EE677

Cost-consequence of using NGS *vs.* single-testing in NSCLC patients at diagnosis – Real-world data from a Portuguese hospital

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INTRODUCTION

Lung cancer (LC) is the **leading cause of death by cancer** in Europe and Portugal[1,2]. In recent years, treatment innovations, such as **therapies targeting specific gene mutations**, have been **transforming the management of LC**, particularly Non-Small Cell Lung Cancer (NSCLC), by **improving the average survival** of patients harbouring specific mutations[3,4].

Characterisation of the genomic profile of NSCLC patients is an **essential step for defining the best treatment strategy**[3]. Given the large number of approved targeted therapies (TT) for NSCLC, **ESMO recommends genetic testing using Next-Generation Sequencing (NGS)**, as it allows for the investigation of a high number of genes in a short timeframe and at a relatively affordable cost[5]. Despite this, the adoption in clinical practice of NGS for diagnosing NSCLC patients is still very low in Portugal.

OBJECTIVES

- **To evaluate, using real-world patient data, the cost-consequence at diagnosis of using NGS *vs.* other single-gene testing methods;**
- **To evaluate the cost-saving potential of performing NGS upfront at diagnosis *vs.* sequential multi-gene testing for all currently actionable mutations.**

METHODS

This was a single-centre cross-sectional study with patients newly diagnosed with NSCLC at IPO Porto (IPOP), which **evaluated the real-world use of two different testing strategies at diagnosis**: strategy 1, implemented between June 2017 and June 2019, consisting of parallel single-gene testing (PSG) for genes EGFR, ALK and ROS1; strategy 2, implemented starting May 2019, consisting of NGS testing with a 17-gene panel (Figure 1).

This study was divided into 5 stages:

1. Process mapping: Exploratory interviews with clinicians, management, genetic technicians and operational support staff;

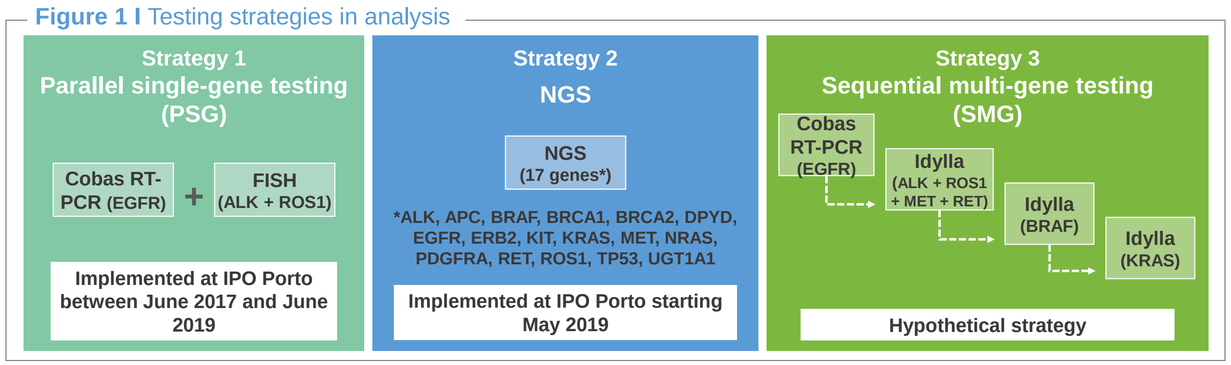
2. Cost determination: Identification of the costs associated with each resource (human and material) used in each technique, using time-driven activity-based costing (TDABC);

3. Data collection and analysis: Collection of relevant data (demographic, clinical and genetic test results) from the IPOP patient database and statistical analysis using RStudio. A significance level of p<0.05 was considered statistically significant;

4. Cost-consequence analysis of NGS: Evaluation of the cost-consequence of NGS at diagnosis *vs.* PSG, by comparing outcomes such as the total number of mutations identified and actionable mutations;

5. Cost-saving potential of NGS: Evaluation of the cost-saving potential of NGS *vs.* sequential multi-gene (SMG) testing - strategy 3 - for all currently actionable genes (with TT approved by EMA) (Figure 1), using the NGS NSCLC cohort population as a case study.

Figure 1 I Testing strategies in analysis



RESULTS

A total of **955 NSCLC patients were identified** that met the inclusion criteria: **486 in the PSG group** and **469 in the NGS group**.

