Original Article | Annals of Dermatology 2022;34(5):349-359 • https://doi.org/10.5021/ad.22.027

Long-Term Effectiveness and Safety of Dutasteride versus Finasteride in Patients with Male Androgenic Alopecia in South Korea: A Multicentre Chart Review Study

Gwang-Seong Choi*, Woo-Young Sim[1]*, Hoon Kang[2], Chang Hun Huh[3], Yang Won Lee[4], Sumitra Shantakumar[5], Yu-Fan Ho[5], Eun-Jeong Oh[6], Mei Sheng Duh[7], Wendy Y. Cheng[7], Priyanka Bobbili[7], Philippe Thompson-Leduc[7], Gary Ong[8]

Department of Dermatology, Inha University College of Medicine, Incheon, [1]Department of Dermatology, Kyung Hee University Hospital at Gangdong, [2]Department of Dermatology, Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, [3]Department of Dermatology, Seoul National University Bundang Hospital, Seongnam, [4]Department of Dermatology, Konkuk University School of Medicine, Seoul, Korea, [5]Vaccines R&D, Medical Affairs, GSK, Singapore, [6]GSK, Seoul, Korea, [7]Analysis Group, Inc., Boston, MA, United States, [8]Pharma Research and Development, Global Medical, GSK, Singapore

Received February 15, 2022
Revised April 27, 2022
Accepted May 17, 2022

Corresponding Author
Gary Ong
Pharma Research and Development, Global Medical, GSK, 23 Rochester Park, 139234 Singapore
Tel: +65-62328338
Fax: +65-62916815
E-mail: gary.p.ong@gsk.com
https://orcid.org/0000-0002-3505-2877
*These authors have equally contributed to the article.

Background: Dutasteride improves hair growth compared with finasteride in male androgenic alopecia (AGA) and is well tolerated. However, real-world evidence for long-term dutasteride use in AGA is lacking.
Objective: To describe baseline characteristics, treatment patterns and long-term safety and effectiveness of dutasteride versus finasteride.
Methods: This was a multicentre, retrospective medical chart review study conducted in South Korea. The index date was the first prescription of dutasteride or finasteride. Baseline characteristics were assessed 6 months prior to index. Safety and effectiveness (improvements in basic and specific [BASP] classification) data were collected from index throughout the observation period.
Results: Overall, 600 male adult patients were included (dutasteride, n=295; finasteride, n=305). Dutasteride-treated patients were older ($p<0.001$) and more likely to have moderate/severe BASP classification at baseline ($p=0.010$) compared with finasteride-treated patients. Among patients treated with recommended, on-label dosing exclusively (n=535: dutasteride, n=250; finasteride, n=285), dutasteride-treated patients showed greater improvement in hair growth than finasteride-treated patients, as measured by the BASP basic M classification (adjusted incidence rate ratio [95% confidence interval]: 2.06 [1.08, 3.95]; $p=0.029$). Among this same subset, overall occurrence of adverse events (AEs) during the observation period were not statistically equivalent between groups (dutasteride 7.6%, finasteride 10.5%; $p=0.201$), although reports of AEs of special interest were equivalent ($p<0.001$).
Conclusion: Dutasteride showed greater effectiveness than finasteride in improving BASP classification in treating male AGA and had a similar or possibly lower occurrence of overall AEs. Dutasteride may provide an effective and safe treatment option for male patients with AGA.

Keywords: Alopecia, Androgenic alopecia, Dutasteride, Epidemiology, Finasteride, Retrospective studies

INTRODUCTION

Androgenic alopecia (AGA) is an androgen-dependent progressive hair loss condition with genetic predisposition, affecting up to 70% of men during their lifetime[1,2]. Male AGA is characterised by receding temporal hairlines and hair loss at the whorl and/or vertex of the head[2]. AGA causes self-image dissatisfaction and impaired overall quality of life[3].

The androgen dihydrotestosterone (DHT) is implicated in the pathophysiology of AGA[1]. Testosterone is converted to DHT

by 5-α-reductase, prompting development of 5-α-reductase inhibitors as AGA treatments. International guidelines recommend topical minoxidil (5%) and oral finasteride (a type II 5-α-reductase inhibitor) for treatment of male AGA[4]. However, dutasteride (an inhibitor of type I and II 5-α-reductase) has demonstrated significantly greater improvement in hair growth compared with finasteride and is well tolerated among male patients with AGA[5-8]. Dutasteride inhibits type II 5-α-reductase three times more potently than finasteride[9] and suppresses serum DHT levels by 98% compared with 71% for finasteride[10].

Dutasteride (0.5 mg/day) is approved for treatment of AGA in South Korea, Japan, and Taiwan[11-13]. However, efficacy and safety data for dutasteride is largely derived from short-term clinical trials and post-marketing surveillance studies[6-8,14-16]. Long-term, real-world evidence for the effectiveness of dutasteride is limited.

We determined the demographic and clinical characteristics of patients receiving dutasteride and finasteride, their treatment patterns, and the long-term effectiveness and safety of each treatment. The study was conducted in South Korea; as dutasteride was approved in South Korea in 2009 it is an appropriate setting for this real-world, long-term data analysis.

MATERIALS AND METHODS

Objectives

This study had four primary objectives: assess the demographic and clinical characteristics of patients with AGA receiving dutasteride or finasteride; describe their treatment patterns; assess the long-term effectiveness of dutasteride and finasteride using the basic and specific (BASP) classification of AGA; and assess and compare the long-term occurrence of adverse events (AEs), AEs of special interest and serious AEs (SAEs).

Study design

This retrospective medical chart review study was conducted across five clinical sites in South Korea. The study was approved by the following institutional review boards: Seoul National University, B-1712/441-103; The Catholic University of Korea, PC19RODI0061; Inha University Hospital, INHAUH 2017-12-001-006; Kyung Hee University Hospital, KHNMC 2018-01-028-009; Konkuk University School of Medicine, KUH1120105.

