J of Nuclear Medicine Technology, first published online February 13, 2024 as doi:10.2967/jnmt.123.266769

# Survey of Clinical Protocols for the Use of $^{177}$Lu-PSMA-617 in the United States

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Although guidelines for the use of $^{177}$Lu-PSMA-617 published by various organizations are important, they do not include all the essential, practical points necessary for a complete institutional protocol. Therefore, a brief survey was performed to assess key components of the $^{177}$Lu-PSMA-617 protocol before, during, and after delivery of therapy. This survey demonstrated the wide variability in many aspects of institutional protocols regarding determination of eligibility for and administration of $^{177}$Lu-PSMA-617 therapy. The real-world protocol details provided here from a variety of institutions may help new and established theranostic programs.

**Key Words:** theranostics; protocol; survey; PSMA; lutetium

**J Nucl Med Technol 2024; 00:1–4**
DOI: 10.2967/jnmt.123.266769

The U.S. Food and Drug Administration's approval of $^{177}$Lu-vipivotide tetraxetan ($^{177}$Lu-PSMA-617) in March 2022 for the treatment of metastatic castration-resistant prostate cancer has launched a proliferation of theranostic programs across the nation (*1*). The prescribing information for $^{177}$Lu-PSMA-617 (Pluvicto; Novartis) is based on the methodology used in the phase 3 registrational VISION trial, which achieved an improvement of overall survival in a highly treatment-refractory patient population (*2*,*3*). Although the prescribing information provides direction on certain protocol issues such as dosing and criteria for selecting patients using prostate-specific membrane antigen (PSMA) PET, it is silent on many other details pertinent to patient selection, treatment, and monitoring (*2*,*4*,*5*). Efforts have been made to fill this gap, such as through a guideline published through the joint efforts of the European Association of Nuclear Medicine, Society of Nuclear Medicine and Molecular Imaging, and International Atomic Energy Agency (*6*,*7*).

Received Sep. 27, 2023; revision accepted Jan. 5, 2024.
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Published online Feb. 13, 2024.


When any new radiopharmaceutical program is started, and even more so for a complex theranostic program, a multitude of factors must be taken into consideration. Such factors include the available number of authorized users, support staff, facilities, delivery times, and travel times for patients—to name just a few. Anecdotally, protocols for the administration of $^{177}$Lu-PSMA-617 show considerable interinstitutional variability. To begin to assess this variability, a brief 10-question survey was conducted. The questions sought to span the $^{177}$Lu-PSMA-617 protocol before, during, and after dose delivery.

## MATERIALS AND METHODS

The purpose of this project was quality improvement, and no patient data were used; thus, no institutional review board review was required.

A 10-question survey was developed to assess the $^{177}$Lu-PSMA-617 protocol before, during, and after delivery of therapy (Fig. 1). We developed these questions to address some of the most common issues that we have been asked about by our nuclear medicine colleagues. In August 2023, faculty at 15 academic institutions were e-mailed the questionnaire. The academic centers represented institutions of various sizes and from various geographic regions throughout the country. The responses were tabulated, compiled into a spreadsheet using Microsoft Excel, and included for analysis only if the responding academic institution had already started a $^{177}$Lu-PSMA-617 program.

## RESULTS

Fourteen responses were received, for a survey response rate of 93% (14/15). Twelve of the 14 responding institutions had started their $^{177}$Lu-PSMA-617 programs and thus had their data included, for a total of 12 of 15 sites included (80%).

Included responses comprise academic institutions in all major geographic regions of the United States as shown in Table 1. The most responses were received from academic centers in the West ($n = 4$), and the fewest responses were from the Midwest ($n = 1$).

Table 2 shows the results of each survey question and also includes additional volunteered comments.

Lu177-PSMA-617 (Pluvicto) Administration Survey

1. Do you pre-hydrate and if so how (PO or IV)? No/Yes (PO or IV)
2. What technique do you use to administer dose (i.e., IV injection, IV push with 3-way stopcock, gravity method, infusion, or specify other)?
3. Do you cover the bathroom floor and if yes (i.e., none, blue chucks, cover large area with plastic sheet, or specify other)?
4. After injection, how long do you keep patient before discharge (if variable, please provide average to the quarter hour)?
5. Do you monitor vital signs? No/Yes (if yes, how often?)
6. How do you provide discharge instructions (i.e., verbal, written, both verbal and written, or specify other)?
7. Any precautions to prevent extravasation other than making as sure as possible that the IV is free flowing? No/Yes (if yes, please specify)
8. Does the authorized user personally administer every dose (understood that the AU is always at least supervising)? No/Yes (if no, then please specify if nurse, nuclear medicine technologist, mid-level, resident, fellow, or specify other)
9. What time frame (in weeks) is typically acceptable between eligibility PSMA-PET and treatment?
10. What time frame (in days) is typically acceptable for obtaining laboratory values before the scheduled dose?

