The efficacy and tolerability of tarafenacin, a new muscarinic acetylcholine receptor M3 antagonist in patients with overactive bladder; randomized, double-blind, placebo-controlled phase 2 study

Junsoo Park[1], Miho Song[1], Jang Hwan Kim[2], Ji-Yeon Han[3], Jeong Zoo Lee[4], Seung-June Oh[5], Ju Tae Seo[6], Jong Bo Choi[7], Kun Suk Kim[1], Sungchan Park[8], Won Hee Park[9], Myung-Soo Choo[1]

[1]Department of Urology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, [2]Department of Urology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, [3]Department of Urology, Pusan National University Yangsan Hospital, Pusan, [4]Department of Urology, Pusan National University Hospital, Busan, Korea, [5]Department of Urology, Seoul National University Hospital, Seoul, Korea, [6]Department of Urology, Cheil General Hospital & Women's Helathcare Center, Kwandong University College of Medicine , Seoul, Korea, [7]Department of Urology, Ajou University Hospital, Suwon, Korea, [8]Department of Urology, Ulsan University Hospital, Ulsan, Korea, [9]Department of Urology, Inha University College of Medicine, Incheon, Korea

Introduction

Tarafenacin is a new quinuclidinol derivative, and has been developed to overcome the limitations of current antimuscarinic agents. It exhibits the highest selectivity of human M3 vs. M2 subtype of any other reference antagonists tested, therefore predicting a safe cardiovascular profile.

Purpose

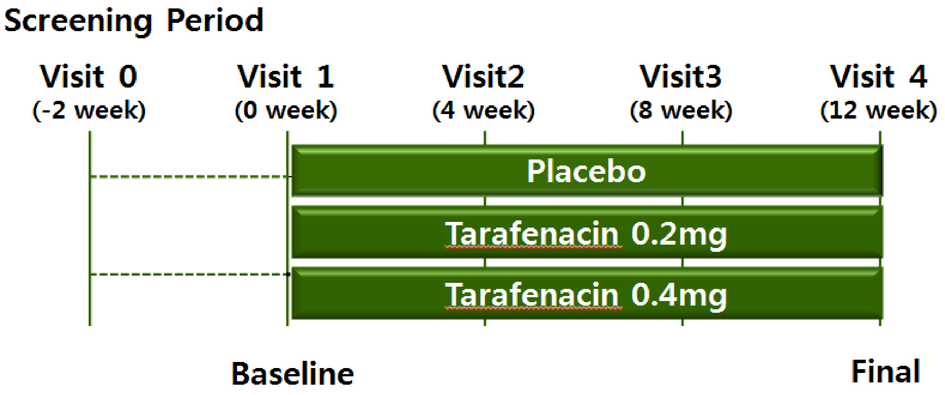
The aim of this study to evaluate the dose-response relationship of tarafenacin, an antimuscarinic agent in development phase, for efficacy and safety, at daily doses of 0.2mg and 0.4mg for the treatment of overactive bladder (OAB)

Materials and Methods

✓A 12-week, multi-center, prospective, double-blinded, randomized, parallel, placebo-controlled phase II study

✓ Institution : Multicenter, 8 General Hospitals in Korea

✓ Trial Period : Sep 2011 ~ Aug 2012



This study was sponsored by Kwang Dong Pharmaceutical Corporation, Ltd.

