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PERSONALISED MEDICINE

Opportunities and Challenges
for European Healthcare



Organisers:



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Personalised medicine

Opportunities and challenges for European healthcare

Introduction

Personalised medicine aims to provide the right diagnosis leading to prevention or treatment at the right dose to the right patient at the right time. Rather than having an unique treatment for each individual, patients can be sub-divided into groups based on their individual biological characteristics. By this stratification of patients with biomarkers, preventative and therapeutic interventions can be tailored to be more effective and have fewer undesirable side effects for this particular group, than the 'one size fits all' medical approach.

Although some personalised medicine has already been introduced into practice we are at an early stage of its implementation and significant paradigm shifts will need to take place in major fields of medical research and health care for this new innovative area of medicine to be fully exploited.

This workshop explored the opportunities and challenges personalised medicine brings, with a particular focus on the bottlenecks that needs to be overcome for the rapid uptake of personalised medicine into clinical practice. The workshop, organised by the Health Research Directorate of the European Commission, was the fourth of a series of preparatory workshops gathering stakeholders interested in personalised medicine. The previous workshops addressed areas such as: The role of –omics technologies for personalised medicine, Stratification biomarkers, Clinical trials and regulatory aspects. The overall aim of the workshops is to build a 2020 vision for Personalised Medicine in Europe and identify the (research) needs for its implementation. The workshops will also begin to identify the most important topics to be addressed in a conference dedicated to the theme of Personalised Medicine to be held in Brussels in 2011.

The panellists in this workshop represented a wide variety of competencies and experiences (see Appendix A). This paper summarises the major issues highlighted during the workshop held at the European Health Forum Gastein, October 2010.

Research and Development

A well developed, strategic science-led programme is one key factor to develop and implement Personalised medicine into clinical practice. Personalised medicine has to build on new levels of insight into the biology of health and disease mechanisms. These insights have to integrate affected individual genes/molecules/targets with interaction factors and functional systems. This will result in a paradigm shift from an organ-based to a biological mechanism-based definition of health and disease.

However, the introduction of new -omics based biomarkers for patient stratification should by no means exclude the use of more traditional biomarkers, such as a patient's age, gender, body composition, physical examination findings, blood pressure, ECG abnormalities, blood biomarkers, histopathology findings, radiological findings etc. for diagnosis of disease and

choice of prevention or treatment. In addition to biomarkers predicting the efficacy and if possible effectiveness of a treatment, sufficient attention must also be given to the use of biomarkers for predicting patient safety and biomarkers used for predicting predisposition to disease. Indeed, personalised medicine research should ideally be fully integrated into more traditional medical fields so that developments are complementary, adding value to patient outcomes rather than introducing gaps in understanding. This is true for medicines and related healthcare technologies, but also in other fields such as nutrition, sports genetics and others.

To progress research in this complex field, well coordinated collaborative research engaging academia and industry as well as patients and clinicians is needed. More public private partnerships for pre-competitive research such as the Innovative Medicines Initiative (IMI) will be necessary for rapid progress. Furthermore the pan-European research infrastructures in the field of biological and medical sciences could play an important role in increasing efficiency of research and by providing a sustainable platform for collaborative research.

Patient involvement

In general, patients welcome the new approach that personalised medicine offers in view of increased effectiveness and better patient safety. Ideally, the development of personalised medicine should take account of patients' needs, views and preferences but, to date, this is not yet achieved generally.

AIDS is one of the few disease areas where personalised treatments already are available and therefore some concrete experiences, both positive and negative, also have been gained. To exemplify what practical issues need to be dealt with, a treatment was given as an example. The prescription of this treatment for patients infected with HIV that is "CCR5 tropic" requires a test to confirm whether a patient is infected with a CCR5-tropic HIV strain or not. The test is expensive and the samples need to be shipped to the US to the one laboratory that has the capacity and capability to perform this test. Patients have to wait 6 weeks for the test results. This particular example raises important issues around ethics, equality, privacy, confidentiality and ownership of data but also key issues related to turn-around time to test result, accessibility to treatment and location of testing facilities. The need for a clear regulatory framework for approval, pricing and reimbursement of drugs and companion diagnostic tests are issues of concern for the patient advocacy groups.

By involvement in new developments from an early stage, patients could, together with the physicians, be the driving force to ensure patient involvement and key clinical input in the design of treatment programmes. Patient empowerment and developing better communications between patients and health professionals is crucial. Patient organisations can play a role in improving health literacy and fostering dialogue with health professionals' bodies. Patients should also be meaningfully engaged in health technology assessments (HTA) and in ensuring effective implementation programmes.

