Joint radionuclide therapy-immunotherapy approach effective in prostate cancer model

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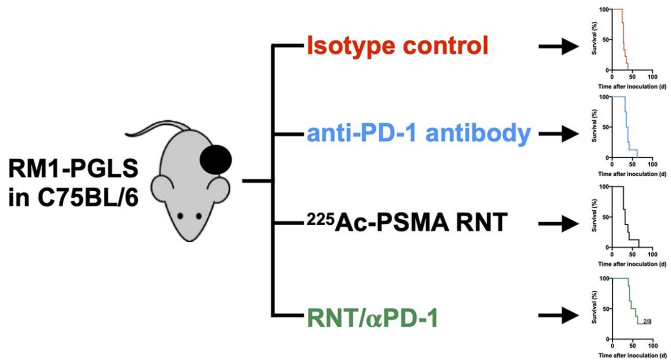

Radionuclide therapy and immune checkpoint blockade synergistically prolong survival in a mouse model of prostate cancer. Credit: Society of Nuclear Medicine and Molecular Imaging

A combination of radionuclide therapy and immunotherapy has proven successful in slowing the progression of prostate cancer and increasing survival time, according to new research published in the February issue of The *Journal of Nuclear Medicine*. The results of the murine study indicate that radionuclide therapy promotes prostate cancer immunogenicity, provoking a cellular response that makes the tumors more receptive to immunotherapy.

"Prostate cancer is generally viewed as an immunological cold cancer in which immunotherapies only have moderate success," said Katharina Lückerath, Ph.D., assistant professor of preclinical theranostics at the University of California Los Angeles in California. "Increasing prostate cancer immunogenicity with prostate-specific membrane antigen (PSMA) radionuclide therapy, however, might render immunotherapies more successful. In our research we sought to exploit this effect by combining radionuclide therapy with immunotherapy in a mouse model of prostate cancer."

In the study, mice bearing prostate cancer tumors received one of four treatments: an isotope control antibody, 225Ac-PSMA617 radionuclide therapy, an anti-PD-1 antibody or both 225Ac-PSMA617 radionuclide therapy and an anti-PD-1 antibody. Therapeutic efficacy was assessed by measuring tumor volume (with computed tomography), time to progression and survival.

While 225Ac-PSMA617 radionuclide therapy and PD-1 blockade alone tended to prolong time to progression as compared to the isotope control (30 days and 33.5 days, respectively, versus 25 days), combining 225Ac-PSMA617 radionuclide therapy and PD-1 blockade significantly improved time to progression (47.5 days). Survival time also increased greatly for the joint therapeutic approach (51.5 days) when compared to225Ac-PSMA617 radionuclide therapy (32 days), anti-PD-1 (37 days) and the control (28 days).

"These findings suggest that radionuclide therapy may have a profound impact on the tumor immune microenvironment that can facilitate immunotherapies in prostate cancer," noted Lückerath. "Radionuclide therapy and immunotherapy combinations are promising therapeutic options for prostate cancer patients, and the data reported in our study support the clinical translation of radionuclide therapy-immunotherapy combination regimens."

In addition to this study, recently launched clinical trials for prostate cancer treatment and new tracers developed to image immune responses underscore the high interest in exploring immunity using molecular imaging and in combining radionuclide therapy with immunotherapy. According to Lückerath, these initiatives might expand the scope of nuclear medicine to immunology and strengthen nuclear medicine's ability to offer powerful and versatile treatment options.

More information: Johannes Czernin et al,

Immune-Checkpoint Blockade Enhances 225Ac-PSMA617 Efficacy in a Mouse Model of Prostate Cancer, *Journal of Nuclear Medicine* (2020). DOI: 10.2967/jnumed.120.246041