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NeoBOMB1, a GRPR-Antagonist for Breast Cancer Theragnostics: First Results of a Preclinical Study with [^{67}Ga]NeoBOMB1 in T-47D Cells and Tumor-Bearing Mice

Aikaterini Kaloudi [1], Emmanouil Lymperis [1], Athina Giarika [1], Simone Dalm [2], Francesca Orlandi [3], Donato Barbato [3], Mattia Tedesco [3], Theodosia Maina [1], Marion de Jong [2] and Berthold A. Nock [1,*]

1 Molecular Radiopharmacy, INRASTES/NCSR "Demokritos", 15310 Athens, Greece; katerinakaloudi@yahoo.gr (A.K.); mlymperis@hotmail.com (E.L.); athina.giarika@gmail.com (A.G.); maina_thea@hotmail.com (T.M.)

2 Department of Radiology, Erasmus MC, 3015 CN Rotterdam, The Netherlands; s.dalm@erasmusmc.nl (S.D.); m.hendriks-dejong@erasmusmc.nl (M.d.J.)

3 Advanced Accelerator Applications, 10010 Colleretto Giacosa TO, Italy; francesca.orlandi@adacap.com (F.O.); donato.barbato@adacap.com (D.B.); mattia.tedesco@adacap.com (M.T.)

* Correspondence: nock_berthold.a@hotmail.com; Tel.: +30-210-650-3908

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Abstract: Background: The GRPR-antagonist-based radioligands [$^{67/68}$Ga/^{111}In/^{177}Lu]NeoBOMB1 have shown excellent theragnostic profiles in preclinical prostate cancer models, while [^{68}Ga]NeoBOMB1 effectively visualized prostate cancer lesions in patients. We were further interested to explore the theragnostic potential of NeoBOMB1 in GRPR-positive mammary carcinoma, by first studying [^{67}Ga]NeoBOMB1 in breast cancer models; Methods: We investigated the profile of [^{67}Ga]NeoBOMB1, a [^{68}Ga]NeoBOMB1 surrogate, in GRPR-expressing T-47D cells and animal models; *Results*: NeoBOMB1 (IC_{50}s of 2.2 ± 0.2 nM) and [^{nat}Ga]NeoBOMB1 (IC_{50}s of 2.5 ± 0.2 nM) exhibited high affinity for the GRPR. At 37 °C [^{67}Ga]NeoBOMB1 strongly bound to the T-47D cell-membrane (45.8 ± 0.4% at 2 h), internalizing poorly, as was expected for a radioantagonist. [^{67}Ga]NeoBOMB1 was detected >90% intact in peripheral mouse blood at 30 min pi. In mice bearing T-47D xenografts, [^{67}Ga]NeoBOMB1 specifically localized in the tumor (8.68 ± 2.9% ID/g vs. 0.6 ± 0.1% ID/g during GRPR-blockade at 4 h pi). The unfavorably high pancreatic uptake could be considerably reduced (206.29 ± 17.35% ID/g to 42.46 ± 1.31% ID/g at 4 h pi) by increasing the NeoBOMB1 dose from 10 pmol to 200 pmol, whereas tumor uptake remained unaffected. Notably, tumor values did not decline from 1 to 24 h pi; Conclusions: [^{67}Ga]NeoBOMB1 can successfully target GRPR-positive breast cancer in animals with excellent prospects for clinical translation.

Keywords: GRPR-antagonist; theragnostics; targeted tumor imaging; PET-imaging; breast cancer