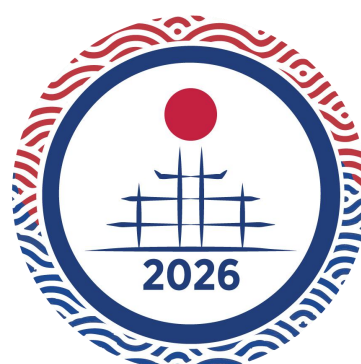




P3.248: Clinical Outcomes for Intrathecal Pemetrexed Plus Systemic Therapy in ERBB2-altered NSCLC Patients With Leptomeningeal Metastases 3018

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INTRODUCTION

Leptomeningeal metastasis (LM) is a devastating complication of advanced non-small cell lung cancer (NSCLC). Patients with ERBB2 alterations represent a distinct molecular subset with unique therapeutic challenges, and optimal management after LM onset remains undefined. This study aimed to evaluate the clinical outcomes of intrathecal pemetrexed (IP) combined with concurrent systemic therapy in ERBB2-altered NSCLC patients with LM.

METHODS

We conducted a retrospective analysis of consecutive ERBB2-altered NSCLC patients with LM who received IP plus systemic therapy at Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University between January 2019 and February 2026. Demographic data, ERBB2 alteration subtypes, treatment details, and survival outcomes were collected. Primary endpoints were overall survival (OS) and intracranial progression-free survival (iPFS) from LM diagnosis. Secondary endpoints included objective response rate (ORR) and safety.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- Intrathecal pemetrexed combined with concurrent systemic therapy demonstrated encouraging efficacy and a manageable safety profile in ERBB2-altered NSCLC patients with leptomeningeal metastases.

Future Direction for Research

- This dual-modality strategy represents a viable therapeutic option for this orphan indication and warrants further prospective validation.

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

- Among 222 NSCLC-LM patients screened, 13 (5.9%) harbored ERBB2 alterations and were included. ERBB2 exon 20 insertions accounted for 69.2% of cases, with the A775_G776insYVMA variant being the most common subtype (77.8%).
- The median OS was 11.7 months, median iPFS was 5.8 months, and ORR was 61.5%.
- The safety profile was manageable, with no treatment-related deaths or chemical meningitis observed.

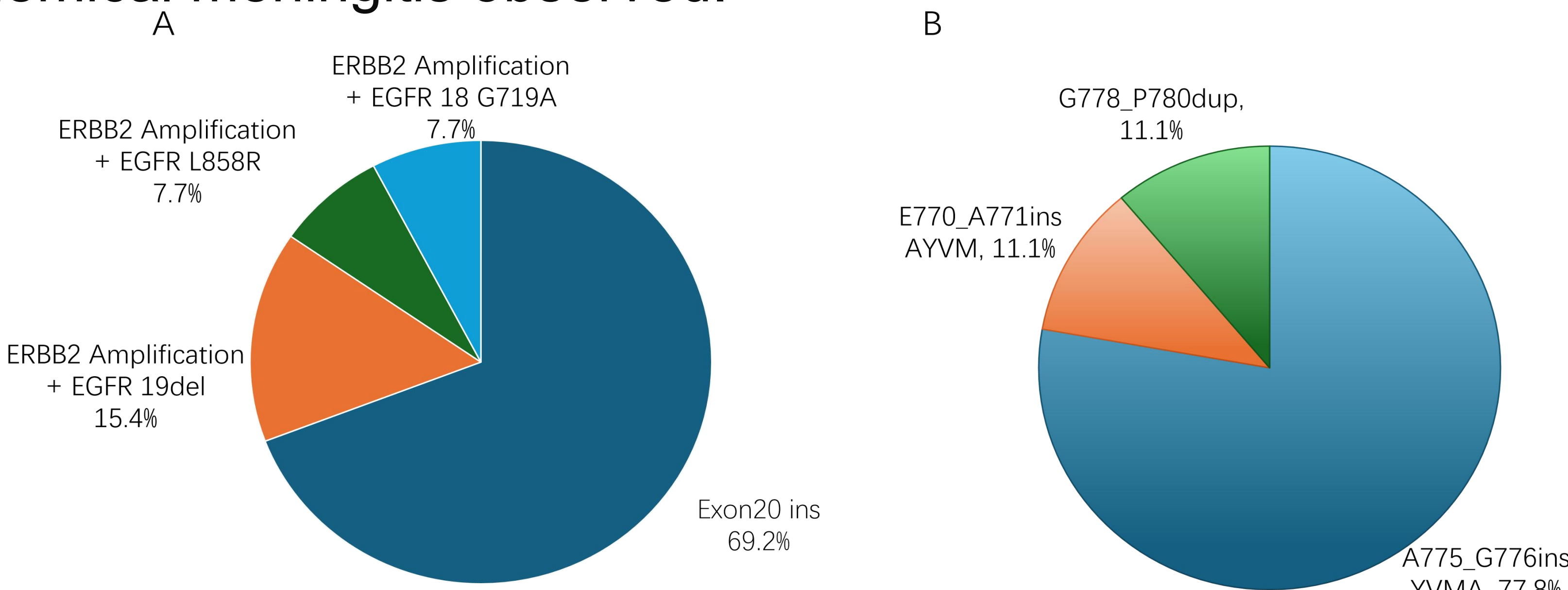


Figure 1: Distribution of ERBB2 alteration types in the study cohort. A: Mutation spectrum of ERBB2 alterations; B: Distribution of ERBB2 ex20ins subtypes.

