Oncidium foundation

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MARCH 19TH, 2024

Radiotheranostics Today

Voicing the Challenges and Opportunities of Radiotheranostics for Cancer Care

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Busy March, Busy Year for Radiotheranostics

Just a few days before World Theranostics Day, celebrated on the 31st of March, we reflect on the pivotal role of radiotheranostics in modern medicine. March holds significant importance for this field, marking a time when advancements and achievements are celebrated, and future pathways are charted. As we commemorate this month, let us recall the pioneering work of Saul Hertz, whose groundbreaking achievements laid the foundation for radiotheranostics.

During this global reminder, we recognize the critical role of radiotheranostics in revolutionizing both therapeutic and diagnostic approaches in medicine. It's a time when we come together globally to acknowledge recent strides in therapy and diagnostics, reflecting on the research and initiatives that drive us forward, but also to highlight the ongoing need for collaboration and advocacy to raise awareness about the availability and potential of radiotheranostics technology. Through collective action, we strive to foster greater understanding and utilization of these innovative tools, ultimately improving patient outcomes and advancing better healthcare for all.

From challenges to opportunities, from awareness to readiness, discover what the voices of Oncidium have to say about bringing forward Radiotheranostics Today.

Ready to talk radiotheranostics with Oncidium foundation?

- Zoom on the radiotheranostics situation in your country
- Evolution, projects and challenges in your region
- Focus on a particular application
- Patient/practitioner interview etc.

Contact us to contribute to the next issue!

Advancing Prostate Cancer Care: Insights and Future Perspectives from the Frontlines of ^{177}Lu Clinical Trials

Interview of Professor Michael Hofman by Dr. Cristiana Gonçalves Gameiro

Professor Michael Hofman, Head of PET/CT and Director of the Prostate Cancer Theranostics and Imaging Centre of Excellence (ProsTIC) at the Peter MacCallum Cancer Centre and University of Melbourne, joins Dr. Cristiana Gameiro, Scientific Advisor at the Oncidium Foundation, in a discussion focusing on ongoing clinical trials involving lutetium-177 (^{177}Lu). Their conversation particularly highlights its application in prostate cancer treatment, showcasing novel combinations, advancements, and a special focus on the TheraP Trial, patient outcomes and quality of life and the place of radiotheranostics in the cancer care setting.

The interview will be in two parts: first an overview of the lutetium-177 (^{177}Lu) trials ongoing and secondly, we will delve into the TheraP trial.

Professor Hofman can you please give us an overview of the clinical trials ongoing with ^{177}Lu?

It's a pleasure to be with you today and thank you for the invitation. I think it's hard to keep track of the number of ^{177}Lu trials currently underway globally. In Australia we've been a leader in ^{177}Lu clinical trials. Australia was an early adopter of ^{177}Lu therapy for treating patients with neuroendocrine tumors. This led to early adoption of ^{177}Lu-PSMA in prostate cancer (PCa). At the Peter MacCallum Cancer Centre, we performed 68Ga-PSMA PET/CT since 2014 and the first prospective trial of ^{177}Lu-PSMA-617 in 2015 and then led an Australian randomized trial, the ANZUP TheraP trial, comparing ^{177}Lu-PSMA-617 to cabazitaxel chemotherapy. More recently, our focus has shifted to looking at novel combinations or to an early line treatment.

I would like to highlight some of the trials that I'm involved in. Recently, Prof. Louise Emmett presented the results of the ENZA-p trial comparing enzalutamide (ENZA) combined with ^{177}Lu-PSMA-617 compared to ENZA alone in men with castration resistant prostate cancer(CRPC). In the castration resistant setting, an androgen targeted drug such as ENZA can result in PSMA upregulation. The hope was that by combining ENZA with ^{177}Lu-PSMA, we will get better targeting of the PSMA receptor. This is in men who have already progressed after ENZA. The results demonstrate that the addition of ^{177}Lu-PSMA-617 resulted in better response and delay in progression of prostate cancer.

