



JMP® Clinical 3

Explore the hidden patterns in clinical trials data.
From SAS, the *de facto* standard for clinical data analysis software.

What is JMP® Clinical?

JMP Clinical software from SAS shortens the drug development process by streamlining safety reviews during clinical trials. Dynamically linking advanced analytics and graphics, JMP Clinical creates reports from CDISC data, the global standard, moving you into a modern review environment. It combines JMP, already a popular tool of choice for medical reviewers, and SAS, the standard analysis and reporting tool for biostatisticians in the pharma industry.

Why is it important?

JMP Clinical helps you migrate from a static, document-centric world to an interactive, data-driven environment optimized for discovery. It screens data from core CDISC domains to enhance safety and efficacy assessments, shortening a drug's time to market or detecting fatal flaws earlier in the process. JMP Clinical depicts analysis results visually, so you can spot trends that spreadsheets and static tables tend to hide. It offers unique and easy access to the data behind the graphics and permits clustering of events, interventions and findings.

Who should use it?

JMP Clinical is designed for medical reviewers, epidemiologists, data monitors, biostatisticians and biometrics groups engaged in analyzing safety data from clinical trials. You can spend more time exploring patterns and testing hypotheses in clinical trials data, without spending time programming or manipulating data.

JMP Clinical software from SAS brings sophisticated analysis and exploration of clinical trials data to a dynamic safety review process. It combines the industry-leading power of SAS® Analytics with the graphical flexibility of JMP, the longstanding tool of choice in the clinical review community.

Medical reviewers, biostatisticians, data monitors and members of biometrics groups need to understand and report clinical trial data accurately and efficiently. JMP Clinical provides a collaborative environment that fosters exploration of medically relevant hypotheses with a statistical perspective.

JMP Clinical dynamically links advanced statistics with exceptional graphics to provide a detailed picture of clinical trial results. Its unsurpassed ease of use puts multifaceted analysis

“It was clear to us early on that JMP Clinical will help us achieve a quicker turnaround in the drug approval process. I believe JMP has hit a home run with this tool.”

Steve Wong, Gilead Sciences Inc.

Senior Director for Statistical Programming
Biometrics Department

options in the hands of all users, regardless of their statistical savvy. Even reviewers without programming experience or statistical training can get started quickly, thanks to simplified dialogs and customized workflows.

A hallmark of JMP Clinical is its fluidity of movement between results for the entire trial and for specific subjects via multifaceted drill-down and swim-up capabilities.

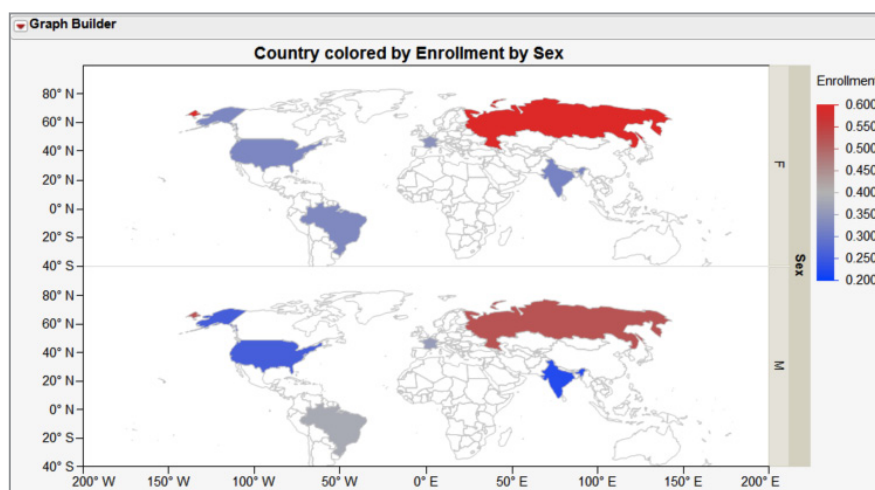


Figure 1. The mapping feature in Graph Builder, new in JMP Clinical 3, lets you choose any variable for geographic display.

