GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

Analysis of 3-Dimensional Volumetric Distribution and Dispersion of the Radioenhancer NBTXR3 in Various Solid Malignancies

489P

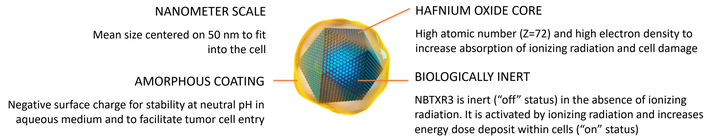
Thierry de Baère[1], Colette Shen[2], Anne Ducassou[3], Sylvie Bonvalot[4], Enrique Chajon[5], Leonard A. Farber[6], Omar I. Vivar[6], Sergio Szyldergemajn[6], Pavel Tyan[6], Laetitia Finzi[6], Eugene J. Koay[7], Steven H. Lin[7], Zhongxing Liao[7], Adam P. Dicker[8], Caroline Hoffmann[4], Christophe Le Tourneau[4]

[1] Institut Gustave Roussy, Villejuif, France; [2] University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA; [3] University Cancer Institute of Toulouse, Toulouse, France; [4] Institut Curie, Paris, France; [5] Mallet Proux Centre, Laval, France; [6] Nanobiotix, Paris, France; [7] MD Anderson Cancer Center, Houston, TX, USA; [8] Thomas Jefferson University Medical Center, Philadelphia, PA, USA

BACKGROUND

What is NBTXR3?

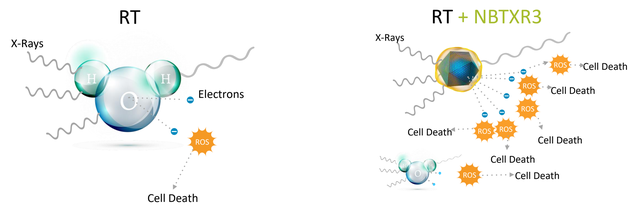
Figure 1: NBTXR3: A First-In-Class Radioenhancer



NBTXR3 is a suspension of nano-sized particles for one-time intratumoral injection

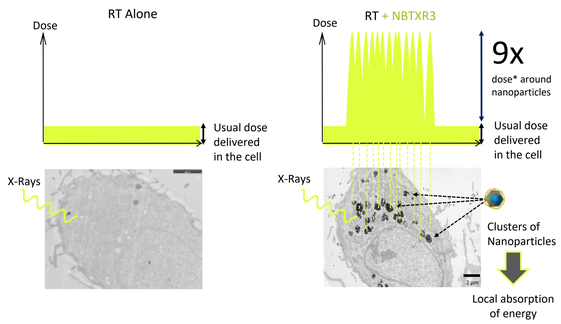
NBTXR3 Universal Mode of Action

Figure 2: NBTXR3 MoA



NBTXR3 Universal MoA Designed to Enhance RT-Cell Death Efficiency

Figure 3: NBTXR3 RT Dose Deposit



*Dose enhancement determined by Monte Carlo simulation[1].

NBTXR3 Safety

To date, intratumoral injection of NBTXR3 has been demonstrated feasible and safe:

- Across 10 phase I studies, 2 phase II studies, 1 phase II-III study and 1 phase III (ongoing NANORAY-312 in LA-HNSCC)
- Over 300 patients treated across all studies in multiple indications
- NBTXR3 is radioopaque due to its high Z value, regardless of anatomic location
- CT scans performed during treatment consistently show NBTXR3 remains localized mainly within the tumor throughout RT treatment

METHODS

NBTXR3 was administered by one-time only intratumoral injection. NBTXR3 dispersion within the tumor was visualized by CT scan post injection and 3D CT scan reconstructions were created.

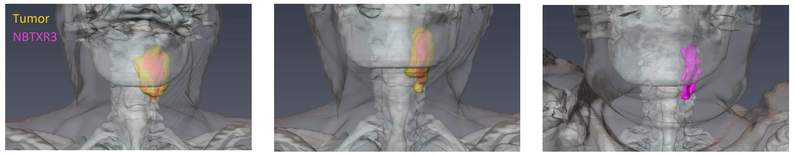
Patients with STS received NBTXR3+RT or RT alone followed by tumor resection in the phase II/III randomized Act.in.Sarc [NCT02379845] trial.

