Increase efficacy of immune checkpoint inhibitors in advanced Non-Small Cell Lung Cancer related to singular immune-related adverse events

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BACKGROUND

Several studies have shown that irAEs are associated with the efficacy of ICIs in different cancers including NSCLC, and it could affect any system organ class (SOC). The goal of this study is to evaluate the prognostic significance of individual SOC IrAEs and effectiveness of PD-1/PD-L1 inhibitors in real-world data of NSCLC patients.

METHODS

This was a retrospective study of the clinical data of patients with NSCLC treated with PD-1/PD-L1 inhibitors as 1a or 2a lines from Marzo 2015 to Marzo 2022 in a single institution. We evaluated association of singular SOC irAEs with efficacy, response and overall survival (Kaplan-Meier and Cox proportional hazard analyses were performed).

RESULTS

A total of 510 patients were included in this analysis. Any grade IrAEs were seen in 321 (63%) patients, are summarized in Table 1. After a median 4-year follow up for patients assessed to efficacy, objective response rate (ORR) to ICIs was higher in patients with irAEs [46% vs 14%] p=0,0001,fig1. In fact, the presence of any irAEs had a significantly improved median OS compared to those without irAEs (19.8vs 6.4 months p = 0.0001) grouped and separated by degree of irAEs (figure 6). Singular SOC toxicities (fig2-5) with OS >30 months were endocrine G1-3, rheumatic G1, cutaneous G2 and hepatitis G3-4; point out toxicities with deleterious effects such as renal G3, rheuma G3 and pneumonitis G4, table 1. We also analyze the influence of different toxicities in the same case. Patients who present more than 1 SOC of toxicity progressively increase the benefit, fig7 (OS in 1SOC 13 m, 2 SOC 23 m, 3 SOC 24 m and 4 SOC 49 m p< 0.0001). Multivariable analysis, including PStatus, PDL1 expresion and IrAEs toxicity demonstrated that the development any irAEs was related to a significantly improved OS (HR 0.44, 95% 0.36-0.54, p = 0.0001); if G3 IrAEs (HR 0.39, 95% 0.29-0.52). Finally, the presence of more than one singular SOC IrAEs; 4 soc (HR: 0.20, 95% 0.10-0.39; p = 0.0001) and 3 SOC (HR 0.33, 95% 0.23-0.46; p = 0.0001) are significantly associated with the greatest benefit of ICIs.

	TYPE OF IrAEs			CUTANEOUS			COLITIS			PNEUMONITIS			HEPATITIS			RHEUMATIC			ENDOCRINE			RENAL			NEUROLOGICAL		
	N	%	OS (95%)	N	%	OS (95%)	N	%	OS (95%)	N	%	OS (95%)	N	%	OS (95%)	N	%	OS (95%)	N	%	OS (95%)	N	%	OS (95%)	N	%	OS (95%)
	321	62.9	19.8 (1.2)	138	27.1	28.3 (3.9)	93	18.2	21.4 (2.7)	91	17.8	16.5(1.8)	84	16.5	20.0(3.7)	82	16.1	25.7 (6.5)	66	12.9	31.6 (7.1)	44	8.6	19.0 (3.4)	15	0.9	21.0 (4.7)
IrAE GRADE 1	134	26.3	18.7 (1.9)	96	18.8	29.0 (3.5)	54	10.6	21.4 (6.3)	29	5.7	18.3 (1.7)	40	9.0	18.0 (2.2)	49	9.6	34.1 (7.0)	43	8.4	37.8 (7.7)	19	3.7	21.4 (6.7)	8	1.6	12.2 (8.1)
IrAE GRADE 2	117	22.9	20.1 (2.2)	30	5.9	31.1 (10.7)	30	5.9	21.4 (3.9)	45	8.8	15.3 (2.6)	18	3.5	20.0 (5.2)	30	5.9	20.1 (4.1)	20	3.9	23.8 (5.1)	16	3.1	28.2 (0.8)	3	0.6	21.0 (4.3)
IrAE GRADE 3	63	12.4	20.6 (2.9)	12	18.8	15.0 (2.3)	9	1.8	13.0 (5.3)	15	2.9	23.7 (14.2)	15	2.9	30.0 (11.1)	3	0.6	5.2 (1.1)	3	0.6	42.0 (--)	7	1.4	9.8 (2.1)	3	0.6	45.8 (--)
IrAE GRADE 4	7	1.4	33.5 (16.8)	—	—	— —	—	—	— —	2	0.4	2.9 (---)	5	1.0	33.5 (22.4)	—	—	— —	—	—	— —	—	—	— —	1	0.2	20.6 (--)
Non IrAE	189	37.1	6.4 (0.8) (pvalue=0.0001)	372	72.9	9.2 (0.8) (pvalue=0.0001)	417	81.8	12.4 (1.2) (pvalue=0.026)	419	82.2	12.8 (1.2) (pvalue=0.425)	426	83.5	12.3 (1.2) (pvalue=0.196)	428	83.9	11.5 (1.0) (pvalue=0.0001)	444	83.9	12.0 (1.0) (pvalue=0.0001)	426	83.5	13.5 (1.1) (pvalue=0.078)	495	99.1	13.1 (1.2) (pvalue=0,836)

Table 1: Descriptive of frequency, percentage and overall survival univariate analysis of each type of toxicity by columns; regarding the severity of the toxicity G1-4 grouped and separated vs non IrAEs.

