

The
Health Policy
Partnership
[research, people, action]

Health system readiness for radioligand therapy in the US

Identified need

Working paper

November 2021

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About this working paper

This working paper is part of a broader piece of work aiming to define what is needed to establish system-level readiness for radioligand therapy in the US. It explores current integration and future readiness for the therapy as it relates to identified need, one of the five domains of the Radioligand Therapy Readiness Assessment Framework (*Figure 1*). The working paper provides answers to questions from the framework, with key findings from relevant subdomains outlined in a summary assessment at the start of each section. It explores whether there are enough epidemiological data, as well as information for patients and healthcare professionals, to predict the number of people who may use radioligand therapy. Throughout the paper, we focus on the situation in neuroendocrine tumors, lymphoma, and prostate cancer.

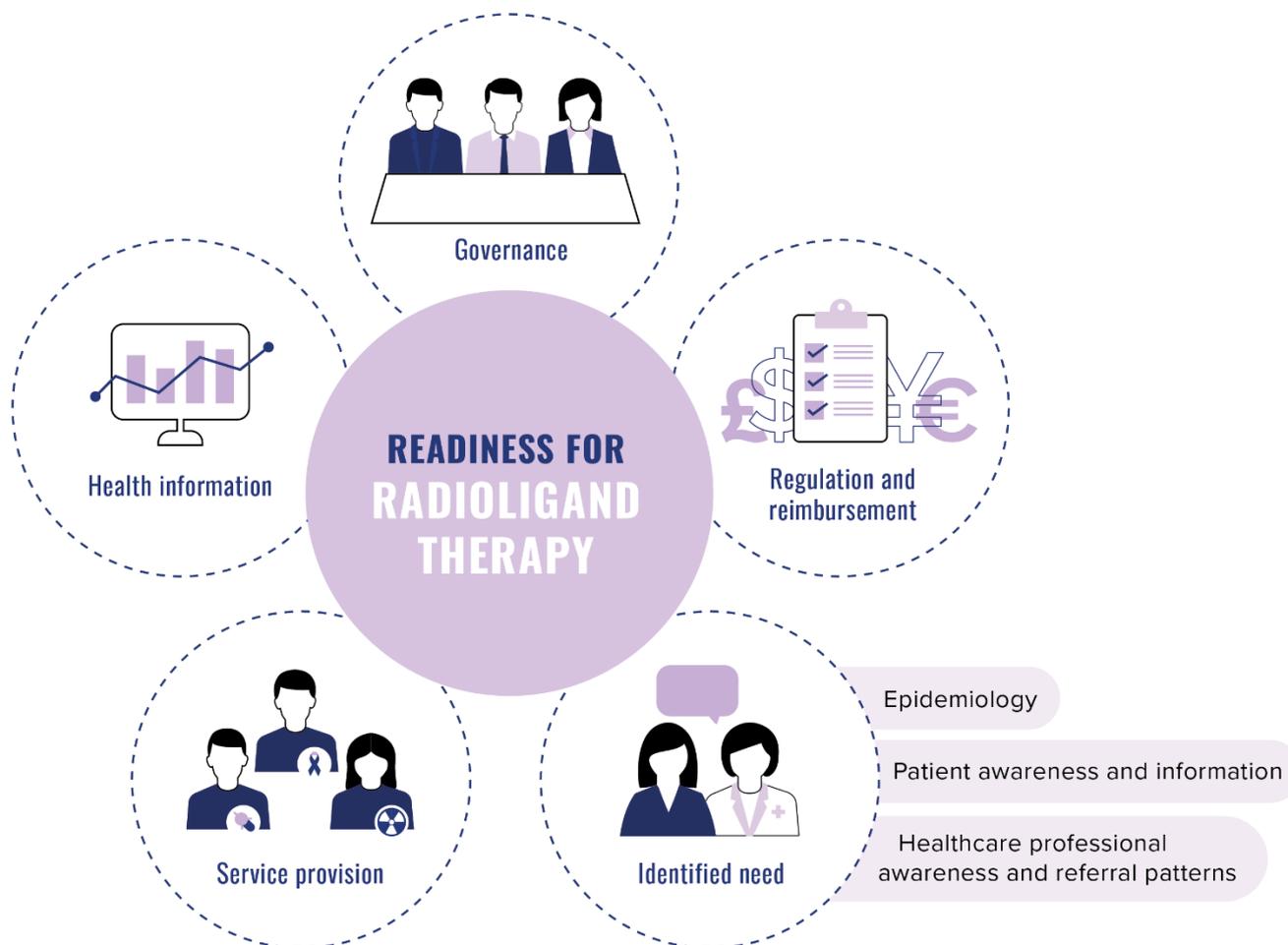
- This working paper is supported by other documents on health system readiness for radioligand therapy in the US. For more details, please visit: www.radioligandtherapy.com/framework/US

