# Event Report: EHC Round Table of Stakeholders on 'The Future of Comprehensive Care and Outcomes'

***About the event***

On Wednesday 20 February 2019, the European Haemophilia Consortium (EHC) held its first Round Table of Stakeholders event of the year on the topic of *the future of comprehensive care and outcomes*. The event was held at the European Parliament in Brussels and gathered patient representatives, healthcare professionals, members of the European Parliament (MEPs) and representatives from the pharmaceutical industry.

The event's agenda, pictures, a video and a written account of the day can be consulted online on the EHC website.

The event was organised and hosted by Mrs. Norica Nicolai (Romania/ALDE) and chaired by Mrs. Gesine Meissner (Germany/ALDE). Dr. Miroslav Mikolášik (Slovakia /EPP) also attended the event.

***On the future of comprehensive care and outcomes***

Haemophilia and other rare congenital bleeding disorders are rare disorders caused by a genetic defect, resulting in a lack of, or insufficient levels of, coagulation factors in the body. In affected individuals, this causes an inability to clot blood, leading to bleeds in the joints, muscles and soft tissues. Although haemophilia and other rare bleeding disorders may be perceived, at first, as haematological disorders, these conditions also severely impact the musculoskeletal system and therefore a comprehensive approach to their treatment is required. Furthermore, the complex, chronic and rare nature of these conditions require life-long monitoring and support by specialised health care professionals, traditionally located within a comprehensive care centre (CCC). This is considered as the gold standard of care and it is widely acknowledged that CCCs should include a series of specialised medical services and health specialists besides the haematologist, such as nurses, orthopaedic surgeons, physiotherapists, laboratory technicians, hepatologists and infectious disease specialists, dental surgeons and psychologists. In Europe, guidelines for the certification of haemophilia centres have been developed through EUHANET, a partly EU-funded project. These guidelines were developed in collaboration between the European Association for Haemophilia and Allied Disorders (EAHAD) and the EHC. Besides providing specialised care, CCCs also fulfil an essential role in furthering clinical research and monitoring post-marketing use of medicinal products. Finally, in some countries CCCs also have a pivotal role in the management and distribution of treatment products as well as tracking treatment use through, for example, patient registries. This information can be used in turn by both the scientific community to further research these conditions and national governments to prepare and plan for future treatment procurement.

With the introduction of novel therapies (extended half-life products, non-replacement therapies, cell and gene therapies) and their current or future arrival on the European market, there is a concern that CCCs may be undermined. This is because these novel therapies have the potential to transform patients' phenotype from severe into mild or moderate, hence reducing the number of bleeds (including potentially subclinical bleeding episodes) and minimising further joint damage. The concern is that patients will be less likely to visit the CCCs and reduce the utilisation of specialised services. As a result, these centres may lose

expertise and may no longer be able to offer specialised services. Another concern is that novel therapies may be distributed more widely and will be prescribed by general healthcare professionals who may not be specialised in neither rare bleeding disorders, nor in the technologies behind these novel treatments. This is raising concerns amongst healthcare professionals and patients as these medicines, although tested through clinical trials, will be used regularly and over a life-time. This is worrying as clinical trials are only carried out for a few years and this means that the full safety profile of these medicines and their long-term effects are still unknown. This is why it is critical that patients using these novel medicines continue to be closely monitored by specialist healthcare professionals.

It is also expected that the use of these novel therapies will allow a more personalised treatment approach, as well as achieve higher trough levels and less frequent injections. This is likely to lead to better joint protection, which leads the community to question whether haemophilia treatment outcomes, which have traditionally relied on joint health score for assessment, need to change.

**Findings and discussions**

Speakers noted that CCCs' goal is to improve quality of life and participation by preventing joint damage through tailored treatment and other services such as physiotherapy, management of bleeds and the rehabilitation of patients until full recovery. CCCs are essential in managing complications such as inhibitors, as well as in tailoring the treatment to the patient to try to minimise inhibitor development. Furthermore, CCCs play a key role in providing patients with psycho-social support. Speakers also noted the crucial role of CCCs in distributing products. This ensures that patients are regularly monitored by specialised healthcare professionals. In addition, it allows the centre to keep all necessary documentation concerning the treatment, which is crucial for post-marketing surveillance. Currently, draft legislation has been prepared in Germany that would remove the role of CCCs in the distribution of treatment. There is fear amongst patients and healthcare providers, that this may directly impact patients' quality of life and even harm patients because they will no longer regularly meet with specialised healthcare professionals and in the case of any complications, they may seek medical support from general practitioners and non-specialist hospitals. Furthermore, there is also a concern that this will decrease data collection, which in turn may weaken the national registry, prevent further establishment of clinical protocols and research advances as the centres will no longer be able to track treatment and its effect on patients.

