

REPORT

IPOPI 11th PID Forum

Access to paediatric medicines: the case of PIDs Towards the revision of Paediatric Regulation



27 June 2018, European Parliament

**Co-chaired by MEP José Inácio Faria (EPP, Portugal)
and
MEP Dr Elena Gentile (S&D, Italy)**

Introduction

On June 27th, 2018, the International Patient Organisation for Primary Immunodeficiencies (IPOPI) organised its 11th PID Forum called “Access to paediatric medicines: the case of PIDs / Towards the revision of Paediatric Regulation” at the European Parliament in Brussels (Belgium). The event was co-chaired by the Member of the European Parliament (MEP) Mr José Inácio Faria (EPP, Portugal) and by MEP Dr Elena Gentile (S&D, Italy), and supported by MEP Mr Tomáš Zdechovský (EPP, Czech Republic). The meeting brought together representatives of the European Commission, parents of patients and patients, academics, healthcare professionals and research project leads and was aimed at addressing the challenges of access to medicines for children with Primary immunodeficiency (PID). With the European Commission reviewing the impacts of the Paediatric Regulation, the PID community gathered on this occasion to shed light on the various hurdles the patients undergo to gain access to treatment as well as to show, from a healthcare professionals’ perspective, how to improve pathways for providing new treatments and diagnosis.

Opening remarks

José Inácio Faria MEP opened the 11th EU PID Forum, thanking IPOPI for the organisation of the event and for the invitation to host the PID Forum for the second time. Due to an urgent mission, MEP Faria joined the Forum via a video link and thanked MEP Gentile for co-hosting the 11th Forum with him. He also emphasised his support for the work IPOPI has done so far and expressed his willingness to continue his commitment in helping to raise the awareness of the needs of the PID community inside and outside the European Parliament. Since the overarching theme of the 11th PID Forum was the review of the Paediatric Regulation, the MEP called the EU legislator to take all necessary steps for the inclusion of proper provisions which will allow for wide access to paediatric medicines for the treatment of PIDs, inclusive of the provisions that affect the development. Furthermore, at this Forum a common ground was pursued for the right approach on the revision of the Paediatric Regulation with all the different stakeholders attending. MEP Faria invited all stakeholders to give their opinions and the position of their community on the potential revision and concluded by looking forward to a fruitful discussion.



Tomáš Zdechovský MEP underlined that with the health budgets in many Member States decreasing, it is the role of the politicians to make sure this does not happen at the expense of patients, and especially not of the most vulnerable patients: children. He highlighted his desire to know more about the specific situations that PID patients face and the positions of the different stakeholders and expressed his hope that the discussion would be focused on quality instead of quantity. MEP Zdechovský concluded by emphasising his willingness to act on behalf of the PID community and his commitment to mobilise other MEP colleagues for this cause.



PID and the Paediatric Regulation

Setting the scene



Martine Pergent (IPOPI Vice-Chair) explained that IPOPI is an association of national organisations of patients with PIDs and has four objectives: 1) To promote early diagnosis and ensure optimal access to care, 2) To develop, strengthen and support National Member Organisations, 3) To raise PID awareness globally, and 4) To stimulate stakeholder collaboration. She elaborated the aim of this 11th EU PID Forum: to better understand the situation for therapies for children with PIDs and to shape IPOPI's position for future discussions on the revision of this legislation. Ms Pergent warned that, despite a growing range of treatments, there still are unmet medical needs that require investment in research and the development of new therapies and conditioning methods which will

improve the life of children and adults with PIDs. According to the European Clinical Trial Register, only 1/6th of the clinical trials (CTs) are for paediatric treatment. Therefore, a few asks can be made on behalf of patients on paediatric therapy development:

- Develop optimal and effective treatments and curative therapies for children with PIDs
- Take into consideration also quality of life improvement
- Help setting up treatments where the knowledge/medicine is travelling, not patients
- Improve transparency & information (developments in the pipeline, current on-going CTs)
- Avoid the conduct of unnecessary CTs in paediatric populations
- ERNs & Centres of Reference to partner with patient groups
- Involve patients in CT design and information development
- Support to post-marketing data collection to increase knowledge and safety

- Legislation to ensure that patients enrolled in CTs are not left untreated after the CT (if successful)
- Increase cooperation between EMA and FDA & other international bodies
- Speed up the process, simplify the CT conduct

