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Assessment of ^{68}Ga-PSMA-11 PET Accuracy in Localizing Recurrent Prostate Cancer

A Prospective Single-Arm Clinical Trial

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Key Points

Question

What is the accuracy of ^{68}Ga-PSMA-11 positron emission tomographic (PET) imaging for localization of recurrent prostate cancer?

Findings

In this prospective single-arm trial of 635 men, ^{68}Ga-PSMA-11 PET demonstrated 84% to 92% positive predictive value at 75% overall detection rate in patients with biochemically recurrent prostate cancer and median prostate-specific antigen of 2.1 ng/mL. Agreement among 3 readers of the PET images was substantial.

Meaning

^{68}Ga-PSMA-11 PET has high positive predictive value, detection rate, and interreader agreement for localization of recurrent prostate cancer; ^{68}Ga-PSMA-11 PET provides early detection of metastases and contributes highly relevant information in a biochemical recurrence setting.

This single-arm prospective trial assesses the positive predictive value, detection rate, inter-reader reproducibility, and safety of ^{68}Ga-PSMA-11 positron emission tomographic (PET) imaging for detection of biochemically recurrent prostate cancer compared with conventional imaging.

Abstract

Importance

In retrospective studies, ^{68}Ga-PSMA-11 positron emission tomographic (PET) imaging improves detection of biochemically recurrent prostate cancer compared with conventional imaging.

Objective

To assess ^{68}Ga-PSMA-11 PET accuracy in a prospective multicenter trial.

Design, Setting, and Participants

In this single-arm prospective trial conducted at University of California, San Francisco and University of California, Los Angeles, 635 patients with biochemically recurrent prostate cancer after prostatectomy (n = 262, 41%), radiation therapy (n = 169, 27%), or both (n = 204, 32%) underwent ^{68}Ga-PSMA-11 PET. Presence of prostate cancer was recorded by 3 blinded readers on a per-patient and per-region base. Lesions were validated by histopathologic analysis and a composite reference standard.

Main Outcomes and Measures

Endpoints were positive predictive value (PPV), detection rate, interreader reproducibility, and safety.

Results

A total of 635 men were enrolled with a median age of 69 years (range, 44-95 years). On a per-patient basis, PPV was 0.84 (95% CI, 0.75-0.90) by histopathologic validation (primary endpoint, n = 87) and 0.92 (95% CI, 0.88-0.95) by the composite reference standard (n = 217). ^{68}Ga-PSMA-11 PET localized recurrent prostate cancer in 475 of 635 (75%) patients; detection rates significantly increased with prostate-specific antigen (PSA): 38% for <0.5 ng/mL (n = 136), 57% for 0.5 to <1.0 ng/mL (n = 79), 84% for 1.0 to <2.0 ng/mL (n = 89), 86% for 2.0 to <5.0 ng/mL (n = 158), and 97% for ≥5.0 ng/mL (n = 173, $P < .001$). Interreader reproducibility was substantial (Fleiss κ, 0.65-0.78). There were no serious adverse events associated with ^{68}Ga-PSMA-11 administration. PET-directed focal therapy alone led to a PSA drop of 50% or more in 31 of 39 (80%) patients.

Conclusions and Relevance

Using blinded reads and independent lesion validation, we establish high PPV for ^{68}Ga-PSMA-11 PET, detection rate and interreader agreement for localization of recurrent prostate cancer.

Trial Registration

ClinicalTrials.gov identifiers: NCT02940262 and NCT03353740

Introduction

Treatment of patients with biochemically recurrent prostate cancer is guided by disease location and extent. Major guidelines recommend computed tomography (CT), magnetic resonance imaging (MRI), and/or bone scintigraphy at biochemical recurrence. However, these guidelines acknowledge limited sensitivity at low prostate-specific antigen (PSA) levels.[1,2,3] Novel positron emission tomography (PET) radiotracers promise to overcome this limitation, most recently with the approval of ^{18}F-fluciclovine.[2,4,5] Among the various PET probes available, ^{68}gallium-labeled ligands of the prostate-specific membrane antigen (PSMA) were associated with unprecedented accuracy and effect on treatment in several meta-analyses of retrospective studies.[6,7,8] Although ^{68}Ga-PSMA-11 PET has been used extensively on a compassionate use basis and reported in numerous retrospective case series outside of the United States, prospective data are lacking.

