



# Trends and challenges for cancer drug development (Part 1)



Improving cancer treatments is a priority for many drug developers, academic researchers and funding bodies. This has led to a wealth of innovative new therapies and increased survival rates, but there are still types of cancers with massive unmet needs. New breakthroughs will possibly add further to the complexities and challenges within drug development to meet the increased need for and goal of precision medicine. Such challenges and complexities could include high costs, competition for eligible patients in certain disease settings, safety complexities and lack of understanding about disease biology. Here we discuss some of the current trends and future considerations for oncology therapeutics. In part 2 of this article series, we will consider how pharma companies can reduce unnecessary costs and optimise their clinical research through working with an effective clinical research organisation.

**Text by:** PCG Clinical Services team, with contributions from Antaros Medical AB

## INTRODUCTION

The healthcare burden of cancer is increasing worldwide. It has been estimated that there were 14.1 million new diagnoses in 2012 and 8.8 million deaths from cancer in 2015<sup>1</sup>. By 2030, the incidence is expected to increase by almost 70 % to 23.6 million new cases per year. Although the number of oncology drugs available is increasing, there are still types of cancers with massive unmet needs. The combined global cost of oncology drugs and supportive treatments was \$83 billion in 2015 and is projected to reach \$190 billion by 2022<sup>2</sup>. With the increase in cancer incidence and thereby rapidly escalating costs, improving oncology diagnostics and therapeutics is a high priority for both patients and for society as a whole.

Accordingly, there has been a great deal of innovation in oncology research and development, enhanced by simultaneous advances in digitalised healthcare, technology and the availability of and ability to process huge data sets. Some exciting new tools for precise cancer diagnostics are in development, such as liquid biopsies, biomarker-based disease prediction, innovative imaging methodologies and tumour staging based on automated disease modelling. In the future, more precise diagnostics might allow tumours to be detected at such early stages that chemotherapies

will no longer be required. However, in the meantime, pharmaceutical companies, academia and non-governmental organisations globally will jointly be focusing on improving anti-cancer therapies.

## TRENDS IN FINDING EFFECTIVE TREATMENTS

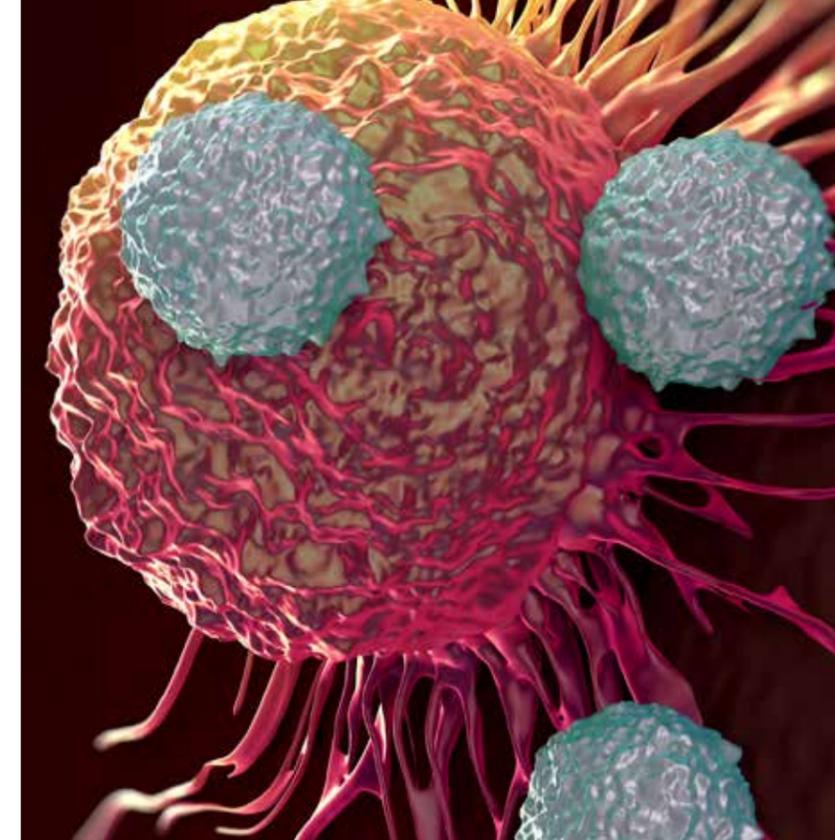
Some revolutionary anti-cancer treatments have emerged over the last couple of decades, including immunotherapies. More drugs have been approved within oncology than in any other therapy area since 2000<sup>3</sup>, and there were 70 new oncology approvals between 2010-2015, for use in over 20 different tumour types<sup>2</sup>. To put this into context, there were only 63 oncology drugs available in total on the UK market, prior to the year 2000<sup>4</sup>. This upsurge of new approvals and oncology drugs coming to market has been helped by regulatory initiatives such as the FDA's Breakthrough Therapy Designation and Accelerated Approval, and the EMA's Priority Medicine (PRIME) scheme<sup>5</sup>. In 2016, four new cancer drugs were approved by the FDA, and all were accelerated approvals. Despite slightly fewer approvals in 2016<sup>5</sup>, the rise in new oncology therapies is expected to continue over the coming years<sup>3</sup>.

