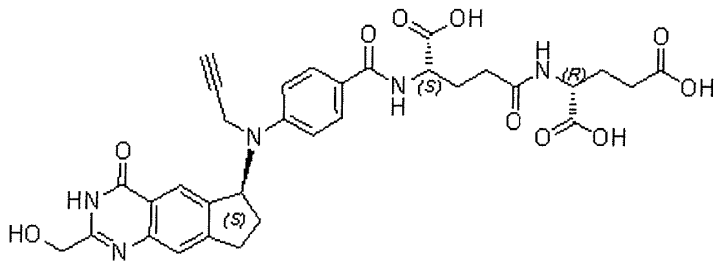
CLAIMS.

1. A compound of formula I



or a pharmaceutically acceptable salt or ester thereof for the treatment of cancer wherein

(i) the cancer is one that has the characteristic of being a type prone to being or becoming refractory or resistant to platinum drug based therapy and

(ii) the treatment is with a dose of between 1mg/m^2 and 30mg/m^2 of compound per patient body surface area per administration.

2. A compound for treatment as claimed in claim 1 characterised in that the cancer is platinum refractory or resistant.

3. A compound for treatment as claimed in claim 1 characterised in that the cancer is selected from ovarian, endometrial, mesothelial, non-small cell lung and cancers derived from one of these.

4. A compound for treatment as claimed in claim 1, 2 or 3 characterised in that is selected from those expressing α-folate receptors (FR-α).

5. A compound for treatment as claimed in claim 4 characterised in that the cancer expresses higher than background non-cancerous tissue levels of α-folate receptors.

6. A compound for treatment as claimed in any one of the preceding claims characterised in that the cancer is an ovarian cancer.

7. A compound for treatment as claimed in claim any one of the preceding claims characterised in that the cancer is epithelial ovarian, fallopian tube or peritoneal cancer.

8. A compound for treatment as claimed in claim 6 or claim 7 characterised in that the cancer is serous ovarian cancer.

9. A compound for treatment as claimed in claim 8 characterised in that the cancer is High-Grade Serous Ovarian Cancer (HGSOC).

10. A compound for treatment as claimed in any one of the preceding claims characterised in that the dose is administered intraperitoneally (IP) or intravenously (IV).

11. A compound for use as claimed in any one of the preceding claims characterised in that the dose is 3mg/m^2 to 30mg/m^2 of compound per patient body surface area per administration,

12. A compound as claimed in any one of the preceding claims characterised in that the treatment administers each dose as individual infusions spaced between 10 and 28 days apart.

13. A compound as claimed in claim 12 characterised in that the infusions are spaced between 10 and 21 days apart.

14. A compound as claimed in claim 13 characterised in that the infusions are administered at dosing interval of about 14 days.

15. A compound as claimed in claim 14 characterised in that the treatment is with a cumulative maximum of 150mg/m^2 of compound per patient body surface area over the course of all the infusions.

16. A compound as claimed in claim 15 characterised in that the maximum cumulative dose is 144mg/m^2.

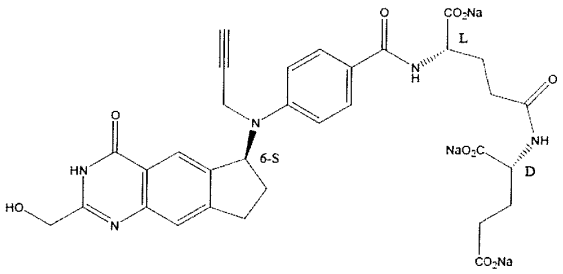
17. A compound as claimed in any one of the preceding claims characterised in that the treatment is with an infusion of 1mg/m^2 to 20mg/m^2 per administration.

18. A compound as claimed in claim 17 characterised in that the treatment is with an infusion of 10mg/m^2 to 15mg/m^2 per administration.

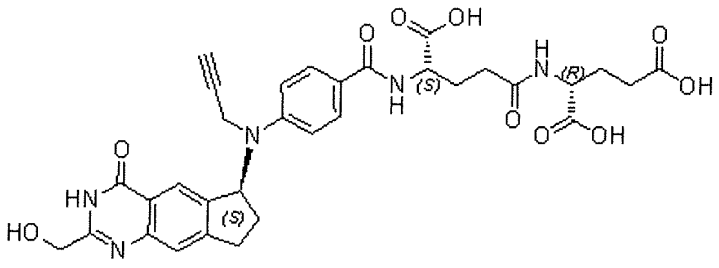
19. A compound as claimed in claim 16 characterised in that the treatment is with an infusion of about 12mg/m^2 per administration.

