Assessing the Value of Next Generation Sequencing in NSCLC

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Overview

Objectives: Next-generation sequencing (NGS) has emerged as a powerful diagnostic tool in precision oncology, enabling personalized treatment for cancer patients. Due to the significant potential impact of NGS on patient care, it is important to understand its full value, which includes the relative impact of comprehensive testing versus single and sequential testing. We conducted a targeted review of the clinical and economic impacts of comprehensive testing (CT) via NGS in non-small cell lung cancer (NSCLC).

Methods: We reviewed select literature focused on the five largest European countries to assess available data on the clinical and economic value of CT in NSCLC (e.g., improved decision making, outcomes, accuracy, cost-effectiveness). The identified studies included retrospective analyses of empirical data and modelbased projections of the impact of CT versus sequential or single-gene methods.

Comprehensive testing is defined as the evaluation of all driver or actionable mutations using both NGS panels and IHC, rather than single gene tests that evaluate individual biomarkers

Table 1. Incremental Cost Effectiveness Ratios of Comprehensive Testing for Advanced and Metastatic NSCLC in EU Countries

Author & Year	Study Country	, Study Design	Estimated ICER*
Loubiere 2018 ³	FR	Prospective study of 843 advanced NSCLC patients across 19 French hospitals	~€13.2 K / LY
Arriola 2023 ¹	SP	Joint decision tree and partitioned survival model of metastatic NSCLC leveraging values from Spanish databases and literature	~ €25.9 K / QALY



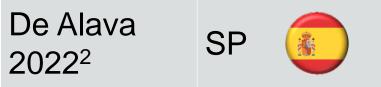
Results: We identified studies that implemented systematic analysis and review of the economic value of CT compared to sequential or single gene testing. These studies demonstrate that CT vs. sequential or single gene methods meets the incremental cost-effectiveness ratio (ICER) thresholds of these countries, which range from €20 – 30 K. CT can also result in direct cost savings, reducing costs related to testing, hospitalization, and personnel costs by up to $\in 5$ K per patient. In many studies, CT was also associated with improved treatment decisions for NSCLC patients, resulting in longer progression-free survival (PFS) and overall survival rates.

Conclusions: Significant progress has been made in recent years in terms of defining and articulating the value of NGS-based CT. Adoption of NGS has the potential to substantially improve patient outcomes and reduce healthcare costs. Overall, this research highlights the importance of understanding the value of NGS to optimize its use and improve patient outcomes in NSCLC. Given most studies focus on late-stage NSCLC, the additional challenges associated with early-stage disease should also be evaluated to determine the utility of NGS across NCSLC stages.

Introduction

- Precision medicine has become critical to improving outcomes for many patients with NSCLC, allowing for identification of specific genomic alterations that will respond to targeted therapies
- NGS allows for greater identification of such patients; however, it is often used in only a small proportion of NSCLC patients, due to lack of awareness of the potential clinical and economic benefits associated with CT
- Several recent studies have specifically evaluated the economic implications of CT for NSCLC patients, especially those with advanced (aNSCLC) or metastatic (mNSCLC) disease

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Decision tree model of metastatic NSCLC using clinical inputs from literature and expert interviews

