CLAIMS

1. Use of a composition comprising aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for treating CRC in a patient, wherein the composition is for simultaneous administration.

2. Use of a composition comprising aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for treating CRC in a patient, wherein the composition is for sequential administration.

3. Use of a composition comprising aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for treating CRC in a patient, wherein the composition is for administration spaced out over a period of time so as to obtain the maximum efficacy of the combination.

4. Use of any one of claims 1 to 3, wherein said patient has previously been treated with chemotherapy, radiotherapy or surgery.

5. Use of any one of claims 1 to 4 wherein said patient has previously been treated with therapy based on oxaliplatin or on bevacizumab.

6. Use of any one of claims 4 and 5 wherein said patient has failed with chemotherapy, radiotherapy or surgery.

7. Use of any one of claims 1 to 6 wherein CRC is a Metastatic CRC.

8. Use of any one of claims 1 to 7 wherein folinic acid at a dosage comprised between about 200 mg/m^2 and about 600 mg/m^2, 5-fluorouracil (5-FU) at a dosage comprised between about 2000 mg/m^2 and about 4000 mg/m^2, irinotecan at a dosage comprised between about 100 mg/m^2 and about 300 mg/m^2 and aflibercept at a dosage comprised between about 1 mg/kg and about 10 mg/kg are to be administered to patient.

9. Use of any one of claims 1 to 8 wherein folinic acid at a dosage of about 400 mg/m^2, 5-fluorouracil (5-FU) at a dosage of about 2800 mg/m^2, irinotecan at a dosage of about 180 mg/m^2 and aflibercept at a dosage of about 4 mg/kg are to be administered to patient.

10. Use of any one of claims 1 to 9 wherein folinic acid is to be administered intravenously at a dosage of about 400 mg/m^2, 5-fluorouracil (5-FU) is to be administered intravenously at a dosage of about 2800 mg/m^2, irinotecan is to be administered intravenously at a dosage of about 180 mg/m^2 and aflibercept is to be administered

intravenously at a dosage of about 4 mg/kg and wherein the combination is to be administered every two weeks.

11. Use of any one of claims 1 to 10 wherein the folinic acid, 5-fluorouracil (5-FU), irinotecan and aflibercept are to be administered intravenously every two weeks for a period comprised between 9 and 18 weeks.

12. Use of any one of claims 2 to 11 wherein the folinic acid is to be administered intravenously immediately after aflibercept administration.

13. Use of any one of claims 2 to 12 wherein the folinic acid is to be administered intravenously immediately after aflibercept administration over a period of about 2 hours.

14. Use of any one of claims 2 to 13 wherein the irinotecan is to be administered intravenously immediately after aflibercept administration.

15. Use of any one of claims 2 to 14 wherein the irinotecan is to be administered intravenously immediately after aflibercept administration over a period of about 90 minutes

16. Use of any one of claims 2 to 15 wherein the 5-fluorouracil (5-FU) is to be administered immediately after aflibercept administration.

17. Use of any one of claims 2 to 16 wherein a first quantity of 5-fluorouracil (5-FU) is to be administered intravenously immediately after aflibercept administration and a second quantity of 5-FU is to be administered intravenously after the first quantity in continuous infusion.

18. Use of any one of claims 2 to 17 wherein about 400 mg/m^2 of 5-fluorouracil (5-FU) is to be administered intravenously over a period of 2 to 4 minutes after aflibercept administration and wherein 2400 mg/m^2 of 5-FU is to be administered intravenously over almost 46 hours after the administration of the 400 mg/m^2 in continuous infusion.

19. Use of any one of claims 1 to 18 wherein the patient has liver metastases.

CLAIMS

1. Use of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for treating Colorectal Cancer (CRC) or Colorectal Cancer (CRC) symptom in a patient.

2. Use of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for increasing Overall Survival (OS) in a patient afflicted with CRC.

3. Use of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for increasing Progression Free Survival (PFS) in a patient afflicted with CRC.

4. Use of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for increasing Overall Response Rate (ORR) in a patient afflicted with CRC.

5. Use of any one of claims 1 to 4, wherein the medicament is safe and effective.

6. Use of any one of claims 1 to 5, wherein said patient has already been treated for the CRC or CRC symptom.

7. Use of any one of claims 1 to 6, wherein said patient has previously been treated with chemotherapy, radiotherapy or surgery.

8. Use of any one of claims 1 to 7 wherein said patient has previously been treated with therapy based on oxaliplatin or on bevacizumab.