20. A compound as claimed in any one of claims 1 to 19 characterised in that the dose is added to a saline drip.

21. A compound for use as claimed in any one of the preceding claims characterised in that it is the trisodium salt of formula II



22. A method for treating a patient suffering from a cancer that has the characteristic of being a type prone to being or becoming refractory or resistant to platinum drug based therapy and wherein the treatment is with a dose of between 1mg/m^2 and 30mg/m^2 of compound per patient body surface area per administration of a compound of formula I



or a pharmaceutically acceptable salt or ester thereof for the treatment of cancer.

23. A method as claimed in claim 22 wherein the treatment is as described in any one of claims 1 to 21.

24. A method as claimed in claim 22 or 23 wherein the treatment with the compound of the formula I is given in combination with a regimen administering a therapeutically effective amount of one or more further anticancer agents.

25. A method as claimed in claim 24, wherein the treatment comprises administering a composition comprising the compound of the formula I and the one or more further anticancer agents.

26. A method as claimed in claim 24, wherein the compound of the formula I and the one or more further anticancer agents are administered separately.

27. A method as claimed in claim 24, wherein the administration of the compound of the formula I and the administration of the one or more further anticancer agents are separated by 12 hours.

28. A method as claimed in claim 24, wherein the administration of the compound of the formula I and the administration of the one or more further anticancer agents are separated by 24 hours.

29. A method as claimed in claim 24, wherein the administration of the compound of the formula I and the administration of the one or more further anticancer agents are separated by 36 hours.

30. A method as claimed in claim 24, wherein the administration of the compound of the formula I and the administration of the one or more further anticancer agents are separated by 38 hours.

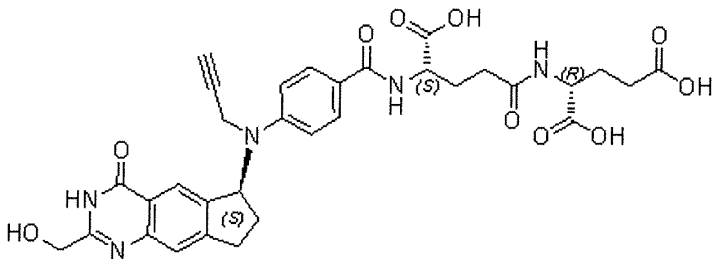
31. A method as claimed in claim 24, wherein the administration of the compound of the formula I and the administration of the one or more further anticancer agents are performed on alternate weeks of a 7 day dosing schedule.

32. A method as claimed in claim 24, wherein the administration of the compound of the formula I and the administration of the one or more further anticancer agents are performed on alternate weeks of a 14 day dosing schedule.

33. A method as claimed in claims 24 to 32 wherein the one or more further anticancer agents used in this combination therapy are selected from Cisplatin, Carboplatin, Doxorubicin, Bevacizumab Gemcitabine, Topetecan, Paclitaxel, Docetaxel, Etoposide, Nanoparticle albumin-bound paclitaxel, Lynparza (olaparib), Rubraca (rucaparib), Zejula (niraparib). Tecentriq (atezoizumab), Bavercio (avelumab).

34. A method as claimed in claims 24 to 32 wherein the treatment includes combinations of the compound of formula I administered together with a regimen administering bevacizumab in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan.

35. A dosage form of a compound of formula I



comprising a single dosage unit containing said compound or a pharmaceutically acceptable salt or ester thereof characterised in that the amount of said compound in the dosage unit is between 0.5mg and 40mg.

36. A dosage form as claimed in claim 35, containing from 0.5mg to 40mg of the compound of formula I or salt or ester thereof.

37. A dosage unit as claimed in claim 35 or 36 containing between 1mg and 30mg of the compound of formula I or salt or ester thereof.

38. A dosage unit as claimed in claim 35, 36, 37 containing between 5mg and 26mg of the compound of formula I or a salt or ester thereof.

39. A dosage unit as claimed in claim 35, 36, 37, or 38 containing between 10 and 24mg of the compound or salt or ester of formula I.

40. A dosage form as claimed in any one of claims 35 to 39 characterised in that it comprises a container of the compound of formula I or its salt or ester.

41. A dosage form as claimed in claim 40 characterised in that it comprises the sodium salt, as a sterile solid or aqueous solution.

