

# ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

Section Editor: Mark J. Ratain, MD

## How Direct-to-Patient Research Can Improve Interest in Clinical Trials



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**H&O** What are the challenges involved in patient recruitment and retention in traditional clinical trials?

**DC** There are so many challenges. For example, most traditional clinical trials do not plan for recruitment. Decades of research have shown that successful clinical trials include an organized recruitment and retention plan. Some plans detail challenges for patients, providers, referral bases, and the trial itself, along with thoughtful action steps to resolve them.

When people are diagnosed with cancer, they develop physiologic and psychologic shock, which makes it extremely difficult for them to comprehend their options, let alone the processes behind cancer research. Also, patients are often directed toward treatment before being informed about the availability of clinical trials. Physicians should be aware of what relevant clinical trials exist, and help their patients understand that a trial may be an option, depending on enrollment criteria. Another way to improve enrollment is to develop online informed consent. The US Food and Drug Administration (FDA) recently provided guidance in this area.

Trial designs often fail to accommodate the patient's needs. Retention may be decreased by too many test procedures and unrealistic follow-up procedures. It can be difficult logistically for patients to attend these appointments, especially if they work or care for family members. Studies might not provide crossover designs or quality-of-life components. Adverse events may also lead patients to discontinue participation in a trial. Clinical trials that do not collect patient-reported outcomes will never find out about these issues.

**H&O** What is direct-to-patient research, and how does it address these challenges?

**DC** Patient-directed research focuses on steps within a clinical trial that can increase convenience for the patient to ultimately foster better enrollment and retention. For example, the numerous trips to an academic center for tests or treatment can be replaced by visits to a more local site. Sometimes, patients can receive tests or treatments, or even provide biospecimens, in their home. This type of research can make the clinical trial experience easier for the patients and their families, which means they are more likely to join the trial and stay involved with it. Some of these trials have also tried to use new technology to help collect patient data. These types of studies have been referred to as “virtual” or “community” trials.

**H&O** What are the advantages and disadvantages of direct-to-patient research?

**DC** There are advantages for both patients and investigators. Eliminating frequent travel to an investigational site is helpful for patients, allowing them to focus on the steps they need to complete treatment, miss less work, and spend more time with family and friends. Patients feel more valued and that their contributions mean more, and they feel more like a participant in the process. Investigators gain happier patients who are more likely to remain in the clinical trial. Investigators may also be able to find eligible patients more quickly since they do not need to rely solely on proximity to the sites conducting the trial.

A disadvantage is that more time may be needed to set up the trial initially. It may be necessary for researchers

to collaborate with many local sites. However, upfront planning can help the trial run more smoothly. There are also emerging companies that manage the logistical processes.

### H&O What has been learned from early attempts at direct-to-patient research?

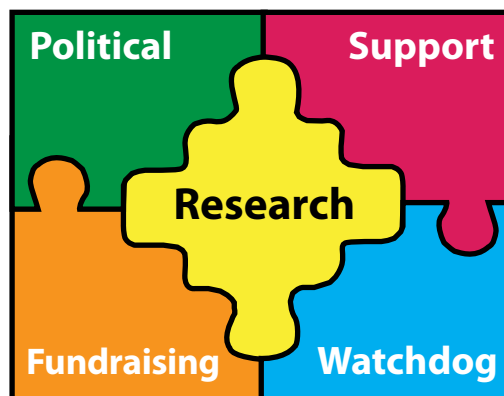
**DC** These trials are not appropriate for all settings. They work well for patients who are sicker and older, and in settings where more frequent visits are required. They are especially beneficial when patients can receive treatments and collect data in their own homes. The direct-to-patient approach can also be good for pediatric trials, especially for rare diseases, which tend to have difficulties recruiting enough participants. These trials work best when focused on treatment. Direct-to-patient research can also be effective when incorporated into registries that are collecting data over time.

### H&O What motivates patients to enroll in clinical trials, and how can more patients be encouraged to participate?

**DC** When patients receive a cancer diagnosis, enrollment in a clinical trial is not an obvious choice, especially when their doctors may not inform them about the option. Many researchers find it challenging to find other ways of reaching patients, but this can be transformed when they think more like a patient who is

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being diagnosed. For patients with cancer, the oncology office is the last place they end up; they have already taken many other steps along their medical path before arriving there. Why not provide information about clinical trials earlier? For example, when a patient visits a radiologist for a scan, information can be provided about clinical trials on screening. Information can also



**Figure.** Components of patient advocacy.

be given when the patient visits the surgeon. Even in the primary care setting, there could be information about what past studies have done for prevention, screening, or behavior modification. With earlier messages about clinical trials, patients will not be shocked when the idea of enrollment is raised later.

Another important area is to ensure that patients understand that there are clinical trials for all stages of cancer. Trials are not solely focused on metastatic or advanced disease. Patients should hear about trials early and often, so that when the possibility of enrollment is raised, they do not think, “Oh, a clinical trial—I must be dying.”

I would also like to clarify the idea of altruism. People diagnosed with cancer want to get better. Even patients with late-stage disease hope that enrollment in a trial will help them live better and longer. They also want to help other patients so that their life has as much meaning as possible, even if the treatment does not help them.

