Comparison of the treatment outcomes: percent change in the sum of longest diameters (RECIST) and percent change of the lesion with the highest SUL (PERCIST) between standard therapy plus Lu-177 PSMA ligand therapy and standard therapy alone among patients with prostatic cancer status-post castration using Ga-18 PET-CT as an outcome indicator

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ABSTRACT

Introduction:

Prostate cancer is the third most common cancer among Filipino males. Ga-68 PSMA PET-CT and Lu-177 PRLT have been introduced in the Philippines for the diagnostics and therapy of prostate cancer.

Objective:

The aim of this study is to compare treatment outcomes of standard therapy plus Lu-177 PSMA radioligand therapy and standard therapy alone among patients with prostatic cancer status-post castration using Ga-68 PET-CT as an outcome indicator.

Methodology:

This is an ambispective cohort study on Ga-68 PSMA PET-CT scans performed between January 1, 2018 and July 31, 2021. Serum PSA data taken within one month of the PET-CT scans were also collected when available. The PET-CT images were reviewed by a radiologist for RECIST response, and by a nuclear medicine physician for PERCIST response .

Results:

A total of 11 participants were included in the study. Six participants (55.5%) received standard therapy, while five participants (45.5%) received Lu-177 PSMA radioligand therapy plus standard therapy. There was no significant difference in the baseline and follow-up CT as shown by all p values > 0.05. A trend towards higher number of participants with non-complete/non-progressive RECIST response was noted in the control group than the treatment group, as well as higher number of participants with progressive or stable disease using the PERCIST response.

Conclusion:

There were no significant differences noted in the clinical outcomes of participants who received Lu-177 PRLT and those with standard therapy alone. A trend towards decreasing serum PSA, CT and PET measurements were noted among patients given Lu-177 PRLT than those with standard therapy.

Keywords*: Lu-177 PSMA, Ga-68 PSMA, prostate cancer*

INTRODUCTION

Prostate cancer is the third most common cancer among Filipino males when non-melanoma skin cancer is excluded [1]. Prostate cancer in Filipinos occurs mainly in the elderly with the average age of 64 years old at the time of diagnosis. It typically presents with more adverse pathological features if compared to prostate cancer seen in American populations [2].

Various prognostic factors must be considered in the management of prostate cancer. Radical prostatectomy and radiotherapy are typically used for definitive treatment with curative intent. However, castration – achieved either through surgery (bilateral orchiectomy) or hormonal therapy – is also considered as part of the standard treatment options offered for Stage II to IV disease [3]. On the other hand, progressive disease with poor castration response is conventionally managed using a variety of treatment modalities such as systemic chemotherapy, immunotherapy and palliative radiotherapy, among others [4].

Prostate cancer follow-up involves biochemical recurrence monitoring through serum prostate-specific antigen (PSA) levels, and radiologic recurrence monitoring using imaging modalities such as multiparametric MRI [5]. In recent years, given the conventional imaging limitations, there has been an emerging role for Gallium-68 (Ga-68) prostate-specific membrane antigen (PSMA) positron emission tomography-computed tomography (PET-CT) for disease monitoring, particularly to check for metastasis, and treatment response evaluation [6]. Imaging entails using a small biomolecule that binds to the transmembrane protein PSMA – which is overexpressed in prostate cancer tissues [7].

Likewise, Ga-68 PSMA PET-CT may be used to determine novel therapy eligibility using beta-emitting radionuclides such as Lutetium-177 (Lu-177). The Lu-177 PSMA radioligand therapy (PRLT) delivers targeted radiation to PSMA-overexpressed prostate cancer lesions [8]. A large, German multicenter study involving advanced prostate cancer patients who received Lu-177 PRLT showed that 45% of patients demonstrated a biochemical decline of at least 50% in their PSA, while a PSA decline of any amount was observed in 60% of patients [9]. The same study showed significant hematologic toxicity in approximately 12% of participants, thus, due caution must be exercised between cycles especially when considering dose escalation [10]. Similar efficacy of PRLT was noted in a smaller Iranian prospective study with no incidence of hematologic toxicity observed [11]. More recently, the international, open-label, phase 3 VISION trial [12] demonstrated that the addition of Lu-177 PRLT to standard therapy not only yielded significant biochemical response identical to the aforementioned studies, but also significantly prolonged imaging-based progression-free survival and overall survival in advanced metastatic castration-resistant prostate cancer patients. The VISION trial relied on Ga-68 PSMA PET-CT scans for the initial participant assessment and Lu-177 PRLT eligibility determination. However, follow-up imaging was mainly done through CT, MRI, and bone scintigraphy. Radiologic response was measured using Response Evaluation Criteria in Solid Tumors (RECIST) relying mainly on morphologic changes between scans [13]. Over the years, other systems for evaluating response have also been established, including the PET Response Criteria in Solid Tumors (PERCIST) [14] which depends molecular activity changes. PERCIST has been found to perform better than morphologic criteria for Ga-68 PSMA PET-CT response evaluation [15].

