Clinical dose ranging studies with finasteride, a type 2 5α-reductase inhibitor, in men with male pattern hair loss

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Background: Androgenetic alopecia is a common condition of adult men. Finasteride, a type 2 5α-reductase inhibitor, decreases the formation of dihydrotestosterone from testosterone.

Objective: Two separate clinical studies were conducted to establish the optimal dose of finasteride in men with this condition.

Methods: Men from 18 to 36 years of age with moderate vertex male pattern hair loss received finasteride 5, 1, 0.2, or 0.01 mg/day or placebo based on random assignment. Efficacy was determined by scalp hair counts, patient self-assessment, investigator assessment, and assessment of clinical photographs. Safety was assessed by clinical and laboratory measurements and by analysis of adverse experiences.

Results: Efficacy was demonstrated for all end points for finasteride at doses of 0.2 mg/day or higher, with 1 and 5 mg demonstrating similar efficacy that was superior to lower doses. Efficacy of the 0.01 mg dose was similar to placebo. No significant safety issues were identified in the trials.

Conclusion: Finasteride 1 mg/day is the optimal dose for the treatment of men with male pattern hair loss and was subsequently identified for further clinical development. (J Am Acad Dermatol 1999;41:555-63.)

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Androgenetic alopecia (male pattern hair loss) in men is the result of the effects of androgens in genetically susceptible individuals.[1] Dihydrotestosterone (DHT), which is formed from testosterone (T) by the action of the enzyme steroid 5α–reductase (5αR), is the specific androgen implicated in the pathophysiology of this disorder, as well as implicated in the pathogenesis of other androgen-mediated diseases. This is based on the observation that men with genetic deficiency of the 5αR enzyme have reduced levels of circulating DHT and do not experience male pattern hair loss or prostate disease, despite normal or elevated circulating levels of T.[2] Further studies with the 5αR enzyme have revealed two isoenzymes, designated types 1 and 2, in man and most other species studied.[3-5] In man, type 1 5αR is found predominantly in sebaceous glands of the skin, including the scalp,[6,7] whereas type 2 5αR, the isoenzyme affected in patients with genetic 5αR deficiency, is found in scalp hair follicles[8] and the prostate.[7]

Finasteride is an orally active, selective inhibitor of the human type 2 isoenzyme with no affinity for the human androgen receptor. In vitro, finasteride has no androgenic, antiandrogenic, estrogenic, antiestrogenic, or progestational effects.[9,10] In vivo, inhibition of the type 2 enzyme blocks peripheral conversion of T to DHT, resulting in significant reductions in serum,[11] prostate,[12] and scalp[13,14] DHT levels. Since 1992, finasteride has been used at a dose of 5 mg/day (Proscar) for the treatment of patients with symptomatic benign prostatic hyperplasia (BPH), and the clinical experience with the drug has established an excellent safety profile in men.[11,15] In 1997, finasteride at a lower dose of 1 mg/day (Propecia) was approved in the United States for the treatment of men with male pattern hair loss.

This article describes the clinical studies providing the rationale for the selection of the 1 mg dose for the treatment of men with male pattern hair loss.

PATIENTS AND METHODS

Patient population (Table I)

Healthy men between the ages of 18 and 36 years with moderate male pattern hair loss in the vertex area (grades III vertex and IV, according to the Norwood-Hamilton classification scale),[16] were enrolled into two separate studies. Principal exclusions to study entry included previous surgical correction of scalp hair loss, use of topical minoxidil within 1 year of study entry, any use of finasteride or other 5αR inhibitors, or hair loss from causes other than androgenetic alopecia. Participants were instructed not to alter their hair style, dye their hair, or use any hair enhancement products or procedures during the studies.

Study protocols (Fig 1)

The first clinical study (pilot study), conducted in 13 centers in the United States, randomized 227 men into a 12-month, double-blind, placebo-controlled study to evaluate the effects of finasteride 5 mg/day on male pattern hair loss. The second clinical trial (dose range study), conducted in 23 centers in the United States, randomized 466 men into a 6-month, double-blind, placebo controlled study to evaluate the effects of low doses (1, 0.2, and 0.01 mg/day) of finasteride. Men completing the 6-month dose range study were eligible to continue into a double-blind extension study without placebo for an additional 6 months. In the 6-month dose range extension study, patients continued on the same therapy they received during the first 6 months or, if initially randomized to placebo, were rerandomized to one of the 3 doses of finasteride.