42. A dosage form as claimed in claim 41 characterised in that the aqueous solution is of compound in water for injection or saline.

43. A dosage form as claimed in any one of claims 35 to 42 characterised in that it is a vial containing an aqueous solution of the compound, salt or ester.

44. A dosage form as claimed in claim 43 containing from 1mg to 40mg of the compound of formula I or salt or ester thereof.

45. A dosage form as claimed in any one of claims 35 to 44 characterised in that it comprises a vial containing between 1 and 40mg of a compound of formula I or a salt or ester thereof in dried solid or aqueous solution form.

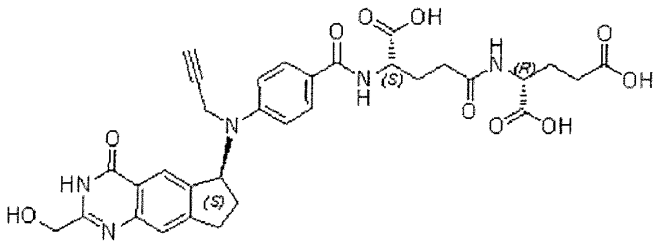
46. A dosage form as claimed in claim 45 containing from 5mg to 30mg of the compound of formula I or salt or ester thereof.

47. A dosage form as claimed in any one of claims 35 to 46 characterised in that it comprises a vial containing 5mg to 30mg of a compound of formula I or a salt or ester thereof in dried solid or aqueous solution form.

48. A dosage form as claimed in claim 47 containing from 10mg to 24mg of the compound of formula I or salt or ester thereof.

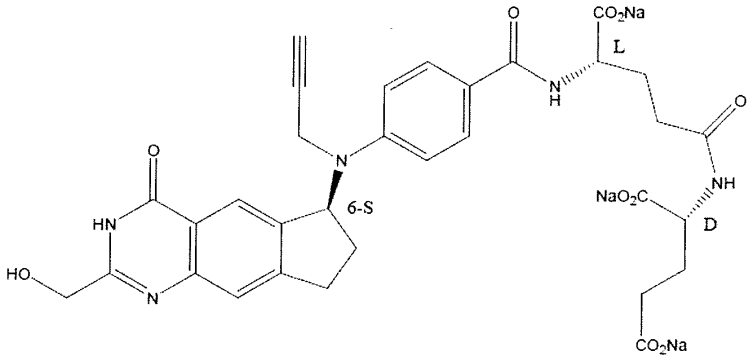
49. A dosage form as claimed in any one of claims 35 to 48 characterised in that it comprises a vial containing 10 to 24mg of a compound of formula I or a salt or ester thereof in dried solid or aqueous solution form.

50. A compound chosen from formula I



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formula II



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and pharmaceutically acceptable salts or esters thereof, for the treatment of cancer,

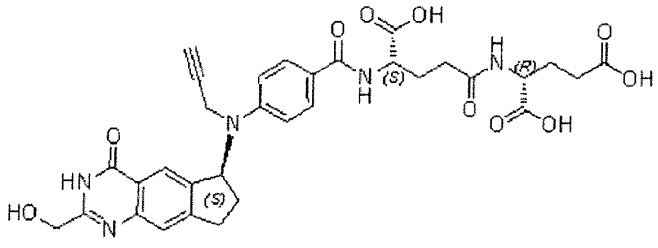
wherein

(i) the cancer is one that has the characteristic of being a type prone to being or becoming refractory or resistant to platinum drug based therapy;

(ii) the treatment is with a dose of from 1mg/m^2 to 30mg/m^2 of compound per patient body surface area per administration; and

(iii) the dose is administered intraperitoneally (IP).

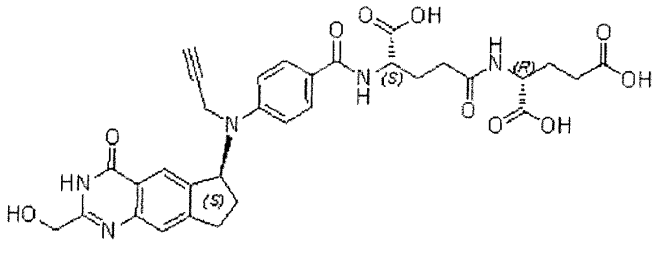
51. A method for treating a patient suffering from a cancer that has the characteristic of being a type prone to being or becoming refractory or resistant to platinum drug based therapy and wherein the treatment is with a dose of from 1mg/m^2 to 30mg/m^2 of compound per patient body surface area per administration of a compound of formula I



or a pharmaceutically acceptable salt or ester thereof for the treatment of cancer, wherein the dose is administered intraperitoneally (IP).