In recent years, Ga-68 PSMA PET-CT and Lu-177 PRLT have been introduced in the Philippines for the diagnostics and therapy of prostate cancer, respectively [16]. To date, there are no published studies that demonstrate the outcomes of PRLT in local settings.

Significance and Rationale of the Study

Prostate cancer is one of the more common cancers affecting elderly Filipino males. There are limited therapeutic options for those who have undergone castration but still demonstrate progressive disease. Lu-177 PRLT is emerging as a promising treatment for patients who have poor response to standard therapy. The findings of this study will provide local treatment outcomes for Lu-177 PRLT in the Philippines and may aid clinicians in the overall management of prostate cancer.

OBJECTIVES

General Objective

To compare treatment outcomes of standard therapy plus Lu-177 PSMA radioligand therapy and standard therapy alone among patients with prostatic cancer status-post castration using Ga-68 PET-CT as an outcome indicator.

Specific Objectives

- To compare the clinical profile of patients with prostatic cancer status-post castration who had

standard therapy plus Lu-177 PRLT versus those who underwent standard treatment alone

- To compare the levels of PSA (baseline and follow up) among patients with standard therapy plus Lu-177 PRLT versus those who underwent standard treatment alone
- To compare the CT and PET measurements (baseline and follow up) among patients with standard therapy plus Lu-177 PRLT versus those who underwent standard treatment alone
- To determine frequency of RECIST responses based on CT and frequency of PERCIST responses based on PET among patients with standard therapy plus Lu-177 PSMA radioligand therapy versus those who underwent standard treatment alone

METHODOLOGY

Type of Study, Time and Period, Setting and Study Population

This is an ambispective cohort study on the treatment outcomes of standard therapy plus Lu-177 PSMA radioligand therapy and standard therapy alone among patients with prostate cancer status post castration who underwent Ga-68 PET-CT between January 1, 2018 and July 31, 2021 at St. Luke's Medical Center-Quezon City.

Inclusion Criteria

- Patient was previously diagnosed with prostatic cancer.
- Patient must have baseline and follow-up PET-CT scan at SLMC-QC.
- Patient must have follow-up PET-CT scan within 6 months to 1 year post treatment.

Exclusion Criteria

Patient did not undergo chemical or surgical castration

Study Maneuver

All PET CT scans of patients with prostate cancer with castration history between January 1, 2018 and July 31, 2021 were reviewed for study inclusion. All baseline and follow-up PET-CT scans of eligible patients were anonymized for both the nuclear medicine physician and radiologist. They were also blinded to the treatment given to the patient.

Ga-68 PSMA PET-CT Scan Protocol

Initial emission imaging of the pelvis was done 50 minutes after intravenous injection of Ga-68 PSMA, followed by subsequent whole-body emission images using a PET-CT scanner 60 minutes after Ga-68 PSMA administration. Furosemide 20 mg was given intravenously shortly after tracer injection. CT contrast was also given when applicable.

Evaluation of Imaging and Biochemical Response

Imaging Evaluation

All baseline and follow up PET-CT studies were anonymized and were reviewed independently by the radiologist and nuclear medicine physician. Any discrepancy in the findings were resolved by consensus agreement of the readers. The radiologist evaluated the CT images using RECIST (see Appendix A) while the nuclear medicine physician evaluated the PET images using PERCIST (see Appendix B).

