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DARIFENACIN PROVIDES CLINICALLY MEANINGFUL QUALITY OF LIFE IMPROVEMENTS IN PATIENTS WITH OVERACTIVE BLADDER ASSESSED BY MINIMAL IMPORTANT DIFFERENCE (MID) ANALYSIS

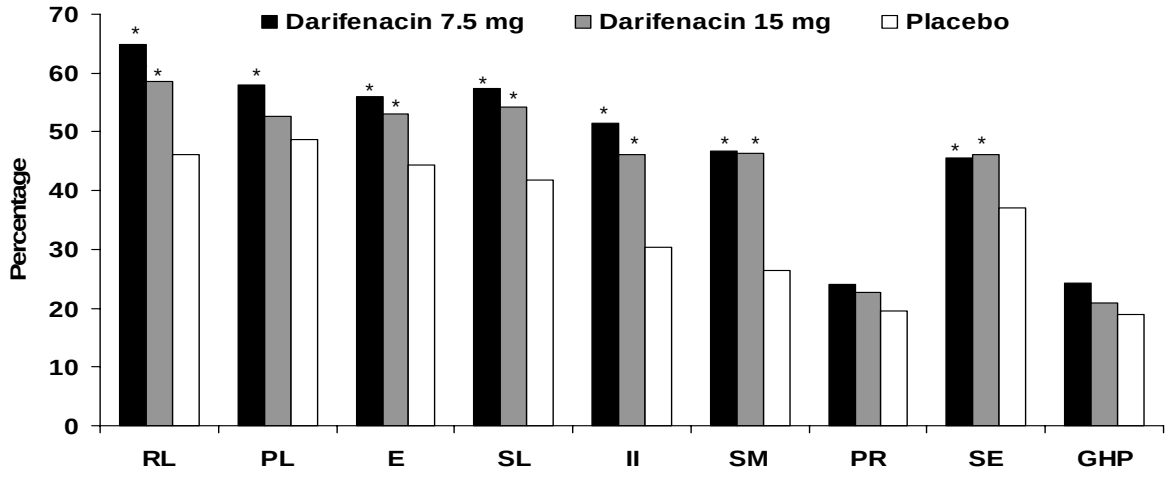
Hypothesis / aims of study
The efficacy, tolerability and safety of darifenacin in the treatment of overactive bladder (OAB) has been confirmed in clinical trials (1). Quality of life (QoL) assessments, using the King's Health Questionnaire (KHQ), have also showed significant patient benefit for darifenacin vs placebo. In the analysis presented here, improvements from baseline in QoL with darifenacin, observed using the KHQ, were further assessed by establishing a Minimal Important Difference (MID).

Study design, materials and methods
The results from three multicentre, double-blind, placebo-controlled studies of 1,059 adults with OAB, randomised to 12 weeks' once-daily (qd) treatment with darifenacin 7.5 mg (2 studies only, n=337), 15 mg (n=334) or placebo (n=388) were pooled for this analysis (1).

QoL was evaluated at baseline and after 12 weeks' treatment using the validated KHQ, incorporating seven multi-item domains: Role Limitations, Physical Limitations, Social Limitations, Personal Relationships, Emotions, Sleep and Energy, and Severity (Coping) Measures and an additional two questions addressing Incontinence Impact and General Health Perceptions. The change in QoL scores from baseline to Week 12 was determined, and the proportion of patients who exceeded the MID for each KHQ domain was calculated for darifenacin (pooled 7.5 and 15 mg qd) and placebo. MID criteria, obtained from a study in which patients received prolonged-release tolterodine (2), were calculated using Juniper's anchor-based technique that determined the mean decrease in KHQ domain scores for those patients reporting a 'small improvement in bladder condition' as described (3).

Results
A significantly higher proportion of darifenacin-treated than placebo-treated patients met or exceeded the MID for seven of the nine KHQ domains (see figure). The domains showing the greatest incremental benefit over placebo were the Incontinence Impact and Severity (Coping) Measures. Darifenacin also provided a significant benefit over placebo in four other domains affected by OAB (Role Limitations, Social Limitations, Emotions and Sleep and Energy). A significant difference compared with placebo was also observed in the Physical Limitations domain for darifenacin 7.5 mg qd. The two domains least likely to change in response to OAB treatment (Personal Relationships and General Health Perceptions) showed a smaller, non-significant benefit over placebo.

Figure. Percentage of darifenacin-treated patients exceeding the MID = small improvement in bladder condition.



Darifenacin 7.5 mg	64.9	58.0	56.0	57.4	51.5	46.7	24.1	45.5	24.3
Darifenacin 15 mg	58.5	52.7	53.0	54.2	46.1	46.4	22.6	46.1	20.9
Placebo	46.2	48.8	44.4	41.8	30.4	26.5	19.6	37.1	19.0

RL = Role Limitations; PL = Physical Limitations; E = Emotions; SL = Social Limitations; II = Incontinence Impact; SM = Severity Measures; PR = Personal Relationships; SE = Sleep and Energy; GHP = General Health Perception.
*Significantly different ($p<0.05$) from placebo using logistic regression.
MIDs are based on data from reference (2)

Adverse events were mostly mild to moderate; all-causality incidences were 54.0% (7.5 mg), 65.6% (15 mg) and 48.7% (placebo).

Interpretation of results

Darifenacin treatment resulted in a higher proportion of patients achieving or exceeding the MID for all nine KHQ domains compared with placebo. The difference between darifenacin and placebo was statistically significant for seven of the domains (Incontinence Impact, Severity Measures, Role Limitations, Physical Limitations [darifenacin 7.5 mg qd only], Social Limitations, Emotions, and Sleep and Energy). These findings support the clinical relevance of the improvements in KHQ achieved with darifenacin treatment.

Concluding message

Darifenacin resulted in statistically significant improvements in health-related QoL in patients with OAB compared with placebo, which met or exceeded MID values. Therefore, the proportion of patients achieving a clinically meaningful treatment response was significantly greater for the darifenacin group compared with the placebo group.

References

1. A pooled analysis of three phase III studies to investigate the efficacy, tolerability and safety of darifenacin, a muscarinic M_3 receptor antagonist, in the treatment of overactive bladder. BJU Int 2005;95(7):993–1001.
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