The Rise of Real World Evidence (RWE) in EU Marketing Authorization Decisions – Past, Present, and Future

HPR56

Jennifer Scarlet Haas, Dominic Meise, Sebastian Braun
Xcenda GmbH, Hannover, Germany

BACKGROUND

- Traditionally, real-world evidence (RWE) is used in post-authorization studies for safety assessments and risk management.
- However, the interest in RWE in the pre-authorization phase of medicines development is increasing.
- The recent initiative of the European Medicines Regulatory Network to create an EU-wide distributed network of real-world data named the Data Analytics and Real World Interrogation Network (DARWIN EU) (1) has the potential to further amplify this trend.
- The European Medicines Agency (EMA) publishes detailed information on the medicines assessed in the form of a so called European public assessment report (EPAR). (2)
- EPARs are published for every human (or veterinary) medicine application and include the product information, and amongst others, a description of the studies conducted (and planned) for the marketing authorization application. (3)

OBJECTIVES

- To allow an assessment of RWE use trends, this study aimed at identifying RWE use in new EMA marketing authorization applications (MAA) that resulted in authorized medications in the year 2021.

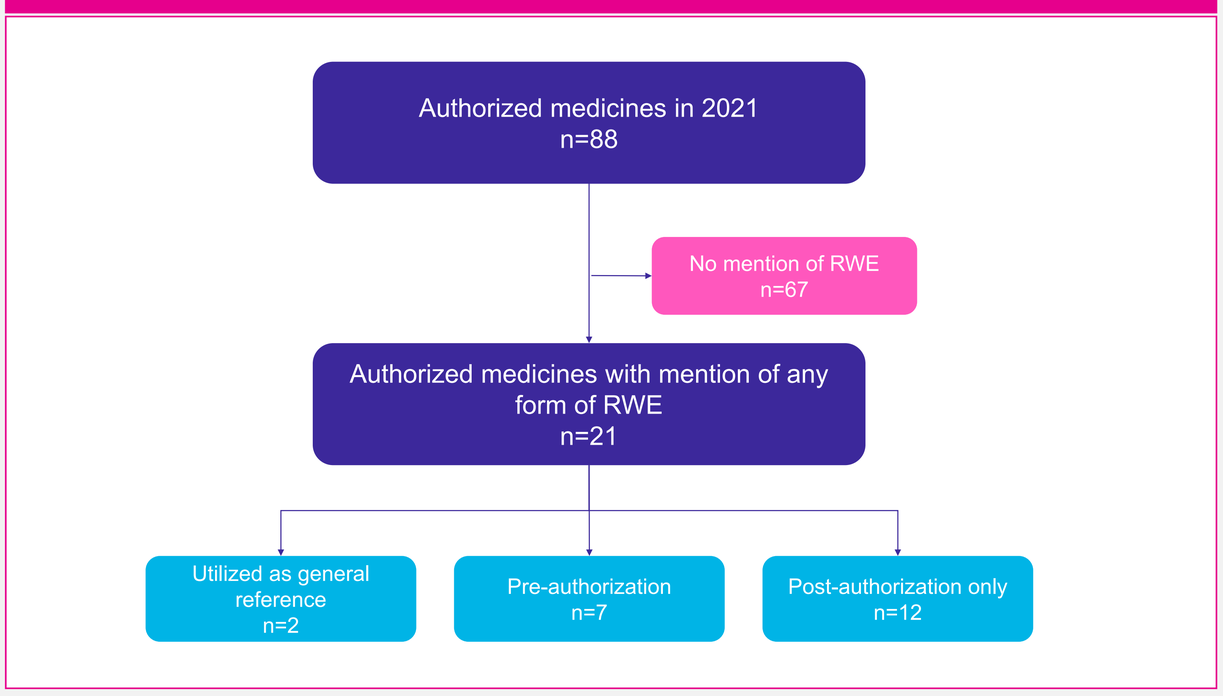
METHODS

- The EMA website search engine was utilized to identify all human medicines which were granted a marketing authorization in 2021. Based on the identified human medicines the EPARs were scanned for the respective RWE use, if applicable.
- Keywords used for identifying real-world data use in the reports were “real-world”, “registry/registries”, “claims”, “administrative”, “health records”, “medical charts”, “synthetic” and “hospital data”.
- The search was limited to the chapters “clinical aspects”, “clinical efficacy” and “clinical safety” as these were considered the main sections that would describe any pre-authorization studies. It is generally assumed that these pre-authorization studies aim to evaluate the safety and efficacy of the product in scope and hence, would include any information on clinical trials or other studies that might potentially include any real-world data use.
- EPARs including RWE were assessed with respect to characteristics such as indication, RWE data source used, and methodological approaches.

RESULTS

- Overall, 88 human medicines received marketing authorization in 2021. For each medicine, the EPAR was reviewed in terms of the respective RWE use.
- Based on the specified search terms, 21 human medicines were identified where RWE was mentioned. The differentiation of pre- and post-authorization RWE use yielded n=7 pre-authorization reports and n=12 post-authorization reports (n=2 only mentioned RWE as a general reference).
- Human medicines with RWE use post marketing approval included Bimzelx, Bylvay, Cibinqo (post and pre RWE use), Elzonris, Evkeeza, Evrysdi, Imcivree, Lumoxiti, Ogluo, Orladeyo, Skysona, Voxzogo, and Vumerity.

