

INTRODUCTION

- We evaluated the real-world outcomes of a contemporary population of patients (pts) with non-small cell lung cancer (NSCLC) and leptomeningeal disease (LMD) and assessed their outcomes with different treatments.

METHODS

- We retrospectively analyzed data at 6 centers of pts diagnosed with NSCLC after December 1, 2017, who developed LMD.
- Overall survival (OS) was compared between groups using Cox proportional hazards models, adjusting for ECOG performance status (PS) and additional confounders, as specified in Table 2.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- Use of systemic molecularly guided treatments was associated with improved OS among patients with NSCLC and LMD, including use of immunotherapy among patients without *EGFR* or *ALK* alterations.
- Although traditional chemotherapy is known to have poor CNS penetration, receipt of platinum-based chemotherapy or pemetrexed after LMD diagnosis was associated with improved OS, even after adjustment for ECOG PS and prior chemotherapy exposure.
- These findings should be interpreted in the context of the study's retrospective design, which is subject to potential selection bias and immortal time bias.

Future Direction for Research

- Larger, prospective studies are needed to better define the survival benefit of individual systemic therapies and to identify which molecular and clinical subgroups derive the greatest benefit from specific treatment strategies.

RESULTS

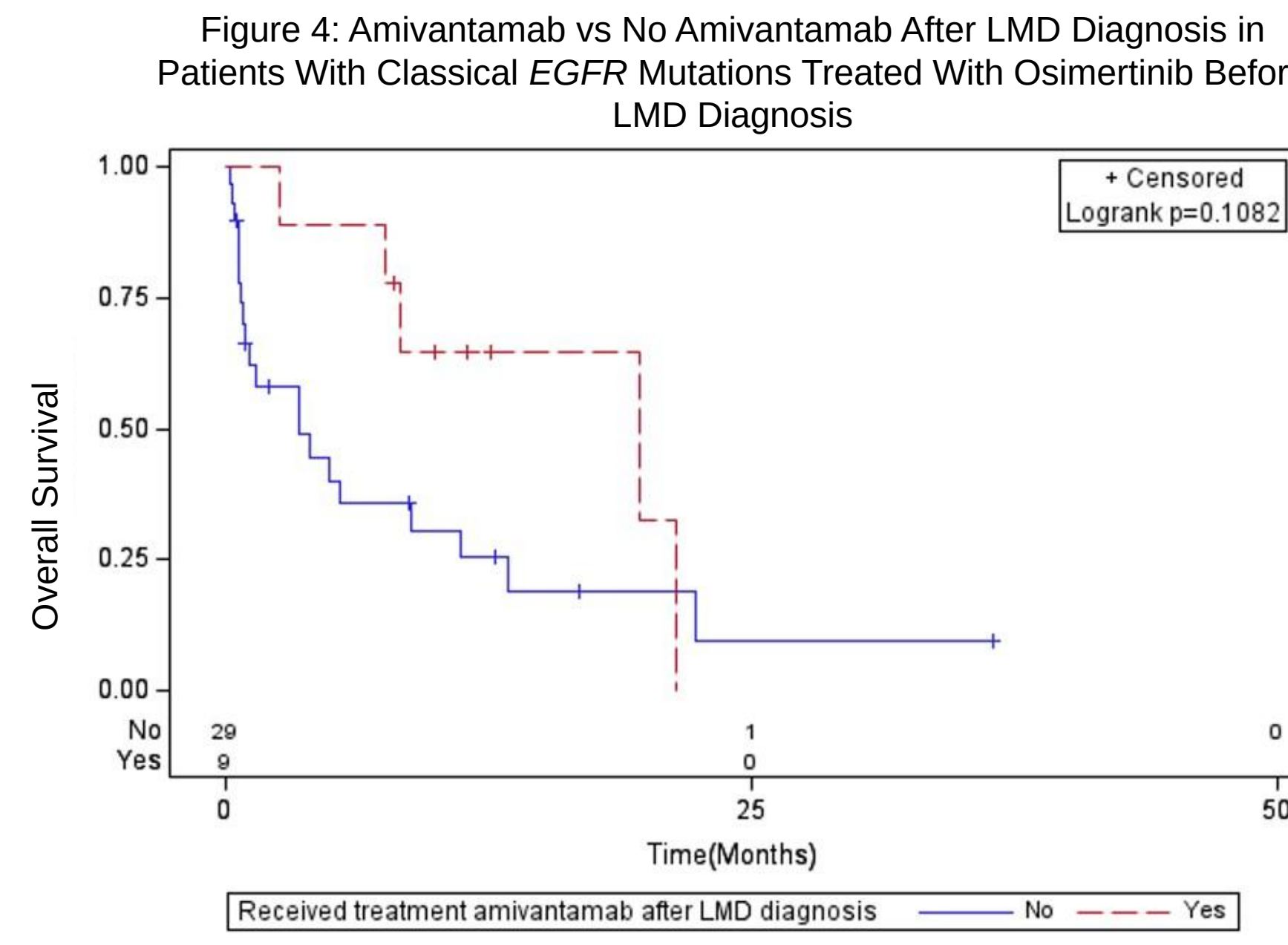
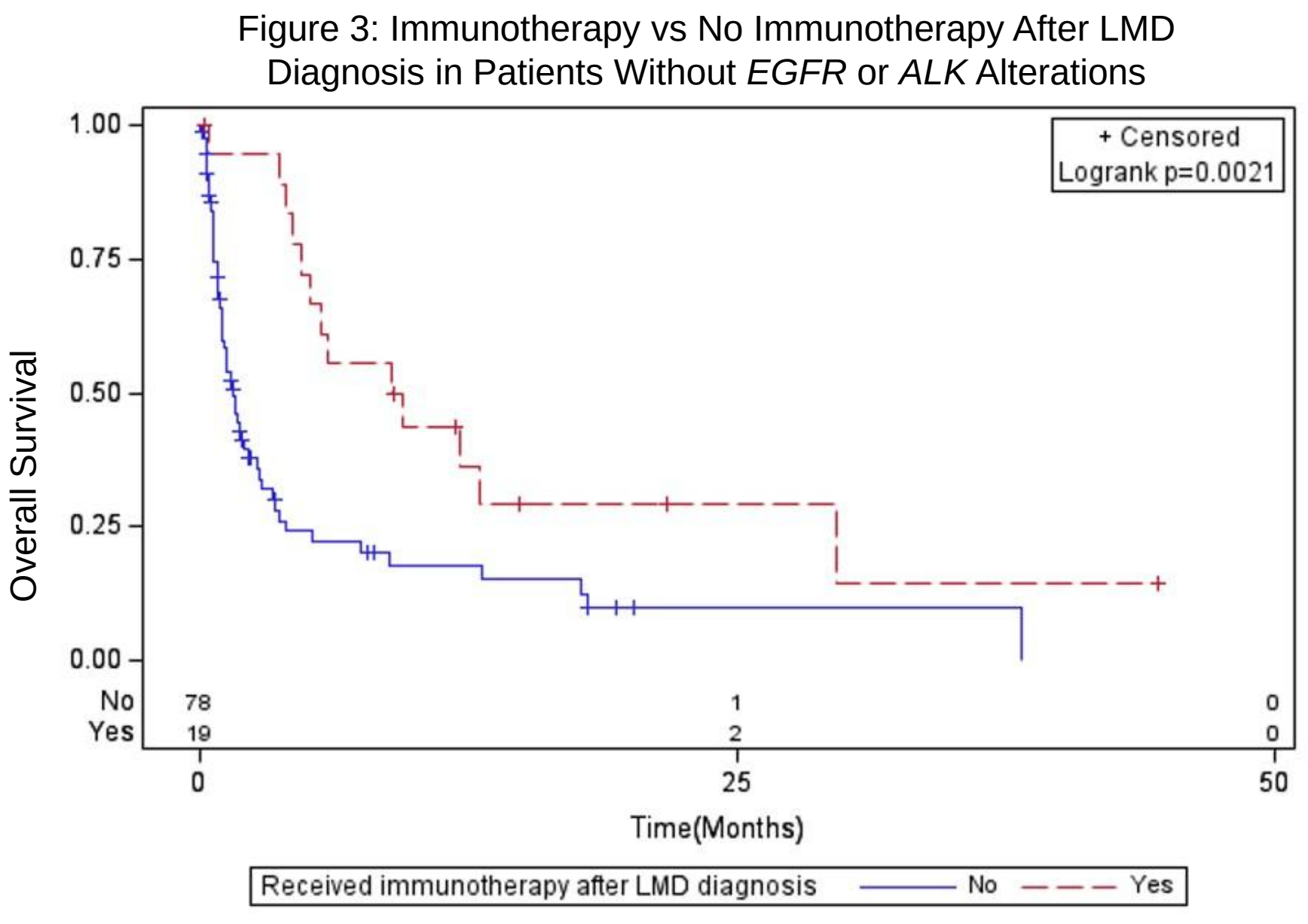
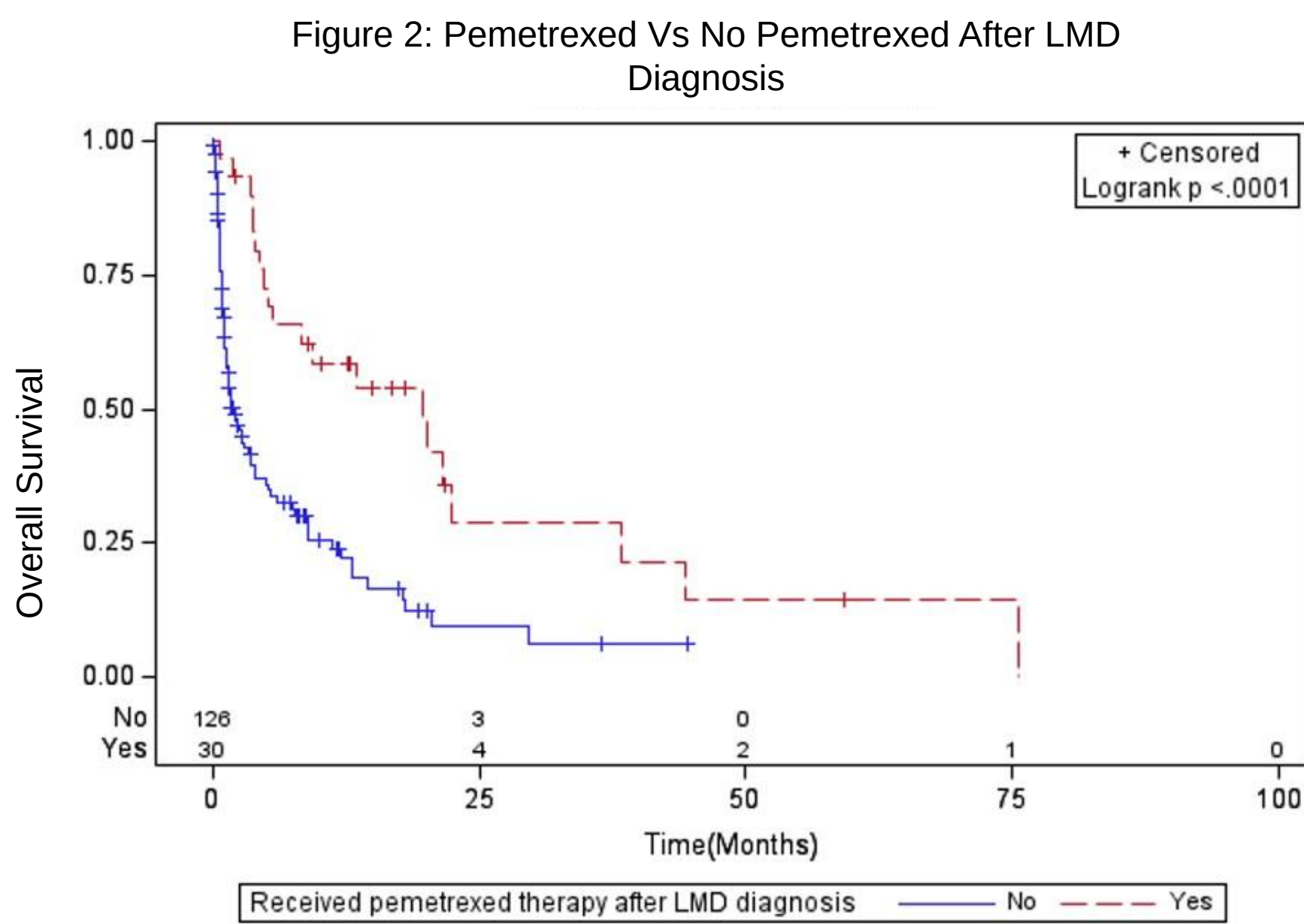
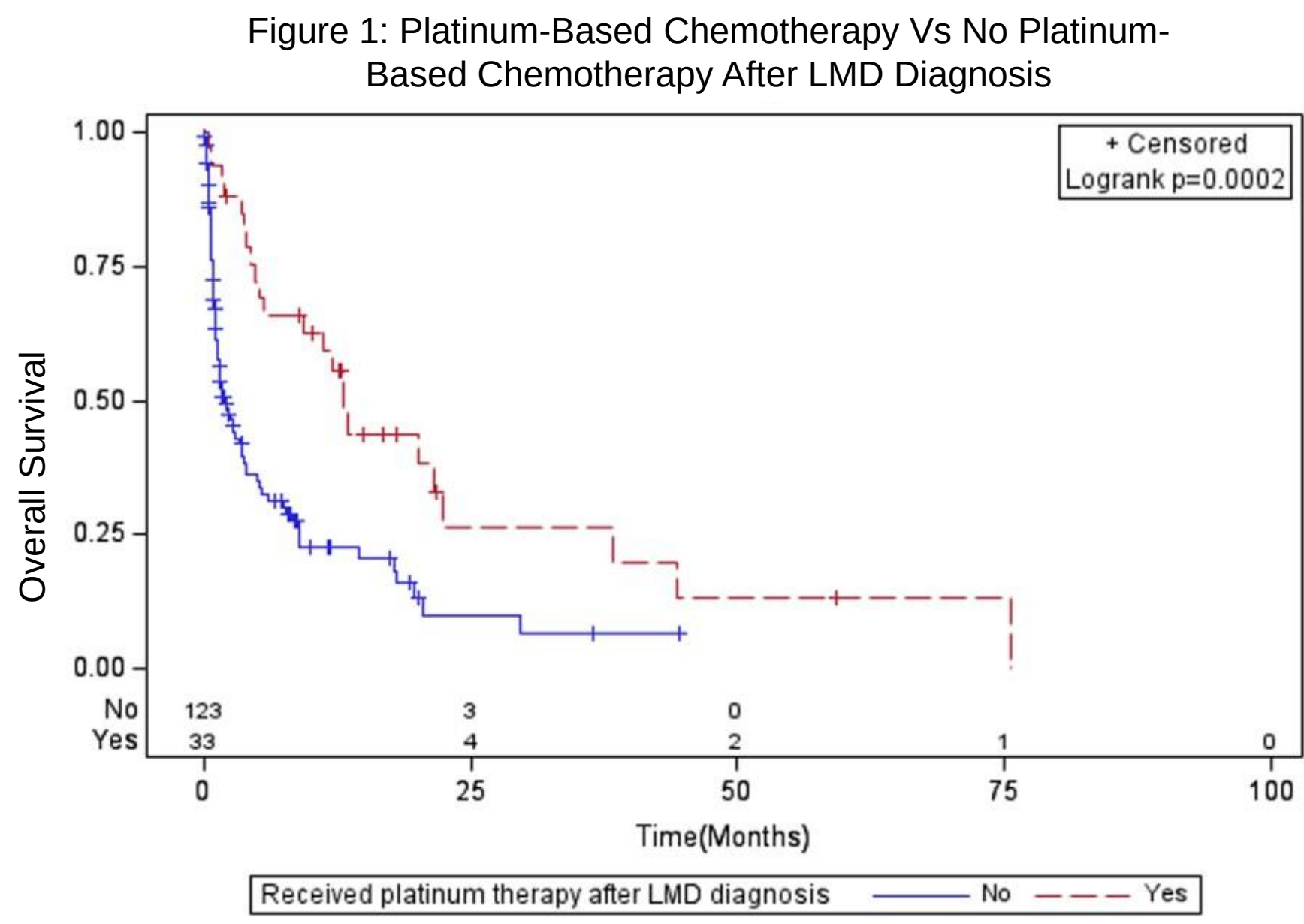
Table 1: Baseline Characteristics (N=156)