The software supports nine core CDISC domains for safety and efficacy review: demographics, adverse events, medical histories, disposition, exposure, concomitant medications, lab results, electrocardiograms and vital signs. With simple configuration, it can analyze results from other CDISC domains as well.

You can rely on JMP Clinical to:

- Explore data visually and interactively, replacing static tables and listings.
- Examine relationships between events, findings and interventions using dashboard visualizations of distributions and incidence screen analyses by demographic interactions.
- Select specific time windows for almost any analysis.
- Share reports easily, streamlining communications between internal reviewers, and then between sponsor organizations and regulatory agencies.
- Fit advanced statistical models, including those with time windows.

JMP Clinical uses CDISC data, the globally recognized standard for clinical analysis and reporting. It organizes the review process, working behind the scenes to automate the analytics and reporting, allowing you more time to interpret and understand the results. As one of the first tools that inherently understands ADaM data, JMP Clinical is a great option for clinicians and biostatisticians migrating into the modern review environment. Its optional 64-bit platform brings

even more power to the analysis of vast data sets.

A new Clinical Starter menu (Figure 2) helps you load CDISC data and follow FDA reporting guidelines in logical sequence. A customizable, menu-driven desktop system lets you see and explore safety and efficacy data from every angle, and then easily share findings with others. You also can use dialogs to manipulate data on the fly and streamline interactions between collaborating groups.

JMP Clinical offers effortless access to the statistical analyses behind the graphics – a benefit not usually found in similar software tools. For example, JMP Clinical makes it easy to generate patient profiles by selecting individual subjects from any graph and to

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examine analysis results by groups – according to race, sex or other characteristics. Just summarize, elect, zoom in and drill down to the details.

JMP Clinical features industry-standard visualizations as well as novel graphics for displaying safety and efficacy data. Space-constrained views allow easy identification of differences between items in a graph in a single dashboard. A new mapping feature allows you to compare results across testing sites or countries.

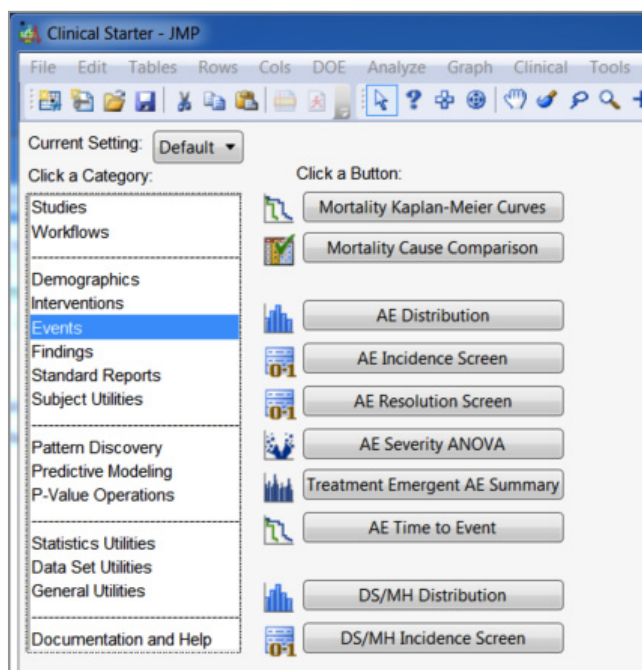


Figure 2. A simplified Starter menu in JMP Clinical 3 helps users easily choose specific reports and analyses for dynamic visual exploration.

Even reviewers without programming experience or statistical training can get started quickly, thanks to simplified dialogs and customized workflows.

Interventions

The new Exposure Summary process identifies differences in dose and duration of exposure across treatment groups, providing context for all downstream analyses (Figure 3). JMP Clinical includes options to choose the number of dosing groups and the duration of the time window.

Incidence screens of concomitant medications allow clinicians to identify drug-drug, drug-demographic and drug-disease interactions.