Figure 1. Assessment of RWE use in human medicines with marketing authorization in 2021

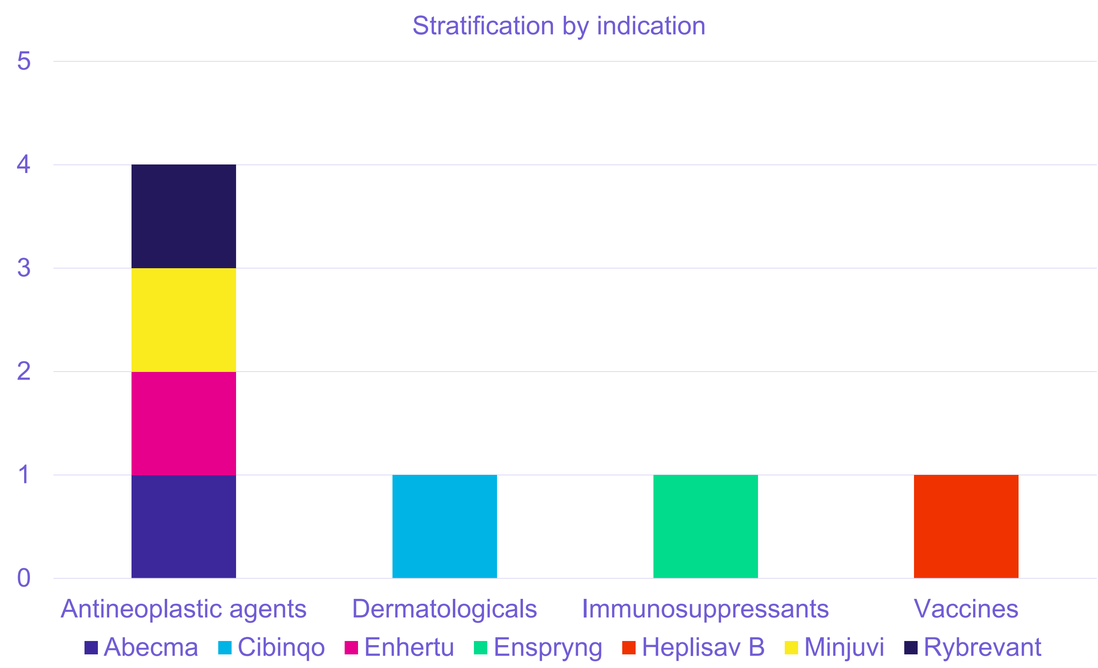


- The majority of post-authorization RWE use was related to Post Authorization Safety Studies (PASSs) labeled as category 3, e.g., Cibinqo, Elzonris, or Orladeyo. Generally, PASSs are either imposed or voluntary. Imposed PASSs refer to studies where the marketing-authorization holders have a specific obligation for a marketing authorization granted under exceptional circumstances and the other studies requested by Pharmacovigilance Risk Assessment Committee (PRAC). Voluntary PASSs (category 3) include non-imposed studies that are requested in risk management plans. (4)

RESULTS (CONTINUED)

- Human medicines with a reference to RWE use prior to marketing authorization were namely Abecma, Cibinqo, Enhertu, Enspryng, Heplisav B, Minjuvi, and Rybrevant.
- In the EPAR of Enhertu individual patient data was referenced, for Rybrevant claims reimbursement data and electronic health records (EHRs) were mentioned, and for Enspryng clinical sites were utilized for pre-authorization submission.
- The assessment of indications showed that cancer was the most prevalent with multiple myeloma (Abecma), breast cancer (Enhertu), diffuse large B-cell lymphoma (DLBCL) (Minjuvi), and non-small lung cancer (NSCLC) (Rybrevant).
- Heplisav B was the only vaccine (preventing hepatitis B virus infection in adults) with RWE use prior to authorization. Cibinqo is indicated for treating adults with moderate to severe atopic dermatitis, and Enspryng is indicated for neuromyelitis optica spectrum disorders (NMSOD).
- Overall, three of the seven agents are designated for an orphan disease. Hence, the majority was a non-orphan designation.

Figure 2. Stratification of the human medicines by marketing authorization indication



- From these seven human medicines, 42.9% (n=3) utilized registry data, namely Cibinqo, Abecma, and Minjuvi. However, for Abecma also clinical sites and research databases were referred to.
- RWE was mainly used to assess safety related events in non-clinical populations as well as to provide external control arms that were compared via matching or inverse probability of treatment weighting to populations from the clinical studies (Abecma, Enhertu, Minjuvi).

DISCUSSION

- Our assessment showed that RWE use is not only limited to orphan designations but rather is considered of value in more prevalent indications with larger sample sizes (and potentially less limited data).
- The use of RWE in EMA marketing authorization submissions is still quite limited. However, there is an increasing trend of utilizing real-world data not only in the post-authorization safety studies but also to support market access.
- An environment with increased focus on utilizing the benefits of RWE is being established but still requires further research and case examples beyond post-authorization utilization.
- Further, the results show an increased importance to enhance real-world data collection and allow accessibility to a wider research community. In turn, it is anticipated that this would also improve the evidence quality of newly marketed medicines.

CONCLUSIONS

- Our results show that the use of real-world data to support marketing authorization in the EU is gaining traction not only in post-authorization studies but also in pre-authorization studies.
- In light of the changes in acceptance of regulators, advancements in RWE generation in terms of accessible data sources and statistical methods, it is anticipated that hybrid approaches including clinical and real-world data for evidence generation will be required.
- Further advancing the knowledge on RWE and accelerating the acceptance in the field of early drug development is of utmost importance given the rapidly changing landscape.

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