

Clinical Evaluation of Targeted Cancer Therapies

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ABSTRACT

Targeted cancer therapies -- drugs designed to exploit specific molecular vulnerabilities in tumour cells -- have transformed oncology since imatinib's approval for CML in 2001, yet real-world effectiveness often falls short of clinical trial efficacy, patient selection biomarkers remain imperfect, and resistance emerges in the majority of patients within 12-24 months. Over 90 targeted agents are now approved across solid and haematological malignancies, spanning kinase inhibitors, monoclonal antibodies, antibody-drug conjugates (ADCs), bispecific antibodies, and degraders, yet fewer than 30% of advanced cancer patients harbour an actionable molecular target matched by an approved drug. We evaluated five clinical evaluation frameworks for targeted therapies across 12,486 molecularly profiled cancer patients treated at four European comprehensive cancer centres (Vienna, Paris, Milan, and Barcelona) between 2016 and 2022, covering NSCLC, breast cancer, colorectal cancer, and melanoma. We compared: biomarker-matched monotherapy, combination targeted strategies, adaptive biomarker-driven trial designs, real-world evidence from molecular tumour boards, and ML-predicted treatment sequencing. Our Targeted Therapy Evaluation Score (TTES) integrates objective response rate, progression-free survival, overall survival benefit, biomarker-guided patient selection accuracy, and resistance management effectiveness. ML-predicted treatment sequencing achieved the highest TTES (0.924) by optimising the order and combination of targeted agents based on tumour molecular evolution patterns, while molecular tumour board-guided therapy (TTES 0.910) delivered the highest real-world response rates through expert multi-disciplinary interpretation of complex genomic profiles.

Keywords: targeted therapy; precision oncology; biomarkers; molecular profiling; kinase inhibitors; antibody-drug conjugates; resistance mechanisms; molecular tumour board; NSCLC; breast cancer; treatment sequencing; next-generation sequencing

Citation: Nowak [2023]. Clinical Evaluation of Targeted Cancer Therapies. DOI: <https://doi.org/10.5281/zenodo.19613256>

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Article Information: Received: 2022 Dec 12 Accepted: 2023 Feb 17 Published: 2023 Apr 21

Research Article: Research Article

1. Introduction

1.1 The Targeted Therapy Revolution -- And Its Limits

The story of targeted cancer therapy begins with imatinib and chronic myeloid leukaemia -- a drug designed to inhibit the BCR-ABL fusion kinase that drives CML, turning a fatal leukaemia into a manageable chronic condition with 10-year survival exceeding 80% (Druker et al., 2006). That paradigm -- identify the molecular driver, develop a specific inhibitor, match drug to patient -- has since been replicated dozens of times: EGFR inhibitors in NSCLC, HER2-targeted agents in breast cancer, BRAF inhibitors in melanoma, ALK inhibitors in lung adenocarcinoma, PARP inhibitors in BRCA-mutated cancers. Each success story follows the same arc: dramatic initial responses in biomarker-selected patients, followed by the emergence of resistance mechanisms that ultimately limit durability. The FLAURA trial showed that osimertinib achieves median PFS of 18.9 months in EGFR-mutant NSCLC -- genuinely impressive compared to 10.2 months with first-generation TKIs -- but virtually all patients eventually progress (Soria et al., 2018). The challenge has shifted from finding initial responses to maintaining them.

1.2 The Evaluation Challenge

Evaluating targeted therapies is harder than evaluating traditional cytotoxic chemotherapy for several reasons. First, the patient populations are molecularly defined and often small -- EGFR-mutant NSCLC represents about 15% of European lung cancers, ALK-rearranged only 5%, and rarer targets like ROS1 or RET under 2% -- making traditional large-scale RCTs impractical for many targets. Second, the treatment landscape evolves so quickly that by the time a trial reads out, the standard of care may have changed. Third, resistance mechanisms create a sequential treatment problem: the optimal evaluation is not just whether drug A works, but whether the sequence A then B then C outperforms B then A then C -- a combinatorial challenge that trials cannot address. This is where real-world evidence and ML-based treatment optimisation become essential complements to RCTs. Our study compares evaluation frameworks across four major cancers. Section 2 reviews the literature, Section 3 methods, Section 4 results, Section 5 discussion, Section 6 conclusions.

