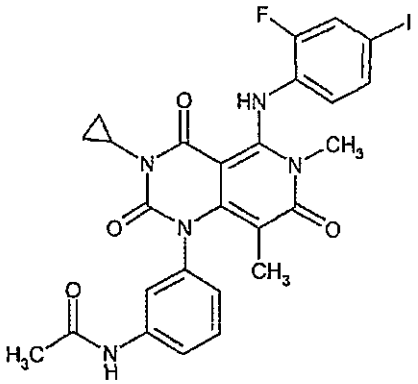
CLAIMS

1. Compound of Structure (I):

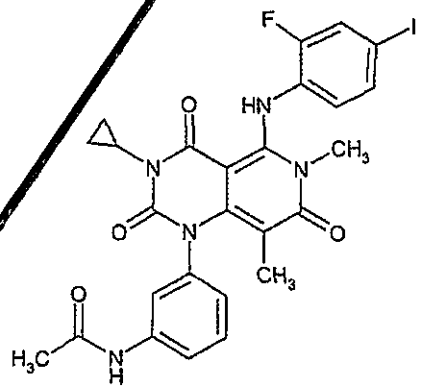


(I)

or a pharmaceutically acceptable salt or solvate thereof; and

an mTOR inhibitor; together in combination, for use in the treatment of cancer and/or precancerous syndromes.

2. A compound of Structure (I):



(I);

or a pharmaceutically acceptable salt or solvate thereof; and

an mTOR inhibitor; when used according to claim 1 where the compound of Structure (I) is in the form of a dimethyl sulfoxide solvate.

3. A combination kit when used in the treatment of cancer and/or precancerous syndromes comprising a combination according to claim 1 or claim 2 together with a pharmaceutically acceptable carrier or carriers.

4. Use of a combination according to claim 1 or claim 2 or a combination kit according to claim 3 in the manufacture of a medicament or medicaments for the treatment of cancer, and/or precancerous syndromes.

5. A therapeutically effective amount of N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide and an mTOR inhibitor, together in combination for use in the treatment of cancer or precancerous syndromes,
wherein the combination is to be administered within a specified period, and
wherein the combination is to be administered for a duration of time.

6. The therapeutic combination according to claim 5 wherein N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide is to be administered once a day, and the mTOR inhibitor is everolimus which is administered twice a day.

7. The therapeutic combination according to claim 5 or claim 6 wherein the amount of N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide is selected from about 0.125mg to about 10mg, and the mTOR inhibitor is everolimus which is to be administered in an amount selected from about 2.5mg to about 20mg.

8. The therapeutic combination according to claim 7 wherein the amount of N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide is selected from about 0.25mg to about 9mg, and that amount is administered once per day, and the amount of everolimus is selected from about 3mg to about 15mg, and that amount is to be administered twice per day.

9. The therapeutic combination according to claim 8 wherein N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-

2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide and everolimus, are to be administered within 12 hours of each other for from 1 to 3 consecutive days followed by administration of N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide for from 3 to 7 consecutive days, optionally followed by one or more cycles of repeat dosing.

10. The therapeutic combination according to any one of claims 5 to 8 wherein N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide and mTOR or a pharmaceutically acceptable salts thereof, are to be administered for at least 7 consecutive days.

11. The therapeutic combination according to any one of claims 5 to 8 wherein N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide and mTOR or a pharmaceutically acceptable salts thereof, are to be administered within 12 hours of each other for at least 5 consecutive days.

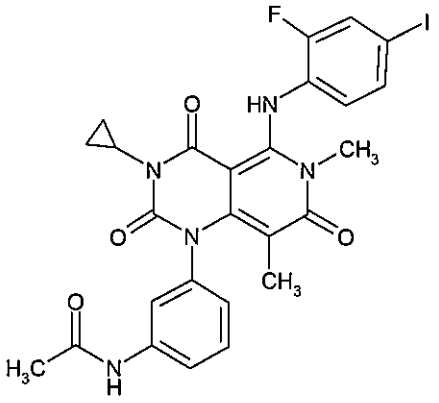
12. The therapeutic combination according to any one of claims 5 to 10 wherein N-{3-[3-cyclopropyl-5-(2-fluoro-4-iodo-phenylamino)-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin-1-yl]phenyl}acetamide dimethyl sulfoxide and mTOR or a pharmaceutically acceptable salts thereof, are to be administered for at least 10 consecutive days.

13. A use according to claim 4, or the therapeutic combination according to any one of claims 5 to 12, wherein the cancer is either wild type or mutant for Ras/Raf and either wild type or mutant for PI3K/PTEN.

14. A use according to claim 4, or the therapeutic combination according to any one of claims 5 to 12 wherein the cancer is selected from the group consisting of ovarian, breast, pancreatic and prostate.

CLAIMS

1. A compound of structure (I):



(I);

and everolimus together in combination, for use in the treatment of cancer and/or precancerous syndromes where the compound of structure (I) is in the form of a dimethyl sulfoxide.

2. The use of a combination according to claim 1, in the manufacture of a medicament or medicaments for the treatment of cancer, and/or precancerous syndromes.

3. A combination as claimed in claim 1 or the use as claimed in claim 2, wherein a therapeutically effective amount of the combination is to be administered within a specified period, and wherein the combination is to be administered for a duration of time.

4. The combination or use according to claim 3, wherein the compound of structure (I) in the form of a dimethyl sulfoxide is to be administered once a day, and everolimus which is to be administered twice a day.

5. The combination or use according to claim 3 or claim 4, wherein the compound of structure (I) in the form of a dimethyl sulfoxide is selected from about 0.125mg to about 10mg, and the everolimus is to be administered in an amount selected from about 2.5mg to about 20mg.

6. The combination or use according to claim 5, wherein the amount of the compound of

structure (I) in the form of a dimethyl sulfoxide is selected from about 0.25mg to about 9mg, and that amount is administered once per day, and the amount of everolimus is selected from about 3mg to about 15mg, and that amount is to be administered twice per day.

7. The combination or use according to claim 6, wherein the compound of structure (I) in the form of a dimethyl sulfoxide and everolimus, are to be administered within 12 hours of each other for from 1 to 3 consecutive days followed by administration of the compound of structure (I) in the form of a dimethyl sulfoxide for from 3 to 7 consecutive days, optionally followed by one or more cycles of repeat dosing.

8. The combination or use according to any one of claims 3 to 6, wherein the compound of structure (I) in the form of a dimethyl sulfoxide and everolimus are to be administered for at least 7 consecutive days.

9. The combination or use according to any one of claims 3 to 6, wherein the compound of structure (I) in the form of a dimethyl sulfoxide and everolimus are to be administered within 12 hours of each other for at least 5 consecutive days.

10. The combination or use according to any one of claims 3 to 8, wherein the compound of structure (I) in the form of a dimethyl sulfoxide and everolimus are to be administered for at least 10 consecutive days.

11. A use according to any one of claims 2 to 10, or the combination according to any one of claims 3 to 10, wherein the cancer is either wild type or mutant for Ras/Raf and either wild type or mutant for PI3K/PTEN.

12. A use according to any one of claims 2 to 10, or the combination according to any one of claims 3 to 10, wherein the cancer is selected from the group consisting of ovarian, breast, pancreatic and prostate.