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EFFICACY, TOLERABILITY AND SAFETY OF LONG-TERM DARIFENACIN TREATMENT IN OLDER PATIENTS WITH OVERACTIVE BLADDER: ANALYSIS OF RESULTS FROM A 2-YEAR, OPEN-LABEL EXTENSION STUDY

Hypothesis / aims of study

Overactive bladder (OAB) is a chronic condition that increases in prevalence with advancing age in both men and women. Drug therapy for OAB usually involves treatment with antimuscarinic agents, which are thought to act by blocking the M_3 muscarinic receptors in the bladder that mediate detrusor contractions. However, there are many potential challenges and difficulties faced by physicians when prescribing these antimuscarinic medications to older patients. For example, this subgroup are thought to tolerate anticholinergics less well than younger patients, and are frequently prescribed multiple co-medications, which could lead to high anticholinergic burden. Since data on OAB treatments in older patients are limited, this analysis was conducted to determine the long-term efficacy, tolerability and safety of darifenacin, a muscarinic M_3 selective receptor antagonist, in patients with OAB aged ≥65 years.

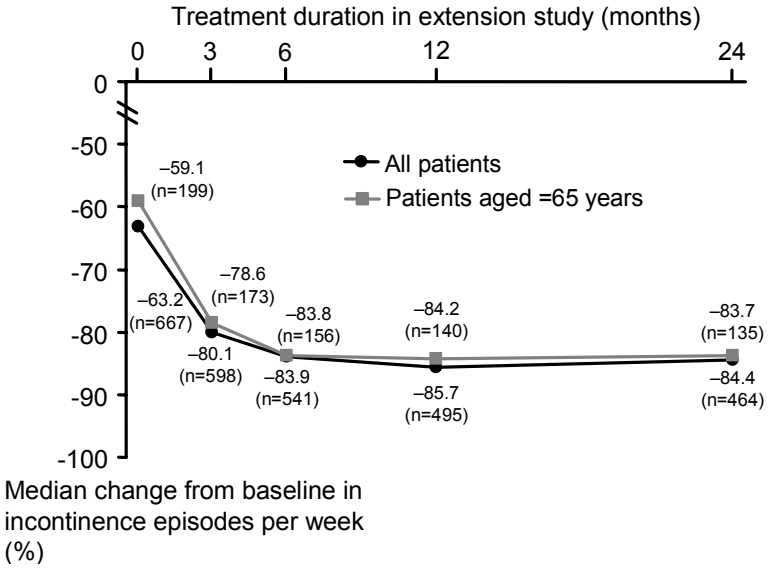
Study design, materials and methods

This was a subgroup analysis, in older patients aged ≥65 years, of a multicenter, open-label, non-comparative, 2-year extension study, in which the efficacy, tolerability and safety of darifenacin prolonged-release 7.5 or 15 mg once daily (od) was evaluated in patients aged ≥18 years with OAB symptoms for ≥6 months. Eligible patients had completed one of two Phase III 12-week, placebo-controlled, double-blind feeder studies [1, 2]. Following this, patients received darifenacin 7.5 mg od for the first 2 weeks of the extension and were then offered the option to increase their dose to 15 mg od if greater efficacy was required and the lower dose was well tolerated. Subsequent dose titration between 7.5 and 15 mg od was permitted according to clinical need and tolerability, following discussion with the investigator. Efficacy was assessed from patient diary data, and tolerability and safety were evaluated at various intervals throughout the extension study.

Results

214 patients aged 65–89 years entered the extension and 137 (64.0%) completed, resulting in a total of 308 patient-years of drug exposure. Darifenacin produced significant median reductions in incontinence episodes (IEs)/week over the 2-year extension period (p<0.001), which were comparable to the reductions seen in the overall OAB population **(Figure 1).**

Figure 1. Median percentage change in incontinence episodes (treatment difference vs feeder-study baseline) during 24 months' treatment with darifenacin 7.5 and 15 mg od



Furthermore, darifenacin significantly reduced the median number of micturitions/day by –1.2 [–12.4%; p<0.001 vs feeder study baseline] and the median number of urgency episodes/day by –3.7 [–52.0%; p<0.001vs feeder study baseline] in older patients with OAB at the end of the extension study. Again, these results were consistent with the efficacy observed in the overall population where median reductions were –1.4 [–13.9%; p<0.001] for micturitions/day and –3.9 [–56.4%; p<0.001] for urgency episodes/day [3]. Compared to feeder-study baseline, responder rates of ≥50%, ≥70% or ≥90% reductions in IEs/week at feeder-study and extension-study end in the older population were also comparable with those of the overall population **(Figure 2)**.

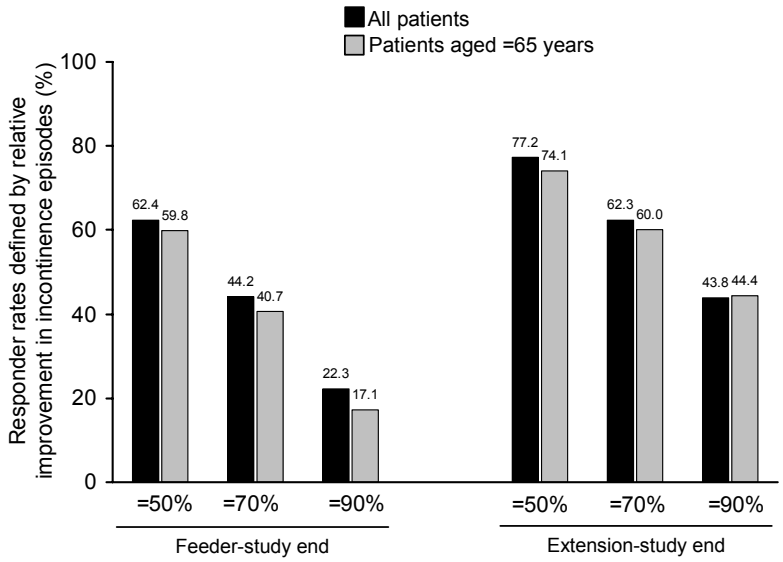


Figure 2. Responder rates of overall and older population to treatment with darifenacin 7.5 and 15 mg od, compared to feeder-study baseline

Importantly, darifenacin was well tolerated in the older OAB population and the most common all-causality adverse events (AEs) were constipation (24.3%) and dry mouth (23.8%), as expected with this drug class. The AE profile in the older population was consistent with that of the overall OAB population, where the incidence of constipation and dry mouth was 20.9% and 23.3% respectively.

Interpretation of results

This analysis demonstrates that the efficacy, tolerability and safety of the M_3 receptor antagonist, darifenacin, is maintained during 2 years of open-label treatment for OAB in patients aged ≥65 years, which is the first 24-month data reported with a prolonged-release antimuscarinic in this older patient population. Furthermore, darifenacin produced high sustained responder rates, and the efficacy, tolerability and safety results were consistent with those in the overall population [3], showing that darifenacin treatment is effective and well tolerated irrespective of age.

Concluding message

Darifenacin was associated with significant improvements in OAB symptoms with high, sustained responder rates and a favourable tolerability profile during 2 years of treatment in older patients, suggesting that darifenacin is an attractive choice for treating OAB in older patients.

References: [1] Haab F, et al. Eur Urol 2004;45:420–9; [2] Steers W, et al. BJU Int 2005;95:580–6; erratum in BJU Int 2005;95:1385–6; [3] Haab F, et al. BJU Int 2006; in press.

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HUMAN SUBJECTS: **This study was approved by the an independent ethics committee or independent review board at each trial centre and followed the Declaration of Helsinki Informed consent was obtained from the patients.**