



#1999: The resistance mechanism and genomic profile of EGFRm NSCLC patients progressed on 1L osimertinib+CTx (SURPASS study)

Yuqing Lou¹, Shuang Li², Qiming Wang³, Minglei Zhuo⁴, Xiaomei Liu⁵, Yu Zhang⁶, Kejing Tang⁷, Jie Li⁸, Yunjian Huang⁹, Li, Lin¹⁰, Tangfeng Lv¹¹, Xinqing Lin¹², Hong Lu¹³, Yuanyuan Ji¹⁴, Jun Jiang¹⁵, Bi Chen¹⁶, Fangling Ning¹⁷, Jianwen Qin¹⁸, Lingxiang Chen¹⁹, Hongmin Lu²⁰, Bo Zhang¹, Baohui Han¹

¹Shanghai Chest Hospital, ²Shanghai Gobroad Cancer Hospital, ³Henan Cancer Hospital, ⁴Beijing Cancer Hospital, ⁵The First Affiliated Hospital of Jinzhou Medical University, ⁶Nanjing Brain Hospital, The Affiliated Brain Hospital of Nanjing Medical University, ⁷The First Affiliated Hospital of Sun Yat-Sen University, ⁸Jining No.1 People's Hospital, ⁹Fujian Cancer Hospital, ¹⁰Zhangzhou Hospital, ¹¹General Hospital of Eastern Theater Command, ¹²Guangzhou Medical University, ¹³Huaihe Hospital of Henan University, ¹⁴Anyang Cancer Hospital, ¹⁵The First People's Hospital of Foshan, ¹⁶The Affiliated Hospital of Xuzhou Medical University, ¹⁷Binzhou Medical University Hospital, ¹⁸Tianjin Chest Hospital, ¹⁹Jiangsu Cancer Hospital, ²⁰Renji Hospital, Shanghai Jiao Tong University School of Medicine

Correspondence: Baohui Han 18930858216@163.com



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INTRODUCTION

- Osimertinib plus chemotherapy (CTx) has become the preferred first-line (1L) treatment option in patients with EGFR-mutant advanced NSCLC, as this combination regimen showed statistically significant and clinically meaningful improvements of PFS and OS compared with osimertinib monotherapy in the Phase III FLAURA2 study.
- Resistance mechanism in FLAURA2 study was assessed exclusively via plasma ctDNA, lacking tissue-based testing.
- Comparative analyses on resistance mechanism detection between tissue and plasma have demonstrated lower sensitivity of plasma-based Next-Generation Sequencing (NGS) in detecting genomic alterations, particularly copy number variations and gene fusions compared with tissue-based NGS.
- To more comprehensively characterize resistance mechanisms and genomic profiles of post 1L osimertinib plus CTx progression, the SURPASS study, which further generates the data of resistance mechanism in tissue and plasma paired samples in real-world setting to address this data gap.

METHODS

Objective

This real-world, multicenter prospective study characterized resistance mechanisms and genomic profiles in patients with EGFR-mutant (ex19del/L858R) advanced NSCLC who had progressed on 1L osimertinib plus CTx

Study Design

Key inclusion criteria

- Age≥18 years old
- Pathologically confirmed non-squamous NSCLC with documented EGFR sensitive mutation(19del and L858R) before 1L treatment
- Evidence of disease progression following 1L initial treatment with osimertinib plus chemotherapy
- Agree to provide adequate tissue and whole blood for testing

• NGS/
Histopathologic
testing

N=100*, 20 sites

Endpoints

Primary endpoint:

- Genetic profile post 1st line osimertinib+CTx resistance(tissue and plasma)
- Acquired resistance mechanism post 1L Osimertinib+CTx (Paired tissue samples)

Secondary endpoint:

- The percentage of MET overexpression and the percentage of pathology transformation from NSCLC to SCLC or SCC
- Resistance mechanism across different chemotherapy cycles(Paired tissue sample)
- Subsequent treatment regimens

Exploratory endpoint:

- Tumor immune microenvironment such as PD-L1 expression (TPS/CPS), tumor-infiltrating lymphocytes (CD8+/CD4+/FoxP3+), et al.

*About 40 participants among 100 participants will provide baseline tissue samples

Study Objective

Primary objectives

- Integrating tissue and blood samples provides a more comprehensive understanding of genetic profile.
- To evaluate the comprehensive molecular mechanisms of resistance following first-line treatment with Osimertinib in combination with chemotherapy progression by paired tissue samples (at pre-1L treatment and progression disease)

Secondary objectives

- To assess Met overexpression and pathology transformation status
- Comparison of Resistance Mechanisms Across Different CTx Combination Cycles
- To evaluate subsequent treatment regimen

Exploratory objectives

- Assessment of Tumor Immune Microenvironment for the NSCLC participants who had disease progression on first-line treatment with Osimertinib in combination with chemotherapy.

Statistical Analysis

Descriptive statistics will be provided for all variables, as appropriate. Continuous variables will be summarized by the number of observations, mean, standard deviation, median, interquartile range (Q1, Q3), minimum, and maximum. Categorical variables will be summarized by frequency counts and percentages for each category. The 95% confidence interval (CI) will be calculated as appropriate.

Conclusion

To our knowledge, this is the first study to explore resistance mechanisms to 1L osimertinib combined with CTx in a real-world setting through tissue samples, which can provide a more comprehensive understanding of resistance mechanisms, and provides more precise information to support second-line treatment strategies.

REFERENCES & ACKNOWLEDGEMENTS

REFERENCES

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Conflict of interest

The authors have no potential conflict of interest to disclose.
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