

CLINICAL PREDICTORS OF LONG-TERM RESPONSES TO IMMUNE CHECKPOINT INHIBITORS IN A MULTI-TUMOR COHORT

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BACKGROUND

- ✓ **Long-term responses** to immune checkpoint inhibitors (ICI) can be observed in various **solid tumors**, even in pre-treated patients with advanced disease.
- ✓ While extensive research has been conducted to identify molecular **biomarkers**, additional efforts are needed to **optimize patient selection** in our clinical practice.

METHODS

- ✓ Real-world study of patients treated with ICI at a tertiary hospital (2015-2022). Patients with **progression-free survival (PFS) >24 months (m)** were selected.
- ✓ Baseline **clinical features**, exposure to **steroids (ST)**, ICI treatment characteristics, and immune-related adverse events (irAEs) were analyzed.

RESULTS

Clinical characteristics of the cohort

- ✓ **475 patients** (66.7% males) were evaluated (median age: 67.5). Distribution of **tumor subtypes**: NSCLC (34.5%), urothelial (17.3%), renal (13.7%), melanoma (11.2%), HNSCC (10.7%), others (12.6%, mainly GI and gynecologic).
- ✓ Most patients (84.8%) received **anti-PD1/anti-PDL1**, followed by **anti-PD1+anti-CTLA4** (13.3%), and **anti-CTLA** (1.9%) (42.1% 1st line, 43.2% 2nd line, 14.7% further lines).
- ✓ **71 patients** (14.9%) had a **PFS >24m**, most of them (69%) having discontinued ICI (26.5% due to irAEs) after a median follow-up of 42.9 months.
- ✓ **Median duration of ICI treatment** in this subgroup was **21.3 months**. Only 15 patients (**21.4%**) developed **progressive disease** after 24 months.



Figure 1. Characteristics of the cohort and comparison between patients with PFS>24m and PFS<24m: baseline ECOG (A), disease burden (B), type of ICI (C), treatment line (D), best radiological response (E), moment of exposure to ST (F), ST indication (G), and incidence of irAEs (H).

RESULTS

Clinical features of long-term responders (PFS>24m)

- ✓ Among patients with **PFS>24m**, there was a higher proportion of **baseline PS=0** (53.5% vs 27%, $p<0.01$), and **exclusive lymph node metastases** (22.5% vs 12.9%, $p=0.03$), contrary to liver (18.3% vs 26.5%) and bone metastases (21.1% vs 29.1%).
- ✓ ICI were more frequently administered in the **1st line setting** among patients with PFS>24m (54.9% vs 39.9%, $p=0.017$).
- ✓ Best radiological response for patients with PFS>24m (vs those with PFS<24m) were: **CR** (33.8% vs 1.2%), **PR** (53.5% vs 22.5%), and **SD** (11.3% vs 14.4%) ($p<0.01$).
- ✓ The prevalence of previous **autoimmune disorders** tended to be higher in long-term responders (9.9% vs 5.9%, $p=0.22$).

Immune-related toxicity and exposure to steroids

- ✓ Patients with PFS>24m had a significantly **higher incidence of irAEs** (54.9% vs 29.5%, $p<0.0001$).
- ✓ **Late exposure to ST** (after 6 m from ICI initiation) prevailed in patients with PFS>24m (54.9% vs 35%, $p<0.01$), and this group was more exposed to **ST for irAEs** (38% vs 17.6%).
- ✓ On the contrary, the **early use of ST** was **less frequent** in patients with PFS>24m, both within 30 days (11.3% vs 26.5%, $p<0.01$) and 3 m (16.9% vs 35.4%, $p<0.01$) after ICI initiation.

CONCLUSIONS

- ✓ Our results from a multi-tumor cohort suggest that **baseline PS=0**, the use of ICI in the **1st line**, **exclusive lymph node disease**, **CR/PR** as best response, and occurrence of **irAEs** are significantly correlated with **long-term responses (PFS>24m)**.
- ✓ The **early use of ST (<3m)** is **negatively associated** with **PFS>24m**, unlike the late use (>6m) of ST and the exposure to ST for the management of immune-related toxicity.