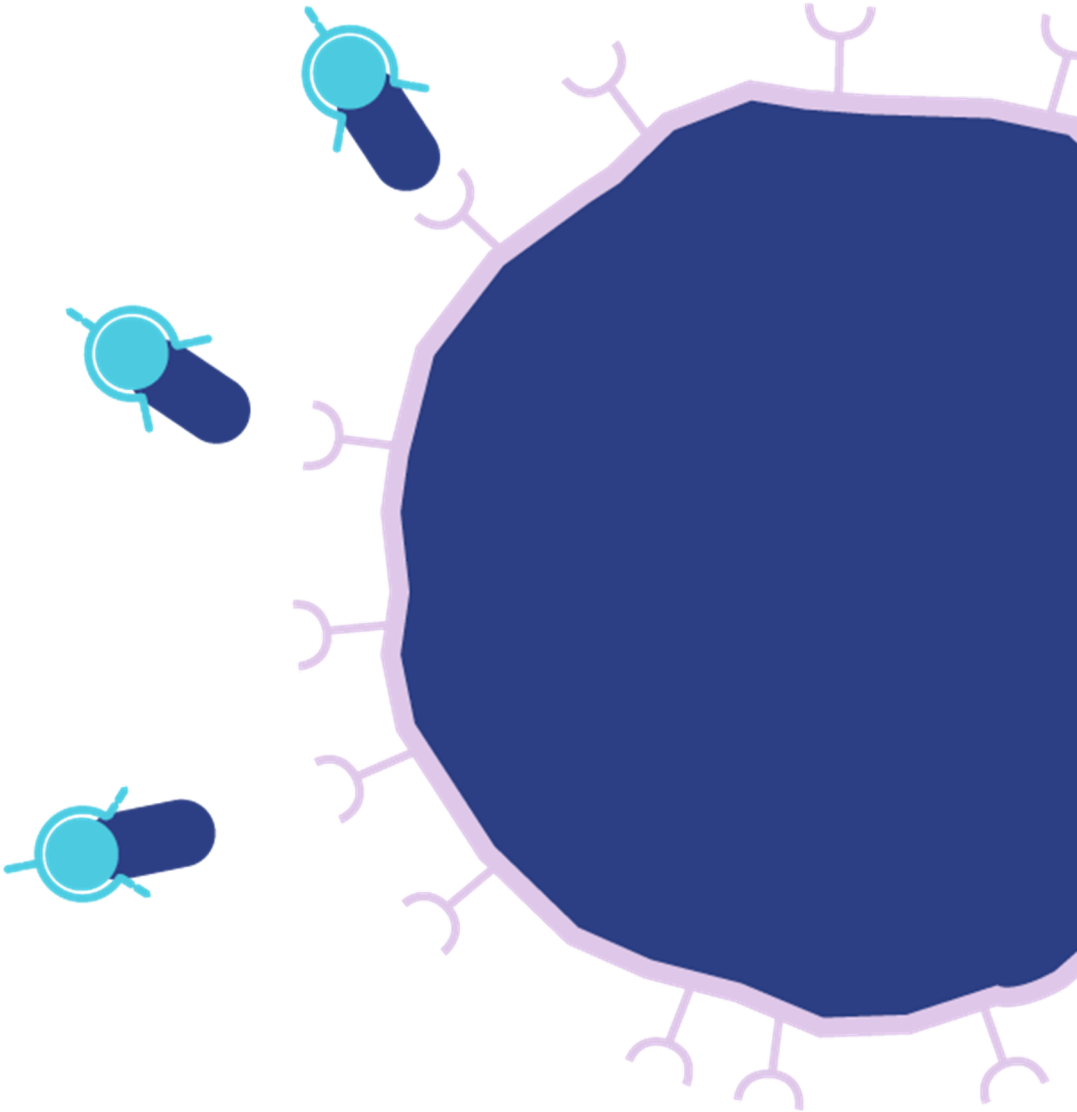


The Health Policy Partnership
[research, people, action]

Health system readiness for radioligand therapy in the US

Health information

Working paper

November 2021

This working paper has been developed by The Health Policy Partnership and Avalere Health in collaboration with a US Expert Advisory Group. The group has had full editorial control over all national-level outputs. The project is supported with funding from Advanced Accelerator Applications, a Novartis Company, with additional support from Nordic Nanovector.

Contents

Please cite as: The Health Policy Partnership. 2021. *Health system readiness for radioligand therapy in the US: health information (working paper)*. London: The Health Policy Partnership.

