First-in-Human Total-Body PET/CT Imaging Using ^{89}Zr-Labeled MUC5AC Antibody in a Patient with Pancreatic Adenocarcinoma

Harshad R. Kulkarni[1,2], Kevin A. Maupin[1,2], Tina Brennan[1], Jens Forsberg[1,2], Dan Rogers[1], Mark Olson[1], Brandon R. Mancini[1,2], Anthony Chang[1], Sreenivasa R. Chandana[3], and Ryohei Kobayashi[4]

[1]BAMF Health, Grand Rapids, Michigan; [2]Department of Radiology, Michigan State University College of Human Medicine, East Lansing, Michigan; [3]The Cancer & Hematology Centers, Grand Rapids, Michigan; and [4]Nihon Medi-Physics Co., Ltd., Tokyo, Japan

We report on a 54-y-old man with stage pT3pN1pM1(HEP) pancreatic-head adenocarcinoma and liver metastasis. After diagnosis 20 mo previously, he underwent Whipple surgery and multiple chemotherapy regimens including folinic acid, fluorouracil, irinotecan hydrochloride, and oxaliplatin; gemcitabine/capecitabine; and gemcitabine/nab-paclitaxel. He recently underwent first-in-human imaging with ^{89}Zr-hNd2 (NMK89; Nihon Medi-Physics Co., Ltd.) for a phase 1 trial (NCT06129422) targeting mucin 5AC (MUC5AC)–positive pancreatic cancer. Of pancreatic adenocarcinomas, 64%–89% express MUC5AC, which is a secreted type of mucin and has a low normal-organ expression (*1*–*3*). In vitro studies of human pancreatic cancer tissue showed retention of MUC5AC around cancer cells and in the stroma (*4*). Therefore, radiolabeled antibodies binding to MUC5AC could potentially be used for molecular imaging and targeted radiomolecular therapy.

Biodistribution of the antibody at 1, 24, 72, and 168 h after injection was assessed using total-body PET/CT (Fig. 1). There were no adverse effects or lab changes up to 14 d after injection of ^{89}Zr-hNd2. Early results with ^{89}Zr-hNd2 suggest its potential in identifying candidates for MUC5AC-targeted treatments, including a theranostic approach with ^{225}Ac, meriting continued investigation in clinical trials (*4*).

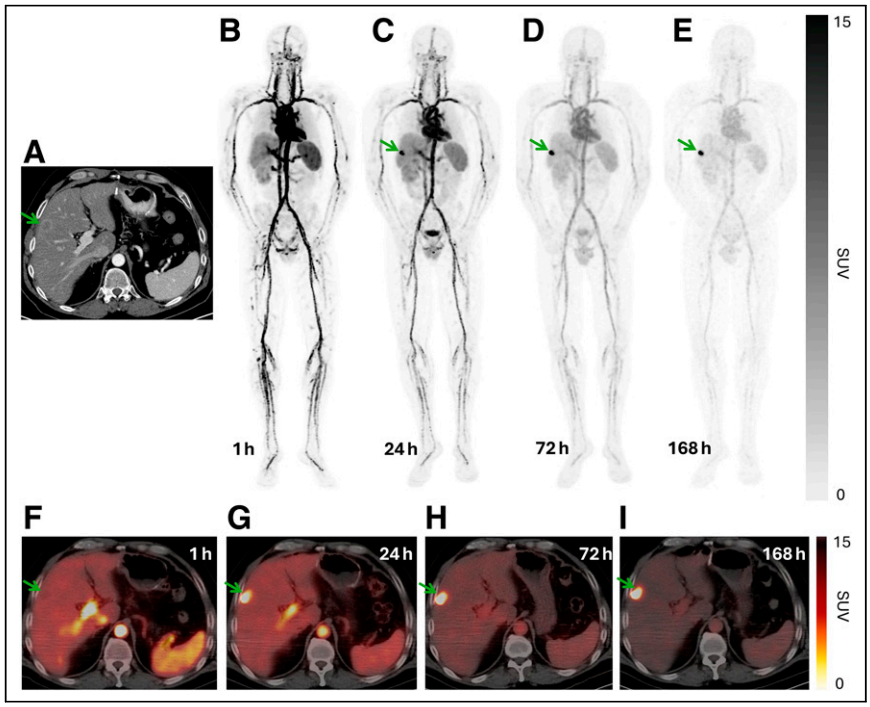

FIGURE 1. Latest contrast-enhanced CT (A) revealed stable single liver metastasis (arrows), which was biopsied and stained positively for MUC5AC. Subsequent ^{89}Zr-hNd2 PET/CT series (B–E, maximum-intensity projections; F–I, axial PET/CT images) at 1, 24, 72, and 168 h after injection of 37 MBq of ^{89}Zr-hNd2 shows lesion SUV_{max} of 36.7 (24 h), 37.0 (72 h), and 35.3 (168 h), with increasing metastasis-to-liver SUV_{max}/SUV_{mean} ratios of 7.6, 14.2, and 27.2, respectively. Stable single liver metastasis was subsequently resected followed by stereotactic radiotherapy because of positive resection margin.

DISCLOSURE

This research was supported by AMED under grant JP17pc0101014. No other potential conflict of interest relevant to this article was reported.

Received May 13, 2024; revision accepted Aug. 8, 2024.
For correspondence or reprints, contact Harshad R. Kulkarni (harshad.kulkarni@bamfhealth.com).
Published online Sep. 5, 2024.

DOI: 10.2967/jnumed.124.268074

REFERENCES

1. Jinfeng M, Kimura W, Hirai I, Sakurai F, Moriya T, Mizutani M. Expression of MUC5AC and MUC6 in invasive ductal carcinoma of the pancreas and relationship with prognosis. *Int J Gastrointest Cancer.* 2003;34:9–18.
2. Wang Y, Gao J, Li Z, Jin Z, Gong Y, Man X. Diagnostic value of mucins (MUC1, MUC2 and MUC5AC) expression profile in endoscopic ultrasound-guided fine-needle aspiration specimens of the pancreas. *Int J Cancer.* 2007;121:2716–2722.
3. Rico SD, Mahnken M, Büscheck F, et al. MUC5AC expression in various tumor types and non-neoplastic tissue: a tissue microarray study on 10 399 tissue samples. *Technol Cancer Res Treat.* 2021;20:15330338211043328.
4. Nakata N, Kobashi N, Okumura Y, et al. Radiation dosimetry and efficacy of an ^{89}Zr/^{225}Ac-labeled humanized anti-MUC5AC antibody. *Nucl Med Biol.* 2022; 108–109:33–43.