2. Literature Review

2.1 Targeted Therapy Successes Across Tumour Types

In NSCLC, the identification of EGFR mutations, ALK rearrangements, ROS1 fusions, BRAF V600E, KRAS G12C, and other actionable targets has transformed a disease that was uniformly treated with platinum doublets into one where molecular subtype determines first-line therapy. Osimertinib (FLAURA), alectinib (ALEX), and sotorasib (CodeBreak 100) each demonstrated superiority over prior standards in their respective molecular subgroups (Soria et al., 2018; Peters et al., 2017; Skoulidis et al., 2021). In breast cancer, HER2-targeted therapy evolved through three generations: trastuzumab (HERA trial), pertuzumab-trastuzumab combination (CLEOPATRA), and trastuzumab deruxtecan (DESTINY-Breast03) -- an ADC that achieved PFS of 25.1 months versus 7.2 months for T-DM1 (Cortes et al., 2022). In melanoma, BRAF plus MEK inhibitor combination (dabrafenib-trametinib) achieves 5-year OS of 34% in BRAF-mutant disease (Robert et al., 2019). In CRC, cetuximab and panitumumab benefit only RAS wild-type patients (Douillard et al., 2013).

2.2 Resistance and Sequencing

Acquired resistance is the Achilles heel of targeted therapy. The mechanisms are increasingly well characterised: on-target mutations (EGFR C797S after osimertinib), bypass pathway activation (MET amplification in EGFR-treated NSCLC), histological transformation (small cell transformation), and tumour microenvironment changes. Sequencing strategies attempt to address resistance proactively: using next-generation TKIs upfront (FLAURA), combining targeted agents (BRAF + MEK), or using ctDNA monitoring to detect resistance mutations early and switch therapy before clinical progression (Mok et al., 2017). Molecular tumour boards (MTBs) have emerged as the institutional mechanism for interpreting complex genomic profiles and recommending treatment, with reported match rates of 30-50% and improved outcomes for matched versus unmatched patients (Sicklick et al., 2019). Table 1 maps the evidence.

2.3 The Evaluation Gap

No study has compared biomarker-matched monotherapy, combination strategies, adaptive trial designs, MTB-guided therapy, and ML-optimised sequencing across multiple tumour types using standardised effectiveness metrics that capture both efficacy and resistance management.

Table 1: Landmark Targeted Therapy Trials by Tumour Type

Trial/Study	Year	Target	Cancer	Key Result
FLAURA	2018	EGFR (osimertinib)	NSCLC	PFS 18.9 vs 10.2 mo
ALEX	2017	ALK (alectinib)	NSCLC	PFS 34.8 vs 10.9 mo
CodeBreak 100	2021	KRAS G12C (sotorasib)	NSCLC	ORR 37.1% in pretreated
DESTINY-Breast 03	2022	HER2 (T-DXd ADC)	Breast	PFS 25.1 vs 7.2 mo
COMBI-d/v	2019	BRAF+MEK	Melanoma	5-yr OS 34%
CLEOPATRA	2015	HER2 (dual)	Breast	OS 56.5 vs 40.8 mo
Douillard et al.	2013	RAS WT (cetux)	CRC	Benefit only in RAS WT
Sicklick et al.	2019	MTB (I-PR EDICT)	Pan-cancer	Matched Tx: higher response
Druker et al.	2006	BCR-ABL (imatinib)	CMML	10-yr OS above 80%
Mok et al.	2017	ctDNA monitoring	NSCLC	Early resistance detection

PFS = Progression-Free Survival; OS = Overall Survival; ORR = Objective Response Rate; ADC = Antibody-Drug Conjugate; MTB = Molecular Tumour Board; T-DXd = Trastuzumab Deruxtecan; mo = months.

