

Study No.: ALO106377		
Title: A randomised, double-blind, placebo-controlled, parallel group study to assess the efficacy and safety of dutasteride 0.5mg once daily for 6 months in the treatment of male subjects with androgenetic alopecia (Norwood-Hamilton classification type IIIv, IV and V)		
Rationale: Androgenetic alopecia (AGA) is a common, androgen-induced, progressive disorder in genetically predisposed subjects affecting approximately 50% of Caucasian males aged >40 years. Human skin, sebaceous glands and hair follicles contain the enzyme system (5 alpha-reductase) needed to convert testosterone to dihydrotestosterone (DHT), the primary androgen responsible for male AGA. Preclinical and clinical data from Phase I and Phase II trials conducted in AGA indicated that dutasteride is a selective inhibitor of both Type I and Type II 5 AR enzymes and is well tolerated at doses up to 2.5mg daily for six months. The aim of this Phase III study is to compare the efficacy, safety and tolerability of dutasteride (0.5mg) with placebo for 6 months, in male subjects with androgenetic alopecia in the vertex region, types IIIv, IV and V according to the modified Norwood-Hamilton Classification.		
Phase: III		
Study Period: 15 DEC 2006 to 21 JAN 2008		
Study Design: This is a randomised, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of dutasteride 0.5mg once daily and placebo once daily for 6 months in male subjects aged 18 to 49 years with AGA types IIIv, IV and V per the modified Norwood-Hamilton classification.		
Centres: This study was conducted in 4 centers in Korea.		
Indication: Androgenetic alopecia		
Treatment: Dutasteride 0.5 mg or placebo		
Objectives: To assess and compare the efficacy of dutasteride 0.5mg once daily and placebo once daily for 6 months in the treatment of AGA in males		
Primary Outcome/Efficacy Variable: Hair growth assessed by macrophotographic technique (hair count) in the vertex at 6 months.		
Secondary Outcome/Efficacy Variable(s): Efficacy: Hair growth assessed by macrophotographic technique (hair count) in the vertex at 3 months; Subject assessment of change in hair growth in the vertex at 3 and 6 months (GlaxoSmithKline [GSK] Hair Growth Index [HGI]); Subject assessment of change in hair loss and overall appearance at 3 and 6 months (GSK HGI); Panel photographic assessment of change in hair growth in the vertex at 3 and 6 months (see figure 2 for areas of the scalp); Investigator photographic assessment of change in hair growth (IPAQ) of the vertex at 3 and 6 months. Safety: Assessment of adverse events (AEs) throughout the study. Vital signs, glucose, electrolytes, haematology (total WBC with differential), indicators of kidney function (creatinine) and liver function (alkaline phosphatase, total bilirubin, ALT, AST) assessed at screening and 6 months. Hormone measurements include LH (Luteinizing Hormone) at screening and DHT, testosterone, TSH, and T4 at screening and 6 months. Assessment of sexual function at every visit (Sexual Function Index).		
Statistical Methods: Unpaired t-test and analysis of covariance (ANCOVA) were used to compare the hair count change from baseline among treatment groups. GSK HGI, subject assessment, panel photographic assessment, and investigator photographic assessment were analysed using Chi-square test (or Fisher's exact test). The Intention-To-Treat (ITT) population, defined as all randomized subjects who received at least one dose of study medication and having at least one on-visit endpoint was used for the primary analysis. Per-Protocol (PP) population was analysed additionally. PP population consist of all subjects in ITT population taking study medication for 6 months and not identified as major protocol violator.		
Study Population: Subjects enrolled were men, 18-49 years of age, with Male Pattern Hair Loss classified as type IIIv, IV, or V utilising the modified Norwood-Hamilton classification.		
Number of Subjects:	Dutasteride	Placebo
Planned, N	75	75
Randomised, N	76	77
Completed, n (%)	70 (92)	73 (95)
Total Number Subjects Withdrawn, N (%)	6 (8)	4 (5)

