In Vivo Imaging of Prostate Cancer Using $[^{68}\text{Ga}]$-Labeled Bombesin Analog BAY86-7548

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Abstract

Purpose: A novel $[^{68}\text{Ga}]$-labeled DOTA-4-amino-1-carboxymethyl-piperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH$_2$ peptide (BAY86-7548) having high affinity to bombesin receptor subtype II to detect primary and metastatic prostate carcinoma using positron emission tomography/computed tomography (PET/CT) was synthesized and evaluated for prostate cancer.

Experimental Design: In this first human study with BAY86-7548, 14 men scheduled for radical prostatectomy (n = 11) or with biochemical recurrence after surgery or hormonal therapy (n = 3) were enrolled. The patients received an intravenous injection of BAY86-7548 followed by over 60-minute dynamic imaging of prostate gland (n = 10) and/or subsequent whole-body imaging (n = 14). The visual assessment of PET/CT images included evaluation of intraprostatic (12 subsextants) and pelvic nodal uptake of BAY86-7548 in 11 surgical patients and detection of potential metastatic foci in all patients. In patients with biochemical recurrence, results were compared with those of either $[^{11}\text{C}]$-acetate (n = 2) or $[^{18}\text{F}]$-fluoromethylcholine (n = 1) PET/CT.

Results: We found a sensitivity, specificity, and accuracy of 88%, 81% and 83%, respectively, for detection of primary PCa and sensitivity of 70% for metastatic lymph nodes using histology as gold standard. BAY86-7548 correctly detected local recurrence in prostate bed and showed nodal relapse in accordance with $[^{11}\text{C}]$-acetate PET/CT in 2 patients with biochemical relapse. In the third hormone refractory patient, BAY86-7548 failed to show multiple bone metastases evident on $[^{18}\text{F}]$-fluoromethylcholine PET/CT.

Conclusion: BAY86-7548 PET/CT is a promising molecular imaging technique for detecting intraprostatic prostate cancer. Clin Cancer Res; 1–10. ©2013 AACR.
Translational Relevance

Overexpression of bombesin receptors has been observed in several neoplastic diseases, including prostate cancer, thus offering a promising target for in vivo imaging. Anatomic imaging often fails to detect local disease with sufficient specificity for emerging focal therapies for prostate cancer. Therefore, novel techniques showing the dominant intraprostatic lesion are becoming increasingly important. This study shows that 68Ga-labeled DOTA-4-aminol-carboxymethylpiperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH2-peptide (BAY86-7548) positron emission tomography/computed tomography (PET/CT) detects organ-confined prostate cancer with an accuracy of 83%, which is at least comparable with multiparametric MRI and PET/CT using radiolabeled choline or acetate. Autoradiography (ARG) findings obtained from surgical specimens indicated that BAY86-7548 indeed detects bombesin receptor subtype II (gastrin-releasing peptide receptor; GRPr)-positive lesions and could assist in planning of focal treatment of prostate cancer.

the reported sensitivities and specificities remains high (7, 8).

PET is frequently used in oncology but its role in diagnosis of primary prostate cancer is not well established. The most common tracer, [18F]fluoro-2-deoxy-D-glucose (FDG), has a low sensitivity for detecting early prostate cancer due to the low glucose consumption (9, 10), limiting the possibility to detect clinically localized disease. Other tracers, such as [18F]- or [11C] labeled choline and [11C]-acetate, are used mainly for the diagnosis of recurrent (11–13) or metastatic (14) prostate cancer. Their feasibility in primary diagnosis is limited because of uptake in benign tissue such as benign prostatic hyperplasia (BPH; refs. 15, 16).