Terminology

This working paper uses the term radioligand therapy to refer to peptide-receptor radionuclide therapy (PRRT), prostate-specific membrane antigen (PSMA) therapy, and radioimmunotherapy. We appreciate that there are a variety of other terms that may be used for radioligand therapy.

Radioligand therapy is a specific subtype of radiopharmaceutical therapies. Where possible, this working paper includes data relating to radioligand therapy. However, where research about radioligand therapy is not specifically available, we may refer more broadly to radiopharmaceutical therapies.

Figure 1. Domains of the Radioligand Therapy Readiness Assessment Framework: US



What is identified need?

Identifying the need for health services lays the groundwork for system-level changes that can benefit patients and wider society. The identified need for radioligand therapy is the potential demand for the therapy among people with cancer. This is influenced by the number of people eligible for the therapy, both now and in the future, and the level of understanding and awareness of the therapy among healthcare professionals and people with cancer.

How is the need for radioligand therapy effectively identified?

Up-to-date epidemiological data, as well as clinician and patient awareness, are needed to ensure health systems can plan for and deliver radioligand therapy to the appropriate people. Reliable and detailed epidemiological data are needed to quantify the number of people with cancer who may be eligible for radioligand therapy, and to plan and supply the service accordingly. These data should be considered in the context of information about relative therapeutic efficacy and optimal sequencing of treatments to gain an accurate image of the number of people who could be referred for the therapy. Awareness of the approach among healthcare professionals is also crucial to ensure that people who would benefit from radioligand therapy are identified and referred at the appropriate time. For patients, the availability of clear, accurate, consistent, and timely information on radioligand therapy can help ensure people fully understand the approach, and its potential benefits and risks. This will help them be involved in therapeutic decision-making, ensuring that they can make informed decisions about their care and that treatment meets with their personal goals and priorities.

- For more information on research into therapeutic efficacy, read the working paper on [health information](#).
- For more information on guidelines for the delivery of radioligand therapy, read the working paper on [governance](#).

1 Epidemiology

Summary assessment

Indicator	Assessment
What is the current burden of disease in the US?	<p>Radioligand therapy is currently approved for use and under investigation in specific types of neuroendocrine tumors (NETs), lymphoma and prostate cancer. Where data on prevalence of these specific subtypes is not readily available, we have provided data on the broader indication.</p> <p>NETs: Although the incidence and prevalence are on the rise in the US, NETs are still considered a rare disease. In 2014, an estimated 0.048% of the US population, more than 170,000 people, were living with NETs. Approximately 12,000 people are diagnosed with NETs each year.</p> <p>Lymphoma: An estimated 90,390 people will be diagnosed with a type of lymphoma in 2021, approximately 4.8% of all cancer cases in the US. In 2018, an estimated 962,304 people were living with a type of lymphoma.</p> <p>Prostate cancer: In 2017, more than 3.1 million people in the US were living with prostate cancer. The prevalence of metastatic prostate cancer is on the rise, with an expected prevalence of over 15,000 by 2025.</p>

1.1 Neuroendocrine tumors

Epidemiological data for neuroendocrine tumors (NETs) suggest that the incidence and prevalence of the condition have increased over time; however, most data are outdated. The most recent formally published data on prevalence for this patient population is from 2012,¹ and data are not updated or reported with sufficient frequency to accurately inform ongoing efforts to address patient needs on a national level. There are more recent informal estimates of prevalence and incidence: data from 2020 suggest that more than 12,000 people are diagnosed with NETs each year.² It was estimated that 171,321 people were living with NETs in 2014, up from 103,312 in 2004.¹ Improvements in diagnostic capacity, such as better imaging tests and endoscopy, as well as increased awareness of NETs among healthcare professionals have contributed to increases in the number of people diagnosed.

Although not all people with NETs will be eligible for radioligand therapy, the treatment is commonly used in this indication.³ Rare diseases are classified as those affecting fewer than 200,000 people in the US; given the increase in incidence of NETs, there is a risk that it could lose its “rare disease” classification. This would have negative implications on accessibility of treatments and research funding, such as that for orphan drugs.