Here we report findings from a prospective multicenter trial investigating the positive predictive value (PPV), detection rate, reproducibility, and safety of ^{68}Ga-PSMA-11 PET imaging in patients with biochemically recurrent prostate cancer.

Methods

Patients

This is a single-arm prospective multicenter trial. Conduction and data acquisition under separate but clinically identical Investigational New Drug (IND) protocols (attached in the Supplement) was defined at baseline. Patients were recruited at the University of California, Los Angeles (UCLA, NCT02940262) and the University of California, San Francisco (UCSF, NCT03353740). Patients were eligible if they had a history of histopathology-proven prostate adenocarcinoma and biochemical recurrence. Biochemical recurrence was defined as a PSA of 0.2 or more ng/mL measured more than 6 weeks after prostatectomy or a PSA of 2 or more ng/mL rise above nadir following radiation therapy (ASTRO-Phoenix consensus definition).[9] Patients were enrolled irrespective of prior conventional imaging findings. Exclusion criteria were investigational therapy for prostate cancer, inability to tolerate a PET scan, and another concurrent malignant condition.

Study Design

The Standards for Reporting of Diagnostic Accuracy (STARD) checklist is included in Supplement 1; the STARD flow diagram is shown in Figure 1. The study was initiated, planned, conducted, analyzed, and published by the investigators. No financial support was received

from commercial entities. The study was approved by local institutional review boards at UCSF and UCLA, and written informed consent was obtained from all patients. Data were collected in a central REDCap database.

PET Imaging

^{68}Ga-PSMA-11 was produced with harmonized release criteria (included in the clinical trial protocol in Supplement 2). Scans were acquired in accordance with the international guideline.[10] In brief, patients received an average of 5.1 (standard deviation, 1.1) mCi of ^{68}Ga-PSMA-11 and 20 mg of furosemide at a mean (SD) 64 (13) min before the scan. Furosemide was given to 588 (93%) of 635 patients to minimize pelvic scatter artifacts. Whole-body PET was acquired starting from pelvis to vertex. Depending on patient weight and bed position, emission time was 2 to 5 minutes per bed position. The UCLA investigators performed PET and or computed tomographic (CT) imaging. The UCSF investigators performed PET/CT or PET/MRI based on availability and contraindications. For PET/CT, a diagnostic CT was obtained with the use of a standard protocol (80 to 100 mA, 120 kV) before the PET scan. Intravenous iodinated contrast was administered to 613 (97%) patients.

For PET/MRI, an abbreviated pelvis PET/MRI was obtained following a whole-body protocol after the PET scan, and the PET/MRI protocol was reported previously.[11]

The PET scan was reconstructed by ordered subset expectation maximization (OSEM)-based algorithms. Data from the CT or MRI scan were used for attenuation correction. All imaging devices used underwent successful American College of Radiology Accreditation.

Safety

Patients were monitored for adverse events during and for 2 hours after radiotracer administration. Heart rate and blood pressure were assessed before and after injection of the radiotracer. Patients were also contacted by phone to assess for the development of delayed adverse events.

Image Interpretation

The cases were divided randomly between 9 readers, not involved in study design and data acquisition, to obtain 3 independent reads per patient (O.S., L.E., H.Z., H.I., A.W., C.R., M.E., I.B., H.S.). Readers with more than 5 years PET/CT experience were assigned to PET/CT, readers with more than 5 years PET/MRI experience were assigned to PET/MRI data sets. At baseline, all readers were trained by reviewing 30 PSMA PET biochemical recurrence cases from a previously published data set.[12] Training cases were reviewed in a blinded fashion before the reference standard was revealed. Correct quantification and image display was confirmed for the local workstations. Images were interpreted by visual criteria published previously.[13] In brief, any focal tracer uptake higher than the surrounding background and not associated with physiological uptake was considered suspicious for malignant abnormality. Stage and PSMA expression were categorized in accordance with Prostate Cancer Molecular Imaging Standardized Evaluation (PROMISE) guidelines.[14]

Data sets for reader interpretation included whole-body PET (attenuation corrected and non-corrected), whole-body postcontrast CT, or whole-body postgadolinium T1 and pelvic T2 MRI. Readers were provided recent PSA level and type of primary therapy (prostatectomy vs radiation therapy), but were blind to all other information. Presence of prostate cancer (positive vs negative) was recorded for 4 regions (prostate bed, pelvic nodes, extrapelvic nonbone, bone), and a total of 21 subregions. Findings were entered directly into the central database. For analysis, majority vote was used in cases of reader disagreement.

