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A Phase II, Open-label study to assess safety and management change using ^{68}Ga-THP PSMA PET/CT in patients with high risk primary prostate cancer or biochemical recurrence after radical treatment: The PRONOUNCED study.

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Short title:

^{68}Ga-THP PSMA PET/CT in prostate cancer

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Abstract

Objectives:

To assess the safety and clinical impact of a novel, kit-based formulation of ^{68}Ga-THP PSMA positron emission tomography/computed tomography (PET/CT) when used to guide the management of patients with prostate cancer (PCa).

Methods:

Patients were prospectively recruited in to one of:

Group A: high-risk untreated prostate cancer; Gleason score ≥4+3, or PSA >20 ng/mL or clinical stage >T2c.

Group B: biochemical recurrence (BCR) and eligible for salvage treatment after radical prostatectomy with two consecutive rises in prostate-specific antigen (PSA) with a three-month interval in between reads and final PSA >0.1 ng/mL **or** a PSA level ≥0.5 ng/mL.

Group C: BCR with radical curative radiotherapy or brachytherapy at least three months prior to enrolment, and an increase in PSA level >2.0 ng/mL above the nadir level after radiotherapy or brachytherapy.

Patients underwent evaluation with PET/CT 60 minutes following intravenous administration of 160±30 MBq of ^{68}Ga-THP PSMA. Safety was assessed by means including vital signs, cardiovascular profile, serum haematology, biochemistry, urinalysis, PSA, and Adverse Events (AEs). A change in management was reported when the predefined clinical management of the patient altered as a result of ^{68}Ga-THP PSMA PET/CT findings.

Results:

Forty-nine patients were evaluated with PET/CT; 20 in Group A, 21 in Group B and 8 in Group C. No patients experienced serious AEs discontinued the study due to AEs, or died during the study. Two patients had Treatment Emergent AEs attributed to ^{68}Ga-THP-PSMA (pruritus in one patient and intravenous catheter site rash in another). Management change secondary to PET/CT occurred in 42.9% of all patients; 30% in Group A, 42.9% in Group B and 75% in Group C.

Conclusions:

^{68}Ga-THP PSMA was safe to use with no serious AE and no AE resulting in withdrawal from the study. ^{68}Ga-THP PSMA PET/CT changed the management of patients in 42.9% of the study population, comparable to studies using other PSMA tracers. These data form the basis of a planned Phase III study of ^{68}Ga-THP PSMA in patients with prostate cancer.

Introduction

Prostate Specific Membrane Antigen (PSMA) imaging with PET/CT has undergone rapid clinical acceptance across a variety of centres throughout the world within several years of first in man studies (**1**). There is growing evidence of superiority over typical standard of care imaging such as CT and bone scan as well as over other PET tracers such as choline but currently market authorisation for use is still lacking (**2,3,4**).

Despite the growing number of articles published, relatively few studies have been performed in a clinical trial format. There is also limited systematically collected data on safety of PSMA PET/CT (**5**).

There are several types of ^{68}Ga-PSMA PET tracer which are being used worldwide (**6**). The greatest use has been with ^{68}Ga-HBED PSMA but other types include PSMA I&T and PSMA 617. The most common method of producing ^{68}Ga PSMA tracers for clinical use includes a manual/ semi-automated multi-step process requiring heating and strict pH conditions to facilitate a multi-step process which can take approximately 25 minutes to produce a dose (**7**). Cold-kit formulations such as 68Ga-tris(hydroxypyridinone) (THP) PSMA involve a single step manufacturing process without the need for heating, requiring approximately 5 minutes to produce a dose (**8**).

^{68}Ga-THP PSMA has been investigated in a Phase I trial which evaluated 14 patients (**9**). Of these, 8 patients went on to have prostatectomy and the tracer was able to identify tumour which was positive for PSMA expression on histopathology. In addition, in 6 patients who had a positive ^{68}Ga-HBED PSMA PET/CT, THP PSMA was able to demonstrate concordance in number

of metastases. Some initial safety data was collected with no adverse events reported. Despite lower absolute uptake, there was a similar tumour to liver uptake ratio when compared with HBED PSMA (**9**).

Aim

The aims of this study were to evaluate PSMA PET/CT in three clinical settings using a cold kit formulation; ^{68}Ga-THP PSMA. The primary objective of the trial was to assess the safety of 68Ga-THP PSMA in prostate cancer and the secondary objective was to evaluate clinical impact by assessing the change in management of patients with prostate cancer after 68Ga-THP PSMA PET/CT.

Materials and Methods

This study, using ^{68}Ga-THP PSMA PET/CT was a prospective open label Phase II clinical trial in patients with newly diagnosed and recurrent prostate cancer (ClinicalTrials.gov Identifier: NCT03617588). The Institutional Review Board (Research and Ethics Committee) approved this study (reference 18/LO/0370) and all subjects signed a written informed consent. The primary end point was evaluation of safety of PSMA PET/CT (specifically adverse events related to ^{68}Ga-THP PSMA use) and the secondary end point was of a change in management plan after PET/CT.

Patients were identified from clinic and tumour board meetings from the primary site and from 3 other hospitals in London.

Patients

Inclusion Criteria

The study group consisted of men >18 years old diagnosed with prostate cancer, an Eastern Oncology Group (EOG) performance status of 0-2 (**10**), who had not received hormone therapy related to prostate cancer within the past three months. The following criteria divided the study cohort in to three distinct groups based on clinical setting.