Events

Following FDA Reviewer Guidance principles and ICHE3 guidelines, JMP Clinical enables analysis of event rates and estimations of risk over time, while helping you explore possible differences in subgroups and identify risk factors linked to serious events. You can easily estimate adverse event frequency and count information with the highly visual mosaic plot (Figure 7).

Using industry-standard or customized views, you can select any serious and/or severe adverse event and drill down for an in-depth view of subject details (Figures 4, 5 and 6). An enhanced workflow adds subject clustering and subject filtering to existing analysis options for patient profiles.

JMP Clinical reduces false-discovery rates, mitigating the risk of over-reporting adverse events with the Severity ANOVA process. This simple, visual approach uses graphical elements to show significance, correlation and

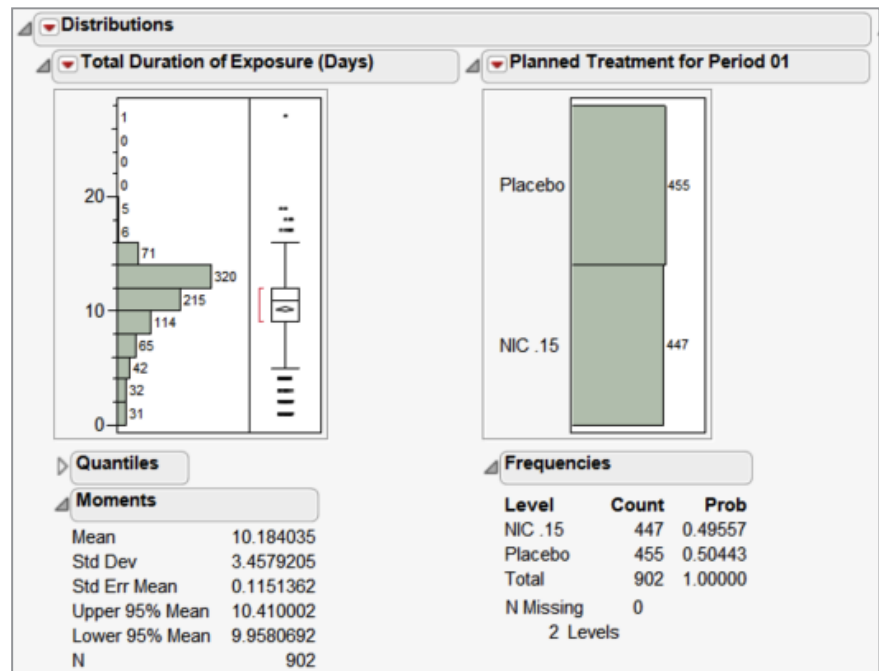


Figure 3. This distribution shows duration of exposure for all subjects in the trial.

trends, along with modern methods for adjusting for multiple testing. You can display and explore data in a variety of ways, including volcano plots, parallel plots, heat maps, bubble plots, and trellises.

The software follows industry-standard analysis methods to measure time-to-event for any adverse event in a clinical trial. You can effectively screen all Standard MedDRA Query (SMQ) terms to discern adverse event patterns across treatment groups. Following analysis, you can generate multiple reports that provide a comprehensive evaluation of risk information based on predictive factors.

Findings

Determining treatment compliance and establishing baseline values for lab measurements is important for all clinical reviewers. Often these data provide the means to determine both efficacy and safety evaluations. JMP Clinical supports baseline determination, shift plots and box plots for all labs, vital signs and electrocardiograms as well as more specific analyses such as Hy's Law Screening (Figures 8 and 9). The Data Filter tool makes it possible to subset distributions of these Findings domains by demographic and derived subject level data.

Sophisticated graphics in JMP Clinical make it easy to spot and select one or more outlying laboratory values, and then drill down quickly to subject-level details using patient profiles.

Baseline ANOVA analysis measures the change from baseline for any specific laboratory test in the trial. Interactive bubble plots show the rate of change for multiple lab tests, measuring trends over time across treatment groups or other categories of interest. The default view for bubble plots in JMP Clinical uses Hy's Law analysis to assess hepatotoxicity, a focus of the US Food and Drug Administration's safety review.