- For more information on the use of radioligand therapy in NETs, read the working paper on [service provision](#).

1.2 Lymphoma

The number of people living with lymphoma is increasing, highlighting the importance of appropriate treatments being available. Lymphoma makes up an estimated 4.8% of all cancer diagnoses, and the Surveillance, Epidemiology, and End Results (SEER) program estimates that 90,390 new cases will be diagnosed in 2021.^{4 5} Between 1975 and 2015 the number of people living longer than five years after diagnosis increased by over 20%^{4 5} – as a result, the number of people living with lymphoma is rising. In 2018, an estimated 962,304 people were living with lymphoma,^{4 5} a notable increase from 690,993 people in 2010.^{6 7} Radioligand therapy will only be appropriate for a subset of these people. It is currently approved for certain types of follicular lymphoma,^{8 9} and is under investigation in this indication as well as in certain types of diffuse large B-cell lymphoma.¹⁰⁻¹² Together, these types account for more than half of lymphoma cases in the US.¹³ As more people live with lymphoma for longer, it will be increasingly important that health systems have adequate capacity for a variety of suitable therapies, such as radioligand therapy, for ongoing management of the diverse presentations and experiences of this condition.

- For more information on the licensing of radioligand therapy in lymphoma, read the working paper on [regulation and reimbursement](#).

1.3 Prostate cancer

The proportion of the US population diagnosed with prostate cancer every year appears to be decreasing, but this may be due to changes in screening and diagnosis procedures. As of 2017, an estimated 1.96% of the male population, representing 3,170,339 people, were living with prostate cancer.¹⁴ Recent incidence data show that 207,430 people are

diagnosed with prostate cancer each year.¹⁵ Between 2007 and 2016, the incidence rate of prostate cancer decreased by 3.8% per year, on average.¹⁶ This is probably because the United States Preventive Services Task Force screening guidelines for prostate cancer were changed owing to worries over false positive results and overtreatment. The guidelines' recommendation against prostate-specific antigen-based screening in men aged 70 and over¹⁷ has likely led to reduced identification of prostate cancer patients. Limited screening means that prostate cancer may be at an advanced stage by the time it is diagnosed, making the availability of effective treatments at that stage even more critical.

Despite the decreasing incidence of prostate cancer overall, metastatic prostate cancer is on the rise. Incidence of metastatic prostate cancer is projected to grow by 1.03% between 2015 and 2025.¹⁸ Prevalence is also expected to increase, from 10,615 in 2015 to 15,097 in 2025.¹⁸ This is attributed to a range of factors, including an aging population, reduced screening initiatives, and delayed diagnosis. Radioligand therapy is currently under investigation in certain types of metastatic prostate cancer,^{19 20} though it may have uses in other types of prostate cancer in future.

- For more information on data and research, read the working paper on [health information](#).

2 Patient awareness and information

Summary assessment

Indicator	Assessment
Is there information for patients on radioligand therapy as a treatment option?	<p>Neuroendocrine tumors (NETs): Information on radioligand therapy as a treatment option for NETs is typically provided by research/advocacy organizations and national cancer organizations. The terminology, type and content of patient information varies between sources.</p> <p>Lymphoma: Information on radioligand therapy for lymphoma is produced by patient advocacy and research organizations. Most information mentions currently licensed radioligand therapy but does not consider novel applications of the approach that are under investigation.</p> <p>Prostate cancer: Advocacy and patient organizations inform patients of ongoing clinical trials for radioligand therapy, but detailed information about the approach is limited.</p>

2.1 Neuroendocrine tumors

Although there is a lot of information about radioligand therapy for people with NETs, the content is inconsistent. A number of research and advocacy organizations,²¹⁻²⁵ professional societies,²⁶⁻²⁸ and healthcare providers²⁹⁻³¹ produce materials about radioligand therapy for people with NETs. There is substantial variation in the type and amount of information provided, which may be confusing for people with NETs or their caregivers. Ultimately, this could mean that people who might benefit from the therapy may not have the appropriate information to make an informed decision about it. For example:

- Information on treatment eligibility criteria can be inconsistent. Cancer Treatment Centers of America states that radioligand therapy is a second-line treatment and that imaging is used to determine eligibility.³⁰ Meanwhile, the National Comprehensive Cancer Network discusses eligibility based on patient indicators related to disease progression,²⁶ and The Healing Net outlines that grade and stage influence patient selection.²⁴

- Information on how radioligand therapy works is provided by different organizations with varying levels of detail. Greater information on the safety of radiation would be beneficial, as experts have mentioned that use of radiation remains a concern for many people.³² Notably, few patient materials provide reassurances about the safe use of therapeutic radiation.

