

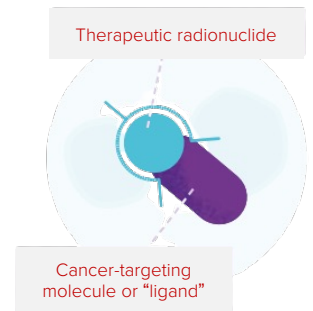


Creating a ready health system for radioligand therapy in the ROK

POLICY ACTION BLUEPRINT

What is radioligand therapy?

Radioligand therapy inhibits the growth and replication of cancer cells by destroying their DNA. A radioligand is made of two parts: a ligand, which targets cancer cells with a particular surface molecule, and radioisotope (RI), which is injected to kill cancer cells with radiation.¹² There are many terms for radioligand therapy, including molecular radiotherapy, peptide-receptor radionuclide therapy (PRRT), or when the ligand used as an antibody, radioimmunotherapy.



Radioligand therapy can deliver the radioisotope and selectively treat targeted cancer cells with radiation, minimizing damage to surrounding healthy cells.^{11 12} This makes radioligand therapy distinct from previous conventional biological and chemical agents, and it has been proven to improve survival and quality of life for patients with certain types of neuroendocrine tumors (NETs).³⁻¹⁰

Readiness for radioligand therapy

To increase accessibility to radioligand therapy within the ROK, we must first ensure **readiness** for the introduction of radioligand therapy and **integration** of radioligand therapy into the existing health system. Therefore, the government should implement a multidisciplinary approach to promptly accept the newly developed treatment at the national level. It should also make sustained effort to ensure that these treatments are properly integrated into the existing system so that they are made available to all people who may benefit from it.

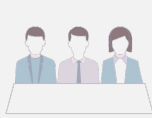
→ **INTEGRATION** is the adoption and assimilation of radioligand therapy into every aspect of a health system (i.e., governance, regulation, reimbursement, funding, and service delivery frameworks) in order to ensure its availability to all people who may benefit from it

→ **READINESS** is the ability of the health system to rapidly and sustainably adapt policies, processes, and infrastructure to support integration of a new radioligand therapy.

6 KEY STRATEGIC CHALLENGES must be addressed to improve the current integration and future readiness for radioligand therapy in the ROK:



Awareness



Cooperation and governance



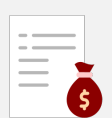
Clinical guidelines and data



Infrastructure and licensing

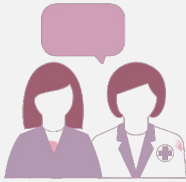


Product approval process



Financial support

6 KEY STRATEGIC CHALLENGES



Awareness

Patients fear treatments that involve radiation, and physicians are not well aware of radioligand therapy. This low awareness of radioligand therapy among patients and physicians result in low awareness within the policymakers of the safety, effectiveness and excellence of the treatment.

WE NEED:

- **Government and relevant associations** to work together to spread correct information and improve negative perceptions of radiation therapy as a whole in the ROK, and actively utilize media to promote the effectiveness of radioligand therapy
- **Multidisciplinary care physicians related to radioligand therapy** to
 - Expand knowledge of treatment by actively attending overseas conferences
 - Form a research group to promote radioligand therapy in the ROK
- **Patient groups associated with Korean Association of Neuroendocrine Tumor (KANT)** to cooperate with each other to build consensus so that policymakers promote policies benefiting patients
- **The National Cancer Center** to promote research by establishing treatment-specific tasks to expand radioligand therapy



Cooperation and governance

Currently, domestic policies related to radioligand therapy are not managed within the Ministry of Health and Welfare (MOHW)'s cancer management policy framework but are overseen by the Ministry of Science and ICT (MSIT) under the existing radioisotope technology support policy. Treatments using radioisotopes are separately managed under disease treatment and technology promotion.

WE NEED:

- **MOHW and the MSIT to closely communicate with each other**, promoting cross-ministerial cooperation and efforts to rapidly introduce further treatment-related technology such as radioligand therapy to the wider medical field.
 - **Ex 1)** Consider to incorporate requirements such as clinical trials, which may be the basis for future product approval, in MSIT's R&D projects, so that the projects for radioisotope industry development and technical support can connect to drugs for disease treatment
 - **Ex 2)** Integrate the regulations on radioisotope safety, which are currently regulated by the *Nuclear Safety Act*, with the regulations on radiopharmaceuticals under the *Pharmaceutical Affairs Act* for efficiency in management of specific radioisotope-related laws



Clinical guidelines and data

Currently, there are no clinical guidelines related to NETs and lymphoma, indications of radioligand therapy, and there are many difficulties in securing high-level data to develop these domestic clinical guidelines

WE NEED:

- **The National Cancer Center (NCC), the Korean Society of Medical Oncology (KSMO), and the Korean Society of Nuclear Medicine (KSNM)** to encourage participation of professional personnel in writing clinical guidelines for NET treatment by providing sufficient incentives and budget support
- **Related academic societies and the government to cooperate with each other** to actively secure clinical data centered on medical institutions that fully reflect the ROK's medical environment, as a means of making preemptive efforts to develop evidence-based clinical guidelines



Infrastructure and licensing

The infrastructure for treatment using radioisotopes is still insufficient as all radiopharmaceuticals needed for radioligand therapy in the ROK depend on imports. In addition, the standards for issuing licenses for radioisotope handling are too high, so for nuclear medicine and radiation oncology specialists, there are numerous redundant regulations pointed out. This ultimately results in a continuous decline in the number of related care professionals.

