



Utilizing Visualizations Developed in R Shiny for Exploratory Safety Analysis

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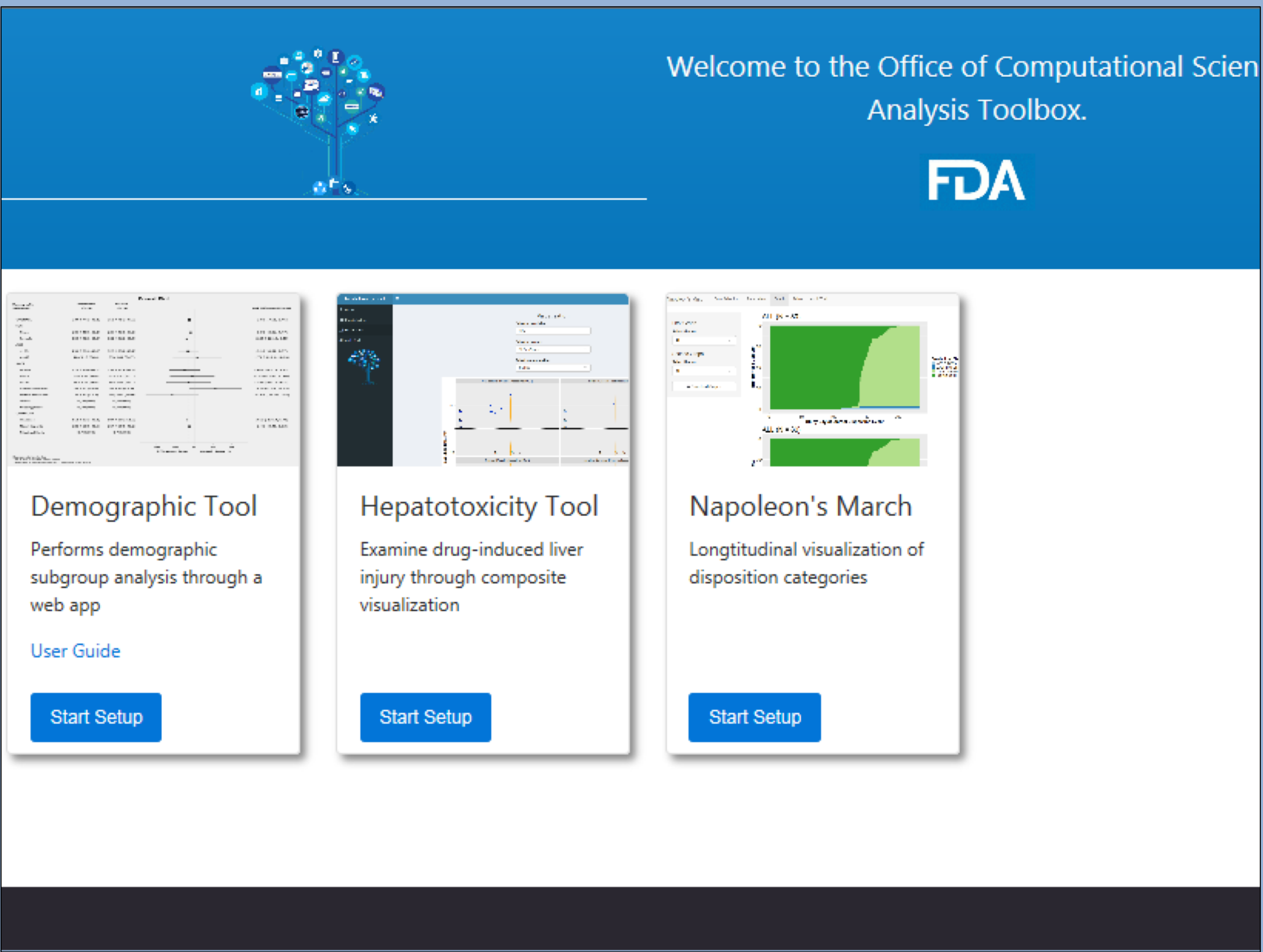
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Background