2.2 Lymphoma

Most patient information about radioligand therapy for lymphoma is out of date, which may impact awareness of current and novel applications of the therapy. Information from advocacy and research organizations, such as the Lymphoma Research Foundation and the Leukemia & Lymphoma Society, explain what radioligand therapy is and how it is delivered.³³⁻³⁶ Many of the resources about radioligand therapy for people with lymphoma are at least five years old, and focus on currently licensed therapies. As such, information may not be readily available to people seeking to learn about investigational lymphoma treatments. A notable exception is the Lymphoma Research Foundation's 2017 information sheet, which contains detailed information about not just currently licensed radioligand therapy but therapies currently under investigation. More clear, accurate, and readily available information on radioligand therapy for people with lymphoma would be beneficial to increase awareness and familiarity with the approach.

2.3 Prostate cancer

Patient information on prostate cancer treatments is widely available, but rarely mentions radioligand therapy. However, some patient advocacy organizations, such as Us TOO International, guide people to radioligand therapy clinical trials for which they may be eligible.³⁷ Beyond this, educational information for patients about investigational radioligand therapy remains limited. Given the recent announcement that the US Food and Drug Administration has granted radioligand therapy breakthrough status in prostate cancer, it is likely that this therapy will garner more attention. It may then be incorporated into the well-established pool of patient information about the use of targeted radiation therapies in prostate cancer.³⁸⁻⁴⁷

- For more information about the breakthrough status of radioligand therapy, read the working paper on [regulation and reimbursement](#).

3 Healthcare professional awareness and referral patterns

Summary assessment

Indicator	Assessment
Are relevant healthcare professionals aware of radioligand therapy as a treatment option?	<p>High awareness of radioligand therapy among healthcare professionals can help to ensure that people who might benefit from the therapy are quickly identified and referred for treatment.</p> <p>Physicians eligible to become Authorized Users receive training about radiopharmaceutical therapies. However, awareness of radioligand therapy is lower among other physicians involved in patient referral, as the therapy is not covered in the requirements for training programs or board certification. The lead physician’s awareness of the therapy and understanding of how it can be used may be further challenged by unclear treatment pathways.</p>

Nuclear medicine physicians, radiation oncologists, nuclear radiologists, and nuclear medicine technologists have a high level of awareness of radioligand therapy; however, they are not consistently trained in its use in all relevant indications. These healthcare professionals are broadly trained in the use of radiopharmaceuticals for therapy,⁴⁸ and most are specifically trained in the use of radioligand therapy in lymphoma.⁴⁹⁻⁵² Most board certification standards do not yet directly refer to use of radioligand therapy in NETs.^{48-50 52} However, in 2022, NETs will be added and lymphoma removed from some technologist exams. Regardless of specialty training, after board certification nuclear medicine physicians, radiation oncologists, and nuclear radiologists are eligible to become further certified as Authorized Users (AUs), who are licensed by the US Nuclear Regulatory Committee to deliver radiopharmaceutical therapies. AUs undergo rigorous additional training where they are likely to become very knowledgeable about the use of radioligand therapy for NETs. Given the important role of these professionals in delivering radioligand therapy, their awareness and understanding of the therapy is essential.

- [For more information about the regulation of AUs, read the working paper on regulation and reimbursement.](#)

Training curricula for referring physicians do not always include radioligand therapy, which limits the number of physicians who are aware of the therapy. People with cancer who would benefit from radioligand therapy must be first identified by their referring physician, typically an oncologist, endocrinologist, gastroenterologist, hematologist, or urologist. Ensuring that referring physicians have a good awareness of novel therapies' potential and eligibility criteria is therefore critical. However, neither the standards for graduate education nor the board certification test topics for the above specialties address radioligand therapy.⁵³⁻⁶² As such, lymphoma experts have suggested that many prospective or newly licensed hematologists may have no experience with radioligand therapy, or may not even have heard of it.⁶³

Referring physicians may become familiar with radioligand therapy on an ad hoc basis after board certification. Some physicians may become aware of the therapy through engagement with professional societies, publications, conferences, and pharmaceutical representatives. Physicians working in large academic institutions are likely to be involved in clinical trials and multidisciplinary tumor boards, giving them the opportunity to learn about investigational therapies. Informal multidisciplinary working patterns, such as ad hoc consultations or informal meetings, and formal tumor boards can also help referring physicians learn about therapies from outside their specialty, such as radioligand therapy. Through the combination of these methods, an expert has suggested that many healthcare professionals treating NETs and prostate cancer are aware of the therapy.⁶⁴ However, these learning opportunities may not be consistently taken up or available, resulting in variable awareness of radioligand therapy.

