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Smarter trials. Faster cures.

WHY FLAWS ARE BEING SCALED NOT SOLVED IN AI-DRIVEN CANCER TRIALS

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Introduction

Oncology drug development is advancing at unprecedented speed, driven by a convergence of advanced molecular understanding, technological innovation, and urgent patient needs.

AI offers the potential to fundamentally transform drug development and bring safe and effective therapies to patients faster - providing the right data foundations are in place. Insights from Phesi's new global analysis reveal the systemic use of historical templates without patient data and context to guide protocol design leads to flaws being scaled, rather than solved by AI. Clinical development needs to start and end with real patients and be powered by AI that harnesses curated, contextualized data.

Less than a third of protocols are linked to patient data

Phesi's new global analysis of more than 600,000 clinical trial protocols shows that fewer than one in three (29.3%) protocols are linked to publicly documented patient data and outcomes.

This trend is consistent across oncology trials, where just 30.9% of 116,746 protocols are linked to usable patient data. With historical protocols often used as the basis for future trial design, the findings highlight a significant risk of flawed decision-making in clinical development.

Further analysis into breast cancer, the world's most studied disease over the past five years, shows that just 31.2% of 15,977 protocols are linked to trials with usable patient data. Even in the most data-rich disease area, high volumes of research do not automatically create the reliable, outcome-driven evidence base needed for future trial design or AI models. This is a systemic issue in drug development.

AI leads to flaws being scaled, not solved

It is standard practice to design protocols based on existing, similar protocols, but when those templates are disconnected from the target patient population, they contribute to amendments and recruitment challenges.

AI leads to flaws being scaled, not solved

In the past, protocol writers could be selective about the protocols they used and apply human judgment to the connection between design and the target patient population. AI can ingest far more historical templates, but without the right logic or judgment it may fail to make that connection. A clinical protocol is effectively a business plan for an investment of tens or hundreds of millions of dollars, so AI must be guided by the right data foundations. In essence, flaws are being scaled, not solved.

Closing the gap between protocols and patients

The reasons why protocols are not linked to patient data are complex. Some trials fail to recruit or complete because design issues restrict the ability to enroll, while others may enroll patients and collect data that never sees the light of day, despite legal reporting requirements. This creates a gap between protocol intent and what happens in patients, making it harder to understand which designs work, which fail and why. Without this visibility, sponsors risk reusing protocol designs that have already contributed to recruitment challenges, amendments or failed studies.

In severe cases, failure of a development program can lead to sponsor financial distress or even bankruptcy. For example, after the FDA limited the use of Clovis Oncology's cancer drug Rubraca, the company faced severe financial pressure, resulting in a 2022 bankruptcy filing and subsequent exit from business in 2023. OncoSec Medical filed for bankruptcy in 2023 after a key phase 2b trial for its cancer drug TAVO-EP failed to meet primary endpoints.

The gap between what protocols are designed to do and what actually happens in patients is the missing link in both current clinical development processes and emerging AI approaches. Datasets must account for the full patient population, not just narrow subsets from late-phase trials or large protocol datasets disconnected from patient treatment outcomes.

Similarly, patient population data extracted from electronic health records may or may not align with the patient population targeted by a protocol. Only curated and contextualized data enables sponsors to identify meaningful oncology subpopulations and surface risk factors.

Opportunities for AI to optimize clinical development

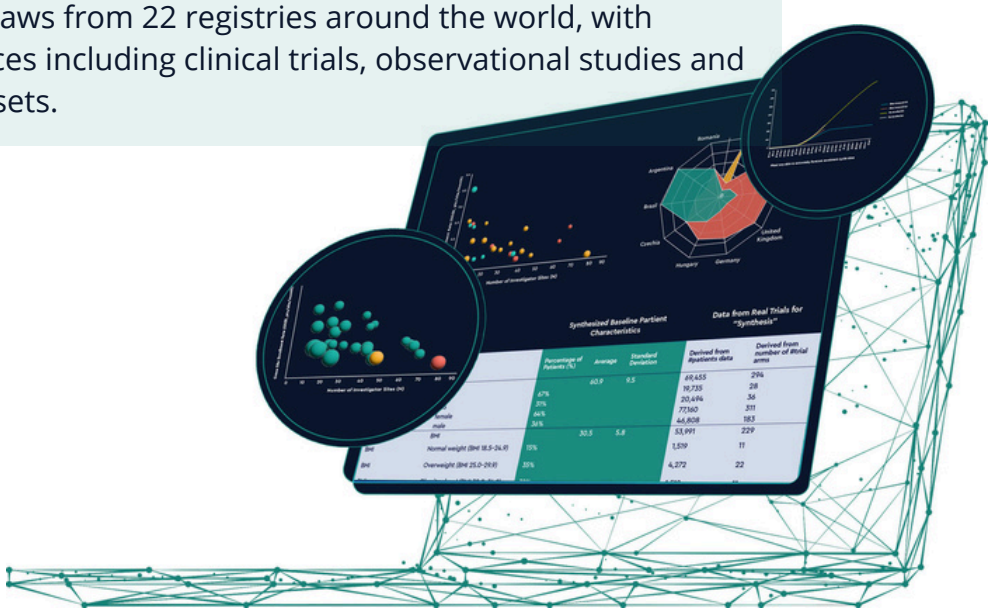
There is huge opportunity for AI to optimize clinical development, but only when the platform being used as the basis for AI can identify protocols with patients and outcomes reported.

