# The Growing Role of Real-World Evidence (RWE) to Support Efficacy in EMA Oncology Approvals: Light at the End of the Tunnel

HTA317

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FOCUSED VALUE

## BACKGROUND

- Despite growing regulatory interest and emerging frameworks in Real-World Evidence (RWE), including the publication of several European Medicines Agency (EMA) guidance documents since 2021,[1-3] the absence of harmonized international standards creates regulatory uncertainty around how RWE can support regulatory submissions.
- In rare cancers, ethical considerations, small patient populations preclude the conduct of adequately powered and controlled trials, thereby creating critical gaps in efficacy assessment.

## METHODS

- Identified oncology medicines granted marketing authorization by the EMA from January 1, 2023, and August 31, 2025; excluding biosimilars, generics, and supportive care.
- Conducted a structured review of European Public Assessment Reports (EPARs) to identify RWE use.
- RWE use was categorized independently by two reviewers, applying an adapted framework by Zhong et al. (2025)[4] based on role (primary vs supportive), intended purpose, and regulatory acceptability **(Fig 1)**.
- Types of RWE were noted and included patient registries, electronic health records, natural history data, survey database, and observational cohort studies.
- Descriptive analysis was conducted on RWE categorization.

## RESULTS

- The EMA approved 40 oncology therapies across 42 indications between Jan 1, 2023 and August 31, 2025.
- RWE was used in only 10 approvals (25.0%), exclusively as supportive rather than primary evidence **(Fig 2)**.
- Among the 10 therapies using RWE:
  - 4 (40.0%) employed RWE for formal comparison (external control arm), while 6 (60.0%) used it for benchmarking trial outcomes **(Fig 3)**.
  - EMA deemed half of these submissions inadequate due to methodological issues and data limitations **(Fig 3, Fig 7)**.
  - The most common real-world data sources were electronic health records (40.0%) and patient registries (30.0%) **(Fig 4)**.
- Among the overall study cohort:
  - 14 therapies out of 40 therapies received orphan drug designation (35.0%), and higher utilization of RWE was observed in this subgroup (5/14, 35.7%) **(Fig 5)**.
  - Hematologic malignancies accounted for 14 of 42 indications (33.3%), but RWE was used for only 4 therapies (4/14, 28.6%) **(Fig 6)**.
- Three case examples illustrate RWE was accepted across distinct contexts: rare-disease benchmarking (Welireg), pediatric single-arm validation (Spexotras), and refractory multiple myeloma trial outcomes comparison (Elrexfio) **(Fig 7)**.

**Figure 3. Purpose & Regulatory Acceptability of RWE Use (n = 10)**

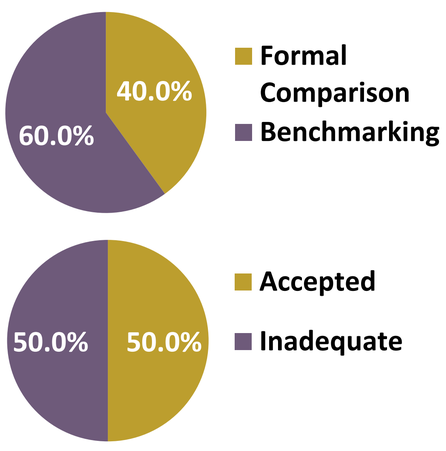
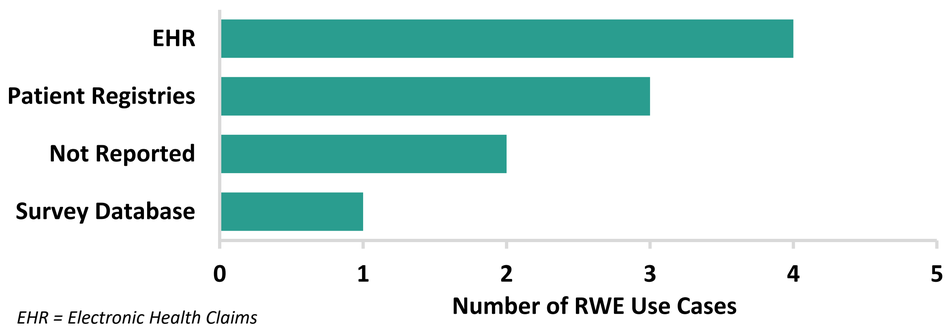



