



## Letter to the Editor

## Establishing treatment optimisation as part of personalised medicine development



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Received 6 March 2019; accepted 8 March 2019

Available online 15 April 2019

Dear Editor

Despite numerous therapeutic strategies authorised on the market, survival and quality of life of cancer patients remain as major public health issues [1]. This can be partly explained by the multiplication of agents with the same mechanisms of action, instead of true innovation. There is limited knowledge on how to use anticancer agents for dose, sequence, combination with surgery and/or radiotherapy and duration of treatment [2]. Suboptimal administration of costly treatments may generate unnecessary toxicity for the patients and negatively affects national healthcare budgets. In Europe, most clinical research focuses primarily on drug development for regulatory approval, instead of addressing patient and public health needs [2]. Once a drug enters the common market, each European Union (EU) member state determines its real-world application based on its own criteria—pricing, reimbursement and clinical indications—leading to disparities between EU citizens.

Such a regulatory drug approval-centred, clinical development, landscape may neglect patient-relevant issues in a real-world setting, such as comparative effectiveness of distinct treatment options or long-term safety monitoring. Therefore, only partial data sets without technology benchmarking are available to clinicians for developing clinical guidelines, for regulators, policymakers and health technology assessment (HTA) bodies, who have to decide ultimately on pricing and therapeutic guidelines for national markets. Treatments with effectiveness uncertainty cannot be offered to patients because of the lack of evidence on how to use them in daily clinical practice. The EU health systems should define their choices based on strong medical and scientific rationale. Society cannot fund expensive treatments with high uncertainty.

How do we move to more patient and society-centred drug development, taking all stakeholders' perspective and needs into account? It is about bridging the gap between two dimensions that are often misunderstood—efficacy, which is demonstrated under controlled conditions in classical clinical drug trials, and effectiveness—and how a drug performs in the real world of widely varying patients and doctors in different types of hospitals and clinics. The development of new treatments and market access need to be re-engineered.

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This means that clinical research must be designed to meet clinical practice needs and not drug development in isolation. Optimising therapeutic and pragmatic clinical research into health care to treat patients in daily care must be factored into the process of access [2]. There should be conditional approval for clinical use. This means bringing level I evidence clinical utility into the drug development pathway so that health technology assessment agencies will have a wealth of new data from new types of trials and research that go beyond the basic risk/benefit analysis that regulators typically apply. Thus, there is a need for investigating the optimal way to use medicines, through applied research, better defined as treatment optimisation (TO) [3].

There is a call for reforming the current system to a truly ‘patient-centred’ paradigm with systematically coordinated TO in conjunction with drug development [4]. The question is how to make it happen in the fragmented Europe where health is a national matter. The first step is to gain stakeholders’ support for making TO a standard step in medicine development in Europe. This is the purpose of a *Manifesto* for ‘a new approach for better medicine in Europe—establishing treatment optimisation as part of personalised medicine development’, developed by the European Organisation for Research and Treatment of Cancer [5], launched during an event in the European Parliament in Brussels [6]. Many stakeholders have joined in supporting the platform, such as Members of the European Parliament, patient organisations, scientific societies and biotech and pharma industry representatives. This initiative follows an informal meeting of EU Health Ministers in September 2018, where the lack of structured information exchange between regulators and national authorities and lack of patient benefit for high-priced medicines highlighted the need for integration of TO investigation [7]. The *Manifesto* emphasises, among other points, (i) the need for the EU—in partnership with Member States—to make TO research a mandatory step in the treatment access path to market; (ii) the inclusion in national legislation provisions allowing for publicly funded international research to address collective therapeutic challenges and (iii) assuring that the next EU Framework Programme for research and innovation provides funding opportunities specifically aimed at supporting TO.

In conclusion, there is a need to raise awareness of the urgency for a better TO as part of personalised medicine development in Europe. This requires efforts that need

to go beyond the clinical audience, addressing patients and their care-givers, politicians, research funders, industry and other stakeholders. However, it is leadership at the policy-making level that will ultimately determine how well health systems are prepared to implement TO in personalised medicine. The course of action to establish a TO in personalised medicine development should be driven by political leaders who are able to invest in the future of public health, even though the results of such action will stretch beyond their policy cycle.

### Conflict of interest statement

The authors declare no competing interests.

### Disclaimer

Views expressed in this letter are the sole responsibility of the authors and do not necessarily reflect the views of the affiliated organisations.

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