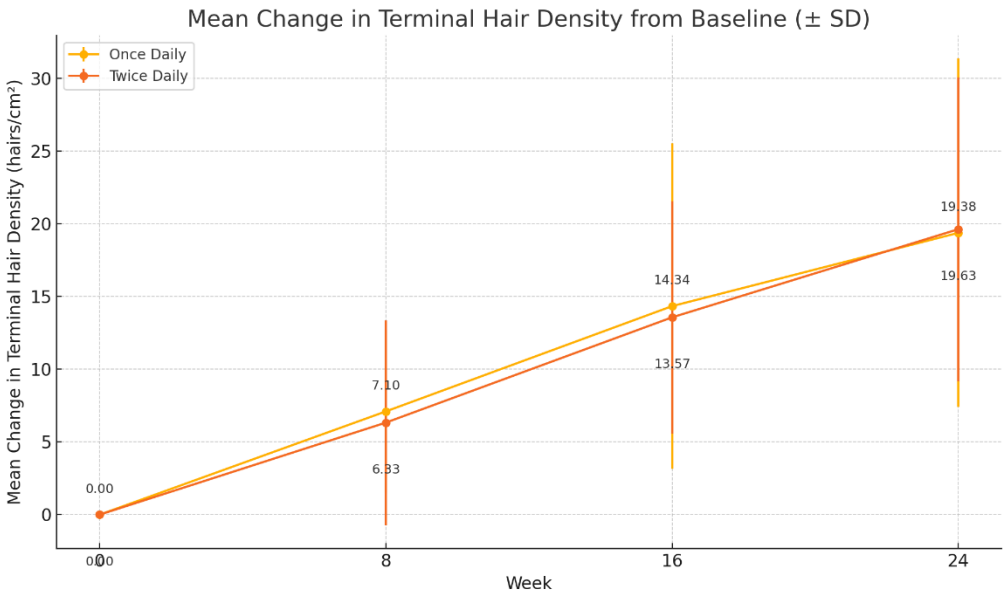

Figure 4.7 Line graph showing the mean change in terminal hair density over time based on intention-to-treat (ITT) analysis.

At week 8, the mean increase in terminal hair density from baseline was 7.10 hairs/cm² (SD = 5.57) in the once-daily group and 6.33 hairs/cm² (SD = 7.04) in the twice-daily group. The between-group difference was 0.77 hairs/cm² (95% CI: –2.55 to 4.09; p = 0.643), indicating no statistically significant difference between the two dosing schedules. While both groups demonstrated early improvements, the twice-daily

application did not provide a significant advantage over once-daily use at this time point.

By week 16, the once-daily group showed a mean increase of 14.34 hairs/cm² (SD = 11.20), compared to 13.57 hairs/cm² (SD = 8.08) in the twice-daily group. The mean difference was 0.78 hairs/cm² (95% CI: –4.30 to 5.86; p = 0.760), again indicating no statistically significant difference. Although the once-daily group exhibited a slightly higher numerical gain, the results suggest comparable efficacy between the two regimens.

At week 24, the mean increase in terminal hair density was 19.38 hairs/cm² (SD = 11.99) for the once-daily group and 19.63 hairs/cm² (SD = 10.46) for the twice-daily group. The between-group difference was minimal, at 0.25 hairs/cm² (95% CI: –6.11 to 5.61; p = 0.931), confirming no statistically significant difference in treatment effect.

In conclusion, both once-daily and twice-daily applications of topical finasteride produced similar improvements in terminal hair density throughout the 24-week period. Increasing the frequency of application did not confer any additional benefit for this specific parameter.

Non-Terminal Hair Density

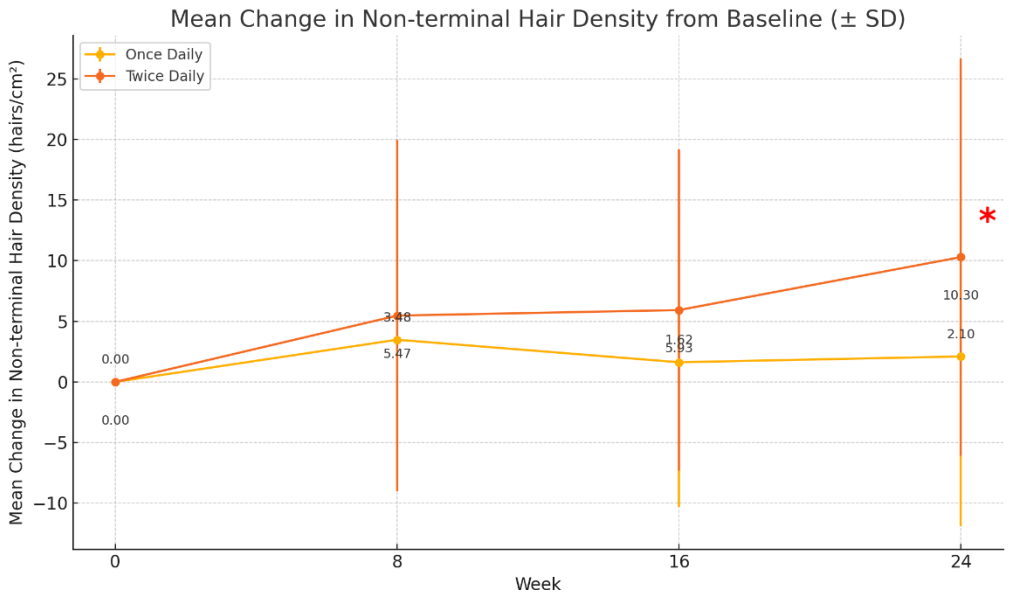

Figure 4.8 Line graph illustrating the mean change in non-terminal hair density over time based on intention-to-treat (ITT) analysis; *P=0.044.

At week 8, the mean increase in non-terminal hair density from baseline was 3.48 hairs/cm² (SD = 11.64) in the once-daily group and 5.47 hairs/cm² (SD = 14.49) in the twice-daily group. The between-group difference of 1.98 hairs/cm² (95% CI: –8.85 to 4.88; p = 0.565) was not statistically significant, indicating that both dosing regimens yielded comparable early improvements in non-terminal hair density.

By week 16, the once-daily group showed a mean increase of 1.62 hairs/cm² (SD = 11.95), while the twice-daily group demonstrated a mean increase of 5.93 hairs/cm² (SD = 13.26). The mean difference between groups was 4.31 hairs/cm² (95% CI: –10.90 to 2.27; p = 0.195), which did not reach statistical significance. Although the twice-daily group showed a numerically greater gain, the difference remained inconclusive.

At week 24, the final assessment, the once-daily group had a mean increase of 2.10 hairs/cm² (SD = 13.98), compared to 10.30 hairs/cm² (SD = 16.38) in

the twice-daily group. The mean intergroup difference was 8.20 hairs/cm² (95% CI: –16.15 to –0.24; p = 0.044), indicating a statistically significant advantage in favor of the twice-daily application.

In conclusion, although both regimens led to modest improvements in non-terminal hair density over time, only the twice-daily application demonstrated a statistically significant benefit by week 24. This suggests that increasing the frequency of topical finasteride may offer superior efficacy in promoting non-terminal hair growth in the long term.

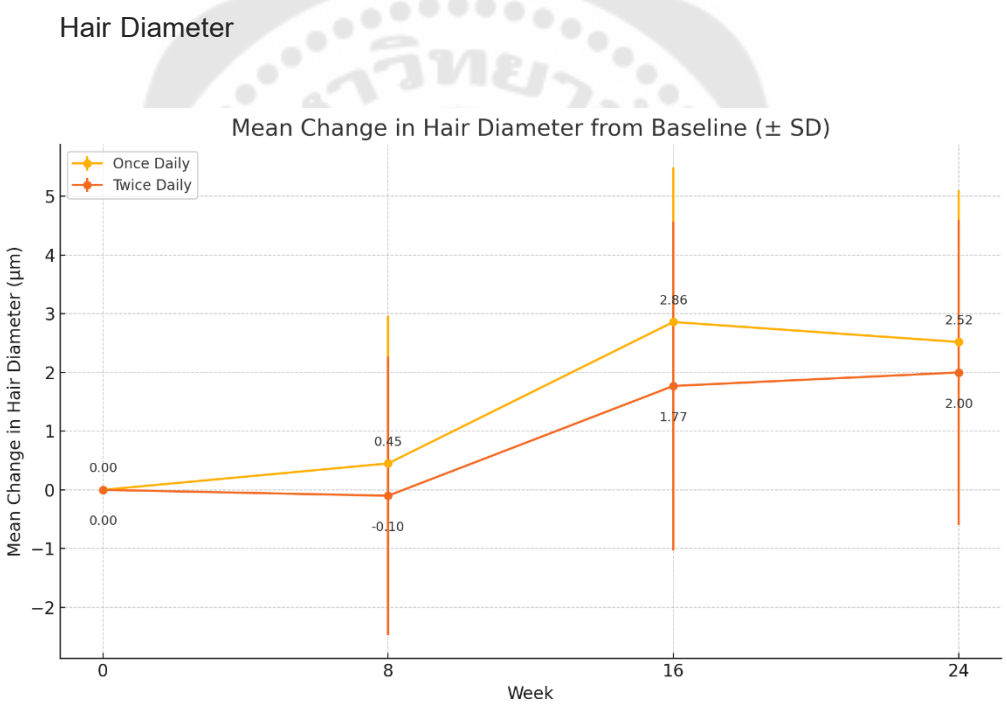

Figure 4.9 Line graph showing the mean change in hair diameter over time based on intention-to-treat (ITT) analysis.

At week 8, the mean change in hair diameter from baseline was 0.45 µm (SD = 2.52) in the once-daily group and –0.10 µm (SD = 2.37) in the twice-daily group. The between-group difference was 0.55 µm (95% CI: –0.73 to 1.82; p = 0.392), indicating no statistically significant difference in hair diameter improvement between

the two regimens. Despite a slightly higher numerical increase in the once-daily group, this difference was not statistically meaningful.

