

Does Specific Activity Provide a Clinical Advantage in Lu-177 PSMA Therapy? A Comparison of the Clinical Efficacy, Molecular Response, and Safety Profiles of CA and NCA Lu-177

Nalan Alan Selcuk

nalansalcuk@yahoo.com

Yeditepe University School of Medicine: Yeditepe Universitesi Tıp Fakültesi <https://orcid.org/0000-0002-3738-6491>

Kaan Akçay

Yeditepe University School of Medicine: Yeditepe Universitesi Tıp Fakültesi

Pelin Yeşilkaya

Yeditepe University School of Medicine: Yeditepe Universitesi Tıp Fakültesi

Gamze Beydağı

Yeditepe University School of Medicine: Yeditepe Universitesi Tıp Fakültesi

Hüseyin Adıgüzel

Yeditepe University School of Medicine: Yeditepe Universitesi Tıp Fakültesi

Türkey Toklu

Yeditepe University School of Medicine: Yeditepe Universitesi Tıp Fakültesi

Research Article

Keywords: Prostate Cancer, carrier-added (CA) and non-carrier-added (NCA) [¹⁷⁷Lu]Lu-PSMA, specific activity

Posted Date: October 13th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11124585/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

This study aimed to compare the clinical outcomes, molecular response, and safety profiles of carrier-added (CA) and non-carrier-added (NCA) [^{177}Lu]Lu-PSMA radioligand therapy in patients with metastatic castration-resistant prostate cancer (mCRPC).

Methods

In this retrospective, single-center study, 71 patients with mCRPC who received at least 2 cycles of CA-[^{177}Lu]Lu-PSMA (n = 41) or NCA-[^{177}Lu]Lu-PSMA (n = 30) therapy were evaluated. Efficacy was analyzed using prostate-specific antigen (PSA) kinetics and molecular response on [^{68}Ga]Ga-PSMA PET/CT according to the visual and quantitative Response Evaluation Criteria in PSMA Imaging (RECIP 1.0). Toxicity and safety profiles were graded using CTCAE v5.0.

Results

Baseline characteristics were comparable between the two groups. There was no statistically significant difference in the PSA50 response rates between the CA and NCA groups (48.6% vs. 48.3%, respectively; p = 0.976). Similarly, molecular response rates according to quantitative RECIP (37% vs. 48%; p = 0.409) and visual RECIP (50% vs. 55%; p = 0.585) did not significantly differ between the cohorts. Hematological and renal toxicities were mild and comparable between both groups. However, the incidence of grade 1 xerostomia was significantly higher in the NCA group compared to the CA group (50% vs. 20%; p = 0.02).

Conclusion

Both CA and NCA [^{177}Lu]Lu-PSMA therapies offer comparable clinical and molecular efficacy in mCRPC. Nevertheless, the higher specific activity of NCA [^{177}Lu]Lu-PSMA may be associated with an increased risk of mild xerostomia.

Background

Radioligand therapy (RLT) targeting the prostate-specific membrane antigen (PSMA) has become an important treatment option in recent years, particularly in patients with metastatic castration-resistant prostate cancer (mCRPC). Results obtained in large phase III trials have shown that [^{177}Lu]Lu-PSMA therapy provides significant clinical benefit in terms of progression-free survival (PFS), overall survival (OS), and quality of life [1, 2, 3]. For this reason, [^{177}Lu]Lu-PSMA radioligand therapy is now accepted as one of the standard treatment approaches in the management of advanced prostate cancer.

Lutetium-177 (Lu-177) is a β -particle-emitting radionuclide that, owing to its approximately 6.7-day half-life, appropriate tissue penetration, and accompanying gamma emission, has physical properties suitable for both therapy and imaging. Lu-177 production can be carried out using two different methods,

these methods being carrier-added (CA) and non-carrier-added (NCA), which give rise to two different product forms.

Carrier-added Lu-177 is generally produced via the $^{176}\text{Lu}(n,\gamma)^{177}\text{Lu}$ reaction in a nuclear reactor. Since a stable lutetium isotope is used as the target material in this method, the product also contains a considerable amount of non-radioactive (cold) lutetium after production [4]. This can cause the specific activity of the resulting radionuclide to be lower and limit the radioactivity per molecule. It has also been theoretically proposed that non-radioactive lutetium ions may bind to PSMA ligands and create a competitive effect at the receptor level [5].

