Claims

1. Use of an anti-androgen in the manufacture of a medicament for treating metastatic castration-sensitive prostate cancer in a patient, wherein a therapeutically effective amount of the anti-androgen is to be administered in combination with androgen deprivation therapy to the patient, wherein the anti-androgen is

4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N- methylbenzamide, and

wherein administration of the anti-androgen in combination with androgen deprivation therapy provides an increase in overall survival of the patient, relative to the overall survival rate of a population of patients with metastatic castration-sensitive prostate cancer, wherein said population is one that have been administered a placebo in combination with an androgen deprivation therapy, and administration of the anti-androgen in combination with androgen deprivation therapy provides an increase in progression-free survival of the patient, relative to the progression-free survival rate of a population of patients with metastatic castration-sensitive prostate cancer, wherein said population is one that have been administered a placebo in combination with an androgen deprivation therapy.

2. The use according to claim 1, wherein the patient is one that has received at least one prior therapy for the treatment of cancer, wherein the prior therapy for the treatment of cancer is radiation, surgical intervention or docetaxel therapy.

3. The use according to claim 1, wherein the patient is treatment naïve.

4. The use according to any one of the preceding claims, wherein 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be administered daily to the patient.

5. The use according to any one of the preceding claims, wherein 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be administered orally to the patient, optionally on a continuous daily dosing schedule.

6. The use according to claim 5, wherein 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be administered orally to the patient at a dose of 30 mg per day to 480 mg per day, optionally at a dose of 180 mg per day to 480 mg per day.

7. The use according to claim 6, wherein 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be administered orally to the patient at a dose of:

(a) 30 mg per day;

(b) 60 mg per day;

(c) 90 mg per day;

(d) 120 mg per day; or

(d) 240 mg per day.

8. The use according to claim 7, wherein 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be administered orally to the patient at a dose of 240 mg per day.

9. The use according to claim 8, wherein if the patient experiences a greater than or equal to Grade 3 toxicity or an intolerable side effect, dosing of 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be held until symptoms of the greater than or equal to Grade 3 toxicity improve to less than or equal to Grade 1 or original grade; and daily oral administration of 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide in an amount of 240mg, 180 mg, or 120 mg is to be resumed.

10. The use according to claim 1, wherein

(a) a daily oral dose of 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be administered in an amount of 240 mg;

(b) if the patient experiences a greater than or equal to Grade 3 toxicity or an intolerable side effect, dosing of 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be held until symptoms of the greater than or equal to Grade 3 toxicity improve to less than or equal to Grade 1 or original grade; and daily oral administration of 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide in an amount of 240mg, 180 mg, or 120 mg is to be resumed.

11. The use according to any one of the preceding claims, wherein administration of the anti-androgen in combination with androgen deprivation therapy provides an increase in overall survival and a 33% reduction in risk of death or an increase in progression-free survival and a 52% reduction in risk of radiographic progression or death.

12. The use according to any one of the preceding claims, wherein 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be administered in combination with at least one gonadotropin-releasing hormone (GnRH) agonist or antagonist.

13. The use according to claim 12, wherein the at least one GnRH agonist or antagonist is or comprises leuprolide, buserelin, naferelin, histrelin, goserelin, deslorelin, degarelix, ozarelix, ABT-620 (elagolix), TAK-385 (relugolix), EP-100, KLH-2109 or triptorelin.

14. The use according to any one of claims 1 to 11, wherein 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is to be used in combination with bilateral orchiectomy.

15. The use according to any one of the preceding claims, wherein the 4-[7-(6-cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide is not to be co-administered with:

(a) a medication that is a CYP2C8 or CYP3A4 inhibitor;

(b) a medication that is primarily metabolized by CYP3A4, CYP2C19, or CYP2C9;

(c) a medication that is a substrate of UDP-glucuronosyl transferase; or

(d) a medication that is a substrate of P-glycoprotein, breast cancer resistance protein or organic anion transporting polypeptide 1B1.