The availability of significant volumes of contextualized patient data enables precise profiling of the patient, greater precision in protocol design and investigator site selection, and opens up the potential to generate digital twins in oncology to accelerate and modernize clinical development.

A data-led, precision approach to clinical development has already been proven to transform oncology clinical trials. For example, precision profiling of patients in breast cancer through biomarkers such as HER2, PIK3CA, BRCa1 and BRCa2. Meanwhile, the successful KEYNOTE trials for the immunotherapy Keytruda harnessed real-world data and performance scores to aid investigator site and patient targeting.

The Phesi data advantage

Phesi is focused on connecting real-world and clinical patient data with trial execution to support precise study design and decision-making. Our Trial Accelerator™ is built on this foundation, drawing on contextualized data from 375 million patients in 232 countries and territories, produced from 719,183 clinical research and clinical development projects guided by protocols and other study plans. The platform draws from 22 registries around the world, with additional sources including clinical trials, observational studies and real-world datasets.



Four ways real-world patient data improves oncology trial design and patient outcomes

1. **Profiling the patient to understand them better**

Using Trial Accelerator™ to analyze real-world patient data, we can build a Digital Patient Profile (DPP) for any indication that provides a statistical view of the patient attributes for the patient population specifically targeted by the protocol – including demographics, outcomes and concomitant medications. This is the starting point for all our clinical data science solutions. The DPP ensures trials are designed with the relevant patients in mind, preventing misalignment between the target patient population and the actual population recruited in a study.

Get in touch to access our Digital Patient Profile catalog with oncology Digital Patient Profiles including:

- Breast cancer: PIK3CA, HER2-Positive
- NSCLC: general NSCLC and KRAS mutated G12C and G12D NSCLC, and NSCLC-EGFR
- Prostate cancer: metastatic, Castration Resistant
- Pancreatic cancer: KRAS mutated, G12D

2. **Optimizing protocol design**

Oncology trial protocols are often overcomplicated with high numbers of outcome measures which increases patient burden and causes recruitment difficulties. Meanwhile, not all the data collected are used in the final submission. Comparing a trial's protocol against real-world data as well as historic trial protocol designs allows sponsors to assess whether their number of outcomes measures is too far above average. This ensures protocol design is optimized against the medical, scientific and commercial objectives.

Four ways real-world patient data improves oncology trial design and patient outcomes ... cont

3. **Greater precision in Investigator site selection**

Creating a Digital Patient Profile helps identify the expert physicians treating the target patient population. In conjunction with Phesi's Patient Access Score (PAS) it is possible to measure the probability of an investigator site accessing the patient population as defined in the protocol. This use of contextualized patient data improves precision in investigator site selection above and beyond historical clinical trial experience, driving higher enrollment rates and shorter enrollment cycles.

4. **Using digital twins to improve the efficiency of clinical trials**

The FDA is becoming increasingly supportive of digital twins in clinical trials. It is important to engage early and ensure good data governance and documentation.

To generate a digital twin, Phesi first builds a precise Digital Patient Profile. This forms the foundation for the digital twin using real-world patient data guided by the protocol. It replicates baseline patient characteristics and predicts the efficacy and safety outcomes of the control arm, allowing researchers to simulate how patients in the control arm are likely to respond to a treatment (or lack thereof) in a clinical trial. A Phesi digital twin has the potential to reduce the size of the control arm or completely replace it, among other use cases.

A Digital Twin of RAS Wildtype Metastatic Colorectal Cancer to Evaluate the Efficacy of Standard-of-Care

We recently published our fourth paper, this time with Harvard University/Dana-Farber Cancer Institute showing how digital twin technology can simulate stand-of-care treatment and provide reliable outcomes for RAS wild-type metastatic colorectal cancer. Read here

View here:

Conclusion

The biopharmaceutical industry is at an exciting inflexion point where we have the patient data and technology required to power precision oncology, reduce patient burden, and get safe and effective treatments to patients faster. AI offers the ability to process at speed and make timely decisions and the good news is that the FDA is increasingly open to its use, if they are involved early. However, in order to realize the potential of AI, current clinical development practices need to evolve to embrace contextualized patient data, otherwise the use of AI will merely scale existing flaws.

To learn more visit phesi.com

About PHESI

Phesi's patient-centric, AI-powered solutions deliver smarter trials and faster cures. Its award-winning Trial Accelerator™ platform draws on real-world data from more than 375 million patients across 223 countries and 4,000 indications. Using Digital Patient Profiles and the unique Patient Access Score, Phesi's precision insights help sponsors optimize protocol design, forecast enrollment rate and select lead enrolling countries and investigator sites to reduce patient burden and cycle times. From enabling Digital Twins and External Control Arms, Phesi is transforming the future of clinical development. To learn more visit phesi.com or book an exploratory meeting via info@phesi.com

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