A phase I dose-escalation study of intratumoral injection of NBTXR3 in combination with IMRT in patients with locally advanced HNSCC

Authors LE TOURNEAU, Christophe, Institut Curie, PARIS, France (Presenting author)
MORENO, Victor, START Madrid- FJD Fundación Jiménez Díaz, Madrid, Spain
CALUGARU, Valentin, Institut Curie, PARIS, France
JOUFFROY, Thomas, Institut Curie, Paris, France
RODRIGUEZ, José, Institut Curie, PARIS, France
HOFFMANN, CAROLINE, Institut Curie, PARIS, France
DODGER, Bernard, START Madrid- FJD Fundación Jiménez Díaz, Madrid, Spain
DIMITRIU, Mikaela, NANOBIOTIX, PARIS, France
LEVY, Laurent, NANOBIOTIX, PARIS, France
CALVO, Emiliano, START Madrid- FJD Fundación Jiménez Díaz, Madrid, Spain
Topic Nonsurgical treatments in head and neck cancer

Background:

Loco-regional control in head and neck cancer has been improved by combining radiotherapy (RT) with chemical agents, radiosensitizers and monoclonal antibodies. However, these associations come with challenging limitations in terms of pharmacology, local control, clinical outcome benefits or patient quality of life. In addition, high doses of radiation may result in several undesired reactions which underline the need for new therapeutic approaches. Functionalized hafnium oxide nanoparticles (NBTXR3) is a new class of material with high electron density, designed in the form of crystalline 50nm-particles (HfO2-NP) to efficiently absorb ionizing radiation and allow the absorption/deposition of a high radiation dose within the cancer cells, to physically kill the cells and modify the tumor immune profile.

Methods:

An increase of cancer cell death in vitro and marked antitumor efficacy in vivo in presence of these nanoparticles (HfO2-NP) exposed to RT have been demonstrated, when compared to RT alone. Hafnium oxide nanoparticles efficacy was assessed in epithelial and mesenchymal tumor models and on patient-derived tumor xenografts in nude mice, showing superior antitumor effects over radiation therapy alone in terms of complete response and overall survival.

HfO2-NP (NBTXR3), administered as a single intratumoral injection and activated by radiotherapy, is currently evaluated in a phase I clinical trial for head and neck cancer [NCT01946867] in elderly and frail patients that cannot receive the standard of care.

Results:

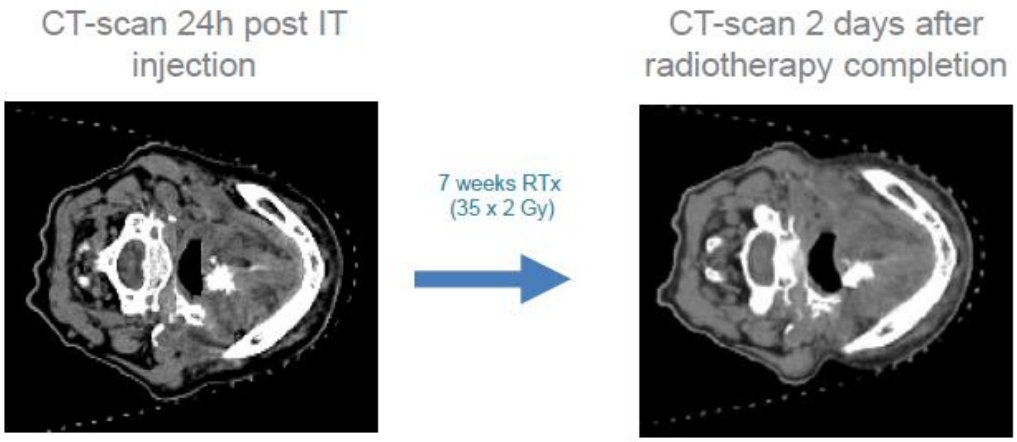
So far, patients treated in this phase I trial showed good local and systemic tolerance to the product up to the highest dose level and received radiotherapy as planned, confirming a very good local safety profile.
Regarding the preliminary efficacy evaluation, the local Complete Response rate is 83 % (dose

level15% and 22%), with a duration of response of 22 months, for a median follow-up of 16 months.

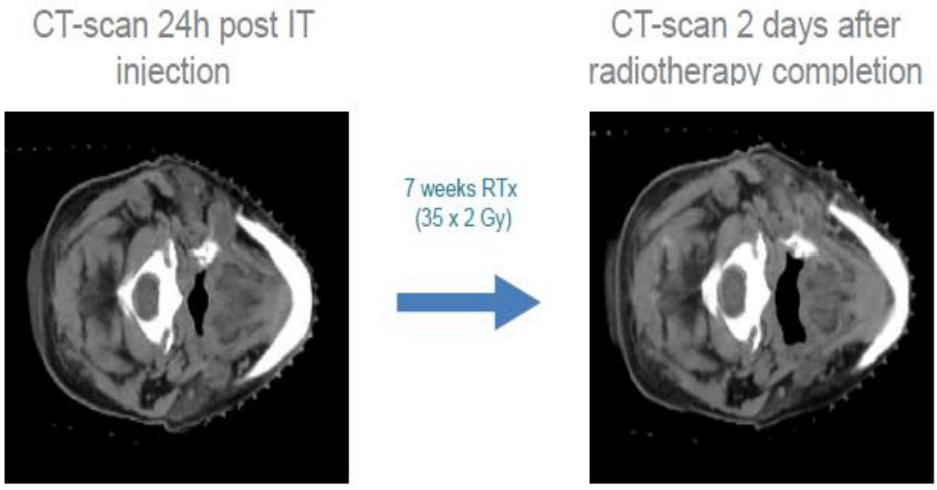
Discussion/ Conclusion:

NBTXR3 nanoparticles may lead to a decrease in the long-term adverse effects of RT and an improvement in quality of life, associated with strong and durable locoregional control and thereby constitute a rising hope for head and neck cancer patients.

In addition, NBTXR3 + RT is being also evaluated in several other cancer indications (soft tissue sarcoma, prostate, liver and rectum cancer). Promising results in terms of safety and efficacy opena bright perspectives for the treatment of head and neck squamous cell carcinoma.



Dispersion of NBTXR3 nanoparticles and intratumor bioavailability of NBTXR3 - 1



Dispersion of NBTXR3 nanoparticles and intratumor bioavailability of NBTXR3 - 2