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First blood-based biomarker in response to the treatment of the most aggressive prostate cancer

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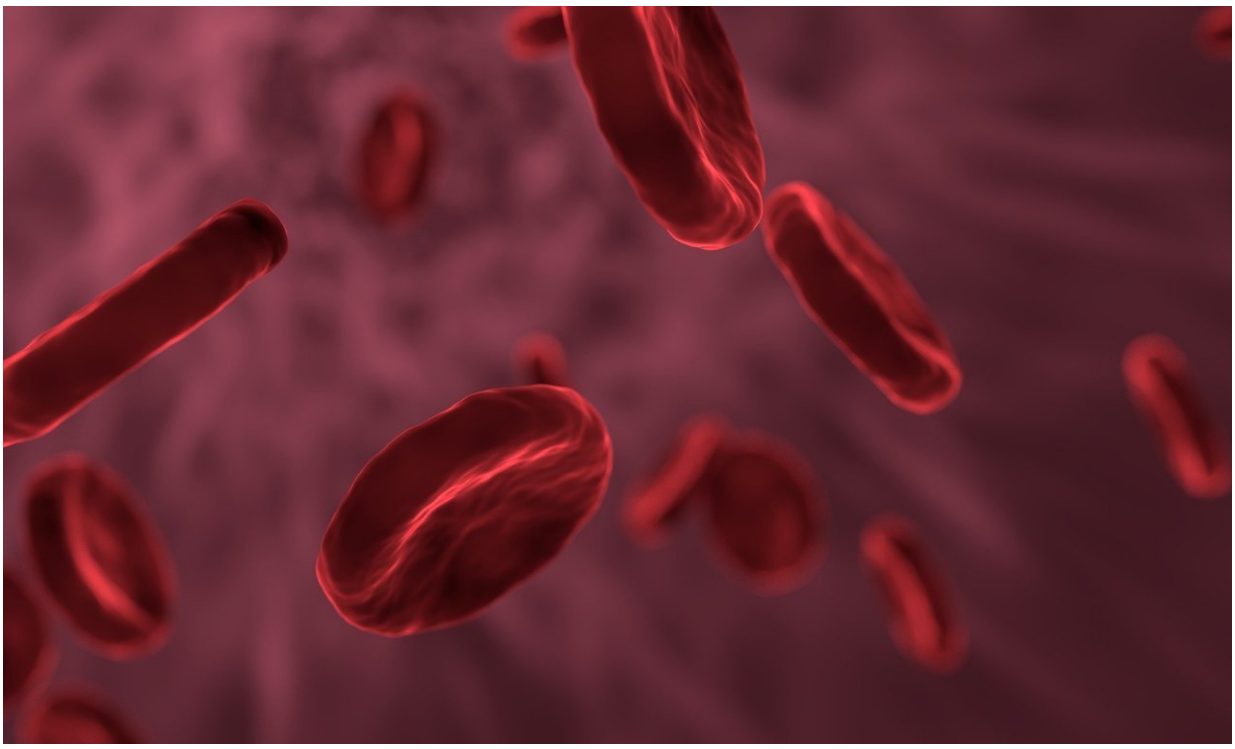

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The most aggressive type of prostate cancer, castration-resistant prostate cancer, can be treated via two therapies: taxanes or hormone treatment. Until recently, there were no comparative studies between the two, and

the decision on which treatment to use was done empirically and based on the patient's preferences. Now, a study co-led by the Spanish National Cancer Research Center (CNIO) and researchers from Italy and the United Kingdom, and published in *European Urology* has identified a biomarker that, via liquid biopsy, can determine which of the two treatments would extend the life expectancy of each patient.

Prostate cancer is one of the most common cancers in men, and has one of the highest five-year survival rates when diagnosed in the localised stage. When diagnosed in the advanced stage or when a localised tumour relapses after the initial local treatment, the usual procedure is to fight it using male hormone (androgen) deprivation therapy. It can be done either by surgical removal of the testicles or using medication that eliminates the testosterone production (chemical castration). However, up to 90 percent of castration patients develop subsequent aggressive, castration-resistant forms, and their survival rate is around two years.

Among the treatments used to extend the life expectancy in patients with castration-resistant prostate cancer, the taxanes docetaxel and cabazitaxel work by blocking cell division and cell proliferation. The new generation hormone therapy, abiraterone and enzalutamide, on the contrary, act on androgen (male hormone) production: abiraterone inhibits its synthesis, while enzalutamide blocks the nuclear testosterone receptor.

"At this moment there are no comparative studies between hormones and taxanes," explains David Olmos. "There are only studies in similar populations and the selection of the adequate treatment is done empirically. The treatment usually starts off with a hormone therapy, but it also depends on the patient's preference, after duly informing the patient of his options."

The study results show that castration-resistant prostate cancer patients with a normal number of copies of the gene encoding the androgen

receptor (AR) in circulating tumour DNA who are treated with abiraterone/enzalutamide have a lower risk of disease progression and higher life expectancy, with a 50 percent higher survival rate compared to docetaxel, where the average life expectancy was around 24 months. On the other hand, the patients with more copies of the androgen receptor gene respond slightly better to docetaxel, with a higher life expectancy, around 9 months, compared to abiraterone/enzalutamide.

The presence of AR in circulating tumour DNA is the first biomarker to define the best first-line therapy. The study also indicates the urgency to develop new treatments for the patients with a higher level of AR, as they respond worse to the existing therapies.

Liquid biopsy has proven to be a reliable, fast and non-invasive method to determine the alterations of a specific tumour and to be able to decide the best treatment in each case. Olmos explains: "Using bioinformatics tools we can calculate the fraction of the tumour DNA present in the total free DNA in the plasma and in that fraction, we calculate the number of AR copies."

For this study, the liquid biopsy has been used to "confirm that a marker that has a prognostic value can also have a predictive use. The next step will be to make a random study that can confirm the results."

More information: Vincenza Conteduca et al, Plasma Androgen Receptor and Docetaxel for Metastatic Castration-resistant Prostate Cancer, *European Urology* (2018). DOI: 10.1016/j.eururo.2018.09.049

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