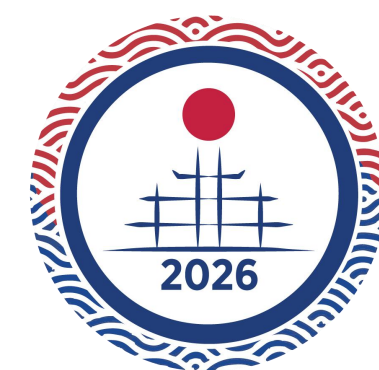




P3.225: Phase 2 Study of High-Dose Furmonertinib Plus Bevacizumab and Intrathecal Pemetrexed in EGFRm NSCLC Patients with Leptomeningeal Metastases (Abstract# 1916)



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INTRODUCTION

- Leptomeningeal metastases (LM) predominantly occurs in patients with epidermal growth factor receptor (EGFR) mutated non-small cell lung cancer (NSCLC) following TKIs resistance, which means a devastating complication with poor prognosis.
- In this prospective study, we evaluated the efficacy and safety of high-dose furmonertinib combined with bevacizumab and intrathecal pemetrexed in patients with EGFR-mutated NSCLC and LM.

METHODS

Study Design:

Inclusion criteria:

- Age 18 to 75 years;
- Histological or cytological confirmed NSCLC with an EGFR mutation;
- LM diagnosed according to the EANO-ESMO guideline, based on at least two of the following criteria: clinical symptoms of intracranial hypertension, radiographic findings, or positive CSF cytology;
- Newly diagnosed LM;
- ECOG PS of 0 to 2 maintained for 2 weeks before enrollment.

Furmonertinib
(160 mg orally once daily)
+
Bevacizumab, intravenous
(7.5mg/kg on day 1, Q3W)
+
Pemetrexed, intrathecal
(50mg on day 1, Q3W)

Disease progression;
Unacceptable toxicities;
Withdrawal of consent;
Death.

- Patients received furmonertinib (160 mg, orally once daily), combined with bevacizumab (7.5mg/kg, intravenously on day 1 of each 3-week cycle) and pemetrexed (50mg, intrathecally on day 1 of each 3-week cycle) until disease progression or unacceptable toxicity.
- The primary endpoint was intracranial progression-free survival (iPFS), secondary endpoints included LM and extracranial objective response rate (ORR), overall survival (OS) and safety.
- Serial cerebrospinal fluid (CSF) samples were also collected for exploratory biomarker analyses.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- High-dose furmonertinib combined with bevacizumab and intrathecal pemetrexed showed promising efficacy and tolerable safety profile, and could be an optional treatment strategy in patients with EGFR-mutated NSCLC and LM.

Future Direction for Research

- High-dose furmonertinib combined with bevacizumab and intrathecal pemetrexed has promising efficacy and a tolerable safety profile in patients with EGFR-mutated NSCLC and LM, which warrants further validation in a randomized clinical trial.
- Dynamic monitoring of CSF may help predict treatment response and prognosis.

