

## Impact of Platinum Dosing Intensity in Patients with Advanced Lung Cancer Treated with Palliative Chemotherapy or Chemo-Immunotherapy

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### Background:

Lung cancer is a leading cause of cancer death worldwide, especially among elderly patients. Platinum-based chemotherapy with or without immunotherapy is a standard treatment for advanced/metastatic lung cancer. Most clinical trials exclude frail and geriatric patients with comorbidities and/or poor performance status, limiting evidence for this group. Preemptive dose reductions of chemotherapy are common in clinical practice despite the lack of any evidence regarding optimal dosing in these populations.

### Methods:

We retrospectively analyzed patients with advanced/metastatic lung cancer aged  $\geq 60$  years treated with platinum based palliative chemotherapy with or without checkpoint inhibitor from 2016-2025 at our institution. Patients were grouped by platinum dosing intensity, AUC  $>5$  being defined as 100%: A) 90-100%, B) 70-89%, C)  $<70\%$ . Primary endpoint was OS. Secondary endpoints included PFS, time to next treatment (TTNT), ORR and toxicity.

### Results:

170 patients were included, 75 belonging to group A, 80 to group B, and 15 to group C. Median age was 72 years across all groups. 47% of patients had adenocarcinoma, 29% SCLC, 19% squamous and 5% other histology. 32% of patients had ECOG PS  $\geq 2$ . Only 2 of 170 patients received cisplatin-based therapy, the rest receiving carboplatin.

Median follow-up for OS was 42 months. No significant differences in median OS (Group A: 12 months (95% CI 7.1-16.9); group B: 10 months (95% CI 8-12), group C: 8 months (95% CI 1-15),  $p=0.34$ ), PFS (median 6/6/5 months, respectively,  $p=0.25$ ), or TTNT (median 7/8/4 months, respectively,  $p=0.08$ ) were observed.

ORR was comparable across groups with no significant dose-dependency detectable (group A 48%, group B 56%, group C 40%,  $p=0.41$ ).

Treatment discontinuation rates were similar across groups ( $p=0.38$ ).

Subgroup analyses and multivariate regression showed that factors such as ECOG PS, histology, cardiovascular comorbidity, brain metastases and treatment kind (with or without immunotherapy) significantly influenced outcomes regardless of dosing.

### Conclusions:

Reduced platinum dosing intensity in patients with advanced lung cancer did not significantly impact survival or response in this real-world cohort. These data support individualized dosing and argue for broader clinical trial inclusion criteria to improve representation of frail populations.

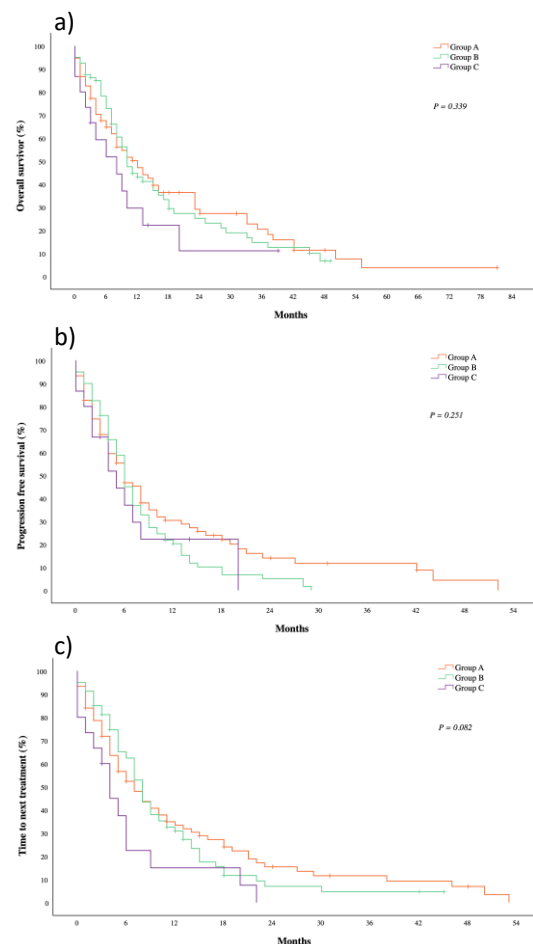


Figure 1: Overall survival (a), progression-free survival (b), and time to next treatment (c) in 170 patients with advanced/metastatic lung cancer treated with palliative platinum-based chemotherapy or chemo-immunotherapy, grouped by platinum dosing intensity: Group A) 90-100%, Group B) 70-89%, Group C)  $<70\%$ .

Characteristics, n (%)	Group A: Dose 90-100% (n=75)	Group B: Dose 70-89% (n=80)	Group C: Dose $<70\%$ (n=15)	p
<b>Median age (range)</b>	71 (61-86)	72 (60-83)	72 (63-83)	0.16
<b>Sex</b>				
Male	47 (63)	47 (59)	12 (80)	
Female	28 (37)	33 (41)	3 (20)	0.3
<b>ECOG PS</b>				
0	25 (33)	15 (19)	0 (0)	
1	32 (43)	36 (45)	8 (53)	
2	14 (19)	25 (31)	5 (33)	
3 – 4	4 (5)	4 (5)	2 (13)	<b>0.03</b>
<b>Previous curative therapy</b>				
Surgery	3 (4)	5 (6)	2 (13)	0.31
Radiochemotherapy	17 (23)	31 (39)	3 (20)	<b>0.07</b>
<b>Treatment kind</b>				
Cisplatin-based	0	0	2	
Carboplatin-based	75	80	13	
Chemo only	16 (21)	15 (19)	4 (27)	
Combined Chemo – ICI	49 (65)	60 (75)	11 (73)	0.38
<b>Reason discontinuation</b>				
Regular (4 - 6 cycles)	46 (68)	44 (63)	6 (50)	
Toxicity	6 (9)	11 (16)	1 (8)	
Progress	9 (1)	6 (9)	2 (17)	
Death	7 (1)	7 (10)	2 (17)	
Patient wish	0	2 (3)	1 (8)	0.38
<b>Subsequent therapy</b>				
2nd line	31 (41)	32 (40)	3 (20)	0.29
3rd or later line	11 (15)	13 (1)	1 (7)	0.63

Table 1: Baseline- and treatment-characteristics of 170 patients with advanced/metastatic lung cancer treated with palliative platinum-based chemotherapy or chemo-immunotherapy, grouped by platinum dosing intensity: Group A) 90-100%, Group B) 70-89%, Group C)  $<70\%$ . ECOG PS= Eastern Cooperative Oncology Group performance status. ICI=Immune checkpoint inhibitor.