68Ga-labeled DOTA-4-aminol-carboxymethylpiperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH2 (BAY86-7548) is a synthetic bombesin receptor antagonist, which targets gastrin-releasing peptide receptors (GRPr; ref. 17). GRPr proteins are highly overexpressed in several human tumors, including prostate cancer (18). Because of their low expression in BPH and inflammatory prostatic tissues (19, 20), imaging of GRPr has potential advantages over current choline- and acetate-based radiotracers. Indeed, preclinical studies using BAY86-7548 have shown a high and persistent tracer uptake in mice bearing PC-3 tumor xenografts, which represent androgen-independent human prostate cancer with high GRPr expression (21).

The aim of this prospective, multisite study was to investigate the safety, tolerability, and accuracy of BAY86-7548 in detection of primary prostate cancer and lymph node metastases in patients scheduled for radical retroperitoneal or robot-assisted laparoscopic prostatectomy. In addition, feasibility of detecting recurrent prostate cancer in comparison with [18F]-fluoromethylcholine, [11C]-acetate positron emission tomography/computed tomography (PET/CT), or MRI was examined in 3 patients with increasing PSA after radical or palliative treatment. Finally, the potential of BAY86-7548 to study GRPr expression in human prostate cancer was studied.

Materials and Methods

Patients and study design

Eleven patients (mean age, 63 years; range, 48–72 years) with histologically confirmed prostate adenocarcinoma, diagnosed through systematic TRUS-guided biopsies, and 3 patients (mean age, 67 years; range, 51–82 years) with biochemical recurrence of prostate cancer were prospectively enrolled. Individual patient characteristics are presented in Table 1. Thirteen patients were studied in Turku, Finland and 1 patient was studied in Zurich, Switzerland. Additional inclusion criteria for patients undergoing radical prostatectomy was presence of cancer in at least 20% of biopsy material and patient preference to undergo radical surgery including pelvic lymphadenectomy after discussion of the treatment options with the study urologist (E. Kähkönen). None of the patients studied in Turku had received any hormonal therapy or radiotherapy, whereas the patient in Zurich was in androgen-resistant phase after pelvic radiotherapy, several local palliative radiotherapies, and antiandrogenic therapy. In addition, a multiparametric 3T MRI using surface coil was conducted for 3 patients (no. 9, 11, and 12) and [11C]-acetate PET/CT in 3 patients (no. 11, 12, and 13). The patient in Zurich (no. 14) underwent [18F]-fluoromethylcholine PET/CT. Multiparametric 3T MRI consisted of anatomic T2- and T1-weighted images, dynamic contrast-enhanced MRI, and diffusion-weighted imaging.

The study protocol was approved by the local ethics committees in Turku and Zurich as well as the respective authorities and each patient gave written informed consent for participation in the study. The entire study was carried out according to the guidelines of the Declaration of Helsinki.

Synthesis of BAY86-7548

The precursor, DOTA-4-aminol-carboxymethylpiperidine-D-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH2 (BAY86-7547), was obtained from Bayer HealthCare Pharmaceuticals. All the other reagents were purchased from commercial suppliers and were synthesized or analytically graded.

Turku. The radiosynthesis was conducted with fully automated synthesis device (Modular Lab, Eckert & Ziegler Eurotope GmbH). 68Ga was obtained from a 68Ge/68Ga generator [IGG-100; 50 mCi (1,850 MBq); Eckert & Ziegler Isotope Products] by eluting the generator with 7 mL of 0.1 mol/L HCl. The radioactive fraction of the 68Ga eluate (1.6 mL) was collected and the HEPES–buffered BAY86-7547 (28 μg; 17 nmol) was added. The reaction mixture was incubated at 100°C to 120°C for 12.5 minutes followed by SepPak purification, sterile filtration, and formulation with sterile PBS. The identity and the radiochemical purity of the...
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**Abbreviations:** PCa, prostate cancer; TNM, tumor—node—metastasis.

**Final Gleason score** is based on the whole-mount prostatectomy, whereas ARG Gleason score is from the particular tissues section used for ARG.
product (BAY86-7548) were evaluated by radio-high-performance liquid chromatography (radio-HPLC). The identity was confirmed by comparing the retention times of the peaks obtained from BAY86-7548 and BAY86-7547. The in vitro stability of BAY86-7548 was tested in formulation solution (PBS) by incubating for 2 hours at room temperature followed by radio-HPLC analysis.

