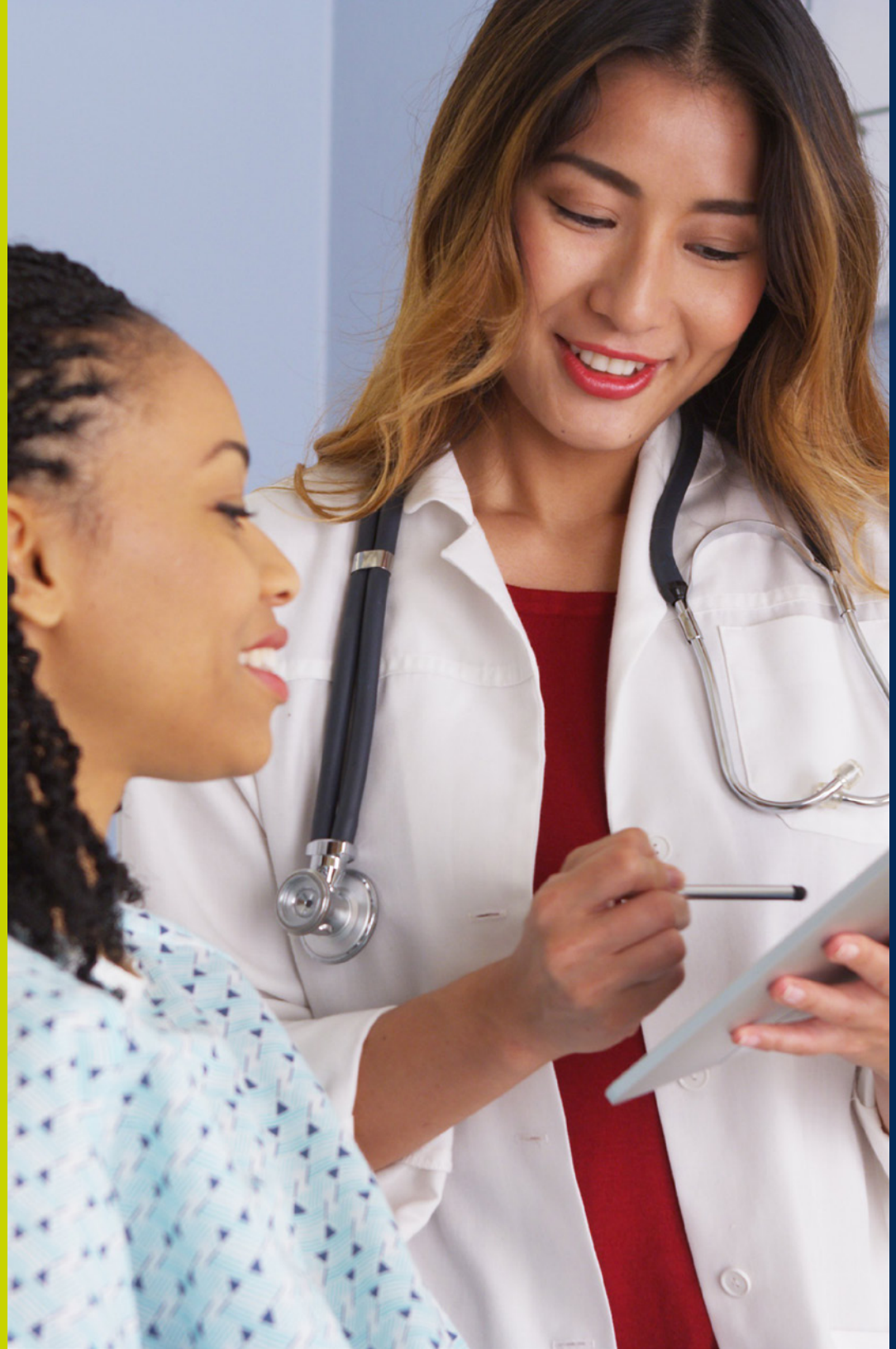


MEDIDATA

Shorten the Path

From Discovery to Approval of Novel Therapies

Use Medidata Trial Design to gain additional insights and evidence for the patient populations studied in your trial and accelerate time to market, lower risk, cut costs, and reduce patient burden.

Table of Contents

Introduction

The race to develop therapies, obtain approval by regulators, and provide new treatments to patients has never been more competitive nor more important, yet the obstacles encountered along the path from discovery to approval threaten the successful launch of novel therapies.

