

## Dosimetry Prediction of <sup>225</sup>Ac-NOTA-Trastuzumab Based on <sup>64</sup>Cu-NOTA-Trastuzumab in Breast Cancer: Preliminary Microdose Clinical Trial

Purpose: To predict the internal dosimetry of <sup>225</sup>Ac-1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA)-trastuzumab and <sup>225</sup>Ac-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)-trastuzumab in breast cancer using <sup>64</sup>Cu-NOTA-trastuzumab, a novel PET tracer for the HER2 and <sup>64</sup>Cu-DOTA-trastuzumab.

### Methods:

Prior to injecting the radiotracer, 45 mg of cold trastuzumab was administered for 15 mins. Five patients with breast cancer were injected with 296 MBq of <sup>64</sup>Cu-NOTA-trastuzumab. Six patients with breast cancer were injected with 370 MBq of <sup>64</sup>Cu-DOTA-trastuzumab. PET/CT was performed 24 and 48 hours after injection. The mean standardized uptake (SUV<sub>mean</sub>) was evaluated from the blood, liver, kidney, muscle, spleen, bladder, lung, and bone. Furthermore, the radiation activity of <sup>64</sup>Cu-NOTA-trastuzumab and <sup>64</sup>Cu-DOTA-trastuzumab for each organ was evaluated at imaging time points and the residence time of radiotracer was calculated from the activity of each organ. The internal dosimetry for <sup>64</sup>Cu-NOTA-trastuzumab and <sup>64</sup>Cu-DOTA-trastuzumab was evaluated using OLINDA/EXM software with an adult female model, which was used for evaluating the internal dosimetry for <sup>225</sup>Ac-NOTA-trastuzumab and <sup>225</sup>Ac-DOTA-trastuzumab.

### Results:

The overall values of SUV<sub>mean</sub> in each organ decreased with time on both <sup>64</sup>Cu-NOTA-trastuzumab and <sup>64</sup>Cu-DOTA-trastuzumab PET images. However, the bladder showed an increasing pattern of SUV<sub>mean</sub> over time. In the liver, <sup>64</sup>Cu-NOTA-trastuzumab showed relatively lower SUV mean (24 hours;  $4.64 \pm 0.28$ , 48 hours;  $4.26 \pm 0.50$ ) compared to <sup>64</sup>Cu-DOTA-trastuzumab (24 hours;  $6.66 \pm 1.57$ , 48 hours;  $7.05 \pm 1.72$ ). <sup>64</sup>Cu-DOTA-trastuzumab showed an increasing pattern of the SUV<sub>mean</sub> in the liver over time. In the blood pool, <sup>64</sup>Cu-NOTA-trastuzumab showed relatively higher SUV mean (24 hours;  $9.32 \pm 1.23$ , 48 hours;  $7.42 \pm 1.85$ ) compared to that of <sup>64</sup>Cu-DOTA-trastuzumab (24 hours;  $7.85 \pm 1.76$ , 48 hours;  $6.25 \pm 1.64$ ). Other tissues showed similar SUV<sub>mean</sub> values on both PET images. Any adverse was not reported. The calculated effective doses for <sup>64</sup>Cu-NOTA-trastuzumab and <sup>64</sup>Cu-DOTA-trastuzumab were 14.3 uSv/MBq and 53.1 uSv/MBq, respectively. <sup>64</sup>Cu-NOTA-trastuzumab showed relatively lower radiation burden (46.4 uSv/MBq) compared to that of <sup>64</sup>Cu-DOTA-trastuzumab (254 uSv/MBq). The predicted effective doses for <sup>225</sup>Ac-NOTA-trastuzumab and <sup>225</sup>Ac-DOTA-trastuzumab were 2.19 mSv/MBq and 7.83 mSv/MBq, respectively. In the case of the liver, <sup>225</sup>Ac-NOTA-trastuzumab showed lower absorbed dose (8.44 mSv/MBq) compared to that of <sup>225</sup>Ac-DOTA-trastuzumab (47.0 mSv/MBq).

### Conclusions:

In the normal liver, lower uptake of <sup>64</sup>Cu-NOTA-trastuzumab was observed compared to <sup>64</sup>Cu-DOTA-trastuzumab. It may be more helpful to detect metastatic lesions in the liver. Furthermore, when the <sup>64</sup>Cu is replaced with <sup>225</sup>Ac for treatment purpose, liver damage may be reduced when using NOTA-trastuzumab compared to when using DOTA-trastuzumab.

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