Supplementary Materials

Table S1. Standard delineation protocol

1. Reconstruction method

According to Makris et al. [1]

2. Analysis plan

PET image analysis of scans performed 4 days post tracer injection.

Targets to select for PET quantification:

- Tumor lesions
- Background regions (=healthy organs/tissue)
- Whole organs

PET quantification parameters

- Background regions: %ID/kg
- Tumor lesions: volume (mL)
- Whole organs: %ID/kg

Software

- A medical imaging data examiner (AMIDE, [2])

Targets

Lesions

- All visible lesions on PET and/or on diagnostic CT scan

Background regions

- For each background organ a background area should be quantified.
- Use an sphericalVOI (location and/or size of VOI might be adapted in case of tumor locations) in at least 3 consecutive axial planes:
    - Brain 5 cm (left hemisphere, parietal)
    - Lung 5 cm (right upper lobe, mediolateral)
    - Aortic blood pool 2 cm (Aortic arch or thoracic aorta, highest region)
    - Muscle 5 cm (region right gluteus maximus/medius)
    - Spleen 5 cm (representative region; 4 cm if 5 cm VOI is too big) and 2 cm (highest region)
    - Liver 5 cm (representative region)
    - Kidney 2 cm (cortex of left kidney, highest region)
    - Bone marrow 2 cm (L4 or L5)

- Bone cortex 1 cm (femur cortex, right)
- Intestine 2 cm (highest region)
- Fat tissue 2 cm (abdominal region)

Whole organ analysis

- Only assess organs when there is no metastatic disease located in this certain organ
- Organs of interest for whole organ analysis:
  - Liver

Calculations

AMIDE output (mean activity concentration in Bq/cc) was used to calculate the percentage injected dose per kilogram (%ID/kg) tissue of every VOI with the following formula:

$$\%ID/kg = \frac{Activity\ concentration\ (Bq/kg)}{Injected\ activity\ (Bq)} * 100\%$$

Injected activity was corrected for decay between moment of tracer injection and time of scanning (under the assumption of a tissue density of 1 kg/L).

Percentage organ and fat tissue tracer uptake was calculated using the following formula:

$$Organ\ uptake\ (\%) = \frac{Activity\ concentration\ (Bq/gr) * Organ\ volume\ (gr)}{Injected\ activity\ (Bq)} * 100\%$$

Table S2. Detailed information antibody and tracer characteristics

	^{89}**Zr-lumretuzumab**	^{89}**Zr-MMOT0530A**	^{89}**Zr-bevacizumab**	^{89}**Zr-trastuzumab**
Pharmacokinetic parameters of monoclonal antibody				
Monoclonal antibody	Lumretuzumab	MMOT0530A	Bevacizumab	Trastuzumab
IgG class	Humanized glycoengineered IgG1κ	Humanized IgG1	Humanized IgG1	Humanized IgG1
Target	HER3	Mesothelin	VEGF	HER2
Molecular weight (kDa)	150	150	150	150
Linear kinetics	Elimination of lumretuzumab across dose range 100 - 400 mg is predominantly target mediated; PK approached linearity at 400 – 2,000 mg	Modest degree of target mediated clearance at doses < 1 mg/kg; linear clearance across tested dose range of 0.2 to 2.8 mg/kg for the q3w schedule	Linear pharmacokinetics for doses 1 - 10 mg/kg	Non-linear elimination
Clearance	1.04 L/d (100 mg); 0.264 L/d (>2000 mg)	27 mL/d/kg	0.188 L/d - 0.220 L/d	0.111 L/d
Volume of distribution	3.64 L (100 mg); 4.4 L (>2000 mg)	Vss = 68 mLl/kg	2.73 - 3.28 L	2.91 L
Elimination half-life time	2.4 d (100 mg); 12 d (>400 mg)	2.1 - 3.7 d	18-20 d	28.5 d
Reference	Meulendijks et al. [3]	Weekes et al. [4]	European public assessment report of Herceptin [5]	European public assessment report of Avastin [6]

Table S2. Continued.

