Personalized Cancer Vaccine Plus Tecentriq Shows Activity Against Solid Tumors

Combining a custom cancer vaccine and a checkpoint inhibitor generated tumor-specific immune responses in a majority of patients.

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Treatment with the personalized cancer vaccine RO7198457 in combination with the PD-L1 inhibitor atezolizumab (Tecentriq) was well tolerated and showed clinical benefit in patients with advanced solid malignancies, according to results from a phase Ib clinical trial presented at the AACR Virtual Annual Meeting II, held June 22-24.

“Many cancers are able to successfully avoid the immune system, and we are only starting to understand the myriad ways in which cancers can do this,” said Juanita Lopez, MB BChir, PhD, a consultant medical oncologist at The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, London. “Because many mutations are not shared between cancers, a personalized treatment approach that targets individual tumor neoantigens may be a viable immunotherapeutic strategy for numerous patients with cancer.”

RO7198457 is a messenger RNA (mRNA)-based cancer vaccine that is manufactured on a per-patient basis, Lopez explained. To produce the vaccine, tumor and blood samples are sequenced and tumor-specific neoantigens are identified. Following the selection of up to 20 neoantigens, the corresponding mRNA is generated, making the backbone of the vaccine, which is then encapsulated in a liposomal formulation to enable intravenous administration, she said. Once the vaccine is administered, the mRNA provides two functions: One is to stimulate the innate immune system, and the other is to encode the neoantigens, which are expressed, processed, and displayed on antigen-presenting cells, with the goal of stimulating an antitumor immune response.

Results evaluating RO7198457 as a monotherapy in 31 patients, which will also be presented during the AACR Virtual Annual Meeting II, showed that the vaccine had a manageable safety profile, with one patient having a complete response and 11 patients having stable disease.

In this trial, 144 patients with advanced solid tumors were enrolled, with the most common tumor types being non-small cell lung cancer (NSCLC), melanoma, triple-negative breast cancer, and urothelial cancer. The median number of prior therapies in this patient population was three, and

nearly 40 percent of patients had received prior immunotherapy. The majority of patients had low levels of PD-L1 expression on both tumor cells and immune cells.

During the induction phase of treatment, patients received one of the different doses of RO7198457 ranging from 15 to 50 micrograms once per week for six weeks; the seventh and eighth doses were administered fortnightly. Atezolizumab was given on a 21-day cycle. Patients received a booster dose of the vaccine during the seventh cycle of atezolizumab, along with a maintenance dose of the vaccine every 24 weeks following the induction phase.

The treatment regimen was well-tolerated, as the majority of adverse events were grade 1 or grade 2. While no dose-limiting toxicities were observed, seven patients discontinued treatment due to adverse events related to study drugs.

Of the 108 patients who had at least one tumor assessment, nine responded, representing an overall response rate of 8 percent. One patient with colorectal cancer had a complete response, and 53 patients, representing 49 percent of evaluable patients, had stable disease.

When the researchers evaluated the peripheral blood of 63 patients, they observed neoantigen-specific T-cell responses induced by the vaccine in 73 percent of patients.

“In this trial, we show that we were able to generate tumor-specific immune responses in the majority of evaluable patients using a personalized cancer vaccine approach in combination with immune checkpoint blockade,” Lopez said. “While the clinical response rate overall was low, this is likely because many of the patients treated in our study had very advanced disease, and were heavily pretreated,” she added. Lopez noted that this therapeutic strategy is being explored in patients with previously untreated melanoma and in patients with resected early-stage NSCLC.

Limitations of the study include its small sample size. Further, due to the single-arm nature of this study, these results cannot be directly compared with atezolizumab monotherapy.

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