#55P

MOREL: A Multi-Center Observational Retrospective Study to Evaluate the Clinical Management of Patients with Newly Diagnosed Locally Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) and to Characterize and Describe how PD-L1 Expression is Performed in Spain.

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Background:

- First-line treatment of advanced NSCLC has undergone a great change in recent years[1,2].
- Immunotherapies that focus on the PD-1/PD-L1 pathway have become part of standard of care for patients with advanced or metastatic NSCLC[1,2].
- PD-L1 testing landscape is complex, with multiple PD-L1 immunohistochemistry (IHC) assays being available, different cutoffs for PD-L1 positivity being utilized and, considerable differences in level of expertise between laboratories evaluating PD-L[1-3].
- The variety of available treatment options as well as new biomarkers add complexity to the selection of the best therapy for each patient[1-3].
- It is of relevance to know how newly diagnosed metastatic NSCLC patients are clinically managed and how immunotherapy is integrated in the first-line NSCLC treatment landscape. In addition, it is considered very important to describe how the PD-L1 testing is being performed in Spain in order to identify points that could be improved.
- The primary objective of this study is to describe patterns of clinical management of newly diagnosed stage IV NSCLC patients in Spain and to characterize and describe how PD-L1 expression is performed in representative medical centers in Spain.

Methods:

Study design:

- This is a multi-center, non-interventional, retrospective study based on secondary use of data collected from healthcare professionals.

Study population:

- The study enrolled patients aged 18 years or older, who were diagnosed with stage IV NSCLC with no tumor activating EGFR and BRAF mutations and/or ALK or ROS1 rearrangements attending to their routine clinical practice from 1st January 2019 to 31st December 2019 in 10 Spanish centers. Patients suitable for radical local treatment were not included in the study.

Statistical methodology

- Given the descriptive nature of the study, mean, median, standard deviation, 25th and 75th percentiles, minimum and maximum, and mean 95% confidence intervals were calculated for continuous variables, and absolute and relative frequencies for categorical variables (missing values were not considered for the calculation of percentages).
- Comparisons between groups, for continuous variables, were performed by means of parametric (Student's t) or non-parametric tests (U Mann-Whitney or Kruskal-Wallis), based on the characteristics of the study variables. For categorical variables, the chi-squared test or Fisher's exact test were applied.
- Statistical significance was considered for p<0.05. All statistical analyses were performed using the SAS version 9.4 statistical package.

Results:

- From January 2020 to May 2020, 308 patients from 10 centers in Spain were included in the study, 297 out of them met all inclusion criteria and none of the exclusion criteria.
- Overall, median age was 67 years (range: 37-89), 77.1% were male. ECOG 0, 1 or ≥2 was 27.8%, 46.4%, and 25.8%, respectively. 17.8 % had squamous NSCLC. The main sites of metastases were lung, bone and brain (42.4%, 39.1% and 21.9%, respectively). **(Table 1).**
- More than half of the patients (58.2%) reported comorbidities, most frequently cardiac disorders (21.2%), followed by respiratory disorders (14.5%), vascular disorders (14.5%) and metabolic and nutritional disorders (13.1%). Renal and urinary disorders were reported in 4.7% of patients.
- Five patients had an autoimmune disease reported at the time of diagnosis.

Treatment description

- 265 patients (89.2%) received systemic treatment for the Stage IV disease **(Figure 1)**, 9.4% as part of a clinical trial. Treatment was initiated approximately one month after histological diagnosis of Stage IV NSCLC (median: 31 days, P25;P75: 22-43 days) and after PD-L1 testing results in most cases (92.6%).
- Almost a third of all patients (28.3%) received complementary treatments for stage IV disease. Radiotherapy was the most frequent treatment (94.0%).
- Nearly half of all patients (46.1%) received systemic corticosteroids one week before or during the initiation of cancer treatment, two thirds of them (66.4%) as standard of care for their chemotherapy treatment
- The treatment regimen by clinicopathological characteristics is described in **Table 2.**

