Alliance for Regenerative Medicine Calls for the European Commission to Fast-Track Real World Evidence for ATMPs

RWE is key to ensuring continued European patient access to Advanced Therapy Medicinal Products (ATMPs)

Real World Evidence (RWE) is a critically important component in the advancement of ATMPs and ensuring patient access to these transformative therapies. The Alliance for Regenerative Medicine (ARM) calls on the European Commission to fast-track the use of RWE for ATMPs by convening a multi-stakeholder forum on the issue – which would include subject matter experts from ARM, manufacturers and patient advocacy groups – in order to establish a European framework for regular RWE use.

Efforts to advance RWE for ATMPs should focus on:

1) *Adopting common standards and data requirements*
2) *Creating an implementation roadmap for healthcare centres across Europe, ensuring cross-border consistency of RWE usage and interoperability through registries and other collection and analysis vehicles*
3) *Complying with legal requirements including GDPR*

We believe this collaborative approach will benefit regulators, HTA bodies, payors, manufacturers, healthcare professionals and most importantly – patients.

Advanced therapies, comprising gene therapies, cell therapies and tissue-engineered products, aim to alter the current practice of medicine by treating the root causes of disease and disorders. Since most of these therapies are administered just as one or very few doses and exert a long-lasting, profound, potentially curative effect, the generation of RWE is a critical component in the assessment of ATMPs across their whole lifecycle, from the early phases of their clinical development. In addition, a significant number of ATMPs are expected to obtain European marketing authorization in the years to come, resulting in an increasingly urgent need to address inefficiencies coming from a fragmented, inconsistent and often unusable RWE ecosystem in Europe.

RWE is the clinical evidence derived from the analysis of Real World Data (RWD), i.e. routinely collected data of a patient's health status or the delivery of care from a variety of sources that is beyond conventional clinical trials, including electronic health records, claims, registries, patient-generated data and other data sources that can generate health status information such as mobile devices. RWE can help to address uncertainties about the long-term effect, safety, health-related quality of life and use of healthcare resources from ATMP treatments, as well enabling comparisons with standard of care. RWE is also helpful in providing natural history datasets in key disease areas and can be used for the indirect detection of a product's therapeutic effect when direct comparisons are not feasible. By providing evidence on the clinical and economic value of a new ATMP product that could not be fully evaluated at the time of marketing authorisation, RWE is instrumental in allowing timely patient access to these therapies through marketing authorization and reimbursement solutions such as conditional marketing authorisation, conditional reimbursement and pay-for-performance agreements, including annuity-based schemes.

However, several challenges may limit the acceptance and use of RWE by payers and regulators, including:

- Potential bias and confounding factors due to methodological flaws in local registries
- The lack of universally accepted methodological standards for the design, conduct, analysis and reporting
- The lack of a technologically advanced, reliable, international and interoperable infrastructure to capture clinical and patient outcome data
- Inconsistency in inputting and keeping data quality standards within databases.

RWE, often generated using product or disease registries, also requires the active participation of many different stakeholders, such as healthcare professionals and patients.

In July 2019, ARM published recommendations for timely access to ATMPs in Europe. The consensus report recommended several key measures, including the development and use of ATMP-relevant RWE infrastructure to obtain and use RWE most effectively.

There is a critical need to develop RWE infrastructure for ATMPs and a common framework at the European level to support long-term evidence generation and procedures to enhance the quality of RWE collected specifically for ATMPs, both for regulatory and payer purposes. The data generated through RWE should meet the needs of all: regulators, HTA bodies, payers, manufacturers, healthcare professionals and patients. Investment in pan-European RWE infrastructure will be particularly effective if ATMP clinical assessment were to be coordinated at the EU level (joint clinical assessment), while adapting national Health Technology Assessment (HTA), pricing and reimbursement processes to capture and value the long-term benefits of ATMPs. An integrated RWE infrastructure, collecting evidence of ATMP use and effectiveness across Europe, will also facilitate cross-border treatments, which are of vital importance in cases when only a limited number of specialised centers across Europe can administer the treatment.

The need for more frequent and effective use of RWE is widely recognized, as illustrated by the many different initiatives and projects that have been launched in Europe during the last few years to improve and facilitate the generation and use of RWE. These include: IMI GetReal project, EMA Adaptive Pathways Pilot and IMI ADAPT-SMART initiative, EMA patients registries initiative including guidelines on indication specific registries, EUnetHTA JA2's Work Package 5 on Post-Launch Evidence Generation, RWE4Decisions project, Eurordis' Rare Impact project, the HMA/EMA Joint Big Data Task Force and the DARWIN platform. The multiplication of these initiatives and projects – not only in Europe but also in other geographies, as demonstrated by initiatives from the US FDA[1] - demonstrates how critically important it is to develop structures and processes and to reach common agreement on ways to develop high quality and robust RWE.

Recently, the European Commission published the roadmap to a new EU pharmaceutical strategy. The objectives of the new pharmaceutical strategy which will be put forward in 2020 include ensuring greater access and availability of pharmaceuticals to patients, and enabling innovation in a way that harnesses the benefits of digital and emerging science and technology and reduces the environmental footprint.

[1] https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

In addition, one of the priorities set out in the new Commission mandate is the creation of a European Health Data Space (EHDS), which would foster the exchange and sharing of different kinds of health data (electronic health records, genomics, registries, etc.) in Europe.

Therefore, ARM advocates for the creation of pan-European infrastructure and processes to develop standards for the collection, analysis and use of RWE as part of the European Commission's pharmaceutical strategy, and fully integrated in the future establishment of a European Health Data Space. The COVID-19 pandemic has highlighted even further the importance and urgency of having a common RWE infrastructure across Europe, in order to ensure critical data is available in times of crisis, when the access to healthcare centres and the conduct of traditional clinical trials are hampered.

In order to achieve success, ARM calls for the European Commission to engage a multi-stakeholder forum, including subject matter experts from ARM, to establish a European framework for the collection and analysis of RWE for ATMPs that could meet the needs of all relevant parties such as regulators, HTA bodies, payers, manufacturers, healthcare professionals and patients. This common framework will allow for a multifaceted approach to address the many challenges of adopting common standards, reaching consensus on data requirements, facilitating implementation in healthcare centres across Europe and complying with GDPR and other legal requirements. Different workstreams could be set up to evaluate the different dimensions, reach consensus, and develop indication-specific pilots to test and refine infrastructure, processes and principles

As the voice of the ATMP sector, ARM looks forward to being part of an inclusive and solution-driven dialogue with the European Commission and other relevant stakeholders in shaping the path forward. With a wave of innovative therapies under development, we applaud Europe's leadership position in continuing to ensure patient access to these durable and potentially curative ATMPs.

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About the Alliance for Regenerative Medicine (ARM)

The Alliance for Regenerative Medicine (ARM) is the leading international advocacy organisation dedicated to realizing the promise of advanced therapy medicinal products (ATMPs). ARM promotes legislative, regulatory and reimbursement initiatives in Europe and internationally to advance this innovative and transformative sector, which includes cell therapies, gene therapies and tissue-based therapies. Early products to market have demonstrated profound, durable and potentially curative benefits that are already helping thousands of patients worldwide, many of whom have no other viable treatment options. Hundreds of additional product candidates contribute to a robust pipeline of potentially life-changing ATMPs. In its 11-year history, ARM has become the voice of the sector, representing the interests of 360+ members worldwide and 70+ members across 15 European countries, including small and large companies, academic research institutions, major medical centres and patient groups. To learn more about ARM or to become a member, visit http://www.alliancerm.org. Transparency register number ID: 244710319190-73