Lesion Validation

All patients were followed up for histopathologic analysis, conventional imaging (CT, MRI, and/or bone scan) or serum PSA after focal salvage therapy acquired during clinical routine. Combination of (in descending priority) histopathologic analysis, imaging, and PSA follow-up after local/focal therapy was taken as composite reference standard. Validation was performed by the unblinded local investigators after reviewing images and reports, following prespecified criteria of the study protocol included in Supplement 2. In patients with follow-up, positive ^{68}Ga-PSMA-11 PET findings were validated as true or false-positive results. Region negative on ^{68}Ga-PSMA-11 PET, but with subsequently confirmed prostate cancer by histopathologic analysis, were considered false-negative results. True negative was not defined.

Statistical Analysis

The primary endpoint was positive predictive value (PPV) on a per-patient and per-region basis of ^{68}Ga-PSMA-11 PET for detection of tumor location confirmed by histopathologic analysis. The null hypothesis was that the true PPV is 0.50, whereas the alternative hypothesis was that the true PPV is at least 0.70. Enrollment was completed when 114 patients had biopsy and/or surgery follow-up, fulfilling protocol requirements for analysis of the per-patient–based primary endpoint (≥107 patients with biopsy and/or surgery follow-up, 90% power, 1-sided .01 significance level). The study was ended before target accrual of 1500 patients to allow for analysis of the primary endpoint for FDA New Drug Application (NDA) submission.

Secondary endpoints were per-patient and per-region PPV confirmed by composite validation, per-patient and per-region sensitivity (SE) confirmed by histopathologic validation, per-patient detection rate stratified by PSA and PSA doubling time, interreader agreement, and safety. Impact on treatment was reported previously for a subset of the UCLA cohort.[15] Detection rate was defined as proportion of patients with PSMA PET positive results, independent of the reference standard. The PPV confidence interval (CI) in the region-based analysis was calculated using logistic random-effects models.[16] All other PPV and SE confidence intervals were calculated using the Wilson score method.[17] Detection rates were compared by χ^2 analysis with a 2-sided significance level of .05. Inter-reader agreement was determined by Fleiss' κ and interpreted by criteria of Landis and Koch.[18] For logistic random-effects models, SPSS statistical software was used (version 24, IBM Inc). Other statistical analyses were performed with R statistical software (version 3.5.1, R Foundation).

Results

Baseline Characteristics and Follow-up

From September 2016 through October 2017, a total of 635 patients were enrolled (n = 250 [39%] at UCLA; n = 385 [61%] at UCSF). Table 1 shows the clinical characteristics of all patients and the efficacy endpoint cohorts separately. Patients underwent either PET/CT (n = 443 [70%]) or PET/MRI (n = 192 [30%]).

Of 635 patients, 269 (42%) had composite follow-up at a median duration of 9 months. Of the 635 patients, 114 (18%) had histopathologic follow-up. Forty-six of 269 patients (17%) were excluded from efficacy analysis based on PET vs follow-up location mismatch (on a subregion basis) or absence of prostate cancer both on PET and histopathologic analysis (true negative not defined in the study protocol). Thus, efficacy cohorts were 223 patients with composite validation and 93 patients with histopathologic validation (eFigure 1 in Supplement 1).

Detection Rate and Accuracy

Based on independent reads, PET detection rate among all patients was 75%. Detection rate stratified by PSA is given in Table 2 and shown in Figure 2. Two patients with prior PSA levels of 0.2 or more at enrollment but less than 0.2 ng/mL at time of imaging had negative PET results. There was a significant increase in detection rate across the predefined PSA ranges: 38% for <0.5 ng/mL (n = 136); 57% for 0.5 to <1.0 (n = 79), 84% for 1.0 to <2.0 ng/mL (n = 89), 86% for 2.0 to <5.0 ng/mL (n = 158), and 97% for ≥5.0 ng/mL (n = 173) ($P < .001$). The PSA doubling time and PSA nadir were not significantly associated with PET detection rate. In patients with PSA levels of 1 ng/mL or higher, disease was spread more often to multiple regions and less often confined to the pelvis (Figure 2). Minimum, median, and maximum PSMA expression score of positive lesions was 1, 2, and 3, respectively, for each of the 4 regions.[14]

In total, 223 patients had lesion validation (n = 217 PET positive, n = 6 PET negative). The PPV/SE contingency tables are shown in eFigure 1 in Supplement 1.

