

DARIFENACIN EFFECTIVELY RELIEVED OVERACTIVE BLADDER SYMPTOMS AS EARLY AS 6–8 DAYS OF INITIATING TREATMENT

Hypothesis / aims of study

Overactive bladder (OAB) is characterised by urgency and other bothersome symptoms such as incontinence episodes (IEs), frequent micturition and nocturia [1,2]. OAB is associated with a significant negative impact on patients' quality of life. Hence, rapid onset of effect is desirable in OAB therapy and knowledge about onset of treatment effects can be important for clinicians when setting a patient's expectations of OAB therapy. This retrospective analysis of data from completed phase III studies was designed to assess time-to-effect with darifenacin treatment.

Study design, materials and methods

Efficacy and safety data were pooled from three, double-blind 12-week studies of 1,059 patients (19–88 years, 85% women) with symptoms of OAB for ≥ 6 months (5–50 IES/week; ≥ 8 voids/day; ≥ 1 urgency episodes/day) randomised to receive darifenacin 7.5 mg (two studies) or 15 mg (all studies) once daily, or placebo [3]. Electronic bladder symptom diaries were completed daily for 1–2 weeks prior to each visit (baseline, Week 2, Week 6, Week 12) by recording number of IEs/week, micturitions and urgency episodes/day. To minimise day-to-day variability, early available diary data (for IEs, micturitions and urgency episodes/day) were analysed by averaging 3-day periods starting with Days 12–14. If statistical significance was found in this period then Days 9–11 were subsequently analysed; using this method, earlier time segments were explored. Non-parametric statistical methods were applied to each segment and by visit analysis (Week 2, Week 6, Week 12).

Results

The analysis population included 1,053 patients. Statistically significant improvements versus placebo were observed with darifenacin 7.5 mg and 15 mg in OAB symptoms analysed at Weeks 2, 6 and 12 (Table 1). At the earlier timepoints analysed, Days 6–8, 9–11 and 12–14, both doses of darifenacin resulted in statistically significant improvements in OAB symptoms compared with placebo as shown in Table 2. Adverse events were generally mild-to-moderate in severity and infrequently resulted in treatment discontinuation.

Interpretation of results

Darifenacin 7.5 mg and 15 mg produced statistically significant reductions in bothersome OAB symptoms from as early as Week 2, which were maintained throughout the study. Furthermore, analysis of earlier data demonstrated significant improvements in specific OAB symptoms within 6–8 days of initiating treatment.

Concluding message

Darifenacin 7.5 mg and 15 mg have a rapid onset of effect in significantly reducing bothersome symptoms of OAB.

Table 1. Median change from baseline for OAB symptoms analysed at weekly timepoints: absolute and (per cent) values

	Weeks	Placebo 7.5 mg	for Darifenacin 7.5 mg	Placebo 15 mg	for Darifenacin 15 mg
IEs/week, (%)	n 2	-3.9 (-27.6)	-5.5 [‡] (-39.3) [‡]	-4.4 (-32.9)	-8.1 [‡] (-55.9) [‡]
	6	-5.4 (-42.8)	-8.1 [‡] (-58.8) [‡]	-6.5 (-49.5)	-9.8 [‡] (-71.0) [‡]
	12	-7.2 (-54.9)	-9.0 [‡] (-69.1) [‡]	-7.9 (-58.6)	-11.0 [‡] (-77.9) [‡]
Micturitions/ day, n (%)	2	-0.3 (-3.2)	-0.9 [‡] (-8.2) [‡]	-0.3 (-3.2)	-0.9 [‡] (-8.8) [‡]
	6	-0.9 (-8.8)	-1.4 [‡] (-13.9) [‡]	-1.0 (-8.8)	-1.6 [‡] (-14.0) [‡]
	12	-1.0 (-9.5)	-1.8 [‡] (-17.2) [‡]	-1.1 (-10.5)	-1.9 (-17.5) [‡]
Urgency episodes/day, n (%)	2	-0.5 (-6.0)	-1.1 [‡] (-15.0) [‡]	-0.6 (-6.3)	-1.2 [‡] (-15.9) [‡]
	6	-1.0 (-12.8)	-1.6 [‡] (-23.4) [‡]	-1.1 (-13.7)	-2.0 [‡] (-25.0) [‡]
	12	-1.1 (-15.4)	-2.0 [‡] (-29.1) [‡]	-1.3 (-18.5)	-2.4 [‡] (-31.1) [‡]
UUIE/week	2	-3.2 (-31.6)	-5.0 [‡] (-41.4) [‡]	-3.9 (-35.1)	-7.2 [‡] (-59.6) [‡]
	6	-5.0 (-50.0)	-7.4 [‡] (-60.0) [‡]	-5.6 (-54.9)	-9.1 [‡] (-74.9) [‡]
	12	-6.3 (-58.4)	-8.0 [‡] (-71.0) [‡]	-7.1 (-63.2)	-9.3 [‡] (-80.3) [‡]
Severity of urgency, ^a (%)	2	-1.0 (-1.8)	-4.6 [‡] (-7.5) [‡]	-1.4 (-2.2)	-6.4 [‡] (-11.0) [‡]
	6	-3.0 (-5.7)	-7.6 [‡] (-13.3) [‡]	-3.3 (-5.8)	-8.3 [‡] (-14.8) [‡]
	12	-4.6 (-8.1)	-8.5 [‡] (-14.5) [‡]	-4.6 (-8.1)	-9.5 [‡] (-17.0) [‡]

IEs=incontinence episodes; UUIEs=urinary urge incontinence episodes; ^avisual analogue scale; [‡]p≤0.01; [‡]p≤0.001 for treatment difference vs placebo (Wilcoxon Rank Sum test stratified by study)

Table 2. Median treatment difference between darifenacin (7.5 mg and 15 mg) and placebo for OAB symptoms analysed in 3-day periods: absolute and (per cent) values

OAB symptom	Darifenacin dose	Median difference			
		Days (n=244–354)	6–8 Days (n=250–360)	9–11 Days (n=241–351)	12–14 Days
IEs/day	7.5 mg	-0.2 [‡] (-6.0) [‡]	-0.3 [‡] (-4.5) [‡]	-0.3 [‡] (-7.7) [‡]	
	15 mg	-0.5 [‡] (-13.2) [‡]	-0.5 [‡] (-11.5) [‡]	-0.6 [‡] (-12.2) [‡]	
Micturitions/day	7.5 mg	-0.3 [‡] (-3.6) [‡]	-0.6 [‡] (-5.8) [‡]	-0.5 [‡] (-5.1) [‡]	
	15 mg	-0.5 [‡] (-5.0) [‡]	-0.8 [‡] (-7.3) [‡]	-0.7 [‡] (-6.3) [‡]	
Urgency episodes/day	7.5 mg	-0.5 [‡] (-9.3) [‡]	-0.7 [‡] (-9.7) [‡]	-0.6 [‡] (-8.3) [‡]	
	15 mg	-0.9 [‡] (-11.1) [‡]	-1.1 [‡] (-13.5) [‡]	-1.0 [‡] (-13.1) [‡]	

IEs=incontinence episodes; [‡]p≤0.01; [‡]p≤0.001 for treatment difference vs placebo (Wilcoxon Rank Sum test stratified by study)

References

1. Irwin DE, et al. BJU Int 2006;97(1):96–100
2. Irwin DE, et al. Eur Urol 2008;53(5):1029–1037
3. Chapple C, et al. BJU Int 2005;95:993–1001

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Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	No
This study did not require ethics committee approval because	This study is a post-hoc analysis
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes