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Clinical Trial Protocol for PRIMARY2: A Multicentre, Phase 3, Randomised Controlled Trial Investigating the Additive Diagnostic Value of [^{68}Ga]Ga-PSMA-11 Positron Emission Tomography/Computed Tomography in Men with Negative or Equivocal Multiparametric Magnetic Resonance Imaging for the Diagnosis of Clinically Significant Prostate Cancer

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Abstract

Background: Multiparametric magnetic resonance imaging (mpMRI) has an established role for the diagnosis of clinically significant prostate cancer (sPCa). The PRIMARY trial

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demonstrated that [^{68}Ga]Ga-PSMA-11 positron emission tomography/computed tomography (PET/CT) was associated with a significant improvement in sensitivity and negative predictive value for sPCa detection.

Objective: To demonstrate that addition of prostate-specific membrane antigen (PSMA) radioligand PET/CT will enable some men to avoid transperineal prostate biopsy without missing sPCa, and will facilitate biopsy targeting of PSMA-avid sites.

Design, setting, and participants: This multicentre, two-arm, phase 3, randomised controlled trial will recruit 660 participants scheduled to undergo biopsy. Eligible participants will have clinical suspicion of sPCa with a Prostate Imaging-Reporting and Data System (PI-RADS) score of 2 and red flags, or a PI-RADS score of 3 on mpMRI (PI-RADS v2). Participants will be randomised at a 1:1 ratio in permuted blocks stratified by centre. The trial is registered on ClinicalTrials.gov as NCT05154162.

Intervention: In the experimental arm, participants will undergo pelvic PSMA PET/CT. Local and central reviewers will interpret scans independently using the PRIMARY score. Participants with a positive result will undergo targeted transperineal prostate biopsies, whereas those with a negative result will undergo prostate-specific antigen monitoring alone. In the control arm, all participants undergo template transperineal prostate biopsies. Participants will be followed for subsequent clinical care for up to 2 yr after randomisation.

Outcome measurements and statistical analysis: sPCa is defined as Gleason score 3 + 4 (≥10%) = 7 disease (grade group 2) or higher on transperineal prostate biopsy. Avoidance of transperineal prostate biopsy will be measured at 6 mo from randomisation. The primary endpoints will be analysed on an intention-to-treat basis.

Conclusions: Patient enrolment began in March 2022, with recruitment expected to take 36 mo.

Patient summary: For patients with suspected prostate cancer who have nonsuspicious or unclear MRI (magnetic resonance imaging) scan findings, a different type of scan (called PSMA PET/CT; prostate-specific membrane antigen positron emission tomography/computed tomography) may identify men who could avoid an invasive prostate biopsy. This type of scan could also help urologists in better targeting of samples from suspicious lesions during prostate biopsies.

1. Introduction

Multiparametric magnetic resonance imaging (mpMRI) has an established role in the diagnosis of prostate cancer, with better diagnostic accuracy in comparison to transrectal ultrasound (TRUS)-guided prostate biopsy. PROMIS [1] demonstrated better accuracy with an mpMRI targeted approach over TRUS, with higher sensitivity for International Society of Urological Pathology (ISUP) grade group (GG) ≥3 disease. However, if clinically significant prostate cancer (sPCa) was defined as GG ≥2, approximately 25% of men with negative mpMRI findings had malignancy that was missed. PRECISION [2] took this approach one step further, omitting biopsy for men with an mpMRI Prostate Imaging-Reporting and Data System (PI-RADS) score of 2 (28% of the population). The proportion of participants with sPCa, defined as GG ≥2, was higher on mpMRI than on standard TRUS biopsy. Nevertheless, owing to concerns regarding missed sPCa cases among men with negative mpMRI findings, implementation of an mpMRI-targeted approach remains difficult for many, resulting in an ongoing role for template biopsy for participants with negative mpMRI findings and a persisting suspicion of malignancy [3]. There is also concern regarding interobserver variability for mpMRI [4], especially as it is broadly adopted in lower-volume centres [5].

Prostate-specific membrane antigen (PSMA) is a large transmembrane glycoprotein that is highly overexpressed in prostate adenocarcinoma [6] and PSMA intensity on immunohistochemistry increases with higher pathological grade [7,8]. Results from two retrospective studies [9,10] and one prospective database [11] favour PSMA positron emission tomography/computed tomography (PET/CT) for detection of sPCa, although these studies probably overestimated test accuracy as they were limited by few patients without cancer or with GG 1 disease on biopsy. Whether PSMA PET/CT should play a clinical role in diagnosis has been evaluated by the PRIMARY trial, a prospective, multicentre, single-arm trial among men at high clinical risk of sPCa undergoing both mpMRI and transperineal prostate biopsy [12]. PRIMARY found a significant improvement in both negative predictive value (NPV) (91%, 95% confidence interval [CI] 80–97% vs 72%, 95% CI 61–80%; $p < 0.001$) and sensitivity (97%, 95% CI 93–99% vs 83%, 95% CI 77–89%; $p < 0.001$) for PSMA PET/CT in addition to mpMRI versus mpMRI alone. The most significant additional value of PSMA PET/CT was for participants with high clinical risk and PI-RADS 2 or 3 lesions. In this group, 38% (56/148) of men had true-negative findings on PSMA PET/CT, representing a subset who could avoid transperineal prostate biopsy (Fig. 1).

According to the results from PRIMARY, PSMA PET/CT and mpMRI appear to be a powerful combination for

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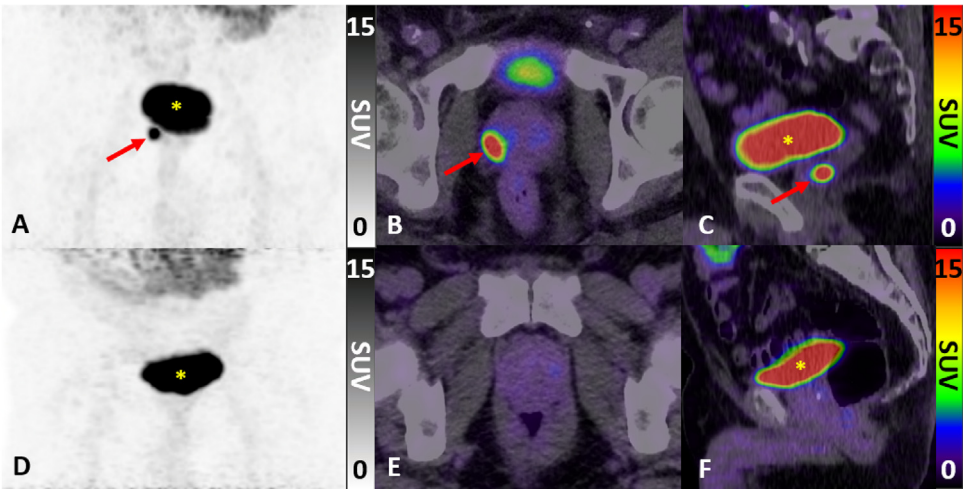

Fig. 1 – PSMA PET/CT examples from the PRIMARY trial. (A–C) Patient with PSA 5.0 ng/ml, prostate volume of 36 ml and PI-RADS 2 score on MRI, and PSA density 0.139 ng/ml^2. PSMA PET/CT revealed a PRIMARY score of 5 with a highly avid focus (SUVmax 25) in the right peripheral zone at mid level shown on (A) MIP, (B) fused transaxial and (C) sagittal planes. Transperineal prostate biopsies revealed prostate adenocarcinoma, Gleason score 4 + 3 = 7 (85% pattern 4). (D–F) Patient with PSA 6.3 ng/ml, prostate volume of 46 ml and PI-RADS score 2 on MRI, and PSA density of 0.137 ng/ml^2. PSMA PET/CT revealed a PRIMARY score of 1 without any PSMA-avid foci as shown on (D) MIP, (E) fused transaxial, and (F) sagittal planes. Transperineal prostate biopsies did not reveal any sites of malignancy. * = bladder (physiological); CT = computed tomography; MIP = maximum-intensity projection; MRI = magnetic resonance imaging; PET = positron emission tomography; PI-RADS = Prostate Imaging-Reporting and Data System; PSMA = prostate-specific membrane antigen; PSA = prostate-specific antigen; SUVmax = maximum standardised uptake value.

identification of significant malignancy, particularly for PI-RADS 2 or 3 lesions with high clinical risk, that could potentially increase the detection of sPCa and reduce both the number of biopsies undertaken and the diagnosis of insignificant malignancy requiring additional follow-up.

