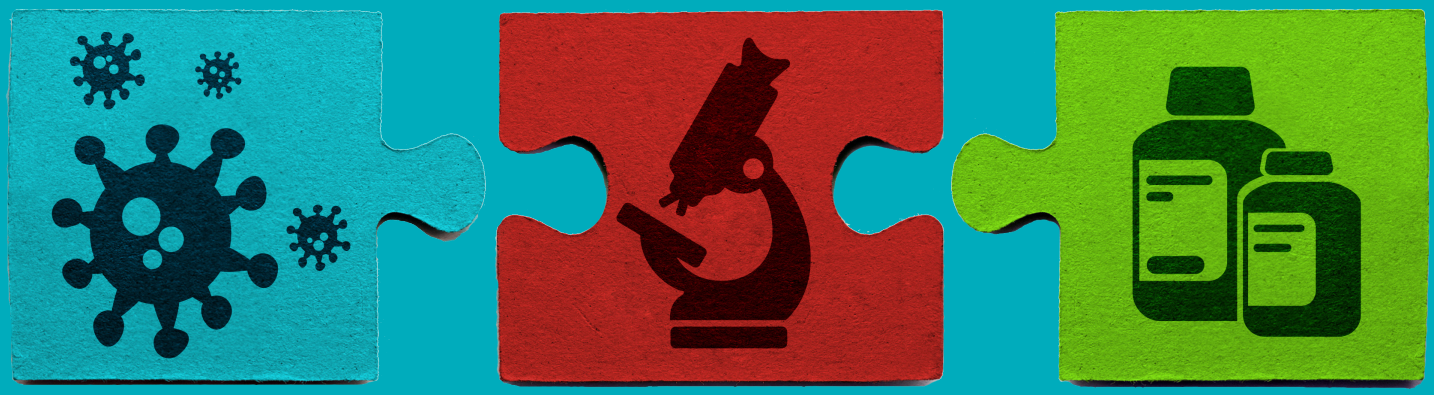
# Managing complexity in cancer trials



Trends, challenges and strategies for successful clinical trials in oncology research

## Introduction

Oncology is the fastest-growing therapeutic area for clinical research, with the value of the global drug market forecasted to reach over $150 billion by 2020.[1] Despite significant breakthroughs in the understanding, prevention, and treatment of cancer, the disease continues to affect millions of people worldwide. On a global level, cancer is now one of the world's most pressing health challenges. By the year 2030, deaths from oncology could increase globally by as much as 80%, according to World Health Organization.[2]

The next decade will see the pharmaceutical industry and their clinical research partners face increasing challenges in turning a range of promising scientific ideas into safe, effective medicines to extend the lives of cancer patients.

*Oncology is the fastest-growing area for clinical research.*

In this article, we discuss some of the current trends, challenges and strategies for increasing the likelihood of success in clinical oncology trial research, and put a spotlight on four ground breaking trials from around the world.

## Oncology trials lead innovation and specialisation

Recent analysis of the worldwide drug development landscape shows that oncology is currently the highest therapeutic class for increased clinical innovation and specialisation.[1] But oncology research is also highly complex.

Therefore, pharmaceutical companies are starting to look closely at each aspect of their clinical trials to make sure they are as smooth and efficient as possible, while meeting all safety and quality measures. A useful place to start is to look at the issues that affect complexity among cancer trials.

# Current factors in cancer trial complexity

Trial complexity varies greatly depending on therapeutic area. Oncology trials, on average, are the most complex trials. They have evolved from relatively simple active agent versus placebo designs to more extensive study designs that involve an increasing number of research arms. These trials require more patients, sites, countries, additional drugs, different dosing schedules, clinical investigators and supply chain variables.

