Paper Summary

<!--META_START-->

Title: Genomically matched therapy in refractory colorectal cancer according to ESMO Scale for Clinical A

Authors: Núria Mulet Margalef, Carmen Castillo, Miguel Mosteiro, Xavier Pérez, Susana Aguilar, Fiorella

DOI: 10.1002/1878-0261.13444

Year: 2023

Publication Type: Journal Article

Discipline/Domain: Oncology

Subdomain/Topic: Precision oncology; colorectal cancer; genomic profiling; clinical actionability

Eligibility: Eligible

Overall Relevance Score: 78

Operationalization Score: 72

Contains Definition of Actionability: Yes (via ESCAT framework)

Contains Systematic Features/Dimensions: Yes (ESCAT levels I–IV)

Contains Explainability: No

Contains Interpretability: Partial (linked to molecular classification)

Contains Framework/Model: Yes (ESCAT classification)

Operationalization Present: Yes

Primary Methodology: Quantitative (retrospective cohort study)

Study Context: Expanded genomic profiling (EGP) for refractory metastatic colorectal cancer (mCRC) pa

Geographic/Institutional Context: Catalan Institute of Oncology and Vall d'Hebron Institute of Oncology, S

Target Users/Stakeholders: Oncologists, molecular tumor boards, clinical trial designers, precision oncolo

Primary Contribution Type: Empirical results and application of ESCAT in clinical setting

CL: Yes

CR: Yes

FE: Yes

TI: No

EX: No

GA: Partial

Reason if Not Eligible: N/A

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Genomically matched therapy in refractory colorectal cancer according to ESMO Scale for Clinical Action

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Year:

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Publication Type:

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Discipline/Domain:

Oncology

Subdomain/Topic:

Precision oncology; colorectal cancer; genomic profiling; clinical actionability

Contextual Background:

The study assesses the feasibility and clinical utility of expanded genomic profiling (EGP) in refractory me

Geographic/Institutional Context:

Catalan Institute of Oncology and Vall d'Hebron Institute of Oncology, Spain.

Target Users/Stakeholders:

Oncologists, molecular tumor boards, clinical trial coordinators, policymakers in precision oncology.

Primary Methodology:

Quantitative – retrospective cohort analysis.

Primary Contribution Type:

Empirical evidence applying ESCAT to real-world mCRC genomic profiling.

General Summary of the Paper

This paper reports on a cohort of 187 heavily pretreated mCRC patients enrolled in an expanded genomi

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Eligibility

Eligible for inclusion: **Yes**

How Actionability is Understood

Actionability is conceptualized through the ESCAT framework, which ranks genomic alterations based on

> “The clinical value according to ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT) cla

> “ESCAT I… validated in clinical trials… ESCAT IV… preclinical data” (Table 1, p. 2)

What Makes Something Actionable

- Validation in prospective clinical trials (ESCAT I)
- Evidence of response in phase I/II or retrospective studies (ESCAT II)
- Validated in other malignancies (ESCAT III)
- Supported only by preclinical data (ESCAT IV)
- Molecular relevance to drug targeting
- Potential inclusion in biomarker-guided clinical trials

How Actionability is Achieved / Operationalized

- **Framework/Approach Name(s):** ESCAT (ESMO Scale for Clinical Actionability of Molecular Targets)
- **Methods/Levers:** Classification of genomic alterations; NGS profiling; molecular tumor boards; clinica
- **Operational Steps / Workflow:** Patient selection → FFPE tumor sample → NGS mutation, CNA, fusio
- **Data & Measures:** Prevalence of ESCAT I–IV alterations; trial inclusion rates
- **Implementation Context:** Precision oncology in a comprehensive cancer center

> “EGP programmes in patients with advanced CRC are feasible and identify a subset of patients with po

> “Final inclusion rate in biomarker-guided clinical trials was 2.7%” (p. 2)

Dimensions and Attributes of Actionability (Authors’ Perspective)

- **CL (Clarity):** Yes — classification provides a clear, evidence-ranked hierarchy of targets.
- **CR (Contextual Relevance):** Yes — alterations are linked to mCRC therapeutic decisions.
- **FE (Feasibility):** Yes — NGS profiling is feasible in reference centers with adequate tumor tissue.
- **TI (Timeliness):** No explicit link.
- **EX (Explainability):** No explicit link.
- **GA (Goal Alignment):** Partial — aim to align profiling with targeted therapy inclusion.
- **Other Dimensions Named by Authors:** Evidence tier, molecular target druggability.

Theoretical or Conceptual Foundations

- ESCAT framework (Mateo et al., 2018) for ranking targets.
- ESMO guidelines on mCRC management and molecular profiling.

Indicators or Metrics for Actionability

- ESCAT category prevalence per patient cohort.
- Percentage inclusion in biomarker-guided trials.
- Mutation prevalence by sidedness and RAS status.

Barriers and Enablers to Actionability

- **Barriers:** Low prevalence of high-tier alterations; trial slot unavailability; sample insufficiency; absenc
- **Enablers:** Centralized high-quality NGS analysis; multidisciplinary molecular boards; established clin

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Relation to Existing Literature

Aligns with prior reports on low prevalence of high-evidence druggable alterations in mCRC and low trial

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Summary

The study applies the ESCAT framework to a real-world cohort of refractory mCRC patients undergoing e

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Scores

- **Overall Relevance Score:** 78 — Strong explicit definition via ESCAT and systematic features, though
- **Operationalization Score:** 72 — Clear application of ESCAT in workflow and measurable outputs, bu

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Supporting Quotes from the Paper

- “The clinical value according to ESMO Scale for Clinical Actionability of molecular Targets (ESCAT) clas
- “EGP programmes in patients with advanced CRC are feasible and identify a subset of patients with pot
- “Final inclusion rate in biomarker-guided clinical trials was 2.7%” (p. 2)
- “Reducing tissue and economical costs… reshaping NGS panels periodically… implementing liquid biop

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Actionability References to Other Papers

- Mateo J. et al., 2018 — Original ESCAT framework definition.
- Mosele F. et al., 2020 — ESMO NGS recommendations.
- ESMO Clinical Practice Guidelines for mCRC (Cervantes et al., 2023).