Next Generation Sequencing: benefit analysis to support a strategic adoption model in the Italian NHS

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1. INTRODUCTION & OBJECTIVES

The evolution of tumor genomic profiling in personalized medicine requires a strategic management of genetic testing. Among the available technologies, Next Generation Sequencing (NGS), allows simultaneous testing for a wide range of genes. However NGS test benefits still need to be assessed and compared to the single-gene test (SGT) approach to provide recommendations for a strategic adoption in the Italian NHS setting.

The study aims to assess the differential impact of NGS and single-gene tests on the diagnostic-therapeutic process of patients with advanced non-small-cell lung cancer (aNSCLC) in a selection of Italian hospitals. On this purpose, we designed a decision model structured in two arms, SGT and NGS approaches, and three stages i.e. diagnostic biopsy, genetic testing and therapy initiation *(See Figure 1).*

2. METHODS

The analysis intends to compare the impact of NGS vs SGT on hospital organization, patient and disease management. Specifically we have measured the following indicators:

- **Resource use**: estimating the differential costs in terms of personnel time absorption (full time equivalent -FTEs- converted by personnel hourly cost), consumables, capital equipment and other relevant direct and indirect costs
- **Time to treatment**: comparing the average time to treatment from biopsy, as a result of the different procedures, machine processing times and number of genes that can be tested simultaneously given capacity constraints
- **Access to advanced therapies**: assessing the proportion of patient that could be eligible for personalized medicine or clinical trials (should no approved treatment already be available as a targeted response to the identified mutations) as a result of the different number of genetic alterations tested

The patient testing path was designed according to the clinical practice of the three Italian hospitals enrolled in the data collection. Three scenarios *(See Table 1)* have then being defined according to number of genes tested and frequency for aNSCLC patients:

1. **Mandatory**: only includes genes reimbursed by NHS through regional tariffs or strongly recommended by AIOM clinical guidelines
2. **Clinical practice**: genes tested as part of current clinical practice in advanced oncological centers
3. **Clinical Evolution**: expected clinical practice evolution according to gene testing and tumor mutational burden (TMB) research trends

For each gene we defined the associated testing techniques (e.g. Sanger, FISH, PCR, Real-time PCR), the operational activities required (e.g. DNA extraction, purification, library set-up) and the resources absorbed. A specific drill down was conducted on personnel, tracking the time dedicated to each operational activity.

Data on costs (consumables, equipment depreciations, maintenance), time to treatment and access to advanced therapies is still under collection.

Table 1. - Scenarios

SCENARIOS	TESTED GENES	TMB
MANDATORY	3[1]	NO
CLINICAL PRACTICE	8[2]	NO
CLINICAL EVOLUTION	9[2]	YES (only feasible with NGS)

1. EGFR, ALK, ROS-1
2. EGFR, ALK, ROS-1, BRAF, MET exon 14 skipping, HER2, RET, PD-L1, KRAS

3. RESULTS

Preliminary results based on available data demonstrate NGS advantages in terms of personnel time absorption in all the three scenarios considered, with a progressive benefit proportional to the increasing number of tested mutations.

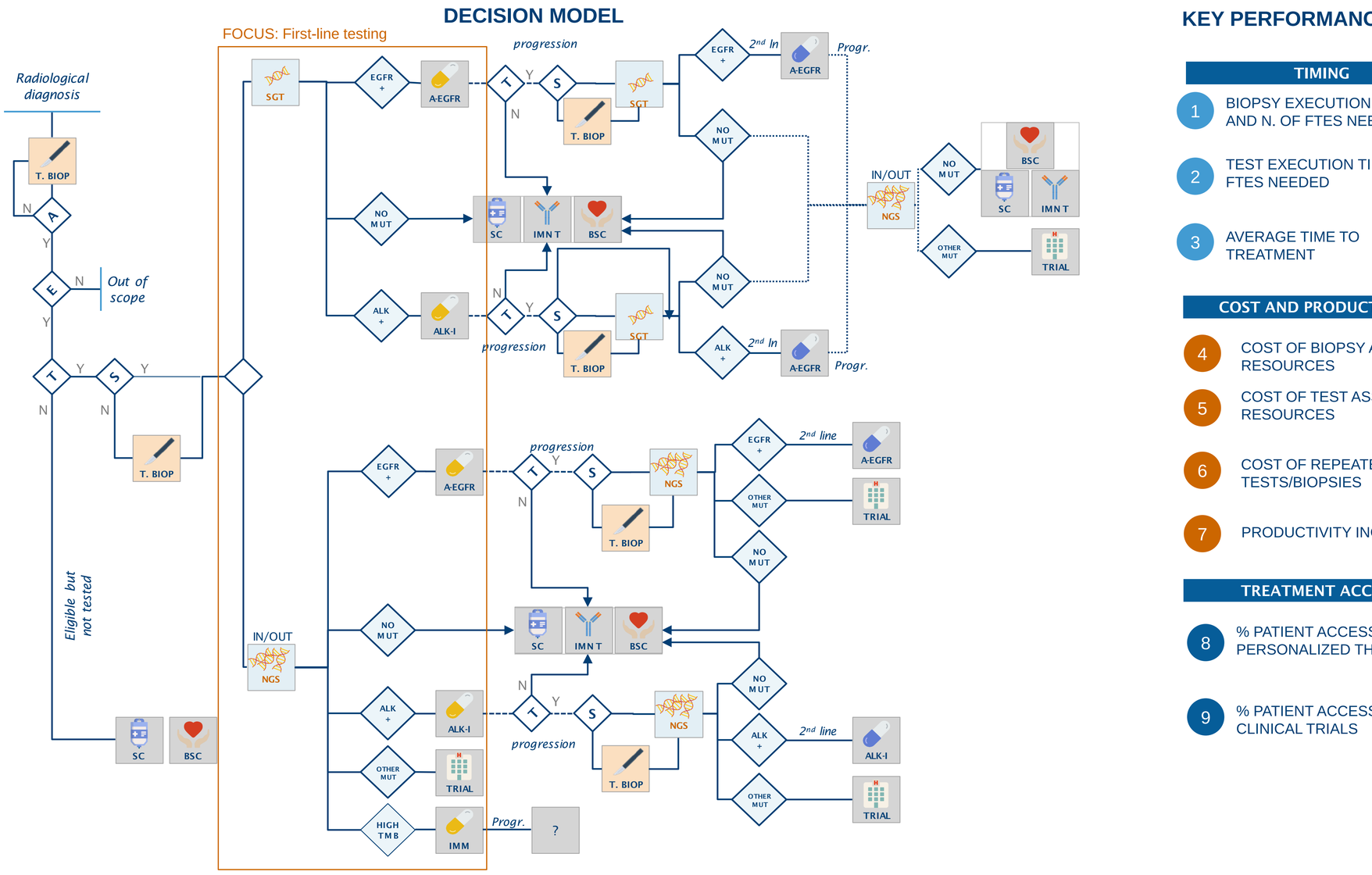
In the "**mandatory scenario**", the use of NGS instead of SGT leads to a saving of **9,7%**, in terms of required laboratory personnel time.

In the "**clinical practice scenario**", given the increase in genes tested (from 3 to 8), the time savings reaches **16,2%**.

In the "**clinical evolution scenario**", considering a set of 9 genes and the TMB evaluation, the saving might reach **53,7%.** In this scenario we should also consider that SGT would not really be a viable alternative, since TMB can be performed with NGS only.

Once the data collection has been completed, a set of strategic recommendations will be developed in order to support the NGS roll-out across the wider Italian NHS.

Figure 1. - Testing path for Advanced NSCLC



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