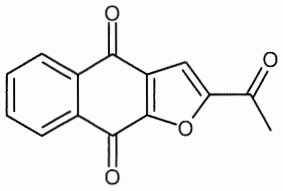
Claims

1. A compound having the structure

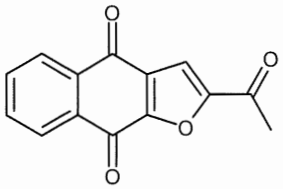


or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, for use in the treatment of cancer, wherein in use the compound is to be administered to a subject in need thereof a therapeutically effect amount of the compound and a therapeutically effective amount of paclitaxel.

2. The compound according to claim 1, wherein the compound is to be administered to the subject at a total daily dose:

a) in a range from about 80 mg to about 2000 mg; or
b) of about 960 mg;

3. A compound having the structure

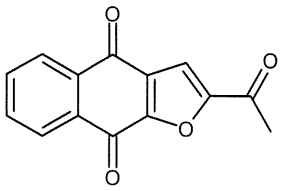


or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, for use in the treatment of cancer wherein the compound is to be administered to the subject at a total daily dose:

a) in a range from about 80 mg to about 2000 mg; or
b) of about 960 mg;

or wherein the compound is to be administered to a subject in need thereof a therapeutically effect amount of the compound and a therapeutically effective amount of paclitaxel.

4. A compound having the structure



or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, for use in the treatment of cancer in a selected patient population, wherein the use comprises the steps of:
(a) measuring a level and/or subcellular localization of one or more cancer sternness markers selected from phosphorylated STATS (p- STAT3), β-catenin, and NANOG in a biological sample obtained from a patient candidate diagnosed of a cancer;
(b) confirming that the patient candidate's cancer sternness marker level and/or subcellular localization is above a benchmark level; and
(c) administering to the patient candidate a therapeutically effective amount of the compound.

5. The compound according to any one of claims 1 to 3, wherein the compound is to be administered to the subject in two daily doses.

6. The compound according to claim 3 or claim 5, wherein each dose is about 480 mg.

7. The compound according to any one of claims 3, 5 or 6, wherein the compound is to be administered to the subject as a tablet or capsule.

8. The compound according to claim 7, wherein the tablet or capsule comprises a dose of about 80 mg.

9. The compound according to any one of claims 1 to 3 or 5 to 8, wherein the interval between administrations of the compound is:

a) in the range from about 4 hours to about 16 hours; or

b) selected from the group consisting of at least about 4 hours, at least about 5 hours, at least about 6 hours, at least about 7 hours, at least about 8 hours, at least about 9 hours, at

least about 10 hours, at least about 11 hours, at least about 12 hours, at least about 13 hours, at least about 14 hours, at least about 15 hours and at least about 16 hours; or c) or about 12 hours.

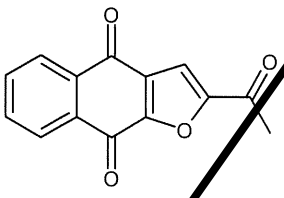
10. The compound according to any one of claims 1 to 3 or 5 to 9, wherein the compound is to be administered to the subject at a dose selected from the group consisting of about 80 mg BID, about 160 mg BID, about 320 mg BID, about 400 mg BID, about 480 mg BID, about 500 mg BID, and about 600 mg BID.

11. The compound according to any one of claims 1 to 3 or 5 to 10, wherein each dose is about 480 mg BID and the interval between administrations is about 12 hours, about 80 mg BID and the interval between administrations is about 12 hours, about 400 mg BID and the interval between administrations is about 12 hours, or about 320 mg BID and the interval between administrations is about 12 hours.

12. The compound according to any one of claims 1 to 3 or 5 to 11, wherein the compound is to be administered orally in conjunction with a fluid, preferably milk or water, on an empty stomach.

13. The compound according to claim 1, wherein the treatment further comprises detecting nuclear β-catenin expression in a patient's tissue, where such nuclear β-catenin expression is used as a biomarker for patient selection.

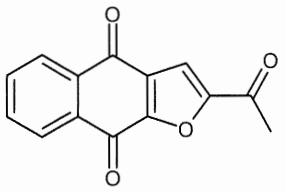
14. A first agent having the structure



or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof; and
an antimitotic agent or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof.
for use in the curative or prophylactic treatment of cancer.

