

# Study of Novel Radioenhancer NBTXR3 Plus Radiotherapy in Patients With Locally Advanced Soft Tissue Sarcoma: Results of the Long-Term Evaluation in the Phase II/III Act.In.Sarc Trial

Sylvie Bonvalot<sup>1</sup>, Piotr L. Rutkowski<sup>2</sup>, Juliette Thariat<sup>3</sup>, Sébastien Carrère<sup>4</sup>, Anne Ducassou<sup>5</sup>, Marie-Pierre Sunyach<sup>6</sup>, Peter Agoston<sup>7</sup>, Angela Hong<sup>8</sup>, Augustin Mervoyer<sup>9</sup>, Marco Rastrelli<sup>10</sup>, Cécile Le Péchoux<sup>11</sup>, Victor Moreno<sup>12</sup>, Rubi K. Li<sup>13</sup>, Béatrice Tiangco<sup>14</sup>, Zsusanna Papai<sup>15</sup>, All Act.in.Sarc investigators

1. Institut Curie, PSL Research University, Paris, France; 2. Maria Sklodowska-Curie Institute – Oncology Centre, Warsaw, Poland; 3. Centre François Baclesse, Caen, France; Centre Lacassagne, Nice, France. 4. Unicancer - Montpellier Cancer Institute (ICM), Montpellier, France; 5. Institut Claudius Regaud (ICR), Institut Universitaire du Cancer de Toulouse-Oncopole (IUCT-O), Toulouse, France; 6. Unicancer - Léon Bérard Cancer Center, Lyon, France; 7. Országos Onkológiai Intézet, Budapest, Hungary; 8. Chris O'Brien Lifehouse and The University of Sydney, Camperdown, Australia; 9. Institut de Cancerologie de l'Ouest- Rene Gauducheau, Saint-Herblain, France; 10. Istituto Oncologico Veneto IRCCS, Padova, Italy; 11 Department of Radiation Oncology, Gustave Roussy, Villejuif, France; 12. Hospital Fundación Jimenez Diaz, Madrid, Spain; 13. St. Luke's Medical Center, Quezon City, Philippines; 14. The Medical City APS Cancer Institute, Pasig City, Philippines; 15. Hungarian Defence Forces Military Hospital, Budapest, Hungary

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# Disclosures

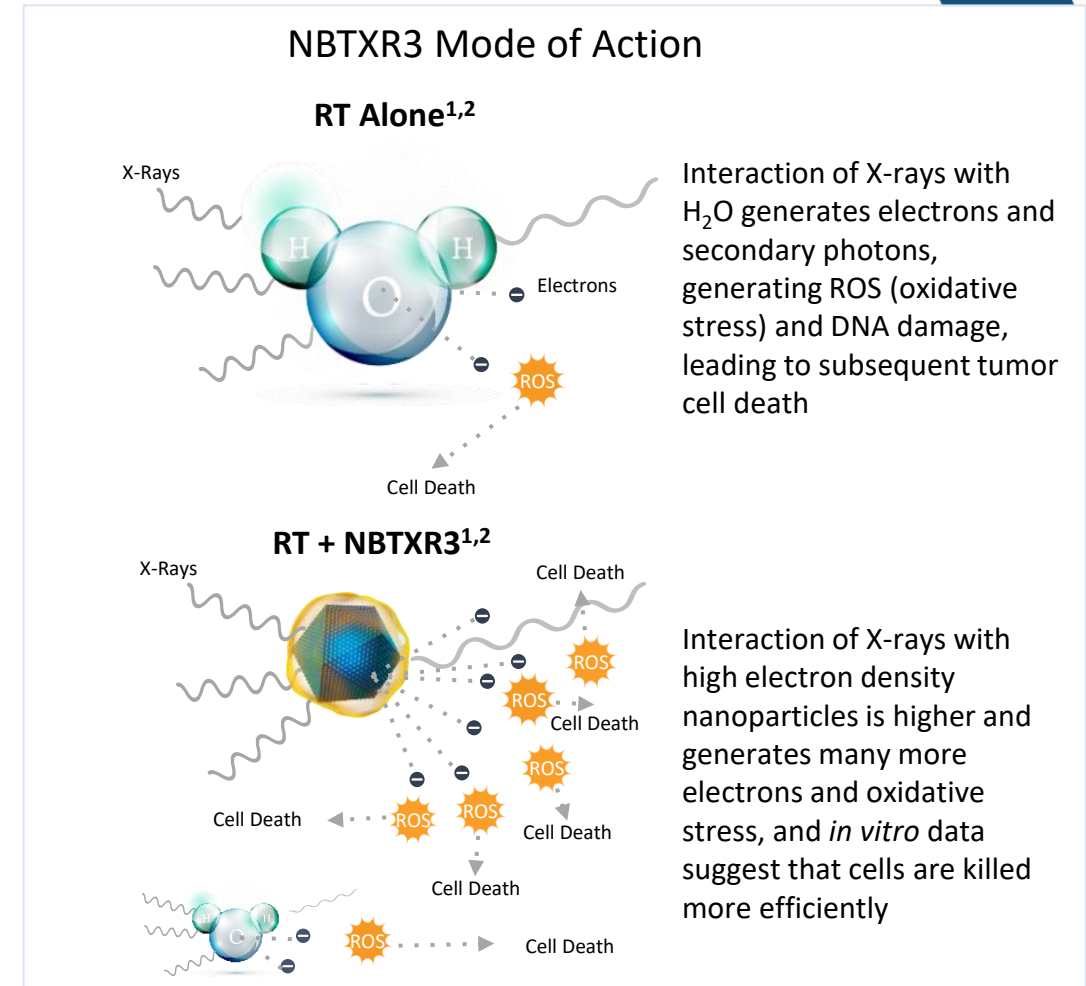
|                                         |            |
|-----------------------------------------|------------|
| <b>Honoraria</b>                        | Nanobiotix |
| <b>Research Funding</b>                 | Nanobiotix |
| <b>Travel, Accommodations, Expenses</b> | Nanobiotix |

