

Real-World Evidence: Leveraging Electronic Health Records to Improve Patient Outcomes

September 2017



Personalized care is shaping today's healthcare industry and fueling the interest of using real-world evidence (RWE) to evaluate and approve individualized treatment options for even the rarest of medical conditions. In December 2016, the bipartisan 21st Century Cures Act, established by President Obama, charged the Food and Drug Administration (FDA) to evaluate the expanded use of RWE, including its potential to support the approval of new drugs as well as expansions for previously approved drugs.¹ The goal of the act was to use RWE to authenticate the value of pharmaceuticals and tailor healthcare decision-making more closely to the characteristics of individual patients for better efficiency and efficacy.

Through McKesson Specialty Health's oncology-focused electronic health record (EHR), iKnowMedSM, supporting treatment and management for 900,000+ patients annually, researchers have been able to analyze data and produce RWE in order to achieve the goal of the 21st Century Cures Act. McKesson Specialty Health partnered with pharmaceutical manufacturer EMD Serono to publish RWE and submit findings to the FDA for an expedited first-line therapy approval for a rare yet aggressive type of skin cancer, metastatic Merkel cell carcinoma (mMCC).

What is RWE?

While the definition of RWE is constantly evolving, it is best described as reflecting data already collected, (i.e., a patient EHR) that researchers review and analyze retrospectively.² Once collected, it can be integrated and analyzed to yield evidence, which in turn, can be used to guide decision-making.

Traditionally, evidence has been derived from randomized clinical trials where patients are recruited and the data collected is closely controlled and monitored. RWE complements clinical trials by reflecting the actual utilization of drugs, devices and other products in clinical practice, outside of randomized controlled trials. Together they provide a more comprehensive view of patient response to medications, a better understanding of disease patterns, greater patient safety information, and the utilization of data for economic analyses in a more varied patient population. In addition to informing clinicians, medical researchers and drug manufacturers, RWE also helps keep policy leaders informed.

Benefits of RWE

The generation of RWE provides numerous benefits. Collectively, RWE:

- Supports more efficient drug development
- Provides insight into disease epidemiology for overall population and important subgroups
- Shapes policy decisions and evidence-based practices by identifying risk factors, medication side effects and contraindications for therapies
- Establishes targets for preventive healthcare



Applications of RWE

RWE supports various phases of the therapeutic innovation process in healthcare, including:

- **Clinical research:** RWE can help expedite the generation of research hypotheses for clinical research or the recruitment of patients for clinical trials.
- **Pre-regulatory approval:** RWE analysis may augment conventional data with data from patients whose diversity reflects real-world practice, resulting in better insight on safe and effective use of innovations
- **Post-approval:** Analysis of patient outcomes from the use of health technology innovations in real-world settings generates further insight on safety and efficacy.³

The Ecosystem of Drug Approvals and Expansions

There are many disease states that have limited options for treatments in today's healthcare arena, and metastatic Merkel cell carcinoma (mMCC) is no exception.

mMCC Statistics

mMCC is a rare, aggressive skin cancer that occurs most frequently in elderly and immunocompromised patients.⁴

- There are approximately 2,500 new cases of Merkel cell carcinoma (MCC) per year in the United States, and the incidence has dramatically increased over the last 20 years.⁵
- MCC typically presents as painless growths that are clinically unremarkable in appearance and are usually found on sun-exposed areas, such as the head and neck.⁶
- Risk factors include ultraviolet light exposure, immunosuppression and advanced age.⁷
- These tumors grow rapidly and tend to metastasize early, leading to a relatively poor prognosis with this aggressive disease.⁴
- The 5-year overall survival rate is 40 percent and the mortality rate of mMCC is greater than that of other skin cancers.⁶

Historically, there was no FDA approved therapy or standard of care. Treatment for mMCC was centered on a chemotherapy primarily based on evidence from observational or case series studies. This changes with the approval of avelumab, which belongs to a medication group known as immune checkpoint inhibitors. These agents "remove the brakes" on the immune system, allowing the body's immune cells to more effectively strike and kill cancer cells. The protein targeted by avelumab, called PD-L1, is overexpressed in many mMCC tumors.⁸

"With iKnowMed, we have access to more patients than you typically find at a comprehensive cancer center," said Jennifer Frytak, senior director of Business Development at McKesson Specialty Health.



Real-World Evidence Case Study

In order to evaluate the benefit of avelumab for treatment of mMCC, there was a need to obtain data on the outcomes of patients with mMCC treated with chemotherapy. This required using the potential of the iKnowMed EHR for outpatient medical histories from community oncology practices across the country. Through iKnowMed, 686 patients with a Merkel cell diagnosis were identified; of which approximately one third of the patients had evidence of metastases. There were 67 of those patients who were determined to meet final eligibility for the study after applying the similar eligibility criteria as per the clinical trial that was being conducted in mMCC.⁶

The study involved collecting existing structured information from iKnowMed patient medical records, and performing a supplemental retrospective review for additional specific information in the progress notes and imaging tests to determine historical responses to previously used treatments. From there, researchers were able to conduct an analysis of the clinical outcomes of historic treatment therapy responses.

