PAGANZ Intermediate Population Approach Workshop

PAGANZ 2014

8:30 am – 5:30 pm January 29, 2014

Presenters: Helen Moore, PhD; Nick Holford, MBChB, FRACP

Two half-day intermediate workshops:

1) Overview of population estimation algorithms, PKPD models and modelling tools using the Pharsight software Phoenix NLME.

2) Population PKPD modelling of QT interval.

The target audience would range from graduate students in pharmacometrics to experienced professionals. Both workshops assume some prior exposure to population PK modeling, and the 2nd Workshop assumes attendance at the 1st Workshop or familiarity with Phoenix NLME.

Workshop 1: Estimation Algorithms, PKPD Models and the Phoenix NLME graphical/textual modelling methodology

08:30 Introduction and Brief Overview of Topics. Presenter: Nick Holford/Helen Moore

09:00 Estimation algorithms (based on White Paper by Bob Leary. (1) Presenter: Helen Moore

09:45 Phoenix NLME – a user's perspective of graphical models and the Phoenix Modeling Language. Presenter: Nick Holford

10:30 Break

11:00 Principles of PKPD Modelling. Presenter: Nick Holford

11:45 Hands-on Phoenix NLME: PKPD models for warfarin (immediate, effect compartment, turnover), bootstrap, VPC . Presenter: Helen Moore

12:30 Lunch

Workshop 2: PKPD Modeling of QT interval

13:30 The QT interval: What is it? Why is it measured? How is it modeled (QT "correction", effect compartment, placebo/active control response, disease progression)? (2-4) Presenter: Nick Holford

14:30 Hands-on 1: Example with baseline- and placebo-corrected QT interval data using Phoenix QT+ to compare models using heart rate as covariate. (5, 6) Presenter: Helen Moore

15:30 Break

16:00 PKPD and Thorough QT Studies. Presenter: Nick Holford/Helen Moore

16:30 Hands-on 2: Concentration-QT interval modelling Population PK with QT modelling. Presenter: Helen Moore

17:00 Summary/Wrap-up and Q&A. Presenter: Helen Moore/Nick Holford

17:30 End of workshop

Reference Materials for Distribution to Participants

1. Leary B, Dunlavey M, Chittenden J, Matzuka B, Guzy S. QRPEM – A New Standard of Accuracy, Precision, and Efficiency in NLME Population PK/PD Methods: Pharsight; 2012. Technical Report.
2. Holford NH, Coates PE, Guentert TW, Riegelman S, Sheiner LB. The effect of quinidine and its metabolites on the electrocardiogram and systolic time intervals: concentration--effect relationships. Br J Clin Pharmacol. 1981;11(2):187-95.
3. Garnett CE, Beasley N, Bhattaram VA, Jadhav PR, Madabushi R, Stockbridge N, et al. Concentration-QT relationships play a key role in the evaluation of proarrhythmic risk during regulatory review. J Clin Pharmacol. 2008;48(1):13-8.
4. Garnett CE, Zhu H, Malik M, Fossa AA, Zhang J, Badilini F, et al. Methodologies to characterize the QT/corrected QT interval in the presence of drug-induced heart rate changes or other autonomic effects. Am Heart J. 2012;163(6):912-30.
5. Grosjean P, Urien S. Moxifloxacin versus placebo modeling of the QT interval. J Pharmacokinet Pharmacodyn. 2012;39(2):205-15.
6. Grosjean P, Urien S. Reevaluation of moxifloxacin pharmacokinetics and their direct effect on the QT interval. J Clin Pharmacol. 2012;52(3):329-38.