### H&O Could you please describe the work of Patient Advocates In Research?

**DC** Patient advocacy means many different things to different people (Figure). In the early 1990s, few patient advocates were involved in research discussions. They were engaged in more traditional types of advocacy, such as direct patient support, fundraising, and political advocacy. There was some watchdog advocacy, as seen in the AIDS movement, but no one was really involved in research projects. Some of us realized that to obtain better results for patients, it was necessary to change the way the research system worked, by focusing more on outcome and less on exploring scientific questions that did not improve peoples’ lives. As the founder of Patient Advocates In Research (PAIR), I have helped people become involved in research advocacy through programs such as

**Table.** Guiding Principles of Health Literacy

<ul style="list-style-type: none"> <li>• Ensure that public health information and services are appropriate, actionable, and easy to understand and use</li> </ul>
<ul style="list-style-type: none"> <li>• Involve representatives from your target audiences in planning, implementing, disseminating, and evaluating health information and services</li> </ul>
<ul style="list-style-type: none"> <li>• Develop key partnerships to help facilitate change, influence behavior, and generate interest in health literacy</li> </ul>
<ul style="list-style-type: none"> <li>• Support changes to improve public health professionals' health literacy skills</li> </ul>

Data from the Centers for Disease Control and Prevention. <https://www.cdc.gov/healthliteracy/training/page1619.html>. Accessed February 27, 2017.

the National Cancer Institute (NCI) cooperative group system. I also helped to establish the NCI translational research program, known as Specialized Programs of Research Excellence (SPORE), and other epidemiology and health delivery research projects. PAIR was founded in 1996 as an international communication network of patient advocates in cancers and other diseases, who are involved in health research.

### **H&O** What barriers stand between research and clinical application?

**DC** One barrier involves communication; research results are reported in scientific journals, often in esoteric language. It can be difficult to identify how results could actually change clinical practice. It is also important to have result summaries, written in plain language, that are focused on what the research found, what it means, and how it may impact clinical care.

Another barrier concerns the costs of treatment. Information regarding clinical implications is needed not only for clinicians and for patients, but also for payers. Patients and their families often pay a tremendous price for treatments that may not work. I am often asked, "Why should we support research that only produces drugs that people can't afford?" It is very difficult to answer that question!

### **H&O** Why should study results be conveyed to patients, and what is the best approach?

**DC** When patients provide informed consent to enroll in a study, they are told that they will receive important information about it. That should, of course, include the results of the study. The immense contributions that patients make to clinical trials can include their very lives. They (and their families) should be able to find out what

happened. Federal regulations in the United States and Europe require that trial sponsors create public result summaries.

It is imperative to explain findings in plain language and with health-literate principles (Table). That means more than just simple language. It includes graphics that help orient patients and give them context for the information. I have helped the Alliance for Clinical Trials in Oncology (and Cancer and Leukemia Group B before them) provide such summaries for their published clinical trials. I am also working with an organization called Health Literacy Media (HLM) to create health-literate, plain-language research summaries that provide information in a clear manner. These summaries include information such as the study population, the disease setting, and the clinical relevance.

### **H&O** Are there any recent changes in the design of clinical trials that aim to address the needs of patients?

**DC** There is a push within the research community, as well as the patient advocate community, to include patient-reported outcomes and quality-of-life factors in every clinical trial. The FDA has approved some treatments based on patient-reported outcomes, even when efficacy was equivalent or inferior to existing agents.

There is also increased interest in direct-to-patient research. When involved in the design of a clinical trial, patient advocates question whether a study can utilize local centers and which parts of the study could be locally distributed. An important improvement that patient advocates have supported since 1996 has been adaptive design that is planned before the study is initiated. In addition, crossover or treatment-switching trial designs offer the patient an opportunity to benefit from another therapy if the first one does not work for them.

### **H&O** Do you have any recommendations from the patient perspective that would improve clinical trial design?

**DC** We need to treat patients who enroll in clinical trials like gold. Their contributions should be highly valued and used to answer as many questions as possible, including questions that are important to them. This not only requires multiple endpoints, it embraces tissue collection and data sharing. During the design of a clinical trial, all aspects of a patient's involvement should be closely considered. Dogma regarding eligibility criteria and follow-up procedures should be questioned. All obligations required of patients should be allowed only if deemed necessary for that specific trial, and not included just

because they are traditionally found in other trials. There should be consideration of whether new technologies, such as smartphones and tablets, can facilitate data collection. When possible, multifactorial arms can improve clinical trial design and create more interest for patients by providing additional opportunities for new treatments. One last thought: please remember that patients never fail treatments. Unfortunately, treatments fail patients all too often. Let's work together to create clinical trials that answer important questions for patients, and hopefully produce better results in the process.

### Disclosure

*Ms Collyar is a member of the Alliance for Clinical Trials in Oncology, is the president of Patient Advocates In Research (PAIR), and consults with Health Literacy Media on their Plain Language Research Summary line.*

### Suggested Readings

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