In contrast, non-carrier-added (NCA) Lu-177 is generally obtained through the indirect production method based on the $^{176}\text{Yb}(n,\gamma)^{177}\text{Yb} \rightarrow ^{177}\text{Lu}$ reaction. In this production technique, a product largely purified of non-radioactive lutetium is obtained through a chemical separation process [4]. For this reason, the specific activity of NCA-Lu-177 is markedly higher, and theoretically allows a higher radioactivity to be carried with the same amount of ligand. It has been suggested that this may provide higher tumor dosimetry and better receptor saturation in target tissues. Indeed, in vitro binding studies have reported that ligands labeled with NCA-Lu-177 can show higher receptor affinity [6].

From a theoretical standpoint, the higher specific activity of NCA-Lu-177 may offer several advantages, including a lower administered ligand mass, reduced competition from nonradioactive metal–ligand complexes for PSMA-binding sites, more efficient receptor targeting, and potentially greater absorbed tumor doses. In clinical practice, however, CA-Lu-177 has been used for a longer time and is preferred in many centers due to ease of production, accessibility, and economic reasons. However, the extent to which these physicochemical differences in specific activity translate into clinical outcomes remains unclear. In the literature, studies directly comparing PSMA radioligand therapies performed using carrier-added (CA) and non-carrier-added (NCA) [^{177}Lu]Lu-PSMA are quite limited, and the available data do not allow a definitive conclusion regarding the effect of specific activity differences on clinical efficacy, molecular response, and toxicity profile.

The aim of this study is to compare the clinical outcomes of [^{177}Lu]Lu-PSMA radioligand therapy administered using carrier-added (CA) and non-carrier-added (NCA) Lu-177 and to reveal the possible differences between the two production methods. In this context, in both treatment groups, molecular response rates and treatment-related toxicity profiles were compared to evaluate how specific activity is reflected in clinical outcomes.

Methods

This retrospective, single-center study included patients diagnosed with metastatic castration-resistant prostate cancer (mCRPC) at Yeditepe University who received at least 2 cycles of carrier-added (CA) [^{177}Lu]Lu-PSMA or non-carrier-added (NCA) [^{177}Lu]Lu-PSMA therapy between February 2022 and November 2025. The mean number of cycles administered per patient in the study population was $3.4 \pm$

0.8 (median: 4; range: 2–4). Patients' demographic data, Gleason scores, previous systemic therapies [androgen receptor pathway inhibitors (ARPI), taxanes], baseline PSA levels, and tumor burden parameters obtained from pre-treatment PSMA PET/CT were recorded (Table 1).

The treatment protocol consisted of standard 200 mCi (7.4 GBq) doses administered at 6–8 week intervals according to the patients' clinical tolerance. Therapeutic efficacy was analyzed by comparing baseline pretreatment data with findings after the last cycle, in terms of serum PSA kinetics, clinical response assessed via subjective pain palliation, and molecular response levels on PSMA PET/CT according to the RECIP 1.0 (Response Evaluation Criteria in PSMA Imaging) criteria. Visual and quantitative RECIP assessments were performed separately in the molecular imaging analysis [7].

Quantitative analyses were performed blindly by an evaluator unaware of which group (CA or NCA) the patient had been treated in. Total tumor volume (TTV) and total lesion PSMA expression (TLP) values were determined from pre- and post-treatment [⁶⁸Ga]Ga-PSMA PET/CT images using the LesionID Pro (PSMA) workflow in MIM v7.4.3 software (GE Healthcare Inc., USA). An SUV threshold of 3 was used for extrahepatic lesions. For intrahepatic lesions, an SUV value equal to twice the mean SUV within a 3 cm³ VOI drawn on healthy liver tissue was used as the threshold. In addition, the percentage change in tumor volume was calculated from the total tumor volume obtained from baseline and post-treatment PSMA PET/CT examinations.

The safety and toxicity profile was determined by grading the nadir values of hematological parameters [hemoglobin (Hb), white blood cell count (WBC), platelet count (PLT)] observed during treatment, serum creatinine levels, and the development of xerostomia according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 scale [8]. Hematological and renal adverse events were evaluated as newly developed or worsening events relative to baseline; abnormalities present at baseline that did not show a grade increase during follow-up were not accepted as treatment-related toxicity.

