18 December 2019

Anticancer Fund

Increasing our options for cancer treatment in Europe

Recommendations to the Cancer Mission Board

Whereas previous European research framework programmes have been driven by the creation of economic growth, Horizon Europe represents an opportunity to reset priorities and to deliver a cancer mission that brings real added value to Europe's citizens. Reducing the societal burden of cancer requires a paradigm shift in the way research is organized and funded, and this paper offers recommendations for the Cancer Mission Board as it paves the way for a much-anticipated European programme for cancer research.

Urgent need for effective and affordable anticancer treatment options

The development of new medicinal products for the treatment of cancer is resource-intensive and relatively slow, taking around 8 to 12 years on average from preclinical testing to marketing authorisation. In addition, the pharmaceutical industry has to deal with increasing productivity issues and low success rates of oncology medicines in clinical trials [1]. Due to high development costs and the risk of failure in clinical trials, new oncology medicines are often very expensive, and on top of that there seems to be a high willingness to pay which leads to extremely high prices [2–4]. Furthermore, anticancer medicines that enter the market may appear effective based on surrogate endpoints, but almost half of them later fail to show positive effects on overall survival and/or quality of life in real-world clinical practice [5].

FACT SHEET: Urgent need for effective and affordable anticancer treatments

- With about 4.2 million new cases and about 1.9 million deaths from cancer in Europe in 2018, the urgent medical need to develop affordable anticancer treatments is clear [16]. By 2030, there will be over 22 million new cases of cancer a year globally, which is almost double the number in 2012 [17].
- The total global spending on therapeutic oncology medicines is increasing every year and will likely exceed $200 billion by 2023 [2].

Untapped potential of independent clinical research with potential societal benefit

The current biomedical discovery ecosystem is mainly driven by creating intellectual property and securing other exclusive rights such as data and marketing protection. Even though big pharma is still the main operator in bringing new medicines to the market, academic and public institutions are the major source of innovation today [6]. However, most of the products that originate from academic or public organizations are out-licensed for clinical development and commercialization to SME's and/or pharmaceutical companies.

High quality, independent clinical research is being conducted worldwide, supported by public and philanthropic funds, and has an important impact on cancer treatment protocols especially when the research is conducted by collaborative groups [7,8]. This independent cancer research aims to answer clinical questions that may not be addressed by companies and has the potential to provide patients with affordable and effective treatments. These treatments comprise not only drugs but also combinations with surgery and radiotherapy. In order to allow cost savings and to deliver valuable treatment options to cancer patients in a timely manner, challenges hindering the translation of independent clinical research into marketed products must be overcome.

FACT SHEET: Underexploited opportunities in independent clinical research

- An analysis of marketing authorization applications approved by EMA between 2010 and 2012 demonstrated that 17% of products originated from academic institutions, public bodies or public-private partnerships. However, none of these organisations retained the product through to the stage of approval [6].
- Of the 58127 clinical trials included in the EudraCT database in September 2019, 21% were non-commercial, while 79% were commercial.
- Of the 190 late-stage clinical trials of repurposed drugs in oncology reported in 2018, only seven (3.7%) were sponsored by a pharmaceutical company, with the vast majority being sponsored directly by a university/hospital (n=127, 67%) or by a research institute, network or foundation (n=53, 28%) [9].
- In the US, the National Cancer Institute's investment in its cancer cooperative group research programme has been proven to provide exceptional value and benefit to the public. A study of the 23 positive Southwest Oncology Group trials sponsored by the NCI from 1965 to 2012 estimated that 3.34 million life-years were gained through to 2015, with return on investment of US $125 per life-year gained [18].

Drug repurposing, which means finding new therapeutic uses for existing medicines, is one area in which a lot of independent cancer research is ongoing [9]. Various drugs already widely used for non-cancer diseases have shown promise for the treatment of cancer. Repurposing these drugs could allow new cancer treatments to be introduced relatively quickly and at low cost, thereby meeting the unmet needs of patients and healthcare payers alike [10,11]. Drug repurposing can be a valuable parallel pathway to the pharmaceutical industry development pipeline, and deserves to be given high priority.

Besides drug repurposing, independent research could also play an essential role in the development of **autologous cell therapy**. The first two autologous T cell therapies that are approved for cancer in the EU are CAR-T cells (Kymriah and Yescarta) and come with a high cost for society. Consequently, several Member States are reluctant to reimburse these therapies, and academic researchers and payers are looking for alternative development options. Autologous cell therapy leans close to autologous transplantation as treatment, which occurs today in Europe on-site in specialised accredited centres. Public funding can support upcoming innovations, such as automated production platforms, available on-site to independent researchers and allowing independent clinical research. This will in time make production at the bedside feasible for these very personalised therapies, ensuring timely access for patients and decreasing the cost for society in the long run.

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Our recommendations to the Cancer Mission Board to optimize cancer treatment in Europe

1. Increase and rethink funding options for independent research

We recommend **making public funds available for independent research** and clinical trials where interest from pharma industry is missing because of lack of monetary incentives and where potential patient benefit is high. One specific research area that would significantly benefit from public funding is the repurposing of existing medicines in oncology, since this could lead to safe, timely and effective new treatment options for cancer patients. Recent advances in genomic and RNA sequencing, advanced technology to analyse the tumour microenvironment and integrated data analysis can lead to innovative new therapeutic uses of existing drugs. Precision oncology is only a limited part of the solution and a more holistic approach including other "-omics" could lead to more innovative treatment options.