NBTXR3 IT injection feasibility and safety has being evaluated in different phase I/II/III trials: HNSCC [NCT01946867], HCC or liver metastases [NCT02721056], advanced cancers (NSCLC/HNSCC or others included) in combination with anti-PD-1 [NCT03589339], Pancreatic cancer [NCT04484909], esophageal cancer [NCT04615013], and prostate adenocarcinoma [NCT02805894].

RESULTS

Head & Neck Squamous Cell Carcinoma (HNSCC) (CT or US-Guided IT Injection)

Complete Tumor Response (RECIST1.1)



CT-scan 24h post IT injection
29 JUNE 2016

CT-scan post radiotherapy
17 AUGUST 2016

CT-scan 7 months after RT
21 MARCH 2017

Study 102 is a Phase I dose escalation/dose expansion study in elderly patients unfit to cisplatin with locally advanced head and neck squamous cell carcinoma (HNSCC).

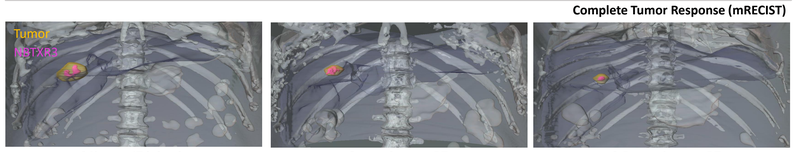
NBTXR3 remaining in tumor cavity

Scan	NBTXR3 Volume (mm^3)	Tumor Volume (mm^3)	NBTXR3 Volume / Tumor Volume (%)
D02	4 931.1	30 659.4	16.1%
End of RT	4 204.4	18 049.6	23.3%
7 months post RT	5 204.7	NA	NA

Figure at 15% NBTXR3, RP2D 22%, MTD not reached

Hepatocellular Carcinoma (HCC) or Liver Metastases (Imaging-Guided IT Injection)

Complete Tumor Response (mRECIST)



24h post IT injection
6 JANUARY 2017

3 months post RT
21 APRIL 2017

9.5 months post RT
24 OCTOBER 2017

Complete response by mRECIST – absence of tumor vasculature

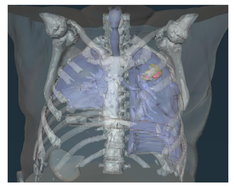
Study 103 (NCT02721056) was a phase I/II dose-escalation and dose-expansion study of NBTXR3 activated by SBRT in adult patients with hepatocellular carcinoma (HCC) or liver metastasis.

Scan	NBTXR3 Volume (mm^3)	Tumor Volume (mm^3)	NBTXR3 Volume / Tumor Volume (%)
D02	3 411.3	27 220.0	12.5%
End of RT	975.7	5 207.1	18.7%
Follow-Up	861.2	3 605.9	23.9%

Figure at 15% NBTXR3 , RP2D defined as 42%, MTD not reached

Lung Metastases (CT or US-Guided IT Injection)

Study 1100 (NCT03589339) is a multicenter, open-label, phase I dose escalation/dose expansion study to evaluate the safety and tolerability of NBTXR3 activated by RT in combination with anti-PD-1 therapy.

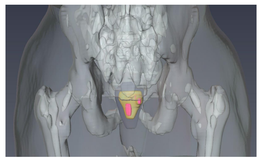


Scan	NBTXR3 Volume (mm^3)	Tumor Volume (mm^3)	NBTXR3 Volume / Tumor Volume (%)
Day 2	1 518.6	31 164.1	4.9%

Study 1100: Figure at 22% of GTV NBTXR3, RP2D defined as 33% MTD not reached

Prostate Adenocarcinoma (Transrectal Ultrasound Guidance)

Study 104 (NCT02805894) was a phase I/II dose escalation/dose expansion study evaluating NBTXR3 activated by EBRT or EBRT with brachytherapy in patients with newly diagnosed unfavorable intermediate or high risk prostate adenocarcinoma treated with androgen deprivation.