**Zurich.** The radiosynthesis was comparable with that in Turku except for the $^{68}$Ga eluate, which was trapped onto a cation-exchange cartridge (Strata-X-C, Phenomenex). Then, 0.4 mL of 98% acetone/0.02 mol/L HCl was used to elute $^{68}$Ga from the cartridge. The peptide BAY86-7547 (28 µg; 17 nmol) and uric acid were dissolved in 2 mL of 0.2 mol/L sodium acetate buffer and were prefilled into the reaction vessel. This was followed by incubation of the reaction mixture at 95°C for 6 minutes and 40 seconds, and formulation and in vitro stability testing was carried out in saline instead of PBS. Otherwise, the procedures were similar.

**BAY86-7548 PET/CT imaging**

The patients were imaged in supine position using a GE Discovery VCT (Turku) or ST16 (Zurich) PET/CT Scanner (General Electric Medical Systems). Low-dose CT protocol (120 kV, 10–80 mA, noise index 25, slice thickness, 3.75 mm in Turku; and 140 kV, 10–80 mA, noise index 11.75, slice thickness, 3.75 mm in Zurich) was conducted and also used for attenuation correction. A median dose of 147 MBq (range, 108–161 MBq) of BAY86-7548 was injected as an intravenous bolus. During imaging, the vital signs were monitored including a 12-lead electrocardiogram, and blood and urine chemistry. The performance liquid chromatography (radio-HPLC). The identity of BAY86-7548 and BAY86-7547 was determined in all ROIs. Tumors with the largest diameter of more than 0.5 cm were included in the analysis. The diagnostic accuracy of BAY86-7548 PET/CT was assessed using whole-mount prostatectomy sections. In patients with biochemical recurrence, additional imaging modality was conducted to clarify the findings of BAY86-7548 PET/CT.

**Surgery**

Open radical retropubic ($n = 2$) or robot-assisted laparoscopic prostatectomy ($n = 9$) and bilateral extended iliac lymphadenectomy was conducted 4 to 34 days after BAY86-7548 imaging. Preoperative risk of lymph node metastasis was estimated using Briganti nomograms (22). The surgeon (E. Kähkönen) was aware of the result of BAY86-7548 imaging and was encouraged to harvest especially the PET/CT-positive lymph nodes. The routine area resected was defined as follows: lateral border of excised fibrofatty tissue was pelvic wall and external and common iliac artery to the ureteral crossing, medial border was perivesical fat, inferior border was femoral canal, and superior border was ureter. In addition, the fibrofatty tissue from both obturator fossa and next to internal iliac artery was removed. Patient no. 3 had incomplete lymphadenectomy due to cardiopulmonary instability at the end of operation. Patient no. 8 showed suspicious metastatic lymph nodes outside routine lymphadenectomy area, just above aortic bifurcation on BAY86-7548 PET/CT and also had these nodes resected. These nodes were not detected on preoperative CT.
Histopathologic analysis

Histologic slides were analyzed by two experienced pathologists (K. Alalen and M. Kallajoki). After radical prostatectomy, the prostate glands were fixed in 10% buffered formalin for 24 to 48 hours. After fixation, the left, right, and anterior surfaces were inked with different colors to preserve the orientation of the prostate gland and to allow correlation with PET/CT images. Whole-mount axial macrosections were obtained at 8-mm intervals transversely in a plane perpendicular to the long axis of the prostate gland in superior–inferior direction. The most apical macrosection was further sectioned in coronal orientation for easier evaluation of the capsular status of the inferior region. The first transversal section at the base was further sectioned in sagittal orientation for easier evaluation of the margin and seminal vesicles. Four micrometer whole-mount sections from each macrosection were stained with hematoxylin and eosin. The presence and location of cancer foci, high-grade prostate intraepithelial neoplasm (HGPIN), prostatitis, BPH, capsular status, and seminal vesicle invasion were determined. Gleason score was assessed as combination of the most common and the second-most common type of Gleason grading for each tumor focus.

