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Using Real-World Data to Examine Long-Term Safety and Effectiveness in Extension Studies

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Leveraging RWD can lessen the strain normally put on investigators and sites.


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Extension studies, or 'rollover studies' conducted after RCTs, allow clinical trial patients to 'roll-over' into a longer term follow-up study, where researchers continue to observe and measure long term safety, tolerability, and/or effectiveness.Extension studies provide insight into the long-term benefits and risks associated with products, though they can be difficult to develop and costly to carry out. However, the growing use of real-world data (RWD) has helped to offer lighter touch approaches to follow up. By designing extension studies that leverage RWD and/or direct to patient follow-up, it is possible to measure outcomes with less burden on investigators and sites.

Designing fit-for-purpose studies

The key to generating real-world evidence (RWE) on long-term safety and effectiveness in extension studies is to ensure that critical information from the parent study is captured and integrated with the study data for the extension study and approaches to minimize burden on investigators and sites are employed. Some methodologies include:

- *Leveraging direct-to-patient technologies.* Smartphone apps, digital tokens, wearable or sensor devices, and/or telemedicine can make it easier for patients to report symptoms and outcomes without the inconvenience or the expense of traveling to a clinical site and reducing dropout rates.
- *Combining related RCTs.* Most extension studies are specific to the site and patients who participated in the parent trial. By incorporating patients from related RCTs studying the same product, researchers can facilitate the collection of longer term outcomes across a number of studies, leading to reduced costs, and optimizing the research results (e.g., rare outcomes can be assessed when more patients are included).
- *Adopting a range of data collection strategies.* Some regions allow researchers to follow up directly with patients to assess outcomes, while other countries have electronic health records (EHRs), claims administration databases, and other data sources that can be used to follow patients and measure events of interest. Depending on the country and region, the data collection approach may need to vary to take advantage of efficient approaches to follow up.

Steps to follow

To design an extension study to measure long-term safety and effectiveness, researchers should start by defining objectives and stakeholder requirements. From there, they can outline steps to follow, such as:

Identify critical time points

For an extension study to deliver accurate analysis, it must reflect a clear timeline starting with the date a patient is randomized into the parent clinical trial and then following the patient throughout extension follow-up. Other key data points that need to be captured from the clinical trial and used for the extension study include the date of diagnosis, treatment assignment, baseline demographic and clinical information, and outcomes of interest throughout the clinical trial. Changes in the treatment regime or discontinuation should also be on the record, as well as patient death or the end of the study period and the reason for it.

Rollover *all* trial patients

To gather meaningful follow-up data, all trial patients should be eligible to rollover into the extension study. Avoid including only patients who responded positively during the parent trial. This selection bias leads to skewed results that favor the product and are not necessarily reflective of the true longer term outcomes. Researchers can provide information on the absolute number of clinical trial patients enrolling in the extension study compared to the number who participated in the parent trials. They can also include descriptions and response outcomes of those who did and did not enroll to understand the extent to which this bias may be a concern.

Include a comparison group

To generate comparable results from the data collected in an extension study, include a control group for the comparison. An internal control arm may not always be possible, and can be challenging when the extension study includes more than one parent trial. In some instances, researchers might benefit from using external (or historical) controls based on RWD.

Choose objective outcomes

Researchers should measure objective, hard outcomes that can be easily measured over longer periods of time and verified using health records. Often, trial outcomes may be measured or recorded differently from the post-trial outcomes recorded in RWD, such as hospital or clinic charts, insurance billing records, or EHRs.

Minimize participant drop-out

There are many reasons why researchers lose access to patients during follow-up extension studies, including dropout because of a lack of response to the treatment or a change in insurance companies. A high dropout rate can compromise the findings of the study. One way to combat this is with a hybrid approach, linking data sources such as the National Death Index with other health databases, and combining this with annual check-ins via telehealth or digital communications.