15. The first agent according to claim 14, and an antimitotic agent, wherein the antimitotic agent is selected from the group consisting of paclitaxel (Abraxane/Taxol), docetaxel (taxotere), BMS-275183, xyotax, tocosal, vinorlebine, vincristine, vinblastine, vindesine, vinzolidine, etoposide (VP-16), teniposide (VM-26), ixabepilone, larotaxel, ortataxel, tesetaxel, and ispinesib; preferably is paclitaxel (Abraxane/Taxol).

16. A compound having the structure



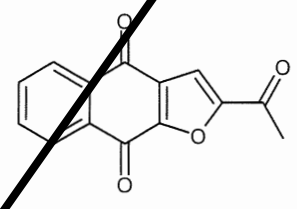
or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, for use in the treatment of cancer, wherein the cancer is colorectal cancer, colon adenocarcinoma or rectal adenocarcinoma.

17. The compound according to claim 16, wherein the compound is to be administered to the subject in two daily doses totaling in a range from about 80 mg to about 2000 mg; preferably about 480 mg.

18. The compound according to claim 16 or claim 17, wherein the interval between administrations of the compound is in the range from about 4 hours to about 16 hours.

19. The compound according to any one of claims 1 to 6 or 11, wherein the compound is to be administered to the subject at a dose selected from the group consisting of about 80 mg BID, about 160 mg BID, about 320 mg BID, about 400 mg BID, about 480 mg BID, and about 500 mg BID.

20. A pharmaceutical composition, comprising:
a therapeutically effective amount of an active ingredient having the structure



a surfactant comprising sodium lauryl sulfate (SLS) or sodium dodecyl sulfate (SDS); Gelucire (lauroyl polyoxylglycerides); and Labrafil (linoleoyl polyoxylglycerides).

21. The pharmaceutical composition according to claim 20, consisting of, by weight, about 27.18% in the active ingredient, about 0.27% in the surfactant, about 14.51% in Gelucire, and about 58.04% in Labrafil.

22. The pharmaceutical composition according to claim 20, consisting of:

a) about 125 mg of the active ingredient, about 1.2 mg of the surfactant, about 66.8 mg of

Gelucire, and about 267 mg of Labrafil; or

b) about 80 mg of the active ingredient, about 0.8 mg of the surfactant, about 42.7 mg of Gelucire, and about 170.9 mg of Labrafil.

23. An item of manufacture comprising the pharmaceutical composition of any one of claims 20 to 22 housed in a capsule; or a capsule of size 1 or smaller.

24. The compound according to claim 3, wherein the cancer is selected from the group consisting of colorectal adenocarcinoma, breast cancer, ovarian cancer, head and neck cancer, melanoma, gastric/gastroesophageal adenocarcinoma, esophageal adenocarcmoma, and adrenocorticoid carcinoma; preferably colorectal adenocarcinoma.

25. The compound according to any one of claims 1 to 2 or 5 to 6 or 9 to 12, wherein the paclitaxel is to be administered to the subject at a total weekly dose in a range from about 40 mg/m^2 to about 100 mg/m^2, preferably a total weekly dose of about 80 mg/m^2.

26. The compound according to claim 25, wherein the paclitaxel is to be administered to the subject through IV.

27. The compound according to any one of claims 1 to 3 or 5 to 12 or 25 to 26, wherein the cancer is selected from the group consisting of gastric and gastroesophageal adenocarcinoma, breast cancer, ovarian cancer, head and neck cancer, melanoma, and esophageal adenocarcinoma; preferably gastric and gastroesophageal adenocarcinoma.

28. The compound according to any one of claims 1 to 3 or 5 to 12 or 25 to 26, wherein the cancer is selected from the group consisting of colorectal adenocarcinoma, breast cancer, ovarian cancer, head and neck cancer, melanoma, gastric adenocarcinoma, and adrenocorticoid carcinoma.

29. The compound according to any one of claims 1 to 3 or 5 to 12 or 25 to 28, wherein the cancer is refractory, recurrent, or/and metastatic.

30. The compound according to any one of claims 1 to 3 or 5 to 12 or 25 to 29, wherein the cancer is associated:

a) with overexpression of STATS; or

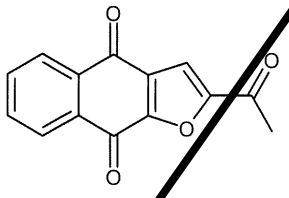
b) with nuclear β-catenin expression.

