ONCODAILY MEDICAL JOURNAL

Article

Harnessing Real-World Evidence to Support Precision Oncology

Authors: C. Benedikt Westphalen

Corresponding author: Christoph_Benedikt.Westphalen@med.uni-muenchen.de

Association: Department of Medicine III, University Hospital, LMU Munich, Munich, Germany; German Cancer Consortium (DKTK), Partner Site Munich, Munich, Germany; Comprehensive Cancer Center (CCC Munich LMU), LMU University Hospital Munich, Munich, Germany

Published: September 2, 2025

doi.org/10.69690/ODMJ-019-0829-4588

ONCODAILY MEDICAL JOURNAL

Article

Harnessing Real-World Evidence to Support Precision Oncology

Authors: C. Benedikt Westphalen

Corresponding author: Christoph_Benedikt.Westphalen@med.uni-muenchen.de

Association: Department of Medicine III, University Hospital, LMU Munich, Munich, Germany; German Cancer Consortium (DKTK), Partner Site Munich, Munich, Germany; Comprehensive Cancer Center (CCC Munich LMU), LMU University Hospital Munich, Munich, Germany

Published: September 2, 2025

ABSTRACT

Despite substantial progress in biomarker-driven therapeutic strategies, precision oncology continues to face significant evidence generation challenges, particularly within molecular tumor boards (MTBs) and off-label treatment contexts. Real-world evidence (RWE) provides a vital complementary source to traditional clinical trials by capturing clinical outcomes directly from routine healthcare settings. Major initiatives like PRIME-ROSE, the Drug Rediscovery Protocol (DRUP), and the AACR Project GENIE demonstrate the potential of RWE in clinical decision-making, regulatory processes, and policy development. Nevertheless, substantial hurdles in data standardization, interpretation, and regulatory recognition remain. Systematic policy frameworks, international collaboration, and rigorous validation are crucial to enhancing RWE's integration, thus fostering sustainable advancements in precision oncology.

INTRODUCTION

As highlight by recent recommendations by the American Society of Clinical Oncology (ASCO) and the European Society of Clinical Oncology (ESMO), comprehensive genomic profiling (CGP) via next-generation sequencing (NGS) for advanced cancers can now be considered standard of care across a broad spectrum of malignancies[1,2]. However, beyond standard of care, particularly within molecular tumor board (MTB) settings and for off-label therapeutic applications, the individualized and exploratory nature of treatments presents significant limitations for traditional randomized controlled trials (RCTs). Patient populations in these scenarios are often heterogeneous and characterized by rare genomic alterations, complicating traditional clinical trial approaches[3].

These intrinsic limitations underscore the necessity for alternative evidence generation methods. Real-world evidence (RWE), derived from routine clinical care, thus provides a critical means to bridge the evidence gap, reflecting practical patient management complexities and outcomes. Comprehensive RWE integration is essential for addressing unanswered clinical questions in precision oncology[4].

USE REAL-WORLD EVIDENCE

Real-world data (RWD) includes various patient-related sources such as electronic health records (EHRs), cancer registries, administrative claims, patient-reported outcomes (PROs), and genomic

information obtained from MTBs[3,4]. In the future, structured analyses of RWD might yield robust RWE, ideally informing clinical decisions, regulatory approvals, and reimbursement strategies, particularly when traditional clinical trial evidence is unavailable or insufficient.

European initiatives, such as PRIME-ROSE, aim to utilize synthetic control arms derived from RWE, informing regulatory processes and reimbursement discussions, particularly in rare or molecularly defined cancers[5]. The Drug Rediscovery Protocol (DRUP) in the Netherlands systematically assesses off-label drug use guided by genomic profiling, exemplifying the clinical utility and practicality of RWE in precision oncology[6,7].

Finally, the AACR Project GENIE, a global consortium pooling genomic and clinical data from over 110,000 tumor samples, significantly enhances genomic biomarker validation, clinical trial enrollment predictions, and the discovery of genomic drivers, particularly in rare cancers. This large-scale international collaboration illustrates RWE's transformative role in global precision oncology efforts[8,9].

