Biomarker may predict if immunotherapy is right choice for colorectal cancer patients

2 May 2019

Foundational research by a City of Hope physician-scientist and his colleagues could one day help metastatic colorectal cancer patients decide whether to choose immunotherapy or chemotherapy as their first treatment option.

"Immunotherapy is the new, hot thing, but sometimes traditional chemotherapy can be a better choice," said Marwan Fakih, M.D., senior author of the new study and co-director of the Gastrointestinal Cancer Program at City of Hope. "Our study suggests tumor genomics could help doctors decide what kind of treatment will benefit each patient most. Taking this kind of personalized medicine approach, we will be able to provide patients with options that yield better outcomes and are more cost-effective."

The study, published on April 30 in the journal *Annals of Oncology*, found that the degree of tumor mutation a patient with metastatic colorectal cancer had was associated with varying responses to immunotherapy when considered in combination with an established biomarker called "microsatellite instability (MSI)."

"Comprehensive genomic profiling is critical to assess the underlying genomic drivers of a tumor, as well as important biomarkers that require broad DNA interrogation like tumor mutational burden (TMB) and microsatellite instability (MSI)," said Alexa Schrock, Ph.D., associate director of clinical development at Foundation Medicine. "In this study, we've seen the importance of evaluating both TMB and MSI when making treatment decisions for metastatic colorectal cancer patients."

At the moment, doctors rely only on MSI status to determine which metastatic colorectal cancer patients receive immunotherapy, Fakih said. He's working to refine the markers that predict patient response to immunotherapy to improve the prognosis for colorectal cancer, the third most commonly diagnosed cancer in the world, according to the World Health Organization. Although this type of cancer has been on the decline, it is on the rise among young adults.

"Finding methods to identify the right, personalized treatment for a patient is top-of-mind, especially in today's precision medicine landscape," Fakih said. "This study is the first to use degree of tumor mutation as a predictor of response to immunotherapy in metastatic colorectal cancer patients with MSI. For cancer patients, timely, appropriate treatment is imperative."

Fakih and his colleagues retrospectively analyzed the data of 22 patients—all of whom had high MSI, a biomarker that indicates they're a good candidate to receive immune checkpoint inhibitor treatment. The patients received either pembrolizumab or nivolumab, both of which are U.S. Food and Drug Administration-approved for metastatic colorectal cancer patients.

The scientists looked at tumor characteristics, tumor genomics and outcome data and compared those analyses to a database containing 18,140 metastatic colorectal cancer patients.

The patients whose tumor cells had a mutation score less than a cut-off point of 37 were less likely to respond to immunotherapy and more likely to have their disease quickly worsen. Those who had a tumor mutation score above the cut-off point of 41 were more likely to respond to pembrolizumab or nivolumab. Notably, the patients who responded to immunotherapy appeared to have durable responses, with the majority experiencing ongoing major shrinkage beyond 1.5 years (the time of study analysis).

The implication is that patients with MSI and a high tumor mutation score should consider receiving immunotherapy as their first treatment, Fakih said. Those with MSI and a low tumor mutation score

(less than 37) should be considered for chemotherapy rather than immunotherapy as their first treatment option, Fakih added. Of course, more research is needed to validate these important findings.

More information: A B Schrock et al, Tumor mutational burden is predictive of response to immune checkpoint inhibitors in MSI-high metastatic colorectal cancer, *Annals of Oncology* (2019). DOI: 10.1093/annonc/mdz134

Provided by City of Hope