Biochemical Evaluation

Serum PSA done within a month from the time of the scan

Data Collection

The following data of eligible participants were collected through Healthcare, Carestream and Medical Records:

1. Age
2. Date of surgery or biopsy
3. Date of starting treatment and type of treatment
4. Baseline and follow-up PSA
5. Baseline and follow-up PET-CT

Outcome Measures

A. Dependent variables:

a) Based on RECIST:
- i) Percent change in sum of longest diameters
- ii) Presence of new lesions
- iii) Frequency and proportion of:
  1. Complete Response
  2. Partial Response
  3. Stable Disease
  4. Progressive Disease

b) Based on PERCIST:
- i) Percent change in highest SUL
- ii) Presence of new PSMA-avid lesions
- iii) Frequency and proportion of:
  1. Complete Response
  2. Partial Response
  3. Stable Disease
  4. Progressive Disease

B. **Independent variables:**
   a) Age
   b) Time to starting treatment
   c) Type of treatment
   d) PSA level

Statistical Analysis

Descriptive statistics were used to summarize the demographic characteristics as well as clinical outcomes of the patients. Frequency and proportion were used for nominal variables, as well as mean and SD for interval/ ratio variables. Non-parametric tests such as Mann Whitney U test, Wilcoxon Signed rank test and Chi-square test were used to analyze data. SPSS version 23 for Windows was used in the data analysis. The missing values will neither be replaced nor estimated. Null hypotheses will be rejected at 0.05α-level of significance .

RESULTS

A total of 11 participants were deemed as eligible participants in the study. Six participants (55.5%) were classified into the control arm, having received standard therapy, while five participants (45.5%) were classified into the interventional arm consisting of Lu-177 PSMA radioligand therapy plus standard therapy.

The mean age of participants in the control arm was 70.67 years, while the mean age in the interventional arm was 63.40 years. There was no significant difference in the age as shown by all p values > 0.05 (see Table 1.). From initial tissue diagnosis of prostate carcinoma, the time to starting therapy in those who received standard therapy was 7.7 years, while the time to starting therapy in those who received Lu-177 PSMA radioligand therapy on top of standard therapy was 5.0 years. There appears to be greater range for participants in the control arm compared to those in the interventional arm.

Not all eligible participants had documented records of serum PSA at the time of the initial and follow-up PET-CT scans. In the control arm, only three out of six (50%) participants have their initial serum PSA on record with a mean cut-off of 3.80 ng/mL, and only 2 (33%) have follow-up serum PSA with a mean cut-off of 32.26 ng/mL. On the other hand, in the interventional arm, five out of the five (100%) participants have their initial serum PSA with a mean cut-off of 451.52 ng/mL, but only 4 (80%) participants have their follow-up serum PSA, yielding 137.20 ng/mL. It must be noted, however, that there is a substantial collected data range in both groups, particularly in the interventional arm. In terms of serum PSA change, there appears to be a greater average serum PSA percentage increase among the proportion of patients in the control arm (459.22%) compared to the interventional arm (10.16%).

Table 2 shows the comparison of baseline and follow-up serum PSA between the two groups. There was no significant difference in the baseline and follow-up serum PSA as shown by all p values > 0.05. Similarly, in each group, there were no significant differences in the serum PSA measurements (p > 0.05). However, a trend towards decreasing PSA was noted in the Lu-177 PRLT than the standard therapy group.

Table 3 shows the comparison of baseline and follow-up CT between the two groups. There was no significant difference in the baseline and follow-up CT as shown by all p values > 0.05. Similarly, in each group, there were no significant differences in the CT measurements (p > 0.05). However, a trend towards decreasing CT measurement was noted in the Lu-177 PRLT than the standard therapy group.

Table 4 shows the comparison of baseline and follow-up PET between the two groups. There was no significant difference in the baseline and follow-up CT as shown by all p values > 0.05. Similarly, in each group, there were no

TABLE 1. Comparison of the demographic profile of patients between the standard therapy group and Lu-177 + standard therapy group

	Standard Therapy (n=6)	**Lu-177 PSMA + Standard Therapy** (n=5)	**p-value**
	Mean ± SD; Frequency (%)		
Age (in years)	70.67 ± 11.57	63.40 ± 4.04	0.20 (NS) †

** p>0.05- Not significant; p ≤0.05-Significant*
† Mann Whitney U -test

TABLE 2. Comparison of the baseline and follow-up serum PSA between standard therapy group and Lu-177 + standard therapy group

