Hypothyroidism caused by apalutamide

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1 Apalutamide is a common treatment for prostate cancer

Apalutamide is an oral, nonsteroidal anti-androgen drug that delays disease progression and improves metastases-free and overall survival when added to androgen deprivation therapy in patients with non-metastatic castration-resistant and metastatic castration-sensitive prostate cancer.[1,2] Apalutamide is commonly dosed at 240 mg/d and continued for a median duration of 3.5 years.[1,2]

2 Hypothyroidism is a common adverse effect of apalutamide

Hypothyroidism occurs in 5.7%–8% of patients taking apalutamide.[3] Patients with pre-existing hypothyroidism are more susceptible to the drug's thyroid effects; worsening hypothyroidism was observed in 30% of these patients.[3] The development of hypothyroidism does not necessitate a dose decrease of apalutamide.[3]

3 A thyroid-stimulating hormone (TSH) level should be checked before and during apalutamide therapy

Most patients' TSH levels rise at a median time of 113 days.[1,2] Baseline TSH should be checked before apalutamide is initiated.[3] In clinical trials, TSH levels were monitored every 4 months.[1,2] Repeating a TSH level sooner is appropriate if signs or symptoms of hypothyroidism develop.

4 Treatment is with levothyroxine

If patients develop hypothyroidism, levothyroxine should be initiated at 1.6 µg/kg. A TSH level should be repeated in 4–6 weeks with levothyroxine dose increases of 12.5–25 µg to target a TSH level in the normal range. Levothyroxine requirements vary among patients and may change over time despite stable apalutamide doses. The required dose of levothyroxine may decrease to pretreatment levels after apalutamide is stopped.[4]

5 Apalutamide-induced hypothyroidism can markedly increase levothyroxine requirements in patients with pre-existing hypothyroidism

Apalutamide induces uridine diphosphate–glucuronyltransferases, catalyzing the attachment of glucuronic acid to levothyroxine and promoting biliary excretion of thyroid hormones, which increases TSH levels through negative feedback.[3,5] Small case series have shown that a 2- to 3-fold increase in levothyroxine may be needed to achieve a euthyroid state in patients with pre-existing hypothyroidism.[4]

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