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Evaluating PARP and ER Targeting in ER+/HER2– Breast Cancer

Dr. Chalasani:
This is *Project Oncology* on ReachMD. I'm Dr. Pavani Chalasani, and joining me to discuss his research on the combination of saruparib and camizestrant in ER-positive, HER2-negative advanced breast cancer is Dr. Timothy Yap. Dr. Yap is a Ransom Horne, Jr. Endowed Professor for Cancer Research, Vice President and Head of Clinical Development in the Therapeutic Discovery Division, and a professor in the Department of Investigational Cancer Therapeutics, which is the Phase I program at the University of Texas MD Anderson Cancer Center. He recently presented this research as a poster at the 2025 San Antonio Breast Cancer Symposium.

Dr. Yap, thanks for being here today.

Dr. Yap:
Thanks so much for having me, Dr. Chalasani.

Dr. Chalasani:
To get started with some background, Dr. Yap, can you review the rationale to explore the combination of saruparib and camizestrant in this patient population?

Dr. Yap:
Yeah, thanks so much. That's a great question. Both of these are great drugs in themselves, but the rationale behind this particular combination lies in the preclinical evidence linking PARP1 activity to estrogen-dependent transcription. And therefore, by inhibiting PARP1 and simultaneously degrading the estrogen receptor, we aim to achieve deeper and more durable responses than with other agents, so either saruparib or with camizestrant alone.

Dr. Chalasani:
With that in mind, could you tell us a little more about the design of the PETRA study?

Dr. Yap:
So this was really module six of the phase 1 and phase 2A open-label PETRA trial, and 38 patients received saruparib at 60 mg once daily together with camizestrant given at 75 mg once daily until disease progression, unacceptable toxicity, or withdrawal of consent, and the primary objective was safety and tolerability of this particular combination.

Patients were heavily pretreated, receiving a median of 3.5 prior lines of therapy, and 10 patients tested positive for homologous recombination repair mutations. In other words, eight patients tested positive for BRCA1 or BRCA2 mutations, and two patients tested positive for PALB2 mutations.

Dr. Chalasani:
I would like to dive into some of the findings now, starting with safety. What did the profile of this combination look like, and how does it compare, do you think, with either agent?

Dr. Yap:
Yeah, great question. So the combination, I must say, was very well tolerated overall. The most commonly occurring treatment-emergent adverse events were anemia at 50 percent, nausea at 47 percent, and neutropenia at 29 percent. Grade three or higher adverse events occurred in approximately 40 percent of patients, but discontinuations due to adverse events were very rare. Only one patient stopped saruparib, and only two patients stopped camizestrant. And importantly, there were no deaths related to adverse events during the study. And so when you compare the combination versus monotherapy, I really think that there wasn't too much by way of

overlapping toxicities, and the toxicity overall was pretty similar.

Dr. Chalasani:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Pavani Chalasani, and I'm speaking with Dr. Timothy Yap about the PETRA study, which investigated saruparib and camizestrant for ER-positive, HER2-negative advanced breast cancer.

So, Dr. Yap, to continue on our discussion on the trial's findings, can you comment on efficacy? What are the early signals you observed in the combination arm? And how would you compare these results to what you're seeing in monotherapy or potentially in other standard options in this setting?

Dr. Yap:
So 35 patients on this clinical trial were evaluable for response, amongst whom the overall response rate was 23 percent, all being RECIST partial responses, and the median duration of response was 5.5 months. But of interest, in a subset of nine evaluable patients with BRCA or PALB2 mutations, the overall response rate was 33 percent, and median PFS, whilst 4.4 months in the overall population, was actually 6.1 months in the mutated subpopulation.

It is difficult to compare it right now with each monotherapy component, just given the potential line of sight eventually that is currently being investigated in the ongoing phase three EvoPAR-BREAST01 trial, which investigates outcomes in patients with ER-positive, HER2-negative, but with HRR mutations in the breast cancer. I would say that these data, however, with an overall response rate of 33 percent and a medium PFS of 6.1 months, is certainly promising.

Dr. Chalasani:
Okay. All right. So before we wrap up our program, do you have any final thoughts you would like to leave with our audience today?

Dr. Yap:
I think this is a very promising combination, not just from an efficacy point of view with an overall response rate of 33 percent observed in our phase one trial and a median PFS of 6.1 months in patients with either BRCA1 or 2 or PALB2 mutations, but it was also very well tolerated with really no overlapping toxicities between both drugs. And so that really provided the rationale and evidence to proceed to this ongoing randomized phase three EvoPAR-BREAST01 trial, which will investigate outcomes in patients with ER-positive, HER2-negative, and HRR-mutated breast cancer.

Dr. Chalasani:
Thank you, Dr. Yap. It's very important for us to investigate novel regimens and this combination for this patient population.

I want to thank my guest, Dr. Timothy Yap, for joining me to discuss the treatment of ER-positive, HER2-negative advanced breast cancer with saruparib and camizestrant.

Dr. Yap, it was great having you on the program.

Dr. Yap:
Thanks so much for having me.

Dr. Chalasani:
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