

Ivonescimab as Later-Line Therapy for NSCLC Patients with CNS Metastases: A Multicenter Retrospective Study

Jiefei. Han¹, Kai Chen², Yi Lin³, Xun Kang³, Gen Lin¹

¹Beijing Chest Hospital, Capital Medical University, Beijing, China; ²Cancer Center, San Huan Cancer Hospital, China; ³Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Introduction

- Central nervous system (CNS) metastases, predominantly brain metastases (BM) with concurrent leptomeningeal disease (LMD) in high-risk cases, occur in 40–60% of advanced NSCLC, with median overall survival (OS) <6 months in ≥3rd-line settings.
- The PD-1/VEGF bispecific antibody ivonescimab has shown intracranial activity in prospective trials; relevant real-world evidence in later-line NSCLC with CNS metastases remains scarce.
- This study evaluated the intracranial efficacy, clinical benefit, and safety of ivonescimab as ≥3rd-line therapy for NSCLC with BM.

Study Design

- Multicenter retrospective study, approved by the IRB of each center.
- 40 consecutive advanced NSCLC patients with MRI-confirmed BM (11 with CSF cytology-proven LMD), treated with ivonescimab (20 mg/kg q3w) as ≥3rd-line systemic therapy, Jan 2024–Dec 2025.
- Eligibility: ECOG PS 0–2; ≥3 prior systemic lines; prior cranial radiotherapy with radiologically confirmed progression ≥4 weeks pre-enrollment was allowed.
- Treatment: ivonescimab monotherapy (n=14) or combined with chemotherapy (n=26).
- Primary endpoints: intracranial ORR (IC-ORR) and DCR (IC-DCR) per RANO/RANO-LM. Secondary endpoints: IC-PFS, OS, neurological symptom response, and safety (NCI-CTCAE v5.0). Survival analyzed by Kaplan–Meier.