Equality and ethical aspects

Health inequality in Europe is a reality. There is a perception that new and more expensive technologies may contribute to further inequalities. Although new science and novel technologies are conceived within academic centres, many countries may not yet have the priority setting or technological capacity or capability to implement new approaches such as personalised medicine into mainstream clinical practice. One proposal for how this situation can be improved could be the establishment of EU wide initiatives to develop guidelines for best practices on how to implement personalised medicine.

Both innovative research and targeted treatment delivering safe, effective and timely healthcare will depend on the access to well-equipped infrastructure with high-level of expertise in key areas such as diagnostic testing, interpretation of test results, biobanking and bioinformatics. In Europe several pilot projects are already developing such infrastructure trying to gather expertise across EU in areas like biobanks, clinical trials or translational medicine. IMI plays also an important role in fostering collaboration between academia and the pharmaceutical industry in the pre-competitive field. Such efforts could be even more facilitated by breaking barriers in the regulatory environment for performing multinational clinical studies.

These initiatives should be embraced, but with some degree of caution and based on evidence. Personalised medicine, like any other research field, is characterised by not one or two ground-breaking developments, but rather a series of important but iterative steps forward, usually one disease at the time. While efforts should obviously be made to incorporate innovative health technology into clinical practice, for large investments, the strength of the evidence supporting the implementation of the technology into clinical practice should be considered. Evidence should be gathered showing the relative utility of these programmes in comparison to other needed investments in public health and take into account the added clinical and cost effectiveness of using a companion diagnostic test and eventually medicine compared with current practice. Likewise, the principles of equality and access should be applied to avoid implementing programs which increase health inequity rather than encourage the equitable use of healthcare resources, realizing that this may be a stepwise approach in which innovation is not always available to all at introduction, but with the aim to realize equality over time.

Health care professionals

Personalised medicine should be seen as a process to reduce the number of unnecessary interventions and adverse effects in patients and to deliver more added value for patients. But personalised medicine as a new concept entails a paradigm shift that must be understood and accepted by all healthcare professionals.

The uptake of personalised medicine into clinical practice is expected to happen, however practitioners will need to understand and access the right test at the right time and correctly interpret the test result and change their prescription behaviour accordingly. Many doctors are already concerned about the large volume of data and information they are expected to work with. Therefore, it is important to consider the training needs of all clinicians so that they feel empowered by the additional information rather than overwhelmed by it. In particular,

specialists and general practitioners should be adequately trained, not only in the scientific advances but also in the accompanying ethical aspects. Easy access to specialists in personalised medicine will be essential and the introduction of decision support systems would make the implementation easier. Continuing Medical Education (CME) courses on the personalised medicine could be made available to introduce practicing physicians to the latest technological developments, while elements of medical curricula should be updated frequently to adequately train medical students.

The recent survey done by Science Business in partnership with Karolinska Institutet on personalised health care (Health for all, Care for you, The promise of Personalised Health Care in Europe¹) showed that the perception of both the public and the healthcare professionals is that personalised approaches can reduce medical errors and provide a better clinical outcome with reduced costs in the future.

Health care systems

The rapid scientific progress facilitating personalised approaches has not been accompanied at the same speed by discussions of appropriate ethical frameworks. A structured approach should therefore be put in place in order to overcome the potential "ethical barriers" which may delay the acceptance of personalised medicine. Technology can advance very rapidly and furthermore, patients can easily access information via the internet. There is, therefore a need to develop a coherent approach that takes both of these factors into account. Issues to be addressed include, for example: how to inform the patient on his/her risk of developing disease in the context of testing results or not, and who should have the role to provide such information? In addition ethics education and training will be needed at many levels.

A very important issue for the implementation of personalised medicine will be how the stratification tests will be provided in practice. Such tests could be either diagnostic tests (using companion diagnostics developed in the context of a specific drug by the private sector) or 'in house' (pathology) assays developed in the hospital laboratory. Critical aspects to reflect on for the implementation of such tests and testing facilities will be the speed of the testing process i.e. time it takes since the sample is taken until the results can be delivered to the patient. Another vital point is that one has to be sure that only ' tests with clinical utility ' are used, i.e. that the test actually measures what it should test, that the test is robust and that false negatives or false positives are minimized. In addition laboratories providing the testing services should be accredited and should participate in relevant external quality assurance schemes.

Proposed improvements in this area include closer collaboration between pathology and other diagnostic laboratories and the treating clinicians to validate the added value of new tests before they are put into clinical practice and harmonised procedures to ensure the robustness, sensitivity and selectivity of the developed stratification assays and diagnostic tests. Another aspect suggested was the importance of ensuring that the actual performance of a diagnostic test is not controlled by the company producing a medicine for which the test would be a companion.

