Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/project-oncology/predicting-immunotherapy-outcomes-in-head-and-neck-cancer-the-role-of-genetic-signatures/32998/

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Predicting Immunotherapy Outcomes in Head and Neck Cancer: The Role of Genetic Signatures

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. George Laliotis, who's a physician-scientist specializing in translational medicine and biomarker research. He'll be discussing his poster on the molecular landscape of immunotherapy in advanced disease in head and neck squamous cell carcinoma, which he co-authored and presented at the 2025 Annual Meeting of the American Society of Clinical Oncology. Here's Dr. Laliotis now.

Dr. Laliotis:
Head and neck squamous carcinoma is a very difficult-to-treat tumor. Historically, patients actually have very high mortality with very few surgical and chemotherapy solutions. So over the last five to six years, some new agents that are called immunotherapy actually attack the tumor to eradicate the immune response. But due to high adverse effects, high costs, and huge diversity of responses, in many cases, clinicians administer this potentially toxic and expensive drug without actually knowing if a patient is going to respond or not. So this study tries to explore specific genetic mutations or transcriptomic RNA signatures that can predict who can benefit and have a lower chance of adverse effects from immunotherapy, so this actually matches a clinical question along with the translational and genetic need from the research perspective.

This study included around 500 patients with advanced head and neck cancer—so stage III and IV—that have been previously treated with different types of immunotherapy, predominantly the first- and second-generation immunotherapy drugs pembrolizumab and nivolumab, which are already FDA approved, and those that were actually pulled from several publicly available datasets through the GEO dataset and cBioPortal portal. And out of these data sets, the patients had available clinical data and also sequencing data from all whole exome sequencing and RNA sequencing from the tumors that allowed us then to have a meta-analysis to merge specific genomic signatures and transcriptomic signatures, i.e. RNA signatures, with the clinical outcomes. Apart from the long-term outcomes, response data based on the RECIST 1:1 criteria were also available.

We actually explored between the patients that responded—i.e., the responders versus the non-responders—the specific genetic mutations that are enriched or amplified or are most commonly found in those that have not responded. So we found the unique signature of 20 genes that span along some very known genes, such as TP53, PIK3CA, Notch1, and CDK1, some major mutations that are not to be associated with tumor progression in general. That was the first step to identify the genetic signature.

Then we actually made a combined signature of these 20 genes, and we found that if you combine this one and you have two groups, patients that have the mutated signatures have shorter overall survival and DFS survival. And notably, the five-year OS is less than 20 percent for those that have it; so basically for up to five years, only 20 percent of the patients are going to be alive.

Another important aspect is that we show downstream impacts of these mutations. We wanted to explore why this oncogenic signature is so deadly for the tumors. So then, we employed the RNA sequencing analysis, and basically, we show differentially expressed genes, so RNA signatures that are associated with the genes. And when we got a deeper look on that one, we saw that patients that have these top 20 genes and signature, they have enrichment of cell cycle progression, so basically, how rapidly the tumor grows, how rapidly it can create new vessels, and also how they respond to hypoxia. So we saw that not only does this genomic signature have poor outcomes to the patients that have some very distinct RNA signatures and genes that are upregulated or downregulated, but they actually justify why this tumor signature is so deadly.

Announcer:
That was Dr. George Laliotis reviewing his research on the molecular landscape of immunotherapy for advanced disease in head and neck squamous carcinoma, which he discussed at ASCO 2025. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!