A pilot study conducted prior to the full study, with a sample size of 50 patients, assessed the availability and quality of medical record data needed to populate the case report form (CRF), with data retrieved for the full observation period of January 2010 to December 2019. The index date was defined as the first prescription of dutasteride or finasteride, as recorded in medical charts, among patients with a confirmed AGA diagnosis. The baseline period was the 6 month-period prior to the index date, during which the inclusion and exclusion criteria were applied. The schematic study design is shown in Supplementary Fig. 1. The observation period spanned from the index date until death, loss to follow-up, or data cut-off date, whichever occurred first. All patients were followed for at least 3 years post-index; based on results of the pilot study and discussions with the participating clinical sites this was the longest duration for which sufficient patient data would be available for meaningful analysis (Supplementary Fig. 1). Patient demographics and clinical characteristics were assessed during the baseline period. Treatment patterns, effectiveness and safety data were assessed during the observation period.

Study data were collected retrospectively from existing patient medical charts, using an electronic CRF (eCRF). Clinical staff abstracted patient information from medical charts into the eCRF. The study protocol was reviewed and approved by institutional review boards at each site.

Inclusion/exclusion criteria

Male patients with a confirmed AGA diagnosis were included if they had ≥1 prescription for either treatment, ≥18 years of age at index and ≥3 years of available medical charts during the observation period whilst receiving the treatment prescribed on the index date. Patients were excluded if they received any prescription of dutasteride ≤12 weeks prior to finasteride initiation or any prescription of finasteride ≤8 weeks prior to dutasteride initiation. Additional exclusion criteria were prior surgical correction of scalp hair loss, history of malignancy other than non-melanotic cancers, systemic cytotoxic therapy, any diagnosis of global hair thinning, scarring of the scalp, hair loss not caused by AGA, or any other condition of the scalp or hair.

Outcomes

Effectiveness and safety data were extracted from patient charts at the index date and at each patient visit during the observation period. The main effectiveness outcome was BASP classifications of AGA. Improvement in BASP classification was defined as any decrease in grades of the basic (e.g. M3 to M2) or specific (e.g. V3 to V1) type compared with baseline[14,16,17].

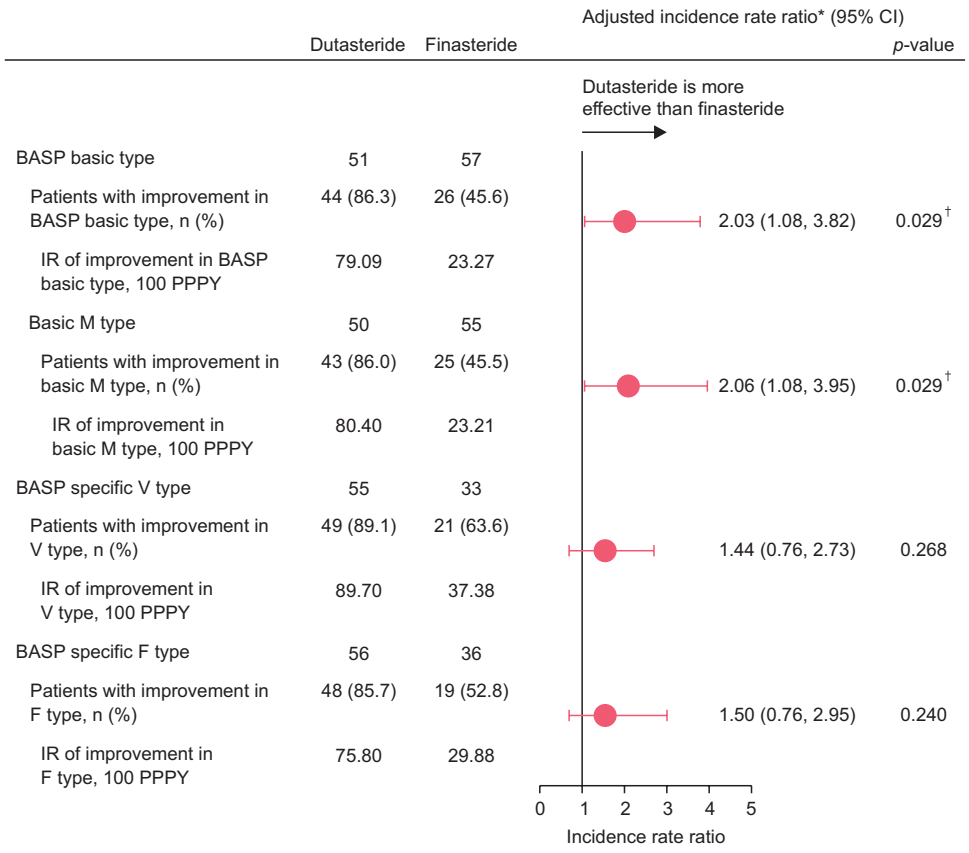

Fig. 1. Comparative analysis of effectiveness, as measured by first observed improvement in BASP classification, among patients prescribed the recommended doses of dutasteride (0.5 mg daily) and finasteride (1 mg daily). AGA: androgenic alopecia, CI: confidence interval, BASP: basic and specific classification, IR: incidence rate, PPPY: per-person per-year. *Multivariate models were adjusted for age at index date, study site, index year, any recent hair loss at baseline, any comorbidities at baseline, use of any treatment during baseline, and baseline severity of AGA. Missing and 'no' values were combined into a single category for each variable. †Significant at the 0.05 level.

AEs were defined as any untoward medical occurrence temporally associated with the use of dutasteride or finasteride, whether or not considered related to treatment. SAEs were defined as any AE that resulted in death or significant disability/incapacity, was life-threatening, or required hospitalisation. Clinical staffs were asked about specific AEs on the eCRF and could also record additional AEs as free text. AEs of special interest included sexual dysfunction (decreased libido, erectile dysfunction, ejaculation disorders), testicular pain, breast tenderness, gynaecomastia, depression and diabetes mellitus. Other AEs investigated in this study were abdominal pain, allergic reactions/swelling of lips and face/rash/urticaria, back pain, diarrhoea, dizziness, dyspepsia, fatigue, headache, influenza, pharyngitis, upper respiratory tract infections. SAEs included death, cancers, and serious cardiovascular events.

