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Assessing Response to [^{177}Lu]PSMA Radioligand Therapy using modified PSMA PET Progression Criteria

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Running Title:

Prognostic implication of PPP criteria

ABSTRACT

Introduction

Positron emission tomography/computer tomography (PET/CT) targeting the prostate specific membrane antigen (PSMA) plays a key role in staging of patients with prostate cancer (PCa). Moreover, it is not only used for the assessment of adequate PSMA expression of PCa cells before PSMA-targeting radioligand therapy (PSMA RLT) but also for re-staging during the course of therapy to evaluate response to treatment. Whereas no established criteria exist for systematic response evaluation so far, recently proposed PSMA PET Progression (PPP) criteria might fill this gap. The aim of this study was to assess the feasibility of PPP criteria in patients undergoing PSMA RLT and their prognostic implications.

Methods

In this retrospective analysis, PSMA PET/CT scans of 46 patients acquired before and after completion of PSMA RLT were analyzed separately by two readers using modified PPP criteria. After interobserver agreement assessment, consensus results (progressive vs. non-progressive disease) were compared in a multivariate cox regression model (endpoint overall survival, OS).

Results

Interobserver agreement on modified PPP criteria was substantial (Cohens $\kappa = 0.73$) with a concordance in 87% of patients. Median OS of all patients after PSMA RLT (n = 46) was 9.0 [95% confidence interval (CI) 7.8 - 10.2] months. Progression according to modified PPP criteria was found in 32 patients and was a significant ($p \leq 0.001$) prognostic marker for OS with a hazard ratio of 15.5 [95% CI 3.4 - 70.2].

Conclusion

Response assessment in patients undergoing PSMA RLT using modified PPP criteria are reproducible and highly prognostic for OS. Modified PPP criteria should be validated in future prospective trials.

Key words: PSMA PET/CT, radioligand therapy, PPP, response assessment

INTRODUCTION

Positron emission tomography/computer tomography (PET/CT) targeting prostate specific membrane antigen (PSMA) has become a key role in staging of patients with prostate cancer (PCa). In order to develop systematic and reproducible evaluation criteria, several proposals for assessing PSMA PET/CT have been made (*1*–*3*). However, no established criteria for therapy response assessment by PSMA PET/CT exist so far, and response assessment in patients with PCa is still based on serum prostate specific antigen (PSA) level as well as on bone scintigraphy and CT scans as recommended by e.g. the Prostate Cancer Working Group 3 (*4*).

Especially in the context of PSMA radioligand therapy (RLT), PSMA PET/CT is frequently used to assess adequate PSMA expression of PCa cells not only before but also during the course of therapy to evaluate response to treatment (*5*). Therefore, an evaluation system, which is easy to implement, simple to use, and reproducible is desirable not only for clinical routine but also for clinical trials. While different approaches have already been suggested for assessing response to treatment in metastatic PCa using response evaluation criteria in solid tumors (RECIST (*6*)) 1.1 criteria (*7,8*), (adapted) PERCIST criteria (*9,7,8*), or the quantification of whole body tumor burden (*10*–*15*), they have not yet been clinically implemented.

Obviously, there is a need for an easy, fast, and reproducible validation system to assess response to PSMA RLT. Fanti et al. recently published the PSMA PET Progression (PPP) criteria, which include PSMA PET/CT, biochemical response as well as clinical parameters. They focused on disease progression which is defined by three categories (*16*). Although promising, these response assessment criteria have not yet been tested for feasibility in patients with advanced PCa receiving PSMA RLT.

The aim of this retrospective analysis was to evaluate the feasibility of PPP criteria in patients undergoing PSMA RLT and to assess their prognostic implications. Therefore, PSMA PET/CT scans before and after completion of RLT were analyzed and the results were correlated to overall survival (OS).

MATERIALS AND METHODS

Patient Cohort

All patients treated on compassionate use basis with at least on cycle of PSMA RLT between February 2016 and April 2020 at our department were screened for eligibility. In suitable patients, both initial and follow-up PET/CT had to be performed with the same PSMA radioligand (68Ga-PSMA-11 or 18F-PSMA-1007), but not necessarily on the same PET/CT scanner. Other inclusion criteria were in-house assessment of imaging and laboratory data and the availability of survival data. Patients without a follow-up PET/CT scan (i.e. in case of clinical progress) were excluded from the study. Time points of the PET/CT scans were before therapy and after the final cycle of PSMA RLT. Last follow-up was in October 2020 and 33 patients had deceased at this time point. The median time of follow-up of surviving patients was 14 [95% confidence interval (CI) 12.9 - 15.1] months. The review board of the University of Freiburg (protocol no. 562/15) approved this study and all subjects signed a written informed consent.

Imaging and Treatment Protocol

Whole-body PSMA PET scans were acquired 1 hour (68Ga-PSMA-11) or 2 hours (18F-PSMA-1007) after injection of the respective tracer from skull to mid-thigh with a scan duration of 2 minutes per bed position. A contrast-enhanced diagnostic CT (120 kVp, 100 - 400 mAs) with dose modulation was performed for anatomic correlation and attenuation correction. Scans were performed with either a VEREOS Digital PET/CT, a GEMINI TF 64 PET/CT, or a GEMINI TF 16 Big-Bore PET/CT (all Philips Healthcare, USA). All patients were asked to void before PET. Images were reconstructed with a vendor-specific time-of-flight iterative reconstruction algorithm (BLOB-OS-TF) with 3 iterations and 9 subsets (relaxation parameter 0.35) and a voxel size of 2 x 2 x 2 mm^3 (VEREOS Digital PET/CT) or with 3 iterations and 33 subsets (relaxation parameter 0.35) and a voxel size of 2 x 2 x 2 mm^3 (GEMINI TF 64 PET/CT and GEMINI

TF 16 Big-Bore PET/CT). The spatial resolution of the reconstructed PET image is about 5 mm (VEREOS) to 7 mm (both GEMINI TF) full width half maximum.

