elcc European Lung Cancer Conference

38O: PD-L1 and PD-1 expression in molecularly selected non-small-cell lung cancer (NSCLC) patients

Armida D'Incecco[1], Mariacarla Andreozzi[2], Vienna Ludovini[3], Elisa Rossi[1], Lorenza Landi[1], Gabriele Minuti[1], Gabriella Fontanini[4], Lucio Crinò[3], Luigi Terracciano[2], and Federico Cappuzzo[1]

[1]Istituto Toscano Tumori, Oncologia Medica, Ospedale Civile, Livorno, Italy; [2]Department of Pathology, Basel Hospital University, Basel, Switzerland; [3]S.C. Oncologia Medica, Ospedale S. Maria della Misericordia, Perugia, Italy; [4]Azienda Ospedaliera Universitaria Pisana, Pisa, Italy

Disclosure

- **Armida D'Incecco**: nothing to disclose
- **All co-authors**: nothing to disclose

Background and Rationale

- PD-1 and its ligand, PD-L1, negatively regulate immune responses
- Recents studies indicate that PD-L1 expression on tumor cells leads to cancer progression and metastasis
- Expression of PD-L1 has been correlated with poor clinical outcomes in a number of human cancers, including NSCLC
- PD-L1 expression may correlate with response to treatment with PD-1 inhibitors
- Aim of the present study was to assess whether PD-1 and PD-L1 were differently expressed in NSCLC patients according to presence or absence of *EGFR* mutations, *KRAS* mutations or *ALK* translocations

Patient selection

- This retrospective study was conducted in a cohort of 125 NSCLC patients, fully characterized for *EGFR* mutations, *KRAS* mutations and *ALK* translocations
- *EGFR* mutations and *KRAS* mutations were evaluated using Polymerase Chain Reaction (PCR) and direct sequencing. Presence of *ALK* translocations was detected using fluorescence *in situ* hybridization (FISH)
- Main inclusion criteria included: availability of additional tumor tissue from the same tumor sample previously used for *EGFR*, *KRAS* and *ALK* assessment; full clinical data including previous therapies and survival

Methods

- PD-L1 and PD-1 expression were assessed by immunohistochemistry (IHC) with primary antibodies PD-L1 (CD274) ab58810 (Abcam) and PD-1 760-4448 (Ventana). Staining intensity was scored considering 0 as negative or trace, 1 as weak, 2 as moderate and 3 as strong. All cases with staining intensity ≥ 2 in more than 5% of tumor cells were considered positive
- A semi-quantitative approach was used to generate a score for each tissue core. The percentage of stained cells (0% to 100%) was multiplied by the dominant intensity pattern of staining ranging from 0 to 3. Therefore, the overall semiquantitative score ranged from 0 to 300

