Rajiv Gandhi Cancer Institute and Research Centre

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Simultaneous Tissue and Liquid Next-generation Sequencing after First-line EGFR Tyrosine Kinase Inhibitors Resistance in Advanced NSCLC

NTU Cancer Center 台大癌醫中心

Simultaneous Tissue and Liquid Next-generation Sequencing after First-line EGFR Tyrosine Kinase Inhibitors Resistance in Advanced Non-small Cell Lung Cancer

Yen-Ting Lin;[1,2,3,*] Chao-Chi Ho;[2] Wei-Hsun Hsu;[4] Wei-Yu Liao;[2] Ching-Yao Yang;[2] Kien Thiam Tan;[5] Wen Hsiao;[5] Jin-Yuan Shih[1,2]

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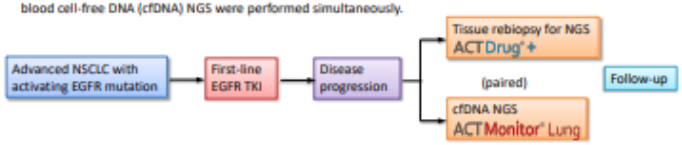
Poster #365

Background

T790M testing is recommended after resistance to first or second-generation EGFR tyrosine kinase inhibitors (TKIs). However, the role of simultaneous tissue and liquid next-generation sequencing (NGS) after first-line EGFR TKI resistance is still unclear.

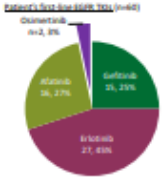
Method

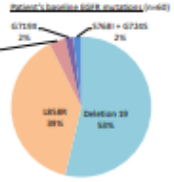
We prospectively enrolled patients with resistance with first-line EGFR TKI. Paired tissue rebiopsy NGS and blood cell-free DNA (cfDNA) NGS were performed simultaneously.



Result

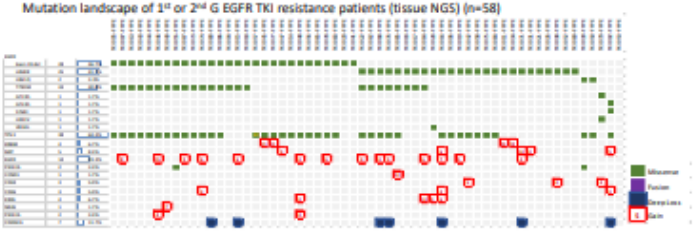
86 patients were enrolled, but 26 of them did not have adequate tissue for NGS. Among the 26 patients, 5 had T790M from cfDNA. Total 60 patients had pairs of tissue and cfDNA NGS were further analyzed.



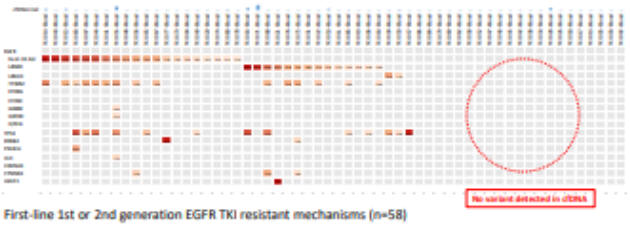


Concordance Rate	
Exon 19 del	87%
L858R	78%
T790M	68%

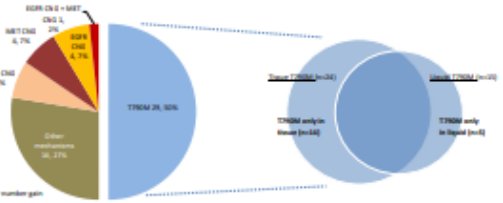
Mutation landscape of 1st or 2nd G EGFR TKI resistance patients (tissue NGS) (n=58)



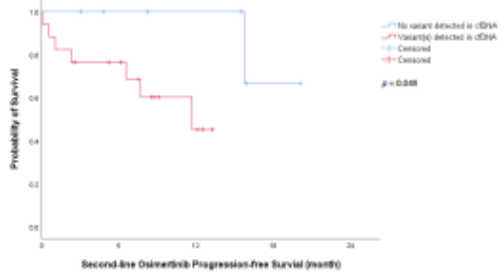
Mutation landscape of 1st or 2nd G EGFR TKI resistance patients (cfDNA NGS) (n=58)



