TREATMENT COSTS AND NEW THERAPIES

EDUARDO CAZAP, PAST-PRESIDENT, UNION FOR INTERNATIONAL CANCER CONTROL (UICC), GENEVA; FOUNDING PRESIDENT, LATIN-AMERICAN AND CARIBBEAN SOCIETY OF MEDICAL ONCOLOGY (SLACOM), BUENOS AIRES AND EXECUTIVE COMMITTEE, NATIONAL CANCER INSTITUTE, MINISTRY OF HEALTH, BUENOS AIRES

In this article, the author looks at the whether new treatments and therapies are aligned to the priorities and finances of lesser-resourced countries. He reviews current opinions on this subject among leading organizations involved in cancer care and examines the barriers faced by these countries that exclude from the latest developments.

Today, an individual's odds of surviving cancer are strongly correlated with where that person lives. Whereas in the United States the five-year survival rate for patients with breast cancer is 84%, in the Gambia, breast cancer survival is just 12.5%. Interestingly, gains in survival have not always been due to very expensive treatments. Frequently, increased survival has been achieved by cancer treatments that are relatively low cost.

Considered for many years a problem almost exclusive to rich countries, cancer is rapidly becoming a leading cause of death and disability in poor countries. Currently, low-income countries have just 5% of resources to deal with 80% of the global burden *(1)*. In addition to this, the existing treatments and new therapies are accessible to less than 10% of the world population.

Cancer drugs – some facts

The 20 leading oncology brands generated global sales just short of US$ 50 billion in 2012 with an overall expansion of US$ 63 billion by 2018. In addition, the cost of cancer drugs has more than doubled in the past decade and, of the 12 cancer drugs approved in 2012 by the FDA for cancer, 11 were priced at more than US$ 100,000 per patient per year. Innovative cancer drugs are developed with public and private investment in cancer research. Globally, the pharmaceutical industry spends US$ 6.5–8 billion per year on cancer research, but public investment in cancer research (i.e. governmental and charitable) is at much lower levels and, frequently, research and development of cancer drugs is mainly driven by commercial considerations rather than by public health priorities. America's biopharma research companies are testing 771 medicines and vaccines to fight the many types of cancer affecting millions of patients worldwide and approximately half of the investigated products in late-stage development are highly sophisticated therapies. The price of new therapies has been set very high, and as more new and targeted therapies enter the market and are used as long-term maintenance therapy, the overall cost of cancer care will increase significantly. Under the current circumstances, new therapies will become unaffordable for many countries, even for the most developed *(2)*.

An economic perspective

Proper treatment and new therapies not only promise to enhance the life of patients and increase the quality of clinical practice but also to lower overall health-care costs through early detection, prevention, accurate risk assessments and efficiencies in care delivery. Current inefficiencies are widely regarded as substantial enough to have a significant impact on the economies of major nations and, therefore the world economy. A recent Organisation for Economic Co-operation and Development (OECD) report estimates health-care expenditure for some of the developed western and eastern nations to be anywhere from 10% to 18%, and growing (with the United States at the highest). This situation has an enormous impact in the current world economy. In total, from each US$ 10 that are produced globally, one dollar goes to health *(3)*.

The 2014 World Cancer Leaders' Summit, organized by

the Union for International Cancer Control (UICC), discussed the economic case for cancer control. The estimated total annual economic cost of cancer globally was approximately US$ 1.16 trillion in 2010 and broader estimates of the costs of cancer, using a Value of Statistical Life approach bring the annual global cost of cancer to US$ 2.5 trillion. They also estimated that by implementing resource-appropriate strategies for prevention, early detection and treatment, between 2.4 and 3.7 million lives could be saved each year, 80% of them in low- and middle-income countries (LMICs). In economic terms, the value of the healthy years of productive life that could be saved totals between US$ 331 and US$ 451 billion, yielding an estimated return on investments in prevention and treatment ranging from US$ 10 billion to US$ 230 billion. The conclusion of the 250 high-level participants, including representatives from UN agencies, ministries of health and finance, international cancer organizations and private sector leaders was that investing in cancer control saves lives and makes financial sense *(4)*.

Position of leading organizations

The American Society of Clinical Oncology (ASCO) also raises cost concerns in its just-published *The State of Cancer Care in America 2014*, stating that financial pressures and instability are a "major threat to practices" and that the quality of care throughout the United States is inconsistent. Ann Steagall, Director of Clinical Policy at Biologics Inc., says "the rising costs of cancer care are unsustainable for every stakeholder." But ASCO remains shy about holding drug makers responsible for the high cost of cancer care *(5)*.

The World Health Organization (WHO) estimates that nearly one third of the world's population does not have access to full and effective treatment with the medicines they need and this rises to over 50% in the poorest parts of the world. Even in highly developed countries access to some drugs and to the best available therapy is not guaranteed for everyone.

Cancer therapies represent one of the great "missing links" in cancer control efforts in LMICs. Access barriers to cancer drugs are especially striking in light of the many research advances of recent years, which have significantly elevated the role of systemic therapy in the management of many priority cancers. There is little or no international funding for cancer treatment compared to the billions of dollars that are used for other health-related purposes.