By week 16, the once-daily group showed a mean increase of 2.86 μm (SD = 2.63), compared to 1.77 μm (SD = 2.80) in the twice-daily group. The mean difference of 1.10 μm (95% CI: –0.32 to 2.51; p = 0.127) remained statistically non-significant. While the once-daily application demonstrated a greater numerical improvement in hair diameter, the result did not reach statistical significance, suggesting comparable efficacy between regimens at this time point.

At week 24, the mean increase in hair diameter was 2.52 μm (SD = 2.59) in the once-daily group and 2.00 μm (SD = 2.60) in the twice-daily group. The mean difference of 0.52 μm (95% CI: –0.83 to 1.87; p = 0.447) was again not statistically significant.

In conclusion, both once-daily and twice-daily applications of topical finasteride led to improvements in hair diameter over the 24-week period. However, no statistically significant differences were observed at any time point, indicating that increasing the frequency of application did not provide additional benefit in enhancing hair diameter.

Comparison of Mean Change from Baseline Between Two Groups Using Complete Case Analysis

Table 4.10 Mean change from baseline in hair density and hair diameter at each follow-up visit, based on the complete case analysis

Mean Change	Hair density (hairs/cm^2), mean ± SD						Hair diameter (μm), mean ± SD	
	Total hair		Terminal hair		Non-terminal hair			
	Once Daily (N = 25)	Twice Daily (N = 23)	Once Daily (N = 25)	Twice Daily (N = 23)	Once Daily (N = 25)	Twice Daily (N = 23)	Once Daily (N = 25)	Twice Daily (N = 23)
Week 8	9.28 ± 9.18	12.78 ± 12.17	6.00 ± 5.13	6.00 ± 6.37	3.36 ± 10.95	6.83 ± 14.34	0.24 ± 2.65	-0.13 ± 2.38
p-value	0.264		1.0		0.349		0.614	
Week 16	13.80 ± 11.06	21.00 ± 12.84	12.84 ± 8.98	14.09 ± 7.45	0.88 ± 12.29	6.74 ± 13.57	2.56 ± 2.43	1.83 ± 2.87
p-value	0.043		0.605		0.123		0.343	
Week 24	20.08 ± 10.35	34.30 ± 15.31	18.68 ± 10.75	22.00 ± 9.47	1.44 ± 14.61	12.43 ± 16.99	2.16 ± 2.32	2.13 ± 2.60
p-value	< 0.001		0.264		0.020		0.967	

Total Hair Density

Throughout the 24-week treatment period, both once- and twice-daily applications of topical finasteride led to progressive improvements in total hair density. At week 8, no statistically significant difference was observed between groups, although the twice-daily regimen demonstrated a numerically greater increase. By week 16, a statistically significant benefit emerged in favor of the twice-daily application ($p = 0.043$), which became more pronounced by week 24 ($p < 0.001$). These results indicate that while both dosing regimens are effective, twice-daily application confers a significantly greater improvement in total hair density over time. Importantly, the findings from this complete case analysis were consistent with those of the intention-to-treat analysis, reinforcing the robustness and reliability of the observed treatment effect.

Terminal Hair Density

Over the 24-week treatment period, both once-daily and twice-daily applications of topical finasteride led to progressive increases in terminal hair density. At week 8, both groups exhibited an identical mean increase of 6.00 hairs/cm², with no observed difference between them (95% CI: –3.35 to 3.35; p = 1.0), suggesting that dosing frequency had no early impact. By week 16, the once-daily group achieved a mean increase of 12.84 hairs/cm² (SD = 8.98), while the twice-daily group showed a slightly higher gain of 14.09 hairs/cm² (SD = 7.45); however, the between-group difference of 1.25 hairs/cm² (95% CI: –6.07 to 3.57; p = 0.605) remained statistically non-significant. At week 24, the mean increases were 18.68 hairs/cm² (SD = 10.75) and 22.00 hairs/cm² (SD = 9.47) in the once- and twice-daily groups, respectively, with a non-significant difference of 3.32 hairs/cm² (95% CI: –9.23 to 2.59; p = 0.264). Although the twice-daily regimen consistently yielded numerically higher improvements, none of the differences reached statistical significance at any time point. These results suggest comparable efficacy between the two dosing strategies in enhancing terminal hair density. Moreover, the findings were consistent with the intention-to-treat analysis, underscoring the robustness and reliability of the outcomes.

Non-Terminal Hair Density

Both treatment regimens led to modest increases in non-terminal hair density over time. At week 8, the once-daily group showed a mean increase of 3.36 hairs/cm² (SD = 10.95), while the twice-daily group achieved a slightly higher gain of 6.83 hairs/cm² (SD = 14.34); however, the between-group difference of 3.47 hairs/cm² (95% CI: –10.84 to 3.91; p = 0.349) was not statistically significant. At week 16, the mean increase was 0.88 hairs/cm² (SD = 12.29) for the once-daily group and 6.74 hairs/cm² (SD = 13.57) for the twice-daily group, yielding a non-significant difference of 5.86 hairs/cm² (95% CI: –13.37 to 1.65; p = 0.123), suggesting a trend toward greater efficacy with twice-daily application. By week 24, a statistically significant benefit was observed in the twice-daily group, which showed a mean increase of 12.43 hairs/cm² (SD = 16.99) compared to 1.44 hairs/cm² (SD = 14.61) in the once-daily group. The between-group difference of 10.99 hairs/cm² (95% CI: –20.18 to –1.81; p = 0.02)

favored the twice-daily regimen. These results indicate that while early differences were not significant, twice-daily application was significantly more effective in enhancing non-terminal hair density by the end of the study. This pattern was concordant with findings from the intention-to-treat analysis, underscoring the consistency and robustness of the treatment effect.

Hair Diameter

Both once- and twice-daily applications of topical finasteride produced modest improvements in hair diameter throughout the study period. At week 8, the once-daily group showed a slight mean increase of 0.24 μm (SD = 2.65), while the twice-daily group demonstrated a small decrease of –0.13 μm (SD = 2.38). The between-group difference of 0.37 μm (95% CI: –1.10 to 1.84; p = 0.614) was not statistically significant, indicating comparable early effects on hair thickness. By week 16, mean hair diameter increased by 2.56 μm (SD = 2.43) in the once-daily group and 1.83 μm (SD = 2.87) in the twice-daily group. The between-group difference of 0.73 μm (95% CI: –0.81 to 2.28; p = 0.343) remained non-significant. At week 24, both groups demonstrated similar improvements—2.16 μm (SD = 2.32) in the once-daily group and 2.13 μm (SD = 2.60) in the twice-daily group—with a negligible difference of 0.03 μm (95% CI: –1.40 to 1.46; p = 0.967). These results suggest that both dosing regimens were equally effective in increasing hair diameter, with no statistically significant differences observed at any time point. The findings were consistent with the intention-to-treat analysis, supporting the overall reliability of the treatment effect on hair diameter.

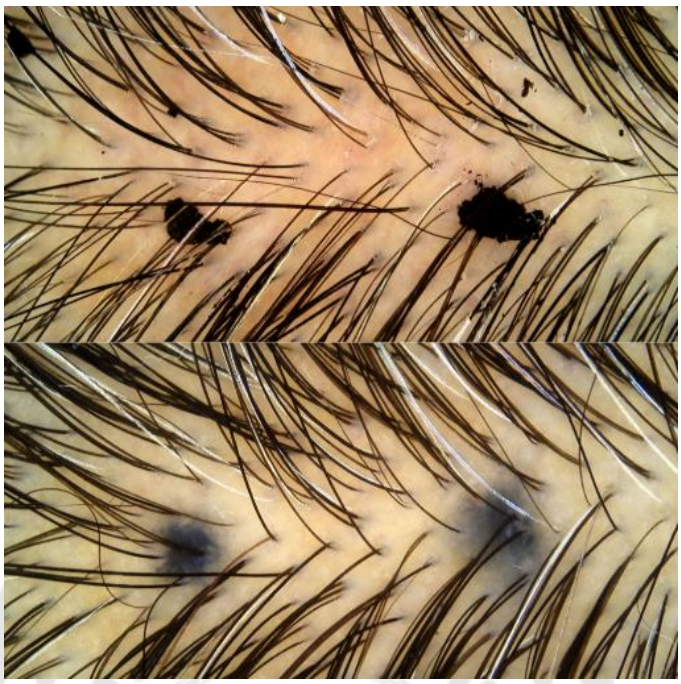

Figure 4.10 Hair density assessed by videodermoscopy at baseline and week 24 in the once-daily application group.

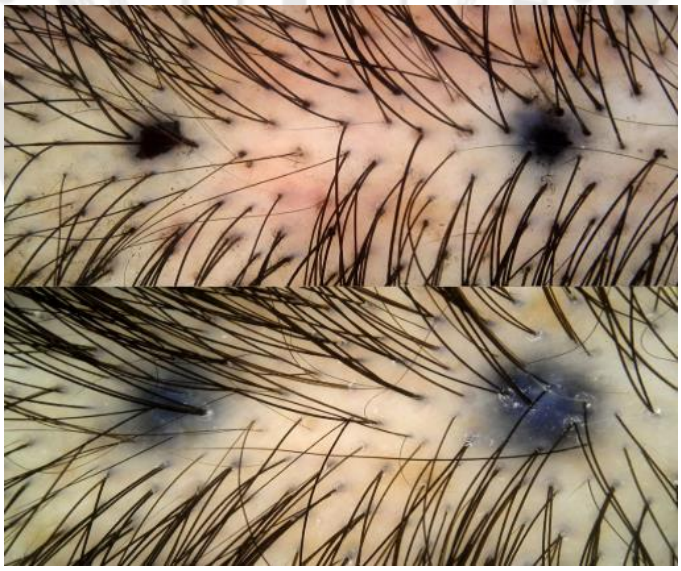

Figure 4.11 Hair density assessed by videodermoscopy at baseline and week 24 in the twice-daily application group.

Table 4.11 Change in global photographic assessment following treatment.

Global Photographic Assessment	Once Daily Group (N = 25)	Twice Daily Group (N = 23)
Global photographic assessment, n (%)		
Greatly decreased	0 (0)	0 (0)
Moderately decreased	0 (0)	0 (0)
Slightly decreased	0 (0)	0 (0)
Unchanged	6 (24.00)	3 (13.04)
Slightly increased	9 (36.00)	6 (26.09)
Moderately increased	7 (28.00)	12 (52.17)
Greatly increased	3 (12.00)	2 (8.70)

Inter-Rater Reliability of Global Photographic Assessment

The global photographic assessment (GPA) was independently evaluated by two dermatologists. To quantify the level of agreement between the two raters, both percent agreement and Cohen's Kappa coefficient were calculated.

