Androgen receptor abnormality may not be associated

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Findings from a small prospective study suggest that androgen receptor V7 (or AR-V7) status does not significantly affect response to taxane chemotherapy in men with metastatic castration-resistant prostate cancer (mCRPC). Treatment outcomes were largely similar for the 17 patients with AR-V7-positive prostate cancer and the 20 patients with AR-V7-negative disease included in this analysis. The study will be presented at the upcoming 2015 Genitourinary Cancers Symposium in Orlando.

"We urgently need markers to predict which therapies are going to be effective and which will not be effective in individual patients with advanced prostate cancer," said lead study author Emmanuel Antonarakis, MD, an assistant professor of oncology and urology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins in Baltimore, Md. "AR-V7 testing may be extremely valuable in guiding treatment decisions for men with hormone-resistant disease in the near future."

AR-V7 is a truncated form of the androgen receptor (AR) that is detected in about a third of patients with castration-resistant prostate cancer. A recent clinical study by Dr. Antonarakis and colleagues showed that mCRPC in men who had AR-V7 in circulating tumor cells was resistant to the hormone drugs enzalutamide and abiraterone.

Prior research in prostate cancer mouse models has also linked AR-V7 with resistance to taxane chemotherapy. Thus, the current study was carried out to see if these findings from preclinical experiments would

be validated in patients with mCRPC.

Given that AR-V7 has been associated with resistance to hormone therapy but not chemotherapy, the authors speculated that AR-V7-positive patients should probably be offered chemotherapy rather than hormone therapy as initial treatment for mCRPC. Patients who are AR-V7-negative, however, can safely choose either regimen.

This is the first clinical study to explore the association between AR-V7 status and outcomes after treatment with taxane chemotherapy (either docetaxel or cabazitaxel) in patients with mCRPC. AR-V7 status was assessed through an experimental blood test that measures AR-V7 mRNA in circulating tumor cells. Seventeen out of 37 men (46 percent) who were enrolled in the study were AR-V7 positive.

Study participants had comparable responses to therapy irrespective of their AR-V7 status. PSA responses were achieved in 41 percent of AR-V7-positive men and in 65 percent of AR-V7-negative men (the difference was not statistically significant). This 41 percent PSA response rate to taxane therapy is notable because the PSA response rate to abiraterone or enzalutamide in AR-V7-positive patients was 0 percent in the authors' prior study.

The median progression-free survival to taxane therapy was also comparable in AR-V7-positive (5.1 months) and AR-V7-negative men (6.9 months; the difference was not statistically significant).

The AR-V7 abnormality occurs more frequently among patients who have undergone multiple lines of hormone therapies. Scientists believe that the AR-V7 abnormality is triggered by chronic low testosterone levels and may be an adaptive response of the cancer to maintain AR signaling when the normal AR is inhibited.

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