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 health information, one of the five domains of the Radioligand Therapy Readiness Assessment Framework (*Figure 1*).[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 looks at how different types of data are collected and used for radioligand therapy, and how well current data collection approaches meet the needs of US decision-makers, healthcare providers and people with cancer. Throughout the paper, we focus on the situation in neuroendocrine tumors, lymphoma, and prostate cancer.

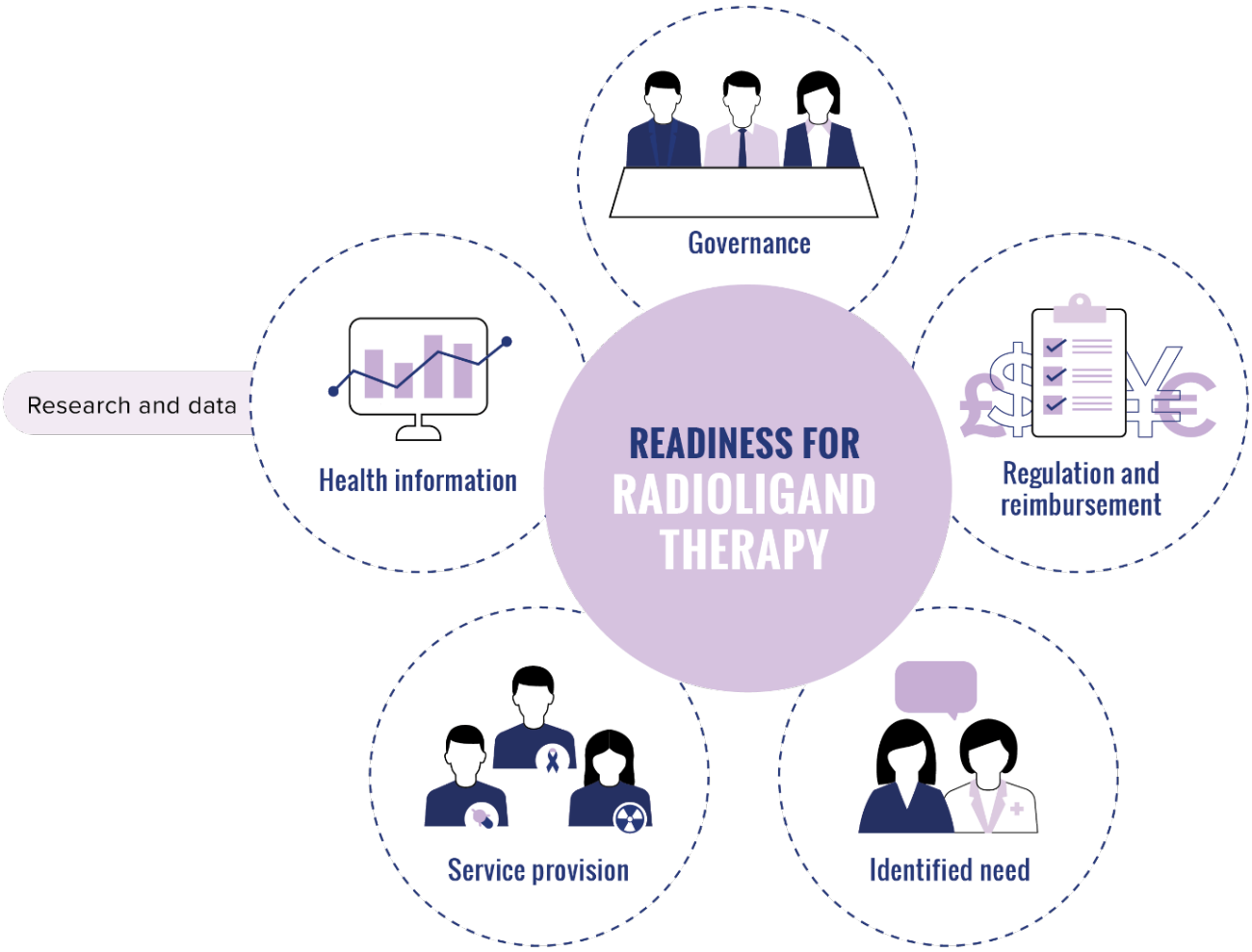
- This working paper is supported by other documents on health system readiness for radioligand therapy in the US. For more details, please visit: www.radioligandtherapy.com/framework/US

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 health information?

Data collection and analysis are key components of high-quality healthcare. The US has a complex network of public and private health data collection systems across national, state, provider, and payer levels.[2] Data may be collected through mechanisms including: medical records from hospitals, physicians and health plans; health surveys; disease registries; and administrative or billing records.[2] Insights drawn from these data can help providers, decision-makers and policymakers improve existing healthcare delivery and prepare for future challenges.[3]

What does good health information look like for radioligand therapy?