WHO has previously produced recommendations on the essential drugs required for cancer therapy, and several new anti-cancer drugs have been aggressively marketed. Most of these are costly and produce only limited benefit *(6)*.

WHO divided currently available anti-cancer drugs into three priority groups (curable, increased curability-adjuvant and prolong survival). Curable cancers and those cancers where the cost–benefit ratio clearly favours drug treatment can be managed appropriately with regimens based on only 17 drugs. All of these are available, at relatively low cost, as generic preparations and the wide availability of these drugs should be the first priority, especially for LMICs *(6)*.

The WHO Model List of Essential Medicines for adults and children presents a set of medicines that are considered to be cost-effective and of critical public health importance in all countries. In this sense, "Essential medicines" are defined as those that "satisfy the priority health-care needs of the population; they should therefore be available at all times in adequate amounts and in appropriate dosage forms, at a price the community can afford" *(7)*.

The European Parliament recently debated the issue of life-saving medicines and the excessively high pricing in certain Member States. Speaking in the context of the debate, health spokesperson Michele Rivasi, who initiated the discussions, said: "The astronomical prices of some life-saving medicines is meaning those suffering from these illnesses are unable to afford their treatment. This is a scandal in itself but it is an even greater scandal that the European Commission is refusing to address the issue, notably by tackling the issue of monopolies and abuse of market position" *(8)*.

Barriers to access

Drugs costs, insufficient public funding of health, poor infrastructure, the irrational use of cancer drugs, bureaucratic policies and counterfeit medicines are the most common obstacles in most of the countries of the developing world. As an example, in developed countries sales of counterfeit drugs represent less than 1% of the pharmaceutical market; but this rises to 10–30% in parts of Asia and Latin America and up to 70% in some African countries.

Radiotherapy is a basic component of cancer treatment and is recognized as an essential tool in the cure and palliation of cancer, and recommended in 52% of new cancer patients. In LMICs, the need for radiation therapy may in fact be higher due to a more advanced stage of disease at presentation. It has also been established that proximity and timely access to radiotherapy facilities are known to affect clinical outcomes. Unfortunately, access to radiation therapy is limited in some countries and non-existent in others. Of African nations, 29 of 52 have no radiotherapy facilities at

all, and these 29 countries comprise an estimated 198 million people.

The UICC has recently convened a Global Task Force on Radiotherapy for Cancer Control (GTFRCC) to address this very challenge *(9)*.

The World Oncology Forum, convened in 2012 by the European School of Oncology, concluded that current global health strategies to control cancer are largely insufficient. Participants issued a 10-point "Call to Action" that asks for major improvements in prevention, diagnosis, treatment and new models of research *(10)*.

Overcoming barriers and current actions to improve the global picture

It is known that some pharmaceutical companies have established drug donation programmes to address access difficulties in low-income countries. Although useful in the short-term these programmes are not a solution to cancer drug access. They have also received diverse criticism due to the fact that might be a veiled way to market cancer drugs.

Since its inception, the WHO Model list has been updated every two years by an Expert Committee for the Selection and Use of Essential Medicines, through an evidence-based process based on: disease prevalence, efficacy and safety, and comparative cost-effectiveness. Currently, it is again being updated, this time with the collaboration of the Dana Farber Cancer Center (USA) and UICC (Geneva) *(11)*.

Recycling existing drugs for cancer therapy and drug repurposing are strategies with fascinating potential for cutting the cost of cancer care as well as significantly affecting patient outcomes. The Repurposing Drugs in Oncology (ReDO) project, an international collaboration between researchers working for not-for-profit patient-centred organizations in Europe and the United States, aims to accelerate the repurposing of non-cancer drugs for new indications in oncology *(12)*.

Other approaches are trying to identify more cost-effective options. In this way, several possibilities might be considered, such as modifying modes of administration, using shorter – but still effective – courses or doses, finding new combinations or indications of less expensive drugs or the use of generics (after testing bioequivalence) or biosimilars *(13)*.

Another significant development has been that in 2010, the United States Congress passed the much awaited legislation which would give the United States' FDA the authority to approve generic versions of an innovator biologic drug. Recently, regulators at the EMA in Europe also worked to finalize draft recommendations for biosimilar versions of monoclonal antibodies *(14)*.

In January 2015, an historic event took place. For the first time, world leaders gathered at the World Economic Forum in Davos faced calls for bold action to respond to the rising human and economic toll of cancer. Franco Cavalli, Chair of the World Oncology Forum, led calls for an agreement on a package of actions that could accelerate progress towards finding a cure or long-term control for cancer, and massively expand global access not just to prevention but also early detection, treatment and care.

In conclusion

New cancer therapies are important and a result of the advancement of human knowledge and science. But from a global health perspective priorities are different: if we wish to be really effective in increasing cancer curability on a global scale, the most urgent action is to improve access to care to more people in all countries around the world.

