# PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

## ARTICLE DETAILS

### Title (Provisional)

European Registry of Next Generation Imaging in Advanced Prostate Cancer (RING): protocol for an international, prospective registry study

### Authors

Chernysheva, Daria; Fanti, Stefano; Bjartell, Anders; Afferi, Luca; Breda, Alberto; Palou, Joan; Padhani, Anwar R.; Sanguedolce, Francesco

## VERSION 1 - REVIEW

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| **Reviewer** | **1** |
| **Name** | **Urso, Luca** |
| **Affiliation** | **Santa Maria della Misericordia University Hospital** |
| **Date** | **05-Sep-2025** |
| **COI** | **None** |

Chernysheva and colleagues propose the protocol named "The European Registry of Next-Generation Imaging in Advanced Prostate Cancer (RING)", which is a no profit, non interventional, multicentre, international, prospective registry aiming to collect real life data on how different imaging techniques are used in advanced prostate cancer patients. The registry has a good potential to explore real world use and relevance of PSMA PET in prostate cancer patients, which is an unmet need since literature still lacks of data regarding the impact of this imaging on patients' story of disease.

The protocol is well described, well designed and has a high clinical relevance. It is some way related to the PROMISE registry, which aims to collect real world data of PSMA PET with different aims.

The only comment I can recommend to consider is relative to the sample size. The authors arbitrarily chose 600 patients as a satisfying sample to analyze. However, I recommend to to estimate the sample size based on power analysis. This could guarantee that the authors' efforts do not fail to provide the expected results.

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| **Reviewer** | **2** |
| **Name** | **Pepe, Pietro** |
| **Affiliation** | **Cannizzaro Hospital, Urology** |
| **Date** | **07-Sep-2025** |
| **COI** | **None** |

The multicentric study is very interesting but some points regarding literature data about the emergent role of PSMA PET/TC in diagnosing and staging PCa could be added

1. The Authors should report the advantage of PSMA PET/TC as a single procedure for the diagnosis and staging of high-risk PCa (Pepe P, Pennisi M. Targeted Biopsy in Men High Risk for Prostate Cancer: 68Ga-PSMA PET/CT Versus mpMRI. Clin Genitourin Cancer. 2023 Dec;21(6):639-642. doi: 10.1016/j.clgc.2023.06.007. Epub 2023 Jun 19. PMID: 37394379)

2. The Authors should report the advantages of PSMA PET/TC in the reevaluation of men enrolled in Active Surveillance protocols especially in men who can not perform mpMRI (i.e., claustrophobia, cardiac pacemaker) (Pepe P, Roscigno M, Pepe L, Panella P, Tamburo M, Marletta G, Savoca F, Candiano G, Cosentino S, Ippolito M, Tsirgiotis A, Pennisi M. Could 68Ga-PSMA PET/CT Evaluation Reduce the Number of Scheduled Prostate Biopsies in Men Enrolled in Active Surveillance Protocols? J Clin Med. 2022 Jun 16;11(12):3473. doi: 10.3390/jcm11123473. PMID: 35743547; PMCID: PMC9225630)

3. The Authors should report also discuss the low accuracy of PSMA PET/CT in diagnosing and staging ductal carcinoma

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| **Reviewer** | **3** |
| **Name** | **Chang, Yifan** |
| **Affiliation** | **Shanghai Changhai Hospital, Department of Urology** |
| **Date** | **20-Sep-2025** |
| **COI** | **None** |

This is a well-designed protocol for an observational study that takes advantage of PSMA-PET/CT to investigate the survival benefit and need for treatment adjustment for prostate cancer patients, with a clear study objective.

## VERSION 1 - AUTHOR RESPONSE

Reviewer: 1
Dr. Luca Urso, Santa Maria della Misericordia University Hospital
Comments to the Author:
Chernysheva and colleagues propose the protocol named "The European Registry of Next-Generation Imaging in Advanced Prostate Cancer (RING)", which is a no profit, non interventional, multicentre, international, prospective registry aiming to collect real life data on how different imaging techniques are used in advanced prostate cancer patients. The registry has a good potential to explore real world use and relevance of PSMA PET in prostate cancer patients, which is an unmet need since literature still lacks of data regarding the impact of this imaging on patients' story of disease.

The protocol is well described, well designed and has a high clinical relevance. It is some way related to the PROMISE registry, which aims to collect real world data of PSMA PET with different aims.

- The only comment I can recommend to consider is relative to the sample size. The authors arbitrarily chose 600 patients as a satisfying sample to analyze. However, I recommend to to estimate the sample size based on power analysis. This could guarantee that the authors' efforts do not fail to provide the expected results.

We thank Dr. Luca Urso for pointing out the importance of power analysis for confirmatory studies. However, our study is designed as a prospective observational registry. In such study designs, the primary objective is the collection of real-world evidence, and the sample size is not calculated based on a single primary hypothesis test. Instead, it is set to ensure a comprehensive representation of the patient population and to allow for meaningful descriptive and exploratory analyses. The target of 600 patients was set to be feasible and to provide a substantial dataset that aligns with the primary descriptive objective.

We are confident that this approach is methodologically sound for a registry study and will yield valuable clinical insights.

Reviewer: 2
Dr. Pietro Pepe, Cannizzaro Hosp
Comments to the Author:
The multicentric study is very interesting but some points regarding literature data about the emergent role of PSMA PET/TC in diagnosing and staging PCa could be added

1. The Authors should report the advantage of PSMA PET/TC as a single procedure for the diagnosis and staging of high-risk PCa (Pepe P, Pennisi M. Targeted Biopsy in Men High Risk for Prostate Cancer: 68Ga-PSMA PET/CT Versus mpMRI. Clin Genitourin Cancer. 2023 Dec;21(6):639-642. doi: 10.1016/j.clgc.2023.06.007. Epub 2023 Jun 19. PMID: 37394379)

2. The Authors should report the advantages of PSMA PET/TC in the reevaluation of men enrolled in Active Surveillance protocols especially in men who can not perform mpMRI (i.e., claustrophobia, cardiac pacemaker) (Pepe P, Roscigno M, Pepe L, Panella P, Tamburo M, Marletta G, Savoca F, Candiano G, Cosentino S, Ippolito M, Tsirgiotis A, Pennisi M. Could 68Ga-PSMA PET/CT Evaluation Reduce the Number of Scheduled Prostate Biopsies in Men Enrolled in Active Surveillance Protocols? J Clin Med. 2022 Jun 16;11(12):3473. doi: 10.3390/jcm11123473. PMID: 35743547; PMCID: PMC9225630)

We thank Dr. Pietro Pepe for suggesting additional literature data, that is for sure very valuable and of great interest; however, to maintain focus on imaging role for metastatic work-up we prefer not to include the aforementioned references in the introduction part.

3. The Authors should report also discuss the low accuracy of PSMA PET/CT in diagnosing and staging ductal carcinoma

Reviewer: 3
Mr. Yifan Chang, Shanghai Changhai Hospital
Comments to the Author:
This is a well-designed protocol for an observational study that takes advantage of PSMA-PET/CT to investigate

the survival benefit and need for treatment adjustment for prostate cancer patients, with a clear study objective.