Group A (new diagnosis high risk): Men with newly diagnosed (histopathologically proven) prostate cancer of Gleason 4+3 or above or PSA >20 or clinical stage >T2c and potentially operable.

Group B (Biochemical Recurrence (BCR) post radical prostatectomy (RP)): The initial criteria for inclusion in the study was any patient with 3 rises in PSA following RP. This was amended to

include first diagnosis of BCR with two consecutive rises in prostate-specific antigen (PSA) with a three-month interval in between reads and final PSA >0.1 ng/mL **or** a PSA level >0.5 ng/mL at time of recruitment.

Group C (BCR post radiotherapy (RT)): First diagnosis of BCR with the following: previous radical curative therapy with radiotherapy or brachytherapy at least three months prior to enrolment, and with BCR based on an increase in PSA level >2.0 ng/mL above the nadir level after radiotherapy or brachytherapy.

Exclusion criteria:

Receiving another Investigational Medical Product from one month before to one month after administration of ^{68}Ga-THP PSMA, known hypersensitivity to 68Ga-THPPSMA or any of its constituents, estimated glomerular filtration rate <20 mL/min /1.73 m^2.

Protocol

Patients were recruited from June 2018 to July 2019. Study participants underwent 4 visits as outlined in **Table 1**.

Safety

Adverse events (AEs) regardless of suspected relationship to study treatment were recorded throughout the study, from the ^{68}Ga-THP PSMA administration until 30 days after the

administration of ^{68}Ga-THPPSMA. All AEs were followed up until resolution or until Visit 4. Common Terminology Criteria grading was used for Adverse Events (CTCAE) (**11**).

Any related SAEs that occurred at any time following 30 days after the administration of ^{68}Ga-THP PSMA were reported.

Safety was assessed by means of physical examination, vital signs, cardiovascular profile (including 12 lead ECG), performance status, laboratory evaluations; haematology, biochemistry and urinalysis.

68Ga-THP PSMA PET/CT

Radiopharmaceutical production of the 68Ga-THP PSMA was performed in accordance with Good Manufacturing Practice and using a kit-based formulation, in a method previously described (**12**).

No patient preparation was required prior to the scan. The target administered activity of ^{68}Ga-THP PSMA was 250MBq ± 20% intravenously via a right upper limb vein.

PET/CT was performed on a GE Discovery 710 TOF scanner with Q.Clear reconstruction algorithm.

Imaging evaluation

All images were reviewed on GE Advantage workstations by 2 nuclear medicine radiologists/ physicians in consensus, both with over 3 years' experience in reporting PSMA PET/CT and who

had undergone training with review of 50 cases of ^{68}Ga-THP PSMA PET/CT which had been performed at another site.

Criteria for a positive scan were as follows: Focal areas of increased tracer uptake above background activity which could not be explained by physiological activity were attributed to prostate cancer or prostate cancer metastases.

Criteria for a negative scan were: No abnormal increased uptake attributable to prostate cancer or prostate cancer metastases above background activity.

Disease distribution was classified into the following sites; prostate (or prostate bed), pelvic lymph nodes, extra-pelvic lymph nodes, bone metastases and 'other' sites e.g. parenchymal disease in the liver. The reviewing nuclear medicine radiologist was permitted to request additional imaging to clarify equivocal areas or potential synchronous pathologies. Image reviewers were not blinded to any existing standard of care imaging which had occurred e.g. bone scan, CT, MRI and were aware of all clinical details including PSA value.

Criteria for a management plan:

Management plans were created by the primary clinician evaluating the patient (Urologist or Oncologist). The initial management plan relied on standard of care clinical and imaging details as per local, national and international guidelines. The revised management plan took all of the above factors in to account with the additional information from the 68Ga-THP PSMA PET/CT. A change in management needed the plan to be influenced by or altered directly in response to the findings from the 68Ga-THP-PSMA PET/CT study. Where a management plan was changed

primarily as a result of non PET factors e.g. co-morbidities etc, this was not included as a management change.

Statistics

The sample size was based on the degree of uncertainty in the estimation of the percentage of patients with a change in management, as measured by the confidence interval. Due to the phase of the study, relatively wide confidence intervals were allowed.

For Group A, previous literature suggested that approximately 25% of patients would change management (**13**). Assuming a 95% confidence level, it was calculated that 20 patients would be sufficient to obtain an estimate of the secondary outcome that was within ±20% of the population value.

For Groups B+C, previous literature suggested that approximately 45% would change management (**14**). With a 95% confidence level, a sample size of 40 patients in the two groups combined would be sufficient to obtain an estimate of the outcome that was within ±15% of the population value. The two-sided 95% Clopper-Pearson exact confidence interval and the two-sided 80% Clopper-Pearson exact confidence interval were calculated.

Validation

Validation included a combination of histology correlation and follow up of PSA levels beyond trial participation where available. Histopathological validation was available in 22 patients and PSA follow up in 31 patients.

Results

Patients

Forty-nine patients underwent evaluation with ^{68}Ga-THP PSMA PET/CT and 48 patients completed all visits including the final safety visit. Median age of recruited patients was 67 (43-80) years.

Figure 1 outlines the number of patients at each stage of the trial and **Table 2** shows patient demographics and clinical characteristics.

Safety

No Serious Adverse Events (SAEs) were reported in this study. No patients were withdrawn from the trial due to Adverse Events (AEs). No deaths were reported during this study.^{68}Ga-THP PSMA was well tolerated.

