dysfunction, shrinking of the male sexual organs, hot flashes, osteoporosis, anemia, reduced muscle mass, decreased muscle strength, increase in body fat, and weight gain, due to the changes in the levels of the hormones testosterone and estrogen. Current treatments for the side effects associated with ADT are known in the art. See US 2009/0143344 (hot flashes – 5HT2A or D2R antagonist); US 2007/0281977 (hot flashes – muscarinic receptor antagonist); US 2008/0080143 (osteoporosis, bone fractures, loss of BMD, hot flashes gynochomastia, hair loss – torimifene). However, there remains a need in the art for alternate therapies wherein certain side effects of ADT may be reduced. In fact, until recently, intermittent androgen deprivation (IAD) was recommended to attempt to minimize the adverse effects of medical castration by withdrawing treatment in patients who have responded to ADT and then reinstituting ADT when there is evidence of recurrent or progressive disease. However, a trial of 1749 patients randomized to continuous ADT versus IAD for a median follow-up of 9.8 years demonstrated that continuous ADT is superior to IAD. A therapy to improve tolerability of the side effects of ADT could lead to improvements in compliance and result in better outcomes to patients.

Summary

In one aspect of the present disclosure, there is provided a use of a compound of (S)-(7-cyano-4-pyridin-2-ylmethyl-1,2,3,4-tetrahydro-cyclopenta[b]indol-2-yl)-carbamic acid isopropyl ester, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating the symptoms as a result of secondary hypogonadism induced by androgen deprivation therapy.

Description

Selective androgen receptor modulators (SARMs) have been found to display a differentiated profile of activity in androgenic tissues. In particular, such agents preferably display androgen agonist activity in anabolic tissues such as muscle or bone, yet are only partial agonists or even antagonists in other androgenic tissues such as the prostate or seminal vesicles. Thus, the use of an androgen receptor (AR) modulator may alleviate the symptoms of ADT for prostate cancer patients.

Figure 1 illustrates that Example 1 resulted in no significant accrual of seminal vesicle weight after treatment of 8 weeks in a rat orchidectomized for 8 weeks and which was hyper responsive to any androgenic stimulation.

Figure 2 illustrates that Example 1 resulted in significant accrual of, lumbar vertebra trabecular bone mineral density (LV-TBMD) and showed a trend towards increase in lumbar vertebra trabecular bone mineral content (LV-TBMC), and cross-sectional area (LV-TA) after treatment of 8 weeks in a rat orchidectomized for 8 weeks.

WE CLAIM:

1. Use of a compound of (S)-(7-cyano-4-pyridin-2-ylmethyl-1,2,3,4-tetrahydro-cyclopenta[b]indol-2-yl)-carbamic acid isopropyl ester, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating the symptoms as a result of secondary hypogonadism induced by androgen deprivation therapy.
2. The use according to Claim 1 wherein the symptoms are loss in bone mass, bone strength, muscle mass, or muscle strength.
3. The use according to Claim 2 wherein the symptoms are loss of libido and hot flashes.