

Title: Hafnium oxide nanoparticles as an emergent promising treatment for solid tumors

Key words: Nanomedicine, radiotherapy, clinical trial, safety, efficacy

Authors: M. Dimitriu¹, A. Pottier¹, C. Le Tourneau², P. Sargos³, C. Le Pechoux⁴, G. Kantor³, T. De Baere⁴, A. Le Cesne⁴, V. Moreno Garcia⁵, E. Calvo⁵, S. Bonvalot²

1. Nanobiotix, Paris
2. Institut Curie, Paris
3. Institut Bergonié, Bordeaux
4. Institut Gustave Roussy, Villejuif
5. START, Madrid

To improve tumor control, radiotherapy has been combined with chemical agents, chemotherapeutics or monoclonal antibodies potentially acting as radiosensitizers. However, the complexity of these associations in terms of pharmacology, local control, clinical outcome benefits or patient quality of life underlines the need for the development of new therapeutic approaches.

A new class of material with high electron density, hafnium oxide, was designed at the nanoscale in the form of crystalline 50nm-particles to efficiently absorb ionizing radiation and increase the radiation dose deposited - "hot spots" of energy deposit - from within the tumor cells for efficient cell killing.

Hafnium oxide nanoparticles (NBTXR3), administered as a single intratumoral injection and activated by radiotherapy, is currently evaluated in a phase II/III clinical trial in soft tissue sarcoma (STS) [NCT02379845], and in phase I/II clinical trials for head and neck [NCT01946867], prostate [NCT02805894], liver [NCT02721056; NCT02721056] and rectum cancers [NCT02465593]. So far, patients treated with NBTXR3 received radiotherapy as planned and showed a very good local safety profile. All data generated have shown interesting transferability across different cancer indications.

To date, 142 patients have been treated with NBTXR3 and radiotherapy. These first-in-class nanoparticles show promising results in terms of anti-tumor efficacy in patients with locally advanced STS and head and neck squamous cell carcinoma. Data from ongoing clinical trials will be presented.