The complexities of clinical trial design often result in lengthy timelines, added costs, increased risk, and greater patient burden.

- Spending on research and development (R&D) has increased more than 50% between 2015-2019 and by more than 10x since the 1980s[1]
- Yet, drug approval rates have remained consistently around 8-12%[2]

One way organizations can improve this is to employ external evidence and insights. This can come from a variety of sources including real world data (RWD), information relating to patient health status and healthcare delivery, as well as the clinical evidence of usage, potential benefits, and predicted risk. However, RWD can introduce bias and lack the patient-level specificity required to answer the hardest of clinical development challenges.

Medidata Trial Design allows sponsors to access unparalleled cross-industry, curated, historical clinical trial data from 30,000 trials across more than 9 million patients, combined with advanced analytics and deep industry and regulatory expertise to help clinical development teams use novel and proven approaches. As a result, teams can reduce trial planning uncertainty and increase the probability of trial and regulatory success as they design trials. This enables teams to accelerate time to market, lower risk, cut costs, and reduce patient burden.

COMMON CHALLENGES

- Investment in R&D has gone up over 50% since 2015, while trial successes have remained constant around 12%
- RWD offers breadth, but lacks specificity

MEDIDATA TRIAL DESIGN SOLUTIONS

Trial Design combines one-of-a-kind cross-sponsor, regulatory-grade, patient-level clinical trial data with pre-integrated real-world data to help clinical developers make critical, data-driven decisions throughout the product development lifecycle and increase their probability of success.

- Improving the probability of technical and regulatory success (PTRS) of your trial by accessing the best available historic clinical trial data (HCTD) to design safer, more effective trials and using predictive modeling to uncover risks before they become trial failures
- Delivering unparalleled access to historical trials and peer-reviewed research proving the efficacy of benchmarking common lab markers against our data to help understand which patients are most likely to experience adverse events to allow clinical developers to design proactive risk mitigation strategies and prevent trial failure
- Offering indication-specific, patient-level past clinical trial data that is highly relevant and contains all the covariates and endpoints as they were designed and captured within their original trials

