

# Long-Term (Over 10 Years) Evaluation of Efficacy and Safety of Finasteride in Japanese Men with Androgenetic Alopecia: Summary of Three Investigations

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## ABSTRACT

**Introduction:** Finasteride has been the standard medical treatment for androgenetic alopecia (AGA) for over 20 years. We started AGA treatment with finasteride in 1999 in Japan, and have demonstrated 3 investigations as long-term and/or large-scale studies (3,177 cases in 2.5 years, 801 cases in 5 years, 532 cases in 10 years, respectively). The objective of this study is to summarize the three investigations, and to consider it as a base for future studies over the next 20 to 30 or more years.

**Methods:** Vertex photographs and/or forehead photographs were taken and recorded for every patient at each examination and used for evaluation for more than 20 years. Efficacy was assessed using the Norwood-Hamilton scale (N-H) and the modified global photographic assessment (MGPA) score, which is the standardized 7-point rating score using scalp photographs. Adverse reactions were assessed through self-reported evaluations by patients in two investigations

**Results:** All three of the investigations demonstrated high evaluations of improvement (MGPA $\geq$ 5; 87.1%, 99.4%, and 91.5%, respectively), and higher evaluations of prevention of disease progression (MGPA $\geq$ 4; 99.6%, 100%, and 99.1%, respectively). Furthermore, the early-stage AGA group (N-H I-III at first visit) and the younger group (less than 40 years of age at first visit) showed more improvement with long-term AGA treatment with finasteride than the other groups did. Two of the investigations showed safety of long-term AGA treatment with finasteride, revealing the low onset rates of adverse reactions (adverse reactions: 0.7% in 2.5 years and 6.8% in 10 years, respectively). Neither of the two investigations recognized Post Finasteride Syndrome adverse reaction at all.

**Conclusion:** Long-term (greater than 10 years) AGA treatment with finasteride 1mg/day demonstrated a high efficacy and safety based on large-scale studies in Japanese men. For patients at the early stage of classification of AGA (within N-H I-III or earlier) and/or younger than 40 years of age, we recommend starting treatment with 1mg/day finasteride.

**Keywords:** androgenetic alopecia, finasteride, Japanese, modified global photographic assessment score, Norwood-Hamilton scale

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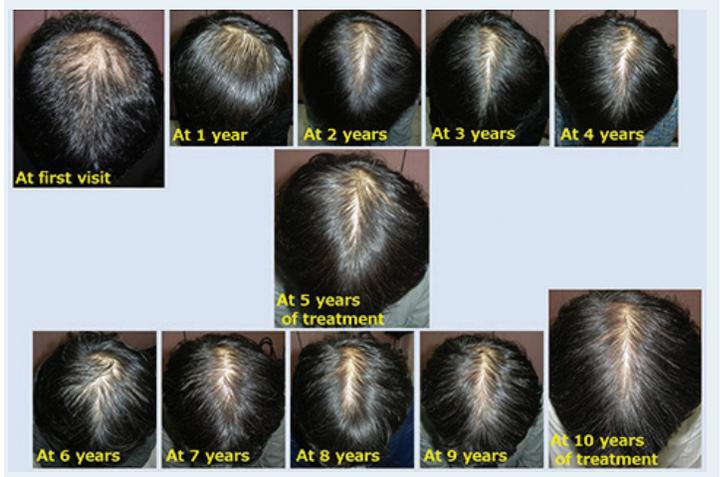
## INTRODUCTION

In 1997, U.S. Food and Drug Administration (FDA) authorized the use of finasteride for the treatment of androgenetic alopecia (AGA); subsequently, the treatment was approved all over the world, and has been in use for more than 20 years. Presently, finasteride is authorized in over 60 countries and is administered to more than 3 million patients for AGA. Dihydro-testosterone (DHT) has a key role in mediating progressive scalp hair loss in men with AGA, and finasteride blocks the conversion of testosterone to DHT as a selective type II 5 $\alpha$ -reductase inhibitor, which justifies its use in AGA treatment.<sup>1-3</sup> Although finasteride has been globally used for more than 20 years, only a few investigations for up to 10 years have been demonstrated worldwide.<sup>4,5</sup> The authors have previously demonstrated three investigations of efficacy and safety of large-scale and long-term AGA treatment with finasteride (3,177 cases in 2.5 years, 801 cases in 5 years, and 532 cases in 10 years, respectively).<sup>5-7</sup> The objective of this article is to summarize the three investigations, and to consider them as a base for future studies over the next 20 to 30 years or more.

## METHODS

Tokyo Memorial Clinic (hereafter, "The clinic") started AGA treatment with finasteride in 1999 (the first in Japan, to our knowledge). Vertex photographs and/or forehead photographs were taken and recorded for every patient at each examination and used for evaluation for over 20 years (Figures 1 and 2). Efficacy was assessed using the

FIGURE 1. Vertex photographs at the first visit and yearly were evaluated using the MGPA score and N-H scale.



Norwood-Hamilton scale (N-H)<sup>8,9</sup> and the modified global photographic assessment (MGPA) score,<sup>10,11</sup> which is the standardized 7-point rating score using scalp photographs. The study period for each of the three investigations is as follows: The first investigation, "Evaluation of Efficacy and Safety of Finasteride 1mg in 3177 Japanese men with Androgenetic Alopecia," was evaluated from January 2006 to June 2009.<sup>7</sup> The second investigation, "Five-Year Efficacy of Finasteride in 801 Japanese Men with Androgenetic Alopecia," was evaluated from January 2000 to November 2008.<sup>6</sup> The third investigation, "Long-Term (10-Year) Efficacy

FIGURE 2. Forehead photographs (same patient from Figure 1) at the first visit and yearly were evaluated using the MGPA score and N-H scale.



of Finasteride in 523 Japanese Men with Androgenetic Alopecia,” was evaluated from December 2005 to January 2009.<sup>5</sup> The same patients were included in the three investigations, but each study period was completely different. In two of the investigations, adverse reactions were assessed through self-reported evaluations by patients.

