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INTRODUCTION

Some studies, including a meta-analysis¹, observed that the circadian rhythm of immune cell's^{2,3} proliferation and destruction may influence progression-free and overall survival in metastatic cancer treated with immunotherapy (IO).

This study aims to evaluate the time of IO administration in patients with locally advanced non-small-cell lung cancer (NSCLC) undergoing curative concurrent chemo/radiotherapy (CRT) followed by IO consolidation.

METHODS

For this retrospective study, all the patients with histologically confirmed unresectable NSCLC PDL1 ≥1% treated with radical concurrent CRT who received at least 1 cycle of IO consolidation (PACIFIC protocol) from 2018 to 2023 at three hospitals of the Institut Català d'Oncologia (ICO) were included.

These patients were categorized depending on the most frequently time of IO administration in two groups: Before 3 pm (receiving 50% or more doses before 15:00h) or after 3 pm (receiving less than 50% doses before 15:00h).

Real-world Progression Free Survival (PFS) and Overall Survival (OS) was calculated using the Kaplan-Meier method with the log-rank test.

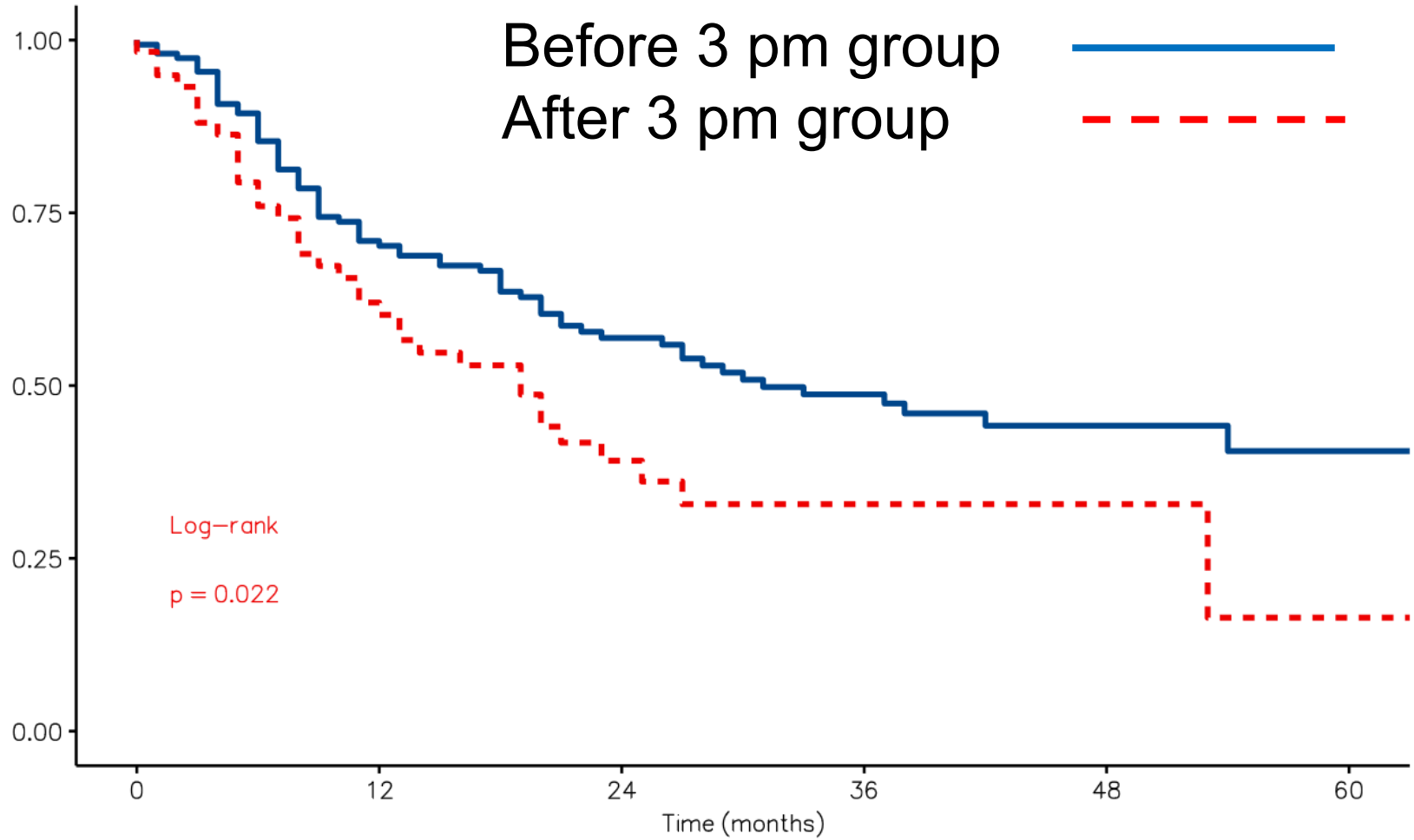
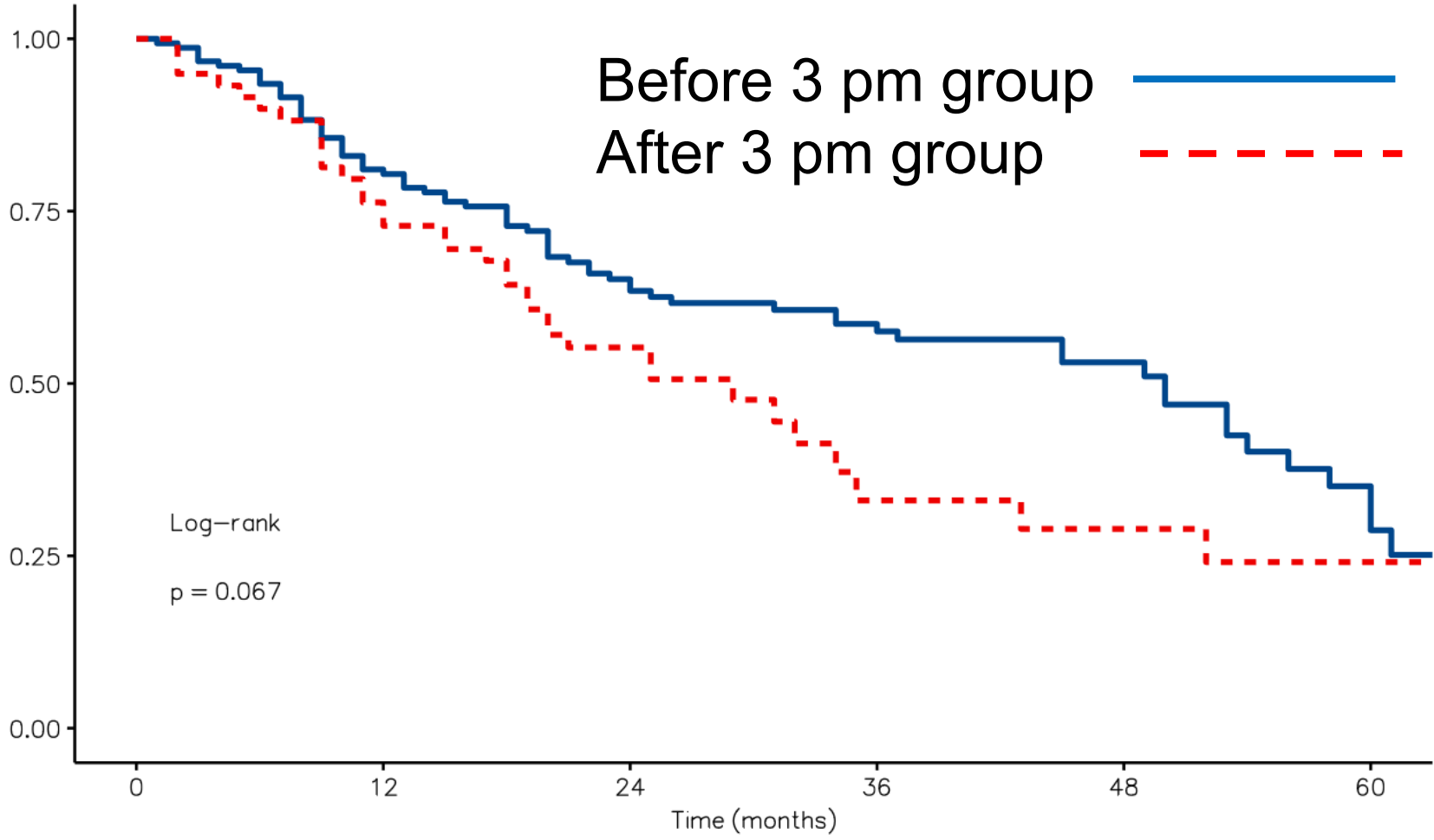
Median follow-up was 24 months.