Subject clustering and profiling

Nearly all analyses in JMP Clinical allow you to cluster subjects, profile subjects or apply subject filters. Subject clustering allows you to look for patterns across all safety domains

and easily identify similarities within a subset of subjects, then apply filters that focus all future analyses only on the selected subset of individuals.

Subject clustering fosters easy exploration of interactions across safety domains.

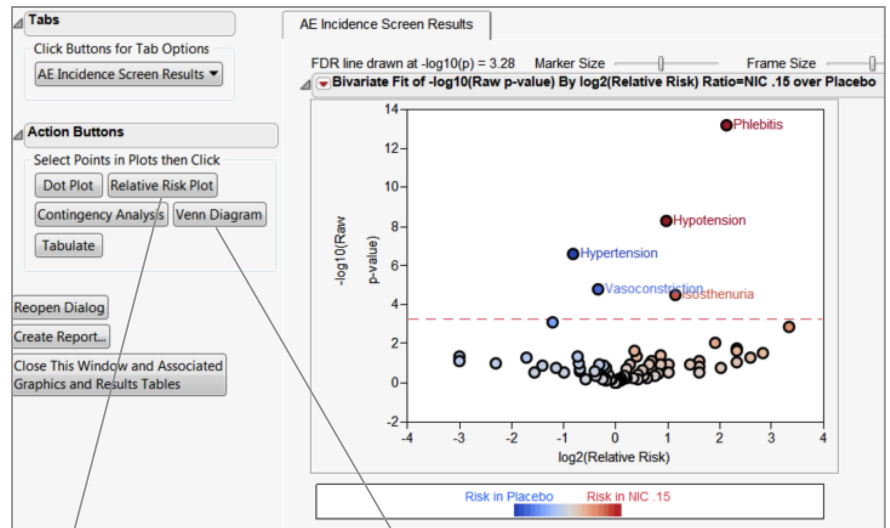


Figure 4. A volcano plot (above) reveals significant adverse events across treatment groups. Focus on the upper left and right corners of the graph to identify the significant adverse events. From this dashboard display, select an Action Button and drill down for details.

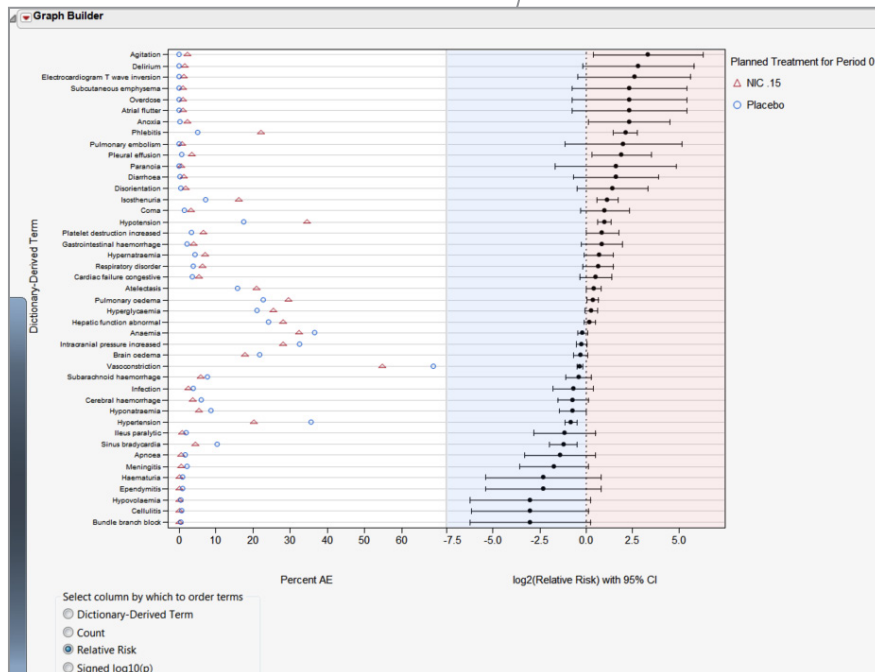


Figure 5. From the volcano plot, drill down to a relative risk plot to sort easily by count, relative risk, significance or dictionary-derived terms.

