

QT Assessment in Early Clinical Development

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Break Out Sessions

- Three Sessions
- About 1 hour
- Discuss key issues and develop a concrete plan to move the ball towards increased practical use of Phase 1 data, in lieu of the TQT
- Deliverable: 2-3 slides
 - Summary of discussion
 - Next steps

Breakout Session 1

- Role of Concentration Effect Modeling in Assessing a Drug's Effect on the QTc Interval
- **Moderator:** Christine Garnett / Steve Riley
- What work remains to be done to convincingly demonstrate that concentration effect modeling applied to early clinical data can exclude mild QTc prolongation (e.g. an effect on $\Delta\Delta\text{QTc}$ around 5 ms) with the same level of confidence as the E14 'time-matched QTc analysis'?

Breakout Session 2

- How Can Assay Sensitivity be Established in Early Clinical Trials without the use of Moxifloxacin?
- **Moderator:** Charles Benson/ Philip Sager
- Which alternative approaches to demonstrate assay sensitivity seem most promising and how should these be prospectively tested in early clinical questions.
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Breakout Session 3

- Can an approach integrating non-clinical and early clinical QT assessment replace the thorough QT Study?
- **Moderator:** Borje Darpo/ Krish Prasad
- Which level of QTc effect should we need to exclude with confidence in early clinical studies to provide an alternative to TQT studies for at least some NCEs?
- Can the results of non-clinical assay influence the level of clinical QT assessment and if so, how?

ICH E14 and Afterwards

- ✓ How do perform a TQT
- ✓ Use of active controls and blinding issues
- ✓ Statistical approaches to central tendency analysis
- ✓ Parallel-designed studies
- ✓ Nested-designed studies
- ✓ Individualized corrections
- ✓ Baseline definition

PK/PD Modeling during early clinical studies- can the predictive value be similar to that of a TQT study?

Think-Tank

- Goal: to come out of the meeting with tangible plans for collaborative work that can advance the science in a measurable manner over the next 12-18 months
- Highly interactive; the key to a Think-tank is focused discussion
 - Need to stay focused on the discussion points
 - Moderator will move the topics along if needed
- Talks are short and must stay on time
- Raise card to be recognized or stand at microphone
- Break-out sessions

QT Evaluation in Drug Development



- This Think-Tank
- Several work-streams
- Significant impact using early clinical data in lieu of the TQT in certain circumstances