The observed percent agreement between the two dermatologists was 81.25%, indicating that in more than four out of five cases, the raters provided identical assessments. However, since percent agreement may overestimate reliability due to agreement occurring by chance, Cohen's Kappa was also computed.

The calculated Kappa coefficient was 0.7241, indicating substantial agreement between the two evaluators, as classified by the Landis and Koch interpretation scale. The expected agreement by chance was 32.03%, suggesting that the observed concordance was unlikely to have occurred randomly. Given this substantial level of inter-rater reliability, the final global photographic assessment (GPA) utilized for analysis in this study was based on consensus ratings between the two dermatologists.

Correlation Between Global Photographic Assessment and Total Hair Density

The Global Photographic Assessment (GPA), based on consensus between two dermatologists with substantial inter-rater reliability (Cohen's Kappa = 0.72), showed a consistent pattern with objective measurements of hair regrowth. Participants in the twice daily application group who demonstrated higher GPA scores also exhibited a statistically significant increase in total hair density at week 24 compared to the once daily group. This concordance between visual clinical evaluation and quantitative videodermoscopic data supports the GPA as a reliable supplementary tool for assessing treatment efficacy in male androgenetic alopecia.

Participants with a global photographic assessment (GPA) score of 2 (moderately increased) or 3 (greatly increased) were classified as responders, indicating a clinically significant outcome. In the once-daily group, 10 out of 25 participants (40.0%) demonstrated a clinical response, compared to 14 out of 23 participants (60.87%) in the twice-daily group. Although the twice-daily regimen showed a higher response rate, the difference was not statistically significant ($p = 0.248$)

Despite the lack of statistical significance, the notably greater proportion of clinical responders in the twice-daily group may suggest a trend toward superior efficacy with more frequent application. This observation supports the potential clinical relevance of the twice-daily regimen, particularly for patients seeking more pronounced improvement in hair density.

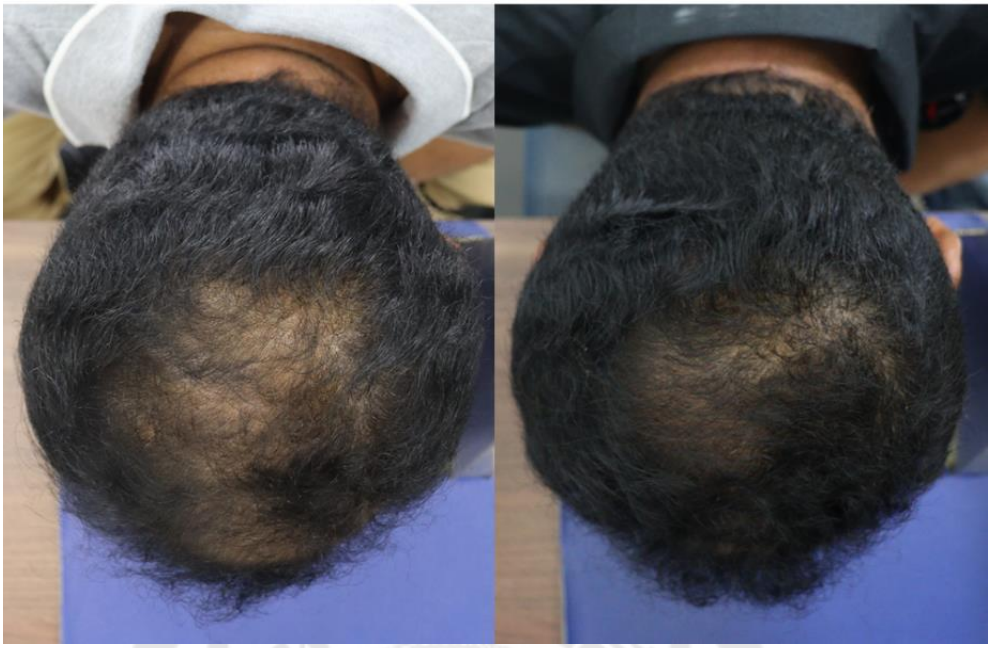

Figure 4.12 Global photographic assessment from a 90-degree angle in the once-daily application group at baseline and at week 24, demonstrating a greatly increased response.

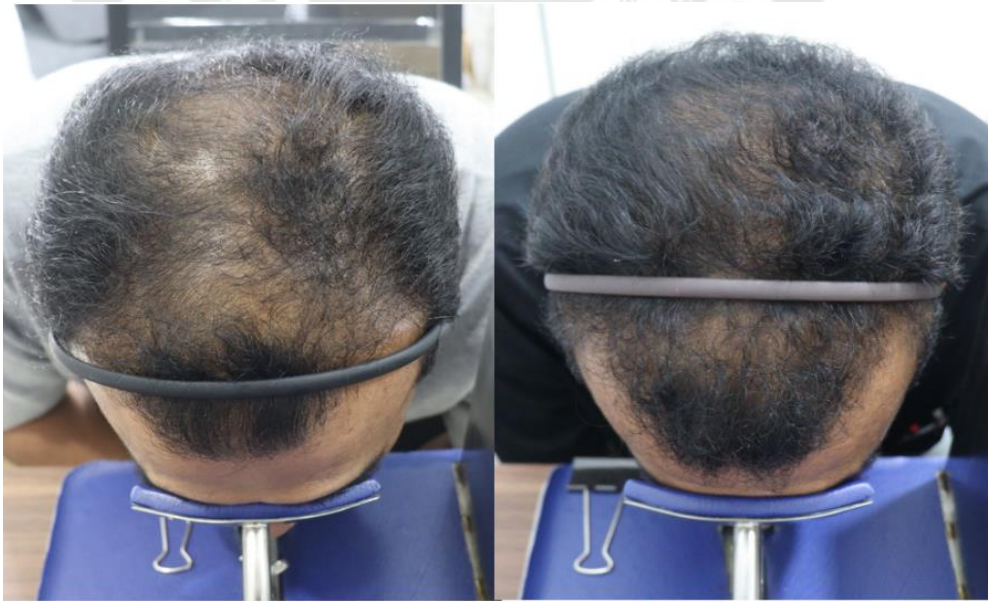

Figure 4.13 Global photographic assessment from a 45-degree angle in the once-daily application group at baseline and at week 24, demonstrating a greatly increased response.

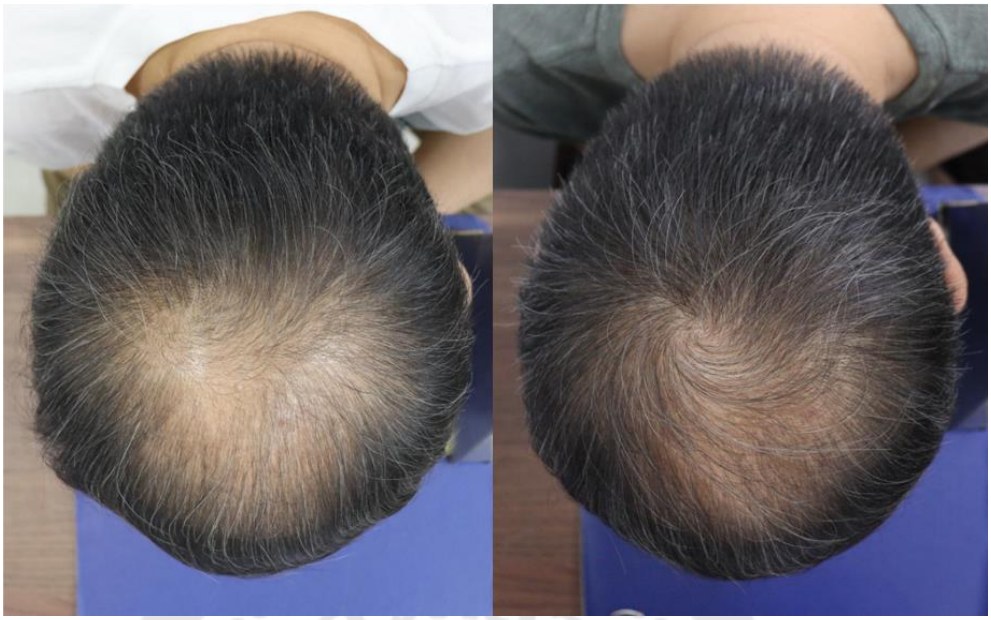

Figure 4.14 Global photographic assessment from a 90-degree angle in the once-daily application group at baseline and at week 24, demonstrating a moderately increased response.

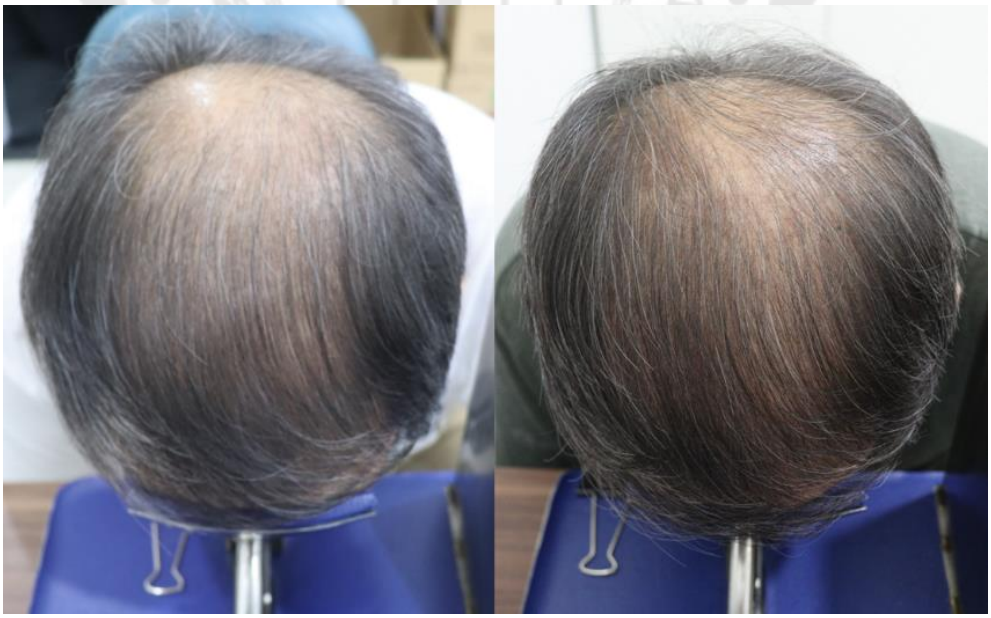

Figure 4.15 Global photographic assessment from a 45-degree angle in the once-daily application group at baseline and at week 24, demonstrating a moderately increased response.

