Clinical Data Like You´ve Never Seen It Before: Why Spotfire is the Leading Tool for Clinical Analytics

Clinical development organizations face a wide array of challenges when it comes to data, many of which can impact the operational effectiveness of their clinical trials. To address these issues, clinical trial teams must leverage advanced analytics platforms that afford them verifiable results, standard-ized views, and intuitive collaboration mechanisms to avoid risks that compromise a trial's progress.

In a recent webinar, "Clinical Data Like You've Never Seen It Before: Why Spotfire is the Leading Tool for Clinical Analytics," experts from PerkinElmer Informatics explored how solutions like its TIBCO Spotfire platform enable better, more streamlined studies. The event also featured a success story from Ambrx, a leading biopharmaceutical company in the area of protein therapeutics, on how it has leveraged Spotfire to tackle data quality and collaboration challenges as part of its clinical trials.

Panelists for the event included:

• Brent Meyers, Director of Clinical and Translational Analytics
• Glenn Guthrie, Principal Product Lead for Clinical Analytics
• Dong Xu, Ph.D., Vice President and Head of Biostatistics & Data Science, Ambrx

The proliferation of decentralized clinical trials has created new complexities for life sciences research – selecting and managing multiple sites, parsing new data sources, and enlisting more diverse participants necessitates best practices aimed at connecting and optimizing data. Surmounting these challenges requires delivering solutions that enable greater collaboration and connectivity, as well as facilitating greater data review, domain expertise, and overall operations management.

Modular analytics, tailored to a use-case, are key to advancing this data optimization for clinical development and generating faster, more actionable insights. PerkinElmer Informatics' Clinical Solutions, coupled with the advanced analytics of Tibco Spotfire, represent an integral tool in helping biopharma-companies and trial sponsors tackle data quality and collaboration challenges and enable more streamlined, better managed studies.

Taking Control of Data with Advanced Analytics

Recent history points to an ever-increasing number of data sources in the average clinical trial. While this volume varies by therapeutic area, the challenges inherent to managing excess data are present across the landscape.

Many clinical trial teams are overburdened with manually importing, cleaning, and plotting this data, impacting the time and resources needed to meaningfully investigate and interpret it.

Many of these teams rely on one-size-fits all consumer products like Microsoft Excel to track data. Building safety and efficacy plots, as well as other forms of visualization, in applications like Excel require significant time and effort, potentially impeding time-sensitive decisions.

Safety signals buried within hundreds of lines of inert data are easy to miss. Transitioning from traditional, data-handling practices to more holistic, agile approaches is critical to improving this paradigm. By utilizing the tools emerging across the space today to inform study design or developmental strategies, trial teams can safeguard their progress and make more informed decisions.

The need to transition to more comprehensive data analytics platforms will only increase as clinical trials become more complex: over the last 10 years, clinical trials have experienced a 60% increase in protocol amendments. While there are expenses associated with these changes, the implication of this upward trend is an industry keen on adapting to new challenges as trials progress.

In terms of maximizing investment in clinical trials, sponsors have increased their investment in trial endpoints by 86% in the same time-frame, and have experienced a 63% increase in the number of sites involved in trials.

The incumbent analytical tools and processes employed by many of these trial teams are insufficient to address this increased complexity, due to relative inflexibility or even a lack of relevancy in interpreting the data involved.

Case Study: ARX788-1711 Phase I Pan-Tumor Study

Ambrx, a pioneer and leader in engineered precision biologics – therapies created using its expanded genetic code technology platform – is focused on overcoming the inherent limitations of conventional conjugation approaches.

The company has achieved this by innovating on the site-specific modification of proteins to create novel, best-in-class biologics.