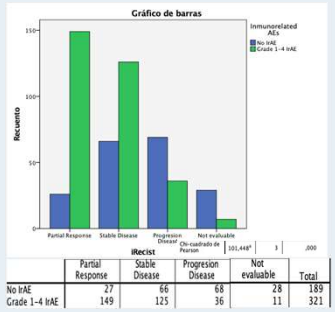

Fig1.iRECIST and correlation with IrAE.

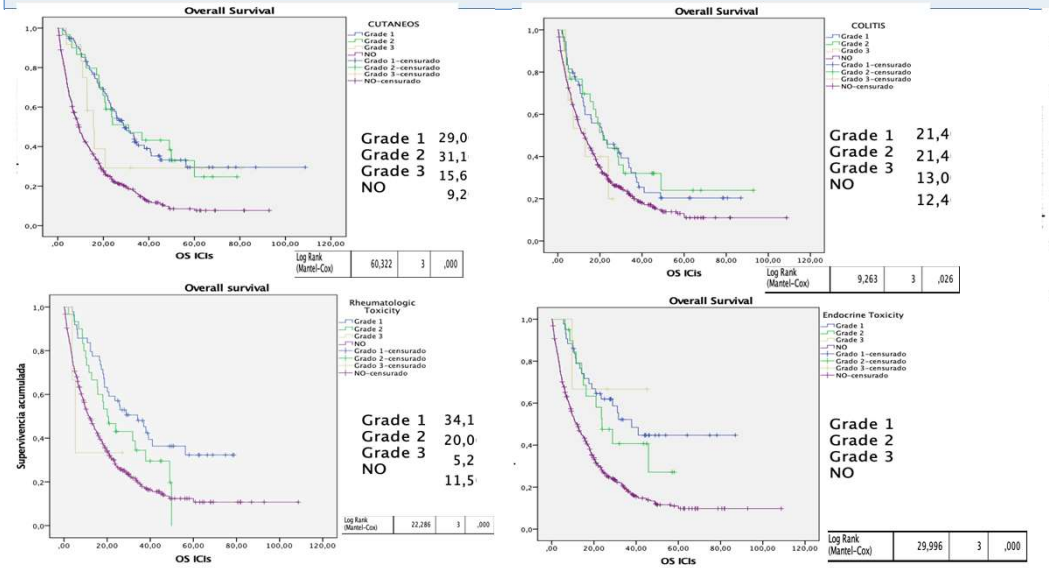

Fig.2-5 – Kaplan-Meier curves according to the type of IrAE with significant univariate analysis for overall survival.

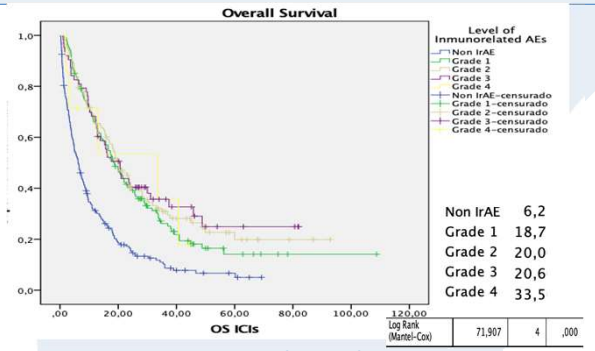

Figure 6 : Kaplan Meier curve for OS of patients treated with ICIs according the severity G1-4 of any IrAE.

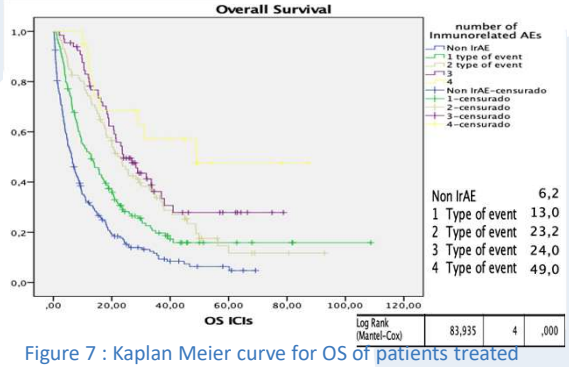

Figure 7 : Kaplan Meier curve for OS of patients treated with ICIs according the number SOC of any IrAE.

CONCLUSIONS

This study confirms that irAEs could be used as a potential marker of ICIs in NSCLC. The development of singular SOC irAEs may better predict treatment efficacy.