Standardized institutional protocol for RLT was applied according to current guidelines (*17*). In-house labeling was carried out for 177Lu-PSMA 617. The standard PSMA RLT protocol consisted of infusion of 6.0 GBq of the radioligand every 6-8 weeks with up to a maximum of 4 cycles depending on response to treatment, as assessed by PSMA PET/CT and laboratory data 6-8 weeks after every second cycle. In case of only three treatment cycles, an additional PET/CT scan was carried out 6-8 weeks after the third cycle.

Response Assessment using Modified PPP Criteria

PET/CT images were retrospectively analyzed by two readers (CK and KM, with one and four years of PSMA PET/CT reading experience) using the local PACS system IMPAX EE (Agfa Health Care, Bonn, Germany). For response assessment, the following three categories defining progression adapted from PPP criteria (*16*) were used (Table 1). Exclusion of these three categories was defined as non-progressive. After the assessment of interobserver agreement, a final consensus was reached and used for further comparisons.

The original category C had to be changed from "increase in size or uptake of one or more lesions" to a "visually assessed distinct increase of the PSMA positive tumor volume" as the original category was not applicable in case of diffuse bone marrow involvement and no validated quantification assessment of the whole-body tumor burden on 18F-PSMA-1007 PET/CT exists so far. However, recent studies report promising results for the manual and semiautomatic quantification of whole-body tumor burden on 68Ga-PSMA-11 PET/CT using $PSMA_{TV50}$ (*14,15*). Hence, $PSMA_{TV50}$ was assessed in all patients without new lesions on PSMA PET/CT (e.g. category C and all patients rated "non-progressive") by one reader (KM) in order to test the suitability of category C. For this, the Beth Israel plugin for FIJI (*18*) from the Beth Israel Deaconess Medical Center (Boston, MA, USA) was used. A relative threshold of 50% of the maximum standardized

uptake value within a segmented volume was applied and the volumes of the segmented lesions were summed to $PSMA_{TV50}$.

Since the increase of laboratory data is not defined by PPP criteria, an arbitrary cut-off value of ≥25% (in analogy to PCWG3 criteria (*4*)) was chosen for PSA, lactate dehydrogenase (LDH), and alkaline phosphatase (ALP) according to results of Yordanova et al. (*19*). Changes of neuron-specific enolase (NSE) were included in order to detect possible neuroendocrine dedifferentiation.

Response of serum PSA level

Response of serum PSA level was assessed in all patients, comparing PSA values from the time of first cycle administration and the time of the last PET/CT (i.e. end of therapy), respectively. In analogy to PCWG3 criteria (*4*), biochemical progression was defined as a rise of serum PSA level of ≥25% and patients were dichotomously divided into "progressive" or "non-progressive" accordingly.

Finally, OS of progressive and non-progressive patients as assessed with both categorization systems (PPP and PSA-level only) was compared in uni- and multivariate analysis with the following possible confounders: time since initial diagnosis, number of lines of therapy before PSMA RLT, total injected activity for PSMA RLT, number of therapy cycles, and serum PSA level before application of the first cycle.

Statistical Analysis

Statistical analyses were performed using SPSS software ver. 27.0 (IBM, Armonk, NY, USA). Descriptive data are presented as mean ± standard deviation and range in parentheses. Survival data are represented by Kaplan-Meier-curves and analyzed via log-rank comparisons for univariate analysis as well as cox regression models for multivariate analysis. For comparison between two cox models, the Gönen & Heller concordance probability estimate (*20*) (CPE) was calculated using R software ver. 4.0.3. with a probability of 0.5 indicating a random discrimination and 1 a perfect discrimination. A landmark analysis

for OS was performed, starting with the time point of the final follow-up PSMA PET/CT after RLT until death or last follow-up. OS is presented as median with the 95% confidence interval in square brackets. Cohens κ was used to assess interrater reliability (based on Landis and Koch criteria (*21*)). For comparisons between subgroups of the volumetric analysis a paired or unpaired t-test was performed when indicated. A p value less than 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

46 patients out of 87 receiving PSMA RLT were included in this analysis. Detailed characteristics are given in Table 2. In total, 129 cycles of RLT were administered with a mean activity of 5.9 ± 0.7 (3.0 – 7.5) GBq. 18 patients received all 4 cycles of PSMA RLT. In 2 patients PSMA RLT was limited to three cycles due to therapy-associated side effects (progression of pre-existing renal insufficiency, xerostomia, and fatigue). In the remaining 26 patients only 2 cycles of PSMA RLT were performed (Figure 1), either due to a very good response (n = 5) or a distinct progression (n = 21) as assessed by PSMA PET/CT and laboratory data (based on clinical decision). Time intervals between initial PSMA PET/CT and first cycle of PSMA RLT as well as last cycle and re-staging PSMA PET/CT were 46 ± 26 (5 - 126) days and 53 ± 12 (23 - 77) days, respectively. In 27 patients RLT was monitored using 68Ga-PSMA-11 PET/CT and 19 patients were examined with 18F-PSMA-1007 PET/CT.

