

ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

Section Editor: Mark J. Ratain, MD

Novel Sources of Funding for Clinical Trials in Oncology



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H&O What are the traditional sources of funding for clinical trials in oncology, and how have they evolved over time?

GS Traditional sources of funding for clinical trials in oncology include both industry and governmental funding agencies, with input from academic institutions. However, pharmaceutical companies have become the primary sponsors of clinical trials in recent years, with drug development occurring primarily in the industry setting rather than in the academic setting. In addition, there has been a growing trend toward drug development on a more global level, with more countries from South America, Asia, and Eastern Europe participating in clinical trials.

H&O What are the advantages and disadvantages of traditional sources of funding for clinical trials in oncology?

GS Industry sponsorship of clinical trials offers clear advantages, primarily owing to the size and financial resources of pharmaceutical companies. However, there are also downsides to such sponsorship, including a potential dependence on industry and a focus not only on improving patient care, but also on making a profit. In contrast, academic research generally has more limited financial opportunities, but allows for greater independence in trial design and a focus on optimizing drug usage rather than maximizing financial gain for the sponsoring companies.

H&O What are the major challenges associated with funding of clinical trials in oncology, and what are some possible solutions to these challenges?

GS Clinical trials are becoming increasingly complicated and expensive, which poses a significant challenge. Additionally, the dependence of academia on the pharmaceutical industry is intensifying. Furthermore, participating in a trial is getting more complex for hospitals and doctors because the requirements set to participate are becoming more difficult to meet. Short timelines to conduct trials have resulted in an increased number of sites participating in industry trials, with fewer patients per site. If the number of patients involved from a hospital in the trial is limited, it can be a burden on that hospital system to open a trial and ensure that everybody is trained and up to speed for such a small number of patients. As a result, some hospitals may not be able to participate in trials. This challenge is not just related to funding but also in running a trial at individual sites.

One potential solution could be to establish a minimum number of patients per site, or a maximum number of sites allowed for each trial. From a pharmaceutical industry perspective, increasing the number of sites is advantageous for running trials quickly. However, there is a trade-off between these 2 considerations, and establishing a minimum number of patients per site could be a viable solution. Another issue is that clinical trials are getting more complex each year. The amount of data that sites are required to enter and the data that

need to be collected are becoming more complicated and demanding. To address this, it may be beneficial to simplify protocols and collect only the data necessary to answer primary and secondary questions. This approach would also benefit the sites participating in the trials.

H&O What are some innovative and novel sources of funding for clinical trials in oncology, and how effective have they been at supporting research?

GS Crowdfunding is one option, although the scale and scope of the trial must be taken into consideration. Crowdfunding for large comparative trials is not common; most successful examples of crowdfunding in medical research involve small proof-of-concept studies. On the other hand, insurance companies and other payers may be more interested in funding trials that focus on cost-effective use of a drug, which presents an interesting avenue for further exploration. There are even more opportunities to explore in this area, as mentioned in a recent paper by Dr Mark Ratain and colleagues, which includes an example in a US setting.

The argument we and others make is that government- and payer-funded trials need to address drug dosing postmarketing.

H&O Could you go into that paper a bit more?

GS The argument we and others make is that government- and payer-funded trials need to address drug dosing postmarketing. In the past, it was assumed that higher drug doses would lead to better effects, but this is not true for modern treatments such as biologics and immunotherapy. Many drugs are still being used at high and potentially excessive levels, causing additional side effects without proven additional benefit. The opinion paper mentioned above by Dr Ratain as well as another paper by Dr Annemiek van Ommen-Nijhof and colleagues provide examples, such as osimertinib (Tagrisso, AstraZeneca) in lung cancer, to demonstrate the types of trials that could

be conducted to optimize drug dosing and scheduling and general cost savings. The potential savings make it desirable for payers to support such trials. If such trials are funded by the agency that is paying for care, they are self-funding.

It is important to keep in mind that the type of health care system can affect the ability to have insurance companies or government pay for these types of trials. For example, a system where there is general health insurance for all patients is different from a system where there is optional health care insurance or where there are many insurance companies that have to collaborate.

H&O Does trial sponsorship differ among therapeutic modalities or cancer types, and if so, what factors influence these differences?

GS I do think that trial sponsorship differs among therapeutic modalities or cancer types. Industry is focused mostly on medicines, and less so on radiotherapy or surgery. Additionally, industry is mostly interested in tumor types with higher incidences and a larger potential for revenue. Smaller, rarer subtypes are more difficult to fund, which is true from both an industry and an academic point of view. So yes, there is a difference between tumor types and modalities.

H&O How have patient advocacy groups and nonprofit organizations become involved in funding clinical trials in oncology, and what effect has this had on the field?

GS Patient participation and support from patient advocacy groups are necessary to trials funded by academic institutions. This type of participation and support has had a large effect on the design of trials and the types of questions being asked, which is a very positive development. I have not seen this level of patient involvement in industry-sponsored trials, where it also would be beneficial to have patient advocacy groups involved. It is important to note that some of the rare cancer types have few patient advocacy groups. It is crucial to ensure that these tumor types get enough attention in industry-sponsored trials.

H&O How have changes in health care policy affected the global funding landscape for clinical trials in oncology?

GS Clinical trials are being run more internationally than ever before. This means that there is increased involvement of a global patient population, given that trials are now being run in countries where they were not

traditionally run. I think this is a positive step forward, and provides more data on differences in treatment effect between regions. However, it is important that trials use contemporary regimens in the control arm for optimal comparison.

H&O What are some future directions for clinical trials in oncology?

GS Personalized medicine is already with us and will become even more important in the future, but it involves ever-smaller populations and therefore makes trials more challenging to run. Trials in personalized medicine require either an active referral system for rare patients or an investment in bringing more hospitals up to speed in performing high-standard clinical trials. Another direction is tissue-agnostic trials, which focus on a specific mutation, characteristic, or biomarker, irrespective of the tumor type of origin. One example is the use of trials within a *NTRK* gene fusion population. A tissue-agnostic approach, however, must be further developed because neither the medical community nor regulatory agencies have established criteria for this type of trial.

One way to improve trials is to simplify them. Rather than a case report form with 1000 data points or more per patient, it is better to keep the form as simple as possible and limit the burden on sites and patients. The real question that needs to be answered typically only involves only a couple of variables, not 1000. Only a small minority of all collected data ever end up in scientific publications.

It would also be beneficial to have a more controlled scientific advice process for trials that ultimately lead to a US Food and Drug Administration (FDA) or European Medicines Agency (EMA) dossier or request for approval. Requesting scientific advice from FDA/EMA is currently

optional for companies, as is translating such advice into the design of the pivotal trial. Having requirements for scientific advice and following it could improve the quality of the trials and ultimately benefit patients.

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Suggested Readings

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