Statistical analyses

Baseline demographic and clinical characteristics were described using means, standard deviations (SDs) and medians for continuous variables; and frequencies and proportions for categorical variables. Baseline demographic and clinical characteristics were compared between groups using a chi-squared test for categorical variables and a Wilcoxon rank-sum test for continuous variables. Statistical significance was defined as a p-value <0.05.

Treatment patterns were described using means, SDs and medians for continuous variables; and frequencies and percentages for categorical variables. No comparison between patients receiving finasteride and dutasteride was performed.

For effectiveness data, comparative analyses were performed using incidence rate (IR) analysis to account for different lengths of follow-up time (during the observation period) to the first observed improvement in BASP classification. The IR of improvement for treatments were compared using IR ratios (IRRs) derived from Poisson models in univariate and multivariate analyses. Multivariate analyses adjusted for confounders including age at index date, study site, index year, any recent hair loss at baseline, any comorbidities at baseline, use of any treatment (such as minoxidil) during baseline, and baseline severity of AGA.

The occurrence of AEs was collected from patients' medical charts; the IRs (number of events per person-time of observa-

tion) was calculated using these data. Statistical inference was made based on equivalence testing. For frequencies of AEs and SAEs, *p*-values were estimated from two one-sided tests to determine if the differences in proportions were within a prespecified equivalence region of ±5%. Equivalence was indicated by a *p*-value <0.05. The IRs of total and specific AEs and SAEs were compared using Poisson models in univariate and multivariate analyses. Multivariate analyses were adjusted for age at AGA diagnosis, time from AGA diagnosis to index date as well as those detailed for multivariate analysis of effectiveness data. The IR difference (IRD) was generated and equivalence was indicated if both bounds of the 90% confidence interval (CI) of the IRD were inside the ±5% equivalence region.

Sensitivity analyses were conducted for effectiveness and safety data, whereby only patients who received the recommended, on-label doses of dutasteride (0.5 mg/day) and finasteride (1.0 mg/day) throughout the duration of the observation period were included.

RESULTS

Baseline clinical and demographic characteristics

The overall population consisted of 600 South Korean patients, 295 of whom received dutasteride and 305 of whom received finasteride as their index medication. Within these groups, 250 dutasteride-treated patients (84.7%) and 285 finasteride-treated patients (93.4%) received exclusively on-label dosages throughout the observation period.

Patients receiving dutasteride were older than those receiving finasteride at index (mean±SD: dutasteride, 41.7±10.6 years; finasteride, 36.8±11.2 years; $p<0.001$). Smoking status and alcohol consumption were similar between groups ($p=0.712$ and $p=0.317$, respectively) (Table 1).

Over three-quarters of patients with available data had a family history of AGA (dutasteride n=163 of 213 [76.5%]; finasteride, n=108 of 140 [77.1%]; $p=0.893$). Fewer dutasteride-treated patients had recent hair loss (n=86 of 255 [33.7%]) versus finasteride-treated patients (n=103 of 195 [52.8%]; $p<0.001$). Moderate and severe AGA (according to BASP classification) was more common in dutasteride-treated patients (n=24 of 101 [23.8%] and n=2 of 101 [2.0%], respectively) versus finasteride-treated patients (n=9 of 94 [9.6%] and n=0 of 94 [0.0%], respectively) ($p=0.010$). Among patients with available BASP measurements at index, most exhibited basic M type hair loss (n=93 of 101 [92.1%] for dutasteride-treated and n=87 of 94 [92.6%] for finasteride-treated patients). At baseline, comorbidities were significantly higher among dutasteride-treated patients (n=14 of 109 [12.8%]) versus finasteride-treated patients (n=4 of 199 [2.0%]; $p<0.001$). A greater proportion of dutasteride-treated patients (n=210 of 263 [79.8%]) were receiving a form of AGA treatment at baseline than finasteride-treated patients (n=131 of 222 [59.0%]; $p<0.001$) (Table 1).

Treatment patterns

The mean duration of the observation period was similar across both treatment groups (dutasteride, 3.4±0.6 years; finasteride 3.4±0.7 years). Both cohorts had a similar mean number of prescriptions for the index medication during the observation period (dutasteride, 8.1±2.7; finasteride, 7.8±2.4) (Table 2). The mean number of days between visits was also similar (dutasteride, 218.5±109.6; finasteride, 217.1±108.1). Throughout the observation period, 96.6% (dutasteride) and 98.7% (finasteride) of all prescriptions were for the recommended dose (0.5 mg/day of dutasteride and 1.0 mg/day of finasteride). Only one patient (among dutasteride-treated patients) discontinued treatment. Low rates of treatment halt were reported (dutasteride, n=7 [2.4%]; finasteride, n=10 [3.3%]). Minoxidil use was greater in dutasteride-treated patients during the observation period (n=226 [76.6%]) than finasteride-treated patients (n=145 [47.5%]).

Effectiveness

The adjusted IRR analysis significantly favoured dutasteride treatment for most BASP types, excluding BASP specific F type (Supplementary Fig. 2). A total of 63 of 78 (80.8%) dutasteride-treated patients and 32 of 67 (47.8%) finasteride-treated patients exhibited an improvement in BASP basic type (adjusted IRR [95% CI]: 1.84 [1.07, 3.17]; $p=0.028$). For basic M type hair loss, the corresponding values were 61 of 76 (80.3%) and 31 of 65 (47.7%) patients (adjusted IRR [95% CI]: 1.84 [1.06, 3.21]; $p=0.031$). For BASP specific V type hair loss the corresponding values were 73 of 79 (92.4%) and 23 of 37 (62.2%) patients (adjusted IRR [95% CI]: 1.95 [1.12, 3.43]; $p=0.019$); and for BASP specific F type the corresponding values were 69 of 81 (85.2%) and 22 of 39 (56.4%) patients (adjusted IRR [95% CI]: 1.41 [0.76, 2.60], $p=0.271$).

