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Investigating a Therapy for Brain Metastases: A Growing Problem

Dr. Turck:
Welcome to Project Oncology on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Priscilla Brastianos who is an associate professor of medicine at Harvard Medical School and the Director of the Central Nervous System Metastasis Center at Massachusetts General Hospital. Today, we'll be discussing her recent research on pembrolizumab for the treatment of brain metastases, which are the most common type of brain tumor.

Dr. Brastianos, welcome to the program.

Dr. Brastianos:
Thank you so much. I'm looking forward to this.

Dr. Turck:
Well, before diving into your research, Dr. Brastianos, would you give us an overview of the prevalence of brain metastases and the associated prognosis?

Dr. Brastianos:
Brain metastases have truly emerged as a growing problem in oncology, and much of that has to do with their increasing incidence, as well as the morbidity and mortality associated with brain metastases. So approximately, 100,000 to 400,000 cases in the U.S. are diagnosed every year, and up to 25 percent of cancer patients will develop brain metastases, so it is truly an unmet need in oncology. And unfortunately, prognosis is still limited and can range from a few months to a few years, and treatment options typically still are limited for this patient population.

Dr. Turck:
Now looking at your ASCO presentation, what was the goal of your research into pembrolizumab? What was the impetus for the study?

Dr. Brastianos:
The goal was to evaluate the potential efficacy of pembrolizumab in patients with brain metastases. So recent work has suggested that the brain metastasis tumor microenvironment is more immunosuppressive compared to that of the extracranial tumor microenvironment, thus we wanted to evaluate the efficacy of pembrolizumab for patients with brain metastases. So this was a single-stage single-arm phase II clinical trial looking at pembrolizumab, and this was in patients with brain metastases of diverse histologies.

Dr. Turck:
And how was the trial designed?

Dr. Brastianos:
It was an open-label, single-stage, single-arm phase II study. The target accrual was 58 patients to achieve at least 52 evaluable patients, and we defined evaluable patients as patients who received at least one dose of pembrolizumab. The primary endpoint was intracranial benefit, which we defined as best response of complete response, pressure response, or stable disease during treatment, and the study design compared a null intracranial benefit rate of 10 percent against an alternative of 24 percent. And at the end of the study, if at least eight patients among the total of 52 had intracranial benefit, the primary efficacy endpoint would be met, and pembrolizumab would be considered worthy of further study in this patient population. And the design had a type I error of 10 percent and a power of 89 percent with a target type II error of 15 percent.

Dr. Turck:
For those just tuning in, you're listening to Project Oncology on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Priscilla Brastianos about her research on pembrolizumab for the treatment of patients with brain metastases.

So delving further into your research, Dr. Brastianos, what else can you tell us about the patients you enrolled? Would you give us an overview of the baseline characteristics?

Dr. Brastianos:
Sure. So in the 57 evaluable patients, the median age was 53 with a range of 28 to 80,and 81 percent of patients were female. Tumor histologies included breast, non-small cell lung cancer, melanoma, small cell lung cancer, sarcoma, ovarian, pituitary carcinoma, pituitary neuroendocrine, esophageal adenocarcinoma, prostate, and other histologies as well.

For the patients with breast cancer, 16 patients had HER2-positive disease, 17 patients had hormone-receptor-positive disease, and 11 patients had the triple-negative subtype. And patients were allowed to enroll into the study if they either had untreated brain metastases or recurrent and progressive brain metastases, so we had two cohorts. We had patients with untreated brain metastases, as I mentioned, and recurrent or progressive brain metastases in the other cohort.

Dr. Turck:
And what were the key findings from your research?

Dr. Brastianos:
The study met its primary endpoint and achieved an intracranial benefit rate of 42 percent, and seven patients—and encompassing breast, melanoma, and sarcoma histologies—had an overall survival greater than two years. Thirty patients did have one or more grade 3 or higher adverse events that were at least possibly treatment-related, and two patients had grade 4 adverse events, cerebral edema, that were deemed at least possibly treatment-related.

Dr. Turck:
Now with all that in mind, what can your study mean for the future use of checkpoint inhibitors in this patient population?

Dr. Brastianos:
These results do suggest that pembrolizumab or checkpoint blockade may benefit a select group of patients with brain metastases, and further studies are needed to identify biomarkers and mechanisms of resistance in this patient population.

Dr. Turck:
And finally, Dr. Brastianos, from your vantage point, what further research needs to be done in this area?

Dr. Brastianos:
That's a fantastic question. In this study, we did identify a subset of patients that did have durable intracranial stability. I think further evaluation is needed to understand—what are the biomarkers of response in this patient population? Also, further larger studies are needed to evaluate pembrolizumab in specific patient subsets. And finally, we need to look at combination approaches as well. So combination immunotherapy approaches are warranted, as well as looking at combination of pembrolizumab with other systemic therapies or with radiation. I think those are all promising next-step approaches for improving outcomes for patients with brain metastases.

Dr. Turck:
Now these are certainly promising findings for the treatment of patients with brain metastases. And I want to thank my guest, Dr. Priscilla Brastianos, for joining me to share her research.

Dr. Brastianos, it was a pleasure speaking with you today.

Dr. Brastianos:
Thank you so much.

Dr. Turck:
I'm Dr. Charles Turck. To access this and other episodes in our series, visit ReachMD.com/ProjectOncology where you can Be Part of the Knowledge. Thanks for listening.