EUROPEAN MULTIPLE SCLEROSIS PLATFORM

Summary Report – (plus post scriptum from recent EMA workshop)

EMSP Spring Conference 2017
Interactive workshop on Real World Evidence Data, held on 18 May 2017

Patient-based evidence and its growing importance for Regulatory Bodies, HTA/Payor agencies, Researchers and Patients

On the 18th May, EMSP held a workshop on Real World Evidence (RWE) data as part of its Annual Spring Conference, gathering experts in the field. Some 50 participants came from EMSP, the Multiple Sclerosis Society in Italy, the Multiple Sclerosis International Federation, the European Medicines Agency, the Haute Autorité de Santé (French HTA agency) and included MS researchers and MS societies/patient representatives from all over Europe.

The **main objectives** of the workshop were:

1. **To contribute to a basic understanding** of technical terms and recent evidence on patient data collection and its current use in healthcare
2. **To raise awareness** on patient relevant outcomes and patient reported outcomes – representing a vital contribution to evidence-based outcomes needed by decision makers at all level (from payers to regulators, including researchers and patients advocates)
3. **To start a broader discussion within the MS patient community** on the impact of patients' data collection on the quality of care in their countries.
4. **To promote an active involvement by patients and patient advocates** in current activities and future initiatives on patient generated evidence.

In support of this workshop and understanding the current states and challenges related to this broad and technical topic, EMSP used two background documents:

1. Essay on Patient- and person-reports on healthcare: preferences, outcomes, experiences, and satisfaction, K Klose and all (Health Econ Rev. 2016; 6: 18, published online 2016 May 21. doi: 10.1186/s13561-016-0094-6)

2. Observations and recommendations raising from the EMA workshop on Patient Registries, 28 October 2016.

Experts from the main relevant stakeholders presented the perspective on real world evidence data and the current state of play:
- Patients' perspective: Christoph Thalheim, Director External Affairs EMSP and Paola Zaratin, Director of Scientific Research, Italian MS Society AISM and MSIF
- Regulator's perspective: Mireia Castillon, Patient Initiative Registry Coordinator at the European Medicines Agency
- HTA's perspective: Chantal Guilhaume, Scientific Project Coordinator at the French National Authority for Health (Haute Autorité de Santé)
- MS Data Connect, Flanders MS patient registry, a recent initiative: Dr. Ir. Liesbet Peeters, University of Hasselt

Introduction

What do we mean by "Real World Evidence data"? "Big data"?
From the patients' and physicians' perspective, the term "Big Data" implies all recorded (health) data in larger volumes.

While the "gold standard" of patient data is traditionally generated within well-defined clinical trials, as a vital part of pre-authorisation work for new therapies, the so called "real world evidence" (RWE) data is generated in the patient's journey after the end of the clinical trial. Most RWE data comes from patients without clinical trial experience.
The data is collected through patient registries and cohorts, on local, regional, national and sometimes even international, level. Those registries can be either drug specific or disease specific.

Although the value of patients' and caregivers' perspectives on healthcare is given more recognition in our days then a couple of years ago, the measurement and implementation of those data presents a lasting challenge to payers, regulators, clinicians and researchers.

A new classification system is needed:
From a patient's perspective, we recommend including **patient- and caregiver-reported preferences, experiences, outcomes and satisfaction related to healthcare status and health outcomes.** These are commonly being addressed by the terms "Patient Reported Outcome " (PRO) data or Patient Reported Outcome Measure (PROM), if referring to the measuring scale.

As a very first step towards the expansion of the evidence based health policy and healthcare decisions, EMSP and its partners have achieved a proof of concept for cross-border registry collaboration: the '**European Register for MS' (EUReMS) initiative**. This could ultimately lead to commonly used "Sets of Core Outcomes" being collected through registries all over Europe, as proposed in literature, e.g. by the COMET (International Classification of Functioning and Core Outcome Measures in Effectiveness Trials) Initiative.
Within the first phase of EUReMS, EMSP developed a system for temporary data sharing and pooling for central analysis together with 13 national or regional MS registries. In addition to this, a second initiative was developed by the Big MS Data group, composed of five major MS registries; this second group developed their own data sharing protocols for joint research projects among the five registries.