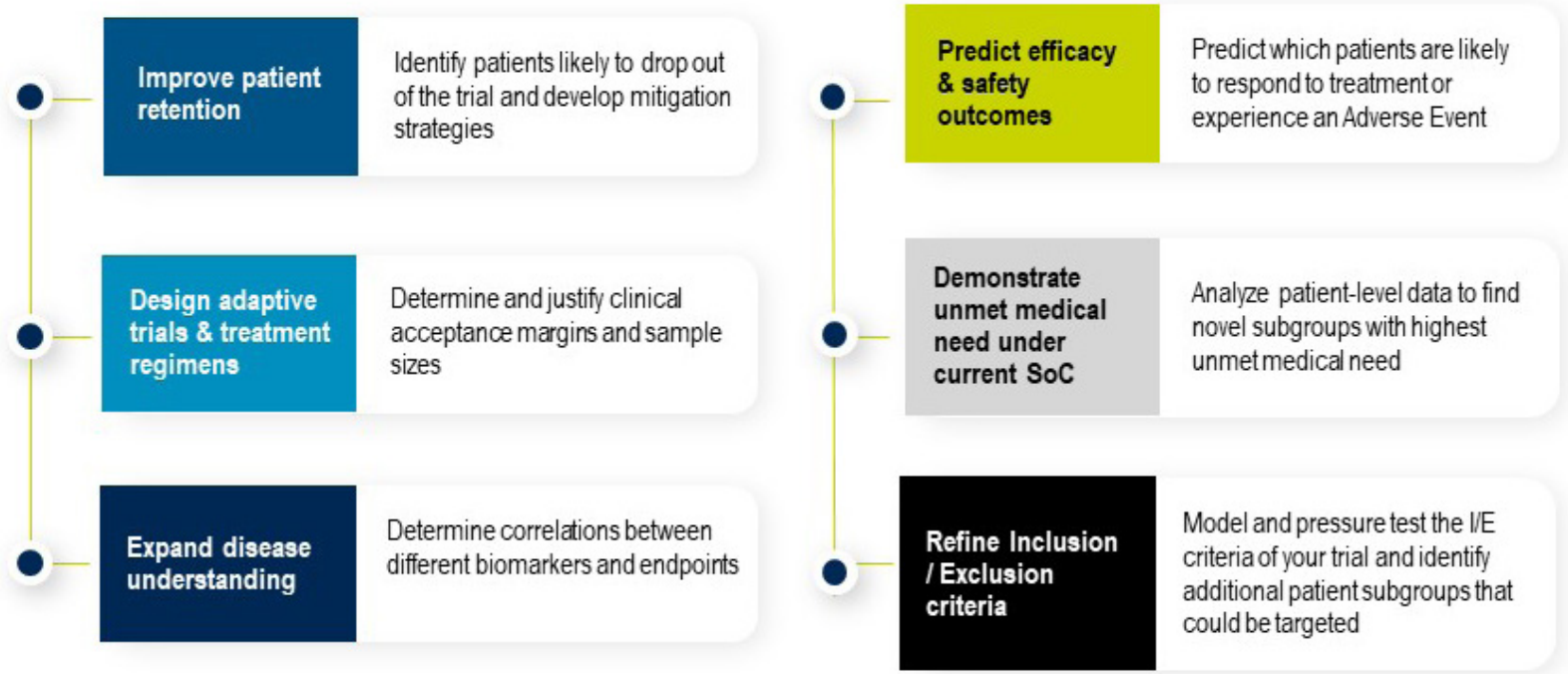
SUMMARY OF TRIAL DESIGN BENEFITS

- Providing powerful insights to better predict therapeutic efficacy
- Informing evidence-based decisions leading to safer trial design
- Increasing the probability of success, minimizing the risk of trial failures

Together, this allows sponsors to access unparalleled cross-industry, curated, historical clinical trial data combined with advanced analytics and deep industry and regulatory expertise to help clinical development teams.

Introduction

6 key uses of historical data to support R&D



MEDIDATA

DASSAULT SYSTEMES

This eBook examines applications of historical trial data and presents examples—in varied indications across the clinical development lifecycle—that illustrate how Medidata Trial Design helps organizations overcome potential hindrances and accelerate their therapies' path to market.

Use Case

01

Identifying patients likely to respond to an investigational aldosterone synthase inhibitor and defining target population for Phase III trial using historical CTD

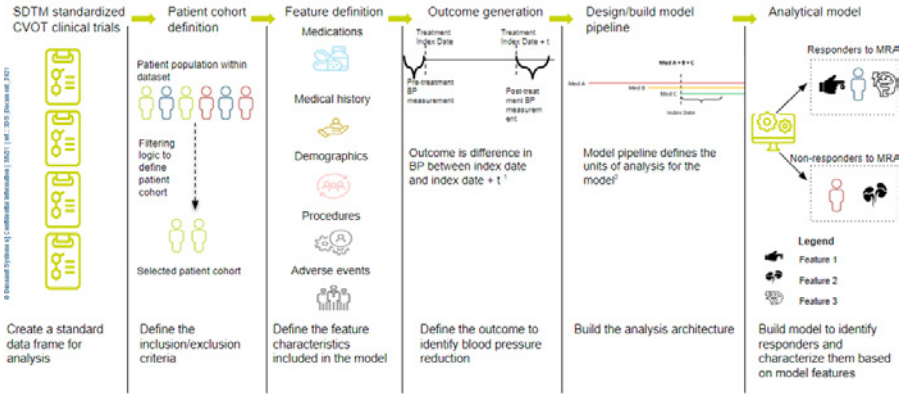
01

CHALLENGE

In trials where an expanded patient population might be eligible for participation, clearly defining inclusion and exclusion criteria can avert difficulties with patient recruitment, enrollment, retention, and identification of likely responders, which might otherwise lead to trial failure.

SITUATION

A biotechnology company is seeking market approval for a novel, highly selective aldosterone synthase inhibitor (ASI) for the treatment of resistant hypertension. Characterizing responders to mineralocorticoid receptor antagonists (MRAs), the closest available analog to ASIs, enables refinement of inclusion/exclusion criteria for future clinical trials which improves the probability of technical and regulatory success. This information will also inform market access strategy.



