

Outcomes to first-line pembrolizumab in patients with advanced NSCLC and high PD-L1 expression: updated results from a spanish multicentric study

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Background. Pembrolizumab stands as a first-line option for patients (p) with advanced NSCLC (Non-small cell lung cancer) and **high PD-L1 expression** ($\geq 50\%$). Several factors influenced outcomes such as antibiotic (AB) exposure, low body mass index (BMI), certain metastatic location (e.g. bone), or ECOG-PS of 2.

Methods. Multicenter retrospective study. Stage IV high PD-L1 expression NSCLC treated with first-line pembrolizumab in clinical practice between August 2017 and July 2022. Descriptive statistics to report baseline characteristics. Kaplan-Meier to estimate survivals, long-rank-test to compare median survivals. Multivariate analyses, using Cox regression.

Results. Survival and treatment outcomes (N=494)

Median follow-up: 14.3m.

Age - years	N (%)
Median	67.29
Sex - n (%)	
Male	379 (76.7%)
Female	115 (23.3%)
Histology - no (%)	
Non-squamous	373 (75.5%)
Squamous	114 (23.1%)
Dedifferentiated	7 (1.4%)
AB exposure - no (%)	
Yes	175 (35.4%)
No	319 (64.6%)
BMI - no (%)	
<24,9	230 (46.6%)
≥ 25	234 (47.3%)
Unknown	30 (6.1%)

Table 1. Patient characteristics.

**Exposure to corticosteroids (>10mg prednisone/equivalent) PPI (Proton Pump Inhibitors) and AB (antibiotics): during treatment with pembrolizumab or 4 weeks before initiation.

	Median OS - months (95% CI)	p-value (univariate analysis)	Median PFS - months (95% CI)	p-value (univariate analysis)
ECOG PS (Figure 3)				
0 (N=138, 27.9%)	36.7 (19.2-54.3)		14.4 (9.6-19.1)	
1 (N=269, 54.5%)	14.8 (12.0-17.5)		10.8 (8.4-13.3)	
2 (N=81, 16.4%)	2.5 (1.5-3.4)		2.5 (0.5-4.5)	
3 (N=6, 1.2%)	0.3 (0.2-0.3)	< 0.001*	0.3 (0.0-1.3)	< 0.001
Corticosteroid exposure** (Figure 4)				
No (N=284, 57.5%)	22.1 (17.8-26.4)		10.1 (7.5-12.7)	
Yes (N=210, 42.5%)	10.6 (7.2-14.0)	< 0.001*	9.3 (5.7-13.0)	0.082
Reason for treatment with corticosteroids				
irAEs (immuno-related adverse events) (N=57, 11.5%)	NR		24.6 (8.8-40.5)	
Baseline conditions/symptom management (N=153, 31.0%)	4.7 (1.6-7.8)	< 0.001	4.5 (1.8-7.3)	< 0.001
PPI exposure** (Figure 5)				
No (N=186, 37.7%)	23.7 (18.4-29.0)		11.5 (7.6-15.4)	
Yes (N=308, 62.3%)	12.7 (10.0-15.3)	0.003	8.5 (5.8-11.3)	0.041
Bone metastases (Figure 6)				
No (N=336, 68.0%)	18.7 (14.7-22.8)		11.1 (8.8-13.3)	
Yes (N=158, 32.0%)	10.2 (5.9-14.6)	0.001	7.3 (5.2-9.4)	0.164
Best response to IO				
CR (N=30, 6.1%)	57.8 (51.9-63.8)		55.4 (42.0-68.7)	
PR (N=184, 37.2%)	NR		35.9 (27.2-44.5)	
SD (N=113, 22.9%)	15.2 (13.2-17.1)		15.9 (13.6-18.3)	
PD (N=117, 23.7%)	4.0 (3.1-5.0)	<0.001	4.1 (3.1-5.0)	<0.001
Not evaluated (N=50, 10.1%)				

Table 2. Variables associated with survival outcomes.