Institutional review board approval and patient written informed consent were obtained before enrollment of patients into each study. Prospective patients were screened for eligibility, which included a physical examination and laboratory safety tests. In both studies, patients

Table I. Baseline characteristics of men randomized in pilot and dose range studies

	Pilot study		Dose range study			
	5 mg (n = 111)	Placebo (n = 116)	1 mg (n = 117)	0.2 mg (n = 115)	0.01 mg (n = 117)	Placebo (n = 117)
Age (y; mean ± SE)	30 ± 0.4	30 ± 0.3	30 ± 0.4	30 ± 0.4	30 ± 0.4	30 ± 0.4
Age at which hair loss began (y; mean ± SE)	23 ± 0.4	23 ± 0.4	24 ± 0.4	23 ± 0.3	23 ± 0.4	23 ± 0.4
No. (%) of patients with family history*	87 (78)	95 (82)	94 (81)	91 (81)	88 (78)	88 (78)
Baseline hair count (mean ± SE)†	862 ± 23	953 ± 23	945 ± 26	905 ± 21	902 ± 25	906 ± 19
No. (%) of patients with hair loss pattern‡						
III vertex	71 (64)	87 (75)	67 (57)	62 (54)	60 (51)	65 (56)
IV	40 (36)	29 (25)	50 (43)	53 (46)	57 (49)	52 (44)

*Family history = Parents or siblings with androgenetic alopecia.
†Measured in a 1-inch diameter circular area (5.1 cm^2) at anterior leading edge of vertex balding scalp.
‡According to the Norwood-Hamilton scale.