State of Paediatric Medicines in the EU

Florian Schmidt (Deputy Head of Unit “Medicines: Policy, Authorisation and Monitoring”, DG SANTE, European Commission), gave an overview of the state of paediatric medicines in the EU. He explained that the Paediatric Regulation has governed the development and authorisation of medicines for paediatric use since entering into force in 2007. In October 2017 the Commission presented to the European Parliament and the Council a comprehensive report on progress made in children's medicines 10 years after the Paediatric Regulation came into force: [State of Paediatric Medicines in the EU - Report from the Commission to the European Parliament](#). This was further complemented by a technical [10-year report to the European Commission prepared by the European Medicines Agency](#) together with its Paediatric Committee, and by a [Study on the economic impact of the Paediatric Regulation](#). These documents established that there were three areas of improvement over the last 10 years: there is more research for paediatric treatments, there are more authorised products for children on the market and there is more information available about the products themselves. However, there were also challenges identified: there are major discrepancies between the various therapeutic areas, the incentives are not always working as hoped (positive results do not evenly spread among all therapeutic areas, but concentrate in some, often linked to research priorities in adults rather than children), the Paediatric Use Marketing Authorisation (PUMA) concept with its specific reward of market and data exclusivity has failed to deliver and in diseases that are rare and/or unique to children and which in many cases are equally supported through the orphan legislation, major therapeutic advances often failed to materialise. The Commission will undertake multiple actions to address these challenges. In the short-term, the Commission will develop together with EMA an action plan, to be expected in summer 2018. In the medium-term, the Commission is performing a gap analysis study for the evaluation of orphan medicinal products (OMPs), which is taking place in 2018 and 2019. With the combined conclusions from the before mentioned three reports and the undergoing combined gap analysis of the Orphan and Paediatric Regulation, the Commission will take an informed decision in 2019 about the steps to take in the Paediatric Regulation reformulation.



Stakeholder perspectives

Industry perspective

Dominika Misztela (Director PPTA Regulatory Policy Europe) explained that the mission of Plasma Protein Therapeutics Association (PPTA) is to promote the availability of and access to safe and effective plasma protein therapies (PPTs) for all patients. She presented also the key challenges for developing medicinal products for children with PIDs, from the industry perspective. Firstly, because of the low number of patients, it is difficult and time consuming to conduct efficacy studies. It is also very common that companies have to perform similar studies with similar protocols investigating similar issues, thus duplication of research is often present (and thus inefficient utilisation of funds). Secondly, regulatory approaches and requirements differ globally. For example, in the EU it takes more time to complete trials than in the USA. Thirdly, patient recruitment is local and happens by informed consent, which means there are different provisions, requirements and expertise in each of the different national ethical committees. Therefore, PPTA would recommend: (1) to use real-life settings complimentary to trials, (2) a common scientific approach to global trial conduct and collaboration between all involved stakeholders. Furthermore, (3) a globally aligned regulatory approach would be helpful. And finally, (4) an early industry-regulator dialogue on key scientific data should be ensured.



Healthcare and Research perspective



Prof Isabelle Meyts (President Elect of the European Society for Immunodeficiencies) presented her first-hand experiences in treating children with PIDs from her role as paediatric haematologist-oncologist at the University Hospital Leuven. Prof Meyts opened her intervention stating that the Hematopoietic Stem-Cell Transplantation (HSCT) is the only curative treatment for many PIDs (>30%). However, this treatment brings child-specific challenges: the child and the parent have different questions, anxieties and expectations. Therefore, an age-specific approach is needed to inform the child. Also, the long-term effects are gaining importance in the consideration of the parents, for example the effect on fertility,

secondary cancers, autoimmunity, overall development of the child and any unknown effects. Treating a child with HSCT has a social and emotional impact which is caused by living in the hospital for months, which leads to social isolation. Therefore, optimal conditions must be ensured for treatment of patients. Most importantly, the first priority should be ensuring equal access to HSCT in all Europe, inclusive of equal reimbursement conditions. Prof Meyts concluded by highlighting that the standardization of treatment and monitoring after the treatment is crucial to guarantee an equal treatment quality.

Dr Frank Staal (Leiden University Medical Centre)

opened the speech by warning that there is a lack of donors that could provide patients with HSCT. Therefore, Dr Staal and his team are working on the Recomb project, financed under the framework of Horizon 2020, on the development of a complementary treatment: autologous gene therapy. With this therapy, stem cells are harvested in patients' own country, then shipped to Leiden (the Netherlands), where the stem cells are genetically corrected. Subsequently, the stem cells are shipped back to the centre where the patient is based and transfused back into the patient and cured for life. This treatment is still very much under development and fortunately received subsidies via the EU Horizon2020 funding programme to implement RAG1-SCID gene therapy. Currently, the research is in the clinical phase - in which the clinical protocol is tested- and the regulatory documentation is getting prepared. Dr Staal also warned that most difficulties have been encountered in the regulatory phase of the finalization of the project/treatment. New EU legislation is needed to guarantee the harmonization of legal requirements at EU level which will make the use of gene therapy a reality. The advantages of stem cell-based gene therapies are that there is no need for donors, no use of foreign material (making it safer) and the treatment is travelling while the family can stay home.