*After multivariate analysis, corticosteroid treatment (HR 1.41) and ECOG (HR 2.40) maintained a prognostic impact.

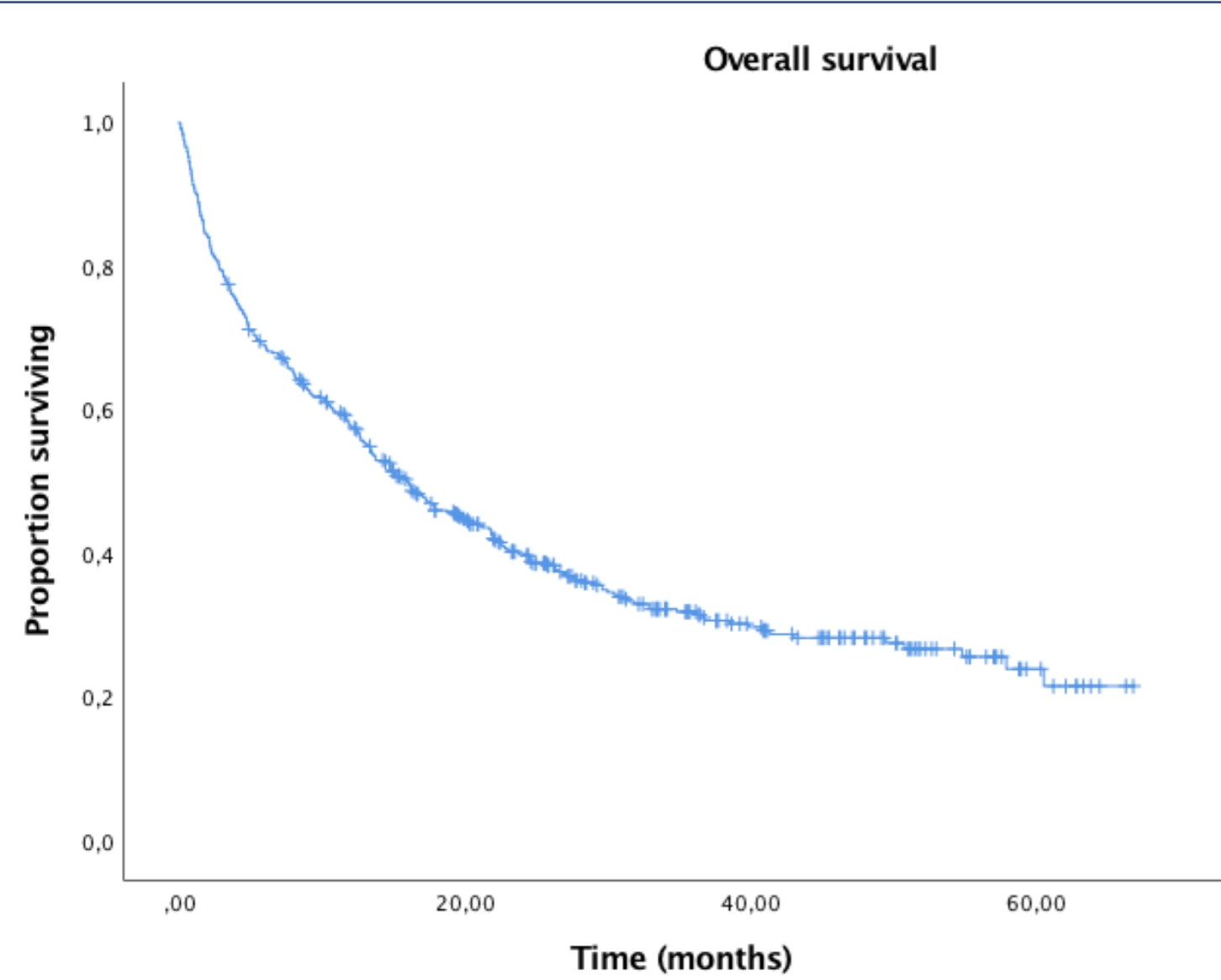


Figure 1. Median OS in the overall population.