Planning for the broader integration of radioligand therapy into cancer care requires consistent collection and careful analysis of data, which can then be used to guide decision-making. To better understand when radioligand therapy could be most beneficial, we need to collect various types of data on the cancers in which the therapy is used, as well as on potentially eligible patients. Relevant data should be collected in trials and real-world settings to learn more about the impact of radioligand therapy. Additionally, information from disease registries that collect data on radioligand therapy should be published regularly to allow for comparisons of trends over time. Patient-reported experience and outcomes data should also be collected and used to inform clinical decision-making and guide service improvements. Economic data should be collected to understand the cost-effectiveness and impact of the approach, providing a foundation for improved funding and reimbursement approaches over time.

1 Research and data

Summary assessment

Indicator	Assessment
Is there sufficient data collection on radioligand therapy in the US to guide future planning and practice?	Data collection practices in the US are fragmented and do not adequately capture how radioligand therapy is used in clinical practice. There is no data collection mechanism that is specific to radioligand therapy. Disease-specific health information sources for smaller populations, such as neuroendocrine tumors (NETs) and lymphoma, capture information on treatment patterns but lack information specific to radioligand therapy. For both of these indications, clinical trial data on radioligand therapy continue to evolve. There are many prostate cancer registries that collect various types of health data for different purposes and populations. These registries do not include radioligand therapy as it is not approved by the US Food and Drug Administration (FDA). However, data on patterns of care for radioligand therapy are being collected in the clinical trial setting. While there are some economic data for early radioligand therapies for lymphoma, economic data are otherwise limited. Patient-reported data are lacking, although some health information sources have recently begun to investigate such data for prostate cancer and NETs.

1.1 Clinical trial data

More clinical trial data are needed to fully understand who might benefit from radioligand therapy and at what stage of their disease. Various trials are underway in the US:

- Clinical trial data for radioligand therapy in neuroendocrine tumors (NETs) are rapidly evolving. Data from the NETTER-1 trial have built an important foundation for clinical knowledge.[4 5] Additional clinical trials in radioligand therapy for NETs, such as NETTER-2 and COMPETE, are in the recruitment phase.[6 7]
- Data on currently licensed therapies have provided evidence of the potential value of radioligand therapy in lymphoma.[8-10] Ongoing clinical trials are exploring the use

of innovative radioligand therapies for various types of lymphoma, such as the phase 1 and 1/2 LYMRIT-37 trials.[11-13]

- Results from phase 2 and 3 clinical trials in advanced prostate cancer have recently been published, notably including the TheraP and VISION trials.[14 15] Evidence from these trials will be vital for approval by the US Food and Drug Administration (FDA). Based on evidence from the VISION trial, the FDA has granted breakthrough therapy designation to lutetium-177–PSMA-617 for the treatment of people with metastatic castration-resistant prostate cancer.[16]

    - For more information about the role of clinical trial data in influencing regulation on radioligand therapy in the US, read the working paper on regulation and reimbursement.

1.2 Registry data

Population-based cancer registries collect comprehensive data for many different indications, but it is not clear whether they include radioligand therapy. The two largest registries are the Surveillance, Epidemiology, and End Results program and the National Program of Cancer Registries (*Box 1*).[17 18] Together, they collect data on all people with cancer in the US, and their data form the basis for the US Cancer Statistics, the official repository for federal cancer data.[17 19] Radioligand therapy data may not always be captured, as these databases typically collect information only on first-line treatments and categorize approaches like radioligand therapy under “other”.

Box 1. Population-based cancer registries

Surveillance, Epidemiology, and End Results (SEER) is governed by the National Cancer Institute and covers around 48% of people with cancer in the US.[18] Data are gathered from various registries and collect information on demographics, primary tumor site, tumor pathology and stage at diagnosis, first course of treatment, and survival.[18] SEER is considered representative of the diverse US population.[18]

The **National Program of Cancer Registries** comprises 48 state and territory registries that are supported by the Centers for Disease Control and Prevention.[20] It represents 97% of people with cancer in the US. Data collected via the constituent registries include demographics, therapies, and patient outcomes.[17]

These registries are sometimes linked with other data sources to enhance our understanding of how cancer therapies are used:

- A linkage between the SEER registry and Medicare-claims data means that an individual's service use and cost data are easily connected and evaluated based on their cancer diagnosis.[21]
- Links between SEER and the Medicare Health Outcomes Survey allow examination of health status, longitudinal treatment, and additional health outcomes information.[22]

As of October 2021, the most recently published data from both databases are from 2018.