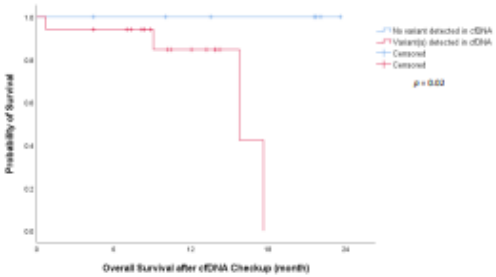
First-line 1st or 2nd generation EGFR TKI resistant mechanisms (n=58)



24 of 29 patients with T790M received second-line osimertinib (n=24)



24 of 29 patients with T790M received second-line osimertinib (n=24) (cont'd)



Conclusion

- Simultaneous tissue rebiopsy NGS and liquid NGS at first-line first or second generation EGFR TKI progression detect more T790M mutation than tissue NGS or liquid NGS only.
- At first-line first or second generation EGFR TKI progression, patients with "no variant detected" in cfDNA NGS may have longer second-line osimertinib PFS and longer OS after cfDNA checkup.
- EGFR, HER2 and MET amplification might contribute to the vast majority of resistance in T790M negative patients.
- NGS at EGFR TKI progression provides more information for sequential anticancer therapy.

Disclosure

✓ This study is sponsored by ACTGenomics.
✓ Yen-Ting Lin has received speaking honoraria from ACTGenomics, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Chugai Pharmaceutical, Eli Lilly, Janssen, Manudipharma, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Takeda and TTY Biopharm; and travel expense from Pfizer.

Reference

- Lin YT et al. *Int J Cancer*. 2019 Jun 1;144(11):2887-2896.
- Wu SG et al. *Mol Cancer*. 2018 Feb 19;17(1):38.
- Rolfo C et al. *J Thorac Oncol*. 2018 Sep;13(9):1248-1268.

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Presented at the ELCC 2022, 30 March – 02 April 2022

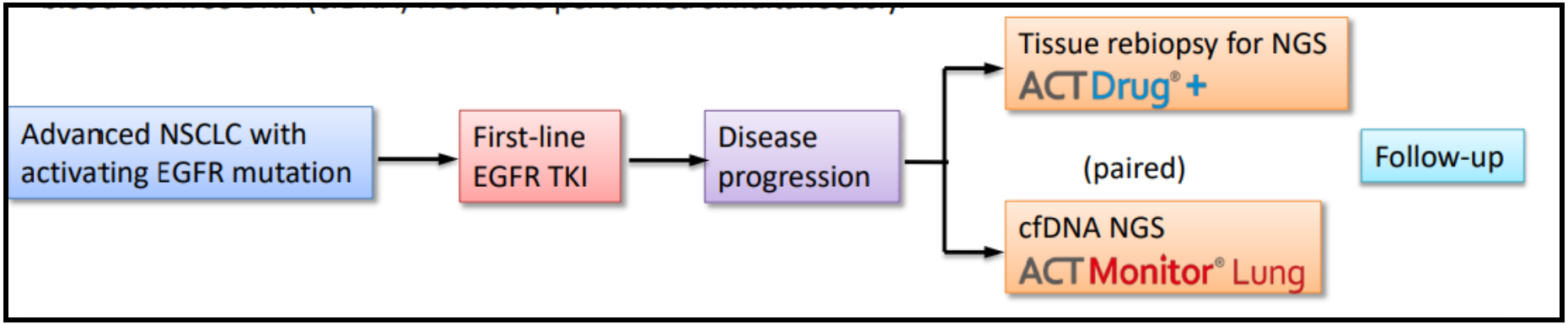
Yen-Ting Lin et al; Presented at the ELCC 2022, 30 March – 02 April 2022; Poster #365

Background

- EGFR mutations are the most robust predictive biomarkers for response to EGFR-TKIs
- Unfortunately, resistance to TKI's are inevitable
- T790M testing is recommended after resistance to first or second-generation EGFR tyrosine kinase inhibitors (TKIs)
- Several studies supports the use of plasma genotyping as a first line testing to detect T790M
- However, the role of simultaneous tissue and liquid next-generation sequencing (NGS) after first-line EGFR TKI resistance is still unclear.

