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Across the Continuum of Real-World Data Use Cases in Oncology: From Early Signals to Regulatory Decision Making

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Across the Continuum of Real-World Data Use Cases in Oncology: Introduction & Setting the Stage

- Real-World Data (RWD) and Real-World Evidence (RWE) have become popular terminology over the past decade
- While FDA mandates well-controlled interventional trials be the basis for new drug approvals, there is recognition that this is not enough
  - Interventional trials are well controlled studies executed according to specific protocols
  - Protocols dictate a specific patient population; pre-determined monitoring/visit schedules, dosing, & endpoints
  - Typically not representative of what will take happen in real-world clinical settings

Primary Use of RWD & RWE Before 2016

- Historically, FDA has utilized real-world data through post-marketing commitments to monitor safety once a drug is on the market
- Heath-care payers also request/require real-world data from manufacturers to inform their reimbursement and access decisions
  - Payers know products do not typically perform the same way in real-world clinical settings as they do in well-controlled clinical trials
- Health-care providers use real-world data in the practice of medicine, often relying on previous experience with similar patients to inform their decision making, and making retrospective observations through case studies

21st Century Cure Act

- The 21st Century Cures Act (“Cures Act”) was signed into law December 2016
- Cures Act designed to help accelerate product development & bring innovations to patients faster & more efficiently
- In response to Cures Act, FDA created a Framework for evaluating use of RWE to help support
  - Approval of a new indication for a drug already approved, or
  - Satisfy drug post-approval study requirements

Real World Data*

Data relating to patient health status and/or the delivery of health care that are routinely collected from a variety of sources, eg:

- Electronic health record (EHR) data
- Medical claims data
- Product or disease registry data
- Data obtained from digital health technologies
- Data gathered from other sources that can inform on health status, such as questionnaires

Real World Evidence*

Clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD

*US Health & Human Services. Framework for FDA’s Real-World Evidence Program. December 2018

21st Century Cure Act (2)

- Since Cures Act, Center for Drug Evaluation and Research (CDER) at FDA has published 7 Draft Guidance documents concerning use of RWE to support drug and biological products
  - Despite the number of Guidance documents published, examples of RWE used for regulatory purposes are few and far between
- However, there exists a range of study types leveraging RWD which can inform life science companies and regulatory agencies on the use and outcomes of therapies in real-world settings

Across the Continuum of Real-World Data Use Cases

Observational Cohort Study

- A non-interventional design in which specific patient cohorts receiving care during routine medical practice are identified according to pre-determined criteria, and subsequent health outcomes are assessed
- Can be used to evaluate treatment landscape pre-approval or support/ confirm product effectiveness and safety

Use Case Examples

- ***Label expansion:*** Use of EHR data to support a label expansion for a product that is already approved
- ***Registry[1]:*** An organized system that collects clinical & other data in a standardized format for a population defined by a particular disease, condition, or exposure.
- Data from registries can be used to inform design & support the conduct of either clinical trials or observational studies

Hybrid clinical trial or pragmatic study

- A study that includes some elements that more closely resemble routine clinical practice
- Results will be more representative of product effectiveness, rather than pure efficacy

Externally controlled trial[2]

- Outcomes in participants receiving the intervention according to a protocol are compared to outcomes among people external to the trial who did not receive intervention
- External control arm can be a cohort from an earlier time (historical control), or during the same time period (concurrent control) but another setting
- Could be used in the situation of a rare disease where randomized clinical trials are not suitable

[1]FDA. Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry
[2]FDA. Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products

Real-World Data Use Cases in Oncology

- Observational cohort study: RWE confirmation of clinical trial results
- Observational cohort study: RWE for FDA label expansion
- External control arm: RWE for first-line FDA approval

CASE STUDIES

RWE confirmation of clinical trial results

RWE for FDA label expansion

RWE for first-line FDA approval

Confirmed clinical trial results of breast cancer therapy in real-world setting

Approach: Use EHR data to assess HER2+ metastatic breast cancer patients treated in real-world setting with same regimen as in clinical trial

Results: Outcomes in real-world setting and data were replicated and proven similar to clinical trial results

