Existing evidence from clinical trial data suggests that a positive placebo effect occurs in overactive bladder (OAB) patients [1]. Researchers also confirmed that the placebo response in OAB clinical trials was substantial by a meta-analysis based on the change from baseline (CFB) outcomes at the end of the study period [2]. However, the time course of the placebo response in OAB clinical trials has not been systematically investigated via model-based analysis.

**Aims**

- To describe the time course of the placebo effect in OAB.
- To quantitatively investigate the covariates for the placebo response.

**Methods**

- We conducted a search of public data sources including new drug application (NDA) materials which had been published online for the study-level (mean) micturition frequency (MF) to develop the placebo effect model.
- Mean patient age, mean male proportion, baseline MF, and ethnicity (non-Japanese or Japanese) were tested as covariates.
- The parameter estimation was performed using NONMEM® 7.1.2 with the FOCE-I method.

**Data used for modelling**

- As a result of our search, study-level (mean) and longitudinal MF data were obtained from 17 clinical studies for anti-cholinergic (anti-muscarinic) agents and a beta-3 adrenergic agonist with 3,580 (from 36 to 508 in each study) placebo-arm patients.

**Results - Modelling**

- The exponential models rather than linear ones adequately described the time course of placebo effect with objective function value (OFV) reduction of 46.
- Placebo mean response (change from baseline) in MF for study i at week j with Nij placebo-arm patients can be written as

  \[
  \text{Mean } CFB \text{ } MF_{ij} = \left(-P_{max} \times (1 - \exp(-k \times \text{week}))+\frac{\sigma}{\sqrt{N_{ij}}} \times \varepsilon_{ij}\right)
  \]

  \[
  \varepsilon_{ij} \sim N(0,1)
  \]

- Ethnicity (non-Japanese or Japanese) was detected as a covariate on the rate constant for onset of the placebo effect (ki) with OFV reduction of 8 (Figure 2), which had already been suggested in clinical studies of fesoterodine, one of the anti-muscarinic agents [3].
  - Smaller k in Japanese.

**Conclusions**

- The (big) placebo effect in the OAB clinical trials is adequately described by an exponential model over time.
- The developed model could be the useful tool for the drug effect evaluation as well as the decision of clinical study period.

**Background**

- The existing evidence from clinical trial data suggests that a positive placebo effect occurs in overactive bladder (OAB) patients [1].
- Researchers also confirmed that the placebo response in OAB clinical trials was substantial by a meta-analysis based on the change from baseline (CFB) outcomes at the end of the study period [2].

**Aims**

- To describe the time course of the placebo effect in OAB.
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**References**

1. Mangera et al, Nat Rev Urol 2011;8(9):495-503
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