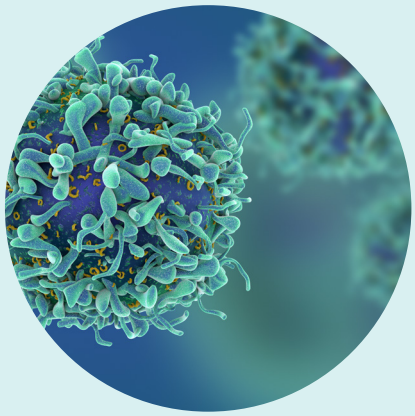
Other major factors that add to the existing complexity of clinical research in oncology include:

**Low patient enrolment:** The supply of adult cancer patients willing to participate in clinical trials remains relatively stagnant at around 5%, and threatens to slow cancer development.[3]

**High treatment demand:** This low enrolment is matched with a high demand for treatments of various cancers. Over the past five years, 70 new oncology treatments have been launched and are being used to treat over 20 different tumour types.[1]

**Reduced development time:** Biopharmaceutical companies are under huge pressure to reduce the time required for oncology drug development in order to get effective therapies licensed as soon as possible.

**Patent expiration:** Ongoing patent expiration of cancer drugs can also lead to a reduction in the revenue generated by pharmaceutical companies, adding to the pressure to reduce drug development time.



**Late stage cancers:** One of the biggest challenges for pharmaceutical companies in oncology research is late stage cancers, which often involve more precarious patient populations, who may be severely ill and require more frequent monitoring of symptoms and treatment side effects.

**Regulatory requirements:** More complex regulatory requirements imposed over the past 15 years may complicate efforts to launch and carry out clinical oncology studies.

**Increased research cost:** The annual global growth rate for oncology drug spending is predicted to be 7.5%-10.5% through 2020. As such, biopharmaceutical sponsors are seeking assurance of the value that results from their spending on these drugs.[1]

**Globalisation:** The globalisation of large, pivotal cancer trials raises logistical challenges that need particular attention, such as harmonising regulatory standards in different countries and ensuring the smooth, efficient coordination of the trial at all research sites and stages.

# Ground breaking oncology trials

Below, we review the significant results of four ground breaking cancer clinical studies that are opening opportunities for future oncology therapies, despite the current challenges involved in this research area.

**Fast-track approval of new therapy for paediatric leukaemia**

The use of global supply logistics played a major role in the success of a 2016 Novartis clinical trial (ELIANA) that evaluated efficacy and safety of an investigational chimeric antigen receptor T cell (CAR T) therapy, in relapsed/refractory paediatric and young adult patients with B-cell acute lymphoblastic leukaemia.[4]

The study involved patients from 25 centres in the US, Europe, Canada, Australia, and Japan. Each patient in the trial underwent leukapheresis – a treatment that can temporarily lower the number of leukaemia cells in the blood – and blood extracts were sent to a Novartis facility in the US, where the personalised CAR T-cell therapy was manufactured for each individual. The therapies were then returned to the treatment centres in each country for administration to the patients. Because the new Novartis CAR T product filled unmet medical needs, it was given priority designation for FDA approval before the end of 2017.

**Pioneering pancreatic cancer trial launched to shrink tumours**

In August 2016, Cancer Research UK launched a first-of-its-kind pancreatic cancer clinical trial to make cancer cells more responsive to chemotherapy and radiotherapy.[5] The trial will treat pancreatic cancer patients whose cancer has grown too big to be removed by surgery but has not yet spread to other parts of the body.

Prof Jeff Evans, chief investigator at the University of Glasgow, said: "This is the first time we're looking at ways to make pancreatic cancer cells more sensitive to radiotherapy. One way to do this is to shrink the pancreatic tumour enough to make surgery a possibility and we hope to see that happen in this trial."

These cancer patients will receive a drug called olaparib, in addition to the standard treatment of chemotherapy and radiation, known as chemoradiation. Cancer Research UK funding helped to develop olaparib, which is already approved by NICE and the European Medicines Agency for the treatment of certain types of advanced ovarian cancer.

The first part of the trial will focus on finding the safest dose of olaparib to use with chemoradiation. The second part of the trial will investigate whether this combination will make the tumour small enough to be removed by surgery in these patients.

**Immunotherapy drug a 'game changer' for head and neck cancer**

An immunotherapy drug was hailed as a potential "game-changer" in promising results presented at the European Society for Medical Oncology congress in October 2016.[6]

Advanced head and neck cancer has very poor survival rates. However, in the study of 350 patients with head and neck cancer, 36% of patients taking the drug nivolumab survived for longer compared with 17% of those who were treated with chemotherapy. In a separate study, combining nivolumab with another drug also shrank tumours in advanced kidney cancer patients.