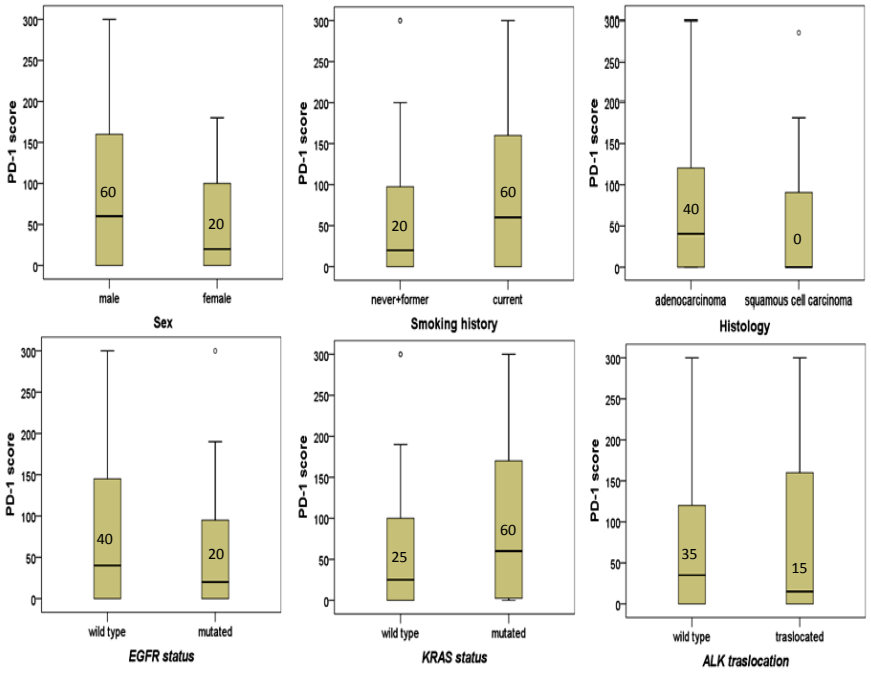
Patients characteristics

Characteristic	Total (N)	%
Total number of patients	125**	100
Median age (years - range)	64	41-84
Gender		
Male/Female	67/58	53.6/46.4
Histology		
Adenocarcinoma/Squamous-cell carcinoma/Other*	83/23/19	66.4/18.4/15.2
Smoking history		
Never/Former/Current/ Unknown	37/58/17/13	29.6/46.4/13.6/10.4
EGFR status		
Mutated#/ Wild type	56/69	44.8/55.2
KRAS status		
Mutated^/ Wild type	29/96	23.2/76.8
ALK status		
Translocated/ Wild type	10/115	8.0/92.0
Triple negative	30	24.0

*Other histologies included: large cell=4 (3.2%), NAS=3 (2.4%), mixed histology= 2 (1.6%), unknown= 10 (8.0%)
#EGFR mutations included: exon 18= 3 (2.4%); exon 19= 30 (24.0%); exon 20= 4 (3.2%); exon 21= 14 (11.2%); other= 5 (4.0%)
^KRAS mutations included: codon 12= 26 (20.8%); codon 13= 2 (1.6%); other= 1 (0.8%)
****99 cases was treated with EGFR-TKIs, including gefitinib (N=30, 30.3%) or erlotinib (N=69, 69.7%)**

PD-1 results

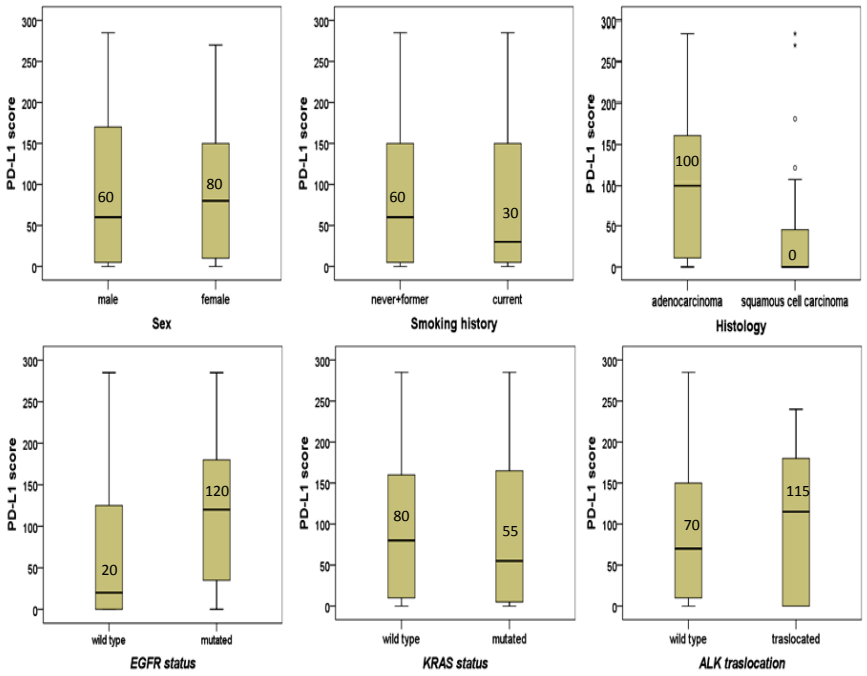
	PD-1 (N/%)
	122/100
Positive	43/35.2
Negative	79/64.8



Characteristic	PD-1+ (N/%)	PD-1 – (N/%)	p-value
Male	24/55.8	41/51.9	0.68
Female	19/44.2	38/48.1	
Never/Former smokers	27/73.0	65/90.3	**0.02**
Current smokers	10/27.0	7/9.7	
Adenocarcinoma	29/85.3	52/75.4	0.25
Squamous cell carcinoma	5/14.7	17/24.6	
***EGFR* mutated**	17/39.5	38/48.1	0.36
***EGFR* wild type**	26/60.5	41/51.9	
***KRAS* mutated**	16/37.2	12/15.2	**0.006**
***KRAS* wild type**	27/62.8	67/84.8	
***ALK* translocated**	3/7.0	7/8.9	1.00
***ALK* wild type**	40/93.0	72/91.1	

