The experience of an outsourced Comprehensive Genomic Profiling service in Italy

C. Viviani Anselmi, PhD[1], R. Cipelli, PhD[1], F. Heiman PhD[1], A. Lugini, MD, PhD[2], M. Montrone, MD, PhD [3], F. Pagni, MD[4], A. Avitabile[5], A. D'Ambrogio[5], L. Lattanzi[5]

1. IQVIA Solutions Italy Srl, Milan, Italy; 2. UOC Oncologia Azienda Ospedaliera San Giovanni Addolorata, Roma, Italy; 3. IRCCS Istituto Tumori "Giovanni Paolo II", Bari, Italy; 4. Department of Medicine and Surgery, University Milan Bicocca, Italy ; 5. Roche S.p.A., Monza, Italy

INTRODUCTION

Foundation Medicine® (FM) Comprehensive Genomic Profiling (CGP) is a Next Generation Sequencing solution that, unlike others, analyzes the genome extensively, from tissue or blood, to detect the major classes of genomic alterations as well as genomic signatures such as Micro-Satellite Instability (MSI) and Tumor Mutational Burden (TMB) that help predict response to immunotherapy[1]. This approach is growing in importance and its impact is well exemplified in the management of non-small cell lung cancer (NSCLC)[2] patients. Since lung cancer is the leading cause of cancer-related death in the world (2.5 out of 10)[3] and personalized treatments are becoming available, a comprehensive biomarker-driven therapeutic approach is of utmost importance in clinical practice[4-5]. This project is aimed at investigating the experience of a group of Italian FM users -both oncologist and pathologist- and how FM impacted their clinical practice in 2019.

OBJECTIVE

The aim of the project was to analyze FM broader customer experience, from service logistics and support to the clinical impact through the experience of real FM users.

METHODS

STUDY DESIGN

A modular approach was designed to capture the impact of FM in clinical practice. Initially, a desk research was conducted to understand FM CGP role in lung cancer management. Three therapeutic area experts (two oncologists and one pathologist) were then involved in a dedicated workshop to define the key FM metrics to be investigated in a Real World Evidence (RWE) survey. After the interview of 25 clinicians, the same three experts reviewed and discussed the output of the survey.

RWE SURVEY DESIGN

Two different RWE surveys were designed: one for oncologists and one for pathologists. The involvement of both was essential to understand the key therapeutic and procedural aspects of FM CGP. Both RWE surveys had four focus areas: i) the definition of FM services patient profile (i.e. demographic, clinical characteristics); ii) the sample management process; iii) the impact on therapeutic choice; iv) the overall customer satisfaction (innovation, support, timeliness, areas of improvement);. Data were collected from 19 oncologists and 6 pathologists through Computer Assisted Web Interviewing (CAWI).The surveys were completely anonymous, and no identifiable personal details were collected from the respondents.

RESULTS

TARGET PATIENT PROFILE

The majority of participants [N.14; 56%] used both FoundationOne CDx and FoundationOne Liquid [mean number of samples sent to FM per participant (μ): 23]. 32% [N.8] used only "FoundationOne CDx" [μ: 26] and 12% used only [N.3] "FoundationOne Liquid" [μ: 41]. FM services have been used equally for patients in the 41-60 and 61-70yrs old highlighting the usage of the test for a very broad age range (Fig. 1, top panel). The vast majority of patients analyzed had primary NSCLC, while only a small fraction [4.8%] had secondary lung cancer (Fig. 1, panel 2). Also, most patients analyzed [89.4%] had stage IV cancer and most patients [73,9%] were naïve or had maximum one line of treatment (Fig. 1, panel 3 and 4, respectively).

SAMPLE MANAGEMENT

The failure rate was 9.3% for FoundationOne Liquid (Fig. 2, panel A) and 8.5% for FoundationOne CDx (Fig. 2, panel B). It is important to highlight that failure rate is mostly due to tissue that is either insufficient or not of enough good quality for nucleic acid extraction. In case the tissue was not sufficient for analysis, the majority of participants also praised the possibility offered by FM to organize a new shipment with new specimens [Liquid: 53,6%; Tissue: 42,8%] (Fig. 2, A-B).

