

CLAIMS

1. Nanoparticles and/or aggregates of nanoparticles for use in the treatment of cancer in a human patient ineligible to undergo a standard-of-care treatment involving radiotherapy (RT) or in a patient at high risk of intolerance to a standard-of-care treatment involving RT, wherein the nanoparticles and/or aggregates of nanoparticles comprise more than 30% by weight of at least one chemical element having an atomic number (Z) between 20 and 83, and wherein the treatment of cancer involves a step of administering the nanoparticles and/or aggregates of nanoparticles to said patient, and a step of exposing the patient who has been administered with the nanoparticles and/or aggregates of nanoparticles to a total dose of ionizing radiation that is equal to or less than 85% of the total dose delivered in the standard-of-care treatment involving RT for said cancer.
2. Nanoparticles and/or aggregates of nanoparticles according to claim 1, wherein the patient is ineligible to undergo a standard of care treatment involving RT because said treatment is contraindicated for said patient.
3. Nanoparticles and/or aggregates of nanoparticles according to claim 1 or 2, wherein the patient fulfils at least one of the following criteria:
- a. is vulnerable or frail according to the comprehensive geriatric assessment (CGA),
 - b. has a high comorbidity index score as evaluated using the Adult Comorbidity Evaluation 27 (ACE-27) and the Charlson Comorbidity Index (CCI),
 - c. has grade 2 or more organ dysfunction based on the National Cancer Institute Common Toxicity Criteria (NCI CTC),
 - d. has poor functional status as measured as an ECOG performance status of 2 or more, or as an equivalent Karnofski performance status,
 - e. is exposed to more than 4 distinct prescribed drugs,
 - f. is elderly and evaluated as “fit”, according to part or full components evaluation of CGA, but presents cumulative exposure to risk factors for being intolerant to treatment,
 - g. has a locally advanced tumor observed at clinical staging,
 - h. has an inoperable stage IIIA or IIIB Non-Small Cell Lung Carcinoma (NSCLC) tumor at clinical staging.
4. Nanoparticles and/or aggregates of nanoparticles for use according to any of claims 1 to 3, wherein the human patient has a locally advanced tumor at clinical staging.

5. Nanoparticles and/or aggregates of nanoparticles for use according to any of claims 1-4, wherein the cancer is selected from a skin cancer, a central nervous system cancer, a head and neck cancer, a lung cancer, a breast cancer, a gastrointestinal cancer, a male genitourinary cancer, a gynecologic cancer, an adrenal and/or retroperitoneal cancer, a sarcoma of bone and soft tissue, or a pediatric cancer.
6. Nanoparticles and/or aggregates of nanoparticles for use according to claim 5, wherein the patient has a locally advanced stage III or IV squamous cell carcinoma of the head and neck (SCCHN) at clinical staging, and receives a total dose of radiation of equal to or less than 59.5 Gy, preferably equal to or less than 56 Gy, more preferably equal to or less than 52.5 Gy, even more preferably equal to or less than 50 Gy, delivered as a stand-alone treatment or in combination with chemotherapy or any other relevant systemic modality.
7. Nanoparticles and/or aggregates of nanoparticles for use according to claim 5, wherein the patient has a stage IIIA or stage IIIB non-small cell Lung Carcinoma (NSCLC) tumor evaluated as inoperable at clinical staging, and receives a total dose of radiation equal to or less than 56.1 Gy, preferably equal to or less than 52.8 Gy or 51 Gy, more preferably equal to or less than 50 Gy, even more preferably equal to or less than 49.1 Gy, 48 Gy or 42 Gy, delivered as a stand-alone treatment or in combination with chemotherapy or any other relevant systemic modality.
8. Nanoparticles and/or aggregates of nanoparticles for use according to claim 5, wherein the patient has an operable locally advanced esophageal cancer tumor, preferably a squamous cell esophageal cancer tumor, and receives a preoperative total dose of radiation equal to or less than 35.2 Gy, preferably equal to or less than 33.1 Gy or 31.1 Gy, more preferably equal to or less than 30 Gy, even more preferably equal to or less than 29 Gy, delivered as a stand-alone treatment or in combination with chemotherapy or any other relevant systemic modality .
9. Nanoparticles and/or aggregates of nanoparticles for use according to claim 5, wherein the patient has glioblastoma and receives a total dose of radiation equal to or less than 51 Gy, preferably equal to or less than 48 Gy, more preferably equal to or less than 42 Gy, delivered as a stand-alone treatment or in combination with chemotherapy or any other relevant systemic modality,
10. Nanoparticles and/or aggregates of nanoparticles for use according to any one of claims 1-9, wherein each nanoparticle comprises at least one chemical element selected from La,

Ce, Pr, Nd, Pm, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu, Hf, Ta, W, Re, Os, Ir, Pt, Au and Bi.

- 5 11. Nanoparticles and/or aggregates of nanoparticles for use according to any one of claims 1-10, wherein the nanoparticles are inorganic nanoparticles.
- 10 12. Nanoparticles and/or aggregates of nanoparticles for use according to any one of claims 1-10, wherein each nanoparticle and/or aggregate of nanoparticles further comprises a biocompatible surface coating.
- 15 13. Nanoparticles and/or aggregates of nanoparticles for use according to any one of claims 1-12, wherein the nanoparticles are selected from a HfO₂ nanoparticle, a Au nanoparticle, a ReO₂ nanoparticle and any mixture thereof.
- 20 14. Pharmaceutical composition comprising nanoparticles and/or aggregates of nanoparticles as described in any one of claims 1-13 and a pharmaceutically acceptable carrier or support for use in the treatment of cancer in a human patient ineligible to undergo a standard-of-care treatment involving RT or in a patient at high risk of intolerance to a standard-of-care treatment involving RT, wherein the nanoparticles and/or aggregates of nanoparticles
- 25 14. Pharmaceutical composition comprising nanoparticles and/or aggregates of nanoparticles as described in any one of claims 1-13 and a pharmaceutically acceptable carrier or support for use in the treatment of cancer in a human patient ineligible to undergo a standard-of-care treatment involving RT or in a patient at high risk of intolerance to a standard-of-care treatment involving RT, wherein the nanoparticles and/or aggregates of nanoparticles comprise more than 30% by weight of at least one chemical element having an atomic number (Z) between 20 and 83, wherein the treatment of cancer involves a step of administering the nanoparticles and/or aggregates of nanoparticles to said patient, and a step of exposing the patient who has been administered with the nanoparticles and/or aggregates of nanoparticles to a total dose of ionizing radiation that is equal to or less than
- 30 15. Nanoparticles and/or aggregates of nanoparticles for use according to any one of claims 1-13, or a pharmaceutical composition for use according to claim 14, wherein the ionizing radiation is selected from X-rays, gamma-rays, electrons and protons.
- 35 16. Nanoparticles and/or aggregates of nanoparticles for use according to anyone of claims 1-13 and 15, or a pharmaceutical composition for use according to claim 14 or 15, wherein the treatment further comprises administering at least one distinct therapeutic agent to the human patient, either simultaneously or separately.

17. Nanoparticles and/or aggregates of nanoparticles for use, or a pharmaceutical composition for use, according to claim 16, wherein the at least one distinct therapeutic agent is an immunotherapeutic agent selected from a monoclonal antibody, a cytokine and a combination thereof.

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18. Nanoparticles and/or aggregates of nanoparticles for use, or a pharmaceutical composition for use, according to claim 17, wherein the at least one distinct therapeutic agent is selected from a biological compound, a small molecule targeted therapeutic, a cytotoxic compound and a combination thereof.

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