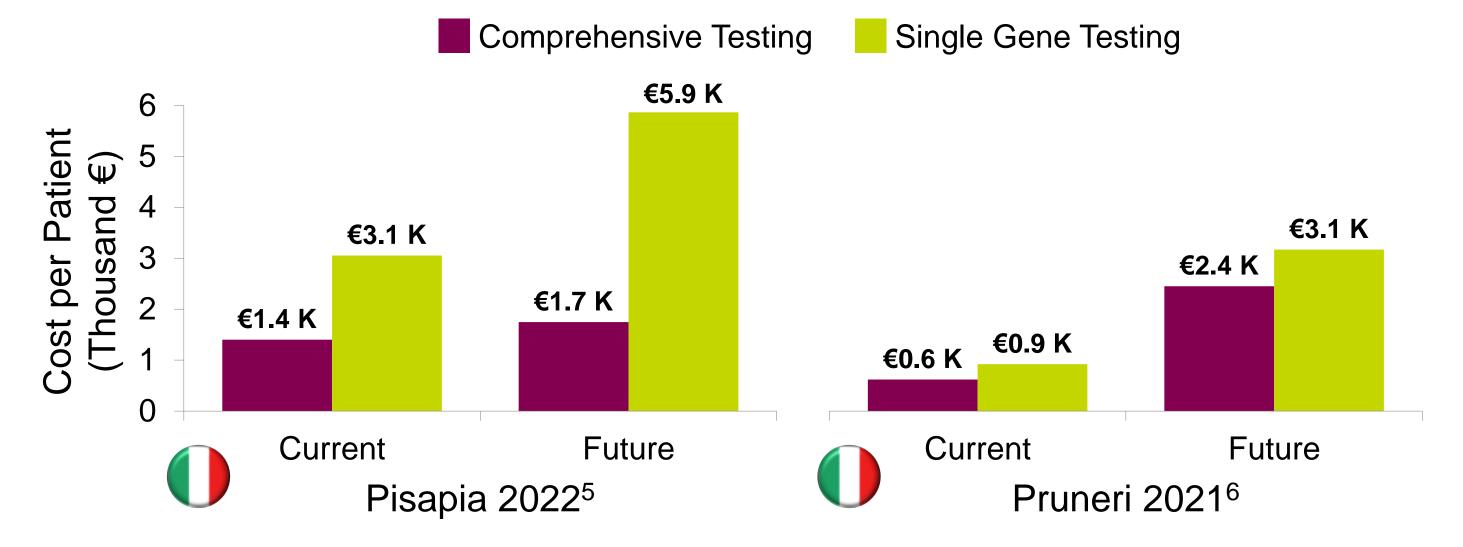
~€9.1 K / QALY

(*) ICER thresholds for countries in the EU tend to be in the range of €20 – 30 K per QALY.^{4,8} While this is a commonly cited range, it should be noted that there may be variation in official thresholds across countries.

Recent Studies Suggest Comprehensive Testing is Cost-effective in the EU

Three studies evaluating the cost-effectiveness of comprehensive testing in France³ and Spain^{1,2} demonstrated that additional costs associated with CT fall well below established cost-effectiveness thresholds in each country. These studies suggest that the cost-effectiveness of CT in metastatic and advanced NSCLC is driven by earlier, broader diagnostic results and improvement in outcomes.

Figure 2. Cost Per Patient for Comprehensive vs. Single Gene Testing in aNSCLC



Comprehensive Testing is Anticipated to Reduce Advanced NSCLC Patient Costs

Although the extent of cost reduction may differ, recent studies suggest CT is less expensive than multiple single-gene tests in current practice.^{5,6} This cost differential is expected to increase in the future as genetic testing becomes more ubiquitous due to additional NSCLC-associated genes and respective treatments being developed, with potential future savings of approximately $\in 1 - 4$ K per patient.^{5,6}

• The aim of this study was to collect and evaluate existing evidence for the cost savings and cost-effectiveness of CT for NSCLC in the EU

Concise Methods

We conducted a targeted PubMed search of English-language publications within the last 5 years on the impact of CT in all stages of NSCLC across economic and clinical metrics in major EU markets. Studies identified were evaluated to select those that were relevant to NSCLC specifically and Europe and to eliminate those with lowerstrength evidence.

Results & Findings

Recent publications include economic evaluation of comprehensive testing

Our search yielded 60 publications, published from 2018 to 2023, demonstrating the value of CT in NSCLC, of which we identified 6 focused on economic impacts. We included publications on a variety of economic metrics, such as cost effectiveness and cost savings, as well as those on outcome improvement.

Figure 1. Prioritization of Studies to Include in Analysis.