Methodology

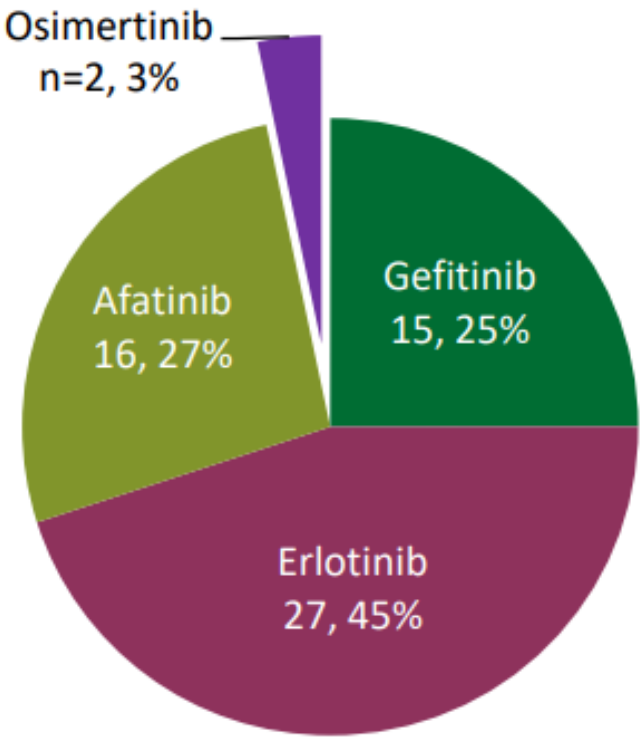
- The patients with resistance with first-line EGFR TKI were prospectively enrolled
- Paired tissue rebiopsy NGS and blood cell-free DNA (cfDNA) NGS were performed simultaneously.



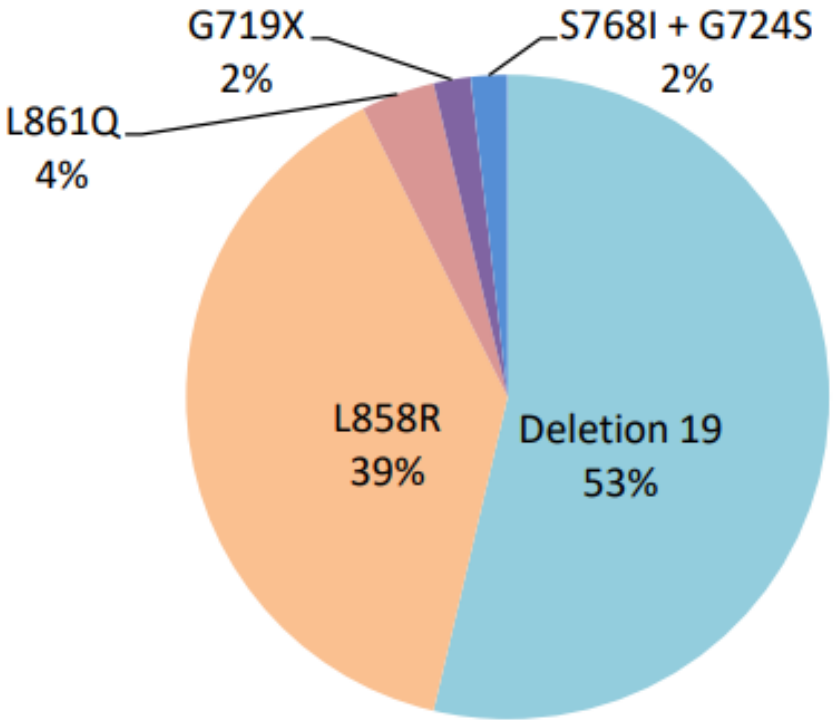
Results

- 86 patients were enrolled
- 26 out of them did not have adequate tissue for NGS
- Among these 26 patients, NGS on cfDNA had revealed T790M in 05 patients
- Total 60 patients had pairs of tissue and cfDNA NGS for comparison and which were further analyzed.