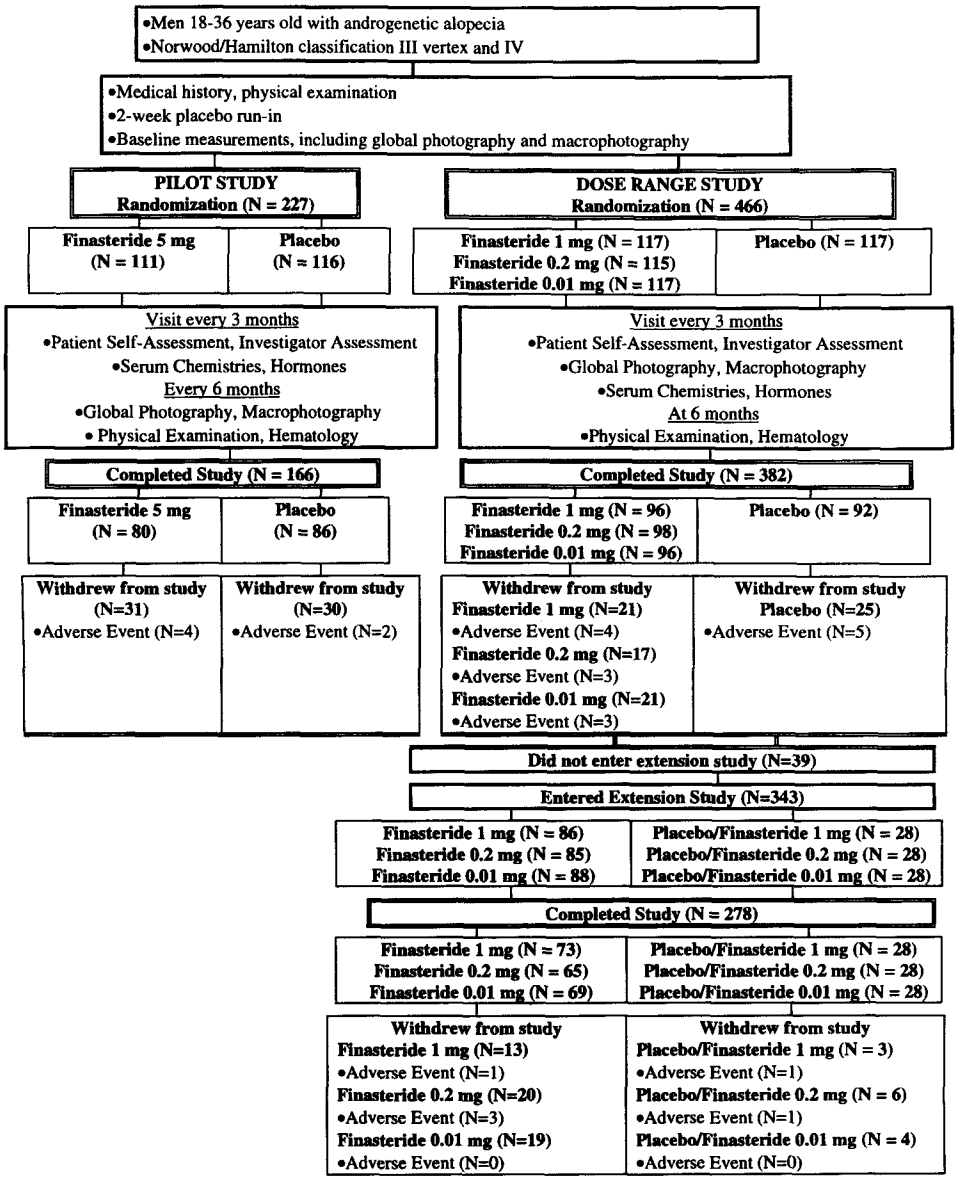

Fig 1. Trial profile. Shows main inclusion criteria and evaluation procedures, number of patients who were randomized, who completed studies, and who discontinued prematurely for each of the two studies (pilot and dose range) by treatment group.

completed a 2-week, single-blind, placebo run-in period before randomization to therapy. Patients were randomized equally to finasteride 5 mg or placebo in the pilot study, and to finasteride 1 mg, 0.2 mg, 0.01 mg, or placebo in the dose range study. Patients were instructed to use the supplied study shampoo (Neutrogena T/Gel, Neutrogena Corp, Los Angeles, Calif) to prevent scalp seborrheic dermatitis, which might affect scalp hair growth.[17]

Clinic visits were scheduled every 3 months. At each visit, patients completed a hair growth questionnaire and the investigator assessed the change in the patient's scalp hair growth from baseline. Macrophotographs for scalp hair count and global photographs for clinical assessment by an expert panel were taken at month 3 (dose range study only) and at months 6 and 12. Patient adverse events were recorded at every visit.

Efficacy evaluation

Hair count. At the beginning of each study, a small dot tattoo was applied at the anterior leading edge of the patient's vertex balding area of the scalp. Hair within a 1-inch (2.54-cm) diameter circle (area = 5.1 cm^2), centered at the tattoo, was clipped short (approximately 1-mm length), using a circular scalp template. This circular area, which defined a representative area of active hair loss, was then photographed by means of a specialized camera fitted with a macrolens.[18] Film emulsion (Kodak T-Max 100), lighting, framing, exposure, and reproduction ratio were

Table II. Hair growth questionnaire

Question	Response options
Since beginning the study, I can see my bald spot getting smaller.	Strongly agree (1) → Strongly disagree (5)
Because of the treatment I have received since the start of the study, the appearance of my hair is:	A lot better (1) → A lot worse (7)
Since the start of the study, how would you describe the growth of your hair?	Greatly increased (1) → Greatly decreased (7)
Since the start of the study, how effective do you think this treatment has been in slowing down your hair loss?	Very effective (1) → Not effective at all (4)
Compared to the beginning of the study, which statement best describes your satisfaction with the appearance of the hairline at the front of your head?	Very satisfied (1) → Very dissatisfied (5)
Compared to the beginning of the study, which statement best describes your satisfaction with the appearance of the hair on top of your head?	Very satisfied (1) → Very dissatisfied (5)
Compared to the beginning of the study, which statement best describes your satisfaction with the appearance of your hair overall?	Very satisfied (1) → Very dissatisfied (5)

held constant. Macrophotographs were evaluated at a central photography quality assurance center (Canfield Scientific, Inc, Fairfield, NJ), enlarged into 8 × 10 inch black and white prints and, by means of a random number system, blinded to time, study center, patient, and treatment before dot mapping for determination of hair count. Dot mapping was conducted at a single site (University of Texas San Antonio, Department of Dermatology) where a trained technician placed a clear acetate transparency over each enlarged macrophotographic print and placed a black dot over each visible hair. Hair counts were obtained from dot map transparencies by means of computer-assisted image analysis.

