

Supplemental Figure 1. Four patients (from left to right: patient #1 in arm A, and patient #2, #7, #16 in arm B) with fulminant hepatic metastases.

## **Inclusion Criteria**

- Written informed consent.
- Patients of either gender, aged ≥ 18 years.
- Histologically confirmed diagnosis of Metastatic, well-differentiated neuroendocrine tumor.
- A diagnostic computed tomography (CT) or magnetic resonance imaging (MRI) of the tumor region within the previous 6 months prior to dosing day is available.
- At least 1 measurable lesion based on RECIST v1.1.
- Blood test results as follows (White blood cell:  $\geq 3*10^9$ /L, Hemoglobin:  $\geq 8.0$  g/dL, Platelets:  $\geq 50x10^9$ /L, Alanine aminotransferase / Aspartate aminotransferase / Alkaline phosphatase:  $\leq 5$  times upper limit of normal (ULN), Bilirubin:  $\leq 3$  times ULN)
- Serum creatinine: within normal limits or < 120  $\mu$ mol/L for patients aged 60 years or older.
- Calculated Glomerular filtration rate (GFR) ≥ 45 mL/min.

## **Exclusion Criteria**

- Known hypersensitivity to Gallium-68, to NODAGA, to DOTA, to LM3, or to any of the excipients of Gallium-68 DOTA-LM3 or Gallium-68 NODAGA-LM3.
- Presence of active infection at screening or history of serious infection within the previous 6 weeks.
- Therapeutic use of any somatostatin analog, including long-acting Sandostatin (within 28 days) and short-acting Sandostatin (within 2 days) prior to study imaging. If a patient is on long-acting Sandostatin, then a wash-out phase of 28 days is required before the injection of the study drug. If a patient is on short-acting Sandostatin, then a wash-out phase of 2 days is required before the injection of the study drug.
- Prior or planned administration of a radiopharmaceutical within 8 half-lives of the radionuclide used on such radiopharmaceutical including at any time during the current study.
- Pregnant or breast-feeding women.
- Current history of any malignancy other than neuroendocrine tumor; patients with a secondary tumor in remission of > 5 years can be included.
- Any mental condition rendering the patient unable to understand the nature, scope and possible consequences of the study, and/or evidence of an uncooperative attitude.

Supplemental Table 2. The SUVmax and tumor-to-background ratios of 38 reference lesions

Time after	$^{68}$ Ga-NODAGA-LM3 ( $N = 18$ )	$^{68}$ Ga-DOTA-LM3 ( $N = 20$ )	P value		
injection (minutes)	SUVmax				
5	$31.3 \pm 19.7$	$36.6 \pm 23.6$	0.455		
15	$40.4 \pm 25.9$	$41.9 \pm 26.5$	0.860		
30	$47.1 \pm 31.0$	$45.3 \pm 29.3$	0.858		
45	$54.9 \pm 37.3$	$46.6 \pm 31.2$	0.461		
60	$57.5 \pm 39.4$	$47.2 \pm 32.6$	0.385		
120	$74.6 \pm 56.3$	$46.1 \pm 30.9$	0.058		
	Tumor-to-blood-pool ratio				
5	$16.4 \pm 11.7$	$15.5 \pm 10.0$	0.803		
15	$28.0 \pm 20.1$	$22.8 \pm 14.7$	0.366		
30	$45.5 \pm 38.6$	$24.6 \pm 15.8$	0.044		
45	$58.8 \pm 46.4$	$32.0 \pm 24.4$	0.038		
60	$57.1 \pm 38.9$	$38.4 \pm 29.1$	0.099		
120	$74.8 \pm 67.2$	$41.5 \pm 41.4$	0.071		
	Tumor-to-kidney ratio				
5	$1.3 \pm 0.7$	$4.8 \pm 3.4$	< 0.001		
15	$2.0 \pm 1.1$	$7.6 \pm 5.9$	< 0.001		
30	$2.4 \pm 1.4$	$8.4 \pm 6.3$	< 0.001		
45	$3.0 \pm 1.8$	$10.3 \pm 8.2$	0.001		
60	$3.1 \pm 1.9$	$11.0 \pm 9.6$	0.002		
120	$4.0 \pm 2.5$	$10.3 \pm 9.2$	0.008		
	Tumor-to-liver ratio				
5	$4.2 \pm 2.8$	$12.5 \pm 7.7$	< 0.001		
15	$6.2 \pm 4.3$	$16.4 \pm 9.2$	< 0.001		
30	$7.8 \pm 5.8$	$17.6 \pm 9.9$	0.001		
45	$9.4 \pm 7.1$	$18.6 \pm 11.6$	0.006		
60	$10.0\pm7.4$	$18.5 \pm 11.5$	0.011		
120	$12.6 \pm 9.5$	$20.7 \pm 12.9$	0.035		

Supplemental Table 3. Residence times and absorbed doses of liver.

	Patient #*	Arm	Residence time (h)	Absorbed doses (mGy/MBq)
Patients with fulminant liver diseases	1	A	0.448	0.124
	2	В	0.536	0.147
	7	В	0.546	0.150
	16	В	0.719	0.196
Patients without fulminant liver diseases	4	В	0.092	0.028
	5	A	0.144	0.042
	6	A	0.172	0.050
	9	A	0.160	0.046
	10	A	0.165	0.048
	11	A	0.110	0.033
	12	В	0.198	0.052
	13	A	0.169	0.049
	14	A	0.181	0.052
	15	В	0.053	0.017

<sup>\*</sup> Patient #3 and #8 were dropped out.