Patient's first-line EGFR TKIs (n=60)



Patient's baseline EGFR mutations (n=60)



1st or 2nd G EGFR TKI resistance patients (n=58)

Concordance between tissue and cf DNA NGS (n=60)

Concordance Rate	
Exon 19 del	87%
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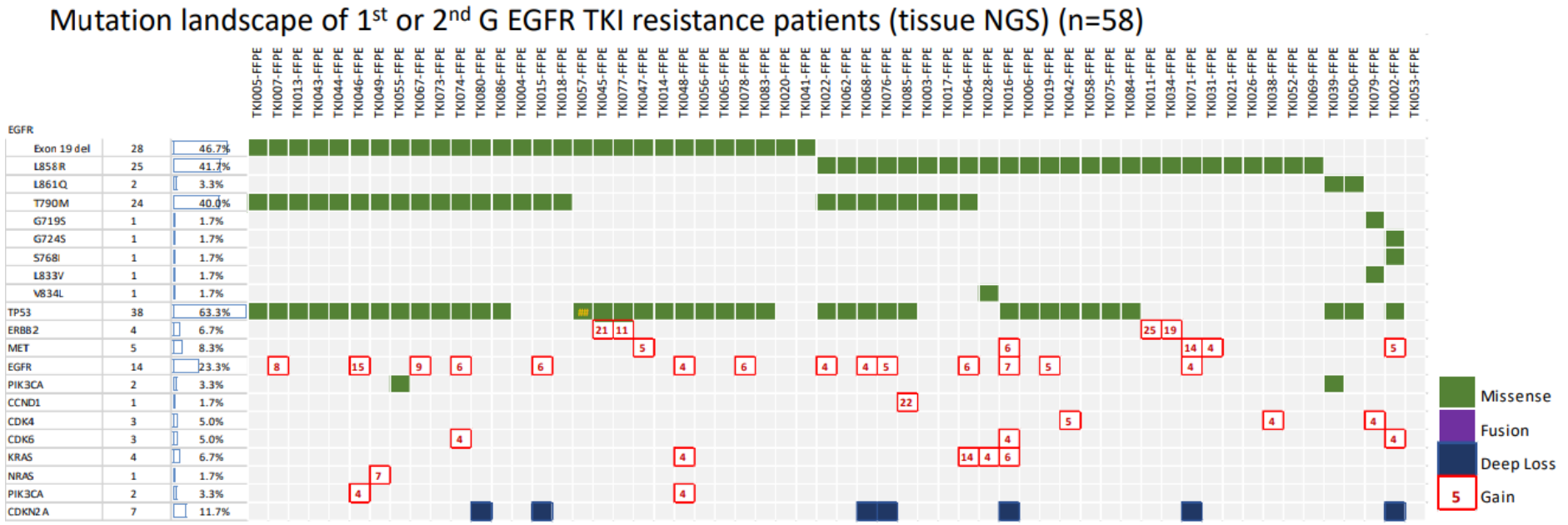
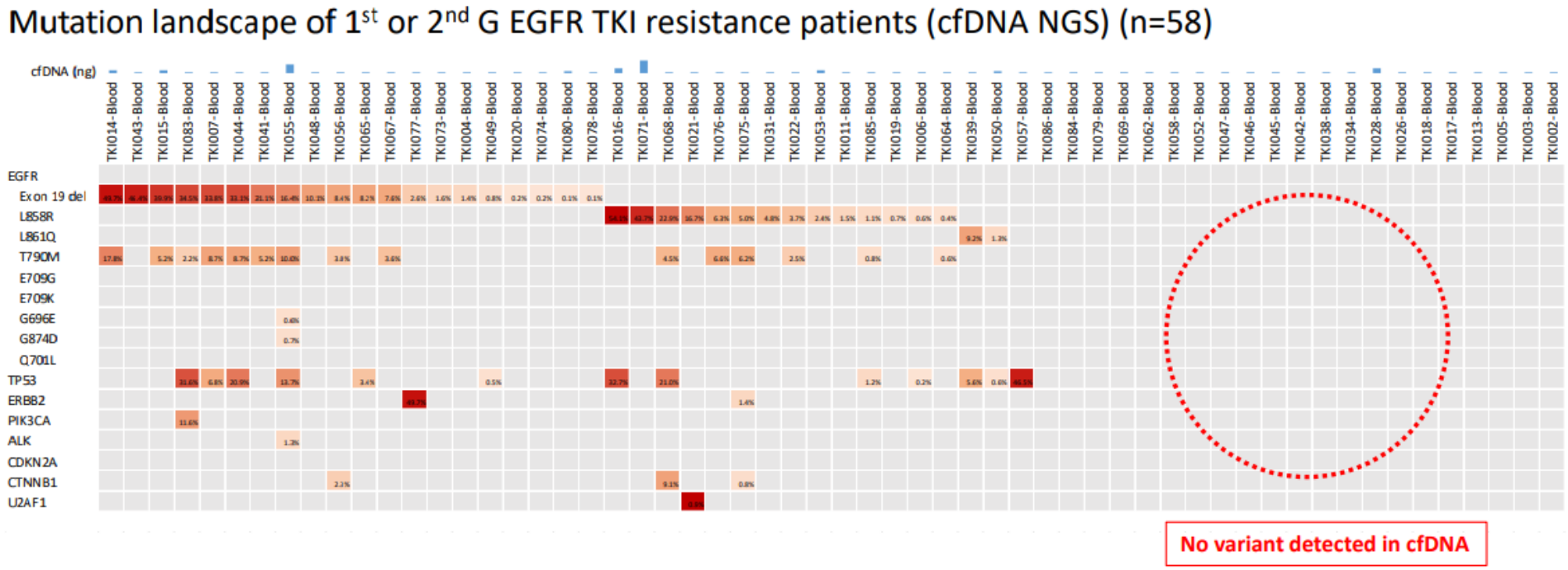
Mutation landscape of 1st or 2nd G EGFR TKI resistance patients (tissue NGS) (n=58)