	Standard Therapy (n = 3)	**Lu-177 PRLT Group** (n = 5)	**p-value**
	Mean ± SD		
Baseline serum PSA (ng/mL)	3.80 ± 3.37	451.52 ± 716.92	0.24 (NS) †
Follow-up serum PSA (ng/mL)	32.26 ± 36.97	137.20 ± 186.84	0.35 (NS) †
p-value	0.22 (NS) §	0.28 (NS) §	---

** p>0.05- Not significant; p ≤0.05-Significant*
† Mann Whitney U -test; §Wilcoxon Signed test

TABLE 3. Comparison of the baseline and follow-up CT measurement (percent change in sum of longest diameters) using RECIST criteria between standard therapy group and Lu-177 + standard therapy group

	Standard Therapy (n = 6)	**Lu-177 PRLT Group** (n = 5)	**p-value**
	Mean ± SD		
Baseline CT Measurement	2.42 ± 2.26	8.95 ± 12.14	0.36 (NS) †
Follow-up CT Measurement	3.58 ± 4.21	5.52 ± 6.12	0.60 (NS) †
p-value	0.22 (NS) §	0.28 (NS) §	---

** p>0.05- Not significant; p ≤0.05-Significant*
† Mann Whitney U -test; §Wilcoxon Signed test

significant differences in the CT measurements (p > 0.05). However, a trend towards decreasing PET measurement was noted in the Lu-177 PRLT than the standard therapy group.

Table 5 and 6 shows the comparison of RECIST and PERCIST response between the two groups. There were no significant differences noted as shown by all p values > 0.05. However, it can be seen that a trend towards higher number of patients with non-complete/non-progressive RECIST response was noted in the control group than the treatment group, as well as higher number of patients with progressive or stable disease using the PERCIST response.

Using the RECIST response on the Ga-68 PSMA PET-CT scans, participants in the control arm on average showed a 10% increase in the sum of longest diameters of the measurable target lesions. For the frequency of overall RECIST response among participants in the control arm, the following were noted: 1 PD, 1 SD, 1 PR, 2 non-CR / non-PD, and 1 unevaluable. On the other hand, in the interventional arm, there is a mean increase of 59% in the sum of longest diameters of the measurable target lesions. Overall RECIST response in the interventional arm were as follows: 3 PD, 1 PR, and 1 unevaluable.

Meanwhile, using PERCIST on the Ga-68 PSMA PET-CT scans, participants in the control arm showed a mean change of 36% in the highest SUL. For the overall PERCIST response in the control arm, there was 4 PD and 2 SD. On the other hand, in the interventional arm, there is a mean change of -30% in the highest SUL with overall PERCIST response in the interventional showing 3 PD and 2 PR.

DISCUSSION

From the 11 eligible participants, it was observed that the study mainly involves older males above 60 years old. This is consistent with the demographics that are typically diagnosed with prostate cancer [2]. Moreover, the data showed that the time to starting therapy from

TABLE 4. Comparison of the baseline and follow-up PET measurement (percent change of the lesion with the highest SUL) using the PERCIST criteria between the standard therapy group and Lu-177 + standard therapy group.

	Standard Therapy (n = 6)	**Lu-177 PRLT Group** (n = 5)	**p-value**
	Mean ± SD		
Baseline PET Measurement	16.48 ± 10.41	16.04 ± 6.43	0.93 (NS) †
Follow-up PET Measurement	24.50 ± 16.30	14.84 ± 5.51	0.20 (NS) †
p-value	0.22 (NS) §	0.68 (NS) §	---

** p>0.05- Not significant; p ≤0.05-Significant*
† Mann Whitney U -test; §Wilcoxon Signed test

TABLE 5. RECIST response based on Ga-68 PSMA PET-CT

	Standard Therapy	**Lu-177 PSMA + Standard Therapy**	**p-value**
Overall RECIST Response			
Progressive Disease (PD)	1 (16.7%)	3 (60.0%)	0.41 (NS) ‡
Stable Disease (SD)	1 (16.7%)	0	
Partial Response (PR)	1 (16.7%)	1 (20.0%)	
Complete Response (CR)	0		
Non-CR / Non-PD	2 (33.3%)	0	
Unevaluable	1 (16.7%)	1 (20.0%)	