# Background

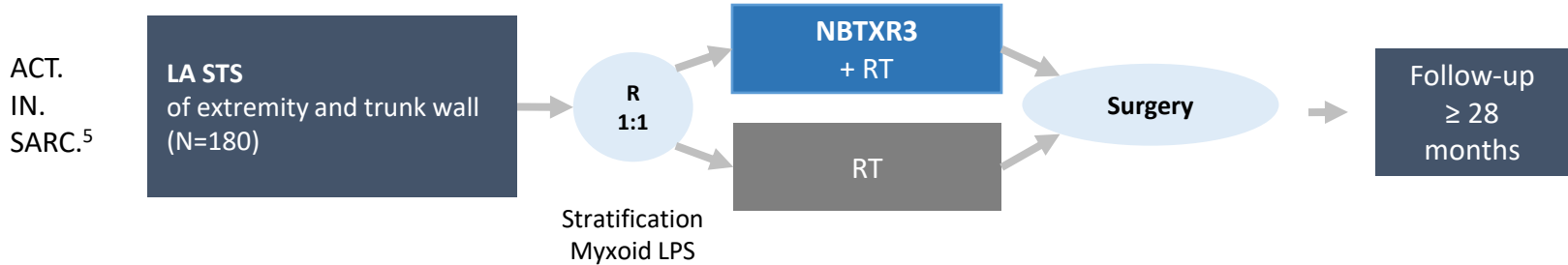
- NBTXR3 is a new first-in-class radio enhancer
- It is a hafnium oxide (HfO<sub>2</sub>) nanoparticle activated by radiotherapy (RT) <sup>1,2</sup>
- Designed at the nanoscale to increase RT dose deposition with subsequent increase in tumor cell killing
- Administered by a one-time direct intra tumoral injection <sup>1-3</sup>
- No increase in toxicity to normal tissue <sup>1-4</sup>

## References

- <sup>1</sup> Marill et al. Radiother Oncol. 2014;9:150.
- <sup>2</sup> Maggiorella et al. Future Oncol. 2012;8:1167-81.
- <sup>3</sup> Zhang et al. Int J Nanomedicine. 2020;15:3843-50.
- <sup>4</sup> Bonvalot et al. Clin Cancer Res. 2017;23(4):908-917



# Study Design



**Primary Endpoint:**  
Pathological complete response rate (pCRR)  
Evaluated by an independent central Pathological Review Board following EORTC guidelines

