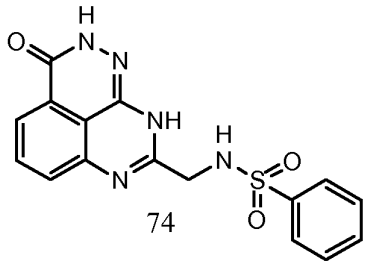
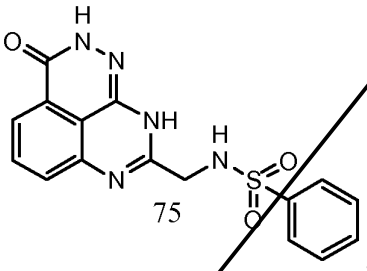
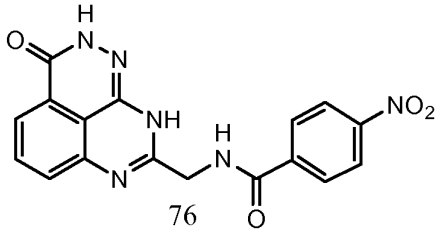

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, and pharmaceutically acceptable salts thereof.

[0033] The present invention also provides means to treat chemotherapy-induced peripheral neuropathy. According to an aspect of the invention, the compounds of the present invention are administered prior to, or together with, the administration of at least one chemotherapy agent to prevent the development of neuropathy symptoms or to mitigate the severity of such symptoms. According to a further aspect, the compounds of the present invention are administered after the administration of at least one chemotherapeutic agent to treat a patient for the symptoms of neuropathy or to mitigate the severity of such symptoms. In another aspect, the present invention provides a method to retard, delay, or arrest the growth of cancer cells in a mammal, comprising the administration of a chemotherapeutic agent, and further comprising the administration of a compound of Formula (I) or a pharmaceutically acceptable salt thereof in an amount sufficient to potentiate the anticancer activity of said chemotherapeutic agent.

[0034] Still other aspects and advantages of the present invention will become readily apparent by those skilled in the art from the following detailed description, wherein it is shown and described preferred embodiments of the invention, simply by way of illustration of the best mode contemplated of carrying out the invention. As will be realized the invention is capable of other and different embodiments, and its several details are capable of modifications in various obvious respects, without departing from the

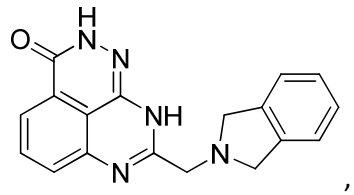
[0083] Salts, hydrates, esters, or solvates may also be formed with organic bases. Organic bases suitable for the formation of pharmaceutically acceptable base addition salts, hydrates, esters, or solvates of the compounds of the present invention include those that are non-toxic and strong enough to form such salts, hydrates, esters, or solvates. For purposes of illustration, the class of such organic bases may include mono-, di-, and trialkylamines, such as methylamine, dimethylamine, triethylamine and dicyclohexylamine; mono-, di- or trihydroxyalkylamines, such as mono-, di-, and triethanolamine; amino acids, such as arginine and lysine; guanidine; N-methyl-glucosamine; N-methyl-glucamine; L-glutamine; N-methyl-piperazine; morpholine; ethylenediamine; N-benzyl-phenethylamine; (trihydroxy-methyl)aminoethane; and the like. See, for example, "Pharmaceutical Salts," J. Pharm. Sci., 66:1, 1-19 (1977). Accordingly, basic nitrogen-containing groups can be quaternized with agents including: lower alkyl halides such as methyl, ethyl, propyl, and butyl chlorides, bromides and iodides; dialkyl sulfates such as dimethyl, diethyl, dibutyl and diamyl sulfates; long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides; and aralkyl halides such as benzyl and phenethyl bromides.

[0084] The acid addition salts, hydrates, esters, or solvates of the basic compounds may be prepared either by dissolving the free base of a compound of the present invention in an aqueous or an aqueous alcohol solution or other suitable solvent containing the appropriate acid or base, and isolating the salt by evaporating the solution. Alternatively, the free base of a compound of the present invention can be reacted with an acid, as well as reacting a compound of the present invention having an acid group thereon with a base, such that the reactions are in an organic solvent, in which case the salt separates directly or can be obtained by concentrating the solution.