2. Patients and methods

2.1. Study design and hypothesis

PRIMARY2 is a multicentre (up to 10 Australian centres), two-arm, phase 3, randomised controlled trial evaluating the addition of PSMA PET/CT to standard mpMRI for detection of sPCa. The hypothesis is that addition of PSMA PET/CT is noninferior to the standard of care with mpMRI alone, and provides the advantages of significantly reducing biopsies, reducing diagnosis of insignificant malignancy, and limiting targeted-only biopsies to men with high clinical suspicion of PCa and PI-RADS 2 or 3 lesions on mpMRI.

2.2. Study population

Participants with a clinical suspicion of prostate cancer and PI-RADS 2 or 3 lesions on mpMRI (PI-RADS v2) within 9 mo who have never undergone a prostate biopsy and who meet all of the inclusion and none of the exclusion criteria (Table 1) will be eligible for the trial.

Table 1 – Eligibility criteria

Inclusion criteria
1. Males aged ≥18 yr at the time of consent
2. No previously diagnosed prostate cancer
3. No previous prostate biopsy
4. Magnetic resonance imaging examination within 9 mo before randomisation meeting one of the following criteria:
• PI-RADS 2 AND at least one red flag, defined as:
○ PSA density >0.1 ng/ml^2
○ Abnormal DRE
○ Strong family history (1 first-degree relative or ≥2 second-degree relatives)
○ *BRCA* mutation
○ PSA >10 ng/ml
○ PSA doubling time <36 mo
○ PSA velocity >0.75 ng/ml/yr
• PI-RADS 3
5. Intention for prostate biopsy
6. Willing and able to comply with all study requirements
Exclusion criteria
1. PSA >20 ng/ml
2. Stage ≥cT3 on DRE. Tx (not assessed) is permitted in the context of virtual consultations, such as during the COVID-19 pandemic.
3. Significant morbidity that, in the judgement of the investigator, would limit compliance with the study protocol.

DRE = digital rectal examination; PI-RADS = Prostate Imaging-Reporting and Data System; PSA = prostate-specific antigen.

2.3. Objectives

The co-primary objectives are to estimate the percentage difference in sPCa between the experimental and control arms, and the percentage of men who avoid transperineal prostate biopsy in the experimental arm. The main secondary objectives are the percentage difference between arms in insignificant prostate cancer, complications following biopsy, health-related quality of life, generalised anxiety, cancer worry, and the health economics impact. The primary and secondary objectives are listed in Table 2.

2.4. Randomisation and interventions

Eligible participants will be randomised at a 1:1 ratio in permuted blocks stratified by centre. In the control arm, all participants will undergo template transperineal prostate biopsy. They will be followed for subsequent clinical care for 6 mo after randomisation. In the experimental arm,

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Table 2 – Study objectives

Joint primary objectives
To estimate the:
1. Percentage difference in sPCa between the experimental arm (with targeted-only biopsy) and the control arm (with transperineal template biopsy), defined as the presence of a single biopsy core indicating Gleason score 3 + 4 (≥10%) = 7 disease (grade group ≥2).
2. Percentage of men who avoid transperineal prostate biopsy in the experimental arm.
Secondary objectives
To assess the:
1. Percentage difference in clinically insignificant prostate cancer between the experimental arm (with targeted-only biopsy) and the control arm (with transperineal template biopsy).
2. Health economics impact of the experimental and control arms.
3. Estimated mean difference in change from baseline in health-related quality of life between the experimental and control arms.
4. Estimated mean difference in generalised anxiety between the experimental and control arms at each time point.
5. Estimated mean difference in cancer worry between the experimental and control arms at each time point.
6. Number of biopsy cores in each arm.
7. Complications following transperineal prostate biopsy.
8. Percentage of men who have sPCa detected only with PSMA PET (MRI PI-RADS 2).
9. Interobserver variability of PSMA PET interpretation between local and central interpretation.
10. Percentage grade group change from biopsy (stratified by biopsy approach) for men who undergo radical prostatectomy.
11. Diagnostic accuracy of PSMA PET in detecting sPCa with a composite of targeted biopsy results and the 2-yr follow-up for PSMA PET negative studies.
12. Percentage of men with sPCa on targeted biopsy in the experimental arm or transperineal template biopsy in the control arm, using alternative sPCa definitions: a. Men who undergo or are recommended for curative-intent treatment (radical prostatectomy, external beam radiotherapy, or brachytherapy). b. Grade group ≥2. c. Grade group ≥3.
13. Estimate of the mean difference in decisional conflict related to participation in a randomised study between the experimental and control arms at baseline.
14. Estimate of the mean difference in decisional regret related to participation in a randomised study between the experimental and control arms at each follow-up time point.

MRI = magnetic resonance imaging; PET = positron emission tomography; PI-RADS = Prostate Imaging-Reporting and Data System; PSMA = prostate-specific membrane antigen; sPCa = significant prostate cancer.

participants will undergo pelvis-only PSMA PET/CT. Participants with positive PSMA PET/CT findings will undergo targeted transperineal prostate biopsy, whereas those with a negative PSMA PET/CT will undergo surveillance. The latter will forego prostate biopsy unless future tests indicate a need for further investigation, such as rising prostate-specific antigen (PSA), for a minimum of 6 mo after randomisation. Participants in the experimental arm will be followed for subsequent clinical care until the commencement of curative-intent treatment or 24 mo after randomisation, whichever comes first. The trial schema is presented in Figure 2.

2.5. Sample size

The sample size required is based on demonstration of noninferiority in the proportion of men with sPCa in the experimental arm in comparison to the control arm. The proportion of participants with sPCa is expected to be 30%, considering the PI-RADS 2 and 3 subset in PRIMARY [12]. A total sample size of 627 participants is required, calculated to demonstrate noninferiority with a margin of 10%, intraclass correlation of 5%, power of 80%, and a one-sided type 1 error of 2.5%. To allow for a patient dropout rate of up to 5%, 660 participants will be accrued to the study (330 participants per arm). Given that 38% of men are expected to avoid biopsy, the total sample size of 627 (and hence >310 participants in the experimental arm), and a one-sided type 1 error of 2.5%, there is greater than 90% power of rejecting the null hypothesis that 20% of men will avoid biopsy in favour of the alternative hypothesis that this proportion is greater than 20%.

2.6. PSMA PET/CT technique

Before site activation, accreditation of PET cameras will be undertaken by the Australasian Radiopharmaceutical Trials Network (ARTnet). To harmonise the image quality and quantitative parameters, standardised acquisition and reconstruction of gallium-68 will be performed using an IEC/NEMA-NU2 body phantom with fillable spherical inserts of varying size to check the accuracy of the dose calibrator [13]. [^{68}Ga]Ga-PSMA-11 production must be validated with ARTnet certification before study commencement.

All participants in the experimental arm will undergo pelvis-only PSMA PET/CT within 28 d after randomisation. The recommended [^{68}Ga]Ga-PSMA-11 activity for administration is 1.8–2.2 MBq/kg, subject to any variation that may be required owing to variable elution efficiencies obtained during the lifetime of the ^{68}Ge/^{68}Ga generator. Furosemide 20 mg (oral or intravenous) is strongly recommended at the time of radiotracer injection.

PSMA PET/CT acquisition is performed between 60 and 70 min, with a minimum bed-step acquisition time of 180 s. A limited field of view of the pelvis will be used with two bed steps, from the iliac crests and downward. The ordered subset expectation maximisation (OSEM) algorithm should be used for tomographic reconstruction. A low-dose CT technique will be used without intravenous or oral contrast. The pelvis-only PSMA PET/CT images will be reviewed by the nuclear medicine team before the patient is discharged. If there is a site of intraprostatic uptake with a maximum standardised uptake value of ≥12, seminal vesicle invasion, or nodal and/or distant metastases in the limited field of view, whole-body PSMA PET/CT will be performed for staging purposes.

2.7. PSMA PET/CT interpretation

Local and central interpretations of PSMA PET/CT will be conducted independently and blinded to mpMRI and clinical details, with reporting according to the PRIMARY score [14]. An imaging examination is considered negative for PRIMARY scores 1–2 versus positive for PRIMARY scores 3–5. In the event of discordance, a second central reviewer will independently interpret the study as a tie-breaker.

