Re-innovate cancer treatment

Tapping into the potential of re-purposed drugs

European Parliament, JAN6Q1 | 27 February 2018 | 17:00-18:30

A roundtable discussion organised with the MEPs Against Cancer Group and the Anticancer Fund

PROGRAMME

17:00 - 17:10	**Introduction** • MEP Alojz Peterle (EPP, SL) President, MEPs Against Cancer • MEP Lieve Wierinck (ALDE, BE)
17:10 - 17:20	**What is drug repurposing & the ACF** • Dr Lydie Meheus, Managing Director, Anticancer Fund
17:20 - 17:40	**Better, more affordable treatments through repurposing research** • Prof Richard Sullivan, Professor of Cancer & Global Health at Kings College London
17:40 - 17:55	**Independent research** • Prof Silvio Garattini, Founder, L'IRCCS - Istituto di Ricerche Farmacologiche Mario Negri
17:55 - 18:10	**European Commission's position** • Olga Solomon, Deputy Head of Unit Medicinal products - authorisations, EMA; DG SANTE
18:10 - 18:20	**Patient perspective : Unmet needs in paediatric cancer** • TBC
18:20 - 18:25	**Questions and wrap-up**
18:20 - 18:30	**Concluding remarks by hosting MEPs**
18:30-19:00	**Cocktail / networking reception outside room**

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SUMMARY REPORT

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Anticancer Fund

MAC MEPs Against Cancer

epp european people's party

alde PARTY ALLIANCE OF LIBERALS AND DEMOCRATS FOR EUROPE

Introduction

MEP Peterle, explained the importance of addressing the untapped potential of innovation in cancer treatment for the benefit of cancer patients in Europe. He also identified the social responsibility of policy-makers to raise awareness of the added value of drug-repurposing for cancer treatment and to stimulate concrete actions to overcome existing burdens for patients and national healthcare systems. This is in line with the MEPs Against Cancer group's work on several strategic issues, such as promoting equal access to high-quality care.

MEP Wierinck, as a previous cancer patient, outlined the need to enhance further research into promising cancer therapies. She recognised the importance of establishing a parallel pathway for re-purposed drugs, which may be complementary to approved cancer medicines, targeted therapies and novel drug development. She also acknowledged the role that non-commercial parties may play with regard to meeting those public health-related needs disregarded by the pharmaceutical industry. Subsequently, she encouraged further exploration of clinical and regulatory framework in this direction.

Dr Lydie Meheus, in her capacity as Managing Director of the Anticancer Fund, delivered a presentation on the purpose of drug repurposing and the role of the ACF in this area. The ACF is a privately-funded foundation focused on research on non-commercial treatment options and independent clinical trials for cancer patients.

In her presentation, Dr Meheus expressed that drug repurposing can be a confusing label, often referred to as drug repositioning or recycling. It consists of finding new indications for existing medicines, specifically new uses outside the label of original medical indications for marketed drugs. She explained that drug repurposing includes the extension of labels or market for off-patent or near to patent expiry medicines through a public campaign, rather than a commercial marketing promotion.

This treatment option is currently not maximised due to the lack of financial incentives for pharmaceutical industries. However, the untapped potential for patients is huge: no changes are required for currently available medicines to help cancer patients, but so far no generic drug has been approved for a new indication.

Several generic medicines have proved to help the treatment of cancer, for example aspirin prevents the immune destruction, heparin opposes the invasion process of metastatic cells, and minocycline combats genome instability and mutation, for example.

Independent clinical trials play a fundamental role in testing the potential of these medicines. The Anticancer Fund recruiting trial portfolio for drug repurposing includes the following:

Aspirin for recurrence and survival in colon cancer;

- Pre-operative hormone treatment for ER+ breast cancer patients;
- Combination of 9 repurposed drugs with low-dose chemotherapy in brain cancer;
- Advanced bone cancer treatment with a combination of chemotherapy and immunosuppressants;
- Immunotherapy, radiation and an immune modulatory combination in cervical and uterine cancer;
- Vitamin D treatment for melanoma;
- Combination of 3 repurposed drugs after chemotherapy failure in lung cancer;
- Anti-inflammatory and cholesterol inhibitor as repurposed drugs for children's optic nerve cancer;
- Treating leukaemia patients with chemotherapy and 2 repurposed drugs.

Repurposing opportunities are mainly found through knowledge mining and clinical observations, such as the case of propranolol as an anticancer agent for angiosarcoma.

According to the existing regulatory pathway, the market authorisation for new therapeutic indications is granted via the label extension by a MA holder or by third parties' marketing authorisation applications (MAA). At the same time, producers cannot implement a new indication without investing in clinical development which will lead to substantial high pricing of the authorised repurposed product and a significant threat of off-label use.