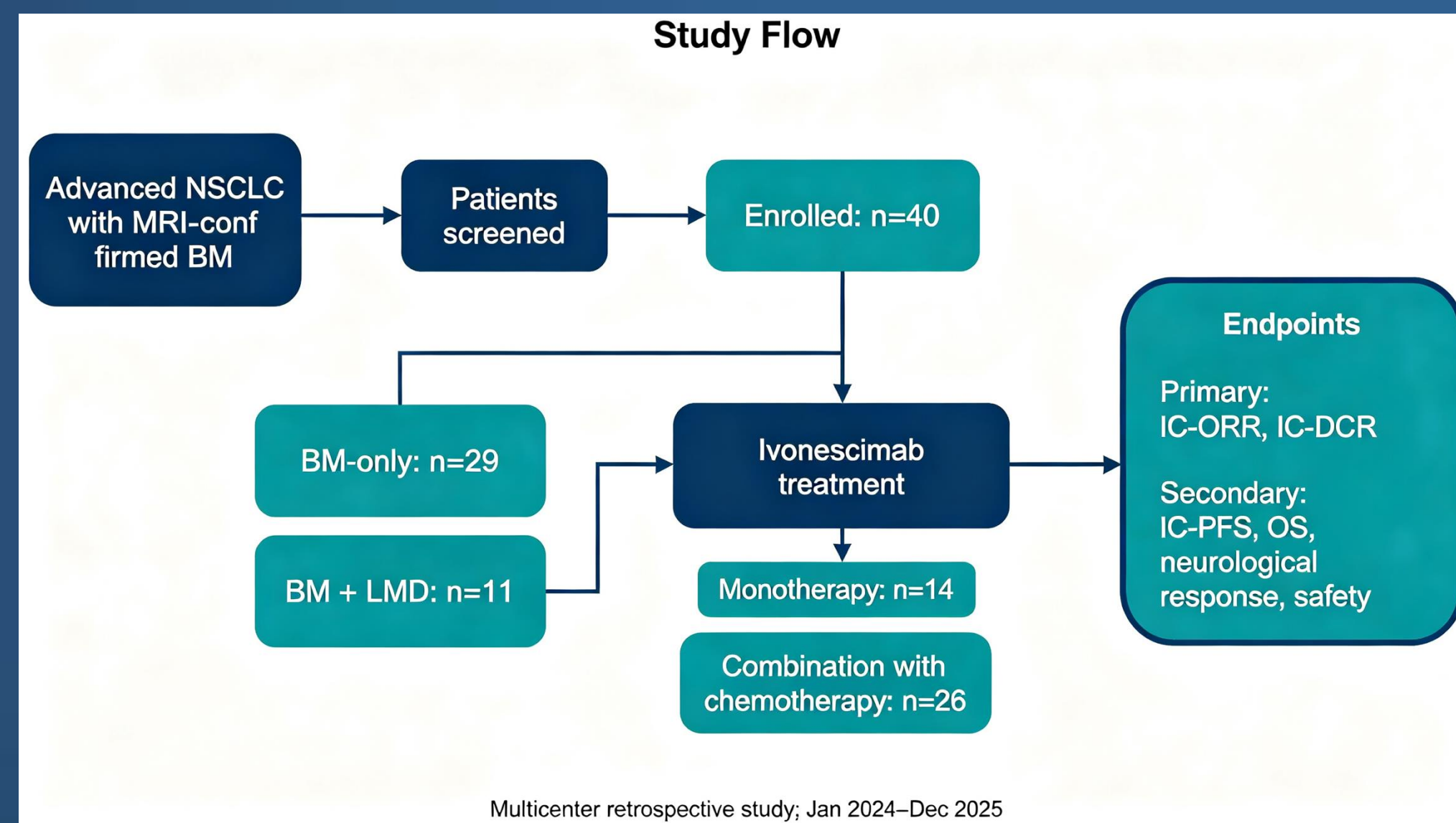


Figure1. Overview of study design

Results

Table 1. Baseline Patient Characteristics (N=40)

Characteristic	Ivonescimab monotherapy (n=14)	Ivonescimab + chemotherapy (n=26)	Total (N=40)
Age, median (range), yr	60 (38–76)	58 (37–75)	59 (37–76)*
Male sex, n (%)	8 (57.1)	14 (53.8)	22 (55.0)†
ECOG PS, n (%)			
0	2 (14.3)	4 (15.4)	6 (15.0)†
1	7 (50.0)	15 (57.7)	22 (55.0)†
2	5 (35.7)	7 (26.9)	12 (30.0)†
Histology, n (%)			
Adenocarcinoma	12 (85.7)	22 (84.6)	34 (85.0)†
Squamous / other	2 (14.3)	4 (15.4)	6 (15.0)†
EGFR-sensitive mutation, n (%)	6 (42.9)	11 (42.3)	17 (42.5)*
CNS disease pattern, n (%)			
BM-only	10 (71.4)	19 (73.1)	29 (72.5)*
BM + concurrent LMD	4 (28.6)	7 (26.9)	11 (27.5)*
Prior cranial radiotherapy, n (%)	9 (64.3)	17 (65.4)	26 (65.0)*
Baseline corticosteroids, n (%)	7 (50.0)	12 (46.2)	19 (47.5)*
Prior systemic lines, median (range)	3 (3–6)	3 (3–6)	3 (3–6)*