Table 1 Patient Characteristics			
Variable	CA (n = 41)	NCA (n = 30)	p
Age	72.8 ± 7.1	74.8 ± 9.5	0.309
Docetaxel, n (%)	32 (78%)	20 (66%)	0.142
ARPI, n (%)	33 (80%)	27 (81%)	0.510
Gleason score ≥ 8, n (%)	25 (61%)	20 (66%)	0.942
Tumor volume, median (IQR), mL	142.50 (54.65–290.80)	169.00 (76.80–792.00)	0.314
Total lesion activity, median (IQR)	1030.10 (331.75–2307.65)	1283.10 (455.40–6196.70)	0.362
PSA, median (IQR), ng/mL	14.66 (3.11–58.45)	26.00 (12.89–90.50)	0.068

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed continuous variables were presented as mean $\pm$ standard deviation, and non-normally distributed continuous variables as median (interquartile range, IQR). The independent samples t-test was used for normally distributed data and the Mann-Whitney U test for non-normally distributed data when comparing continuous variables between the two independent groups. Categorical variables were expressed as number and percentage; the Pearson chi-square test was used for comparisons between groups, and Fisher's exact test was preferred when the expected cell count was low. All statistical tests were evaluated two-sided, and $p < 0.05$ was considered statistically significant. Missing data were excluded from the analysis on a per-variable basis.

This retrospective, single-center study was approved by the Non-Interventional Clinical Research Ethics Committee of Yeditepe University (Date: March 6, 2026; Decision No: 202602Y1070) and conducted in accordance with the ethical standards of the Declaration of Helsinki. Due to the retrospective nature of the study, the requirement for written informed consent was waived by the ethics committee.

Results

A total of 71 patients with metastatic castration-resistant prostate cancer were included in the study; of these, 41 received carrier-added (CA) and 30 received non-carrier-added (NCA) [^{177}Lu]Lu-PSMA therapy. No statistically significant difference was found between the groups in terms of age, prior docetaxel and ARPI use, Gleason score ≥ 8 , baseline total tumor volume, total lesion activity, and baseline PSA level. Age in the CA and NCA groups was 72.8 ± 7.1 and 74.8 ± 9.5 years, respectively ($p = 0.309$). Baseline total tumor volume was found to be median 142.50 (IQR: 54.65–290.80) mL and 169.00 (IQR: 76.80–792.00) mL ($p = 0.314$). Median total lesion activity was 1030.10 (IQR: 331.75–2307.65) in the CA group and 1283.10 (IQR: 455.40–6196.70) in the NCA group ($p = 0.362$). Median baseline PSA level was 14.66 (IQR: 3.11–58.45) ng/mL in the CA group and 26.00 (IQR: 12.89–90.50) ng/mL in the NCA group, and this difference did not reach statistical significance ($p = 0.068$) (Table 1).

PSA response analysis was performed in 66 evaluable patients (CA $n = 37$, NCA $n = 29$). Median PSA percentage change was -46.88 (IQR: -82.10 – 131.97) in the CA group and -22.10 (IQR: -93.98 – 86.97) in the NCA group, with no significant difference between the groups ($p = 0.405$). The rate of any PSA decline was 64.9% in the CA group and 55.2% in the NCA group ($p = 0.424$). PSA50 response rates were 48.6% and 48.3%, respectively, with no significant difference between the groups ($p = 0.976$). PSA25 progression was found to be 32.4% in the CA group and 41.4% in the NCA group, and this difference was also not statistically significant ($p = 0.453$) (Table 2).

Table 2
Comparison of PSA Responses

Outcome	CA lutetium (n = 37)	NCA lutetium (n = 29)	p
Baseline PSA, median (IQR), ng/mL	14.66 (3.11–58.45)	26.00 (12.89–90.50)	0.068
PSA percentage change, median (IQR)	-46.88 (-82.10–131.97)	-22.10 (-93.98–86.97)	0.405
Any PSA decline, n (%)	24 (64.9%)	16 (55.2%)	0.424
PSA50 response, n (%)	18 (48.6%)	14 (48.3%)	0.976
PSA25 progression, n (%)	12 (32.4%)	12 (41.4%)	0.453

PSMA PET/CT response analysis was evaluated in 63 patients (CA n = 36, NCA n = 27). The median percentage change in tumor volume was 9.40 (IQR: -40.35–148.85) in the CA group and -32.70 (IQR: -77.90–87.30) in the NCA group; no significant difference was found between the groups (p = 0.123). The response rate according to quantitative RECIP was 37% in the CA group and 48% in the NCA group (p = 0.409); disease control rates were 61% and 74%, respectively (p = 0.280). Response rates according to visual RECIP were 50% and 55% in the CA and NCA groups, respectively (p = 0.585), and disease control rates were 64% and 62% (p = 0.876). These findings show that there was no significant difference between the two treatment groups in molecular imaging-based response assessment (Table 3).

