HOW TO MAXIMIZE PATIENT RECRUITMENT IN ONCOLOGY TRIALS

DIVE BRAND STUDIO

COVANCE
SOLUTIONS MADE REAL®

A **BIOPHARMA DIVE** PLAYBOOK

Over the last several decades, patient recruitment for clinical trials has remained a major barrier to rapid execution of drug development programs. Currently, less than 20% of studies are on-time, meaning the majority are failing to meet initial plans and expectations. Sponsors are also spending 20% to 60% of their time recruiting patients and about 40% of their study budgets on this task.

This problem is particularly acute in oncology. As the number of oncology trials has risen, the industry still has not been able to overcome the patient-recruitment problem to meet the increased demand for patients. It is estimated that only 3% of cancer patients participate in clinical trials,[1] but over 12,000 interventional cancer trials are currently recruiting or planning to recruit, according to the website clinicaltrials.gov.

Despite many attempts to improve the process, "most of our time is spent in identifying and recruiting trial participants," says Dr. Brett Bishop, global vice president and general manager of Oncology at Covance. "And as the various studies become more complex and the specificities of the disease become more granular, recruiting patients is becoming ever more challenging and costly."

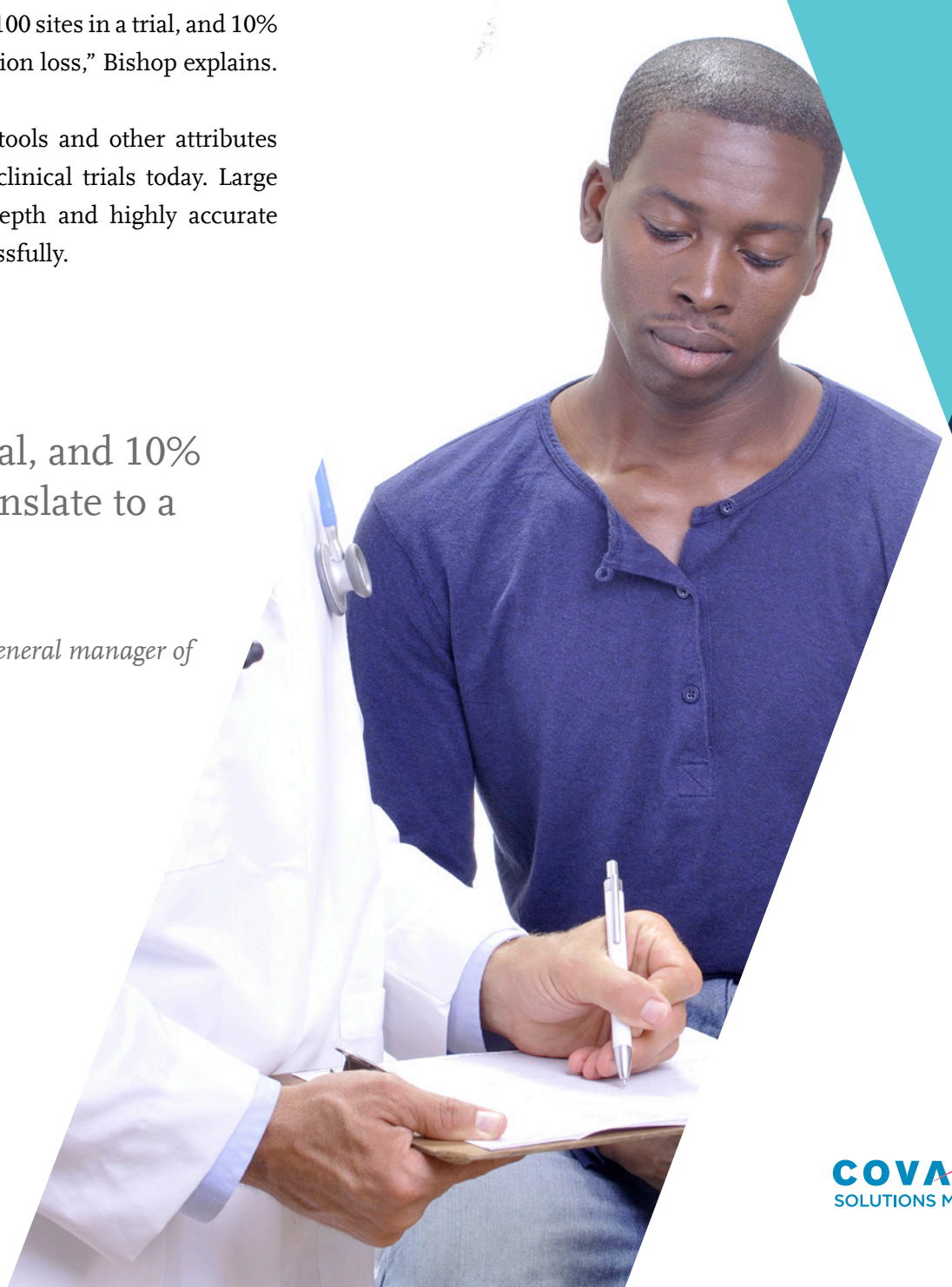
There is also an increase in the number of global trials, raising further challenges. "We are tracking data on over 175,000 investigators all over the world," says Bishop. And the disparities between sites is still striking, with many doing a very poor job of recruiting patients.