Patient self-assessment (hair growth questionnaire). A hair growth questionnaire, self-administered by the patient at each visit, measured the patient's perception of changes in his hair growth. The multi-item questionnaire was validated[19] during the course of the two studies and, subsequently, 7 questions that assessed change from baseline were deemed valid and used in the data analysis. The 7 questions, which were introduced into the questionnaire just before the month 12 time point of the pilot study, included 4 questions related to the efficacy of treatment and 3 questions related to patient satisfaction with the appearance of his scalp hair (Table II).

Investigator assessment. Each investigator assessed the change in the patient's scalp hair growth as compared with baseline at each visit, by means of a standardized 7-point rating scale: greatly decreased (-3), moderately decreased (-2), slightly decreased (-1), no change (0), slightly increased (+1), moderately increased (+2), greatly increased (+3).

Global photographic assessment. Clinical photographs of the patient's vertex balding area were taken with the head in a fixed position by means of a stereotactic device.[18] Film emulsion (Kodak KR-64 color slide film), exposure, lighting, and reproduction ratio were held constant. At various time points during the studies, paired baseline and follow-up photographic slides of each patient were projected under standardized conditions, and the change in hair growth was assessed independently by means of the standardized 7-point rating scale (see above), by an expert panel of dermatologists (E. Olsen, R. Savin, D. Whiting) blinded to treatment, study center, and patient.

Safety evaluation

Vital signs and reports of any adverse event were collected at every visit. A physical examination was performed at baseline and at months 6 and 12. Hematology, urinalysis, serum chemistries including prostate-specific antigen (PSA), and serum hormones (T, DHT, luteinizing hormone [LH] and follicle-stimulating hormone [FSH]) were measured at baseline and during follow-up, including end of study (Fig 1).

Serum chemistries, LH, and FSH were assayed in a central laboratory (Medical Research Laboratories, Highland Heights, Ky), and hematology and urinalysis were performed in either the central laboratory or in the investigator's laboratory. Serum DHT was assayed at Endocrine Sciences (Calabasas Hills, Calif), and serum T was assayed at Medical Research Laboratories (pilot study) or at Endocrine Sciences (dose range study).

Statistical methods

The primary analysis for both studies included all patients who had measurements at both baseline and one or more on-treatment time points, that is, the intention-to-treat population. Missing data were estimated by substituting the last on-treatment value for a given patient. In the dose range study, the adjusted form of the Tukey-Ciminera-Heyse trend test was used to address the progressiveness of response in hair growth with increasing dose.[20,21] This approach examines the dose-response relationship for the 1, 0.2, and 0.01 mg doses of finasteride and

Table III. Summary of efficacy data from pilot and dose range studies

	Month 6: Change from baseline						Month 12: Change from baseline				
	Study						Study				
	Pilot		Dose range				Pilot		Dose range extension*		
End point	5 mg	Placebo	1 mg	0.2 mg	0.01 mg	Placebo	5 mg	Placebo	1 mg	0.2 mg	0.01 mg
Scalp hair count in 1-inch diameter circle (mean number of hairs)	66	-20	69	55	-9	-15	93	-20	85	65	-18
Patient self-assessment (No. of questions significantly different vs placebo†/total)	‡	NA	7/7	4/7	0/7	NA	7/7	NA	7/7	6/7	NA
Investigator clinical assessment (% improved)	68	46	75	67	50	51	77	46	91	81	65
Global photographic assessment (% improved)	51	10	52	38	12	11	48	3	54	38	10