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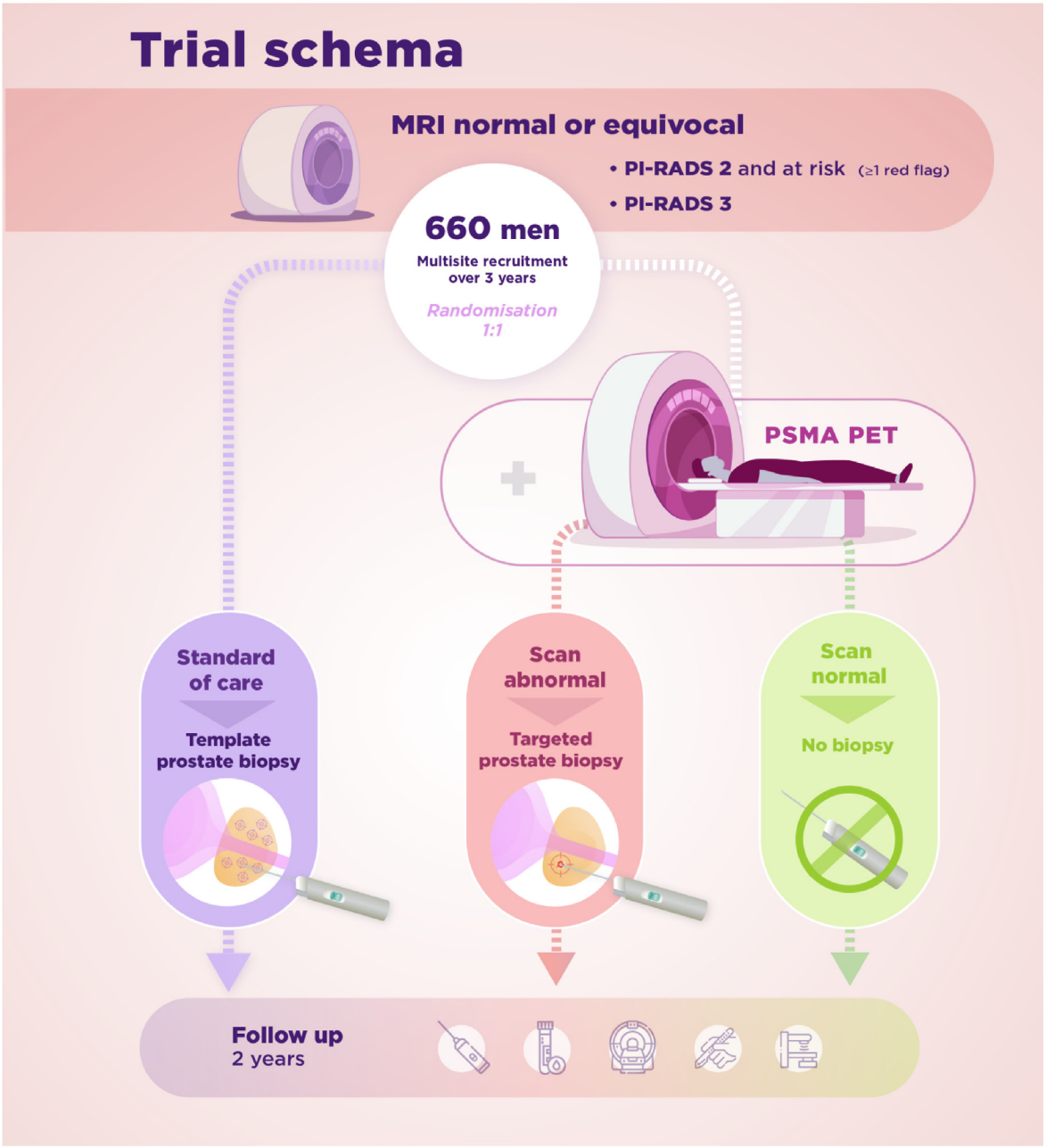

Fig. 2 – Trial schema. The trial will recruit 660 eligible men and randomise them at a 1:1 ratio. Participants in the standard-of-care arm will undergo template transperineal prostate biopsies. Those in the experimental arm will proceed with PSMA PET/CT, which guides the decision on whether to proceed or not with targeted transperineal biopsies. Participants will be followed for up to 2 yr to collect clinical information about subsequent prostate biopsies, prostate-specific antigen results, subsequent PSMA PET/CT and MRI, and curative-intent treatments with radical prostatectomy or radiation therapy. CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography; PI-RADS = Prostate Imaging-Reporting and Data System; PSMA = prostate-specific membrane antigen

2.8. Transperineal prostate biopsy

In the experimental arm, participants with positive PSMA PET/CT findings will undergo targeted transperineal prostate biopsy. A detailed report with PSMA PET/CT images and a simplified prostate diagram identifying the sites to target will be made available to the treating urologist (Fig. 3). Up to four lesions identified on PSMA PET/CT ± mp MRI will be targeted, with a minimum of five cores sampled.

In the control arm, template transperineal prostate biopsy will be performed according to the treating urologist's usual practice. A minimum of 12 cores is required for template sampling of the prostate, depending on the prostate volume. mpMRI will be available for any additional targeted biopsies.

