CLAIMS

1. Use of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinocetan 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 irinocetan 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 irinocetan 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 irinocetan 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 , irinocetan 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 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, irinocetan at a dosage of about 180 mg/m^2 and aflibercept at a dosage of about 4 mg/kg are 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, irinocetan is 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 comination is administered every two weeks.

14. Use of any one of claims 1 to 13 wherein the folinic acid, 5-fluorouracil (5-FU), irinocetan and aflibercept are 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 administered intravenously immediately after aflibercept administration.

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

18. Use of any one of claims 1 to 17 wherein the irinocetan is 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 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 administered intravenously immediately after aflibercept administration and a second quantity of 5-FU is administered intravenously after the first quantity in continous infusion.

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

a) a packaging material

b) aflibercept, 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 irinocetan is effective for the treatment of CRC.

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

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

29. An article of manufacture 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 irinocetan and comprising a pharmaceutically acceptable carrier for treating patients with CRC.

31. A kit for treating patients with CRC comprising:

a) at least one compound chosen from the list consisting of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinocetan; 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 irinocetan (FOLFIRI) or that folinic acid, 5-fluorouracil (5-FU) and irinocetan (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 irinocetan.

CLAIMS

1. A method of treating Colorectal Cancer (CRC) or Colorectal Cancer (CRC) symptom in a patient in need thereof, said method comprising administering to said patient therapeutically effective amounts of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinocetan.

2. A method of increasing Overall Survival (OS) in a patient afflicted with CRC, said method comprising administering to said patient therapeutically effective amounts of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinocetan.

3. A method of increasing Progression Free Survival (PFS) in a patient afflicted with CRC, said method comprising administering to said patient therapeutically effective amounts of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinocetan.

4. A method of increasing Overall Response Rate (ORR) in a patient afflicted with CRC, said method comprising administering to said patient therapeutically effective amounts of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinocetan.

5. A method according to any one of claims 1 to 4 which is safe and effective.

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

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

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

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

10. A method according to any one of claims 1 to 9 wherein CRC is a Metastatic CRC.

11. A method according to 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 , irinocetan 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 administered to patient.

12. A method according to 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, irinocetan at a dosage of about 180 mg/m^2 and aflibercept at a dosage of about 4 mg/kg are administered to patient.

13. A method according to 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, irinocetan is 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 comination is administered every two weeks.

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

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

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

17. A method according to any one of claims 1 to 16 wherein the irinocetan is administered intravenouslyimmediately after aflibercept administration.

18. A method according to any one of claims 1 to 17 wherein the irinocetan is administered intravenously immediately after aflibercept administration over a period of about 90 minutes

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

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

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

22. A method according to any one of claims 1 to 21 wherein the patient has liver metastases.

23. Composition comprising therapeutically effective amounts of aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinocetan for treating patients with CRC wherein the composition is for simultaneous administration.

24. Composition comprising therapeutically effective amounts of aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinocetan for treating patients with CRC wherein the composition is for sequential administration.

25. Composition comprising therapeutically effective amounts of aflibercept in combination with folinic acid, 5-fluorouracil (5-FU) and irinocetan for treating patients with CRC wherein 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 comprising:

a) a packaging material

b) aflibercept, 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 irinocetan is effective for the treatment of CRC.

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

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

29. An article of manufacture 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 irinocetan and comprising a pharmaceutically acceptable carrier for treating patients with CRC.

31. A kit for treating patients with CRC comprising:

a) at least one compound chosen from the list consisting of aflibercept, folinic acid, 5-fluorouracil (5-FU) and irinocetan; 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 irinocetan (FOLFIRI) or that folinic acid, 5-fluorouracil (5-FU) and irinocetan (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 irinocetan.