- For more information about multidisciplinary working for radioligand therapy, read the working paper on [service provision](#).

Clear referral pathways can help physicians identify people who are eligible for radioligand therapy and direct them to the appropriate services. This is particularly important in management of lymphoma and prostate cancer, which are often treated in community settings, where access to tumor boards and multidisciplinary working may be disproportionately low.⁶⁵ No standard referral pathways were identified for NETs and lymphoma, and processes differ between settings.⁶⁶ Moreover, guidelines do not include information about how referring physicians can be involved throughout the treatment process.⁶⁶⁻⁶⁹ Although referring physicians may be involved in patient follow-up between

cycles and after treatment, this seems to be uncommon. As a result, referring physicians may not know the appropriate time to consider radioligand therapy, and may be reluctant to recommend it for fear of losing the patient to another institution.

Conclusion

More timely collection and analysis of epidemiological data would help the US health system better prepare for the anticipated increase in demand for radioligand therapy.

Rare diseases such as NETs often do not receive ready funding for research or as much attention on the national healthcare agenda as more prevalent conditions. But accurate and up-to-date epidemiological data and evidence-based models of future cancer prevalence for people with NETs, as well as those with lymphoma and prostate cancer, will be an important component of ensuring equitable and timely access to needed therapy. It is important to ensure these data are considered in the context of wider information about therapeutic efficacy and optimal timing of usage. Combined, this information should feed into health system planning to secure sufficient resources to meet the need for innovative, targeted therapies such as radioligand therapy.

Demand for novel therapies is driven by people who are eligible and knowledgeable.

Information on radioligand therapy is more readily available for people with NETs than for people with lymphoma or prostate cancer. This is unsurprising given that the therapy is commonly used in NETs, whereas its use in lymphoma is limited and it is still under investigation in prostate cancer. However, the variability of information presented through different sources may reduce understanding of radioligand therapy among people with NETs and lymphoma. The preparation of clear and consistent patient information will be important as new therapies are explored in prostate cancer and lymphoma. Moreover, organizations may benefit from providing information that helps patients better understand the role of radioligand therapy amid other treatment options available to them.

Although experts involved in nuclear medicine and radiation oncology are trained in radiopharmaceutical therapies, referring physicians are not consistently aware of these therapies. Unclear referral pathways for radioligand therapy in NETs and lymphoma may further limit understanding of and familiarity with the therapy. As a result, medical oncologists, gastroenterologists, endocrinologists, and hematologists may not readily consider radioligand therapy as an appropriate option for their eligible patients. Clear guidance on the timing for consideration of radioligand therapy, and the engagement of healthcare professionals throughout the process, may reduce barriers to integrating the approach into care. Guidance should apply to and be clearly communicated in both

community settings and large hospitals, to ensure equitable access to radioligand therapy across the country.