The adjusted sensitivity analysis of the effectiveness of treatments among patients receiving the recommended doses of each treatment are shown in Fig. 1. A total of 44 of 51 (86.3%) dutasteride-treated patients and 26 of 57 (45.6%)

Table 1. Table of baseline demographic and clinical characteristics

Characteristic	Dutasteride (n=295)	Finasteride (n=305)	*p*-value
Baseline demographic characteristics			
Age at index (yr)	41.7±10.6 (42.9)	36.8±11.2 (35.1)	<0.001*
Smoking status	n=91[§] (30.8)	n=32[§] (10.5)	
Never (<100 cigarettes during lifetime)	43 (47.3)	14 (43.8)	0.712
Former	18 (19.8)	5 (15.6)	
Current	30 (33.0)	13 (40.6)	
Alcohol consumption	n=8[§] (2.7)	n=5[§] (1.6)	
No alcohol consumption	1 (12.5)	1 (20.0)	0.317
Light to moderate (≤14 drinks/wk)	2 (25.0)	3 (60.0)	
Heavy (>14 drinks/wk)	5 (62.5)	1 (20.0)	
Baseline clinical characteristics			
Family history of AGA	n=213[§] (72.2)	n=140[§] (45.9)	
Yes	163 (76.5)	108 (77.1)	
Mother only	21 (12.9)	12 (11.1)	0.893
Father only	127 (77.9)	86 (79.6)	0.908
Both parents	15 (9.2)	10 (9.3)	
No	50 (23.5)	32 (22.9)	
Recent hair loss	n=255[§] (86.4)	n=195[§] (63.9)	
Yes	86 (33.7)	103 (52.8)	<0.001*
No	169 (66.3)	92 (47.2)	
Age at which hair loss was first observed (yr)	n=33[§] (11.2)	n=52[§] (17.0)	
	40.3±15.3 (38.0)	35.2±20.3 (30.5)	0.004[‡]
Baseline BASP classification	n=101[§] (34.2)	n=94[§] (30.8)	
Severity[†]			
No hair loss (L, M0, C0)	0 (0.0)	0 (0.0)	0.010[‡]
Mild (M1-2, C1, V1-2, F1-3)	75 (74.3)	85 (90.4)	
Moderate (M3, C2, V3)	24 (23.8)	9 (9.6)	
Severe (C3, U1-3)	2 (2.0)	0 (0.0)	
Basic type			0.087
L	0 (0.0)	4 (4.3)	
M	93 (92.1)	87 (92.6)	
M0	17 (16.8)	11 (11.7)	
M1	29 (28.7)	33 (35.1)	
M2	33 (32.7)	40 (42.6)	
M3	14 (13.9)	3 (3.2)	
C	7 (6.9)	3 (3.2)	
U	1 (1.0)	0 (0.0)	
Specific type			
V	80 (79.2)	48 (51.1)	<0.001*
F	81 (80.2)	46 (48.9)	<0.001*

Table 1. Continued

Characteristic	Dutasteride (n=295)	Finasteride (n=305)	p-value
Diagnoses of comorbidities	109 (36.9)	199 (65.2)	
Any	14 (12.8)	4 (2.0)	<0.001*
None	95 (87.2)	195 (98.0)	<0.001*
Use of treatments related to AGA	263 (89.2)	222 (72.8)	
Any	210 (79.8)	131 (59.0)	<0.001*
Topical minoxidil	207 (78.7)	129 (58.1)	<0.001*

Values are presented as number (%) or mean±standard deviation (median). AGA: androgenic alopecia, BASP: basic and specific classification. *p*-values were computed using a global chi-squared test (or Fisher's exact test as appropriate) for binary or categorical variables and a Wilcoxon rank-sum test for continuous variables. Statistical significance was defined as a *p*-value <0.05. *Significant at the 0.001 level. †Severity was determined by the more severe of basic type or specific type. For example, if a patient had M1 (mild) as basic type and V3 (moderate) as specific type, he would be classified as moderate. ‡Significant at the 0.05 level. §Patients with known information from which percentages were calculated.

Table 2. Treatment patterns among dutasteride- and finasteride-treated patients

Treatment pattern characteristic	Dutasteride (n=295)	Finasteride (n=305)
Duration of observation period (yr)	3.4±0.6 (3.2)	3.4±0.7 (3.2)
Index medication prescriptions during the observation period*		
Number of index medication prescriptions	8.1±2.7 (7.0)	7.8±2.4 (7.0)
Number of index medication prescriptions, PPPY	2.5±0.9 (2.3)	2.3±0.8 (2.2)
Duration between visits (day)	218.5±109.6 (195.0)	217.1±108.1 (197.4)
Any minoxidil use during the observation period	226 (76.6)	145 (47.5)
Most frequent prescription of index medication		
0.5 mg/day	285 (96.6)	N/A
1.0 mg/day	N/A	301 (98.7)
Discontinued medication use	1 (0.3)	0 (0.0)
Had a treatment halt at any time	7 (2.4)	10 (3.3)

Values are presented as mean±standard deviation (median) or number (%). N/A: not applicable, PPPY: per-person per-year. *Includes prescriptions on index date.

finasteride-treated patients exhibited an improvement in BASP basic type (adjusted IRR [95% CI]: 2.03 [1.08, 3.82]; p=0.029); for basic M type hair loss, the corresponding values were 43 of 50 (86.0%) and 25 of 55 (45.5%) patients (adjusted IRR [95% CI]: 2.06 [1.08, 3.95]; p=0.029). Rates of improvement were numerically, but not significantly, greater for dutasteride-treated patients in BASP specific V type (adjusted IRR [95% CI]: 1.44 [0.76, 2.73]; p=0.268) and BASP specific F type hair loss (adjusted IRR [95% CI]: 1.50 [0.76, 2.95], p=0.240).