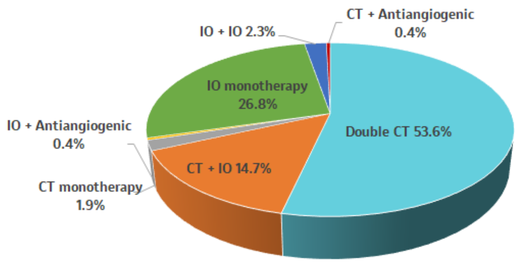
Table 1. Baseline demographics and clinicopathological characteristics

Total Patients	297
Gender n (%)	
Male	229 (77.1)
Female	68 (22.9)
Age n (%)	
Mean (SD)	67.1 (9.9)
≤75 years	237 (79.8)
>75 years	60 (20.2)
Cigarette smoking history n (%)	
Never smoker (≤100 cigarettes/lifetime)	30 (10.1)
Former smoker (≥1 year)	149 (50.2)
Smoker	115 (38.7)
Years smoking. Mean (SD)	42.8 (10.8)
ECOG n=295 *(%)*	
0	82 (27.8)
1	137 (46.4)
≥2	76 (25.8)
Status of Stage IV n=296 *(%)*	
M1a	64 (21.6)
M1b	58 (19.6)
M1c	174 (58.8)
Histological subtype n (%)	
Squamous	53 (17.8)
Non squamous	244 (82.2)

Total Patients	297
Site metastases [1] n (%)	
Lung	126 (42.4)
Bone	116 (39.1)
Adrenal glands	61 (20.5)
Brain (active)	52 (17.5)
Liver	45 (15.2)
Pleura	36 (12.1)
Lymph nodes	32 (10.8)
Brain (not active)	13 (4.4)
Muscular	12 (4)
Other[2]	32 (10.8)
Autoimmune disease at the time of diagnosis n (%)	**5 (1.7)**
Crohn's disease	2 (0.7)
Ulcerative colitis	1 (0.3)
Rheumatoid arthritis	2 (0.7)
Viral infections n (%)	**7 (2.4)**
HIV	1 (0.3)
Hepatitis B	3 (1)
Hepatitis C	3 (1)

[1] A single patient might report more than one localization of metastases.
[2] Other localization of metastases (n:32): Peritoneum n=7; Soft tissue n=5; Spleen n=3; Kidney n=3; Pancreas n=2; Pericardium n=2; Coeliac trunk n=1; Kidney. small intestine n= 1; Mediastinum n=1; Pancreas. intestine n=1; Peritoneum and soft tissue n=1; Pancreas n=1; Skin and peritoneum n=1; small intestine n=1; Soft tissue and Hypothalamic pituitary n=1; Thyroid n=1.

Figure 1. Type of systemic treatment (n=265)[1]



[1]Double Chemotherapy (CT): 142 (53.6%) : *Carboplatin + Nab-paclitaxel: 2 (0.8%); Cisplatin + Pemetrexed: 38 (14.3%); Carboplatin + Pemetrexed: 50 (18.9%); Cisplatin + Paclitaxel: 1 (0.4%); Carboplatin + Paclitaxel: 14 (5.3%); Cisplatin + Gemcitabine: 8 (3%); Carboplatin + Gemcitabine: 8 (3%); Carboplatin + Vinorelbine: 14 (5.3%) ; Cisplatin + Vinorelbine: 4 (1.6%); Carboplatin + Etoposide: 1 (0.4%); Cisplatin + Etoposide: 1 (0.4%); Carboplatin + Docetaxel: 1 (0.4%).*

CT monotherapy: 5 (1.9%): *Vinorelbine: 1 (0.4%); Docetaxel 1 (0.4%); Pemetrexed: 1 (0.4%), Carboplatin: 2 (0.8%).*

CT + Antiangiogenic: 1 (0.4%)*: Carboplatin + Pemetrexed + Bevacizumab: 1 (0.4%).*

IO (Immunotherapy) monotherapy: 71 (26.8%): *Pembrolizumab: 66 (24.9%); Atezolizumab: 2 (0.8%); Eftilagimod: 1 (0.4%); INCMGA0012: 2 (0.8%).*

