2022 ASCO® ANNUAL MEETING

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

Ouissam Al Jarroudi[1,2], Coralie Williams[3], Rita Santos[2], Armelle Dufresne[4], Valéry Attignon[5], Anthony Ferrari[6], Sandrine Boyault[5], Laurie Tonon[6], Séverine Tabone-Eglinger[7], Philippe Cassier[4], Nadège Corradini[8], Armelle Vinceneux[4], Aurélie Swalduz[4], Alain Viari[6], Sylvie Chabaud[8], David Pérol[8], Mohammad Afshar[2,3], Jean-Yves Blay[4,10], Olivier Trédan[4], Pierre Saintigny[1,4,10]

1- Department of translational medicine, Centre Léon Bérard, Lyon, France; 2- OmiCure Inc, Paris, France; 3- Ariana Pharma, Paris, France; 4- Department of Medical Oncology, Centre Léon Bérard, Lyon, France; 5- Platform of Cancer 10 Genomics, Centre Léon Bérard, Lyon, France; 6- Platform of Bioinformatics Gilles-Thomas, Centre Léon Bérard, Lyon, France; 7- Biobank, Centre Léon Bérard, Lyon, France; 8- Department of Pediatric Oncology, Institute of Pediatric Hematology and Oncology, Centre 13 Leon Bérard, Lyon, France; 9- Department of Clinical Research, Centre Léon Bérard, Lyon, France; 10- Univ Lyon, Claude Bernard Lyon 1 University, INSERM 1052, CNRS 5286, 15 Centre Léon Bérard, Cancer Research Center of Lyon, Lyon, France.

Background: Precision oncology aims to guide patient (pts) treatment decisions by matching biological features with available drugs. Extensive genomic analysis allows to identify an actionable alteration in 40-60% of patients. In a recent study of 50 pts with advanced refractory diseases included in PROFILER (NCT01774409), whole exome and fusion transcripts had a limited value over a 90-tumor gene panel (TGP) to increase molecular-based treatment recommendations (MBTR). Herein, we evaluated the feasibility, in the same cohort of pts, of the AI-transcriptional-based therapeutic recommendation-tool Onco KEM® to guide treatment recommendations. **Methods:** 77 fresh frozen (FF) and/or FFPE samples including paired specimens for 53 pts with available RNA-Seq gene expression profiles were included. For each pts, a tumor transcriptional profile (TTP) was generated by identifying differentially expressed genes between the pts tumor and a cohort of matched healthy tissue. A large database of drug transcriptional signatures (DTS) was queried in order to identify a "reversal relationship" between the TTP and a DTS. A total of 205 drugs were ranked, including a subset of 61 FDA and/or EMA approved targeted therapies (aTT). **Results:** Most common diagnoses were breast cancers (21% of which 63% were TNBC), followed by ovarian cancers (OC, 18%) and soft-tissue sarcomas (STS, 13%). The median number of previous treatment lines was 4 (range: 1 - 10). Among the 77 tumor samples analyzed, 54 (70%) specimens led to the generation of an OncoKEM ® report, with no differences between FF and FFPE samples (p=0.85). The overlap between the top 10 proposed drugs between paired FF and FFPE samples was 56% on average. All patients had at least 2 propositions (range: 2-9) of aTT among the top 10 ranked drugs in the Onco KEM® reports. Most frequently proposed drugs among the top 10 were palbociclib, talazoparib, infigratinib in TNBC; bosutinib, sapanisertib, SAR125844 in OC; ipilimumab, cabozantib, sapanisertib in STS. Among the 30 pts (79%) without any MBTR based on TGP/WES/fusion transcript analysis, all had at least 2 proposed aTT in the Onco KEM® report (median: 4, range: 2-9). Top ranked drugs were MET (18%), VEGFR (12%), Abl (12%), FGFR (11%), PI3K/AKT/mTOR (11%), PARP (10%) and CDK4/6 inhibitors (7%). **Conclusions:** AI-transcriptional-based therapeutic recommendation-tool Onco KEM® is feasible in real-world pts and has the potential to expand personalized cancer treatment in pts with advanced & refractory diseases without tractable genomic alterations. The clinical relevance remains to be evaluated.