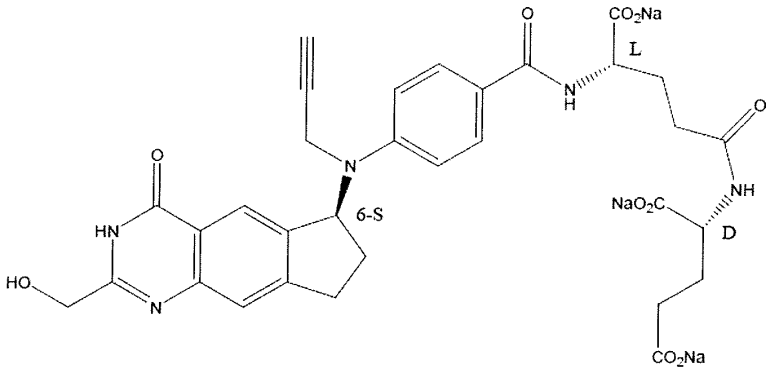
52. A method as claimed in claim 51 wherein the treatment with the compound of the formula I is given in combination with a regimen administering a therapeutically effective amount of one or more further anticancer agents.

53. A compound chosen from formula I



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formula II



,

and pharmaceutically acceptable salts or esters thereof, for the treatment of cancer, wherein

(i) the cancer is one that has the characteristic of being a type prone to being or becoming refractory or resistant to platinum drug based therapy;

(ii) the treatment is with a dose of from 1mg/m^2 to 30mg/m^2 of compound per patient body surface area per administration; and

(iii) wherein at least one side effect associated with classical thymidylate synthase inhibitors or alpha folate receptor antibody drug conjugates is not observed.

54. The compound according to claim 53, wherein the at least one side effect is chosen from neutropenia, diarrhoea, hair loss, blurred vision or nausea.

55. A compound for treatment as claimed in claim 53 or 54 characterised in that the cancer is selected from ovarian, endometrial, mesothelial, non-small cell lung and cancers derived from one of these.

56. A compound for treatment as claimed in claim 53, 54, or 55 characterised in that it is selected from those expressing α-folate receptors (FR-α).

57. A compound for treatment as claimed in claim 56 characterised in that the cancer expresses higher than background non-cancerous tissue levels of α-folate receptors.

58. A compound for treatment as claimed in any one of claims 53 to 57 characterised in that the cancer is an ovarian cancer.

59. A compound for treatment as claimed in any one of claims 53 to 58 characterised in that the cancer is epithelial ovarian, fallopian tube or peritoneal cancer.

60. A compound for treatment as claimed in claim 58 or claim 59 characterised in that the cancer is serous ovarian cancer.

61. A compound for treatment as claimed in claim 60 characterised in that the cancer is High-Grade Serous Ovarian Cancer (HGSOC).

62. A compound for treatment as claimed in any one of claims 53 to 61 characterised in that the dose is administered intraperitoneally (IP) or intravenously (IV).

63. A compound for use as claimed in any one of claims 53 to 62 characterised in that the dose is 3mg/m^2 to 30mg/m^2 of compound per patient body surface area per administration,

64. A compound as claimed in any one claims 53 to 63 characterised in that the treatment administers each dose as individual infusions spaced between 10 and 28 days apart.

65. A compound as claimed in claim 64 characterised in that the infusions are spaced between 10 and 21 days apart.

66. A compound as claimed in claim 65 characterised in that the infusions are administered at dosing interval of about 14 days.

67. A compound as claimed in claim 66 characterised in that the treatment is with a cumulative maximum of 150mg/m^2 of compound per patient body surface area over the course of all the infusions.

68. A compound as claimed in claim 67 characterised in that the maximum cumulative dose is 144mg/m^2.

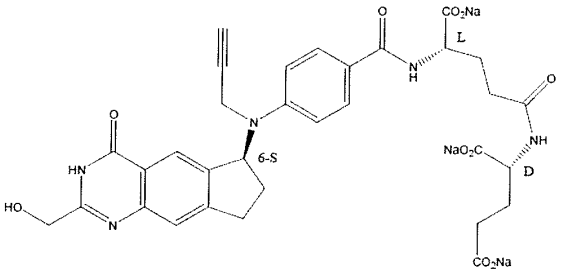
69. A compound as claimed in any one of claims 53 to 68 characterised in that the treatment is with an infusion of 1mg/m^2 to 20mg/m^2 per administration.

