Robin Robinson

Payers Play Larger Role In POSTLAUNCH STRATEGIES

The focus of postlaunch activities has changed dramatically in just a few short years.

Due to the increased power of payers and managed care companies, Phase IV studies have become more imperative to sustaining a successful postlaunch campaign. Companies have had to reprioritize the need for surveillance and Phase IV studies, which prove the safety and value of new drugs to payers and move them to the top of the list.

Electronic health records (EHR) data can be extremely helpful in verifying value and safety post launch, because monitoring patients allows the discovery of real-world use and the ability to proactively identify safety concerns. Using EHR data is likely to change the tactical attributes of postmarketing surveillance as well as the strategy for Phase IV trials. Other challenges include executing correct research strategies, effectively monitoring patient reported outcomes (PRO) and adverse events, and re-evaluating the initial course taken using the myriad data available.

There are many significant challenges involved with postmarketing research, but one of the more critical is determining which approach to use most effectively for the new brand.

Interventional trials, prospective observational studies and registries, and existing data from administrative and health records all have different strengths and limitations, but are critical to the success of any postapproval study, says Richard Gliklich, M.D., president, Outcome, and global head of late phase, Quintiles. In the beginning phases when discussing the implementation of a new study, researchers should consider all of these approaches and how they may enhance or detract from the quality of data that are generated and if the evidence gained will answer the primary study questions.

"Researchers should also keep in mind that these approaches can be complementary," Dr. Gliklich says. "It's not always one or the other, but more a question of which one is appropriate at the right time and for the right question."

Another challenge related to postmarketing research is patient-reported outcomes.

Many gray areas remain with regard to regulatory guidance, and those conducting the research have concerns about misclassification, bias, and confounding factors in any type of non-randomized control study.

Another hurdle to overcome is making sure that those designing the postlaunch studies don't make the mistake of applying the same structure as used in prelaunch studies.

"Postlaunch studies require a strong internal or external advocate to stand up for the appropriate approach or, in many cases, either the study won't be undertaken, or it will be overengineered and overly expensive," says Jeffrey Trotter, executive VP, Phase IV development, PharmaNet/i3. "Perhaps the biggest issue in the postlaunch research environment is the imposition of pre-launch study components. Researchers comfortable with the operational requirements for randomized clinical trials often inadvertently impose such structure onto Phase IV studies that, being commissioned for far different reasons, must be designed differently."

Moreover, he says, most sponsors are not optimally organized to ensure that the rationale underlying postapproval studies is effectively executed through an appropriate design and practical operational plan.

Adverse Events, Market Research, Patient Enrollment, and Other Postmarket Challenges

One of the more difficult tasks during post launch is ascertaining the divide between a product's own clinical focus and the competition's. This information is vital to the overall planning of products and resources. According to Melissa Hammond, managing director, Snowfish, this is especially true during the mid-later stages of a product's life cycle.

"It is critical to re-evaluate the product's direction, while taking into consideration developments in the clinical practice environment as well as in the competitive landscape," she says. "Knowledge of the clinical focus among the competition will allow for a deeper understanding of the direction that is being taken. An understanding of how the data are perceived by the clinical community will determine if this is indeed the appropriate path. This helps to set a product's course and uncover hidden opportunities."

LOU SHAPIRO ▪ *PhoneScreen*

"While social media can quickly raise awareness of a study with a specific patient population, there are unanswered questions about the potential impact of recruiting patients in this manner."

Best Practice Tips for Postlaunch Strategies

While the challenges are numerous, there are many solutions to improve Phase IV and postlaunch activities. According to our thought leaders, early planning, transparency, and validating study results are just a few factors that improve postlaunch activity outcomes.

As payers become more crucial to the success of a new launch, it is essential to communicate the value story to payers with credible and persuasive ambassadors.

"Postapproval studies have continued to expand measurably in number, size, and complexity in recent years," says Carol Collins, Ph.D., corporate VP and worldwide head of PACE, Parexel. "As a result, biopharmaceutical companies require much greater efficiency in managing the high-volume throughput of data while controlling the costs related to these programs."

The focus needs to be on achieving greater efficiency by gathering more data at a significantly lower cost per patient. Experts say a variety of late-phase studies, including observational studies and patient registries, are being used as either primary or adjunct vehicles for pharmacovigilance and health evaluation activities to meet increasing regulatory and payer demands for long-term safety and health outcomes data.

"It is important to generate more robust product safety and health outcomes profiles," Dr. Collins says. "Sponsors need to collect precise data to prove the value of their products to multiple stakeholders, and better position their products for commercial success. Observational research has become increasingly important as a means to demonstrate product value in a real-world clinical setting."

However, optimal execution of a postlaunch research agenda requires planning well before product approval, Mr. Trotter says.

"Effective planning must begin as early as Phase II or else the postlaunch agenda for establishing product safety and value will be seriously constrained," he says. "Ideally, a variety of pre-approval activities will accommodate the need to explore pharmacoeconomic issues so as to serve as an appropriate foundation for postlaunch, real-world research activities. Without this foundation, postlaunch research initiatives can often be weighed down with having to capture too much information."