	^{89}Zr-lumretuzumab	**^{89}Zr-MMOT0530A**	**^{89}Zr-bevacizumab**	**^{89}Zr-trastuzumab**
Information on the ^{89}Zr-labeled antibodies				
Chelator	TFP-*N*-sucDf	TFP-*N*-sucDf	TFP-*N*-sucDf	TFP-*N*-sucDf
Chelator:mAb conjugation ratio	1.5 ± 0.1	1.5 ± 0.1	1.5 ± 0.1	1.3 ± 0.1
In vitro serum stability	Stable in serum; < 5% decrease in radiochemical purity (rcp) after 168 h	2% decrease in rcp after 168 h in normal saline at 20°C	6% decrease rcp after 168 h in serum	0.39 ± 0.02% decrease in rcp/day in serum
Radiochemical purity (%)	> 98	> 98	> 98	> 98
pH	4 - 7	5 - 8	6 - 7	5-8
Immunoreactivity (%)	Preserved	> 70	> 60	> 70
Appearance	Colorless to light yellow	Colorless to light yellow liquid	Colorless	Colorless
Bacterial endotoxins (EU/mL)	< 2.5	< 2.5	< 1.0	< 2
Aggregates (%)	< 5	< 5	< 3	< 5
Sterility	Sterile	Sterile	Sterile	Sterile

^{89}Zr, Zirconium-89; IgG, Immunoglobuline gamma; HER, Human epidermal growth factor receptor; mAb, monoclonal antibody; rcp, radiochemical purity; TFP-*N*-sucDf, tetrafluorophenol-N-succinyldesferal; VEGF, Vascular endothelial growth factor receptor; Vss, steady state volume of distribution.

Table S3. Details on deposited data and curation process

Data deposit

An overview over the deposited datasets including details on the dataset, contact information, information on requesting and depositing data can be found online under www.imagingwarehouse.eu.

Deposited data

Information on the individual subject and imaging data per individual subject will be deposited.

Specification of the deposited data for the four ^{89}Zr-mAb tracers analyzed in the current manuscript:

Patient related information:

Weight, height, total tumor load (PET based, mL), injected [netto] dose, time between tracer injection and start of PET scan, activity on the day of tracer injection.

PET imaging data per individual patient:

AMIDE output and SUV calculations for blood and normal organ VOI's: aorta, liver, kidney, fat tissue, muscle, brain, lung, spleen, intestine, femur cortex and bone marrow.

AMIDE output per VOI includes median, mean, variance, standard deviation, minimum, maximum and size (mm^3).

SUV calculations include SUVmean and SUVmax.

Data to be deposited by external parties should include at least above mentioned patient related information and PET related information. Thereby, the administered radiation dose is not restricted to 37 MBq, as the dose can vary. Information on the used analysis tool and/or algorithm should also be deposited. Throughout time, requirements on which data to be deposited might change, therefore, it is recommended to consult the website for further instructions (www.imagingwarehouse.eu).

Data request

All data will be provided upon request. Requests can be send by email to the imaging warehouse group (imagingwarehouse@onco.umcg.nl). Data can be requested by health care professionals and all scientific personnel. Data is provided for research purpose only.

Re-processing of imaging data with other reconstruction protocols and additional information can be requested. Whether requested data can be provided, will be decided by the for the dataset responsible researcher or delegates (*e.g.* based on privacy laws).

Request format

All requests need to contain a specification of the requested data set, information on the requesting person or group including name of the responsible investigator, function and institution. Furthermore, a short description of the intended aim/research question is preferred.

Public disclosure and publication policy

Provenance of the data must be stated and data needs to be referenced to in all publications in written form, oral presentation or publication in any other form.