Response Assessment

Response According to modified PPP Criteria

32 of 46 patients were considered progressive according to modified PPP criteria (70%). Of these patients, 21 had undergone 2 cycles of PSMA RLT, 2 patients were treated with 3 cycles of PSMA RLT, and

9 patients had received 4 cycles of RLT. In most cases (27/32, 84%) progression was due to the appearance of two or more new metastases on PSMA PET (category A). In four patients a distinct increase of tumor volume was seen in addition to a rising serum PSA level of ≥25% (category C), and in one patient a distinct increase of tumor volume was seen in addition to a rising ALP of ≥25% (category C). Category B (one new metastasis and rising laboratory values) did not occur in any patient. Interobserver agreement of categorization was substantial, as indicated by Cohens κ = 0.73 with a concordance in 87% of patients. Examples for category A and C are shown in Figure 2.

The volumetric assessment of the patients who were rated with category C (n = 5) or as non-progressive (n = 14) showed a significant difference of the percentual change of $PSMA_{TV50}$ between the two groups (C: $\Delta PSMA_{TV50}$ 96 ± 73%, range: 31% - 200% vs. non-progressive: $\Delta PSMA_{TV50}$ -51 ± 35%, range: -87% - 16%; p <0.001). $PSMA_{TV50}$ decreased significantly in patients rated as non-progressive (from 135.6 ± 172.1 ml to 81.2 ± 171.3 ml; p = 0.02), but no significant change of $PSMA_{TV50}$ was found in the 5 patients rated with category C (from 198.6 ± 271.5 ml to 325.3 ± 390.4 ml; p = 0.086).

Median OS of all patients (n = 46) was 9.0 [95% CI 7.8 - 10.2] months. Patients with progression according to modified PPP criteria (n = 32) had a median OS of 7.0 [95% CI 4.0 – 10.0] months only. Those patients who were not progressive had a significant longer median OS with 29.0 [95% CI 8.2 - 49.8] months (p ≤0.001; Figure 3).

Response of serum PSA level

Progression of serum PSA level at time of final PET/CT was found in 18 of 46 patients (39%). Of these patients, 14 had been treated with 2 cycles, and 4 patients with 4 cycles of PSMA RLT. These patients (n = 18) had a median OS of 8.0 [95% CI 6.9 – 9.1] months compared to those patients (n = 28) with a non-progressive serum PSA level with a median OS of 9.0 [95% CI 0 - 19.1] months (p = 0.046; Figure 3).

Comparison of Biochemical and Imaging Findings

13 patients who were rated as category A did not show a progression of serum PSA level. Mean relative change of serum PSA in these patients was -33 ± 24% (-69% - 5%). These patients had a significantly shorter median OS of 11.0 [95% CI 8.2 – 13.8] months than those patients with a non-progressive serum PSA level (n = 15, median OS was not reached at the end of the follow-up period; p ≤0.001). Conversely, all patients with a progressive serum PSA showed also a progression on PSMA PET/CT (category A or C).

After PSMA RLT, 8 patients presented with new visceral sites of disease. Of these, 2 patients presented with new liver metastases which were only visible on CT (apart from many progressive PSMA-positive bone and lymph node metastases). The other new visceral metastases were concordantly detectable on PET and CT (a detailed comparison of biochemical and imaging findings can be found in the Supplemental Table 1).

In a multivariate analysis, progression according to modified PPP criteria remained a significant prognostic marker (p ≤0.001) with a hazard ratio (HR) of 15.5 [95% CI 3.4 - 70.2]. In contrast to response of serum PSA level, which was not significant after stratification (p = 0.12). Modified PPP criteria showed a better discriminatory power with a CPE of 0.76 compared to response of PSA with a CPE of 0.66.

DISCUSSION

In our patient cohort, median OS of all patients (n = 46) was 9.0 months, which at first appears to be shorter than the OS reported in other published retrospective (11.0 months) (*22*) and prospective studies (13.3 months) (*23*) receiving PSMA RLT. However, this discrepancy is not surprising as we performed a landmark analysis starting with the follow-up PSMA PET/CT and not with the administration

of the first cycle of therapy in order to assess the association of post-therapy PPP criteria and further patient survival. The binary categorization of patients into progressive and non-progressive by modified PPP criteria was superior to the binary categorization of serum PSA level as judged by Gönen & Heller's CPE. This was probably due to 13 of 46 patients, who had a non-progressive serum PSA level, but showed two or more new lesions on PSMA PET/CT (i.e. category A), which was associated with a significantly reduced median OS of 11.0 months compared to patients with a corresponding biochemical and imaging response. In this respect, discrepant developments of PSA and PSMA PET have previously been observed after PSMA RLT (*24*) and might indicate the loss of adequate PSA expression and the transition to a more aggressive stage of disease (*25*). Moreover, none of the patients was attributed to Category B (one new metastasis and rising laboratory values), which was probably due to the advanced disease stage of the patients with disseminated metastases or even diffuse bone marrow involvement.