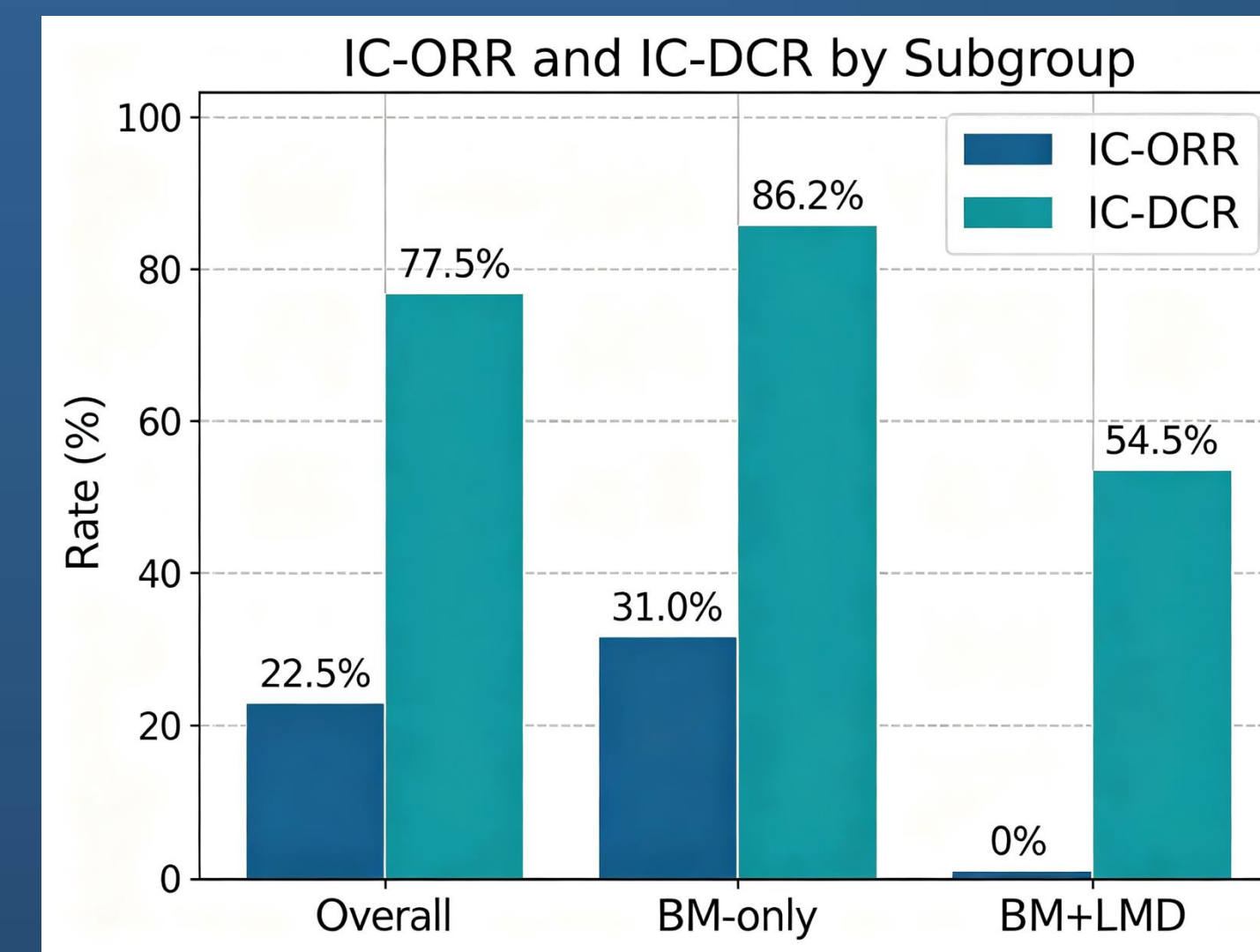


Figure 2. Intracranial objective response rate (IC-ORR) and intracranial disease control rate (IC-DCR) in subgroups. IC-ORR (dark blue) and IC-DCR (teal) are presented for overall cohort, BM-only and BM+LMD patients. Response was assessed by RANO-BM criteria.