References

1. Dasari A, Shen C, Halperin D, *et al.* 2017. Trends in the incidence, prevalence, and survival outcomes in patients with neuroendocrine tumors in the United States. *JAMA Oncol* 3(10): 1335-42
2. Cancer.Net. Neuroendocrine tumors: Statistics. Available from: <https://www.cancer.net/cancer-types/neuroendocrine-tumors/statistics#:~:text=Overall%2C%20it%20is%20estimated%20that,has%20been%20increasing%20for%20years> [Accessed 12/22/20]
3. Strosberg J. 2020. Interview with Partnership MBaAaCMaTHP [Telephone]. 10/12/20
4. Surveillance Epidemiology and End Results Program. Cancer stat facts: Hodgkin Lymphoma. Available from: <https://seer.cancer.gov/statfacts/html/hodg.html> [Accessed 07/06/21]
5. Surveillance Epidemiology and End Results Program. Cancer stat facts: Non-Hodgkin lymphoma. Available from: <https://seer.cancer.gov/statfacts/html/nhl.html> [Accessed 07/06/21]
6. Surveillance Epidemiology and End Results Programme. Table 9.1 Hodgkin Lymphoma. Available from: https://seer.cancer.gov/archive/csr/1975_2010/results_merged/sect_09_hodgkins.pdf [Accessed 07/29/21]
7. Surveillance Epidemiology and End Results Program. 2013. Table 19.1 non-Hodgkin Lymphoma. Available from: https://seer.cancer.gov/archive/csr/1975_2010/results_merged/sect_19_nhl.pdf [Accessed 07/29/21]
8. Grillo-López AJ. 2002. Zevalin: the first radioimmunotherapy approved for the treatment of lymphoma. *Expert Rev Anticancer Ther* 2(5): 485-93
9. Spectrum Pharmaceuticals. FDA Approves ZEVALIN(R) Expanded Label as Part of First-Line Therapy in Treatment of Follicular Non-Hodgkin's Lymphoma. Available from: <https://investor.sppirx.com/news-releases/news-release-details/fda-approves-zevalinr-expanded-label-part-first-line-therapy> [Accessed 07/16/21]
10. Clinicaltrials.gov. A Phase I/II Study of Betalutin for Treatment of Relapsed Non-Hodgkin Lymphoma (LYMRIT-37-01). [Updated 04/01/21]. Available from: <https://clinicaltrials.gov/ct2/show/NCT01796171> [Accessed 07/02/21]
11. ClinicalTrials.gov. Study of Betalutin for Treatment of Relapsed or Refractory Non-Hodgkin Lymphoma (LYMRIT-37-05). [Updated 01/12/21]. Available from: <https://www.clinicaltrials.gov/ct2/show/NCT02658968> [Accessed 07/02/21]
12. Kolstad A, Madsbu U, Beasley M, *et al.* 2018. LYMRIT 37-01: A phase I/II study of ¹⁷⁷Lu-lilotomab satetraxetan (Betalutin[®]) antibody-radionuclide-conjugate (ARC) for the treatment of relapsed non-Hodgkin's lymphoma (NHL) — analysis with 6-month follow-up. *Blood*: 10.1182/blood-2018-99-110555

13. American Cancer Society. Types of B-cell lymphoma. [Updated 01/29/19]. Available from: <https://www.cancer.org/cancer/non-hodgkin-lymphoma/about/b-cell-lymphoma.html> [Accessed 08/25/21]
14. Surveillance Epidemiology and End Results Program. Table 23.1 Cancer of the Prostate (Invasive). Available from: https://seer.cancer.gov/archive/csr/1975_2017/results_merged/sect_23_prostate.pdf [Accessed 08/09/21]
15. U.S. Cancer Statistics Working Group. U.S. cancer statistics data visualizations tool, based on 2019 submission data (1999-2017). [Updated 06/15/20]. Available from: <https://gis.cdc.gov/Cancer/USCS/#/AtAGlance/> [Accessed 09/12/20]
16. American Cancer Society. 2020. *Cancer facts & figures 2020*. Atlanta, GA: American Cancer Society
17. US Preventive Services Task Force. Screening for Prostate Cancer: US Preventive Services Task Force Recommendation Statement. Available from: <https://www.uspreventiveservicestaskforce.org/home/getfilebytoken/zYdjLaTCTBVUwgJTn zpVXr> [Accessed 06/24/21]
18. Kelly S, Anderson W, Rosenberg P, *et al.* 2018. Past, current, and future incidence rates and burden of metastatic prostate cancer in the United States. *Eur Urol Focus* 4(1): 121-27
19. ClinicalTrials.gov. A Trial of 177Lu-PSMA617 Theranostic Versus Cabazitaxel in Progressive Metastatic Castration Resistant Prostate Cancer (TheraP). [Updated 09/26/19]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03392428> [Accessed 07/02/21]
20. Clinicaltrials.gov. Study of 177Lu-PSMA-617 In Metastatic Castrate-Resistant Prostate Cancer (VISION). [Updated 07/27/21]. Available from: <https://www.clinicaltrials.gov/ct2/show/NCT03511664> [Accessed 08/03/21]
21. NorCal CarciNet. Northern California CarciNET community website. Available from: <https://norcalcarcinet.org/component/tags/tag/prrt> [Accessed 09/18/20]
22. The Carcinoid Cancer Foundation. Treatment options. Available from: <https://www.carcinoid.org/for-patients/treatment/treatment-options/> [Accessed 09/19/20]
23. Neuroendocrine Tumor Research Foundation. Treatment of neuroendocrine tumors: nuclear medicine treatments for neuroendocrine tumors. Available from: <https://netrf.org/for-patients/nets-info/net-treatment/nuclear-medicine/> [Accessed 09/19/20]
24. The Healing Net Foundation. Nuclear medicine - peptide receptor radionuclide therapy (PRRT). Available from: <https://www.thehealingnet.org/nuclearmedicine-prrt> [Accessed 12/22/20]
25. PRRTInfo.Org. What is PRRT? Available from: <http://prrtinfo.org/prrt> [Accessed 24/05/21]
26. National Comprehensive Cancer Network. 2018. *Neuroendocrine tumors: guidelines for patients*. Plymouth Meeting, PA: National Comprehensive Cancer Network