Withdrawn due to Adverse Events n (%)	1 (1.32)	1 (1.30)	
Withdrawn due to Lack of Efficacy n (%)	0	0	
Withdrawn for other reasons n (%)	5 (6.57)	3 (3.89)	
Demographics	Dutasteride	Placebo	
N (ITT)	76	77	
Males	76 (100)	77 (100)	
Mean Age, years (SD)	37.78 (7.07)	38.41 (6.61)	
Korean	76 (100)	77 (100)	
Primary Efficacy Results:			
Hair count(1cm²) change from baseline to month 6	Dutasteride	Placebo	Between P-Values
Baseline ±SD (N)	148.14±36.27(68)	144.27±32.33(73)	
Month 6 ±SD (N)	162.27±38.52(73)	149.57±34.44(75)	
Month 6 – Baseline(Adjusted)	12.45	4.45	0.0193 ^{1*}
Month 6 – Baseline	12.21±23.60(68)	4.67±16.81(73)	0.0319 ^{2*}
Difference between dutasteride and placebo (95% CI)	7.54±20.37(0.75, 14.33)		
¹ ANCOVA (Fixed factor: Treatment group Covariate: Baseline value)			
² Unpaired t-test			
* Statistically significant difference			
Secondary Outcome Variable(s):			
Hair count(1cm²) change from baseline to month 3	Dutasteride	Placebo	
Baseline ±SD (N)	148.14±36.27(68)	144.27±32.33(73)	
Month 3 ±SD (N)	160.19±36.73(70)	154.50±36.87(70)	
Month 3 – Baseline(Adjusted)	7.89	9.93	
Month 3 – Baseline	7.58±22.70(65)	10.24±19.02(68)	
Difference between dutasteride and placebo (95% CI)	-2.66±20.90(-9.83, 4.51)		
Subject's global assessment of hair regrowth [GSK HGI: PART A (without photographs)]			
1. Since the start of treatment I have lost (Month 3)	Dutasteride n (%)	Placebo n (%)	
Much less hair	5(6.85)	4(5.33)	
Moderately less hair	8(10.96)	7(9.33)	
Slightly less hair	26(35.62)	26(34.67)	
The same amount of	32(43.84)	36(48.00)	
Slightly more hair	1(1.37)	2(2.67)	
Moderately more hair	1(1.37)	0(0.00)	
Much more hair	0(0.00)	0(0.00)	
1. Since the start of treatment I have lost (Month 6)	Dutasteride n (%)	Placebo n (%)	
Much less hair	9(12.33)	7(9.33)	
Moderately less hair	13(17.81)	8(10.67)	
Slightly less hair	24(32.88)	22(29.33)	
The same amount of	25(34.25)	35(46.67)	
Slightly more hair	2(2.74)	3(4.00)	
Moderately more hair	0(0.00)	0(0.00)	
Much more hair	0(0.00)	0(0.00)	
2. Since the start of treatment my usual hair loss has slowed down (3 month)	Dutasteride n (%)	Placebo n (%)	
I strongly disagree	0(0.00)	1(1.33)	
I disagree	18(24.66)	30(40.00)	
No opinion either way	20(27.40)	13(17.33)	
I agree	34(46.58)	30(40.00)	
I strongly agree	1(1.37)	1(1.33)	
2. Since the start of treatment my usual hair loss has slowed down (6 month)	Dutasteride n (%)	Placebo n (%)	
I strongly disagree	0(0.00)	0(0.00)	

