Biopharm Safety Monitoring Working Group: Bayesian and Graphics Approaches Based on Regulatory Guidance — Topic Contributed Papers

Discussion
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Statistical Challenges in Drug Safety Monitoring

- Not all safety outcomes are known at the design stage
- False positive discovery – multiplicity issue
- Low power in detecting rare safety events during the pre-marketing stage
- A dynamic process

Contemporary Approaches in Drug Safety Monitoring

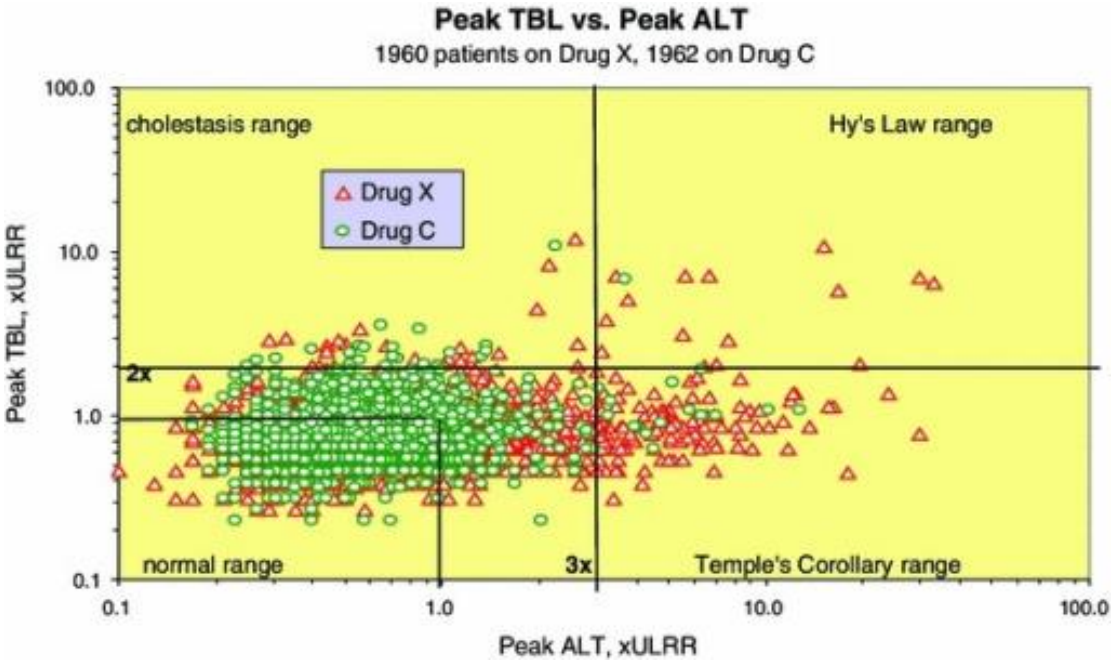
- Dr. Kefei Zhou - overview
  - Enhancing Visual Analytics
  - Bayesian Analytic Graph
- Dr. Michael Fries – type I error control
  - New double false discovery rate (NDFDR)
  - Bayesian hierarchal model
- Dr. Brian Waterhouse – assessing risk of a known event
  - A novel Bayesian methodology (SDRIBS)
  - Contour plots and interactive graphics

Graphics Are Excellent Tools

- Main stream graphs
  - Dot plot
  - Bar plot
  - KM plot
  - Bubble plot
  - Relative risk plot
  - Volcano plot
  - Word Cloud
  - Others..
- Novel graphs before the trial
  - Contour plots
  - Shiny SDRIBS : interactive tool allows flexibility in terms of
    - Change in control event rate
    - Amount of exposure accruement
    - RR cut-point

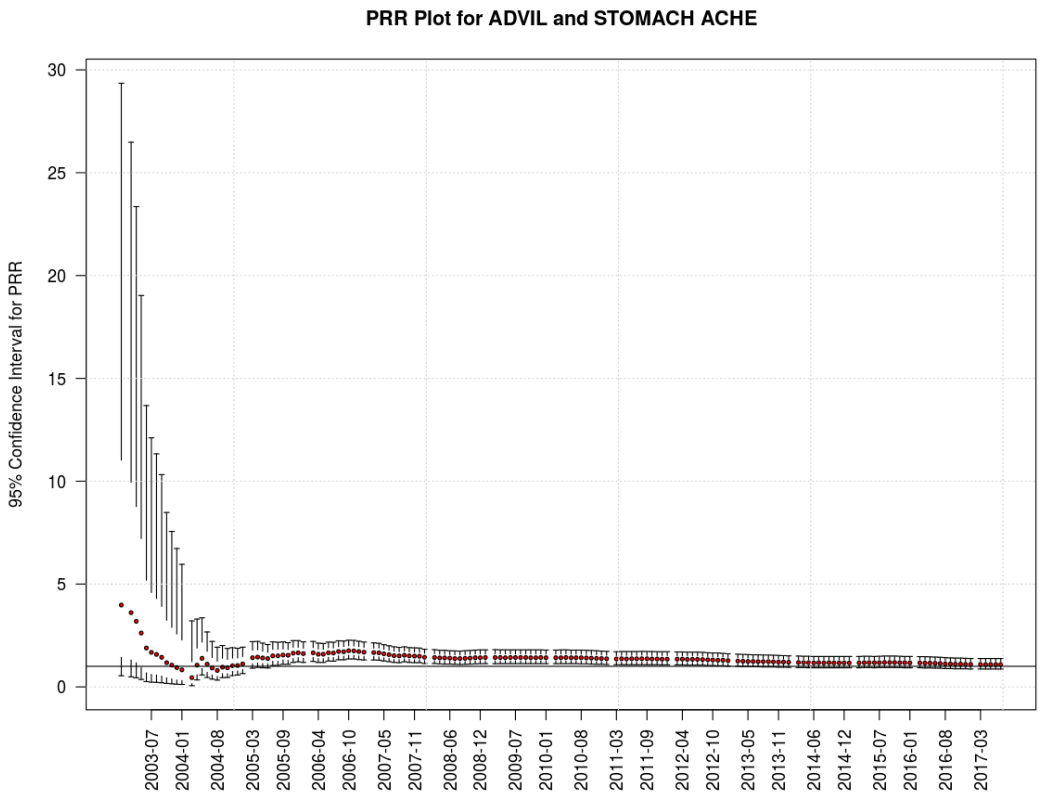
Some Graphic Tools Developed at the FDA

- eDISH (evaluation of Drug-Induced Serious Hepatotoxity plot) -- developed to monitor drug-induced liver injury



Some Graphic Tools Developed at the FDA

- OpenFDA:
  - Dynamic PRR (proportional reporting ratio) to show event over time



Bayesian Methods Come to the Rescue

- Not all safety outcomes are known at the design stage
  - Hierarchical mixture models by Berry & Berry (2004)
- False positive discovery – multiplicity issue
  - Simulation showed that the FWERs/FDRs for Bayes model results are much lower
- Low power in detecting rare safety events during the pre-marketing stage
  - Does not rely on asymptotic properties in dealing with rare events
- A dynamic process
  - Bayesian method incorporate prior information

Safety monitoring is a multidisciplinary effort at the FDA

- Offices involved:
  - OND
  - OSE
  - OB
- Good statistical tools help the communications between us and the clinicians/epidemiologists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