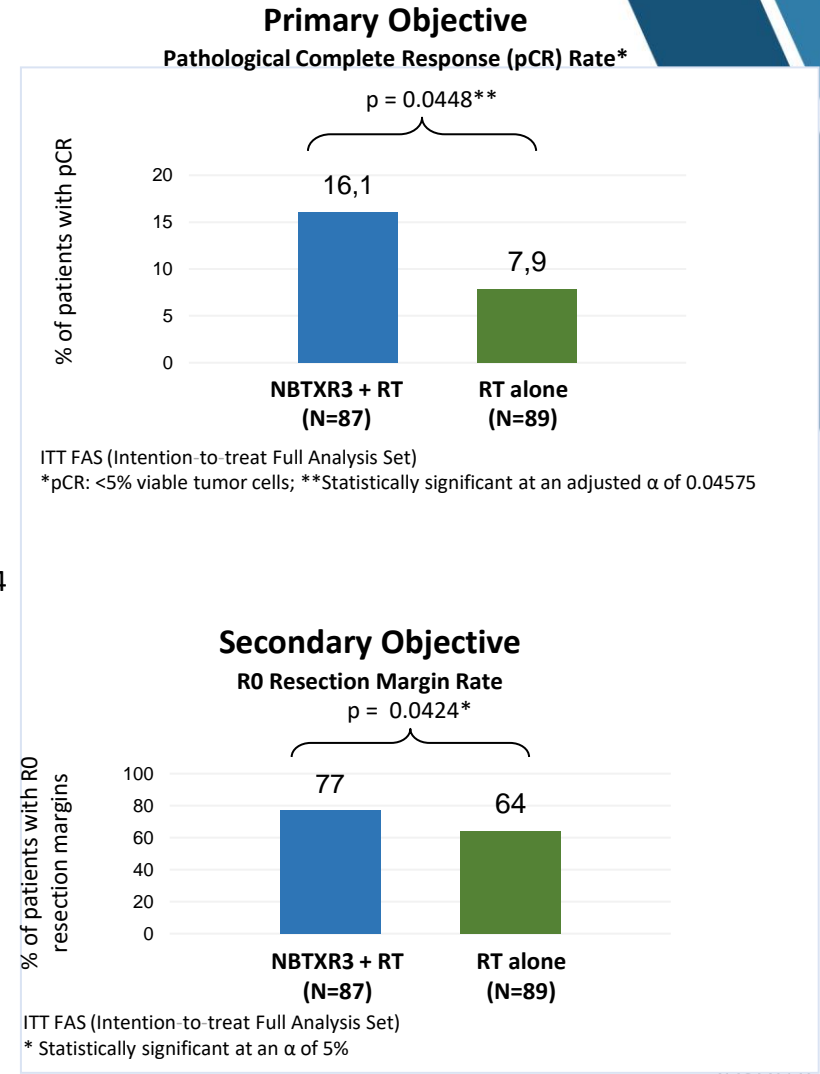
**Secondary Endpoints:**  
Safety Profile, wound complications, oncologic resection, amputation rate, QoL

- Phase II/III Act.In.Sarc (NCT02379845) achieved primary and secondary endpoints<sup>4</sup>
- No impact on early safety profile of RT by addition of NBTXR3
- Market authorization in the EU (CE marking)
- **Here, we evaluated NBTXR3 long-term safety, impact on limb function, and QoL**

References <sup>4</sup> Bonvalot et al. Lancet Oncol. 2019;20:1148-59.

<sup>5</sup> <https://clinicaltrials.gov/ct2/show/NCT02379845>.

Notes LA STS, locally advanced soft tissue sarcoma.



# Baseline Characteristics

## Patient Characteristics.<sup>6</sup>

|                              | NBTR3 + RT<br>N=87 | RT <i>alone</i><br>N=89 |
|------------------------------|--------------------|-------------------------|
| <b>Sex, n (%)</b>            |                    |                         |
| Female                       | 34 (39.1)          | 42 (47.2)               |
| Male                         | 53 (60.9)          | 47 (52.8)               |
| <b>Age, years</b>            |                    |                         |
| N                            | 84                 | 85                      |
| Mean (SD)                    | 60.5 (14.1)        | 60.0 (14.7)             |
| Median                       | 63.5               | 64.0                    |
| Min ; Max                    | 22 ; 83            | 21 ; 86                 |
| <b>ECOG/WHO PS, n (%)</b>    |                    |                         |
| 0                            | 57 (65.5)          | 56 (63.6)               |
| 1                            | 27 (31.0)          | 29 (33.0)               |
| 2                            | 3 (3.4)            | 3 (3.4)                 |
| <b>Disease status, n (%)</b> |                    |                         |
| Primary locally advanced STS | 79 (90.8)          | 83 (93.3)               |
| Locally relapsed             | 8 (9.2)            | 6 (6.7)                 |
| Metastatic                   | 2 (2.3)            | 2 (2.2)                 |