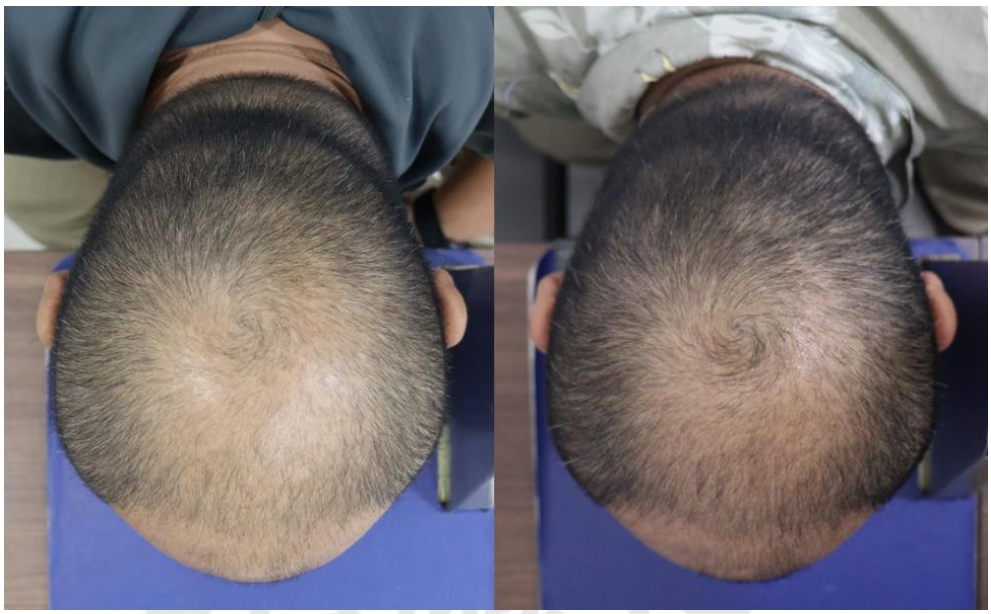

Figure 4.16 Global photographic assessment from a 90-degree angle in the once-daily application group at baseline and at week 24, demonstrating a mildly increased response.

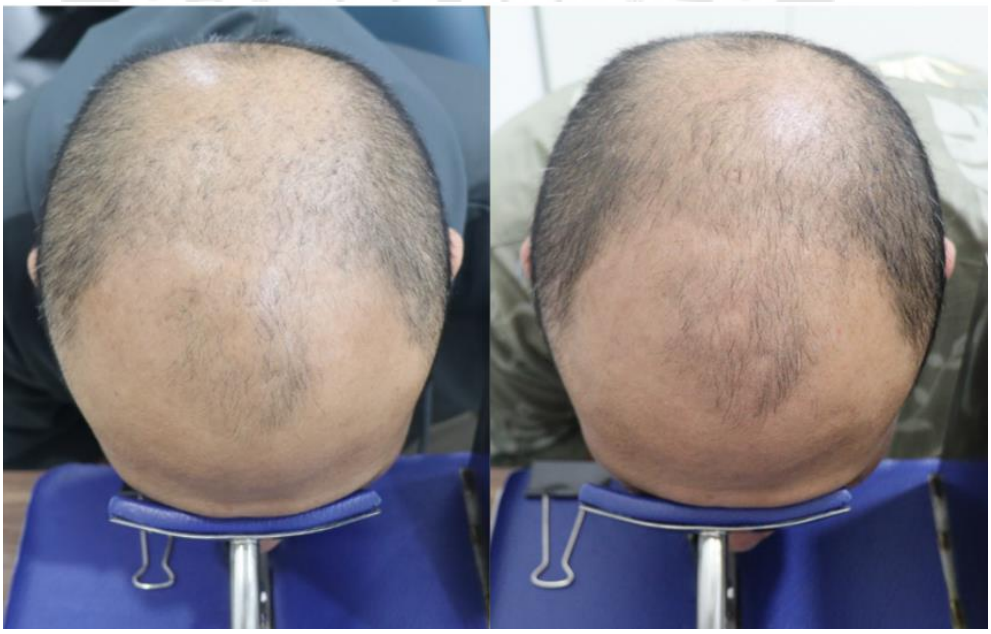

Figure 4.17 Global photographic assessment from a 45-degree angle in the once-daily application group at baseline and at week 24, demonstrating a mildly increased response.

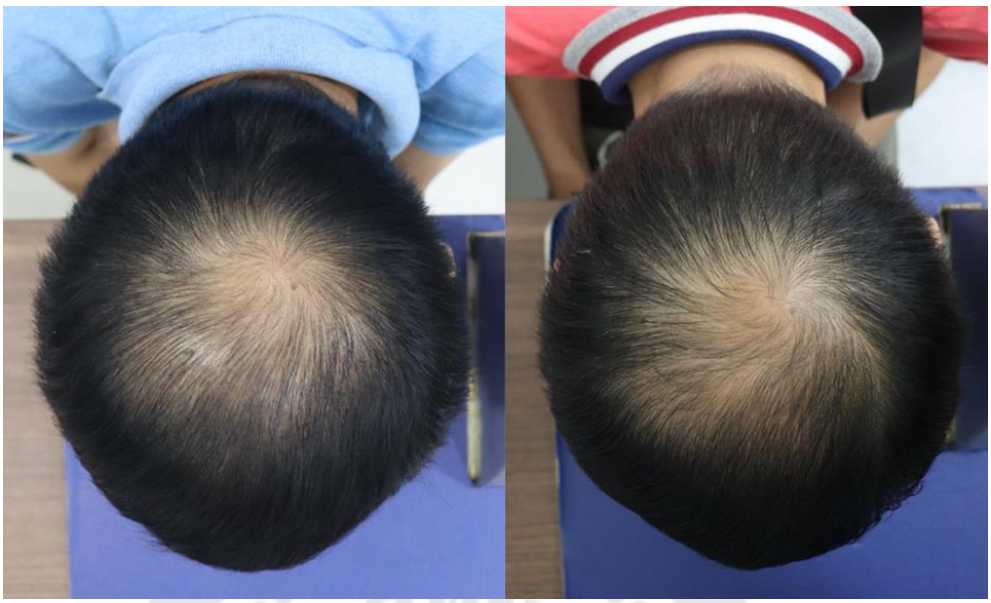

Figure 4.18 Global photographic assessment from a 90-degree angle in the once-daily application group at baseline and at week 24, demonstrating an unchanged response.

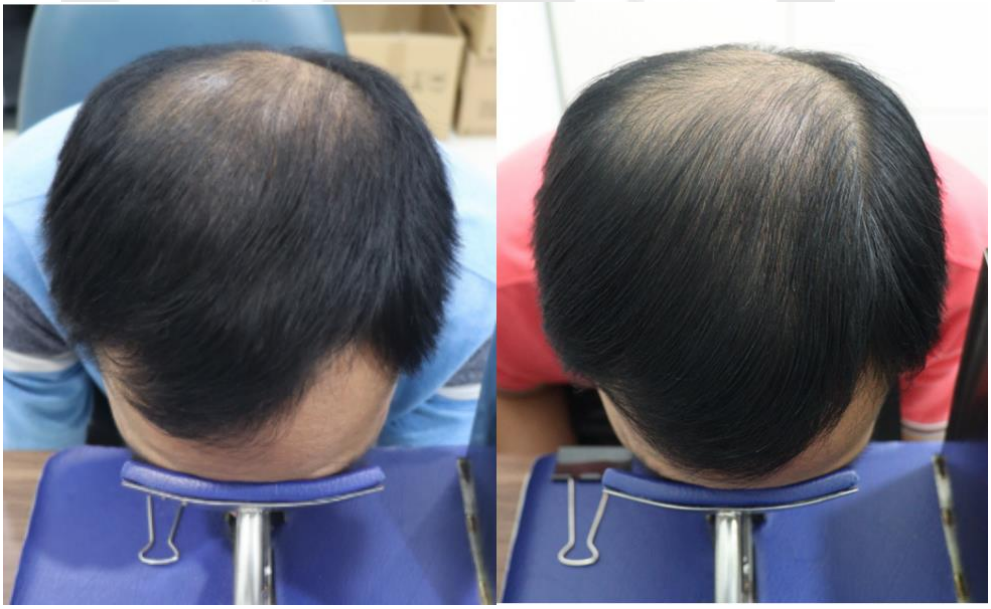

Figure 4.19 Global photographic assessment from a 45-degree angle in the once-daily application group at baseline and at week 24, demonstrating an unchanged response.