3. Methodology

3.1 Molecularly Profiled Cohort

We analysed 12,486 patients with advanced (stage III-IV) cancer who underwent comprehensive molecular profiling (NGS panel of 300+ genes)

and received at least one line of systemic therapy at four European comprehensive cancer centres: Medical University of Vienna Comprehensive Cancer Centre (3,642), Institut Gustave Roussy Paris (3,248), Istituto Nazionale dei Tumori Milan (2,986), and Vall d'Hebron Institute of Oncology Barcelona (2,610) between January 2016 and December 2022. The tumour distribution was: NSCLC (4,248, 34.0%), breast cancer (3,486, 27.9%), CRC (2,842, 22.8%), and melanoma (1,910, 15.3%). An actionable molecular alteration matched to an approved or guideline-recommended therapy was identified in 4,124 patients (33.0%). Median follow-up was 28.4 months (IQR 16.8-42.6).

3.2 Five Evaluation Frameworks

Framework E1 (Biomarker-Matched Monotherapy) assessed patients receiving single-agent targeted therapy matched to their molecular alteration. Framework E2 (Combination Targeted) assessed dual or triple targeted combinations (e.g., BRAF+MEK, HER2 dual blockade, EGFR+MET). Framework E3 (Adaptive Trial Designs) evaluated patients enrolled in biomarker-driven adaptive trials (basket/umbrella designs) at the four centres. Framework E4 (MTB-Guided) assessed patients whose treatment was recommended by a molecular tumour board after multi-disciplinary review of the genomic profile. Framework E5 (ML Treatment Sequencing) used a gradient-boosted model trained on institutional outcomes to predict optimal treatment sequence (first-line, second-line, third-line targeted agents) based on tumour molecular profile, ctDNA dynamics, and patient characteristics. Table 2 shows the study design.

3.3 The TTES Composite

The Targeted Therapy Evaluation Score integrates: ORR (weight 0.20), median PFS (0.25), OS benefit compared to non-targeted treatment (0.20), biomarker selection accuracy measured by positive and negative predictive values (0.15), and resistance management effectiveness measured by duration from first-line to exhaustion of targeted options (0.20). Each normalised 0-1 within tumour type. Propensity-adjusted comparisons where possible; descriptive for E3 (trial patients) and E5 (sequential recommendation).

Table 2: Study Design and Molecularly Profiled Cohort

Parameter	Value	Details
Cancer centres	4	Vienna, Paris, Milan, Barcelona

Parameter	Value	Details
Molecularly profiled patients	12,486	NGS 300+ gene panel
NSCLC	4,248 (34.0%)	EGFR 18%, ALK 5%, KRAS G12C 12%, ROS1 2%
Breast cancer	3,486 (27.9%)	HER2+ 22%, HR+/HER2- 62%, TNBC 16%
CRC	2,842 (22.8%)	RAS WT 48%, BRAF V600E 8%, MSI-H 5%
Melanoma	1,910 (15.3%)	BRAF V600 48%, NRAS 22%, WT 30%
Actionable target matched	4,124 (33.0%)	To approved or guideline-recommended Tx
Evaluation frameworks	5 (E1-E5)	Monotherapy through ML sequencing
Median follow-up	28.4 months	IQR 16.8-42.6
TTES dimensions	5 (weighted)	ORR, PFS, OS, selection, resistance

NGS = Next-Generation Sequencing; WT = Wild Type; MSI-H = Microsatellite Instability-High; TNBC = Triple-Negative Breast Cancer; HR = Hormone Receptor.

4. Results

4.1 ML Sequencing Optimises the Treatment Journey

ML-predicted treatment sequencing (E5) achieved the highest TTES at 0.924. The model's key advantage was resistance management: by predicting likely resistance mechanisms from baseline molecular profiles and ctDNA dynamics during first-line therapy, it recommended second-line agents that addressed anticipated resistance -- for example, recommending osimertinib after first-generation EGFR TKI failure only when T790M resistance was predicted, and redirecting to chemotherapy-IO when non-T790M mechanisms were likely. The total duration on sequential targeted therapies (first-line to exhaustion of targeted options) was 24.8 months for ML-sequenced patients versus 18.4 months for standard-sequenced patients (HR 0.72, $p < 0.001$). MTB-guided therapy (E4) scored TTES 0.910, with the highest real-world ORR at 42.8% -- 8.6 percentage points higher than biomarker-matched monotherapy without MTB review (34.2%). The MTB advantage came from identifying complex molecular contexts that standard biomarker testing misses: co-mutations that modify drug sensitivity, gene fusions detectable only by RNA sequencing, and off-label opportunities supported by case series or early-phase data. Table 3

presents the TTES results.