That leads to much higher costs. “If there are 100 sites in a trial, and 10% perform poorly, that can translate to a $1 million loss,” Bishop explains.

This playbook highlights unique expertise, tools and other attributes that can help companies excel in oncology clinical trials today. Large amounts of data and the ability to do in-depth and highly accurate analysis are key to implementing trials successfully.

“If there are 100 sites in a trial, and 10% perform poorly, that can translate to a **$1 million loss.”**

Dr. Brett Bishop, global vice president and general manager of Oncology at Covance



Immuno-Oncology Adds a Twist

With a new focus on immuno-oncology, both recruitment and study design have become even more challenging. Although the first such products, called checkpoint inhibitors, just started to reach the market a few years ago, immuno-oncology is expected to generate approximately $14 billion in drug sales annually within the next several years and then more than $30 billion within a decade,[2] thus providing a serious competition to develop novel immuno-oncology products and/or explore combinations with such products. Fully one-third of oncology trials currently include immuno-oncology products – which represents a twenty-fold increase in the number of trials with immuno-oncology products since 2010.[3] The success of these drugs has clearly ignited an intense race within the pharmaceutical industry to launch the next breakthrough immuno-oncology products.

However, it's still not clear why only a small proportion (10% to 50%)[4] of patients respond to these new drugs and how to select the most appropriate patients for a particular trial. As a result, there is a growing interest in biomarkers. The hope is that such markers will better match patients to available treatments.

Fully one-third of oncology trials currently include immuno-oncology products – which represents **a twenty-fold increase in the number of trials** with immuno-oncology products since 2010.[3]

Combination trials have also become increasingly important, as researchers aim to attack cancers from multiple vantage points. Checkpoint inhibitors essentially hobble the system that allows cancers to evade immune detection. Now, researchers hope that once they disengage that system, they can also elevate other means of attack, such as targeted therapies and immune stimulators. In fact, drugs that have been in development for years are now getting new interest as they are being tested in combination with new immuno-oncology products. Surgery and chemotherapy will also continue to be used. Again, it will be crucial to know which patients need which treatment and when is the best time to deliver it.

It's a whole new paradigm. The recent rapid evolution of immuno-oncology has thus led to the increased need to be nimble and able to quickly test hypotheses and then build upon them with robust follow-up trials. Companies are excited about the initial dramatic results from these new drugs, but they now want to boost response rates. To do that, they need optimally designed trials and the appropriately selected patient populations.

Patient recruitment is a key industry pain point that demands innovative new approaches. "Despite all the best efforts of the last 20 years, this has remained a major problem," says Bishop.

Data-Driven Study Recruitment and Design

One of the critical early steps is to select the best-performing investigators. Being able to identify top-performing investigators saves time and money by including only sites where the quantity of patients and quality of the work are appropriate for a robust trial. "About 10% of all sites fail to enroll even a single patient," says Bishop. Simply eliminating these sites will dramatically reduce costs and potentially speed recruitment. It's also important to be able to identify sites that make a lot of errors, such as sending in non-viable samples, making mistakes on requisition sheets or showing other signs of poor quality.

This type of analysis can only be done by companies that already have troves of data about current investigators and sites. Incorporating other data, including that available from public sources, can greatly enhance capabilities.

"About **10%** of all sites fail to enroll even a single patient."

Dr. Brett Bishop, global vice president and general manager of Oncology at Covance

Breast Cancer Case Study: The High Value of Data Layering

By layering the World Health Organization's breast cancer prevalence data in Europe with the Covance proprietary data on patient recruitment and investigator performance, it's possible to locate the most advantageous sites to include in a clinical trial. In one case, a trial had 116 sites, but only 42 sites were active and it had taken 15 months to enroll just 77 patients.

Using the Covance proprietary Xcellerate® Informatics Suite, the company was able to optimally leverage its Historical Performance Database. Covance has access to data on over 40% of industry trials at any one time and information on more than 16,000 protocols.