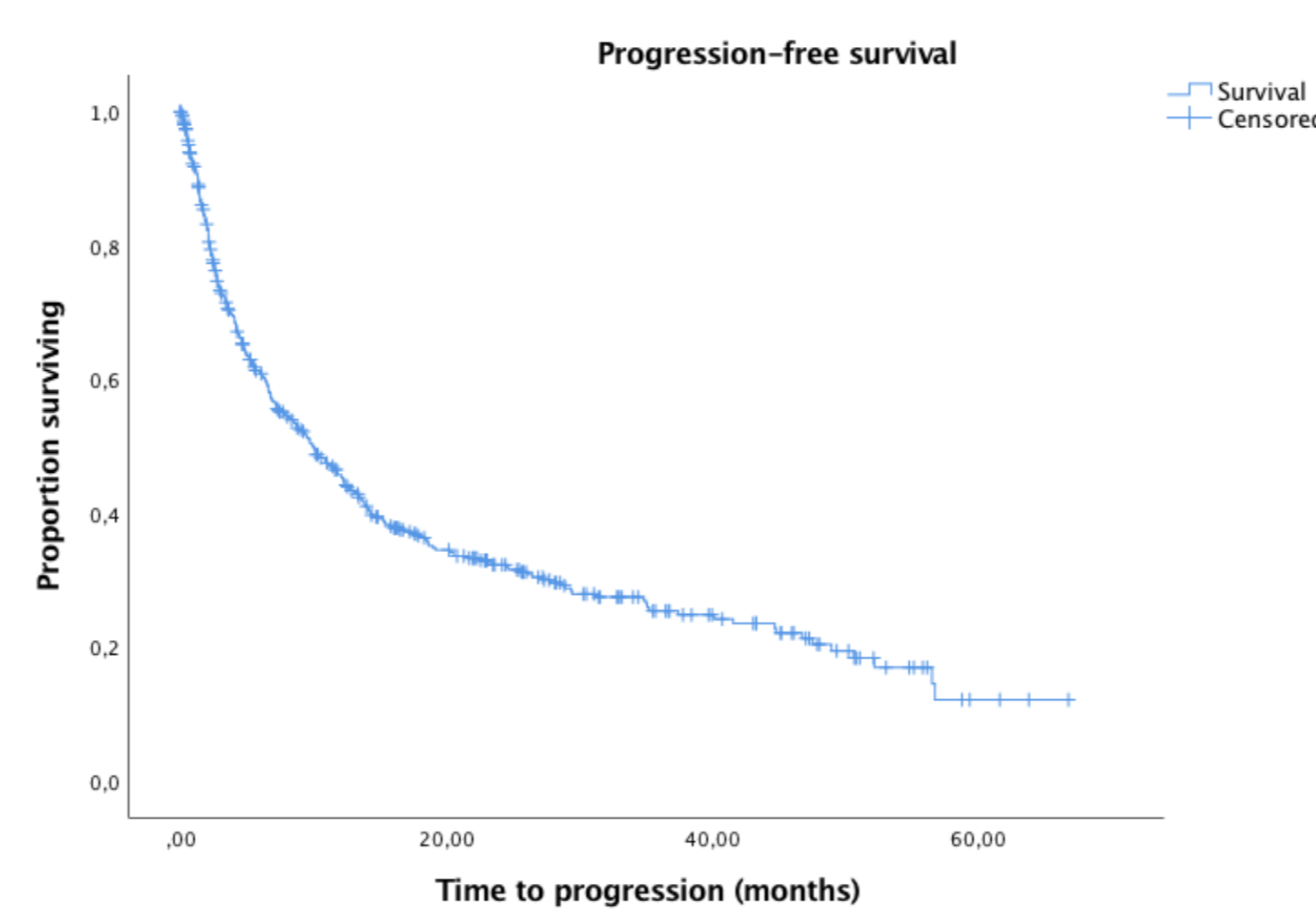


Figure 2. Median PFS in the overall population.