Its internal pipeline is focused on creating antibody drug conjugates (ADCs) and immune-oncology conjugates; its most advanced internal ADC candidate is ARX788, which is currently being studied broadly in multiple phase 1, 2, and 3 studies. The target patient population covers breast cancer, gastric cancer, non-small cell lung cancer, and many other solid tumors.
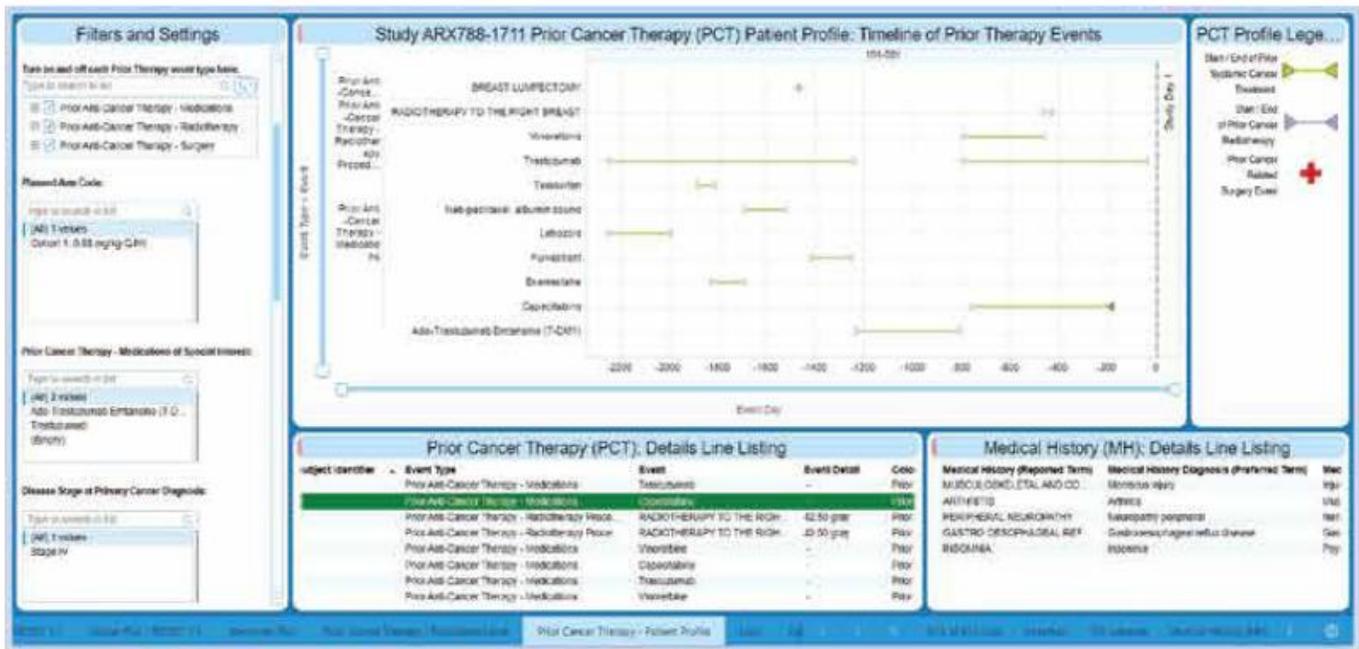

Figure 1. Prior Therapy

With collaboration from PerkinElmer, Ambrx began employing Spotfire more than a decade ago, and its success with the platform has extended to its trials involving ARX788.

Ambrx's Phase 1 pan-tumor study of ARX788-1711 has leveraged Spotfire's functionality – in particular, PerkinElmer's Clinical Data Review and Oncology Efficacy modules – to great success. For this study, the primary goal is to assess the dose-limiting toxicity (DLT) of ARX788 and determine its maximum tolerated dose (MTD). The study's design is a straightforward 3 + 3 dose-escalation, and many of the variables that constitute its key data points, from demographics to individual patient profiles to adverse events, are up-to-date, filterable, and comparable using the Spotfire platform.

For example, users can know the trial's enrollment status in real time, without downloading raw data from a data-base and calculating it themselves, and can perform any subgroup analysis by specifying various filters and variables using Spotfire's control panel.

Performing subset analyses based on cohort, prior cancer therapy, disease stage, or some combination of these or other variables is core to Spotfire's value in trials like ARX788-1711.

This tailored analysis is particularly important for cohorts like the trial's breast cancer population; because Ambrx is interested in studying the efficacy of ARX788 on breast cancer patients who have failed other available therapies **(Figure 1)**.

Being able to analyze this data more closely informs its future development strategy for these patients. This evaluation capability extends to the individual patient level – users can see a participant's prior surgeries, radiotherapies, and medications, which in turn helps inform a more holistic understanding of Ambrx's target patient population.

