

## Advancements in Non-Small Cell Lung Cancer

# Biomarker testing in patients with advanced non-small cell lung cancer: the never-ending story

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In the era of precision oncology, a rapidly increasing number of predictive biomarkers have been routinely implemented to define the advanced non-small cell lung cancer (NSCLC) patients' treatment decision making process. The Clinical Practice Guidelines of the European Society for Medical Oncology (ESMO) for NSCLC in the advanced stage suggest a panel of mandatory testing genes including *EGFR*, *KRAS* (p.G12C), *BRAF* (p.V600), *ERBB2*, and *MET* (exon 14 skipping) mutations, *MET* amplifications, *ALK*, *ROS1*, *RET*, and *NTRK1/2/3* fusions, and PD-L1 expression.<sup>1</sup> However, there is suggestive evidence that routine testing of predictive biomarkers is not evolving along with approval of new treatments.

Two papers published in *The Lancet Regional Health—Europe* for the Series on “Advancements in Non-Small Cell Lung Cancer” provide an overview of the major recent developments in targeted therapy treatment for advanced NSCLC, the differences in predictive biomarker testing rates and targeted therapy availability for patients across Europe<sup>2</sup> and a future perspective of the application of molecular testing in advanced stage NSCLC.<sup>3</sup>

As reported in the first paper by Jager et al.,<sup>2</sup> it is now strictly necessary to implement routine large-panel next-generation sequencing (NGS) for all patients with advanced stage NSCLC to enable testing of all clinically relevant biomarkers, both for biomarkers relevant at the present time as well as for those who will be relevant in the near future. Unfortunately, in the real world setting the access to this type of approach is still limited, as highlighted by Bayle et al. in the ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe.<sup>4</sup> The adoption of comprehensive genome profile (CGP) strategies in clinical trials enhanced the list of “promising biomarkers” that could play a pivotal role as prognostic or predictive players in the practice of

predictive molecular pathology. Among them, *NRG1* fusions; *MAP2K1*, *ERBB2*, *BRCA1/2* mutations, *BRAF* non-p.V600 and *KRAS* non-p.G12C mutations are currently being investigated in clinical trials as potential drug-susceptible alterations and represent only a small part of this never ending story.<sup>2</sup>

To transfer the power of this knowledge into daily clinical practice and to decode in a routine setting the role of co-occurring mutations in different biomarkers, several barriers need to be overcome. In particular, as described by Jager et al. in their Viewpoint,<sup>3</sup> one of the main barriers is represented by a harmonized access to the drug across the European countries, and this is even more difficult taking into account that National guidelines of European countries already contain recommendations for predictive biomarker testing in patients with NSCLC, but only partially align with current ESMO guidelines. In addition, to make effective the power of CGP, National Knowledge Base Database—collecting in one place the data coming from the different institutions—represents a milestone needed to be reached.<sup>5</sup> Furthermore, the Molecular Tumor Board (MTB) must be implemented in daily practice, overcoming the barriers due to the lack of national guidelines in most European countries. MTB represent the key weapon to decodify the power of CGP making effective the access to the new therapeutic options for NSCLC patient.

Moreover, in this complex but fascinating scenario, to ensure a sustainability of the system, predictive molecular testing using large-panel NGS should be centralized in experienced institution fully integrated in an oncological network, as this is the keystone to ensure equal access to biomarker, testing to all patients. Considering all the topics discussed in these two papers and the need to run at the same speed as the evolution of NSCLC biomarker testing landscape, an additional barrier that need to be overcome, allowing the fully transfer of the knowledge from clinical trial to clinical setting, will be represented by our ability to “embrace” a fully digital revolution of our recording system.

#### Contributors

Both authors contributed equally.



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## Declaration of interests

Nothing to declare.

## References

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