Jury still out on cardiovascular safety of prostate cancer treatments

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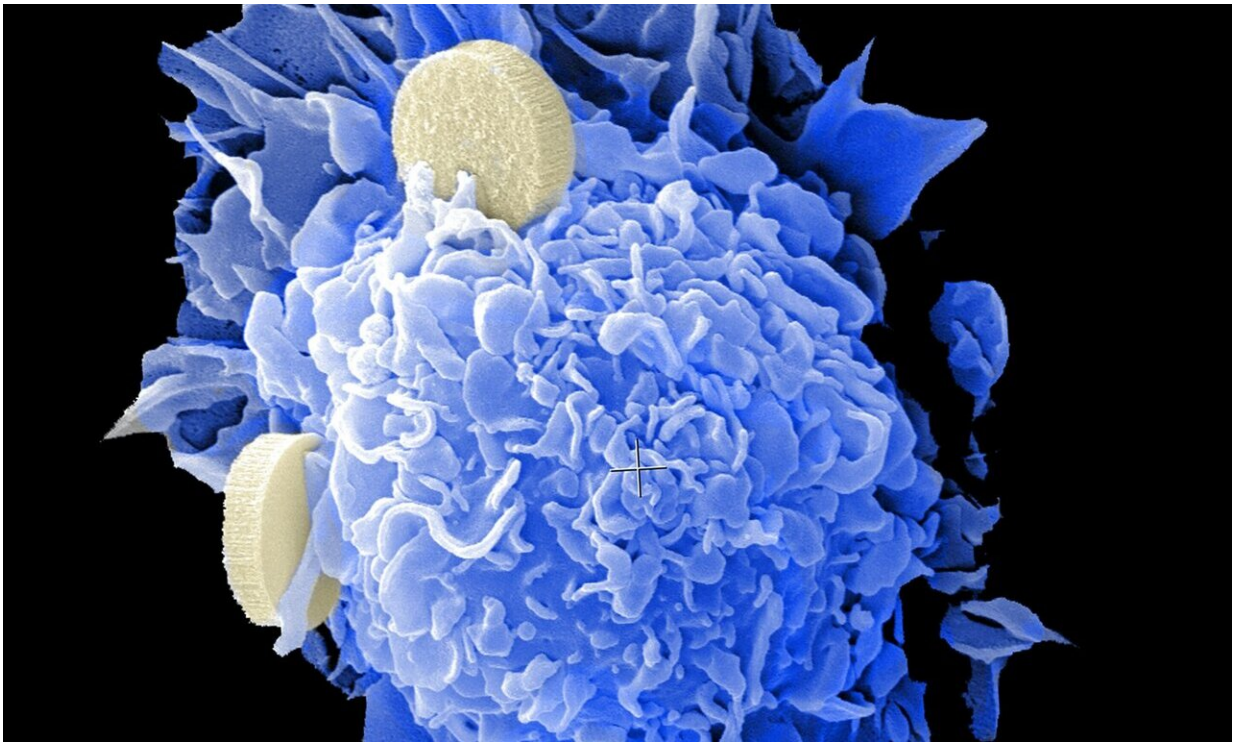

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The relative cardiovascular safety of different types of androgen deprivation therapy (ADT) for prostate cancer remains unresolved after the PRONOUNCE trial was terminated early. The late breaking research is presented in a Hot Line session today at ESC Congress 2021.

More than one million men are diagnosed with prostate cancer worldwide every year. These patients are at high risk of developing cardiovascular disease and are more likely to die from cardiovascular disease than their healthy peers.

Approximately 50% of all patients with prostate cancer will be prescribed ADT at some point in their illness. ADT has been associated with heart disease and stroke, particularly in men with pre-existing cardiovascular disease. However, it is unclear whether this is driven by the method of androgen deprivation—i.e. orchiectomy, testosterone antagonists, or modulation of the gonadotropin-releasing hormone (GnRH) receptor. Previous research has suggested that GnRH antagonists may be associated with a preferable cardiovascular safety profile.

PRONOUNCE was the first randomized clinical trial to prospectively compare the cardiovascular safety of a GnRH antagonist versus GnRH agonist in patients with prostate cancer. This was also the first interdisciplinary, multinational cardio-oncology outcomes-based trial that has involved close collaboration between urologists, oncologists and cardiologists.

The trial was initially designed to enroll 900 men with prostate cancer and concomitant atherosclerotic cardiovascular disease. Participants were randomized 1:1 to the GnRH antagonist degarelix or the GnRH agonist leuprolide for 12 months. The primary outcome was the time to first occurrence of a major adverse cardiovascular event (MACE), defined as a composite of death, myocardial infarction or stroke through 12 months.

Enrolment was slower than anticipated and the trial was terminated prematurely with fewer than half of the planned 66 endpoint events in 545 randomized patients.

The analysis included 545 men with an average age of 73.2 years. At 12 months, no statistically significant difference in the rate of MACE was observed between patients treated with degarelix compared with those treated with leuprolide. There were 15 (5.5%) and 11 (4.1%) primary endpoint events in the degarelix and leuprolide groups, respectively (p=0.53).

Principal investigator Professor Renato Lopes of Duke University Medical Center, Durham, US says that "PRONOUNCE is the first, international, randomized clinical trial to prospectively compare the cardiovascular safety of a GnRH antagonist and a GnRH agonist in patients with prostate cancer. The study was terminated prematurely due to smaller than planned numbers of participants and events and no difference in MACE at one year between patients assigned to degarelix or leuprolide was observed. Thus, the relative cardiovascular safety of GnRH antagonists and agonists remains unresolved. There is an ongoing need to understand the cardiovascular effects of oncological treatments as cancer survivorship increases and competing non-cancer death becomes more likely."

He concluded that "PRONOUNCE provides a model for the interdisciplinary collaboration between oncologists and cardiologists with a shared goal of evaluating the impact of cancer therapies on cardiovascular outcomes."

More information: ESC Congress: www.escardio.org/Congresses-&-Events/ESC-Congress

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