Effect of ALK-TKI in ALK-rearranged with PD-L1-negative versus ALK-rearranged with PD-L1-positive NSCLC: a target trial emulation study

Yijin Qiu[1], Yexin Chen[1], Yunwu Zhong[1], Tiantian Zhang[1*]

1Jinan University, School of Medicine, Guangzhou, China

*Corresponding author. Jinan University, School of Medicine, Guangzhou, 510632, China. Electronic address: zhangtiantian@jnu.edu.cn.

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INTRODUCTION

- ALK-TKIs were standard treatment for patients with ALK-rearranged non-small cell lung cancer (NSCLC). [1]
- Patients with ALK rearrangement often coexist with other positive biomarkers, and the efficacy of ALK-TKIs in these patients remains to be proven.
- This study aimed to explore the effect of alectinib as first-line treatment in patients with NSCLC who have ALK rearrangement combined with PD-L1 negativity or PD-L1 positivity.

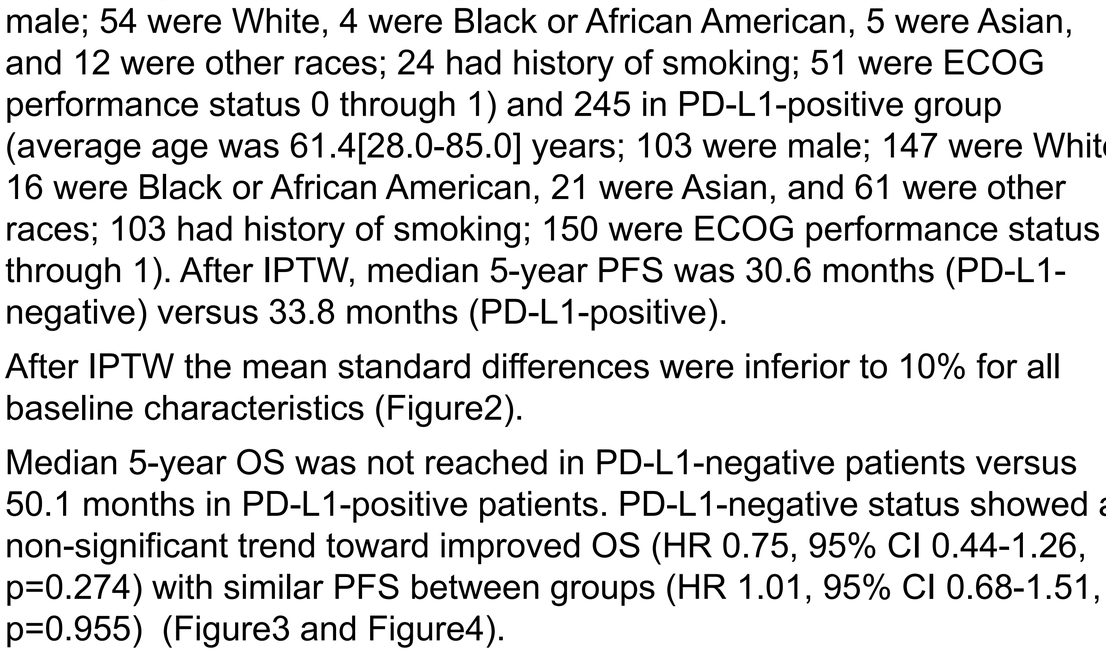
METHODS

- This retrospective study conducted target trial emulation to compared progression-free survival (PFS) and overall survival (OS) in patients had ALK–rearranged NSCLC with PD-L1 negativity or with PD-L1 positivity.[2, 3]
- Inverse probability of treatment weighting (IPTW) was employed to minimize imbalances in baseline characteristics.
- Time-to-first-event analysis was performed using Cox proportional hazards and Kaplan–Meier survival analysis, with the hazard ratio and 95% confidence interval calculated.
- Deidentified patient-level data were selected from a United States Flatiron Health oncology database of electronic health records. Patients were received aletinib as first-line treatment. Data were analyzed from April 2004 to March 2025.
- Subgroup analyses was done to assess the consistency of the treatment effect on PFS and OS by concomitant variable.