The Office of Computational Science (OCS) has begun to leverage open source programming languages to aid exploratory safety analysis within the clinical review through the development of new analytical tools. These tools incorporate varying levels of complexity, in terms of analysis, but are all executed and presented in a simple user-friendly web-interface. By leveraging R Shiny and various web languages (e.g., JavaScript), the analytical outputs are delivered with flexible parameters that eliminate the need for overly-complicated coding or navigation. End-users can execute and review the analysis from start to finish with little or no training. In addition to enhancement in the functionality, these tools can showcase effective and highly customized visualizations not readily available elsewhere.

Streamlining Distribution

The tools developed in R Shiny are distributed through the OCS Analysis Toolbox. The toolbox provides a simple and intuitive way for end-users to download the necessary components and launch the analysis. The toolbox includes a user guide for each tool to assist end-users in launching and understanding the analysis. If the end-user requires additional assistance, the OCS Service Desk is available to assist through phone or email communication.



Acknowledgements: Eileen Navarro Almario, Kathryn Matto

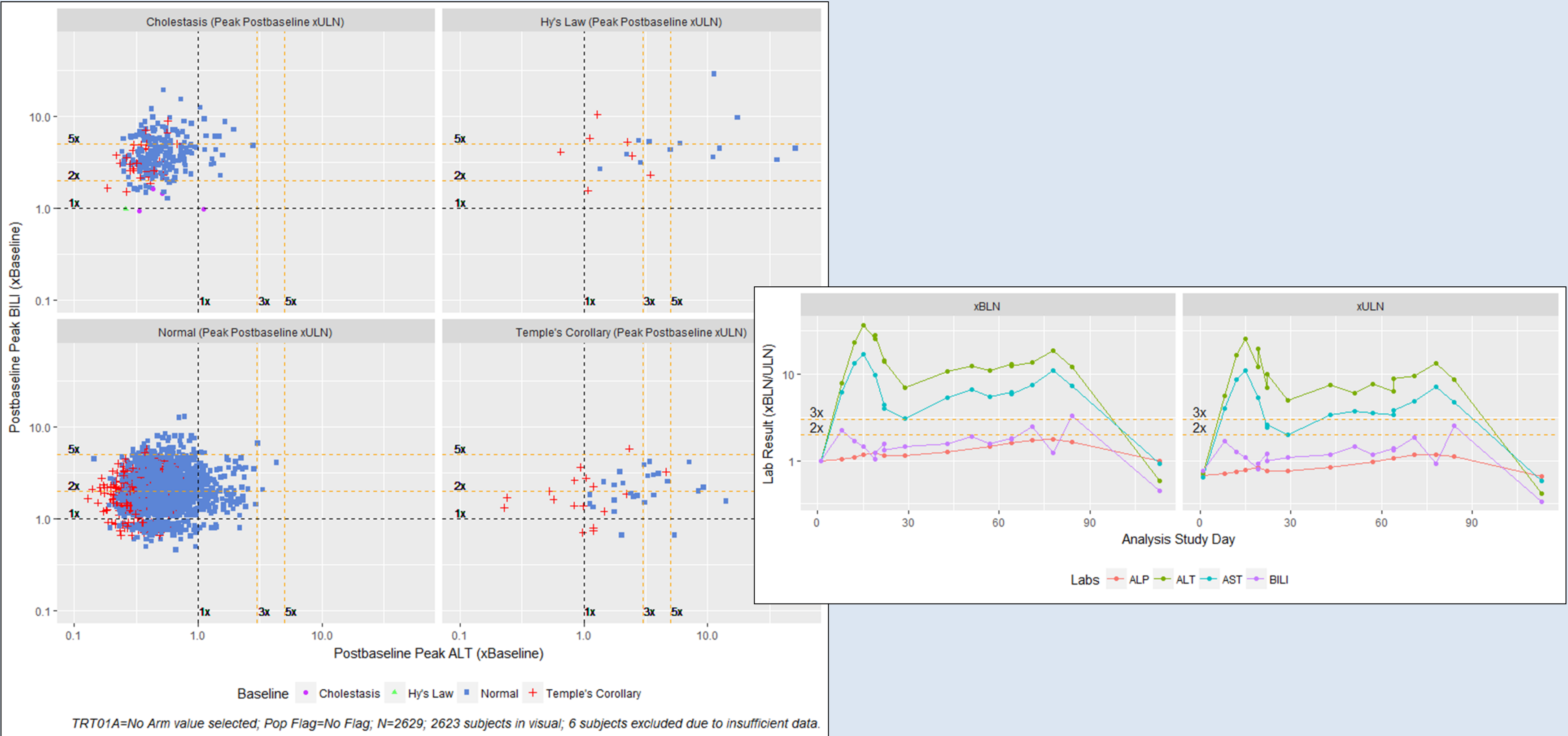
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Exploratory Safety Visualizations