These patients' treatments were evaluated systematically by mimicking a measurement tool called RECIST, or Response Evaluation Criteria in Solid Tumors (the same tool used in clinical trials.) In this study, the response rate with second line therapy was 28.6 percent and the median duration of response was 1.7 months. In the avelumab clinical trial, after the median follow-up of 16.4

months in a similar population of patients, the response rate was 33 percent, but the median duration of response was not reached yet with 72 percent of patients having ongoing responses.⁵

"With iKnowMed, we have access to more patients than you typically find at a comprehensive cancer center," said Jennifer Frytak, executive director of Business Development at McKesson Specialty Health. "Identifying eligible participants for a targeted study like this is easier when you can look at patients in the communities or rural areas where a common EHR is used."

"Without the RWE from iKnowMed, this type of study could have taken several years," added Janet Espirito, PharmD, associate director of Outcomes Research at McKesson Specialty Health.

"Instead, we were able to identify eligible patients and complete the study within several months."

Case study results indicated that although responses were observed with chemotherapy, the duration of such responses was brief and was associated with poor overall outcomes in patients with mMCC. These results underscored the need for novel therapeutic approaches, with initial evidence suggesting that immune checkpoint inhibitors have the potential to improve treatment outcomes.



FDA Approval of Avelumab

On March 23, 2017, less than a year after the McKesson Specialty Health research study concluded, the FDA granted accelerated approval to avelumab⁹ for the treatment of patients with mMCC. This was the first FDA-approved product to treat this type of cancer and was even featured on the FDA's Drug Information Soundcast in Clinical Oncology (D.I.S.C.O) on the day of the approval.⁹

"This is the first FDA-approved treatment for the disease," said Nicholas Robert, MD, medical oncologist with The US Oncology Network and medical director for Health Economics and Outcomes Research (HEOR) at McKesson Specialty Health. "The therapy represents an important advancement for our patients with this type of cancer."

"This example of analyzing our EHR and utilizing real-world evidence to help establish a first-line therapy approval is significant," said Dr. Robert. "The growing trend of using RWE, coupled with the FDA allowing such data to be submitted as part of the drug approval process, will ultimately allow patient access to new therapies. It will improve health outcomes more effectively and efficiently, and most importantly, in a more timely manner."

Conclusion

RWE development is shaping up to be the new normal.

"There is a new appreciation for accessing patient records more easily through an EHR such as iKnowMed" said Dr. Robert. "It's exciting to have valid information in electronic records that can provide evidence for either using a drug or expanding the approval of drugs."

In addition, analyzing iKnowMed data allows researchers to discover patterns that may not be visible in smaller sample sizes, helping them to support potential new indications for medicines. As the trend toward individualized medicine continues to shape the healthcare landscape, the demand for individualized treatment options will naturally increase. The ability to quickly gather RWE from EHRs can assist in drug development, ultimately improving patient outcomes.

McKesson Specialty Health

10101 Woodloch Forest
The Woodlands, TX 77382

DataInsights@mckesson.com

www.mckesson.com/heor

©2017 McKesson Specialty Health. All rights reserved.



"This is the first FDA-approved treatment for the disease," said Nicholas Robert, MD, medical oncologist with The US Oncology Network and medical director for Health Economics and Outcomes Research (HEOR) at McKesson Specialty Health "The therapy represents an important advancement for our patients with this type of cancer."



References:

1. Hills B, Zegarelli B. 21st Century Cures Act Requires FDA to Expand the Role of Real World Evidence. Dec. 19, 2016. <https://www.healthlawpolicymatters.com/2016/12/19/21st-century-cures-act-requires-fda-to-expand-the-role-of-rwe/>
2. Califf R, Sherman R. What We Mean When We Talk About Data. Dec. 10, 2015. <https://blogs.fda.gov/fdavoices/index.php/tag/real-world-evidence/>
3. Hubbard T, Paradis R. Real-world evidence: a new era for health care innovation. Network for Excellence in Health Innovation. 2. (2015).
4. Lemos BD, Storer BE, Iyer JG, et al. Pathologic nodal evaluation improves prognostic accuracy in Merkel cell carcinoma: analysis of 5823 cases as the basis of the first consensus staging system. J. Am. Acad. Dermatol. 63(5), 751-761 (2010).
5. Kaufman HL, Russell JS, Hamid O, et al. Durable responses to avelumab (anti-PD-L1) in patients with Merkel cell carcinoma progressed after chemotherapy: 1-year efficacy update. American Association for Cancer Research Annual Meeting. (2017).
6. Cowey L, Mahnke L, Espirito J, et al. Real-world outcomes in patients with metastatic Merkel cell carcinoma treated with chemotherapy in the USA. Future Oncology. 1-11. (2017).
7. Schadendorf D, Lebbé C, Hausen A, et al. Merkel cell carcinoma: Epidemiology, prognosis, therapy and unmet medical needs. European Journal of Cancer. 53-69. (2017).
8. Kaufman HL, Russell J, Hamid O, et al. Avelumab in patients with chemotherapy-refractory metastatic Merkel cell carcinoma: a multicenter, single-group, open-label, phase 2 trial. Lancet Oncology. 1-2. (2016).
9. <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm559876.htm>