**Figure 4. RWE Use by Data Source Type (n = 10)**




*EHR = Electronic Health Claims*

**Figure 5. RWE Use in Therapies with Orphan Drug Designation (n = 14)**

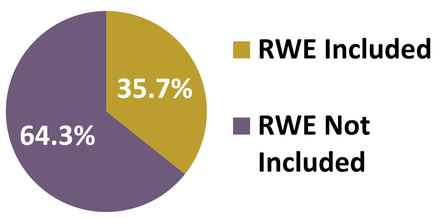
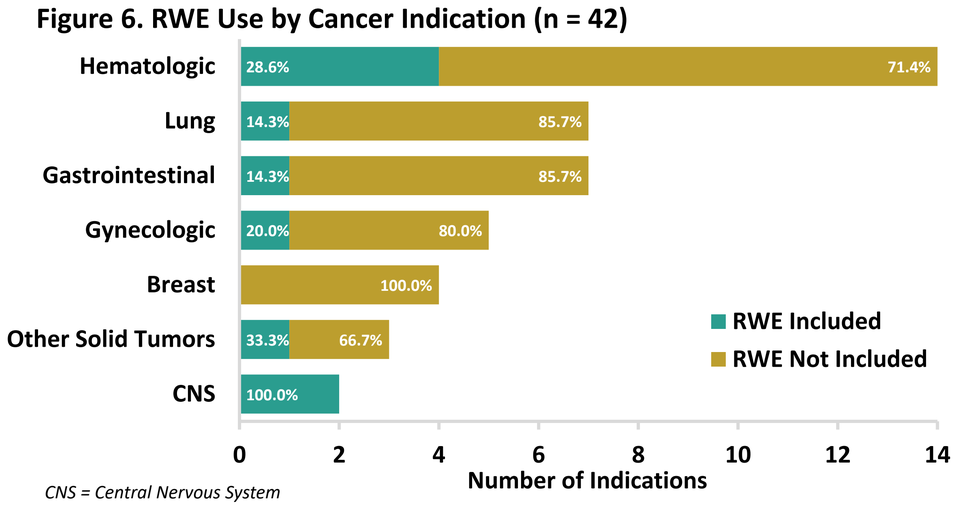