PD-L1 results

	PD-L1 (N/%)
	123/100
Positive	68/55.3
Negative	55/44.7

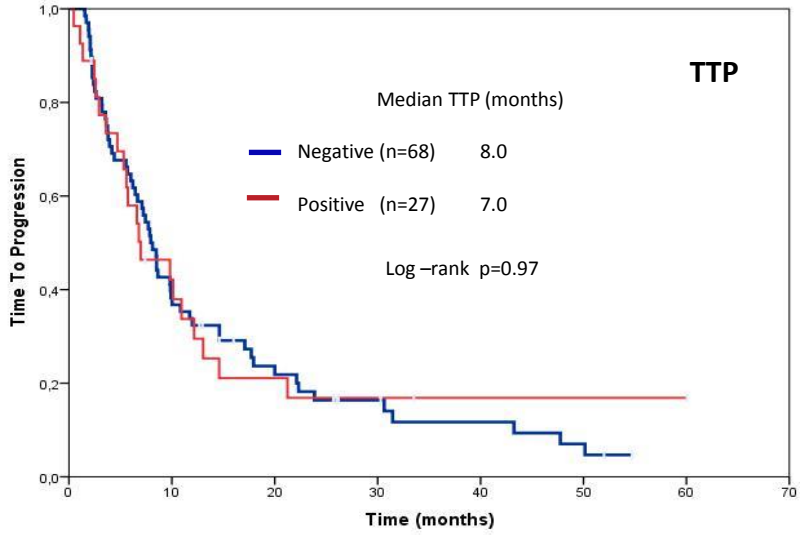


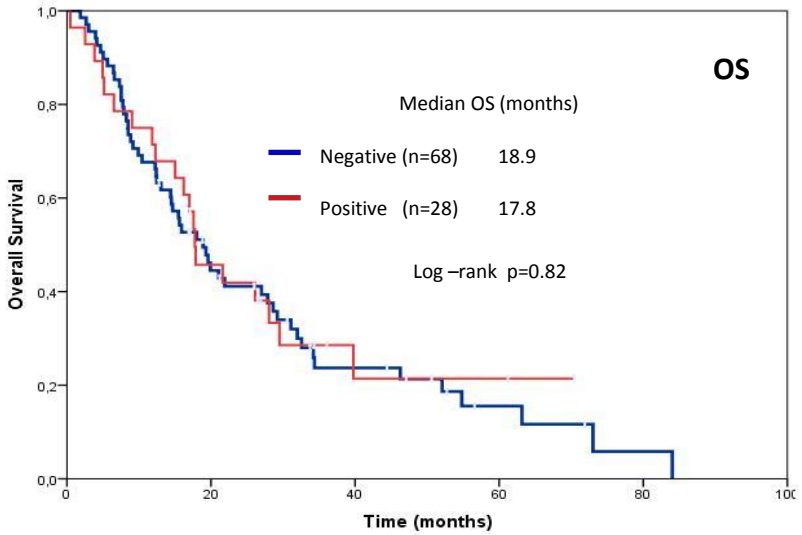
Characteristic	PD-L1+ (N/%)	PD-L1 – (N/%)	p-value
Male	36/52.9	30/54.5	0.86
Female	32/47.1	25/45.5	
Never/Former smokers	53/86.9	41/82.0	0.48
Current smokers	8/13.1	9/18.0	
Adenocarcinoma	52/88.1	30/65.2	**0.005**
Squamous cell carcinoma	7/11.9	16/34.8	
***EGFR* mutated**	40/58.8	16/29.1	**0.001**
***EGFR* wild type**	28/41.2	39/70.9	
***KRAS* mutated**	15/22.1	13/23.6	0.84
***KRAS* wild type**	53/77.9	42/76.4	
***ALK* translocated**	6/8.8	4/7.3	1.00
***ALK* wild type**	62/91.2	51/92.7	

