

# Dutasteride improves male pattern hair loss in a randomized study in identical twins

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## Summary

**Objectives** This study compared the efficacy of dutasteride vs. placebo in the treatment of male pattern hair loss (androgenetic alopecia) in 17 pairs of identical twin males with androgenetic alopecia over a 1-year period.

**Methods** In this randomized, double-blind, placebo-controlled, single-center study, one twin from each identical twin pair received dutasteride 0.5 mg/day for 12 months while the other received placebo for 12 months. Hair growth was evaluated using standardized clinical photographs, hair counts, and patient self-assessment questionnaires.

**Result** Dutasteride significantly improved hair growth at 1-year compared to placebo based on the analysis of the investigator assessment and the patient self-assessment questionnaires. Sixteen of 17 sets of twins completed the study, of which 15 sets correctly predicted the use of dutasteride. Only one set could not determine the active drug from the placebo.

**Conclusion** Through the use of identical twins, this randomized trial provides evidence that dutasteride significantly reduces hair loss progression in men with male pattern hair loss.

**Keywords:** androgenetic alopecia, dutasteride, identical twins

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## Introduction

Male pattern hair loss (MPHL) affects 50% of men by the age of 50.<sup>1,2</sup> This condition is thought to be genetically controlled, occurring in males with an inherited propensity to the effects of dihydrotestosterone on scalp hair follicles.<sup>3,4</sup>

Studies in monozygotic twins are commonly conducted to examine the influence of genetic and environmental factors on phenotypic traits.<sup>5</sup> Similarly, monozygotic twins are ideally suited to determine the extent of drug efficacy in the treatment of a condition, such as MPHL, whose expression is determined by genetics.<sup>6</sup> Identical twins share the same genetic makeup, so that comparison between

the responses of each subject in a twin pair, such as when one receives active drug and the other placebo, allows for rigorous examination of the effects of drug treatment. This approach has been used for over 20 years.<sup>6-9</sup>

Dutasteride is a potent, selective, orally active inhibitor of the enzyme 5 $\alpha$ -reductase type 2 in humans, lowering serum and scalp dihydrotestosterone levels without having intrinsic androgenic, antiandrogenic, estrogenic, antiestrogenic, or progestational effects.<sup>10-15</sup> Dutasteride has been shown to significantly increase hair count and hair weight, improve the ratio of anagen to telogen hairs, improve scalp coverage based on assessment of standardized clinical (global) photography, and improve patients' satisfaction with the appearance of their hair.<sup>16-20</sup>

In this unique study, the efficacy of dutasteride was compared with placebo in genotypically identical twins with MPHL. The primary efficacy objective was to determine whether dutasteride reduced hair loss as determined by assessments of standardized clinical photographs in

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comparison to placebo. Secondary efficacy objectives were to determine the effects of dutasteride on hair count and patient self-assessment changes in scalp hair at study initialization. This study thus assessed the effects of dutasteride treatment by monitoring the changes in phenotype in genotypically identical twins.

## Patients and methods

### Patients

Seventeen pairs of Caucasian identical twin males between the ages of 18 and 50 participated in the study. These identical twins had a vertex grade of II, III, IV, or V MPHL, according to a modified Norwood/Hamilton classification scale.<sup>1,17</sup> As would be expected in a study of identical twins, demographics and baseline characteristics were similar between the two treatment groups. Both twins in each pair had the same Norwood/Hamilton classification and were in good physical and mental condition. Major exclusion criteria included a history of any significant illness or condition that might confound the results of the study or pose an additional risk in administering dutasteride to the patient; surgical correction of scalp hair loss; and the use of minoxidil or any 5 $\alpha$ -reductase inhibitor within 12 months of study initiation.

Institutional review board approval of the protocol was obtained prior to study initiation and all patients provided written informed consent prior to entry in the study.

### Study design

This was a randomized, placebo-controlled, double-blind study conducted in a single center in the United States. After screening, each patient in each pair of twins was randomized to receive either dutasteride or placebo for 1 year.

Patients were instructed not to alter their hairstyle or dye their hair during the study period. The primary efficacy assessment was by comparison of pre- and posttreatment standardized clinical (global) photographs of the vertex scalp,<sup>17,20</sup> using the Canfield photography system<sup>20</sup> at baseline, month 6, and month 12. This technique has been previously validated to generate reproducible results.<sup>21</sup> An experienced dermatologist assessed changes from baseline using a 7-point rating scale, ranging from "greatly decreased hair growth" to "greatly increased hair growth," centered at no change.<sup>17</sup>

Macrophotography for hair counts was done at baseline, month 6, and month 12 with the Canfield photography system.<sup>20</sup> A small dot tattoo was placed on the scalp at

baseline to identify the center of a 1 cm<sup>2</sup> circular target area on the anterior leading edge of the vertex hair loss region to be used for hair counts.<sup>22</sup> Hair counts were obtained from macrophotographs at Canfield Scientific Inc. (Fairfield, NJ), using a technique that has been previously described.<sup>17,20</sup>

Patients assessed the changes in their scalp hair using a validated, self-administered hair growth questionnaire<sup>17,23</sup> consisting of four questions on treatment efficacy and three questions on satisfaction with appearance of scalp hair. These questionnaires were completed at months 6 and 12.

Any reports of adverse events were collected at each clinic visit during the 1-year treatment period. The intensity and the relationship to treatment of any reported adverse events were evaluated.