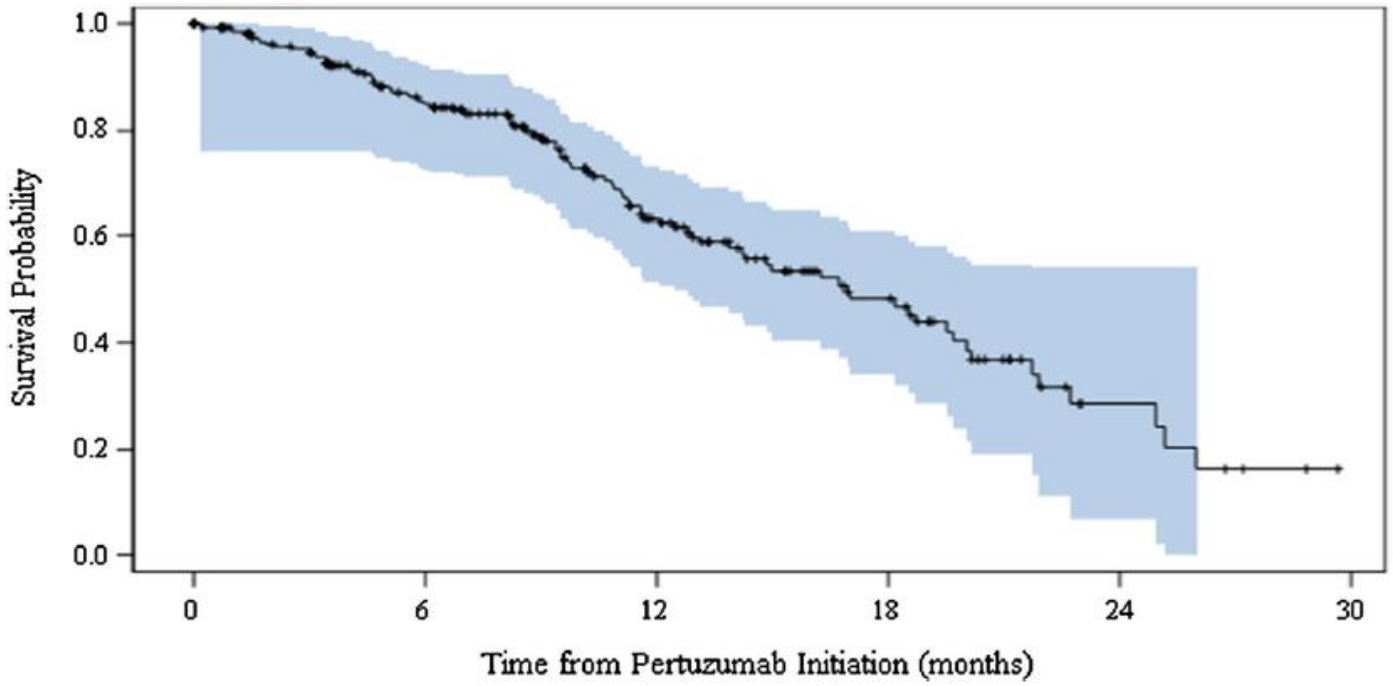
Example of confirmatory RWE study

Drugs - Real World Outcomes (2017) 4:1–7
DOI 10.1007/s40801-016-0102-5

ORIGINAL RESEARCH ARTICLE

HER2-Positive Metastatic Breast Cancer Patients Receiving Pertuzumab in a Community Oncology Practice Setting: Treatment Patterns and Outcomes

Nicholas J. Robert[1] · Hans-Peter Goertz[2] · Pooja Chopra[3] · Xiaolong Jiao[3] · Bongin Yoo[2] · Debra Patt[4] · Vincent Antao[2]



Number of Patients at Risk	221	149	75	35	7	0

Number of Patients	Number of PFS events	Median PFS (95% CI) (months)	Mean PFS (Std Err) (months)	PFS Rate (95% CI) 6-month	9-month	12-month	18-month
221	86	16.9 (13.9-20.1)	16.2 (0.7)	84.3% (78.2-88.7)	78.4% (71.6-83.8)	62.5% (54.2-69.7)	46.7% (37.1-55.7)

Fig. 2 Progression-free survival from initiation of pertuzumab (Kaplan–Meier analysis)—sensitivity analysis population

Breast Cancer Res Treat . 2021 Jun;187(3):903-913.
doi: 10.1007/s10549-021-06137-3. Epub 2021 Mar 1.

Recurrence rates in patients with HER2+ breast cancer who achieved a pathological complete response after neoadjuvant pertuzumab plus trastuzumab followed by adjuvant trastuzumab: a real-world evidence study

Joyce O'Shaughnessy[1,2], Nicholas Robert[3], Srinivas Annavarapu[4], Jie Zhou[3], Jesse Sussell[5], Anna Cheng[5], Anita Fung[5]

Abstract

Conclusions: Consistent with previous studies, this real-world study observed that patients with HER2+ BC showing pCR with nPT remain at risk for IDR, especially with node-positive disease at diagnosis. Alternatives to adjuvant trastuzumab alone, including combined trastuzumab and pertuzumab, should be considered to improve outcomes for initially N+ patients showing pCR with nPT.

