Introduction

- At the Division of Pharmacometrics at the FDA, a web-based tool is currently under development for performing exposure response analyses of integrated summary of safety (ISS) data.
- A tool that would allow reviewers to explore potential safety signals in submissions, while standardizing analyses from rich datasets.

Goals

- Time Efficient Reviews
- Broad Data Format Support
- Smart Data Loading
- Easy and User Friendly

Results

Data Loading and Visualization

- Automatic mapping of datasets adhering to the CDISC standard
- Filtering and selection of risk factors to include in analyses
- Visualize domains with standard tables e.g.:
  - Demographic
  - AEs by Preferred Term
  - Descriptive Statistics by Exposure Group

Interactive Analysis

- Analysis Types
  - Logistic Regression
  - Kaplan-Meier
  - Cox Proportional Hazards
  - Linear Regression
  - Non-linear Regression
  - Other

Project Organization

- Group analyses
- Decisions displayed for easy navigation

Decision Tree

- Add new decision points based on current analysis
- Systematically screen safety events
- Pass sequential through decision points

Example:

- Data Loading (ADaM / SDTM)
  - > 1000 events
- AE Table / Time Course of Event
  - ~ 100 events
- Safety signals of interest?
  - ~ 10 events
- Logistic regression

Implementation

- The user interface was developed in C#, JavaScript and HTML5
- SAS 9.2 was used to generate all analyses and output

Conclusions

A tool to automate exposure response analysis from ISS data is currently under development at the FDA. It provides reviewers with the opportunity to explore potential safety signals in New Drug Applications (NDA), generate standardized exposure response analyses output, minimizes data management and let the reviewers focus on result based decision making.

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