



EP10.04: A Multicenter, Real-World Data Analysis of T-DXd Efficacy in Acquired ERBB2 Alterations After Resistance to Osimertinib

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INTRODUCTION

Trastuzumab Deruxtecan(T-DXd) has demonstrated significant survival benefits in advanced patients with ERBB2-mutant non-small cell lung cancer (NSCLC). However, evidence of its efficacy in patients with acquired ERBB2 alterations following resistance to EGFR-TKIs is limited to case reports, and data supporting targeted therapy in this setting remain scarce.

METHODS

This multicenter, real-world study included 17 patients with unresectable NSCLC harboring acquired EGFR-ERBB2 co-alterations after Osimertinib resistance, enrolled from five centers across China. Endpoints included time-to-treatment failure (TTF), overall survival (OS), objective response rate (ORR), disease control rate (DCR), 2-year survival rate, and toxicity.

DISCUSSION AND CONCLUSION

In conclusion, T-DXd-based therapy may represent a potential strategy to overcome acquired ERBB2 alterations after Osimertinib resistance.

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RESULTS

Among the 17 patients with acquired ERBB2 alterations, 9 received ERBB2-directed therapy as first-line treatment post-resistance, while 8 received no ERBB2-directed therapy. Median TTF (mTTF) (9.4 vs. 4.2 months, $p=0.073$) and median OS (mOS) (31.2 vs. 15.5 months, $p=0.532$) were numerically longer in patients receiving ERBB2-directed therapy. Of the 9 patients treated with ERBB2-directed therapy, 5 received T-DXd plus Osimertinib, 2 received T-DXd monotherapy, and 2 received dacomitinib plus Osimertinib. In patients treated with T-DXd, ORR and DCR were 14.3% and 100%, respectively, both numerically higher than those not receiving T-DXd (ORR: 0%; DCR: 50.0%). mTTF was significantly longer in T-DXd-treated patients (9.4 months; 95% CI, 2.9–15.9) compared with those not receiving ERBB2-directed therapy ($p=0.015$). Although mOS data were immature, the 24-month OS rate was numerically higher in ADC-treated patients with acquired ERBB2 alterations versus those not receiving ERBB2-directed therapy (85.7% vs. 66.7%). Only one grade 3 treatment-related adverse event (20.0%) was observed in the T-DXd plus Osimertinib group.

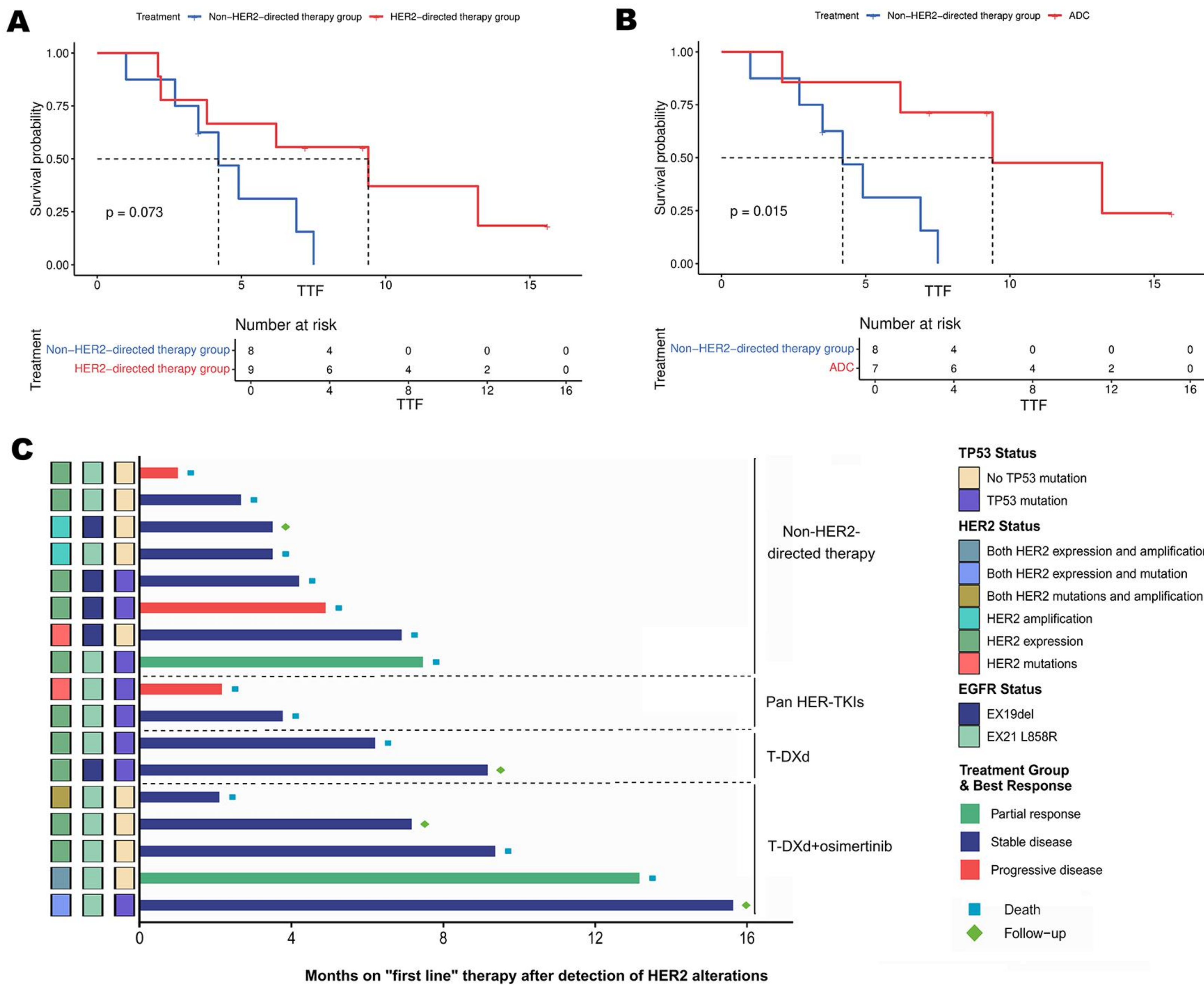


Figure A. Kaplan-Meier estimates of TTF and OS in patients harboring acquired EGFR-ERBB2 co-alterations treated with and without ERBB2-directed therapy.

Figure B. Kaplan-Meier estimates of TTF and OS in patients harboring acquired EGFR-ERBB2 co-alterations treated with T-DXd and non-ERBB2-directed therapy.

Figure C. A swimming's plot of duration of first-line therapy after detection of HER2 alterations.