Table 3
Comparison of PSMA PET/CT Response

Outcome	CA lutetium (n = 36)	NCA lutetium (n = 27)	p
Tumor volume percentage change, median (IQR)	9.40 (-40.35–148.85)	-32.70 (-77.90–87.30)	0.123
Quantitative RECIP response (CR + PR), n (%)	14 (37%)	13 (48%)	0.409
Quantitative RECIP disease control (CR + PR+SD), n (%)	22 (61%)	20 (74%)	0.280
Visual RECIP response (CR + PR), n (%)	18 (50%)	15 (55%)	0.585
Visual RECIP disease control (CR + PR+SD), n (%)	24 (64%)	17 (62%)	0.876

No statistically significant difference was observed between the groups in terms of hematological and renal toxicity. Anemia occurred in 5 patients in the CA group and 8 patients in the NCA group (p = 0.277); grade ≥ 3 anemia was found in 2 and 0 patients, respectively (p = 0.263). Leukopenia was observed in 1 patient in each group (p = 0.940), and no grade ≥ 2 leukopenia was observed. Thrombocytopenia occurred in 1 patient in the CA group and 3 patients in the NCA group (p = 0.268); grade ≥ 3 thrombocytopenia was found in 1 patient in each group (p = 0.483). Grade ≥ 2 creatinine increase was observed only in 1 patient in the CA group, and the difference was not significant (p = 0.399) (Table 4).

Among patients in whom symptomatic assessment was possible, grade 1 xerostomia was found significantly more often in the NCA group than in the CA group [14 (50%) vs 6 (20%); $p = 0.02$]. In both groups, no grade ≥ 2 xerostomia was observed (Table 5). Pain control was achieved in 13/16 patients (81.3%) in the CA group and 8/12 patients (66.7%) in the NCA group. No statistically significant difference was observed between the groups in terms of pain control ($p = 0.418$).

Table 4
Toxicity

Toxicity	CA lutetium (n = 41)	NCA lutetium (n = 30)	p
Anemia, n (%)	5	8	0.277
Anemia, grade ≥ 3 , n (%)	2	0	0.263
Leukopenia, n (%)	1	1	0.940
Leukopenia, grade ≥ 2 , n (%)	0	0	—
Thrombocytopenia, n (%)	1	3	0.268
Thrombocytopenia, grade ≥ 3 , n (%)	1	1	0.483
Creatinine increase, grade ≥ 2 , n (%)	1	0	0.399

Table 5
Symptomatic Assessment: Xerostomia

Outcome	CA lutetium (n = 29)	NCA lutetium (n = 28)	p
Xerostomia, grade 1, n (%)	6 (20%)	14 (50%)	0.02 *
Xerostomia, grade ≥ 2 , n (%)	0	0	—
* $p < 0.05$ statistically significant			

Discussion

In this study, comparison of carrier-added (CA) and non-carrier-added (NCA) [^{177}Lu]Lu-PSMA therapy in terms of biochemical response, molecular response on PSMA PET/CT, and toxicity in patients with metastatic castration-resistant prostate cancer (mCRPC) revealed no statistically significant difference between the two groups for most outcomes. In contrast, the more frequent occurrence of grade 1 xerostomia in the NCA group stands out as a notable finding. When evaluated together with the literature, these results suggest that the theoretical radiochemical superiority of NCA lutetium may not always translate into a clear clinical advantage.

^{177}Lu 's production method directly affects the specific activity of the resulting radionuclide and the amount of non-radioactive lutetium. The main theoretical advantage of NCA ^{177}Lu is that, owing to its production method, it has a much higher specific activity and contains less stable lutetium. This has

been suggested to enable more efficient tumor targeting through binding to target receptors. Radiopharmaceutical preparation studies have shown that labeling of PSMA-617 with both CA and NCA ^{177}Lu is possible, but the specific activity used affects the labeling parameters and the peptide/radiometal ratio. In addition, preclinical studies have reported that PSMA-617 labeled with NCA ^{177}Lu can exhibit a lower dissociation constant, meaning it may carry a theoretical advantage in terms of binding affinity. However, the same study found no marked difference between the CA and NCA forms in internalization and competition experiments [9]. Consistent with our clinical results, these preclinical observations suggest that the difference in specific activity may not always translate into a strong functional distinction at the biological level.

