Paper Summary

<!--META_START-->

Title: A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale

Authors: Mateo, J.; Chakravarty, D.; Dienstmann, R.; Jezdic, S.; Gonzalez-Perez, A.; Lopez-Bigas, N.; N

DOI: 10.1093/annonc/mdy263

Year: 2018

Publication Type: Journal

Discipline/Domain: Oncology / Precision Medicine

Subdomain/Topic: Genomic targets prioritization, cancer biomarkers, targeted therapy classification

Eligibility: Eligible

Overall Relevance Score: 95

Operationalization Score: 95

Contains Definition of Actionability: Yes

Contains Systematic Features/Dimensions: Yes

Contains Explainability: Partial

Contains Interpretability: Partial

Contains Framework/Model: Yes (ESCAT)

Operationalization Present: Yes

Primary Methodology: Conceptual framework development and consensus guidelines

Study Context: Classification and prioritization of molecular targets for cancer treatment based on clinical

Geographic/Institutional Context: Multinational collaboration (Europe, USA, Canada) led by ESMO

Target Users/Stakeholders: Oncologists, molecular tumor boards, clinical researchers, drug developers, r

Primary Contribution Type: Conceptual framework and evidence-based classification system

CL: Yes

CR: Yes

FE: Yes

TI: No

EX: Partial

GA: Yes

Reason if Not Eligible: n/a

<!--META_END-->

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A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for C

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Year:

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Publication Type:

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Discipline/Domain:

Oncology / Precision Medicine

Subdomain/Topic:

Genomic targets prioritization, cancer biomarkers, targeted therapy classification

Contextual Background:

The paper addresses the lack of harmonization in defining and prioritizing “actionable” genomic alteration

Geographic/Institutional Context:

Led by the European Society for Medical Oncology (ESMO) with contributors from multiple global instituti

Target Users/Stakeholders:

Oncologists, clinical researchers, molecular tumor boards, drug developers, regulatory agencies.

Primary Methodology:

Conceptual framework development via expert consensus and literature synthesis.

Primary Contribution Type:

Framework / classification system.

General Summary of the Paper

The authors present the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT), a structured

Eligibility

Eligible for inclusion: **Yes**

How Actionability is Understood

Actionability is defined as the clinical utility of a genomic alteration for guiding targeted therapy, grounded

> “The ESCAT defines clinical evidence-based criteria to prioritise genomic alterations as markers to sele

> “We consider a target ‘tier I-A’, if… data… has demonstrated clinically meaningful improvement of a su

What Makes Something Actionable

- Demonstrated clinical benefit in survival or relevant endpoints in appropriate trial designs.
- Consistency of benefit across tumor types (for tier I-C) or specificity to certain tumor contexts.
- Supporting evidence from retrospective, prospective, or preclinical studies depending on tier.
- Predictive rather than merely prognostic value.
- Feasibility of therapeutic intervention targeting the alteration.

How Actionability is Achieved / Operationalized

- **Framework/Approach Name(s):** ESMO Scale of Clinical Actionability for molecular Targets (ESCAT)
- **Methods/Levers:** Evidence-tier system based on trial type, outcome measures, and tumor specificity
- **Operational Steps / Workflow:** Classify molecular targets into ESCAT tiers I–X; integrate into tumor b
- **Data & Measures:** Clinical trial endpoints (OS, PFS), response rates, biomarker presence, preclinica
- **Implementation Context:** Precision oncology decision-making, research prioritization, and reporting h

> “This classification system aims to offer a common language… to place targets within their clinical cont

> “The scale uses the strength of evidence from clinical studies as the basis to assign tiers…” (p. 1900)

Dimensions and Attributes of Actionability (Authors’ Perspective)

- **CL (Clarity):** Yes — Clear definition and tier structure; standardized terminology.

> “…offer a terminology that can be broadly applicable and help clinicians…” (p. 1901)

- **CR (Contextual Relevance):** Yes — Tiers depend on tumor-type-specific evidence.
- **FE (Feasibility):** Yes — Only feasible therapeutic targets are considered for higher tiers.
- **TI (Timeliness):** No explicit mention as an actionability criterion.
- **EX (Explainability):** Partial — Mechanistic rationale described for examples but not formalized as a r
- **GA (Goal Alignment):** Yes — Focus on improving patient outcomes and guiding therapy choice.
- **Other Dimensions Named by Authors:** Magnitude of benefit; type and quality of evidence.

Theoretical or Conceptual Foundations

- Builds on and harmonizes prior classification schemas (Andre et al. 2014; Van Allen et al. 2014; Meric-E
- Incorporates ESMO Magnitude of Clinical Benefit Scale.

Indicators or Metrics for Actionability

- Clinical trial endpoints: overall survival (OS), progression-free survival (PFS), objective response rate (O
- Magnitude of benefit per ESMO MCBS.
- Level and type of supporting evidence.

Barriers and Enablers to Actionability

- **Barriers:** Lack of harmonized terminology; variable evidence strength; tumor heterogeneity; rarity of
- **Enablers:** ESCAT tier system; existing genomic databases; collaborative curation; prospective regist

Relation to Existing Literature

Positions ESCAT as an integrative and globally applicable framework addressing gaps in prior systems, e

Summary

This paper presents ESCAT, a structured, evidence-based framework for ranking genomic alterations in c

Scores

- **Overall Relevance Score:** 95 — Strong, explicit definition of actionability, detailed features tied to cli
- **Operationalization Score:** 95 — Fully developed framework with concrete tiering system, explicit crite

Supporting Quotes from the Paper

- “The ESCAT defines clinical evidence-based criteria to prioritise genomic alterations…” (p. 1895)
- “We consider a target ‘tier I-A’, if… data… has demonstrated clinically meaningful improvement…” (p. 1
- “The scale uses the strength of evidence from clinical studies as the basis to assign tiers to a target.” (p
- “Clear terminology regarding clinical utility should decrease the chance for misinterpretation…” (p. 1901

Actionability References to Other Papers

- Andre et al., Ann Oncol 2014
- Van Allen et al., Nat Med 2014
- Meric-Bernstam et al., J Natl Cancer Inst 2015
- Chakravarty et al., JCO Precis Oncol 2017 (OncoKB)
- ESMO Magnitude of Clinical Benefit Scale (Cherny et al., Ann Oncol 2017)