2.9. Statistical considerations

The primary endpoints will be analysed on an intention-to-treat basis according to the arm to which the patient was randomised, regardless of whether the patient received their assigned diagnostic intervention or not. sPCa is

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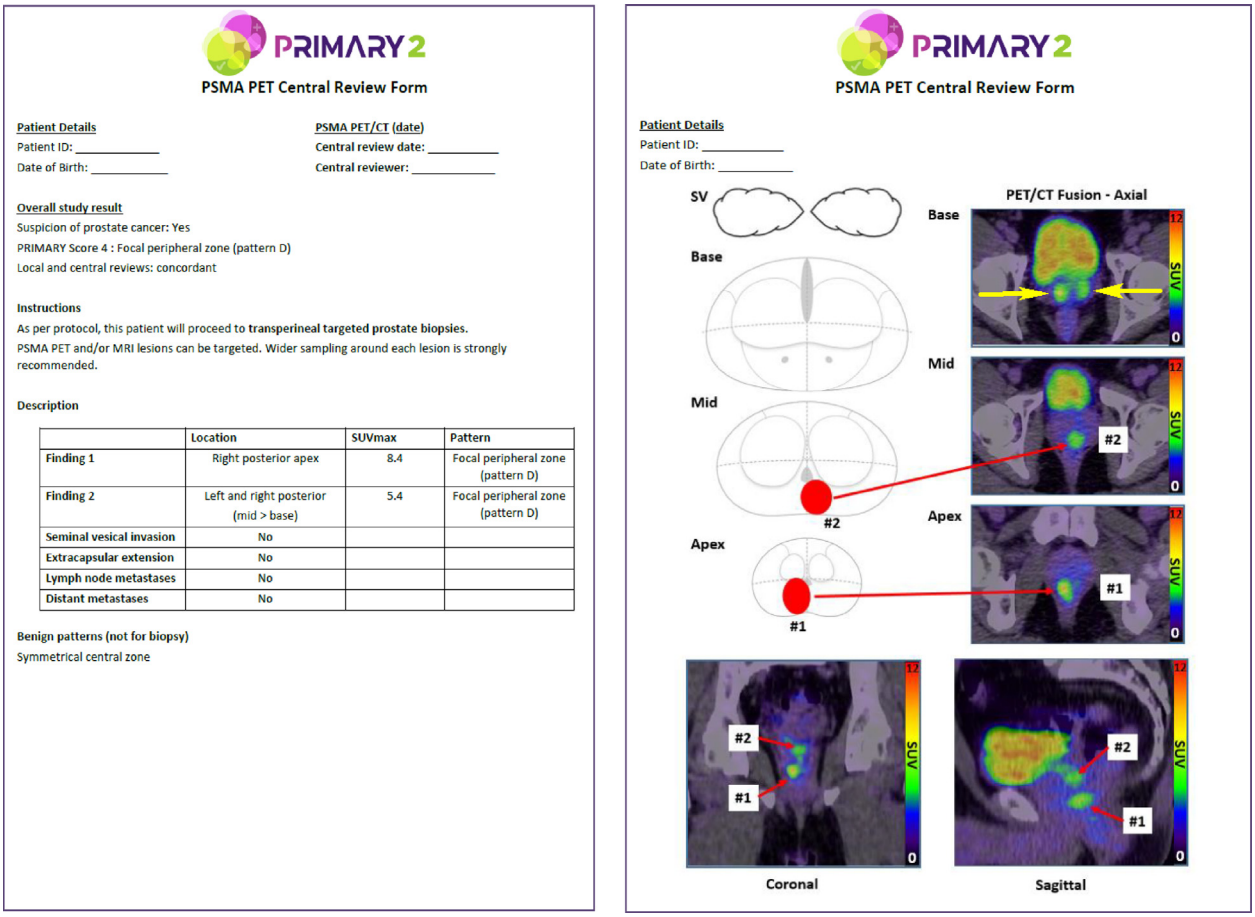
PRIMARY 2

PSMA PET Central Review Form

Patient Details
Patient ID: _____
Date of Birth: _____

PSMA PET/CT (date)
Central review date: _____
Central reviewer: _____

Overall study result
Suspicion of prostate cancer: Yes
PRIMARY Score 4 : Focal peripheral zone (pattern D)
Local and central reviews: concordant

Instructions
As per protocol, this patient will proceed to **transperineal targeted prostate biopsies.**
PSMA PET and/or MRI lesions can be targeted. Wider sampling around each lesion is strongly recommended.