PD-1 expression and outcome in patients treated with EGFR-TKIs

PD-1	Total (N)	%
	96	100
Positive	28	29.2
Negative	68	70.8

Total evaluable for response : N= 93	CR+PR	SD+PD	p-value
PD-1 positive (N=26)	46.2% (N=12)	53.8% (N=14)	0.70
PD-1 negative (N=67)	50.7% (N=34)	49.3% (N=33)	

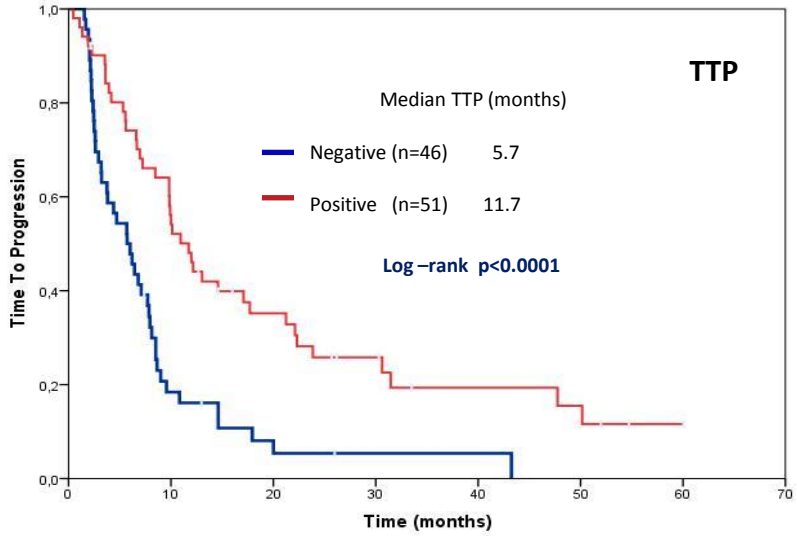


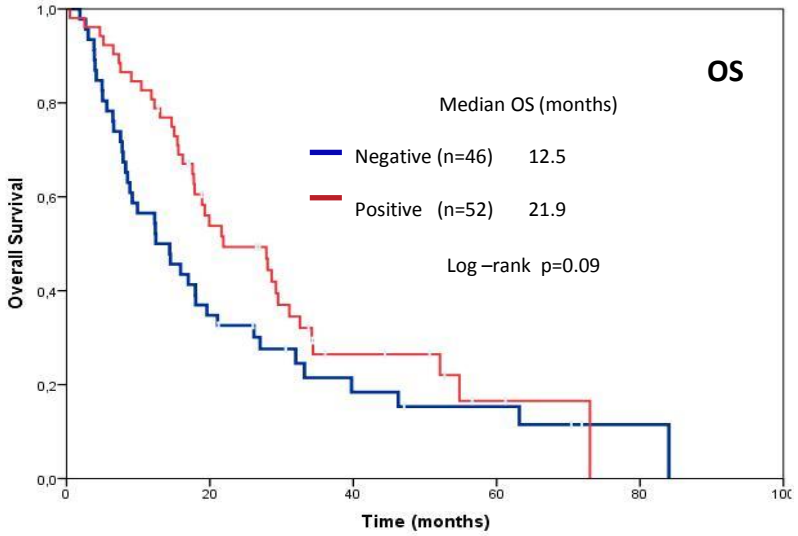


PD-L1 expression and outcome in patients treated with EGFR-TKIs

PD-L1	Total (N)	%
	98	100
Positive	52	53.1
Negative	46	46.9

Total evaluable for response : N= 95	CR+PR	SD+PD	p-value
PD-L1 positive (N=49)	**61.2%** (N=30)	38.8% (N=19)	**0.01**
PD-L1 negative (N=46)	34.8% (N=16)	65.2% (N=30)	