The cumulative proportions of patients with improvement in BASP classification in patients receiving the recommended dose were significantly higher for dutasteride-treated patients compared with finasteride-treated patients for basic type (at 12 months; p<0.001), basic M type (at 12 months; p<0.001), V type (at 12 months; p<0.05) and F type (at 18 months; p<0.05) (Fig. 2). Similar results were observed in the overall population (Supplementary Fig. 3).

Safety

Results of the sensitivity analysis comparing occurrence of AEs between dutasteride- and finasteride-treated patients prescribed at the recommended doses showed that AEs were reported for 19 (7.6%) dutasteride-treated patients and 30 (10.5%) finasteride-treated patients (Table 3). Equivalence testing indicated these proportions were not equivalent (proportion

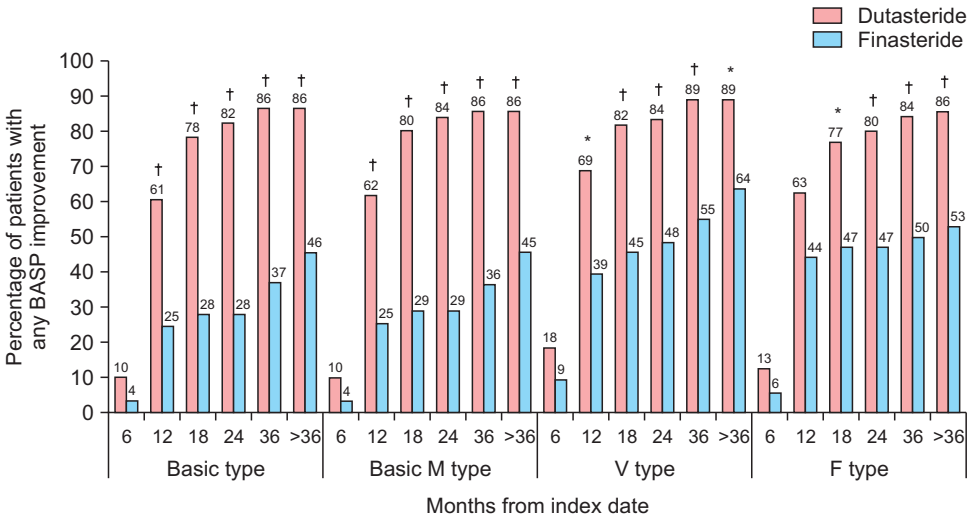

Fig. 2. Cumulative proportions of improvement in BASP classification among patients prescribed recommended doses of dutasteride (0.5 mg daily) and finasteride (1 mg daily). BASP: basic and specific classification. *Significant at the 0.05 level. †Significant at the 0.001 level.

Table 3. On-treatment adverse events reported for dutasteride and finasteride among patients prescribed the recommended doses of dutasteride (0.5 mg daily) and finasteride (1 mg daily)

Adverse event	Dutasteride (n=250)	Finasteride (n=285)	Equivalence?*
Any adverse event	19 (7.6)	30 (10.5)	No
Any adverse event of special interest	4 (1.6)	3 (1.1)	Yes
Sexual adverse events	4 (1.6)	3 (1.1)	Yes
Decreased libido	3 (1.2)	2 (0.7)	Yes
Impotence/erectile dysfunction	1 (0.4)	0 (0.0)	Yes
Other sexual dysfunction	0 (0.0)	1 (0.4)	Yes
Any other adverse event	17 (6.8)	27 (9.5)	No
Allergic reactions/swelling of lips and face/rash/urticaria	1 (0.4)	2 (0.7)	Yes
Back pain	1 (0.4)	0 (0.0)	Yes
Diarrhoea	1 (0.4)	2 (0.7)	Yes
Dyspepsia	1 (0.4)	1 (0.4)	Yes
Fatigue	1 (0.4)	0 (0.0)	Yes
Other†	12 (4.8)	24 (8.4)	No
Skin disorders‡	11 (4.4)	17 (6.0)	Yes
Any SAE	0 (0.0)	2 (0.7)	Yes
Serious cardiovascular event (e.g. cardiac failure, stroke)	0 (0.0)	1 (0.4)	Yes
Other SAE§	0 (0.0)	1 (0.4)	Yes

Values are presented as number (%).SAE: serious adverse event. *Equivalence was determined from two one-sided tests to determine whether the 90% confidence interval for the differences in proportions were within the equivalence region, defined as ±5%. †Other adverse events were reported as open-ended responses and included skin disorders, herpes simplex, shoulder pain/herniated disc, ureter stone, abdominal wall lipoma, fever, gastroesophageal reflux and transient ischemic attack. ‡Skin disorders included acne, eczema, erythema, erythematous papules, epidermal cyst, folliculitis, itching, psoriasis, rash, seborrheic dermatitis, seborrheic keratosis and tinea pedis. §Other SAEs included abdominal pain, acute colitis and schwannoma on the left neck, all of which resulted in hospitalizations.

difference [90% CI]: 2.9% [–1.1, 7.0]; p=0.201) (Supplementary Fig. 4).

AEs relating to sexual dysfunction were equivalent between groups: occurring in 4 (1.6%) and 3 (1.1%) dutasteride- and finasteride-treated patients, respectively (proportion difference [90% CI]: –0.5% [–2.2, 1.1]; p<0.001). The most frequently

	Dutasteride (n=250)	Finasteride (n=285)	Unadjusted IRD (90% CI)	Adjusted IRD* (90% CI)
All AEs, per 100 PY	2.33	3.32	0.984 (−0.346, 2.314) *Equivalent*	3.765 (−0.559, 8.089) *Not equivalent*
AEs of special interest, per 100 PY	0.48	0.31	−0.166 (−0.660, 0.327) *Equivalent*	-
Other AEs, per 100 PY	2.07	2.95	0.878 (−0.370, 2.126) *Equivalent*	1.561 (−0.825, 3.948) *Equivalent*
SAEs, per 100 PY	0.00	0.21	0.207 (−0.034, 0.447) *Equivalent*	-