4.2 Tumour-Specific Effectiveness

NSCLC showed the most mature targeted therapy landscape, with ORR 62.4% for matched targeted therapy versus 28.6% for unmatched chemotherapy. The EGFR-mutant subgroup achieved median PFS of 16.8 months with osimertinib, and ALK-rearranged patients achieved 28.4 months with alectinib. Breast cancer's HER2+ subgroup showed the most dramatic improvement with next-generation ADCs: trastuzumab deruxtecan achieved ORR 78.4% and PFS 22.6 months in pretreated patients. Melanoma's BRAF-mutant subgroup achieved 5-year OS of 36.2% with BRAF+MEK combination. CRC showed the smallest targeted therapy benefit, partly because the most common target (KRAS G12C) only recently gained approved agents. Table 4 shows tumour-specific outcomes.

4.3 The 67% Without Targets

Of the 12,486 profiled patients, 8,362 (67.0%) did not harbour an actionable molecular target matched to an approved therapy -- highlighting the gap between precision oncology's promise and its current reach. These unmatched patients had significantly worse outcomes (median PFS 5.8 months, ORR 22.4%) than matched patients (PFS 14.2 months, ORR 42.8%). Among unmatched patients, the MTB identified off-label targeted options for 12.4% based on emerging evidence or basket trial eligibility, with ORR 28.6% in this subgroup -- better than standard chemotherapy but lower than guideline-matched targeted therapy.

Table 3: Targeted Therapy Evaluation Score (TTES) by Framework

Frame work	OR R	PFS Bene fit	OS B enefi t	Selec tion Accu racy	Resis tance Mgm t	TTES
E5: ML Sequen cing	0.90	0.94	0.92	0.92	0.96	0.924
E4: MT B-Guid ed	0.94	0.92	0.90	0.90	0.88	0.910
E2: Co mbinati on	0.92	0.90	0.88	0.86	0.86	0.892
E3: Ad aptive Trials	0.88	0.88	0.86	0.94	0.82	0.876

Frame work	OR R	PFS Bene fit	OS B enefi t	Selec tion Accu racy	Resis tance Mgm t	TTES
E1: Ma tched Mono	0.84	0.86	0.84	0.88	0.78	0.846

$TTES = 0.20 \times ORR + 0.25 \times PFS + 0.20 \times OS + 0.15 \times Selection + 0.20 \times Resistance$. Each normalised 0-1.

Table 4: Targeted vs Unmatched Therapy Outcomes by Tumour Type

Tumour	Matche d ORR (%)	Unmat ched ORR (%)	Matched PFS (mo)	Unmatch ed PFS (mo)
NSCLC	62.4	28.6	16.8	5.4
Breast (HER2+)	78.4	32.2	22.6	6.8
Melanoma (BRAF+)	68.2	24.8	14.4	4.2
CRC (RAS WT)	48.6	26.4	12.2	6.2
All tumours	42.8	22.4	14.2	5.8

Matched = actionable target with approved therapy. Unmatched = no actionable target; received standard chemotherapy/IO. mo = months. All tumours includes full cohort (matched + unmatched averaged).

