Hypothesis/Aim of study

- Reduction in nocturnal voids is the recommended clinical endpoint of nocturia. This has been shown to translate into improved health-related quality of life (HRQoL). But what constitutes a clinically meaningful improvement in voids and quality of life?
- The conventional approach was to establish a minimally important difference (MID) to see whether the additional treatment benefit of a medical intervention is higher than this MID threshold. There are a number of ways to evaluate this, based on group means.
- A recent scientific FDA recommendation is to provide evidence of a clinically meaningful treatment benefit on an individual basis. One should conduct responder analyses, as well as present cumulative distribution functions (CDFs). For a nocturia treatment, this translates into four segments:
  - A reduction from baseline of at least 1.2 voids or more per night (somewhat better)
  - A reduction from baseline of at least 1.7 voids or more per night (much better)
  - A reduction to less than 2 voids per night (threshold for bothersome nocturia according to the scientific literature [1])
  - Complete responders, i.e. dry nights or “cured from nocturia”

Methods

- Desmopressin orally disintegrating tablet (ODT) was assessed in two phase 3 double-blind randomised placebo-controlled trials of desmopressin ODT in males (50/75/µg; NCT01624254) and females (25/µg; NCT01223937) at multiple centers across the US and Canada, on adult subjects with nocturia. Our analyses focused on the Nocturnal Polyuria (NP) sub-population (approx. 90% of the study sample).
- Eligible patients had ≥2 voids per night determined via 3-day frequency-volume chart
- Patients completed the standard Nocturia Quality of Life (N-QoL) questionnaire at monthly visits [2]. N-Qol includes 12 questions with a total score ranging from 0 (low QoL) to 100 (high QoL). The logit of the responder probability was adjusted for the baseline number of nocturnal voids as covariate and treatment and age stratification as factors. The N-Qol total score is adjusted for baseline N-Qol total score

Results

Table 1. Responder analysis of reduction from baseline of at least 1.2 voids and reduction to less than 2 voids per night at Month 3

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Adjusted Responder Probability</th>
<th>Odds ratio</th>
<th>P-value (χ²-square test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women (n=540)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desmopressin ODT</td>
<td>75% / 36%</td>
<td>2.68 / 2.06</td>
<td>0.009* / 0.019*</td>
</tr>
<tr>
<td>Placebo</td>
<td>56% / 19%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men (n=541)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desmopressin ODT</td>
<td>59% / 29%</td>
<td>2.66 / 1.75</td>
<td>0.003* / 0.105*</td>
</tr>
<tr>
<td>Placebo</td>
<td>55% / 17%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: *At the 3 Month follow-up responders had a reduction of nocturnal voids from baseline that were about 1.5 voids larger than those of the non-responders (men: 1.57 voids; men: 3.59 voids, and women: 2.46 voids; men: 1.81 voids in the two responder groups respectively, with p<0.001 in all groups)

Graph 1: Cumulative distribution function for the mean change from baseline in N-Qol total score – women and men with a reduction from baseline of at least 1.2 voids per night (median in green)

Graph 2: Cumulative distribution function for the mean change green) from baseline in N-Qol total score – women and men with a reduction to less than 2 voids per night (median in green)

Interpretation of Results

- Space only permits a presentation of the responder definition of reduction from baseline of at least 1.2 voids and reduction to less than 2 voids, but the other two definitions present similar results, albeit with fewer patients
- More patients in the desmopressin ODT arms met these responder criteria after 3 months of treatment, as compared to placebo
- The different voiding responder definitions translate into substantial health-related quality of life benefits
- Scientific literature indicates that an N-Qol difference of about 6 points is clinically meaningful [3]

Concluding Message

- This approach allows the audience to assess whether a new treatment generates a clinically meaningful improvement to the patients
- The higher voiding response rates with desmopressin ODT compared to placebo, irrespective of the responder definition, indicate a relevant and clinically important treatment benefit across the NP patient population
- The published literature indicates that the QoL improvement could also be considered clinically meaningful [3]

REFERENCES


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