The tumor inflammation signature is predictive of anti-PD1 treatment benefit in the CERTIM pan-cancer cohort

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OBJECTIVES
Robust biomarkers predicting immune checkpoint inhibitor (ICI) sensitivity are needed for current management of patients. One such biomarker, the Tumor Inflammation Signature (TIS), is an 18 gene signature that measures the presence of a preexisting suppressed immune response within the tumor. It was developed as a predictor for response to the anti-PD1 therapy pembrolizumab (1).

Validation of the 18-gene Tumor Inflammation Signature (TIS) in FFPE tumor samples, in a real-life cohort of patients with various tumor types, including a majority of NSCLC (Non-Small Cell Lung Carcinoma), treated with anti-PD1 in routine clinical care.

RESULTS 1 - all tumors

• Patients: Consecutive various metastatic cancer treated with anti-PD1 in the CERTIM (2.3.4)
• CERTIM is a collaborative French network of physician involved in oncology and research and located in Cochin Hospital (Paris, France)
• Materials: FFPE tumor blocks from surgical resection and small biopsies
• Methods: RNA extraction with High Pure FFPE RNA isolation Kit (Roche). 25-100 ng RNA hybridized to a pilot version of the NanoString® PanCancer Immuno-oncology 360 Panel (beta version)*

Statistics: logistic regression model, LogRank tests and Cox model to assess the association between individual gene expression (GE), TIS and other GE signatures with outcome (response to therapy and overall survival).

RESULTS 2 - NSCLC

In the NSCLC cohort, clinical response (PR or CR versus SD or progression) was significantly associated with TIS score [OR=1.96, 95%CI(1.18, 3.25), p=0.042]

In the whole cohort, clinical response (PR or CR versus SD or progression) was significantly associated with TIS score [OR=1.66, 95%CI(1.13, 1.41), p=0.012]

Overall response rate is significantly associated with specific signatures: TIS, IFNγ, IDO1, PD-L2.

Overall survival is associated with high TIS expression (first tertile)

CONCLUSIONS

• Tumor Inflammation Signature (TIS) predict clinical benefit (ORR, OS) for patients treated with immune checkpoint inhibitors (anti-PD1)
• TIS may be used in routine samples (FFPE and small biopsies)
• NanoString PanCancer Immuno-oncology 360 Panel, including TIS, allows identification of key processes involved in anti-tumor immune response and immune evasion.

REFERENCES