ISCTM
THE INTERNATIONAL SOCIETY FOR CNS CLINICAL TRIALS AND METHODOLOGY

Adaptive Design Working Group

- Chair - Ginger Haynes ginger.haynes@lilly.com
- Prior Accomplishments
  - Feedback to FDA draft guidance on adaptive design (AD)
  - Dinners and Workshops 2011-2013, Poster (2012)
  - Invited manuscript accepted for publication in Therapeutic Innovations and Regulatory Science (in press January 2014)
- Current Objectives
  - Demonstrate two approaches to designing Phase IIIB/IV population enrichment studies in migraine to test for superior efficacy vs. an active comparator

Workshop 2013

- Ron Marcus shared a two stage adaptive population enrichment design for Phase IIIB/IV study in migraine
  - Medication had graduated from successful Phase III indicating superior efficacy vs. placebo in all patients and enhanced efficacy in biomarker positive (bio +ve) patients
  - Hypothesis – bio +ve group has greater efficacy than active comparator. Stage 1 – all patients, Stage 2 – biomarker only
  - Adaptations included sample size re-estimation, stopping early for futility if bio +ve did not show superiority vs. active
- Tom Parke shared designs for the same case
  - Traditional – randomize all patients and test for bio +ve at end
  - AD – following enrollment of ½ the patients, let data guide early stopping for success (in all or bio +ve) or futility (no diff in either)
  - AD required fewer patients, had greater power to test bio +ve in the moderate effect scenario, but did have slightly higher estimated loss in the null scenario of no superiority vs. active

- Discussion
  - Brisk discussion of the use of biomarkers in an enrichment adaptive design study, when adaptive design methodology would be advantageous/ disadvantageous, and the operational issues associated with it