Safety is the central concern of any clinical trial. Monitoring a study's safety in real-time in order to understand it in the context of the trial's overarching goals is critical.

For the ARX788-1711 trial, Spotfire has enabled Ambrx to track adverse events from a number of vantage points, including outcomes, the action taken, and number of adverse events by toxicity grade **(Figure 2)**. Users can drill down from there: from the "action taken" visualization, for example, researchers can access additional levels of detail, such as the summary statistics for interactions, delays, reductions, and discontinuations of treatment.

These key parameters help the trial team understand, in real time, the overall safety profile for patients. As with other metrics, Ambrx is able to drill down to patient-level data for adverse events and tailor its results for optimal utility.

Ambrx also has a customized presentation for its efficacy endpoint data in Spotfire, the result of collaboration between Ambrx and the PerkinElmer team to create a comprehensive tool that captures the wide range of factors that impact a treatment's effectiveness. The result is a comprehensive swimmer plot that
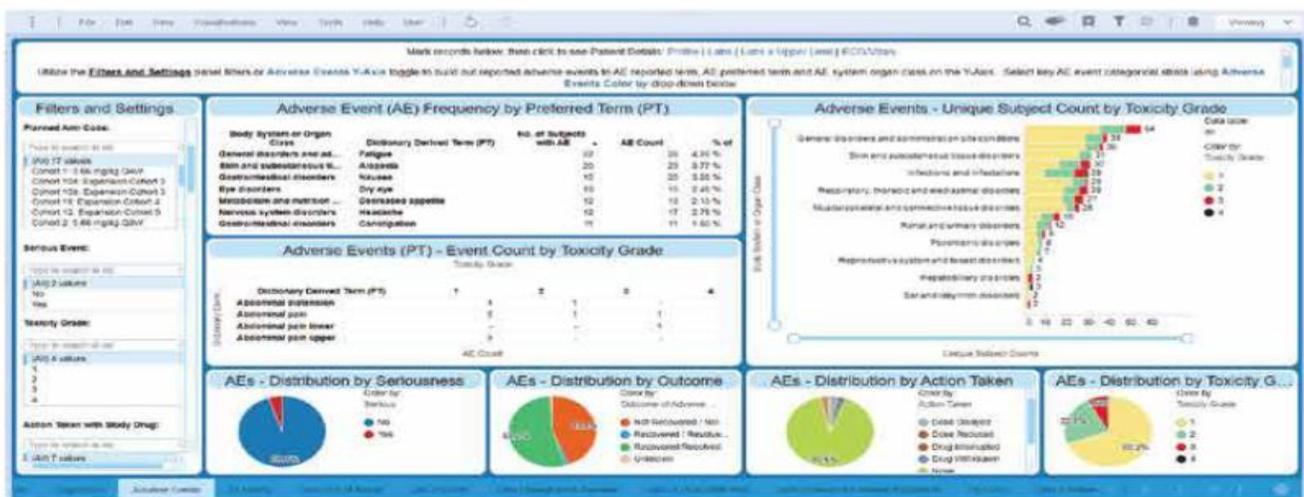

Figure 2. Adverse Event

Figure 3. Comprehensive Swimmer Plot

combines tumor assessment data with dosing information, color coded and organized to make comparing the efficacy of the treatment with patient dosage and track the relationship between them and other key factors **(Figure 3).**

Ultimately, Spotfire is a powerful tool for medical data review. Once connected with Ambrx's RAVE database, its real-time data presentation offers users like Ambrx a seamless solution, able to integrate data from different domains. Each page can be easily tailored to fit reviewer needs. With just a click, users can produce different subgroup analyses to assess the robustness of data across different subgroups and identify any outliers. The platform is very intuitive and easy to use, and with training support from PerkinElmer, Ambrx's entire cross-functional team is able to use this tool on a daily basis to improve productivity and drive better trial outcomes.

Modular, Flexible Solutions for Advanced Analytics

Any existing configuration in Tibco Spotfire can be further extended to address additional questions users might have, including those associated with pharmacokinetics, related analytics, or issues linked to specific therapeutic areas - PerkinElmer frequently fulfills requests to add analytics for Oncology and create supplementary Swimmer, Spider, and waterfall plots, for example. The system is designed to be flexible and agile enough to address changing analytical needs.

