Tumor Mutation Burden and Cancer Treatment

What Is Tumor Mutation Burden?
The goal of cancer treatment is to kill cancer cells while not hurting the body’s healthy cells. One way this is done is by using a drug to target a specific genetic change (also referred to as a mutation) in the cancer cells that is not seen in healthy cells. Historically, many of these mutations have been associated with an aggressive biology and sometimes resistance to cancer treatments, such as chemotherapy. But with immunotherapy, which is treatment given to stimulate or remove inhibition of the immune system to help combat a cancer, a higher number of mutations in a tumor can also be associated with a greater probability of response to treatment. This is because the immune system has a better opportunity to attack the cancer effectively if it can recognize it, and the body’s immune system may better identify cancer cells that have a higher number of mutations.

Here, the number of mutations is like lottery tickets. Although buying a large number of lottery tickets does not mean you will always have a winning ticket, it increases the chance of winning compared with only buying 1 or 2 tickets. Similarly, if a tumor has many different mutations, the odds are greater that the immune system will be able to recognize at least 1 of these mutations and kill the cancer (win the lottery). The number of mutations in a tumor cell is commonly referred to as the tumor mutation burden (TMB) of the cancer.

Measuring TMB
- The TMB can be measured by a laboratory test that uses next-generation sequencing of tumor tissue, which looks broadly for a wide range of mutations.
- Although not as established as measuring TMB from a biopsy sample of tumor tissue, studies are now evaluating measuring TMB from circulating tumor DNA in the plasma, making it potentially possible to test TMB from blood in the future.
- The TMB is reported as the number of mutations seen in a section of DNA and reported as mutations per megabase (mut/Mb).
- Cancers with a TMB of 10 mut/Mb or greater (called TMB-high) may be more likely to respond to drugs called immune checkpoint inhibitors that help activate the immune system to better recognize cancer cells.

Current Role of TMB in Cancer Therapy
The TMB can be helpful in predicting response to immune checkpoint inhibitor treatment across many cancer types. However, it may be a better predictor for some cancers and not as helpful for others. Clinical trials are being conducted now to understand which cancers with high TMB respond best to drugs that help turn on the immune system. The immune checkpoint inhibitor pembrolizumab is approved for treating both adults and children with advanced cancers that have a high TMB (defined as ≥10 mut/Mb) after other drugs have been tried.

FOR MORE INFORMATION

Authors: Michael J. Fusco, PharmD; Howard (Jack) West, MD; Christine M. Walko, PharmD
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Author Affiliations: Department of Individualized Cancer Medicine, Moffitt Cancer Center, Tampa, Florida (Fusco, Walko); Department of Medical Oncology and Therapeutics Research, City of Hope Comprehensive Cancer Center, Duarte, California (West).
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