More choice for cancer patients

www.anticancerfund.org

Anticancer Fund

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Emerging from the Swiss-based organisation Reliable Cancer Therapies, founded in 2009 by Belgian entrepreneur Luc Verelst, the Belgian-based Anticancer Fund (ACF) is a private not-for-profit foundation dedicated to expanding the range of treatment options available to cancer patients. It is this central focus on patients which is the common theme that runs through the diverse activities of the ACF – both in terms of its day to day activities and also in its approach to scientific and clinical research.

While the ACF is a relatively small organisation, employing mainly scientists and medical doctors, it has an international reach which extends well beyond the borders of Belgium. This manifests itself both in terms of supporting projects in a number of different countries and also in making available scientifically accurate information to the public in multiple languages. These twin tracks of scientific and public engagement are apparent in the range of projects and activities that the ACF is engaged in.

Public Engagement

The most visible form of public engagement is in the provision of scientifically accurate information to members of the public via the ACF website (www.anticancerfund.org). Here patients, family and carers can find information on different cancer types, current cancer treatments, including the ESMO (European Society for Medical Oncology) guidelines rewritten for the lay-person, a gateway to search for clinical trials and a range of guides on relevant topics, including non-conventional treatments, diet and exercise, information for newly diagnosed or advanced cancer patients and so on (http://www.anticancerfund.org/guides/topics). This information is available in English, French, Dutch and Spanish and includes downloadable leaflets in addition to the information on the site. Also available is information on some of the 'alternative' therapies that many cancer patients may come across on the web. This is of particular importance given the range of 'alternatives' which are available on the internet, much of it based on a rejection of science or on wishful thinking and a belief in miracles.

The ACF takes seriously the task of 'quack busting', and has been active in exposing the activities of fraudsters who seek to exploit vulnerable and desperate cancer patients seeking 'miracle cures'. For example there is a very active group of people in Europe selling a fake cancer cure called GcMAF – which claims to be an immunological treatment for cancer, autism, chronic fatigue, HIV and other serious and life-threatening conditions. The ACF has been active in informing the authorities about the fraudsters, in publishing factual information about GcMAF on the web and has also been working to expose the scientific wrong-doing of individuals who have published in the peer-reviewed literature, leading to the retraction of a number of journal articles to date. The ACF is also interested in exploring, at the European level, mechanisms by which action can be taken against fraudsters operating in multiple jurisdictions.

However, the ACFs engagement with the public goes beyond publishing information and extends to direct support for individual patients seeking new therapeutic options. The ACFs medically and scientifically trained staff provide personalised information to cancer patients based on their case histories and current disease status. Patients are able

to email (info@anticancerfund.org) the ACF and take part in a dialogue to identify potential treatment options – this information is supplied to the patient who can share it with his or her oncology team. In some cases the ACF staff engages directly with the treating physicians to explore these options. Since 2010 over 500 patients, primarily from France, Belgium, the Netherlands and the United Kingdom have used this service.

Finally, there is another form of public engagement in which the ACF is becoming increasingly involved and that takes the form of public policy intervention – most notably this arises from the ACF research agenda and the need to move from positive results to clinical implementation.

Scientific Research

The ACF believes that as a society we need to ensure that no treatment option is left untapped. To this end there are three major strands of research, focused primarily on non-mainstream treatments: drug repurposing, non-commercial immunotherapies and non-pharmaceutical interventions. This broad research portfolio has another common characteristic – it is based on patient-relevant outcomes rather than on primary academic research. The objective is to bring these non-mainstream treatments into mainstream clinical practice as quickly as is possible.

Drug Repurposing

The Repurposing Drugs in Oncology (ReDO) project is an on-going collaboration with the US not-for-profit organisation GlobalCures. The aim of the project is straightforward – it seeks to identify a range of existing non-cancer drugs which show strong evidence of anti-cancer activity and which have the potential to be used clinically in cancer treatments. There is a broad spectrum of drugs that the ReDO project has identified as potential candidates, many of them available as cheap generics, including antibiotics (clarithromycin), antifungals (itraconazole), antiparasitics (mebendazole) and so on. Taking evidence from pre-clinical (test tube and animal data) and clinical sources, including small clinical trials and individual case reports, the ReDO project has reviewed and summarised the data on these drugs and then published the results in peer-reviewed journals. In addition the ReDO project has identified specific cancer types and clinical situations in which these repurposed drugs might be evaluated in the first instance.

The ACF also aims to confirm these promising data by supporting well-designed clinical trials in a number of different countries. Examples include a pioneering trial of ketorolac (used to treat post-operative pain) in women undergoing breast cancer surgery, and the addition of nitroglycerin patches (used to treat angina) with chemo-radiotherapy in non-small cell lung cancer. The promise of drug repurposing is the delivery of new therapeutic agents in a relatively short time frame and at lower cost than de novo drug design. The ACF is committed to delivering on this promise but the ultimate goal is to persuade other foundations, European and national governmental organisations to start mining this relatively unexplored field of affordable, non-toxic and potentially breakthrough opportunities that could be of benefit to patients.