In cases with composite validation, 200 of 217 (92%) PET-positive patients and 229 of 249 (92%) PET-positive regions were characterized as true positive. This resulted in a ^{68}Ga-PSMA-11 PET PPV of 0.92 (95% CI, 0.88-0.95) (Table 3). In PET-positive patients with histopathologic validation (n = 87), PPV was 0.84 on a per-patient and per-region basis (primary endpoint; 95% CI, 0.75-0.90 and 95% CI, 0.76-0.91, respectively) (Table 3).

In cases with histopathologic validation, 73 of 79 (92%) confirmed patients and 76 of 84 (90%) confirmed regions were PET positive resulting in an SE of 0.92 (95% CI, 0.84-0.96) on a per-patient and 0.90 (95% CI, 0.82-0.95) on a per-region basis (Table 3). eFigure 2 in Supplement 1 demonstrates examples for PET true and false-positive findings. Detection rate and PPV for individual readers are given in eTable 1 in Supplement 1.

There were 8 regions where findings of PET were judged negative by the blinded readers but biopsy and/or surgery confirmed prostate cancer (PET false-negative, eFigure 1C in Supplement 1). Biopsy and/or surgery was triggered by local reads based on faint focal uptake (n = 4, mean maximum standardized uptake value [SUV_{max}], 5.1), CT/MRI lesions (n = 3; mean size, 0.9 cm), or clinical suspicion (n = 1). Details for PET false-negative regions are given in eTable 2 in Supplement 1.

PSA Response to Focal Salvage Therapy in the Validation Data Set

The association of PET with tumor control was not the focus of this study; however, PSA response was collected as part of the lesion validation in 39 patients with focal therapy. Patient characteristics are given in eTable 3 in Supplement 1. Radiation therapy, surgery, or cryoablation was performed for PET lesions in 20 (51%), 16 (41%), or 3 (8%) of 39 patients, respectively. Treatment was not standardized. Patients were identified during follow-up file review by confirming lesion removal and/or targeting in absence of systemic therapy. Surgical specimens confirmed prostate cancer in 16 of 16 (100%) patients. eFigure 3 in Supplement 1 presents a waterfall plot of best PSA response stratified by type of focal therapy. The PSA follow-up was recorded at a median duration of 6 months (range 1-12 months) after treatment.

Following focal therapy to PET lesions, any PSA decline was seen in 36 of 39 patients (92%). PSA decline was 50% or higher in 31 (80%) patients (PET true positive). In 10 (26%) of these patients, PSA was undetectable.

PET Disease Extent and Reader Agreement

The PET disease extent, categorized by PROMISE is given in eTable 4 in Supplement 1. Prostate cancer was localized in the pelvis only in 219 of 635 patients (35%). Of the 635 patients, 256 (40%) had extrapelvic disease, including nodal/soft tissue metastases (105 [17%]), bone metastases (104 [16%]), or involvement of both (47 [7%]). Inter-reader agreement was substantial for all 4 regions (prostate bed, $\kappa = 0.65$; 95% CI, 0.61-0.70; pelvic nodes, $\kappa = 0.73$; 95% CI, 0.69-0.78; extrapelvic soft tissue, $\kappa = 0.70$; 95% CI, 0.65-0.74; bone, $\kappa = 0.78$; 95% CI, 0.73-0.82).

Safety

There was no grade 2 or higher event (eTable 5 in Supplement 1). Grade 1 events were noted in 15 of 635 (2%) patients after the PET scan. None of the events required intervention.

Discussion

Prospective proof of accuracy of a new diagnostic test is prerequisite for approval and reimbursement. This prospective multicenter trial demonstrates high accuracy, reproducibility, and safety of ^{68}Ga-PSMA-11 PET in patients with biochemically recurrent prostate cancer. The primary endpoint (PPV≥0.70) was met: the positive predictive value for prostate cancer localization ranged from 0.84 to 0.92. The overall detection rate was 75% with significant correlation with PSA. There were no notable adverse events.