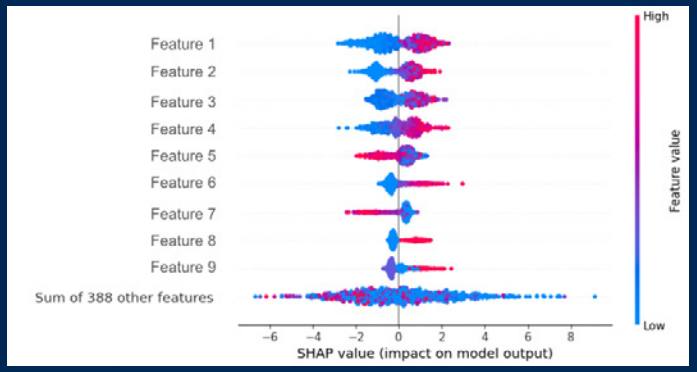
The figure captures the schematic of the approach used to create the model to identify responders vs. non-responders

APPROACH

Historical clinical trial data was standardized to create a dataset of ~100,000 patients across 6 cardiovascular disease trials. A model was developed to characterize blood pressure responders and non-responders to MRA initiation.

The Approach included:

- Defining clinically relevant features and the endpoints to capture BP response
- Validating the model with sponsor data



The figure shows SHAP values, which describe a feature's impact on a prediction, here the prediction is whether or not the patient responds to MRAs.

KEY

Features are ranked according to importance in descending order:

- Red = large feature values
- Blue = low feature values
- SHAP values show whether the effect of that feature value is associated with a higher or lower prediction for the outcome

IMPACT

Medidata delivered results in weeks to support high-paced decision-making:

- Leveraging the model to define characteristics for super-responders and refine eligibility criteria for a Phase III trial
- Helping inform the design of subgroup analysis within Phase III trials to support post-approval payer discussions
- Supporting the design of data capture requirements to generate market access evidence (QALYs, adverse event rates) for payers and decision support tool for clinicians

Use Case

02

Demonstrating that CR could be a viable primary endpoint for treatment efficacy for high-risk DLBCL patients

02

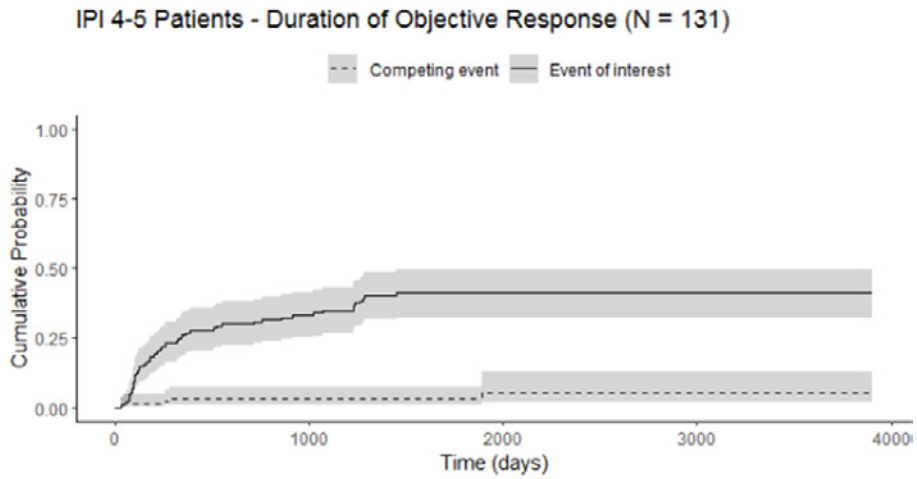
CHALLENGE

Establishing endpoints that demonstrate treatment efficacy is necessary to adequately assess the value of novel therapies under investigation. Further, it can help run shorter trials if a surrogate endpoint can be demonstrated to be a good indicator of long-term benefit.

SITUATION

A biotechnology company is planning a clinical trial (CT) evaluating the efficacy of using CAR-T therapy as a first line therapy (1L) in Diffuse Large B-Cell Lymphoma (DLBCL).

Establishing a clear link between post-treatment complete response (CR) by six months in 1L DLBCL with event-free survival (EFS) and overall survival (OS) may convince regulators to accept CR attained by 6 months as a primary endpoint for registrational studies on CAR-T.