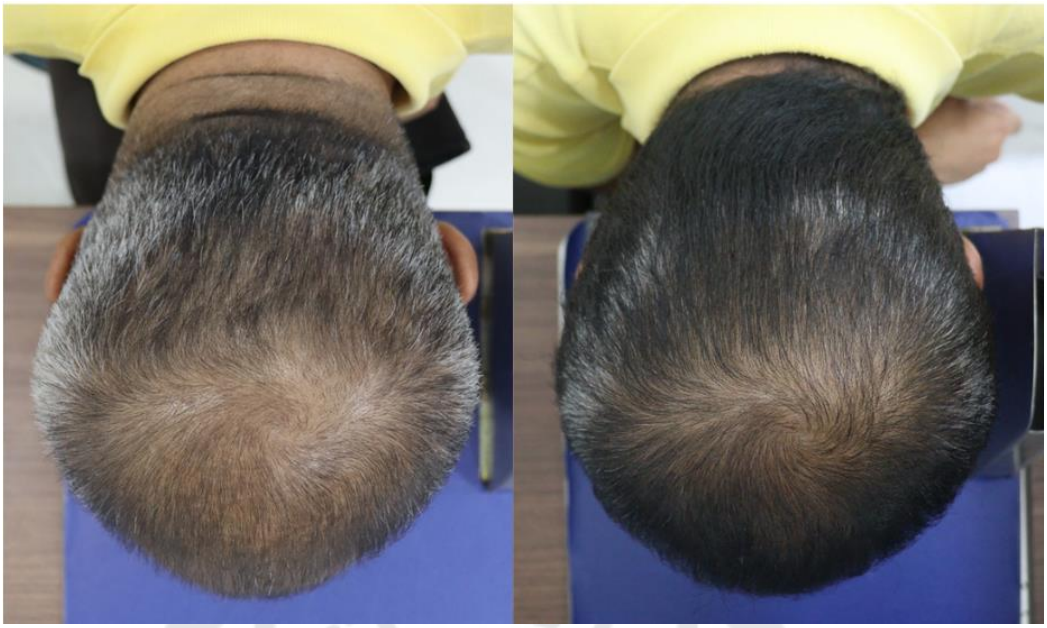

Figure 4.20 Global photographic assessment from a 90-degree angle in the twice-daily application group at baseline and at week 24, demonstrating a greatly increased response.

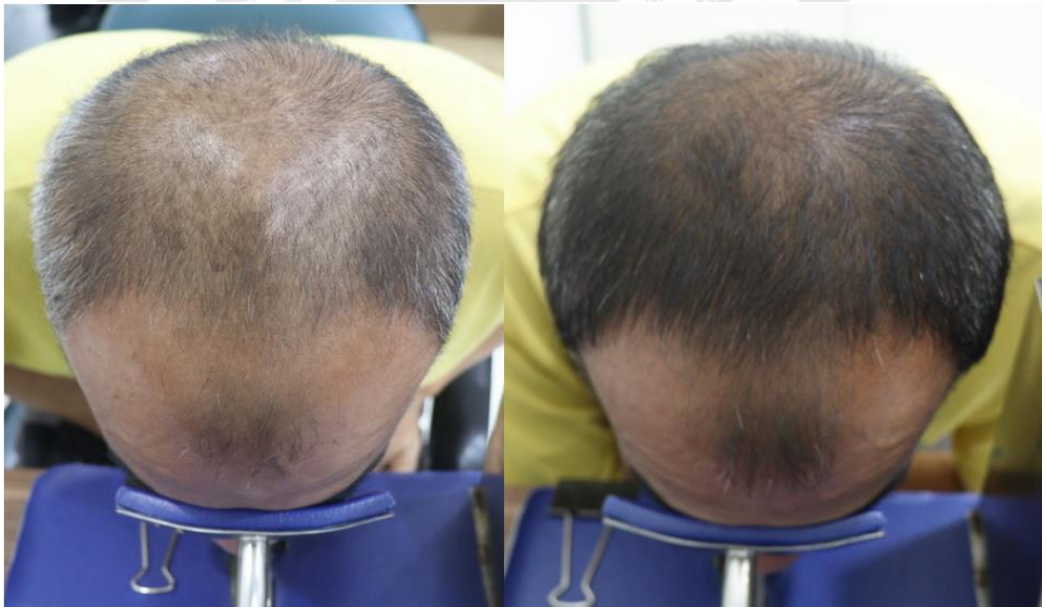

Figure 4.21 Global photographic assessment from a 45-degree angle in the twice-daily application group at baseline and at week 24, demonstrating a greatly increased response.

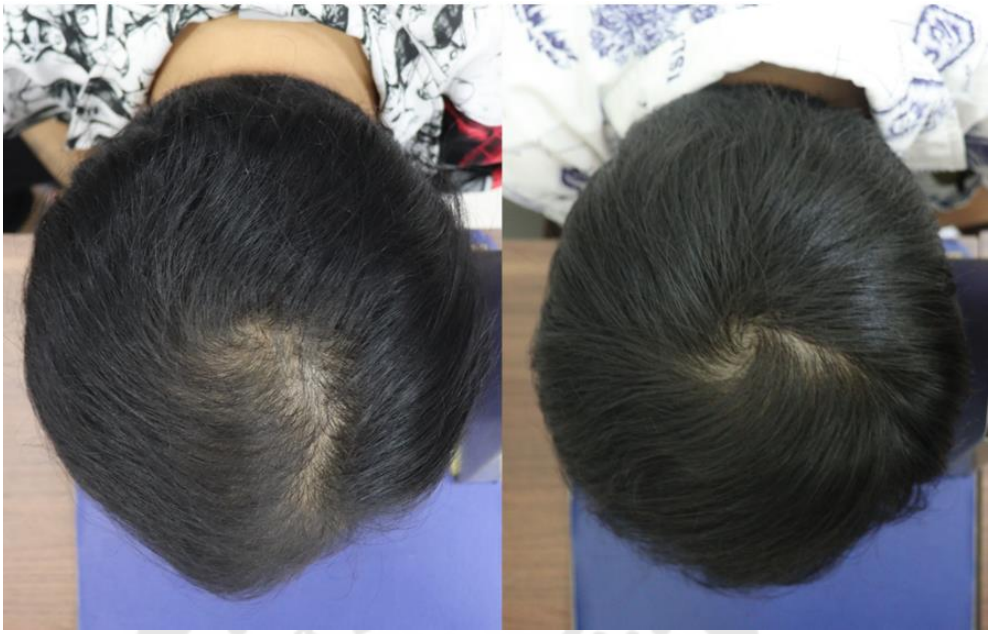

Figure 4.22 Global photographic assessment from a 90-degree angle in the twice-daily application group at baseline and at week 24, demonstrating a moderately increased response.

Figure 4.23 Global photographic assessment from a 45-degree angle in the twice-daily application group at baseline and at week 24, demonstrating a moderately increased response.

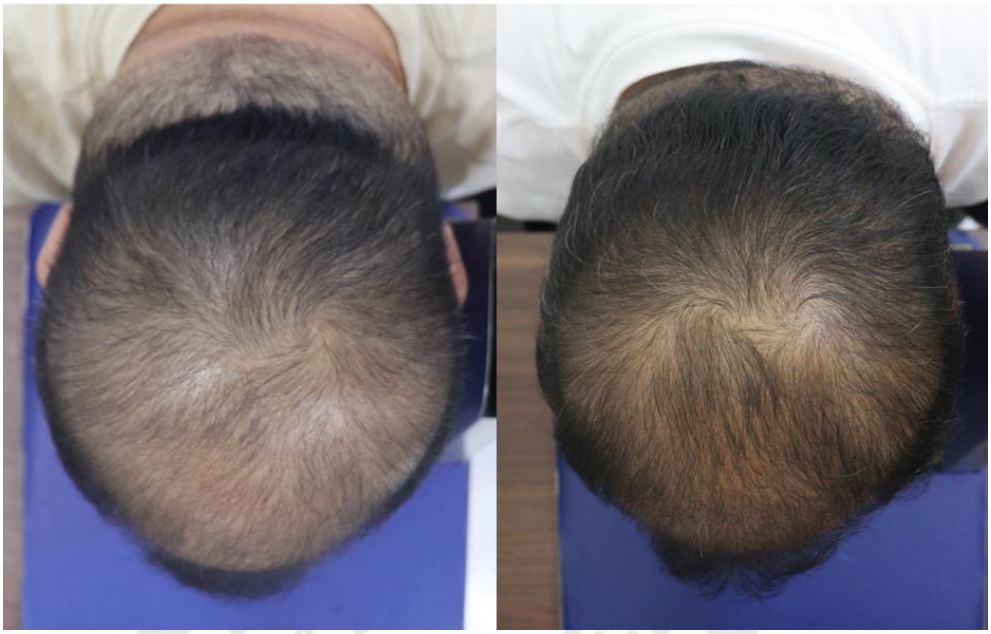

Figure 4.24 Global photographic assessment from a 90-degree angle in the twice-daily application group at baseline and at week 24, demonstrating a mildly increased response.

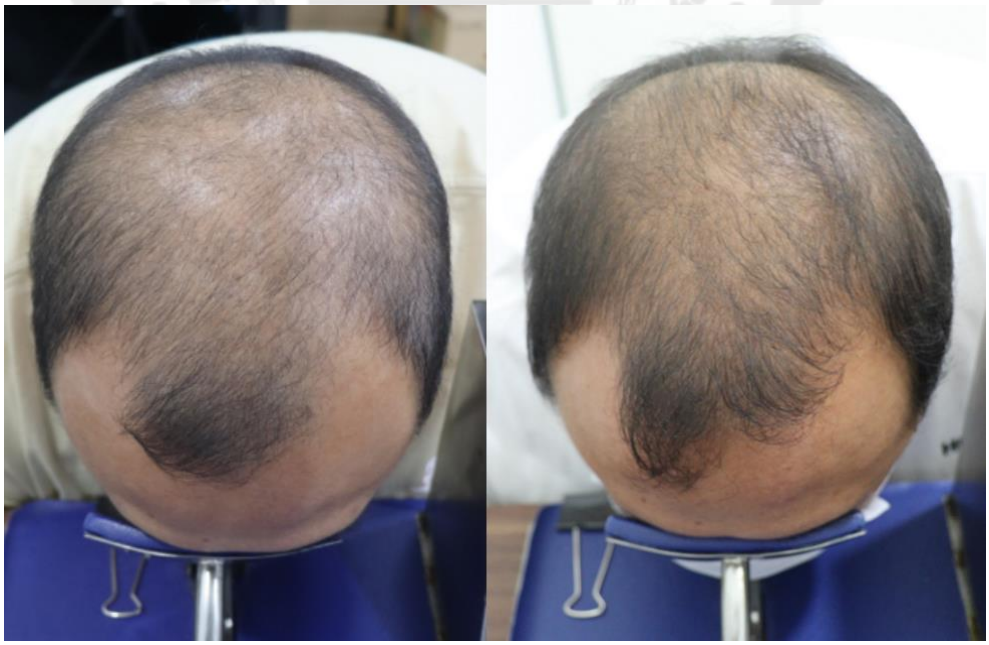

Figure 4.25 Global photographic assessment from a 45-degree angle in the twice-daily application group at baseline and at week 24, demonstrating a mildly increased response.