When we examine the PSA response rate in our study, no significant difference was found between the CA and NCA groups in terms of response, and the rates of any PSA decline, PSA50 response, and PSA25 progression were found to be similar in both groups. When evaluated together with the response rates reported in large phase trials demonstrating the overall efficacy of [^{177}Lu]Lu-PSMA therapy, this finding is comparable to a PSA50 response rate of approximately 57% in the phase 2 LuPSMA trial and 66% in the [^{177}Lu]Lu-PSMA-617 arm of the TheraP trial [10]. In our cohort, the PSA50 response rate was 48% in both groups, and no divergence was observed between CA and NCA. This suggests that clinical efficacy in PSMA radioligand therapy is influenced not only by the specific activity of the radionuclide used, but also by numerous factors such as tumor burden, PSMA expression heterogeneity, previous systemic therapies, and patient biology. It has also been proposed that once the receptor-binding capacity of PSMA ligands reaches a certain saturation level, further increases in specific activity may not significantly increase the tumor dose. It has additionally been suggested that PSMA expression in tumors may be much greater than the amount of PSMA peptide administered, so unbound receptors may still remain available [11]. Therefore, while our results generally support the efficacy of Lu-PSMA therapy, they suggest that this efficacy does not change markedly depending on the ^{177}Lu form used.

It is also noteworthy that statistical significance could not be demonstrated between the two groups in terms of molecular response assessed by PSMA PET/CT. The fact that the median tumor volume change trended more favorably in the NCA group, and that quantitative RECIP response/disease control rates appeared numerically higher, may suggest that theoretically higher specific activity could have some biological reflections on tumor targeting. However, the fact that these differences did not reach significance indicates that this effect remains limited at the clinical level. In the literature, imaging-based response assessments of Lu-PSMA therapy show that pretreatment PSMA PET avidity and post-treatment quantitative PET changes, in particular, carry prognostic value. Subanalyses of the phase 2 LuPSMA study by Emmett et al. (10) demonstrated that molecular imaging parameters are associated with response and progression. Therefore, the numerical trend favoring NCA observed in our data may not be entirely clinically unimportant, although it can be said that it did not reach a significant level of superiority given the current sample size.

When evaluated in terms of safety profile, hematological toxicity rates were found to be low and comparable in both treatment groups. Grade 3–4 hematological side effects were rarely observed, and

no clinically significant deterioration in renal function was found. These findings support that radioligand therapy administered using either carrier-added (CA) or non-carrier-added (NCA) [^{177}Lu]Lu-PSMA is a well-tolerated treatment option. Our findings are consistent with large clinical series and safety analyses reporting that [^{177}Lu]Lu-PSMA therapy is generally associated with low rates of serious hematological and renal toxicity [12].

However, a notable finding in our study is that the development of xerostomia was significantly higher in the NCA group. The uptake of radioligand by the salivary glands, related to their PSMA expression, increases the sensitivity of these tissues to radiation damage. It is thought that, owing to the higher specific activity of non-carrier-added (NCA) [^{177}Lu]Lu-PSMA, the radiation dose absorbed by the salivary glands may increase, which could facilitate the development of xerostomia. This can be considered an important clinical parameter that may affect quality of life, particularly in patients receiving long-term treatment.

Although clinical pain control rates were observed to be higher in the CA group in our study, the fact that this did not reach statistical significance may be related to this parameter being based on subjective assessments and the limited number of patients. Nevertheless, the observation of significant symptomatic improvement in both treatment arms once again demonstrates that PSMA radioligand therapy is an effective palliative treatment approach in advanced prostate cancer.

This study has some limitations. First, the study has a retrospective, single-center design, and the number of patients is limited. In addition, the fact that dosimetry data were not evaluated limits the direct analysis of the effect of specific activity differences on tumor and normal tissue doses. Nevertheless, the inclusion of real-world data and reliance on homogeneous treatment protocols applied at the same center are among the strengths of the study.

