Hafnium oxide nanoparticles NBTXR3 activated by radiotherapy as a new therapeutic option for elderly/frail HNSCC patients.

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Author(s): Christophe Le Tourneau, Victor Moreno, Sebastien Salas, Xavier Mirabel, Emiliano Calvo, Bernard Doger, Carmen Florescu, Juliette Thariat, Jacek Fijuth, Tomasz Rutkowski, Nicolas Magné, Xavier Liem, Nicolas Fakhry, Stéphanie Wong-Hee-Kam, Valentin Calugaru, Caroline Hoffmann; Institut Curie, Paris, France; START Madrid-FJD, Madrid, Spain; CEPCM Assistance Publique des Hôpitaux de Marseille, Marseille, France; Oncology, Oscar Lambret Center, Lille, France; START Madrid-CIOCC, Madrid, Spain; START Madrid, FJD, Madrid, Spain; Centre François Baclesse, Caen, France; Provita Prolife, Tomaszów Mazowiecki, Poland; Maria Skłodowska-Curie Institute of Oncology, Gliwice, France; Medical Oncology Department, AP-HP, Salpetriere Hospital, University Paris VI, Paris, France; Centre Oscar Lambret, Lille, France; Hôpital Timone, AP-HM, Marseille, France; INSERM Unit U932 Immunity and Cancer, Institut Curie, Paris, France

Abstract Disclosures

Abstract:

Background: New therapeutic approaches are needed for elderly or frail head and neck squamous cell carcinoma (HNSCC) patients (pts) ineligible for standard of care treatment. NBTXR3, a crystalline solution of hafnium oxide nanoparticles may represent such an option. Injected intratumorally, NBTXR3 enters tumor cells and yields an increased cell-localized energy deposit upon exposure to radiotherapy (RT), leading to increased tumor cell death compared to the same dose of RT alone. **Methods:** Phase I study of NBTXR3 activated by RT in pts ≥70 years old or ≥65 years old and unable to receive cisplatin, eligible for exclusive RT with stage III or IV HNSCC of the oral cavity or oropharynx [NCT01946867]. A 3+3 dose escalation design was implemented with dose levels corresponding to 5%, 10%, 15% and 22% of baseline tumor volume, followed by an expansion phase. Pts received an intratumoral (IT) injection of NBTXR3 and intensity modulated RT (IMRT; 70 Gy/35

fractions/7 weeks). Determination of Recommended Phase 2 Dose (RP2D) and Dose Limiting Toxicities (DLT) were primary endpoints of phase I. Absence of NBTXR3 leakage and preliminary efficacy using RECIST 1.1 principles were also evaluated. **Results:** The dose-escalation is complete. Nineteen pts were enrolled: 3 at 5%, 3 at 10%; 5 at 15% and 8 at 22% with no observed DLT or SAE related to NBTXR3 or IT injection. One grade 1 NBTXR3-related AE (asthenia at 22%) and four IT injection-related AE (grade 2 oral pain; grade 1 tumor hemorrhage; grade 1 asthenia, and grade 1 injection site hemorrhage) were reported. RT-related toxicity was as expected with IMRT. RP2D has been determined to be 22%. CT-scan assessment between 24h and 7 weeks post-IT injection demonstrated absence of NBTXR3 leakage in the surrounding tissues. Among 13 evaluable pts treated at doses ≥10%, 9 achieved a complete response of the injected lesion. **Conclusions:** These results show that NBTXR3 activated by RT is safe and well tolerated at all doses with preliminary encouraging efficacy results. It thus represents a promising future treatment for frail and elderly pts with locally advanced HNSCC with limited therapeutic options. Expansion phase has started at the RP2D. Clinical trial information: NCT01946867