** p>0.05- Not significant (NS); p ≤0.05-Significant (S)*
‡ Chi-square test

TABLE 6. PERCIST response based on Ga-68 PSMA PET-CT

	Standard Therapy	**Lu-177 PSMA + Standard Therapy**	**p-value**
Overall PERCIST Response			
Progressive Disease (PD)	4 (66.7%)	3 (60.0%)	0.13 (NS) ‡
Stable Disease (SD)	2 (33.3%)	0	
Partial Response (PR)	0	2 (40.0%)	
Complete Response (CR)	0	0	

** p>0.05- Not significant (NS); p ≤0.05-Significant (S)*
‡ Chi-square test

the initial tissue diagnosis took more than 5 years. This may be reflective of the more conservative approach of watchful observation during the early stages of prostate cancer, and the more aggressive treatment modalities only being pursued later in the course of the disease [3].

Serum PSA plays a crucial role in the monitoring and response assessment for prostate cancer. The nature of the present study limited the collection of biochemical data from available records. It must also be noted that both baseline and follow-up serum PSA were obtained in close temporal relation to the Ga-68 PSMA PET-CT scans rather than to each arm's therapies. Data from clinical trials [9,11,12] reported that substantial serum PSA reduction was seen in Lu-177 PSMA radioligand therapy-treated prostate cancer patients. In particular, the recently concluded VISION trial showed greater serum PSA reduction when Lu-177 PSMA radioligand therapy was added to standard therapy [12]. Such dramatic reductions in serum PSA were not observed in the present study likely due to the gathered data's limitations. Also, the present study showed that the

proportion of participants in the interventional arm appear to have higher mean serum PSA cut-off compared to those in the control arm. This is consistent with the notion that Lu-177 PSMA radioligand therapy is typically used for more advanced prostate cancer. Although serum PSA increased in both arms of the study, the control arm appeared to have greater mean percentage increase on follow-up compared to the interventional arm. This may suggest that the addition of Lu-177 PSMA radioligand therapy to standard therapy stalls biochemical progression better than standard therapy alone. However, no statistical difference can be inferred from the present data.

Apart from biochemical markers, imaging plays a major role in response assessment for prostate cancer. Radiologic response assessment in the VISION trial [12] used RECIST in objective radiologic response determination, primarily through follow-up CT, MRI and radionuclide bone scans. In contrast, the present study evaluated the role of Ga-68 PSMA PET-CT in determining treatment response. Given the trove of information being provided by hybrid imaging, using both RECIST and PERCIST allowed for post-treatment evaluation of both morphologic and molecular response. It must be noted that using both criteria, progressive disease was the most common response seen in the participants of both arms of the study. Based on the RECIST, more cases of progressive disease were detected in the interventional arm. This may be interpreted as either reflective of poor treatment response after Lu-177 PSMA radioligand therapy, or simply secondary to overall more aggressive disease among participants who received Lu-177 PSMA radioligand therapy. It must be emphasized, however, that the inherent limitations of RECIST – particularly concerning osseous lesions – may affect overall response assessment in some participants. A closer look at individual data revealed that most of the cases in the control arm involved non-measurable RECIST lesions. In contrast, when PERCIST was utilized, there were more participants with progressive disease in the control arm than in the interventional arm. Apparent concordance in PERCIST and biochemical response can be observed in the two study groups with more aggressive progression seen in those who received standard therapy alone. Although RECIST has long been established in response assessment, Gupta and colleagues [15] reported the superiority of PERCIST in treatment response assessment for Ga-68 PSMA PET-CT. Albeit there were no significant difference in both treatment arms using both RECIST and PERCIST, the concomitant use of both criteria in response evaluation may nevertheless help clinicians evaluate treatment response in prostate cancer patients whenever hybrid imaging in the form Ga-68 PSMA PET-CT is available.

The first limitation of this study was small sample size within the study period of 43 months. Second, the PSA levels of three participants on the standard treatment was done in another institution. Third, the study setting was done in a private tertiary hospital with high cost of PRLT and PET/CT study.

We recommend collaborative local study with larger populations to compare for the biochemical and radiologic outcomes between standard therapy and standard therapy plus Lu-177 PRLT among castrate-resistant prostate cancer. Both RECIST and PERCIST should be utilized when evaluating radiologic response in Ga-68 PSMA PET-CT, and serum PSA should likewise be monitored for biochemical response assessment.