RESULTS

- 320 ALK–rearranged NSCLC patients were enrolled (Figure1), with 75 in PD-L1-negative group (average age was 60.7[30.0-85.0] years; 39 were male; 54 were White, 4 were Black or African American, 5 were Asian, and 12 were other races; 24 had history of smoking; 51 were ECOG performance status 0 through 1) and 245 in PD-L1-positive group (average age was 61.4[28.0-85.0] years; 103 were male; 147 were White, 16 were Black or African American, 21 were Asian, and 61 were other races; 103 had history of smoking; 150 were ECOG performance status 0 through 1). After IPTW, median 5-year PFS was 30.6 months (PD-L1-negative) versus 33.8 months (PD-L1-positive).
- After IPTW the mean standard differences were inferior to 10% for all baseline characteristics (Figure2).
- Median 5-year OS was not reached in PD-L1-negative patients versus 50.1 months in PD-L1-positive patients. PD-L1-negative status showed a non-significant trend toward improved OS (HR 0.75, 95% CI 0.44-1.26, p=0.274) with similar PFS between groups (HR 1.01, 95% CI 0.68-1.51, p=0.955) (Figure3 and Figure4).
- Subgroup analysis revealed that among patients aged <60 years, PD-L1-negative status was associated with significantly better OS outcomes.

Figure1 Study population flowchart



RESULTS CONT'D

Figure2 Love plots for standardized mean differences comparing covariate values before and after IPTW

