IMPACT OF STEROIDS INDICATION ON THE OUTCOMES OF IMMUNOTHERAPY IN A MULTI-TUMOR COHORT: TIME AND DOSE-DEPENDENT EVALUATION

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BACKGROUND

- ✓ The detrimental impact of **steroids** (ST) on the efficacy of **immune checkpoint inhibitors** (ICI) has been described in several studies.
- ✓ However, the influence of indication, time of administration and dosage is more controversial.

METHODS

- ✓ This is a retrospective study of **patients** with **advanced solid tumors** treated with **ICI in monotherapy** (2015-2022). Data regarding baseline characteristics and outcomes were collected.
- ✓ For each patient, the **indication for ST** and the **daily ST dose** (in mg/kg of prednisone) were registered until progression or death.
- ✓ Patients were divided into **quartiles** (Q) based on the cumulative dose (CD) of ST received within 30 days after the first cycle (C1) (**D1-30**), 90 days after C1 (**D1-90**) and after 6 months from C1 in long-responders (**>6m**).
- ✓ The impact of ST dose and indication on the objective response rate (**ORR**) and progression-free survival (**PFS**) was analyzed.

RESULTS

Clinical characteristics

- ✓ **475 patients** were evaluated (median age: 67.5). **ECOG PS** prior to C1 was: 0 (31%), 1 (53.6%), ≥2 (15.4%). 33.5% had ≥3 metastatic locations (15.6% in CNS, 25.3% in liver, 45.6% in lung).
- ✓ The most frequent **tumor subtypes** were NSCLC (34%), urothelial (17%), renal (14%), melanoma (11%) and HNSCC (11%) (*fig 1A*).
- ✓ Most patients received **anti-PD1** monotherapy (64.4%), followed by **anti-PDL1** (20.4%) and **anti-PD1/CTLA4** (13.3%) (*fig 1B*). 42.1% received ICI in **1st line** (43.1% in 2nd line, 14.8% in further lines).
- ✓ **49.5%** of patients **received ST** during ICI treatment (**20.6%** for **irAEs**, **33.9%** for **other indications**). The proportion exposed to ST for irAE was 5.7% in D1-30, 10.7% in D1-90, and 12% >6m (*fig 1C*).

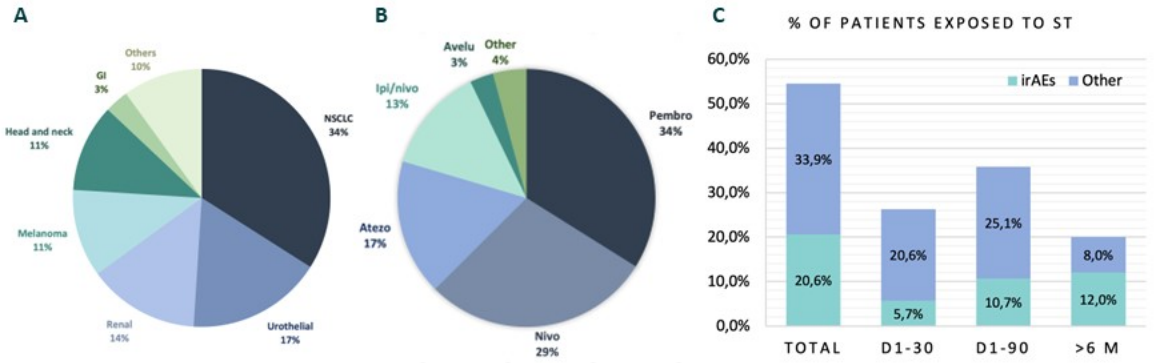

***Figure 1**. Clinical characteristics regarding tumor subtypes (**A**), ICI distribution (**B**) and exposure to steroids depending on clinical indication –immune-related adverse events (irAEs) vs. other– within D1-30, D1-90 and >6m (**C**).*