Focused Literature Review of

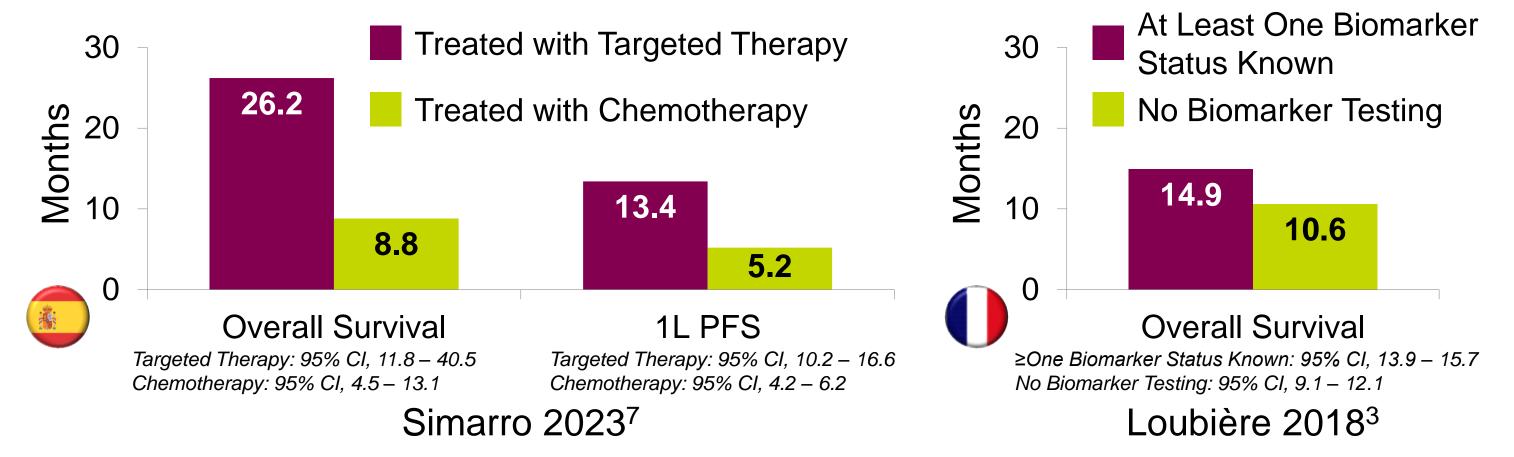
60 Studies



Inclusion

Studies

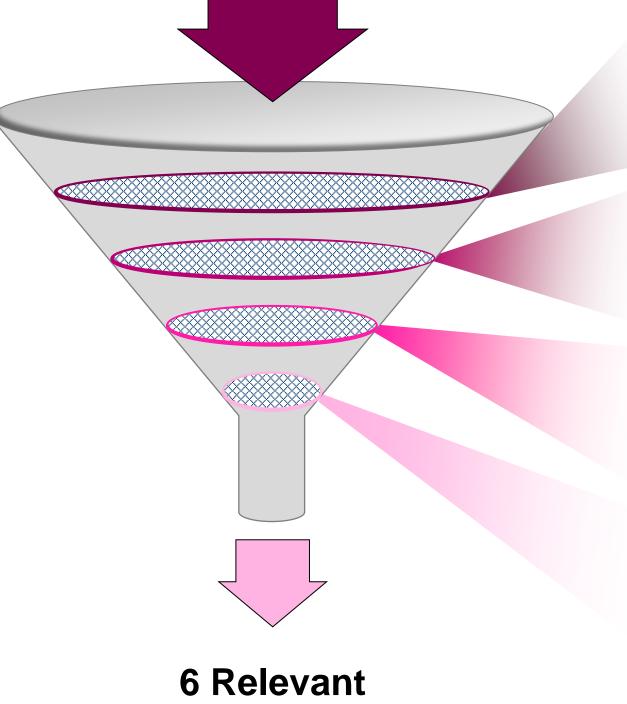
Figure 3. Impact of Comprehensive Testing and Targeted Therapy on Clinical **Outcomes of NSCLC Patients**



Targeted Therapy Results in Improved Outcomes for NSCLC Patients

A recent study of >200 NSCLC patients of all stages in Spain⁷ clearly demonstrated that patients who received targeted therapy aligned with their NGS analysis had better outcomes in terms of both overall and progression-free survival. These results are supported by a French study³ of >800 advanced NSCLC patients which found that patients with at least one identified biomarker had longer mean survival than patients without biomarker testing.

Conclusions



EU-focused Studies

Criteria	Eliminated
Studies that focused on the economic impacts of comprehensive testing	34
Inclusion of NSCLC in indications evaluated	5
High evidence strength (e.g., study design, direct vs. indirect evidence)	2
EU-based studies	13

This research identifies two key themes on the impact of CT on NSCLC in the EU: 1) initial studies strongly suggest that CT is not only cost-effective but may also confer cost savings for NSCLC patients, and 2) targeted therapy enabled by CT improves outcomes for NSCLC patients. These are important insights which support additional investigation in future studies, such as a systematic review across geographies on the value of CT in NSCLC, and investigation into the value of CT for early-stage NSCLC patients.

Based on the limited evidence available today, CT could improve care for patients in a cost-effective manner. Additional research is needed to fully understand the value of NGS and CT in NSCLC.

References)
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1. Arriola, et al. JCO Precis Oncol. 2023 Mar;7:e2200546. 2. de Alava, et al. Expert Rev Pharmacoecon Outcomes Res. 2022 6. Pruneri, et al. Pharmacoecon Open. 2021 Jun;5(2):285-298. Sep;22(6):1033-1042. 3. Loubière, et al. Eur Respir J. 2018 Mar 15;51(3):1701467.

- 4. Pichon-Rievere. Lancet Glob Health. 2023 Jun;11(6):e833-e842.
- 5. Pisapia, et al. Crit Rev Oncol Hematol. 2022 Jan;169:103525.
- 7. Simmaro, et al. Cancers (Basel). 2023 Mar; 15(6): 1705. 8. Vallejo-Torres, et al. Health Econ. 2018 Apr;27(4):746-761.