## Tumor Characteristics.<sup>6</sup>

|                                                                                 | NBTR3 + RT<br>N=87 | RT <i>alone</i><br>N=89 |
|---------------------------------------------------------------------------------|--------------------|-------------------------|
| <b>Tumor site, n (%)</b>                                                        |                    |                         |
| Lower limb                                                                      | 64 (73.6)          | 66 (74.2)               |
| Trunk                                                                           | 14 (16.1)          | 14 (15.6)               |
| Upper limb                                                                      | 9 (10.3)           | 9 (10.1)                |
| <b>Tumor histologic type, n (%)</b>                                             |                    |                         |
| Myxoid liposarcoma                                                              | 14 (16.1)          | 15 (16.9)               |
| Other                                                                           | 73 (83.9)          | 74 (83.1)               |
| <b>Histologic grade, n (%)</b>                                                  |                    |                         |
| 1                                                                               | 15 (17.2)          | 16 (18.0)               |
| 2                                                                               | 36 (41.4)          | 44 (49.4)               |
| 3                                                                               | 30 (34.5)          | 23 (25.8)               |
| Undetermined                                                                    | 6 (6.9)            | 6 (6.7)                 |
| <b>Tumor longest diameter by MRI (mm) as per RECIST 1.1</b>                     |                    |                         |
| Median                                                                          | 80.0               | 91.0                    |
| Min ; Max                                                                       | 25 ; 191           | 33 ; 152                |
| <b>Target theoretical tumor volume (mL) (centralized reading)<sup>a,b</sup></b> |                    |                         |
| Median                                                                          | 525.0              | 717.8                   |
| Min ; Max                                                                       | 16 ; 6326          | 29 ; 4117               |

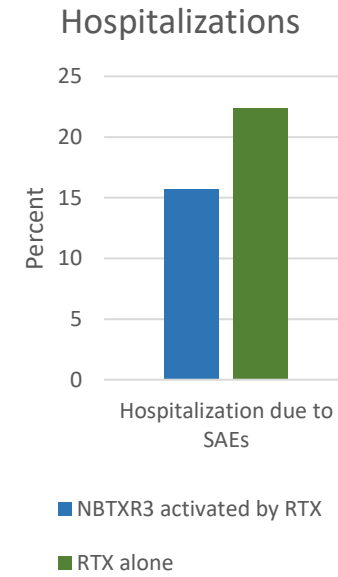
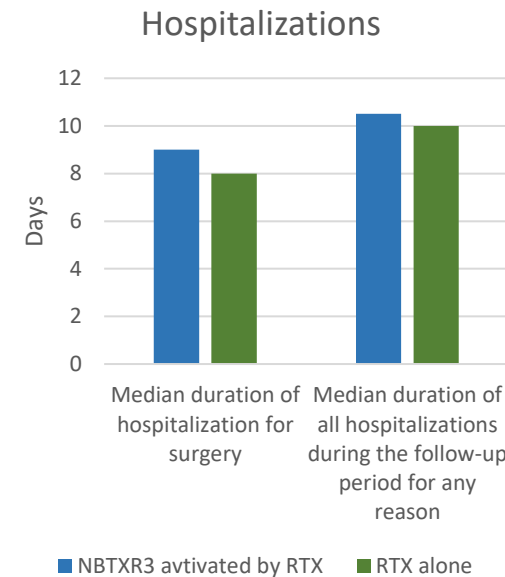
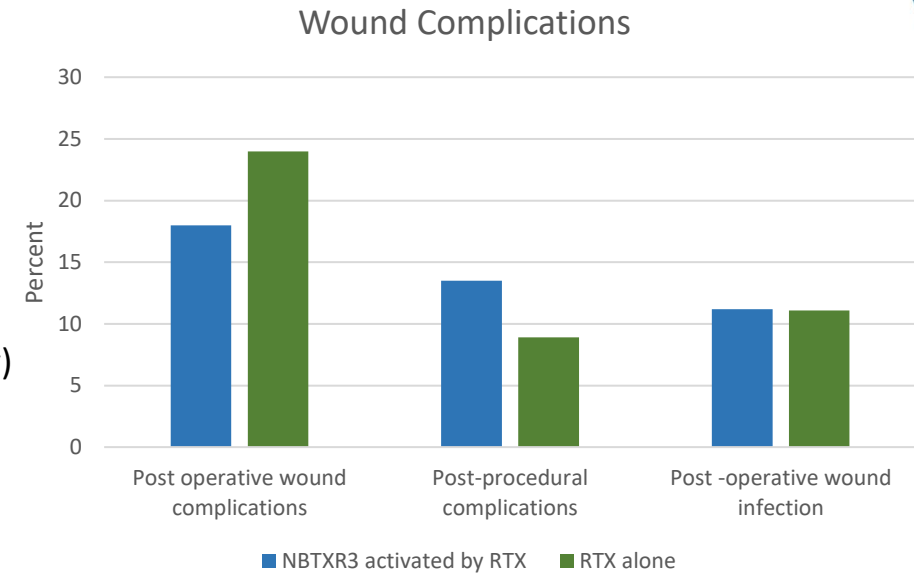
<sup>a</sup> Tumor volume at baseline is the theoretical tumor volume estimated by the product of the three longest dimensions (Length x Width x Depth), measured by MRI.