Another trial that I'm involved in is the UpFrontPSMA trial, where men with newly diagnosed high volume PCa who haven't received any treatment but have extensive metastatic disease. They are randomized to ^{177}Lu-PSMA-617 followed by standard of care (SoC) chemotherapy, which is docetaxel or just the SoC docetaxel alone. Both arms get hormone treatment. This trial is led by A/Prof Arun Azud and we hope to present the first results in 6-9 months' time.

There is also LuCAB trial,a trial of ^{177}Lu-PSMA-617 in combination with cabazitaxel chemotherapy to see if it's safe and well tolerated, and whether we can deliver this combination at the same time and if it would be more efficacious. On the same theme, we have a trial using ^{177}Lu-PSMA I&T combined with ^{223}Ra (the AlphaBet trial), again hoping that the combination will be more effective.

The LuPARP is a study combining ^{177}Lu with a PARP inhibitor, Olaparib. It's been running for a few years now. Before we started this trial we were concerned that this combination may be quite toxic therefore we started with a very low dose of the PARP inhibitor, and we've been slowly increasing the dose up to a sort of a standard dose. We now treat patients with a standard dose of PARP inhibitor and the combination has a remarkably low side effect profile.

Then we have had two trials combining ^{177}Lu with immunotherapy. The PRINCE trial, reported at ESMO 2021 by Prof. Shahneen Sandhy, which combined ^{177}Lu-PSMA-617 with pembrolizumab. This study showed that the combination was safe and we didn't see any additional toxicities. That was a small trial and it led to a multi-center trial called the ANZUP EVOLUTION trial, combining ^{177}Lu-PSMA-617 with two immunotherapy drugs, nivolumab (CTLA-4 inhibitor) and ipilimumab, (PD-1 inhibitor).

So just in Australia, we have so many clinical trials underway that are all going to read out one by one over the next 1 to 4 years- very exciting!

To be continued page 03

How do you see these trials in the current and future landscape of cancer care, with a special focus on PCa?

At the moment, the current positioning is in the castration-resistant setting after use of an antiandrogen drug and after use of docetaxel chemotherapy. However, it's already moving earlier in many places. In our center, we have elderly patients or patients with comorbidities who simply aren't suitable for chemotherapy and we treat these patients with ^{177}Lu-PSMA and have good results. We also have some industry sponsored trials, PSMAfore from Novartis, but this is in the pre-chemotherapy setting. It won't be long before ^{177}Lu-PSMA is at least positioned prior to chemotherapy after an antiandrogen drug. There's a lot of interest in moving it earlier, but we need to await the clinical trials and evidence-based results.

"It won't be long before ^{177}Lu-PSMA is at least positioned prior to chemotherapy after an antiandrogen drug. (…) but we need to await the clinical trials and evidence-based results."

Let's dive into the second part of the interview, focusing on TheraP. Could you discuss the design rationale ?

TheraP is a randomized trial of ^{177}Lu-PSMA-617 compared to cabazitaxel chemotherapy in the post androgen receptor blockade and post-docetaxel population. We did the first prospective trial of ^{177}Lu-PSMA-617 in 2015 and this 30-patient trial, very early on, was producing similar results to what was coming from Germany; unprecedented responses in men who had failed all existing forms of therapy for PCa. So, we have put forward this randomized trial against chemotherapy and we did it together with the The Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) cooperative trial group.

We put ^{177}Lu-PSMA-617 head-to-head against what was the SoC at the time in this population and the results showed that, ^{177}Lu-PSMA 617 had doubled the response rates in terms of PSA responses, RECIST responses, shrinkage of tumors and it also resulted in prolongation of progression free survival. By one year in this population, almost everyone on cabazitaxel had progressed, but around 20% of men who received ^{177}Lu-PSMA 617 had not progressed in 12 months.

We recently published the three-year overall survival (OS) and there was not a significant difference in OS between the two groups. This tells us that cabazitaxel is quite an effective therapy. Despite the similar survival, we looked at more than 50 symptoms that patients were reporting every 3 weeks and certainly there were multiple domains where patients' QoL was superior with ^{177}Lu compared to cabazitaxel.

If you want to make oncology trials very simple in this advanced population, there's only two things that matter, which is: will I live longer or will I live better.

"How early can we move ^{177}Lu-PSMA? If we can cure men with external beam radiation, the hypothesis is that we can cure men with ^{177}Lu-PSMA instead."