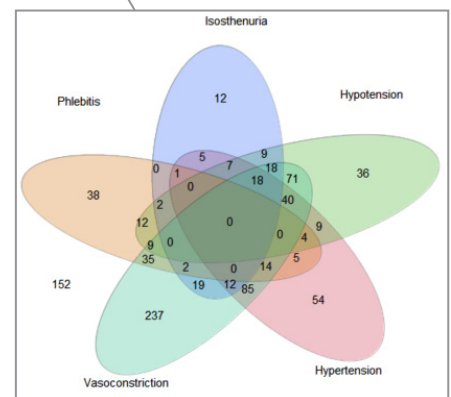


Figure 6. From the volcano plot, a Venn diagram helps identify co-occurring adverse events for subjects in the study. Then select subjects for clustering or profiling.

A new feature in JMP Clinical 3 makes it easier to compare information about multiple subjects by overlaying their profiles on a single time line (Figures 10 and 11). Reviewers and medical writers can now also record and save unstructured text about any subject or group, noting, among other things, cases of death, serious adverse events and reasons for discontinuation. You can furthermore customize patient profiles, displaying data from any combination of the core safety domains.

JMP® Clinical now facilitates time windowing in most analyses, making it easy for you to compare interventions, events and findings for two or more time windows.

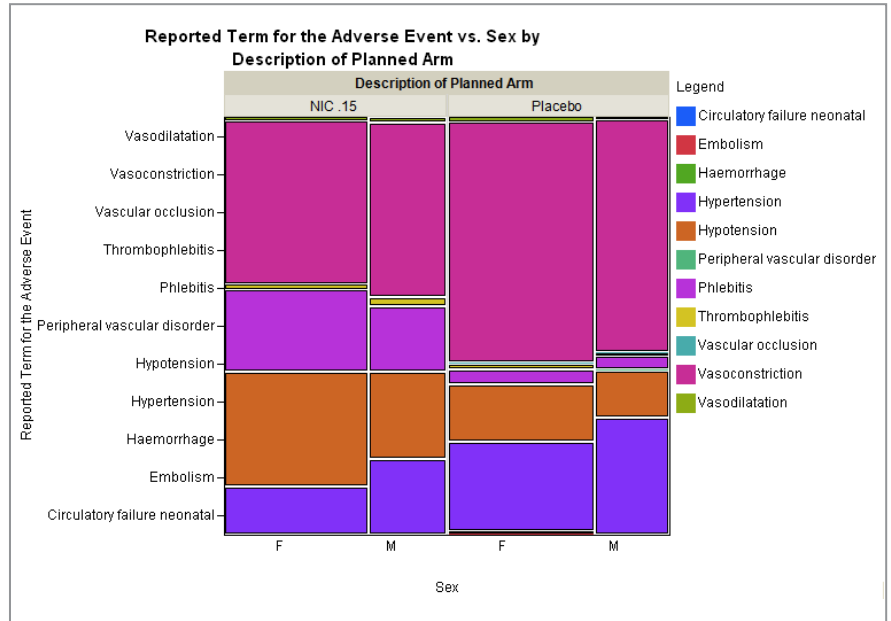


Figure 7. Use Graph Builder's Mosaic Plot to compare adverse events, here from the vascular body system, by sex across treatment groups.