For this particular breast cancer study, Covance compared the performance of various investigators and then made recommendations to close out 31 non-performing sites and add 51 more, some in countries that had not previously been involved in the trial. The result was a doubling of the recruitment rate: In effect, this rescued the trial and the trial was delivered according to the projections

Continues on next page

COVANCE
SOLUTIONS MADE REAL®

Excellent trial design and implementation are also essential, and having data from thousands of previous trials ensures better results. Study design has evolved very rapidly, even over the last couple of years. So being able to visualize the patient distribution and track trends in diagnostic test use are invaluable in protocol design. To do this ideally, it is necessary to have sufficient data to model and test the consequences of specific protocol choices. The patient pool, for example, can be narrowed or broadened, depending on how that will impact the validity of study results.

This ability will become increasingly important as biomarkers play a greater role in oncology study design. Those designing protocols will need to determine the specific diagnostic criteria for patients eligible for trials and how that criteria may evolve as the trial progresses.

Data, Experience and Scope Make the Difference

How can we finally break the 20% barrier and reach a point where the majority of oncology trials are recruited sufficiently according to plan? "We now have the ability to optimize protocols that can be implemented in the real world, with patients that actually exist," says Bishop.

generated at the time of the intervention (18 months antecedent to last patient enrolled in the trial).

With its recent acquisition by LabCorp, Covance is now also capable of analyzing millions of data points from de-identified patient care test data, along with information from clinical trial protocols. "LabCorp is the leading diagnostic testing lab in the world," says Frank Makosiej, executive director, operational strategy and planning at Covance. "We've been very excited by what we can do combining this data with what we already have, and the growing wealth of public data."

LabCorp processes more than 500,000 samples per day. The company has analyzed tests for more than 190,000 patients with breast cancer alone. This type of data can be used to pinpoint geographic areas that have many of a specific type of patient. Sometimes entirely new sites, never before used by the client, can be identified by analyzing the testing data and finding concentrations of patients with a particular type of cancer. Additionally, referral of patients to sites with ongoing clinical trials in a recruitment phase can also be effectively achieved.

The most successful oncology developers in the future will have access to **the right data to determine how to best evaluate their drugs,** alone and in combination, particularly with immunotherapies.

By layering proprietary data with public data, modeling and testing their hypothesis in silico, investigators can make certain their trials are on the path to success. This is the type of data-driven, intelligent trial design, recruitment and performance that's needed to power the next generation of oncology products. This process takes much of the guesswork out of clinical trial design and should lead to faster trials, lower costs and better options for patients.

A growing number of experts believe that the future of oncology will revolve around the breakthrough immuno-oncology products now reaching the market. Learning how to harness the body's own immune system to fight cancer represents a turning point for the field. The most successful oncology developers in the future will have access to the right data to determine how to best evaluate their drugs, alone and in combination, particularly with immunotherapies. They'll also have ideal tools to select the most appropriate patients for their trials.

After decades of struggle, too many Phase III disappointments and huge gaps in our knowledge, oncology research is finally delivering the type of truly effective treatments that can possibly turn many cancers into chronic diseases, if not deliver actual cures. But it will be the quality and amount of data that companies have access to, as well as the best analytics, that will do the most to accelerate the field.

COVANCE®
SOLUTIONS MADE REAL®

Maximize the Value of Your Molecule

Covance is the only company that can – from product development through commercialization – partner with you to grow your product's market potential. We work with you to provide the best available resources to maximize the commercial opportunities for your product by:

- Providing the necessary insight that will save you time and resources and yield invaluable information for critical product development decisions
- Giving you the critical advantage to stay ahead of your competition and maximize the commercial potential of your product
- Helping maximize the acquisition price for your product, improve licensing opportunities and increase the value of your company
- Helping your product gain favorable coverage and reimbursement

Learn More

Sources

1. Mooney, M and Mayer, M. Chapter 3, in Transforming Clinical Research in the United States: Challenges and Opportunities: Workshop Summary. Institute of Medicine (US) Forum on Drug Discovery, Development and Translation. National Academies Press, 2010. **https://www.ncbi.nlm.nih.gov/books/NBK50895/**

2. Roberts, D. Multi-blockbuster drugs will drive immuno-oncology market to $34B. Drug Discovery and Development Magazine. April 19, 2016. **http://www.dddmag.com/article/2016/04/multi-blockbuster-drugs-will-drive-immuno-oncology-market-34b**

3. Kiernan, B. Clinical trends and challenges in immuno-oncology. Thomson Reuters. **http://stateofinnovation.thomsonreuters.com/clinical-trends-and-challenges-in-immuno-oncology**

4. Kleponis, J, Skelton, R and Zheng, L. Fueling the engine and releasing the break: combinational therapy of cancer vaccines and immune checkpoint inhibitors. Cancer Biology and Medicine, September, 2015; 12(3): 201-208). **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4607816/**

COVANCE
SOLUTIONS MADE REAL®