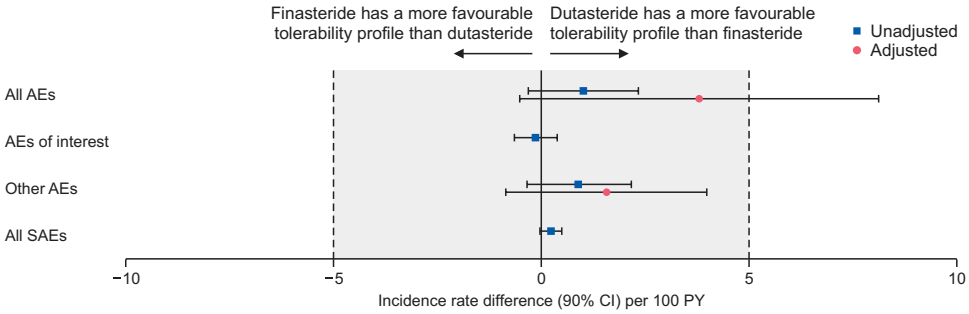

Fig. 3. Incidence rates of AEs reported for dutasteride and finasteride among patients prescribed the recommended doses of dutasteride (0.5 mg daily) and finasteride (1 mg daily). *Multivariate models were adjusted for age at androgenic alopecia diagnosis, time from diagnosis to index date, study site, index year, baseline hair loss (recent hair loss), presence of any comorbidities, baseline basic and specific classification (BASP) severity, presence of any treatment during baseline. Missing values among the covariates were used as separate categories in models. Adjusted IR differences could not be produced for AEs of special interest and SAEs as there were very few events and models did not converge when covariates were included. AE: adverse event, IRD: incidence rate difference, CI: confidence interval, PY: person-year, SAE: serious adverse event.

reported sexual AE was decreased libido (dutasteride, n=3 [1.2%]; finasteride, n=2 [0.7%]).

The overall incidence of AEs categorised as 'Other AEs' were not equivalent between groups; they were reported in 17 (6.8%) and 27 (9.5%) of dutasteride-treated and finasteride-treated patients, respectively (proportion difference [90% CI]: 2.7% [–1.2, 6.5]; p=0.162). However, among the 'Other AEs', some events such as skin disorders were equivalent; reported in 11 (4.4%) and 17 (6.0%) of dutasteride-treated and finasteride-treated patients, respectively (proportion difference [90% CI]: 1.6 [–1.6, 4.7,]; p=0.036). Only two SAEs were reported among finasteride-treated patients (0.7%), none were reported among dutasteride-treated patients.

IRs for all AEs (per 100 person-years) in patients receiving the recommended doses were 2.33 and 3.32 for dutasteride and finasteride, respectively; the adjusted IRD was not equivalent (3.765, 90% CI: –0.559, 8.089). For AEs of special interest (sexual AEs), IRs were 0.48 and 0.31, respectively. For all other AEs, the IRs were 2.07 and 2.95, respectively, and the adjusted IRD was equivalent (1.561 [90% CI: –0.825, 3.948]) (Fig. 3). The analysis of the adjusted IRD for some categories of AEs could not be conducted because there were too few events. No deaths were reported in either treatment group. Similar results were observed in the overall population (Supplementary Fig. 5, 6).

DISCUSSION

The safety and efficacy of dutasteride and finasteride treatment for male AGA has been compared in randomized controlled trials (RCTs)[18]. The current study provides, to our knowledge, the first real-world evidence comparing the long-term effectiveness and safety of these treatments in male AGA. The sample size was sufficiently large to explore multivariable models, accounting for baseline differences between treatment groups. Dutasteride was more effective than finasteride in improving hair growth, based on the BASP classification, especially among BASP M type (the most common type of male AGA[17]). Safety profiles were largely equivalent, with equivalence demonstrated in several AEs, including skin disorders. Data from this study suggest that dutasteride may be more beneficial compared with finasteride in the treatment of AGA in some male patients, in line with results from prior RCTs[7,8,19]. Our results indicate that dutasteride is effective and well tolerated when prescribed at the recommended dose (0.5 mg/day).

For the overall patient population, significantly greater improvements were observed in dutasteride-treated patients over finasteride-treated patients (even after adjusting the analysis for confounders including age); specifically, in BASP basic, basic M and specific V types of hair loss. These data were largely consis-

tent among patients prescribed the recommended doses of each medication. Significantly improved adjusted IRs of improvements were observed in BASP basic and basic M type hair loss among dutasteride-treated patients. However, this improvement was not significant for specific V and F type classifications after adjusting for confounders. The results should be interpreted considering the lower number of patients with specific F and V types among finasteride-treated patients, resulting in reduced statistical power. Results from the overall population are possibly more representative of the real world, as patients may not always be prescribed the recommended doses.

Most patients with a BASP classification available at baseline exhibited basic M type hair loss at treatment initiation (~92%); results from the effectiveness analysis in this group have the highest statistical power. Proportions presented here are similar to previously reported estimates of its prevalence in South Korea (80%~85%)[17,20]. M type classification is characterised by hair loss predominantly in the frontotemporal hairline[17]. Data from the present report are consistent with findings from a RCT in which patients treated with dutasteride showed similar improvements in hair growth, particularly in the frontal area[7]. Our combined findings, along with published research elsewhere, indicate that the drug may bind more strongly to receptors in the frontal area of the scalp[7].

The effectiveness results reported here are consistent with a systematic review of three clinical trials investigating the efficacy of dutasteride and finasteride in male AGA over 24 weeks. Among 576 participants, dutasteride showed significantly better efficacy than finasteride, as measured by total hair count and investigators' assessment of the vertex and frontal views[18]. A recent meta-analysis, using data from 30 RCTs, also identified dutasteride as a more efficacious treatment than finasteride for the treatment of male AGA, as measured by mean change in hair count from baseline following treatment[21]. Our efficacy findings are in agreement with data from a post-marketing surveillance study, conducted in Japan, in which, patients treated with dutasteride exhibited an increase in mean target area hair count and hair restoration over a 52-week period[16].