Patients also experienced fewer side effects from immunotherapy.

So far, nivolumab has only been approved for treating skin cancer (melanoma) and in June 2016, it became one of the fastest medicines ever approved for NHS use, in combination with ipilimumab, for melanoma. Prof Paul Workman, chief executive of The Institute of Cancer Research, said nivolumab was one of a new wave of immunotherapies that were beginning to have an impact across cancer treatment.

*Oncology trials are the most complex of all therapeutic areas.*

**Breakthrough breast cancer drug 'is best for 20 years'**

In December 2016, breakthrough research findings from the largest cancer trial ever undertaken, showed that post-menopausal women who took the drug Arimidex (anastrozole) daily for two and a half years after early breast surgery were 77% less likely to develop cancer in the unaffected breast.[7] The results showed a significantly better chance of anastrozole-treated women surviving their disease, compared with those women who remain on treatment with tamoxifen, the current 'front-line' drug for breast cancer. Using tamoxifen over a similar period cut the risk by 54%.

Experts have hailed the drug as the biggest step forward in 20 years. Dr Jeffrey Tobias of University-College Hospital, London, who as one of the trial investigators, called the results 'exceptional'. "The reduction in the development of new cancers was very much greater than we had anticipated," he said. "This is the first time a largescale clinical trial has proved another treatment superior to tamoxifen."

The international trials of the new drug involved more than 9,300 women. Arimidex is currently licensed for treatment of early breast cancer only in Japan, but manufacturers Astra-Zeneca are expecting early approval of their application for an EU licence.

## Summary

Some of the challenges for clinical researchers within oncology include the complexity of the disease, clinical trial enrolment, product demand, expense, patent expiration and regulatory roadblocks.

One of the options that may help pharmaceutical companies face these challenges is moving their clinical trial equipment supply and logistics to third parties to overcome some of these barriers, without affecting the quality of the trials.

Continued progress against cancer will require a sustained, collaborative, and global effort. This will include investing in a well-designed scientific protocol and development strategy, and the right partners to help optimise the likelihood of success in various phases of oncology trials.

***Continued progress against cancer will require a sustained, collaborative and global effort.***


**References:**

1. IMS Health Study: Outlook for Global Medicines through 2021. http://www.imshealth.com/en/about-us/news/ims-health-study-global-market-for-cancer-treatments-grows-to-107-billion-in-2015-fueled-by-record-level-of-innovation. Accessed December, 2016.
2. Cancer Media Fact Sheet. http://www.who.int/mediacentre/factsheets/fs297/en/. Accessed December, 2016.
3. Wiener, M et al. Bring Your Oncology Drug To Market Quicker. Life Science Leader, July 2009.
4. Novartis presents results from first global registration trial of CTL019 in pediatric and young adult patients with r/r B-ALL. https://www.drugs.com/clinical_trials/novartis-presents-results-first-global-registration-trial-ctl019-pediatric-young-adult-patients-r-r-17264.html. Accessed December 2016.
5. Cancer Research UK. Pancreatic cancer trial to make tumours more sensitive to treatment. http://www.cancerresearchuk.org/about-us/cancer-news/press-release/2016-08-29-pancreatic-cancer-trial-to-make-tumours-more-sensitive-to-treatment#VvSkQcYA8ScUBZHZ.99. Accessed December 2016.
6. Immunotherapy cancer drug hailed as 'game changer'. http://www.bbc.co.uk/news/health-37588541. Accessed December 2016.
7. Jenny Hope and James Chapman. Breast cancer drug 'is best for 20 years'. http://www.dailymail.co.uk/health/article-115350/Breast-cancer-drug-best-20-years.html#ixzz4SjXkcgCL. Accessed December 2016.

# Sooner.
# Smoother.
# Smarter.

We're here to help you create positive patient outcomes and control the total cost of your trial. Wherever you are in the world, we manage the whole product life-cycle allowing you to focus on the objectives of your study. At every step of the way there's a trusted expert guaranteeing you a reliable, flexible and prompt solution-focused service.

For more information please visit mesm.com/resources

mesm

Marketing Code: MESM140
Date of preparation: Jan 2017