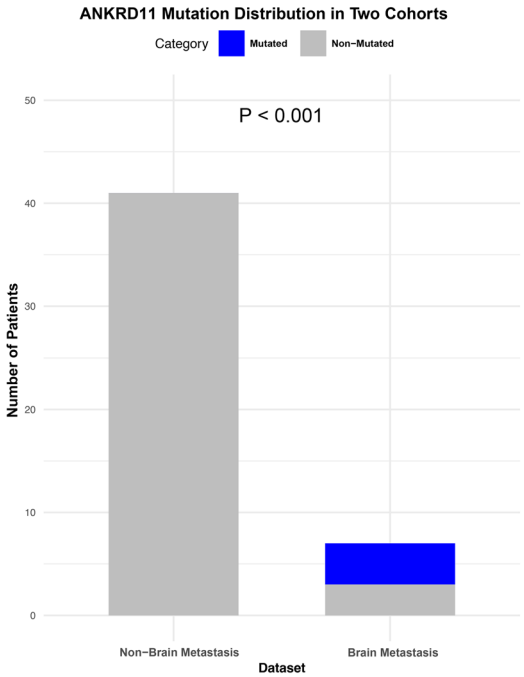

Figure S1 Comparison of *ANKRD11* mutation rates between brain metastasis (BM) and non-brain metastasis (non-BM) cohorts. The data show a significantly higher prevalence of *ANKRD11* mutations in the brain metastasis cohort compared to the non-brain metastasis cohort (P<0.001).

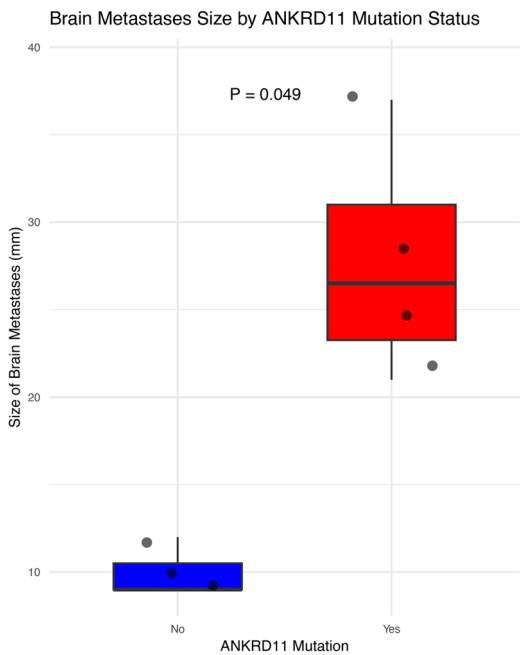

Figure S2 Comparison of brain metastasis lesion size between patients with and without *ANKRD11* mutations. Patients with *ANKRD11* mutations exhibited significantly larger brain metastatic lesions (P=0.049).

https://dx.doi.org/10.21037/tlcr-24-800

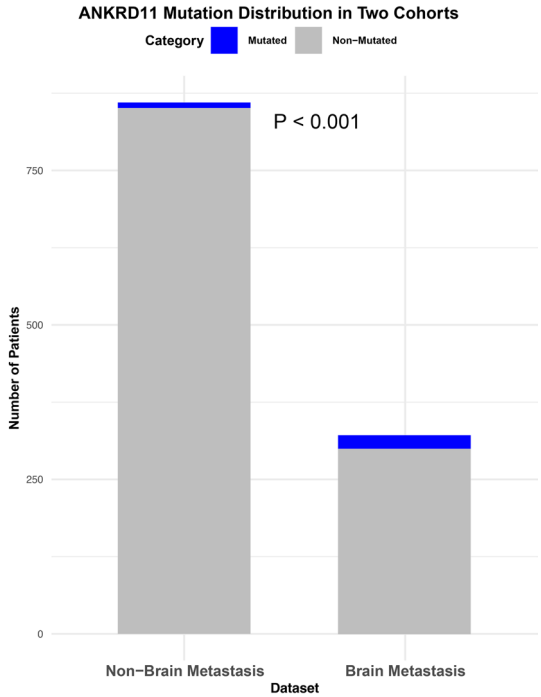

Figure S3 Comparison of *ANKRD11* mutation rates between brain metastases and nonbrain-metastatic sites in large public dataset cohorts. *ANKRD11* mutations were significantly more frequent in brain metastases (7%) compared to non-brain metastatic sites (1%) (P<0.001).

https://dx.doi.org/10.21037/tlcr-24-800

Table S1 Inclusion and Exclusion Criteria

Inclusion Criteria:

1. Patients must have a confirmed diagnosis of non-small cell lung cancer (NSCLC) with evidence of brain metastases, including treated and stable metastases, active metastases, or leptomeningeal metastases.

2. Participants must be between 18 and 75 years of age at the time of enrollment.

3. Patients with treated and stable brain metastases must exhibit neurological stability, defined as the absence of new neurological symptoms and the use of a stable or tapering dose of corticosteroids at the time of enrollment.

4. Sufficient cerebrospinal fluid (CSF) samples must be available for liquid biopsy analysis.

5. Patients must provide written informed consent before participating in the study.

Exclusion Criteria:

1. Patients with a history of other primary malignancies that could interfere with the interpretation of study results will be excluded.

2. Patients presenting with clinically significant intracranial hemorrhage, symptomatic brain edema, or uncontrolled seizures at the time of enrollment are ineligible.

3. Patients whose CSF samples are of insufficient quality or quantity for genetic testing will be excluded.

4. Patients who are taking medications that may interfere with the investigational drugs, such as CYP-inducing antiepileptic drugs or high-dose corticosteroids, will not be eligible.

5. Women who are pregnant or actively breastfeeding will be excluded from the study.

6. Patients with a high risk of severe CNS complications, including significant bleeding, seizures, or other CNS-related risks associated with the investigational drug, will not be eligible for participation.

CYP, cytochrome P450; CNS, central nervous system.

Table S2 Summary of patient clinical and pathological characteristics.

Patient	Age (years)	Sex	Smoking history	Stage	Pathological subtype	Treatment types	Brain metastasis site	Size of brain metastases (mm)	EGFR status	Response	ANKRD11 mutation
1	70	Male	Active	IVB	Adeno	Targeted therapy + radiotherapy	Right cerebellar hemisphere	29	Mutated	PD	Yes
2	56	Female	Non-smoker	IVB	Adeno	Chemotherapy + immunotherapy	Left parietal lobe	24	Wild-type	SD	Yes
3	69	Male	Active	IVB	Adeno	Targeted therapy + radiotherapy	Left frontal lobe	9	Mutated	PD	No
4	58	Male	Active	IVB	Adeno	Targeted therapy + radiotherapy	Right frontal lobe	21	Mutated	PD	Yes
5	58	Female	Non-smoker	IVB	Adeno	Chemotherapy + immunotherapy	Junction of the parietal, temporal, and insular lobes	9	Wild-type	SD	No
6	66	Female	Non-smoker	IVB	Adeno	Chemotherapy + immunotherapy	Right cerebellar hemisphere	37	Wild-type	SD	Yes
7	68	Female	Non-smoker	IVB	Adeno	Targeted therapy + radiotherapy	Left frontoparietal lobe	12	Mutated	PR	No

PD, progressive disease; SD, stable disease; PR, partial response; EGFR, Epidermal Growth Factor Receptor.

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