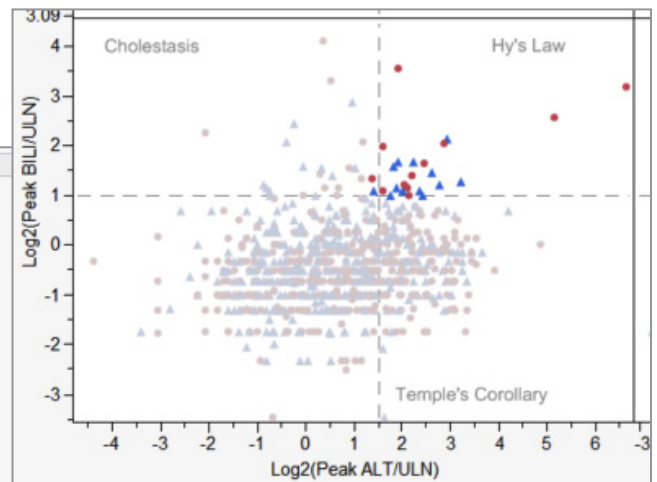
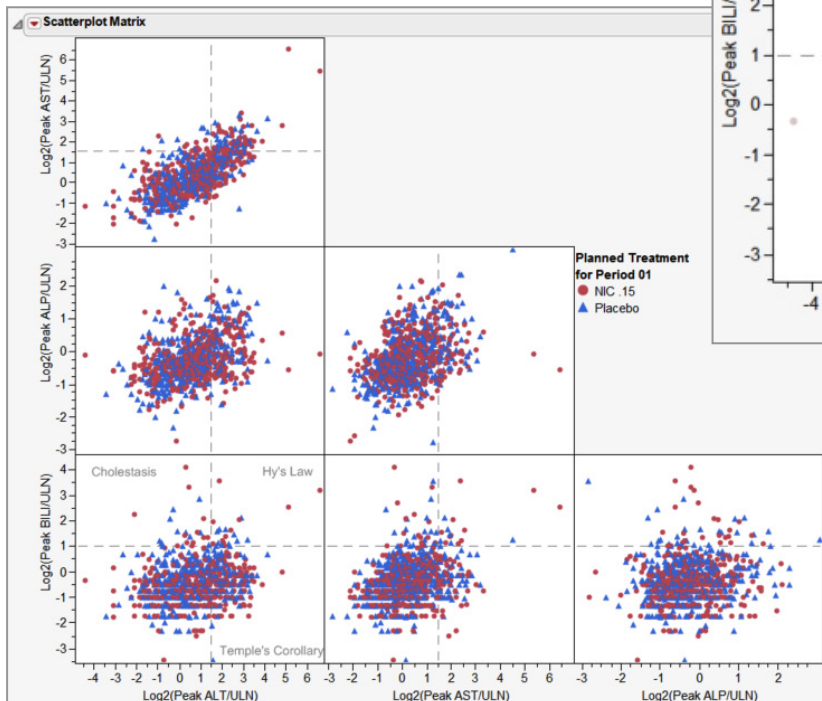


Figure 8. Zoom in to select subjects in the Hy's Law region. Drill down on selected subjects to see patient profiles or subject clusters.

Figure 9. The industry-standard Hy's Law display in JMP Clinical is interactive for selection of subjects. A scatterplot matrix of lab measurements associated with liver failure includes labels for Hy's Law, cholestasis and Temple's Corollary regions.

Time windows

JMP Clinical now facilitates time windowing in most analyses, making it easy for you to compare interventions, events and findings for two or more time windows. AE Resolution Screen, also new, lets you monitor the outcome of adverse events during a specified time window.

Corporate, government and academic licenses for JMP Clinical are available by annual subscription. For more information about our software and complimentary Webcast training for prospective customers, please visit our Web site: jmp.com/clinical

