

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 ≥ 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 ≥ 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.

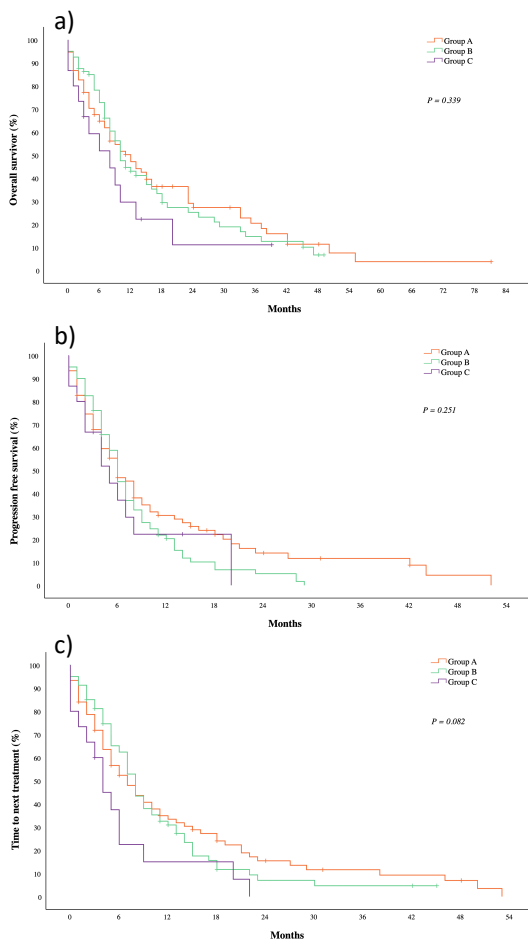


Figure 1: Overall survival (a), progression-free survival (b), and time to next treatment (c) in 170 patients with advanced/metastatic lung cancer treated with palliative platinum-based chemotherapy or chemo-immunotherapy, grouped by platinum dosing intensity: Group A) 90-100%, Group B) 70-89%, Group 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
Median age (range)	71 (61-86)	72 (60-83)	72 (63-83)	0.16
Sex				
Male	47 (63)	47 (59)	12 (80)	0.3
Female	28 (37)	33 (41)	3 (20)	
ECOG PS				
0	25 (33)	15 (19)	0 (0)	0.03
1	32 (43)	36 (45)	8 (53)	
2	14 (19)	25 (31)	5 (33)	
3 – 4	4 (5)	4 (5)	2 (13)	
Previous curative therapy				
Surgery	3 (4)	5 (6)	2 (13)	0.31
Radiochemotherapy	17 (23)	31 (39)	3 (20)	0.07
Treatment kind				
Cisplatin-based	0	0	2	0.38
Carboplatin-based	75	80	13	
Chemo only	16 (21)	15 (19)	4 (27)	
Combined Chemo – ICI	49 (65)	60 (75)	11 (73)	
Reason discontinuation				
Regular (4 - 6 cycles)	46 (68)	44 (63)	6 (50)	0.38
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)	0.29
Subsequent therapy				
2nd line	31 (41)	32 (40)	3 (20)	
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.