NA, Not applicable.
*There was no placebo group in the dose range extension study.
†Versus the finasteride 0.01 mg treatment group in the dose range extension study at month 12.
‡Data for the 7 hair growth questions in the pilot study are available only at month 12.

provides for a more effective comparison of finasteride doses with the placebo group and within the finasteride doses. Analysis of variance (ANOVA) was used for pairwise between-treatment group comparisons for all the efficacy and biochemical end points in both studies. The ANOVA model included terms for both treatment and study center. In addition, in the dose range study the Cochran-Armitage trend test was used to test trend between the placebo group and the finasteride dose groups for categorical response variables in the safety analyses. Fisher's exact test was used for all pairwise between-treatment group comparisons in the safety analyses in both studies.

For the extension to the dose range study, analysis of data included all patients who had measurements at both baseline and an on-treatment time point during the extension. This analysis evaluated two separate cohorts: (1) those patients who received finasteride (1, 0.2, or 0.01 mg) during the initial, 6-month, placebo-controlled dose range study and who continued this therapy during the 6-month blinded extension (up to 12 months finasteride therapy; n = 259) and (2) patients who initially received placebo for 6 months and who were rerandomized to finasteride (1, 0.2, or 0.01 mg) at the beginning of the 6-month extension study (up to 6 months finasteride therapy; n = 84). Missing data for the extension study were estimated by using the last measurement on-treatment during the extension, but data were not carried forward across studies (ie, from the initial placebo controlled portion of the dose range study into the extension study).

The primary hypothesis for hair counts was assessed by the difference between the count at each time point and the accompanying baseline count. The hypothesis for patient self-assessment was assessed by a global test across the 7 validated questions of the hair growth questionnaire, using a generalized least squares procedure that accounts for the different scales of, and covariance among, the 7 questions.[22,23] For investigator and global photographic assessments, hypotheses were assessed by rating scores at each time point. Hypothesis testing for hair counts, individual patient self-assessment questions, and investigator and global photographic assessments was performed by means of the statistical methods as described above.

Safety analyses concentrated on the biochemical parameters and on adverse event reports. Comparison of the proportion of patients with an adverse event was done by means of the Cochran-Armitage trend test in the dose range study to assess any trend in the incidence of adverse events with increasing dose. In both studies, Fisher's exact test was used for the pairwise between-treatment group comparisons regarding the incidence of adverse events.

RESULTS

Baseline summary data, demonstrating similarity between groups and between studies, are shown in Table I, and clinical efficacy data are summarized in Table III.

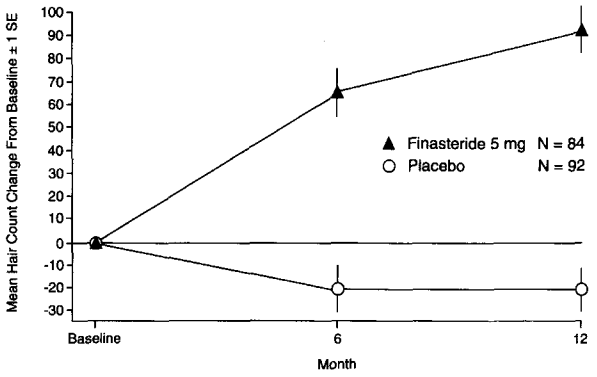

Fig 2. Hair count mean change from baseline (± 1 SE) for men in pilot study.

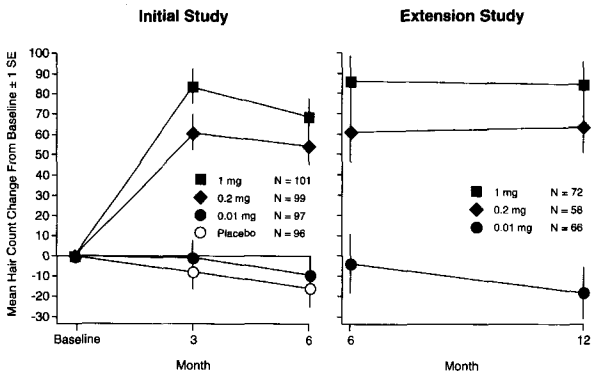

Fig 3. Hair count mean change from baseline (± 1 SE) for men in dose range study (initial and extension phases).