Two patients (4.1%) had a Treatment Emergent Adverse Event (TEAE) that was considered related to ^{68}Ga-THP PSMA PET/CT. These were CTCAE Grade 1 pruritus (Duration: 22 days) (Group A) and CTCAE Grade 1 catheter site rash (Duration: 4 days) (Group B). An additional 9 TEAEs were reported, not related to ^{68}Ga-THP administration .

No clinically significant variation in serum haematology, clinical chemistry or urinalysis parameters were detected and no AEs were identified from these parameters.

There were no clinically significant changes in vital signs for any patients during the study. No AEs were recorded from ECG findings.

Imaging findings

All imaging was of diagnostic quality. In two patients, images were more challenging to interpret due to high body mass index, lower end of the range of acceptable injected activity and arm down position in a patient who was not able to elevate their arms above the head.

Minor halo artefact was frequently encountered but images could be reviewed without scatter correction to reduce the effect of this.

^{68}Ga-THP PSMA PET/CT was positive in 27 patients (55.1%). The vast majority of patients in Group A had focal uptake of tracer in the prostate gland. In two of these cases, focal increased tracer uptake in the prostate was difficult to localise on PET/CT, leading to a positivity rate of 90% in this group. Fifteen of Group A had prostate-disease only, 1 prostate + Seminal vesicle involvement, 1 prostate + pelvic lymph nodes, 1 prostate with lymph nodes below and above the diaphragm. **(Figure 2).**

Only 3 of 21 patients in Group B were positive for disease (14.3%). Only 1 of 21 patients in Group B had uptake in the prostatectomy bed. There was 1 patient with prostate disease and pelvic lymph nodes (PSA 1.77), 1 patient with pelvic and bone metastasis (PSA 0.6) and 1 with bone metastases only (PSA 2.54).
Positive scans in this group were only demonstrated when PSA at the time of the scan was >0.5ng/ml. **(Figure 2 and 3).**

Patients in Group C tended to have a higher proportion of positive scans than in Group B (6/8, 75%). Disease was identified in the treated prostate in 50% of the cases in this group, and in a relatively greater proportion in lymph nodes (pelvic and extra pelvic) and bones when

compared with Groups A and B. In 3 patients, the ^{68}Ga-THP was positive in the prostate only, 1 prostate and lymph nodes above and below the diaphragm, 1 with pelvic and retroperitoneal lymph nodes and 1 with pelvic, extra-pelvic and bone metastases. **(Figure 2).**

In three cases, additional imaging was requested; a HBED PSMA as short interval follow up to evaluate a small volume mildly avid pelvic node - also negative on HBED PSMA, MRI of the liver for solitary focal uptake in the liver revealed imaging features typical for a haemangioma and MRI spine performed for focal uptake in the L5 vertebral body. The latter showed no metastases and the uptake at L5 was deemed to be secondary to degenerative change.

Patients demonstrated the typical physiological distribution of this tracer which has been described previously (**9**).

In some cases, areas of uptake were relatively mild in the prostate and this required manipulation of the window setting to evaluate further. This feature was also noted during training with ^{68}Ga-THP PSMA cases prior to the trial, suggesting both background and tumour activity may be less than in patients being evaluated with HBED PSMA.

Change in management

There were 21 changes from the original management plans in total across all three groups. Of these, 6 occurred in group A (30%), 8 in group B (42.9%) and 6 in group C (75%), giving a combined recurrence group (B+C) management change of 51.7% **(Table 3).**

Most of the changes throughout the three groups were inter-modality (16/21) e.g. from prostatectomy to radiotherapy, or from radical or salvage local treatment to systemic

treatment. Salvage treatment of the prostate bed to surveillance was also considered as inter modality change.

A minority of change were inter-modality i.e. changing prostatectomy with lymph node dissection to prostatectomy alone or adjusting radiotherapy fields to include lymph nodes.

Management changes occurred at all PSA levels (**Figure 4**).

An example of a positive ^{68}Ga-THP PSMA PET/CT with resulting change in management is shown in **Figure 5**.

Validation

In all 22 patients with histopathological reference standard (n=6 prostatectomy, n= 16 biopsy) within 3 months of the date of ^{68}Ga-THP PSMA PET/CT, disease within the prostate identified on ^{68}Ga-THP PSMA PET/CT could be correlated with a site of disease on histology. In patients where follow up PSA was available post-trial participation, (n=14 with management change and n=17 without), PSA reduced in all patients.

In the two group A patients where disease was difficult to identify, prostatectomy was performed in one which revealed pT2 Gleason 4+3 acinar adenocarcinoma with a tumour volume of 0.2cm^2. The second patient has a pre-trial biopsy demonstrating Gleason 4+5 maximum tumour length 7mm, 40% and was ultimately treated with radiotherapy.

Discussion

This is the first Phase II clinical trial using ^{68}Ga-THP PSMA (a kit-based formulation) which showed lack of SAE and lack of patients discontinuing the study due to AEs. The confirmed safety profile when reviewing serum haematology, chemistry, urinalysis, vital signs and ECG, further fortified the safety profile of this tracer. These were all important findings when considering a phase III study with this tracer.