[0085] "Pharmaceutically acceptable prodrug" refers to a derivative of the inventive compounds which undergoes biotransformation prior to exhibiting its pharmacological effect(s). The prodrug is formulated with the objective(s) of improved chemical stability, improved patient acceptance and compliance, improved bioavailability, prolonged duration of action, improved organ selectivity, improved formulation (e.g., increased hydrosolubility), and/or decreased side effects (e.g., toxicity). The prodrug can be readily prepared from the inventive compounds using methods known in the art, such as

CLAIMS

1. The use of the compound 37



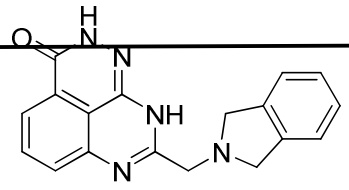
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or a pharmaceutically acceptable salt, ester, solvate or hydrate thereof for the manufacture of a pharmaceutical composition for treating a mammal having a cancer characterized by having a defect in the homologous recombination (HR) pathway of double-stranded DNA repair

2. The use of claim 1, wherein said mammal is a human.

3. The use of claim 1 or 2, wherein the cancer cells are selected from the group consisting of ACTH-producing tumors, acute lymphocytic leukemia, acute nonlymphocytic leukemia, cancer of the adrenal cortex, bladder cancer, brain cancer, breast cancer, cervical cancer, chronic lymphocytic leukemia, chronic myelocytic leukemia, colorectal cancer, cutaneous T-cell lymphoma, endometrial cancer, esophageal cancer, Ewing's sarcoma, gallbladder cancer, hairy cell leukemia, head and neck cancer, Hodgkin's lymphoma, Kaposi's sarcoma, kidney cancer, liver cancer, lung cancer (small and/or non-small cell), malignant peritoneal effusion, malignant pleural effusion, melanoma, mesothelioma, multiple myeloma, neuroblastoma, non-Hodgkin's lymphoma, osteosarcoma, ovarian cancer, ovary (germ cell) cancer, prostate cancer, pancreatic cancer, penile cancer, retinoblastoma, skin cancer, soft-tissue sarcoma, squamous cell carcinomas, stomach cancer, testicular cancer, thyroid cancer, trophoblastic neoplasms, uterine cancer, vaginal cancer, cancer of the vulva and Wilm's tumor.

4. The use of the compound 37



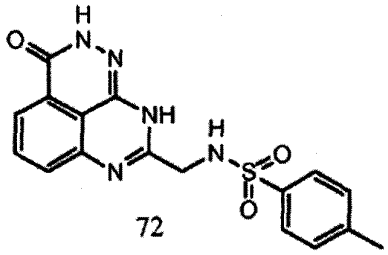
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or a pharmaceutically acceptable salt, ester, solvate or hydrate thereof for the manufacture of a pharmaceutical composition for treating a mammal having a cancer characterized by having a defect in the homologous recombination (HR) pathway of double-stranded DNA repair.

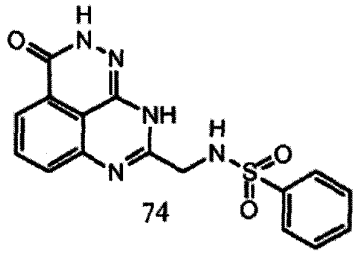
5. The use of claim 4, wherein said mammal is a human.

6. The use of claim 4 or 5, wherein the cancer has a phenotype selected from the group consisting of i) a BRCA-I defect, ii) a BRC A-2 defect, iii) a BRCA-I and BRCA-2 defect, and iv) Fanconi anemia.

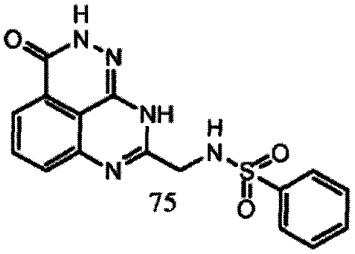
7. The use of any one of claims 4-6, wherein the cancer is selected from breast cancer or ovarian cancer.



