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Title:

Hafnium oxide nanoparticles activated by radiotherapy for the treatment of solid tumors

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Background:

To improve radiotherapy (RT) in terms of tumor response and to reduce irradiation of healthy tissues, innovative therapeutic approaches are needed. In response, NBTXR3, injectable hafnium oxide nanoparticles, was developed for the treatment of solid tumors.

Once injected intratumorally, NBTXR3 can deposit high energy within tumors only when activated by an ionizing radiation source, like current standard RTs. Upon activation, the high energy radiation physically kills the tumor cells by triggering DNA damage and cell destruction improving clinical outcomes.

Since its first successful clinical evaluation in a completed phase I trial in patients with locally advanced soft tissue sarcoma, NBTXR3 is currently evaluated in numerous indications worldwide (EU, Asia, US).

Methods:

NBTXR3 was the object of numerous in vitro and in vivo tumor models to determine its mechanism of action, performance and biocompatibility profile. Once they were assessed, NBTXR3 entered clinical development and was administered as a single intratumoral (IT) injection activated by RT.

NBTXR3 is clinically evaluated in head and neck [NCT01946867; NCT02901483], prostate [NCT02805894], liver [NCT02721056] and rectum cancers [NCT02465593] with the scope of determining the Recommended Dose or observing any Dose Limiting Toxicities (DLTs) in each indication. A phase II/III trial in soft tissue sarcoma of the trunk and extremities [NCT02379845] is about to be finalized.

Results

Preclinically, in vitro results showed an increase of cancer cells death and in vivo results demonstrated antitumor efficacy with NBTXR3 + RT compared to RT alone. This physical cell killing could open a potential systemic activity through immune response by triggering immunogenic cell death, reinforcing local effect.

Clinically, across the 7 clinical trials and 6 indications, NBTXR3 demonstrated an overall positive safety profile. The numerous types of tumors and different body locations involved in these trials confirmed feasibility of IT injection and persistence of NBTXR3 in the tumor, with no leakage in the surrounding healthy tissues.

NBTXR3 antitumor activity is currently evaluated in its first phase II/III in patients with STS. Besides, analysis of tumor biopsies collected pre- and post-radiotherapy suggested a release of tumor antigens during cancer cell death and stimulation of local immunological effects.

Conclusion

NBTXR3 have shown promising results in non-clinical studies with marked antitumor efficacy and in clinical development in terms of safety and preliminary evaluations of efficacy. Considering the preliminary results of the 145 patients injected across all clinical trials, these first-in-class nanoparticles have already proven to be an encouraging innovative treatment in various types of tumors.

The last patient of the phase II/III trial in STS was included and the results of this study regarding efficacy and safety will soon be disclosed.

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