Non-pharmaceutical Interventions

Another key area is non-pharmaceutical interventions, which covers nutritional, lifestyle and other non-drug and non-surgical approaches to cancer. While these interventions are gaining more and more public attention there are important issues to tackle in order to allow proper evaluation of these as additions to current standard of care treatments or, as claimed by some proponents, as alternatives to standard of care therapies. The quality of supplements and plant extracts need to be guaranteed, the contents have to be standardised (for example there are numerous forms of curcumin available from multiple manufacturers, all of them different) and manufacturing to medicinal standards undertaken.

Similarly mind body interventions, such as meditation or yoga, even when delivered by experts, need to be standardised so that the same treatment can be administered in different centres in clinical trials. And finally it is important that clinical trial guidelines are adapted to deal with this type of intervention. In terms of non-pharmaceutical interventions the ACF supports a UK trial exploring dietary changes in advanced breast cancer; another, in Belgium, is investigating mindfulness meditation in young adults during and after their cancer treatment.

Immunotherapy

Finally, the ACF is also active in the field of immunotherapy – with an emphasis on commercially neglected areas, such as non-patentable, cellular immunotherapy or combinations of the latest generation of highly expensive immunomodulatory drugs with low-cost interventions. For example there is a trial of adoptive T-cell transfer – which uses patient derived immune cells – in ovarian cancer and a planned trial which combines the newest generation of anti-PD1 drugs with low-cost treatments such as radiotherapy and repurposed drugs.

While there have been recent impressive results with the commercial anti-PD1/PDL1 checkpoint inhibitors there are numerous challenges to overcome. For example, there is the scientific challenge to improve the duration of clinical responses and the number of patients who show response. In terms of commercial challenges these include difficulties in running trials with combinations of agents from different companies and also the very high costs associated with these treatments. The trials that the ACF is supporting in this area address some of these issues directly, but more remains to be done.

Clinical Trials

The patient focus of ACF is also reflected in the support of clinical trials in patient populations with high unmet needs – particularly rare, refractory or metastatic cancers. Some of these trials utilise drugs identified by the ReDO project, or adopt a similar approach of combining a range of repurposed agents with existing metronomic or standard of care treatments. Examples include the combination of celecoxib and fluvastatin in paediatric optic nerve gliomas, another is a multicentre trial in France with four repurposed drugs in advanced pre-treated osteosarcoma. These are a start but ideally these types of trial should be organised at a European level to minimise problems of slow patient accrual and improve the speed at which results can be generated. It is often the case that in rare cancers progress is slowed down considerably by the relatively small number of patients in each country.

It should be noted that the ACF selection criteria for supporting clinical trials does not focus on specific phases of trial. The emphasis is on supporting trials which have the highest potential to change practice – these are pivotal trials of break-through treatments rather than Phase II or Phase III. End-points are designed to be clinically relevant rather than being geared towards academic interest.

The support model for trials varies by project, and can include intellectual input, study design and protocol development in addition to financial support. In all cases the ACF works closely with the principal investigators. ACF-supported clinical trials are currently scheduled to include over 1250 patients.

Barriers to Change

Another instance of the ACF commitment to public engagement is to look at the institutional and regulatory obstacles to advancing these non-mainstream treatments. These treatments need to be compared to standard of care in order to prove benefit, but this is not always a simple task. For example, trials using herbal extracts or nutraceuticals as a monotherapy are problematic due to current European clinical trial directives. There is also a lack of standardised extracts or Good Manufacturing Practices (GMP) compliant manufacturing of agents – and manufacturers are unwilling to invest to gain accreditation.

Trials in drug repurposing are easier to initiate, but there are obstacles to the adoption when positive results are reported. For example there have been a number of instances where repurposed drugs have shown evidence of efficacy – for example the common antacid cimetidine in colorectal cancer – but which have not then been licensed for cancer nor been adopted clinically. Regulatory hurdles include difficulties licensing a generic drug for a new indication when the original license holder has no interest in going forward, or indeed has newer and more costly drugs which they wish to pursue. Re-licensing is one part of a broader process required to change practice – but it is not the only one. Also important is the updating of clinical guidelines, recommendations from expert groups and so on.

Not all the barriers are economic; there are social issues at play too. For example, work in drug repurposing or non-pharmaceutical interventions may not be judged as scientifically engaging or as interesting as work using the latest technologies or theoretical constructs. Scientists respond to incentives in the same way that other sections of the community do; the result is that potentially beneficial treatments may be ignored in favour of newer, more expensive but academically rewarding commercial developments.

Changing practice is hard and the ACF believes it needs the involvement of regulators, insurers, clinicians, patients and other stakeholders to make it happen. In particular there is an opportunity to broaden the participation of non-commercial and non-academic actors in the medical research process – to the benefit of society as a whole.