70. A compound as claimed in claim 69 characterised in that the treatment is with an infusion of 10mg/m^2 to 15mg/m^2 per administration.

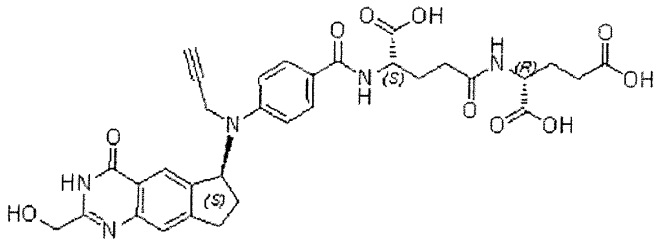
71. A compound as claimed in claim 68 characterised in that the treatment is with an infusion of about 12mg/m^2 per administration.

72. A compound as claimed in any one of claims 53 to 71 characterised in that the dose is added to a saline drip.

73. A compound for use as claimed in any one of claims 53 to 72 characterised in that it is the trisodium salt of formula II

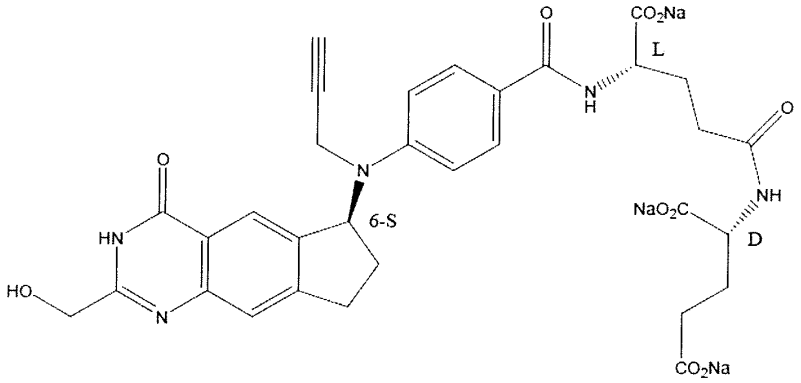


74. A compound chosen from formula I



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formula II



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and pharmaceutically acceptable salts or esters thereof, for the treatment of cancer, wherein

(i) the cancer is one that has the characteristic of being a type prone to being or

becoming refractory or resistant to platinum drug based therapy;

(ii) the treatment is with a dose that achieves a concentration of about 0.5 μM or greater of the compound for at least 72hrs.

75. The compound according to claim 74, wherein the treatment is with a dose that achieves a concentration of about 0.7 μM or greater of the compound for at least 36hrs.

76. The compound according to claim 74, wherein the treatment is with a dose that achieves a concentration of about 0.9 μM or greater of the compound for at least 24hrs.

77. A compound for treatment as claimed in claim 74, 75 or 76 characterised in that the cancer is selected from ovarian, endometrial, mesothelial, non-small cell lung and cancers derived from one of these.

78. A compound for treatment as claimed in claim 74, 75, 76, or 77 characterised in that it is selected from those expressing α-folate receptors (FR-α).

79. A compound for treatment as claimed in claim 78 characterised in that the cancer expresses higher than background non-cancerous tissue levels of α-folate receptors.

80. A compound for treatment as claimed in any one of claims 74 to 79 characterised in that the cancer is an ovarian cancer.

81. A compound for treatment as claimed in any one of claims 74 to 80 characterised in that the cancer is epithelial ovarian, fallopian tube or peritoneal cancer.

82. A compound for treatment as claimed in claim 80 or claim 81 characterised in that the cancer is serous ovarian cancer.

83. A compound for treatment as claimed in claim 82 characterised in that the cancer is High-Grade Serous Ovarian Cancer (HGSOC).

84. A compound for treatment as claimed in any one of claims 74 to 83 characterised in that the dose is administered intraperitoneally (IP) or intravenously (IV).

85. A compound for use as claimed in any one of claims 74 to 84 characterised in that the dose is 3mg/m^2 to 30mg/m^2 of compound per patient body surface area per administration,

86. A compound as claimed in any one claims 74 to 85 characterised in that the treatment administers each dose as individual infusions spaced between 10 and 28 days apart.