Proprietary registries can also be used to examine treatment patterns and health outcomes in other settings, but access to these data are restricted.[23] Proprietary registries are owned by private companies and contain data that are typically used for commercial purposes. Data for these registries can be collected from hospitals, or any other healthcare facility, physician practice, or research organization.[23] There is often a fee for external institutions to access the data, but the registry-owning companies may publish reports on topics of their choosing. Data collection through proprietary registries may become important for the analysis of radioligand therapy should healthcare facilities deliver the therapy currently and in the future.

1.2.1 Electronic health record data

Electronic health records (EHRs) are a valuable tool for hospitals and hospital networks, though information collected in them may not always be consistent or comparable. Hospital-based registries draw data from EHRs for people who use that particular hospital,[24] [25] and would likely include radioligand therapy if the approach were provided there. Data from hospital registries are primarily used to inform improvements in patient care, physician education, research, and facility resource utilization.[10] However, an expert has highlighted that the data specific to radioligand therapy may be difficult to extract and, therefore, not readily analyzed.[26] For hospital-based registries that involve multiple institutions, these data help establish common care standards and performance benchmarking information across facilities.[10] Flatiron Health has developed a nationwide cancer-specific EHR, which has been used to assess treatment patterns of patients in an effort to improve treatment and quality of life (*Real-world example 1*). However, an expert has noted that the collection of data specific to radioligand therapy is limited in oncology-focused databases because these therapies are often not considered a standard part of medical oncology.[27]

Real-world example 1. Flatiron Health electronic health record

The Flatiron Health EHR collects real-world data from community practices, medical centers, and hospitals, with the aim of using those data to drive improvements in cancer care.[28] The system has approximately three million patient records from more than 280 community sites and seven major academic cancer centers across the US.[28]

Many researchers and healthcare providers have used data from Flatiron Health to investigate treatment patterns and improve treatment options for certain types of cancer.[28] For example, Peter Martin from the Lymphoma Program at Cornell along with co-authors used data from the Flatiron Health EHR to evaluate treatment and outcomes for more than 3,000 people with mantle cell lymphoma.[29] The study found that real-world treatment patterns did not always follow guideline recommendations, and highlighted the need to develop treatment regimens that can be delivered effectively in community practices where the majority of lymphoma care occurs.[29] The study also highlighted some limitations of the data from Flatiron Health, including a lack of response and progression data, and the reason for treatment selection was not captured.

Studies have leveraged the real-world data from EHRs to assess treatment patterns and outcomes of people with NETs. Recently, the Patient-Centered Outcomes Research Institute awarded funding to the University of Iowa to conduct a comparative effectiveness research study focused on therapy options for NETs.[30] One of the aims of the study is to compare effectiveness of radioligand therapy regimens on outcomes of renal toxicity, disease progression, and quality of life. Given that there are currently no large-scale national prospective studies of patients with NETs, this study is a positive step in collecting real-world data on NETs outcomes and use of radioligand therapy.[30]

The siloed nature of cancer registries limits their use for health planning, but initiatives are underway to create more unified EHR systems. The variety of EHR operating systems, alongside institution-specific data collection, creates discrepancies and inconsistencies in available data.[31] An expert has suggested that some companies have found it difficult to collect data that are useful in EHRs, with a lot of data missing or 'messy', making them difficult to extract and analyze.[27] Ultimately, this limits the value of such registries for health research and planning. Given the prevalence of cancer in the US and its high priority on the nation's healthcare agenda, efforts are ongoing to aggregate and unify cancer data from the various EHR sources into larger patient data sets.[32] The COVID-19 pandemic has prompted rapid action on EHR unification, with the National COVID Cohort Collaborative emerging as a possible model for future data harmonization in other areas of the health system (*Real-world example 2*).

Real-world example 2. National COVID Cohort Collaborative

During the COVID-19 pandemic, fragmented data and data collection systems have made it difficult to understand aspects such as patient outcomes and risk factors. The National Institutes of Health created the National COVID Cohort Collaborative (N3C) to become a centralized data source for the research community.[33]

The N3C collects, cleans and standardizes data from EHRs across the US, and grants access to de-identified data to academic researchers, clinicians, and citizen scientists investigating COVID-19.[34] [35] To date, the database has 8.6 million patient records, mostly from hospital-based settings.[35]

The initiative is a successful example of how a broad range of clinical data can be harmonized and safely shared. The N3C could become a model for future interoperability and data integration in radioligand therapy and beyond.

