516 CLINICAL TIER GRADING OF CANCER STEM CELLS ACCORDING TO CLINICAL CHARACTERISTICS FOR IMMUNE CHECKPOINT INHIBITORS GUIDED BY MRNA STEMNESS INDEX

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Background Cancer stems cells are cells in tumors that have self-renewing capabilities and proliferation, and are partly responsible for tumor growth, metastasis and drug resistance, and have been associated with multidrug resistance and epithelial-mesenchymal transition. Recent studies have shown that cancer stemness is capable of being targeted by immunotherapies.[1]

mRNAsi, or mRNA stemness index, is a tool that has been developed to analyze prognostic significance for immunotherapy response for cancer stemness in lung adenocarcinoma, adrenocortical carcinoma and gastric cancer, among other carcinomas[2,3,4] This abstract proposes to apply the prognostic signatures as determined by mRNAsi to create a clinical tier grading system that categorizes cancer stemness presenting characteristics based on studies by for ICI (nivolumab, (anti-PD-1) ipilumumab (anti-CTLA-4), pembrolizumab (anti-PD-L1), atezolizumab (anti-PD-L1)) treatment. [5]

Methods A literature search will be conducted using the keywords "cancer stem cells" OR "cancer stemness" AND "immunotherapies" AND "mRNAsi" AND "immune checkpoint inhibitors efficacy". Additional keywords include "prognostic signatures" AND "metastasis" AND "clinical features" AND "clinical presentation."

Results mRNAsi-guided tools determined differentially expressed genes in tumors and generated prognostic signatures which in turn reflected clinical characteristics that could be grouped into a tiered list, creating grading categories for ICI treatment efficacy (table 1). Low-risk and high-risk survival groups, tumor mutational burden, TNM pathological stages, overall survival were generated from prognostic gene signatures through mRNAsi. They also could predict 1-year, 3-year, and 5-year overall survival in certain cancers. Based on this clinical presentation, guidance for ICI therapy could be developed.

Conclusions A clinical tier grading list may be an effective way to guide oncologists in applying mRNAsi tools to cancer stemness for treatment through ICIs. Future studies could focus on stratifying patients through the prognostic signatures generated by these tools.

Abstract 516 Table 1 Clinical Tier Grading List According to Prognostic Signatures as Determined by mRNAsi (adapted from Shi 2021, Li 2021, Mao 2021, Santoro 2022)

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Tier 1		
Signature	Clinical Characteristics	ICI Efficacy
High-mRNAsi Low PD-L1 Low PD-1 Low CTLA-4	High risk Low OS High TMB	Low
Tier 2		
Signature	Clinical Characteristics	ICI Efficacy
Low-mRNAsi High PD-L1 High PD-1 High CTLA-4	Low to moderate risk High OS	High

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