A possible pitfall of PPP criteria is their assumption of a persistent PSMA-expression throughout the course of disease. Neuroendocrine dedifferentiation and progression with a loss of PSMA expression (*26*) (which is more likely to occur in advanced disease stage) is not defined, and progression without a finding on PSMA PET or CT is not included in PPP criteria. In our patient cohort, two patients presented with new liver metastases after PSMA RLT, which could be solely detected on CT. Unfortunately, CT-based criteria in advanced prostate cancer are known to be of limited value (*8,7*), especially since diffuse sclerotic bone lesions are difficult to measure and to quantify (*27*). In this sense, it is imaginable that the additional use of 18F-fluorodeoxyglucose (18F-FDG) PET might help to detect more aggressive tumor manifestations (*28,29*). Discordant 18F-FDG-positive, but PSMA-negative lesions are a known negative prognostic marker before initiation of PSMA RLT (*30*). Neuroendocrine biomarkers have shown to be not prognostic for OS before PSMA RLT (*31*). However, distinct elevated or rising NSE level during the course of PSMA RLT are reported to be associated with discordant 18F-FDG-positive lesions (*32*). If this association can be

confirmed and a prognostic relation can be found for both parameters, NSE level might be implemented into PPP criteria to be evaluated even in case of a “non-progressive” PSMA PET/CT scan.

Limitations

As this analysis was retrospective, there were some limitations, which resulted in modified PPP criteria without confirmatory biopsy or correlative imaging within 3 months. However, this affected only 11% (5/46) of the included patients, who were rated as category C, and it is more likely in clinical routine. Second, in contrast to published PPP criteria, our evaluation was primarily done visually as our analysis included PSMA PET scans with two different tracers (68Ga-PSMA-11 and 18F-PSMA-1007), and no validated quantification assessment of the whole-body tumor burden on 18F-PSMA-1007 PET/CT exists so far. In particular, a liver based threshold as proposed for 68Ga-PSMA-11 PET (*12*) cannot be directly adapted to 18F-PSMA-1007 PET due to the hepatobiliary excretion of 18F-PSMA-1007 (*33*). However using the recently proposed quantification of whole-body tumor burden on 68Ga-PSMA-11 PET/CT using $PSMA_{TV50}$ (*14*) we found a significant difference of the percentual change of $PSMA_{TV50}$ between patients rated with category C and those patients who did not show a progression on PSMA PET/CT. Further research which evaluates $PSMA_{TV50}$ in larger patient cohorts with 18F-PSMA-1007 PET scans might help to implement this approach into PPP criteria. Third, although the patients included in this study were not treated with the same number of therapy cycles it must be emphasized, that the aim of this analysis was not to evaluate the effectiveness of PSMA RLT but the assessment of progression using (modified) PPP criteria. Therefore, the number of therapy cycles was part of the multivariate analysis with modified PPP criteria also showing a significant impact on OS after stratification, despite the admitted limitation of a rather small patient population. Fourth, an important limitation of (modified) PPP criteria is that they cannot be used in clinical trials for assessing radiographic progression free-survival, as they contain also laboratory data. Fifth, even though the authors of the PPP criteria mentioned that a correlation between

PPP assessment and OS might be of limited value because of the bias of further treatments (*16*), it has to be acknowledged that PSMA RLT often represents the last line treatment with restricted further therapeutic options. Thus, in our opinion there is no or only a little bias to our observation that PPP assessment accurately reflects response to PSMA RLT. Finally, a prospective validation of the present modified PPP scheme is warranted.

CONCLUSION

Response assessment in patients undergoing PSMA RLT using modified PPP criteria are reproducible and highly prognostic for OS. Modified PPP criteria should be validated in future prospective trials.

KEY POINTS

QUESTION: Evaluation of the feasibility of PPP criteria in patients undergoing PSMA RLT and to assess their prognostic implications.

PERTINENT FINDINGS: In this retrospective analysis, PSMA PET/CT scans of 46 patients acquired before and after completion of PSMA RLT were analyzed separately by two readers using modified PPP criteria. Progression according to modified PPP criteria was found in 32 patients and was a significant ($p \leq 0.001$) prognostic marker for OS with a hazard ratio of 15.5 [95% CI 3.4 - 70.2].

IMPLICATIONS FOR PATIENT CARE: Response assessment in patients undergoing PSMA RLT using modified PPP criteria are reproducible and highly prognostic for OS.