RESULTS

		Before 3pm group (n= 153)	After 3pm group (n= 59)	TOTAL (n= 212)
Age years	median (range)	68 (42-86)	66 (43-89)	67 (42-89)
Sex n° (%)	Male	122 (79.8%)	43 (72.9%)	165 (77.8%)
	Female	31 (20.2%)	16 (27.1%)	47 (22.2%)
Smoking n° (%)	Current	84 (54.9%)	29 (49.2%)	113 (53.3%)
	Former	64 (41.8%)	25 (42.3%)	89 (42%)
	Never smoker	5 (3.3%)	5 (8.5%)	10 (4.7%)
Histology n° (%)	Squamous	84 (54.9%)	32 (54.2%)	116 (54.7%)
	Adenocarcinoma	49 (32%)	19 (32.2%)	68 (32.1%)
	Others	20 (13.1%)	8 (13.6%)	28 (13.2%)
Stage n° (%)	II	14 (9.1%)	5 (8.5%)	19 (8.9%)
	III	134 (87.6%)	51 (86.4%)	185 (87.3%)
	IV	5 (3.3%)	3 (5.1%)	8 (3.8%)

Progression-free survival (PFS)

- PFS was significantly better in the before 3pm group compared to the after 3pm group with a median PFS was of 31 vs 19 months respectively (Hazard Ratio = 0.62; 95% CI 0.42-0.94; p=0.02).
- The 1-year and 3-year PFS rates were 70.2% vs. 60.2% and 48.7% vs. 32.8% respectively.



Overall survival (OS)

- A trend toward longer OS was observed in the before 3 pm group, but these differences were not statistically significant with a median OS was 50 vs. 29 months respectively (Hazard Ratio 0.69; 95% CI 0.46-1.03; p=0.07).
- The 1-year and 3-year OS rates were 80.4% vs. 72.9% and 57.6% vs. 33.0%, respectively.

CONCLUSIONS

- This is the **first retrospective analysis** in which has been observed that patients treated **preferentially before 3pm** exhibit a **better disease control** than those treated onwards in **radical treatment** with concurrent Chemo/radiotherapy followed by immunotherapy in patients with **locally advanced non-small-cell lung cancer**.
- Preferential treatment before 3pm** may **enhance disease control** and **improve OS**.
- These findings **support the need for prospective clinical trials** to further explore the **impact of circadian timing** on treatment outcomes.

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