

EP12.55: Intracranial Outcomes and Treatment Response in *HER2* (*ERBB2*)-Mutated Non-Small Cell Lung Cancer with Brain Metastases

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Introduction

- HER2* (*ERBB2*) mutations occur in ~2-4% of patients with non-small cell lung cancer (NSCLC)¹
- Until recently, effective *HER2*-directed targeted therapies have been lacking²⁻⁴
- Additional data is needed to further our understanding of intracranial outcomes in these patients
- We aimed to assess outcomes in patients with *HER2*-mutated NSCLC with brain metastases, with a focus on type of therapy received and progression to leptomeningeal disease

Methods

- Retrospective chart review study
- Utilized the Stanford STARR database
- Patients with metastatic *HER2*-mutated NSCLC with brain metastases at any time point were included
- Data related to demographics, therapy, and treatment response was collected
- Kaplan-Meier survival analysis was used to calculate time to intracranial progression
- Analysis focused on pemetrexed-based therapy, trastuzumab deruxtecan (T-DXd), and other *HER2*-directed therapies

References

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Results

Patient Demographics

- N=22

Table 1. Demographic and Disease Characteristics of Patients

Characteristics	Category	Value
Age	Median (Range)	56 (19-82)
Sex	Male	36%
	Female	64%
Race/Ethnicity	White	41%
	Hispanic/Latino	14%
	Asian	41%
	Black	0%
	Native American/Pacific Islander	0%
	Other/Unknown	5%
Smoking History	Never	91%
	Current	4.50%
	Former	4.50%
Stage at Diagnosis	I-III	24%
	IV	76%
Genetic Mutation	Y772_A775dup	32%
	A775_G776insYVMA	23%
	G776delinsVC	14%
	S778_P780dup	9%

Treatment lines

Table 2. Treatment and Radiation Exposure within the Cohort

Category	Subcategory	Value
Medical Therapy	Pemetrexed-based therapy	95%
	Trastuzumab deruxtecan (T-DXd)	59%
	Any other <i>HER2</i> -targeted therapy	55%
	Afinib	27%
	TDM-1	27%
	Trastuzumab	27%
	Immunotherapy	82%
Radiation Therapy	Received Any Radiation	95%
	Stereotactic Radiosurgery (SRS)	82%
	Whole Brain Radiation Therapy (WBRT)	27%

- Pemetrexed-based therapy was first-line treatment after developing brain metastases in 68% of patients

Results Continued

Leptomeningeal Disease (LMD) and Overall Survival

- Progression to LMD occurred in 41% of patients
- Median time from LMD to death was 4.6 months
- 5-year overall survival (OS) rate was 24% with a shorter median OS for those patients having brain metastases at the time of diagnosis (2.5 v 3.6 years)
- Median time to intracranial progression was 7.4 months for pemetrexed-based therapy

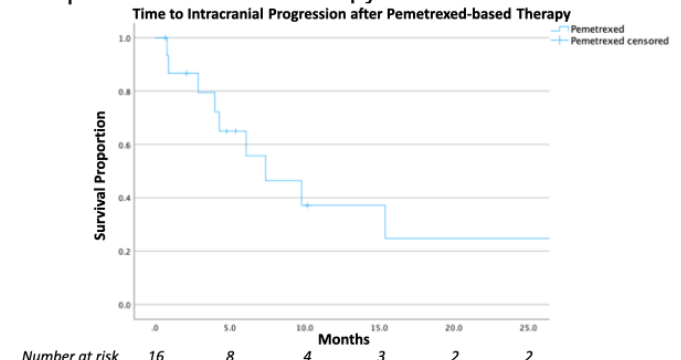


Figure 1. Kaplan-Meier survival analysis for pemetrexed-based therapies.

- Median time to intracranial progression was 3.2 months for T-DXd

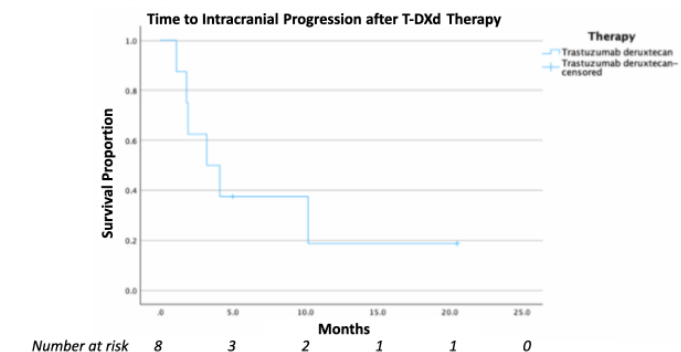


Figure 2. Kaplan-Meier survival analysis for T-DXd.

Conclusion

- All therapies achieved only modest CNS disease control
- Therapies with better CNS activity for *HER2*-mutated NSCLC are needed, potentially with newly-approved zongertinib and sevabertinib