CONCLUSION

There were no significant differences noted in the demographic characteristics as well as the clinical outcomes of patients who received Lu-177 PRLT and those with standard therapy alone. However, using PERCIST for the evaluation of Ga-68 PET-CT, there was a greater proportion of participants with progressive disease in those who received standard therapy alone compared to those who received Lu-177 PRLT with standard therapy. The inverse was true when using RECIST with more patients demonstrating progressive disease after the addition of Lu-177 PRLT to standard therapy. In line with the PERCIST findings, greater serum PSA progression was observed in the proportion of patients who were only given standard therapy. Also, a trend towards decreasing serum PSA, CT and PET measurements were noted among patients given Lu-177 PRLT than those with standard therapy.

Disclosure

The authors have no conflicts of interest to declare.

REFERENCES

1. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Global Cancer Observatory: Cancer Today [Internet]. International Agency for Research on Cancer. [cited 2021 Jul 4]. Available from: https://gco.iarc.fr/today.
2. Grageda M, Choy B, Paner G, So J. Prostate cancer: a presentation of clinicopathologic prognosticators among Filipino and American men at radical prostatectomy. Asian J Androl [Internet]. 2021 [cited 2021 Jul 5];0

https://pubmed.ncbi.nlm.nih.gov/33753582/

3. PDQ Adult Treatment Editorial Board. Prostate Cancer Treatment (PDQ®): Health Professional Version. PDQ Cancer Inf Summ [Internet]. 2017 Feb 12 [cited 2021 Jul 5];1–115. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26389471.
4. Akaza H, Procopio G, Pripatnanont C, Facchini G, Fava S, Wheatley D, et al. Metastatic Castration-Resistant Prostate Cancer Previously Treated With Docetaxel-Based Chemotherapy: Treatment Patterns From the PROXIMA Prospective Registry. J Glob Oncol [Internet]. 2018 Mar 1 [cited 2021 Aug 1];4(4). Available from: /pmc/articles/PMC6223517/
5. Sarkar S, Das S. A Review of Imaging Methods for Prostate Cancer Detection. Biomed Eng Comput Biol [Internet]. 2016 Jan [cited 2021 Jul 20];7(Suppl 1):1. Available from: /pmc/articles/PMC4777886/
6. Fendler WP, Eiber M, Beheshti M, Bomanji J, Ceci F, Cho S, et al. 68Ga-PSMA PET/CT: Joint EANM and SNMMI procedure guideline for prostate cancer imaging: version 1.0. Eur J Nucl Med Mol Imaging. doi: 10.1007/s00259-017-3670-z; PMID: 28283702.
7. Bois F, Noirot C, Dietemann S, Mainta IC, Zilli T, Garibotto V, et al. [68Ga]Ga-PSMA-11 in prostate cancer: a comprehensive review. Am J Nucl Med Mol Imaging [Internet]. 2020 [cited 2021 Jul 21];10(6):349. Available from: /pmc/articles/PMC7724278/
8. Kratochwil C, Fendler WP, Eiber M, Baum R, Bozkurt MF, Czernin J, et al. EANM procedure guidelines for radionuclide therapy with 177Lu-labelled PSMA-ligands (177Lu-PSMA-RLT). Eur J Nucl Med Mol Imaging 2019 4612 [Internet]. 2019 Aug 22 [cited 2022 Jun 11];46(12):2536–44. Available from: https://link.springer.com/article/10.1007/s00259-019-04485-3.
9. Rahbar K, Ahmadzadehfar H, Kratochwil C, Haberkorn U, Schäfers M, Essler M, et al. German Multicenter Study Investigating 177Lu-PSMA-617 Radioligand Therapy in Advanced Prostate Cancer Patients. J Nucl Med [Internet]. 2017 Jan 1 [cited 2021 Jul 21];58(1):85–90. Available from: https://jnm.snmjournals.org/content/58/1/85.
10. Kratochwil C, Giesel FL, Stefanova M, Benešová M, Bronzel M, Afshar-Oromieh A, et al. PSMA-Targeted Radionuclide Therapy of Metastatic Castration-Resistant Prostate Cancer with 177Lu-Labeled PSMA-617. J Nucl Med [Internet]. 2016 Aug 1 [cited 2021 Aug 1];57(8):1170–6. Available from: https://jnm.snmjournals.org/content/57/8/1170.
11. Aghdam RA, Amoui M, Ghodsirad M, Khoshbakht S, Mofid B, Kaghazchi F, et al. Efficacy and safety of 177 Lutetium-prostate-specific membrane antigen therapy in metastatic castration-resistant prostate cancer patients: First experience in West Asia - A prospective study. World J Nucl Med [Internet]. 2019 Jul [cited 2022 Jun 12];18(3):258–65. Available from: https://pubmed.ncbi.nlm.nih.gov/31516369/
12. Sartor O, de Bono J, Chi KN, Fizazi K, Herrmann K, Rahbar K, et al. Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med [Internet]. 2021 Sep 16 [cited 2022 Jun 11];385(12):1091–103. Available from: https://www.nejm.org/doi/full/10.1056/nejmoa2107322
13. Schwartz LH, Litière S, De Vries E, Ford R, Gwyther S, Mandrekar S, et al. RECIST 1.1 – Update and Clarification: From the RECIST Committee. Eur J Cancer [Internet]. 2016 Jul 1 [cited 2022 Jun 12];62:132. Available from: /pmc/articles/PMC5737828/
14. O JH, Lodge MA, Wahl RL. Practical PERCIST: A Simplified Guide to PET Response Criteria in Solid Tumors 1.0. Radiology [Internet]. 2016 Aug 1 [cited 2022 Jun 12];280(2):576. Available from: /pmc/articles/PMC4976461/
15. Gupta M, Choudhury PS, Rawal S, Goel HC, Rao SA. Evaluation of RECIST, PERCIST, EORTC, and MDA Criteria for Assessing Treatment Response with Ga68-PSMA PET-CT in Metastatic Prostate Cancer Patient with Biochemical Progression: a Comparative Study. Nucl Med Mol Imaging (2010) [Internet]. 2018 Dec 1 [cited 2022 Jun 12];52(6):420. Available from: /pmc/articles/PMC6261863/
16. Bautista PA. The Emergence of Theranostics in the Philippines: Overcoming Challenges and Bringing Hope. Nucl Med Mol Imaging (2010) [Internet]. 2019 Feb 1 [cited 2021 Aug 1];53(1):30. Available from: /pmc/articles/PMC6377579/