Cumulative Probability: Duration of Objective Response

APPROACH

Medidata aggregated a novel clinical trial dataset of 160 high-risk DLBCL patients (International Prognostic Index [IPI] score 4 or 5):

- Establishing the rate of achieving and sustaining CR by 6 months
- Evaluating the association between achieving and sustaining CR by 6 months post-treatment and EFS and OS among patients with IPI 4–5 DLBCL treated with 1L CIT
- Generating the evidence for post-treatment use, to achieve and sustain CR by 6 months post-treatment as a viable endpoint to be used for a registrational trial in 1L DLBCL

IMPACT

Medidata delivered results in weeks to support high-paced decision-making for clinical trial:

- Providing evidence that CR achieved by 6 months of 1L CIT was associated with longer OS among high-risk DLBCL patients
- Demonstrating that CR can be an informative early endpoint for assessing the value of novel therapies
- Revolutionizing oncology clinical trial design by enabling trial timelines to be cut by 2 years, saving an estimated $10-15 million

Use Case

03

Top-20 pharma company leveraging anonymized patient-level data to investigate to inform a successful and differentiated CAR-T product development program

03

CHALLENGE

In trials involving a high-risk patient population, refining trial protocols is crucial in reducing the risk of treatment-emergent adverse events.

SITUATION

CAR-T therapy has rapidly become one of the most promising areas of immuno-oncology. Their development and adoption have been impeded by treatment-emergent adverse events (TEAEs), complexity of pre-conditioning regimens, dosing, patient selection, and other factors.

By leveraging Medidata Trial Design's pooled historical clinical trial data, a biotech company can set up their program for success and deliver optimal, safe, and effective therapies to patients and become a leader in the rapidly growing market space.

Data coverage by domain in Medidata CRS data
Days relative to experimental treatment start (i.e., TCE, CAR-T)

APPROACH

Using 3,000+ NHL, ALL, and solid tumor patients treated with CD19 Auto CAR-Ts and Bispecifics, a high-fidelity synthetic dataset was created for CAR-T trials. Having access to this cohort of synthetic patients has enabled the biotech company to investigate generalizability across heme-onc indications.

Example: Are the risk factors of ALL generalizable to NHL and ALL+NHL and Solid Tumor populations?

The high fidelity of the data allows the biotechnology company to run analyses relating to TEAEs. Treatment outcomes can be analyzed across multiple indications, treatments, and cohorts of patients.

IMPACT

Insights from analyses on the high-fidelity synthetic data allowed the biotechnology company to:

- Refine their trial protocols to reduce the risk of CAR-T/Bispecific TEAEs (CRS, ICANS)
- Identify optimal treatment patterns among each indication in relation to patients' clinical outcomes
- Refine their inclusion/exclusion criteria by analyzing patient characteristics and generating greater understanding of dosing schedules and AE management

This combination of insights greatly increased the probability of technical and regulatory success for their treatment development program.

Use Case

04

Using anonymized patient-level data to investigate to investigate patients pre- and post-CAR-T therapy with a top-20 pharma company

04

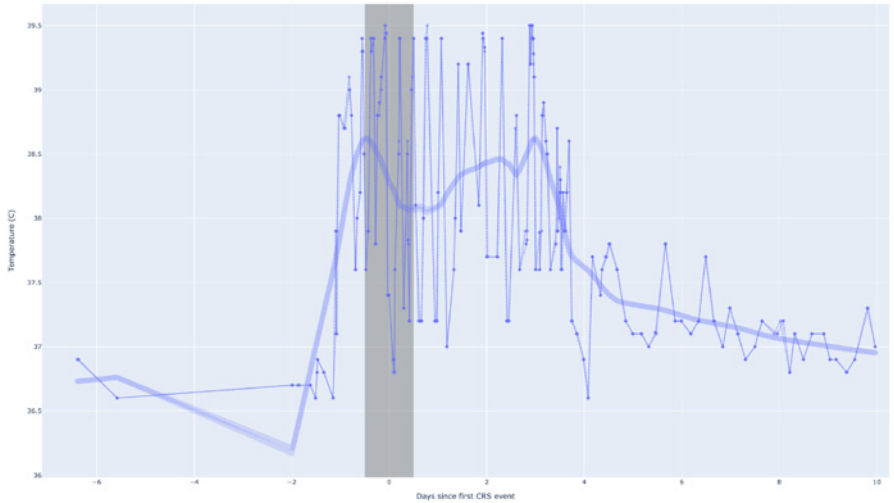
CHALLENGE

Without access to a substantial pool of historical clinical trial data, investigations could be hindered by unpredictable patient responses, including low treatment efficacy, increased adverse events, and high rates of failure.

SITUATION

CAR-T therapy has rapidly become one of the most promising areas of immuno-oncology. Historically, developers have had no longitudinal dataset available to them to conduct an in-depth analysis.

