The negative prognostic role of opioids in patients with NSCLC treated with immunotherapy

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Background: Opioids seem to interfere with immune response.¹⁻³ We analysed the prognostic and predictive impact of opioids in Non Small Cell Lung Cancer (NSCLC) patients treated with immunotherapy.

Methods: We retrospectively collected and analyzed data about NSCLC patients treated with anti-PD-1/anti-PD-L1 agents at our Institution. Progression free survival (PFS) and overall survival (OS) were estimated using Kaplan-Meier method. A Cox regression model was carried out for univariate and multivariate analyses.

Results: Sixty-six patients were enrolled, 50 male (75.8%) and 16 female (24.2%). Median age was 72 years (range 25-88). Thirty-one patients (47%) received opioids at the beginning and/or during immunotherapy. (Table 1) This setting of patients had a poorer prognosis (mOS 5.37 months vs not reached, $p=0.0009$; mPFS 3.83 months vs not reached, $p=0.0001$). (Figure 1) Performance Status (PS) according to Eastern Cooperative Oncology Group (ECOG) had a prognostic and predictive role (mOS 3.23 months vs not reached, $p=0.0059$; mPFS of 1.7 vs 3.8 months, $p=0.0089$). (Figure 2) Sex, age (cut-off 70 years), lymphopenia, PD-L1 expression did not result as prognostic and predictive factors. Multivariate analysis confirmed that opioids had a negative prognostic and predictive role and ECOG-PS ≥ 2 had a negative prognostic impact. Patients requiring higher opioids doses or opioids switch had a lower survival (OS 4.9 vs 16.5 months; $p=0.0030$). A trend of worse prognosis was observed in patients receiving morphine (mOS 4.1 vs 8.6 months, $p=0.059$) and fentanyl (mOS 4.17 vs 8.63 months).

Conclusion: Opioid treatment and its escalation at the beginning and during immunotherapy are negative prognostic factors in advanced NSCLC.

	N. of patients	(%) of patients
Total	66	
Gender		
Male	50	75.8
Female	16	24.2
Histology		
Squamous	30	45.5
Non-squamous	34	51.5
NOS	2	3
Age at diagnosis		
< 70 years	31	47
≥ 70 years	35	53
Smoking		
Smoker	18	23.3
Non-smoker	5	7.6
Past-smoker	43	65.1
ECOG-PS		
≥ 2	8	12.1
<2	57	84.4
NOS	1	1.5
Immunotherapy, which line		
First-line	15	27.8
Second-line	44	66.7
Third-line	6	9
Forth-line	1	1.5
Lymphopenia		
Yes	19	28.8
No	47	71.2
Elevated N/L		
Yes	16	24.2
No	50	75.8
Exitus		
Yes	29	44
No	37	56

Table 1. Patients' clinical-laboratoristic characteristics. NOS= Not Otherwise Specified; ECOG-PS = Eastern Cooperative Oncology Group Performance Status

Fig 1. OS and PFS of patients according to opioids' treatment (1: yes, 2: no).

Fig 2. OS and PFS of patients according to ECOG-PS (1: ≥ 2 , 2: <2).

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