



EP10.03: First-Line T-DXd vs. Conventional Therapy in HER2-Altered Advanced NSCLC: Real-World Outcomes by HER2/EGFR Co-Alteration Status

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IASLC 2026 World Conference on Lung Cancer

SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

Research on HER2-altered NSCLC has been ongoing for years. However, breakthrough first-line therapies for unresectable HER2-altered NSCLC remained lacking. This was particularly evident in cases with co-occurring HER2-EGFR co-alterations, where clinical evidence continued to be scarce.

METHODS

We included HER2-altered advanced NSCLC patients who had received first-line systemic therapy across six medical centers, and evaluated outcomes following chemotherapy-based combinations, TKIs, and T-DXd. Endpoints included PFS, ORR, DCR, one-year and two-year survival rates, and toxicity.

DISCUSSION AND CONCLUSION

First-line T-DXd showed promising activity signals in only HER2-altered NSCLC. In EGFR-HER2 co-altered patients, the EGFR-TKI monotherapy showed limited efficacy. The findings underscored the urgent need for prospective randomised trials.

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RESULTS

A total of 69 patients were enrolled, comprising 45 with only HER2 alterations and 24 with HER2-EGFR co-alterations. In patients with only HER2-altered NSCLC, those receiving first-line T-DXd had an mPFS of 15.7 months (95% CI, 12.5-18.9), an ORR of 85.7%, and a DCR of 100.0%. The mPFS for patients receiving chemotherapy-based regimens, pan-HER TKIs, and chemotherapy plus pan-HER TKIs were 7.6 (95% CI, 6.6-8.5) months, 4.4 (95% CI, 4.0-4.9) months, and 7.0 (95% CI, 6.1-9.1) months, respectively. The ORR for the three groups above was 33.3%, 0, and 0, respectively. In subgroup analysis, patients with only HER2 alterations who did not harbor TP53 mutations had a longer PFS than those with TP53 co-mutations (8.7m vs. 7.2m; HR: 0.35; 95% CI: 0.11-0.99; P = 0.048). In patients with EGFR-HER2 co-alterations, first-line EGFR-TKI monotherapy yielded an mPFS of 9.7 (95% CI, 8.6-10.8) months, an ORR of 40.0%, and a DCR of 93.3%. Regarding safety, we did not observe Grade $\geq$ 3 TRAEs in first-line T-DXd treatment.