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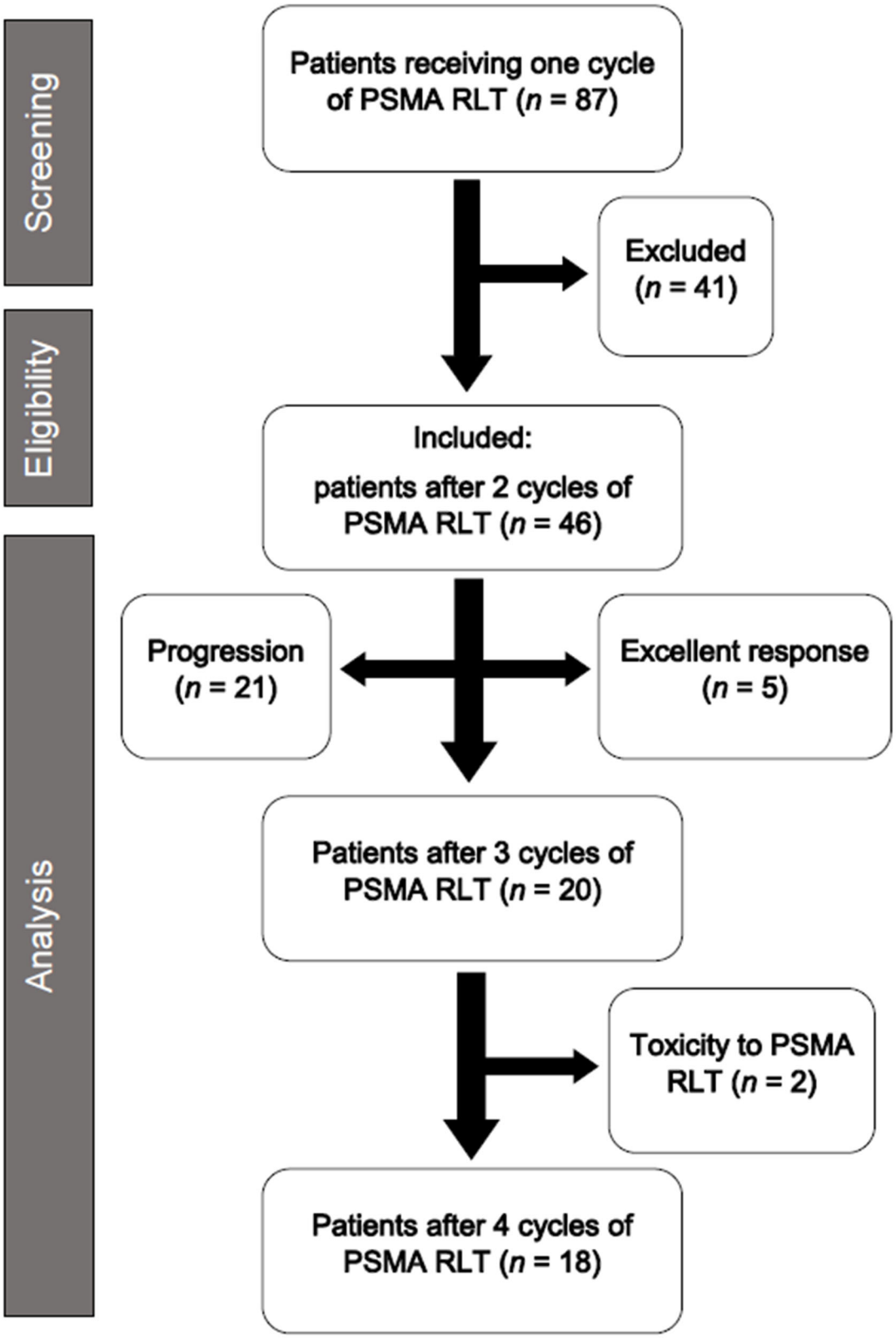


Figure 1 Flow diagram of patients included in this analysis undergoing PSMA radioligand therapy (RLT).

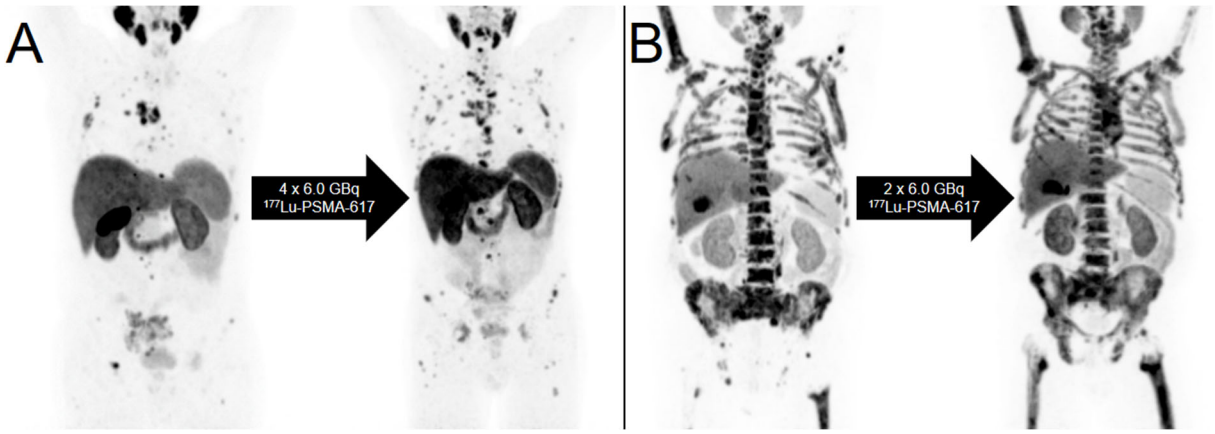
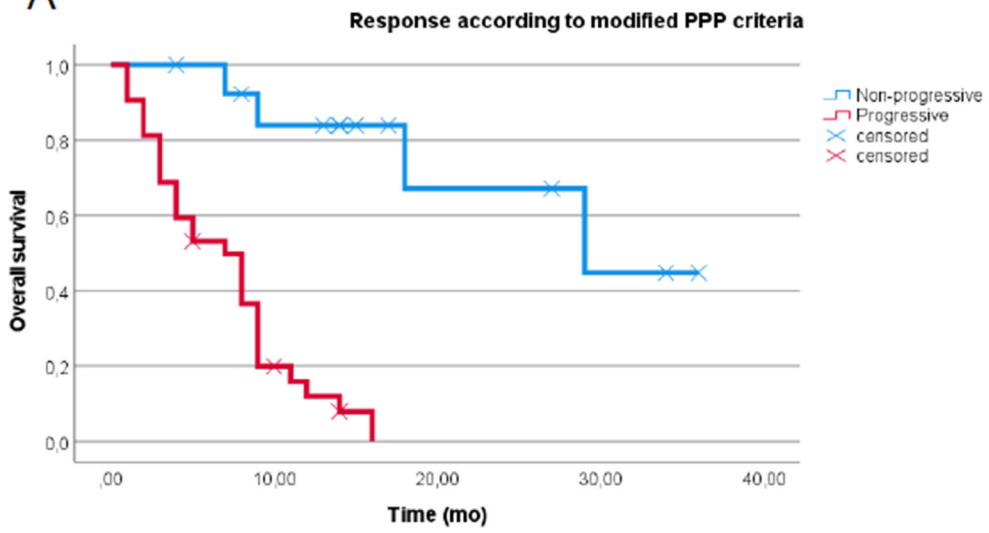


