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Feasibility of an explainable AI-based therapeutic recommendation-tool utilizing tumor gene expression profiles for precision medicine in advanced & refractory solid tumors

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Background

- Precision oncology aims to guide patient treatment decisions by matching biological features with available drugs.
- Extensive genomic analysis allows to identify an actionable alteration in only 40-60% of patients **[1]**.
- Recently, a study of 50 pts with advanced refractory diseases included in PROFILER trial ***(NCT01774409)*** **[2]**, whole exome and fusion transcripts had a limited value over a 90-tumor gene panel to increase molecular-based treatment recommendations (MBTR).

Objective

- To evaluate the feasibility of the AI-transcriptional-based therapeutic recommendation-tool Onco KEM® to guide treatment recommendations for patients without tractable DNA-alterations.

Methods

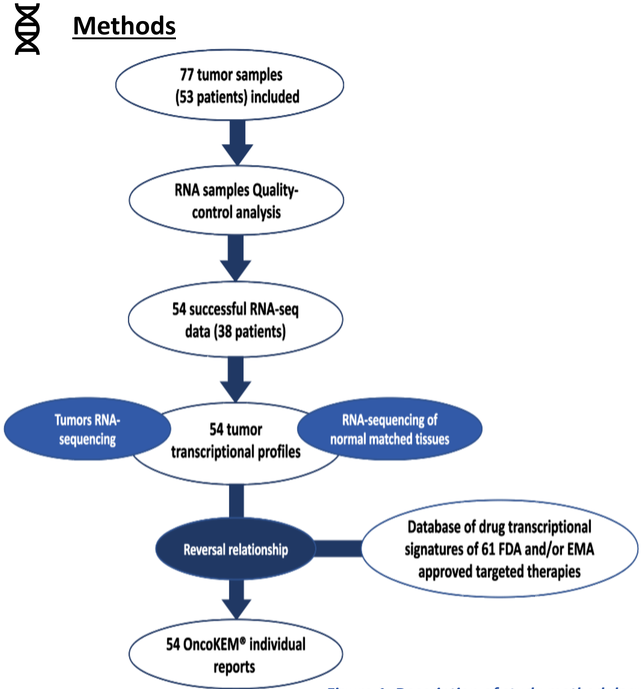
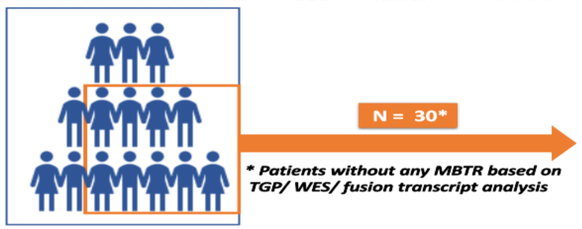


Figure 1: Description of study methodology

Results

Most common diagnoses were gynecological cancers (23.6% of which 77.8% were ovarian cancers), followed by breast cancers (21% of which 66.7% were triple-negative breast cancer [TNBC]), digestive cancers (18.4% of which 71.4% were colorectal cancers [CRC]), and soft tissue sarcomas [STS] (13.1%) *(Table1)*.

- Most frequently proposed drugs among the top 10 were ***palbociclib, talazoparib, infigratinib*** in TNBC; ***bosutinib, sapanisertib, SAR125844*** in OC; ***SAR125844, osimertinib, onartuzumab*** in CRC; ***ipilimumab, cabozantinib, sapanisertib*** in STS *(Figure 2)*.
- Even in the 30 patients cohort (79%) without any MBTR based on TGP/WES/fusion transcript analysis, all had at least 2 proposed targeted therapies in the Onco KEM® report (Median: 4) *(Figure 3)*.



Variable	%
Number of therapeutic propositions by OncoKEM Median (Range)	4 (2 – 9)
Top ranked drugs pathway	
MET inhibitors	18%
VEGFR inhibitors	12%
Abl inhibitors	12%
FGFR inhibitors	11%
PI3k/AKT/mTOR inhibitors	11%
PARP inhibitors	10%
CDK4/6 inhibitors	7%
Others	19%

Figure 3: Description of most ranked drugs pathway

Table 1: Baseline characteristics

Characteristics	%
Age: Median (Range)	53 (21 – 70)
Gender	
Female	60.5%
Male	39.5%
Primary tumor site	
Gynecological	*23.6%*
Breast	*21%*
Digestive	*18.4%*
Sarcomas	*13.2%*
Others	23.8%
Disease stage	
Metastatic	92.1%
Locally advanced	7.9%
Number of metastasis sites: Median (Range)	2 (1 – 5)
Number of previous treatment lines: Median (Range)	4 (1 – 11)

Only ***21%*** of patients had a recommendation (Molecular Based Treatment Recommendation based on TGP/WES/fusion transcript analysis).

For all patients, at least 2 (median 4) targeted therapies were proposed using the ***AI-transcriptional-based therapeutic recommendation-tool OncoKEM®.***

This tool has the ***potential to expand*** personalized cancer treatment in patients with advanced & refractory diseases ***without tractable genomic alterations.***

Its ***clinical relevance*** assessment is planned in an ***upcoming clinical trial.***

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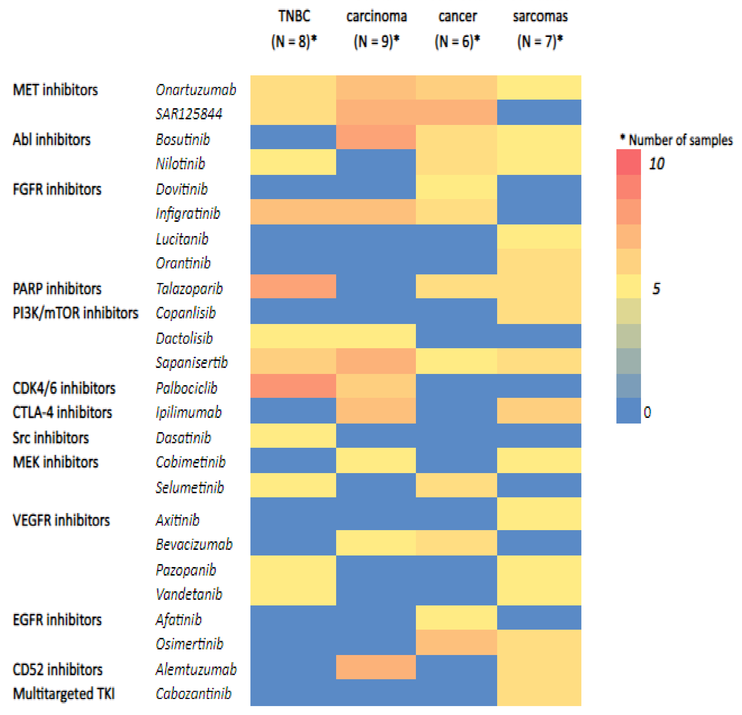

Figure 2: Ranking of targeted therapies in the 4 most frequent types of cancer

References: 1. Malone ER, *et al.* Molecular profiling for precision cancer therapies. *Genome Med* 12, 8 (2020).
2. Trédan O, et al. Molecular screening program to select molecular-based recommended therapies for metastatic cancer patients: analysis from the ProfiLER trial. Annals of Oncology, 2019