2022 ASCO ANNUAL MEETING

# 1554

# 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

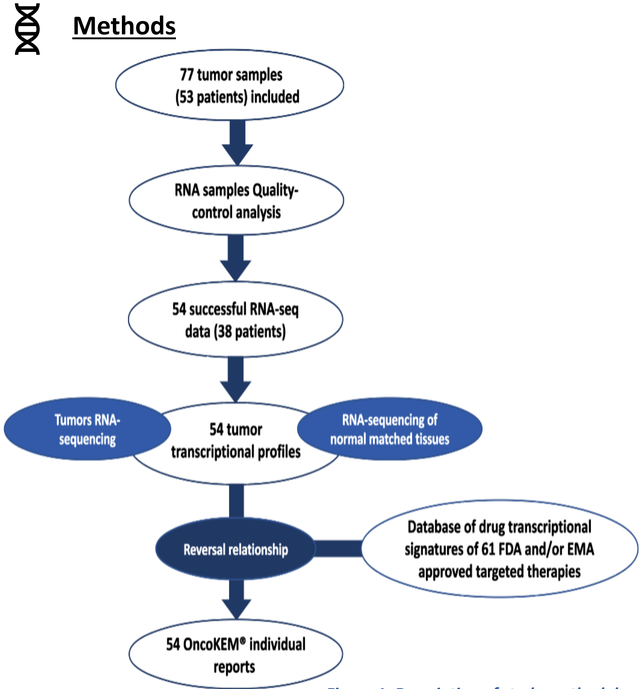
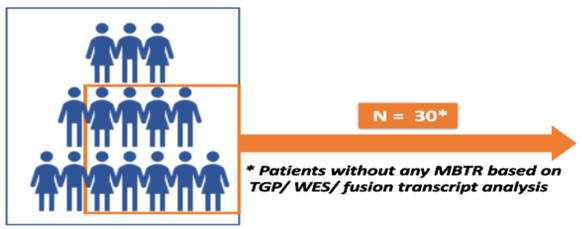



*Figure 1: Description of study methodology*

## 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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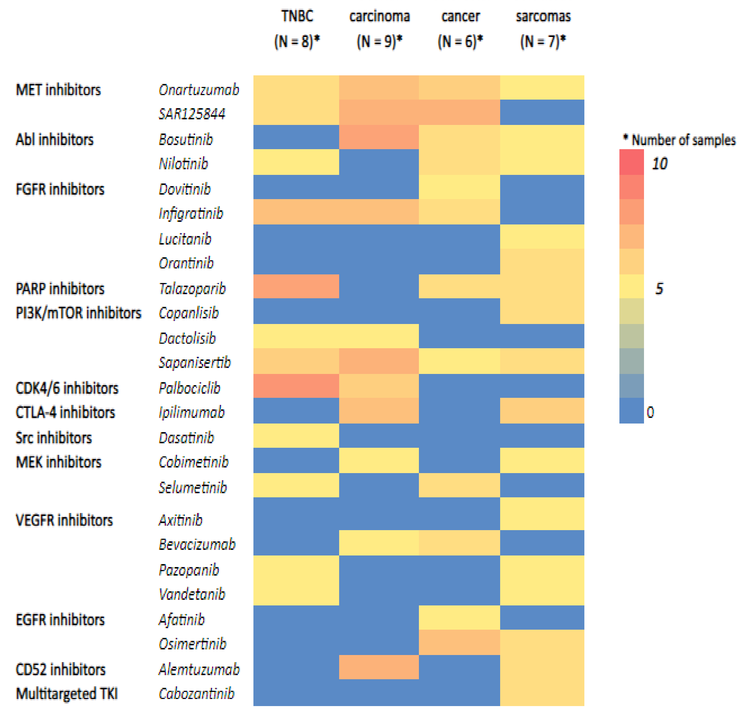


*Figure 2: Ranking of targeted therapies in the 4 most frequent types of cancer*

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

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CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

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LYon Recherche Innovation contre le CANcer

# Background

Patients with advanced & refractory solid tumors

Tumor samples

Genomic analysis

DNA actionable alterations (40-60% of patients)

