Paper Summary

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Title: A framework for genomic biomarker actionability and its use in clinical decision making

Authors: Smruti J. Vidwans, Michelle L. Turski, Filip Janku, Ignacio Garrido-Laguna, Javier Munoz, Richa

DOI: 10.18632/oncoscience.104

Year: 2014

Publication Type: Journal

Discipline/Domain: Oncology, Genomics

Subdomain/Topic: Biomarker actionability, targeted cancer therapy

Eligibility: Eligible

Overall Relevance Score: 95

Operationalization Score: 90

Contains Definition of Actionability: Yes

Contains Systematic Features/Dimensions: Yes

Contains Explainability: Yes

Contains Interpretability: Yes

Contains Framework/Model: Yes

Operationalization Present: Yes

Primary Methodology: Conceptual framework

Study Context: Genomic biomarkers in cancer diagnosis and treatment planning

Geographic/Institutional Context: USA, Spain (multi-institutional collaboration)

Target Users/Stakeholders: Oncologists, molecular pathologists, clinical researchers

Primary Contribution Type: Conceptual framework and practical categorization

CL: Yes

CR: Yes

FE: Yes

TI: Partial

EX: Yes

GA: Yes

Reason if Not Eligible: N/A

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Title:

A framework for genomic biomarker actionability and its use in clinical decision making

Authors:

Smruti J. Vidwans, Michelle L. Turski, Filip Janku, Ignacio Garrido-Laguna, Javier Munoz, Richard Schwa

DOI:

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Year:

2014

Publication Type:

Journal

Discipline/Domain:

Oncology, Genomics

Subdomain/Topic:

Biomarker actionability, targeted cancer therapy

Contextual Background:

The paper addresses the growing use of molecular diagnostics in oncology, particularly genomic biomark

Geographic/Institutional Context:

USA and Spain, involving institutions like MD Anderson Cancer Center, University of California San Dieg

Target Users/Stakeholders:

Oncologists, molecular pathologists, clinical researchers, trial designers.

Primary Methodology:

Conceptual framework development.

Primary Contribution Type:

Proposal of a structured framework for determining biomarker actionability in cancer.

General Summary of the Paper

The authors present a comprehensive framework for evaluating the actionability of genomic biomarkers i

Eligibility

Eligible for inclusion: **Yes**

How Actionability is Understood

Actionability refers to a biomarker being oncogenic and/or differentially expressed in tumor cells such tha

> “A biomarker is actionable if it is oncogenic and/or differentially expressed on tumor cells, and a treatme

> “A gene may be considered theoretically actionable if it has a basis of actionability….” (p. 614)

What Makes Something Actionable

- Functional role in driving malignancy.
- Targetability by approved or investigational drugs.
- Involvement in targetable pathways (directly or indirectly).
- Homology to other actionable biomarkers.
- Differential expression enabling targeted delivery.
- Supportive evidence from clinical guidelines, clinical/pre-clinical studies, or analogous genetic diseases.

How Actionability is Achieved / Operationalized

- **Framework/Approach Name(s):** Basis of Actionability & Rationale for Actionability.
- **Methods/Levers:** Categorization based on functional role, drug targetability, pathway involvement, ho
- **Operational Steps / Workflow:** Identify biomarker → Determine category (basis) → Map rationale (ev
- **Data & Measures:** Clinical trial data, pre-clinical evidence, treatment guidelines, registry data, geneti
- **Implementation Context:** Personalized oncology decision-making.

> “The framework also includes a rationale for actionability in which strength of evidence for a biomarker

> “A biomarker may be considered actionable if it is a direct target of one or more approved drugs…” (p. 6

Dimensions and Attributes of Actionability (Authors’ Perspective)

- **CL (Clarity):** Yes — clearly defined biomarker-drug relationships are necessary for actionability.

> “…standards exist that outline treatments for individuals harboring aberrations in the biomarker…” (p. 6

- **CR (Contextual Relevance):** Yes — considers histology-specific and histology-agnostic evidence.

> “…extrapolating predictive data from the tumor site of origin with the highest strength of evidence to a d

- **FE (Feasibility):** Yes — includes evidence-based categories to guide clinical applicability.
- **TI (Timeliness):** Partial — recognizes rapid adoption of NGS and challenges in matching treatments
- **EX (Explainability):** Yes — detailed rationale for why a biomarker is actionable.
- **GA (Goal Alignment):** Yes — aligns biomarker actionability with optimal patient outcomes.

Other Dimensions Named by Authors:

- Strength of evidence level.
- Functional role versus passenger status.

Theoretical or Conceptual Foundations

- Companion diagnostics in oncology.
- NCCN and FDA treatment guideline frameworks.
- Molecular oncology concepts like oncogenic drivers, passengers, and pathway targeting.

Indicators or Metrics for Actionability

- Approval status of drugs with companion diagnostics.

- Inclusion in treatment guidelines.

- Evidence from clinical trials, pre-clinical studies, or genetic disease contexts.

Barriers and Enablers to Actionability

- **Barriers:** Conflicting data across histologies, novel variants of unknown significance, tumor genomic

- **Enablers:** Systems biology approaches, multi-omic profiling, histology-agnostic trial designs.

Relation to Existing Literature

Builds on existing oncology guidelines and targeted therapy concepts but integrates them into a unified fr

Summary

This paper offers a structured framework for assessing genomic biomarker actionability in cancer therapy

Scores

- **Overall Relevance Score:** 95 — Offers a direct, explicit definition of actionability, detailed categoriza

- **Operationalization Score:** 90 — Provides a clear workflow and categories for applying actionability a

Supporting Quotes from th