## Results

### Hair count – month 6

At month 6, the summary of the hair count data indicated that there was an average of 11 fewer hairs in the placebo-treated group vs. 6.8 more hairs in the dutasteride-treated subjects (Table 1). In 12 sets of twins, the mean hair count reached statistical significance indicating 19.8 more hairs in the dutasteride-treated subjects than in the placebo-treated subjects. Compliance was 94% with placebo and 99% with dutasteride. Because of technical problems related to the hair count evaluation, hair count data were uninterpretable in five sets of twins.

### Month 12

At month 12, there were 3.8 fewer hairs in the placebo-treated vs. 16.5 more hairs in the dutasteride-treated subjects. In 11 sets of twins, the mean hair count indicated 22.2 more hairs in the dutasteride-treated subjects than in the placebo-treated subjects. However, this did not achieve statistical significance ( $P = 0.14$ ) because of the large variability and the technical problems encountered with five sets of twins at months 6 and 12.

**Table 1** Mean change from baseline in hair counts\*.

Mean change	Placebo	Dutasteride
Month 6	-11.0 ( $n = 14$ )	6.8 ( $n = 13$ )
Month 12	-3.8 ( $n = 14$ )	16.5 ( $n = 11$ )

\*Five pairs of twins were not included in this analysis because of technical problems.

**Table 2** Hair growth scoring.

Rank	Definition
1	Greatly worse
2	Moderately worse
3	Slightly worse
4	No change
5	Slightly improved
6	Moderately improved
7	Greatly improved

**Table 3** Mean change from baseline to month 12 in hair growth scores.

Mean change	Placebo	Dutasteride
Month 12	4.07 ( <i>n</i> = 14)	5.00 ( <i>n</i> = 11)

**Figure 1** Twin subjects treated with dutasteride and placebo.

#### Investigators' assessment of hair growth

Hair growth scores were derived from expert evaluation comparing 35-mm photographs from baseline to months 6 and 12. The score range was 1–7 with the ranking as illustrated (Table 2).

The mean difference between the treatment groups in expert assessment of hair growth of 0.90 units achieved statistical significance at month 12 ( $P = 0.016$ ). The mean score in the dutasteride group at month 12 was 5.0 (slightly improved) as indicated (Table 3).

In the two sets of twins pictured in Figures 1 and 2, the dutasteride-treated subjects demonstrate more hair growth than the placebo-treated subject.

#### Subjects' assessment of hair growth

The hair growth index, evaluated by the study subjects, rated perceptions of hair growth improvement via comparison

**Figure 2** Twin subjects treated with placebo and dutasteride.

of photographs from baseline to months 6 and 12. The score range was 1–7 as it related to questions about the subjects' perception of hair growth. The patient questionnaire included an assessment beginning at baseline of their hair thinning, coverage, and appearance. Sixteen of 17 twin sets correctly identified their treatment by month 6.

#### Adverse events

No serious clinical or laboratory adverse experiences occurred during the study and possibly two treatment-related clinical adverse experiences were reported. These were characterized as decreased libido of mild to moderate severity.

#### Discussion

Multiple studies have confirmed the benefit of 5 $\alpha$ -reductase inhibitors in men with male pattern baldness.<sup>17,24</sup> Kaufman *et al.* demonstrated that long-term treatment with finasteride, 1 mg per day over a 5-year period, was well tolerated and led to sustained improvement in scalp hair growth and decreased the progression of hair loss without treatment.

The 5 $\alpha$ -reductase inhibitor finasteride was studied in MPHL in a randomized study involving identical twins.<sup>25</sup> In this study, finasteride significantly improved hair growth at 1 year compared to placebo ( $P < 0.05$ ) based on an analysis of photographs of the vertex and frontal scalp.<sup>25</sup> The hair count change also demonstrated a positive effect compared to placebo ( $P < 0.05$ ).<sup>25</sup> In the above-referenced study with finasteride, photographic endpoints demonstrated that none of the finasteride patients showed deterioration in their hair growth at 12 months. In contrast, the majority of placebo patients demonstrated visible worsening in scalp hair coverage based on global photographic assessment of the vertex scalp at month 4.

The normal course of androgenetic alopecia is progressive over time.<sup>24</sup> In this unique study of male identical twins with androgenetic alopecia (MPHL), treatment with dutasteride slowed the progression of hair loss and enhanced hair growth compared to treatment with placebo. This study supports previously published trials<sup>26</sup> showing that dutasteride significantly improves scalp hair growth based on assessments of standardized clinical photographs, hair count, and patients' assessments of their scalp hair. Based on the two predefined photographic endpoints, none of the dutasteride patients showed deterioration in hair growth at 12 months. In contrast, the majority of placebo patients demonstrated visible worsening in scalp hair coverage based on global photographic assessment of the vertex scalp at month 12.

The validated patient self-assessment hair growth questionnaire demonstrated that treatment with dutasteride, in comparison to placebo, led to improvement in patients' scalp hair growth and increased satisfaction with the appearance of hair.

Because MPHL is under genetic control and identical twins share the same genetic code, the comparison of paired data between twins is a highly efficient way of evaluating the efficacy of a treatment in a limited number of patients, as each twin serves as a control. Thus, despite the necessarily limited sample size of this study, efficacy in favor of dutasteride was demonstrated for the predefined endpoints. The separation between treatment groups was achieved. It should be noted that the phenotypic expression of MPHL, while similar in each twin pair, was not necessarily identical. This was evident by careful examination of baseline global photographs for each pair of twins.

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