CLAIMS

1. Use of a nanoparticle and/or aggregate of nanoparticles for preparing a vaccine composition for treating cancer in a human subject suffering from metastatic cancer and undergoing a palliative radiotherapy, in a human subject suffering from metastatic cancer for whom radiotherapy has been abandoned, in a human subject suffering from a cancer which is not treated by radiotherapy, or in a human subject suffering from a liquid cancer affecting blood or lymphoid cell tissue; wherein ~~the human subject, or~~ a cancer sample of said human subject, comprising the nanoparticle and/or aggregate of nanoparticles, is to be exposed to a fractionated radiotherapy comprising at least one irradiation step wherein the ionizing radiations dose ranges from 1.8 to 30 Gray (Gy), and wherein each nanoparticle consists in a material having a density of at least 7 g/cm^3 and an atomic number (Z) of at least 25 and each nanoparticle or aggregate of nanoparticles is covered with a biocompatible coating allowing the nanoparticle stability between pH 6.5 and 7.5 in a physiological fluid, wherein the at least one irradiation step is to be applied *ex vivo* on a cancer sample of the subject comprising the nanoparticles or aggregates of nanoparticles, and the *ex vivo* lethally irradiated cancer cells and at least part of the associated cell supernatant from the cancer sample when the cancer is a metastatic cancer are, or the *ex vivo* irradiated liquid cancer sample when the cancer is a liquid cancer is, to be at least partly readministered to the subject before any optional subsequent *in vivo* treatment of cancer in said subject.~~.~~

2. The use according to claim 1 wherein the ionizing radiations dose ranges from 1.8 to 20 Gray (Gy).

~~3. The use according to claims 1 or 2 wherein, when the cancer is a metastatic cancer, the at least one irradiation step is to be applied *in vivo* on one, at most two, tumor sites of the metastatic cancer comprising the nanoparticles or aggregates of nanoparticles.~~

~~4. The use according to anyone of claims 1 to 3 wherein, when the cancer is a metastatic cancer, the at least one irradiation step is to be applied *ex vivo* on a cancer sample of the subject comprising the nanoparticles or aggregates of nanoparticles, and the *ex vivo* lethally irradiated cancer cells and at least part of the associated cell supernatant from the cancer sample are to be at least partly readministered to the subject before any optional subsequent *in vivo* treatment of cancer in said subject.~~

~~5. The use according to claim 1 or 2 wherein, when the cancer is a liquid cancer, affecting the blood or lymphoid cell tissue, the at least one irradiation step is to be applied *ex vivo* on a liquid cancer sample of the subject comprising the nanoparticles or aggregates of nanoparticles, and the irradiated liquid~~

~~cancer sample is to be at least partly readministered to the subject before any optional subsequent *in vivo* treatment of cancer in said subject.~~

~~6~~3. The use according to claim ~~5~~ 1 or 2, wherein the liquid cancer sample is a blood sample or the whole blood volume of the subject.

~~7~~4. The use according to anyone of claims ~~4~~ 1 to ~~6~~3, wherein the *ex vivo* lethally irradiated cancer cells or the irradiated liquid cancer sample is to be at least partly readministered to the subject together with at least one additional immunotherapeutic agent; wherein the *ex vivo* lethally irradiated cancer cells or the irradiated liquid cancer sample and the least one additional immunotherapeutic agent are to be administered to the subject either simultaneously or separately.

~~8~~5. The use according to anyone of claims 1 to ~~7~~4, wherein the ionizing radiations dose is selected from 1.8, 2, 2.4, 2.5, 3, 3.2, 3.6, 4, 4.5, 5, 5.5, 6, 7, 8, 10, 15 and 20 Gy per fraction treatment.

~~9~~6. The use according to anyone of claims 1 to ~~8~~5, wherein the metastatic cancer affects (i) a connective tissue and is selected from a fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteosarcoma, chordoma, malignant fibrous histiocytoma, (ii) an endothelium or mesothelium tissue and is selected from hemangiosarcoma, angiosarcoma, lymphangiosarcoma and mesothelioma, (iii) a muscle tissue and is selected from leiomyosarcoma and rhabdomyosarcoma, (iv) an epithelial tissue and is selected from adenocarcinoma, squamous cell carcinoma and epidermoid carcinoma, (v) a neural tissue and is selected from multiform glioblastoma, glioma, neuroblastoma, medulloblastoma, meningioma, neurofibrosarcoma and schwannoma, and (vi) the APUD system and is selected from thyroid carcinoma, pancreas carcinoma, stomach carcinoma and intestine carcinoma; or wherein the metastatic cancer is a melanoma.