27. Cancer.Net. Neuroendocrine tumors: types of treatment. [Updated 04/15/19]. Available from: <https://www.cancer.net/cancer-types/neuroendocrine-tumors/types-treatment> [Accessed 09/19/20]
28. American Society for Radiation Oncology. Additional treatment options. Available from: <https://rtanswers.org/How-does-radiation-therapy-work/Additional-Treatment-Options> [Accessed 22/12/20]
29. Mayo Clinic. 2020. Neuroendocrine tumors: Diagnosis and treatment. [Updated 09/16/20]. Available from: <https://www.mayoclinic.org/diseases-conditions/neuroendocrine-tumors/diagnosis-treatment/drc-20465865> [Accessed 08/11/20]
30. Cancer Treatment Centers of America. Peptide receptor radionuclide therapy (PRRT). [Updated 09/14/21]. Available from: <https://www.cancercenter.com/cancer-types/neuroendocrine-tumors/treatments/peptide-receptor-radionuclide-therapy> [Accessed 05/03/21]
31. MD Anderson Cancer Center. 2020. MD Anderson. 9 things to know about neuroendocrine tumors. [Updated 2/26/2020]. Available from: <https://www.mdanderson.org/cancerwise/neuroendocrine-tumors--9-things-to-know.h00-159379578.html> [Accessed 11/08/20]
32. Lee D. 2020. Interview with Michelle Bruno at Avalere Health [Telephone]. 10/07/20
33. Leukemia & Lymphoma Society. Immunotherapy. Available from: <https://www.lls.org/treatment/types-treatment/immunotherapy> [Accessed 07/09/21]
34. Venugopal P. Treatment Approaches for Low Grade Lymphomas. [Updated 03/01/17]. Available from: <https://www.youtube.com/watch?v=A5y5GNjIDYY> [Accessed 07/29/21]
35. Cutaneous Lymphoma Foundation. 2014. *Understanding treatment options in cutaneous lymphoma*. Birmingham: Cutaneous Lymphoma Foundation
36. Lymphoma Research Foundation. Getting the facts: radioimmunotherapy. Available from: https://lymphoma.org/wp-content/uploads/2017/07/LRF_FACTSHEET_RADIOIMMUNOTHERAPY.pdf [Accessed 07/29/21]
37. Us TOO International. 2021. Home. Available from: <https://www.ustoo.org/> [Accessed 09/14/21]
38. Cancer.Net. Treatment of metastatic castration-resistant prostate cancer. Available from: <https://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/treatment-metastatic-castration-resistant-prostate-cancer> [Accessed 11/10/20]
39. Urology Care Foundation. mCRPC: What you should know fact sheet. Available from: <https://www.urologyhealth.org/educational-materials/mcrpc-what-you-should-know> [Accessed 11/10/20]
40. Prostate Cancer Research Institute. 2018. *The prostate cancer staging guide*. Culver City, CA: Prostate Cancer Research Institute