Table 1 I Demographic and clinical characteristics

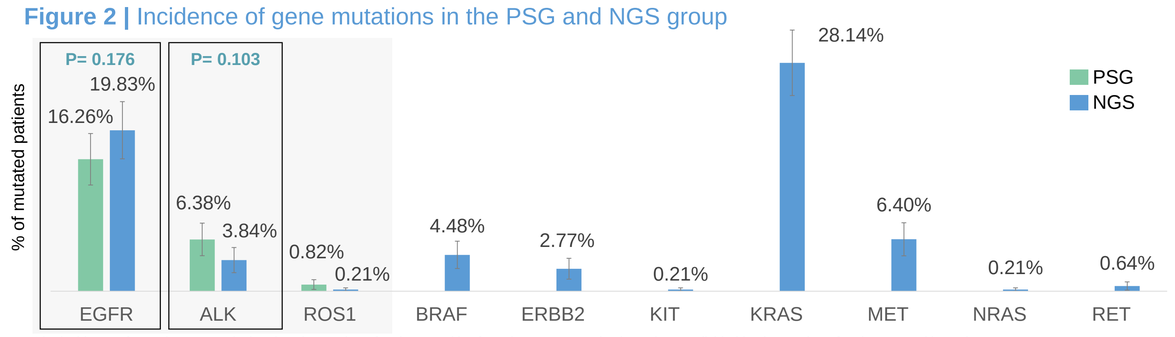
Characteristics	PSG group N=486	NGS group N=469	P-value
	N (%)	N (%)	
Sex			0.612
Male	321 (66%)	318 (68%)	
Female	165 (34%)	151 (32%)	
Age at diagnosis			0.751
Mean (95% CI)	65.9 [65.0, 66.8]	66.1 [65.2, 67.0]	
Disease stage			0.067
Stage I	76 (16%)	93 (20%)	
Stage II	30 (6%)	30 (6%)	
Stage III	95 (19%)	64 (14%)	
Stage IV	277 (57%)	278 (59%)	
No info	8 (2%)	4 (1%)	
Type of NSCLC			0.284
Squamous cell carcinoma	6 (1%)	11 (2%)	
Adenocarcinoma	441 (91%)	413 (88%)	
Other NSCLC	39 (8%)	45 (10%)	

Table 2 I Total and mean tests performed per patient, and time to get a result in each group

Techniques performed	N tests performed	Mean time to get a result (days)
	N Mean [95% CI]	Mean [95% CI]
PSG Group		
FISH – ALK	453 0.93 [0.90, 0.96]	9 [9,9]
FISH – ROS1	446 0.92 [0.89, 0.95]	9 [9,9]
COBAS® RT-PCR – EGFR	496 1.02 [1.00, 1.04]	9 [8,9]
NGS group		
COBAS® RT-PCR – EGFR	2 0.00 [0.00, 0.01]	3 [NA, 22]
NGS – 17 genes	478 1.02 [1.01, 1.03]	13 [13, 14]
FISH – MET	1 0.00 [0.00, 0.01]	8 [NA, NA]
Sanger sequencing – MET	1 0.00 [0.00, 0.01]	6 [NA, NA]

Incidence of gene mutations

Figure 2 | Incidence of gene mutations in the PSG and NGS group

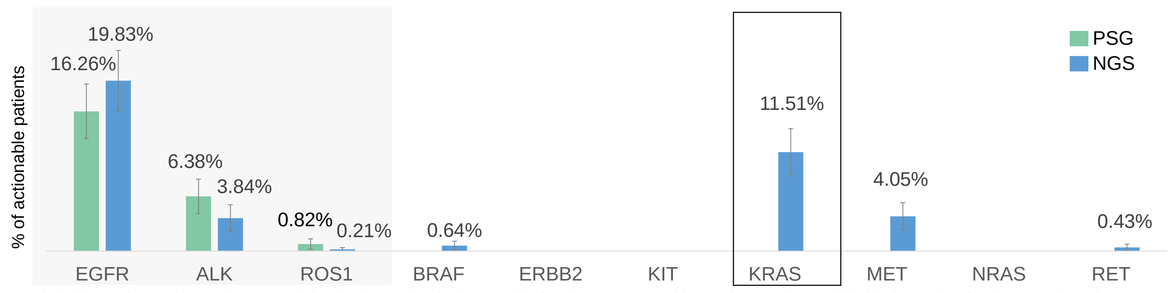


*the incidence of mutations was calculated as the number of patients positive for at least one mutation in each gene divided by the number of patients tested in each group.

The differences in the incidence of mutations in genes EGFR (p=0.176) and ALK (p=0.103) found between the two groups are not statistically significant.

Incidence of actionable gene mutations

Figure 3 | Incidence of actionable gene mutations in the PSG and NGS group



*the incidence of actionable mutations was calculated as the number of patients positive for at least one **actionable** mutation in each gene divided by the number of patients tested in each group.