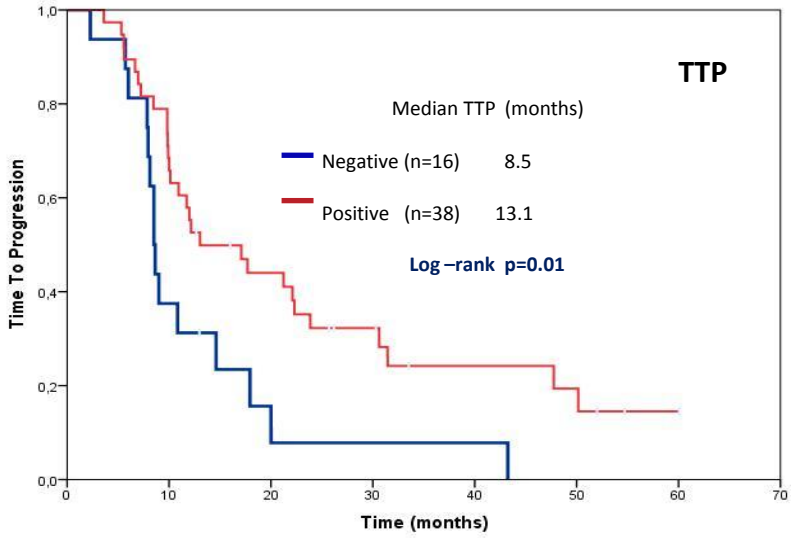


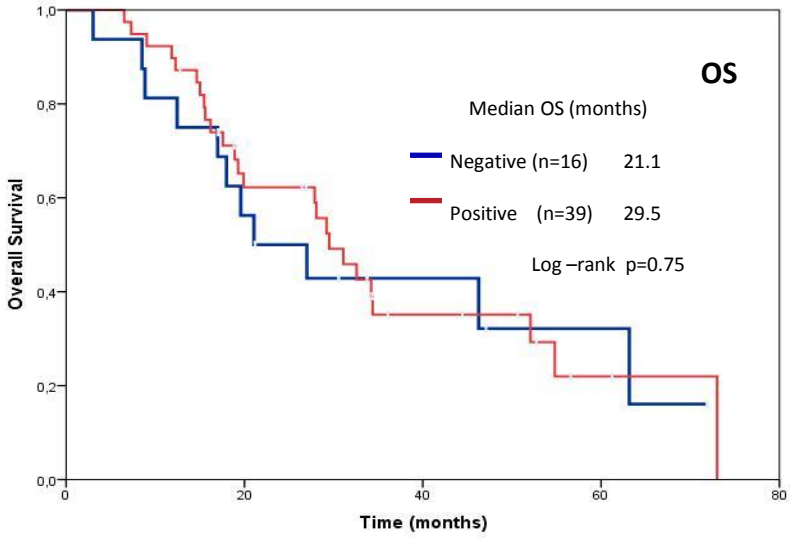


PD-L1 expression and outcome in *EGFR* mutated patients treated with EGFR-TKIs

PD-L1	Total (N)	%
	55	100
Positive	39	70.9
Negative	16	29.1

Total evaluable for response : N= 54	CR+PR	SD+PD	p-value
PD-L1 positive (N=38)	76.3% (N=29)	23.7% (N=9)	1.00
PD-L1 negative (N=16)	75.0% (N=12)	25.0% (N=4)	





Conclusions

- PD-1 and PD-L1 expression differs according to clinical and biological characteristics:

  - PD-1 positive patients are generally male, smokers, with adenocarcinoma histology, *KRAS* mutated

  - PD-L1 positive patients are generally female, never/former smokers, with adenocarcinoma histology, *EGFR* mutated or *ALK* translocated

- Our data and other data strongly support a combination of specific checkpoint inhibitors with targeted therapies

elcc European Lung Cancer Conference

Participating Centers

- **Istituto Toscano Tumori, Dipartimento di Oncologia, Ospedale Civile, Livorno, Italy**

  Federico Cappuzzo, Lorenza Landi, Jessica Salvini, Armida D'Incecco, Gabriele Minuti, Erika Coppi, Elisa Rossi, Carmelo Tibaldi, Roberto Mario Incensati, Maria Elena Filice, Spartaco Sani

- **Department of Pathology, Basel Hospital University, Basel, Switzerland**

  Luigi Terracciano

  Mariacarla Andreozzi

- **S.C. Oncologia Medica, Ospedale S. Maria della Misericordia, Perugia, Italy**

  Lucio Crinò

  Vienna Ludovini

- **Azienda Ospedaliera Universitaria Pisana, Pisa, Italy**

  Gabriella Fontanini

  Antonio Chella

  Alessandra Capodanno

Supported by: Italian Association for Cancer Research (AIRC) and Istituto Tumori Toscano (ITT)