Recently, regulators such as the European Medicines Agency and the health technology assessment (HTA) agencies have shown a strong interest to add RWE data to the assessment of factors influencing their individual decisions. However, in the case of multiple sclerosis, there are no commonly used agreements on suitable measures of RWE data (yet).

What are the next steps for EMSP and EMA?

EMA will be hosting on the 7th July 2017 a workshop on MS registries. The aim of the workshop is to facilitate the understanding and future implementation of the following recommendations:

1. Collect core data elements using the same methodology and using the same scales through as many MS patient registries as possible
2. Ensure good governance as well as reliable quality data delivery
3. Ensure registry interoperability through common terminology and other measures
4. Develop a work plan on the finalisation of these recommendations and their implementation by registry holders, pharma industry, regulatory, HTA and Payors.

Paola Zaratin, Director of Scientific Research at the Italian MS Foundation, reported on the international PROs Initiative promoted by the Multiple Sclerosis International Federation in cooperation also with EMSP, which intends to:

- ✓ Focus on Patient Reported Outcome Measures (PROMs) in real world settings
- ✓ Establish an effective PwMS engagement plan
- ✓ Identify those functional domains that matter most to people with MS (ICF model)– with direct patient help (focus groups) as well as via a literature review - International Classification of Functioning and Core Outcome Measures in Effectiveness Trials Initiative(COMET)
- ✓ Harmonize the existing PROMs globally - using the domains selected above (supported by the International Consortium for Health Outcomes Measurement / ICHOM?)
- ✓ Liaise with parallel efforts of DO-IT! – the IMI support action for Big Data projects

Mireia Castillon Melero, Registries Initiative Coordinator within the Pharmacovigilance and Epidemiology Department (P-PE) of European Medicines Agency opened her presentation by mentioning the EMA Patient Registries Initiative launched in 2015, trying to harmonise the data collection by standardising and creating a more systematic approach to use data registries. The main aim of this initiative was the facilitation of interactions between regulators and registry holders. It appears to be difficult as the range of expectations and standards varies considerably from one registry to another.

Following the developments of new products coming on the market, a request was received to support harmonising the registries in order to allow better exploitation of their current and (in future, expanded) list of patient data.

The idea of the cross-committee task force is to include several stakeholders and to provide a new focus on existing disease profiles; registries being made "fit for regulatory questions" rather than using individual drug specific registries.
Mireia concluded by briefly elaborating on ENCePP, the inventory of existing registries and the importance of making contacts with the registry holders.

ENCePP (European Network of Centres for Pharmacoepidemiology and Pharmacovigilance) is an EU Resource Database, to which registry holders can submit their data for inclusion.

Chantal Guilhaume, Scientific Project Manager, EUnetHTA JA3, Direction de l'Evaluation Médicale, Economique et de Santé Publique (DEMESP / HAS) confirmed that the patient-based evidence is of growing importance for HTA agencies.

Although health technology assessments are still mostly based on data from clinical trials, RWE data and especially PRO data, including quality of life aspects, are finding more and more their way into the assessment process.

One example of HTA relevant data is patient adherence: data on why the patient is taking or not taking the medicine has an impact on judging effectiveness of the drug - so the collection of this data is necessary.
Another example is the measurement of specific disease related symptoms - like mobility problems and fatigue related to MS.

The scales to measure such data need to be precise and to be validated, preferably available in many languages to allow comparability if used in different countries.
An example of a scale often-used by HTA is EQ-5D that allows for calculation of quality-adjusted life years (QALYs) When Qalys outcomes are combined with measurement of health care resource, an evaluation of incremental cost per Qaly can be performed and shared with decision makers.

Dr. Ir. Liesbet M. Peeters, Postdoctoral Researcher at the University of Hasselt/Belgium presented a recent initiative aiming at setting up a multidisciplinary registry with the new inclusion of rehabilitation outcomes: MS Data-Connect.