¹ http://www.sciencebusiness.net/reports/PM_survey_results.pdf

Without underestimating the potential value of personalised approaches to healthcare, it is also important to consider the broader context. The –omics fields and advances in genetics will doubtless transform how treatments are chosen and developed. However, within the larger health system context, personalised medicine is only a part of a comprehensive system aimed at delivering health to populations. Preventive and public health initiatives, health system strengthening, multi-sectoral approaches and health policy research have an immense impact on health indicators before any pathology is developed. Thus, investments in personalized medicine should be balanced with other approaches, using citizen and patient outcomes as a compass to guide policy action.

Putting into use

The need for a clear regulatory framework for personalised medicine was highlighted. The benefits or drawbacks for having separate or joint regulatory frameworks for diagnostic tests and therapeutics respectively need to be evaluated. The current system in the EU with separate frameworks and with the biomarker qualification process by EMA may provide good flexibility. However there may be benefits of doing the evaluation of both therapies and diagnostic tests at the same place, not as today by different entities.

Furthermore, it is important to introduce mechanisms monitoring the safety and clinical added value of innovative treatments after they have reached the market; only then can we have a clear idea of any potential adverse events which may occur throughout the course of the treatment's market life.

The similarities between the field of rare disease and personalised medicine were also mentioned, and inspiration for an appropriate regulatory framework also may be sought from the rare disease and orphan medicinal products area.

Value of personalised medicine

Fears are that personalised medicine may stratify patient groups into smaller and smaller sub-entities for which treatments may not become available or affordable. Small patient groups are a well known problem for rare diseases. In this way, personalised treatments may compare to orphan medicines. In contrast, it is possible that, with better understanding of disease mechanisms, the opposite may also be true. Small patient subsets may be regrouped around common disease biology mechanisms and with drugs that specifically target these biology mechanisms.

A key factor that may determine the uptake of personalised medicine into healthcare will be how it will be valued in the health economics context. In an era of cost containment and limited health care resources there is a need to consider opportunity cost of decisions about which health care interventions to use. There is a need to demonstrate the potential added value personalised approaches bring, in particular the added value of patient stratification in view of improved effectiveness and/or reduction of adverse side effects. While on the one hand potentially beneficial treatments cannot be dismissed by the lack of data at their launch, in the end more evidence of value is required based on conducting economic evaluations of specific examples of personalised medicine, which should also include patient views and should be prepared by including payer input in the clinical trial design. Such evaluations

should compare the costs and benefits of personalised medicine with current practice. It is also important to develop methods to include the notion of added value and benefit from the patient and the health professional point of view.

A comparison between some EU Member States of a personalised therapy and its companion diagnostic tests showed that very different approaches are used to inform reimbursement. For example, diagnostic tests were sometimes seen as research, whereas in other cases they are treated as 'goods'. This shows that approaches towards streamlining and coordination would be desirable. Alongside of this, there is a need to understand current approaches to the health technology assessment for diagnostic tests that are used in conjunction with medicines. The result should be that the approaches for HTA can be developed in a way that furthers the application of personalised medicine approaches in mainstream healthcare.

It should also be evaluated if data supporting a HTA analysis could be collected already at the stage of clinical trials and if collaboration between regulatory and HTA bodies at the stage of the design of the clinical trials could be put in place

Conclusions

In general the panellists believe that Europe is ready to start the paradigm shift towards personalised medicine. However, many conditions still need to be fulfilled. The shift towards personalised medicine should be seen as a process rather than an endpoint.

Personalised medicine builds on a better understanding of disease mechanisms and much more research is needed to progress this area. Structuring efforts are needed to take stock of ongoing research and infrastructure initiatives in all EU member states.

Education and training of professionals in how to deal with the new personalised approaches must be strengthened and ethical aspects should be given a major role.

The engagement of patients, health care practitioners, pathologists already in the early stages of personalised medicine development should ensure that patients' needs are in focus and that developed therapies and stratification diagnostics and assays are useful in the clinical setting and that their results are reliable.

Efforts should be made to ensure a flexible regulatory framework that ideally also provides evidence for reimbursement decision making. Robust methods, using good quality data, are necessary to generate information on the added value of personalised medicines compared with current prescription approaches.

It is vital that patient and citizens outcomes are put first. Personalised medicine shows substantial potential in terms of both extending life but also improving the quality of extra years of life gained.

However, personalised medicine needs to be developed and be introduced into clinical practice in line with the two core principles of European health systems: health equity and universal access, avoiding throwing out innovation too early based on lack of data at the onset.

Healthcare professionals and policy makers must aim to ensure that personalised medicine contributes to the improvement of population health effectively and efficiently with clear and robust evidence of patient value, and a time frame to develop the data to prove it.

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