The lack of SAE is in concordant with published data on safety using other PSMA agents (^{68}Ga PSMA 11, ^{18}F-PSMA-11 and ^{18}F DCFPyL) (5,15,16). The ^{68}Ga PSMA 11 data showed no clinical reported AEs. With 18F PSMA-11, No clinically relevant changes in vital parameters were observed and no patient reported side effects. The DCFPyL study shown no serious adverse events and no adverse events with monitored heart rate of blood pressure. One patient reported two adverse events that were classified as unlikely to be attributable to the radiotracer and another patient had a fall in platelet count attributed to treatment for prostate cancer.

This study demonstrated that clinically significant levels of management changes occurred following ^{68}Ga-THP PSMA PET/CT in high-risk patients and in those with biochemical recurrence (42.9% change in management across all groups).

In the primary high-risk group, management changes occurred in 30% of patients. This is comparable with the findings from a recent study performed with the same tracer which showed management changed in 24% of high-risk patients and the management change rate in high risk patients in a randomised multicenter study using HBED PSMA was 28% (**4,13**).

In the biochemical recurrence groups combined, management changes occurred in 51.7% of patients**.** This was comparable to the findings of the meta-analysis of studies performed with PSMA in the recurrence setting by Han et al and slightly higher than the proportion of management change we had described previously using ^{68}Ga HBED PSMA **(14).**

There were fewer changes in the post prostatectomy group (42.9%) compared with the post radiotherapy group (75%). This may in part have been due to the large proportion of patients scanned at very low PSA levels in group B; 23.8% of patients in this group had a PSA of 0.1-0.2ng/ml and 52.4% had a PSA of 0.2-0.5 ng/ml and associated low number of positive scans. The low PSA levels at the time of scanning in the post-prostatectomy group was driven by the definition of BCR in this group, reflecting clinicians' threshold to consider offering early salvage radiotherapy. In the BCR group evaluated by Kulkarni et al, there were no positive scans in the population with PSA <0.5 and that study reported higher rates of management change at higher PSA levels (**13**). Derlin et al did demonstrate positive studies at very low PSA levels; 20.0% for a PSA value of >0.2 to <0.5, and 22.2% for a PSA value of 0.01 to 0.2 ng/mL **(17).** This is in contrast with the findings from other published data using HBED PSMA which showed 38% of scans were positive when PSA <0.5ng/mL in BCR (**18**). Others have also demonstrated higher positive rates at very low PSA levels and this is one of the key strengths of PSMA over other PET tracer such as ^{18}F/^{11}C Choline. However, our previous study using HBED PSMA demonstrated a positive rate of 15.8% in the range PSA 0.2-0.5 (**19**). Considering possible explanations for this, many studies have not excluded hormone use prior to scan (which would increase PSMA upregulation/ scan positivity) and faster renal clearance of THP and potential lower affinity of ^{68}Ga-THP PSMA compared with HBED PSMA are also important considerations (**13**). The

different PSMA tracers would need to be investigated using both tracers in the same population with low PSA levels or at least in a matched pair analysis to evaluate further.

The higher rate of management change in the post radiotherapy BCR group (group C) may have been in part due to the greater proportion of positive PET/CTs in this group, as well as the greater number of available options to treat these patients including salvage prostatectomy, salvage focal therapy, further salvage radiotherapy/brachytherapy, systemic therapies, or watchful waiting.

The cold-kit manufacturing method of this tracer has several potential benefits if permitted to enter mainstream clinical use. Short manufacture time is helpful in the context of a short half-life radiotracer and less complex radiopharmacy production may allow more patients to be scanned with produced doses.

Limitations.

The end point chosen for this trial of management change has been used in multiple studies evaluating PSMA PET/CT (**20-22**). This allows potential progression of PSMA tracers towards regulatory approval when conducted in a well-designed clinical trial as although survival/progression end points are more objective, they may take years to reach. There remains a lack of evidence that the management change improves survival or another surrogate endpoint. However, the increased accuracy of disease detection implies more personalised and appropriate management for the stage of disease and reduction of risks and side effects of ineffective treatments.

There is a lack of full validation within this and many studies on PSMA PET/CT (**20-22**). Although histology was available in a proportion of patients, mainly those with recent biopsy and those who underwent prostatectomy soon after the PET/CT, this was not available in all patients and other sites of disease e.g. lymph nodes were not sampled to provide systematic validation. This is often not feasible, particularly in the biochemical recurrence setting. Diagnostic accuracy assessment was not within the scope of this Phase II trial, but is planned to be evaluated in a larger Phase III study.

The study design involved recording the intended management plan after and on the basis of ^{68}Ga-THP PSMA PET/CT and there may have been factors related to clinician-patient consultations which led to a difference in executed management from that recorded in the study.

In the case of one patient where lymph node dissection was not performed, the lack of uptake in nodes formed part of the decision process not to proceed with lymphadenectomy, even though the clinician and patient were aware a negative scan did not exclude disease entirely. This touches on the complex issue of PSMA guided targeted therapy and the need for robust histopathological studies to confirm the limits of disease detection within nodes.

Conclusion

^{68}Ga-THP PSMA (kit formulation) was well tolerated and safe to use with no SAE and no AE resulting in withdrawal from this Phase II study. ^{68}Ga-THP SMA PET/CT changes the management of patients with prostate cancer, in biochemical recurrence (42.9%) and, to a lesser degree in primary high-risk disease. The levels of management changes described in this prospective trial are comparable to others who have evaluated PSMA in these prospective and retrospective clinical settings. These data form the basis of a planned Phase III study of ^{68}Ga-THP PSMA in patients with prostate cancer.