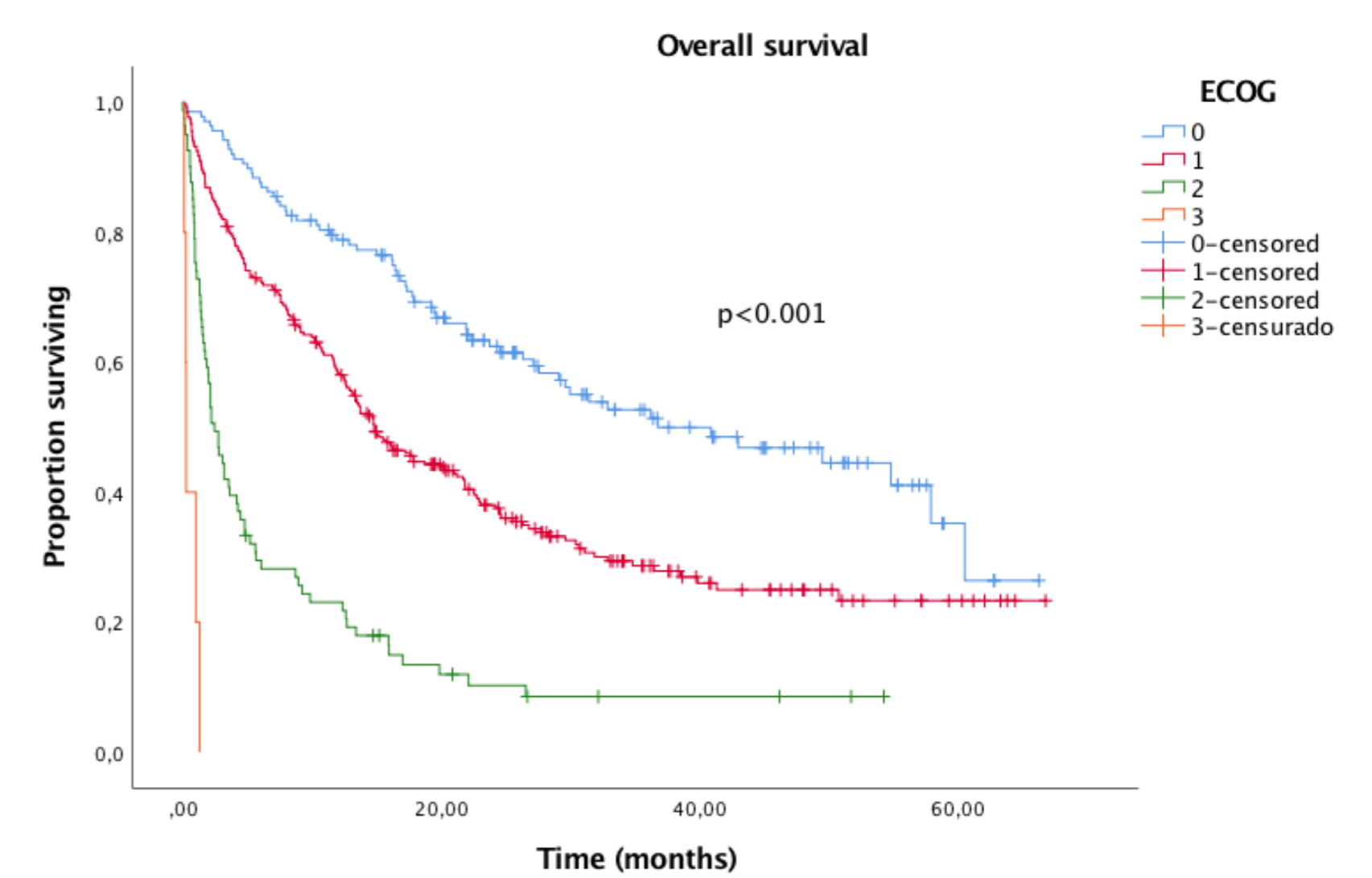


Figure 3. OS according to ECOG.

