The Use of Real-World Data to Optimize Oncology Drug Development and Access

CDDF Multi-Stakeholder Workshop

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Views of regulators, HTA bodies, industry, clinicians, patients, and researchers on how to increase the use of RWD converged on true value for patients

Cancer is increasingly becoming a rare disease

At the time of licensing, knowledge on true benefit–risk balance is frequently limited, as marketing authorization is often based on a single pivotal trial

RWD/RWE have the potential to transform the drug development process

Early discussion with relevant stakeholders and prospective planning of RWE studies for collection of the right data for the right purpose are important

New data sources without accepted analysis methods and clear purpose will not have a noticeable effect on regulatory decision-making. Seek scientific advice to support qualification procedures for novel methodologies

RWD open up opportunities for patient-centered research

There are limitations to RWD

Upfront planning of RWD together with clinical study protocols substantiated by real-world (RW) epidemiology data would help address these limitations

The empathy for building good RWD repositories is missing

EHR data have the potential to provide research-/regulatory-grade evidence and supplement evidence from clinical trials

From an HTA perspective, cost containment is crucial. Each new treatment product is associated with opportunity cost

EHR, electronic health record; HTA, Health Technology Assessment; RW, real world; RWD, real-world data; RWE, real-world evidence.

Leveraging RWD/RWE to inform oncology drug development and healthcare decision making (Executive Summary)

Precision medicine offers new opportunities for patients; however, it does pose challenges for healthcare decision-making. RCTs may not be feasible in rare cancers (small number of patients, ethical considerations, lack of standard of care, etc.). While RCTs remain the gold standard, RWD can play an important role as sources of supplementary evidence for HA/HTA decision-making. It was recommended that RWD should be considered early and repeatedly during drug development in dialogue with all stakeholders. Additional opportunities for RWD include assessment of optimal treatment approaches in terms of sequencing and combination use, patient access to new therapies, adherence to oral medication, guiding RCT design and post-marketing assessment of safety and effectiveness.

There are multiple sources of RWD. Disease- and product-based registries provide valuable information to help understand the natural history of disease and inform optimal study design. The Cancer Registry of Norway showcased the importance of registries in collecting observational data on outcomes. Inclusion of treatment information in private–regulatory–registry collaboration can be used to generate evidence supporting individual approvals/appraisals. Pan-cancer trials and registries will likely change the paradigm of cancer treatment by identifying common molecular targets across cancers. Trials in the clinical practice setting that rely on RWD include pragmatic trials, randomization within observational studies, or registries. A range of novel, non-RCT analytical methodologies have been proposed (e.g. construction of external control arm, reweighing of RCTs to reflect real-life, replacing RCTs with RWD analysis, etc.). Mitigating bias, data quality and consistency, and privacy issues were highlighted as important common considerations across sources.

Digital health is an exciting and rapidly evolving field. EHRs are emerging as an important source of RWD that can complement RCT evidence through design of hybrid controls. Linking clinical RW patient data with genomic data, creates rich clinico-genomic databases with enormous potential for pan-tumor research and drug development. Wearable technology and mobile devices provide possibilities for patient-centered research and collection of outcomes relevant for the patient (i.e. PROs), through a sustainable and longitudinal route; however, wearable technology is underutilized in oncology.

Despite increased regulatory and HTA focus globally, there is a lack of understanding of the minimum requirements for fit-for-purpose RWD. Clinicians and patients struggle with lack of clear definitions and meaningful endpoints, such as OS and QoL. Overall, there is a need to establish best practices for RW study conduct. Harmonization of data collection approaches (e.g. common data models) and need to identify global solutions beyond the EU or country level were emphasized.

HA, Health Assessment; PRO, patient-reported outcome;
RCT, randomized controlled trial.

The lively discussion at the intersection of disciplines called for innovative approaches in oncology drug development, integrating RWD*

Globally, there is a need for:

- Regulatory/HTA frameworks on the use of RWD/RWE for oncology drug development featuring key considerations for decision-making
- **Harmonization,** ideally led by the European Commission or the ICH. Establishment of best practices for RW study conduct
- **Categorization of evidence** of RWE to help prioritize and plan studies according to the hierarchy of evidence (e.g. establishing the gold standard of RWE)
- **Data quality standards** and strategies to ensure data consistency and completeness (endpoint definitions and assessment, linkage to genomic data, capturing of comorbidities)
- **Guidelines** on data collection and analysis, including (minimum set of) sensitivity analyses and adjustment for confounders
- Efforts to overcome fragmentation of data and access to data through a common data model. One of the fundamental challenges is heterogeneity of data coming from various sources. Cultural differences and privacy issues across the EU present another set of challenges
- A new concept of informed consent may be required

Practical recommendations:

- Clearly specify study objectives and establish a **rigorous statistical analysis plan** aimed at testing and adjusting for bias prior to study initiation, and mitigation of missing data and false positive results
- **Plan RWE studies prospectively** (e.g. pragmatic clinical trials, observational studies), especially if conditional approval is the goal
- Train investigators to ensure adherence to data quality requirements
- Preferably use contemporaneous control (vs historic) in RCTs for rare cancers where external control is the only option
- Ensure early **patient involvement** in study design – patient input on relevant outcomes is critical
- Engage in **ongoing dialogue with regulators and payers** on RWD/RWE requirements
- **Seek scientific advice to support qualification procedures** for novel methodologies to harmonize approaches in the EU
- Provide **better information** to support patients in coping with the disease
- Make an inventory of existing registries to optimize use of existing frameworks both at the national and international level
- Share success stories and learning

*Highlights of breakout sessions. ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use.