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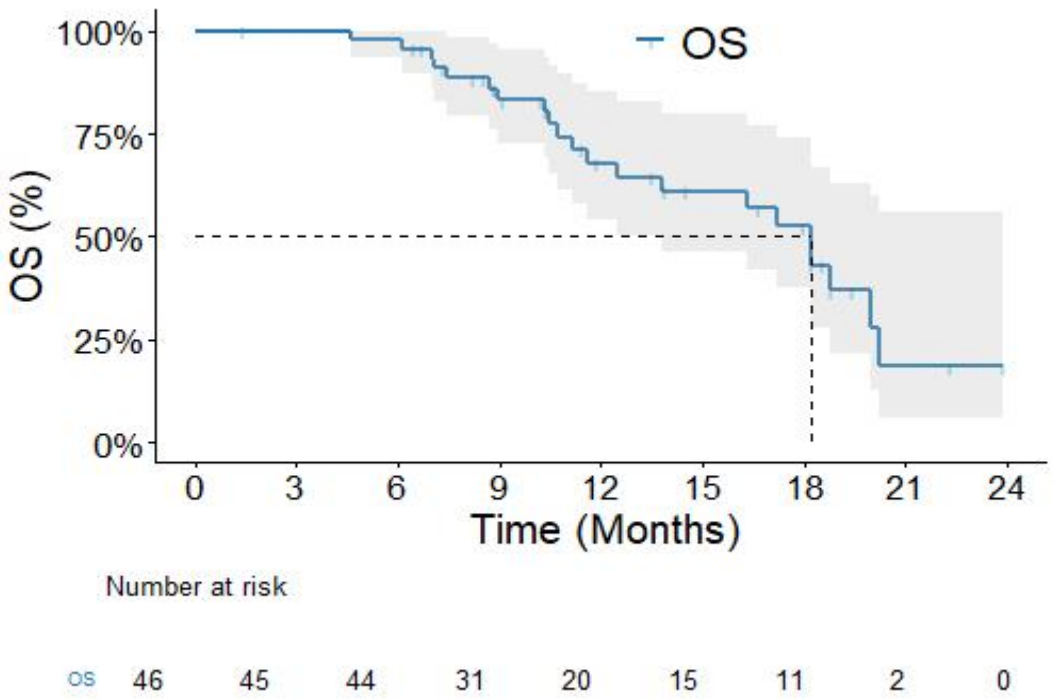
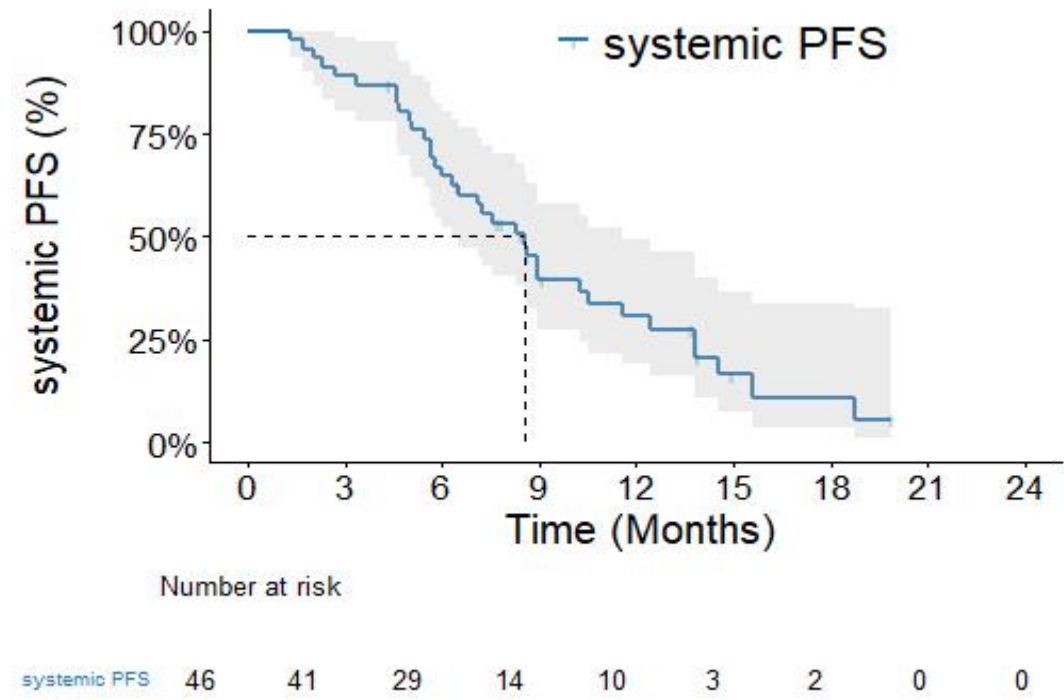
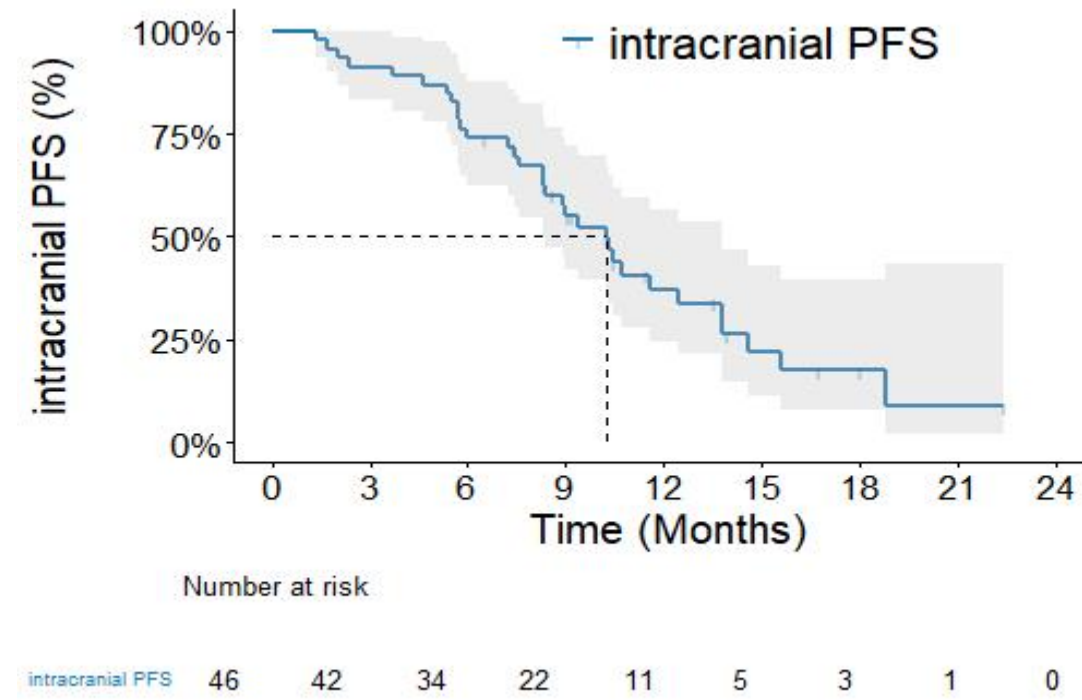
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RESULTS

