Prognostic value of Thyroid Transcription Factor-1 expression in lung adenocarcinoma in patients treated with anti PD-1/PD-L1.

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BACKGROUND

Anti-PD1/PD-L1-directed immune checkpoint inhibitors (ICI) are game changers in advanced non-small-cell lung cancer (NSCLC) [1], but biomarkers are lacking. The aim of our study was to find clinically relevant biomarkers of the efficacy of ICI in non-squamous NSCLC.

METHODS

We conducted a retrospective study of patients receiving ICI for advanced non-squamous NSCLC in two cohorts (Dijon and Caen, France). For a subset of patients, RNAseq data were generated on tumor biopsy taken before ICI. The primary end point was progression-free survival (PFS) under ICI. Secondary end point was overall survival (OS) from ICI initiation.

RESULTS

In Dijon cohort, we studied 231 patients. Clinico-pathological characteristics included KRAS mutant status (n=88), TTF1-positive expression (n=136), LIPI (Lung Immune Prognostic Index) score of 0 (n=116) [2] . In our cohort, lack of TTF1 expression, LIPI score >0, line of treatment >1, and liver metastases were associated with poorer PFS. TTF1 (or LIPI score), KRAS status and PD-L1 status could be combined in a composite score that could be used to stratify survival (PFS or OS) and improve the AUC (Area Under the Curve) for prediction of prognosis in comparison with the only PD-L1 gold standard (Figure A-D) [3]. Using an external cohort (Caen) of 154 patients, we confirmed the independent prognostic role of TTF1.

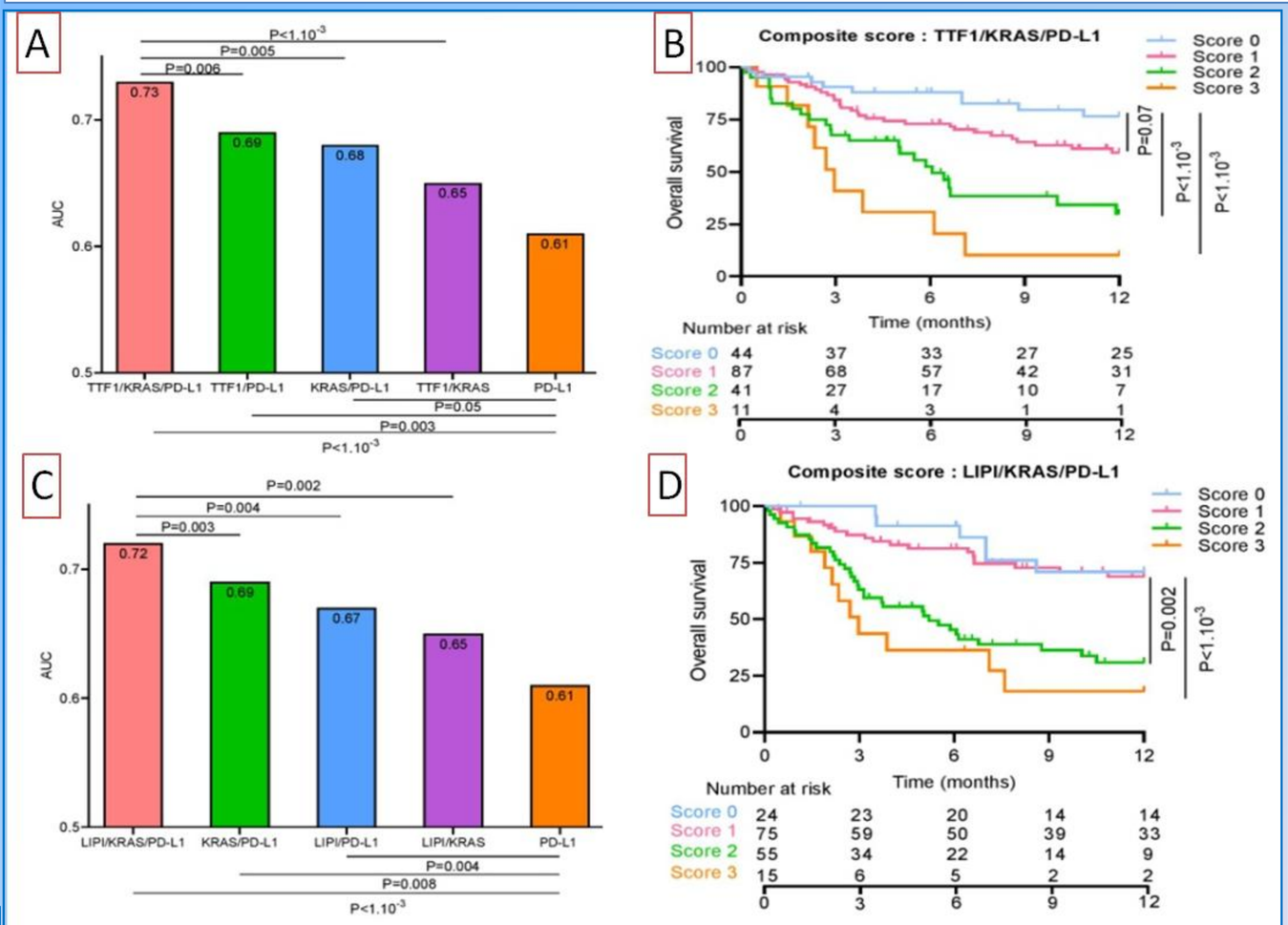

Fig A-D : **Association between overall survival, and TTF1 (or LIPI), KRAS, and PD-L1 status.**
4 groups, classified by a score ranging from 0 to 3, where scores were computed as the sum of each the 3 variables: variables were scored 1 in case of KRAS mutated status, absence of TTF1 (or LIPI score ≥1) and absence of PD-L1 positive tumor cells.

CONCLUSIONS

TTF1 expression and PD-L1 could be used to stratify risk and predict PFS and OS in patients treated with ICI for non squamous-NSCLC.

PARIS 2021 ESMO congress

Presentation number : 78P

AKNOWLEDGEMENT

We thank Caen hospital and Anne-Laure Lepage for the external cohort.

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Author contact : fghiringhelli@cgfl.fr - ePoster presented at the Virtual 2021 ESMO congress, 16-21 September 2021 - This research received no external funding - No author has any conflicting financial interest to declare.