PerkinElmer's core modules are typically its Clinical Data Review Module, which can answer a variety of biostatistical, data management, and safety questions its Medical Review Module, which offers a tailored workflow to address medical monitor specific questions, and its Operations module, which allows clinical project managers, CRAs, and other site monitoring teams to monitor their studies remotely or centrally **(Figure 4)**

For specific needs, PerkinElmer can also add capabilities to track line listing review or data status, add study-specific efficacy analyses, and directly connect to a multitude of data sources to receive a near-real-time view of data

Spotfire features superior capabilities when it comes to data wrangling. Its Clinical Data Review Module exemplifies the power of this data wrangling: Spotfire can connect to virtually any data at its source, transform disparate data structures to easily create clinically-relevant visuals from SDTM and raw data sources alike.

Although the visuals "out of the box" have proven their utility over hundreds of clinical studies, they are also capable of being customized quickly and easily to suit particular study team needs, as is the case with Ambrx's Spotfire implementation. PerkinElmer's services team, in collaborating with sponsors to tailor the Clinical Data Review Module, centers its configuration on some key
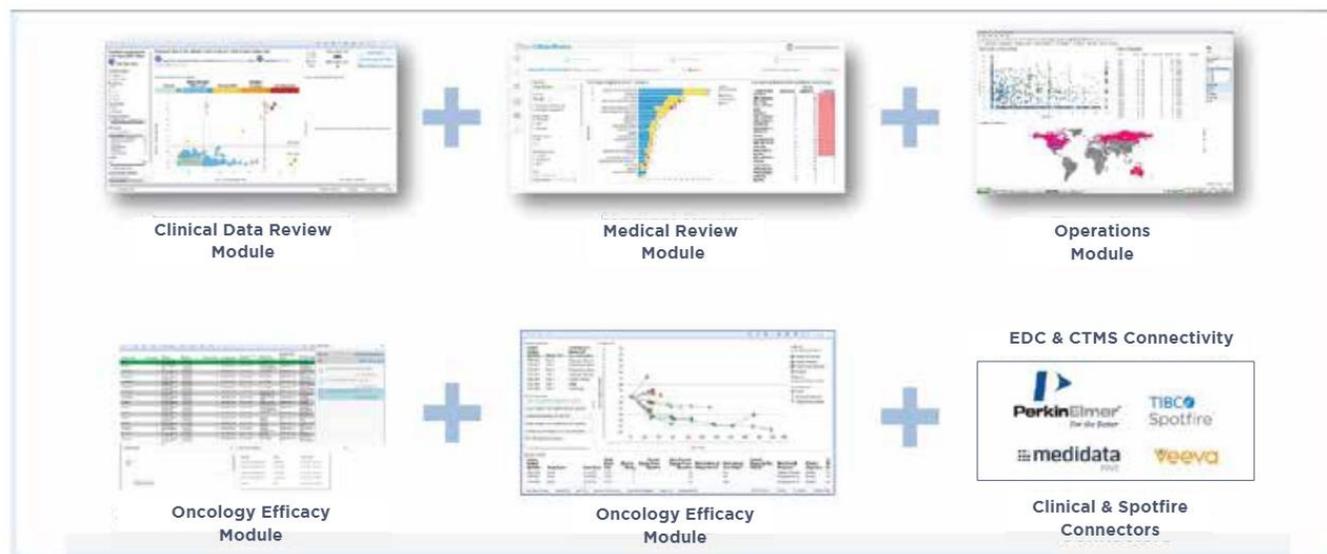
Figure 4: Use case in which the client needed data, medical review, and operational oversight into their pivotal solid tumor oncology investigational products.

variables with particular emphasis on biostatistics, data management and safety.

By working to understand the endpoints and challenges of the trial in question, PerkinElmer Informatics' Clinical practice can help facilitate workflows for sponsor trial teams that inform approaches and flag issues quickly and precisely. One example of this is PerkinElmer Informatics Oncology visualizations, which feature a slew of efficacy-based data visualizations tailored for oncological trial applications.

Waterfall, spider and swimmer plots are standard visualizations that can be improved on in Spotfire. Instead of being static visuals, in Spotfire one can color and filter the visuals to correlate outcomes with demographics, biomarkers, prior therapy, cancer type or patient specific information.