Results

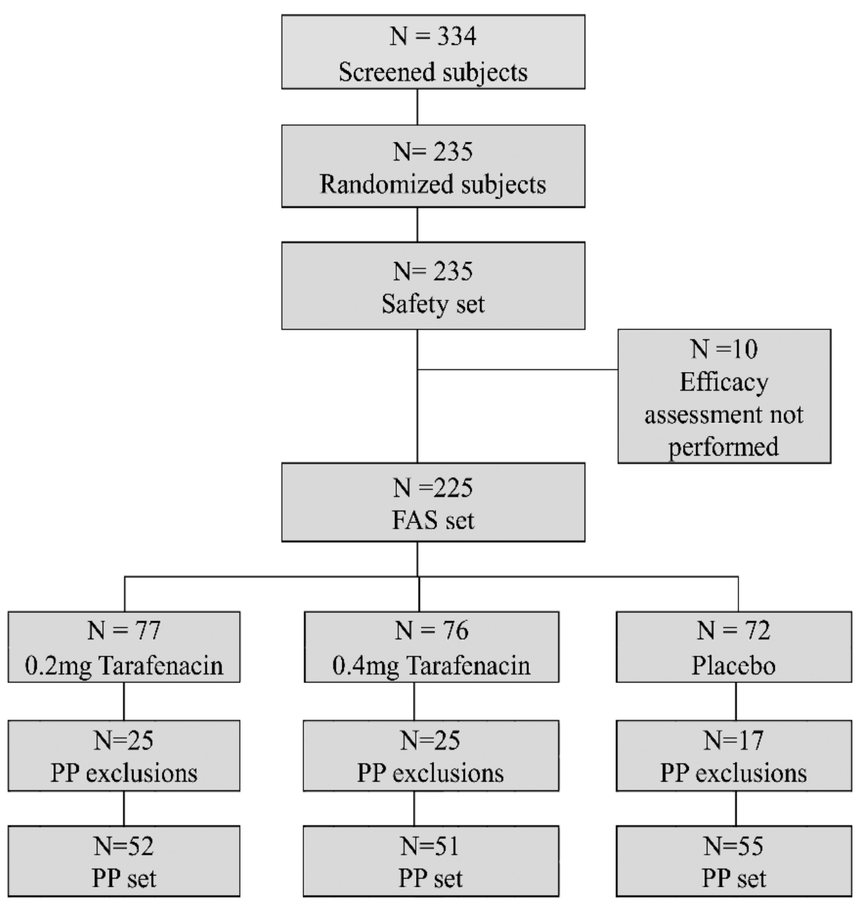


Figure 1. Patient disposition

		Tarafenacin 0.2mg(N=77)	Tarafenacin 0.4mg(N=76)	Placebo (N=72)	P-value
Age (years)	Mean±SD	59.00±10.59	60.18±10.84	58.35±12.44	0.605
	Min~Max	20.05~79.39	29.33~78.94	22.20~78.84	
Gender	Male	29	26	21	0.546*
	Female	48	50	51	
OAB symptom duration (yr)	Mean±SD	7.53±8.92	7.12±8.63	7.29±7.27	0.954
	Min~Max	0.50~42.39	0.54~42.02	0.53~30.26	
frequency	Mean±SD	11.40±2.63	11.42±3.98	12.10±4.32	0.426
	Min~Max	7.67~18.67	7.33~32.67	8.00~29.33	
Urgency	Mean±SD	5.51±3.70	5.95±4.96	6.30±4.62	0.559
	Min~Max	2.00~17.00	1.33~32.67	2.00~23.33	
Urge incontinence	Mean±SD	0.94±1.86	0.95±1.90	1.21±2.15	0.637
	Min~Max	0.00~9.00	0.00~12.00	0.00~10.00	
Nocturia	Mean±SD	1.32±0.94	1.61±1.19	1.62±1.42	0.207
	Min~Max	0.00~4.33	0.00~8.33	0.00~8.00	

Table 1. Patient demographics at baseline.

