RWE4Decisions REAL WORLD EVIDENCE

Webinar Report

Real-World Evidence over the lifecycle of ATMPs to meet the HTA Regulation Needs

Tuesday, 10 October 2023

Keynote speaker

Ana Hidalgo-Simon
Associate Professor, Leiden University Medical Center (reNEW consortium)

Panellists

Alexander Natz
Secretary-General, European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)

Christoph Rupprecht
Head of the Health Policy & Health Economics Department, Allgemeine Ortskrankenkasse (AOK)

Niklas Hedberg
Chief Pharmacist, Swedish Dental and Pharmaceuticals Benefits Agency (TLV)

Simone Boselli
Public Affairs Director, Rare Diseases Europe (EURORDIS)

Co-moderators

Eric Sutherland
Senior Health Economist, OECD

Karen Facey
RWE4Decisions Facilitator

The RWE4Decisions webinar series in 2023 focuses on the products that will be the first to undergo Joint Clinical Assessment under the new Health Technology Assessment (HTA) Regulation: cancer medicines and Advanced Therapeutic Medicinal Products (ATMPs). As there is often a paucity of clinical evidence available for these innovative treatments, the potential for use of Real-World Evidence (RWE) must be explored, taking into consideration the existing challenges, such as the lack of EU-wide guidance on RWE generation or use.

Advanced Therapy Medicinal Products (ATMPs or advanced therapies) are a wide-ranging category of innovative, complex, high-cost medical therapies that differ from traditional medicines in a variety of ways (one or two administrations, permanent effect, administration in specialised centres, difficult to copy). They include gene therapies, cell therapies, and tissue-engineered products, and are typically used in severe or rare diseases. **Professor Ana Hidalgo-Simon, Leiden University Medical Center (reNEW consortium)** discussed the current state of ATMPs and the value of Real-World Evidence (RWE) for these treatments.

Since the first approval of an ATMP by the European Medicines Agency (EMA) in 2009, 25 ATMPs have received regulatory approval. The majority have been approved in the past four years, but six have also been withdrawn from the market, all for commercial reasons. Most ATMPs have been designated as orphans and despite a relatively small evidence base when compared with classical medicines (often based on phase/II uncontrolled trials), a large proportion of them have received full marketing authorisations.

Advanced therapies often originate from academic centres and so translational research needs to consider the requirements to enter clinical development and how decision-grade evidence can be developed for the regulatory benefit:risk assessment and the HTA evaluation of added value and value for money. This requires multi-stakeholder collaboration with clinicians and the pharmaceutical industry that puts patients at the centre, to better understand their needs and preferences. Early planning dialogues and continuous collaboration between developers, regulators and HTA bodies are essential to ensure that RWE can help resolve uncertainties and support decision-making throughout the lifecycle of ATMPs, from marketing authorization to post-authorization commitments, renewals, and long-term value for society. Consideration must be given to the burden of data collection, especially in academic settings where various data collection systems may be mandated, and the need for better data sharing.

Professor Hidalgo-Simon concluded that a level of uncertainty at the point of decision making will always remain for regulatory and HTA evaluation of advanced therapies, but should be minimised as much as possible through good planning with all stakeholders.

The panellists representing various stakeholders shared their views on the role of RWE over the lifecycle of ATMPs to support decision-making from marketing approval to reimbursement and patient access.

Representing the industry viewpoint, **Dr Alexander Natz, EUCOPE** began by acknowledging significant developments in the use of RWE in recent years, highlighting how RWE has been increasingly incorporated into decision-making processes, moving beyond regulatory considerations to pricing and reimbursement decisions. For advanced therapies, high quality RWD is required, particularly to understand long-term effects. RWE should be seen as complementary rather than a replacement for evidence from traditional randomized controlled trials (RCT). Furthermore, it is essential to collect quality-of-life data over the lifespan of the product, to inform pricing and reimbursement decisions. This may be used in outcome-based agreements, which can help mitigate risks for Payers while ensuring patient access to advanced therapies.

Drawing parallels with the earlier presentation by Professor Hidalgo-Simon, **Niklas Hedberg, TLV** highlighted common HTA challenges associated with advanced therapies. These include the need for agreement on relevant outcomes to demonstrate patient benefit and considerations about how to manage uncertainty, including the potential for outcomes-based managed entry agreements and the importance of RWE. In Sweden, HTA evaluates clinical and cost effectiveness, and for advanced therapies there are often concerns about data quality, relevance of study outcomes, and high cost given size of demonstrated benefit and/or magnitude of uncertainties. In Sweden, three TLV reports have addressed issues related to assessing, paying for, and handling ATMPs - emphasizing the role of uncertainty in each of them. Key themes within these reports included dealing with intangible utilities, assessing evidence gaps, and the conundrum of precision medicines. They also explored the challenges of long-term effectiveness and emphasized the importance of outcome-based agreements. For advanced therapies, close collaboration of HTA bodies and Payers is needed to enhance knowledge and develop capacity. Furthermore, the legal framework for pricing advanced therapies needs to be developed in some countries, especially for combination therapies.