IO + Antiangiogenic: 1 (0.4%)*: Atezolizumab + Bevacizumab: 1 (0.4%).*

Combo IO+ CT : 39 (14.7%): *Carboplatin + Pemetrexed + Pembrolizumab: 24 (9.6%); Cisplatin + Pemetrexed + Pembrolizumab: 11 (4.4%); Carboplatin + Paclitaxel + Pembrolizumab: 1 (0.4%); Carboplatin + Pemetrexed + Atezolizumab: 1 (0.4%); Cisplatin + Pemetrexed + Pembrolizumab + Canakinumab: 1 (0.4%); Pemetrexed + Pembrolizumab: 1 (0.4%).*

Combo IO + IO: 6 (2.3%): *Pembrolizumab + Eftilagimod: 6 (2.3%).*

Table 2. Treatment regimen by clinicopathological characteristics

	Double CT	CT monotherapy	CT + Antiangiogenic	IO monotherapy	CT + IO	IO + IO	IO + Antiangiogenic	P[1]
Overall population n=265	**142 (53.6)**	**5 (1.9)**	**1 (0.4)**	**71 (26.8)**	**39 (14.7)**	**6 (2.3)**	**1 (0.4)**	
Age groups n (%)								
≤75 years	118 (54.1)	3 (1.4)	1 (0.5)	53 (24.3)	37 (17.0)	5 (2.3)	1 (0.5)	0.0757
>75 years	24 (51.1)	2 (4.3)	0 (0.0)	18 (38.3)	2 (4.3)	1 (2.1)	0 (0.0)	
Gender n (%)								
Male	114 (55.9)	4 (2.0)	0 (0.0)	55 (27.0)	26 (12.7)	4 (2.0)	1 (0.5)	0.2666
Female	28 (45.9)	1 (1.6)	1 (1.6)	16 (26.2)	13 (21.3)	2 (3.3)	0 (0.0)	
Smoking history n (%)								
Current/former smoker	129 (54.7)	4 (1.7)	1 (0.4)	63 (26.7)	33 (14.0)	5 (2.1)	1 (0.4)	0.3780
Never smoked	10 (38.5)	1 (3.8)	0 (0.0)	8 (30.8)	6 (23.1)	1 (3.8)	0 (0.0)	
ECOG n (%)								
0-1	109 (52.2)	2 (1.0)	1 (0.5)	54 (25.8)	36 (17.2)	6 (2.9)	1 (0.5)	0.0590
≥2	33 (61.1)	3 (5.6)	0 (0.0)	15 (27.8)	3 (5.6)	0 (0.0)	0 (0.0)	
Histology n (%)								
Squamous	34 (68.0)	1 (2.0)	0 (0.0)	12 (24.0)	1 (2.0)	2 (4.0)	0 (0.0)	**0.0241**
Non squamous	108 (50.2)	4 (1.9)	1 (0.5)	59 (27.4)	38 (17.7)	4 (1.9)	1 (0.5)	
PD-L1 Expression n (%)								
<1%	73 (73.0)	4 (4.0)	0 (0.0)	1 (1.0)	21 (21.0)	0 (0.0)	1 (1.0)	**<0.0001**
1-49%	52 (74.3)	1 (1.4)	1 (1.4)	4 (5.7)	10 (14.3)	2 (2.9)	0 (0.0)	
≥50%	11 (12.9)	0 (0.0)	0 (0.0)	65 (76.5)	6 (7.1)	3 (3.5)	0 (0.0)	
Not evaluable	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)	
Brain Mets n (%)								
Yes	32 (54.2)	1 (1.7)	0 (0.0)	13 (22.0)	11 (18.6)	1 (1.7)	1 (1.7)	0.5466
No	110 (53.4)	4 (1.9)	1 (0.5)	58 (28.2)	28 (13.6)	5 (2.4)	0 (0.0)	
Liver Mets n (%)								
Yes	21 (56.8)	1 (2.7)	0 (0.0)	8 (21.6)	6 (16.2)	1 (2.7)	0 (0.0)	0.8425
No	121 (53.1)	4 (1.8)	1 (0.4)	63 (27.6)	33 (14.5)	5 (2.2)	1 (0.4)	
Comorbidities n (%)								
Yes	92 (58.2)	3 (1.9)	0 (0.0)	41 (25.9)	22 (13.9)	0 (0.0)	0 (0.0)	**0.0155**
No	50 (46.7)	2 (1.9)	1 (0.9)	30 (28.0)	17 (15.9)	6 (5.6)	1 (0.9)	

