COMMENTARY

The type of ADT may matter for testosterone recovery

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Long and colleagues from University of Iowa are applauded for reporting on a clinically important and timely topic. This is a hot subject in light of the recent FDA-approval of Relugolix in advanced prostate cancer.[1] This is a new oral Gn-RH antagonist and is touted to have more rapid recovery of testosterone upon discontinuation. While many patients with advanced prostate cancer merit long term ADT where recovery of testosterone level is not desirable, other men with localized or locally advanced disease receiving primary radiotherapy, receive short term ADT. In these men, recovery of testosterone more rapidly may be desirable to limit side-effects and improve quality of life.

Long and colleagues found that for men who were on parenteral ADT (leuprolide, goserelin, degarelix) for a median of 15 months, it took 19 more months to recover testosterone levels to greater than 240 ng/dL.[2] For men with locally advanced or high risk prostate cancer who receive guideline-based ADT for 18-36 months along with radiotherapy, this delay in testosterone recovery may lead to increased side-effects such as osteoporosis, diabetes, cardiovascular disease, weight gain, and other manifestations of metabolic syndrome.[3,4]

Contrast the findings of Long et al with recently published results of the HERO study comparing oral relugolix to 3 month depot leuprolide in a 2:1 randomization.[1] In 622 men, mean age of 71.4, who received oral relugolix, testosterone was suppressed to less than 50 ng/dL in 96.7% over 48 weeks compared to 88.8% in the 308 men receiving depot 3 month leuprolide. At day 29 of ADT therapy, 95% of relugolix patients were below a testosterone of 20 ng/dL compared to 57% of leuprolide patients. In a testosterone recovery sub study of 184 patients, mean testosterone level was 280 ng/dL 3 months after discontinuation of oral relugolix versus a mean testosterone level of 50 ng/dL in 47 leuprolide patients. The data of Long et al appear similar to the control leuprolide patients in the HERO trial.

The take home message is that parenteral ADT (leuprolide, degarelix, goserelin) are indicated when long term ADT and long term testosterone suppression is desired. On the other hand, oral relugolix may be recommended when short term ADT is preferred such as neoadjuvant or adjuvant ADT (NHT) or in the setting of intermittent hormonal therapy (IHT). The key learning point is that a depot injection of an LH-RH agonist or antagonist lasts much longer than the stated depot time and patients should be counseled appropriately of what to expect. □

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