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Letter to the Editor

Reply to Stephen Shei-Dei Yang and Shang-Jen Chang's Letter to the Editor re: Christopher R. Chapple, Francesco Montorsi, Teuvo L.J. Tammela, et al. Silodosin Therapy for Lower Urinary Tract Symptoms in Men with Suspected Benign Prostatic Hyperplasia: Results of an International, Randomized, Double-Blind, Placebo- and Active-Controlled Clinical Trial Performed in Europe. Eur Urol 2011;59:342–52

Thanks very much for your interesting response to our article [1].

We can see how the entry criteria to the study relating to maximum flow rate (Q_{max}) might appear anomalous to the observer. Table 1 of the paper [1] refers to the demographic and baseline characteristics of the study population (any patient who took at least one capsule as part of the double-blind clinical study). For this reason, the table includes data from protocol violators who were subsequently excluded from the main analysis.

You mention that a responder is defined in our study as a subject who shows a 30% increase in Q_{max}, and you enquired how many patients could therefore be categorised as responders during the washout period. In Table 1, we show the data regarding the Q_{max} responder rate during the run-in period for nonrandomised patients (first column) and for patients randomised to placebo, silodosin, and tamsulosin, respectively, in addition to the overall results (safety population). In Table 2, we show the data regarding the Q_{max} responder rate during the run-in period in the intention-to-treat population.

Because Q_{max} is dependent on voided volume, the question has been raised whether the increase in Q_{max} in both treatment and placebo groups might be secondary to the increase in voided volume rather than to alleviation of bladder outlet obstruction. The response shown in Table 3 includes data relating to voided volume values by treatment and by visit, and Table 4 shows data relating to the voided volume by treatment and at end point.

Table 1 – Maximum flow rate (Qmax) responder during run-in (safety population)

	Treatment (character)								All	
	Nonrandomised		Placebo		Silodosin 8 mg		Tamsulosin 0.4 mg			
	N	%	N	%	N	%	N	%	N	%
Qmax Responder										
Yes	24	15.4	33	17.4	65	17.1	64	16.7	186	16.7
No	132	84.6	157	82.6	316	82.9	320	83.3	925	83.3
All	156	100.0	190	100.0	381	100.0	384	100.0	1111	100.0

Table 2 – Maximum flow rate (Qmax) responder during run-in (intention-to-treat [ITT] population)

ITT population	Treatment (character)						All	
	Placebo		Silodosin 8 mg		Tamsulosin 0.4 mg			
	N	%	N	%	N	%	N	%
Qmax Responder								
Yes	32	17.3	62	16.7	63	16.8	157	16.8
No	153	82.7	309	83.3	313	83.2	775	83.2
All	185	100.0	371	100.0	376	100.0	932	100.0

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Table 3 – Voided volume (intention to treat population)

	Treatment (character)					
	Placebo		Silodosin 8 mg		Tamsulosin 0.4 mg	
	Voided volume		Voided volume		Voided volume	
	N	Mean	N	Mean	N	Mean
Reassigned Visit						
Placebo Run-in	185	229.3	371	223.7	376	222.5
Baseline	185	219.4	371	228.0	375	221.6
Week 1	185	252.3	371	255.2	376	246.9
Week 2	184	240.0	370	264.6	373	256.7
Week 4	182	241.8	368	264.2	370	250.6
Week 8	178	252.2	363	265.8	367	255.7
Week 12	172	248.4	357	269.5	365	254.8

Table 4 – Voided volume at end point (intention-to-treat population)

Treatment (character)					
Placebo		Silodosin 8 mg		Tamsulosin 0.4 mg	
Voided volume		Voided volume		Voided volume	
N	Mean	N	Mean	N	Mean
184	247.6	371	268.6	376	256.7

As you correctly state, experts suggest a voided volume of ≥150 ml to be adequate for interpretation of uroflow study including Q_{max}. You enquire why we chose a smaller volume of 125 ml and question whether the increase of Q_{max} in the placebo group was just secondary to the increase of voided volume. We answer that many important studies, including the Medical Therapy of Prostatic Symptoms study [2], the Combination of Avodart and Tamsulosin study [3], and the phase 2 and 3 trials carried out in Europe to obtain the registration of the tamsulosin oral controlled absorption system formulation [4,5], have all used similar cut-off values. Indeed, as you can see, the mean voided volumes were much higher.

Your final point related to the heterogeneity of the patients, due to inadequate screening of uroflowmetry, accounting for the relatively higher responder rate (50.8% for the International Prostate Symptom Score and 40.5% for Q_{max}) in the placebo group compared with historical series. We feel that adequate randomisation and sample size plus adequate screening of uroflowmetry would have dealt with any heterogeneity, and we feel that the evidence stands as published, based on the findings of this study.

It is certainly interesting that there is a higher responder rate than in many historical series on placebo.

Conflicts of interest: The author has nothing to disclose.

References

[1] Chapple CR, Montorsi F, Tammela TLJ, Wirth M, Koldewijn E, Fernández Fernández E, on behalf of the European Silodosin Study Group. Silodosin therapy for lower urinary tract symptoms in men with suspected benign prostatic hyperplasia: results of an international, randomized, double-blind, placebo- and active-controlled clinical trial performed in Europe. Eur Urol 2011;59: 342–52.

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