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EU Drug Development: The long journey from discovery to patient access

FEAM European Biomedical Policy Forum
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Prior to the arrival of any medicine on the market, each product goes through a lengthy research and development process, focussing on proof of concept, safety and efficacy. Stakeholders at all stages in this process have drawn attention to length, complexity, costs, difficulty in retrieving data for reproduction, a lack of focus on patient needs as well as a disparity between the pace of innovation and regulatory mechanisms.

Within the EU, once the European Medicines Agency (EMA) approves an intervention, distribution and accessability decisions are then the remit of the Member State that set country specific criteria. In oncology, there is a notable gap between marketing-approval development of anti-cancer medicines and their post registration use in clinical practice. With academics, (clinical) researchers, industry, regulators, and treating physicians and patients not fully aligned, any gap in the transfer of evidence based knowledge can and will affect optimal implementation. In light of this, the FEAM European Biomedical Policy Forum – with the support of Novartis - hosted a virtual event on 25th November 2021 discussing and examining drug development within the European Union and beyond.

Current Landscape

A thorough analysis of the current situation in Europe reveals that the drug development process is not only a complex, long and very costly process, but also does not result in universal access.

Building on a recent report published by the Royal Netherlands Academy of Arts and Sciences, a need for more efficient predictive preclinical disease models, and adequate clinical trial models to guarantee the safety and efficacy of a given drug, is nowadays evident. This is further compounded by the high failure rate of proposed compounds, where there are allegedly 10,000 compounds involved in early stages of basic research, yielding only 1 drug for patient access. Therefore, the key issue, amongst many, is to determine how science can contribute to a more efficient process in R&D without compromising safety and efficacy of proposed drugs. The Dutch Committee responsible for the report therefore took an inventory of the scientific techniques in each stage of the process below, in addition to speaking with relevant stakeholders:

- *Basic research*
- *Drug discovery*
- *Preclinical development*
- *Clinical development*
- *Marketing authorisation*
- *Patient access*

The need for more efficient predictive preclinical models is not only to avoid occurrences such as the thalidomide safety disaster of 1961, but additionally, to improve and quantify the predictive value on efficacy of investigated agents.

Looking beyond the discovery stage, at development level, there are limitations between studies and actual clinical use, with poor translation between the two, wasted time and expertise from scientist for projects that are either (predictably) unsuccessful or remain unfinished, as well as the breadth of patient populations not being reflected in the sample sizes of said studies. In addition, patients are not involved in the development and research phase, with academia virtually dropping off after discovery, leaving industry to dominate the remaining stages.

One of the aims of this meeting was to gather and explore the perspectives of different stakeholders in the process with a view to also examine any likely solutions.

EU Parliamentary Perspective

It was noted that the cost of drugs is currently too high, and patients often end up paying out of pocket. With the newly proposed EU Pharmaceutical Strategy, EU authorities will address many aspects of this vocation within the EU framework, yet hopefully examine pricing as one of its key issues to solve. Horizon Europe is said to be well funded in the area of cancer; however, it should be noted that this is not just an issue concerning oncology drugs, but affects all other medical specialties, especially as digitisation and personalised medicine become more visible.

Furthermore, whilst the need to partner with industry was noted, the recognition that it is not possible to meet all of the demands was highlighted. More incentives are needed to look beyond pricing. Indeed, the responsibility to contribute to the streamlining of the drug development process does not only lie within the European stakeholders but is a global exercise.

Patient Priorities

The pandemic has highlighted the inequalities at play across Europe but also globally and exacerbated the disparity regarding patient access to adequate treatments. This issue has the result of negatively affecting patient wellness and health outcomes; crucially patients appear to be left out of the development process despite being the recipients of said treatments. There is a need to include patients in the process to respond to questions on timelines planned for a specific drug approval and its accessibility.

One of the proposed solutions is to conduct robust patient preference studies to ensure a patient centric approach in the development of drugs and devices. Indeed, specifically in the case of cancer patients, the COVID-19 pandemic has resulted in delayed treatments which have had a detrimental effect on patients and therefore their voice is even more central and vital to this debate.

The Role of Health Technology Assessment (HTA)

In addition to considering patient voice as a key element, other important issues identified were quality of care which should include safety, equity, and sustainability. Tone of the key questions is: how effective are these treatments in reality?

