

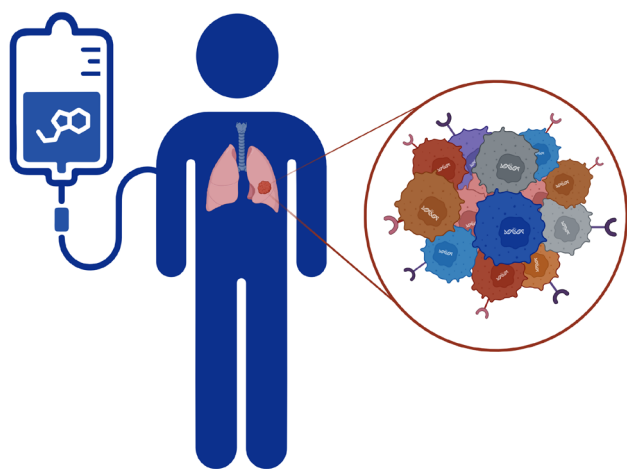
# FAST FACTS: TUMOUR MUTATIONAL BURDEN TESTING



Dr Nicole Rossum

## UNDERSTANDING TUMOUR MUTATIONAL BURDEN TESTING

Tumour Mutational Burden (TMB) is a measure of the total number of somatic mutations found in the DNA of cancer cells. It is usually expressed as mutations per megabase (mut/Mb) of DNA sequenced and reflects how many genetic changes (mutations) have occurred in the tumour's genome.



The rationale for testing for TMB, is that tumours with higher mutational loads are more likely to generate neoantigens, increasing immunogenicity and the likelihood of response to immunotherapy, particularly immune checkpoint inhibitors (anti-PD-1/PD-L1 therapies).

A high TMB is defined by a common cutoff value of  $\geq 10$  mut/Mb, although, some tumour types may benefit at higher cutoffs.

Current consensus is that TMB testing should be considered in the context of advanced, unresectable, or metastatic solid tumours with no satisfactory alternative treatment options, specifically to identify candidates for immune checkpoint inhibitor therapy.

The KEYNOTE-158 trial, evaluated the immune checkpoint inhibitor, pembrolizumab, in patients with previously treated, advanced solid tumours. Patients with TMB-high ( $\geq 10$  mut/Mb) advanced solid tumours had higher response rates to pembrolizumab (29% vs. 6% in non-TMB-high), leading to regulatory approval for pembrolizumab in TMB-high tumours, regardless of histology.



## NEXT GENERATION SEQUENCING (NGS) BASED TUMOUR MUTATIONAL BURDEN TESTING

- Ampath is now offering NGS based Tumour Mutational Burden (TMB) testing.
- TMB can be requested in isolation or as part of the Oncomine™ Comprehensive Assay Plus.

## TUMOUR MUTATIONAL BURDEN NGS TESTING PANEL

|                     |  |
|---------------------|--|
| Test mnemonic       | TMB  |
| Clinical indication | To identify oncology patients that may be candidates for immune checkpoint inhibitor therapy   |
| Specimen type       | Formalin Fixed Paraffin Embedded Tissue (FFPE) 8-12 normal slides (not charged) with 10 micron thick unstained recuts and/or 10 micron thick recuts in an Eppendorf tube and/or paraffin embedded tissue block |
| Turnaround time     | 14 working days  |

For more information contact: [ngs@ampath.co.za](mailto:ngs@ampath.co.za)