**FIGURE 1.** Ten-question e-mail survey focusing on $^{177}$Lu-PSMA-617 protocol before, during, and after delivery of dose. AU = authorized user; IV = intravenous; PO = oral.

## DISCUSSION

The survey demonstrated the wide variability in many aspects of institutional protocols regarding determination of eligibility for and administration of $^{177}$Lu-PSMA-617 therapy. Although guidelines published through the joint efforts of the Society of Nuclear Medicine and Molecular Imaging, European Association of Nuclear Medicine, and International Atomic Energy Agency are important reading, they do not include all the important practical points necessary for a complete protocol (*6*,*7*). We hope that the real-world protocol details provided here will help new and established theranostic programs.

Only a single question had completely concordant responses (question 6), and several questions revealed substantial variability in $^{177}$Lu-PSMA-617 protocols between institutions. The results of this survey are likely to be of interest to institutions looking to either start a $^{177}$Lu-PSMA-617 program or update current protocols for $^{177}$Lu-PSMA-617 therapy. Additionally, this survey may be used to guide larger surveys on this topic or support formal research investigations to determine whether variability in $^{177}$Lu-PSMA-617 procedures and protocols meaningfully impacts patient selection or treatment outcomes for $^{177}$Lu-PSMA-617 therapy.

The evenly split number of responses to whether patients are prehydrated (question 1) exemplifies the lack of uniformity of protocols across the dozen programs. Of the programs that prehydrate, 5 of 6 use intravenous hydration (including the one that uses both intravenous and oral hydration). The VISION trial did not specify any method of hydration. It will be important to compare the long-term effects, if any, of hydration (none, oral, or intravenous) on renal function. For question 2, regarding technique for administering dose, half the sites use an infusion pump whereas the other half were evenly divided between intravenous push with a 3-way stopcock and the gravity method. These numbers suggest that all the recommended methods are successfully used. A nearly even split was also observed for the third question, asking about covering the bathroom floor. Of the 7 sites that responded positively, 4 used blue chucks (disposable absorbent pads). Interestingly, these responses show that a significant percentage of sites do not find it necessary to cover the bathroom to mitigate contamination with radioactivity.

**TABLE 1**
U.S. Geographic Locations of Responding Academic Institutions

| Geographic location | No. of academic institutions |
|---|---|
| Northeast | 3 |
| Southeast | 2 |
| Midwest | 1 |
| Southwest | 2 |
| West | 4 |

The fourth question asks how long after injection the patient is kept before discharge, and the responses ranged widely from immediately to 2.5 h. Nine of 12 responses fell into the range of 0.25–0.5 h. Question 5 concerned monitoring of vital signs, and a third of programs responded that they do not check vital signs. Two of the 8 positive responses were "on arrival only," but the other six were some variations of checking vital signs before and after infusion. Question 6 queried how discharge instructions are provided, and the responses were unanimous that both verbal and written instructions are given. Interestingly, some responders collectively made additional comments that consultation and teaching are done by a physician, nurse, or health physicist (radiation safety).

The seventh question asked whether programs take any precautions to prevent extravasation other than making as sure as possible that the intravenous line is free-flowing. Only 1 site responded with a yes, writing that intravenous patency is tested with 18.5 MBq (0.5 mCi) of $^{99m}$Tc-pertechnetate and that a detector is used to confirm no extravasation. Another site added the comment that radiation is measured at the injection site before the patients are discharged, and if more than 40 mR/h, a scan for potential infiltration is considered. This survey suggests that most of the responding programs do not take any extra precautions to prevent extravasation other than making as sure as possible that the intravenous line is free-flowing. Question 8 queried whether the authorized user personally administers every dose, with the understanding that the authorized user is always at least personally present and supervising the administration. At only 1 site does the authorized user physically administer all the doses. Nuclear medicine technologists administer the doses routinely at 10 of 12 sites, and the resident or fellow gives the dose at the remaining site (under supervision of an authorized user).

