Efficacy and Safety of Propiverine Hydrochloride Extended-Release (ER) in Chinese Patients with Overactive Bladder
—— A Randomized, Double-Blind, Active Controlled Clinical Trial

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Introduction & Objective

- Overactive bladder (OAB) has currently a high incidence in China, especially in the elderly. The disease can seriously impair quality of life.
- Several options of anticholinergic treatment are available; however, blocking of cholinergic receptors may induce adverse effects because the receptors are distributed not only in the bladder but also in other organs.
- Propiverine, a benzylic acid derivative, is unique in having both anticholinergic and calcium-channel blocking effects. The former effects are known to suppress neurogenic detrusor contraction while the latter has a direct spasmylytic effect on the bladder.
- Pellet technology Acid Controlled Extended release System (ACES): sustained release formulation for Propiverine ER.
- The objective of the trial was to evaluate the efficacy and safety of propiverine hydrochloride 30mg ER capsules compared with tolterodine tartrate 4mg ER tablets in the treatment of Chinese patients with overactive bladder.

Methods

PATIENTS
- Male and female outpatients aged between 18 and 75 years old with OAB symptoms for at least 3 months were enrolled in the study.
- Patients were required to show urgency with or without urgency incontinence, frequency of ≥ 8 voidings/24h and voided volume ≤ 200ml during the 3-day voiding diary period before randomization.
- Clinical status of patients at baseline: the changes from baseline in the number of urinary incontinence episodes/24h were not significantly different between the two groups.

STUDY DESIGN AND TREATMENT
- A randomized, multicenter, double-blind, double-dummy, parallel group and active-controlled clinical study.
- After 2 weeks screening period, qualified patients were randomized at a ratio of 1:1 to treatment with 30mg propiverine ER or 4mg tolterodine ER once daily for 8 consecutive weeks.

ASSESSMENTS
- Efficacy was evaluated based on the 3-day voiding diary. Patients used the diaries to record voiding frequency, voided volume, and incontinence episodes.
- Safety was assessed by adverse events, laboratory tests, 12-lead electrocardiograms (ECG), and vital signs.

RESULTS OF PRIMARY EFFICACY ENDPOINT (Table 1, 2)

- The incontinence episodes/24h decreased throughout the treatment period in both groups. In FAS and PP population, the changes from baseline in the number of urinary incontinence episodes/24h were significantly greater in propiverine group compared to tolterodine group at all evaluation time points (2 and 8 weeks).
- In both FAS and PP population, there were no statistically significant differences between the two groups in the changes from baseline in mean number of voidings/24h after 2 weeks treatment, in the voided volume after 2 and 8 weeks of treatment and in the time of onset of drug effect.
- It was shown that a higher benefit proportion in patients’ self-assessment at 8 weeks for propiverine group than tolterodine group (p<0.007, in FAS).

RESULTS OF SECONDARY EFFICACY ENDPOINTS (Table 1, 2)

- The incidence of adverse events (AE) was comparable in 2 groups of FAS and PP.
- There were no significant differences between the propiverine and tolterodine group in the demographic or clinical characteristics at baseline.

Table 1 Efficacy endpoint results of full analysis set population

<table>
<thead>
<tr>
<th></th>
<th>Propiverine ER (n=162)</th>
<th>Tolterodine ER (n=162)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change from baseline in the number of voidings/24h</td>
<td>-4.5 ± 2.80</td>
<td>-4.2 ± 2.78</td>
</tr>
<tr>
<td>Mean voided volume</td>
<td>200 ± 72.17</td>
<td>202 ± 74.27</td>
</tr>
<tr>
<td>Mean incontinence episodes/24h</td>
<td>3.89 ± 2.95</td>
<td>3.58 ± 2.95</td>
</tr>
</tbody>
</table>

Table 2 Efficacy endpoint results of per-protocol population

<table>
<thead>
<tr>
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SAFETY RESULTS

- The incidence of adverse events (AE) was comparable in propiverine and tolterodine treatment groups (45.1% vs. 41.4%, p=0.5010).
- The difference of the incidence of adverse reactions (ADR) between the two groups had no statistical significance (40.7% vs. 39.5%, p=0.8207).
- The most frequent adverse reaction observed in both groups was dry mouth. (Table 3)

Table 3 Main adverse reactions in safety analysis population

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<th>Tolterodine ER (n=162)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>37 (23.0%)</td>
<td>32 (21.5%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (6.8%)</td>
<td>8 (5.4%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>9 (5.6%)</td>
<td>11 (7.2%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>9 (5.6%)</td>
<td>12 (7.9%)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>7 (4.3%)</td>
<td>6 (3.9%)</td>
</tr>
</tbody>
</table>

Conclusions

- The present study was the first randomized, controlled trial (RCT) that confirmed the efficacy and safety of propiverine ER 30mg in Chinese patients with OAB.
- Based on the results of the study, it can be concluded that propiverine, 30mg once daily for 8 weeks, is effective and well-tolerated for Chinese OAB patients. Therefore, propiverine ER is a suitable option for treatment of overactive bladder.

Acknowledgements

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