The aim of this initiative is to develop a proof of concept by 2019/2020, collecting various type of data relevant to patients. It foresees the inclusion of different stakeholders in a multidisciplinary team, all embedded within one centre in Belgium, focusing on optimizing the data and providing a user-friendly and sustainable platform. The novelty is that the data can be inserted in the data-platform while working/talking with the patient. During the patient's visit, the clinical team can add an entry in the registry on a timely, accurate and efficient way. This can be done by MS Nurse, Neurologists, Rehabilitation team and other staff.
There is an **App**lication in development by PXL for patients to complete the questionnaire while they are in the waiting room.

For more information please see www.msdataconnect.com ----------

Questions and Answers session

Paola Zaratin:
Is there any initiative for MS organisation to engage patients in the process of data collection?
Is there also a way to focus on the functional domain, if we do not have enough outcomes in the regulatory process?

Chantal Guilhaume:
HTA bodies are trying to involve more and more patients in the process of evaluation as well as during early advice where plan of development of evidence are discussed with industry. Patients input is informative both at the time of drug launch but also after launch when the health technology/drug is used in real practice. Initiatives such as the "MS Data Connect" would be useful to provide additional patient relevant data from patients participating in one of the various national registries as this data will help completing the picture.

Comments from national MS societies representatives:

Denmark: Ethics and data ownership are major issues in Denmark. Additionally, a person with MS often has other chronic diseases (comorbidity), thus it can be difficult to determine if the symptoms can specifically be attributed to MS or to the other conditions. It would be helpful to have PRO data identified specifically related to MS.
Most of these processes thus far have been developed without any patients' involvement. This is an opportunity to bridge that gap and involve patients in the process.

Malta: There is a small number of MS patients in Malta and it would be interesting to have a MS registry developed. However, it seems that in Malta, neither the patients nor the neurologists are interested in collecting the data. There is an expression of interest of the Maltese MS society representative to set up a registry.

Greece: There is a MS registry in Greece, but it appears that the national MS society representative was not aware of this. There is a lack of communication on the registry, the data collected and its use.
Ireland: There is no registry in Ireland. MS Ireland would be interested in collaborating and investigating how this could be set up.

Portugal: The discussions showed that there are different levels of progress in different countries. There is a need for an individualised approach per country which will take into consideration the different strengths and capacities of the MS societies. It would be helpful to receive guidance on how to build up a national framework to develop a register and initiate a discussion at national level, to reach out to politicians and regulators. MS societies need support to be more effective in setting up and/or use the registries.

Czech Republic: the inclusion of real world evidence data in the decisions related to treatments are encouraging as they include issues important for the quality of life of people affected by MS.

Closing remarks

- ✓ Data collection is an important tool for advocacy! It is one way to make a point that cannot be disputed; research is a unique powerful advocacy tool. This data can be used to fight for the rights of people with MS and for fundraising purposes.
- ✓ EMSP is currently undertaking a mapping exercise of existing MS registries across Europe. The results will be published once they will be ready.
- ✓ Recommendations and next steps will be developed after the EMA workshop, foreseen on the 7th July. EMSP will be working on the development of the next phase for the European Network of MS Registries.

POST SCRIPTUM on July 10,2017:

The discussion at the **EMA workshop on MS registries** (July 7th, 2017, aiming at better exploitation of registry data for regulatory and HTA/payor related decision making) was structured along three main subjects:

1) Common data elements that are needed by all stakeholders and its validation
2) Informed consents, governance data protection and individual vs. aggregated data
3) Common procedures and registry interoperability, quality assurance and data analysis.

Almost fifty experts representing regulatory bodies, HTA agencies and payors, registry holders from across Europe and beyond, national MS patient advocacy groups, European MS Platform, the Progressive MS Alliance and six major MS marketing authorization holders (= industry) discussed the above subjects.

A detailed workshop report and recommendations for action was promised by EMA to come as soon as possible, while the Power Point slides being presented at the workshop can be found here.

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