9. Use of any one of claims 7 and 8 wherein said patient has failed with chemotherapy, radiotherapy or surgery.

10. Use of any one of claims 1 to 9 wherein CRC is a Metastatic CRC.

11. Use of any one of claims 1 to 10 wherein folinic acid at a dosage comprised between about 200 mg/m^2 and about 600 mg/m^2, 5-fluorouracil (5-FU) at a dosage comprised between about 2000 mg/m^2 and about 4000 mg/m^2 , irinotecan at a dosage comprised between about 100 mg/m^2 and about 300 mg/m^2 and aflibercept at a dosage comprised between about 1 mg/kg and about 10 mg/kg are to be administered to patient.

12. Use of any one of claims 1 to 11 wherein folinic acid at a dosage of about 400 mg/m^2, 5-fluorouracil (5-FU) at a dosage of about 2800 mg/m^2, irinotecan at a dosage of about 180 mg/m^2 and aflibercept at a dosage of about 4 mg/kg are to be administered to patient.

13. Use of any one of claims 1 to 12 wherein folinic acid is administered intravenously at a dosage of about 400 mg/m^2, 5-fluorouracil (5-FU) is administered intravenously at a dosage of about 2800 mg/m^2, irinotecan is to be administered intravenously at a dosage of about 180 mg/m^2 and aflibercept is administered intravenously at a dosage of about 4 mg/kg and wherein the combination is to be administered every two weeks.

14. Use of any one of claims 1 to 13 wherein the folinic acid, 5-fluorouracil (5-FU), irinotecan and aflibercept are to be administered intravenously every two weeks for a period comprised between 9 and 18 weeks.

15. Use of any one of claims 1 to14 wherein the folinic acid is to be administered intravenously immediately after aflibercept administration.

16. Use of any one of claims 1 to 15 wherein the folinic acid is to be administered intravenously immediately after aflibercept administration over a period of about 2 hours.

17. Use of any one of claims 1 to 16 wherein the irinotecan is to be administered intravenously immediately after aflibercept administration.

18. Use of any one of claims 1 to 17 wherein the irinotecan is to be administered intravenously immediately after aflibercept administration over a period of about 90 minutes

19. Use of any one of claims 1 to 18 wherein the 5-fluorouracil (5-FU) is to be administered immediately after aflibercept administration.

20. Use of any one of claims 1 to 19 wherein a first quantity of 5-fluorouracil (5-FU) is to be administered intravenously immediately after aflibercept administration and a second quantity of 5-FU is to be administered intravenously after the first quantity in continuous infusion.

21. Use of any one of claims 1 to 20 wherein about 400 mg/m^2 of 5-fluorouracil (5-FU) is to be administered intravenously over a period of 2 to 4 minutes after aflibercept administration and wherein 2400 mg/m^2 of 5-FU is to be administered intravenously over almost 46 hours after the administration of the 400 mg/m^2 in continuous infusion.

22. Use of any one of claims 1 to 21 wherein the patient has liver metastases.

23. Use of a composition comprising aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for treating CRC, wherein the composition is for simultaneous administration.

24. Use of a composition comprising aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for treating CRC, wherein the composition is for sequential administration.

25. Use of a composition comprising aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan in the manufacture of a medicament for treating CRC, wherein the composition is for administration spaced out over a period of time so as to obtain the maximum efficacy of the combination.

26. An article of manufacture for use in treating Colorectal Cancer (CRC) comprising:

a) a packaging material

b) aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinotecan; and

c) a label or package insert contained within said packaging material indicates that aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan is effective for the treatment of CRC in the manufacture of an article for treating CRC.

27. An article of manufacture for use according to claim 26, wherein said treatment of CRC comprises improvement in Overall Survival (OS).

28. An article of manufacture for use according to claim 26, wherein said treatment of CRC comprises improvement in Progression Free Survival (PFS).

29. An article of manufacture for use according to claim 26, wherein said treatment of CRC comprises improvement in Overall Response Rate (ORR).

30. Composition comprising therapeutically effective amounts of aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan and comprising a pharmaceutically acceptable carrier for treating patients with CRC.

31. A kit for use in treating patients with CRC comprising:

a) the compounds aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinotecan; and

b) a label or package insert contained within said kit indicating that aflibercept is to be used in combination with folinic acid, 5-fluorouracil (5-FU) and irinotecan (FOLFIRI) or that folinic acid, 5-fluorouracil (5-FU) and irinotecan (FOLFIRI) is to be used in combination with Aflibercept.

32. A kit comprising in separate containers pharmaceutical compositions for combined use in treating CRC in a patient which comprises (1) a pharmaceutical composition comprising aflibercept , (2) a pharmaceutical composition comprising folinic acid, (3) a pharmaceutical composition comprising 5-fluorouracil (5-FU) and (4) a pharmaceutical composition comprising irinotecan.