Hair counts

At month 6, treatment with the 3 highest doses of finasteride tested (5, 1, and 0.2 mg) significantly increased hair count compared with baseline or placebo ($P < .001$; Table III; Figs 2 and 3). In the dose range study, the trend test across placebo and the finasteride dose groups showed a statistically significant positive trend ($P < .001$) in change in hair counts with increasing dose, with hair count increases evident as early as month 3 with the higher doses tested (1 and 0.2 mg; Fig 3). For the finasteride 5 and 1 mg groups at month 6, the increase in hair count (mean ± SE) in the representative 1-inch diameter circular target area was similar (66 ± 10.2 and 69 ± 8.9 hairs, respectively), and there was a numerically smaller increase for the 0.2 mg group (55 ± 9.0 hairs); patients treated with either finasteride 0.01 mg or placebo had a mean decrease in hair count from baseline. Of note, the net improvement in hair count (finasteride – placebo) observed with finasteride 5 mg (66 – (-20) = 86 hairs) was remarkably similar to that observed with finasteride 1 mg (69 – (-15) = 84 hairs).

At month 12, the finasteride 5, 1, and 0.2 mg groups demonstrated increases in hair count of 93 ± 10, 85 ± 11, and 65 ± 13 hairs, respectively, from baseline ($P < .001$ vs placebo or 0.01 mg) (Table III; Figs 2 and 3). The trend test showed a significant dose response ($P < .001$) across all 3 finasteride dose groups in the dose range extension study. Mean decreases in hair count from baseline were observed for both the finasteride 0.01 mg and placebo groups in the dose range and pilot studies, respectively. In the dose range extension study, the results for the placebo group rerandomized to 1 of 3 finasteride doses (1, 0.2, or 0.01 mg) for 6 months were similar (62 ± 17, 53 ± 18, and -6 ± 18 hairs from baseline, respectively) to the 6-month results observed for patients randomized to these doses in the initial placebo controlled portion of the dose range study.

Patient self-assessment

Because the 7 validated questions of the hair growth questionnaire were introduced into the questionnaire just before the month 12 time point of the pilot study, data with the 5 mg dose were available at end of study only.

In the dose range study, the global test across all 7 questions demonstrated superiority as early as month 3 for the finasteride 1 mg group compared with placebo ($P < .05$), but not for the lower dosage groups. At month 6, there were significant differences between both the 1 and 0.2 mg groups compared with placebo ($P < .001$ and $P < .05$, respectively). However, only the 1 mg group showed significant ($P < .05$) superiority for each of the 7 individual questions compared with the placebo group (Table III).

At month 12, the global test showed that the finasteride 5 mg, as well as finasteride 1 and 0.2 mg, groups were significantly ($P < .001$ for 5 and 1 mg; $P < .05$ for 0.2 mg) superior to the placebo (pilot study) or finasteride 0.01 mg (dose range study) groups. However, only the 5 and 1 mg groups demonstrated significant ($P < .05$ for 5 mg; $P < .01$ for 1 mg) superiority for all 7 individual questions compared with the placebo (or finasteride 0.01 mg) group (Table III).

Investigator assessment

On the basis of the investigator's assessment of change in the patient's scalp hair growth from baseline, treatment with finasteride at the 3 highest doses studied (5, 1, and 0.2 mg) demonstrated significant ($P < .001$, $P < .05$, and $P < .001$, respectively) efficacy compared with placebo at month 3,

and the percentages of patients rated as improved in each of these 3 treatment groups were 50%, 55%, and 65%, respectively. At month 6, the 5, 1, and 0.2 mg groups again demonstrated significant ($P < .001$) efficacy compared with placebo, and similar percentages of patients were rated as improved in each of these 3 treatment groups (68%, 75%, and 67%, respectively) (Table III). The trend test across placebo and all 3 finasteride dose groups in the dose range study showed that there was a statistically significant dose response ($P < .001$).

At month 12, the investigator assessment demonstrated significant ($P < .001$) further improvement for the 5, 1, and 0.2 mg treatment groups, with percentages of patients rated as improved being higher than at month 6 (77%, 91%, and 81%, respectively) (Table III). The trend test showed a significant dose response ($P < .001$) across all 3 finasteride dose groups in the dose range extension study.