The main goal is to ensure equitable and fair access for all patients, but one issue that currently hinders this is where there are successful trials, there is no immediate access to said treatments. On average, Europe approves drugs 8 months later than in the US, and indeed at times there is no access at all in eastern European regions.

The solution is faster administrative processes not only at European levels but internationally. In order to address the pricing issue health technology assessment (HTA) was introduced after the approval of new drugs by the European Medicines Agency (EMA). HTA is a multidisciplinary process that summarises information about social, medical, economic, ethical issues related to the use of a new technology in a systematic and transparent way. The assessment phase of this exercise focuses on clinical outcomes and effectiveness of said therapy; and the appraisal phase examines budgets constraints, equity, value, and patient preferences. Final decisions from this process could be reimbursements or none. There have been small attempts at value-based pricing, yet this is said to have had limited success.

Whilst health technology does not solve the affordability issue as the focus currently weighs heavily towards pricing and discounts; there is also a lack of data to track feasibility. New business and price models are required to rectify the current system, that specifically place a focus on patients and not profits. For example, some treatments currently cost $350k per patient, and clearly perpetuates inequity.

Panel Discussion

Some of the high costs required for a drug development may be considerably reduced by decreasing the number of failed treatments; in addition, there was consensus regarding pricing models and the possibility of promoting public-private partnerships to facilitate solutions.

The issue of early regulation was raised, given the US and UK models, and whilst it can be easier to approve a particular drug where there is a public-private partnership – it was crucial to note that no

one company should have a monopoly on the regulatory process. Such an issue should be discussed at the newly formed European Cancer Forum. In this regard, it was stressed that ethics committees require a balanced membership of general ethics experts and experts in clinical trials to properly assess this question. A centralised ethics committee may be one instrument in speeding up the development process.

Regarding patients that partake in current trials, there was recognition that going forward the small trial population sample should at least reflect the majority of the population in which the drug is intended for use; as whilst diseases are the same for all individuals, their effect can be different based on natural variations in the physiology of each individual. In addition, given the variation in the interaction between a cell, tumour, treatment, and environment, it is clear that human trials are still required for appropriate understanding of efficacy.

The discussion moved on to note that the pharmaceutical industry at times perseveres with projects even where the efficacy and data is marginal and so proper model are required to address this. This is further compounded by the fact that within the education system for doctors, there is no focus during their learning on how drugs are developed, let alone any input they could make towards their clinical use. These challenges can be addressed by supporting thriving research and innovation ecosystems that enable true collaboration and cross-fertilisation between public and private sector. For instance, training the next generation of translational scientists, facilitating novel collaborative models and structuring access to relevant expertise, through local/national bioscience hubs (bioscience parks) and dedicated international biomedical research infrastructures, such as EATRIS, can support in building such research continuum.

Lastly, it was noted that as each country within the EU has its own mechanisms, systems, and pricing, in addition to the language barrier. There is a fractured approach to drug development at the moment with patients having scarce information that prevents them from being an active and knowledgeable participant in the treatment they are receiving. In addition to the inclusion of drug development in the education of practitioners, it was highlighted that more communication between academia and industry is required at all stages to prevent failing projects, as well as the need for a minimum diagnostic criterion that can be applied across the EU.

Webinar organised with the sponsorship of Novartis

Additional material available:

1. ***Agenda and speaker information***
2. ***Full Recording of the event***
3. ***Presentation from Prof. Jaap Verweij***
4. ***KNAW advisory report on "Greater Efficiency through Innovation"***
5. ***EFPIA report on "Improving regulatory timelines to enable patient access to innovative oncology therapies in Europe"***

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Disclaimer: Opinions expressed in this report do not necessarily represent the views of all participants at the event, the Federation of European Academies of Medicine (FEAM) and its Member Academies, or the FEAM European Biomedical Policy Forum partners.

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The FEAM European Biomedical Policy Forum provides a platform for discussion on key policy issues for the biomedical community. The Forum is an initiative from the Federation of European Academies of Medicine (FEAM). It aims to bring together representatives from academia, research charities, industry, European and national trade associations and professional bodies, regulators, public health bodies, and patient and consumers groups. If you would like further information or becoming a partner, please contact elisa.corritore@feam.eu.