Description

	Location	SUVmax	Pattern
Finding 1	Right posterior apex	8.4	Focal peripheral zone (pattern D)
Finding 2	Left and right posterior (mid > base)	5.4	Focal peripheral zone (pattern D)
Seminal vesical invasion	No		
Extracapsular extension	No		
Lymph node metastases	No		
Distant metastases	No		

Benign patterns (not for biopsy)
Symmetrical central zone

Fig. 3 – Central review report. A central review report summarises the study results for the urologist, as well as instructions on whether to proceed or not to transperineal prostate biopsy. A table describes each PSMA-avid site and other key findings, such as the presence of seminal vesicle invasion. The sites to target for transperineal prostate biopsy are identified on a prostate diagram in red. PSMA PET/CT fusion images are provided in axial (base, mid, apex), coronal, and sagittal views. Normal patterns of PSMA uptake, such as symmetrical central-zone uptake at the base (yellow arrows), are not indications for biopsy. CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography; PSMA = prostate-specific membrane antigen.

defined as Gleason score 3 + 4 (≥10%) = 7 (grade group ≥2) in at least one core on transperineal prostate biopsy, regardless of other histopathological characteristics such as volume, length of core infiltration, or percentage of core involved. Avoidance of transperineal prostate biopsy will be measured at 6 mo after randomisation. The 95% confidence intervals for differences between the arms will be calculated for all endpoints. Statistical tests will be two-sided, with the type 1 error level set at 5%.

The study design involves individual randomisation, stratified by centre, of participants to each arm. Therefore, the centre will be taken into account in the analyses, where appropriate. The degree of clustering by centre will be examined by estimating the intraclass correlation. No adjustment for covariates or multiple comparisons will be made unless otherwise specified. A detailed statistical analysis plan will be formulated before the data are locked.

2.10. Health economics analysis

A cost-effectiveness analysis will be undertaken to assess the cost per quality-adjusted life year gained for PSMA PET/CT in addition to mpMRI in comparison to mpMRI alone for the diagnosis of sPCa. Importantly, this analysis will take into consideration the impact on costs and quality of life (EORTC QLU-C10D) associated with the hypothesised reduction in biopsies arising from the better accuracy of PSMA PET/CT. Costs included in the analysis will focus on those for the diagnosis of sPCa, reflecting resource use in both pathways for scans, transperineal prostate biopsy, and associated medical service utilisation (as recorded via Medicare claims data). Prices for the majority of health care service use will be valued on the basis of publicly available sources. In addition, patient travel time associated with visits, imaging acquisition, and biopsies will be collected. Resource use associated with the complications arising from each study arm will also be included.

2.11. Analysis of patient-reported outcome and experience measures

Standardised questionnaires will be used for analyses of the participants' experience, including anxiety and cancer worry, with PSMA PET/CT in addition to mpMRI in comparison to template transperineal prostate biopsy in the control arm at different time points in the study. Quality of life will be assessed using the EORTC QLQ-C30 questionnaire. Complications from transperineal prostate biopsy will be

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measured with the modified PRECISION questionnaire and the Sexual Health Inventory in Men, a five-item version of the International Index of Erectile Function questionnaire. The modified Cancer Worry Scale is a three-item questionnaire used in the context of cancer worry regarding abnormal PSA levels for men participating in community screening programs. The Generalised Anxiety Disorder (GAD-7) scale [15] is a seven-item questionnaire for screening and measuring the severity of generalised anxiety disorder. The Decision Conflict Scale is designed to measure personal perceptions of uncertainty in choosing options and effective decision-making, while the Decision Regret Scale measures distress or remorse after a health care decision.