IMPACT ON THERAPEUTIC CHOICE

FM' CGP was perceived by clinicians as decisive with an average score 3.6 (from 1 "low" to 5 "high") (data not shown). The high concordance of FM CGP with standard methods was also underlined [80,3%]. In case of discrepancy [4,1%], the majority [71,4%] of clinicians chose a therapy based on FM findings and not the standard test (data not shown). For more than half the patients analyzed, FM found a viable therapeutic option: for 23,5% there was an on-label drug, for 18,4% there was an off-label drug, and for 10.7% there was an available clinical trial (Fig. 3, panel A). For 33,1% of the patients there was no druggable mutation and for 14,3% no mutations were found (Fig. 3, panel A). Approximately 3 out of 4 and 2 out of 3 clinicians found the information of genomic signatures predictive of response to immunotherapy useful (for MSI and TMB respectively) (Fig. 3, panel B).

OVERALL SATISFACTION

In general, 66,7% of clinicians were promoter of FM solutions, 29,2% were neutral, 4,2% were detractors (Fig. 4).

Figure 1. Target Patient Profile

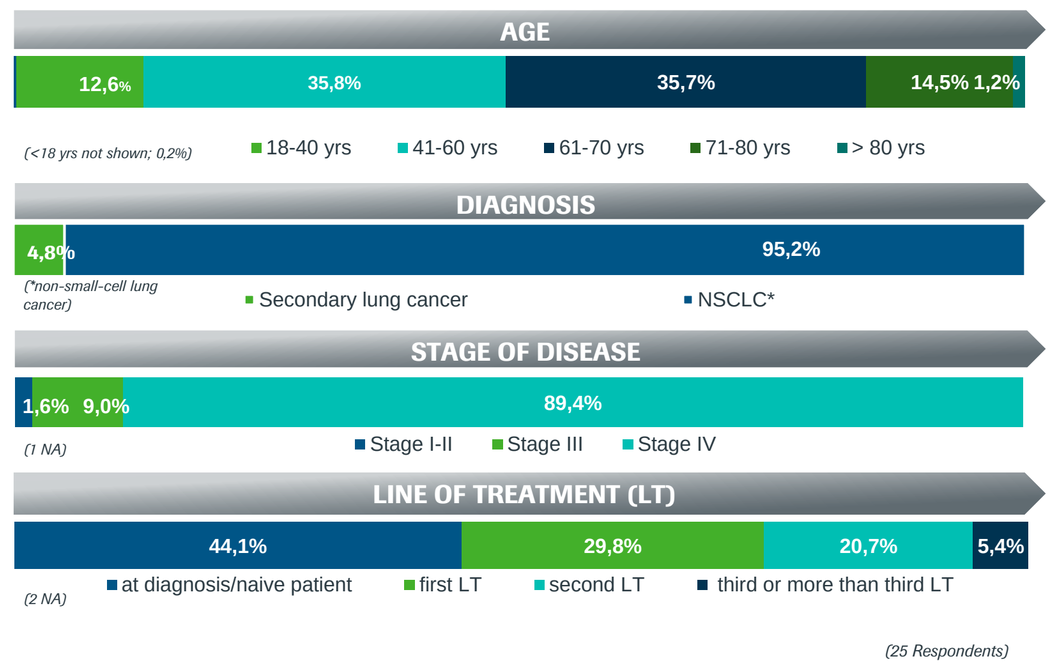


Figure 2. Sample management

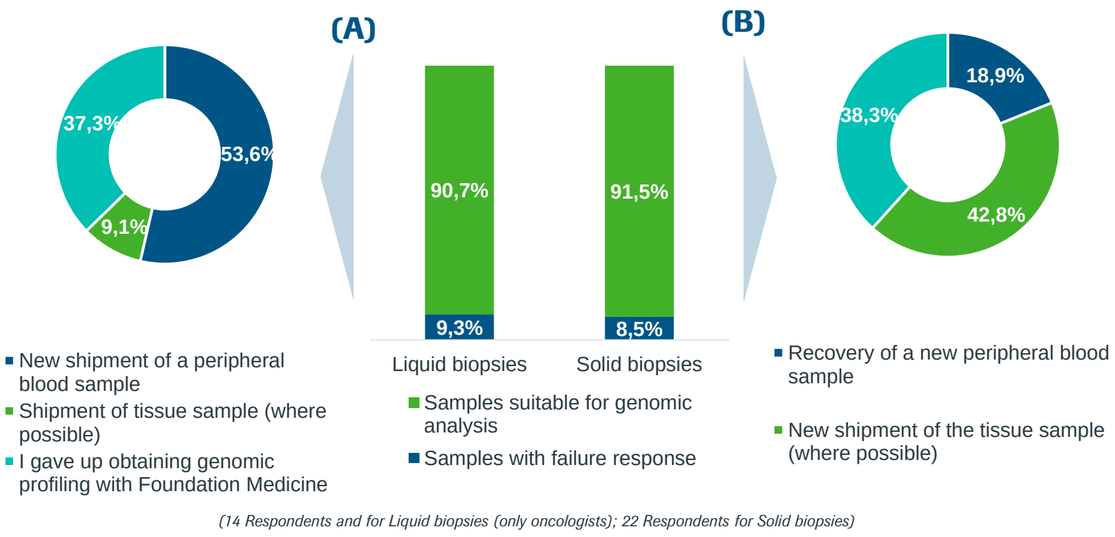


Figure 3. Impact on therapeutic choice

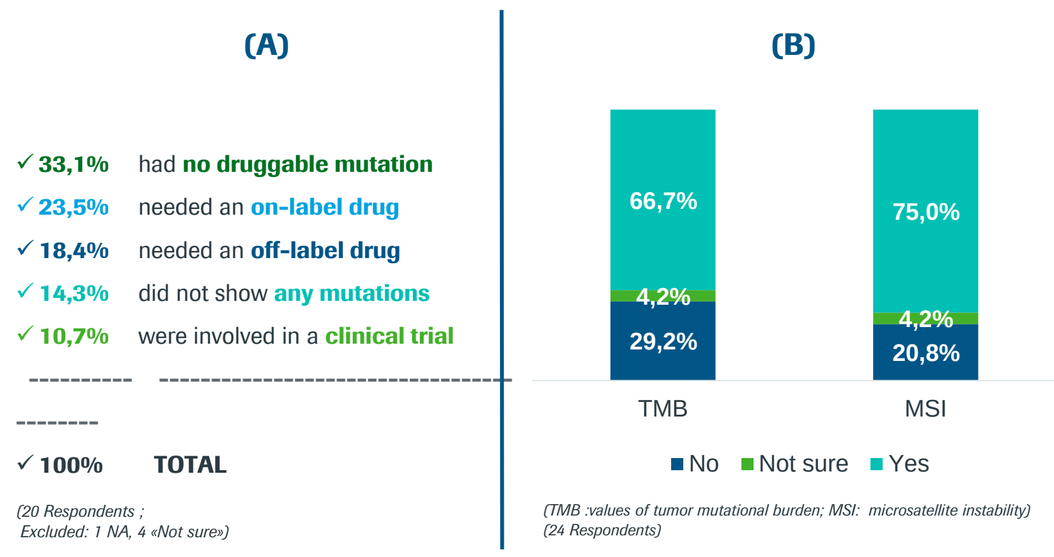
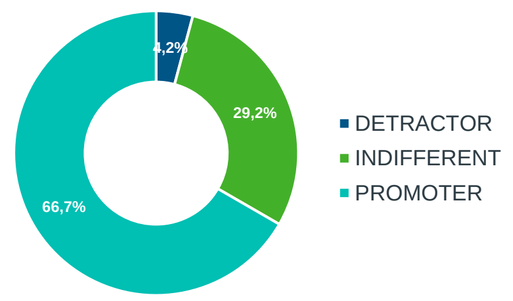


Figure 4. Overall satisfaction



(24 Respondents, Excluded: 1 NA)

(Score from 1 to 10: 0-6 = «Detractor», 7-8 = «Indifferent», 9-10 = «Promoter»)

CONCLUSIONS

This RWE survey is an innovative way of partnering with stakeholders focusing on real needs of final users. FoundationOne CDx –which analyzes tissue biopsies- and FoundationOne Liquid – which analyzes blood- were used equally, suggesting that often tissue is not available in lung cancer patients and clinicians are considering liquid biopsy as a viable alternative for clinical decision making. The fact that clinicians requested CGP at diagnosis highlights the importance of early broad molecular profiling for better therapeutic pathway for patients right form the start.

The small but not negligible failure rates indicate that often the tissue is not collected or stored in a suitable/optimal way for very sophisticated molecular analyses such as next-generation sequencing. The need for standardization of and new pre-analytical procedures is evident.

The impact of CGP on clinical management is remarkable. In fact, in more than half of the tested patients a clinically actionable mutation was detected. Only approximately one fourth of the biomarkers detected had an on-label drug highlighting the need of better and faster clinical studies approval pathways for new drugs or for drug repurposing.

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FOR FURTHER INFORMATION: Please contact Franca Heiman – franca.heiman@iqvia.com - IQVIA, Via Fabio Filzi 29, 20124, Milan Italy

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