Figure 2 Maximum intensity projections of [^{18}F]PSMA-1007 PET scans of 2 patients with metastatic prostate cancer undergoing PSMA radioligand therapy (RLT): A, 75 year-old patient with disseminated bone metastases and multiple lymph node metastases before and after 4 cycles of PSMA RLT; Re-staging PET shows multiple new bone metastases (category A). B, 65 year-old patient with diffuse bone marrow involvement and multiple lymph node metastases before and after 2 cycles of PSMA RLT; re-staging PET shows a distinct increase of the tumor volume (see humerus, pelvis and right femur; $PSMA_{TV50}$ increased by 50%) with a corresponding increase of serum alkaline phosphatase 45%. In turn, serum PSA decreased by 52% (category C).

A


Response according to modified PPP criteria
Overall survival
1,0
0,8
0,6
0,4
0,2
0,0
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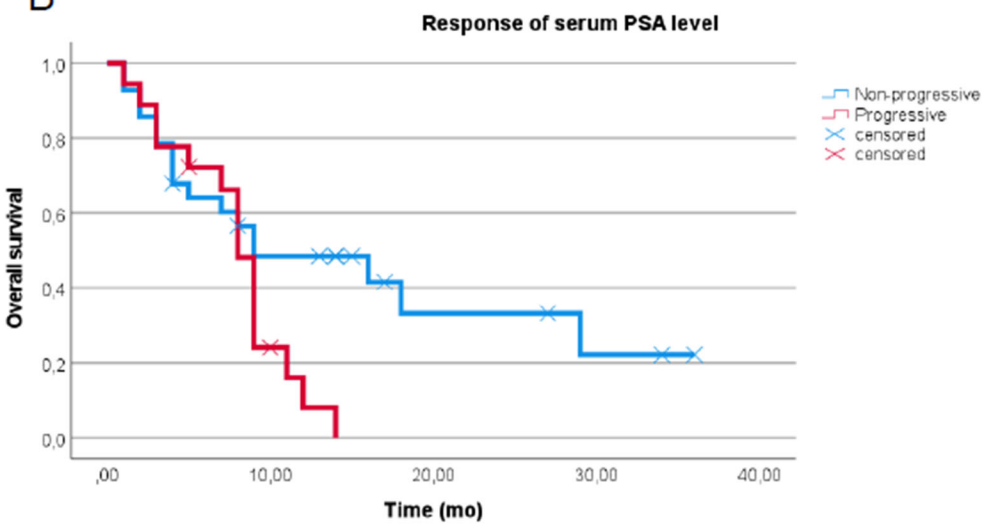
10,00
20,00
30,00
40,00
Time (mo)
Non-progressive
Progressive
censored
censored

B


Response of serum PSA level
Overall survival
1,0
0,8
0,6
0,4
0,2
0,0
,00
10,00
20,00
30,00
40,00
Time (mo)
Non-progressive
Progressive
censored
censored

C

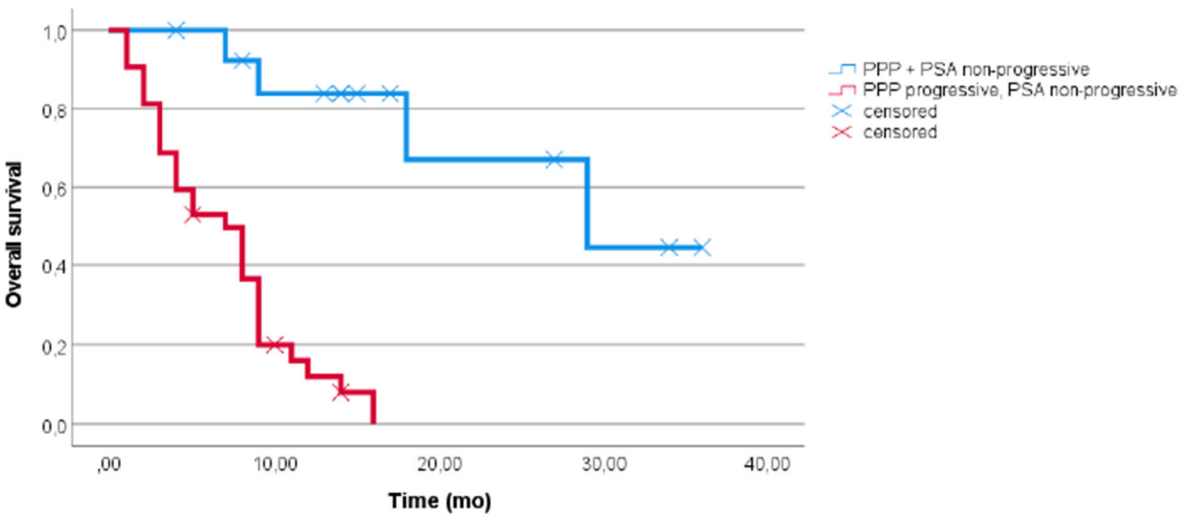

Discordant response according to modified PPP criteria and PSA
Overall survival
1,0
0,8
0,6
0,4
0,2
0,0
,00
10,00
20,00
30,00
40,00
Time (mo)
PPP + PSA non-progressive
PPP progressive, PSA non-progressive
censored
censored