Global photographic assessment

At month 3, the finasteride 0.2 mg group showed significantly better efficacy than placebo ($P < .05$), and there was a trend towards better efficacy in the 1 mg group ($P = .074$ vs placebo). The finasteride 5, 1, and 0.2 mg groups all demonstrated significant ($P < .001$) efficacy compared with placebo at month 6, and the 1 mg group showed superior efficacy over the 0.2 mg group ($P < .05$). The percentages of patients rated as improved were comparable between the 5 and 1 mg groups (51% and 52%, respectively), but higher than the 0.2 mg group (38%) or the placebo groups (10% to 11%) (Table III). The trend test showed a significant dose response ($P < .001$) across placebo and all 3 finasteride dose groups in the dose range study.

At month 12, the finasteride 5, 1, and 0.2 mg groups demonstrated significant efficacy compared with placebo or 0.01 mg finasteride, and the 1 mg group was superior to the 0.2 mg group ($P < .05$). The percentages of patients rated as improved were comparable between the 5 and 1 mg groups (48% and 54%, respectively), but higher than the 0.2 mg group (38%) or the 0.01 mg or placebo groups (3% to 10%) (Table III). The trend test showed a significant dose response ($P < .001$) across all 3 finasteride dose groups in the dose range study.

Serum hormones and PSA

Treatment with finasteride significantly decreased serum DHT levels at all doses (median decrease of $-67.6\% \pm 3.1\%$, $-68.5\% \pm 1.4\%$, $-61.2\% \pm 1.7\%$, and $-10.8\% \pm 4.2\%$ for the 5, 1, 0.2, and 0.01 mg groups, respectively, at month 6; $P < .01$ vs placebo), findings consistent with previous studies.[11] There was a significant ($P < .05$) dose response in DHT reduction between the 1 and 0.2 mg groups, which persisted out to month 12, supporting greater suppression of DHT formation with the 1 mg dose.

The marked reductions in serum DHT at doses of finasteride more than or equal to 0.2 mg/day were associated with small but significant increases in serum T (mean increase of $18.3\% \pm 3.1\%$, $19.4\% \pm 3.6\%$, and $18.1\% \pm 3.6\%$ for the 5, 1, and 0.2 mg groups, respectively, at month 6; $P < .01$ vs placebo). These small increases observed in serum T, associated with marked decreases in serum DHT, were not associated with significant changes in serum LH or FSH from baseline. Consistent with previous studies, serum PSA was decreased slightly (from a baseline of 0.6 to 0.7 ng/mL) at month 6 (-0.2 ± 0.04 and -0.2 ± 0.07 ng/mL for the 5 and 1 mg groups, respectively, $P < .05$ vs placebo; -0.1 ± 0.05 ng/mL for the 0.2 mg group, $P = .078$).

Adverse events

All adverse events that were considered by the investigator to be possibly, probably, or definitely drug related (ie, side effects) and that occurred in at least 1% of patients in any treatment group during the placebo-controlled portion of the pilot and dose range studies are shown in Table IV. On the basis of previous experience with finasteride in older men with BPH, the incidence of sexually related side effects was specifically analyzed for each treatment group. The incidence of these side effects with finasteride therapy was generally comparable to that observed with treatment with placebo, and there was no evidence of dose dependency or increased incidence with longer therapy out to 12 months. In addition, these side effects ceased in some patients while they continued to receive finasteride.