CASE STUDIES

RWE confirmation of clinical trial results

RWE for FDA label expansion

RWE for first-line FDA approval

Supported administration of palbociclib in male patients with breast cancer

Approach: Use EHR data to assess effectiveness and safety of administration in palbociclib in male patients with metastatic breast cancer

Results: Outcomes in real-world setting were replicated and proven to be similar to the clinical trial results in women. This product label change expanded the use of palbociclib to male breast cancer patients

CLINICAL CANCER RESEARCH | CCR DRUG UPDATES

FDA Approval Summary: Palbociclib for Male Patients with Metastatic Breast Cancer

Suparna Wedam[1], Lola Fashoyin-Aje[1], Erik Bloomquist[1], Shenghui Tang[1], Rajeshwari Sridhara[1], Kirsten B. Goldberg[2], Marc R. Theoret[1,2], Laleh Amiri-Kordestani[1], Richard Pazdur[1,2], and Julia A. Beaver[1]

ABSTRACT

On April 4, 2019, the FDA approved a supplemental new drug application for palbociclib (IBRANCE), to expand the approved indications in women with hormone receptor (HR)-positive, HER2-negative advanced or metastatic breast cancer (MBC) in combination with an aromatase inhibitor or fulvestrant, to include men. Palbociclib was first approved in 2015 for use in combination with letrozole for the treatment of estrogen receptor–positive, HER2-negative advanced breast cancer as initial endocrine-based therapy in postmenopausal women and subsequently in 2016 in combination with fulvestrant in women with HR-positive, HER2-negative advanced breast cancer with disease progression following endocrine therapy. The current approval was primarily based on the results of the PALOMA-2 and PALOMA-3 trials and, supported by real-world data from electronic health records and insurance claims. To support the safety evaluation in male patients, data from two phase I studies with palbociclib and safety information from the global safety database, were also reviewed. This article summarizes FDA decision-making and data supporting the approval of palbociclib for the treatment of male patients with HR-positive, HER2-negative advanced or MBC.

CASE STUDIES

RWE confirmation of clinical trial results

RWE for FDA label expansion

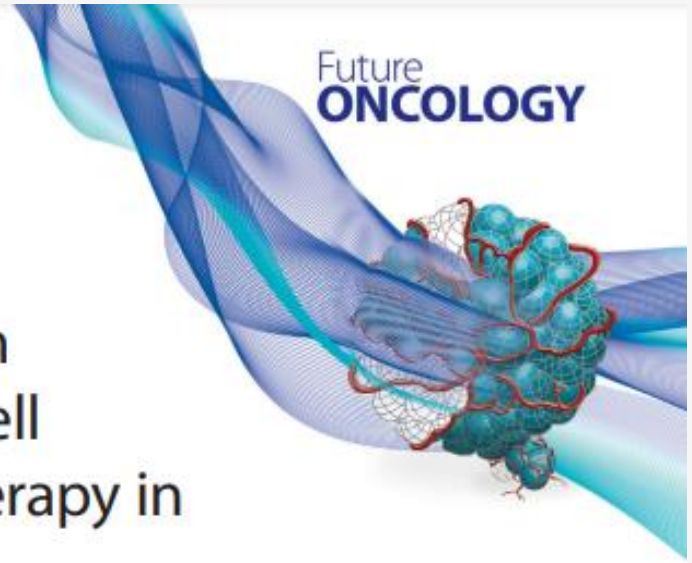
RWE for first-line FDA approval

Supported FDA submission for rare skin cancer indication

Approach: Applied clinical trial eligibility criteria to patients in EHR in real-world setting who served as a historical control

Results: Publication supported first-ever, first-line FDA approval in oncology using retrospective analysis of real-world data

Future ONCOLOGY



RESEARCH ARTICLE

For reprint orders, please contact: reprints@futuremedicine.com

Real-world treatment outcomes in patients with metastatic Merkel cell carcinoma treated with chemotherapy in the USA

C Lance Cowey*[1], Lisa Mahnke[2], Janet Espirito[3], Christoph Helwig[4], Dina Oksen[4] & Murtuza Bharmal[4]

Aim: This retrospective study of patients in the USA with metastatic Merkel cell carcinoma (mMCC) aimed to assess patient responses to second-line and later (2L+) and first-line (1L) chemotherapy. **Patients & methods:** Out of 686 patients with MCC identified in The US Oncology Network, 20 and 67 patients with mMCC qualified for the 2L+ and 1L study, respectively; the primary analysis population was restricted to immunocompetent patients. **Results:** In the 2L+ primary analysis population, objective response rate (ORR) was 28.6%, median duration of response (DOR) was 1.7 months and median progression-free survival was 2.2 months. In the 1L primary analysis population, ORR was 29.4%, median DOR was 6.7 months and median progression-free survival was 4.6 months. **Conclusion:** The low ORR and brief DOR underscore the need for novel therapies.