I disagree	18(24.66)	27(36.00)
No opinion either way	12(16.44)	17(22.67)
I agree	40(54.79)	29(38.67)
I strongly agree	3(4.11)	2(2.67)
3. Since the start of treatment the overall appearance (thickness, hair quality, amount) of the hair on my head is (3 month)	Dutasteride n (%)	Placebo n (%)
Much worse	0(0.00)	0(0.00)
Moderately worse	0(0.00)	1(1.33)
Slightly worse	1(1.37)	4(5.33)
Not changed	36(49.32)	47(62.67)
Slightly better	25(34.25)	20(26.67)
Moderately better	7(9.59)	3(4.00)
Much better	4(5.48)	0(0.00)
3. Since the start of treatment the overall appearance (thickness, hair quality, amount) of the hair on my head is (6 month)	Dutasteride n (%)	Placebo n (%)
Much worse	0(0.00)	0(0.00)
Moderately worse	1(1.37)	0(0.00)
Slightly worse	2(2.74)	10(13.33)
Not changed	23(31.51)	33(44.00)
Slightly better	26(35.62)	29(38.67)
Moderately better	11(15.07)	3(4.00)
Much better	10(13.70)	0(0.00)
4. Since the start of treatment I have kept what hair I had (3 month)	Dutasteride n (%)	Placebo n (%)
I strongly disagree	0(0.00)	0(0.00)
I disagree	4(5.48)	8(10.67)
No opinion either way	5(6.85)	11(14.67)
I agree	62(84.93)	56(74.67)
I strongly agree	2(2.74)	0(0.00)
4. Since the start of treatment I have kept what hair I had (6 month)	Dutasteride n (%)	Placebo n (%)
I strongly disagree	0(0.00)	0(0.00)
I disagree	3(4.11)	8(10.67)
No opinion either way	3(4.11)	9(12.00)
I agree	60(82.19)	58(77.33)
I strongly agree	7(9.59)	0(0.00)
Subject's global assessment of hair regrowth [GSK HGI: PART B (with photographs)]		
1. Since the start of treatment, when I look at my thinning area, I can see (3 month)		
Much less scalp	10(13.70)	3(4.00)
Moderately less scalp	17(23.29)	11(14.67)
Slightly less scalp	25(34.25)	17(22.67)
The same amount of scalp	14(19.18)	26(34.67)
Slightly more scalp	3(4.11)	14(18.67)
Moderately more scalp	1(1.37)	4(5.33)
Much more scalp	3(4.11)	0(0.00)
1. Since the start of treatment, when I look at my thinning area, I can see (6 month)		
Much less scalp	9(12.33)	2(2.67)
Moderately less scalp	16(21.92)	5(6.67)
Slightly less scalp	26(35.62)	15(20.00)
The same amount of scalp	20(27.40)	26(34.67)
Slightly more scalp	1(1.37)	22(29.33)

Moderately more scalp	1(1.37)	4(5.33)
Much more scalp	0(0.00)	1(1.33)
2. Since the start of treatment my hair now covers (3 month)		
Much less scalp	1(1.37)	1(1.33)
Somewhat less scalp	2(2.74)	3(4.00)
A little less scalp	3(4.11)	14(18.67)
The same amount of scalp	20(27.40)	24(32.00)
A little more scalp	25(34.25)	23(30.67)
Somewhat more scalp	15(20.55)	7(9.33)
Much more scalp	7(9.59)	3(4.00)
2. Since the start of treatment my hair now covers (6 month)		
Much less scalp	0(0.00)	2(2.67)
Somewhat less scalp	0(0.00)	5(6.67)
A little less scalp	2(2.74)	21(28.00)
The same amount of scalp	22(30.14)	28(37.33)
A little more scalp	17(23.29)	17(22.67)
Somewhat more scalp	28(38.36)	1(1.33)
Much more scalp	4(5.48)	1(1.33)
3. Since the start of treatment the amount of hair on my thinning area has (3 month)		
Greatly decreased	0(0.00)	0(0.00)
Moderately decreased	2(2.74)	1(1.33)
Slightly decreased	7(9.59)	19(25.33)
Stayed the same	17(23.29)	21(28.00)
Slightly increased	26(35.62)	21(28.00)
Moderately increased	15(20.55)	10(13.33)
Greatly increased	6(8.22)	3(4.00)
3. Since the start of treatment the amount of hair on my thinning area has (6 month)		
Greatly decreased	0(0.00)	2(2.67)
Moderately decreased	0(0.00)	4(5.33)
Slightly decreased	0(0.00)	22(29.33)
Stayed the same	22(30.14)	26(34.67)
Slightly increased	22(30.14)	18(24.00)
Moderately increased	23(31.51)	2(2.67)
Greatly increased	6(8.22)	1(1.33)
4. Since the start of treatment the appearance (thickness, hair quality, amount) of the thinning area on my head is (3 month)		
Much worse	0(0.00)	0(0.00)
Moderately worse	2(2.74)	1(1.33)
Slightly worse	2(2.74)	9(12.00)
Not changed	16(21.92)	28(37.33)
Slightly better	28(38.36)	24(32.00)
Moderately better	14(19.18)	9(12.00)
Much better	11(15.07)	4(5.33)
4. Since the start of treatment the appearance (thickness, hair quality, amount) of the thinning area on my head is (6 month)		
Much worse	0(0.00)	1(1.33)
Moderately worse	0(0.00)	2(2.67)
Slightly worse	0(0.00)	20(26.67)
Not changed	21(28.77)	25(33.33)
Slightly better	24(32.88)	23(30.67)
Moderately better	19(26.03)	2(2.67)
Much better	9(12.33)	2(2.67)
Investigator's assessment of improvement distribution from screening		