Cost-consequence analysis

Table 3 I Theoretical cost per group

Techniques performed	Cost of consumables (€)	Cost of human resources (€)	Total cost (€)
PSG	**208.51 €**	**59.65 €**	**268.16 €**
DNA extraction	9.48 €	5.80 €	15.28 €
COBAS® RT-PCR	47.73 €	16.14 €	63.87 €
FISH (ALK+ROS1)	151.30 €	37.71 €	189.01 €
NGS group	**535.67 €**	**29.71 €**	**565.38 €**
DNA extraction	9.48 €	5.80 €	15.28 €
NGS	526.19 €	23.91 €	550.10 €

In practice, the **mean cost per patient** in the **PSG group was 255.59 €**, while in the **NGS group was 576.93 €** per patient.

The differences in the theoretical and real cost per patient result from the fact that, in reality, clinical practice may differ slightly from strategies 1 and 2.

Figure 4 I Percentage of mutated patients

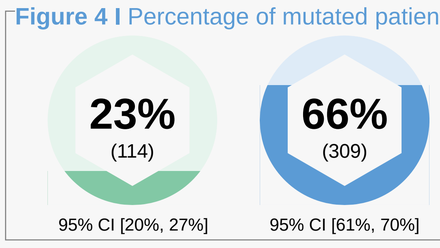
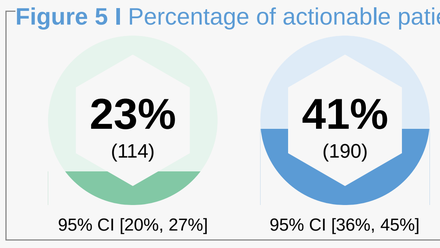


Figure 5 I Percentage of actionable patients

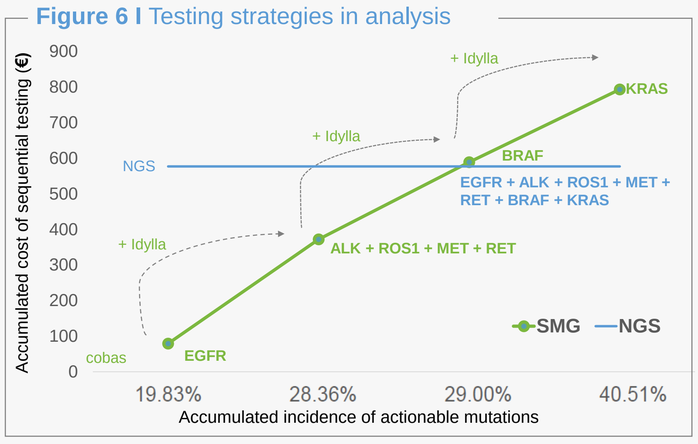


Cost-saving analysis

Table 4 I Cost of each test

Test	Genes being tested	Cost per test (€)	Accumulated cost (€)
SMG group			
COBAS ® RT-PCR	EGFR	79.15 €	79.15 €
Idylla™	ALK, ROS1, MET and RET	292.96 €	372.11 €
Idylla™	BRAF	216.70 €	588.81 €
Idylla™	KRAS	204.40 €	793.21 €

Figure 6 I Testing strategies in analysis



To simulate strategy 3 – SMG testing, the cohort of patients in the NGS group was considered. Based on this hypothetical strategy, each patient in the **SMG group would do, on average, 3.2 tests** [3.1, 3.3], with the **average cost being 614.39 €** [587.99, 640.80 €].

LIMITATIONS

- The cost of each technique is specific to IPOP and could potentially not be representative, hindering the generalizability of the cost-consequence analysis;
- A gene was only considered to be actionable if there were TT approved by EMA, meaning that ERBB2 mutations, which have TT approved by FDA and are currently used off-label in some Portuguese institutions, were not considered actionable, despite being present in 13 patients in the NGS group (2.77%).

TAKE HOME MESSAGES

- **The average cost per patient of performing NGS at diagnosis is superior to the PSG group - 576.93 € *vs.* 255.59 €. However, it allowed for the identification of more mutated patients - 66% (309) vs. 23% (114) and patients potentially eligible for TT - 41% (190) vs. 23% (114);**
- **Given that TT have better clinical outcomes, knowing the mutation status for all actionable mutations is essential to optimise treatment decision;**
- **Sequential testing for all currently known actionable mutations (strategy 3 – SMG testing) is, on average, 37.5 € more expensive per patient than NGS. The cost-saving potential of NGS is only thought to increase in the future.**

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References

[1] OECD/European Union. Health at a Glance: Europe 2022; [2] Globocan 2020 Portugal; [3] Michelotti A.et al.. NSCLC as the Paradigm of Precision Medicine at Its Finest: The Rise of New Druggable Molecular Targets for Advanced Disease. Int J Mol Sci. 2022 Jun 17;23(12):6748; [4] Mosele F. et al. Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group. Annals of Oncology. 2020 Nov;31(11):1491–505.