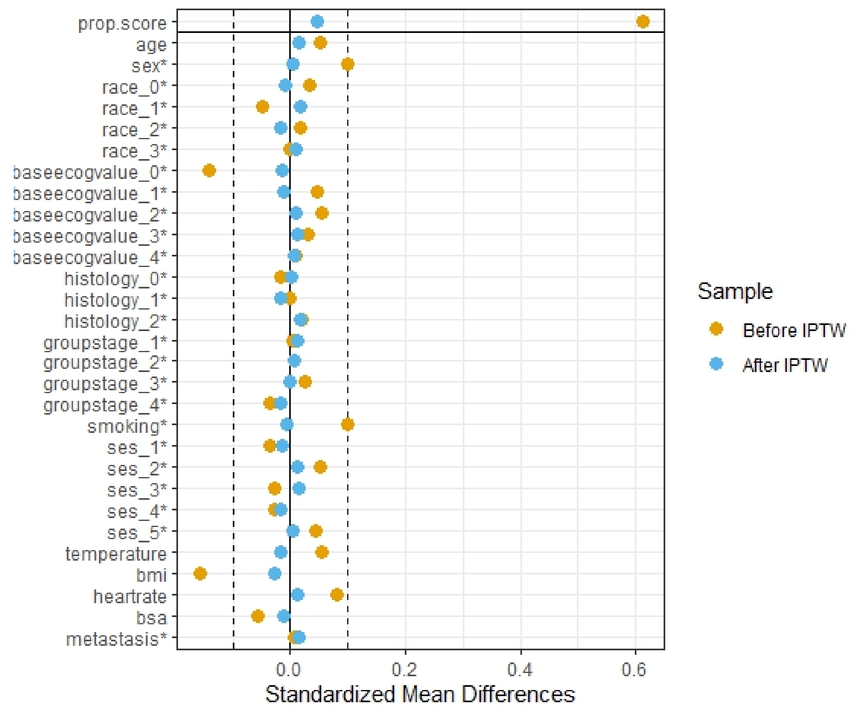


Figure3 Progression-free survival among ALK-rearranged aNSCLC patients

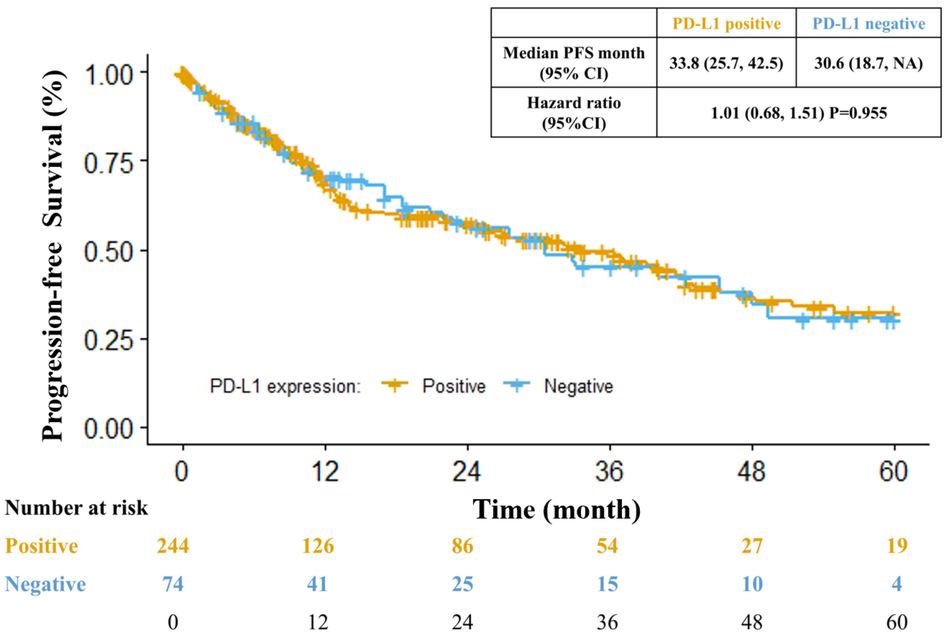
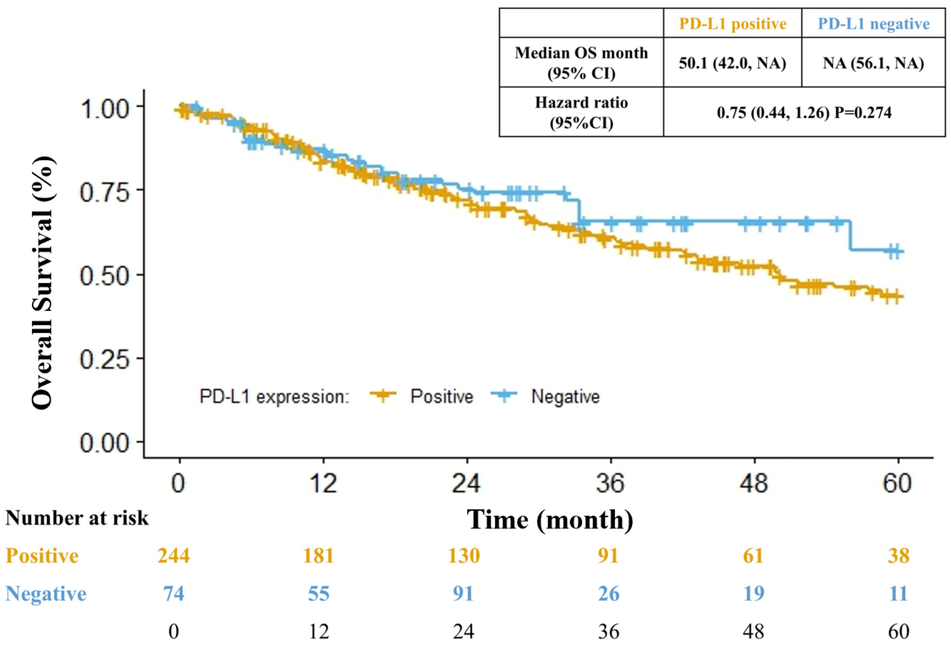


Figure4 Overall survival among ALK-rearranged aNSCLC patients



CONCLUSIONS

- Alectinib as first-line treatment in ALK-rearranged NSCLC with PD-L1 positivity demonstrates no significant difference in efficacy compared to ALK-rearranged and PD-L1 negative patients, and it remains an effective treatment option.

REFERENCES

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CONTACT INFORMATION

- Tiantian Zhang, Ph.D & Associate Professor, E-mail: zhangtiantian@jnu.edu.cn.
- Yijin Qiu, Ph.D Student, E-mail: qyj0726@stu2024.jnu.edu.cn