Mutation landscape of 1st or 2nd G EGFR TKI resistance patients (cfDNA NGS) (n=58)



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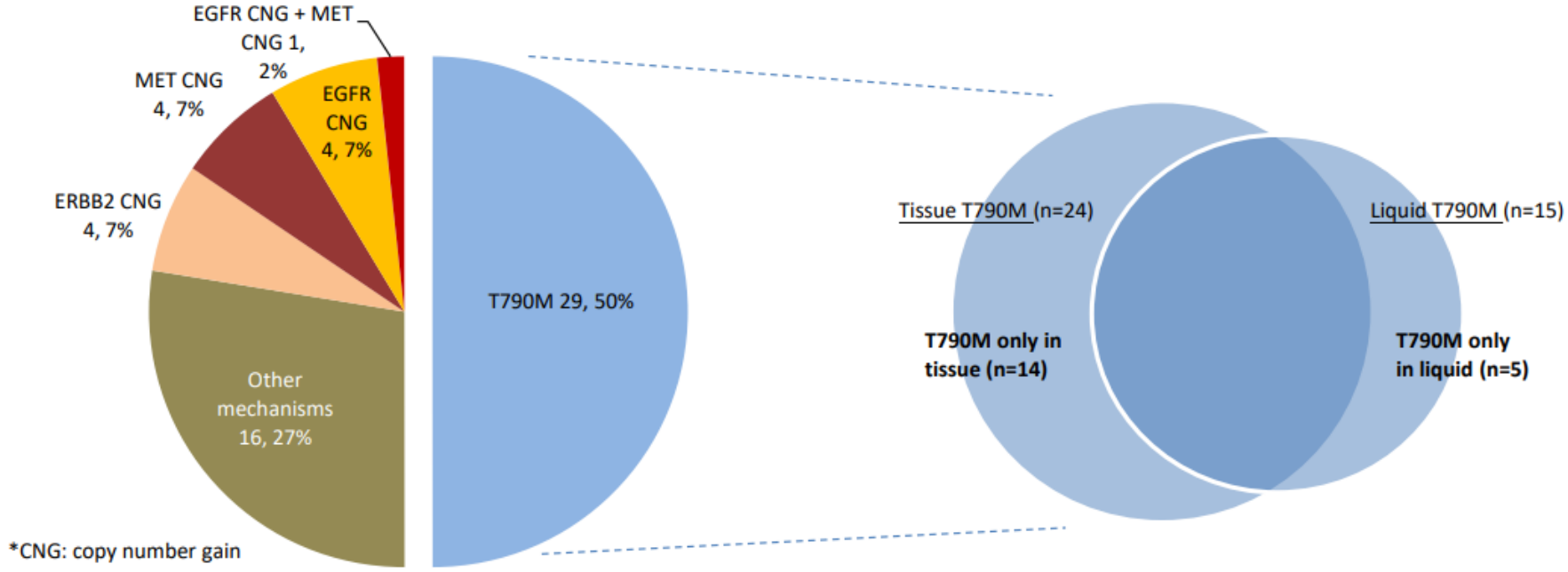