1.2.2 Registry data on NETs

Many registries have been created specifically for people diagnosed with NETs, which may collect different data on radioligand therapy. Some registries are hospital-based, such as the University of Iowa Neuroendocrine Tumor Registry, or are part of larger registries like the Oregon Index of Endocrine Neoplasias (ORION).[24] [36] Alternatively, data may be collected by specific institutions or organizations:

- RegisterNET is a voluntary registry collecting medical history, treatment modalities, quality of life, and other information in a prospective registry.[37]
- University of Nebraska Medical Center Integrated Cancer Repository for Cancer Research (iCaRe2) aggregates data from numerous registries, focusing on small and rural hospitals or cancer centers.[38] One component registry is the Neuroendocrine Tumor Registry (NETR).

Current and prior efforts to create international, national, and local NETs registries have been challenging, with organizations and institutions facing difficulties in cross-institutional data sharing, extracting and obtaining meaningful data, and a lack of funding and staff to update the registry once it is established – leading to a lack of success.[26] [39]

1.2.3 Registry data on lymphoma

Data are collected on lymphoma in the US, but limited information is collected on radioligand therapy specifically. There are a number of disease-specific registries that focus on blood cancers in general or very specific lymphoma subtypes. For example, the Leukemia & Lymphoma Society National Patient Registry gathers information from the medical records of people with blood cancers, including lymphoma, to understand more about treatment patterns, health outcomes, and real-world experiences.[40] If a person who has received radioligand therapy joins the registry, their data would be included. Shorter-term studies that collect data on lymphoma subtypes include the National LymphoCare Study, which looked to better understand treatment regimens, patterns of care, and outcomes of people with follicular lymphoma.[41] This decade-long, multicenter, observational study collected data on treatment choices, including radioligand therapy, and ended in 2014.[42-44] The study highlighted that a diverse range of first-line treatment approaches were used despite clear guidelines on treatment sequencing.[45]

1.2.4 Registry data on prostate cancer

Data collection for prostate cancer is well established in the US, but will require expansion should radioligand therapy be approved for use. There are numerous prostate-cancer-specific registries covering different populations (*Box 2*), but their use in service improvement will vary. It is unclear whether these registries contribute to the national registries or large-scale health system planning initiatives. It is likely that registries collecting state-level data contribute at that level. Unsurprisingly, none of them collect information specific to radioligand therapy, as its use is not yet approved by the FDA.[46] Such registries may, in time, have an important role in collecting data on radioligand therapy, but such efforts will require decision-makers to commit funding and resources.

Box 2. Prostate cancer registries

The following are some examples of the many prostate-cancer-specific registries that have various purposes and cover different populations:

- The **AQUA registry** collects data on diagnosis, treatment, and outcomes from people with urologic conditions including prostate cancer, with the aim of tracking and potentially improving quality measures at the practice and provider level.[46] Some practices that participate in AQUA share their administrative data on radioligand therapy; however, an expert has noted that AQUA may not be actively processing these data.[27]
- The **CaPSURE registry**, from the University of California San Francisco, draws data from 43 community urology practices, academic medical centers, and Veterans Health Administration hospitals throughout the US.[47] The registry includes data on various levels of treatment for people with all stages of prostate cancer.
- The **MPower Prostate Cancer Registry** is one example of many large, state-based registries that collect treatment and outcomes data for people with prostate cancer.[48]
- The international **IRONMAN registry** collects diagnostic, treatment, survival, and patient-recorded outcomes data from people with several types of advanced prostate cancer, in academic and community practices.[49] The registry covers Australia, Brazil, Canada, Ireland, Spain, Sweden, Switzerland, Nigeria, the UK, and the US, and aims to recruit 5,000 patients across 14 countries by 2022.[49 50]

1.3 Economic data

While radioligand therapy has been approved for treatment of NETs for many years, there are very limited economic data publicly available. Researchers speculate that the increased frequency of NETs diagnoses could place a significant burden on the US health system.[51] The lack of available economic data could hinder the ability to establish and utilize innovative approaches to funding and reimbursement of the therapy, therefore impeding the formation of centers of excellence in radioligand therapy throughout the US.[52]

Despite radioligand therapy having been approved for lymphoma longer than for NETs, and the availability of some economic data from previously established radioligand therapies, these data may not reflect the current cost and situation in the US.[26] More concrete data on the cost-effectiveness of radioligand therapy for lymphoma are needed to increase acceptance and improve use of both existing and potential therapies in the US.[52 53]

Conclusion

While several mechanisms for tracking cancer statistics and patterns of care exist, few health information sources collect data on radioligand therapy. As such, there are limited tracking data relating to the use of radioligand therapy or its implications for workforce or system-level planning for cancer care.