## Targeted therapies

Targeted therapies have attracted much interest within oncology R&D: it was recently estimated that these account for 87 % of oncology drugs in late phase clinical development<sup>2</sup>. Targeted therapies include small molecules or monoclonal antibodies that specifically target selected pathways of the tumour cells, as well as antibody-drug conjugates (ADCs) that bind to a particular cell surface protein on tumour cells via the antibody, in order to deliver the linked drug into the cell. Targeting the therapy specifically to cancer cells not only reduces harmful side effects for healthy cells, but can also achieve better clinical effect. Several targeted therapies have been approved over the last decade<sup>6</sup> and are helping many patients. Many more therapies are now in clinical trials<sup>6,7</sup>.

## Immuno-oncology

More recently, there has been considerable scientific progress in the area of activating the patient's immune system to attack tumours. Several promising drugs have been launched since 2011 that use antibodies that bind to and thereby inhibit immune checkpoint proteins and receptors, such as CTLA-4 or PD-1, on tumour cells. Checkpoint inhibitor drugs result in tumour shrinkage as well as prolonging life for patients with a variety of different cancer types<sup>8,9</sup>. The first checkpoint inhibitor drugs to be launched were Yervoy (anti-CTLA-4, 2011), and Keytruda and Opdivo (both anti-PD-1, 2014). Several similar treatments have since been approved and more are in development<sup>6,10</sup>. It has been recognised that the response to novel immuno-oncology treatments does not necessarily follow the chemotherapy dogma that early tumour shrinkage response is predictive of a better clinical outcome. Drug development guidelines have been proposed to recognise this fact<sup>11</sup>. Until recently, these immunotherapies were used in patients that have already been treated with chemotherapy but Keytruda has now been approved for use in patients that have not had any previous chemotherapy. Importantly, one checkpoint inhibitor drug might be effective against multiple different cancer types, and research suggests they could be more powerful when used in combination with one another, or with other treatments<sup>2,12</sup>.



## Biomarkers and personalised medicine

Despite the introduction of many promising anti-cancer therapies, some patients respond for only a short period, or not at all, and in many cases resistance to treatment is developed over time. Through novel biomarkers, researchers hope to be able to provide information that will enable clinicians to link the right drug to the right patient. Such personalised medicine is expected to play a vital role in helping to manage more effective treatments with greater cost efficiency. A significant recent activity in this area is the American Society of Clinical Oncology's Targeted Agent and Profiling Utilization Registry (TAPUR) study<sup>13</sup>.

## Advanced therapy medicinal products (ATMPs)

There is great interest in ATMPs<sup>14</sup>, including gene therapies, stem cells and cell therapies based on gene editing techniques such as CRISPR. These emerging approaches could potentially lead to important novel strategies in oncology. However, ATMPs also bring a number of complications that have yet to be understood, including how to effectively test these products, how best to manage risk and safety, what laboratory support is needed during trials, logistical challenges, and what the long-term treatment effects might be. EMA has introduced specific pharmacovigilance guidelines for ATMPs<sup>15</sup> and there will be increasing demand among sponsors for CROs with experience in ATMP studies.

## Future considerations

Despite the increasing incidence of cancer, its death rates have declined nearly 22% since peaking in the 1990s<sup>16</sup>, but there are still many remaining challenges for drug development in this area. An important focus area is the question of how and why tumours develop resistance to drugs. This has long been a problem and increased understanding of development of resistance is one of many high priority research areas. Hopefully, some questions may be answered as more collaborative studies are carried out, that provide large-scale data sets and broader information about biomarkers.

When continuing the search for new cancer therapies, the same challenges with setting up trials still remain. Cancers can be complicated to treat, and clinical trial design needs to take into account a number of factors that are unique for oncology. For example, where should the proposed new chemotherapy fit with regards to existing surgery and radiotherapy regimes? When testing with Phase I patients who are already very unwell with little remaining life expectancy, how can dose tolerability studies be safely established? When developing new orphan drugs, what's an achievable and adequate sample size for Phase I and Phase II testing? While safety has to be everybody's priority in clinical testing, it's also important that more effective anti-cancer treatments can be made available to patients as quickly and cost-effectively as possible, and this will require smart thinking when it comes to clinical trial designs.

Working with an experienced CRO that has a large network of partners can help pharma companies to identify the optimal design for their clinical study. At PCG Clinical Services, our Advisory board and project managers can provide guidance for streamlining studies while ensuring high quality and meaningful data collection.

The continued successful development of more effective oncology therapeutics will require even greater engagement, open discussion and collaboration between payers, researchers, CROs and the regulatory agencies than has taken place over the past 15 years. In part 2 of this article, we consider some of the challenges of developing anti-cancer drugs, and how working with the right CRO can help to improve clinical trial efficiencies.

At **PCG Clinical Services**, we are experienced in managing many different types of studies within oncology and other therapy areas. We are committed to optimising clinical trials and reducing unnecessary costs through our scientific expertise, progressive EDC technology and more effective ways of working.

Our capabilities range from early study advice and target product profiling through Phase I to Phase IV trials, supported by our flexible global partner network. We continually improve our knowledge to ensure we are equipped to assist with our clients' current and future needs. For example, we are now extending our ATMP experience and study processes so that we can assist with studies in this field. Follow us on Twitter and our LinkedIn company page for company news, updates and relevant articles regarding our industry.

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