CLAIMS

1. Use of interleukin-8 (IL-8) as a biomarker for predicting the outcome of the treatment with aflibercept, or ziv-aflibercept of a patient suspected to suffer from a cancer.

2. A method of determining whether a patient suspected to suffer from cancer is a candidate for aflibercept, or ziv-aflibercept therapy for the said cancer comprising the step of subjecting a patient's biological sample to at least one assay to measure at baseline the IL-8 level, wherein when the biological sample IL-8 level is low relative to a reference level of expression of IL-8, the patient is identified as a candidate for therapy for cancer.

3. A method of determining whether a patient suspected to suffer from cancer is a candidate for aflibercept, or ziv-aflibercept therapy for the said cancer comprising the step of subjecting a patient's biological sample to at least one assay to measure at baseline the IL-8 level, wherein when the biological sample IL-8 level is high relative to a reference level of expression of IL-8, the patient is identified as not being a candidate for therapy for cancer.

4. Use of a therapeutically effective amount of aflibercept, or ziv-aflibercept for the manufacture of a medicament for treating a patient with a cancer, wherein the patient has been identified as having lower IL-8 level in biological sample than a reference level of expression of IL-8.

5. The method according to any of claims 2 to 3 or the use according to claim 4, wherein the relative to a reference level of expression of IL-8 is between around 10 and around 30 pg/ml.

6. The method according to any of claims 2 to 3 of the use according to claims 4 or 5, wherein the relative to a reference level of expression of IL-8 is around 19 pg/ml.

7. Use of aflibercept or ziv-aflibercept for the manufacture of a medicament for optimizing therapeutic efficacy for treatment of cancer in a patient, wherein the level of interleukin-8 (IL-8) in a patient’s biological sample is determined, and

wherein an increase of the interleukin-8 (IL-8) level indicates the need to decrease the amount of aflibercept, or ziv-aflibercept in subsequent administrations.

8. A method of managing the risk to allow a safe use of aflibercept, or ziv-aflibercept in the treatment of a patient suspected to suffer from a cancer, said method comprising the following steps:

(a) before beginning of the treatment with aflibercept, or ziv-aflibercept, determining the interleukin-8 (IL-8) level in a biological sample from the patient;

(b) along the treatment determining the interleukin-8 (IL-8) level in a biological sample from the patient

(c) comparing the interleukin-8 (IL-8) level determined in step (b) with the level determined in step (a),

whereby a higher interleukin-8 (IL-8) level in the sample of step (b) compared to that of level in the sample of step (a) indicates that the patient should be closely monitored.

9. The method according to any of claims 2 to 3 or 5, 6, 8 or the use according to any of claims 4 to 7, wherein the biological sample is chosen from the group consisting of blood, serum and plasma.

10. The method according to any of claims 2 to 3 or 5, 6, 8 or the use according to any of claims 4 to 7, wherein the cancer is colon cancer, a colorectal cancer or a rectal cancer.

11. The method or use according to claim 10 wherein the colorectal cancer is a metastatic colorectal cancer.

12. The method according to any of claims 2 to 3 or 5, 6, 8 or the use according to any of claims 4 to 7, wherein the interleukin-8 (IL-8) level which is determined is the circulating level.

13. Use of therapeutically effective amounts of aflibercept, or ziv-aflibercept, oxaliplatin, 5-fluorouracil (5-FU) and folinic acid for the manufacture of a medicament for treating a patient with a cancer.

14. The use according to claim 13, wherein therapeutically effective amounts of aflibercept, or ziv-aflibercept, folinic acid, 5- fluorouracil (5-FU) and irinocetan is to be administered to the patient.

15. The use according to any one of claims 4 to 6 or 13 to 14, wherein said patient has previously been treated with therapy based on oxaliplatin or on bevacizumab.

16. The use according to any one of claims 4 to 6 or 13 to 14, wherein said patient has failed with chemotherapy, radiotherapy or surgery.

17. The use according to claim 14, 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 to be administered to the patient.

18. The use according to any one of claims 14 or 17, 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 to be administered to the patient.

19. The use according to any one of claims 14, 17 and 18 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, irinocetan 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.

20. The use according to any one of claims 14 and 17 to 19, wherein the folinic acid, 5- fluorouracil (5-FU), irinocetan and aflibercept are to be administered intravenously every two weeks for a period comprised between 9 and 18 weeks.

21. The use according to any one of claims 14 and 17 to 20, wherein the folinic acid is to be administered intravenously immediately after aflibercept administration.

22. The use according to any one of claims 14 and 17 to 21, wherein the folinic acid is to be administered intravenously immediately after aflibercept administration over a period of about 2 hours.

23. Aflibercept, or ziv-aflibercept for use in treating a patient suspected to suffer from cancer, wherein the patient has been identified as having lower IL-8 level in biological sample than a reference level of expression of IL-8.

24. A kit for predicting whether a patient suspected to suffer from cancer is a candidate for aflibercept, or ziv-aflibercept therapy, which kit comprises:

a) means for measuring the interleukin-8 (IL-8) level; and

b) optionally, a label giving instructions for the use of said kit in predicting whether a a patient suspected to suffer from cancer is a candidate for aflibercept, or ziv-aflibercept therapy.

25. An article of manufacture comprising:

a) a packaging material;

b) means for measuring the interleukin-8 (IL-8) level; and

c) a label giving instructions for the use of said kit in predicting whether a a patient suspected to suffer from cancer is a candidate for aflibercept, or ziv-aflibercept therapy.