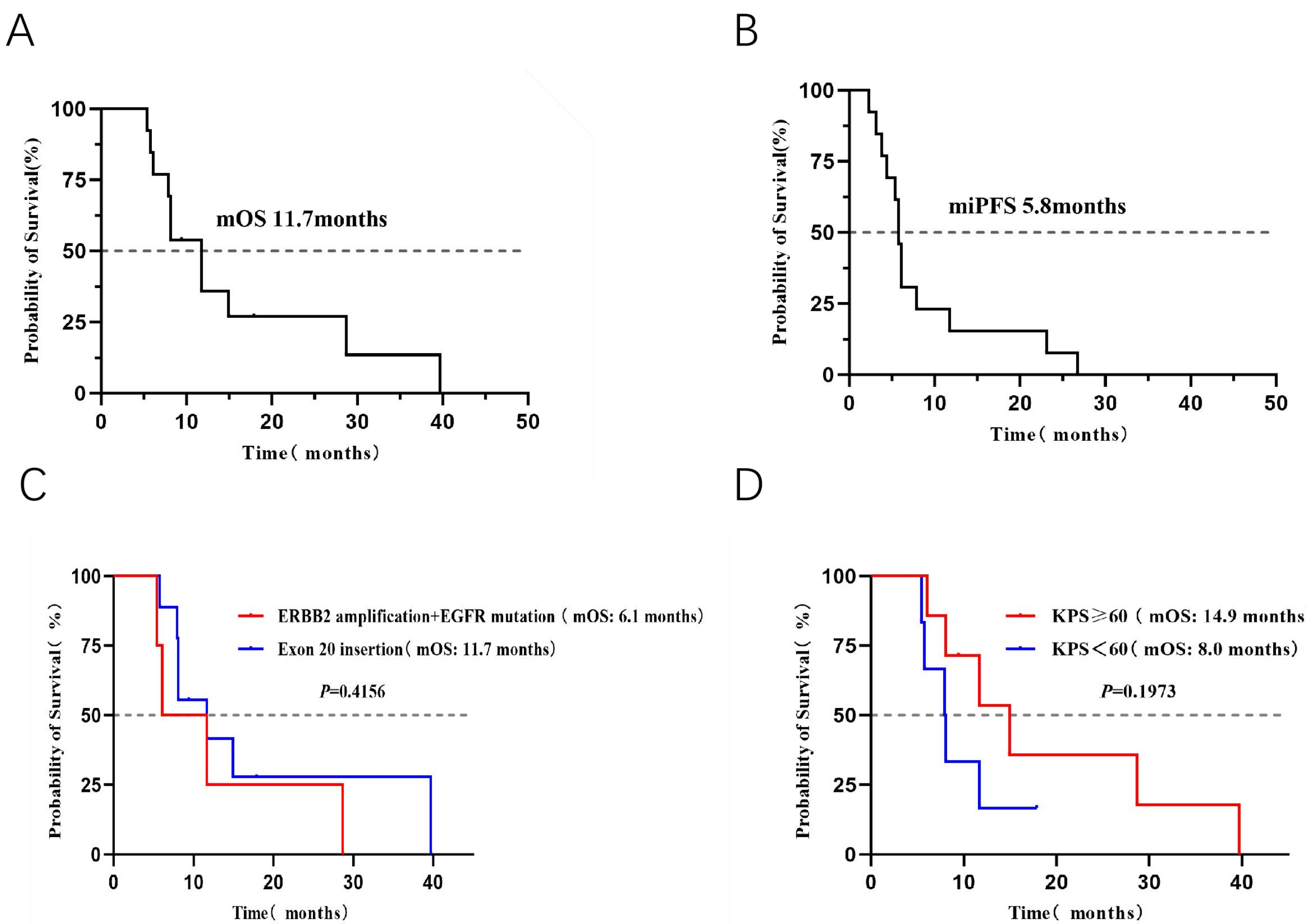


Figure 2: Survival outcomes in ERBB2-altered NSCLC patients with LM treated with IP plus systemic therapy. A: Kaplan-Meier curve of OS for the entire cohort; B: Kaplan-Meier curve of iPFS for the entire cohort; C: OS stratified by ERBB2 alteration subtype; D: OS stratified by KPS.