[1] Fisher's exact test (ƒ) in categorical variables

Characterization and description of the PD-L1 expression test performed

- PD-L1 test was performed in 287 pts (96.6%) **(Figure 2).** Most of the institutions performed PD-L1 testing in House (95.1%) and 4.9% of tests were done in a centralized laboratory. There were statistically significant differences in the time between PD-L1 testing request and testing results, depending on the institution that performed the PD-L1 test: median (P25; P75) of 5.00 (0.00 ; 12.00) days in-house vs 15.50 (5.50 ; 19.00) days in centralized laboratories (p=0.0079).
- The most frequently used assay was 22C3 pharmDx kit (54.7%) **(Figure 3).**

Figure 2. PD-L1 Expression (n=287)

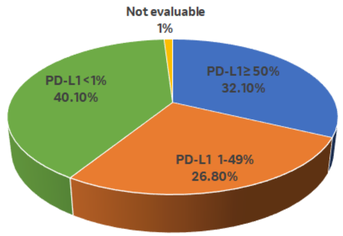
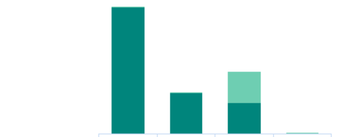


Figure 3. Assay used to test PD-L1 (n=287)



[1] LDT: Laboratory Developed Test

- There were no statistically significant differences in demographic and clinicopathological characteristics per PD-L1 status, except for the histological subtype **(Table 3).**

Table 3. PD-L1 expression by clinicopathological characteristics

	PD-L1 <1%	PD-L1 1-49%	PD-L1 ≥50%	P[1]
Total Patients n=287	**115 (40.1)**	**77 (26.8)**	**92 (32.1)**	
Gender n=284 *(%)*				
Male	89 (40.8)	61 (28)	68 (31.2)	0.7029
Female	26 (39.4)	16 (24.2)	24 (36.4)	
Age n=284 *(%)*				
≤75	93 (41.3)	63 (28)	69 (30.7)	0.4720
>75	22 (37.3)	14 (23.7)	23 (39)	
Smoking history n=284 *(%)*				
Never smoked	11 (39.3)	6 (21.4)	11 (39.3)	0.6989
Smoker	48 (42.1)	34 (29.8)	32 (28.1)	
Former smoker	54 (38.8)	36 (25.9)	49 (35.3)	
ECOG n=282 *(%)*				
0-1	78 (37.3)	59 (28.2)	72 (34.4)	0.1196
≥2	37 (50.7)	18 (24.7)	18 (24.7)	
Histology n=284 *(%)*				
Squamous	16 (31.4)	21 (41.2)	14 (27.5)	**0.0433**
Non-squamous	99 (42.5)	56 (24)	78 (33.5)	

[1] Chi-squared test.

Conclusions

- The implementation of PD-L1 testing is feasible in clinical practice and seems to guide treatment decisions with IO, according to the regulations in Spain.
- Most patients with stage IV NSCLC in Spain, who are referred to the medical oncology units, are subsidiary of active systemic treatment.
- Treatments decisions seem to be guided by histology results, the presence of comorbidities as well as PD-L1 expression.
- The selection of treatments is made according to those that were available in Spain in 2019. Systemic treatments availability varied during the study period.
- For almost all stage IV patients, the PD-L1 expression status is available prior to the treatment decision.
- PD-L1 testing is performed mainly in house and using clinically validated methods.
- PD-L1 percentages in this study are consistent with those previously reported in clinical trials and do not appear to be influenced by different clinicopathological characteristics except for histology.

References:

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