Unleashing the potential of real-world evidence in rare diseases

Recommendations for optimising the use, design and regulation of real-world evidence (RWE) collection based on an expert panel hosted by the Associazione Italiana Miastenia (AIM) on 1 March 2021

PART 1:
SUMMARY OF THE EXPERT PANEL

On 1 March 2021, argenx sponsored a panel event on the potential of RWE in rare diseases hosted by the Italian patient organisation Associazione Italiana Miastenia (AIM).

Real-world evidence is the clinical evidence derived from the analysis of real-world data that is collected outside of randomised controlled trials (RCTs), through routine medical practice.

For instance, real-world data can come from patient-generated data, electronic health records, product and disease registries, as well as data gathered by mobile devices. Generated by different types of study designs and analyses, including observational studies, real-world evidence has the potential to complement the knowledge acquired by RCTs in rare diseases.

The event was aimed at providing a deeper understanding of RWE and its potential benefits in the rare disease space. It also sought to provide additional comprehension on the challenge of gathering patients' perspective on living with a disease and treatments outside of standardized clinical trials.

To uncover some of these insights, we convened a senior multi-stakeholder panel of experts offering medical, scientific, patient, economic and regulatory perspectives. The discussion was grounded on the MyRealWorldTM MG Observational Study.

Anant Murthy, argenx's General Manager Europe, opened the event with commentary on how COVID-19 has illuminated the importance of interconnected healthcare systems and evidence-sharing between them.

Dr. Renato Mantegazza, President of AIM and Director of the Neuroimmunology and Neuromuscular Diseases Unit at the Fondazione Istituto Neurologico "Carlo Besta" of Milan, outlined the value of information when it comes to better understanding and treating rare diseases. He asserted that real-world evidence is a driving force for knowledge and transparency, which can only be achieved through increased connectivity between the industry, healthcare providers, payers and patients.

Mark Larkin, Founder and CEO of Vitaccess, the RWE solutions and analytics platform that developed the MyRealWorldTM MG Observational Study, summarised the initial learnings from the study and underlined the importance of effective collaboration between different stakeholders in recruiting patients for such studies. He also highlighted the role of digital tools in allowing RWE collection to be flexible, to keep track of the impact of external factors on rare disease patients, and more broadly, to gather patients' perspective in such studies.

Marguerite Friconneau, Expert Patient and Patient Advocate on the Scientific Board of the MyRealWorldTM MG Study, focused on the importance of patient-centricity for observational studies. On the MyRealWorldTM MG Study specifically, she explained that the innovative approach to the study involving input from patients early and often enabled the incorporation of patients' expectations and needs.

Lieven Annemans, Senior Professor of Economics of Health and Wellbeing at Ghent University and Brussels University (VUB), noted that real-world evidence can support the entire innovation cycle: from drug development stages by gathering deeper understanding of a disease and its current management; through the patient access stage; and the post market-access stage by helping assess whether a treatment delivers on its promised value from a clinical and a healthcare system perspective.

Brieuc Van Damme, Director-General Healthcare at Belgium's National Institute for Health and Disability Insurance (RIZIV-INAMI), showcased some of the ways in which Belgium has started using RWE. For instance, via the RWE4Decisions platform; and highlighted the need for a common European approach to RWE such as in the context of the European Commission's work on a European Health Data Space.

Tomislav Sokol, Member of the European Parliament (EPP Group, Croatia) called for harmonising the EU regulatory framework on RWE collection, management and ethics in order to increase the value of RWE for patients.

Finally, **Sarah Emond**, Executive Vice President and Chief Operating Officer, Institute for Clinical and Economic Review (ICER), opened the **Q&A discussion**. Sarah stressed the importance of making the outcomes of clinical trials more patient-centred with the support of RWE.

PART 2: RECOMMENDATIONS

I. OPTIMISING THE USE OF RWE THROUGHOUT THE DRUG DEVELOPMENT CYCLE

One of the main challenges faced by biopharmaceutical companies and healthcare systems is the inherent gap between data collection from standardised clinical trials and how things happen in the real world.

RWE can help the sector overcome this "data gap" throughout the drug development cycle, allowing drug developers to better understand a disease and improve R&D. It would also enable healthcare authorities to make more informed decisions while ensuring greater involvement of patients' perspective.

Specifically, the use of RWE should be encouraged and enhanced at three key stages of the drug development cycle:

i. Drug development phase

- RWE does not replace or compete with clinical trial data, but complements it by improving our understanding of diseases and treatments and their everyday impact.
- RWE is critical to improve patient empowerment and better incorporate patients' perspective in drug development by reporting both patients' and clinicians' outcomes.
- In general, information gathered through RWE collection can bring more value to patients because it is shareable and based on their "expertise by experience."

ii. Health Technology Assessment (HTA) and access phase

- The clinical and value appraisal of new drugs by healthcare authorities, especially in rare diseases, is often associated with disease, treatment, and healthcare system-related uncertainties that can impede or delay patients' access to medical innovation. RWE can help overcome such uncertainties and concerns about the value of innovative treatments by providing real-world information before a drug has been approved.
- RWE can also contribute to more comprehensive value assessment by broadening its scope to new, often neglected perspectives such as workers' productivity and caregiver burden.

iii. Post-access phase

- RWE can play a central role in assessing whether and how a new treatment, once in use in a healthcare system, delivers on its promised value both from a clinical and from a healthcare system perspective.
- More generally, high-quality data gathered through RWE can improve the overall management of the healthcare system, for example by enabling hospital-level comparisons and by enhancing transparency and trust for the general public.