GRPr receptor ARG

Fresh tissue samples of 1.5 cm × 1.5 cm × 0.5 cm size for ARG were taken from right and left lobe of prostate gland in 10 patients. Patient no. 2 had two fresh tissue samples from each lobe, whereas the remaining patients had only one per each lobe. The samples were immediately frozen at −70°C. Cryostat sections (20-µm thick) of these samples were processed for receptor ARG as described previously for other peptide receptors (22) using GRPr-specific [125I]-Tyr4-bombesin as radioligand (23). Tissue sections were mounted on precleaned microscope slides and stored at −20°C for at least 3 days to improve adhesion of tissue to the slide. Sections were then processed according to Vigna and colleagues. (23). They were first preincubated in 10 mmol/L of HEPES buffer (pH 7.4) for 5 minutes at room temperature followed by incubation in 10 mmol/L of HEPES, 130 mmol/L of NaCl, 4.7 mmol/L of KCl, 5 mmol/L of MgCl2, 1 mmol/L of ethyleneglycol-bis (β-aminoethylether)-N,N,N,N-tetraacetic acid, 0.1% bovine serum albumin (BSA), 100 mg/mL of bacitracin (pH 7.4), and approximately 100 pmol/L of [125I]-Tyr4-bombesin-14 (81.4 TBq/mmol; PerkinElmer) in the presence or absence of 1 mmol/L of bombesin for 1 hour at room temperature. After incubation, the sections were washed four times for 2 minutes in 10 mmol/L of HEPES with 0.1% BSA (pH 7.4) at 4°C. Finally, the slides were rinsed twice for 5 seconds at 4°C in distilled water, dried at room temperature, and placed in apposition to imaging plates (Fuji Imaging Plate BAS-TR2025; Fuji Photo Film Co. Ltd.) for 14 days for scanning with the Fuji Analyzer FLA-5100. Sections were stained with hematoxylin and eosin to localize the areas of BPH, prostate cancer, and HGPIN.

Statistical analysis

Statistical analysis was conducted with SAS, version 9.3 (SAS Institute Inc.). SUV measurements were compared using Bonferroni multiple comparison test (24). Normal distributions were assessed by the Kolmogorov and Smirnov method. A P value below 0.01 was considered to be statistically significant.

Results

Patients’ clinical findings are summarized in Table 1. No drug-related adverse events were associated with BAY86-7548 and all patients tolerated the imaging procedure well. The mean PSA level of patients with primary prostate cancer was 18 ± 11 ng/mL (range, 6.2–45.0 ng/mL), whereas the 3 patients with biochemical recurrence of prostate cancer had PSA levels of 0.36, 4.7, and 282 ng/mL. On the basis of histopathologic analysis of whole-mount prostatectomy samples, 26 tumor foci were identified in 11 patients, with 19 (73%) of these foci larger than 0.5 cm.

BAY86-7548 showed fast excretion through kidneys with 25% of injected radioactivity dose observed in urine 30 minutes after injection. Plasma pharmacokinetics, whole-body distribution, metabolism, and radiation dosimetry of BAY86-7548 in healthy men have been previously described (25). The highest radioactivity uptake was detected in the urinary bladder and pancreas, which is in the line with the known expression of GRPr and previous preclinical studies with RM2 peptide (21). Maximum peak uptake of the total injected radioactivity was seen in the urinary bladder and liver, 36% and 19%, respectively.