If we are to deliver on the potential benefits of these commercially neglected non-mainstream therapies, particularly in an era with globally rocketing health-system costs, these non-scientific barriers must also be overcome. By keeping patients at the forefront of its work the ACF is moving forward to deliver on its core mission in all areas of activity.

Reducing the burden of cancer

Adjacent Government highlights the work of the National Cancer Institute (NCI), to reduce and treat cancer...

The National Cancer Institute (NCI) is the U.S. Federal government's primary agency for cancer research and training. As part of the National Institutes of Health (NIH) they coordinate with the National Cancer Programme, which conducts and supports research, training, health information dissemination and other programs related to cancer – i.e. diagnosis, prevention, and treatment. Real progress is being made against cancer worldwide, and due to the work of NCI and medical researchers throughout the U.S., in 2012 there were approximately 14 million cancer survivors throughout the country.

The NCI estimated that in 2015, 1,658,370 new cases of cancer will be diagnosed in the U.S. and 589,430 people will die from the disease. Approximately 39.6% of men and women will be diagnosed with cancer at some point in their life, with breast, lung, bronchus, prostate, colon, bladder, melanoma of the skin and rectum cancer named the most common cancers in 2015. [1]

Throughout the U.S. the rate of new cancers overall has been declining for more than a decade. Through new treatments and understanding for the detection and diagnosis, people living with cancer are living longer and with a better quality of life than ever before.

In a blog post [2] by Acting NCI Director, Doug Lowy, M.D, he discusses the critical contribution of basic science in fostering progress against cancer.

"Over the past 2 decades, we have made significant progress in diagnosing and treating cancer- progress that is reflected in the continuing declines in cancer death rates and the increasing numbers of cancer survivors. This progress is only possible because of our efforts to understand the biological mechanisms underpinning cancer.

"When or where the next major advance in cancer research will occur is unknown, but it always begins with basic research – often in areas which a direct application to medicine may not be immediately apparent, including areas such as physics, mathematics and materials science."

Ensuring people receive the right treatment for their cancer is integral to their quality of life. Treatments for cancer can come in many forms. Some people require a combination of measures, whilst others only have one type. The majority of people with cancer do have combination treatment, which could consist of surgery with chemotherapy and/or radiation therapy.

Treatments and new drugs are tested using clinical trials. Cancer patients at any stage of their treatment can take part in these, and they are key to developing new methods to prevent, detect and treat cancer.

Clinical trials can also bring to light new information and outcomes to researchers in regards to the cancer and the way it reacts to drugs. At NCI a clinical trial has recently revealed some interesting results in regards to precision medicine and the most common type of lymphoma.

Lymphoma is a cancer that begins in cells of the lymph system and can being almost anywhere in the body. The joint study conducted by the NCI, and Pharmacyclics Sunnyvale, California revealed that patients with a specific molecular subtype of diffuse large B cell lymphoma (DLBCL) are more likely to respond to a specific drug that patients with another molecular subtype of the disease. [3]

Several years ago, NCI scientists identified two primary subtypes of DLBCL based on characteristic patterns of gene activity with the lymphoma cells. This discover led the researchers to believe that targeted treatments could be developed.

Louis Staudt from the NCI Centre for Cancer Genomics, who co-led the study, said: "Clinical trials such as this are critical for translating basic molecular findings into effective therapies."

Study co-leader Wyndham Wilson of the NCI added: "This is the first clinical study to demonstrate the importance of precision medicine in lymphomas."

Target therapy is the foundation of precision medicine and works by targeting the changes in cancer cells that help them grow, divide and spread. Most cancers patients will have a target for a certain drug, so they can be treated with that drug. However, most of the time the tumour will need to be tested to see if it contains markers for which we have drugs. Most targeted therapies help the immune systems destroy cancer cells; stop the cancer cells from growing; stop signals that help for blood vessels; deliver cell-killing substances to cancer cells; cause cancer cell death; and starve cancer of the hormones it needs to grow. [4]

However, there are some drawbacks to targeted therapy, as there is with most cancer treatments. Cancer cells may become resistant to them and drugs for targets are hard to develop.

With detailed research and funding, cancer treatments have come a long way over the years. However, the questions still remains: why haven't we found a cure yet? Treatments available can extend life, and if caught at the right time many people do survive cancer. Due to the complicated nature of cancer and the number of types there are, it is still proving a difficult task to find that cure to eliminate this awful and life changing disease.

Organisations like the NCI play a pivotal role in getting us closer to finding that cure. Ongoing cancer research and clinical trials to test and develop new drugs could be that crucial step to help patients live a longer and happier life, with or without cancer.

1 http://www.cancer.gov/about-cancer/what-is-cancer/statistics

2 http://www.cancer.gov/news-events/cancer-currents-blog/2015/bypass-basic-science

3 http://www.cancer.gov/news-events/press-releases/2015/ibrutinib-lymphoma-subtype

4 http://www.cancer.gov/about-cancer/treatment/types/targeted-therapies

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