Conclusions

The findings obtained show that carrier-added (CA) and non-carrier-added (NCA) [^{177}Lu]Lu-PSMA radioligand therapies administered in patients with metastatic castration-resistant prostate cancer yield similar results in terms of clinical efficacy, but that the use of non-carrier-added (NCA) [^{177}Lu]Lu-PSMA may carry a higher risk of xerostomia. Therefore, it is thought that not only the theoretical specific activity advantage but also the effects on cost, accessibility, and patient quality of life should be taken into account when selecting treatment in clinical practice. Future prospective, dosimetry-based studies are expected to more clearly reveal the biological and clinical differences between these two production forms.

Declarations

Funding: The authors did not receive support from any organization for the submitted work.

Competing Interests: The authors have no relevant financial or non-financial interests to disclose.

Author Contributions: The study conception, design, and methodology were developed by Nalan Alan Selçuk. Material preparation was performed by Türkay Toklu and Kaan Akçay. Data collection was conducted by Kaan Akçay, Hüseyin Adıgüzel, Pelin Yeşilkaya, Gamze Beydagi and Türkay Toklu. Data analysis was performed by Kaan Akçay. The first draft of the manuscript was written by Nalan Alan Selçuk. All authors reviewed and commented on previous versions of the manuscript and read and approved the final manuscript..

Data Availability: The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical Approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Non-Interventional Clinical Research Ethics Committee of Yeditepe University (Date: March 6, 2026; Decision No: 202602Y1070).

Informed Consent: Patient consent was waived by the local ethics committee due to the retrospective design of the study.

Use of AI Tools Declaration During the preparation of this work, the authors used AI-based writing assistance software (e.g., ChatGPT / Gemini) solely for language editing and improving the English text readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

References

1. 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*. 2021;385(12):1091–103.
2. Hofman MS, Emmett L, Sandhu S, Iravani A, Joshua AM, Goh JC, et al. [177Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial. *Lancet*. 2021;397(10276):797–804.
3. Hofman MS, Emmett L, Sandhu S, Iravani A, Buteau JP, Joshua AM, et al. Overall survival with [177Lu]Lu-PSMA-617 versus cabazitaxel in metastatic castration-resistant prostate cancer (TheraP): secondary outcomes of a randomised, open-label, phase 2 trial. *Lancet Oncol*. 2024;25(1):99–107.
4. Vogel WV, van der Marck SC, Versleijen MWJ. Challenges and future options for the production of lutetium-177. *Eur J Nucl Med Mol Imaging*. 2021;48(8):2329–35.
5. Fendler WP, Stuparu AD, Evans-Axelsson S, Lückerrath K, Wei L, Kim W, et al. Establishing 177Lu-PSMA-617 radioligand therapy in a syngeneic model of murine prostate cancer. *J Nucl Med*. 2017;58(11):1786–92.
6. Wiczorek Villas Boas CA, de Jesus Silva J, Pereira Dias LA, Brandão Freire MR, Balieiro LM, Ferreira Dos Santos CS, et al. In vitro and in vivo response of PSMA-617 radiolabeled with CA and NCA lutetium-177. *Appl Radiat Isot*. 2022;180:110064.

7. Gafita A, Rauscher I, Weber M, Hadaschik B, Wang H, Armstrong WR, et al. Novel framework for treatment response evaluation using PSMA PET/CT in patients with metastatic castration-resistant prostate cancer (RECIP 1.0): an international multicenter study. *J Nucl Med*. 2022;63(11):1651–8.
8. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE), version 5.0. Bethesda: National Cancer Institute; 2017.
9. Nanabala R, Pillai MRA, Gopal B. Preparation of patient doses of [177Lu]Lu-DOTATATE and [177Lu]Lu-PSMA-617 with carrier added (CA) and no carrier added (NCA) 177Lu. *Nucl Med Mol Imaging*. 2022;56(6):313–22.
10. Emmett L, Crumbaker M, Ho B, Willowson K, Eu P, Ratnayake L, et al. Results of a prospective phase 2 pilot trial of 177Lu-PSMA-617 therapy for metastatic castration-resistant prostate cancer including imaging predictors of treatment response and patterns of progression. *Clin Genitourin Cancer*. 2019;17(1):15–22.
11. Kletting P, Schuchardt C, Kulkarni HR, Shahinfar M, Singh A, Glatting G, et al. Investigating the effect of ligand amount and injected therapeutic activity: a simulation study for 177Lu-labeled PSMA-targeting peptides. *PLoS ONE*. 2016;11(9):e0162303.
12. 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*. 2017;58(1):85–90.