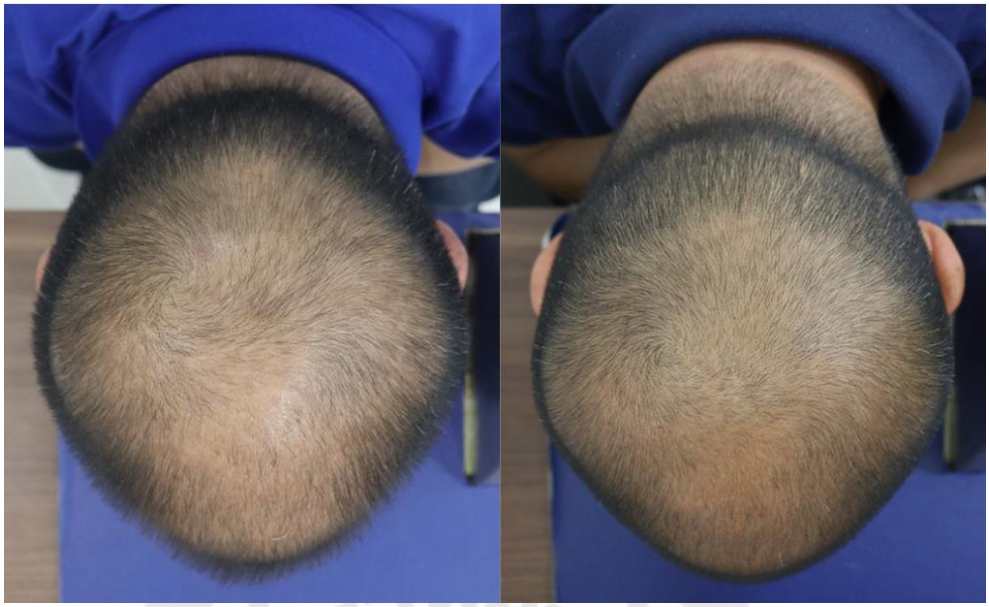

Figure 4.26 Global photographic assessment from a 90-degree angle in the twice-daily application group at baseline and at week 24, demonstrating an unchanged response.

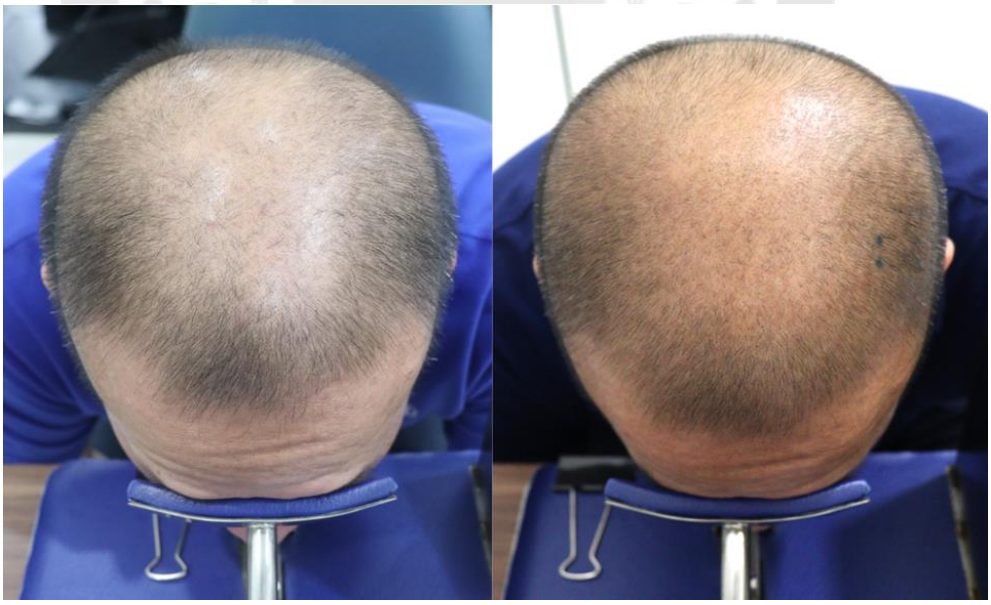

Figure 4.27 Global photographic assessment from a 45-degree angle in the twice-daily application group at baseline and at week 24, demonstrating an unchanged response.

Patient satisfaction

At the end of the 24-week treatment period, patient satisfaction was assessed and compared between the once daily and twice daily application groups. The mean satisfaction score in the once daily group was 8.84 ± 1.13, while the twice daily group reported a slightly higher mean score of 9.07 ± 0.89. The scores in both groups ranged from 7 to 10. A two-sample *t*-test was performed to evaluate the statistical significance of this difference, revealing no significant difference between the groups ($p = 0.44$). These findings indicate that both treatment regimens were highly satisfactory to patients, and the frequency of application did not significantly influence patient-reported satisfaction levels (Table 4.12).

Table 4.12 Patient satisfaction after treatment.

Patient Satisfaction	Once Daily Group (N = 25)	Twice Daily Group (N = 23)	*p*-value
Patient satisfaction, n (%)	8.84 ± 1.13	9.07 ± 0.89	0.44
Minimum – maximum	7 - 10	7 - 10	

Adverse Events

All participants were assessed for both local and systemic adverse events using a standardized evaluation form. To ensure privacy and encourage accurate reporting, assessments were conducted confidentially, particularly regarding sensitive issues such as sexual and psychiatric side effects.

Throughout the 24-week treatment period, adverse events were monitored and compared between the once-daily and twice-daily application groups. A total of four participants (8.33%) in each group reported experiencing at least one adverse event. In the once-daily group, two participants (8%) developed folliculitis. In the twice-daily group, three participants (13.04%) reported pruritus and two participants (8.70%) also reported folliculitis. Notably, no systemic adverse events were observed in either group,

including dizziness, depression, breast tenderness, testicular pain, or sexual dysfunction. All reported events were mild and confined to local skin reactions at the application site. Statistical analysis showed no significant difference in the incidence of adverse events between the two groups ($p > 0.99$). These results suggest that both dosing regimens were well tolerated, with only minor and localized side effects and no systemic safety concerns identified during the study (Table 4.13).

Table 4.13 Adverse events.

Adverse Events	Once Daily Group (N = 25)	Twice Daily Group (N = 23)	*p*-value
Adverse events, n (%)			
Pruritus	0 (0)	3 (13.04)	> 0.99
Erythema	0 (0)	0 (0)	
Folliculitis	2 (8.00)	2 (8.70)	
Dizziness	0 (0)	0 (0)	
Breast tenderness or enlargement	0 (0)	0 (0)	
Testicular pain	0 (0)	0 (0)	
Depression	0 (0)	0 (0)	
Sexual dysfunction	0 (0)	0 (0)	

CHAPTER 5
SUMMARY DISCUSSION AND SUGGESTION

Conclusion

This randomized, investigator-blinded trial demonstrated that twice-daily application of 0.5% topical finasteride resulted in significantly greater hair regrowth compared to once-daily use. By week 24, the twice-daily group exhibited a larger increase in total hair density (mean change $\Delta \approx 34$ hairs/cm²) than the once-daily group ($\Delta \approx 20$ hairs/cm²), with the difference reaching statistical significance ($p = 0.036$). Non-terminal hair density also showed a more pronounced increase with twice-daily dosing ($p = 0.044$ at week 24). In contrast, terminal hair density and hair diameter improved comparably in both groups, with no significant between-group differences observed at week 24 for terminal hair count ($p = 0.931$) or mean hair diameter ($p = 0.447$). Notably, both treatment regimens were associated with significant improvements from baseline across all hair parameters over the 24-week period (all within-group $p < 0.001$), confirming the efficacy of topical finasteride in promoting scalp hair growth. Global photographic assessment responses categorized as “moderately” or “greatly increased” were more frequent in the twice-daily group (60.87%) compared to the once-daily group (40%), aligning with the observed objective improvements.

Comparison with Previous Research

These findings corroborate and extend prior studies of topical finasteride. A recent systematic review noted that topical finasteride consistently increases both total and terminal hair counts in AGA and reduces the rate of hair loss, while also lowering scalp and plasma DHT levels without altering serum testosterone [44]. In particular, Piraccini *et al.*’s phase III RCT [13] found that 0.25% topical finasteride significantly improved target-area hair count versus placebo (mean 20.2 vs 6.7 hairs, $p<0.001$), with efficacy comparable to oral finasteride. Likewise, the therapeutic effect of 1% finasteride gel (twice daily) was shown to be equivalent to 1 mg daily oral finasteride in another trial.

These data agree with our observation that topical finasteride can drive meaningful hair regrowth in men.

However, our finding that twice-daily 0.5% outperformed once-daily differs from certain pharmacodynamic reports. Caserini et al. [15] reported that a 0.25% solution applied once daily achieved a greater reduction in scalp dihydrotestosterone (DHT) levels (approximately 70%) than twice-daily application (approximately 50%), suggesting a potential plateau effect or diminishing returns with increased dosing frequency at that concentration. Several factors may explain this discrepancy. First, our study employed a 24-week clinical trial, considerably longer than the short-term pharmacodynamic studies, which typically lasted seven days. Second, the studies differed in their primary endpoints: while pharmacodynamic studies primarily assessed hormonal suppression, our study evaluated clinical outcomes such as total hair density. Although pharmacokinetic data have suggested that more frequent application may interfere with optimal drug absorption or scalp bioavailability, particularly at lower concentrations, this limitation may not apply when using a higher-concentration formulation over a longer treatment period. Therefore, while once-daily application may be sufficient for short-term DHT suppression, twice-daily application of a 0.5% solution may offer superior clinical efficacy in promoting hair regrowth over extended durations.

Clinical Implications: Once versus Twice Daily Application

Clinically, our data suggest that increasing application frequency of topical finasteride can improve efficacy in AGA. Men using 0.5% solution twice daily achieved greater overall hair density gains without any added systemic risk, indicating that a twice-daily regimen may be preferable for maximizing results. This is especially relevant for patients seeking faster or more robust improvement. Importantly, adherence was similarly high in both groups (≈98%), and no compliance issues arose with the twice-daily schedule. In practice, physicians might therefore consider twice-daily application of 0.5% when treating recalcitrant cases or where optimal regrowth is desired.