Start early to plan your extension study

Extension studies are complex and take a concerted effort to design and implement. Start planning early to ensure a smoother transition to the extension study after the trial ends and obtain advanced consent from trial participants on issues such as:

- Including patient-reported outcomes or other information in the trial for later use in the study
- Permission to store biospecimens
- Agreement to link trial participants with their records through administrative claims, EHRs, death, and other registries
- Provision of financial or other incentives for participating in ongoing follow-up after the trial
- Potential reimbursement for services, depending on marketing authorization status
- Consent to using flexible and hybrid models of follow-up
- Developing protocols to use across different geographical regions, depending on the method of follow-up

Since most RCTs have a global focus, it is vital to use simple, standardized data collection methods to account for different time zones.

The use of RWD ultimately offers a solution to the many barriers that have historically arisen in the execution of extension studies, such as time, cost, and access to patients. As these challenges are diminished, RWD simultaneously allows researchers to garner more comprehensive understanding of long term risks and benefits. By developing a hybrid approach to data collection that optimizes use of related studies, researchers can ultimately support improved delivery of safe and high-performing medical products that drive better patient health outcomes.

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Novartis Reveals New Collaborators to Beacon of Hope Initiative

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Expansion aims to continue to create programs that address health and education inequities.

Image Credit: Adobe Stock Images/freshidea

With the goal of diversifying clinical trials, breaking down economic and educational barriers, and creating greater trust across research and development, Novartis announced on July 12, 2023 the inclusion of six new organizations to its Beacon of Hope Initiative. The company selected the new organizations to provide tools and expertise to enable the Historically Black Medical School Centers of Excellence to accelerate progress on increasing diversity, equity, and inclusion in clinical trials and support new research into healthcare disparities.

Those organizations include:

- Advarra
- Virb
- BeeKeeperAI
- Amgen
- Alnylam
- Global Black Economic Forum (GBEF)

According to the Novartis press release,[1] Advarra will support clinical trial-site management, BeeKeeperAI is providing a privacy-preserving collaboration platform that enables protected algorithms to compute on real-world data, and Virb will help with the sourcing and training of clinical trial coordinators and research study staff. Amgen and Alnylam will run clinical trials through the Centers of Excellence. Alnylam, specifically, also intends to offer an opportunity for under-represented students who want to pursue careers in drug development to attend a summer fellowship program.

Lastly, GBEF joins the Beacon of Hope to empower the next generation of diverse leaders in STEM while working to address economic disparities. They will offer career training and leadership development programs to students enrolled in Novartis and Thurgood Marshall College Fund scholarship and mentorship programs.

"Our relentless commitment to the success of Beacon of Hope led us to undertake a comprehensive assessment of where we have made important progress and where we still have gaps to fulfilling the mission of the program," said Linda Armstrong, US Novartis Foundation President, head of Novartis US corporate responsibility, in the company press release. "We actively sought out collaborations with organizations that both possess the expertise necessary to bridge these gaps—particularly on the technology front—and that share our unwavering mission to tackle the fundamental factors that contribute to health and education disparities."