There are a number of strengths of this study in comparison to prior retrospective trials evaluating ^{68}Ga-PSMA-11 PET. Our prospective study is strengthened by a large cohort size, implementation of blinded reads, and independent lesion validation. Image interpretation was defined by a statistical consensus of trained, international readers randomly assigned to the data sets. Validation of findings was performed locally based on predefined reference standard criteria.

The detection rate reported in this prospective trial falls within the 95% confidence interval of a meta-analysis of previously published detection rates.[7] In 2015, Eiber et al[21] and Afshar-Oromieh et al[22] reported somewhat higher detection rates, likewise associated with PSA at biochemical recurrence. In their studies, findings were summarized retrospectively in an unblinded manner, which may have led to a higher confidence for prostate cancer detection. Detection rate was similar in a recent expanded cohort of more than 1000 patients.[23]

Afshar-Oromieh et al[22] and smaller trials employed pathologic correlation in part of their patient cohorts. In line with our findings, ^{68}Ga-PSMA-11 PET PPV for localization of prostate cancer was consistently 0.80 or more.[21,22,24,25,26,27,28] We demonstrate in this prospective multicenter trial that ^{68}Ga-PSMA-11 PET positivity identifies with very high likelihood of prostate cancer. High rates of biochemical response (≥80%) in patients with PET-directed focal therapy indicates potential value of the PET information for treatment planning. However, this study focuses on the diagnostic performance of ^{68}Ga-PSMA-11 PET. The PSA response was recorded as part of the lesion validation only. The association of PET with tumor control needs to be carefully weighed against potential morbidity and complexity of salvage procedures in clinical trials on patient outcomes.[29]

Overall, PET false-positive lesions were reported in few patients, most often in the prostate or prostate bed (11 of 17 patients [65%]). False-positive reports may be owing to urinary tracer excretion, inflammation, or posttherapeutic remodeling.[30]

Half of PET false-negative lesions demonstrated faint tracer uptake. Unblinded local reads, guided by clinical need, triggered biopsy and/or surgery, whereas blinded consensus was negative. Low or absent PSMA expression, small lesion size, and adjacent uptake in the urinary bladder (5 of 8 lesions were in the prostate bed) may have resulted in false-negative findings.[30,31]

We demonstrate substantial reproducibility of the PET interpretations across 9 randomly assigned international readers for all 4 evaluated regions. Reproducibility is similar to previous findings of our group,[12] which identified optimal experience level and allowed creation of a reader training, which was implemented in this prospective study. High reproducibility of ^{68}Ga-PSMA-11 PET interpretation is in line with findings for the approved ^{68}Ga-somatostatin-receptor PET.[32,33] ^{68}Ga-PSMA-11 PET Fleiss' κ values (0.65 to 0.78) were higher than those reported for the recently approved ^{18}F-fluciclovine PET (0.36 to 0.57).[34]

Limitations

Development of a reference standard in patients with biochemically recurrent prostate cancer is challenging. In patients with low PSA levels (304 [48%] of our patients had PSA levels lower than 2 ng/mL), positive lesions are frequently subcentimeter and difficult to biopsy. Therefore, performing biopsies in this population is frequently not possible or bears high risk of target mismatch. Furthermore, previous retrospective studies document high accuracy of ^{68}Ga-PSMA-11 PET, and so mandated biopsy of PET-positive and PET-negative regions was deemed both not feasible and unethical by the investigators. Instead, lesion validation was based on a composite reference standard comprised of histopathologic analysis, PSA levels, and imaging data acquired during clinical routine. As anticipated, owing to current guideline recommendations, few patients received biopsy and/or surgery or imaging under first-line treatment for bio-

chemical recurrence.[2,3] This may have introduced a selection bias for the lesion validation. Other factors may have negatively impacted the accuracy of the reference standard: size criteria with potentially limited sensitivity and specificity were applied. Based on our validation framework, true negative lesions were not defined and specificity as well as negative predictive value were not determined. ^{18}F-fluciclovine PET, which may have complemented the reference standard, was not approved at the time of study initiation. Comparison of ^{68}Ga-PSMA-11 vs ^{18}F-fluciclovine PET is currently under investigation in a subsequent trial at UCLA (ClinicalTrials.gov identifier, NCT03515577).