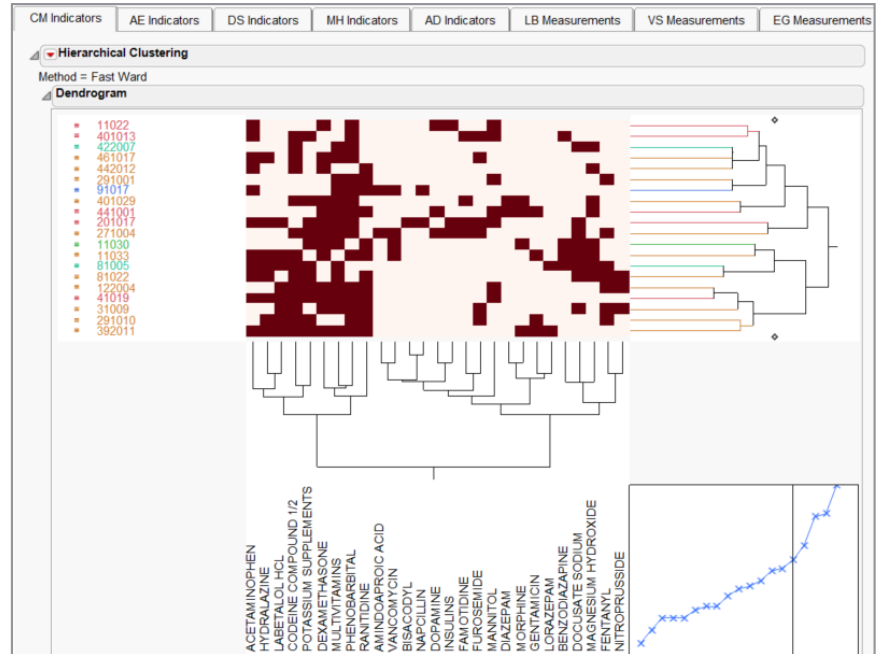


Figure 10. A Hierarchical Cluster report with two-way clustering identifies relationships between individual subjects and the events, findings and interventions included in the safety analyses for the study.

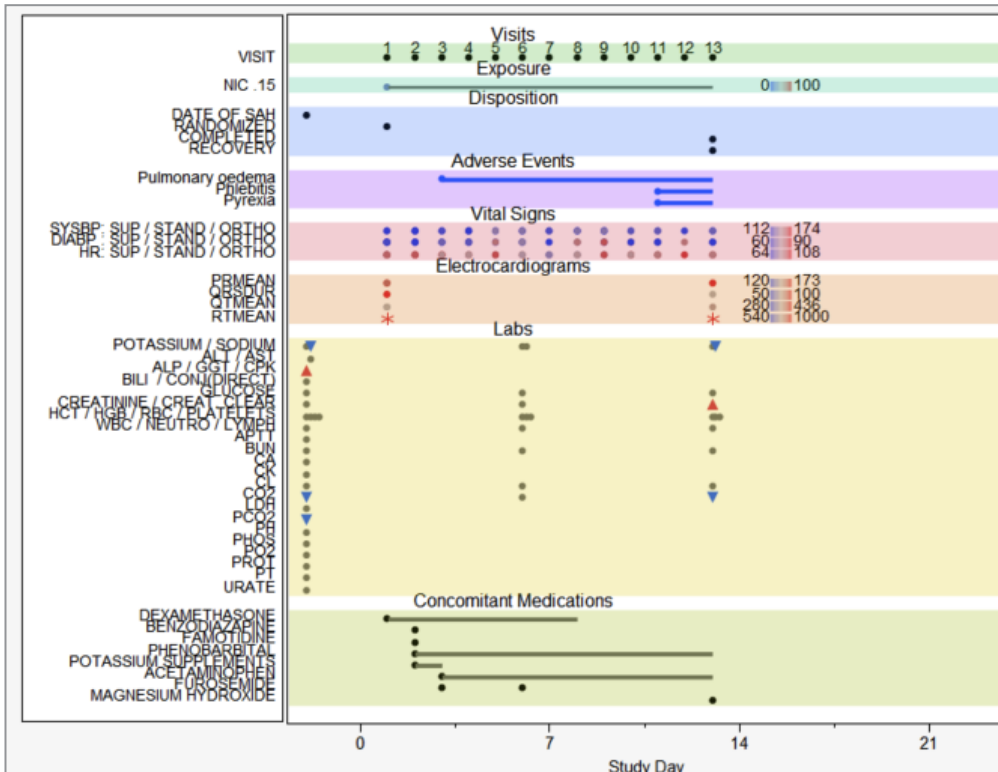


Figure 11. A patient profile reveals the onset of interventions, events and findings during the trial.

JMP® Clinical Features

Linking dynamic JMP® visualizations with robust SAS® Analytics, JMP Clinical includes:

- A new Starter menu that allows rapid and focused point-and-click access to all reports.
- Wide-ranging advanced statistical analysis, pattern discovery and predictive modeling using well-documented methods.
- An audit trail that tracks your analysis path.
- Capabilities for adding your own analyses with tailored dialogs and customized analysis processes. A programmers' guide is available.
- Open architecture that provides access to all SAS code, macros and JMP scripts, so you can see exactly what is being done. No more black box!
- Shared architecture with JMP Genomics facilitates research combining traditional clinical data with analysis of genomic biomarkers.

Interactive JMP software provides:

- Zoom-and-filter capabilities for drilling down into the data underlying statistically significant events.
- Discovery-driven integration of dynamic graphics and statistical detail not possible in other software offerings.
- Unparalleled flexibility for point-and-click creation of custom graphics: 2-D and 3-D scatterplots; tree maps; and mosaic, parallel, overlay, contour and bubble plots.
- Dynamic, click-and-drag interface for visual exploration of data patterns with Graph Builder.
- Built-in JMP Scripting Language (JSL) and auto-generated, reusable graphics scripts that make it easy to capture and share important findings.

Space-constrained displays of visual analytics allow:

- Four-dimensional reports in one dynamic volcano plot/bubble plot.
- Data movies that show effects of interventions over time.
- Efficient depictions of overlapping factors in five-way Venn diagrams.

Intuitive dashboards make it easy to get started and include:

- Easy-to-understand visual summaries of large data sets.
- Basic Safety Workflow that lets you perform a complete set of standard analyses with only a few mouse clicks.
- Behind-the-scenes data manipulation that makes it easy to take full advantage of statistical analysis features.
- On-the-fly error mitigation. If recommended variables are missing from data, JMP Clinical automatically searches for them in other locations.
- Workflow Builder, which lets expert users create custom workflows.
- Connections that link graphics and data for point-and-click selection and easy creation of subset data tables.
- A data filter that tailors views of your data using complex queries.

CDISC data optimization that:

- Offers easy migration to CDISC, the worldwide standard for clinical reporting and analysis.
- Checks automatically for required variables to assess data for CDISC compliance.

- Enables management of information derived from SDTM data as the first ADaM-aware tool on the market.
- Creates ADSL data sets and other types of ADaM data on the fly by collecting relevant slices of SDTM data.

Subject clustering that shows:

- Views of interventions, events and findings within or across domains to search for hidden patterns.
- Drug-drug, drug-demographic and drug-disease interactions by screening concomitant medications and medical histories, respectively.

Time windowing lets you:

- Break down an analysis into arbitrary time windows to easily identify time trends that are masked by overall summary reports.
- Dynamically plot data over time and/or create animations with bubble plots.

Examine patient profiles from many perspectives:

- Open any CDISC domain and create a patient profile for any subject.
- Drill down for details on significant adverse events and other domains.
- Create customized patient profile templates to select display of relevant safety domains.
- See the medical history for any subject.
- Profile multiple subjects simultaneously, side by side.

Apply trusted statistical methods with flexible options to:

- Screen and compare all safety results for every major CDISC domain using such methods as Fisher's Exact Test, Kaplan-Meier curves and mixed-model ANOVA.
- Discover statistically significant differences in data while correcting for multiple tests: Employ the latest multiple testing methods (e.g., Adaptive Holm, Adaptive Hochberg, Adaptive FDR and Dependent FDR) for multiple testing correction in ANOVA-related and other processes.

Use sophisticated pattern-discovery capabilities to:

- Perform interactive partial correlation analysis on clusters of events to adjust for potential confounding.
- Employ dimension-reduction techniques such as principal components and multidimensional scaling to highlight major structural trends in your data.
- Create interactive Venn diagrams with up to five variables.

Apply advanced predictive modeling analysis tools to allow:

- Comparison of results across eight different major predictive modeling methods, with numerous options and tuning capabilities.
- Customized predictor filtering during model construction.
- Predictive modeling for survival analysis.
- Sophisticated cross-validation with adjustable hold-out and iteration options to enable comparison of relative performance across multiple models.
- Learning Curve analysis assessing the impact of sample size.



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