Nevertheless, these conclusions must be balanced against convenience and patient preference. Many patients default to once-daily routines, and it remains unknown whether twice-daily use of lower concentrations (e.g. 0.25% applied twice a day) could achieve comparable efficacy. Our study did not compare concentrations, so it is unclear whether 0.5% once daily might match 0.25% twice daily in effect. Until more data emerge, clinicians should weigh patient lifestyle, cost of extra doses, and personal tolerability. As with oral finasteride, combination with other therapies (e.g. minoxidil) may also influence the choice of regimen. Overall, our findings point toward twice-daily 0.5% as a safe way to enhance outcomes when maximum hair increase is the goal.

Safety Profile

Both application regimens were well tolerated and associated only with mild local reactions. Over 24 weeks, the incidence of scalp irritation was low and did not differ between groups (overall ~8% in each). Reported adverse events were limited to mild pruritus, erythema or folliculitis at the application site. Crucially, no systemic side effects occurred: there were zero reports of dizziness, depression, sexual dysfunction, testicular pain or other endocrine complaints in either group. Statistical comparison confirmed no difference in overall adverse event rates ($p > 0.99$), suggesting that doubling the daily dose did not increase toxicity.

These clinical safety observations align with pharmacokinetic evidence that topical finasteride yields minimal systemic exposure. For example, Piraccini *et al.* [13] measured plasma finasteride levels over 100-fold lower with topical use than with oral dosing, and serum DHT fell only ~35% with topical versus ~56% with oral. By extension, the risk of systemic 5α-reductase inhibition (and related sexual AEs) is greatly reduced with topical application. Our finding of no psychiatric or sexual side effects mirrors the consensus that topical finasteride is safe for patients concerned about oral side effects. In summary, twice-daily 0.5% finasteride did not increase systemic risk compared to once-daily, while yielding greater hair growth, a reassuring combination for clinical use.

Limitations of the Study

Several limitations should be acknowledged. First, the calculated sample size was relatively small (n = 25 per group), and this single-centre design of the study may limit the generalizability of the findings to broder populations. Second, the trial design did not include a placebo control or patient blinding; instead, it compared two active regimens. Consequently, the net therapeutic effect of topical finasteride relative to natural progression or vehicle alone cannot be determined.

Third, although the 24-week duration was adequate to capture early changes in hair growth, it may be insufficient to evaluate long-term efficacy or the durability of results, as well as the potential for delayed adverse events. Extended follow-up would be necessary to confirm sustained benefits and monitor late-onset side effects.

Fourth, pharmacokinetic and hormonal parameters, such as plasma or scalp DHT levels, were not measured. As a result, we cannot directly correlate the observed differences in hair regrowth with the degree of systemic or local DHT suppression. Future studies incorporating biochemical assays are warranted to elucidate how dosing frequency influences 5α-reductase inhibition.

Fifth, only a 0.5% concentration was evaluated; therefore, it remains unclear whether lower concentrations administered with the same or different frequencies would yield comparable outcomes.

Lastly, while our primary endpoints included objective measures such as hair counts and shaft diameter, we did not assess quality-of-life outcomes. Although participant satisfaction was recorded, these subjective measures should be interpreted with caution.

Despite these limitations, this study offers valuable head-to-head data on dosing frequency and provides a foundation for future research in optimizing topical finasteride therapy.

Future Directions for Research

Our results open several avenues for further investigation. Larger, multicenter RCTs should confirm whether the superiority of twice-daily 0.5% finasteride holds in more diverse populations and over longer treatment periods. Studies incorporating placebo and oral finasteride control arms would provide clearer benchmarks. It would also be valuable to directly compare different concentrations: for example, is 0.25% twice daily as effective (or safer) as 0.5% once daily or vice versa?

Pharmacokinetic or pharmacodynamic studies are needed to map how dosing frequency and concentration translate into scalp and systemic DHT levels. Measuring drug levels in blood, scalp and possibly hair follicles could optimize the dose that maximizes local effect while minimizing systemic absorption. Additionally, combination trials (e.g. topical finasteride plus minoxidil, or other 5α-reductase inhibitors) may explore synergistic regimens. Research into patient adherence and preference between once- vs twice-daily regimens would clarify real-world feasibility. Finally, investigation in women with pattern hair loss could broaden therapeutic options. In summary, the ideal topical formulation, concentration, and application frequency will require further studies.

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Appendix

Case Record Form

Part 1

Patient demographic information

ID number ……..

Age ……. years, date of birth …….. /…….. /……..

Underlying disease ○ No ○ Yes

……

Current medication ○ No ○ Yes

……

Smoking ○ No ○ Yes

Part 2

History of male androgenetic alopecia (AGA)

Onset ……. years ……. months

Family history of male androgenetic alopecia (AGA) ○ No ○ Yes

☐ 1. Paternal ☐ 2. Maternal

Previous treatment ○ No ○ Yes

☐ 1. Topical medication

……

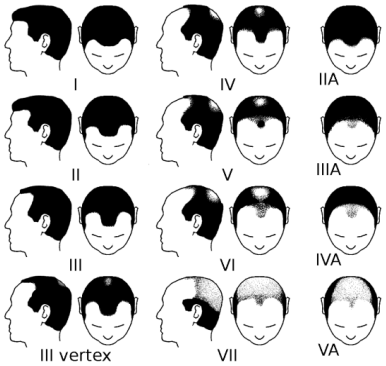
☐ 2. Oral medication

……

☐ 3. Others

……

Hamilton-Norwood classification



Part 3: Outcome Measurement

Hair Density and Hair Diameter Record Form

Visit	Week	Hair Density (hairs/circular 1 cm^2)	Average Hair Diameter (μm) (60 μm)	Compliance	Adverse Events
0	0	Total hair ..... hairs Terminal hair ..... hairs Non-terminal hair ..... hairs	Total hair ø ..... μm Terminal hair ø ..... μm Non-terminal hair ø ..... μm		
1	8	Total hair ..... hairs Terminal hair ..... hairs Non-terminal hair ..... hairs	Total hair ø ..... μm Terminal hair ø ..... μm Non-terminal hair ø ..... μm	○ finished ○ missed ..... applications (.....%)	○ pruritus ○ erythema ○ dizziness ○ breast enlargement, or tenderness ○ testicular swelling, or pain ○ sexual dysfunction ○ depression ○ .....
2	16	Total hair ..... hairs Terminal hair ..... hairs Non-terminal hair ..... hairs	Total hair ø ..... μm Terminal hair ø ..... μm Non-terminal hair ø ..... μm	○ finished ○ missed ..... applications (.....%)	○ pruritus ○ erythema ○ dizziness ○ breast enlargement, or tenderness ○ testicular swelling, or pain ○ sexual dysfunction ○ depression ○ .....
3	24	Total hair ..... hairs Terminal hair ..... hairs Non-terminal hair ..... hairs	Total hair ø ..... μm Terminal hair ø ..... μm Non-terminal hair ø ..... μm	○ finished ○ missed ..... applications (.....%)	○ pruritus ○ erythema ○ dizziness ○ breast enlargement, or tenderness ○ testicular swelling, or pain ○ sexual dysfunction ○ depression ○ .....

Global Photography Assessment (GPA) by Dermatologists

ID number.....

Visit ○ 1 ○ 2 ○ 3 Week ○ 8 ○ 16 ○ 24

Assess by Dermatologist ○ 1

○ 2

7-point rating scale

○ -3 greatly decreased

○ -2 moderately decreased

○ -1 slightly decreased

○ 0 unchanged

○ 1 slightly increased

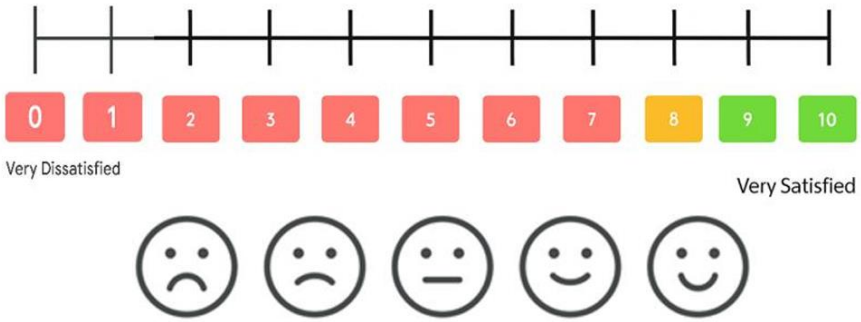
○ 2 moderately increased

○ 3 greatly increased

Patient Satisfaction

ID number.....

Visit 3 Week 24



Others.....

.....

.....

Case Record Form (แบบบันทึกข้อมูลผู้เข้าร่วมวิจัย)

ส่วนที่ 1 ข้อมูลส่วนตัว (Patient demographic information)

ลำดับผู้เข้าร่วมวิจัย (ID number)……

อายุ .....ปี, วัน เดือน ปีเกิด …….. /…….. /……..

โรคประจำตัว ○ 0 ไม่มี

○ 1 มี ระบุ

.....

ยาประจำตัว ○ 0 ไม่มี

○ 1 มี ระบุ

.....

ประวัติการสูบบุหรี่

○ 0 ไม่สูบ

○ 1 เคยสูบ สูบมา.....ปี เลิกแล้ว.....ปี

○ 2 ยังสูบ สูบมา.....ปี

ส่วนที่ 2 ข้อมูลที่เกี่ยวข้องกับภาวะผมบางจากพันธุกรรม [History of male androgenetic alopecia (AGA)]

ระยะเวลาที่ผมเริ่มบาง .....ปี.....เดือน

ประวัติบุคคลในครอบครัวมีภาวะผมบางจากพันธุกรรม

○ 0 ไม่มี

○ 1 มี ☐ บิดา ☐ มารดา ☐ บุคคลอื่น ระบุ.....

การรักษาในอดีต

○ 0 ไม่เคยรักษา

○ 1 เคยรักษา

☐ 2 ยาทา ระบุ

.....