And we certainly show that you will live better. So following the TheraP, in our center we recommend ^{177}Lu to be given prior to cabazitaxel for most men. But it's not a replacement, it's an additional treatment.

I always like to finish the interview with a positive note. When would these types of treatments be available for patients in earlier stages? Could you mention any other trial that is going in that direction?

How early can we move ^{177}LuPSMA? We have run the LuTectomy trial in our center. It is a trial that Professor Declan Murphy and Dr Renu Eapen, our urologists, myself and our medical oncologists have run. It is a boutique small trial, which explores the use of ^{177}Lu-PSMA-617 in patients with a new diagnosis of prostate cancer prior to prostatectomy surgery. We wanted to see if this is safe primarily but also what radiation dose we can get to prostate cancer when we give this as a treatment. We know that both surgery and external beam radiation can cure men with prostate cancer. If we can cure men with external beam radiation, the hypothesis is that we can cure men with ^{177}Lu-PSMA instead.

In this trial, we're really looking at the feasibility of ^{177}Lu-PSMA in this setting. All men proceeded to have a prostatectomy. So, we also have histopathology. I'm hopeful that there is a group of patients where ^{177}Lu-PSMA can be used as a first line treatment, either in combination with surgery or in combination with external beam radiation. The goal is to improve the cure rates. Or maybe in selected men it could be given as a treatment on its own and could be highly efficacious or, even, curative. The results of LuTectomy, recently published in European Urology, will pave the way for groups around the world to further study ^{177}Lu in this very early first line setting and better define what its role is.

From what I hear, LuTectomy is quite unique and quoting Doctor Maurer during the EAU in 2022: "Is LuTectomy the role for ^{177}Lu-PSMA-617 in the future in the prostate cancer therapy landscape?". Do you have an opinion about this question from Doctor Maurer?

I think it is. It's just going to take some time to define it and it is going to be a stepwise process. We do need to be careful that we don't treat men with new treatments when there are proven curative treatments. We have proven uses for ^{177}Lu today, but they are in a later stage, but hopefully when we do another interview, in a few years' time, we'll have some strong evidence for very early use of ^{177}Lu or other theranostics in this setting. And I think it will become another pillar in modern oncology.

To be continued page 04

At the same time, we are exploring radio-isotopes other than Lu-177 for treating patients with prostate cancer. We recently completed recruitment of 30-men in a first-in-human study of Terbium-161 (^{161}Tb) PSMA, the VIOLET study. ^{161}Tb is similar to ^{177}Lu but also emits another type of radiation called Auger electrons. These particles travel very short distances, less than the width of a human cell, compared to around 1mm for ^{177}Lu. We believe this will enable better targeting of microscopic sites of residual cancer, and might be the reason ^{177}Lu fails in some patients.

"TheraP is a randomized trial of ^{177}Lu-PSMA-617 compared to cabazitaxel chemotherapy in the post androgen receptor blockade and post-docetaxel population"

Last but not least, what are your expectations from the Oncidium foundation?

The foundation has a critical role in making people aware of theranostics. Awareness is really important providing both patients and clinicians with information about these new forms of therapy and bringing industry together with the clinicians to make this treatment available to patients by promoting, educating, and increasing some of the infrastructure that is required to deliver theranostics. Theranostics is different from chemotherapy or immunotherapy as - it needs specialized facilities, and people with expertise in using these radioactive substances.

Many patients in many parts of the world are still unable to access either ^{177}Lu-DOTATATE in neuroendocrine tumors or ^{177}Lu-PSMA in prostate cancer, both now proven treatments. We need organizations like yours to advocate, to promote and educate.

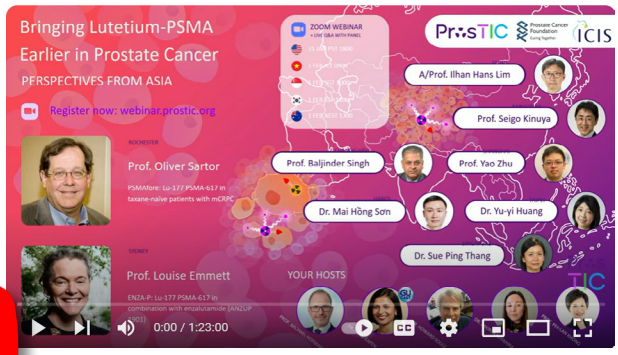
Thank you very much for this interview. I learned a lot.