A waterfall plot can be filtered to see just the subjects in dose expansion vs dose escalation, or to view a particular cohort. The plot can also be colored to see if higher dosing levels during dose expansion are having an impact on tumor growth.

Another optional addition to Spotfire, the Line Listing Review Module, is geared toward the collaborative process of establishing and resolving a medical query in the data. This functionality allows users to initially evaluate questionable variables in the data; and mark that data for further review by collaborators within data management who can then take action in source data systems such as EDC. **(Figure 5).**

Resolving actions from this query from source data systems as well as any updated results can then also be visualized within Spotfire.

This tracking capability, coupled with near real-time updates to data, help ensure that trial teams have access to the most accurate information regarding a trial's progress at any given time, alleviating the hassle of employing a separate workflow to track and resolve medical queries during review.

Ultimately, the ability to collect and visualize safety and efficacy data in a centralized location, in a timely, repeatable fashion, is key to overcoming many of the challenges faced by clinical trial teams. PerkinElmer Informatics' various modules for Spotfire offer advanced analytics solutions for every area of clinical development. By employing the Spotfire platform as part of a clinical trial, researchers can improve efficiency, minimize discrepancies, and streamline collaboration across functional groups.

Spotfire has unparalleled workflow flexibility, allowing users to quickly identify risks, engage in dynamic collaboration, and safely bring therapies to market faster.
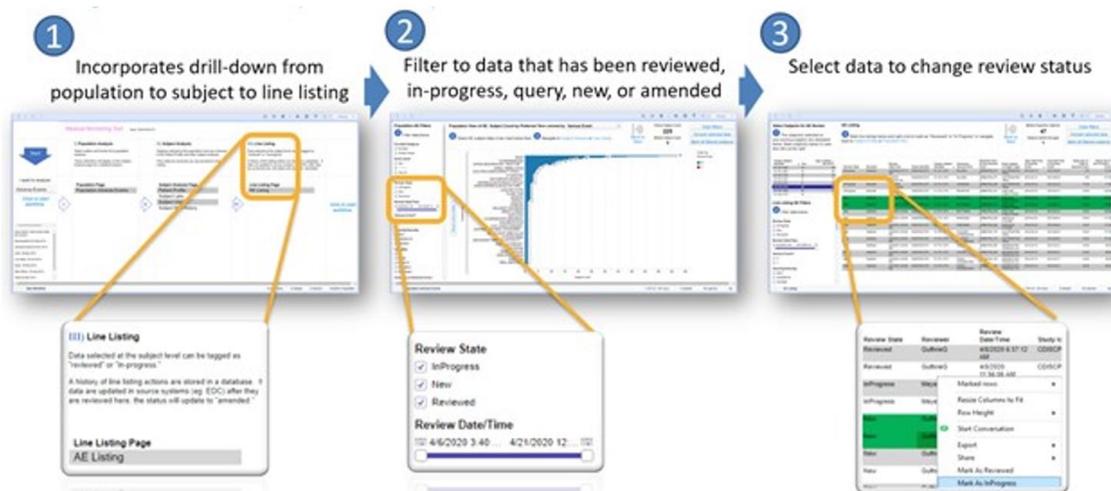
Figure 5: Resolving Medical Query through Line Listing Review

Using Spotfire's® advanced analytics across all areas of clinical development can help users minimize discrepancies, improve efficiency and collaboration among cross functional groups, and collect, visualize, and mine study data to achieve better trial management and overcome fundamental challenges. Ensuring patient safety and streamlining clinical development so important treatments can reach the patients who need them faster are the ultimate goals of any clinical trial, and PerkinElmer's customizable analytics solution empowers sponsors to accomplish these goals.

Achieving more successful, better managed trials hinges on solutions that enable easy data mining and real-time insights, and Spotfire's holistic, flexible platform is primed to help trial teams achieve it. PerkinElmer Informatics Clinical Solutions, powered by TIBCO® Spotfire® provide a unified, scalable data analytics.

To learn more, contact us at clinicalinformatics@perkinelmer.com

or visit us at https://perkinelmerinformatics.com/products/clinical-translational/clinical-solutions

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