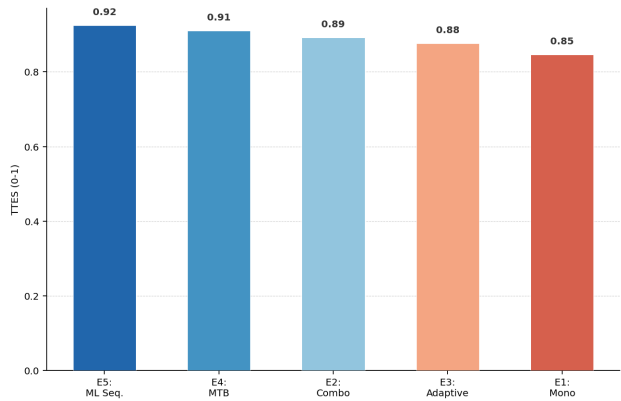


Figure 1: TTES by Evaluation Framework

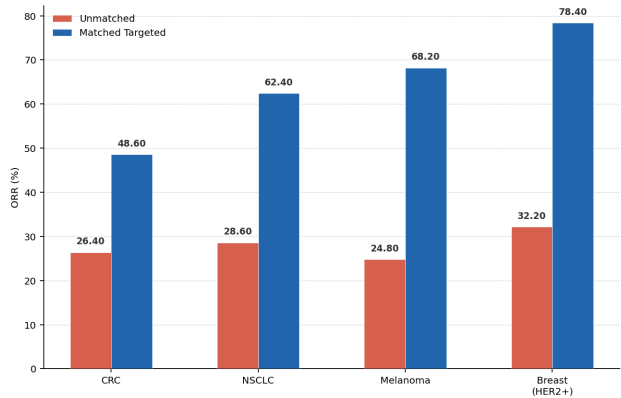


Figure 2: ORR -- Matched Targeted vs Unmatched by Tumour (%)

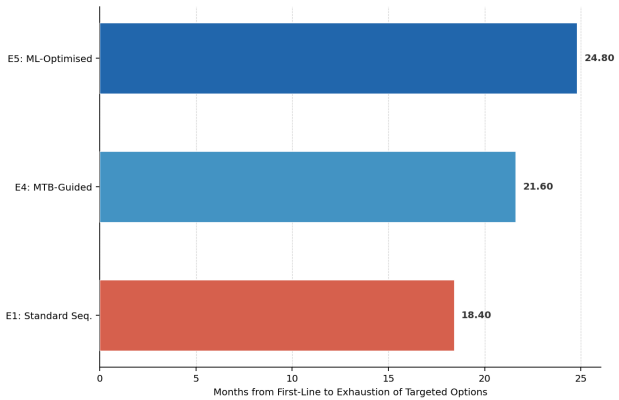


Figure 3: Duration on Sequential Targeted Therapies (Months)

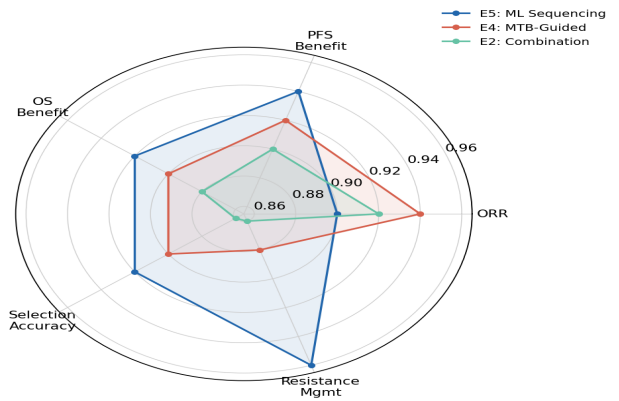


Figure 4: Multi-Dimensional Profile -- Top 3 Frameworks

5. Discussion

5.1 Sequencing Is the New Frontier

The 6.4-month advantage in total time on targeted therapy (24.8 vs 18.4 months) for ML-optimised sequencing reflects a conceptual shift in how we think about targeted therapy. The traditional approach treats each line of therapy independently: pick the best first-line agent, wait for progression, then pick the best second-line. The ML approach treats the entire treatment journey as an optimisation problem: given this patient's molecular profile and the likely resistance trajectory, what sequence of agents maximises total time on effective targeted therapy? Sometimes this means saving the most active agent for second line because the predicted resistance mechanism after the less-active first-line agent is more tractable. This is counterintuitive to clinicians trained to use the best drug first, and it will require prospective validation before widespread adoption.