Each of the visualizations displayed in this section represents a tool, analysis, or solution that has been developed using open source languages (i.e., R). They can be easily launched through a modern browser. The input data for these analyses are standardized clinical trial datasets (i.e., ADaM). The end-user can either upload the datasets or supply a shared-location of the data of their choosing.

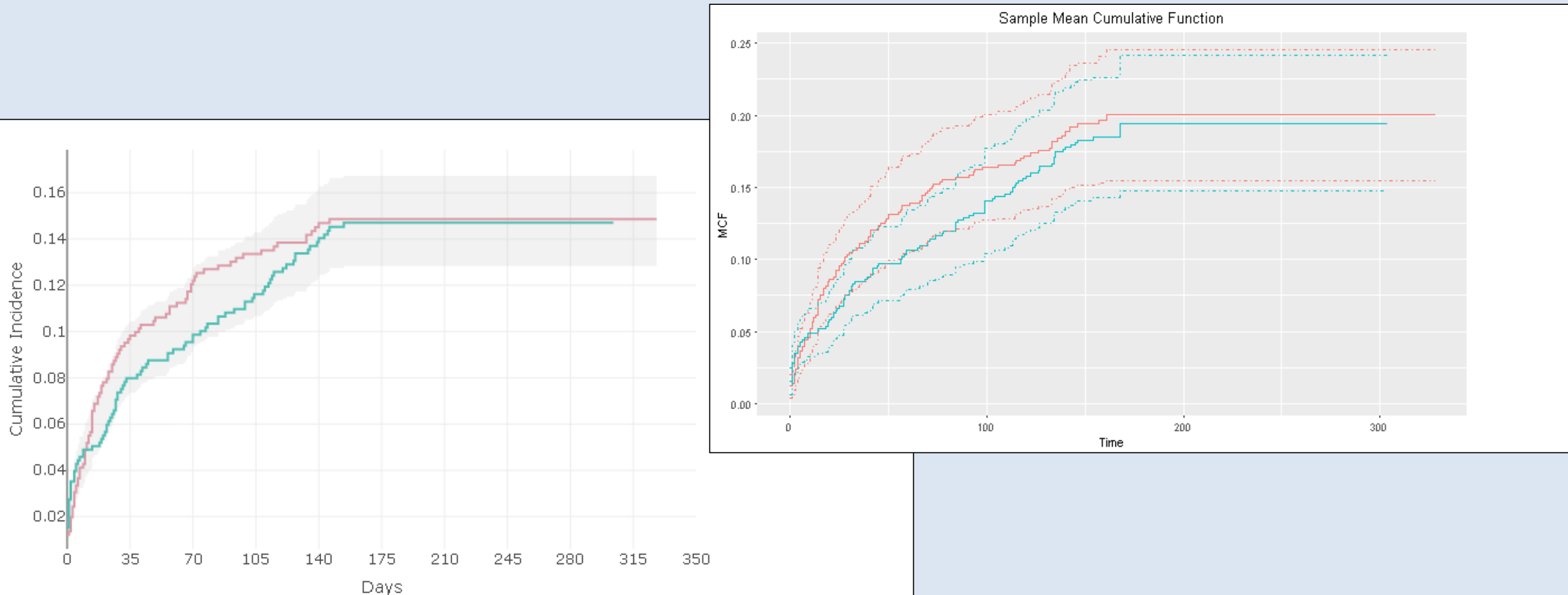
Composite Hepatotoxicity Visualization with Drill-down