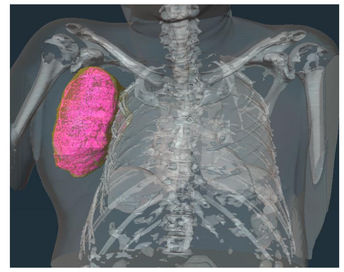
Scan	Prostate Volume (mm^3)	NBTXR3 Volume (mm^3)	NBTXR3 Volume / Prostate Volume (%)
Day 9	20 912.7	3 219.3	15.3%

Study 104: Figure at 5% NBTXR3

RESULTS

Soft Tissue Sarcoma (STS) (Preoperative)

Act.in.Sarc (NCT02379845) was an international, multicenter, open-label, randomized phase II/III study to compare the efficacy of NBTXR3 activated by RT versus RT alone in adult patients with locally advanced STS of the extremity and trunk wall[2].(Bonvalot et al. 2019)

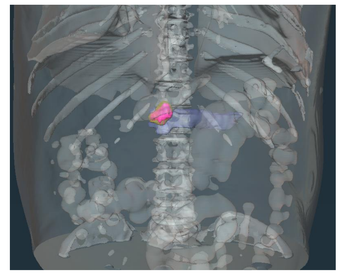


Scan	NBTXR3 Volume (mm3)	Tumor Volume (mm^3)	NBTXR3 Volume / Tumor Volume (%)
Day 2	371 136.7	1 277 130.0	29.1%

Study 301: 10% NBTXR3

Pancreatic Ductal Adenocarcinoma (PDAC) (Endoscopically Injected)

Study 2019-1001 (NCT04484909) is a single institution, single arm, open-label, non-randomized, dose-escalation and dose-expansion phase I study to evaluate NBTXR3 activated by IMRT in patients with locally advanced or borderline resectable pancreatic ductal adenocarcinoma.

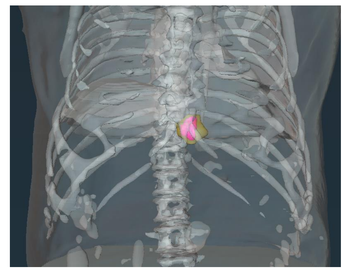


Scan	NBTXR3 Volume (mm3)	Tumor Volume (mm^3)	NBTXR3 Volume / Tumor Volume (%)
Day 2	2 591.6	6 558.9	39.5%

Study 2019-1001: Figure at 33% of GTV NBTXR3

Esophageal Carcinoma (Endoscopically Injected)

Study 2020-0122 (NCT04615013) is a single institution, single arm, open-label, non-randomized, dose-escalation and dose-expansion phase I study to evaluate NBTXR3 activated by IMRT with concurrent chemotherapy (excluding cisplatin regimens) in treatment-naïve patients with stage II–III adenocarcinoma of the esophagus.



Scan	NBTXR3 Volume (mm3)	Tumor Volume (mm^3)	NBTXR3 Volume / Tumor Volume (%)
Day 2	3 868.3	21 597.1	17.9%

Study 2020-0122 Figure at 33% of GTV NBTXR3

CONCLUSION

IT, NBTXR3 single injection was feasible in patients within a variety of solid malignancies, including spread lymph nodes: STS, head and neck squamous cell carcinoma (HNSCC), hepatocellular carcinoma (HCC), liver and lung metastases, pancreatic ductal adenocarcinoma (PDAC), esophageal cancer, rectal and prostate cancer.

NBTXR3 was consistently and easily traceable within the tumor following intratumoral injection, regardless of the injection site.

Dispersion varied by tumor type and NBTXR3 injected dose, and appeared to be a function of the anatomical structure or tumor within.

NBTXR3 remained within the tumor area injected in a patient with HNSCC, after achieving a complete response.

NBTXR3 has shown proof-of concept results, including improved clinical efficacy and QOL outcomes, together with comparable safety in a phase II/III study in patients with non-metastatic STS, confirmatory studies are ongoing in other tumor types and settings.

References

(1) CEA Saclay, France; (2) Bonvalot S, et al., Lancet Oncol. 2019.

Acknowledgements

All participating centers, all site staff, all patients and their families

Contact Information

Leonard A. Farber, MD: leonard.farber@nanobiotix.com

institut Curie
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®
NANOBIOTIX