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Conceptualization of core clinico-molecular variables for registries enrolling patients diagnosed with a solid tumor and profiled with next-generation sequencing (NGS)

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Summary

Our list of core variables provides viable guidance for conducting research- and regulatory-grade real-world precision oncology studies, and facilitating standardized data collection and thus pooling from various datasets

Poster https://bit.ly/3HrCZP5

Supplement https://bit.ly/3Jh0a0A

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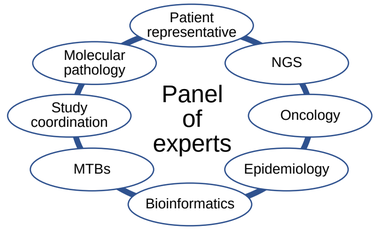
Introduction

- In precision oncology, there is a need for robust linked and longitudinal genomic and clinical data, via purposeful data collection along the entire patient journey.
- To support epidemiologic research, we developed WAYFIND-R, a global registry that enrolls patients diagnosed with a solid tumor and profiled with NGS (NCT04529122; AACR 2022 Abstract 4094).
- Standardizing variables of interest and decision-making processes along the patient journey is critical for data connectivity and understanding their clinical relevance.
- We propose a framework for identifying the core variables that are most critical for oncology-based real-world studies and registries in precision oncology.

Methods



Draft variables list compiled by panel

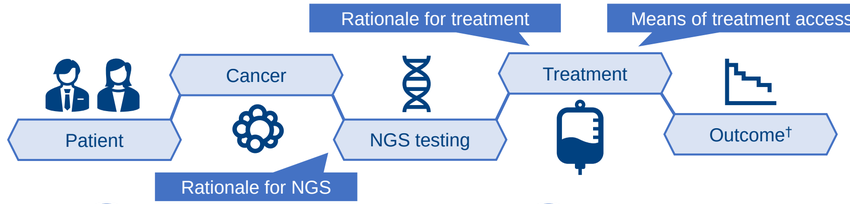
Variables categorized by clinical importance

Aligned with EMA registry guidelines (October 2021)[1] and with internationally harmonized coding dictionaries

Results

- The variables list was created to describe a patient's cancer history and journey effectively (Figure 1); to allow conduct of comparative effectiveness studies and comparisons with clinical trials; and to represent key risk factors or important confounders for prognosis or statistical analysis adjustments.
- The draft list comprised ~500 variables and was reconciled to ~150 (supplement); highest priority was given to patient information (e.g. consent, demographics, risk and prognostic factors, dates of cancer-related events), cancer details (e.g. disease ontology, staging, metastases), NGS testing (e.g. actionable alterations, genomic signatures), and treatment characteristics/outcomes (e.g. treatment information, response, progression, death) (Figure 2).

Figure 1. The variables capture the entire patient journey and decision-making process.*



Patient	Cancer	NGS testing	Tumor/treatment characteristics	Outcomes
All significant dates (e.g. ICF signature, visits, assessments)	All significant dates (e.g. diagnosis, staging)	All significant dates (e.g. biopsy, results)	All significant dates (e.g. start, stop)	All significant dates (e.g. progression, response assessment, death)
Site characteristics	Cancer diagnosis (e.g. topography and morphology)	Actionable alterations	Metastatic status (e.g. localized, regional, distant)	Clinical means of assessing progression
Sex, family history	Cancer stage and staging system used	Types of alterations and corresponding details (e.g. ctDNA change, genomic position, CNV)	Presence of CNS metastases	Clinical response (e.g. PD, SD)
Reasons for visit	Group staging (e.g. I, II, III)	Genomic signatures (e.g. HRD, MSI, TMB)	Treatments (e.g. drug name, line of therapy, regimen, response)	Informal or formal criteria used (e.g. RECIST version 1.1)
Relevant cancer-related biomarkers (e.g. PD-L1, HER2)			Therapies (e.g. radiotherapy, surgery)	Reason for treatment discontinuation
Performance status				
Major risk factors (e.g. alcohol use, smoking)				

Figure 2. Mandatory variables to be collected along the patient journey.

- These variables are most critical because they enable the natural history of the disease across the entire patient journey to be captured (with longitudinal data collection), they allow conduct of comparative effectiveness studies by creating control groups using matched variables (e.g. age, sex, ECOG PS) from, for example, single-arm trials, can be used to assess how study populations and clinical trial results are translatable in the real world, and consider critical risk factors that may bias analyses (e.g. smoking in lung cancer).
- Moderate-to-lower priority variables comprised NGS (e.g. technical, quality criteria), familial cancer history, adherence to MTB recommendations, and primary cause of death (supplement).

Conclusions: how our core variables will aid research-/regulatory-grade real-world precision oncology studies

1. **Harmonizing data collection efforts to bring synergy and dataset connectivity**
2. **Ensuring streamlined data collection for oncology**
3. **Leading RWD collection by example, per all relevant recommendations**

*These data are usually not captured linearly but data collection tools are structured to enable data analyses to recreate this journey, using key event dates; †Until death or loss of follow-up. **Abbreviations:** CNS, central nervous system; CNV, copy number variant; ctDNA, circulating tumor DNA; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EMA, European Medicines Agency; HRD, homologous recombination repair deficiency; ICF, informed consent form; MSI, microsatellite instability; MTB, molecular tumor board; NGS, next-generation sequencing; PD, progressive disease; PD-L1, programmed cell death-ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors; RWD, real-world data; SD, stable disease; TMB, tumor mutational burden.

References: 1. EMA. Guideline on registry-based studies. October 22, 2021.

Acknowledgments
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Conflicts of interest
RD is an employee of Oncoclínicas Grupo, has business ownership in Trialing, has received a grant/contract from Merck, has performed a consulting/advisory role for Roche and Boehringer Ingelheim, and has attended speakers' bureaus for Roche, Ipsen, Sanofi, MSD Oncology, Servier, Amgen, and Libbs. Please refer to the Supplement for all author conflicts of interest. This analysis was sponsored by F. Hoffmann-La Roche Ltd.