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MM: Research radiographer funded by Theragnostics.

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KEY POINTS

QUESTION:

Is ^{68}Ga-THP PSMA PET/CT safe to use and does it change the management of patients with prostate cancer?

PERTINENT FINDINGS:

This phase II open label prospective clinical trial showed ^{68}Ga-THP PSMA PET/CT to be well tolerated and safe to use. Management was changed in 30% of patients with untreated high-risk disease and 51.7% of patients with recurrent disease.

IMPLICATIONS FOR PATIENT CARE: This data shows the potential utility of ^{68}Ga-THP PSMA in untreated and recurrent disease and the safety data serves as a basis of a planned Phase III study.

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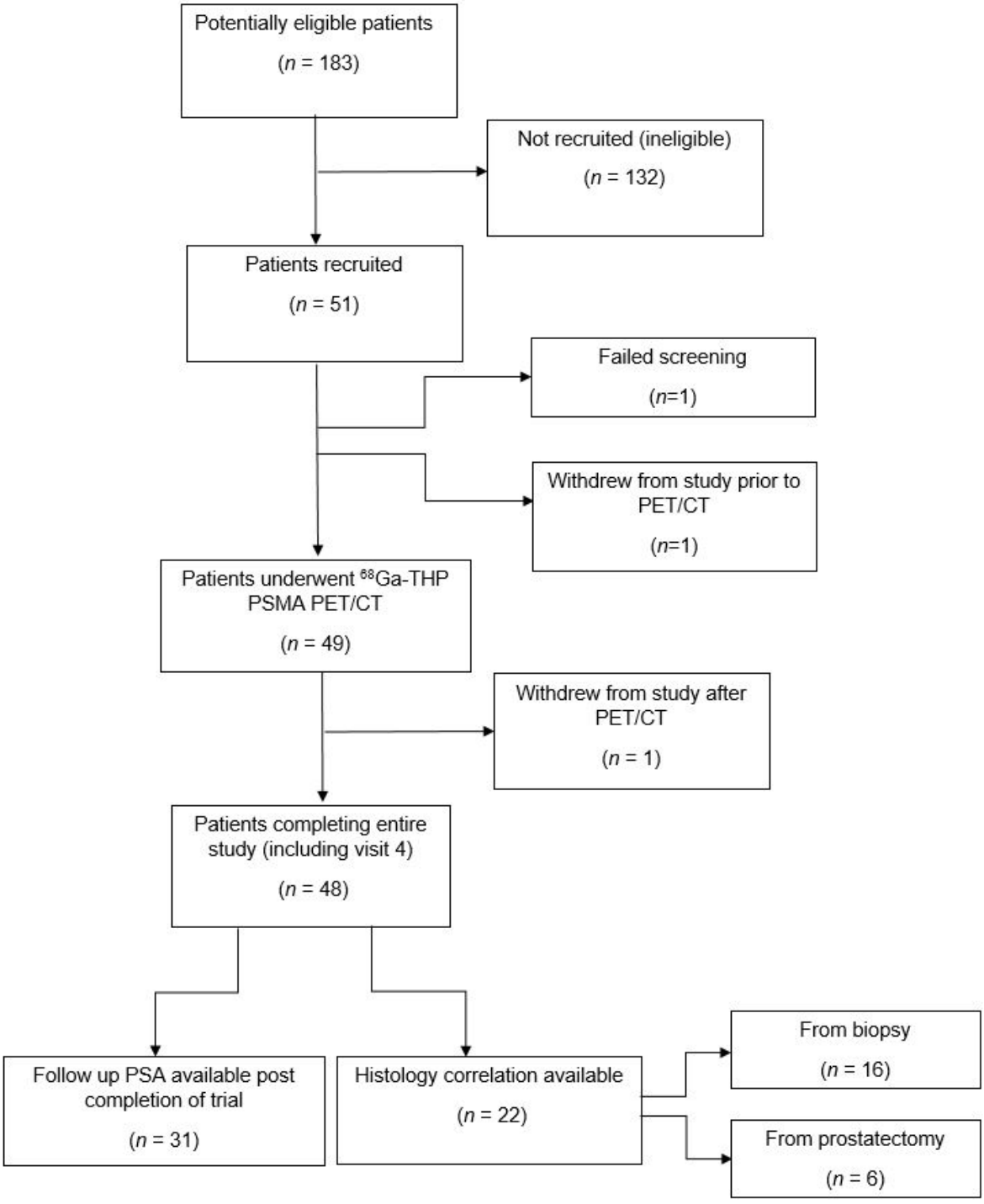