Preparation of BAY86-7548

The radiopharmaceutical BAY86-7548 was obtained with a moderate yield (440 ± 120 MBq; n = 13). Radioactivity concentration and specific radioactivity at end of synthesis (EOS) were 44 ± 13 MBq/mL and 26 ± 7 GBq/µmol, respectively. Radiochemical purity was at least 97% and the difference between retention times of HPLC peaks obtained from BAY86-7547 and BAY86-7548 was 0.19 ± 0.07 minutes. The tracer remained radiochemically stable for 2 hours in formulation solution at room temperature; radiochemical purity was 98% ± 0% at 1 hour after EOS and 98% ± 1% at 2 hours after EOS (mean ± SD; n = 3). Every injected batch of BAY86-7548 fulfilled the release criteria.

Diagnostic accuracy of cancer detection

Region-based analysis of BAY86-7548 PET/CT findings in 132 regions, of which 57 (43%) contained cancer according to histopathologic analysis, revealed 63 regions as positive and 69 as negative. Using histology as gold standard, 49 of these were considered true-positive and 61 true-negative, yielding a sensitivity, specificity, and accuracy of 89%, 81%, and 83%, respectively. Lesion-based analysis of BAY86-7548 PET/CT revealed 15 true-positive tumor lesions, 6 false-positive lesions, and 4 false-negative lesions resulting in a sensitivity of 79%. The 6 false-positive intraprostatic lesions were determined to be BPH based on whole-mount
prostatectomy sections. BAY86-7548 PET/CT successfully detected all dominant lesions except one anterior lesion. However, another smaller peripheral zone tumor of the same patient (no. 2) was detected. Both of the lesions had the Gleason score of 3+4.

**Detection of lymph node metastasis**

Primary prostate cancer with at least one metastatic lymph node was present in 3 (27%) of 11 patients undergoing prostatectomy with lymph node dissection. In total, 135 lymph nodes were histopathologically analyzed with 10 showing the presence of metastatic prostate cancer. Per patient sensitivity was 67% and per node sensitivity was 70% for BAY86-7548 PET/CT. The sizes of the three BAY86-7548–negative metastases were 6 (patient no. 1, left iliac node), 5, and 5 mm (patient no. 6, two right iliac lymph nodes). Patient no. 6 had in addition one correctly detected metastatic left iliac node (size 11 mm). Two normal-sized lymph nodes (less than 10 mm) were removed from patient no. 8 above the aortic bifurcation based on guidance of BAY86-7548 PET/CT (see section Surgery). Both of these were histopathologically confirmed as prostate cancer metastases (Fig. 1).

**Quantitative analysis**

The average SUV\(_{\text{max}}\) and SUV\(_{\text{mean}}\) were 6.6 ± 4.7 and 5.1 ± 3.7, respectively, for histologically confirmed cancer foci as measured 60 to 70 minutes after injection. These values were different from the SUV\(_{\text{max}}\) and SUV\(_{\text{mean}}\) of BPH (2.4 ± 1.5 and 1.8 ± 1.2, respectively) and normal tissue of peripheral zone (1.3 ± 1.0 and 1.0 ± 0.9, respectively; \(P < 0.01\) for all comparisons). No significant difference in SUV\(_{\text{max}}\) and SUV\(_{\text{mean}}\) of BPH and normal tissue of peripheral zone was observed (see Fig. 2).

**Results of ARG**

Prostate cancer was present in 15 (68%) ARG sections. All lesions were positive by ARG. BPH nodules in two tissue sections and HGPIN lesion in one tissue section were positive, indicating the presence of GRPr expression (Fig. 3).