<sup>b</sup> For one patient in Arm B, the tumor volume calculation was based on TAP CT-scan assessments (Length, Width, Depth), at baseline and before tumorectomy.

References<sup>6</sup>In House Data, cut-off date: 26MAR2021.

# Global Safety Profile

- Post-treatment AEs (all grades) were observed in 51.7% and 57.8% of patients treated in the test arm and control arm<sup>7</sup>
- 12.4% (11/89) of patients experienced SAEs related to NBTXR3 (whole study)
- For all study duration, SAEs related to RT (all grades) occurred in:
  - 11.2% (10/89) of patients in NBTXR3 + RT arm
  - 13.3% (12/90) of patients in RT alone arm
- Prevalence of post-surgical wound complications and median duration of hospitalization was similar in both arms across a range of tumor anatomical sites
- 4 AE-related deaths, 2 in each arm
- Deaths in the NBTXR3 +RT arm were unrelated to NBTXR3 or implantation procedure



References <sup>7</sup> In House Data, database lock: 09NOV2020.

# Study Dosimetry Parameters

- Median doses to OARs including femur, femoral head, and spinal cord were equivalent in both arms<sup>7</sup>
- PTV and CTV min, mean, and max doses to respective volumes were equivalent in both arms<sup>7</sup>

|                             | NBTXR3 with RTX<br>(N=89) | RTX alone<br>(N=90) |
|-----------------------------|---------------------------|---------------------|
| PTV50 Vol(mL)               | 1685.2 (1440.2)           | 1539.5 (1022.6)     |
| Min Dose (Gy)               | 30.4 (14.2)               | 31.8 (12.8)         |
| Max Dose (Gy)               | 54.1 (1.5)                | 52.7 (5.0)          |
| Mean Dose (Gy)              | 50.1 (1.1)                | 49.1 (4.6)          |
| CTV50 Vol(mL)               | 1360.3 (1215.2)           | 1197.2 (842.5)      |
| Min Dose (Gy)               | 29.8 (15.9)               | 31.4 (16.1)         |
| Max Dose (Gy)               | 53.7 (1.7)                | 52.5 (5.2)          |
| Mean Dose (Gy)              | 49.9 (3.0)                | 48.8 (5.0)          |
| <b>Values are Mean (SD)</b> |                           |                     |

References <sup>7</sup> In House Data, database lock: 09NOV2020

Notes CTV , clinical tumor volume; PTV, planning target volume; OAR, organs at risk.

# Post treatment evaluation over time – Functional outcomes for STS of the extremity

NBTXR3 did not have a negative impact on patient quality of life (QoL), as evaluated by 4 different patient- and physician-reported methods<sup>7</sup>:

- Toronto Extremity Salvage Score
- Musculo Skeletal Tumor rating Scale
- Euro Qol- 5 Dimensions
- Reintegration to Normal Living Index<sup>7</sup>

| Baseline Value                        |           | ARM A<br>NBTXR3 activated<br>by RTX<br>(N=74) | ARM B<br>RTX alone<br>(N=75) |
|---------------------------------------|-----------|-----------------------------------------------|------------------------------|
| Toronto Extremity Salvage Total Score | N         | 55                                            | 61                           |
|                                       | Mean (SD) | 81.3 (20.6)                                   | 83.1 (19.1)                  |
|                                       | Median    | 89.1                                          | 91.1                         |
|                                       | Min ; Max | 16 ; 100                                      | 23 ; 100                     |
| MSTS-Total Score                      | N         | 50                                            | 49                           |
|                                       | Mean (SD) | 26.9 (7.1)                                    | 27.8 (6.6)                   |
|                                       | Median    | 29.0                                          | 29.0                         |
|                                       | Min ; Max | 2 ; 35                                        | 8 ; 35                       |
| EQ5D02-EQ VAS Score                   | N         | 57                                            | 63                           |
|                                       | Mean (SD) | 77.6 (19.7)                                   | 71.0 (21.3)                  |
|                                       | Median    | 80.0                                          | 72.0                         |
|                                       | Min ; Max | 20 ; 100                                      | 0 ; 100                      |
| RNLI-Total Score                      | N         | 47                                            | 53                           |
|                                       | Mean (SD) | 91.0 (26.2)                                   | 92.6 (21.2)                  |
|                                       | Median    | 100.0                                         | 100.0                        |
|                                       | Min ; Max | 0 ; 110                                       | 20 ; 110                     |