**Figure 6. RWE Use by Cancer Indication (n = 42)**

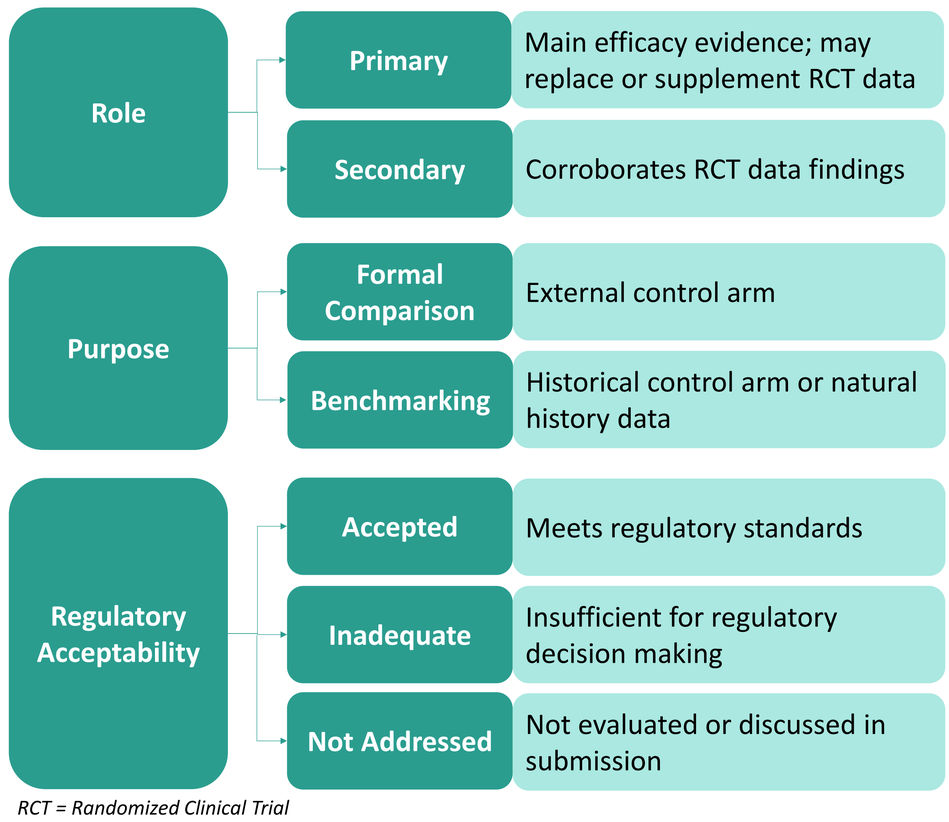



*CNS = Central Nervous System*

## AIM

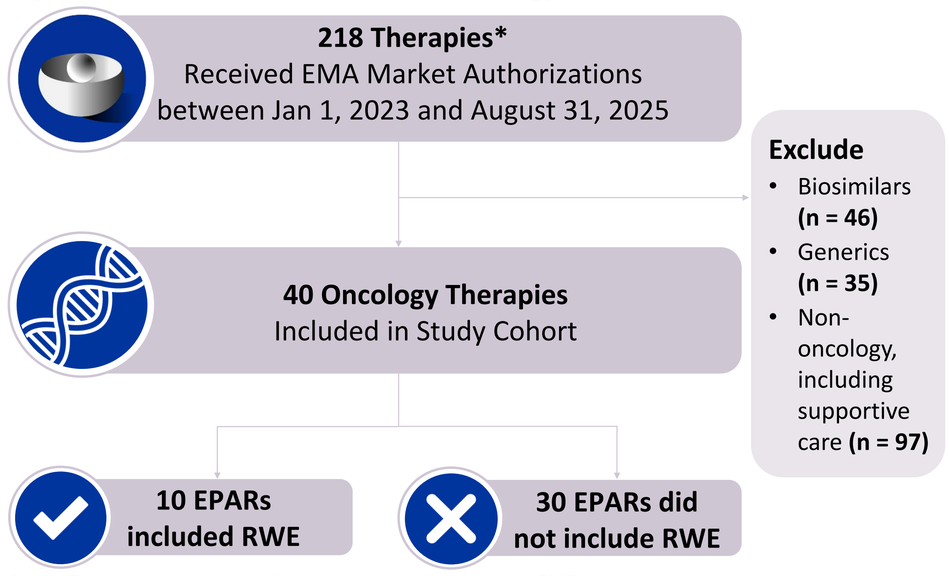
- This study aimed to quantify how RWE has been used to support efficacy evidence in European Medicines Agency (EMA) approvals of oncology medicines.

**Figure 1. Categorization of RWE in EMA Submissions**



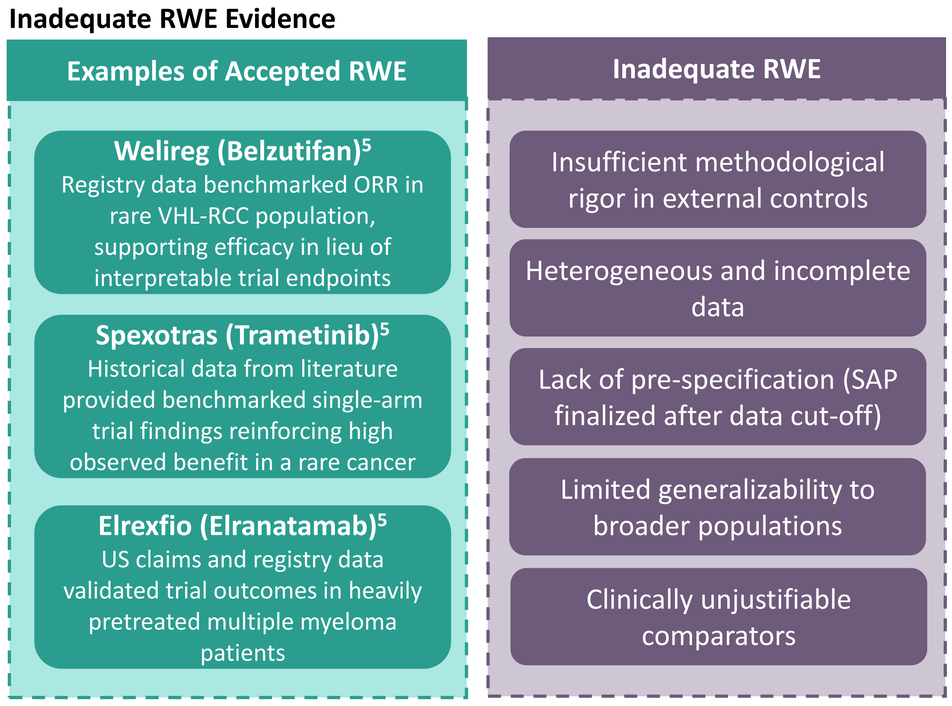

*RCT = Randomized Clinical Trial*

**Figure 2. Flowchart of RWE Use in Oncology EMA Market Authorizations**




*Note: *Two therapies had two indications approved; in both cases, RWE was not included.*
*EMA = European Medicines Agency, EPAR = European Public Assessment Reports*

**Figure 7. Case Studies of RWE Accepted Evidence and Reasons for Inadequate RWE Evidence**




*ORR = Objective Response Rate; RWE = Real-World Evidence, SAP = Statistical Analysis Plan, VHL = on Hippel–Lindau–associated Renal Cell Carcinoma)*

## LIMITATIONS

- The analysis was restricted to publicly available EPARs, rather than the more comprehensive confidential Committee for Medicinal Products for Human Use (CMPH) reports. RWE submitted but not discussed in EPARs may have been missed, potentially underestimating RWE use.
- RWE may have been used in Orphan Maintenance Reports to support orphan drug designation, even if absent from EPARs.
- The study focused solely on RWE supporting efficacy evidence; RWE submitted for safety, unmet need, or other purposes was not systematically captured.

## CONCLUSIONS

- Despite growing emphasis on the importance of RWE, RWE is underused in EMA oncology approvals (25.0%) and only used to support efficacy claims rather than as primary evidence.
- Among orphan drugs for rare cancers, RWE is utilized more frequently (35.7%) but remains underused, even though it could strengthen evidence generation and support regulatory decision-making in this therapeutic area.
- 50.0% RWE applications were judged inadequate, highlighting ongoing implementation and quality issues and the urgent need for clearer, harmonized standards.

## REFERENCES

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