Figure 1: Number of patients in each stage of the trial

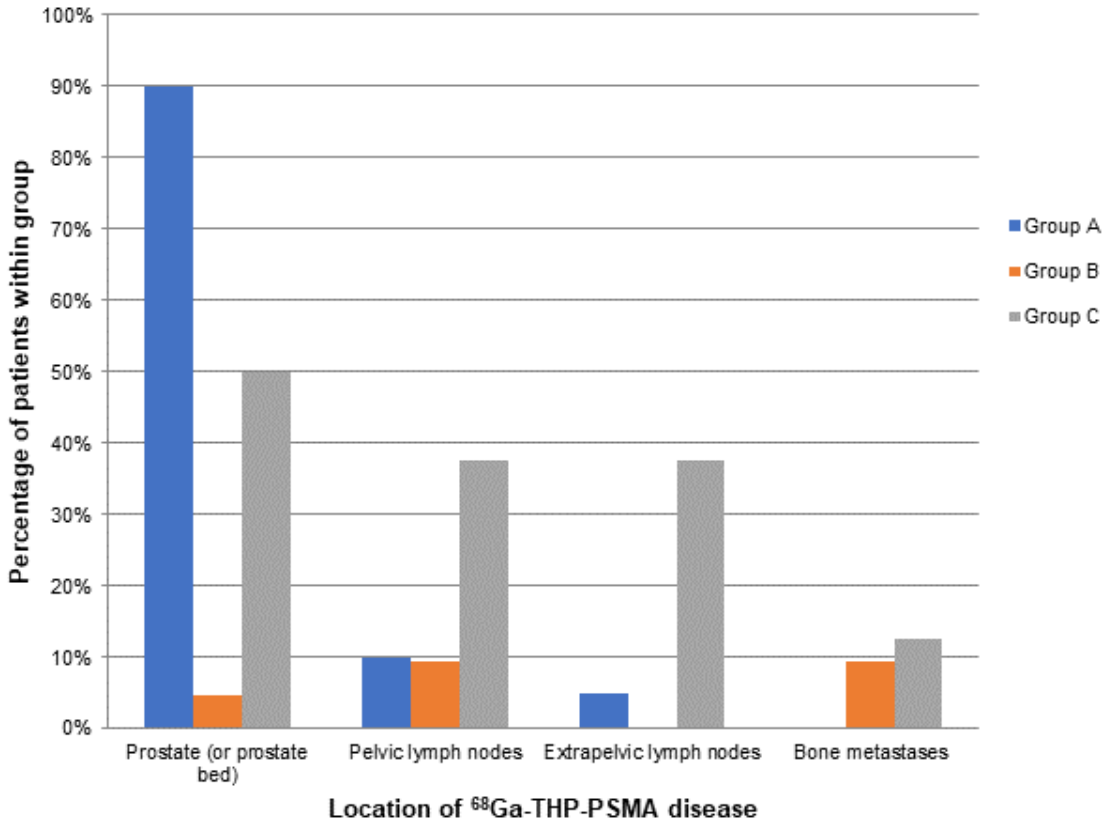

Figure 2: Locations of ^{68}Ga-THP uptake positive for tumour in Group A, B and C.

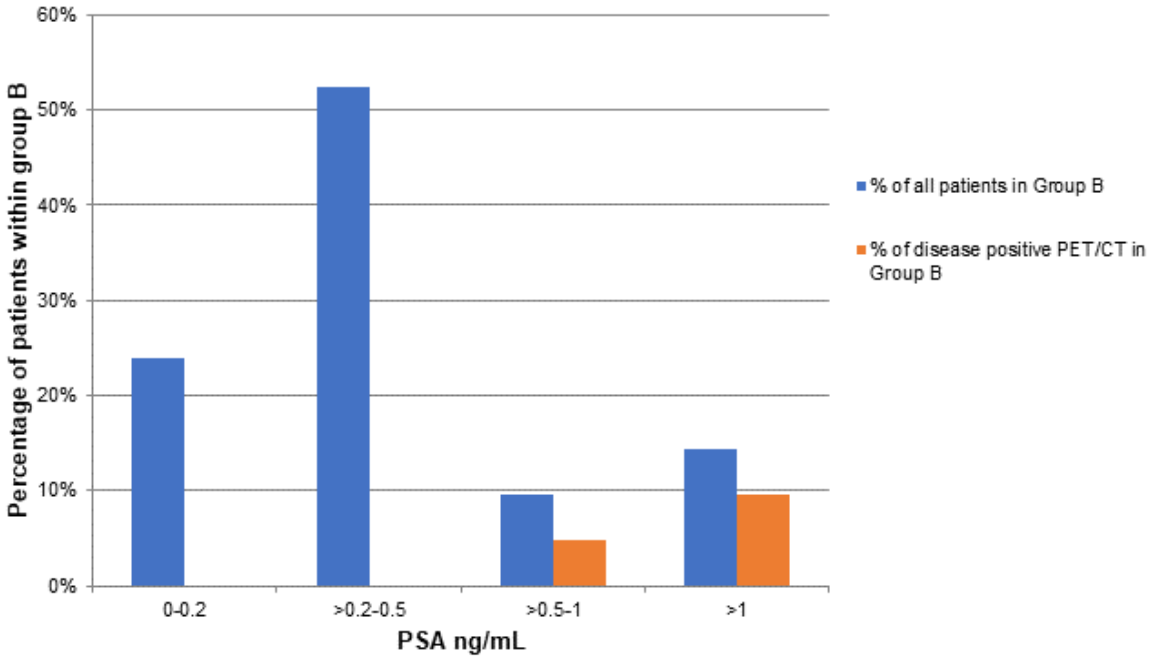

Figure 3: Proportion of patients in Group B and proportion of positive scans in this Group, stratified according to serum PSA level.