3. Discussion

PSMA PET/CT has proven utility in staging [16] and biochemical recurrence [17] settings but is currently not recommended for diagnosis of prostate cancer [18]. The PRIMARY2 trial is designed to demonstrate that addition of PSMA PET/CT can reduce the need for biopsy without compromising detection of sPCa. The selected population of men with high clinical suspicion of sPCa and a PI-RADS score of 2 or 3 on mpMRI represents a clinical challenge. Although mpMRI has high diagnostic accuracy, urologists may have ongoing concern about some patients with negative or equivocal mpMRI findings in the presence of red flags such as high PSA density, strong family history, and *BRCA* mutation. In this selected and triage-enriched cohort, 35% (52/148) had sPCa on biopsy in PRIMARY [12]. Blind reinterpretation of the mpMRI scans from a 100-patient sample in PRIMARY by three experts yielded comparable test performance [19]. In a large public tertiary hospital, 26% (36/138) of patients who proceeded to prostate biopsy regardless of a PI-RADS 2 or 3 result on mpMRI had sPCa [20]. Although PSA density improves the identification of patients with negative MRI requiring biopsy, suggested cutoffs vary (0.10, 0.15, and 0.20 ng/ml^2), with acknowledgment that future studies are required to improve risk prediction [21,22]. The combination of very high sensitivity and NPV for this subset in the PRIMARY trial justifies investigation of PSMA PET/CT to further improve triaging and identify targets for biopsy in this group.

PRIMARY2 will provide a more accurate estimate of the ability of PSMA PET/CT to identify prostate malignancies that require intervention, while reducing overdiagnosis of GG 1 pathology. Expert consensus from the trial steering committee has specified a noninferiority margin of 10%. As there is potential to safely avoid biopsy in a substantial number of participants while potentially identifying sPCa earlier given the very high sensitivity, this appears to be a clinically reasonable margin. Most patients receiving the intervention could benefit from this de-escalation approach. For example, among 10 patients who would otherwise undergo a template biopsy, four patients avoid biopsy and six patients receive a targeted (instead of a template) biopsy. According to the 10% noninferiority margin, the acceptable trade-off to achieve these benefits is one sPCa case is not detected at that moment. Importantly, clinical and PSA follow-up for up to 2 yr in the experimental arm will identify patients with sPCa not initially detected. This approach will provide further information on the proportion of false negatives in the setting of normal PSMA PET/CT, as well as sPCa cases potentially missed by limiting biopsy to a targeted transperineal approach.

The definition of sPCa is contentious: definitions include GG $\geq$2, GG $\geq$3, and additional histopathological features, such as percentage of Gleason pattern 4, percentage of specimens involved, and length [23]. The ISUP 2014 conference separated Gleason score 3 + 4 = 7 and 4 + 3 = 7 into different categories [24]. Multiple studies have demonstrated that the percentage of pattern 4 on biopsy has prognostic significance for biochemical recurrence and adverse pathology on radical prostatectomy [25,26]. However, there can be significant interobserver variability between histopathologists [27]. Minimal Gleason pattern 4 ($\leq$5%) on biopsy has similar pathological parameters to GG 1 on radical prostatectomy histopathology [28] to biochemical recurrence [29]. We therefore defined sPCa as Gleason score 3 + 4 ($\geq$10%) = 7 (GG $\geq$2), in alignment with consensus-based recommendations regarding consideration of active surveillance for selected participants with low-volume, intermediate-risk (Gleason score 3 + 4 = 7; GG 2) localised prostate cancer [30–33].

If the PSMA PET/CT intervention is found to be noninferior, the diagnostic pathway for diagnosis of sPCa will be enhanced by avoiding unnecessary prostate biopsies. Furthermore, PSMA PET/CT guidance for transperineal prostate biopsy could both improve targeting, by identifying sites suspicious for sPCa, and reduce overdiagnosis of GG 1 disease that may be identified on template transperineal prostate biopsy. These approaches could reduce patient anxiety and worry about having prostate cancer, and decrease biopsy complications via better triaging and targeted biopsies. Better use of health care resources may be more cost effective, a key consideration for access to this service in a publicly funded system. If the trial is negative, we will provide high-quality evidence about appropriate use of PSMA PET/CT in this clinical setting.

4. Conclusions

PRIMARY2 (NCT05154162) is a phase 3 trial activated in March 2022. Recruitment is expected to take 36 mo.

The protocol for this study was presented as a poster at the American Society of Clinical Oncology Genitourinary Cancers Symposium, San Francisco, February 16–18, 2023.

Author contributions: James P. Buteau had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Emmett, Hofman, Buteau, Moon, Fahey, Roberts, Thompson, Murphy, Papa, Mitchell, De Abreu Lourenco, Dhillon, Kasivisvanathan, Stricker, Francis.

Acquisition of data: All authors.

Analysis and interpretation of data: Fahey, Emmett, Hofman, Buteau, Moon.

Drafting of the manuscript: Buteau, Emmett, Hofman, Moon, Fahey, Roberts, Murphy.

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