Characteristic	N (%)
Median age at LMD diagnosis	64
Sex	
Male	62 (40)
Female	94 (60)
Race	
White	89 (57)
Black or African American	49 (31)
Asian	9 (6)
Other	6 (4)
Unknown	3 (2)
Smoking status	
Never smoker	59 (38)
Former smoker	73 (47)
Current smoker	24 (15)
Diagnosis of LMD	
MRI alone	107 (69)
Lumbar puncture alone	8 (5)
MRI and lumbar puncture	37 (24)
Resected CNS metastasis pathology	3 (2)
CT head & high clinical suspicion	1 (1)
LMD present at NSCLC diagnosis	47 (30)
CNS symptoms at LMD diagnosis	136 (87)
Histology	
Squamous	10 (6)
Non-squamous	146 (94)
PD-L1 expression	
0	32 (21)
1–49%	64 (41)
≥50%	32 (21)
Unknown	28 (18)
Genomic alterations identified (101/141 patients, 72%)	
<i>EGFR</i> exon 19 deletion or L858R mutation	48 (48)
<i>EGFR</i> exon 20 insertion	6 (6)
Compound <i>EGFR</i> mutation	4 (4)
Atypical <i>EGFR</i> mutation	15 (15)
<i>ALK</i> fusion	4 (4)
<i>KRAS</i> G12C mutation	10 (10)
<i>ROS1</i> fusion	3 (3)
<i>HER2</i> mutation	7 (7)
<i>RET</i> fusion	1 (1)
<i>MET</i> exon 14 skipping mutation	3 (3)
<i>BRAF</i> V600E mutation	2 (2)
Received any therapy after LMD diagnosis (105/156 patients, 67%)	
Radiation therapy	72 (69)
Systemic therapy	79 (75)
Chemotherapy	43 (54)
Immunotherapy	23 (29)
Targeted therapy	47 (59)