## RESULTS

All three investigations demonstrated high evaluations of improvement (MGPA  $\geq$  5; 87.1% (2230/2561), 99.4% (796/801), and 91.5% (487/532), respectively), and higher evaluations of prevention of disease progression (MGPA  $\geq$  4; 99.6% (2550/2561), 100% (801/801), 99.1% (527/532), respectively) (Tables 1 and 2). Furthermore, the early-stage AGA group (N-H: I/II/III at first visit) and the younger group (less than 40 years of age at first visit), demonstrated more improvement with long-term AGA treatment with finasteride than the other groups did.

In the investigation of “801 cases in 5 years,” receiver operating characteristic (ROC) curve analysis was performed to classify patients with sufficient efficacy (MGPA  $\geq$  6) and insufficient (MGPA < 6) condition at year 5 of treatment; the cut-off point was N-H: IV, and 39 years at first visit. (The area under the curve [AUC], which indicates the predictive value, was 0.676). In the investigation of “532 cases in 10 years,” ROC analysis was performed to classify patients with improvement (MGPA  $\geq$  5) and no improvement (MGPA < 5)

TABLE 1. Study Improvement and Prevention Results

Study Period	Study Population	Improvement (MGPA score $\geq$ 5)	Prevention of Disease Progression (MGPA score $\geq$ 4)	Adverse Reactions
2.5 years	3177	87.1% (2230/2561)	99.6% (2550/2561)	0.7% 23/3177
5 years	801	99.4% (796/801)	100.0% (801/801)	no evaluation
10 years	532	91.5% (487/532)	99.1% (527/532)	6.8% 36/532

TABLE 2. Study Conclusions

	Conclusions
3177 cases in 2.5 year	In Japanese men with AGA, long-term treatment with finasteride 1 mg tablets maintained high efficacy without recognized side-effect.
801 cases in 5 year	Younger age and less advanced disease at start of treatment were the key predictors of higher finasteride efficacy. Finasteride has lower efficacy in patients over 40 years old and in patients with advanced N-H scale (over N-H: IV) at the first visit.
532 cases in 10 year	Long-term (10-year) AGA treatment with finasteride 1 mg/day demonstrated a high efficacy and safety based on subjective and objective evaluations in Japanese men. The group with N-H: I/II/III at the first visit showed greater improvement than the group with N-H: IV/V/ VI/VII at first visit, following 10 years of AGA treatment with finasteride.

condition at year 10 of treatment; the cut-off point was N-H III, and 39 years at first visit (AUC was 0.746) (Table 3).

TABLE 3. ROC Results

Receiver Operating Characteristic Curve (ROC) Analysis	Comparison		Cut-off Point		Area Under the Curve
			N-H:	Years	
801 cases in 5 year	sufficient	MGPA $\geq$ 6	IV	39	0.676
	insufficient	MGPA < 6			
532 cases in 10 year	improvement	MGPA $\geq$ 5	III	39	0.746
	no improvement	MGPA < 5			

The two investigations demonstrated the safety of long-term AGA treatment with finasteride, revealing the low onset rates of adverse reactions (0.7% (23/3,177) in 2.5 years, 6.8% (36/532) in 10 years). All adverse reactions were mild and almost all of the patients continued treatment for more than 10 years. Neither of the two investigations recognized Post Finasteride Syndrome adverse reaction at all.

## DISCUSSION

The efficacy of the investigated treatment in Japanese men exceeded that reported in other studies in Caucasians. Differences have been known to occur in the progression of AGA symptoms between Japanese and Caucasian men.<sup>7,12</sup> The superior response of Japanese men with AGA was reported to likely be attributable to their hair characteristics (greater diameter, black color, and lower density), which facilitated the detection of slight changes.<sup>6,13-15</sup>

Though many investigations have been recognized all over the world, most Japanese people still wrongly believe the following: “finasteride has only efficacy of prevention of AGA progression”; “finasteride decreases testosterone”; “finasteride has serious adverse reactions (decreased libido, male infertility, erectile dysfunction, liver dysfunction, etc.).” The cause is thought to be because the package insert of finasteride still includes the following wording: “Efficacy; prevention of AGA progression”; in addition, there are some noted adverse reactions without revision from 2006 in Japan. Possibly, a similar situation may happen in some other countries. Some of our objectives in this study were to dispel rumors and to publicize the true information.

Almost no Post Finasteride Syndrome has been recognized as a result of AGA treatment with finasteride over the 20 years studied by our clinic. Similarly, almost no Post Finasteride Syndrome as adverse reactions were recognized from investigations of finasteride in Japan.<sup>5,7,16</sup>

There are only a few articles that follow AGA treatment with finasteride for 10 years.<sup>4,5</sup> Furthermore, we have continued investigating for greater than 10 years and are preparing for future studies that detail 20, 30, or more years.

In summary, during the 3 investigations, long-term (greater than 10 years) AGA treatment with finasteride 1mg/day demonstrated high efficacy and safety based on large-scale studies in Japanese men. For best efficacy, we recommend that AGA patients should start treatment with 1mg/day finasteride at the early stage of classification of AGA (N-H I-III or earlier) and/or younger than 40 years of age.

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