Given the limited amount of real-world data for rare diseases,[54] and specifically for radioligand therapy in NETs,[55] there is a clear need to increase data collection efforts for existing therapies. None of the national registries for cancer collect data specific to radioligand therapy, and data that could inform future practice or planning for oncology care at the national level are scarce. However, given the broad network of registries across the country, there is a strong rationale to establish a common cancer data set that includes radioligand therapy, which also allows individual institutions, interest groups, and states or regions to collect data that serve their needs. This will require adequate and long-term funding and resources – as well as long-term strategic planning and engagement with many stakeholders to determine the right data elements – as few registries currently include information on radioligand therapy, with most focusing on first-line treatments only.

A concerted effort from the clinical and advocacy communities will be needed to guide the future direction and structure of data collection for radioligand therapy. All stakeholders need to work together to ensure that meaningful and useful data are collected on radioligand therapy – and consider how to include data on patient-reported outcomes, cost-effectiveness, and service delivery. This will be essential to help establish a robust health information system for radioligand therapy, which is useful to decision-makers, payers and providers. It may not require a significant system overhaul; there is much that can be done to improve or expand existing data collection mechanisms. Identifying and establishing the appropriate nomenclature for radioligand therapy data collection will be a first step toward identifying existing use or integrating its inclusion into existing registries. The data housed in many registries have yet to be mined or analyzed in ways that could inform the implementation of radioligand therapy.[27] Until they are, a gap in knowledge around the therapy's application in practice will remain.

Linking disease-specific registries to claims or outcomes data on radioligand therapy could be helpful to improve care in the future. Once radioligand therapy has been fully integrated into existing NETs, lymphoma and prostate cancer registries, further links to claims or outcomes data would be helpful opportunities to gather real-world evidence on the approach. While phase III clinical trial data remain the gold standard, real-world data have the potential to strengthen the radioligand therapy landscape. It is important to capture information on therapy administration, disease management pathways, and retreatment. The development of registries specific to administration of radioligand therapy, health outcomes, and patients' quality of life, can support better adoption across the US. Thorough oversight of the use and impact of radioligand therapy for people undergoing treatment will be vital to ensure the therapy's use in cancer care is optimized and will ultimately benefit all eligible patients in the years to come.

References

1. The Health Policy Partnership. 2021. *Radioligand Therapy Readiness Assessment Framework.* London: HPP

2. Agency for Healthcare Research and Quality. Race, Ethnicity, and Language Data: Standardization for Health Care Quality Improvement: 5. Improving Data Collection across the Health Care System. [Updated May 2018]. Available from: https://www.ahrq.gov/research/findings/final-reports/iomracereport/reldata5.html [Accessed 02/16/21]

3. Institute of Medicine. 2010. *Clinical Data as the Basic Staple of Health Learning: Creating and Protecting a Public Good: Workshop Summary.* Washington DC: National Academies Press

4. Clinicaltrials.gov. A Study Comparing Treatment With 177Lu-DOTA0-Tyr3-Octreotate to Octreotide LAR in Patients With Inoperable, Progressive, Somatostatin Receptor Positive Midgut Carcinoid Tumours (NETTER-1). Available from: https://clinicaltrials.gov/ct2/show/NCT01578239 [Accessed 12/15/20]

5. Zhang J, Kulkarni HR, Singh A*, et al.* 2019. Delayed Response (Partial Remission) 3 Years After Peptide Receptor Radionuclide Therapy in a Patient Participating in the NETTER-1 Trial. *Clin Nucl Med* 44(3): 223-26

6. ClinicalTrials.gov. Study to Evaluate the Efficacy and Safety of Lutathera in Patients With Grade 2 and Grade 3 Advanced GEP-NET (NETTER-2). [Updated 04/01/21]. Available from: https://clinicaltrials.gov/ct2/show/NCT03972488 [Accessed 08/03/21]

7. Clinicaltrials.gov. Efficacy and Safety of 177Lu-edotreotide PRRT in GEP-NET Patients (COMPETE). [Updated 04/13/21]. Available from: https://clinicaltrials.gov/ct2/show/NCT03049189 [Accessed 08/03/21]

8. Davies AJ. 2007. Radioimmunotherapy for B-cell lymphoma: Y90 ibritumomab tiuxetan and I(131) tositumomab. *Oncogene* 26(25): 3614-28