Table 2: OS by Treatment After LMD Diagnosis

Population & Treatment Comparison	N	Median OS (months)	HR	p-value
All pts				
Any systemic therapy vs no systemic therapy [†]	79 vs 77	8.3 vs 0.8	0.12	<0.0001
Platinum-based chemotherapy vs no platinum-based chemotherapy ^{†‡§}	33 vs 123	12.1 vs 1.3	0.38	0.0009
Pemetrexed vs no pemetrexed ^{†§}	30 vs 126	11.4 vs 1.3	0.36	0.0004
Pts with molecular alterations				
Any targeted therapy vs no targeted therapy	46 vs 43	9.4 vs 0.8	0.23	0.0001
Pts who received 1 targeted therapy prior to LMD diagnosis: further targeted therapy vs. no targeted therapy	10 vs 35	12.7 vs 2.5	0.29	0.045
Pts with <i>EGFR</i> mutations who received osimertinib before LMD diagnosis				
<i>EGFR</i> TKI vs no <i>EGFR</i> TKI	20 vs 18	9.4 vs 0.7	0.18	0.002
Amivantamab vs no amivantamab	9 vs 29	10.0 vs 1.5	0.34	0.052
Pts without <i>EGFR</i> or <i>ALK</i> alterations				
Immunotherapy vs no immunotherapy ^{†#}	17 vs 78	9.0 vs 1.2	0.48	0.049

Footnotes: All analyses were adjusted for ECOG PS at LMD diagnosis. Selected analyses were also adjusted for the following variables assessed prior to LMD diagnosis: number of systemic therapy lines (†), presence of a molecular alteration (§), prior platinum exposure (§), prior pemetrexed exposure (||), number of targeted therapy lines (||), and prior immunotherapy exposure (#).



Note: Figures 1–4 show unadjusted survival curves, whereas Table 2 presents results adjusted for potential confounders, including ECOG PS and prior therapy.