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Bone turnover markers predict prostate cancer outcomes

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Biomarkers for bone formation and resorption predict outcomes for men with castration-resistant prostate cancer, a team of researchers from UC Davis and their collaborators have found. Their study, published online in the *Journal of the National Cancer Institute*, also found that the markers identified a small group of patients who responded to the investigational drug atrasentan. The markers' predictive ability could help clinicians match treatments with individual patients, track their effectiveness and affect clinical trial design.

Castration-resistant prostate cancer does not respond to hormone treatments and often metastasizes to bone. This led researchers to wonder if increased bone turnover markers might predict the course of the disease.

"We found that patients with high levels of these markers in the blood had a much shorter lifespan compared to patients with low levels," said lead author Primo Lara, associate director for translational research at the UC Davis Comprehensive Cancer Center. "By measuring bone turnover in prostate cancer patients, we can determine how well they do."

Healthy bone maintains a balance between formation and resorption, generating new bone while recycling old. Prostate cancer throws off this balance. Researchers hoped this mechanism would help them track the cancer. To investigate this potential link, the team tested blood serum in 778 patients for both resorption (N-telopeptide, pyridinoline) and

formation markers (C-terminal collagen propeptide, bone alkaline phosphatase) and found elevated levels of each of the markers predicted poor prognosis.

Perhaps most interesting, elevated marker levels also predicted whether patients would respond to a specific drug. About 6 percent of patients with the highest marker levels responded to atrasentan, and investigational drug abandoned because it failed in clinical trials. Lara and colleagues believe this may be related to study design.

"Atrasentan kept coming up short in randomized trials because the drug only works for a small group," Lara said. "Because certain drugs only succeed in a fraction of patients, drug makers need to factor in these bone metabolism markers in their trial design. They need to target the patients most likely to benefit."

In addition to determining which patients might respond best to a specific treatment, these markers could be used to track their response during treatment. Marker status could also stratify patients equally within different study arms. Balancing these studies could potentially make them more accurate and identify the niche value of drugs like atrasentan whose effectiveness is not evident in large populations.

"I think the days of doing empirical studies on all comers should end," Lara said. "You need to have an appropriate database of patients and perform a rigorous analysis to find the subset who will benefit from an investigational drug."

Provided by UC Davis

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