Regarding how much time is typically acceptable between eligibility PSMA PET imaging and treatment, the responses varied widely from 3 wk to 6 mo, with no specific time frame reported by 2 sites. Similarly, for the time frame that is typically acceptable for obtaining laboratory values before the scheduled dose, the responses varied widely, with no more than 2 programs using the same protocol in response to this

**TABLE 2**
Survey Questions and Responses

| Question and responses | *n* |
|---|---|
| 1. Do you prehydrate and if so how (PO or IV)? | |
| Yes | 6/12 (50%) |
| IV | 4/6 (67%) |
| PO | 1/6 (17%) |
| IV and PO | 1/6 (17%) |
| No | 6/12 (50%) |
| 2. What technique do you use to administer dose (i.e., IV injection, IV push with 3-way stopcock, gravity method, infusion, or other)? | |
| Infusion pump | 6/12 (50% |
| IV push with 3-way stopcock | 3/12 (25%) |
| Gravity method | 3/12 (25%) |
| 3. Do you cover bathroom floor and, if yes, how (i.e., use blue chucks, cover large area with plastic sheet, other)? | |
| Yes | 7/12 (58%) |
| Blue chucks | 4/7 (57%) |
| Cover large area with plastic | 2/7 (29%) |
| Bench-Armor coated paper sheets (Jaece) | 1/7 (14%) |
| No | 5/12 (42%) |
| 4. After injection, how long do you keep patient before discharge (if variable, please provide average to quarter hour)? | |
| 0.5 h | 5/12 (42%) |
| 0.25 h | 3/12 (25%) |
| 0.25–0.5 h | 1/12 (8%) |
| 2–2.5 h | 1/12 (8%) |
| Immediately if dose rate < 5 mrem/h at 1 m | 1/12 (8%) |
| Immediately | 1/12 (8%) |
| 5. Do you monitor vital signs (if yes, how often)? | |
| Yes | 8/12 (67%) |
| Before administration and before leaving clinic | 3/8 (38%) |
| On arrival only | 2/8 (25%) |
| Before and 15 min after infusion | 1/8 (13%) |
| Before and 15–30 min after infusion | 1/8 (13%) |
| Baseline and at end of infusion | 1/8 (13%) |
| No | 4/12 (33%) |
| 6. How do you provide discharge instructions (i.e., verbal, written, both verbal and written, other)? | |
| Both verbal and written* | 12/12 (100%) |
| 7. Do you take any precautions to prevent extravasation other than making as sure as possible that IV line is free-flowing (if yes, please specify)? | |
| No | 11/12 (92%) |
| Yes† | 1/12 (8%) |
| 8. Does authorized user personally administer every dose (it is understood that authorized user is always supervising)? If no, please specify whether nurse, nuclear medicine technologist, mid-level provider, resident, fellow, or other administers doses. | |
| No | 11/12 (92%) |
| Nuclear medicine technologist | 10/11 (91%) |
| Resident or fellow | 1/11 (9%) |
| Yes | 1/12 (8%) |
| 9. What time frame (in weeks) is typically acceptable between eligibility PSMA PET and treatment? | |
| No specific timeframe | 2/12 (17%) |
| 4 wk | 2/12 (17%) |
| 6 mo | 2/12 (17%) |
| 3 wk | 1/12 (8%) |
| 8 wk | 1/12 (8%) |
| 12 wk | 1/12 (8%) |
| 4 wk preferred, up to 3 mo acceptable | 1/12 (8%) |
| 3 mo preferred, up to 6 mo acceptable | 1/12 (8%) |
| 4 mo | 1/12 (8%) |
| 10. What time frame is typically acceptable for obtaining laboratory values before scheduled dose? | |
| 7–10 d | 2/12 (17%) |
| 4 wk | 2/12 (17%) |
| 5–7 d | 1/12 (8%) |
| 7–14 d | 1/12 (8%) |
| Prefer day of therapy for first dose, allowable up to 2 d prior, for subsequent doses up to 7 d prior | 1/12 (8%) |
| Day of administration and time of initial consult, typically 2–4 wk before | 1/12 (8%) |
| 48 h before and 4 wk after dose | 1/12 (8%) |
| 1 wk for first dose and 2 wk for subsequent doses | 1/12 (8%) |
| 0–3 d and midway between treatments at 3 wk | 1/12 (8%) |
| 3 wk ahead and 1 d ahead of scheduled dose | 1/12 (8%) |

*Additional comments report consultation and teaching by combination of physicians, nurses, and medical physicists.