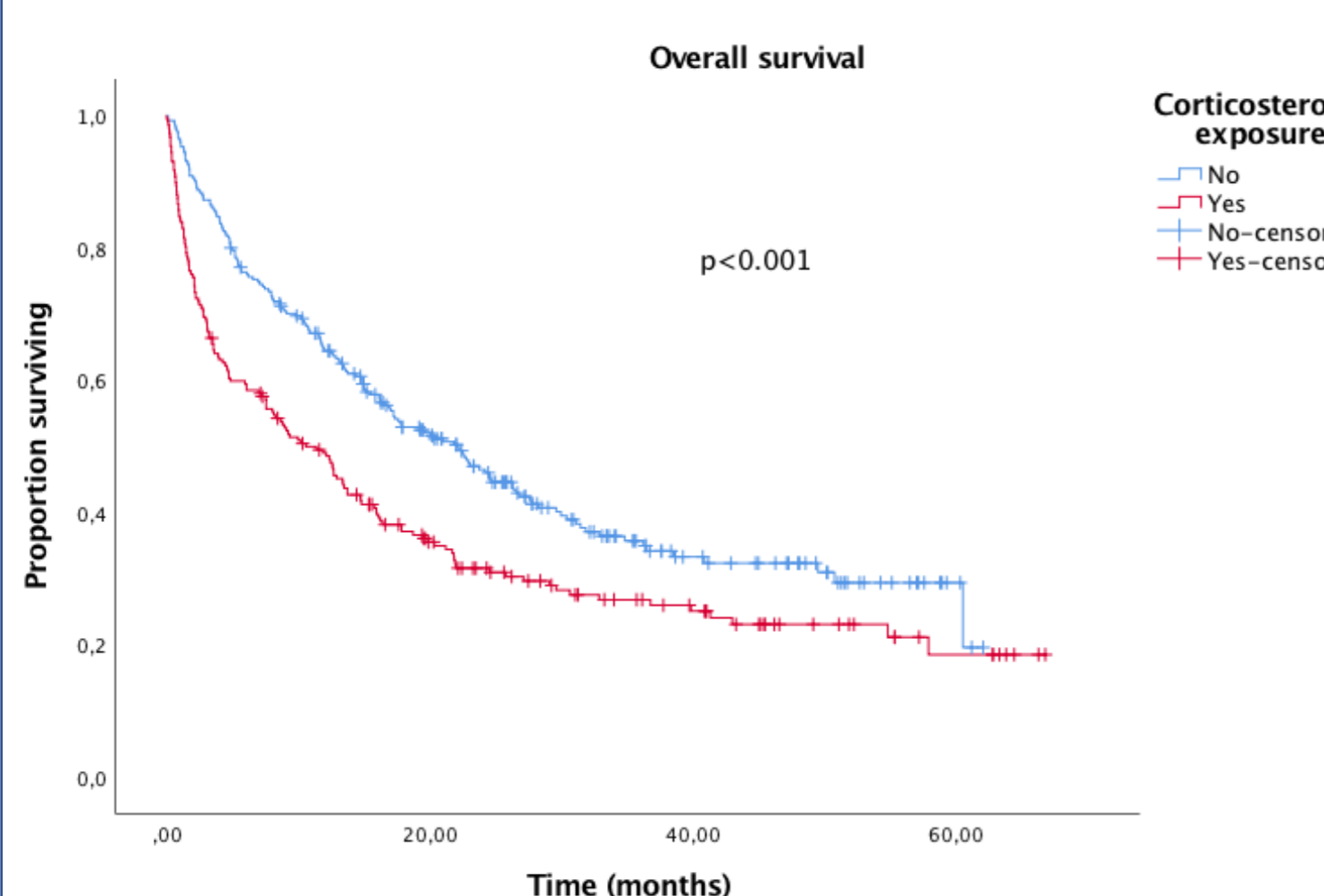


Figure 4. OS according to treatment with corticosteroids.