II. OPTMISING THE DESIGN OF RWE COLLECTION AND OBSERVATIONAL STUDIES

The value of RWE throughout the drug development cycle is only as good as the value of the data collected throughout the process. As a result, RWE collection projects and observational studies should follow best practices, such as:

i. Multi-stakeholder cooperation

- RWE is centred on collecting information about the real-world interplay between disease, treatment and their management in the healthcare system. Its success relies on the effective involvement of and collaboration between a series of stakeholders, from industry to patients, clinicians and healthcare providers.
- Early and active involvement of expert patients, such as seeking their inputs on design of RWE collection studies, is particularly important for two reasons:
  - Collecting information about their perspective on the burden of disease and their medical needs is one of RWE's central objectives.
  - Involving expert patients in the design of such studies is a key pre-condition for their effective participation in such studies. Creating an atmosphere of trust is of utmost importance, in addition to addressing issues such as usability and relevance.

ii. Digital tools

- Digital tools such as app-based observational studies are particularly useful for RWE collection. They allow for the real-time inclusion of unexpected environmental factors (e.g. COVID-19 in the context of MyRealWorldTM MG) and the assessment of their impact on rare disease patients.
- Digital RWE tools generally ease evidence generation and patient recruitment for such studies.

iii. Quantity v. quality of data

- Stakeholders involved in the RWE collection process should focus on the quality rather than on the quantity of the data generated, as the former is the essential variable for the value of the evidence generated.

III. OPTIMISING THE REGULATORY FRAMEWORK FOR RWE AT NATIONAL AND EUROPEAN LEVEL

In addition to the questions on the design of RWE studies and how this type of data can contribute to the drug development cycle, another central issue around RWE relates to the regulatory framework in which it takes places.

More specifically, the challenge remains to what extent do these regulations provide necessary incentives for key stakeholders to participate in RWE collection, without establishing undue regulatory obstacles, particularly in terms of data sharing.

This requires solutions both at the national and EU level:

i. At national level

- **Incentives:** National policymakers should encourage cooperation between RWE stakeholders by providing appropriate incentives, such as healthcare providers to register and share data in a qualitative way.
- **Qualification:** To ensure good quality data, RWE stakeholders and in particular healthcare providers need to be qualified to register it in an appropriate and timely manner. This could be supported, for example, by national healthcare authorities introducing RWE training for practitioners to develop the necessary skills.
- **Regulatory consistency:** In some countries, the processes of data registration on the one hand and of reimbursement on the other are not fully aligned. This could lead to insufficiently incorporating the information provided by a RWE registry into the HTA process and potentially wasting it.

ii. At European level

Especially in rare diseases, the added value of RWE would be strongly enhanced by the possibility to combine data on a European and international scale. Nevertheless, diverging national regulations on the launch of RWE studies and the creation of RWE registries generate significant obstacles.

Any solutions to overcome the current European fragmentation and promote European integration on RWE would be beneficial. Such solutions could take the form of:

- **Regulatory integration:** In the context of the European Commission's work on a European Health Data Space or of the currently discussed EU HTA Regulation, which could be used to ensure interoperability of RWE protocols and standards.
- **Common fundamental infrastructure**, for example in the ongoing work on a European data cloud.

IV. CONCLUSION

Based on the elements above, three concrete recommendations could be made:

RECOMMENDATION 1

RWE should be enhanced throughout the drug development cycle and in particular:

- In the drug development phase, to improve our understanding of diseases by incorporating the patients' perspective.
- In the Health Technology Assessment (HTA) and access phase, to improve our understanding of how a disease and various treatments are managed in a given healthcare system.
- In the post-access phase to assess whether and how a new treatment, once in use in a healthcare system, delivers on its promised value both from a clinical and from a healthcare-system perspective.

RECOMMENDATION 2

To optimise the value of RWE, RWE collection studies should follow best practices in terms of:

- Transparent, trust-based multi-stakeholder cooperation, especially with regards to an early and active involvement of expert patients.
- Using digital tools as a flexible way to incorporate environmental factors and facilitate participation by rare disease patients.
- Privileging the quality over the quantity of the evidence generated.

RECOMMENDATION 3

To optimise the regulatory framework for RWE with a view to supporting both the effective incorporation of RWE into national HTA processes and EU-wide RWE integration, national and European policymakers should:

- Provide the appropriate incentives, qualification and regulatory consistency (mainly at the national level)
- Address potential regulatory fragmentation and encourage EU-wide regulatory integration and infrastructure (mainly at EU level)
- Privileging the quality over the quantity of the evidence generated.