Progress on Prostate Cancer Research

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Advancements in prostate cancer research provide hope for finding a cure and lead to the discovery of new treatments to minimize the impact of a man's prostate cancer and maximize his quality of life. This regular *Hot SHEET* supplement includes some of the latest research from the Prostate Cancer Foundation (www.pcf.org).

The PCF is the world's leading philanthropic organization funding and accelerating prostate cancer research. Founded in 1993, the PCF has raised more than $745 million and provided funding to more than 2,000 research programs at nearly 200 cancer centers and universities.

Promising Results of Phase 1b Trial Lead to Upcoming Phase 3 Trial in mCRPC

At the GU-ASCO meeting held earlier this year, Dr. Neeraj Agarwal of the Huntsman Cancer Center at the University of Utah presented results of a Phase 1b trial of combination therapy with two drugs (cabozantinib + atezolizumab) in metastatic castration resistant prostate cancer (mCRPC).

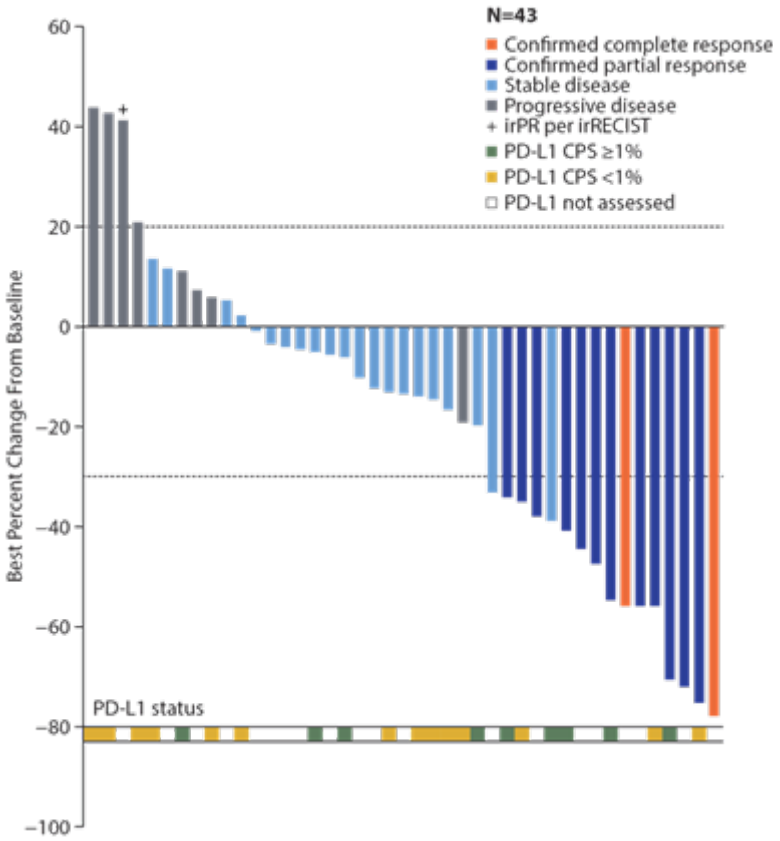
Many treatments for mCRPC exist, but the cancer progresses in almost all men despite therapy, and **more options are needed. Cabozantinib** is an inhibitor of multiple proteins called tyrosine kinases that are involved in cancer processes (tumor growth, angiogenesis, and immune cell regulation). **Atezolizumab** is an immune checkpoint inhibitor that targets the immune-suppressive protein PD-L1 – in other words, the drug prevents the cancer from blocking the body's immune response, allowing the immune system to kill the cancer cells.

These drugs had not been effective on their own, but data suggested that **the combination might be beneficial**, leading to a multinational phase 1b trial across many cancer types. Dr. Agarwal presented the results of one specific cohort of 44 patients: men with mCRPC who had cancer in soft tissues that progressed while on treatment with abiraterone or enzalutamide or both. **These men had significant disease**: 82% were classified as "high risk" mCRPC based on the extent and location of the metastases.

The overall response rate was 32% among all 44 CRPC patients and an additional 48% of patients experienced stable disease. Thus, the clinical benefit rate (response or stabilization of disease) was seen in 80% of patients. The median duration of treatment was 6.3 months, and the median duration of response was 8.3 months. This waterfall plot shows changes in tumor burden for each patient. **Most patients showed a decrease in the amount of tumor as measured on scans**.

The side effect profile of the combination was primarily associated with known effects of cabozantinib. 59% of patients had a Grade 3 or 4 treatment-related adverse event (AE) and 9.1% of patients had an immune-related Grade 3 AE. One grade 4 AE of diverticular perforation was reported. One patient had a Grade 5 AE (dehydration).

The overall response rate of 32% was highly promising. **These results have led to the initiation of an international phase 3 trial** to test the combination of cabozantinib + atezolizumab in men with mCRPC. The trial has already been approved by the FDA and is opening at several sites. The investigators hope to enroll the first patient within months.



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