87. A compound as claimed in claim 86 characterised in that the infusions are spaced between 10 and 21 days apart.

88. A compound as claimed in claim 87 characterised in that the infusions are administered at dosing interval of about 14 days.

89. A compound as claimed in claim 88 characterised in that the treatment is with a cumulative maximum of 150mg/m^2 of compound per patient body surface area over the course of all the infusions.

90. A compound as claimed in claim 89 characterised in that the maximum cumulative dose is 144mg/m^2.

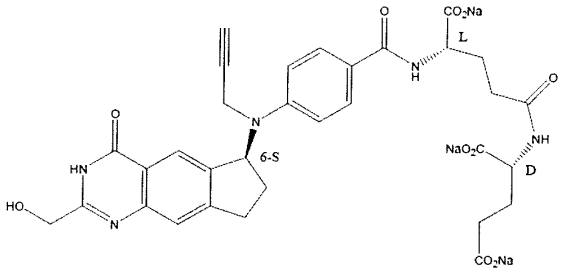
91. A compound as claimed in any one of claims 74 to 90 characterised in that the treatment is with an infusion of 1mg/m^2 to 20mg/m^2 per administration.

92. A compound as claimed in claim 91 characterised in that the treatment is with an infusion of 10mg/m^2 to 15mg/m^2 per administration.

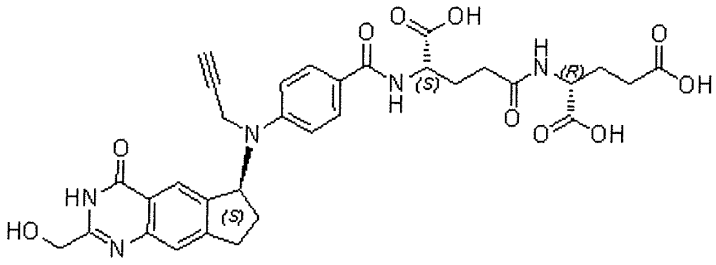
93. A compound as claimed in claim 90 characterised in that the treatment is with an infusion of about 12mg/m^2 per administration.

94. A compound as claimed in any one of claims 74 to 93 characterised in that the dose is added to a saline drip.

95. A compound for use as claimed in any one of claims 74 to 94 characterised in that it is the trisodium salt of formula II



96. Use of a compound of formula I



or a pharmaceutically acceptable salt or ester thereof

for the manufacture of a medicament for the treatment of cancer wherein

(i) the cancer is one that has the characteristic of being a type prone to being or becoming refractory or resistant to platinum drug based therapy and

(ii) the treatment is with a dose of between 1mg/m^2 and 30mg/m^2 of compound per patient body surface area per administration.

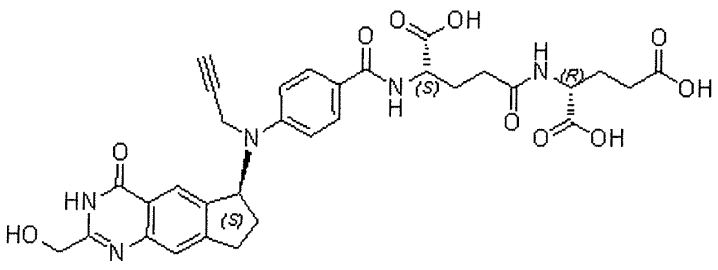
97. A compound as claimed in Claim 1 wherein the treatment is with a dosage regimen selected from the group

- a dose of 1 to 10mg/m^2 administered in a 28 day cycle at 7 day intervals on day 1, 8, 15 and 22.
- a dose of 6 to 14mg/m^2 administered in a 28 day cycle at 14 day intervals on day 1 and 15
- a dose of 10 to 30mg/m^2 administered in a 21 day cycle on day 1.

98. A compound as claimed in Claim 97 wherein the dosage regimen is a dose of 10 to 14mg/m^2 administered in a 28 day cycle at 14 day intervals on day 1 and 15.

99. A compound as claimed in Claim 97 wherein the dosage regimen is a dose of 10 to 14mg/m^2 administered in a 21 day cycle on day 1.

100. A pharmaceutical composition for the treatment of cancer comprising a compound of formula I



or a pharmaceutically acceptable salt or ester thereof for the treatment of cancer wherein

(i) the cancer is one that has the characteristic of being a type prone to being or becoming refractory or resistant to platinum drug based therapy and

(ii) the treatment is with a dose of between 1mg/m^2 and 30mg/m^2 of compound per patient body surface area per administration.