

Combined Analysis of CTC-Derived DNA and Plasma ctDNA Improves Preoperative Detection of Clinically Relevant Genomic Alterations in Early-stage NSCLC

F. Lococo^{*1,2}, Y. Liu^{*3}, J. Evangelista^{4,5}, I. Desitter³, M. Heidary³, K. Vasileiou³, E. De Paolis^{4,5}, C. Sassorossi¹, M. Giannakoulis³, A. Campanella¹, K. Prevost³, A. Decina³, A. Minucci^{4,5}, D. Brechot³, P. Paterlini³

* co-first authors

1 Thoracic Surgery, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, 00168, Italy.

2 Thoracic Surgery, Università Cattolica del Sacro Cuore, Rome, 00168, Italy

3 Rarecells Diagnostics, Cancer Campus, 3 mail du Docteur Nicole Girard-Mangin 94800 Villejuif

4 Departmental Unit of Molecular and Genomic Diagnostics, Genomics Core Facility, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, 00168, Italy

5 Science and Technology Park (G-STeP), Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, 00168, Italy

***Corresponding author:**

Patrizia Paterlini MD, PhD, [E-mail:patrizia.paterlini@rarecells.com](mailto:patrizia.paterlini@rarecells.com)

References:

- Tsuboi, M. *et al.* Neoadjuvant osimertinib with/without chemotherapy versus chemotherapy alone for EGFR-mutated resectable non-small-cell lung cancer: NeoADAURA. *Future Oncology* **17**, 4045–4055 (2021).
- Hong, T. H. *et al.* Clinical Utility of Tumor-Naïve Presurgical Circulating Tumor DNA Detection in Early-Stage NSCLC. *Journal of Thoracic Oncology* **19**, 1512–1524 (2024).
- Driussi, A. *et al.* Clinicopathological Predictors of the Presence of Blood Circulating Tumor DNA in Early-Stage Non-Small Cell Lung Cancers. *Modern Pathology* **38**, (2025).
- Hofman, V. *et al.* Preoperative Circulating Tumor Cell Detection Using the Isolation by Size of Epithelial Tumor Cell Method for Patients with Lung Cancer
- Is a New Prognostic Biomarker. *Clin Cancer Res* **17**, 827–835 (2011).
- Laget, S. *et al.* Technical insights into highly sensitive isolation and molecular characterization of fixed and live circulating tumor cells for early detection of tumor invasion. *PLoS One* **12**, (2017).
- Ilie, M. *et al.* ‘Sentinel’ circulating tumor cells allow early diagnosis of lung cancer in patients with Chronic obstructive pulmonary disease. *PLoS One* **9**, (2014).
- Zer, A. *et al.* Early and locally advanced non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆. *Annals of Oncology* **36**, 1245–1262 (2025).

- Jamal-Hanjani, M. *et al.* Tracking the evolution of non-small-cell lung cancer. *N Engl J Med.* **376**, 2109–2121 (2017).
- He Y. *et al.* Concordance of genomic profiles in matched tissue and plasma samples from Chinese patients with lung cancer. *Cancer Inform.* **16**: 1–9 (2022)
- Kim, W. *et al.* Mutational differences between primary cancer tissue and circulating tumor cells in early-stage non-small cell lung cancer. *Transl. Lung Cancer Res.* **13**, 3026–3038 (2024).
- Wishart, G., Templeman, A., Hendry, F., Miller, K. & Pailhes-Jimenez, A. S. Molecular Profiling of Circulating Tumour Cells and Circulating Tumour DNA: Complementary Insights from a Single Blood Sample Utilising the Parsortix® System. *Current Issues in Molecular Biology* vol. 46 773–787 Preprint at <https://doi.org/10.3390/cimb46010050> (2024).