Conclusions

We established high detection rates, positive predictive value, inter-reader reproducibility, and safety of ^{68}Ga-PSMA-11 PET for localization of biochemically recurrent prostate cancer in a prospective multicenter trial. The primary endpoint was met: ^{68}Ga-PSMA-11 PET demonstrated 84% to 92% positive predictive value at 75% overall detection rate.

Notes

Supplement 1.

eFigure 1. Contingency tables for Positive Predictive Value (PPV) and Sensitivity (SE).

eFigure 2. Examples of true positive (A-D) and false positive (E-H) PET/CT Findings.

eFigure 3. Best PSA response following Focal Therapy to PET lesions.

eTable 1. Positive Predictive Value (PPV) among individual Readers.

eTable 2. PET false negative regions.

eTable 3. Characteristics of the Patients with PSA response following Focal Therapy.

eTable 4. miTNM Stage by PSMA PET.

eTable 5. Safety.

Supplement 2.

Trial Protocol

Supplement 3.

Data Sharing Statement

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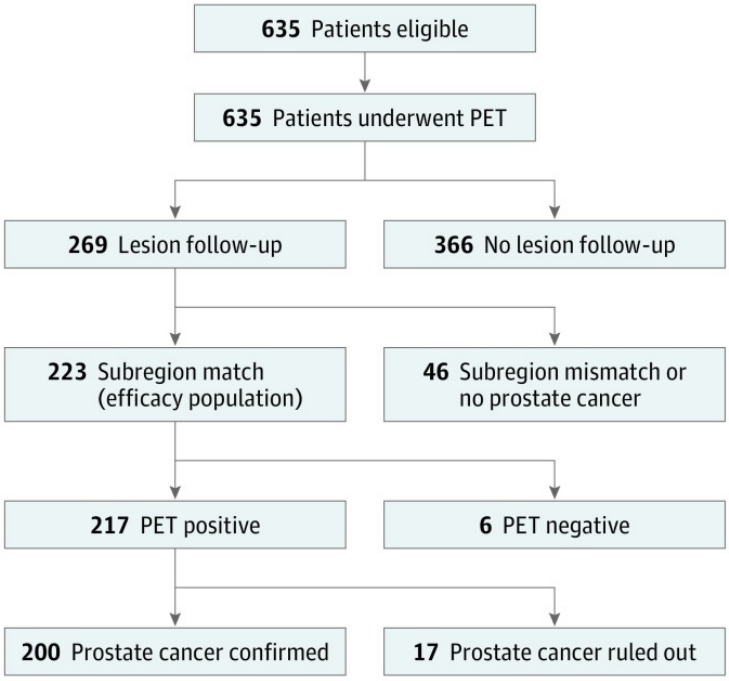
Figures and Tables

Figure 1.



STARD Flow Diagram for the Efficacy Cohort with Composite Validation

PET indicates positron emission tomography.

Table 1.

Characteristics of the Patients at Baseline

Characteristic	No. (%)		
	All Patients (N = 635)	Efficacy Cohort	
		Composite (N = 223)	Histopathologic (N = 93)
Age, median (range), y	69 (44-95)	70 (49-88)	71 (49-88)
Initial therapy			
Prostatectomy only	262 (41)	60 (27)	22 (24)
Radiation therapy only	169 (27)	80 (36)	50 (54)
Prostatectomy and salvage radiation therapy	204 (32)	83 (37)	21 (23)
Other prior therapy			
Local salvage therapy	85 (13)	35 (16)	9 (10)
Androgen deprivation	244 (38)	110 (49)	31 (33)
Abiraterone/enzalutamide	15 (2)	13 (6)	1 (1)
Chemotherapy	14 (2)	12 (5)	1 (1)
Bone-targeted treatment	6 (1)	6 (3)	0 (0)
Other	32 (5)	19 (9)	3 (3)
Time from initial therapy to PET, y			
Median (range)	5 (0-33)	6 (0-29)	6 (0-29)
<5	309 (49)	97 (43)	34 (37)
≥5	307 (48)	118 (53)	57 (61)
Not available	19 (3)	8 (4)	2 (2)
Gleason score			
<8	378 (60)	128 (57)	68 (73)
≥8	202 (32)	82 (37)	21 (23)
Not available	55 (9)	13 (6)	4 (4)
PSA, median (range), ng/mL[a]	2.1 (0.1-1154.0)	3.5 (0.1-1154.0)	3.9 (0.1-70.6)
PSA doubling time, median (range), mo[b]	6 (0->120)	6 (1->120)	10 (1-73)

Abbreviations: PSA, prostate-specific antigen; PET, positron emission tomography.