The Hepatotoxicity tool provides an analysis of Drug Induced Liver Injury (DILI) through a composite visualization that includes both pre-treatment and on-treatment prevalence of ALT and BILI elevations in terms of Hy's Law candidate laboratory Upper Limit Normal (ULN) threshold values as well as the magnitude of these elevations normalized by respective baseline test results. This analysis is particularly useful for studies in which subjects have elevated liver enzyme test results at baseline (e.g., subjects with Chronic Hepatitis C).



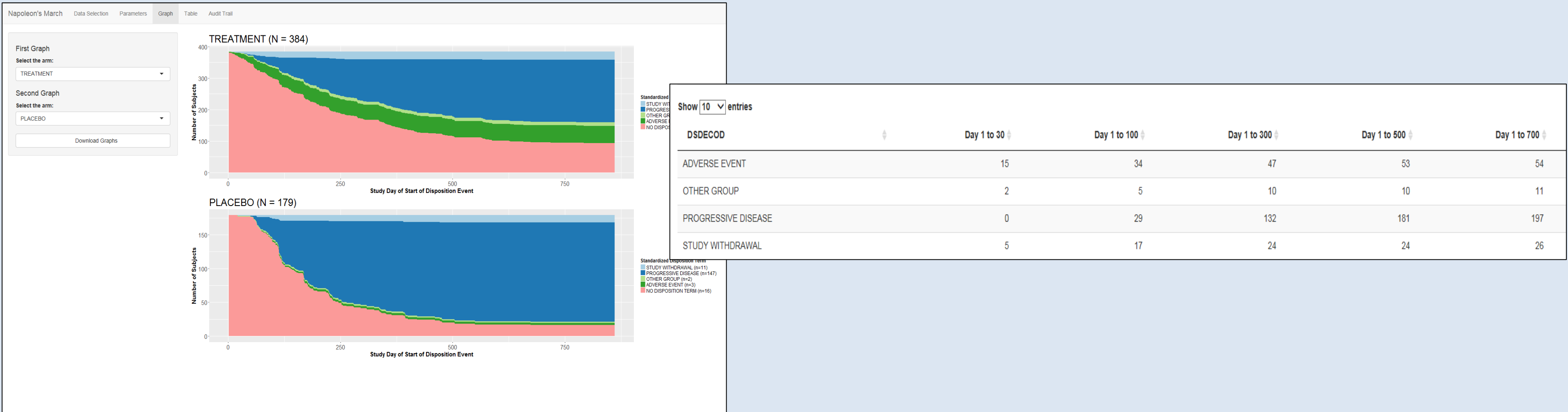
Kaplan Meier and Mean Cumulative Function

The Kaplan Meier is a non-parametric method used in visualizing adverse events longitudinally. This application provides an estimate of the probability of a particular event, or combination of events, over time. The mean cumulative function can do the same, but it accounts for multiple adverse events over the course of a study period. By using the same core parameters for each analysis, end-users can generate both of these analyses to get a better understanding of the temporal characterization of the adverse event signal of interest.



