More choice for cancer patients

www.anticancerfund.org

Anticancer Fund

The Anticancer Fund

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.

Cancer research – 50 years and counting

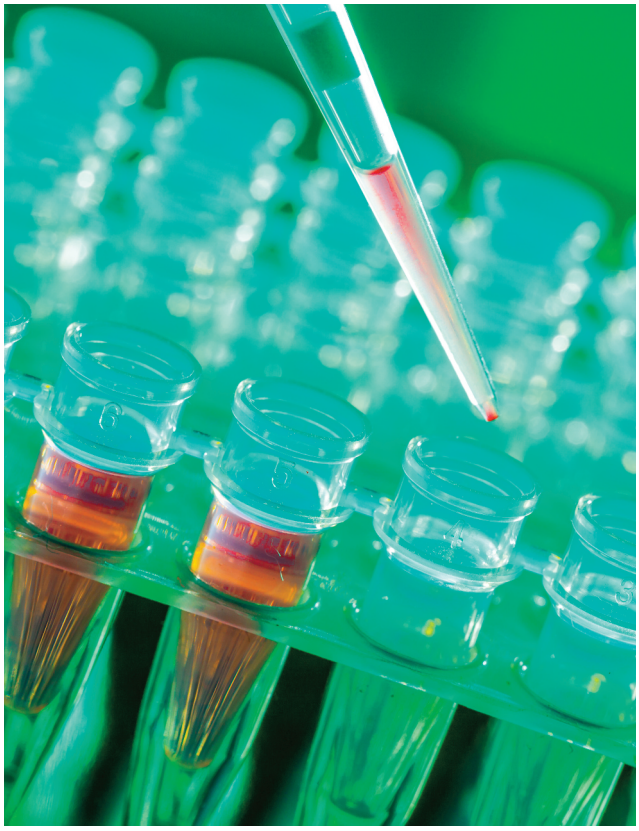
Christopher P. Wild, Director at the International Agency for Research on Cancer (IARC) outlines how 50 years on, prevention still remains key to cancer research...

"Have you found a cure yet?" Which cancer researcher upon revealing their profession has not faced this question? One can respond confidently with examples of major improvements in survival: childhood leukaemia, testicular and breast cancers being notable. One can point to remarkable insights into the previously hidden biology of cancer, with drugs now tailored to exploit the molecular Achilles heel of an individual tumour. These triumphs of scientific creativity and endeavour merit the telling. Yet the disturbing, deeper truth is we cannot treat our way out of the cancer problem.

As people live longer and populations increase, the number of new cancers each year is projected to rise sharply. In 2035, just 20 years from now, there will be an estimated 10 million more people every year facing a cancer diagnosis. Increases are greatest in the developing countries where there is least capacity to treat and care for patients. The spread of risk factors linked to western patterns of individual behaviour and societal structure will exacerbate the problem. Even for the world's richest countries the spiralling cost of cancer means improved treatment alone is an inadequate response. For the world's poorest, the out-of-pocket expenses of treatment for one individual can be financially catastrophic for an extended family. The pain of cancer is far reaching. How did we end up here and what might be done better?

Fifty years ago, when the International Agency for Research on Cancer (IARC) was established, IARC scientists considered the striking global variations in cancer patterns and decided to study the causes of this heterogeneity as an avenue to prevention. Over the last 5 decades IARC played its part, with many others, in discovering human carcinogens. Tobacco remains the pre-eminent culprit. Chronic infections account for 16% of all cancers, one in 4 in the most populous nation, China. Alcohol, radiation including excess sunlight, unhealthy diets, environmental contaminants and occupational exposures all contribute. Imbalances in calorie intake and expenditure are adding to the problem; many people are no longer moving enough to justify the amount they eat and drink.

Estimates vary but one can safely conjecture that some 40-50% of cancers could be prevented by translating this accumulated knowledge into interventions. Further inroads are made by detection of early-stage cancers or pre-cancerous conditions, combined with more effective treatment e.g. for cervical, breast, colorectal and oral cancers. Furthermore, prevention and early detection demonstrably work. Major declines in lung cancer following reduced tobacco consumption are remarkable as are the falls in cervical cancer following introduction of screening. Improved protection against work place carcinogens form part of the successes. Vaccination against hepatitis B virus and human papilloma viruses will in time yield their fruits. Many interventions have added value through reducing other illnesses of aging such as cardiovascular disease and diabetes.



Despite proof and promise, prevention is too often neglected. Commonly less than 5% of cancer research funding goes to prevention, a proportion dwarfed by the investment in basic science and clinical translational research. In addition, the science that is performed too often remains at the stage of proof-of-principle, with a failure to implement. This under-investment in research and in implementation is costly and while the underlying drivers are complex, they merit exploration.

Part of the problem may be time. The benefits of prevention can take many years to manifest. This is incompatible with the duration of a political mandate (at least in most democracies) but also with the immediacy of people's personal experience, where what is sought is a cure. Economics is important, because while new therapeutics offer opportunities for private sector investment and growth, public health interventions are perceived as cost pressures. Complexity is a further element. Prevention requires a multi-sectoral cooperation across health, transport, environment, etc., to address the "causes of the causes".

Responsibility has been too often placed solely on the shoulders of the individual whereas tobacco control has shown how appropriate legislation has been key to success.

Nevertheless, this is an exciting time for cancer prevention. Advances in cancer biology offer fresh impetus to studies of causes, early detection and prevention. Implementation research, close to policy, can better indicate factors which help or hinder the translation of promising interventions into effective national programmes. Thorough analyses of the economic benefits of prevention may yet reduce the unpopularity of the Minister of Health among government colleagues. Prevention, applied at the population level, offers a sustainable approach contributing in turn to reduced inequalities in society.

From a global perspective the necessity of prevention is blindingly obvious. IARC enters its second 50 years with a renewed mandate to conduct cancer research for cancer prevention. As there is an undeniable responsibility to offer the very best in treatments for the patients of today, there is also an undeniable responsibility to prevent the suffering from cancer for the populations of tomorrow. Perhaps eventually, on revealing one's identity as a cancer researcher to a new generation, the question may just occasionally be: "Can you prevent it yet?"

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