WE NEED:

- **MOHW and MSIT to cooperate with each other to**
 - Continuously develop radioisotope-related infrastructure projects and support R&D development of radioisotope-related technologies
 - Support domestic clinical trials after the development of radioisotope-related technologies and enhance the radiation-related expertise of evaluation department at the Ministry of Food and Drug Safety (MFDS) to promote localization of radiopharmaceuticals
 - Revise the *Nuclear Safety Act* and pursuant Sub-Enforcement Decree so that special licenses for radioisotope handlers are automatically granted to nuclear medicine physicians and radiation oncologists, and manage the quality of licenses through specialist training courses and regular academic conferences

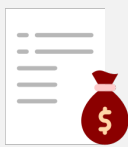


Product approval process

Currently, regulations related to domestic product approvals do not reflect the specificity of the half-life of radiopharmaceuticals. In addition, radiopharmaceuticals are separately managed by the *Pharmaceutical Affairs Act* for their use as pharmaceuticals and the *Nuclear Safety Act* for the safe use of radioisotopes

WE NEED:

- **MOHW and MFDS to**
 - Establish a specific definition of radiopharmaceuticals in the *Pharmaceutical Affairs Act* and include the radioisotope-related safety aspects necessary for drug use
 - Establish and manage an independent and comprehensive product approval process for radiopharmaceuticals based on the amended *Pharmaceutical Affairs Act*



Financial support

National-level reimbursement is confirmed based on the patient's age, tumor appearance location, and degree of anticancer treatment. The number of non-reimbursed treatments is also limited within the health insurance reimbursement standard, so treatment capacity cannot sufficiently meet patient demand. In addition, radioligand therapy in the ROK is currently subject to a restrictively low fee for service, compared to the use of facilities and personnel in hospitals. Therefore, a structural problem persists in which hospitals are unable to recuperate costs as treatment proceeds.

WE NEED:

- **The Health Insurance Review and Assessment Service (HIRA) to**
 - Enhance expertise in the reimbursement decision process by including nuclear medicine physicians in HIRA's Cancer Assessment Committee
 - Establish a separate reimbursement assessment system for patients using radiopharmaceuticals, considering their unique characteristics such as half-lives
 - Relieve or abolish current regulations on non-reimbursement standard on radioligand therapy (i.e., rounds of radioligand therapy)
 - Promote reimbursement of radiopharmaceuticals used for eligibility assessment of radioligand therapy
- **MOHW and healthcare professionals to present sufficient opinions to increase fee for service of radioligand therapy by reflecting valuable resources for the use of personnel, equipment, and facilities in hospitals**



Why does the ROK need to be ready for the wider use of radioligand therapy?

Here, we need to reflect on the need to come up with several measures to expand the implementation of radioligand therapy. Currently, radioligand therapy in the ROK has been approved by the MFDS as a treatment for some NETs and non-Hodgkin's lymphoma^{12 13}, and since then, limited benefits have been applied to patients who meet specific conditions.^{14 15 16} In other words, in the ROK, radioligand therapy is currently conducted only for some NET patients who receive reimbursed treatments, and in the case of non-Hodgkin's lymphoma, the treatment is rarely performed, meaning patient access to the treatment is still limited.^{17 18}

However, given the recent rapid development of genetic research, the emergence of advanced precision medicine, and the increasing demand for personalized treatment at home and abroad, it is expected that customized precision treatment including radioligand therapy will continue to develop rapidly in the future.

In fact, radioligand therapy is currently being actively studied for prostate, breast, and other types of cancer to expand existing treatable indications.¹⁹⁻²³ Further, as a result of these studies, if advanced prostate cancer is added to eligible indications for radioligand therapy in the ROK in the near future, patient demand for the treatment could grow by significant scale. Considering the possibility of expanding treatment to prostate cancer,²⁴ readiness must be ensured in advance through evaluation of models of care, including domestic infrastructure and medical personnel, to continuously expand indications eligible for radioligand therapy.

In doing so, a systematic evaluation of policies for the introduction of radioligand therapy, and a careful identification of areas in the medical field to prepare policy improvement directions will set a precedent for ensuring access to treatment for cancer patients. Furthermore, the ROK will be able to continue and actively respond to the implementation of a wide range of personalized treatments in the future, such as radioligand therapy, and firmly maintain its position as a global leader in the operation of health care systems.

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ABOUT THE RADIOLIGAND THERAPY READINESS ASSESSMENT PROJECT



This policy action blueprint is part of a broader piece of work aiming to define what is needed to establish system-level readiness for radioligand therapy in the ROK. It is supported by other documents including a ROK summary report and an associated national framework, which was adapted from the Radioligand Therapy Readiness Assessment Framework, developed by The Health Policy Partnership.

All documents have been developed by GR Korea in collaboration with the ROK Expert Advisory Group. The project was supported with funding from Advanced Accelerator Applications, a Novartis company. For more details, please visit www.radioligandtherapy.com