

CLAIMS

1. A method for determining, modulating or adjusting a treatment regimen with a chemotherapeutic agent in a patient affected with a colorectal cancer, wherein said agent is able to leverage or promote a tumor-targeted immune response, preferably by causing immunological cell death (ICD), ~~which method comprises quantifying at least two biological markers which are CD8 and CD3 in a tumor sample from the patient.~~
2. ~~The method of claim 1,~~ said method comprising a) quantifying at least two biological markers which are CD8 and CD3 in a tumor sample from the patient, and b) comparing the values obtained in a) to predetermined reference values, and c) deciding to ~~increasing-increase~~ the exposure of the patient to the chemotherapeutic agent by deciding to ~~increasing-increase~~ the dose, the duration of treatment and/or the frequency of administration, when the values obtained in a) are superior to a predetermined reference value;-
3. wherein step a) ~~The method of claim 1 or 2, which comprises~~ is performed by quantifying the density of CD3+ cells in center of the tumor (CT), the density of CD8+ cells in the center of the tumor (CT), the density of CD3+ cells in the invasive margin (IM), and the density of CD8+ cells in the invasive margin (IM);-
4. ~~The method of claim 3,~~ wherein step b) further comprises classifying the patient in groups (Low, Intermediate, or High Immunoscore (IS)) as follows:
 - Low IS corresponds to a mean percentile below 25%,
 - Intermediate IS corresponds to a mean percentile between 25% and 70%,
 - High IS corresponds to a mean percentile above 70%;
 wherein the mean percentile refers to the mean percentile of the 4 individual percentiles of the 4 markers (CD3ct, CD8ct, CD3im, CD8im) corresponding to the density of CD3 cells in CT and IM regions and the density of CD8 cells in CT and IM regions;-

wherein the chemotherapeutic agent is oxaliplatin, optionally combined with 5-fluorouracil (5FU) and/or capecitabine;

wherein, when the patient has been classified as belonging to the intermediate or high IS group, deciding to adjust the duration of the treatment regimen with the chemotherapeutic agent to at least six months, and the oxaliplatin dose to at least a cumulative dose of 700 mg/m².

2. ~~The method of any one of claims 1 to 4, comprising deciding to adjusting the duration of the treatment to at least six months, preferably at least eight months, still preferably at least a year.~~

3. Use of a chemotherapeutic agent in the manufacture of a medicament for the treatment of colorectal cancer in a patient, wherein said chemotherapeutic agent is able to leverage or promote a tumor-targeted immune response, preferably by causing immunological cell death (ICD), wherein said chemotherapeutic agent is oxaliplatin, optionally combined with 5-fluorouracil (5FU) and/or capecitabine; wherein the patient has been classified as belonging to the intermediate or high Immunoscore (IS) group according to the method of claim 1 or 2, and wherein the patient is to be administered a treatment regimen with the oxaliplatin for at least six months, and at a cumulative dose of oxaliplatin of at least 700 mg/m².

4. Use according to claim 3, wherein the oxaliplatin is to be administered for at least six months and at a cumulative dose of at least 700 mg/m².

5. Use according to claim 3 or 4, wherein the oxaliplatin is to be administered in combination with 5-fluorouracil (5FU) and/or capecitabine.

6. ~~The method of any one of claims 1 to 5, comprising modulating the dose, the duration of treatment and/or the frequency of administration, when the patient has been classified as belonging to the intermediate or high IS group.~~

7. ~~The method of any of claims 1 to 6, wherein the chemotherapeutic agent is selected from the group consisting of platinum or a platinum salt, derivative or~~

analog thereof (such as oxaliplatin, cisplatin or carboplatin), bleomycin, bortezomib, alkylating agents (such as cyclophosphamide), anthracyclins such as doxorubicin, alone or in combination.

8. The method of claim 7, wherein the chemotherapeutic agent is platinum or a platinum salt, derivative or analog thereof, such as oxaliplatin, alone or in combination with at least another therapeutic agent, e.g. a fluoropyrimidine, such as 5-fluorouracil (5FU) and/or capecitabine.

9. The method of claim 8, wherein the chemotherapeutic agent is oxaliplatin, optionally combined with 5-fluorouracil (5FU) and/or capecitabine.

10. The method according to any one of the preceding claims, wherein the cancer is a solid cancer.

11. The method of claim 10, wherein the cancer is selected from the group consisting of colorectal cancer, colon cancer, rectum cancer, pancreatic cancer, gastrointestinal carcinoid tumors, stomach cancer, skin cancer, melanoma, lung cancer, bladder cancer, breast cancer, bile duct cancer, laryngeal cancer, hypopharyngeal cancer, nasal cavity cancer, paranasal sinus cancer, nasopharyngeal cancer, oral cavity cancer, oropharyngeal cancer, and salivary gland cancer.

12. The method of claim 11, wherein the solid cancer is colorectal cancer.

13. The method of claim 12, wherein the cancer is preferably a colorectal cancer, the chemotherapeutic agent is platinum or a platinum salt, derivative or analog thereof (preferably oxaliplatin), alone or in combination with another therapeutic agent, e.g. a fluoropyrimidine, such as 5-fluorouracil (5FU) and/or capecitabine, which method comprises a) quantifying at least two biological markers which are CD8 and CD3 in a tumor sample from the patient, preferably by quantifying the densities of CD3⁺ and cytotoxic CD8⁺ T cells in the core tumor (CT) and invasive margin (IM) of the patient and b) comparing the values obtained in a) to predetermined reference values, and c) when the values obtained in a) are superior to a predetermined reference value, modulating the dose, the duration of treatment and/or the frequency of administration, preferably by adjusting the duration of the treatment to at least six months, and/or the dose to at least a cumulative dose of 700mg/m².

14. The method of claim 13, wherein step b) further comprises classifying the patient in groups (Low, Intermediate, or High Immunoscore (IS)) as follows:
 — Low IS corresponds to a mean percentile below 25%;
 — Intermediate IS corresponds to a mean percentile between 25% and 70%;
 — High IS corresponds to a mean percentile above 70%;

wherein the mean percentile refers to the mean percentile of the 4 individual percentiles of the 4 markers (CD3_{ct}, CD8_{ct}, CD3_{im}, CD8_{im}) corresponding to the density of CD3 cells in CT and IM regions and the density of CD8 cells in CT and IM regions; and c)

~~comprising modulating the dose, the duration of treatment and/or the frequency of administration, when the patient has been classified as belonging to the intermediate or high IS group, preferably by adjusting the duration of the treatment to at least six months, and/or the dose to at least a cumulative dose of 700 mg/m².~~