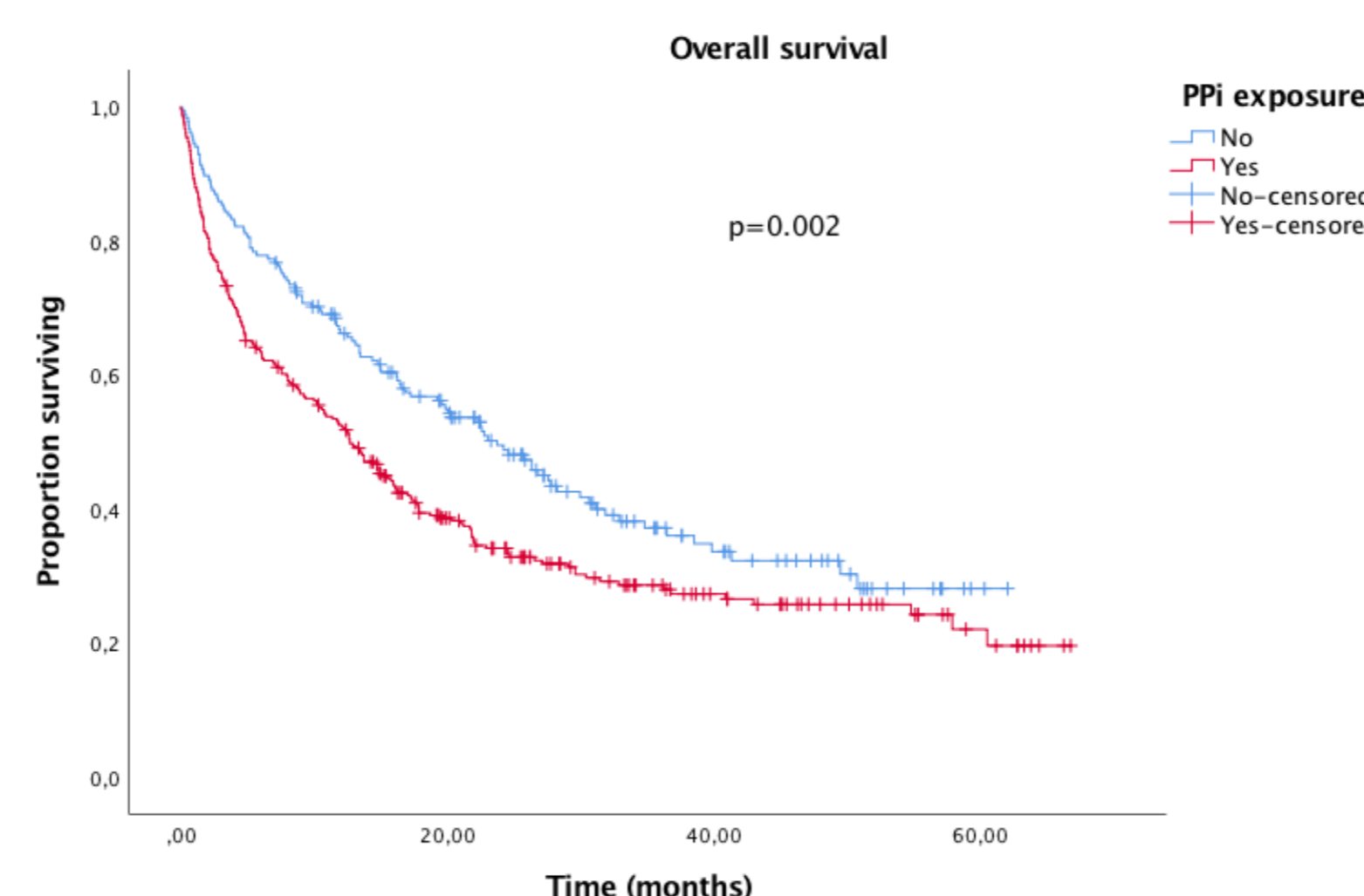


Figure 5. OS according to treatment with PPI.