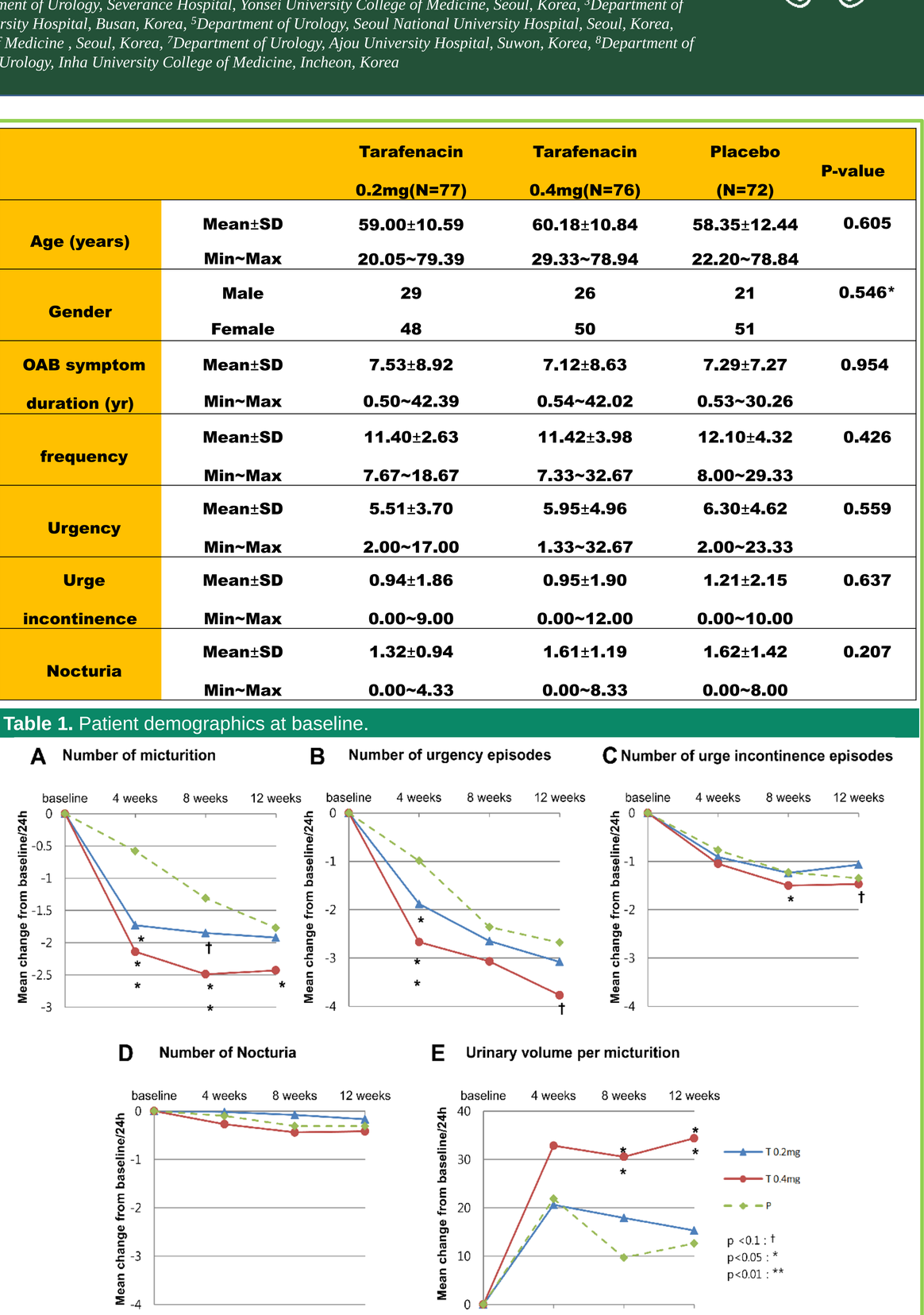


Figure 2. (A) The mean changes in the number of micturitions per 24 hours (B) The mean changes in the number of urinary urgency episodes per 24 hours (C) The mean changes in the number of urinary urge incontinence episodes per 24 hours (D) The mean changes in the number of nocturia incontinence episodes per 24 hours (E) The mean changes in the urinary volume per micturitions

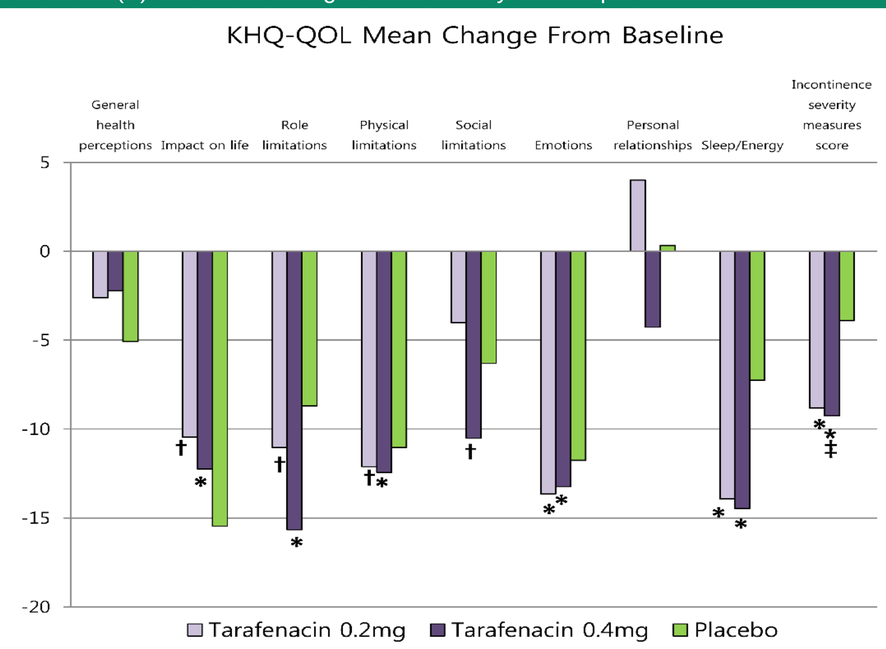


Figure 3. Mean change from baseline to week 12 in Kivieing's Health Questionnaire – Quality of Life. †p<0.005 and *p<0.001 compared to baseline, ‡p<0.005 compared to placebo. KHQ-QOL = King's Health Questionnaire – Quality of Life

Conclusions

Tarafenacin 0.4mg decreased the number of micturitions in patients with OAB after 12 weeks comparing placebo, and the dose-response relationship of tarafenacin 0.2 mg and 0.4 mg was confirmed. Both dose levels of tarafenacin were well tolerated.