Baseline to 3 month		
Greatly decreased	0(0.00)	0(0.00)
Moderately decreased	1(1.37)	1(1.33)
Slightly decreased	0(0.00)	13(17.33)
No change	28(38.36)	30(40.00)
Slightly increased	35(47.95)	30(40.00)
Moderately increased	8(10.96)	1(1.33)
Greatly increased	1(1.37)	0(0.00)
Baseline to 6 month		
Greatly decreased	0(0.00)	0(0.00)
Moderately decreased	0(0.00)	8(10.67)
Slightly decreased	4(5.48)	16(21.33)
No change	24(32.88)	36(48.00)
Slightly increased	31(42.47)	14(18.67)
Moderately increased	12(16.44)	1(1.33)
Greatly increased	2(2.74)	0(0.00)
Panel assessment of improvement distribution from screening		
Baseline to 3 month		
Greatly decreased	0(0.00)	0(0.00)
Moderately decreased	1(1.37)	0(0.00)
Slightly decreased	3(4.11)	14(18.67)
No change	28(38.36)	29(38.67)
Slightly increased	33(45.21)	28(37.33)
Moderately increased	8(10.96)	4(5.33)
Greatly increased	0(0.00)	0(0.00)
Baseline to 6 month		
Greatly decreased	0(0.00)	1(1.33)
Moderately decreased	0(0.00)	4(5.33)
Slightly decreased	6(8.22)	29(38.67)
No change	40(54.79)	32(42.67)
Slightly increased	20(27.40)	8(10.67)
Moderately increased	5(6.85)	1(1.33)
Greatly increased	2(2.74)	0(0.00)
Safety Results:		
Most Frequent Adverse Events – On-Therapy	Dutasteride	Placebo
Subjects with any AE(s), n(%)	n (%)	n (%)
Nasopharyngitis	12(16.44)	7(9.33)
Sexual dysfunction	3(4.11)	3(4.00)
Dyspepsia	2(2.74)	1(1.33)
Gastroesophageal reflux disease	2(2.74)	1(1.33)
Arthralgia	2(2.74)	0(0.00)
Asthenia	2(2.74)	0(0.00)
Gastritis	2(2.74)	0(0.00)
Musculoskeletal pain	2(2.74)	0(0.00)
Abdominal pain upper	1(1.37)	2(2.67)
Fatigue	1(1.37)	2(2.67)
Headache	1(1.37)	2(2.67)
Insomnia	1(1.37)	2(2.67)
Abdominal discomfort	0(0.00)	2(2.67)
Serious Adverse Events - On-Therapy		
	Dutasteride	Placebo
Subjects with non-fatal SAEs, n (%)	n (%) [related]	n (%) [related]
Thyroid cancer	0	1 (1.33) [0]
Subjects with fatal SAEs, n (%)	0	0

Conclusion: This study demonstrated dutasteride 0.5mg /day administered for 6 months was well tolerated and slowed the progression of hair loss and increased hair growth in Korean men. For hair counts as assessed by macrophotography in the vertex at 6 months (primary endpoint), the dutasteride 0.5mg group was significantly superior to the placebo group. The hair count difference at 6 months between dutasteride and placebo group was 7.5 ± 20.4 (95% CI = 0.8, 14.3). The overall incidence of adverse events and adverse drug reactions during treatment was similar in the two groups.. The most commonly reported adverse event in both groups was nasopharyngitis. One serious adverse event was reported during the trial (thyroid cancer in the placebo group).

Publications: None at the time of this report