In the current study, improvement in AGA was defined as a decrease in BASP classification of hair loss. This approach has been implemented elsewhere to describe the effectiveness of finasteride[20]. An alternative approach would have been to group BASP types together to define 'mild' (M1–2, C1, V1–2, F1–3), 'moderate' (M3, C2, V3) and 'severe' (C3, U1–3) AGA, but this lacks the specificity required to detect improvements in AGA. Additional measures of hair loss were investigated, including total hair count and hair diameter (data not shown); however, these data were too sparse to reach adequate statistical power.

The rate of AEs overall was low in both treatment groups, although the calculated IR of AEs were numerically higher among finasteride-treated patients compared with dutasteride-treated patients. This difference was greater after adjusting for baseline differences. In the present study, skin conditions were the most frequently reported AE, and mostly occurred among finasteride-treated patients. The relatively high frequency (compared with the incidence of other AEs) observed in both treatment groups may be attributable to patient treatment by dermatologists. The occurrence of skin conditions should be monitored in future studies as they have been reported in a post-marketing surveillance study conducted in South Korea (2.5% among dutasteride-treated patients)[15]. AEs, relating to sexual dysfunction, were equivalent between treatment groups. Proportions of decreased libido are lower than those reported elsewhere. Two separate meta-analyses show altered libido occurred in 6.7%~18.9% and 1.2%~6.7% of finasteride-treated patients; and 4.8%~22.8% and 1.5%~11.8% of dutasteride-treated patients[18,22]. The lower proportions observed here may be because sexual AEs are not recorded by dermatologists in the real world in the same way as in clinical trials. SAEs were reported infrequently and were equivalent between treatment groups, consistent with the South Korean post-marketing surveillance study, which found SAEs occurred among 0.6% of dutasteride-treated patients[15]. Our study supports a similar or potentially slightly better safety profile of dutasteride compared with finasteride.

The current study had some limitations. Data quality and completeness varied among study sites; large proportions of data were missing among variables of interest, including total hair count and hair width at baseline and during the observation period of the pilot study. To mitigate this, site coordinators aimed to ensure consistent reporting based on patients' available data. In addition, although smoking status and alcohol consumption have been associated with AGA[23], we were unable to account for this as few patients had baseline data available for these factors. Among the patients who did have information available for smoking status and alcohol consumption, the prevalence of each was similar between

treatment groups, so this was unlikely to have contributed to the findings. As in any observational chart review study, there was potential for residual or unmeasured confounding. However, this is expected to have affected both groups equally. Additionally, these results may not be generalizable beyond South Korean populations. Finally, loss of follow-up or treatment change/discontinuation (leading to censorship from analysis) could have affected the results' validity. For example, if finasteride-treated patients discontinued therapy due to ineffective results, then effectiveness results comparing dutasteride versus finasteride may become biased towards the null; we tried to mitigate this by ensuring that all patients were treated for a minimum of 3 years.

In conclusion, findings from this study provide real-world evidence of the effectiveness and safety of dutasteride versus finasteride in the treatment of AGA among patients treated for ≥3 years in South Korea. These results support treatment with dutasteride among patients with various levels of AGA severity, especially those with the most common type of AGA (M type). Therefore, consistent use of dutasteride should be considered for use in clinical practice for the treatment of AGA to improve outcomes in South Korea. This would align with guidelines in Japan, where dutasteride, as well as finasteride, are recommended as first-line treatments for AGA[24]. Importantly, results indicate that, with the recommended dose of dutasteride, patients experience few AEs, which are slightly lower than finasteride-treated patients.

ACKNOWLEDGMENT

The authors would like to thank Mu Cheng, Sonia Cheung, Suna Park, and Heather Sipsma of Analysis Group, Inc., for their help with data analysis. Editorial support (in the form of writing assistance, including preparation of the draft manuscript under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing and referencing) was provided by Robert Bloxham at Fishawack Indicia Ltd., part of Fishawack Health UK.

SUPPLEMENTARY MATERIALS

Supplementary data can be found via http://anndermatol.org/src/sm/ad-22-027-s001.pdf.

CONFLICTS OF INTEREST

GSC, WYS, HK, CHH, YWL have no, real or perceived, direct or indirect conflicts of interest that relate to this manuscript. GO, SS, YFH and EJO are employees of GSK; GO, SS, and YFH hold stocks and shares in the company. MSD, WYC, PB and PTL are employees of Analysis Group, Inc., a consulting firm that has received funding for the conduct of this study.

FUNDING SOURCE

The study was funded by GSK (GSK study number: 206807). GSK contributed to the design of the study and interpretation of the data; and participated in the writing, review and approval of the manuscript.

DATA SHARING STATEMENT

The data that support the findings of this study (individual participant data and study documents) are available from www.clinicalstudydatarequest.com upon reasonable request.

ORCID

Gwang-Seong Choi, https://orcid.org/0000-0002-5766-0179
Woo-Young Sim, https://orcid.org/0000-0001-5300-6869
Hoon Kang, https://orcid.org/0000-0002-9822-4760
Chang Hun Huh, https://orcid.org/0000-0003-3944-7777
Yang Won Lee, https://orcid.org/0000-0003-1268-1248
Sumitra Shantakumar, https://orcid.org/0000-0001-5814-6465
Yu-Fan Ho, https://orcid.org/0000-0003-1943-5533
Eun-Jeong Oh, https://orcid.org/0000-0001-5263-9867
Mei Sheng Duh, https://orcid.org/0000-0001-5035-6687
Wendy Y. Cheng, https://orcid.org/0000-0002-8281-2496
Priyanka Bobbili, https://orcid.org/0000-0002-1343-8314
Philippe Thompson-Leduc, https://orcid.org/0000-0001-9047-3941
Gary Ong, https://orcid.org/0000-0002-3505-2877

REFERENCES

1. Kaufman KD. Androgens and alopecia. Mol Cell Endocrinol 2002;198:89-95.
2. Wolff H, Fischer TW, Blume-Peytavi U. The diagnosis and treatment of hair and scalp diseases. Dtsch Arztebl Int 2016;113:377-386.