**Patients with clinical suspicion of recurrent disease**

BAY86-7548 PET/CT successfully detected recurrence of prostate cancer in the two hormone-naïve patients with biochemical recurrence (no. 12 and 13). The findings were in concordance with \(^{[1]}\text{C}-\)acetate PET/CT and 3T MRI in prostate bed in patient no. 12. In contrast, both \(^{[1]}\text{C}-\)acetate PET/CT and diffusion-weighted MRI suggested the presence of metastatic parailiac lymph node, whereas BAY86-7548 PET/CT did not show any pathologic uptake in this region. The patient subsequently received radiotherapy for PET- and MRI-positive prostatic bed and parailiac nodes bilaterally. In a repeated \(^{[1]}\text{C}-\)acetate PET/CT 3 months from radiotherapy, PSA was 0.068 and the prostate bed had turned \(^{[1]}\text{C}-\)acetate negative, whereas the parailiac lymph node was still positive. On CT, this node measured 6 mm and remained unchanged before and after.
radiotherapy despite rapid decrease in serum PSA. In patient no. 13, BAY86-7548 was positive in one iliac and one mediastinal node, which were similarly positive on [11C]-acetate. In addition, [11C]-acetate showed several positive lymph nodes in unconventional locations such as axillary, parasternal, and inguinal regions. The single patient imaged in Zurich (no. 14) had multiple [18F]-fluoromethylcholine–positive bone metastases and his BAY86-7548 PET/CT was totally negative.

Discussion

With the evolution of local and minimally invasive therapies for prostate cancer such as focal radiotherapy and high-intensity focused ultrasound, a pressure to develop better diagnostic tools to detect primary prostate cancer is evident. Currently, multiparametric MRI is being increasingly used in imaging of local prostate cancer to plan focal therapies (7, 8). Combination of functional and anatomic information using hybrid PET/MRI imaging can be a powerful technique provided that the applied tracer and the chosen MRI acquisition protocol are optimized for each patient individually.

Because none of the currently available positron-emitting tracers can reliably detect early prostate cancer or identify the extent of intraprostatic disease, there is a demand for more specific tracers. An ideal tracer would detect the dominant prostate cancer lesion and differentiate cancer from BPH and inflammatory lesions. We studied a novel 68Ga-labeled bombesin antagonist BAY86-7548 to translate the encouraging preclinical findings (21) to identical results in patients scheduled for radical prostatectomy or with biochemical recurrence. We were specifically interested in the uptake of BAY86-7548 in intraprostatic lesions (Fig. 4) and in the potential of the peptide tracer to detect metastatic lymph nodes. By selecting 68Ga as the radionuclide, we were able to carry out the study without access to cyclotron.

The potential of 68Ga-labeled peptides to target tumor receptors has been previously shown in the case of somatostatin receptor imaging. Because of their higher sensitivity and better biodistribution properties (26, 27), [68Ga]DOTATOC, [68Ga]DOTANOC, and [68Ga]DOTATATE are used for diagnosis of neuroendocrine tumors and are gradually replacing conventional gamma-emitting radioisotope techniques in Europe. In general, peptides provide excellent characteristics for PET imaging due to their easy synthesis, fast and specific targeting features, and rapid clearance from the body mainly via the renal pathway. Much like somatostatin receptors, peptides targeting G-protein–coupled receptors are effectively accumulating in tumors in vivo.

The GRPr, also named bombesin receptor subtype II, is a G-protein–coupled seven-transmembrane receptor belonging to the bombesin receptor family with four subtypes (for review see ref. 17). GRPr proteins are highly overexpressed in several human tumors, including prostate cancer, breast cancer, small cell lung cancer (SCLC), and non-SCLC, as well as renal cell cancer (18). Our results with radiolabeled bombesin antagonist (BAY86-7548) indicate that this tracer could be more prostate cancer-specific than imaging with [18F], [11C]-choline, or [11C]-acetate, which generally

![Figure 3. BAY86-7548 PET/CT (A) of patient no. 10 showing uptake in the left lobe of prostate gland in the area of cancer based on whole-mount prostatectomy sample. B, tumor is outlined in blue. Bar, 1 cm. ARG showed presence of GRPr in the section taken from the left lobe (D, top; bar, 1 cm) in the area of cancer (C, top, tumor is outlined in blue; bar, 1 cm), whereas only small areas of HGPIN in the section taken from the right lobe had positive activity (F and G, bottom, red arrow points to the area of HGPIN; bar, 1 cm). The presence of 1 mmol/L bombesin blocked uptake of [125I]-Tyr4-bombesin-14 in the sections from left (E, top right) and right (H, bottom right) lobe. BAY86-7548 PET/CT image is scaled to SUV, with a minimum at 0 and maximum at 5.](https://www.aacrjournals.org/doi/figure.clincancerres.aacrjournals.org/10.1158/1078-0432.CCR-12-3490)

