

P2.208: ctDNA Predicts Disease Progression in Advanced Non-Small-Cell Lung Cancer Post Immunotherapy

Fang Wu¹, Yue Zeng¹, Yurong Peng¹, Xingxiang Pu², Ping Liu³, Fang Ma¹, Zhenhua Qiu¹, Lemeng Zhang², Yan Zhou⁴, Cheng-Zhi Zhou⁵, Qing Bu⁶, Jie Weng⁷, Juan Yu⁸, Rui Meng⁹, Hailong Liu¹⁰, Zhiqing Zhou¹¹, Zengmei Sheng¹², Chaojiu Xu¹³, Hongke Wang¹⁴, Wei Yang¹⁵
¹The Second Xiangya Hospital of Central South University, ²Hunan Cancer Hospital, ³The First Hospital of Changsha City, ⁴The Third Xiangya Hospital of Central South University, ⁵the First Affiliated Hospital of Guangzhou Medical University, ⁶The First Affiliated Hospital of Guangxi Medical University, ⁷Yueyang Central Hospital, Yueyang, ⁸Zhangjiajie People's Hospital, ⁹Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, ¹⁰Chenzhou First People's Hospital, ¹¹The Second People's Hospital of Huaihua, ¹²The Third Hospital of Changsha, ¹³The hospital of Xiangxi Autonomous Prefecture, ¹⁴Geneplus-Beijing Institute, ¹⁵Geneseeq Research Institute, Nanjing Geneseeq Technology Inc..
Correspondence: wufang4461@csu.edu.cn; Department of Oncology, The Second Xiangya Hospital, Central South University, Changsha, Hunan 410011, China



IASLC 2026 World
Conference on Lung Cancer
SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

- Patients with advanced non-small-cell lung cancer (NSCLC) who experience durable benefit from first-line immunotherapy have heterogeneous outcomes, but effective tools to stratify subsequent progression risk in this population are lacking.
- We aimed to determine whether serial circulating tumor DNA -based post-immunotherapy minimal residual disease monitoring (ctDNA-iMRD) could identify occult molecular progression and refine risk stratification in this setting (NCT05198154).

METHODS

- Design:** Prospective, observational, multicenter study
- Population:** Patients with advanced NSCLC who had received first-line ICIs-based therapy and remained progression-free for 12 months after treatment initiation.
- ctDNA Monitoring:** Serial plasma collection every 2-3 months in year 1 and every 3-6 months thereafter until progression
- Assays:** Tumor-informed and tumor-agnostic ctDNA approaches
- ctDNA-iMRD positive:** Detectable ctDNA by either assay at any surveillance timepoint
- Primary Endpoint:** Investigator-assessed PFS

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- Surveillance by ctDNA-iMRD in patients with sustained benefit from immunotherapy is predictive of survival outcomes, supporting its potential role in risk-adapted early intervention strategies.

Future Direction for Research

- We launched the CR1STAL-Adaptive study (NCT06951646), a randomized, open-label, phase II multicenter trial, evaluating the safety and efficacy of Ivonescimab plus docetaxel versus standard treatment in advanced NSCLC with long-term benefit from first-line immunotherapy with ctDNA-MRD positive.

REFERENCES & ACKNOWLEDGEMENTS

Acknowledgments

We thank the following individuals and groups for their support:

- All patients and their families
- The multidisciplinary team (MDT) of Thoracic Oncology at the Second Xiangya Hospital, Central South University
- All CR1STAL study investigators

Correspondence to :

Fang Wu, MD, PhD; wufang4461@csu.edu.cn;
Website: <http://fangwulab.com/>



Artificial Intelligence (AI) Use Disclaimer

In accordance with ACCME standards, we disclose that no artificial intelligence tools were used in the development of this presentation, including content creation, literature selection, figure generation, or slide assembly. All materials are the sole work of the authors, who take full responsibility for the accuracy, balance, and clinical validity of the content.

RESULTS

Patients and ctDNA-iMRD Status

- 97 advanced NSCLC patients (46 tumor-informed, 51 tumor-agnostic)
- 49 patients (50.5%) with ctDNA-iMRD positive.

Survival, Lead Time & Assay Performance

- PFS: ctDNA-iMRD (+) vs (-) : 10.1 months vs NR (HR=4.85, P<0.001).
- Median lead time: 5.9 months of ctDNA positive before imaging.
- Comparable predictive performance between two methods: Tumor-informed (HR=6.29; P<0.001) ; Tumor-agnostic (HR=3.67; P=0.001).
- OS: ctDNA-iMRD negative associated with longer survival (HR=0.22, P<0.001).

Additional Prognostic Factors

- Rapid vs. slow ctDNA growth rates: mPFS 5.6 vs. 14.5 mo (HR=5.02; P=0.012).
- Clonal mutations vs. non-clonal: mPFS 7.4 vs. 18.0 mo (HR=3.17; P=0.007).