Successful late-phase researchers are focusing on patient reported outcomes these days. According to a 2011 Cutting Edge Information report, PRO activity spending by the biopharma industry has increased more than 50%.

inVentiv Health also conducted a survey that highlighted the importance of PRO to payers. The survey of more than 20 medical and pharmacy directors showed that almost 95% of the respondents confirmed that they are likely or very likely to factor in PRO in future coverage decisions.

As a result, experts say successful late-phase researchers will need a variety of tools to measure the patient experience and translate that into a value message for payers.

DR. RICHARD GLIKLICH ▪ *Outcome*

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Postmarketing Studies

At the heart of postmarket research are postmarket studies and outcomes-based data. Identifying, targeting, and gathering data from this specific patient base continues to be a challenge.

Scott Connor, VP, marketing, at Acurian, says on the most simplistic level, there is often a funding issue with regard to sponsors investing in enrollment and retention services in postmarketing studies.

"The budgets for these requisite services are generally an afterthought, even more so than with Phase III critical path studies," he says. "But it is more than just throwing money at the problem, of course. The strategies for recruiting and retaining patients don't fundamentally differ from Phase III to IV, except that there should be greater emphasis on tightening the relationship between patient and site in the postlaunch world. Many Phase IV studies are endpoint studies. They are long and involved. Patients have to really want to be in the study, and that requires lots of relationship and trust-building over time."

Mr. Connor says providing patients with good information up-front and consistent and meaningful communications throughout the

Patient Enrollment

A study by Cutting Edge Information shows that although patient enrollment is seen by clinical executives as the greatest opportunity to accelerate Phase IV clinical trial timelines, it is at the same time the most time-consuming of all trial activities. The report, Phase IV Clinical Trials: Best Practices in Post-Marketing Study Management found that across five different types of Phase IV studies, patient recruitment consumes up to 30% of trial timelines.

Trials often run beyond their initial timelines due to delays in patient enrollment and the fact that companies end up enrolling an average between 5% and 15% fewer patients than originally planned. Companies struggle to find patients whether they're looking for general population patients or treatment-naive patients and once an appropriate potential population is identified, the competition for those patients makes adequate recruitment extremely difficult. To meet these challenges, some companies are trying new ways to attain and retain trial subjects. To be successful, a company needs to be both creative and systematic in pursuing and keeping Phase IV volunteers, the report says.

process, are paramount to both enrollment and retention.

"There are excellent technologies to help manage these interactions and give sponsors and sites a centralized dashboard to identify and potentially rectify retention issues in a proactive fashion," Mr. Connor says. "Having a system to track retention metrics in real time is fairly new, but without it, there is no way to recover when you uncover a severe patient attrition issue. It's like a tornado. If your first knowledge of a twister is when it's tearing up your barn, you are in a position of no escape. You need to have early-warning systems in place, and the same goes for retention. These technologies are relatively nascent, but they exist and are already gaining traction and credibility for tightening the patient-site relationship while providing a radar-like system to readily check the pulse of the patient, so to speak."

Lou Shapiro, senior VP, business development at PhoneScreen, says at its core patient recruitment involves identifying appropriate patients and enrolling them in a clinical study — a concept that sounds simple and straightforward — however, implementing effective patient recruitment programs is more complicated and time-consuming than appears.

"The primary challenges faced with patient recruitment are reaching appropriate patients, prompting patients to act and get involved in a clinical trial, and on-going support for patients so they stay enrolled in a trial," he says. "A few considerations for effective patient recruitment and retention programs include outreach, screening, quick referral to study sites, etc."

Mr. Shapiro says outreach is key and can be done through traditional media channels such as print, radio, and TV advertising, as well as patient advocacy groups. Screening patients is also critical to expediting patient recruitment and enrollment.

"Screening can be a bottleneck for study sites costing quite a bit of time and providing disappointing results," Mr. Shapiro says. "Companies should use a screening tool that is aligned with their study's inclusion and exclusion criteria. This tool will help speed up screening and identification of appropriate patients. Another option is to consider using a pharmaceutical call center to assist with patient screening."

Another best practice identified by Mr. Shapiro is to quickly refer patients to study sites.

"If it is possible, transfer screened patients directly to study sites for further evaluation," he suggests. "This immediate transfer increases patient enrollment and retention. It is also important to meet all the patients' informational needs. Provide user-friendly and easy-to-understand information on study treatment and risks and develop materials and tools to support patient compliance with study requirements. Patients and their family members are juggling a number of important issues during their treatment and study support mechanisms must be simple, easy, and automatic. Think about generating automated reminders for appointments, pre-visit instructions, and reminders to complete patient logs/diaries. Also, think about the age, demographics and preferences of the patient population."