3. Han SH, Byun JW, Lee WS, Kang H, Kye YC, Kim KH, et al. Quality of life assessment in male patients with androgenetic alopecia: result of a prospective, multicenter study. Ann Dermatol 2012;24:311-318.
4. Kanti V, Messenger A, Dobos G, Reygagne P, Finner A, Blumeyer A, et al. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men - short version. J Eur Acad Dermatol Venereol 2018;32:11-22.
5. Chung HC, Lee S, Lee WS. Long-term efficacy and safety of the dual 5-alpha reductase blocker dutasteride on male androgenetic alopecia patients. J Dermatol 2017;44:1408-1409.
6. Eun HC, Kwon OS, Yeon JH, Shin HS, Kim BY, Ro BI, et al. Efficacy, safety, and tolerability of dutasteride 0.5 mg once daily in male patients with male pattern hair loss: a randomized, double-blind, placebo-controlled, phase III study. J Am Acad Dermatol 2010;63:252-258.
7. Gubelin Harcha W, Barboza Martínez J, Tsai TF, Katsuoka K, Kawashima M, Tsuboi R, et al. A randomized, active- and placebo-controlled study of the efficacy and safety of different doses of dutasteride versus placebo and finasteride in the treatment of male subjects with androgenetic alopecia. J Am Acad Dermatol 2014;70:489-498.e3.
8. Shanshanwal SJ, Dhurat RS. Superiority of dutasteride over finasteride in hair regrowth and reversal of miniaturization in men with androgenetic alopecia: a randomized controlled open-label, evaluator-blinded study. Indian J Dermatol Venereol Leprol 2017;83:47-54.
9. Hirshburg JM, Kelsey PA, Therrien CA, Gavino AC, Reichenberg JS. Adverse effects and safety of 5-alpha reductase inhibitors (finasteride, dutasteride): a systematic review. J Clin Aesthet Dermatol 2016;9:56-62.
10. Clark RV, Hermann DJ, Cunningham GR, Wilson TH, Morrill BB, Hobbs S. Marked suppression of dihydrotestosterone in men with benign prostatic hyperplasia by dutasteride, a dual 5alpha-reductase inhibitor. J Clin Endocrinol Metab 2004;89:2179-2184.
11. MFDS. Avodart Soft Capsule 0.5mg (Dutasteride) [Internet]. Cheongju: MFDS; 2004 [cited 2021 Apr 9]. Available from: https://nedrug.mfds.go.kr/pbp/CCBBB01/getItemDetail?itemSeq=200409982.
12. Food and Drug Administration Ministry of Health and Welfare. Nuvaniv License Details [Internet]. Taipei: Food and Drug Administration Ministry of Helath and Welfare; 2007 [cited 2021 Jan 13]. Available from: https://www.fda.gov.tw/mlms/H0001D.aspx?Type=Lic&LicId=52026888.
13. Pharmaceuticals and Medical Devices Agency. Zagallo Review Report [Internet]. Tokyo: Pharmaceuticals and Medical Devices Agency; 2015 [cited 2021 Jan 13]. Available from: https://www.pmda.go.jp/english/review-services/reviews/approved-information/drugs/0001.html.
14. Stough D. Dutasteride improves male pattern hair loss in a randomized study in identical twins. J Cosmet Dermatol 2007;6:9-13.
15. Choi GS, Kim JH, Oh SY, Park JM, Hong JS, Lee YS, et al. Safety and tolerability of the dual 5-alpha reductase inhibitor dutasteride in the treatment of androgenetic alopecia. Ann Dermatol 2016;28:444-450.
16. Tsunemi Y, Irisawa R, Yoshiie H, Brotherton B, Ito H, Tsuboi R, et al. Long-term safety and efficacy of dutasteride in the treatment of male patients with androgenetic alopecia. J Dermatol 2016;43:1051-1058.
17. Lee WS, Ro BI, Hong SP, Bak H, Sim WY, Kim DW, et al. A new classification of pattern hair loss that is universal for men and women: basic and specific (BASP) classification. J Am Acad Dermatol 2007;57:37-46.
18. Zhou Z, Song S, Gao Z, Wu J, Ma J, Cui Y. The efficacy and safety of dutasteride compared with finasteride in treating men with androgenetic alopecia: a systematic review and meta-analysis. Clin Interv Aging 2019;14:399-406.
19. Olsen EA, Hordinsky M, Whiting D, Stough D, Hobbs S, Ellis ML, et al. The importance of dual 5alpha-reductase inhibition in the treatment of male pattern hair loss: results of a randomized placebo-controlled study of dutasteride versus finasteride. J Am Acad Dermatol 2006;55:1014-1023.
20. Shin JW, Chung EH, Kim MB, Kim TO, Kim WI, Huh CH. Evaluation of long-term efficacy of finasteride in Korean men with androgenetic alopecia using the basic and specific classification system. J Dermatol 2019;46:139-143.
21. Gupta AK, Bamimore MA, Foley KA. Efficacy of non-surgical treatments for androgenetic alopecia in men and women: a systematic review with network meta-analyses, and an assessment of evidence quality. J Dermatolog Treat 2022;33:62-72.
22. Lee S, Lee YB, Choe SJ, Lee WS. Adverse sexual effects of treatment with finasteride or dutasteride for male androgenetic alopecia: a systematic review and meta-analysis. Acta Derm Venereol 2019;99:12-17.
23. Yeo IK, Jang WS, Min PK, Cho HR, Cho SW, Hong NS, et al. An epidemiological study of androgenic alopecia in 3114 Korean patients. Clin Exp Dermatol 2014;39:25-29.
24. Manabe M, Tsuboi R, Itami S, Osada SI, Amoh Y, Ito T, et al. Guidelines for the diagnosis and treatment of male-pattern and female-pattern hair loss, 2017 version. J Dermatol 2018;45:1031-1043.