[a]Most recent before PET.

[b]Determined in accordance with Pound et al.[19]

Table 2.

^{68}Ga-PSMA-11 PET Detection Rate on a Patient Basis

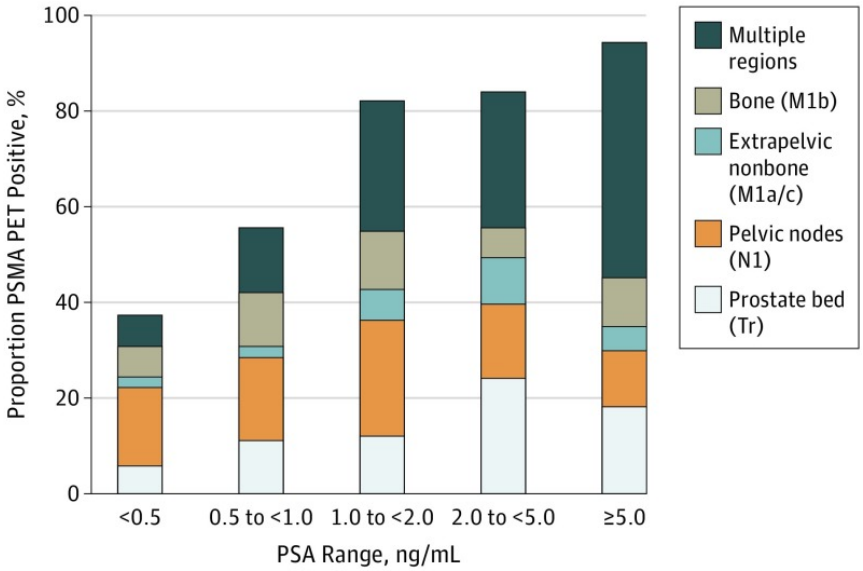
Stratification	No.	PET-Positive Results, No. (%)	χ^2 *P* Value
All patients	635	475 (75)	
PSA			
<0.5	136	52 (38)	
0.5- <1.0	79	45 (57)	
1.0- <2.0	89	75 (84)	<.001
2.0- <5.0	158	136 (86)	
≥5.0	173	167 (97)	
PSA doubling time, mo[a]			
<6	248	191 (77)	
≥6	245	182 (74)	.80
Not available	142	102 (72)	
PSA nadir after prostatectomy[b]			
<0.1	230	146 (63)	
≥0.1	111	81 (73)	.18
Not available	125	92 (74)	

Abbreviations: PSA, prostate-specific antigen; PET, positron emission tomography.

[a]Determined in accordance with Pound et al.[19]

[b]Determined in accordance with Bianchi et al.[20]

Figure 2.



Detection Rate on a Patient Basis Stratified by PSA and Region

Tr indicates prostate bed only; N1, pelvic nodes only; M1, extrapelvic only. Proportion of patients with ^{68}Ga-PSMA-11 PET positive findings were stratified by PSA range and region of disease in accordance with PROMISE.[14]

Table 3.

^{68}Ga-PSMA-11 PET Accuracy

Validation Group	Total Regions/Patients, No.	No. (%)		PPV or SE (95%CI)
		Confirmed	Ruled Out	
Positive Predictive Value				
Composite validation				
PET positive (per-patient)	217	200 (92)	17 (8)	0.92 (0.88-0.95)
PET positive (per-region)	249	229 (92)	20 (8)	0.92 (0.88-0.95)
Histopathologic validation				
PET positive (per-patient)	87	73 (84)	14 (16)	0.84 (0.75-0.90)
PET positive (per-region)	90	76 (84)	14 (16)	0.84 (0.76-0.91)
Sensitivity				
Histopathologic findings				
Confirmed (per-patient)	79	73 (92)[a]	6 (8)[b]	0.92 (0.84-0.96)
Confirmed (per-region)	84	76 (90)[a]	8 (10)[b]	0.90 (0.82-0.95)

Abbreviations: PET, positron emission tomography; PPV, positive predictive value; SE, sensitivity.

[a]PET positive.

[b]PET negative.