- With a median follow-up of 16.5 months, the median iPFS was 10.27 months (95%CI, 8.52-12.02), median systemic PFS was 8.63 months (95%CI, 7.02-10.25), and median OS was 18.23 months (95%CI, 15.43-21.03).



- The confirmed LM ORR and DCR assessed according to RANO-LM criteria were 60.9% and 91.3%, respectively. Grade ≥ 3 treatment-related adverse events occurred in 32.6% (15/46) of patients, and no treatment-related deaths occurred.

	Response, No. (%)		
	LM response by RANO-LM	BM ^b response by RECIST 1.1	Extracranial response by RECIST 1.1
No. of patients (%)	46	34	38
Complete response	0	0	0
Partial response	28 (60.9)	10 (29.4)	5 (13.2)
Stable disease	14 (30.4)	22 (64.7)	31 (81.5)
Progressive disease	4 (8.7)	2 (5.9)	2 (5.3)
Objective response rate, (95% CI), %	60.9 (45.4-74.9)	29.4 (15.1-47.5)	13.2 (4.4-28.1)
Disease control rate, (95% CI), %	91.3 (79.2-97.6)	94.1 (80.3-99.3)	94.7 (82.3-99.4)

- Patients with higher CSF ctDNA concentrations had worse OS, and increasing CSF ctDNA concentrations after three cycles of treatment were associated with worse iPFS and OS.