By leveraging Medidata Trial Design's pooled historical clinical trial data, a biotech company is able to expand their medical affairs and market access for their CAR-T product, support development of new products, and optimize products for clinical trial development.



Obfuscation of the data: Real vs. Simulant

APPROACH

Using 850+ NHL patients treated with CD19 Auto CAR-Ts and Bispecifics, a high-fidelity synthetic dataset was created for CAR-T trials.

This high-fidelity synthetic dataset allowed the pharma company to analyze treatment patterns pre- and post-CAR-T/TCE treatment and observe how those responses impact survival.

Using this synthetic dataset, the company was able to investigate outcomes of patients on subsequent therapies and assess how prior therapy impacts outcomes with CAR-T.

IMPACT

Medidata increased trial efficacy and improved the outcomes of patients treated with CAR-T therapy.

The synthetic data allowed the client to conduct multiple analyses to identify optimal treatment patterns, patient cohorts, and patient-related outcomes. This allowed the client to build optimal treatment regimens and refine their inclusion/exclusion criteria for future trials. And it helped the client design better future trials by considering prior or combination therapies.

Use Case

05

Predicting cytokine release syndrome (CRS) in clinical trials for T cell engager (TCE) therapies

05

CHALLENGE

Life-threatening adverse events are one of the greatest threats to clinical trial success—and in CAR-T therapy, CRS is one of most common and pernicious complications observed.

SITUATION

CRS is one of the principal challenges to the development of Immuno-Oncological agents. CRS is an AE characterized by fever and multiple organ dysfunction that is associated with CAR-T therapy, therapeutic antibodies, and haploidentical allogeneic transplantation. CRS has led to 15+ trial failures since 2016, $7B+ lost investment, and $20B+ lost enterprise value[1].

To avoid trial failure, the leading trial sponsor sought to build an industry-leading capability for the clinical development of TCE therapies using evidence-based and data backed strategies to optimize both the safety and efficacy of anti-neoplastic agents.

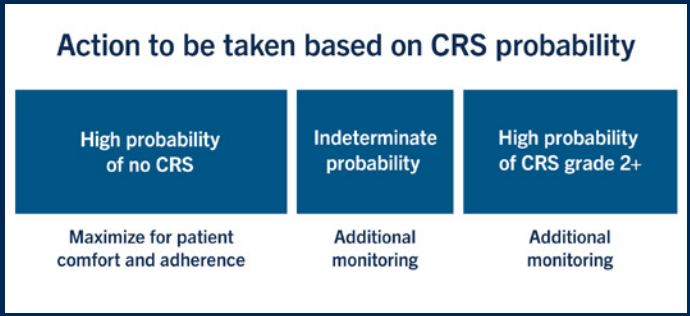
APPROACH

Medidata Trial Design accessed the world's largest cell therapy database and built a standardized clinical trial dataset consisting of >700 patients from 13 historical clinical trials.

TCE trials across multiple indications and sponsors, and with multiple CRS AEs, were standardized, and inclusion/exclusion criteria, data description, table shells, and codes were reviewed.

Various tree models were developed and trained to:

- Assign a risk quartile for CRS grade 2+ in TCE treated patients across multiple indications, based on baseline biomarker values and information available prior to the first dose



IMPACT

Medidata delivered results which support both patient-specific decision making and clinical trial decision making.

- Leveraging the model to identify and predict patients who are likely to have a CRS grade 2+ event
- An additional analysis emerged from early data findings on the correlation between Tumor Burden and CRS risk in the ALL TCE space
- These findings helped the pharma company maximize resource efficiency and treatment efficacy, while maintaining the highest safety standards

Their findings inform future study design and can potentially standardize the TCE space across the industry.

About Medidata

Medidata is leading the digital transformation of life sciences, creating hope for millions of patients. Medidata helps generate the evidence and insights to help pharmaceutical, biotech, medical device and diagnostics companies, and academic researchers accelerate value, minimize risk, and optimize outcomes. More than one million registered users across 1,800 customers and partners access the world's most-used platform for clinical development, commercial, and real-world data. Medidata, a Dassault Systèmes company (Euronext Paris: #13065, DSY.PA), is headquartered in New York City and has offices around the world to meet the needs of its customers. Discover more at www.medidata.com and follow us @medidata, The Operating System for Life Sciences™.

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