31. The compound according to any one of claims 1 to 3 or 5 to 12 or 25 to 30, the method comprising detecting a level of phosphorylated STAT3 (p-STAT3) in a patient tissue, where the level of p-STAT3 is used as a biomarker for patient selection.

32. The compound according to any one of claims 1 to 3 or 5 to 12 or 25 to 29 and 44, the method comprising detecting β-catenin expression in a patient's tissue, where such β-catenin expression is used as a biomarker for patient selection.

33. The compound according to claim 32, wherein significant β-catenin expression is detected in cell nucleus.

34. A compound having the structure

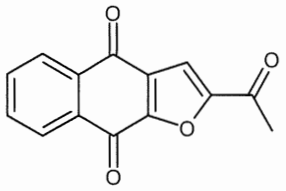


or a pharmaceutically acceptable salt, solvate, hydrate, or prodrug thereof, for use in the treatment of cancer in a patient whose β-catenin expression in cell is detected in cell nucleus.

35. The compound according to claim 34, wherein the β-catenin is at a level of medium to strong expression of β-catenin such that β-catenin is detected in 20% or more tumor cells.

36. A pharmaceutical composition, comprising:

(a) a therapeutically effective amount of an active ingredient having the structure



(b) polyoxylglycerides of which HLB is more than 10; and

(c) polyoxylglycerides of which HLB is less than 10.

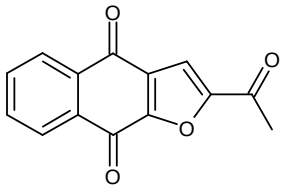
37. The pharmaceutical composition according to claim 36, wherein the composition further comprises a surfactant; preferably sodium lauryl sulfate (SLS) or sodium dodecyl sulfate.

38. The pharmaceutical composition according to claim 36 or claim 37, wherein the polyoxylglycerides of which HLB is more than 10 is selected from the group consisting of lauroyl polyoxylglycerides and stearoyl polyoxylglycerides.

39. The pharmaceutical composition according to any one of claims 36 to 38, wherein the poly-oxylglycerides of which HLB is less than 10 is linoleoyl polyoxylglycerides.

CLAIMS

1. Use of a compound having the structure of



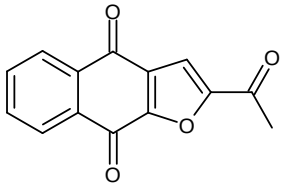
or a pharmaceutically acceptable salt, solvate, or hydrate thereof, in the manufacture of a medicament for use in a combination therapy of cancer in a subject,

wherein the medicament is administered in combination with an antimitotic agent or a pharmaceutically acceptable salt, solvate, or hydrate thereof, and

wherein the compound is administered at a total daily dose in a range from about 80 mg to about 2000 mg.

2. The use according to claim 1, wherein the antimitotic agent is selected from the group consisting of paclitaxel (Abraxane/Taxol), docetaxel (taxotere), BMS-275183, xyotax, tocosal, vinorlebine, vincristine, vinblastine, vindesine, vinzolidine, etoposide (VP-16), teniposide (VM-26), ixabepilone, larotaxel, ortataxel, tesetaxel, and ispinesib.

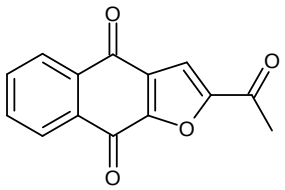
3. Use of a compound having the structure of



or a pharmaceutically acceptable salt, solvate, or hydrate thereof, in the manufacture of a medicament for use in a combination therapy of a cancer in a subject,

wherein the medicament is administered in combination with paclitaxel, and the compound is administered at a total daily dose in a range from about 80 mg to about 2000 mg.

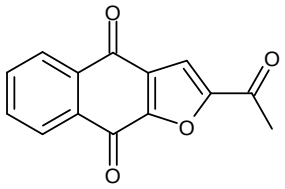
4. Use of a compound having the structure of



or a pharmaceutically acceptable salt, solvate, or hydrate thereof, in the manufacture of a medicament for use in a combination therapy of a cancer in a subject,

wherein the medicament is administered in combination of paclitaxel, the cancer is gastric cancer, gastroesophageal junction cancer, or esophageal cancer, and the compound is administered at a total daily dose in a range from about 80 mg to about 2000 mg.