Molecular tumor board

Targeted therapy

***For the 40 to 60% of patients without any tractable DNA-alteration?***

RNA

RNA sequencing

Tumor gene expression profiles

Gene Expression

Explainable AI analysis

OncoKEM® reports

Proposition of targeted treatments

# **Methodology:** *A global overview of OncoKEM®* algorithm

**Tumor's tissue**

**Matching healthy tissue***

**Treated samples by drugs**

**Untreated samples**

**RNA expression comparison**

**Identification of dysregulated genes**

**Cancer gene expression signature**

**Drug gene expression signatures**

**Reference database**

* **Provided from a reference database**

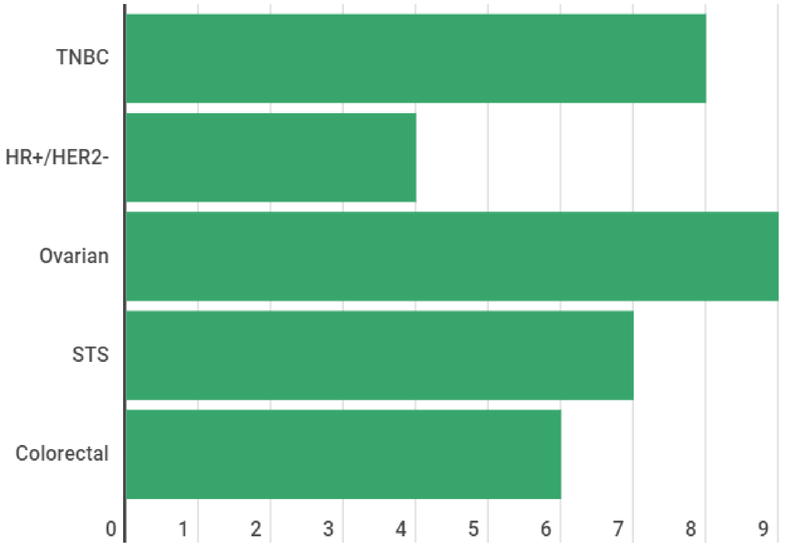
**Compare the cancer gene expression signature to the reference database**

**OncoKEM algorithm**

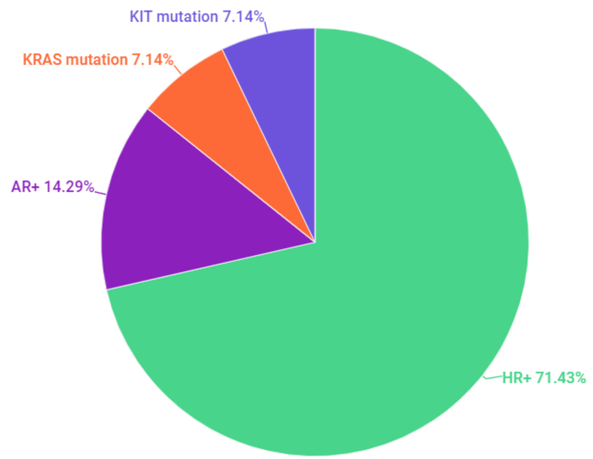
- ✓ A **"reversal relationship"** between cancer and drug gene expression signatures was searched.
- ✓ Drugs will be ranked by their **scores** based on the level of dysregulated target genes implicated in each drug's efficacy in the tumor tissue.
- ✓ Target genes are classified as concordant or discordant according to their contribution by adding or subtracting from the score respectively.

**Produce the OncoKEM report**

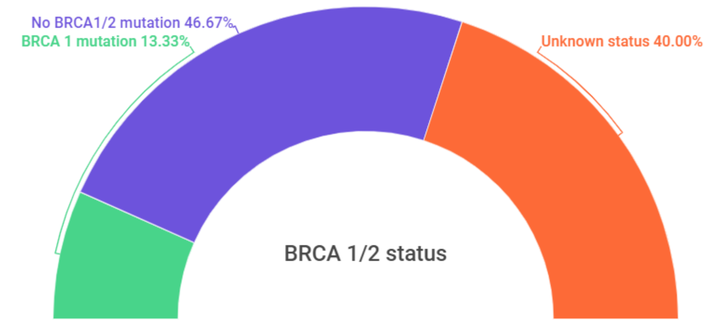
**Report of the 10 highest scored drugs**