| Change from baseline at 2 years (Follow-Up Visit 8) |           | ARM A<br>NBTXR3 activated<br>by RTX<br>(N=74) | ARM B<br>RTX alone<br>(N=75) |
|-----------------------------------------------------|-----------|-----------------------------------------------|------------------------------|
| Toronto Extremity Salvage Total Score               | N         | 27                                            | 26                           |
|                                                     | Mean (SD) | -3.4 (13.4)                                   | -6.1 (17.4)                  |
|                                                     | Median    | -0.5                                          | -2.6                         |
|                                                     | Min ; Max | -38 ; 27                                      | -58 ; 23                     |
| MSTS-Total Score                                    | N         | 25                                            | 24                           |
|                                                     | Mean (SD) | 2.0 (27.4)                                    | 0.0 (26.7)                   |
|                                                     | Median    | 0.0                                           | 0.4                          |
|                                                     | Min ; Max | -69 ; 94                                      | -56 ; 79                     |
| EQ5D02-EQ VAS Score                                 | N         | 31                                            | 28                           |
|                                                     | Mean (SD) | 6.5 (15.9)                                    | 2.3 (22.7)                   |
|                                                     | Median    | 5.0                                           | 10.0                         |
|                                                     | Min ; Max | -28 ; 50                                      | -80 ; 25                     |
| RNLI-Total Score                                    | N         | 19                                            | 15                           |
|                                                     | Mean (SD) | 1.7 (6.1)                                     | 1.2 (6.0)                    |
|                                                     | Median    | 2.0                                           | 2.0                          |
|                                                     | Min ; Max | -14 ; 16                                      | -8 ; 11                      |

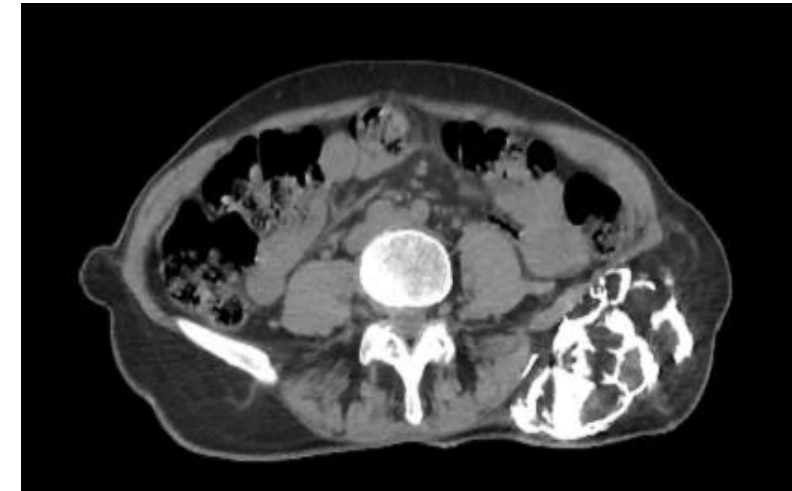
References <sup>7</sup> In House Data, database lock: 09NOV2020.



# Conclusion

- NBTXR3 did not have a negative impact on patient quality of life or long-term morbidity
- This long-term safety profile together with the efficacy of NBTXR3 reinforces its favorable benefit-risk ratio against LA STS
- PTV and CTV min, mean, and max doses to respective volumes were equivalent in both arms suggesting the superior efficacy due to increased energy deposit by NBTXR3
- Potential future indications in sarcoma could include non-resectable tumors, pediatric tumors, and re-irradiation
- NBTXR3 has potential for improved outcomes in other cancers treated by RT alone and is being developed for head and neck SCC, liver, and lung cancers<sup>8</sup>

24h post NBTXR3 injection



5 weeks post Radiotherapy

References <sup>8</sup> Hoffmann C, et al. Eur J Cancer. 2021 Mar;146:135-144.