INDOLEAMINE 2,3 DIOXYGENASE EXPRESSION PREDICTS RESPONSE TO IMMUNE CHECKPOINT BLOCKERS IN ADVANCED NON-SMALL CELL LUNG CANCER

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Background In the era of immuno-oncology, it’s now crucial to identify primary resistance mechanisms to Immune Checkpoint Blockers (ICB) in order to (i) delineate novel pathways that can be targeted to improve current rate of response and to (ii) identify predictive biomarkers to select patients who might benefit from ICB. The Indoleamine 2,3 dioxygenase (Ido) – a tryptophan degrading enzyme – has been well described to exert immunosuppressive functions and is considered as a therapeutic target to improve ICB benefit. However, despite important drug development efforts, little is known about Ido expression and its association with clinical response to ICB.

Methods We analyzed through a digital pathology approach the tumor samples obtained at immunotherapy onset from 55 patients (pts) with stage III/IV NSCLC enrolled in an institutional molecular profiling program (BIP: NCT02534649, sponsor: Institut Bergonié, Bordeaux, France). A multiplexed immunohistofluorescence panel consisting of the following markers PDL1, IDO1, CD8 and PanCK was developed, validated, and applied on each available tissue sample. Images were captured through slide digitization (PhenoImager HT, Akoya Biosciences) and analyzed for correlation with clinical outcome (Progression Free Survival and Overall Survival).

Results High PDL1 expression was correlated with a better PFS (19.60 months vs 4 months, p=0.018) and OS (not reached vs 21.2 months, p=0.017) than PDL1low pts. This study confirmed that pts with a higher abundance of CD8 within the stroma were more responsive to ICB than pts with a lower CD8 infiltration level. Strikingly, high levels of IDO1 expression within the tumor region – as defined through PanCK staining – was associated with a better PFS (not reached vs 4.40 months, p=0.039). Additional image analysis is currently ongoing for the evaluation of the association between the spatial distribution of PDL1+, IDO1+ and CD8 + cells and clinical outcome.

Conclusions Our results indicate that high IDO1 expression in the tumor compartment is associated with improved outcome in patients with advanced NSCLC. Inhibiting IDO may not be a relevant approach to improve ICB efficacy in NSCLC.