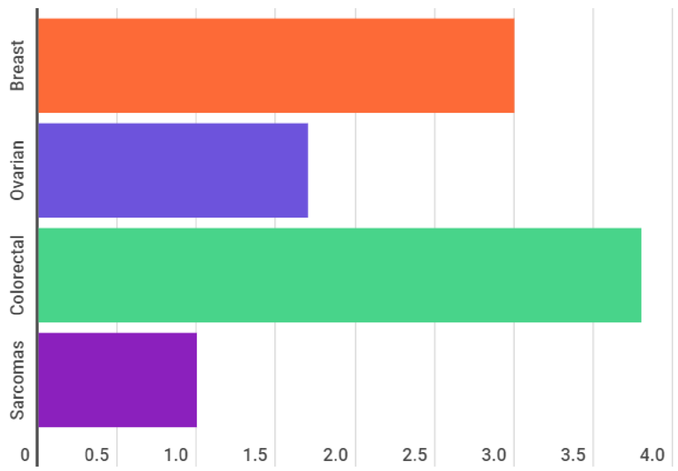

***Number of samples in the most frequent cancer types***



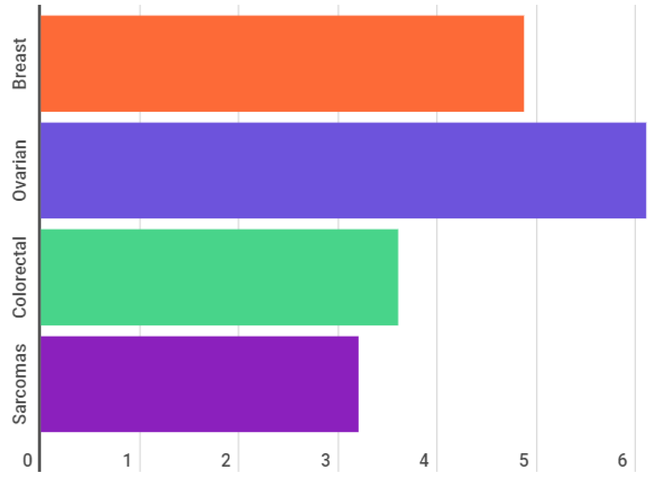

***Molecular profile of the 4 most common types of cancers***



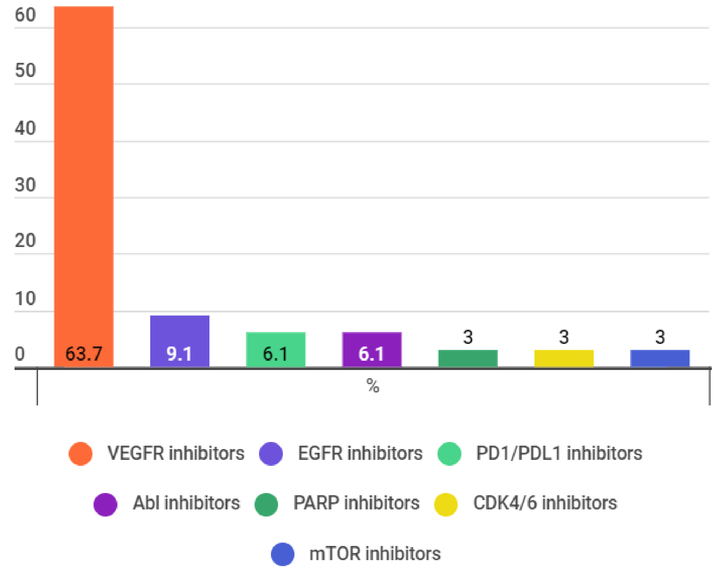

***BRCA1/2 status of patients with breast and ovarian cancers***



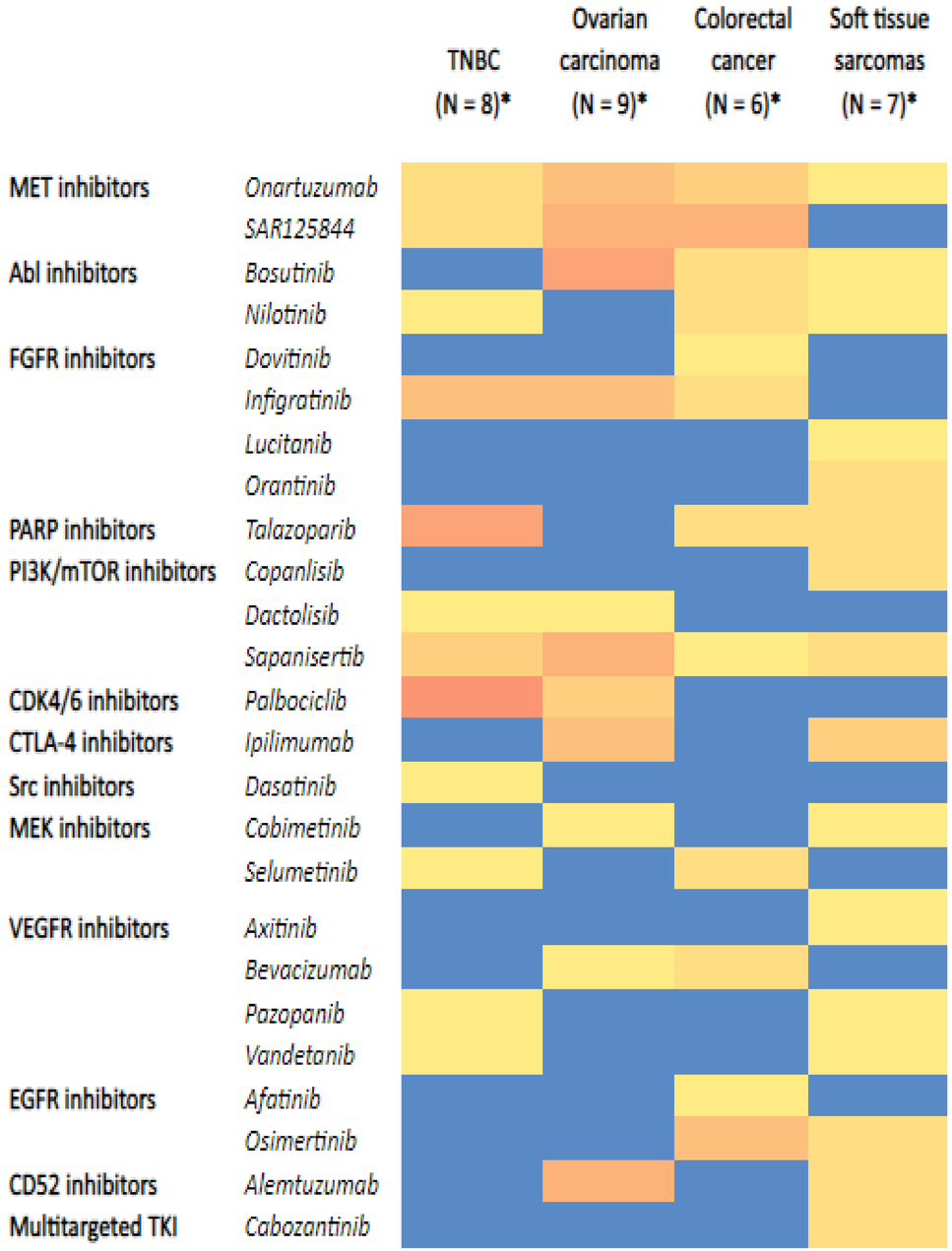

***Average number of metastasis sites***




***Average of previous treatment lines at metastatic setting***

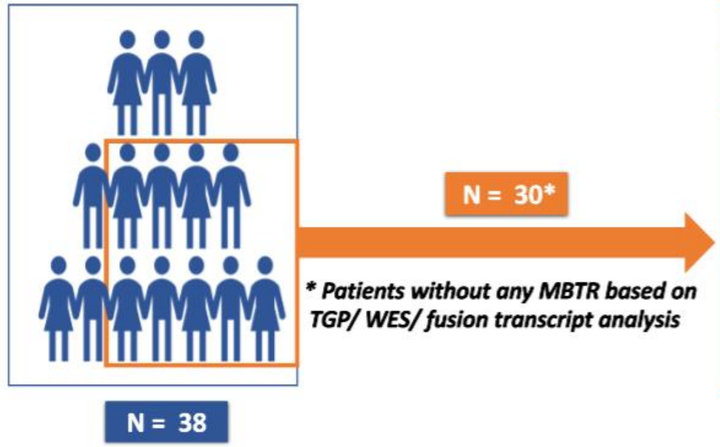



***Ranking of previously used targeted therapies***





*Ranking of targeted therapies in the 4 most frequent types of cancer*

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*Description of most ranked drugs pathway*

AI-based therapeutic recommendation tool OncoKEM® is ***feasible*** in real-world patients and has the ***potential to expand*** personalized cancer treatment in patients with advanced & refractory diseases ***without tractable genomic alterations.***

***Its clinical relevance will be assessed in an upcoming clinical trial***