CHALLENGES IN DATA STANDARDIZATION AND INTERPRETATION

Effective utilization of RWE faces significant challenges due to the variability in genomic data generation, analytical methodologies, and clinical interpretations across institutions. Diverse genomic assays, inconsistent documentation practices, and varied molecular interpretations complicate reliable data aggregation and analysis. Thus, ensuring rigorous quality assurance through standardized and validated procedures is essential.

Addressing these challenges requires harmonized guidelines such as those by the ESMO Precision Oncology Working Group, which advocates standardized genomic assay protocols, consistent use of clinical actionability scales like the ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT)[10], and structured documentation standards within MTBs[11]. These measures significantly enhance data comparability, reliability, and utility, crucial for meaningful clinical interpretation and implementation. Operational challenges identified in MTBs include frequency of meetings, clinician participation, streamlined workflows, and clinician education to improve genomic data interpretation and integration into clinical practice. Addressing these operational and educational aspects is essential for fully realizing precision oncology's potential[11,12,13].

FUTURE PERSPECTIVES

Future developments in precision oncology will increasingly depend on integrating multimodal biomarker data, encompassing genomic, transcriptomic, proteomic, epigenomic, and immune profiling. Combined with robust RWE frameworks, this integrative approach promises significant advancements in patient stratification, clinical decision-making, and personalized treatment strategies, markedly refining therapeutic precision.

Global real-world evidence registries, exemplified by the AACR GENIE initiative, capturing diverse patient populations and clinical outcomes, are critical. These registries will address gaps left by traditional trials, improving generalizability and supporting regulatory acceptance of RWE as complementary evidence, especially for rare diseases and genomic subsets.

Regulatory frameworks must evolve systematically to integrate RWE, requiring clear, harmonized guidelines recognizing RWE's clinical value. Policy-level adaptations and international collaborations are necessary to facilitate seamless integration into clinical practice, regulatory decisions, and health policy.

CONCLUSION

Real-world evidence is essential for sustainable advancements in precision oncology, particularly in scenarios inadequately addressed by traditional clinical trials. Rigorous standardization, comprehensive validation, and multimodal biomarker data integration, supported by global registries and collaborative initiatives, are fundamental. Multi-stakeholder collaboration among clinicians, regulators, academia, and industry is imperative to overcoming barriers, optimizing RWE utilization, and maximizing patient benefits, thereby fully realizing precision oncology's potential.

Competing Interests: C. Benedikt Westphalen has received honoraria from AstraZeneca, Amgen, Bayer, BMS, Chugai, Celgene, Falk, GSK, Lilly, MSD, Merck, Janssen, Ipsen, QuiP GmbH, Roche, Servier, SIRTeX, and Taiho; served on advisory boards for AstraZeneca, Bayer, BMS, Celgene, Janssen, MSD, Servier, Shire/Baxalta, Rafael Pharmaceuticals, RedHill, and Roche; received travel support from AstraZeneca, Bayer, Celgene, Janssen, MSD, RedHill, Roche, Servier, and Taiho; and research grants (institutional) from Roche. He serves as faculty for the European Society of Medical Oncology (ESMO), Deutsche Krebshilfe (DKH), and Arbeitsgemeinschaft Internistische Onkologie (AIO); is a member of the EU Commission expert group: Mission Board for Cancer; and a member of the BFTR steering committee: Strategiekreis Dekade gegen Krebs.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

LICENSE

REFERENCES

1 . *Mosele MF, Westphalen CB, Stenzinger A, Barlesi F, Bayle A, Bièche I, et al. Recommendations for the use of next-generation sequencing (NGS) for patients with advanced cancer in 2024: a report from the ESMO Precision Medicine Working Group. Ann Oncol. 2024 Jul;35(7):588-606. doi: 10.1016/j.annonc.2024.04.005. Epub 2024 May 27. Erratum in: Ann Oncol. 2025 Apr;36(4):472. doi: 10.1016/j.annonc.2024.11.010.*