In light of the above, Dr Lydie Meheus suggests the following next steps and final objectives:

- Adapt regulatory pathways for adding new indications to existing labels;
- Increase funding and create novel finance systems for non-commercial research;
- Support patient recruitment for non-commercial clinical trials;
- Promote knowledge-sharing & establish centres of excellence to perform horizon scanning.

Summary Report

Prof Richard Sullivan, Professor of cancer and global health at Kings College in London, talked about repurposing research to provide better and more affordable treatments.

“New is not always necessarily better!”: according to Prof Sullivan, who stated that the current paradigm in oncological medicine supports new medicines while not paying adequate attention to the issue of affordability. A majority of current cancer drug development is centered around returns on investments within the industry. Conversely, the added value of drug repurposing is that this is entirely focused on health and delivering better outcomes for patients.

Some inconsistencies have emerged including current patient access schemes for high-cost cancer drugs do not deliver enough value to society and many drugs circulate in the market without enough back-up data and evidence on outcomes of survival and improvement of quality of life.

Many European countries, especially countries in Eastern Europe, are under a huge economic burden for cancer but a gap remains between the amount spent and the actual outcomes obtained for the clinical benefits of patients. Little research has been done in the prevention, detection and critical areas. Most research is concentrated where the money is: novel drug development and translation research related to commercially-driven research activities.

Cancer medicines are treated more and more as valuable commodities with distorted effects on healthcare systems and medical priorities. This argument offers a great rationale for re-focusing research innovation into repurposing. Although research and development on repurposing is growing thanks to the EU Member States’ contributions, research endeavours rest on soft money, such as crowdfunding. According to Prof Sullivan, the existing system supports the inequality paradigm: attractive and innovative drug developments, which are very expensive and affordable to only few patients yet they are of no real value to society as a whole. Drug repurposing is part of the solution for a generation focused on health rather than wealth.

Summary Report

Prof Silvio Garattini, Founder of the Institute of Pharmacological Research Mario Negri (IRCCS), discussed the role of independent research in innovation.

Prof Garattini illustrated the advantages of independent clinical research for repurposing old drugs by stating that pharmacy company-sponsored research mostly focuses on the product, with inadequate times and doses and on clinical results. Furthermore, it excludes fragile populations and publishes selective contents. Conversely, independent research values therapeutic innovation, adequate sample size and follow-up, proactive pharmacovigilance, publications of data regardless of results obtained from research, inclusion of fragile population and data-sharing with participants in clinical centres.

He also commented that recently approved anti-cancer agents are very expensive, hardly effective versus best standard of care, toxic, and are not supported by data on overall survival. The merits of repurposing existing drugs do not lie only on low prices, but also on better knowledge of interactions with other drugs as well as risks and benefits, dosage and long-term usage.

He confirmed that there is an unmet need of randomised clinical trials that may be timely and independent from pharmaceutical companies; have no restriction for 3-5 years; address comparative effectiveness and receive adequate financial support.

In addition, he outlined that drug repurposing needs a new policy and new financial framework. For example, he stated that Horizon 2020 has not succeeded in supporting independent clinical trials. He expressed the hope that some of these ambitions could be pursued in the context of the budget capacity under the new Multiannual Financial Framework and through the creation of a special EU fund. Less than 0,3% of the EU pharmaceutical market budget is currently devoted to regular revisions of drugs not covered by patents and to tests their clinical use for anticancer indications.

His conclusions drew attention to the enormous potential for savings through drug repurposing for cancer treatment As an example, the use of tretinoin to treat breast cancer in the place of trastuzumab enable to save 45, 522 euros (according to the sharp price difference between the cost of tretinoin, 4,158.00 €, and the price of trastuzumab 49,680.00 €), namely almost 92%.

Olga Solomon, Head of Unit Medicines: policy, authorisation and monitoring, DG SANTE

Ms Solomon highlighted the position of the European Commission on opportunities and challenges in repurposing, starting from brainstorming discussions of the expert group STAMP on the topic of repurposing.

The STAMP Committee - Safe and Timely Access to Medicines for Patients – has worked on identifying ways to effectively use the existing EU regulatory tools, increasing information-sharing among Member States, improving implementation of EU pharmaceutical legislation and patients' access to innovate and affordable medicines. First internal discussions concerned early access initiatives through conditional marketing authorisation, adaptive pathways and PRIority MEdicines (PRIME). After a meeting in March 2016, the STAMP Committee sent a questionnaire to seek more information on important authorised medicines widely used off-label. No similarities on the patterns of use across Member States have been identified. However, the need to involve stakeholders was set as a priority. Subsequently, a brainstorming session in March 2017 gathered participants from industry, patient and consumer groups, HTA and payers bodies.