9. Morschhauser F, Radford J, Van Hoof A*, et al.* 2008. Phase III trial of consolidation therapy with yttrium-90-ibritumomab tiuxetan compared with no additional therapy after first remission in advanced follicular lymphoma. *J Clin Oncol* 26(32): 5156-64

10. Witzig TE, Gordon LI, Cabanillas F*, et al.* 2002. Randomized controlled trial of yttrium-90-labeled ibritumomab tiuxetan radioimmunotherapy versus rituximab immunotherapy for patients with relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma. *J Clin Oncol* 20(10): 2453-63

11. 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]

12. 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]

13. 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

14. Sartor O, de Bono J, Chi KN*, et al.* 2021. Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. *N Engl J Med*: 10.1056/NEJMoa2107322:

15. Hofman MS, Emmett L, Sandhu S*, et al.* 2021. [(177)Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial. *Lancet* 397(10276): 797-804

16. Novartis. Novartis receives FDA Breakthrough Therapy designation for investigational 177Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer (mCRPC). Available from: https://www.novartis.com/news/novartis-receives-fda-breakthrough-therapy-designation-investigational-177lu-psma-617-patients-metastatic-castration-resistant-prostate-cancer-mcrpc [Accessed 07/20/21]

17. Centers for Disease Control and Prevention. National Program of Cancer Registries (NPCR): about the program. Available from: https://www.cdc.gov/cancer/npcr/about.htm [Accessed 08/03/21]

18. National Cancer Institute. Overview of the SEER Program. Available from: https://seer.cancer.gov/about/overview.html [Accessed 08/03/21]

19. American Cancer Society. Cancer Surveillance Programs in the United States. Available from: https://www.cancer.org/cancer/cancer-basics/cancer-surveillance-programs-and-registries-in-the-united-states.html [Accessed 04/09/21]

20. Center for Disease Control and Prevention. Contact a Local Registry - NPCR Program Contacts by Funding Status. *National Program of Cancer Registries (NPCR).* Available from: https://nccd.cdc.gov/dcpc_Programs/index.aspx#/3 [Accessed 07/27/21]

21. National Cancer Institute. SEER-Medicare: Brief Description of the SEER-Medicare Database. Available from: https://healthcaredelivery.cancer.gov/seermedicare/overview/ [Accessed 08/03/21]

22. National Cancer Institute. About the SEER-MHOS Data Resource. Available from: https://healthcaredelivery.cancer.gov/seer-mhos/overview/ [Accessed 04/09/21]

23. Gliklich RE, Leavy MB, Dreyer NA. 2020. Principles of registry ethics, data ownership, and privacy. *Registries for Evaluating Patient Outcomes: A User's Guide [Internet] 4th edition*. Rockville (MD): Agency for Healthcare Research and Quality (US)

24. Oregon Health & Science University Knight Cancer Institute. Cancer Registries. Available from: https://www.ohsu.edu/knight-cancer-institute/cancer-registries [Accessed 04/09/21]

25. National Cancer Institute. Hospital-Based Registries. Available from: https://training.seer.cancer.gov/registration/types/hospital.html [Accessed 04/09/21]

26. Mittra E. 2021. Personal communication by email: 08/12/21

27. Shelton J. 2021. Interview with Michelle Bruno at Avalere Health [Telephone]. 03/19/21

28. Flatiron Health. About us. Available from: https://flatiron.com/about-us/ [Accessed 07/23/21]

29. Martin P, Wang M, Kumar A*, et al.* Real-world (RW) treatment (tx) patterns and outcomes of 3,455 previously untreated mantle cell lymphoma (MCL) patients (pts) in U.S. routine clinical practice. Available from: https://meetinglibrary.asco.org/record/201548/abstract [Accessed 07/23/21]

30. Patient-Centered Outcomes Research Institute. Comparative Effectiveness Research for Neuroendocrine Tumors (CER-NET). [Updated 05/20/21]. Available from: https://www.pcori.org/research-results/2021/comparative-effectiveness-research-neuroendocrine-tumors-cer-net [Accessed 07/01/21]

31. Reisman M. 2017. EHRs: The Challenge of Making Electronic Data Usable and Interoperable. *P&T* 42(9): 572-75

32. Thompson CA, Jin A, Luft HS*, et al.* 2020. Population-Based Registry Linkages to Improve Validity of Electronic Health Record–Based Cancer Research. *Cancer Epidemiology Biomarkers & Prevention* 29(4): 796-806

33. National Institute of Health. N3C Data Overview. [Updated 06/25/21]. Available from: https://ncats.nih.gov/n3c/about/data-overview [Accessed 07/07/21]

