Web-based Integrated Summary of Safety Exposure Response Analysis

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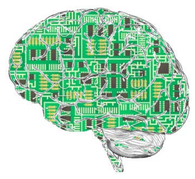
Introduction

- 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

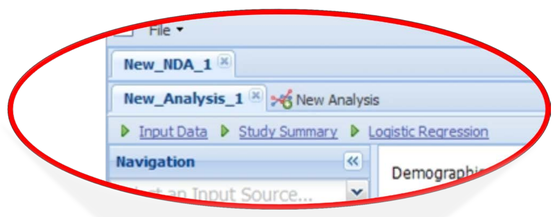
- Automatic mapping of data-sets adhering to the CDISC standard
- Filtering and selection of risk factors to include in analyses
- Visualize domains with standard tables e.g.:
  - Demographic
  - AEs by Preferred Term
  - Descriptive Statistics by Exposure Group

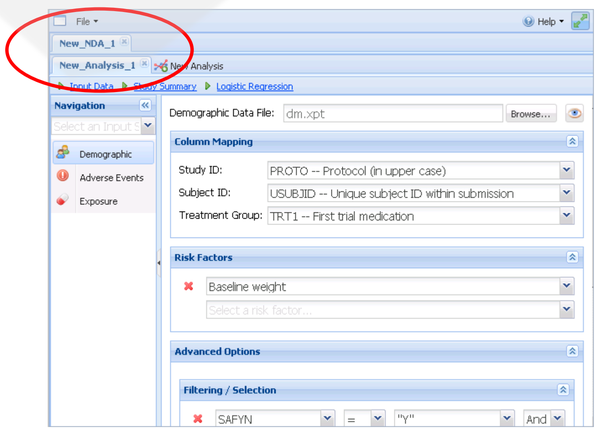
Demographics

	Drug 5 mg		Drug 10 mg		Drug 15 mg		Drug 20 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Number of Subjects	14		23		40		23	
Sex								
F	12	(85.7)	19	(82.6)	26	(65.0)	17	(73.9)
M	2	(14.2)	4	(17.3)	14	(35.0)	6	(26.0)
Race								
Asian	6	(42.8)	8	(34.7)	17	(42.5)	7	(30.4)
Black	4	(28.5)	8	(34.7)	9	(22.5)	4	(17.3)
Other	0		4	(17.3)	10	(25.0)	9	(39.1)
White	4	(28.5)	3	(13.0)	4	(10.0)	3	(13.0)

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

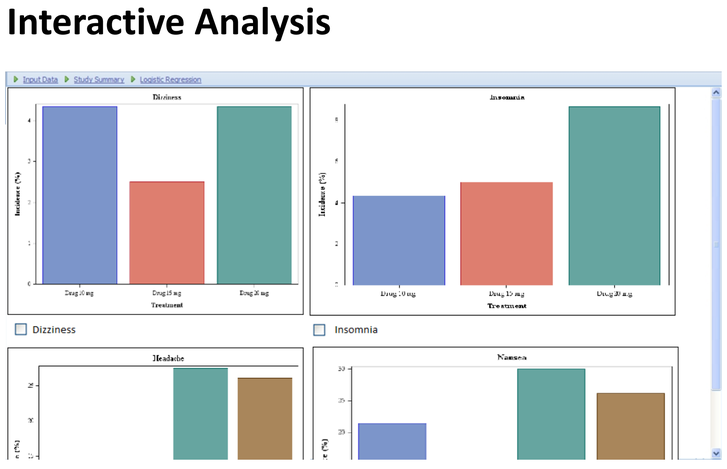
Safety signals of interest?

~ 100 events

Logistic regression

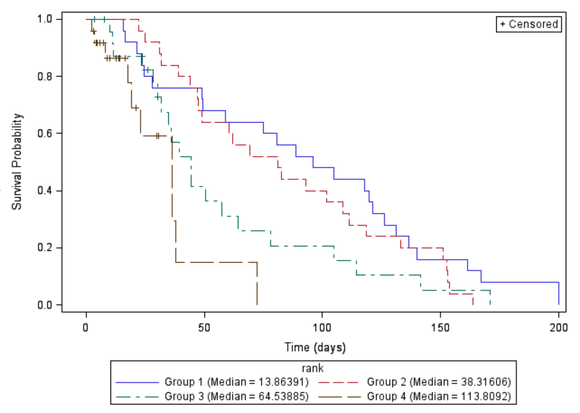
~ 10 events

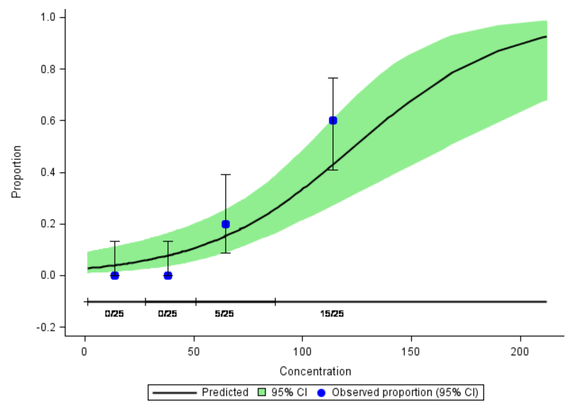
Interactive Analysis



Analysis Types

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





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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