Figure 3: Kaplan Meier curves of overall survival (OS) using log-rank comparison. A, Patients with progression according to modified PSMA PET Progression (PPP) criteria (n = 32) had a short median OS of 7.0 [95% confidence interval (CI) 4.0 – 10.0] months (red line). Those patients who were not progressive (n = 14) had a significant longer OS with 29.0 [95% CI 8.2 - 49.8] months (p ≤0.001; blue line). B, Patients with progression of serum PSA level (n = 18) had a median OS of 8.0 [95% CI 6.9 – 9.1] months (red line) compared to those patients with a non-progressive serum PSA level (n = 28) with an OS of 9.0 [95% CI 0 - 19.1] months (p = 0.046; blue line). C, Patients rated as category A (modified PPP criteria) but with a non-progressive PSA value (n = 13) had a significantly shorter median OS of 11.0 [95% CI 8.2 – 13.8] months (red line) than the patients with a non-progressive serum PSA level and corresponding response according to modified PPP criteria (n = 15, median OS was not reached at the end of the follow-up period; p ≤0.001; blue line).

Table 1 Progression on PSMA PET/CT in accordance to modified PPP criteria.

Category A	**Category B**	**Category C**
≥ 2 new metastases	1 new metastasis	Distinct increase of the tumor volume (visually assessed)
	AND	AND
	increase of ≥25% of	increase of ≥25% of
	- PSA or	- PSA or
	- LDH or	- LDH or
	- ALP or	- ALP or
	- NSE	- NSE

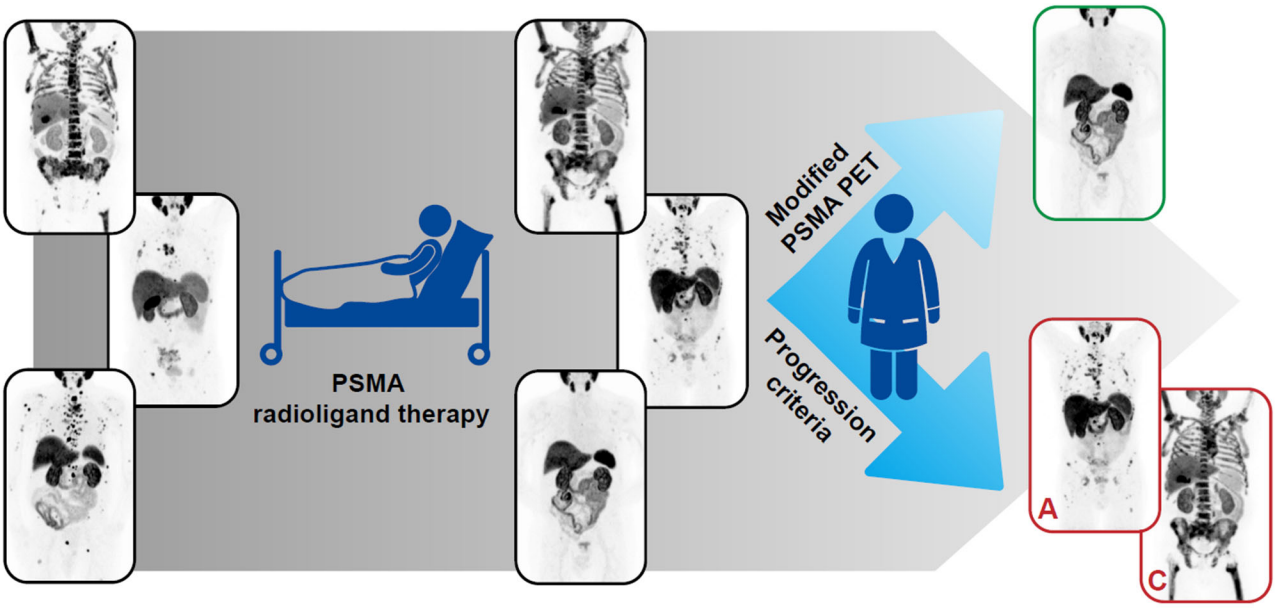
Abbreviations: PPP = PSMA PET Progression, PSA = prostate specific antigen, LDH = lactate dehydrogenase, ALP = alkaline phosphatase, NSE = neuron-specific enolase.

Table 2 Patient characteristics (n = 46).

	mean ± SD (range)	
Age [years]	80 ± 8 (53 - 90)	
Time since diagnosis of prostate cancer [years]	8 ± 6 (2 - 26)	
PSA [ng/ml]	396 ± 674 (0.06 – 3129)	
Gleason score at diagnosis*:	Frequency	%
<8	9/41	22
≥8	32/41	78
Sites of metastatic disease:	Frequency	%
Bone	44/46	96
Lymph node	33/46	72
Visceral sites[†]	15/46	15
Pattern of bone involvement[‡]:	Frequency	%
None	2/46	4
Oligometastatic (≤3)	4/46	9
Disseminated (>3)	33/46	72
Diffuse bone marrow involvement	7/46	15
Previous treatment:	Frequency	%
Prostatectomy	26/46	57
Radiotherapy to prostate/ prostate bed	33/46	72
ADT	46/46	100
Abiraterone	29/46	63
Enzalutamide	15/46	33
Docetaxel	28/46	61
Cabazitaxel	5/46	11
223Ra-Dichloride	7/46	15

Abbreviations: SD = standard deviation, PSA = prostate specific antigen, ADT = androgen deprivation therapy, *unknown in n = 5, [†](lung: n = 8; pleura: n = 3; peritoneal carcinomatosis: n = 2, adrenal gland: n = 1; liver: n = 1), [‡]according to PROMISE criteria (*1*).