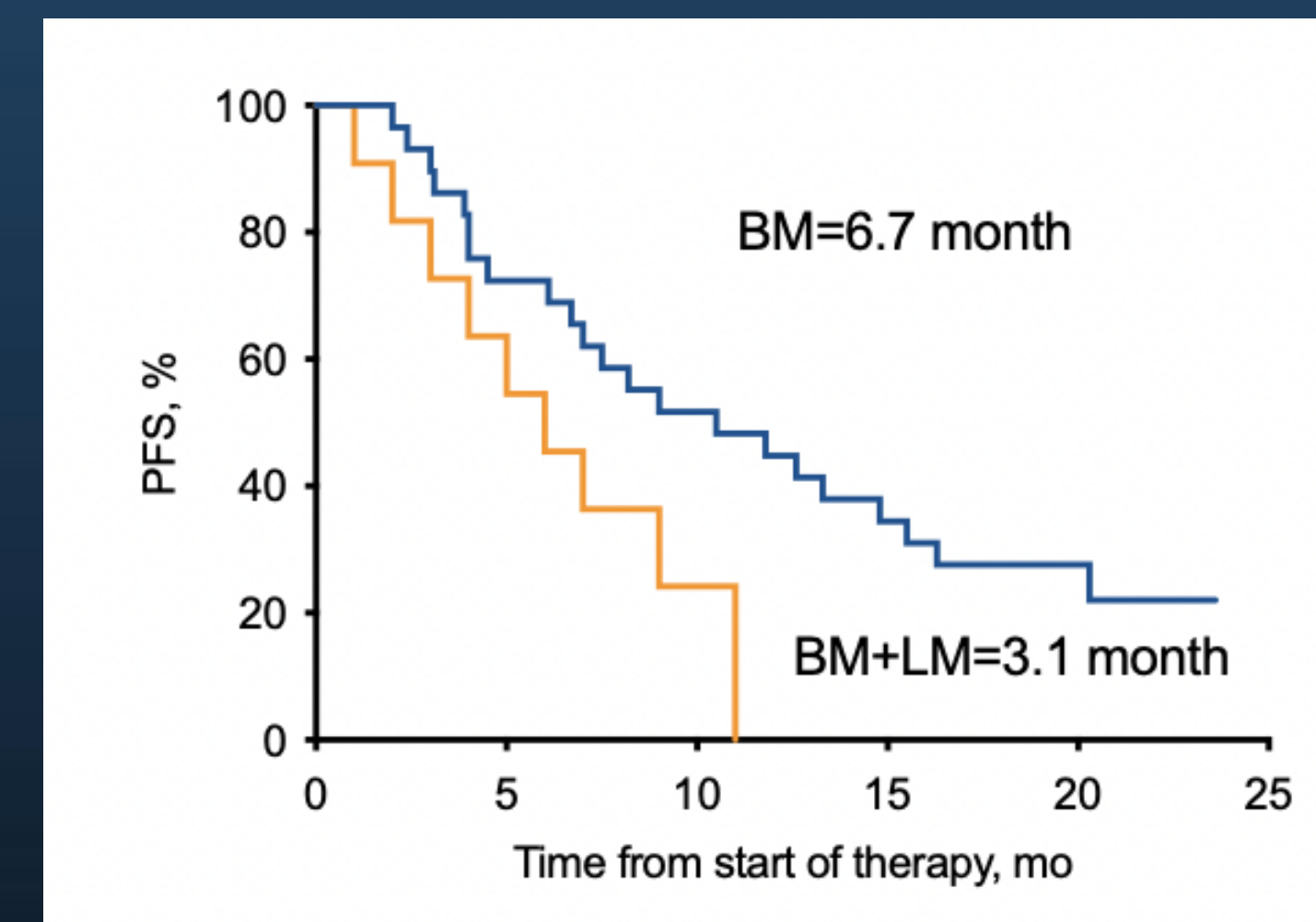


Figure3. Progression-free survival by BM (N=29) and BM&LM (N=11)

Table 2. Treatment-related adverse events

Adverse event, n (%)	Overall (N=40)	Ivonescimab monotherapy (n=14)	Ivonescimab + chemotherapy (n=26)
Any TRAE	30 (75.0)	9 (64.3)	21 (80.8)
Grade ≥3 TRAE	9 (22.5)	2 (14.3)	7 (26.9)
Hematologic			
Neutropenia (any grade)	11 (27.5)	2 (14.3)	9 (34.6)
Neutropenia (grade≥3)	4 (10.0)	0 (0.0)	4 (15.4)
Anemia (any grade)	9 (22.5)	2 (14.3)	7 (26.9)
Thrombocytopenia (any grade)	7 (17.5)	1 (7.1)	6 (23.1)
Hepatic			
Transaminitis (any grade)	8 (20.0)	3 (21.4)	5 (19.2)
Transaminitis (grade≥3)	2 (5.0)	1 (7.1)	1 (3.8)
Cardiovascular			
Hypertension (any grade)	10 (25.0)	4 (28.6)	6 (23.1)
Hypertension (grade≥3)	2 (5.0)	1 (7.1)	1 (3.8)
Immune-related AE			
Hypothyroidism	5 (12.5)	3 (21.4)	2 (7.7)
Hyperthyroidism	2 (5.0)	1 (7.1)	1 (3.8)
Pneumonitis	3 (7.5)	2 (14.3)	1 (3.8)
Neurological			
Cerebral infarction (grade3)	1 (2.5)	1 (7.1)	0 (0.0)

Conclusion

- Ivonescimab provides moderate intracranial disease control with a manageable safety profile in heavily pretreated later-line NSCLC patients with brain metastases.
- Limited by retrospective design and small sample size, these findings offer preliminary real-world reference for this refractory population and require further validation in large-scale prospective trials.