Abstract SIOG 2018

Title

A new treatment option for locally advanced HNSCC in elderly patients: NBTXR3

Authors: Caroline Hoffmann* 1, Valentin Calgaru1, Victor Moreno2, Xavier Mirabel3, Bernard Dodger2, Emiliano Calvo2, Thomas Jouffroy1, Jose Rodriguez1, Anne Chilles1, Meriem Yemi1, Christophe Le Tourneau1

1Institut Curie, Paris, France, 2START Madrid, Madrid, Spain, 3Centre Oscar Lambret, Lille, France

Introduction: Compared to younger individuals, elderly patients with head and neck squamous cell carcinoma (HNSCC) have limited therapeutic options being more burdened by cancer-related symptoms and short/long term treatment related toxicities. HNSCC in those patients lead to highly detrimental impact on quality of life (QoL). Despite representing approximately 47% of the affected population with an increasing incidence, older patients are underrepresented from HNSCC prospective clinical trials further limiting their therapeutic options. They are mostly frail and unfit to chemotherapy, the gold standard concurrent treatment for unresectable tumors treated by radiotherapy, thereby subject to suboptimal treatment due to fears of poor tolerance.

Intensity-modulated radiation therapy (IMRT) represents a viable treatment. Yet, like with all radiation therapy (RT) techniques, the energy dose deposit to tumor cells is limited by the surrounding healthy tissues. Injectable hafnium oxide nanoparticles, NBTXR3, were developed to increase the deposited dose of ionizing radiation within tumor cells when activated by RT. This leads to an increase of tumor- physical killing through DNA damage/cell destruction and boost of the intratumoral immune profile.

Objectives: This phase I clinical study evaluates NBTXR3 in the treatment of locally advanced HNSCC of the oral cavity and oropharynx in frail elderly patients ineligible for surgery and cisplatin, the non-surgical standard of care, or intolerant to cetuximab [NCT01946867].

Methods: Patients aged 65 or more are treated by a single intratumoral injection (IT) of NBTXR3 activated by IMRT (2Gy*35 fractions in 7 weeks) and followed until disease progression or study cut-off date. The design is a 3+3 dose escalation study with NBTXR3 dose levels corresponding to 5%, 10%, 15% and 22% of baseline tumor volume. Primary endpoints include the determination of recommended dose and early dose limiting toxicity (DLT). Presence of NBTXR3 in the surrounding healthy tissues and efficacy per RECIST 1.1 response via MRI are also evaluated, as well as QoL of patients.

Results: So far, 16 patients (median age: 78.5 years) were treated at NBTXR3 volume dose levels 5% (3 patients), 10% (3 patients), 15% (5 patients) and 22% (5 pts). All patients experienced no DLT nor SAE related to NBTXR3 or injection procedure. Two adverse events (AE; asthenia, grade 1; oral pain, grade 2) related to NBTXR3 and four AEs (tumor hemorrhage, grade 1; asthenia, grade 1; oral pain, grade 2; hemorrhage, grade 1) related to the IT injection were reported.

The best response per RECIST 1.1 by investigator assessment, for NBTXR3 doses ≥15% were 5 complete responses (CR), 2 partial responses and 2 stable diseases. Currently, duration of CR is at least 7 months up to 18 months after the end of treatment, with a median follow-up of 12 months, 25 days.

The NBTXR3 injection feasibility and intratumoral persistence with no leakage was confirmed by CT scan before and after the whole radiation therapy.

Conclusion: Overall, NBTXR3 preliminary results show a very good safety profile with favorable signs of efficacy. Hence, they highly indicate NBTXR3 as a promising future treatment for frail and elderly patients with locally advanced HNSCC burdened from limited therapeutic options.

NBTXR3 is evaluated in 6 other clinical trials, including a phase II/III in soft tissue sarcoma [NCT02379845] and phases I/II for recurrent/metastatic HNSCC or metastatic non-small cell lung cancer; HNSCC with cisplatin [NCT02901483]; prostate [NCT02805894], liver [NCT02721056] and rectum cancers [NCT02465593].

Disclosure of Interest: None Declared

Keywords: hafnium oxide, HNSCC, IMRT, Nanomedicine, NBTXR3

https://doi.org/10.1016/S1879-4068(18)30439-9