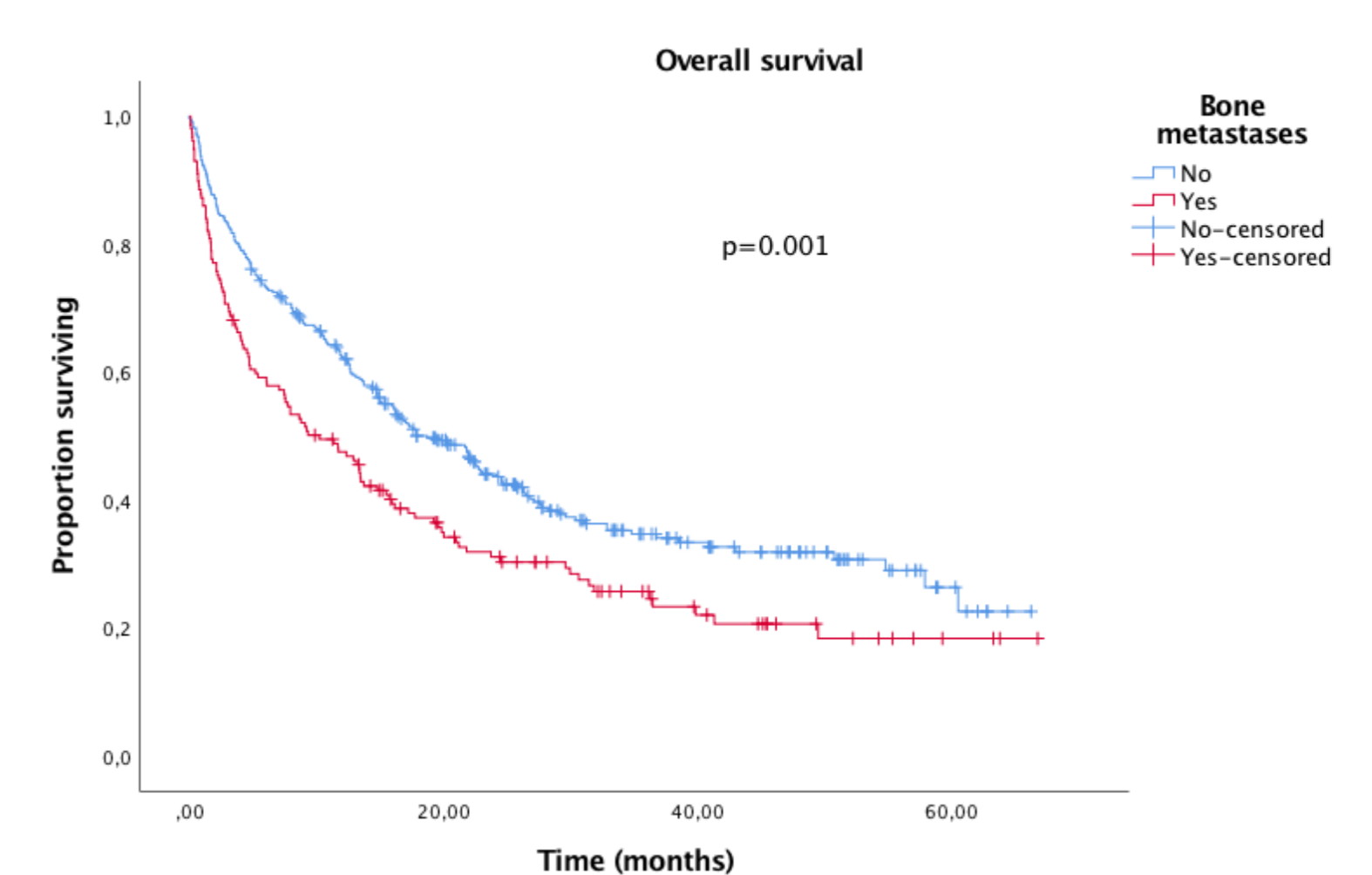


Figure 6. OS according to bone metastases.

Conclusions. First-line pembrolizumab in advanced NSCLC p with high PD-L1 expression should only be used in patients with good PS. Patients with PS 2 are in urgent need of new treatment approaches.

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