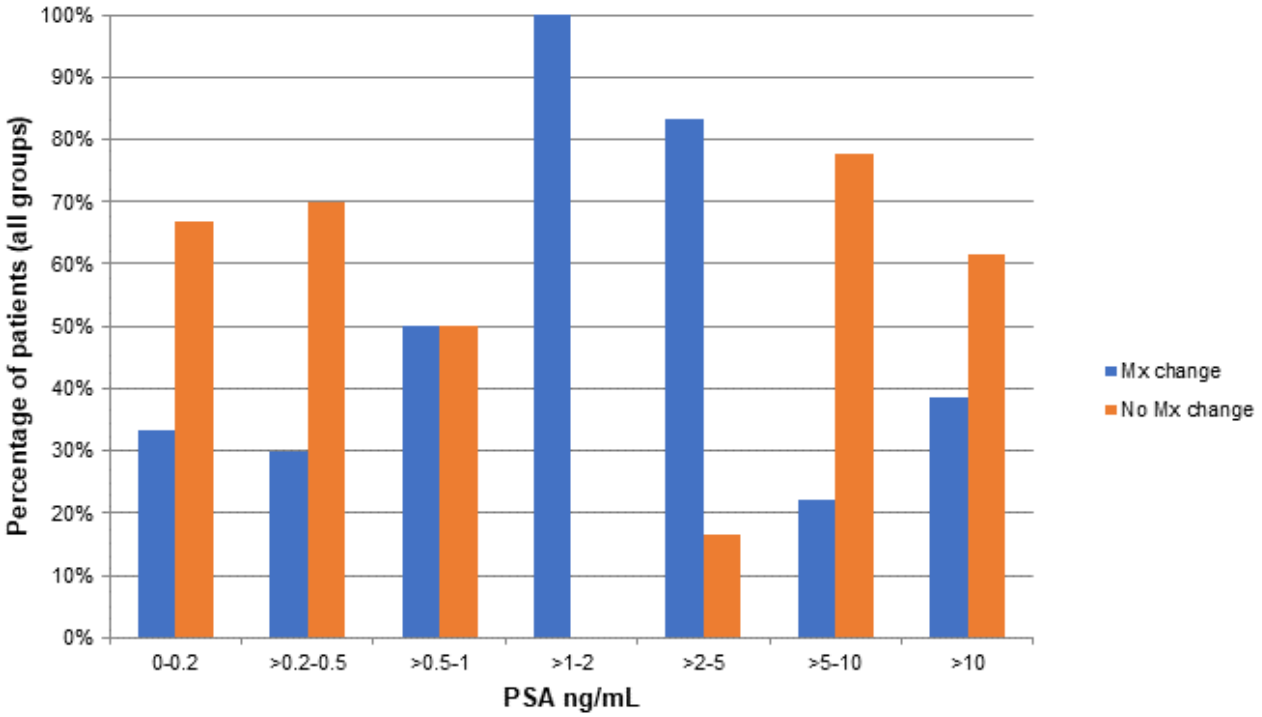

Figure 4: Proportion of patients with a management change (all Groups) stratified according to PSA level.