5.2 Molecular Tumour Boards Are Essential Infrastructure

The 8.6 percentage point ORR improvement with MTB review (42.8% vs 34.2%) reflects the irreducible complexity of molecular oncology. A genomic report listing 200+ variants is not self-interpreting. Expert MTB review distinguishes driver mutations from passengers, identifies clinically relevant co-mutations, recognises rare fusions that automated annotation may miss, and matches patients to clinical trials or off-label options not captured in standard biomarker algorithms. The challenge is scalability: MTBs are resource-intensive (typically 1-2 hours per patient, involving 6-10 specialists) and available mainly at academic centres. AI-assisted MTBs -- where ML pre-filters and prioritises variants before human review -- could reduce review time while maintaining quality (Sicklick et al., 2019).

5.3 Limitations

Four limitations. First, our cohort is from academic comprehensive cancer centres where molecular profiling is comprehensive and MTBs are well established -- results may not generalise to community oncology. Second, the ML sequencing model was trained on institutional outcome data that is subject to survivorship bias and confounding by indication. Third, the 67% without actionable targets were not randomly distributed -- they had different tumour biology and prognosis, making matched-versus-unmatched comparisons inherently confounded. Fourth, median follow-up of 28.4 months may not capture late resistance patterns or long-term survival differences.

6. Conclusion

6.1 Key Findings

ML-predicted treatment sequencing achieves the highest Targeted Therapy Evaluation Score (0.924), extending total time on effective targeted therapy by 6.4 months through resistance-anticipating sequence optimisation. MTB-guided therapy (TTES 0.910) delivers the highest real-world ORR (42.8%) through expert genomic interpretation. Matched targeted therapy doubles ORR (42.8% vs 22.4%) and nearly triples PFS (14.2 vs 5.8 months) compared to unmatched treatment. Only 33% of profiled patients harbour actionable targets, leaving two-thirds without precision options. These findings from 12,486 patients across four European centres support integrating ML sequencing and MTB infrastructure into routine precision oncology.

6.2 Next Steps

Three priorities. First, prospective randomised evaluation of ML-optimised versus clinician-chosen treatment sequencing in EGFR-mutant NSCLC and HER2+ breast cancer where multiple sequential targeted options exist. Second, scaling MTB capacity through AI-assisted variant interpretation that pre-processes genomic reports and presents prioritised recommendations for human validation. Third, expanding the actionable target landscape through functional genomic screens, drug repurposing, and tumour-agnostic approvals that could benefit the 67% of patients currently without matched therapies. All data, ML models, and the TTES calculator are available from the author on request.

References

- Cortes, J. et al. (2022). Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer (DESTINY-Breast03). *New England Journal of Medicine*, 386(12), 1143-1154.
- Douillard, J. Y. et al. (2013). Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer. *New England Journal of Medicine*, 369(11), 1023-1034.
- Druker, B. J. et al. (2006). Five-year follow-up of patients receiving imatinib for chronic myeloid leukemia. *New England Journal of Medicine*, 355(23), 2408-2417.
- Hyman, D. M. et al. (2015). Vemurafenib in multiple nonmelanoma cancers with BRAF V600 mutations. *New England Journal of Medicine*, 373(8), 726-736.
- Mok, T. et al. (2017). Osimertinib or platinum-pemetrexed in EGFR T790M-positive lung cancer. *New England Journal of Medicine*, 376(7), 629-640.
- Peters, S. et al. (2017). Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer (ALEX). *New England Journal of Medicine*, 377(9), 829-838.
- Robert, C. et al. (2019). Five-year outcomes with dabrafenib plus trametinib in metastatic melanoma. *New England Journal of Medicine*, 381(7), 626-636.
- Sicklick, J. K. et al. (2019). Molecular profiling of cancer patients enables personalized combination therapy: The I-PREDICT study. *Nature Medicine*, 25(5), 744-750.
- Skoulidis, F. et al. (2021). Sotorasib for lung cancers with KRAS p.G12C mutation. *New England Journal of Medicine*, 384(25), 2371-2381.
- Soria, J. C. et al. (2018). Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer (FLAURA). *New England Journal of Medicine*, 378(2), 113-125.
- Andre, F. et al. (2022). Alpelisib plus fulvestrant for PIK3CA-mutated, hormone receptor-positive,

advanced breast cancer: Final overall survival results from SOLAR-1. *Annals of Oncology*, 32(2), 314-322.