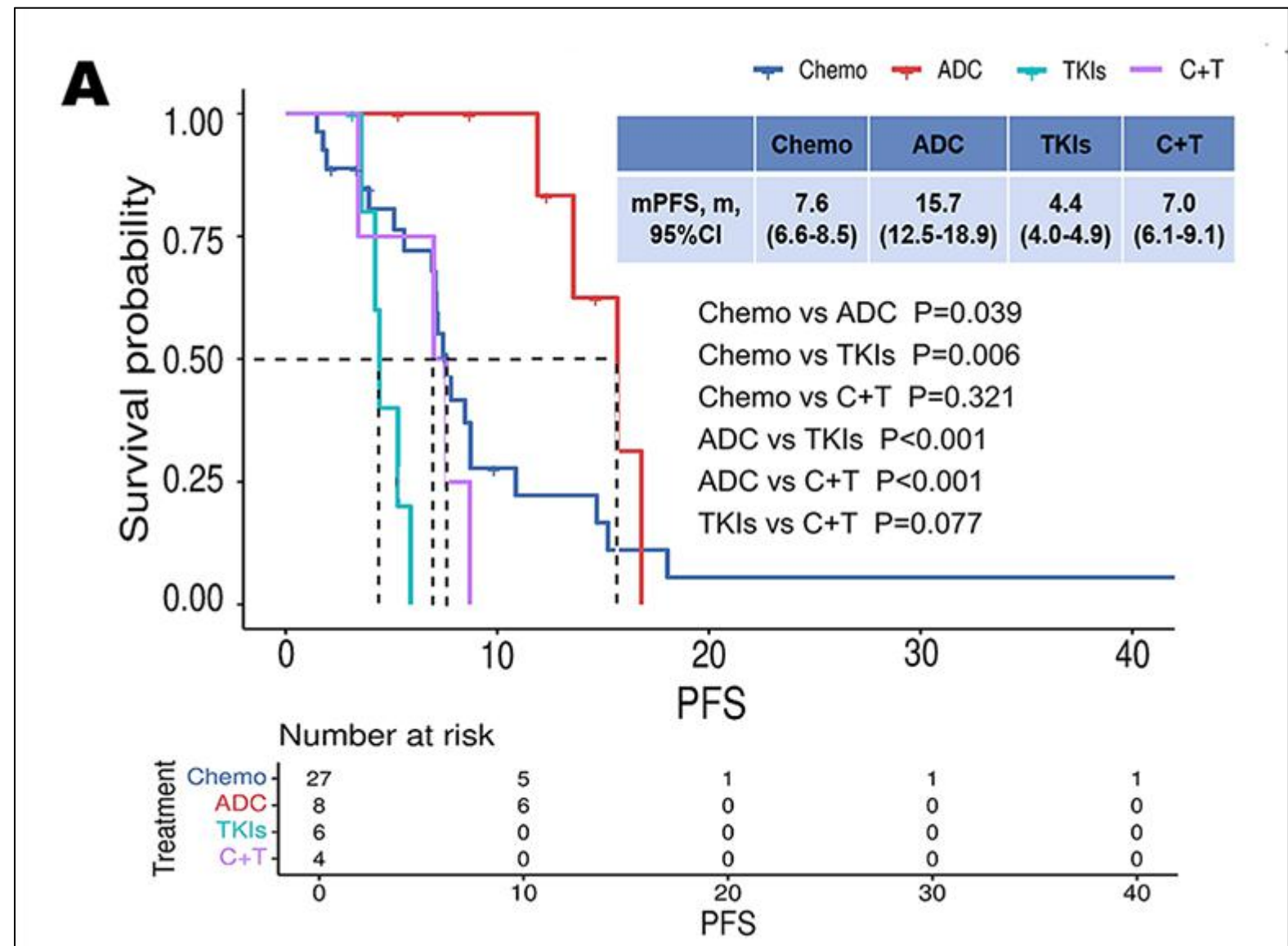


Figure A. Kaplan-Meier estimates of PFS in patients harboring only HER2 alterations receiving chemotherapy, ADCs, TKIs and chemotherapy combined with TKIs (C+T).

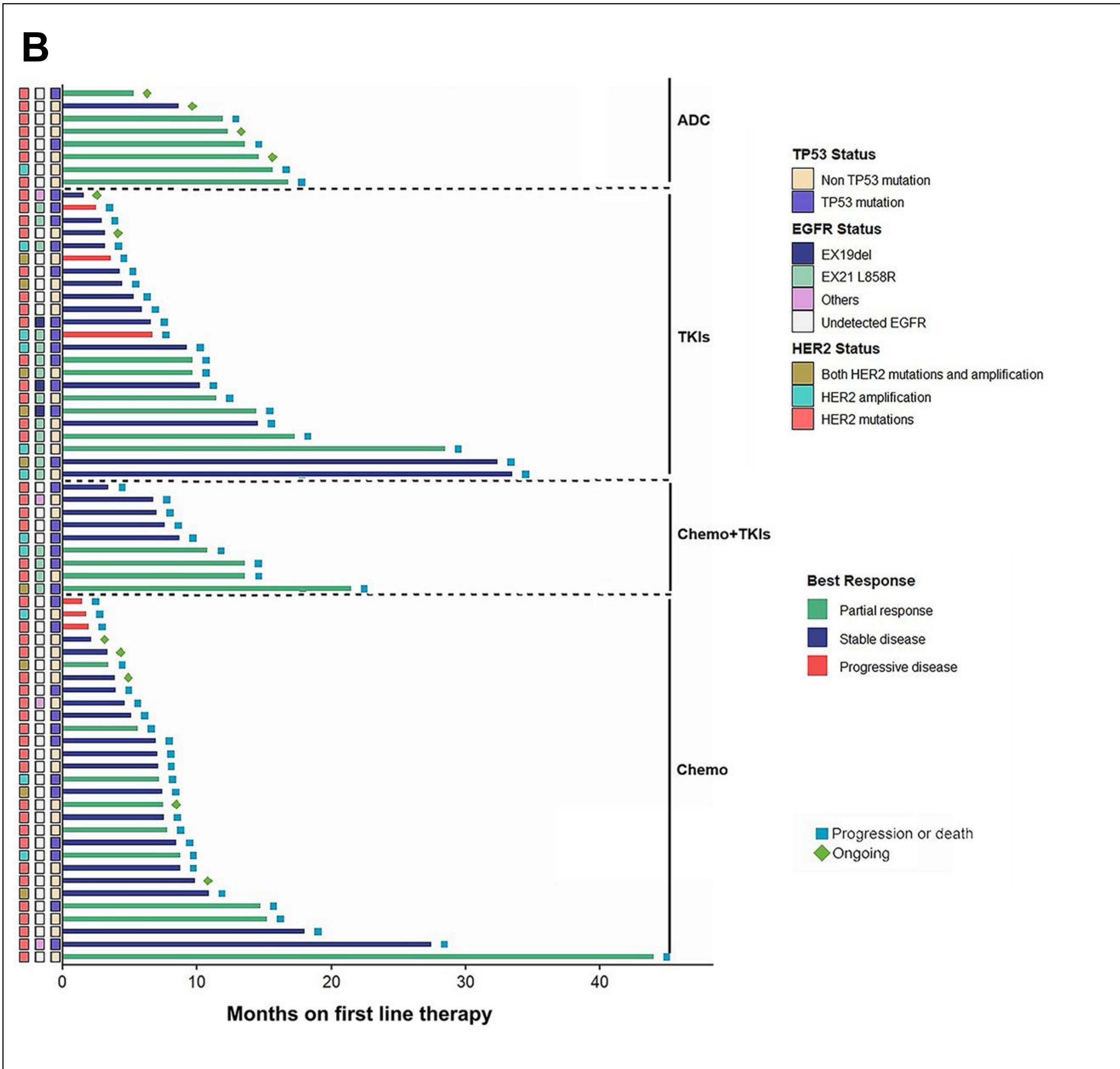


Figure B. A swimming's plot of duration of first-line therapy after detection of HER2 alterations.