DISCUSSION

The development of finasteride for the treatment of men with male pattern hair loss was undertaken after the establishment of an excellent safety profile for the drug at a 5 mg daily dose in older men with BPH. A preliminary biochemical study in balding men undergoing hair transplantation demonstrated that finasteride 5 mg significantly reduced the DHT content of balding scalp after 4 weeks of treatment.[13] Using clinical efficacy measures that assess changes in scalp hair growth, two multicenter, randomized, placebo-controlled clinical trials, the pilot and dose range studies, were subsequently conducted to (1) establish the proof that treatment with finasteride would lead to clinical improvement in men with male pattern hair loss and (2) determine the optimal dose of finasteride for further clinical investigation in

Table IV. Side effects occurring in 1% or more of patients: Placebo-controlled studies

	Month 6: Patient count (%)					Month 12*: Patient count* (%)	
	Study						
	Pilot study	Dose range study			Combined	Pilot study	
	5 mg (n = 111)	1 mg (n = 117)	0.2 mg (n = 115)	0.01 mg (n = 117)	Placebo (n = 233)	5 mg (n = 111)	Placebo (n = 116)
Patients with one or more drug-related sexual AEs	4 (3.6)	5 (4.3)	7 (6.1)	2 (1.7)	8 (3.4)	4 (3.6)	7 (6.0)
Decreased libido	3 (2.7)	2 (1.7)	4 (3.5)	2 (1.7)	7 (3.0)	3 (2.7)	5 (4.3)
Erectile dysfunction	2 (1.8)	3 (2.6)	2 (1.7)	0	0	2 (1.8)	0
Body hair growth increased	0	0	0	2 (1.7)	2 (0.9)		

AEs, Adverse events.
*The dose range extension study (through month 12) was not placebo controlled.

this patient population. The pilot study demonstrated that treatment with finasteride 5 mg/day increased scalp hair counts in men with male pattern hair loss and led to clinically significant improvements in scalp hair growth as determined by 3 separate efficacy end points (patient self-assessment, investigator clinical assessment, and assessment of clinical global photographs by an expert panel) in men with male pattern hair loss.

Whereas the pilot study established proof of concept for the usefulness of finasteride in the treatment of men with male pattern hair loss, a second biochemical study conducted in parallel demonstrated that finasteride at doses as low as 0.2 mg/day for 6 weeks maximally suppressed scalp and serum DHT in balding men.[14] Based on these data and the desire to fully characterize the dose-response relationship below 5 mg/day with clinically meaningful end points, a separate clinical dose range study was undertaken. This study enrolled a similar patient population, and used identical efficacy end points, as in the pilot study, allowing comparison of data from both studies across a wide dose range from 0.01 to 5 mg/day.

Analysis of data from both the pilot and dose range studies demonstrated that (1) increases in hair count observed with treatment with finasteride 1 mg were numerically superior to those observed with the lower 0.2 mg dose but similar to results observed with the higher 5 mg dose, and (2) treatment with finasteride 1 mg resulted in significantly greater efficacy by patient self-assessment and global photographic assessment compared with the lower 0.2 mg dose, supporting the clinical relevance of the superiority observed in the hair count measure. Thus, on the basis of the data from these two studies, finasteride 1 mg was determined to have efficacy similar to that observed at a higher dose but superior to lower doses. These findings related to clinical efficacy and dose are consistent with the findings observed for serum DHT suppression at 6 and 12 months, with 1 mg demonstrating potency similar to the higher 5 mg dose but superior to lower doses.

Comparison of safety data from these studies demonstrated that treatment with finasteride at any of the doses tested resulted in safety profiles that were similar to each other and not significantly different from placebo. As anticipated from previous studies with finasteride in older men with BPH, side effects related to finasteride (or placebo) therapy in these studies were related to sexual dysfunction, with the overall number of patients affected being small and generally similar between treatment groups in the two studies. The absence of significant effect on serum LH or FSH baseline levels indicates that finasteride treatment had no significant effect on the hypothalamic-pituitary-gonadal axis, whereas the effect observed on serum PSA in these young men was small and not clinically significant.

CONCLUSION

The efficacy and safety data from these studies confirmed that finasteride 1 mg was the optimal dose for further clinical investigation in the treatment of men with male pattern hair loss. These studies were continued as open-label extension studies in which all patients received finasteride 1 mg to continue evaluation of the long-term efficacy and safety of the drug in this patient population. Subsequently, finasteride 1 mg was extensively evaluated in 3 multicenter, placebo-controlled, clinical trials for male pattern hair loss

in more than 1800 men from 18 to 41 years old[24,25] to further establish its safety and efficacy profile, leading to approval of the drug as a treatment for men with male pattern hair loss.

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