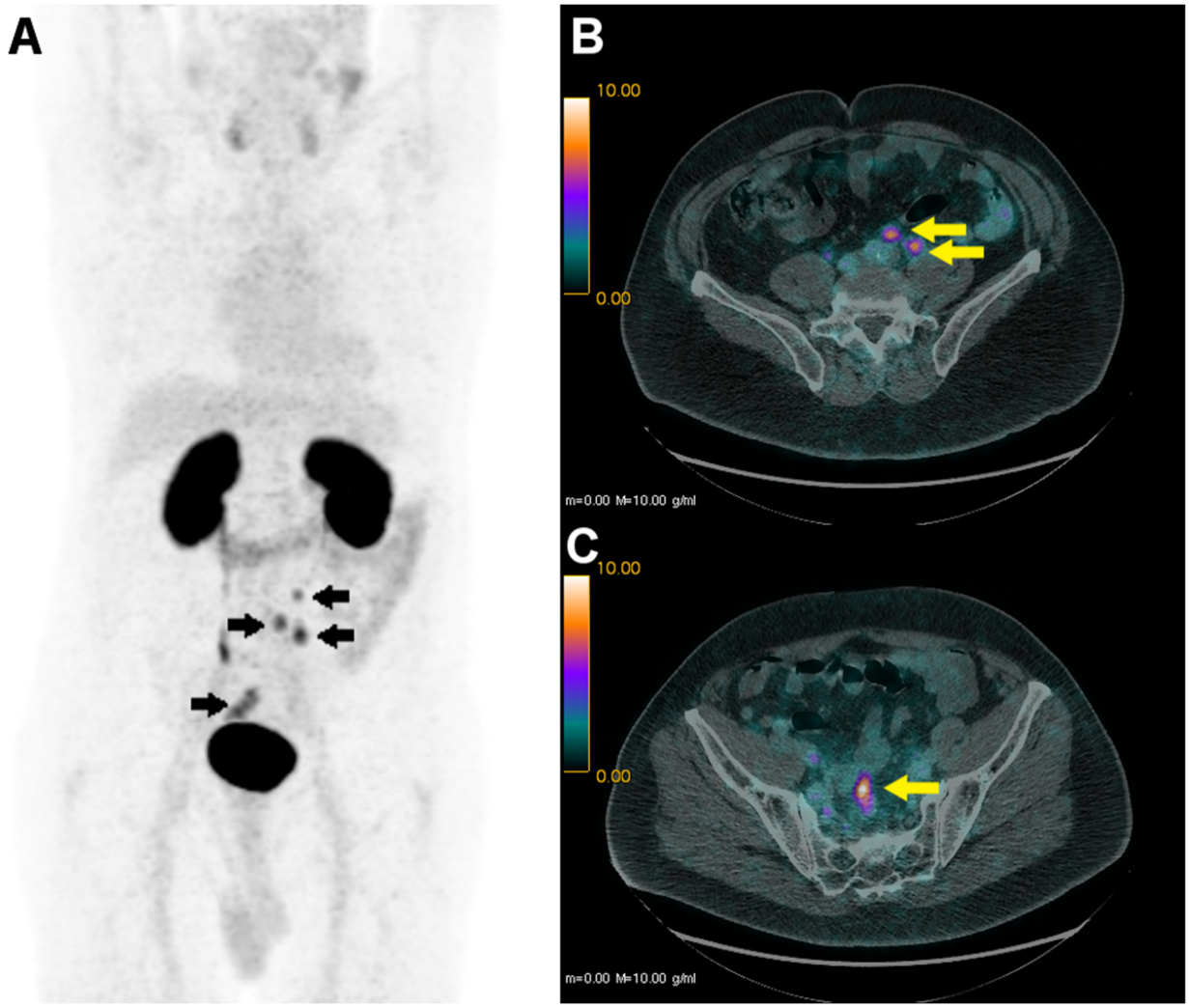

Figure 5: ^{68}Ga-THP PSMA PET/CT in a 62-year-old man in Group C. Left image: MIP, black arrows show 68Ga-THP PSMA avid lymph nodes in the pelvis and retroperitoneum.

Upper right image: Axial fused PET/CT image showing some of the small volume retroperitoneal lymph nodes.

Lower right image: Axial fused PET/CT image showing some of the small volume pelvic nodal disease.

The patient's management changed from potential salvage options (prostatectomy or focal therapy) to systemic treatment with hormones.

Event	Groups A, B and C			
	Visit 1 Pre-scan Data (=< 4 weeks of scan)	**Visit 2** (day of scan)	**Visit 3** by Telephone (next working day)	**Visit 4** Outpatient (approximately 2 weeks post-scan)[a]
Confirm eligibility	X			
Informed consent	X			
Demographics	X			
Medical history including: PCa treatment history/Imaging history	X	X		
Physical examination[b]	X	X		X
ECOG performance status	X			X
Concomitant medications	X	X	X	X
Management plan[c]	X			X
Study registration	X			
Serum full blood count, urea , electrolytes, liver function tests, PSA	X			X
Urinalysis	X			X
Cardiovascular profile (ECG)	X	X[d]		X
Vital signs	X	X[e]		X
^{68}Ga-THP PSMA PET/CT administration and imaging		X		
Adverse events		X	X	X

[a] A window of 0 to 6 weeks was permitted depending on local clinical practice. [b] Comprised height (Visit 1 only), weight, body surface area and description of external signs of cancer. [c] It was recognised that the revised management plan may be decided on before the outpatient appointment and this was permitted. It did not constitute a protocol deviation if the management plan was decided outside of the visit. [d] ECG: Visit 2 – approximately 1 hour pre-scan. [e] Vital signs: Visit 2 – pre-scan, during injection, post-scan for 2 hours after injection and prior to discharge.

Table 1: Study protocol demonstrating data collected at each of the 4 patient visits

Demographic Characteristic	Statistic	Newly Diagnosed (Group A)	BCR (Groups B+C)	Total
Number of Patients	N	20	29	49
Age (years)	N	20	29	49
	Median	68.5	66.0	67.0
	Minimum	49	43	43
	Maximum	76	80	80
Race				
White	n(%)	13 (65.0%)	21 (72.4%)	34 (69.4%)
Afro-Caribbean	n(%)	7 (35.0%)	5 (17.2%)	12 (24.5%)
Asian	n(%)	0 (0.0%)	3 (10.3%)	3 (6.1%)
ECOG Performance Status				
0	n(%)	19 (95.0%)	29 (100.0%)	48 (98.0%)
1	n(%)	1 (5.0%)	0 (0.0%)	1 (2.0%)
PSA prior to scan (ug/L)	N	20	29	49
	Mean	25.2	1.6	11.2
	SD	27.00	2.32	20.70
	Median	13.8	0.4	4.2
	Min, Max	5,90	0,10	0,90
Initial Gleason Score				
=<3+4	n(%)	1 (5.0%)	15 (51.7%)	16 (32.7%)
>=4+3	n(%)	19 (95.0%)	14 (48.3%)	33(67.3%)

Table 2 Summary of Demographics and Baseline Characteristics in Group A (new diagnosis high-risk) and in Group B+C(combined recurrence post radical prostatectomy and post radiotherapy).

Group	Positive	Inter-modality change	Intra-modality change	Other (imaging/ short interval follow up)	Total management change per Group
A	18 (90%)	4	1	1	30.0%
		RP to RT (1) RT to RP (1) RT to RT with field change (1) RP to hormones (1)	RP with LND to RP alone (1)	Spine MRI (1)	
B	3 (14.3%)	6	1	2	42.9%
		RT to surveillance (4) RT to hormones (2)	RT to RT with field change (1)	Liver MRI (1) Short interval repeat PET/CT (1)	
C	6 (75%)	6	0	0	75.0%
		Salvage RP/focal therapy of prostate to hormones/chemotherapy (3) Hormones to template biopsy for consideration of salvage RP/focal therapy (2) Salvage RP/focal therapy of prostate to surveillance (1)			
Total	27 (55.1%)	16	2	3	42.9%

Table 3: Scan positivity and management change per patient Group. RP; radical prostatectomy, RT; radiotherapy, LND; Lymph node dissection.