APPENDIX A. RECIST

Minimum size of measurable lesion	CT: 10 mm
Lymph node	CT: ≥ 15mm short axis (target lesion) ≥ 10 - < 15 mm for (non-target lesion) < 10mm is not pathological
Overall tumor burden	5 lesions (2 per organ)
Response criteria for target lesion	
Complete response (CR)	Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in short axis diameter to < 10mm.
Partial response (PR)	At least 30% decrease in the sum of diameters of the target lesions, taking as reference the baseline sum diameters
Progressive disease (PD)	At least 20% increase in the sum of diameters of the target lesions, taking as reference the smallest sum of the study (this includes the baseline sum if that is the smallest). In addition to relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5mm. The appearance of one or more new lesions is also considered progression.
Stable disease (SD)	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking into reference the smallest sum of diameters while on study.
Response criteria for non-target lesion	
Complete response (CR)	Disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathologic in size (<10mm)
Non-complete response (Non-CR) / Non-progressive disease (Non-PD)	Persistence of one or more non-target lesion(s) and/ or maintenance of tumor marker level above the normal limits.
Progressive disease (PD)	Unequivocal progression of existing lesions or the appearance of the one or more new lesions

APPENDIX B. PERCIST

Quantitative parameter (SUL)	SUV-peak, normalized to lean body mass (SUL)
Progressive metabolic disease	Any of the following: - SUL increase by at least 30% and increase in by at least 0.8 SUL units of target lesion - Development of at least one new lesion - Increase in target lesion size by 30% - Unequivocal progression of target lesion
Stable metabolic disease	Increase or decrease of SUL by less than 30%
Partial metabolic response	All the following: - Decrease of SUL by >=30% and at least 0.8 SUL units difference - No new PSMA-avid lesions - No increase in size >30% of the target lesion - No increase in SUL or size of non-target lesion
Complete metabolic response	All the following: - PSMA uptake indistinguishable from surrounding background - SUL less than liver