†Additional volunteered comment: IV patency is first tested with injection of 18.5 MBq (0.5 mCi) of $^{99m}$Tc-pertechnetate, and detector is used to confirm no extravasation.

PO = oral; IV = intravenous.

question. Three sites check laboratory values twice before each treatment. The laboratory tests closer to the treatment dose ranged from 0 to 3 d before the therapeutic administration. The laboratory checks after the treatment ranged from 2 to 3 wk before the next scheduled dose. The other 9 sites typically check laboratory values just once before the treatment, ranging from 0 d to 4 wk. This wide variation and lack of consensus may be due to a variety of reasons, including lack of data to support a clear recommendation, reimbursement issues, and challenges in access to testing.

Although this survey of a dozen practices was meant neither to provide a complete or detailed representation of all practices across the nation nor to make specific recommendations, the survey does show that there is considerable variation among practices regarding treatment protocols. A take-home message from the results is that no one-size-fits-all approach exists. Practices tailor their $^{177}$Lu-PSMA-617 protocols according to their resources and patient population. The spectrum of responses here may help new theranostic programs or programs looking to adapt their protocols to meet changes in resources or needs. The variation in practices may also inform protocols for future theranostic agents.

Although based on data from a limited number of institutions, this survey incorporates the treatment experience from a large number of patients. The variations in institutional procedures will provide data for future retrospective analyses to relate patient outcomes to treatment procedures and thus help to establish best practices for performing these treatments. This work has the potential to be useful in the development of future surveys. For example, the questions with unanimous or near-unanimous responses, such as the question showing that both verbal and written discharge instruction are uniformly given, may not need to be asked again. This survey was sent to academic centers of a variety of sizes and in various regions of the country, and it would be interesting to include nonacademic practices in the future. Also, as $^{177}$Lu-PSMA-617 programs proliferate around the world, it would be fascinating to compare practices among countries. Although beyond the scope of this project, a future survey could focus on the complex issue of how to follow up patients for response and clinical decision-making.

## DISCLOSURE

Phillip Kuo is a consultant or speaker for Blue Earth Diagnostics, Chimerix, Eli Lilly, Fusion Pharma, GE Healthcare, Invicro, Novartis, Radionetics, and Telix Pharmaceuticals. He is a recipient of research grants from Blue Earth Diagnostics and GE Healthcare and was previously a part-time employee of Invicro. Daniel Lee is an investigator for MedTrace and Novartis/Advanced Accelerator Applications. Terence Wong is a consultant for GE Healthcare, Novartis Pharmaceuticals, Progenics Pharmaceuticals, and Telix Pharmaceuticals. Matthew Covington is a consultant for Invicro, GE Healthcare, and NexEos. He is a recipient of research grants from 5 For the Fight and Fujifilm USA. Neeta Pandit-Taskar has received honoraria from AstraZeneca/MedImmune and Actinium Pharmaceuticals. She is a consultant or advisor for Progenics, Illumina, Imaginab, and Actinium Pharmaceuticals. She has served on the Speakers' Bureau for Actinium Pharmaceuticals and Telix. She has institutional research funding from Imaginab, Regeneron, Bristol Myers Squibb, Janssen, Clarity, and Bayer Health. No other potential conflict of interest relevant to this article was reported.


## ACKNOWLEDGMENTS

We thank the following colleagues for adding their experience to this survey: Dena Abdelhameed, Ryan Avery, Delphine Chen, Ming-Kai Chen, Gagandeep Choudhary, Arash Kardan, Saima Muzahir, Eric Rohren, David Schuster, Marc Seltzer, Gary Ulaner, Ming Yang, and Don Yoo.


## KEY POINTS

**QUESTION:** What is the real-world, institutional variability in key components of the $^{177}$Lu-PSMA-617 protocol before, during, and after delivery of therapy?

**PERTINENT FINDINGS:** The survey demonstrated the wide variability in many aspects of institutional protocols regarding determination of eligibility for and administration of $^{177}$Lu-PSMA-617 therapy.

**IMPLICATIONS FOR PATIENT CARE:** The real-world protocol detailed here from a variety of institutions may help new and established theranostic programs to optimize their own protocols.

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