Results collected by repurposing case studies developed by interested Member States and other bodies in 2017 showed that lack of interest from and difficulties in engaging with the pharmaceutical industry depend engagement with the pharmaceutical industry for timely generation of necessary data; support for non-industry developers on the procedure for registration; and the issue if a market authorisation holder has no particular interest in the repurposing pathway and a new indication cannot be formally considered.

The added value brought by non-commercial drug developers addresses filling the gap of accessible information in the public domain. In this regard, they can obtain all relevant existing historical data for a medicinal product and make use of their expertise of the non-clinical aspects of a dossier and the data that may support dose finding. At the same time, case studies raised awareness of the lack of a regulatory framework that recognises the challenges faced by non-industry researchers, in terms of insufficient regulatory awareness, fee waivers and advice on the use of an authorised, off-patent, medicine in a new indication. Furthermore, regulatory authorities could make a better use of extensive data sets generated in registries to support appropriate product use. It should be explored whether the EMA's registry pilot or HMA/EMA Joint big data task force can offer consensus regarding data collection in the real world setting.

Repurposing of medicines is still an important discussion topic for the STAMP Committee, and one of the current challenges for the group involves the inclusion of new indications for off-patent drugs, while establishing new synergies with the Health Technology Assessment Network. Another challenge is providing better access to data and providing data quality.

In Ms Solomon's opinion, the industry should not be left aside in this process: she expressed that understanding the industry and making data available could increase the level of cooperation. She confirmed her neutral stance when stating that EU Institutions are certainly in favour of facilitating the work of non-commercial parties regarding drug repurposing, within the existing regulatory framework. At the same time, the institutions recognise the efforts made by industry associations. In order to bridge the gap, she stated these questions that need to be answered:

- Why is the industry reluctant towards new indications?
- Do non-industry organisations and academics have adequate knowledge about the regulatory framework for the authorisation of medicines?

She also advised on bringing stakeholders together within a platform to implement mechanisms for support on data quality. This would help to develop guidelines on useful support contacts, access to data that may be compliant with a MA procedure, as well as incentives for the uptake of new indications, including fee exemptions, reward systems and designation opportunities.

The next step she suggested is that industry could submit to the STAMP proposals on what a supportive repurposing framework might look like.

Summary Report

Ian Banks, Chair of the European Cancer Organisation (ECCO), Patient Advisory Committee

Mr. Banks acknowledged the challenge of the unmet needs of patients, including children and stated that innovation should be delivered on the basis of real benefits to patients.

He explained that repurposing is a crucial tool for better meeting patient needs with the medicines we already have. According to his experience, patients seek normality. Unless repurposing addresses this concern, it won't bring added value to patients.

Mr. Banks explained that the advantages of repurposing for patients are:

- To enable patients to maintain, as far as possible, 'normality' in their daily lives;
- to take better account of the needs of carers and older patients;
- to meet the need of paediatric medicine: there are still too many waivers during initial investigation stages and more research is needed for children.

What we should consider while repurposing for the benefits of patients is improving patient safety and assisting patient adherence. In this respect, reduction of side effects or more convenient dosing frequencies could be viable options. The risk of not providing repurposing is that people can go easily online and look for their medicines by themselves with no guidance.

In line with Ms Solomon's call for further cooperation, Mr Banks also emphasised the crucial role of dialogue, collaboration and expert exchange on the nature of the problem. Multi-stakeholders consensus, modifications to the currently operating incentive systems, political will and accountability to achieve a change, especially at EU level, are the prerequisites he identified as further steps.

Closure

The session ended with a question from the audience on the use of common registers for patients' cancer data and off-label use of cancer treatments.

Dr Lydie Meheus answered by mentioning the valuable model of the Joint Action on Rare Cancers registry, where there is a working party on registrations, thus creating room for further innovation on registering data and off-label use of medicines. The Anticancer Fund, which is a member of this network, is committed to fostering the registration of off-label use. At the EU level, other initiatives ,such as the European Reference Network's potential on the collection of data across Europe on rare diseases can also be explored.

MEP Lieve Wierinck concluded the discussion by thanking the participants for their contribution.

Anticancer Fund

Our mission:

Cancer is a threat to society, too many cancer patients suffer or die.

More can be done if we exclude “profit” as a driver in cancer research and focus on patient benefits instead.

The Anticancer Fund is an independent non-profit organisation dedicated to expanding the range of treatment options available to cancer patients, regardless of the commercial value. We support promising non-commercial research, seek new and better treatment options, and engage in comprehensive knowledge sharing. With no commercial shareholders or interference from special interest groups or pharma companies, patients’ interest is our exclusive focus.

Boechoutlaan 221, 1853 Strombeek Bever, Belgium
+32 2 268 48 16
info@anticancerfund.org
www.anticancerfund.org