Graphical Abstract



Supplemental Table 1 Comparison of biochemical and imaging response after PSMA radioligand therapy

Patient	# of cycles	ΔPSA	PPP	$\Delta PSMA_{TV50}$	Sites of metastatic disease		Tracer
					Before PSMA RLT	After PSMA RLT	
1	2	349.9%	1A	n.a.	OSS; LN	OSS; LN; SPLEEN	PSMA-11
2	2	197.5%	1A	n.a.	OSS; LN	OSS; LN	PSMA-11
3	4	-48.2%	1A	n.a.	OSS; LN	OSS; LN	PSMA-11
4	2	3.7%	1A	n.a.	OSS; LN	OSS; LN; HEP	PSMA-11
5	4	-82.3%	n.p.	-80%	OSS; LN; PLEURA	OSS; LN	PSMA-11
6	2	65.4%	1C	31%	OSS; LN; PLEURA	OSS	PSMA-11
7	2	-31.5%	n.p.	-6%	OSS	OSS	PSMA-11
8	2	-46.2%	1A	n.a.	OSS; LN; PUL	OSS; LN; PUL	PSMA-11
9	2	-69.3%	1A	n.a.	OSS; LN; PUL	OSS; LN	PSMA-11
10	2	-35.3%	1A	n.a.	OSS; LN	OSS; LN	PSMA-11
11	4	4.8%	1A	n.a.	OSS; LN	OSS; LN	PSMA-11
12	2	-98.0%	n.p.	-65%	OSS	OSS	PSMA-11
13	4	-47.8%	1A	n.a.	OSS; LN	OSS	PSMA-11
14	2	-88.2%	n.p.	16%	OSS; LN; PeC	OSS; LN; PeC	PSMA-11
15	2	-99.8%	n.p.	-93%	OSS; LN	OSS	PSMA-11
16	4	-31.2%	1A	n.a.	OSS; LN	OSS	PSMA-11
17	2	-98.3%	n.p.	4%	OSS; LN; PLEURA	OSS	PSMA-11
18	2	3.2%	1A	n.a.	OSS; LN; PUL	OSS; LN; PUL	PSMA-11
19	2	68.1%	1C	53%	OSS	OSS	PSMA-11
20	4	-33.3%	n.p.	-62%	OSS; LN; PUL	OSS; LN; PUL	PSMA-11
21	2	87.3%	1A	n.a.	OSS; LN	OSS; LN; AG	PSMA-11
22	3	-67.5%	1A	n.a.	OSS; LN; PUL	OSS; LN; PUL; MUSCLE	PSMA-11
23	2	-89.9%	n.p.	-74%	OSS	OSS	PSMA-11
24	2	-33.5%	1A	n.a.	OSS; LN	OSS; LN	PSMA-11
25	3	-41.4%	1A	n.a.	OSS; LN	OSS; LN; PeC	PSMA-11
26	4	80.9%	1A	n.a.	OSS; LN	OSS; LN	PSMA-11
27	2	60.2%	1A	n.a.	OSS; LN; PUL	OSS; LN; PUL; AG	PSMA-11
28	2	50.5%	1C	146%	OSS	OSS	PSMA-1007
29	2	-52.0%	1C	50%	OSS; LN	OSS; LN	PSMA-1007
30	2	207.5%	1A	n.a.	OSS	OSS; LN	PSMA-1007
31	4	230.8%	1A	n.a.	OSS	OSS; PUL	PSMA-1007
32	4	-95.7%	n.p.	-71%	OSS; LN; PUL	OSS; LN; PUL	PSMA-1007
33	4	-77.3%	n.p.	-64%	OSS	OSS	PSMA-1007
34	4	-17.7%	1A	n.a.	OSS; PeC	OSS; LN; PeC	PSMA-1007
35	4	-95.9%	n.p.	-68%	OSS; LN; PUL	OSS	PSMA-1007
36	2	-99.9%	n.p.	-87%	OSS; LN	OSS; LN	PSMA-1007
37	2	310.3%	1C	200%	OSS; LN	OSS; LN	PSMA-1007
38	2	70.5%	1A	n.a.	OSS	OSS	PSMA-1007
39	4	104.9%	1A	n.a.	OSS; LN	OSS; LN; HEP*	PSMA-1007
40	2	133.8%	1A	n.a.	OSS	OSS	PSMA-1007
41	4	44.5%	1A	n.a.	OSS; AG	OSS	PSMA-1007
42	4	-97.1%	n.p.	-18%	OSS	OSS	PSMA-1007
43	2	351.9%	1A	n.a.	LN; HEP	OSS; LN	PSMA-1007
44	2	64.1%	1A	n.a.	OSS; LN	OSS; LN; HEP*	PSMA-1007
45	4	-98.1%	n.p.	-46%	LN	LN	PSMA-1007
46	2	90.5%	1A	n.a.	OSS; LN	OSS; LN	PSMA-1007

Explanations: PSMA = prostate specific membrane antigen; PSA = prostate specific antigen; PPP = modified PSMA PET criteria; $PSMA_{TV50}$: whole-body tumor volume on PSMA PET; RLT = radioligand therapy; OSS = bone; LN = lymph node; PUL = lungs; PeC = peritoneal carcinomatosis; HEP = liver; AG = adrenal gland; n.p. = non-progressive; n.a. = not applicable; *only seen on CT.