~~10~~7. The use according to claim ~~9~~ 6, wherein the metastatic cancer is or derives from a cancer selected from skin cancer, central nervous system cancer, head and neck cancer, lung cancer, kidney cancer, breast cancer, gastrointestinal cancer (GIST), prostate cancer, liver cancer, colon cancer, rectum cancer, anal cancer, oesophagus cancer, male genitourinary cancer, gynecologic cancer, adrenal and retroperitoneal cancer, sarcomas of bone and soft tissue, pediatric cancer, neuroblastoma, central nervous system cancer and Ewing's sarcoma.

~~11~~8. The use according to anyone of claims 1 to ~~8~~5, wherein the liquid cancer is selected from leukemia, myeloma and lymphoma.

~~12. The use according to anyone of claims 1 to 11, wherein the nanoparticle or aggregate of nanoparticles are to be administered to the subject to be treated together with at least one immunotherapeutic agent, the nanoparticle or aggregate of nanoparticles and the at least one immunotherapeutic agent being administered to the subject either simultaneously or separately.~~

~~13~~9. The use according to anyone of claims 1 to ~~12~~8, wherein the composition further comprises a pharmaceutically acceptable carrier or vehicle.

~~14~~10. The use according to claim ~~13~~9, wherein the composition further comprises at least one immunotherapeutic agent.

~~15. A kit comprising (i) a nanoparticle or aggregate of nanoparticles consisting in a material having a density of at least 7 g/cm^3 and an atomic number (Z) of at least 25, each nanoparticle or aggregate of nanoparticles being covered with a biocompatible coating allowing the nanoparticle stability between pH 6.5 and 7.5 in a physiological fluid, or a composition as described in anyone of claims 1-13, together with (ii) at least one immunotherapeutic agent.~~

~~16~~11. The use according to claim ~~14 10or the kit according to claim 15~~, wherein the at least one immunotherapeutic agent is selected from a monoclonal antibody, a cytokine, and a combination thereof.

~~17~~12. The use ~~or kit~~ according to claim ~~16~~11, wherein the monoclonal antibody is selected from ipilimumab, tremelimumab, nivolumab, prembolizumab, pidilizumab, lambrolizumab, dacetuzumab, lucatumumab, urelumab, fresolimumab and lirilumab.

~~18~~13. The use according to claim ~~14 10or kit according to claim 16~~, wherein the immunotherapeutic agent is an antibody selected from an anti-CTLA-4 antibody, an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-PD-L2 antibody; a monoclonal antibody enhancing CD27 signaling, CD137 signaling, OX-40 signaling, GITR signaling and/or MHCII signaling and/or activating CD40; a monoclonal antibody inhibiting TGF-β signaling or KIR signaling; a cytokine selected from granulocyte-macrophage colony stimulating factor (GM-CSF), a fms-related tyrosine kinase 3 ligand (FLT3L), IFN-α, IFN-α2b, IFNg, IL2, IL-7, IL-10 and IL-15; an immunocytokine; an immune cell presenting or sensitized to a tumor antigen; a cell secreting an immunogenic molecule; a dead tumor cell or a dying tumor cell expressing CRT and/or producing HMGB1 and/or producing ATP in a ICD amount; or a

Toll-like receptor agonist selected from a TLR 2/4 agonist, a TRL 7 agonist, a TRL 7/8 agonist and a TRL 9 agonist.

~~19~~14. The use ~~or kit~~ according to claim ~~18~~13, wherein the immunocytokine is L19-IL2.

~~20~~15. The use ~~or kit~~ according to claim ~~18~~13, wherein the Toll-like receptor agonist is selected from imiquimod, bacillus Calmette-Guérin and monophosphoryl lipid A.