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Study No.: ARIF 4005
Title: Prospective, national, multicentre, non comparative study evaluating the improvement of urinary symptoms, discomfort and quality of life in subjects with benign prostatic hyperplasia (BPH) after 24 weeks of treatment by dutasteride.
Rationale: Benign prostatic hyperplasia (BPH) is a frequent pathology in men aged over 50 years and the low urinary tract symptoms, very often associated with a subject discomfort, are the most representative clinical manifestations of the disease that are able to worsen the quality of life of the affected subjects. Dutasteride is a dual inhibitor of 5- α -reductase enzyme (types 1 and 2), responsible of testosterone conversion to dihydrotestosterone. The aim of this study was to evaluate the change in urinary symptoms, subject discomfort, and quality of life in subjects with BPH following treatment with dutasteride.
Phase: III B
Study Period: From June 2002 to January 2005
Study Design: This was a prospective, non comparative (open label), multicentre study evaluating during 24 weeks the efficacy and safety of dutasteride 0.5 mg per day in symptomatic BPH subjects with a prostate volume of at least 30 cm. ³
Centres: 113 initiated sites and 72 recruiting sites in France
Indication: BPH
Treatment: Oral administration of Dutasteride 0.5 mg, once a day
Objectives: The aim of this study was to evaluate the improvement by dutasteride of urinary symptoms, subject discomfort and quality of life in BPH.
Primary Outcome/Efficacy Variable: The primary endpoint was to identify the proportion of subjects who achieve a reduction of at least 3 points from baseline in the International Prostate Symptom Score (IPSS) after 24 weeks of treatment. Predictive factors of IPSS evolution have been evaluated in a multivariate model.
Secondary Outcome/Efficacy Variable(s): The secondary endpoints evaluated: discomfort and quality of life evolution by IPSS item 8 score, BPH Impact Index (BII) score and by Visual Analog Scales (VAS) at baseline, week 12 and week 24.
Statistical Methods: The primary population for analysis was the Intent to Treat population (ITT). The primary analysis was also performed on the Per Protocol (PP) population to confirm Full Analysis Set (FAS) population results. As it was planned in the Reporting Analysis Plan, that the secondary analyses were only done on the ITT population because the PP population was higher than 80% of the ITT population (83%). The primary efficacy endpoint was the proportion of subjects who achieved a reduction of at least 3 points from baseline in the IPSS score after 24 weeks of treatment. It was described with the associated 95% confidence interval on the ITT population. The probability of a reduction of at least 3 points from baseline in the IPSS score after 24 weeks of treatment was modelised with a multivariate logistic regression with the IPSS score at inclusion as a covariate and any factor recorded at baseline previously judged significant by a univariate logistic. All safety analyses were performed on Safety Population
Study Population: Male outpatients at least 50 years old, with a diagnosis of symptomatic BPH confirmed by medical history and clinical examination, requiring medical treatment by dutasteride according to the urologist, with a benign prostate hypertrophy greater than or equal to 30 grams on digital rectum examination (DRE). Previous history of prostate cancer, previous history of prostate surgery or other invasive procedures to treat BPH, any clinically significant abnormal signs on breast examination, previous history of spontaneous acute urinary retention represented the main exclusion criteria.

Number of Subjects:	
Planned, N	382
Randomised, N	400
Completed, n (%)	328 (82)
Total Number Subjects Withdrawn, N (%)	72 (18)
Withdrawn due to Adverse Events n (%)	44 (11)
Withdrawn due to Lack of Efficacy n (%)	0
Withdrawn for other reasons n (%)	28 (7)
Demographics	
N (ITT) all patients having received at least one dose of study treatment and undergone a primary endpoint evaluation	366
Male	366 (100)
Mean Age, years (SD)	66 (8.1)
Caucasian, %	99%
Primary Efficacy Results:	
Change in IPSS score	Dutasteride N=366
n	313
Mean Baseline IPSS score	15.3 ± 6.4
Mean IPSS score at week 24	9.1 ± 5.6
Mean change from baseline to week 24	-6.2
95% CI	-6.9, -5.5
p-value	<0.001
Secondary Outcome Variables	
Mean baseline BII score	5.1 ± 2.9
Mean baseline discomfort VAS score	48.9 ± 20.0
Change in IPSS score-Item 8	Dutasteride N=366
n	332
Change from baseline to week 12	-5.2
95% CI	-5.8, -4.6
n	349
Change from baseline to endpoint	-5.7
95% CI	-6.4, -5.0
n	311
Change from week 12 to week 24	-0.9
95% CI	-1.3, -0.4
BII score	
Change from baseline to week 12	-2.0
Change from week 12 to week 24	-0.2
Satisfaction	
Mean score week 12	61.7
Mean score week 24	63.4
Discomfort	
Change from baseline to week 12	-17.8
Change from week 12 to week 24	-2.0
Safety Results:	
Most Frequent Adverse Events (AEs) -On-Therapy	

Safety Population	Dutasteride N=399
No. of Subjects with AEs during treatment period, n (%)	157 (39%)
Any adverse event during treatment period	273
Libido decreased	16 (4%)
Erectile dysfunction	12 (3%)
Erection decreased	9 (2%)
Gynecomastia	6 (2%)
Impotence	6 (2%)
Abdominal pain	4 (1%)
Constipation	4 (1%)
Diarrhoea	4 (1%)
Micturition burning	4 (1%)
Pollakiuria	4 (1%)
Serious Adverse Events (SAEs) – On-Therapy N (%) [n considered by the investigator to be related to study medication]	
	Dutasteride N=399
Subjects with non-fatal SAEs, n (%)	22 (6)
Reproductive system and breast disorders	1 (<1) [0]
Gastrointestinal disorders	1 (<1) [0]
Renal and urinary disorders	6 (2) [0]
Respiratory, thoracic and mediastinal disorders	2 (<1) [0]
Vascular disorders	1 (<1) [0]
Cardiac disorders	2 (<1) [0]
Infections and infestations	1 (<1) [0]
Injury, poisoning and procedural complications	1 (<1) [0]
Neoplasms benign, malignant and unspecified (including cysts and polyps)	6 (2) [0]
Hepatobiliary disorders	1 (<1) [0]
Subjects with fatal SAEs, n (%)	5 (1)
Hemiplegia (study discontinued 12 weeks before SAE)	1 (<1) [0]
Heart failure (8 weeks after starting study drug)	1 (<1) [0]
Myocardial infarction (7 weeks after starting study drug)	1 (<1) [0]
Unknown cause of death (11 weeks after starting study drug)	1 (<1) [0]
Myelodysplastic syndrome (study discontinued 12 weeks before SAE)	1 (<1) [0]
Conclusion: In conclusion, these results show that in real-life clinical practice, dutasteride is well tolerated and significantly improves urinary symptoms, quality of life and patient discomfort and satisfaction after 12 and 24 weeks of treatment. Thus, this study adds to the growing body of evidence establishing dutasteride as an effective treatment option for men with BPH.	
Publications: Desgrandchamps F, Droupy S, Irani J, Saussine C, Comenducci A. Effect of dutasteride on the symptoms of benign prostatic hyperplasia, and patient quality of life and discomfort, in clinical practice. BJU International 2006; 98(1): 83-88	

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