5. Use of a compound having the structure

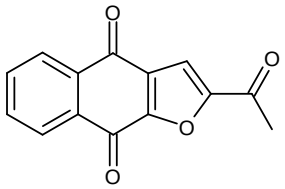


or a pharmaceutically acceptable salt, solvate, or hydrate thereof, in the manufacture of a medicament for use in a combination therapy of a cancer in a subject,

wherein the medicament is administered in combination with paclitaxel, and

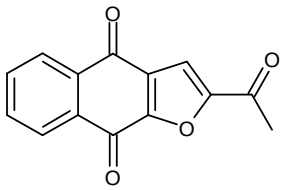
wherein the level of phosphorylated STAT3 (p-STAT3) in the subject's cancer cells is above a benchmark level.

6. Use of a compound having the structure



or a pharmaceutically acceptable salt, solvate, or hydrate thereof, in the manufacture of a medicament for use in the treatment of a cancer in a subject, wherein the level and/or subcellular localization of the cancer stemness markers β-catenin and / or NANOG in the subject's cancer cells is above a benchmark level.

7. Use of a compound having the structure of



or a pharmaceutically acceptable salt, solvate, or hydrate thereof, in the manufacture of a medicament for use in the treatment of a cancer in a patient,

wherein β-catenin is localized to the nucleus of the patient's cancer cells.

8. The use according to any one of claims 5 to 7, wherein the compound is administered at a total daily dose in a range from about 80 mg to about 2000 mg.

9. The use according to claim 8, wherein the compound is administered at a total daily dose of about 960 mg.

10. The use according to claim 8, wherein the compound is administered in two daily doses.

11. The use according to claim 10, wherein the interval between the two daily doses is in the range from about 4 hours to about 16 hours.

12. The use according to claim 10, wherein the interval between the two daily doses is about 12 hours.

13. The use according to any one of claims 1 to 7, wherein the compound is administered at a dose of about 80 mg BID, about 160 mg BID, about 320 mg BID, about 400 mg BID, about 480 mg BID, or about 500 mg BID.

14. The use according to claim 13, wherein the compound is administered at a dose of about 480 mg BID.

15. The use according to claim 13, wherein the medicament consists of about 27.2% by weight of the compound, about 0.3% by weight of a surfactant, about 14.5% by weight of Gelucire, and about 58.0% by weight of Labrafil.

16. The use according to claim 13, wherein the medicament consists of

a) about 125 mg of the active ingredient, about 1.2 mg of a surfactant, about 66.8 mg of Gelucire, and about 267 mg of Labrafil; or

b) about 80 mg of the active ingredient, about 0.8 mg of a surfactant, about 42.7 mg of Gelucire, and about 170.9 mg of Labrafil.

17. The use according to any one of claims 1 to 3 and 5 to 7, wherein the cancer is colorectal adenocarcinoma, breast cancer, ovarian cancer, head and neck cancer, melanoma, gastric adenocarcinoma, gastroesophageal adenocarcinoma, esophageal adenocarcinoma, or adrenocorticoid carcinoma.

18. The use according to any one of claims 1 to 5, wherein the paclitaxel is administered at a total weekly dose in a range from about 40 mg/m^2 to about 100 mg/m^2.

19. The use according to any one of claims 6, 7, and 18, wherein the paclitaxel is administered at a total weekly dose of about 80 mg/m^2.

20. The use according to claim 19, wherein the paclitaxel is administered to the subject through IV.

21. The use according to any one of claims 1 to 7, wherein the cancer is refractory, recurrent, or/and metastatic.

22. The use according to claim 6 or claim 7, wherein the β-catenin is detected in 20% or more of the cancer cells tested in the subject.

23. The use according to any one of claims 1 to 7, wherein the medicament comprises a therapeutically effective amount of the compound, polyoxylglycerides with a hydrophilic lipophilic balance (HLB) value of more than 10, and polyoxylglycerides with a hydrophilic lipophilic balance (HLB) value of less than 10.

24. The use according to claim 23, wherein the medicament further comprises a surfactant, preferably sodium lauryl sulfate (SLS) or sodium dodecyl sulfate (SDS).

25. The use according to claim 23 or claim 24, wherein the polyoxylglycerides with a hydrophilic lipophilic balance (HLB) value of more than 10 comprise lauroyl polyoxylglycerides or stearoyl polyoxylglycerides.

26. The use according to claim 23 or claim 24, wherein the polyoxylglycerides with an HLB value of less than 10 comprise linoleoyl polyoxylglycerides.

27. The use according to any one of claims 1 to 7, wherein the medicament is in a capsule.

28. The use according to claim 27, wherein the capsule comprises about 80 mg of the compound.