Regulatory representation of patients



Jose Drabwell (IPOPI Chair) highlighted three changes introduced by the Paediatric Regulation in 2007. One of these changes was the creation of the Paediatric Committee (PDCO) at the EMA to provide objective scientific opinions on Paediatric Investigation Plans (PIPs). The Paediatric Regulation also introduced a system of obligations, rewards and incentives to encourage manufacturers to research and develop medicines for the specific needs of children. Moreover, in 2008, the European network of paediatric research at the European Medicines Agency (Enpr-EMA) was set-up to facilitate studies to increase the availability of medicinal products authorised for use in paediatric population. IPOPI is well represented at EMA since a very early stage. As PIDs represent a large group of chronic and rare conditions, IPOPI can participate in many different networks within the

EMA. Among others, IPOPI is a member of the Patient and Consumers' Working Party and also participates in discussions regarding patients' issues such as informed consent and assent and is involved in the development of European Reference Networks (ERNs).

Patient perspective

Ellen de Smet (mother of a PID child) shared her personal story in which, after she directed an open letter to the Belgium Minister of Health Maggie de Block, a campaign was catapulted into the Belgian media to raise the problems the PID patients and their families put up with. Ms De Smet is mother of four children, one of which suffers from a PID. In her letter to the Minister, she addressed the challenges faced daily by her family. Ms De Smet explained that financial support is needed to set up a multidisciplinary team to treat a sick child, inclusive of specialists, a secretary, a PID nurse, dietitians, physiotherapists, audiologists and psychologists. Age-tailored psychological support is essential for children and families dealing with PID. However, she warned, this is not covered by the Belgian state. Furthermore, for Belgium specifically, not all treatments are reimbursed while in surrounding countries the same treatments are getting public health coverage. SCID newborn screening is also not available in Belgium via the Guthrie card, while it is already available in other countries, like the United States.



Edith Klapwijk (mother of PID children) expressed her gratitude in seeing many people from different disciplinary backgrounds gathering together in the European Parliament to address the important topic of access to treatment for children with PID. Ms Klapwijk is a mother of three sons, all of which suffer from PIDs and require immunoglobulin replacement therapy. Ms Klapwijk shared that when her children were younger there was hardly any treatment available, and that it was often not suitable for children and not reimbursed. Nonetheless, thanks to the medical staff which wanted to help, her children were treated while not being registered at the hospital to avoid out of pocket payment. Additionally, Ms Klapwijk had to inject the boys herself subcutaneously, which she was taught by

a nurse at the hospital. This type of treatment was not officially available at the time. Ms Klapwijk was happy to see that some progress has been made over the last years but nonetheless she also called for doing more to achieve equal access to treatment for all children with PIDs.

Discussion

After the presentations a brief discussion was held where it was questioned if real world data would be more acceptable in driving the decision making. Real-world data (RWD) is defined as data derived from several sources that are associated with outcomes in a heterogeneous patient population in real-world settings (for instance, the number of adverse reactions experienced by patients after the treatment is approved to be on the market). Analysis of this data generates real-world evidence that, in turn, can generate meaningful insights into unmet needs, interventional pathways and the clinical and economic impact on patients and healthcare systems (for instance, there would be no need to reimburse a treatment that has shown little effect on patients and on their condition's progression or quality of life). Prof Meyts explained that real world data is already very helpful to further develop HSCT and other treatments.

Furthermore, the question was raised if the Commission is considering a more holistic approach for the potential revision of the Paediatric Regulation, taking for into account also early diagnosis and screening. Mr Schmidt stated that the Commission is aware that the new regulation should take into consideration new technologies being developed, such as more personalized treatment therapies. Therefore, for the new Clinical Trial Regulation, the integrated therapy is also considered. There are new legislative pieces being put into place as well including the Medical Devices Regulation. Nonetheless, these still need be rolled out to fully accomplish the wished effects.

Closing Remarks



MEP Gentile closed the 11th EU PID Forum by thanking everyone for attending the meeting and reiterating that the challenges brought up by the speakers must be addressed. The European Union needs to be engaged in reaching its most important target, namely improving the health of children who are the most vulnerable in our societies. The experience, brought in by the stakeholders to this meeting, needs to be put at the centre of the discussion and reflected in a new, revised Regulation. Attention is also needed, the MEP affirmed, to establish a harmonised approach for health at a structural level, for example through new organisations, networks and models. She called the European Commission to think

about the patient stories heard today when drafting a law that must ensure their needs are met. MEP Gentile pointed out that she is not only saying these words as a politician, but also as a paediatrician and most importantly as a mother. The needs of children with a rare disease must be at the centre of the attention and now is the right time to act. She closed the Forum by thanking everyone once again for showing their input and providing suggestions on how to improve the current regulatory framework and confirmed her will to engage in any future actions needed to tackle this challenge.