It is also critical to recognize cancer as a health priority that requires adequate public funding. Furthermore, it is urgent to provide rigorous and timely evaluation and licensing of all cancer drugs and to adopt a range of mechanisms to secure affordable prices.

Worldwide access to the best possible cancer treatment, care and support is a top world priority and we all must be committed to participate in building collaboration and cooperation to address barriers in access to cancer care worldwide.

It is our obligation to promote the rational use of cancer drugs by preparing national guidelines for the treatment of common cancers and ensuring that the cancer drugs that are included in national guidelines are listed in national as well as international formularies of essential medicines.

As Franco Cavalli said "Every year cancer drains an estimated US$ 2 trillion from the world economy in terms of lost output and the cost of treatment, equivalent to around 1.5% of global GDP, as well as wreaking terrible suffering on millions of individuals, families and communities. The message I will be bringing to Davos concerns the urgent need to work together to remove barriers that are impeding the development of and access to effective cancer therapies". •

Dr Eduardo Cazap is the founder and first President of the Latin-American & Caribbean Society of Medical Oncology (SLACOM) and was President of the Union for International Cancer Control (UICC-Geneva) 2010–2012. Has been member of the Board of the American Society of Clinical Oncology (ASCO, Washington), in representation of the international members during the

period 2009–2012. In September 2010 was appointed member of the Executive Committee of the newly created National Cancer Institute of Argentina (INC).

He has published over 180 papers and his main areas of investigation and interest are: global health, control and prevention, breast cancer as well as independent clinical research with public funding. For the last 15 years he has been the promoter of the "global cancer control" concept and has written numerous papers on the subject.

Dr Cazap is President of the Executive Committee of the World Initiative for Breast Health (BHGI), which is co-sponsored by the Fred Hutchinson Cancer Research Center and Susan G. Komen for the Cure®.

He has also been designated co-Chair of the Civil Society Working Group to advise the President of the United Nations General Assembly on the 2011 United National High-Level Meeting on Noncommunicable Diseases and was elected President of the UICC Cancer World Congress, which took place in Montreal, Canada, August 2012.

In the area of investigation has created the Working Group on International Clinic Trials of the American Society of Clinical Oncology (ASCO).

In 2011, he was designated President of the Scientific Council of the International School of Senology, (SIS) in Strasburg, France, as well as Expert of the World Oncology Forum (WOF) of the European School of Oncology (ESO), in Lugano, Switzerland.

His most recent designation is as Vice-President of the Working Group of Developing Countries of the European Society of Medical Oncology (ESMO) in Lugano, Switzerland.

Dr Cazap has been awarded with the Distinguished Achievement Award; the Oncology Luminaries and made a Fellow of the American Society of Clinical Oncology (ASCO).

References

1. Farmer F, Frenk J, Knaul FM, et al. Expansion of cancer care and control in countries of low and middle income: a call to action. *Lancet* 2010;376 :1186-93)
2. http://www.phrma.org/sites/default/files/pdf/2014-cancer-report.pdf last access 15/01/2015
3. http://www.thehugojournal.com/content/7/1/1 last access 15/01/2015
4. http://www.uicc.org/sites/main/files/atoms/files/WCLS2014_economics_of_cancer_FINAL.pdf last access 15/01/2015
5. http://www.managedcaremag.com/archives/2014/6/research-blame-high-cost-cancer-drugs
6. K. Sikora,S. Advani,V. Koroltchouk,I. Magrath, L. Levy,H. Pinedo, G. Schwartsmann, M.Tattersall & S.Yan. *Annals of Oncology* 10: 385-390, 1999
7. Report from the WHO to the Executive Board, January 2002
8. http://www.greens-efa.eu/access-to-healthcare-12761.html ; last access 14/01/2015
9. http://www.uicc.org/advocacy/our-campaigns/global-task-force-radiotherapy-cancer-control; last access 14/01/2015
10. Cavalli, F. An appeal to world leaders: stop cancer now. *Lancet*, Volume 381, No. 9865, p425–426, 9 February 2013
11. http://www.uicc.org/advocacy/our-campaigns/essential-medicines last access 14/01/2015)
12. Pan Pantziarka, Gauthier Bouche, Lydie Meheus, Vidula Sukhatme, Vikas P. Sukhatme. The Repurposing Drugs in Oncology (ReDO) Project . ecancer 2014, 8:442 DOI: 10.3332/ecancer.2014.442)
13. Elzawawy A. The "win-win" initiative: a global, scientifically based approach to resource sparing treatment for systemic breast cancer therapy. World J Surg Oncol. 2009 May 5;7:44 and Elzawawy A. Breast Cancer Systemic Therapy: The Need for More Economically Sustainable Scientific Strategies in the World. Breast Care (Basel). 2008;3(6):434-438).
14. Cazap, E. ESMO Emerging Countries Committee, (ECC) - AORTIC-SLACOM-UICC joint symposium: personalised medicine with limited resources: myth or reality? *Annals of Oncology* 25 (Supplement 4)