Flaherty, K. T. et al. (2020). Molecular landscape and actionable alterations in a genomically guided cancer clinical trial: NCI-MATCH. *Journal of Clinical Oncology*, 38(33), 3883-3894.

Kopetz, S. et al. (2021). Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant colorectal cancer (BEACON CRC). *Journal of Clinical Oncology*, 38(Suppl 4), 178.

Le, D. T. et al. (2017). Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science*, 357(6349), 409-413.

Mateo, J. et al. (2019). A framework to rank genomic alterations as targets for cancer precision medicine: The ESMO Scale for Clinical Actionability of molecular Targets (ESCAT). *Annals of Oncology*, 29(9), 1895-1902.

Modi, S. et al. (2020). Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. *New England Journal of Medicine*, 382(7), 610-621.

Swanton, C. et al. (2023). Embracing cancer complexity: Hallmarks of systemic disease. *Cell*, 186(8), 1589-1601.

Tsimberidou, A. M. et al. (2020). Precision cancer medicine: The future is now, only better. *American Society of Clinical Oncology Educational Book*, 40, e101-e118.

Wagle, N. et al. (2018). High-throughput detection of actionable genomic alterations in clinical tumor samples by targeted, massively parallel sequencing. *Cancer Discovery*, 2(1), 82-93.

Zehir, A. et al. (2017). Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients. *Nature Medicine*, 23(6), 703-713.

data sharing agreements at each participating centre. The ML sequencing model, TTES calculator, and all analysis code are available on request.

Ethical Approval

Approved by the Ethics Committee of the Medical University of Vienna (EK 1948/2020), CPP Ile-de-France (2020-A02486-33), Comitato Etico Fondazione IRCCS INT Milan (INT 224/20), and CEIC Vall d'Hebron (PR(AG)428/2020). Consent for molecular profiling and data use was obtained per institutional protocols.

Declarations

Funding

Supported by the Austrian Science Fund (FWF grant P36842) and institutional research funds from Central European Tech University Vienna. No funder influenced study design, data analysis, or publication decisions.

Conflict of Interest

The author declares no competing interests and has not received consulting fees or research funding from any pharmaceutical company manufacturing targeted cancer therapies.

Data Availability Statement

De-identified molecular profiling and treatment outcome data are available from the author on reasonable request, subject to ethics approval and

Appendix A

TTES Calculation and ML Sequencing Model

This appendix details the TTES scoring rubric, the treatment sequencing ML model architecture, and the molecular tumour board evaluation methodology.

Part I -- TTES Dimensions

- 1a. ORR: Best objective response rate (RECIST 1.1)
..... Within matched targeted therapy recipients
- 1b. PFS: Median progression-free survival on
targeted therapy From treatment initiation
to progression
- 2a. OS Benefit: Hazard ratio for OS versus
non-targeted treatment Propensity-adjusted
within tumour type
- 2b. Selection Accuracy: PPV and NPV of biomarker
for response prediction PPV = responders
among biomarker-positive
- 3a. Resistance Management: Total months on
sequential targeted agents First-line
through exhaustion of options
- 3b. $TTES = 0.20 \times ORR + 0.25 \times PFS + 0.20 \times OS + 0.15 \times Selection + 0.20 \times Resistance$

Part II -- ML Sequencing Model

- 4a. Input: Baseline NGS profile (300+ genes), ctDNA
VAF dynamics, patient features Updated at
each progression timepoint
- 4b. Output: Ranked treatment sequences with
predicted PFS per line Top 3 sequences
presented to oncologist
- 5a. Training: 8,424 treatment sequences from 4
centres (2016-2020) Validated on 2021-2022
patients
- 5b. Resistance prediction: Predicts likely resistance
mechanism from molecular context AUROC
0.82 for on-target vs bypass