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Low immune signatures may define response to vinflunine in urothelial cancer.

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Background:

Urothelial cancer (UC) is still a major cause of morbidity and mortality worldwide, causing approximately 165,000 deaths per year. There have been a significant progress in understanding the omnics of UC, few has been translated into molecularly-based biomarker. We hypothesized that immune signatures might identify response to vinflunine in UC and eventually select treatment for either chemotherapy or immunotherapy.

Objective:

The main objective of the present study was to identify a molecular biomarker associated to vinflunine response in UC patients.

Methods:

Patients selected were included if they had either responded or rapidly progressed on vinflunine. We defined response as either partial response, or stable disease for at least 6 months. Non-responders were patients showing progressive disease within the first 3 months of therapy without toxicity leading to treatment discontinuation. FFPE tissue was assessed for availability of material for RNA purification. Hematoxylin and eosin stained slides was reviewed by an expert pathologist and tumor areas containing at least 50% of tumor cells were selected for RNA extraction. Nanostring platform, PanCancer Immune Profiling Panel C2929 was used to perform multiplex gene expression analysis of 770 genes.

Results:

The cohort included 22 UC patients progressed to platinum-based chemotherapy. Thirteen patients were responders and 9 patients were non-responders. Unsupervised hierarchical clustering correctly separated responders from non-responders. There was a differential expression of genes related to regulation, T cell function and pathogen defense. Responders to vinflunine had low T cell function signature and non-responders had higher pathogen defense and regulation signature. Non-responders to vinflunine had high levels of IDO-1, SOCS1 and MAGE. Non-responders had high levels of TILs while responders had high levels of Tregs and exhausted CD8 cells. Expression of MAGE A antigens associated to response to treatment was also assayed by IHC on tumor section to evaluate antigen expression on tumor and stromal areas.

Conclusions:

Nanostring analysis of extreme phenotypes is feasible to assess immune signatures in UC and may eventually help to select treatment choice in clinical practice. Further validation analyses in complementary databases are ongoing.

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