

IMPACT OF 'DRY DAYS' ON QUALITY OF LIFE IN PATIENTS WITH 'WET' OVERACTIVE BLADDER: RESULTS OF A POOLED ANALYSIS OF THREE PHASE III STUDIES WITH DARIFENACIN

Hypothesis / aims of study

Urge incontinence is a core symptom of overactive bladder (OAB), affecting 37% of patients with OAB (1). Patients with urge incontinence (referred to as 'wet' OAB) typically have poorer health-related quality of life (HRQoL) and seek help from health care professionals (2). This pooled analysis aimed to evaluate the effects of darifenacin on number of 'dry days' and associated HRQoL.

Study design, materials and methods

Efficacy and safety data were pooled from three multicenter, randomized, double-blind, placebo-controlled 12-week studies with fixed-doses of darifenacin. Each study consisted of a 2-week treatment-free or placebo run-in period, followed by 12 weeks' treatment with placebo or fixed-doses of darifenacin 7.5 or 15 mg once daily. Patients were ≥ 18 years with symptoms of overactive bladder for ≥ 6 months. Electronic bladder diaries were used to determine the number of patients with ≥ 3 consecutive dry days. Improvements in HRQoL were assessed using the King's Health Questionnaire (KHQ). The KHQ is fully validated to assess HRQoL in both women and men with lower urinary tract dysfunction, including OAB. KHQ scores were analyzed for patients achieving ≥ 3 consecutive dry days vs. patients with 0–2 consecutive dry days. Tolerability and safety were evaluated from withdrawal rates and adverse events (AEs).

Results

Of 1059 patients randomized to treatment, 1053 were included in the full analysis population evaluated here. After 12 weeks of treatment, significantly more patients on darifenacin had ≥ 3 consecutive dry days, regardless of baseline OAB severity (moderately severe/severe OAB defined as ≥ 14 incontinence episodes/week, mild OAB defined as < 14 incontinence episodes/week) compared with placebo (darifenacin 7.5 mg 49% vs placebo 35.2%, $p < 0.001$; darifenacin 15 mg 56.3% vs placebo 39.8%, $p < 0.001$). When data for all doses were combined, 52.6% of patients achieved ≥ 3 consecutive dry days with darifenacin compared with 39.8% with placebo ($p < 0.001$). Overall, patients receiving darifenacin who achieved ≥ 3 consecutive dry days had statistically significant improvement in KHQ scores versus placebo after 12 weeks of treatment in 5 out of 9 KHQ domains ($p < 0.03$): Scores for Role Limitations, Emotions and Severity Measures domains were statistically significantly greater with both darifenacin doses compared with placebo. In addition, for darifenacin 7.5 mg, statistical significance was also reached for the Incontinence Impact and Social Limitations domains. Patients were further characterized based on those that achieved ≥ 3 consecutive dry days vs those that did not have 3 consecutive dry days. For the patients that have achieved 3 consecutive dry days, substantially greater improvements were seen in all 9 KHQ domains (Fig 1). Furthermore, only patients achieving ≥ 3 consecutive dry days had significant improvements in General Health and Personal Relationships domains of the KHQ. For all 9 KHQ domains, the adjusted mean improvement was statistically significantly higher for patients that achieved 3 consecutive dry days at 12 week compared to those that did not achieve 3 consecutive dry days. The most common all-causality AEs were dry mouth (darifenacin 7.5 mg 20.2%, 15 mg 35.3% and placebo 8.2%) and constipation (darifenacin 7.5 mg 14.8%, 15 mg 21.3% and placebo 6.2%) (3). However, it appears as though patients tolerated these side effects as discontinuation rates due to dry mouth and constipation were low (darifenacin 7.5 mg 0.6%, 15 mg 2.1% and placebo 0.3%).

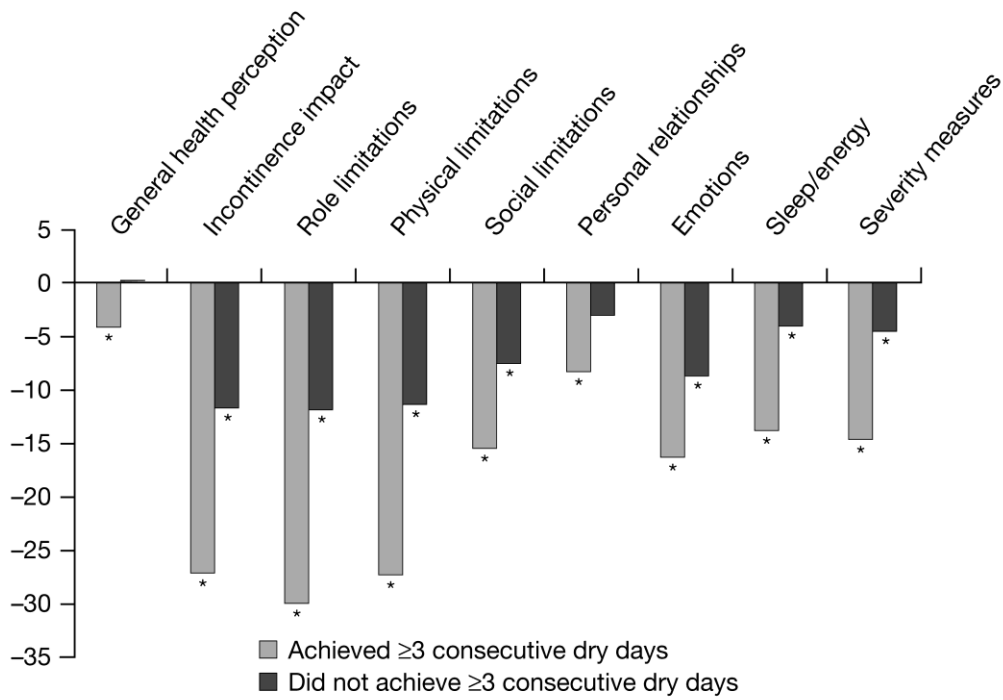
Interpretation of results

A significantly greater proportion of patients receiving darifenacin achieved ≥ 3 consecutive dry days compared with placebo. When results for all treatment groups were pooled in a post-hoc analysis, greater improvements in KHQ domains were observed in patients who had ≥ 3 consecutive dry days compared with those who did not. Notably, the improvements in General Health and Personal Relationships were only significant in patients with ≥ 3 consecutive dry days. Common AEs were mild and infrequently led to discontinuation.

Concluding message

Darifenacin treatment is associated with an increase in the number of patients achieving ≥ 3 consecutive dry days, which is associated with improved HRQoL in patients with 'wet' OAB.

Figure1. Change from baseline in KHQ domains at Week 12 (all darifenacin doses)



*p<0.001 Week 12 vs baseline

References

1. Stewart WF et al. World J Urol 2003;20:327–336
2. Abrams P et al. Am J Manag Care 2000;6:S580–S590
3. Chapple C et al. BJU Int 2005;95:993–1001

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Is this a clinical trial?	Yes
Is this study registered in a public clinical trials registry?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes
Specify Name of Ethics Committee	Data taken from 3 multicentre Phase III trials. The study protocol was approved in writing prior to its start by an independent Ethics Committee whose constitution was appropriate for the countries in which the study was to be performed. Ethical approval was gained for each centre.
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes