Medidata Rave CSA (Centralized Statistical Analytics)

Enabling more insightful clinical trial reviews

Monitoring and reviewing clinical trial data is a critical step to ensuring the success of any clinical development plan. But today's manual processes can often result in errors, compromising data quality and incurring costly study delays.

Rave CSA provides immediate insight into clinical trial site performance and data quality. An integral part of Medidata Rave RBM—our unified solution for risk-based monitoring—Rave CSA integrates data from different systems and provides a comprehensive report for each subject, making it easier for teams to detect and track critical data changes throughout trial execution.

Individual reporting at the subject level

Rave CSA integrates and analyzes data across multiple domains, generating patient-centric reports to allow for quick and easy clinical trial review. The reports are available via a study portal, which leverages trial data to create and display a customized study dashboard, site dashboards, listing tables and interactive visualizations like adverse events and concomitant medications, along with visit dates and time on study drug. The portal also uses our patent-pending statistical algorithms to mine the database and automatically identify anomalies, outliers, potential fraud and procedural issues—enabling sponsors to work more effectively and attain faster, safer clinical trial data reviews.

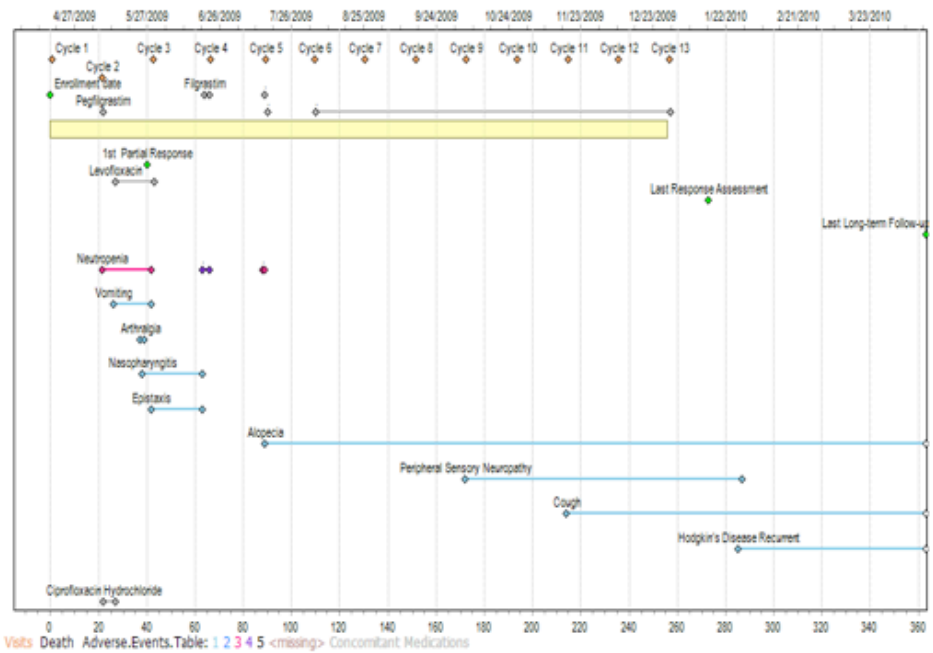
An example of a timeline and lab table from an oncology trial is shown in Figure 1. The time that the patient was on the study drug is highlighted in yellow and the events are color-coded based on user-defined criteria. The data in the table is also color-coded based on normal ranges defined by CDISC's study data tabulation model (SDTM) variables.

Finding inconsistencies in data can be one of the most frustrating and time-consuming parts of assessing clinical trial data. Rave CSA simplifies this process by visually unifying all relevant data for each individual patient. Figure 2 is a representative example of the first page of a patient profile report generated by Rave CSA with errors introduced for illustration.

Rave CSA processes over 1,000,000 data points and finds over 4,000 patterns in less than one hour. Its advanced statistical analytics turn on in days to provide immediate benefits:

- Automatically extracts and maps data from the Medidata Rave Clinical Cloud® to create individual patient profiles
- Statistically analyzes data and identifies anomalies, outliers, unexpected errors, fraud and procedural issues
- Summarizes and presents overall risks and identifies the sites that need further investigation

Figure 1: Example of a timeline and table from an oncology trial



Chemistry & Hematology Labs

Date	*Visit Name*	*ALT*	*AST*	*Hemoglobin*	*Neutrophils*	*Leukocytes*
4/17/2009	Baseline	15	19	10	3.43	4.77
4/17/2009	Cycle 1 Day 1	16	23	10	3.38	4.59
5/8/2009	Cycle 2 Day 1	43	32	11.7	0.66	1.88
5/29/2009	Cycle 3 Day 1	38	30	10.9	2.58	3.67
6/22/2009	Cycle 4 Day 1	27	24	11.6	8.72	11.19
7/15/2009	Cycle 5 Day 1	50	43	11.1	2.48	3.72
8/4/2009	Cycle 6 Day 1	26		11	2.18	3.73
8/25/2009	Cycle 7 Day 1	21	21	10.5	2.53	3.63
9/15/2009	Cycle 8 Day 1	14	18	10.5	2.52	3.43
10/6/2009	Cycle 9 Day 1	13	16	10.4	1.81	2.59
10/27/2009	Cycle 10 Day 1	10	16	10.6	2.37	3.55
11/17/2009	Cycle 11 Day 1	12	19	9.9	2.42	3.64
12/8/2009	Cycle 12 Day 1	12	19	10.1	2.28	3.59
12/29/2009	Cycle 13 Day 1	10	20	10.4	2	3.56
1/29/2010	End of Treatment	12	16	10.7	4.18	5.55

** Red = High; Blue = Low*

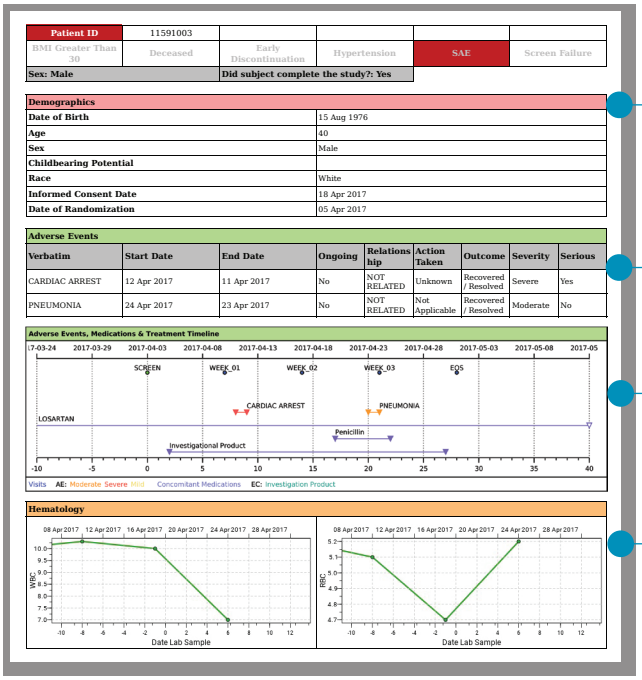
Dataset Date 3/31/2013 Created on 7/7/2014 Patient Profiles Version 7.1.0.1 Study XYZ

Medidata Rave CSA ensures data quality

Rave CSA helps identify areas of risk much faster and more accurately by providing immediate insight into clinical trial performance and data quality. It is specifically designed for centralized statistical monitoring of data across various functional areas. With its sophisticated statistical algorithms, it interrogates the clinical data in a trial for outliers, data anomalies and trends. These algorithms are generated programmatically by the system, so there is zero statistical programming required on the user's end.

Whether you are a small, mid-size or large organization, Medidata has the skills and experience to work hand in hand with your team and ensure success of your RBM vision.

Figure 2: Inside a patient profile report



Set conditions to highlight and flag important patients & events.

Show timeline of imporant events.

Customize to focus on areas of importance.

Summary

The advanced and robust statistical algorithms in Rave CSA provide a comprehensive scan of a clinical trial database for inconsistencies across data domains, sites and patients. With templates for SDTM data, automated processes can be setup so that every clinical study submitted to the FDA can have a study grade calculated for data quality. The overall study grade can be a measure of overall data consistency, and be compared across sponsors, studies, indications and disease areas. Individual site grades can be used to measure data quality within the site, and identify studies and sites at high-risk for procedural problems and data errors.

Rave CSA algorithms

A variety of centralized statistical analytics algorithms automate error detection and flag unusual data within a clinical trial. The statistical methodology uses the full set of data collected, including demographics, efficacy parameters, lab values, adverse events and medications to cluster clinical trial patients. The algorithms identify expected values within clusters, and thus can identify patterns (or rules) and flag data that does not fit those patterns. Rules are identified within each patient cluster and across all patients, with typically over 3,000 rules found in the data of a single trial. Figure 3 represents examples of two different rules identified from a clinical data set.

Figure 3: (a) Box plot of BMI (b) Scatterplot pRBC transfusion

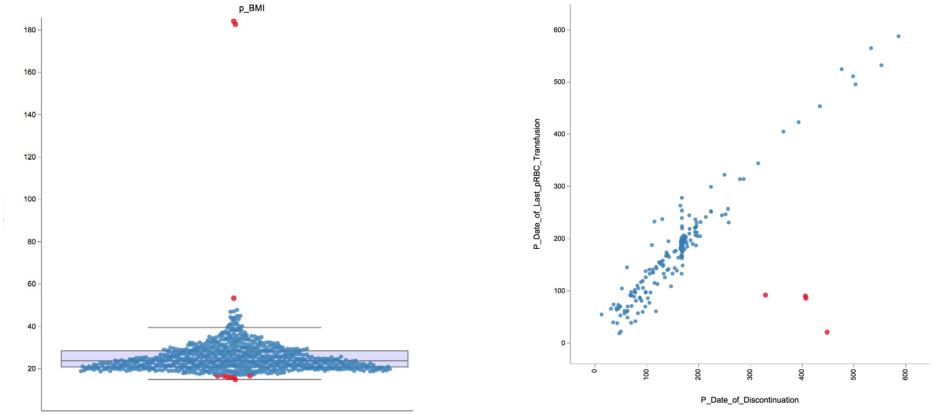


Figure 3 (a) shows a boxplot of body mass index (BMI) in which two patients (from the same site) are flagged as extreme outliers at the top of the graph, as their height was entered in the wrong units. The scatterplot in Figure 3 (b) shows data from the study day of discontinuation vs. the last study day of packed red blood cells (pRBC) transfusion. The four outliers in the graph on the right stand out as unusual because they do not follow the trend of the other data points. These four patients are said to have broken one of the "rules" set by the data. The user does not need to define such rules ahead of time; rather, these rules are identified by the software automatically (not hard-coded in) and alert the user once issues are found.

Individual sites and the overall study are graded for data quality based on the percentage of data points flagged as outliers. As shown in Figure 4, each site has its own dashboard that displays a grade, statistics summary and a list of the patients and variables with the highest percentage of anomalies at that site.

Figure 4: Representative example of a site performance dashboard

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Site Overview

B	A+	High Risk Patients	
Site Grade	*Study Grade*	Patient	% Discrepancies
8	421	4561002	5.16
Total Patients	*Total Patients*		
2.62	2.38	4561008	4.35
Percent Discrepancies	*Percent Discrepancies*		
3.48	3.27	4561007	4.18
Average Discrepancy	*Average Discrepancy*		
		4561010	3

About Medidata

Medidata is leading the digital transformation of life sciences, with the world's most-used platform for clinical development, commercial, and real-world data. Powered by artificial intelligence and delivered by the #1 ranked industry experts, Medidata helps pharmaceutical, biotech, medical device companies, and academic researchers accelerate value, minimize risk and optimize outcomes. Medidata and its companies, Acorn AI and SHYFT, serve more than 1,200 customers and partners worldwide and empower more than 150,000 certified users every day to create hope for millions of patients. Discover the future of life sciences:

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