*CNG: copy number gain

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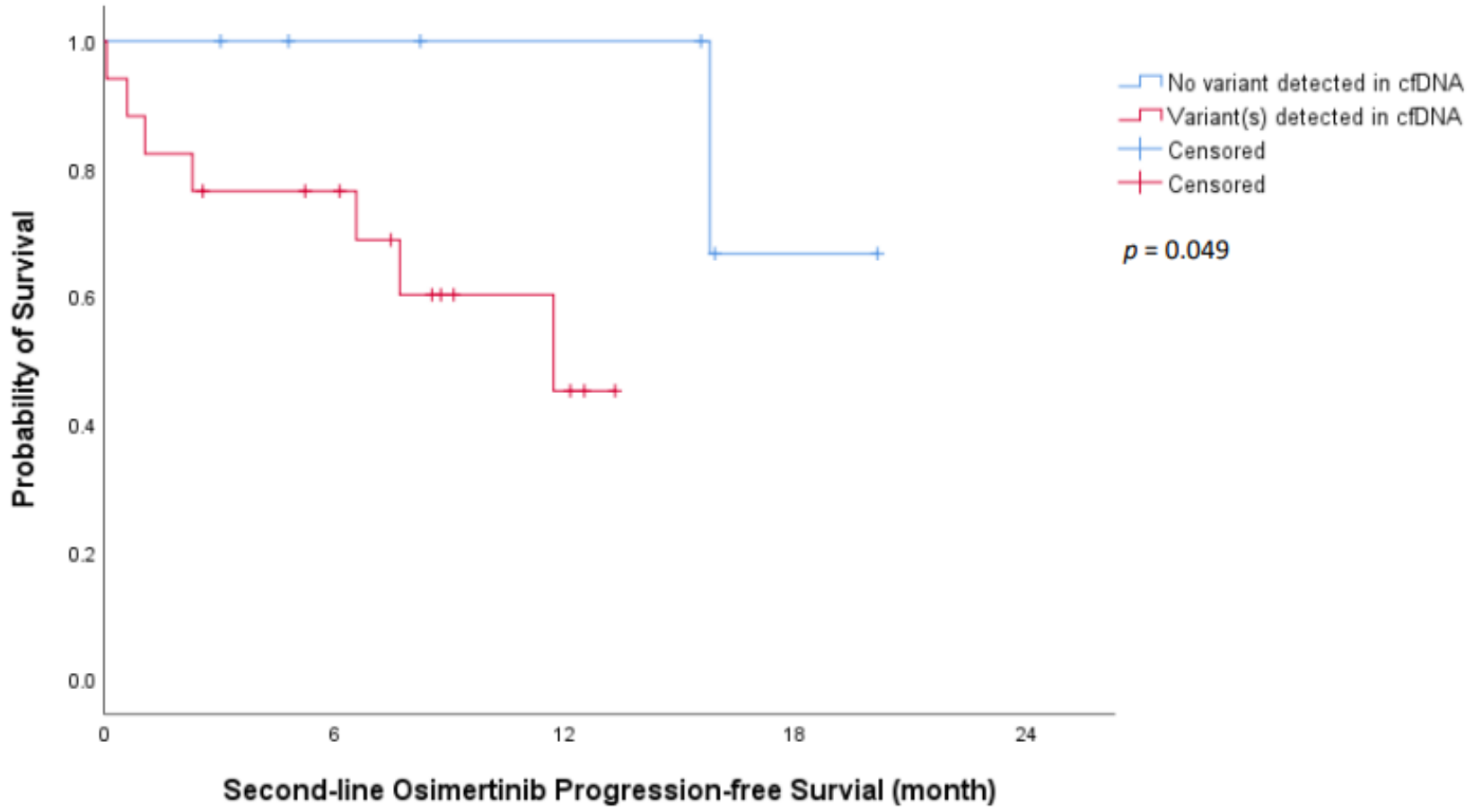
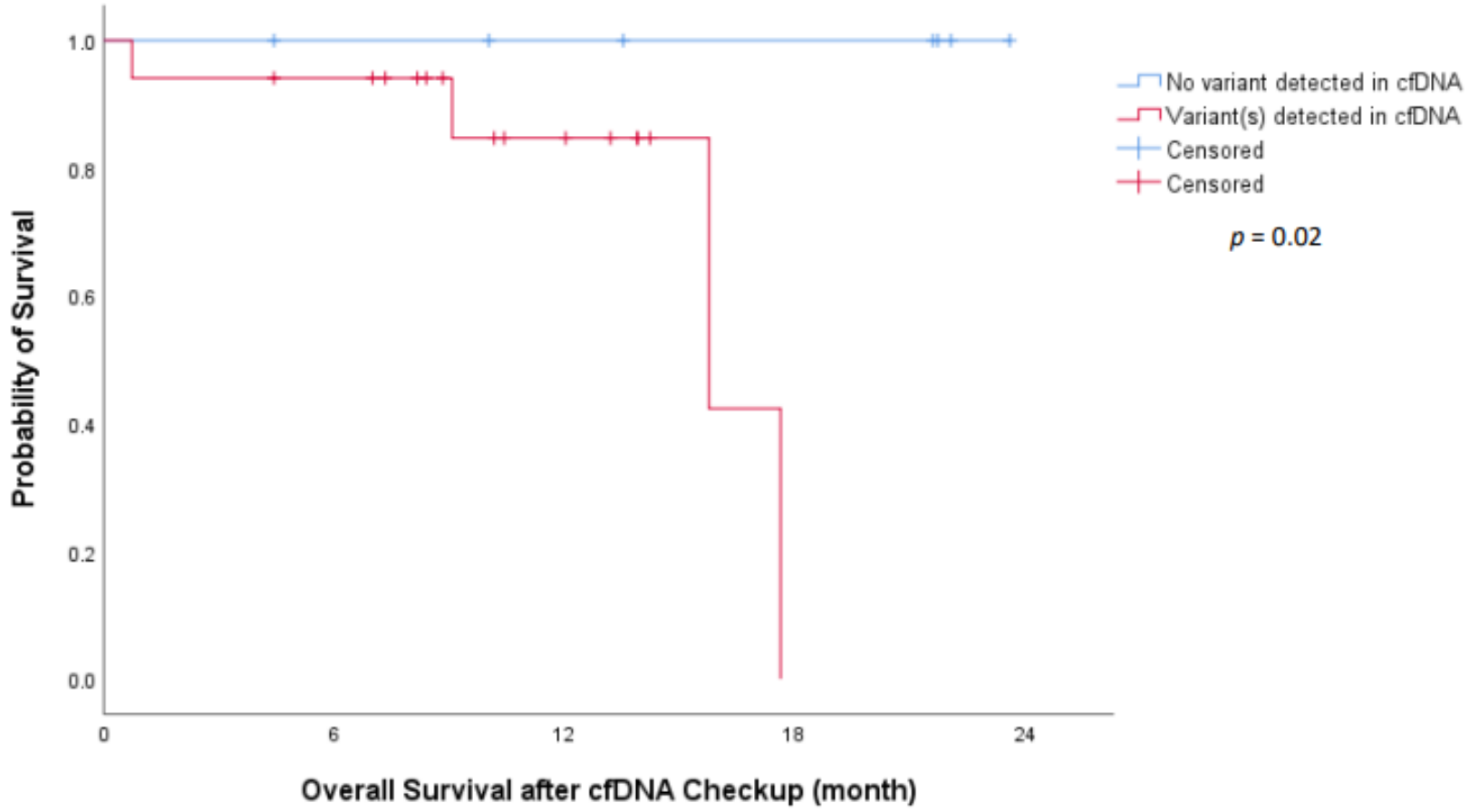


24 of 29 patients with T790M received second-line osimertinib (n=24) (cont'd)



Conclusions

- Simultaneous tissue rebiopsy NGS and liquid NGS at first-line EGFR TKI progression (first or second generation) detect more T790M mutation than tissue NGS or liquid NGS only.

- At first-line EGFR TKI progression (first or second generation) , patients with “no variant detected” in cfDNA NGS may have longer second-line osimertinib PFS and longer OS after cfDNA checkup.

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Thank You