2 . *Chakravarty D, Johnson A, Sklar J, Lindeman NI, Moore K, Ganesan S, et al. Somatic genomic testing in patients with metastatic or advanced cancer: ASCO provisional clinical opinion. J Clin Oncol. 2022 Apr 10;40(11):1231-58. doi: 10.1200/JCO.21.02767. Epub 2022 Feb 17. Erratum in: J Clin Oncol. 2022 Jun 20;40(18):2068. doi: 10.1200/JCO.22.01144.*

3 . *Moscow JA, Fojo T, Schilsky RL. The evidence framework for precision cancer medicine. Nat Rev Clin Oncol. 2018 Mar;15(3):183-92. doi: 10.1038/nrclinonc.2017.186. Epub 2017 Dec 19.*

4 . *Luo J, Solit DB. Leveraging real-world data to advance biomarker discovery and precision oncology. Cancer Cell. 2025 Apr 14;43(4):606-10. doi: 10.1016/j.ccell.2025.03.012. Epub 2025 Mar 27.*

5 . *Christopoulos P, Schlenk R, Kazdal D, Blasi M, Lennerz J, Shah R, et al. Real-world data for precision cancer medicine – A European perspective. Genes Chromosomes Cancer. 2023 Sep;62(9):557-63. doi: 10.1002/gcc.23135. Epub 2023 Mar 9.*

6 . *Hoes LR, van Berge Henegouwen JM, van der Wijngaart H, Zeverijn LJ, van der Velden DL, van de Haar J, et al. Patients with rare cancers in the Drug Rediscovery Protocol (DRUP) benefit from genomics-guided treatment. Clin Cancer Res. 2022 Apr 1;28(7):1402-11. doi: 10.1158/1078-0432.CCR-21-3752.*

7 . *van der Velden DL, Hoes LR, van der Wijngaart H, van Berge Henegouwen JM, van Werkhoven E, Roepman P, et al. The Drug Rediscovery protocol facilitates the expanded use of existing anticancer drugs. Nature. 2019 Oct;574(7776):127-31. doi: 10.1038/s41586-019-1600-x. Epub 2019 Sep 30.*

8 . *Pugh TJ, Bell JL, Bruce JP, Doherty GJ, Galvin M, Green MF, et al. AACR Project GENIE: 100,000 cases and beyond. Cancer Discov. 2022 Sep 2;12(9):2044-57. doi: 10.1158/2159-8290.CD-21-1547.*

9 . *AACR Project GENIE Consortium. AACR Project GENIE: Powering precision medicine through an international consortium. Cancer Discov. 2017 Aug;7(8):818-31. doi: 10.1158/2159-8290.CD-17-0151. Epub 2017 Jun 1.*

10 . *Mateo J, Chakravarty D, Dienstmann R, Jezdic S, Gonzalez-Perez A, Lopez-Bigas N, et al. A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT). Ann Oncol. 2018 Sep 1;29(9):1895-902. doi: 10.1093/annonc/mdy263.*

11 . *Westphalen CB, Boscolo Bielo L, Aftimos P, Beltran H, Benary M, Chakravarty D, et al. ESMO Precision Oncology Working Group recommendations on the structure and quality indicators for molecular tumour boards in clinical practice. Ann Oncol. 2025 Jun;36(6):614-25. doi:10.1016/j.annonc.2025.02.009. Epub 2025 Apr 6.*

12 . *Casolino R, Beer PA, Chakravarty D, Davis MB, Malapelle U, Mazzarella L, et al. Interpreting and integrating genomic test results in clinical cancer care: Overview and practical guidance. CA Cancer J Clin. 2024 May-Jun;74(3):264-85. doi: 10.3322/caac.21825. Epub 2024 Jan 4.*

13 . *Mateo J, Steuten L, Aftimos P, André F, Davies M, Garralda E, et al. Delivering precision oncology to*

patients with cancer. Nat Med. 2022 Apr;28(4):658-65. doi: 10.1038/s41591-022-01717-2. Epub 2022 Apr 19.