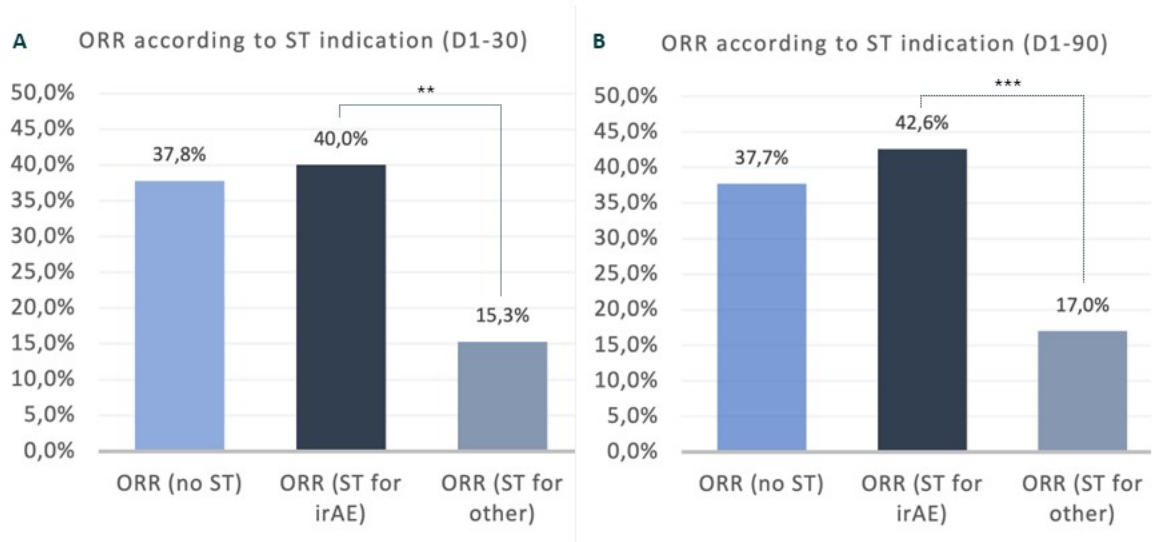

***Figure 2**. Impact of steroids indication on the objective response rate (ORR) in D1-30 (**A**) and D1-90 (**B**). **p<0.05; ***p<0.01.*

RESULTS

Impact of ST indication

- ✓ The **ORR** was **significantly higher** among patients exposed to **ST for irAEs** (vs. other indications), both in D1-30 (40% vs. 15.3%; *p*=0.028) (*fig 2A*) and in D1-90 (42.6% vs. 17%; *p*=0.001) (*fig 2B*).
- ✓ There were not significant differences in the ORR among patients exposed to ST for irAEs and not exposed to ST during ICI treatment.

Impact of ST cumulative dose and time of exposure

- ✓ There was an **inverse correlation** between the **CD of ST** and the **ORR** in D1-30: 37.8% (no ST), 29.6% (Q1), 21.4% (Q2), 11.1% (Q3) and 22.2% (Q4) (*p*<0.05).
- ✓ However, this association was **not observed** among those **exposed to ST for irAEs** in D1-30: 37.8% (no ST), 100% (Q1), 0% (Q2), 33.3% (Q3) and 42.9% (Q4) (p=0.21). Similar results were obtained for D1-90.
- ✓ Among long-responders (>6m), PFS tended to be longer among those exposed to ST, and was similar regardless the indication for ST use.

CONCLUSIONS

- ✓ **Exposure to ST** is correlated with **poorer response rates** in patients treated with immunotherapy.
- ✓ Our study shows that the **impact of ST** is **time and dose-dependent** (only observed within 90 days after C1, and inversely correlated to the cumulative doses).
- ✓ Interestingly, this effect was **not observed** among patients receiving **ST for irAEs**, suggesting that immune-related toxicity may attenuate the detrimental impact of ST in patients treated with ICI.