![Figure 4. The uptake of BAY86-7548 in patient no. 3 was localized in the peripheral (yellow arrow in A) and central zone (red arrow in A). These areas coincide well with cancer (outlined in blue) on corresponding prostatectomy sections (B, bar, 1 cm). The large BPH nodules in the central zone did not show uptake of BAY86-7548. Black arrow points to urinary activity in a urethral catheter. The weight of the prostate gland immediately after prostatectomy was 152 g. Image is scaled to SUV, with a minimum at 0.5 and maximum at 5.](https://www.aacrjournals.org/doi/figure.clincancerres.aacrjournals.org/10.1158/1078-0432.CCR-12-3490)
The potential of BAY86-7548 in diagnosis of recurrent prostate cancer remained inconclusive. Finally, most of our patients undergoing a surgery belonged to the high clinical risk group with high risk of lymph node metastasis. This resulted in relatively high percentage (43%) of regions containing cancer according to histopathologic analysis and a selection bias embedded to the study inclusion criteria could not be completely avoided. Because whole-mount axial macrosections were obtained at 8-mm intervals, some small prostate cancer lesions could have been missed and the diameter of larger cancer lesions could have been underestimated. It is well known that precise correlation of prostate cancer location on whole-mount prostatectomy with PET/CT and MRI is relatively difficult (32). Anatomic landmarks, such as urethra were used to enable the correlations of whole-mount prostatectomy with PET/CT images. Although no cross-calibration of the two PET/CT scanners was conducted, the consequences are considered minimal as only 1 patient was studied using a different PET/CT scanner. Although radiolabeled choline or acetate remain the most commonly used tracers for imaging of biochemical relapse, these tracers have shown only limited accuracy in detection of primary prostate cancer (15, 16). In a recent study, including 39 patients undergoing radical prostatectomy, multiparametric MRI showed a sensitivity of 82% for detection of prostate cancer lesions greater than 0.5 cm, whereas the sensitivity of [11C]-acetate PET/CT was only 62% (33). Similarly, MRI including magnetic resonance spectroscopy has been shown to outperform [11C]-choline PET/CT in evaluation of primary disease (34) and multiple studies have shown low specificity of radiolabeled choline or acetate for prostate cancer imaging due to uptake in BPH (15, 16, 33). Currently, none of these 18F- or 11C-labeled tracers, which are metabolized in the phospholipid synthesis pathway, can be recommended for evaluation of primary prostate cancer (35). Therefore, the 83% accuracy of BAY86-7548 PET/CT observed in this study is indeed encouraging. When combined with multiparametric MRI, BAY86-7548 PET/CT might result in sufficient diagnostic performance to allow focal treatment of intraprostatic lesions of prostate cancer.
Despite the relatively small number of patients, we have shown the feasibility of BAY86-7548 PET/CT for detection of organ-confirmed prostate cancer. Our histopathologic and ARG analyses indicated that $^{68}$Ga-labeled bombesin antagonist BAY86-7548 had high prostate cancer–binding specificity with significantly higher uptake in prostate cancer compared with benign tissue. BAY86-7548 was well tolerated by all patients. This new tracer could be more accurate in detection of primary and recurrent prostate cancer than previously used positron-emitting tracers, although its feasibility in imaging of metastatic disease requires further optimization.

Disclosure of Potential Conflicts of Interest
Ray Valencia is employed as senior experimental medicine expert in Bayer Pharma AG. No potential conflicts of interest were disclosed by the other authors.

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