Another topic of discussion was joint health and prophylaxis. Speakers highlighted that although prophylaxis is the gold standard of treatment, currently it only delays and does not entirely prevent joint bleeds and therefore joint damage still occurs as prophylaxis only slows it down. This is why early prevention and an early start to prophylaxis is critical. Based on current research it is estimated that patients will need to achieve at least a 5% trough level to avoid chronic synovitis, which is the precursor to joint damage. Novel therapies, and in particular therapies with a non-replacement mode of action, have the potential to achieve much higher trough levels. However, speakers noted that trough levels in these therapies were still difficult to quantify given their mode of action bypasses the missing protein instead of replacing it. Another novel therapy is gene therapy, which can achieve almost normal trough levels. However, speakers noted in this regard that this therapy, which is still under development, has great variability in results between different types of therapies but also amongst different patients undergoing the same treatment. Furthermore, there is a lack of long-term data on gene therapy safety and efficacy. Nonetheless, the diverse treatment options that will be available thanks to novel therapies will allow the personalisation of treatment for patients based on age, adherence, bleeding phenotype and venous access, which is hugely positive news for patients.

Another critical element that needs to be considered for treatment personalisation is the level of physical activity performed by the patient as a more active lifestyle will require higher trough levels to preserve joint health. Speakers noted that although these novel therapies prevent further joint bleeds and may help in restoring some joint functionality, they will not restore any previously damaged joint structure, so that a

joint that is severely damaged will likely continue to deteriorate over time despite higher trough levels. Again, the importance of starting prophylaxis at an early age was highlighted. Currently, joint health is assessed using the Haemophilia Joint Health Score (HJHS). This score looks at parameters such as swelling, range of motion, cartilage damage, loss of mobility for each range of motion and attributes points for each of these parameters. The problem with this scoring system is that a patient that already presents with bad joints will not get a higher score if his/her joints are further damaged but scores will remain the same. Therefore, speakers called for the development of more sensitive scoring methods to be used with these novel therapies. It was also noted that for patients with healthier joints, ultrasound is becoming an increasingly cheaper, available and reliable tool to assess joints. The convenience of ultrasound is that it can be used by non-specialist healthcare professionals such as haematologists and physiotherapists. However, this tool is not adequate to assess patients with pre-existing joint damage. Finally, speakers noted that magnetic resonance imaging (MRI) remains a critical assessment tool for joint health as it clearly shows structural damage, however, it is costly, often unavailable and can only be used to examine one joint at the time.

**Conclusions**

Speakers reaffirmed unanimously that CCCs will still be needed in the future. In fact, even if gene therapy becomes widely available, children may not be able to access gene therapy immediately. In addition, not all patients may want to or be eligible for gene therapy.

Furthermore, CCCs will still be needed to provide specialised services such as surgery, and services to other rare bleeding disorders as well as women with rare bleeding disorders. Finally, CCCs will be needed to manage spontaneous bleeds, which may still occur despite novel therapies. Patients with inhibitors and other co-morbidities will also need to continue receiving specialised services. Finally, CCCs will still need to fulfil roles of long-term monitoring for the safety profile of novel treatments. To do so, it is crucial that CCCs are able to continue distributing treatment in the established national framework.

In terms of treatment, speakers noted that the parallel availability of different treatments will allow for greater personalisation, higher trough levels and greater joint protection. It is also hoped that all of these treatments will allow patients to achieve higher trough levels so that joint damage can be avoided altogether.

With regard to joint assessment, tools for such assessments will need to be adapted depending on the patient. For instance, for patients with more intact joints, the use of an ultrasound assessment will be useful to identify synovial hypertrophy and early damage. However, for patients with more advanced arthropathy, an ultrasound assessment will not be sensitive enough and therefore a comprehensive assessment looking at both the structure and function of the joint will need to be done. This will be critical to understand the level of damage and how it impacts the patient's participation in physiotherapy and their quality of life.

The event was concluded by reminding participants of the importance of European collaboration and support for research programmes such as Horizon 2020 to help further research in the area of rare diseases. The present MEP also reminded participants of the current proposal for Health Technology Assessment (HTA) legislation, which may facilitate and speed up availability of novel therapies, in particular in the field of rare diseases.