41. National Cancer Institute. Prostate Cancer Treatment (PDQ®)—Patient version. [Updated 10/09/20]. Available from: https://www.cancer.gov/types/prostate/patient/prostate-treatment-pdq#link/_147 [Accessed 11/10/20]
42. CancerCare. 2016. *Metastatic prostate cancer*. New York, NY: CancerCare
43. American Cancer Society. Treating prostate cancer. [Updated 07/11/20]. Available from: <https://www.cancer.org/cancer/prostate-cancer/treating.html> [Accessed 11/10/20]
44. Us TOO International. Treatment options. Available from: <https://www.ustoo.org/Treatment-Options#AdvancedProstateCancer> [Accessed 09/03/21]
45. Zero Cancer. 2018. *Managing advanced prostate cancer*. Alexandria, VA: Zero Cancer
46. Prostate Conditions Education Council. Advanced disease. Available from: <https://www.prostateconditions.org/about-prostate-conditions/prostate-cancer/advanced-disease> [Accessed 09/19/20]
47. Janssen. My prostate cancer roadmap. [Updated 05/2020]. Available from: <https://www.myprostatecancerroadmap.com/evaluating-your-options.html> [Accessed 11/10/20]
48. Accreditation Council for Graduate Medical Education. 2020. *ACGME program requirements for graduate medical education in nuclear medicine*. Chicago, IL: ACGME
49. Accreditation Council for Graduate Medical Education. 2020. *ACGME program requirements for graduate medical education in radiation oncology*. Chicago, IL: ACGME
50. Accreditation Council for Graduate Medical Education. 2021. *ACGME program requirements for graduate medical education in nuclear radiology*. Chicago, IL: ACGME
51. Nuclear Medicine Technology Certification Board. Component of preparedness. Available from: https://www.nmtcb.org/documents/resources/NMTCB_COPS_2020.pdf [Accessed 10/29/20]
52. American Registry of Radiologic Technologists. Nuclear medicine technology - examination. Available from: <https://assets-us-01.kc-usercontent.com/406ac8c6-58e8-00b3-e3c1-0c312965deb2/a3eb0a18-02a8-420c-b480-1bcd2ecf71ab/Nuclear%20Medicine%20Technology%20Content%20Specifications2017.pdf> [Accessed 07/30/21]
53. American Osteopathic Board of Internal Medicine. Endocrinology certification process. Available from: <https://certification.osteopathic.org/internal-medicine/certification-process-overview/endocrinology/written-exam/> [Accessed 09/28/20]
54. American Osteopathic Board of Internal Medicine. Gastroenterology certification process. Available from: <https://certification.osteopathic.org/internal-medicine/certification-process-overview/gastroenterology/written-exam/> [Accessed 09/28/20]
55. Accreditation Council for Graduate Medical Education. 2020. *ACGME program requirements for graduate medical education in endocrinology diabetes and metabolism*. Chicago, IL: ACGME

56. Accreditation Council for Graduate Medical Education. 2020. *ACGME program requirements for graduate medical education in gastroenterology*. Chicago, IL: ACGME
57. American Board of Internal Medicine. 2020. *Endocrinology, diabetes, & metabolism certification exam blueprint*. Philadelphia, PA: ABIM
58. American Board of Internal Medicine. 2020. *Gastroenterology certification examination blueprint*. Philadelphia, PA: ABIM
59. The American Board of Urology I. 2020. *2021 information for applicants and candidates*. Charlottesville, VA
60. Accreditation Council for Graduate Medical Education. 2020. *ACGME program requirements for graduate medical education in hematology and medical oncology*. Chicago, IL: ACGME
61. Accreditation Council for Graduate Medical Education. 2020. *ACGME program requirements for graduate medical education in urology*. Chicago, IL: ACGME
62. American Board of Internal Medicine. 2020. *Medical oncology certification examination blueprint*. Philadelphia, PA: ABIM
63. Gopal A. 2021. Case study: clinical readiness in the US. Launch of the Radioligand Therapy Readiness Assessment Framework; 06/09/21; Online event
64. Mitra E. 2021. Personal communication by email: 08/12/21
65. Charlton M, Schlichting J, Chioreso C, *et al*. Challenges of rural cancer care in the United States. [Updated 09/15/15]. Available from: <https://www.cancernetwork.com/view/challenges-rural-cancer-care-united-states> [Accessed 08/25/21]
66. Hope TA, Abbott A, Colucci K, *et al*. 2019. NANETS/SNMMI Procedure Standard for Somatostatin Receptor-Based Peptide Receptor Radionuclide Therapy with (177)Lu-DOTATATE. *J Nucl Med* 60(7): 937-43
67. National Comprehensive Cancer Network. 2021. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): B-cell Lymphomas*. Plymouth Meeting, PA: NCCN
68. National Comprehensive Cancer Network. 2021. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Neuroendocrine and Adrenal Tumors*. Plymouth Meeting, PA: NCCN
69. Halfdanarson TR, Strosberg JR, Tang L, *et al*. 2020. The North American Neuroendocrine Tumor Society Consensus Guidelines for Surveillance and Medical Management of Pancreatic Neuroendocrine Tumors. *Pancreas* 49(7): 863-81