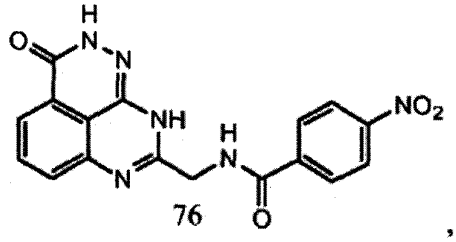
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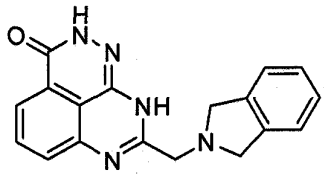
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and pharmaceutically acceptable salts thereof.

[0032a] In another embodiment the invention provides the compound 37



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or a pharmaceutically acceptable salt, ester, solvate or hydrate thereof.

[0033] The present invention also provides means to treat chemotherapy-induced peripheral neuropathy. According to an aspect of the invention, the compounds of the present invention are administered prior to, or together with, the administration of at least one chemotherapy agent to prevent the development of neuropathy symptoms or to mitigate the severity of such symptoms. According to a further aspect, the compounds of the present invention are administered after the administration of at least one chemotherapeutic agent to treat a patient for the symptoms of neuropathy or to mitigate the severity of such symptoms. In another aspect, the present invention provides a method to retard, delay, or arrest the growth of cancer cells in a mammal, comprising the administration of a chemotherapeutic agent, and further comprising the administration of a compound of Formula (I) or a pharmaceutically acceptable salt thereof in an amount sufficient to potentiate the anticancer activity of said chemotherapeutic agent.

[0034] Still other aspects and advantages of the present invention will become readily apparent by those skilled in the art from the following detailed description, wherein it is shown and described preferred embodiments of the invention, simply by way of illustration of the best mode contemplated of carrying out the invention. As will be realized the invention is capable of other and different embodiments, and its several details are capable of modifications in various obvious respects, without departing from the

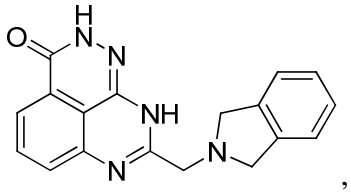
[0083] Salts, hydrates, esters, or solvates may also be formed with organic bases. Organic bases suitable for the formation of pharmaceutically acceptable base addition salts, hydrates, esters, or solvates of the compounds of the present invention include those that are non-toxic and strong enough to form such salts, hydrates, esters, or solvates. For purposes of illustration, the class of such organic bases may include mono-, di-, and trialkylamines, such as methylamine, dimethylamine, triethylamine and dicyclohexylamine; mono-, di- or trihydroxyalkylamines, such as mono-, di-, and triethanolamine; amino acids, such as arginine and lysine; guanidine; N-methyl-glucosamine; N-methyl-glucamine; L-glutamine; N-methyl-piperazine; morpholine; ethylenediamine; N-benzyl-phenethylamine; (trihydroxy-methyl)aminoethane; and the like. See, for example, "Pharmaceutical Salts," J. Pharm. Sci., 66:1, 1-19 (1977). Accordingly, basic nitrogen-containing groups can be quaternized with agents including: lower alkyl halides such as methyl, ethyl, propyl, and butyl chlorides, bromides and iodides; dialkyl sulfates such as dimethyl, diethyl, dibutyl and diamyl sulfates; long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides; and aralkyl halides such as benzyl and phenethyl bromides.

[0084] The acid addition salts, hydrates, esters, or solvates of the basic compounds may be prepared either by dissolving the free base of a compound of the present invention in an aqueous or an aqueous alcohol solution or other suitable solvent containing the appropriate acid or base, and isolating the salt by evaporating the solution. Alternatively, the free base of a compound of the present invention can be reacted with an acid, as well as reacting a compound of the present invention having an acid group thereon with a base, such that the reactions are in an organic solvent, in which case the salt separates directly or can be obtained by concentrating the solution.

[0085] "Pharmaceutically acceptable prodrug" refers to a derivative of the inventive compounds which undergoes biotransformation prior to exhibiting its pharmacological effect(s). The prodrug is formulated for improved chemical stability, improved patient acceptance and compliance, improved bioavailability, prolonged duration of action, improved organ selectivity, improved formulation (e.g., increased hydrosolubility), and/or decreased side effects (e.g., toxicity). The prodrug can be readily prepared from the inventive compounds using methods known in the art, such as

CLAIMS

1. The compound 37



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or a pharmaceutically acceptable salt or ester thereof.