Prof. Michael Hofman
• Head of PET/CT and Director of the Prostate Cancer Theranostics and Imaging Centre of Excellence (ProsTIC)

Cristiana Goncalves Gameiro Ph.D.
• Product Manager at IBA Radiopharma Solutions
• IBA Honorary Fellow
• Scientific Advisor at the Oncidium foundation

The initial results of the studies ENZA-p, PSMAfore, LuTectomy were discussed on the ProsTIC TV webinar "Bringing Lutetium PSMA Earlier: with Perspectives from Asia" aired of February 11th 2024 and accessible on

Youtube : Click here



Radiopharmaceutical Development: From Design to Clinical Impact

By Leila Safavi, PhD

Ever wondered about the fascinating journey radiopharmaceuticals undergo before making their way into medical practice? Join us as we illuminate the intricate process that shapes these groundbreaking agents, ultimately driving advancements in modern healthcare.

Radiopharmaceuticals represent a pivotal intersection of cutting-edge science and medical innovation, driving progress in both diagnostic imaging and targeted therapeutic interventions. These specialized compounds play a crucial role in modern medicine, providing invaluable insights and precise treatment options for a range of conditions. In this article, we will delve into the intricate journey these agents undertake, from their inception in the design and synthesis phase to thorough testing, regulatory approvals, and their profound clinical impact.

Design & Synthesis: The process commences with the meticulous design and synthesis of radiopharmaceutical compounds. Scientists utilize a blend of chemistry, biology, and pharmacology to craft molecules that precisely target specific areas in the body. This involves combining knowledge from different scientific areas. The goal is to create compounds with outstanding properties, ensuring they can effectively deliver radiation to the intended targets.

Radioisotope Production: At the core of radiopharmaceuticals are radioisotopes - tiny particles emitting crucial radiation. These isotopes are created through controlled nuclear reactions in specialized reactors or accelerators. This stage requires expertise in nuclear physics, safety protocols, and engineering. The aim is to produce isotopes with the right balance of stability, half-life, and emission characteristics needed for medical applications.

Precision Testing: After synthesis, each radiopharmaceutical undergoes rigorous testing. These evaluations confirm purity, stability, and binding specificity. Quality checks are put in place to guarantee smooth performance when used in a clinical setting. This phase acts as a filter, allowing only the strongest and most reliable radiopharmaceuticals to move forward, ready to provide precise medical insights.

Navigating Regulations: The regulatory process is a crucial phase in radiopharmaceutical development. These compounds must go through thorough evaluations to demonstrate their effectiveness and safety for patients. Regulatory approvals signal that the compounds have successfully met stringent standards. This phase requires close collaboration with regulatory bodies, meticulous documentation, and strict adherence to guidelines. It showcases a dedicated commitment to patient well-being and the highest medical standards.

Clinical Impact: The culmination of this journey produces radiopharmaceuticals that surpass conventional medical imaging and therapies. They act as guides for surgeons, offering invaluable insights into the complexities of disease. They also open the door to targeted therapies, allowing for precise treatment planning. Radiopharmaceuticals have become indispensable tools in modern medicine, enabling diagnoses and interventions that were once unimaginable.

Revolutionizing Diagnostics: Radiopharmaceuticals have transformed diagnostic imaging. Techniques like positron emission tomography (PET) and single-photon emission computed tomography (SPECT) now benefit from the integration of radiopharmaceuticals. These imaging methods provide clinicians with unparalleled clarity and specificity, enabling early detection and accurate staging of various diseases, including cancer, neurological disorders, and cardiovascular conditions.

Targeted Therapies: Beyond diagnostics, radiopharmaceuticals have revolutionized targeted therapies. Radiopharmaceutical therapy, also known as radiotherapy, uses the specific properties of these compounds to deliver radiation directly to diseased cells while sparing healthy tissue. This approach shows promise for treating cancer and certain non-malignant conditions, offering a more effective and less invasive alternative to traditional therapies.

