Depression is a common, recurrent and potentially serious illness that is associated with notable chronicity and disability. The WHO ranks major depression as one of the most burdensome diseases in the world. A recent U.S. survey of mental disorders revealed lifetime and 12-month prevalence estimates for Major Depressive Disorder of approximately 16% and 6%, respectively, with women exhibiting higher rates than men. Prevalence estimates for European populations suggest similar rates.

Placebo effect is an important component of the efficiency of antidepressant drug that has to be taken into account when predicting the time course and the efficiency of antidepressant drug.

The objective of this investigation was to develop a placebo response longitudinal model in depression as measured with the Hamilton Depression Rating Scale (HDRS) accounting for dropout.

Methods

Data

Data from 8-week double blind, placebo-controlled study were used. The data file comprises 909 observations in 141 subjects. HDRS is the most commonly used measure of depression. It consists of 17 items that are summed up to provide a total score.

Hamilton depression scale measurements were obtained before the start of the treatment and at week 1, 2, 3, 4, 6 and 8 during the treatment period.

Modelling

Indirect-response model was used to describe the time course of the Hamilton depression scale. The time course of HDRS is determined as the net resultant of an onset (kin) and a loss rate (kout) process.

Placebo could produce indirect action on either the inhibition of the onset response rate or the stimulation of the loss rate.

Sigmoid IMax and Weibull functions were evaluated to describe the placebo effect.

Responders and non-responders in the population were differentiate either by an a priori selection (drop of HDRS less than 20% from baseline) or using a mixture model.

Data was fitted using NONMEM first order approximation method. Inter-individual variability (exponential model) was introduced on placebo effect parameters and indirect-response parameters.

A residual error model was used to model residual variability.

\[
\text{Dose Driving Rate } = \text{DK}_{\text{in}} + \text{DK}_{\text{out}}
\]

\[
f(\text{DK}_{\text{in}}) = \frac{\text{DK}_{\text{in}}}{\text{EDK}_{\text{in}}} + \text{DK}_{\text{out}}
\]

\[
\frac{d\text{HDRS}}{dt} = K_{\text{in}}[1 - f(\text{HDRS})] - k_{\text{out}} \cdot \text{HDRS}
\]

 objetives

The objective of the above investigation was to develop a placebo response longitudinal model in depression as measured with the Hamilton Depression Rating Scale (HDRS) accounting for dropout.

CONCLUSIONS

Placebo effect can be characterised by the administration of a "virtual" drug with unknown PK using a K-PD model strategy. This mechanistic approach enables placebo effect to be linked to a dose regimen.

REFERENCES


