A Process for the Emulation of Comparative Oncology Trials with Real-world Evidence (ENCORE)

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Abstract

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Background

With 21% of all drug approvals, oncology was the disease area with the most FDA drug approvals in 2023.[1] Although randomized controlled trials (RCTs) are considered the gold standard, decision-makers increasingly rely on real-world evidence (RWE) generated from routine-care health data such as electronic health records (EHR) to evaluate the comparative safety and effectiveness of novel cancer therapies.**purpura2022role?** Especially in the field of precision oncology, RWE has many essential use cases and plays a critical role in complementing evidence like in patient populations that are underrepresented in RCTs, to construct external control arms in single-arm trials where active recruitment may not be feasible or in drug/biomarker discovery and label extensions among pan-tumor populations that harbor specific genomic signatures. However, to draw causal inferences from such comparisons in non-randomized data, it is pivotal that endpoints and prognostic information can be measured reliably and at scale, which remains a significant challenge in oncological comparative effectiveness research (CER).

...[2]

Methods

Systematic process for understanding the validity of RWE for oncology submissions

Discussion

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Conclusions

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References

1. Senior M: Fresh from the biotech pipeline: Record-breaking FDA approvals. Nature Biotechnology, 2024

2. Weberpals J, Raman SR, Shaw PA, et al: Smdi: An r package to perform structural missing data investigations on partially observed confounders in real-world evidence studies [Internet]. JAMIA Open 7:ooae008, 2024Available from: https://doi.org/10.1093/jamiaopen/ooae008

Table 1: Criteria .

Criteria	Definition
Interventional study	The nature of the investigation or investigational use for which clinical study information is
Randomized allocation	The method by which participants are assigned to arms in a clinical trial.
Interventional study model	The strategy for assigning interventions to participants.
Sponsor/source	The entity (for example, corporation or agency) that initiates the study
Study start date	The estimated date on which the clinical study will be open for recruitment of participants,
Primary purpose	The main objective of the intervention(s) being evaluated by the clinical trial.
Primary outcome	A description of each primary outcome measure (or for observational studies, specific key me
Overall Recruitment Status	The recruitment status for the clinical study as a whole, based upon the status of the indivi
Feasibility and clinical relevance	Are all key variables available to emulate the clinical trial at hand and is the clinical trial co

Tables

Table 2: Tentative list of randomized controlled trials (RCTs) considered for emulation.

NCTID	Acronym	Clinical setting
Non-small cell lung cancer		
NCT02296125	FLAURA	Advanced/metastatic EGFRm+
NCT01673867	CheckMate057	Metastatic non-squamous
NCT03215706	CheckMate9LA	Metastatic
Breast cancer		
NCT01740427	PALOMA-2	Advanced postmenopausal ER-positive and HER2-negative
NCT02819518	KEYNOTE-355	Locally recurrent inoperable or metastatic triple negative
NCT01772472	KATHERINE	HER2-positive
Colorectal cancer		
NCT04737187	SUNLIGHT	Refractory metastatic
NCT01374425	MAVERICC	Metastatic
NCT02563002	KEYNOTE-177	Metastatic microsatellite instability-high (MSI-H) or mismatch repa
Multiple Myeloma		
NCT01568866	ENDEAVOR	Relapsing or progressing disease
NCT02252172	MAIA	Newly diagnosed
NCT01239797	ELOQUENT - 2	Relapsed or refractory

Figures

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Figure 1: Systematic process to understand effectiveness claims of oncology trials using real-world evide