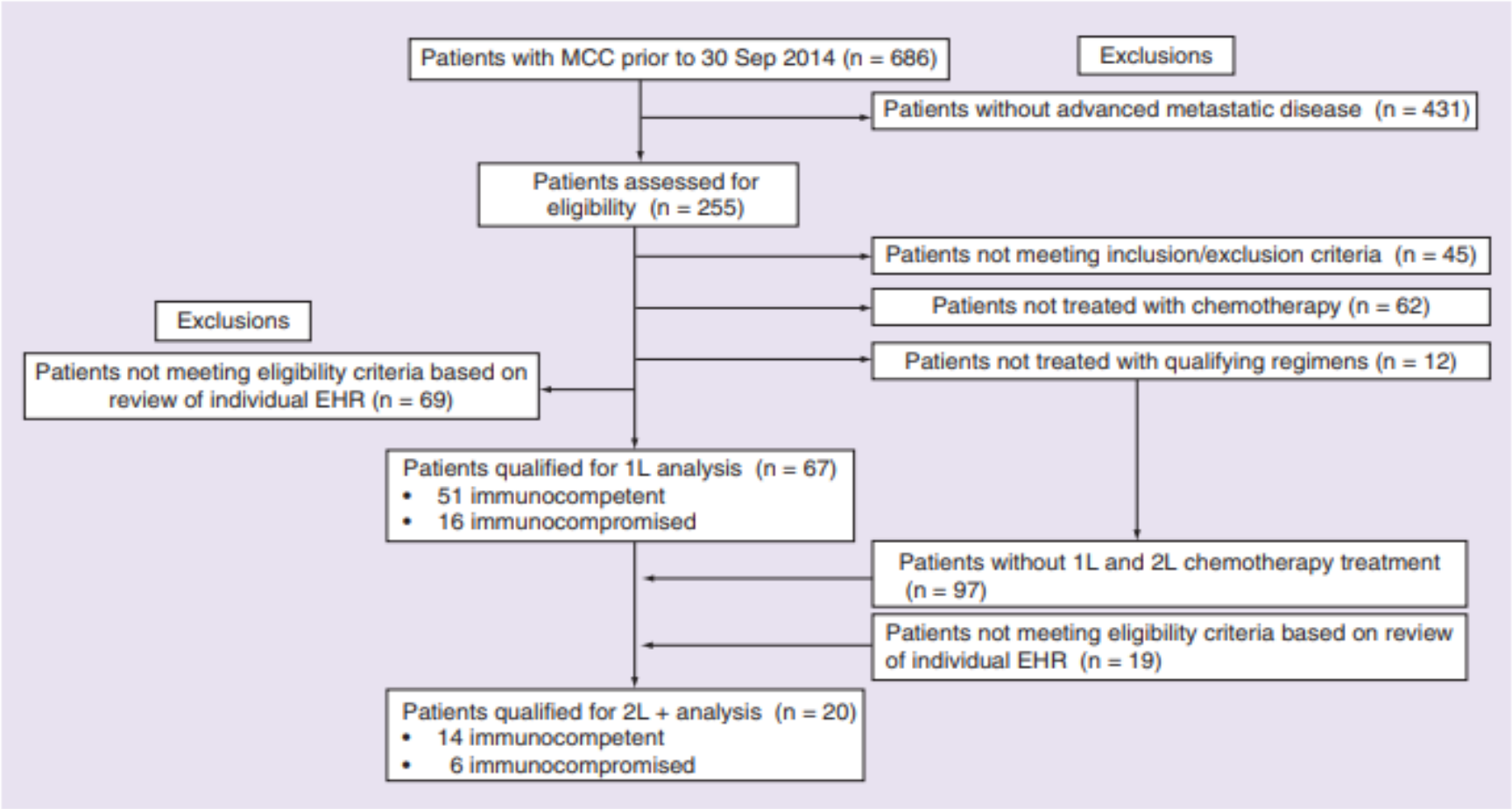


Figure 1. Patient selection.

1L: First line; 2L+: Second line and later; EHR: Electronic health record; MCC: Merkel cell carcinoma; USON: The US Oncology Network.

Conclusions

- Despite the shortage of examples of RWE in regulatory decision making, there are many possible use cases for RWD/RWE in support of product development
  - These range from observational studies to external control arms
- In any of the study designs & use cases, researchers have a responsibility to "ensure the reliability and relevance of the data used"
  - ***Reliability*** includes data accuracy, completeness, provenance, and traceability
  - ***Relevance*** includes the availability of key data elements (exposure, outcomes, covariates) and sufficient numbers of representative patients for the study
- The quality of RWD is only getting better: lots to be excited about!

Thank you