Advancing Research and Development: The journey of radiopharmaceuticals is an ongoing process of innovation and improvement. Researchers are continually exploring new compounds, refining synthesis techniques, and investigating new radioisotopes with enhanced properties. This relentless pursuit of excellence aims to expand the capabilities of radiopharmaceuticals, opening new frontiers in medical imaging and therapy.

Every step of this journey, from design to regulatory approvals, demonstrates the dedication and expertise of scientists, engineers, and healthcare professionals. Their tireless efforts bridge the worlds of science and medicine, ushering in a new era of healthcare possibilities. Radiopharmaceuticals stand as a testament to human ingenuity and our unwavering commitment to advancing medical science for the betterment of patients worldwide. Looking ahead, the continued evolution of radiopharmaceuticals promises even greater breakthroughs in modern medicine.

Leila Safavi, PhD.
Oncidium foundation
Ambassador
Irvine, USA

Actinium-225 Production and the Future Needs for Labeled Drugs

By Dr. Richard Zimmermann

As the R&D and the clinical interest for Actinium-225 labeled molecules increases, questions regarding future availability of industrial-scale quantities of this isotope cast doubt on the marketing viability of ^{225}Ac-labeled drugs. In a recent publication entitled 'Is Actinium Really Happening', the short editorial concludes with an obvious answer "yes, of course excess actinium will be available", however adds a "but" announcing the limit of the success.

The paper emphasizes that, within the next 10 years, an important number of stakeholders will invest substantial sums to expand industrial capacity access to ^{225}Ac for the high number of ^{225}Ac-labeled drugs that are currently under development. More than a dozen of these molecules have already been injected in man and the first of them could reach the market by 2028, coinciding with increased access to high-quality radionuclides produced under Good Manufacturing Practices (GMP). In the following years, the worldwide capacity will even exceed needs, probably resulting in an interesting price competition benefiting the patients. Non-carrier-added quality ^{225}Ac, meaning in this case, ^{225}Ac without ^{227}Ac contamination, will be used exclusively in human. As a consequence of higher yields, the technologies based on accelerators (cyclotrons, linacs, rhodotrons) will remain the only profitable tools, while the presently generator-based production will stay in use until larger amounts of ^{225}Ac can be produced with the newest technologies.

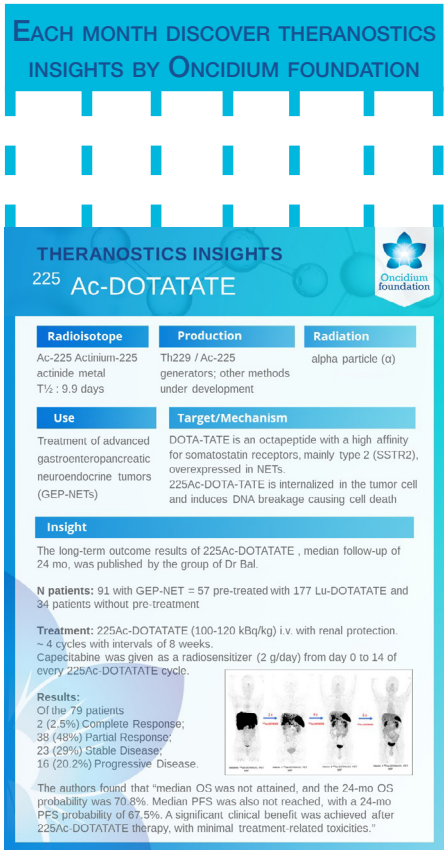
The journey towards the first marketed ^{225}Ac-drug still requires some patience given the time required to develop new tools (2 to 5 years) and source the requisite material, Radium-226, which is common across all production technologies. Encouragingly, almost all players are slowly finding addressing this challenge, which should be resolved within the next three years. As a reminder, the industrial production of ^{226}Ra was stopped in 1954, but during this year more than 2.3 kg of this material was extracted and purified, underscoring the importance of investment priorities and political will.