Additionally, clinical innovations can come from sources other than new molecules or cell therapies, including radiotherapy, surgery or combinations of all modalities. Optimizing those interventions could deliver meaningful clinical benefit to patients and will become part of the solution in the fight against cancer, although they do not always attract industry support. Without improved funding for independent trials, such innovations may be stifled and patients will be denied valuable and affordable treatment options.

2. Create adequate infrastructure and foster cross-country collaboration

We should accept that pharma industry will only invest in research that pays off and for example not in repurposing a generic and cheap drug in a rare cancer indication. In order to drive innovation in academic research neglected by industry, we recommend centralising cancer research in a limited number of specialised institutions/clinics possibly within a framework such as **a European Cancer Institute**, similar to the US National Cancer Institute (NCI). This institute could help organize cancer research in Europe, and could also function as a centre of excellence for horizon scanning and knowledge-sharing on anticancer treatments. The focus of this institute should be on deepening the cooperation across disciplines and stakeholders, including patients, in Europe.

Medicine developers, regulators, payers and other stakeholders are increasingly exploring the use of real-world data in the development and utilisation of medicines as it holds the promise of increasing the efficiency and effectiveness of all processes. Collecting real-world data may be of particular importance for medicines that are currently used off-label in rare or paediatric cancers. However, better infrastructure is urgently needed to systematically capture these data. In the US, the Food and Drug Administration (FDA) and National Institutes of Health (NIH) recently launched a web-based tool called CURE ID that enables health care providers to report novel uses of existing drugs for infectious diseases [12]. We recommend implementing such an innovative **real-world data crowdsourcing approach** in Europe to capture clinical outcomes of anticancer treatments in new indications, in new populations, in new doses or in new combinations.

Finally, we urge the exploration and implementation of innovative trial designs, such as multi-arm/multi-stage or platform trials [13–15], to accelerate clinical development, reduce competition for patients and ensure high-quality results. If **an independent platform clinical trial infrastructure**, potentially driven by existing organisations such as the European Organisation for Research and Treatment of Cancer (EORTC), is in place, both commercial and non-commercial treatments could be evaluated side-by-side in a patient-centric way.

References

1. Scannell JW, Blanckley A, Boldon H, Warrington B. Diagnosing the decline in pharmaceutical R&D efficiency. *Nat Rev Drug Discov*. 2012;11(3):191-200. doi:10.1038/nrd3681.
2. IQVIA Institute for Human Data Science. *Global Oncology Trends 2019*.; 2019.
3. Prasad V, Wang R, Afifi SH, Mailankody S. The Rising Price of Cancer Drugs-A New Old Problem? *JAMA Oncol*. October 2016:2015-2016. doi:10.1001/jamaoncol.2016.4275.
4. Prasad V, Jesús K De, Mailankody S. The high price of anticancer drugs: origins, implications, barriers, solutions. *Nat Rev Clin Oncol*. 2017;14(6):381-390. doi:10.1038/nrclinonc.2017.31.
5. Davis C, Naci H, Gurpinar E, Poplavska E, Pinto A, Aggarwal A. Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13. *BMJ*. 2017;359:j4530. doi:10.1136/BMJ.J4530.
6. Lincker H, Ziogas C, Carr M, Porta N, Eichler H-G. Regulatory watch: Where do new medicines originate from in the EU? *Nat Rev Drug Discov 2014 132*. January 2014.
7. Unger JM, Nghiem VT, Hershman DL, Vaidya R, LeBlanc M, Blanke CD. Association of National Cancer Institute–Sponsored Clinical Trial Network Group Studies With Guideline Care and New Drug Indications. *JAMA Netw Open*. 2019;2(9):e1910593. doi:10.1001/jamanetworkopen.2019.10593.
8. Kesselheim AS, Tan YT, Avorn J. The roles of academia, rare diseases, and repurposing in the development of the most transformative drugs. *Health Aff*. 2015;34(2):286-293. doi:10.1377/hlthaff.2014.1038.
9. Pantziarka P, Verbaanderd C, Sukhatme V, et al. ReDO_DB: the repurposing drugs in oncology database. *Ecancermedicalscience*. 2018;12:886. doi:10.3332/ecancer.2018.886.
10. Breckenridge A, Jacob R. Overcoming the legal and regulatory barriers to drug repurposing. *Nat Rev Drug Discov*. 2018;18(1):1-2. doi:10.1038/nrd.2018.92.
11. Pushpakom S, Iorio F, Eyers PA, et al. Drug repurposing: progress, challenges and recommendations. *Nat Rev Drug Discov*. 2019;18(1):41-58. doi:10.1038/nrd.2018.168.
12. CURE ID. https://cure.ncats.io/#/sign-in. Accessed December 9, 2019.
13. The Adaptive Platform Trials Coalition. Adaptive platform trials: definition, design, conduct and reporting considerations. *Nat Rev Drug Discov*. 2019;18(10):797-807. doi:10.1038/s41573-019-0034-3.
14. Parmar MKB, Carpenter J, Sydes MR. More multiarm randomised trials of superiority are needed. *Lancet*. 2014;384(9940):283-284. doi:10.1016/S0140-6736(14)61122-3.
15. Woodcock J, LaVange LM. Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. *N Engl J Med*. 2017;377(1):62-70. doi:10.1056/NEJMra1510062.
16. International Agency for Research on Cancer. Global Cancer Observatory. http://gco.iarc.fr/. Accessed October 15, 2019.
17. Cancer Research UK - International Agency for Research on Cancer. *World Cancer Factsheet*.; 2012.
18. Unger JM, LeBlanc M, Blanke CD. The Effect of Positive SWOG Treatment Trials on Survival of Patients With Cancer in the US Population. *JAMA Oncol*. 2017;3(10):1345. doi:10.1001/jamaoncol.2017.0762.