34. Ferguson C. It took a pandemic, but the US finally has (some) centralized medical data. Available from: https://www.technologyreview.com/2021/06/21/1026590/us-covid-database-n3c-nih-privacy/ [Accessed 07/07/21]

35. National COVID Cohort Collaborative. N3C Cohort Exploration: N3C Data Enclave Statistics. [Updated 10/28/21]. Available from: https://covid.cd2h.org/dashboard/ [Accessed 10/29/21]

36. Sharma N, Naraev BG, Engelman EG*, et al.* 2017. Peptide Receptor Radionuclide Therapy Outcomes in a North American Cohort With Metastatic Well-Differentiated Neuroendocrine Tumors. *Pancreas* 46(2): 151-56

37. Clinicaltrials.gov. RegisterNET - A Registry for Neuroendocrine Tumors in the USA (RegisterNET). [Updated 06/11/21]. Available from: https://clinicaltrials.gov/ct2/show/NCT02270567 [Accessed 08/03/21]

38. University of Nebraska Medical Center. The integrated Cancer Repository for Cancer Research (iCaRe2). Available from: https://www.unmc.edu/cancercenter/registry/ [Accessed 09/04/21]

39. Mailman J. Interview with Michelle Bruno at Avalere Health [Telephone]. 10/05/20

40. Leukemia & Lymphoma Society. The LLS National Patient Registry, a project of the Michael J. Garil Patient Data Collective. Available from: https://www.ciitizen.com/lls/ [Accessed 07/05/21]

41. Friedberg JW, Taylor MD, Cerhan JR*, et al.* 2009. Follicular lymphoma in the United States: first report of the national LymphoCare study. *J Clin Oncol* 27(8): 1202-8

42. Wagner-Johnston ND, Link BK, Byrtek M*, et al.* 2015. Outcomes of transformed follicular lymphoma in the modern era: a report from the National LymphoCare Study (NLCS). *Blood* 126(7): 851-7

43. Link BK, Day BM, Zhou X*, et al.* 2019. Second-line and subsequent therapy and outcomes for follicular lymphoma in the United States: data from the observational National LymphoCare Study. *Br J Haematol* 184(4): 660-63

44. ClinicalTrials.gov. An Observational Study of Treatment, Outcomes, and Prognosis in Patients With Follicular Non-Hodgkin's Lymphoma. [Updated 03/23/21]. Available from: https://clinicaltrials.gov/ct2/show/NCT00097565 [Accessed 07/06/21]

45. Friedberg JW, Byrtek M, Link BK*, et al.* 2012. Effectiveness of first-line management strategies for stage I follicular lymphoma: analysis of the National LymphoCare Study. *J Clin Oncol* 30(27): 3368-75

46. Fang R. 2020. Interview with Michelle Bruno at Avalere Health [Telephone]. 09/25/20

47. University of California San Francisco. CaPSURE™. Available from: https://urology.ucsf.edu/research/cancer/capsure [Accessed 09/04/21]

48. Fred Hutch Cures Start Here. MPower Prostate Cancer Registry. Available from: https://www.fredhutch.org/en/research/institutes-networks-ircs/institute-for-prostate-cancer-research/mpower-prostate-cancer-registry.html [Accessed 04/09/21]

49. Clinicaltrials.gov. International Registry to Improve Outcomes in Men With Advanced Prostate Cancer (IRONMAN) (IRONMAN). [Updated 07/09/21]. Available from: https://clinicaltrials.gov/ct2/show/NCT03151629 [Accessed 08/03/21]

50. IRONMAN. Home. Available from: https://ironmanregistry.org/ [Accessed 07/21/21]

51. Simoneaux R. 2020. A Look at the Increasing Incidence of Neuroendocrine Tumors. *Oncology Times* 42(6): 1-4

52. Fahey F, Zukotynski K, Capala J*, et al.* 2014. Targeted radionuclide therapy: proceedings of a joint workshop hosted by the National Cancer Institute and the Society of Nuclear Medicine and Molecular Imaging. *J Nucl Med* 55(2): 337-48

53. Thornton S. 2021. Interview with Lucy Morgan and Chris Melson at The Health Policy Partnership [Telephone]. 07/21/21

54. Optum. 2021. *White paper: Using real-world data to close the rare disease data gap.* Minnesota: Optum

55. Konda B, Rogers SC, Grenade CN*, et al.* 2019. First real-world experience of peptide receptor radionuclide therapy (PRRT) in neuroendocrine tumors (NET) since US FDA approval. *J Clin Oncol* 37(15_suppl): e15691-e91