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On the Horizon: Emerging Antigen-Directed Strategies Across Disease Stage

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Dr. Leal:
Welcome to CE with GLC. I'm Dr. Ticiana Leal. Today I'll discuss emerging antigen-directed strategies across disease stage in small cell lung cancer.

In the TIGOS trial, this is a phase 3 trial of an anti-fucosyl IgG antibody in combination with nivolumab, with chemotherapy as a first-line therapy in patients with extensive-stage small cell lung cancer.

In this study, patients will be randomized to the combination of BMS plus nivolumab plus chemotherapy versus atezolizumab plus chemotherapy, with the usual 4 cycles of induction as per standard of care, followed by maintenance, in the maintenance phase, with BMS plus nivolumab versus atezolizumab, and in this study the primary endpoint is overall survival.

We're also investigating this combination in now the limited-stage setting. This is TIGOS-LS, or TIGO-Limited Stage, with a phase 2 study with the combination of BMS-986489 versus durvalumab as consolidation therapy following chemoradiation in patients with limited-stage small cell lung cancer. Here, patients will receive the combination of BMS-986489 or durvalumab intravenously at a fixed dose once every 4 weeks for up to 2 years or until discontinuation criteria are met. The primary endpoint of this study is overall survival, and we'll be including a patient population of 250 patients. Enrollment has already started, and this study is ongoing.

So next I'd like to highlight the phase 3 trials investigating tarlatamab, a DLL3 T-cell engager, in small cell lung cancer. First, I'd like to highlight DeLLphi-312. This is a study that is investigating the combination of tarlatamab in the frontline setting with chemoimmunotherapy, where patients are randomized to the combination of chemoimmunotherapy plus tarlatamab versus a standard of care, followed by maintenance tarlatamab in combination with durvalumab versus the standard of care IO maintenance.

Another study is DeLLphi-305, which is now investigating the combination of tarlatamab plus durvalumab in first-line maintenance versus the standard of care of immunotherapy alone in first-line maintenance.

And now seeing tarlatamab move to the limited-stage setting in the DeLLphi-306 study. In this randomized phase 3 study, patients receive concurrent chemoradiation as per the standard of care and then are randomized to consolidation tarlatamab versus placebo.

The next study I'd like to highlight is IDeate-Lung02 now investigating I-DXd, a B7-H3 ADC with a topo I inhibitor payload in the second-

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line setting. IDeate-Lung02 is a randomized phase 3 trial that included patients with small cell lung cancer who have received 1 prior line of systemic therapy, which must have included platinum-based chemotherapy plus/minus an anti-PD-1/PD-L1 inhibitor. And in this study, 540 patients are randomized 1:1 to I-DXd at 12 mg/kg every 3 weeks or the standard of care, which include treatment of physician's choice chemotherapy.

The primary endpoint of this study is overall response rate and overall survival.

We also have an early-phase trial of I-DXd moving into earlier lines of therapy with IDeate-Lung03. This is a phase 1b/2 trial of first-line I-DXd plus atezolizumab and chemotherapy in extensive-stage small cell lung cancer.

One important thing to consider is all of this progress with these emerging strategies, either in later lines or in frontlines, really has been due to the progress that we've made with enrollment in clinical trials in extensive-stage small cell lung cancer. Small cell lung cancer has been a very difficult-to-treat disease, and clinical trials have really provided our patients with early access to novel therapies that are now becoming the standard of care.

In addition, another advantage of clinical trials in small cell lung cancer is a dedicated support team with our research teams as well as our clinical teams. And importantly, these are contributing to future breakthroughs that hopefully will not only help the patients that are receiving these treatments, but also our broader patient population with small cell lung cancer, which has been in great need of better therapies. And then importantly, being part of a broader community, not only for patients and their caregivers, but also for investigators and our clinical research teams. It's really been amazing to be part of this broader community that is really pushing the needle forward and providing better strategies for our patients, which will hopefully translate into better survival and, importantly, as we move into earlier phases and into the limited-stage setting, perhaps more cures for our patients.

Well, my time's up. I hope you found this bite-sized overview helpful. Thanks for listening.

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