Large Cell Neuroendocrine Carcinoma Care: A Look at Evolving Approaches

Announcer:

Welcome to *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. Balazs Halmos, who will be discussing molecular profiling of neuroendocrine carcinomas. Dr. Halmos is a Professor in the Department of Oncology at the Albert Einstein College of Medicine and the Associate Director of Clinical Science at the Montefiore Einstein Comprehensive Cancer Center in New York City. Here he is now.

Dr. Halmos:

Large cell neuroendocrine carcinoma is so uncommon that there's very few trials focusing on it, so we have to kind of expand our knowledge and translate our knowledge from other cancer types into proper management. And this is where it's important to, first of all, recognize that usually we use small cell type chemotherapy regimens upfront for patients with large cell neuroendocrine carcinoma, such as platinum etoposide, but on top of that, molecular testing is important in this particular subtype. About half of them will have a more small cell type molecular profile with P53 and retinoblastoma abnormalities, but the other half is more like a non-small cell molecular profile, retinoblastoma wild type, potentially KRAS, STK11, and Kip1 abnormalities, and maybe even molecular targeting, such as KRAS G12C inhibitors, can be used for those patients. We need to establish that molecular profile, use appropriate chemotherapy, and build upon that with proper use of immunotherapy and then possibly molecular targeted agents DLL3-targeting BiTEs.

So just because we don't have a lot of clinical trial-based knowledge, we can still translate knowledge from small cell lung cancer and non-small cell lung cancer for the right patient in front of us to find the optimal treatment program.

We have seen tremendous amount of advanced focusing on DLL3. Number one, this is an important molecule in the biology of small cell lung cancer, part of the Notch pathway leading to small cell lung cancer growth, and it's very frequently expressed. About 95 percent of patients with small cell lung cancer will have high level of DLL3 expression. And a little bit less so but still significantly in large neuroendocrine carcinoma.

The biggest focus at the moment is antibody drug conjugates, and very specifically we've seen a lot of excitement about bispecific antibodies such as ivonescimab targeting anti-PD1 VEGF, as well as antibody drug conjugates, such as I-DXd targeting B7H3. So we're seeing a number of clinical trials now focusing on expanding the results of the early trials using both sets of agents, both frontline alongside chemotherapy—thinking about the bispecific PD1 VEGF antibodies—as well as in the second line and beyond setting with I-DXd, the B7H3 targeting ADC.

So a lot of excitement about large classes of molecules with multiple members being developed by a number of excellent sponsors. We're hoping that some of them will actually translate into true clinical impact and we'll be able to use these excellent agents in not just the clinical trial setting, but in standard of care as well. So we will just need to, for now, contribute to these trials by recruiting patients appropriately, and hope for the best that the results will be positive and then we can offer this to our patients in the coming years for even better outcomes than today.

Announcer:

That was Dr. Balazs Halmos talking about how molecular profiling can help diagnose and make treatment decisions for neuroendocrine carcinoma. 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!