As strategies are developed to expedite patient recruitment, Mr. Shapiro says take into consideration patient privacy policies and regulations and study design principles. These impact what pharmaceutical company sponsors can do to expedite patient recruitment.

"An emerging area in patient recruitment is using social media tools to identify potential study volunteers," he says. "Social media sites such as Inspire, Patients Like Me, and Army of Women all provide access to their network and followers. While social media can quickly raise awareness of a study with a specific patient population, there are unanswered questions about the potential impact of recruiting patients in this manner. Specific areas of concern are patient privacy and whether discussing the study and side effects from the treatment arms could harm the integrity of the study. At the heart of this question is whether it is possible for patients to figure which arm of the study they are on, and essentially unblind the study. These are important issues to be discussed and considered when using social media tools for patient recruitment."

Mr. Trotter of PharmaNet/i3, says in his experience, patient enrollment in Phase IV studies is not a serious problem at all.

"Indeed, more and more physicians and patients are interested in participating in real-world observational studies, in part, because of the true lack of burden associated with participating in these studies, if they are designed and executed appropriately," he says. PV

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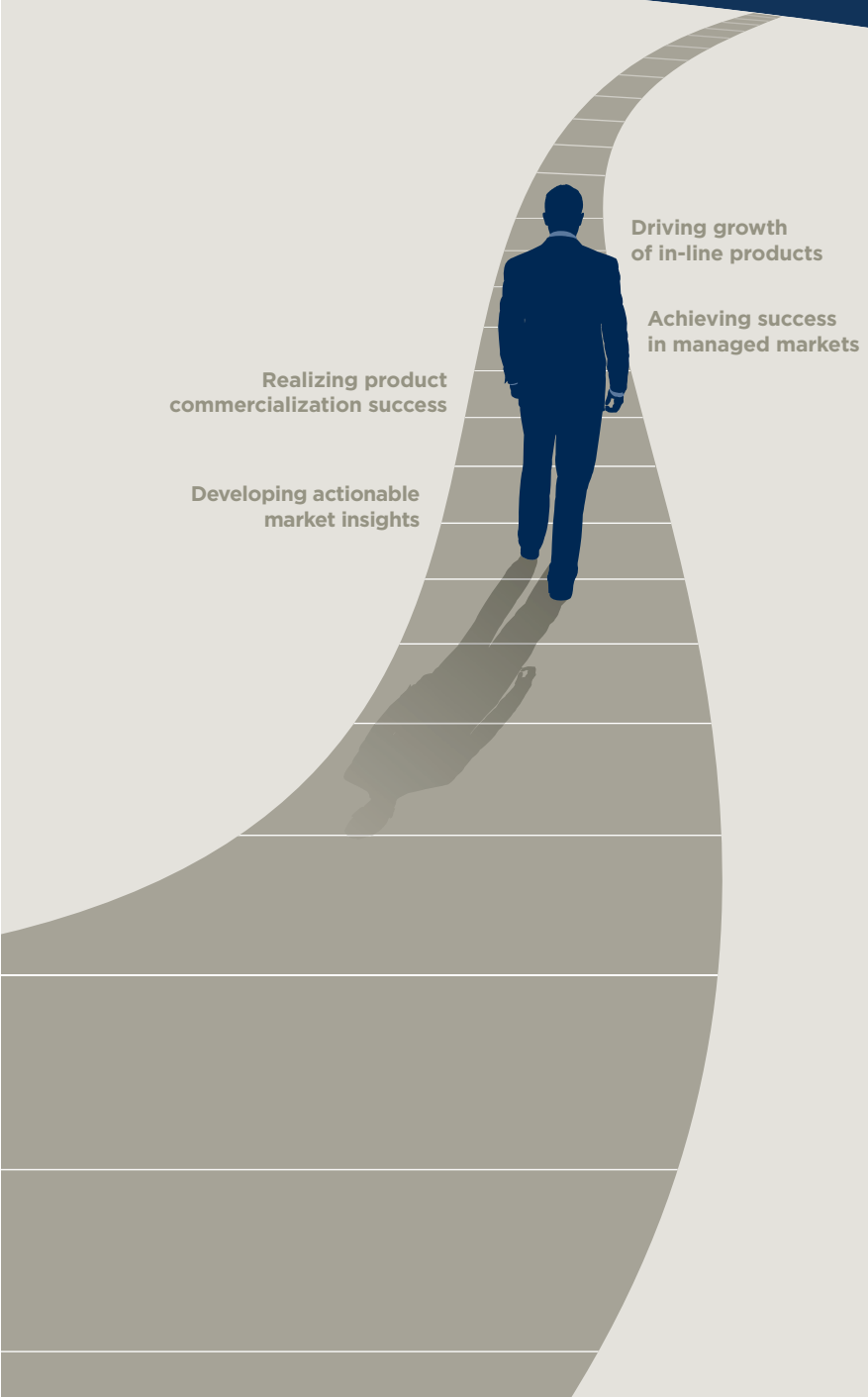

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