SUMMARY OF THE INVENTION

The inventors succeeded in obtaining a suitable animal model for the severe pulmonary adverse events and, then, have surprisingly found that severe toxicological side effects, in particular lung injuries, associated with intra-arterial or intravenous administration of Nanoparticules loaded with a chemotherapeutic agent, can be prevented by intravenous or intra-arterial infusion of said Nanoparticules for several hours.

On this basis, the present ~~invention~~disclosure concerns Nanoparticules comprising at least one chemotherapeutic antitumoral agent, at least one poly(alkylcyanoacrylate) and at least one cyclodextrin, for use for treating a cancer, wherein the Nanoparticules are administered by intravenous or intra-arterial infusion for at least 2 hours. In particular, Nanoparticules can be administered by intravenous or intra-arterial infusion for between 2 and 24 hours, more particularly for between 4 and 12 hours, even more particularly for about 6 hours. In a particular embodiment, the administration is by intravenous infusion.

Preferably, the poly(alkylcyanoacrylate) polymer comprised in the Nanoparticules is a polyisohexylcyanoacrylate polymer.

The Nanoparticules used in the ~~invention~~present disclosure may comprise said at least one chemotherapeutic agent at a concentration from 0.01 to 200 mg/g of Nanoparticules, from 0.1 to 70 % w/w of said at least one cyclodextrin and from 1 to 25 % w/w of said at least one poly(alkylcyanoacrylate).

The chemotherapeutic antitumoral agent comprised in the Nanoparticules may be selected from the group consisting of anthracyclines, topoisomerase inhibitors, spindle poison plant alkaloids, alkylating agents, anti-metabolites, ellipticine and harmine, and any combination thereof. Preferably, the chemotherapeutic antitumoral agent is an anthracycline. More preferably, the chemotherapeutic agent is selected from the group consisting of doxorubicin, daunorubicin, epirubicin, idarubicin, valrubicin, pirarubicin, zorubicin, aclarubicin, detorubicin, carminomycin, morpholinodoxorubicin, morpholinodaunorubicin, methoxymorpholinyldoxorubicin, any pharmaceutically acceptable salt thereof, and any combination thereof. In a particularly preferred embodiment, the chemotherapeutic antitumoral agent is doxorubicin or any pharmaceutically acceptable salt thereof. In this embodiment, the dosage of doxorubicin may be from about 10 to about 75 mg/m^2, from about 10 to about 60 mg/m^2, from about 10

to about 45 mg/m², from about 10 to about 30 mg/m², from about 20 to about 30 mg/m². In a particular embodiment, the dosage of doxorubicin may be about 20mg/m² or 30 mg/m².

The cancer treated with the Nanoparticules may be is a solid tumor or a hematopoietic tumor, preferably selected from the group consisting of hepatocellular carcinoma, acute lymphoblastic leukemia, acute myeloblastic leukemia, chronic myelogenous leukemia, Hodgkin's disease, diffuse large B-cell lymphoma, small cell lung cancer, colorectal cancer, pancreas cancer, breast cancer, ovary cancer, uterine cancer, cervix cancer, head and neck cancer, brain cancer, blade cancer, multiple myeloma, neuroblastoma, Edwing's sarcoma, osteosarcoma, soft tissue sarcoma, thyroid cancer, prostate cancer, stomach cancer, nephroblastoma, Kaposi's sarcoma, and non-Hodgkins lymphoma. In a particularly preferred embodiment, the cancer is a hepatocellular carcinoma.

In another ~~aspect~~example, the present ~~invention~~disclosure concerns a method for treating cancer, wherein the method comprises administering by intravenous or intra-arterial infusion for at least 2 hours, a therapeutically effective amount of Nanoparticules comprising at least one chemotherapeutic agent, at least one poly(alkylcyanoacrylate) and at least one cyclodextrin to a patient in need of such treatment. Preferably, Nanoparticules are administered in the form of a pharmaceutical composition as described above. All ~~embodiments~~examples disclosed above for the Nanoparticules are encompassed in this aspect. In a particular ~~embodiment~~example, the administration is by intravenous infusion.

In one example~~further aspect~~, the present invention concerns the use of Nanoparticules comprising at least one chemotherapeutic agent, at least one poly(alkylcyanoacrylate) and at least one cyclodextrin for the treatment of cancer, said Nanoparticules being administered by intravenous or intra-arterial infusion for at least 2 hours. All examples~~embodiments~~ disclosed above for the Nanoparticules are encompassed in this aspect. In a particular example~~embodiment~~, the administration is by intravenous infusion.

In one aspect, there is provided the use of Nanoparticules comprising at least one chemotherapeutic antitumoral agent, at least one poly(alkylcyanoacrylate) and at least one cyclodextrin, for the manufacture of a medicament for use in treating a cancer, wherein the Nanoparticules are administered by intravenous or intra-arterial infusion for at least 2 hours.

In ~~a last aspect~~another example, the present ~~invention~~disclosure concerns the use of Nanoparticules comprising at least one chemotherapeutic agent, at least one poly(alkylcyanoacrylate) and at least one cyclodextrin, for the manufacture of a pharmaceutical preparation for the treatment of cancer, said pharmaceutical composition being administered by intravenous or intra-arterial infusion for at least 2 hours. All ~~embodiments~~examples disclosed above for the Nanoparticules are encompassed in this ~~aspect~~example. In a particular ~~embodiment~~example, the administration is by intravenous infusion.