Christoph Rupprecht, AOK, shared Payers' perspectives, emphasizing the need for management novel medicines and the quality-assured introduction of new pharmaceuticals, considering the rapid pace of innovation. This should ensure that ATMPs are made available across all European countries. To support this, a network of Centers of Excellence distributed across Europe is needed to ensure that new medicines reach patients without significant delays. Availability of ATMPs in all 27 EU member states is a matter of fairness and an investment in the overall health and well-being of the continent. However, two fundamental challenges remain with ATMPs. The first challenge is the time horizon, especially for ultra-rare diseases with a small number of patients, making comparative studies challenging and benefits

often realised many years after clinical trials are completed. The second challenge is the uncertainty surrounding the safety and efficacy of ATMPs, which can complicate patient acceptance of new treatments. Outcome-based agreements could offer short-term solutions, but they might not be ideal for long-term uncertainties. Importantly, evidence standards should not be reduced for advanced therapies, instead more intelligent tools, new statistical methods and approaches should be used to address the challenges posed. This could also include the use of RWE, provided the validity and quality of the data increases significantly in the future.

Representing patients' perspectives, **Simone Boselli, EURORDIS** emphasized the value of RWE in providing a more comprehensive understanding of treatment outcomes, long-term safety, and improvements in the quality of life for patients with rare diseases. Rare diseases often pose unique challenges, such as difficulties in clinical trial enrollment and limited disease understanding, which can be addressed through use of RWE. A patient-centred approach to generation of RWE is needed, where individuals living with rare diseases actively contribute their experiences and perspectives. This will empower people living with rare diseases to influence the development and accessibility of innovative therapies, ultimately improving care and outcomes for this vulnerable population. A "whole of Europe approach" is needed to generate RWE for these therapies, which addresses the need for infrastructure development that empowers patients and allows their input in the early phases of clinical development and regulatory authorization. Early dialogue and alignment of evidence requirements among decision makers is key, involving stakeholders such as patient representatives, regulators, and Payers to ensure best efforts are made to collect high-quality RWE. Furthermore, in a wider policy setting, interoperability of healthcare data across countries is needed to build stronger RWE for rare diseases.

Discussion among the panellists and audience addressed:

- What advice to give policymakers who are considering adopting the European health data space or similar initiatives to enable cross-border data sharing for RWE and HTA?

- Can we be smarter about giving early advice to health technology developers, that don't have pharmaceutical development experience.

- Can we work earlier to align our data collection requirements with EMA's early scientific advice sessions and agree on a minimum data set that meets the needs of decision-makers?

- What is the one thing we should focus on in the next year to improve RWE for HTA?

In conclusion, several common themes and points of agreement emerged among the speakers. These included a strong emphasis on the importance of collaboration between diverse stakeholders, such as regulators, HTA bodies, Payers, industry, and patient representatives, to improve real-world evidence collection and decision-making. The significance of data quality and validity was widely acknowledged, highlighting the need for robust and representative data. Early engagement and dialogue between industry and decision-makers was seen as valuable in identifying data needs and aligning on endpoints. The challenges of addressing uncertainty, particularly regarding long-term effectiveness, were recognized. European collaboration through initiatives like the European Health Data Space was seen as a way to enhance data sharing and standardization across countries. A comprehensive approach to ATMPs from development to patient access was proposed, as well as the importance of involving patient perspectives in decision-making processes from the onset.

RWE4Decisions is a payer-led multi-stakeholder learning network, which has developed **stakeholder actions** that will better enable the use of real-world evidence in HTA/payer decisions about highly innovative technologies. The work has been commissioned by the Belgian National Institute of Health and Disability Insurance (NIHDI) and is led by a multi-stakeholder Steering Group with a wider community of contributors including HTA bodies and payers, regulatory agencies, patient groups, clinicians, industry, analytics experts and academic experts/researchers. The RWE4Decisions Secretariat is provided by FIPRA, with sponsorship by the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), AstraZeneca, Boehringer Ingelheim, Novartis, Pfizer, Roche and Takeda.

For further information and to watch the recording of the webinar, visit our website at:

https://rwe4decisions.com/event/rwe-over-the-lifecycle-of-atmps-to-meet-the-htarneeds/

What are you are doing to progress learnings on the use of RWE?

Contact us at **secretariat@rwe4decisions.com** to join the RWE4Decisions Learning Network.

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