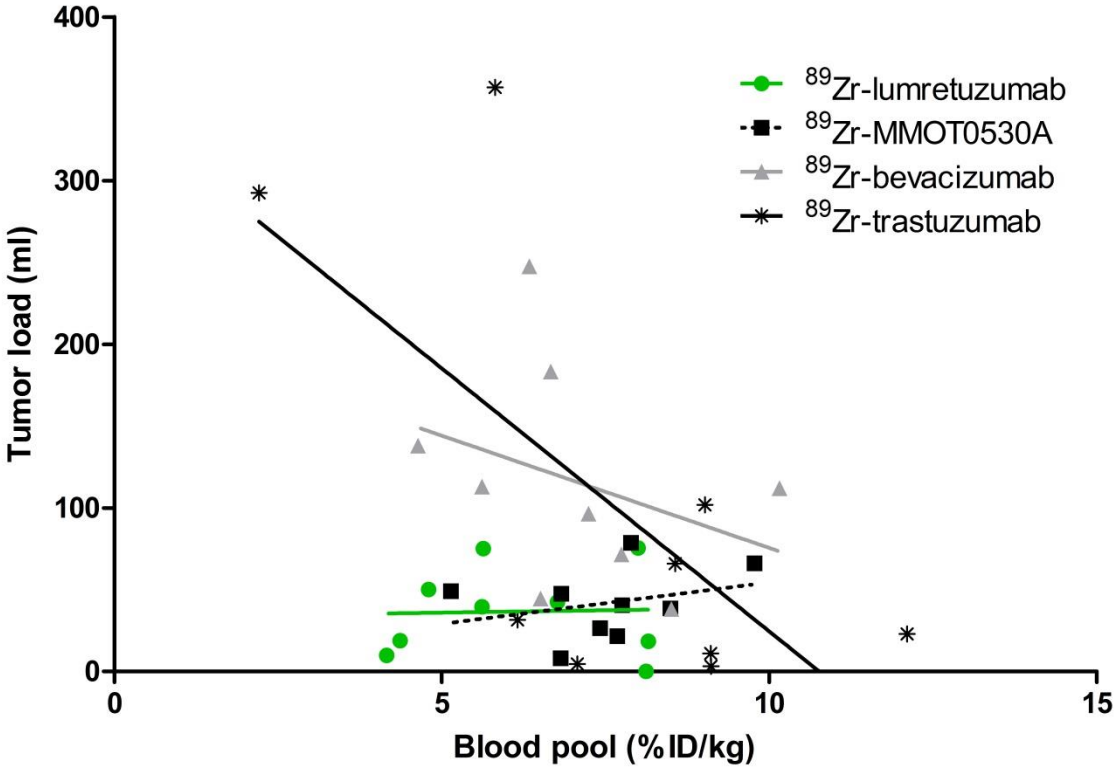

Figure S1. Correlation between activity in the aorta (%ID/kg) and tumor load (ml) for ^{89}Zr-lumretuzumab (r^2=0.00, *P*=0.93), ^{89}Zr-MMOT0530A (r^2=0.09, *P*=0.44), ^{89}Zr-bevacizumab (r^2=0.11, *P*=0.38) and ^{89}Zr-trastuzumab (r^2=0.46, *P*=0.05).

References:

1. Makris NE, Boellaard R, Visser EP, et al. Multicenter harmonization of ^{89}Zr PET/CT performance. J Nucl Med. 2014; 55: 264-267.
2. Loening AM, Gambhir SS. AMIDE: a free software tool for multimodality medical image analysis. Mol Imaging. 2003; 2: 131-137.
3. Meulendijks D, Jacob W, Martinez-Garcia M, et al. First-in-human phase I study of lumretuzumab, a glycoengineered humanized anti-HER3 monoclonal antibody in patients with metastatic or advanced HER3-positive solid tumors. Clin Cancer Res. 2016; 22: 877-885.
4. Weekes CD, Lamberts LE, Borad MJ, et al. Phase I study of DMOT4039A, an antibody-drug conjugate targeting mesothelin, in patients with unresectable pancreatic or platinum-resistant ovarian cancer. Mol Cancer Ther. 2016; 15: 439-447.
5. European Medicines Agency, European public assessment report of Herceptin. Revised 13/12/2017. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000278/human_med_000818.jsp&mid=WC0b01ac058001d124
6. European Medicines Agency, European public assessment report of Avastin. Revised 15/12/2017. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000582/human_med_000663.jsp&mid=WC0b01ac058001d124