Paper Summary

<!--META_START-->

Title: Efficacy of molecularly targeted agents given in the randomised trial SHIVA01 according to the ESM

Authors: A. Moreira, J. Masliah-Planchon, C. Callens, S. Vacher, C. Lecerf, M. Frelaut, E. Borcoman, N. T

DOI: https://doi.org/10.1016/j.ejca.2019.09.001

Year: 2019

Publication Type: Journal

Discipline/Domain: Oncology / Precision Medicine

Subdomain/Topic: Clinical actionability, molecularly targeted agents, ESCAT scale, SHIVA01 trial

Eligibility: Eligible

Overall Relevance Score: 75

Operationalization Score: 70

Contains Definition of Actionability: Yes (explicit via ESCAT framework)

Contains Systematic Features/Dimensions: Yes

Contains Explainability: Partial

Contains Interpretability: Partial

Contains Framework/Model: Yes (ESCAT)

Operationalization Present: Yes

Primary Methodology: Quantitative (retrospective analysis of trial data)

Study Context: Retrospective classification of molecular alterations from SHIVA01 trial according to ESCA

Geographic/Institutional Context: Institut Curie, France

Target Users/Stakeholders: Clinical oncologists, precision medicine researchers, trial designers

Primary Contribution Type: Empirical evaluation of actionability framework (ESCAT) applied to existing tri

CL: Yes

CR: Yes

FE: Yes

TI: No

EX: Partial

GA: Partial

Reason if Not Eligible: N/A

<!--META_END-->

Title:

Efficacy of molecularly targeted agents given in the randomised trial SHIVA01 according to the ESMO Sc

Authors:

A. Moreira et al.

DOI:

https://doi.org/10.1016/j.ejca.2019.09.001

Year:

2019

Publication Type:

Journal

Discipline/Domain:

Oncology / Precision Medicine

Subdomain/Topic:

Clinical actionability, molecularly targeted agents, ESCAT scale, SHIVA01 trial

Contextual Background:

The paper re-evaluates the SHIVA01 precision medicine trial by applying the European Society for Medic

Geographic/Institutional Context:

Institut Curie, France

Target Users/Stakeholders:

Oncologists, trial designers, policy-makers in precision oncology

Primary Methodology:

Quantitative retrospective analysis

Primary Contribution Type:

Empirical reassessment of trial outcomes through an actionability framework

---

General Summary of the Paper

The SHIVA01 trial compared molecularly targeted agents (MTAs) selected by a treatment algorithm base

---

Eligibility

Eligible for inclusion: **Yes**

How Actionability is Understood

Actionability is explicitly framed through ESCAT as the degree of clinical evidence supporting the use of a

> “ESCAT… defined criteria to prioritise molecular alterations (MAs) to select anticancer drugs.” (p. 202)

> “We… classified [MAs] according to the ESCAT by assessing the level of evidence in the literature.” (p.

What Makes Something Actionable

- Supported by clinical trial evidence in the same tumour type (higher ESCAT tier)
- Type of alteration must match that shown to confer benefit (mutation vs amplification)
- Evidence from other tumour types (lower tier) less predictive
- Preclinical or in silico evidence can guide classification when clinical data is lacking
- Drug-target affinity and specificity influence actionability beyond ESCAT tier

---

How Actionability is Achieved / Operationalized

- **Framework/Approach Name(s):** ESMO Scale for Clinical Actionability of molecular Targets (ESCAT)
- **Methods/Levers:** Literature review for evidence of benefit of MA-targeted MTA
- **Operational Steps / Workflow:** Identify MA → Search same-cancer evidence → If absent, search cro
- **Data & Measures:** PFS, OS, ESCAT tier classification, patient demographics
- **Implementation Context:** Retrospective re-analysis of SHIVA01 patient data

> “For each MA, we… searched for clinical trials… in the same tumour type… then… other tumour types.

Dimensions and Attributes of Actionability (Authors’ Perspective)

- **CL (Clarity):** Yes — ESCAT tiers are explicitly defined and applied
- **CR (Contextual Relevance):** Yes — Same vs other tumour type evidence distinguishes tiers
- **FE (Feasibility):** Yes — Relates to whether drugs are usable in context based on evidence strength
- **TI (Timeliness):** No — Not addressed directly
- **EX (Explainability):** Partial — ESCAT rationale is given, but biological mechanisms less discussed
- **GA (Goal Alignment):** Partial — Implicit alignment with precision oncology goals
- **Other Dimensions Named by Authors:** Type of alteration specificity, drug-target affinity

---

Theoretical or Conceptual Foundations

- ESCAT framework (Mateo et al., 2018)
- Prior actionability scales (OncoKB, AMP/ASCO/CAP guidelines)

Indicators or Metrics for Actionability

- ESCAT tier assignment (I–V)
- Clinical endpoints: PFS, OS stratified by tier

Barriers and Enablers to Actionability

- **Barriers:** Low ESCAT tier prevalence, misclassification of alteration type, lack of tumour-type-specifi
- **Enablers:** In vitro/in vivo functional validation, drug specificity, comprehensive molecular profiling

---

Relation to Existing Literature

Positions ESCAT as the latest in a series of actionability frameworks and demonstrates its application to

---

Summary

This paper retrospectively applies the ESCAT actionability framework to the SHIVA01 trial, showing that

---

Scores

- **Overall Relevance Score:** 75 — Strong conceptual clarity through ESCAT, explicit linkage of feature
- **Operationalization Score:** 70 — Detailed process for applying ESCAT tiers; however, not a prospect

---

Supporting Quotes from the Paper

- “[ESCAT] defined criteria to prioritise molecular alterations (MAs) to select anticancer drugs.” (p. 202)
- “Most MAs… were shown to improve outcomes in other tumour types (tier IIIA). Worst outcome… in tier
- “For each MA, we… searched for clinical trials… in the same tumour type… other tumour types… precli
- “This highlights the crucial importance of the type of alteration beyond the gene and/or signalling pathwa

---

Actionability References to Other Papers

- Mateo J et al., 2018 — ESCAT
- Chakravarty D et al., 2017 — OncoKB
- Li MM et al., 2017 — AMP/ASCO/CAP guidelines
- Meric-Bernstam F et al., 2015 — Decision support framework