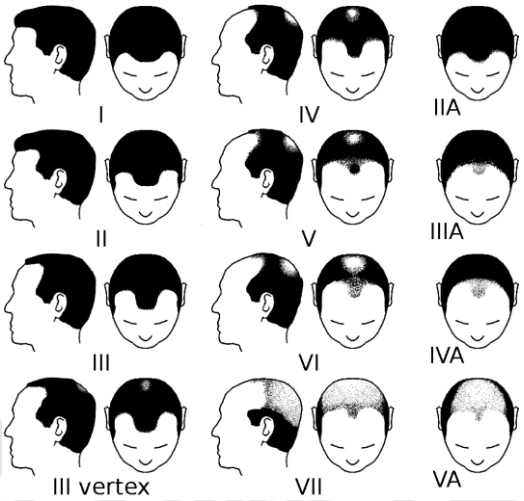
☐ 3 ยารับประทาน ระบุ

.....

☐ 4 อื่นๆ ระบุ

.....

ประเภทของความหนาแน่นของเส้นผมตาม Hamilton-Norwood classification



Part 3: Outcome Measurement

Hair Density and Hair Diameter Record Form

Visit	Week	Hair Density (hairs/circular 1 cm^2)	Average Hair Diameter (μm) (60 μm)	**ความสม่ำเสมอ**	**อาการไม่พึงประสงค์**
0	0	Total hair ..... hairs Terminal hair ..... hairs Non-terminal hair ..... hairs	Total hair ø ..... μm Terminal hair ø ..... μm Non-terminal hair ø ..... μm		
1	8	Total hair ..... hairs Terminal hair ..... hairs Non-terminal hair ..... hairs	Total hair ø ..... μm Terminal hair ø ..... μm Non-terminal hair ø ..... μm	❍ ยาหมด ❍ ลืมทา .....ครั้ง (.....%) ❍ ยาเหลือ..... มล.	❍ คัน ❍ แดง ❍ รูขุมขนอักเสบ ❍ เวียนศีรษะ ❍ เต้านมขยาย หรือเจ็บ ❍ อัณฑะบวมหรือเจ็บ ❍ ความต้องการทางเพศลดลง ❍ อวัยวะเพศไม่แข็งตัว ❍ ซึมเศร้า ❍ อื่นๆ .....

Visit	Week	Hair Density (hairs/circular 1 cm2)	Average Hair Diameter (μm) (60 μm)	**ความสม่ำเสมอ**	**อาการไม่พึงประสงค์**
2	16	Total hair ..... hairs Terminal hair ..... hairs Non-terminal hair ..... hairs	Total hair ø ..... μm Terminal hair ø ..... μm Non-terminal hair ø ..... μm	○ ยาหมด ○ ลืมทา .....ครั้ง (.....%) ○ ยาเหลือ..... มล.	○ คัน ○ แดง ○ รูขุมขนอักเสบ ○ เวียนศีรษะ ○ เต้านมขยาย หรือเจ็บ ○ อัณฑะบวมหรือเจ็บ ○ ความต้องการทางเพศลดลง ○ อวัยวะเพศไม่แข็งตัว ○ ซึมเศร้า ○ อื่นๆ .....
3	24	Total hair ..... hairs Terminal hair ..... hairs Non-terminal hair ..... hairs	Total hair ø ..... μm Terminal hair ø ..... μm Non-terminal hair ø ..... μm	○ ยาหมด ○ ลืมทา .....ครั้ง (.....%) ○ ยาเหลือ..... มล.	○ คัน ○ แดง ○ รูขุมขนอักเสบ ○ เวียนศีรษะ ○ เต้านมขยาย หรือเจ็บ ○ อัณฑะบวมหรือเจ็บ ○ ความต้องการทางเพศลดลง ○ อวัยวะเพศไม่แข็งตัว ○ ซึมเศร้า ○ อื่นๆ .....

Global Photography Assessment (GPA) by Dermatologists

ID number.....

Visit ○ 1 ○ 2 ○ 3 Week ○ 8 ○ 16 ○ 24

Assess by Dermatologist ○ 1

○ 2

7-point rating scale

○ -3 greatly decreased

○ -2 moderately decreased

○ -1 slightly decreased

○ 0 unchanged

○ 1 slightly increased

○ 2 moderately increased

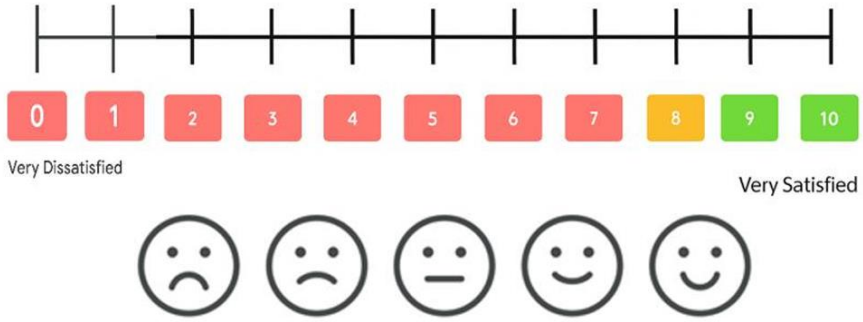
○ 3 greatly increased

ความพึงพอใจของผู้เข้าร่วมวิจัย (Patient Satisfaction)

รหัสผู้เข้าร่วมวิจัย (ID number).....

ติดตามผลครั้งที่ (visit) 3 **สัปดาห์ที่** (week) 24

กรุณาให้คะแนนความพึงพอใจโดยจุดลงในกราฟตามระดับความพึงพอใจที่ตรงกับท่าน



ไม่พึงพอใจมาก **พึงพอใจมาก**

ข้อเสนอแนะเพิ่มเติม.....

.....

ID number .....

แบบสอบถามประเมินด้านเพศ ติดตามสัปดาห์ที่.....

คำชี้แจง

- แบบสอบถามนี้มีวัตถุประสงค์เพื่อประเมินอาการทางด้านเพศที่อาจเกิดขึ้นหลังการใช้ยา
- **ข้อมูลจะถูกเกิดเป็นความลับ** โดยไม่เปิดเผยตัวตนของผู้ตอบแบบสอบถาม
- โปรดทำเครื่องหมาย √ ลงในช่อง ❑ ที่ตรงกับความเป็นจริงของท่านมากที่สุด

การประเมินปัญหาเรื่องสมรรถภาพทางเพศ

ลักษณะของสมรรถภาพ					
ระดับของปัญหา	**เป็นปัญหามาก**	**เป็นปัญหาพอสมควร**	**เป็นปัญหาเล็กน้อย**	**แทบจะไม่เป็นปัญหา**	**ไม่เป็นปัญหา**
ในช่วง 30 วันที่ผ่านมา ท่านคิดว่าความต้องการทางเพศที่ลดลงก่อให้เกิดปัญหากับท่านในระดับใด					
ในช่วง 30 วันที่ผ่านมา ท่านคิดว่าภาวะที่อวัยวะเพศไม่สามารถแข็งตัวได้อย่างเพียงพอก่อให้เกิดปัญหากับท่านในระดับใด					
ในช่วง 30 วันที่ผ่านมา ท่านคิดว่าอาการหลั่งน้ำอสุจิในปริมาณที่ลดลง ก่อให้เกิดปัญหากับท่านในระดับใด					

(Problem Assessment Scale of the Sexual Function Inventory (PAS SFI)

ID number .....

แบบสอบถามผลข้างเคียงทางด้านอารมณ์
ติดตามสัปดาห์ที่.....

คำชี้แจง

- แบบสอบถามนี้เป็นส่วนหนึ่งของงานวิจัย มีวัตถุประสงค์เพื่อประเมินผลข้างเคียงทางด้านอารมณ์ที่อาจเกิดขึ้นหลังจากรับประทานยา

- โปรดทำเครื่องหมาย ✔ ลงในช่อง ❑ ที่ตรงกับความเป็นจริงของท่านมากที่สุด

โปรดตอบแบบสอบถามข้อ 1 และ 2

1. ใน 2 สัปดาห์ที่ผ่านมารวมวันนี้ ท่านรู้สึกหดหู่ เศร้า หรือท้อแท้สิ้นหวัง หรือไม่?

❑ มี ❑ ไม่มี

2. ใน 2 สัปดาห์ที่ผ่านมารวมวันนี้ ท่านรู้สึกเบื่อ ทำอะไรก็ไม่เพลิดเพลิน หรือไม่?

❑ มี ❑ ไม่มี

หากท่านตอบ ไม่มี ทั้งสองข้อ ไม่ต้องทำแบบสอบถามข้อ 3 – 11

หากท่านตอบ มี ข้อใดข้อหนึ่งหรือทั้งสองข้อ โปรดตอบแบบสอบถามข้อ 3 – 11 ต่อหน้า 2

ID number .....

<u>โปรดตอบแบบสอบถามข้อ 3 – 11 ทุกข้อ</u>

คำถามสำหรับข้อ 3 – 11 คือ

ใน 2 สัปดาห์ที่ผ่านมารวมวันนี้ ท่านมีอาการเหล่านี้บ่อยแค่ไหน

1. เบื่อ ไม่สนใจอยากทำอะไร?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

2. ไม่สบายใจ ซึมเศร้า ท้อแท้?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

3. หลับยาก หรือหลับๆ ตื่นๆ หรือ หลับมากไป?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

4. เหนื่อยง่ายหรือไม่ค่อยมีแรง?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

5. เบื่ออาหารหรือกินมากเกินไป?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

6. รู้สึกไม่ดีกับตัวเอง คิดว่าตัวเองล้มเหลวหรือครอบครัวผิดหวัง?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

7. สมาธิไม่ดี เวลาทำอะไร เช่น ดูโทรทัศน์ ฟังวิทยุ หรือทำงานที่ต้องใช้ความตั้งใจ?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

8. พูดช้า ทำอะไรช้าลงจนคนอื่นสังเกตเห็นได้หรือกระสับกระส่ายไม่สามารถอยู่นิ่งได้เหมือนที่เคยเป็น?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

9. คิดทำร้ายตนเอง หรือคิดว่าถ้าตายไปคงจะดี?

❑ ไม่มีเลย ❑ เป็นบางวัน 1 – 7 วัน ❑ เป็นบ่อย > 7 วัน ❑ เป็นทุกวัน

VITA