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.

Tackling childhood cancer

Hollie Chandler, Senior Policy Advisor at Cancer Research UK highlights the work being done to improve treatment for childhood cancers...

In the UK around 3,800 children, teenagers and young adults are diagnosed with cancer each year, that's 73 every week. Thanks to new treatments, survival rates are improving. More than 80% of children and young people with cancer now survive for 5 years or more, compared with just 30% in the late 1960s.

Despite these improvements, cancer remains the leading cause of death in children and the most common cause of death by disease in teenagers and young adults. Some types of children's cancer remain very hard to treat. Many patients suffer long-term physical and psychological consequences of their treatment into adulthood.

At Cancer Research UK, we think more needs to be done. Which is why we launched Cancer Research UK Kids & Teens [1], our campaign to raise money for research into cancers affecting children, teens and young adults. Over the next 5-10 years we aim to double the amount we spend in this area, to accelerate progress finding new cures and kinder treatments. Our ambition is that all young people diagnosed with cancer will survive and go on to live long, fulfilling lives.

Importantly, our commitment is part of a wider UK effort to improve treatment of childhood cancers. The Cancer Strategy for England [2], published by the Independent Cancer Taskforce last year, made several recommendations to

improve the delivery of treatment to children, teens and young adults as well as improving their access to clinical trials. Cancer Research UK is working with NHS England and other organisations to make sure the Taskforce's recommendations are taken forward.

Trials are essential for establishing the best possible treatments for all cancer patients. Children and young people are no exception. By running trials in the UK, patients also get innovative treatments that wouldn't otherwise be available to them.

World class research centres such as Cancer Research UK's Children's Cancer Trials Team at the University of Birmingham coordinate groundbreaking trials across the UK and internationally. This team has had some fantastic successes, including a large international trial that has helped lead to liver cancer death rates in children falling by 26% in the last decade.

For teams like this to operate effectively, they need to be supported by the wider NHS research environment. Government's continued support for NHS research infrastructure is key, which is why we've been really pleased to see plans to improve research and innovation in the NHS as part of its Five Year Forward View [3].

But England is only one part of the puzzle. All cancers occurring in children are rare so recruiting enough patients to a trial can be difficult. For this reason, it is often necessary to run large trials that are run over multiple sites across the UK, or even internationally, in order to reach a larger pool of patients.

Unfortunately, such trials are still taking far too long to set up. Streamlining trial approvals would help get these trials off the ground and deliver the outcomes we need for younger patients sooner.

In the UK, work by the Health Research Authority looks set to make real headway on this and we expect to see much better coordination of trials across Europe when the European Clinical Trials Regulation comes into force. Unfortunately, the timelines for this keep getting pushed back, with the latest estimate suggesting late 2018. The UK Government needs to continue its efforts to support the implementation of this Regulation and ensure there are no further delays.

Creating a supportive environment for research and ensuring trials can be set up in a timely way will attract further investment from industry to conduct trials in the UK. Industry investment in trials for children is limited, although it has increased since the European Paediatric Medicine Regulation was introduced in 2007. This Regulation requires all companies developing new medicines for adults, to develop a plan for how they would investigate the potential of the same drug in children. In some circumstances companies aren't required to complete this plan. And although this can be appropriate, there have been instances where exemptions have been granted to medicines that we believe could be used to treat childhood cancers. This Regulation will be reviewed in 2017 and we'll be working to make sure improvements are made so that it can better support the development of new drugs for children.

Outside of trials, population-based data on how younger patients are being treated and their outcomes can be used to increase our understanding of how best to treat their disease. But to do this effectively, we need to improve the collection of high quality data for research purposes, and we need to ensure that researchers can gain access to these data in a timely way.

Research through clinical trials and using population-based data is essential if we are to develop new cures and kinder treatments for younger cancer patients. Right now, Cancer Research UK is working so that in the future, all young people diagnosed with cancer survive and go on to live long, fulfilling lives.

1 http://www.cancerresearchuk.org/support-us/donate/kids-and-teens

2 http://scienceblog.cancerresearchuk.org/2015/07/19/taskorce-report-achieving-world-class-cancer-outcomes/

3 https://www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf

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