Total Mutational Load – Immune Checkpoint Inhibitors Response

Caris Molecular Intelligence® tumor profiling includes **Total Mutational Load** (TML) status. TML is an emerging indicator for predicting response to immune checkpoint inhibitors across a wide spectrum of tumor types, including CRC, melanoma, NSCLC and urothelial carcinomas (bladder, renal, etc.).

**High TML Across Caris Molecular Intelligence Cases**

Ovarian Surface Epithelial Carcinomas
Breast Carcinoma
Prostatic Adenocarcinoma
Pancreatic Adenocarcinoma
Small Cell Lung Cancer (SCLC)
Liver Hepatocellular Carcinoma
Esophageal & Esophageal Junction Carcinoma
Colorectal Adenocarcinoma
Glioblastoma
Gastric Adenocarcinoma
Cholangiocarcinoma
Neuroendocrine Tumors
Bladder Cancer
Female Genital Tract Malignancy
Non-Small Cell Lung Cancer (NSCLC)
Thymic Carcinoma
Melanoma

**Genomic profiling with Caris Molecular Intelligence can help you make more informed therapy decisions when considering immune checkpoint inhibitors.**

**How It Works**

Total mutational load by Next-Generation Sequencing measures the total number of non-synonymous, somatic mutations identified per megabase (Mb) of the genome coding area (a megabase is 1,000,000 DNA basepairs).

- Non-synonymous mutations are changes in DNA that result in amino acid changes in the protein.
- The new protein changes result in new shapes (neo-antigens) that are considered to be foreign to the immune system.
- Immune checkpoint inhibitors are able to stimulate and allow the immune system to detect these neo-antigens and destroy the tumor.
- Germline (inherited) mutations are not included in TML because the immune system has a higher likelihood of recognizing these alterations as normal.

**TML: Immune Checkpoint Indication for Response**

Tumors with significant numbers of mutations resulting in altered proteins (neo-antigens) may respond more effectively to immunotherapies.
Unlock the Power of Immune Checkpoint Inhibitors

By harnessing the body’s immune system to detect and destroy tumor cells, immune checkpoint inhibitors are rapidly ushering in a new era of precision medicine. Although immune checkpoint inhibitors have demonstrated durable clinical responses across several tumor types, these therapies are costly and may present toxic side effects.

Identify Patients More Likely to Respond to Immune Checkpoint Inhibitors with Biomarker Testing from Caris Molecular Intelligence:

**PD-L1**
- Immunohistochemistry

**Programmed death ligand-1 (PD-L1)** is among the most important checkpoint proteins that mediate tumor-induced immune suppression through T-cell downregulation. PD-L1 expression may indicate response to immune checkpoint inhibitors.

**MSI**
- Fragment Analysis

**Microsatellite instability (MSI)** is caused by failure of the DNA mismatch repair (MMR) system. MSI-High correlates to an increased neoantigen burden, which may respond more favorably to immune checkpoint inhibitors.

**TML**
- Next-Generation Sequencing

**Total mutational load (TML)** measures the total number of non-synonymous somatic mutations identified per megabase of the genome coding area. Tumors with high TML likely harbor neoantigens and may respond more favorably to immune checkpoint inhibitors.

Caris has performed more than 30,000 PD-L1 tests across all lineages.

MSI testing is included for all colorectal and endometrial cancers.

TML is reported for all solid tumors tested with Next-Generation Sequencing (592 genes).

Comprehensive genomic and proteomic profiling with Caris Molecular Intelligence can help you make more informed therapy decisions when considering immune checkpoint inhibitors.