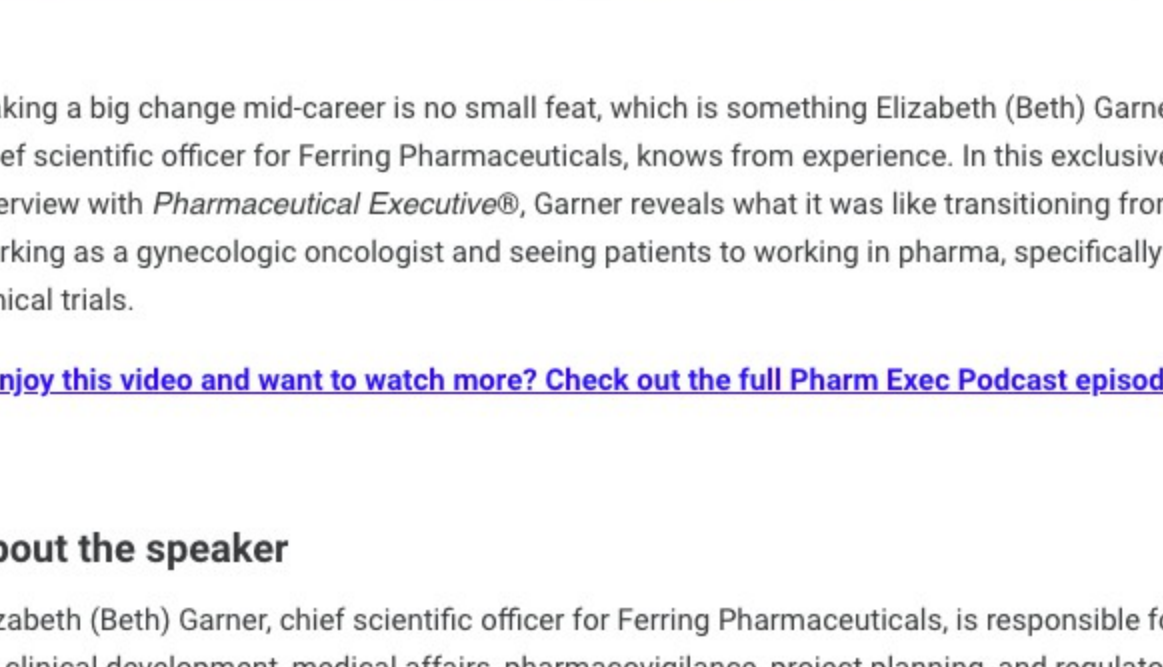
Reference

1. Novartis, "Novartis Strengthens Commitment to Beacon of Hope Initiative, Engages New Collaborators to Support Clinical Trial Diversity, Break Down Economic and Education Barriers," press release, July 12, 2023. https://www.novartis.com/us-en/news/media-releases/novartis-strengthens-commitment-beacon-hope-initiative-engages-new-collaborators-support-clinical-trial-diversity-break-down-economic-and-education-barriers

From Physician to Pharma: Gynecologic Oncologist Enters Clinical Trials Space

Published on: July 12, 2023
Meg Rivers

Elizabeth (Beth) Garner, chief scientific officer for Ferring Pharmaceuticals, discusses what it was like transitioning from working as a gynecologic oncologist and seeing patients to working in pharma, specifically clinical trials.



Making a big change mid-career is no small feat, which is something Elizabeth (Beth) Garner, chief scientific officer for Ferring Pharmaceuticals, knows from experience. In this exclusive interview with *Pharmaceutical Executive*®, Garner reveals what it was like transitioning from working as a gynecologic oncologist and seeing patients to working in pharma, specifically in clinical trials.

Enjoy this video and want to watch more? Check out the full Pharm Exec Podcast episode.

About the speaker

Elizabeth (Beth) Garner, chief scientific officer for Ferring Pharmaceuticals, is responsible for US clinical development, medical affairs, pharmacovigilance, project planning, and regulatory affairs at Ferring Pharmaceuticals US. Garner has nearly 30 years of experience in the medical industry. Prior to joining Ferring in 2022, she held chief medical officer roles for ObsEva, a biotechnology company focused on women's health, and Agile Therapeutics, a women's healthcare company. Earlier, she held leadership roles in medical affairs at Myriad Genetics Laboratories and clinical development at Abbott Laboratories and Merck Research Laboratories. Garner also holds a medical degree from Harvard Medical School and has practiced in obstetrics, gynecology, gynecologic oncology, and internal medicine at Brigham and Women's Hospital and Massachusetts General Hospital. In addition, she holds a master's degree in public health from Harvard's T.H. Chan School of Public Health and a bachelor's degree from Mount Holyoke College in Massachusetts.

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FDA Issues Draft Guidance on Psychedelics

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First guidance in this area from the Agency addresses the unique challenges when designing clinical studies for these drugs

The FDA published its first draft guidance that presents considerations to industry for designing clinical trials for psychedelic drugs.[1] In the guidance, the FDA says the term psychedelic includes classic psychedelics, typically understood to be 5-HT2 agonists such as psilocybin and lysergic acid diethylamide (LSD), as well as entactogens or empathogens such as methylenedioxymethamphetamine (MDMA).[2]