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Event Report: EHC Round Table of Stakeholders on 'Outcome Measures in Haemophilia'

About the event

On Monday 28 November 2016, the European Haemophilia Consortium (EHC) held a Round Table of Stakeholders at the European Parliament in Brussels to discuss outcome measures in haemophilia.

Over 50 participants including patient representatives, healthcare professionals and industry representatives attended the event. The event's agenda, list of speakers and presentations can be consulted online on the EHC website.

The event was kindly supported by Members of the European Parliament (MEPs) Mr Norica Nicolai (Romania/ ALDE) and Mrs Vasilica Dăncilă (Romania/ S&D).

On outcome measures in haemophilia

Haemophilia is a rare and congenital bleeding disorder caused by a genetic defect resulting in a lack of or insufficient coagulation factors VIII or IX in the body. This causes, in affected individuals, an inability to clot blood, leading to bleeds in the joints, muscles and soft tissues. If left untreated, this can cause disability and sometimes death.

Outcomes are effects produced by medical technologies that are measured and reported to assess and quantify the impact of a medical technology. Currently these measurements are used for either regulatory purposes, such as obtaining licenses to market a product, but also for economic purposes, such as obtaining reimbursement of these products from national healthcare services.

Many outcome measurement instruments have been developed to identify, measure and value the effects of new medicinal products. However, these are often developed for use in therapeutic areas covering medical conditions present in larger populations. This means that they can easily be compared to existing data that has been generated with large clinical studies and cohorts. Unfortunately the same outcome measurement instruments are ill-adapted for therapeutic areas in rare diseases such as haemophilia. In fact, due to the limited patient population it is difficult to generate large quality data on outcome measures. This argument is often used, in particular in times of cost-containment, to scrutinise and threaten access to novel therapies in haemophilia.

It is for these reasons that the EHC held a Round Table of Stakeholders on the topic of 'Outcome measures in haemophilia' to determine how this situation can be changed to better reflect which outcomes need to be taken into consideration when developing and evaluating new treatments for haemophilia.

Findings and discussions

Outcome measures are the identification and evaluation of the results of an activity compared to an intended results. They provide useful information on which to base decisions in an environment where resources are finite. These tools and their results are used by a variety of stakeholders to make decisions on treatment protocols, on the organisation and financing of care as well as to decide which novel medical technologies should be developed, licensed and reimbursed. These tools are therefore essential to determine how these finite resources should be allocated in the most efficient way. To do so, outcome measures should evaluate the treatment process in a holistic way and encompass clinical outcomes,

humanistic outcomes, health care resource utilisation outcomes and economic outcomes.

It is therefore important that the interpretation of a specific outcome is adapted to the context and the purpose for which it will be used. For example, in 2016 many novel treatments for haemophilia are either in the final stages of clinical development or being marketed. These treatments are innovative because they provide new ways of tackling and managing the disorder compared to existing treatments. For example, extended half-life products provide a replacement treatment with a longer half-life meaning patients would either get higher protection (with higher trough levels) or longer protection (and would need to infuse less regularly). Other novel treatments tackle the thrombin generation instead of simply replacing the factor, which could provide a solution for patients affected by inhibitors[1] for example. Finally, gene therapy offers the potential to permanently cure this disorder, ridding patients of the need for life-long treatment. All of these novel treatments will need to demonstrate their efficacy against current treatments to different stakeholders. However the use of these outcomes will differ depending on the stakeholder analysing the data. For instance regulators are likely to use these outcomes to identify proof of efficacy and determine whether the medicines should be licensed. Payers, on the other hand, will consider whether these treatments are better than available treatments and therefore justify reimbursement. Patients will look at these new treatments to determine whether they will decrease the burden of illness. Clinicians may look at markers indicating treatment response and disease progression. Finally academia will use the same outcomes to understand the disease mechanisms. This raises a series of questions such as: which outcomes should be measured? How should this data be collected and analysed to provide a satisfactory answer to all of these stakeholder? Finally and most importantly, do these outcomes translate into significant impact on patient's quality of life?

Traditionally, outcome measures such as annualised bleeding rates and musculoskeletal health and functions were looked at to determine the efficacy of novel haemophilia treatments. However, with more adequate treatment protocols, such as prophylaxis, and the use of effective treatments, such as coagulation factors concentrates, the general health status of PWH has increased. Therefore these traditional measurements are no longer viewed as sensitive enough to determine the impact of new therapies on the quality of life of PWH. This is why it is important to involve patients and healthcare professionals to identify new measurements that would be sensitive enough to gather data reflecting the true impact of novel technologies in patients' quality of life. This is particularly crucial when dealing with rare diseases as patients are often the experts on their specific medical area.

This question is even more important now that we are seeing for the first time a considerable number of people with haemophilia (PWH) entering old age. This raises a number of questions with regard to how age-related co-morbidities should be treated in relation to haemophilia but also viral co-infections. In turn this will raise questions of which outcome measures are important to this population segment.

This approach reflects a new paradigm in which care is tailored to patients' needs and expectations. On this note it was considered whether Goal Attainment Scaling (GAS) could replace patient reported outcomes to quantify individual treatment goals. Furthermore, it is expected that this paradigm shift will also result in different methods to procure medicinal products in the future.

Finally speakers and participants considered the question on how to gather real-world data to assess outcomes. Participants discussed whether, besides traditional patient registries, medical software and mobile technologies could be used to collect both objective and self-reported data. This raised questions with regard to data quality and interoperability, data ownership and privacy. It was also noted that patient organisations can provide help in collecting or organising the collection of this data.

Conclusions

Outcome measures should be not only used for regulatory or economic purposes but they should help

[1] Inhibitors are an adverse event to the use of coagulation factors concentrates. They are antibodies to the treatment. People with haemophilia and inhibitors have as a result less therapeutic options and are left vulnerable to bleeds.

determine real impact on the quality of life of patients. In doing so outcome measures can help in bridging political willingness to pay for a treatment with best clinical practices tailored to patients' needs. It is important to involve patients in the process as being the ultimate beneficiary of the treatment, they can provide insightful information on what is expected of a treatment and whether novel technologies meet expectations.

For rare diseases, such as haemophilia, data collection is important and novel ways of collecting information should be looked at.