2. A compound of claim 1, wherein the compound is a pharmaceutically acceptable salt, ester, solvate or hydrate of compound 37.

3. A pharmaceutical composition comprising the compound of claim 1 or claim 2, and a pharmaceutically acceptable carrier.

4. The pharmaceutical composition of claim 3, further comprising a chemotherapeutic agent selected from the group consisting of temozolomide, adriamycin, camptothecin, carboplatin, cisplatin, daunorubicin, docetaxel, doxorubicin, interferon-alpha, interferon-beta, interferon-gamma, interleukin 2, irinotecan, paclitaxel, topotecan, a taxoid, dactinomycin, danorubicin, 4'-deoxydoxorubicin, bleomycin, pilcamycin, mitomycin, neomycin, gentamycin, etoposide, 4-OH cyclophosphamide, a platinum coordination complex, and mixtures thereof.

5. The pharmaceutical composition of claim 4, wherein said chemotherapeutic agent is temozolomide, or a salt thereof.

6. Use of a compound of Claim 1 or Claim 2, or a pharmaceutical composition of any one of claims 3 to 5, for the manufacture of a medicament for use in chemosensitizing cancer cells in a mammal in need of chemotherapy.

7. Use of a compound of Claim 1 or Claim 2, or a pharmaceutical composition of claim 3, for the manufacture of a medicament for use in radiosensitizing cancer cells in a

mammal in need of radiation therapy.

8. The use of claim 6 or claim 7, wherein the cancer cells are selected from the group consisting of ACTH-producing tumors, acute lymphocytic leukemia, acute nonlymphocytic leukemia, cancer of the adrenal cortex, bladder cancer, brain cancer, breast cancer, cervical cancer, chronic lymphocytic leukemia, chronic myelocytic leukemia, colorectal cancer, cutaneous T-cell lymphoma, endometrial cancer, esophageal cancer, Ewing's sarcoma, gallbladder cancer, hariy cell leukemia, head and neck cancer, Hodgkin's lymphoma, Kaposi's sarcoma, kidney cancer, liver cancer, lung cancer (small and/or non-small cell), malignant peritoneal effusion, malignant pleural effusion, melanoma, mesothelioma, multiple myeloma, neuroblastoma, non-Hodgkin's lymphoma, osteosarcoma, ovarian cancer, ovary (germ cell) cancer, prostate cancer, pancreatic cancer, penile cancer, retinoblastoma, skin cancer, soft-tissue sarcoma, squamous cell carcinomas, stomach cancer, testicular cancer, thyroid cancer, trophoblastic neoplasms, uterine cancer, vaginal cancer, cancer of the vulva and the Wilm's tumor.

9. The use of any one of claims 6 to 8, of a compound of Claim 1 or Claim 2 which is a pharmaceutically acceptable salt of compound 37, or of a pharmaceutical composition of any of claims 3 to 5 which comprises a pharmaceutically acceptable salt, wherein said pharmaceutically acceptable salt comprises an organic acid.

10. Use of a compound of Claim 1 or Claim 2, or a pharmaceutical composition of any one of claims 3 to 5, for the manufacture of a medicament for use in treating a mammal having a cancer characterized by having a defect in the homologous recombination (HR) pathway of double-stranded DNA repair.

11. The use of claim 10, wherein said mammal is a human.

12. The use of claim 10 or claim 11, wherein the cancer has a phenotype selected from the group consisting of i) a BRCA-I- defect, ii) a BRC A-2 defect, iii) a BRCA-I and

BRCA-2 defect, and iv) Fanconi anemia.

13. The use of any one of claims 10 to 12, wherein the cancer is selected from breast cancer or ovarian cancer.

14. The use of any one of claims 10 to 13, of a compound of Claim 1 or Claim 2 which is a pharmaceutically acceptable salt, or of a pharmaceutical composition of any of claims 3 to 5 which comprises a pharmaceutically acceptable salt, wherein said pharmaceutically acceptable salt comprises an organic acid.