The Impact of Molecular Tumour Board on Costs and Patient Access to Personalized Medicine

De Micheli V.¹, Pasini S.¹, Baggi A.¹, Vingiani A.^{2,3}, Agnelli L.², Duca M.⁴, Gancitano G.⁵, Ferrario M.⁵, Franzini J.M.¹, De Braud F.^{3,4}, Jommi C.⁶, Pruneri G. ^{2,3}

1. Life Sciences Division, Business Integration Partners S.p.A., Milan, Italy 2. Department of Pathology, Fondazione IRCCS, Istituto Nazionale Tumori, Milan, Italy 3. University of Milan, School of Medicine, Milan, Italy 4. Medical Oncology Department, Fondazione IRCCS, Istituto Nazionale Tumori, Milan, Italy 5. Roche S.p.A, Monza, Italy 6. SDA Bocconi School of Management, Bocconi University, Milan, Italy

INTRODUCTION & OBJECTIVE

The growing availability of target therapies in oncology and the impressive progresses on tumour genomic profiling have significantly improved patients' outcomes and have increased the role of personalized medicine for oncological patients. In most cases, from a clinical perspective, it is crucial to investigate the tumour mutational profile to define which is the most appropriate treatment for the patient. Therefore, treatment choice in oncology nowadays requires a healthcare professionals' team (i.e. oncologists, geneticists, pathologists, bioinformaticians, biologists, pharmacologists, surgeons) with different competences, due to the high level of complexity. In this scenario, the **testing methodology** applied to investigate patient tumour genomic profiling and the possibility of evaluating patient in Molecular Tumour Boards (MTB) significantly influence patients' access to target therapies, therefore potential disease progression and clinical outcomes.

The project aims to quantify the impact of Molecular Tumour Board in accessing target therapies in terms of patients' eligibility and costs, according to different Next Generation Sequencing (NGS) panel sizes and cancer types.

METHODS

We analyzed 676 patients discussed by the institutional Molecular Tumour Board of Fondazione IRCCS Istituto Nazionale dei Tumori of Milan between April 2020 and September 2021, investigating four cancer subtypes: nonsmall cell lung cancer (NSCLC), cholangiocarcinoma (CCA), pancreatic carcinoma (PC) and gastric



Tumour genomic profiling through Next Generation Sequencing (NGS)



carcinoma (GC).

For each tumour, we evaluated three key dimensions (**Figure 1**):

- The eligibility of patients to target therapies by type of treatment (on label, off label, clinical trials) according to the Italian Medicines Agency.
- The total cost of patient diagnostic journey, which includes all the activities from cancer suspect to treatment choice. We divided the overall patient diagnostic journey in three main phases:
 - All the activities before tumour genomic profiling;
 - II. Tumour genomic profiling through Next Generation Sequencing technology;
 - III. MTB evaluation.
- The incremental cost per patient to access target therapies, estimated diving the total cost of performing tumour genomic profiling (Phase II) and evaluating patients in MTB (Phase III) by the number of patients which are eligible to target therapies. Costs of all activities before tumour genomic profiling (Phase I) were not included in the calculation of the incremental cost since they are not differential on the diagnostic pathway.

For each dimension, we compared patients tested with small (≤ 50 biomarkers) and large (>50 biomarkers) NGS **panels** to highlight the consequences of the two different approaches. Immunohistochemical biomarkers for immune therapy eligibility (example, PD-L1) were not included in the study.

We relied on multiple sources of data to perform the analysis:

- an anonymized dataset tracking patients' evaluation by the institutional MTB;
- semi-structured interviews to hospital personnel (oncologists, geneticist, pathologists, bioinformaticians, biologists, laboratory technicians) including the collection of detailed data and open ended questions;
- hospital economic data;
- regional healthcare services tariffs.

FIGURE 1. RESEARCH DESIGN



LKB1 v2 panel Hotspot + Archer sarcoma Hotspot + Oncomine BRCA **Oncomine BRCA** LKB1.v2 panel + OCAplusRNA





RESULTS

The eligibility to target therapies varied across different cancers (NSCLC: 37%; CCA: 39%; PC:18%; GC: 38%) and larger NGS panels significantly enhanced patients' eligibility to personalised medicines compared to smaller NGS panels. The benefits of larger NGS panels increased moving from NSCLC to CCA, PC and GC (NSCLC: 37%) small panel vs. 39% large panel; CCA: 17% vs. 44%; PC: 2% vs. 35%; GC: 0% vs 40%) (Figure 2). A considerable amount of NSCLC patients was eligible to on label therapies, while in case of CCA, PC and GC most patients were eligible to off label and clinical trials treatments.

The overall cost of diagnostic journey was between 3.2K and 7.4K euros per patient (NSCLC: 6.4K small panel) vs. 7.4K large panel; CCA: .3.7K vs. 4.9K; PC: 4.5K vs. 5.8K; GC: 3.2K vs 4.2K) (Figure 3). All the activities before tumour genomic profiling (Phase I), are not differential in the diagnostic pathway and are generally more expensive compared to NGS testing (Phase II) and MTB evaluation (Phase III). The cost of NGS (Phase II) included personnel, equipment, consumables and overheads costs (570-1.015 €/patient - small panels, 1.830-1.984€/patient large panels). The cost of MTB evaluation (Phase III) had a marginal impact on the overall cost of patient diagnostic journey (2-3%), since it was between 113€/patient (small NGS panel) and 118€/patient (large NGS



panels) considering personnel costs.

The **incremental cost** per patient to access target therapies changed using larger NGS panels (NSCLC: 2.8K small panel vs. 5K large panel; CCA: 4.4K vs. 4.4K; PC: 27K vs. 5.5K; GC: not measurable vs. 5.2K) (Figure 4). In case of GC, it was not possible to define the incremental cost for patients tested with small NGS panels, since none of them was eligible to personalized medicines in the analysed sample.

CONCLUSIONS

The evaluation of oncological patients in MTB has a negligible cost compared to the outstanding benefits as accessibility to target therapies. In addition, to combine MTB and Comprehensive Genomic Profiling (NGS with large panels) allows to greatly increase patients' eligibility to personalized medicines and optimize the incremental cost per patient to access target therapies for CCA, PC and GC.

FIGURE 4. THE INCREMENTAL COST PER PATIENT ACCESS TO TARGET THERAPIES



		ALL PATIENTS TESTED WITH SMALL NGS PANEL				ALL PATIENTS TESTED WITH LARGE NGS PANEL			
	Cancer subtype	NSCLC	CCA	PC	GC	NSCLC	CCA	PC	GC
	N° patients included in the simulation	458	64	77	77	458	64	77	77
	Testing cost [€/patient]	930	627	570	1.015	1.856	1.830	1.830	1.984
	MTB evaluation cost [€/patient]	113	113	113	113	118	118	118	118
	% Patients eligible to target therapies	37%	17%	2%	0%	39%	44%	35%	40%
	Total costs of testing + MTB [K€]	477,5	47,3	52,6	86,8	904,1	124,7	149,9	161,9
	N° patients eligible to target therapies	168	11	2	0	179	28	27	31
	Incremental cost to access target therapies per patient [K€/patient]	2,8	4,4	27,3	-	5,0	4,4	5,5	5,2