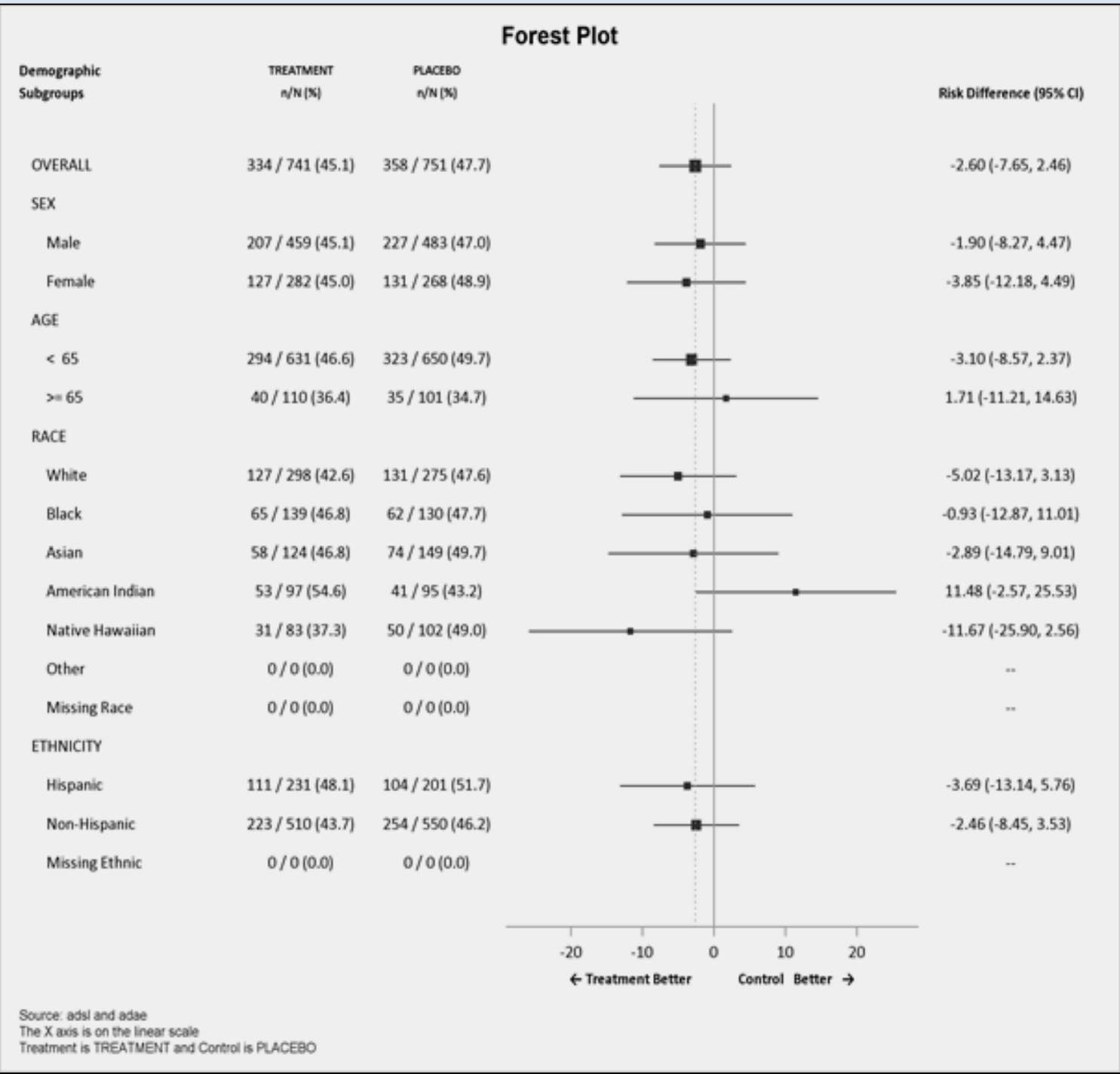
Napoleon's March

This tool counts the number of subjects dropping out of the study over time by treatment arm. This information is displayed dynamically through graphical and tabular representations. Users have the ability to select particular disposition categories as well as group disposition events into user-defined categories.



Demographic Subgroup Analysis

This tool provides targeted descriptive statistics and safety endpoint analysis for demographic subgroups including age, sex, race, and ethnicity. Users have the ability to generate both a table and forest plot of the comparison between two study arms of interest. R Shiny is deployed as the user interface to launch this analysis in SAS.



Future considerations

OCS is looking into further improvements to the end-user experience. The next generation of tools may include more visual representations of adverse event hierarchical data.