Next to solving the access to ^{226}Ra, engineers will have to make sure that the risk of explosion of the targets in these new high-capacity production tools remains close to zero as, with the long half-life of the target material, any accident in such site could lead to a shut-down of the center for hundreds of years and jeopardize the other sites. However, the major issue that needs to be anticipated is rather a political issue and not specific to ^{225}Ac, but applicable for all long half-life radionuclides. As the pharmaceutical industry is aiming at treating several hundreds of thousands of patients a year which translates into millions of doses, a concern will be addressed by green groups looking at preserving the planet and in particular water systems if no action is taken to control the waste generated by the patients that are being treated. Ambulatory treatment can work as long as only a few thousands of patients are being treated, but by 2032, the industry, the hospitals and the authorities will have to propose a solution to minimize the risk of river pollution. There remains no risk for patients or for the population.

With this last point in mind, looking ahead, Actinium-225 (as well as Lutetium-177) holds promise but within a limited timeframe. All the molecules that have entered or are close to entering clinical trials within the next two years stand a high chance of becoming blockbusters. However, if molecules labeled with radioisotopes with shorter half-lives (e.g., labeled with ^{211}At or ^{212}Pb) reach the market in a form that is readily available and demonstrates the same efficacy; it can easily displace the equivalent long half-life radiolabelled molecules.

Short half-life radionuclides will bear a strong ecological marketing advantage which may lead to a switch even before 2035 and lasting over a 10 to 15 years period. While we embrace the decade of ^{225}Ac ,it is now time to prepare for the next generation of radiotheranostics.

Richard Zimmermann Ph.D.
President & Founder at
Oncidium foundation



Introduction to Phase 0 Imaging Studies with Radiopharmaceuticals

By TRACER CRO

Drug development undergoes three primary phases. Initially, there's the research and development phase, focusing on molecule development and selection. Following this, preclinical studies are conducted to evaluate the drug's potential. Upon obtaining promising results in preclinical trials, the subsequent phase involves initiating clinical trials with human participants. These trials are traditionally categorized into Phase I, II, and III studies.

In 2006 the FDA added Phase 0, as a translational clinical trial between preclinical and Phase I. A Phase 0 clinical trial, also known as Exploratory Investigational New Drug applications eIND or Exploratory Clinical Trials, is an early stage clinical trial conducted to assess the Pharmacokinetics and Pharmacodynamics of a drug candidate in a small number of human subjects. Preferably patients that express the drug's target.

Unlike later-phase trials that focus on efficacy and safety, Phase 0 trials involve administering a very low non-therapeutic dose of the drug (microdose) to a small number of participants (usually less than 15). This approach enables drug developers to obtain preliminary insights into the behavior of the drug within the human body. The main objective is to provide data for an early go/no-go decision before moving the drug candidate to the next clinical trial phases which are more costly and time-consuming. Additionally, conducting a Phase 0 study allows drug developers to skip large animal models and move to first-in-human studies faster.

Imaging in clinical trials can provide indisputable proof that the investigational drug reaches and binds to the target, and if applicable, shows uptake in diseased tissue and no or little uptake in healthy tissue. Imaging in clinical trials is not limited to radiopharmaceuticals. Non-radioactive compounds can be labeled with radionuclides to make them suitable for imaging in the drug development process.

Phase 0 using labeled drugs provides data that drug developers can use for further development.

- In-human data regarding Pharmacokinetics and Biodistribution are useful in later phases of development
- The on- and off-target effect (background-to-target ratio) can be determined. This data is especially important for radiopharmaceuticals intended to be used in radioligand therapy (RLT)
- Precision (radioligand) therapy and the corresponding indication(s) can be determined with the right study design. For example, selecting tumor types
- The possibility of studying multiple indications in Phase II and III can be explored
- The path of excretion and potential risk of accumulation can be made visible.

It is important to highlight that Phase 0 does not aim to study toxicity and safety, nor to establish the treatment dose. However, in some cases initial dosimetry can be performed.

One important aspect of Phase 0 is that it can replace large animal studies and instead provide early in-human data. Regarding resources, this means that all or at least a large amount of time and cost normally spent on extensive preclinical experiments can be reallocated. For this reason, in most cases, conducting a Phase 0 study requires minimal additional resources. Further, with early go-/no-go decisions drug developers avoid spending resources on taking non-targeting drugs to the next development stages.

Considerations for clinical trials with radiopharmaceuticals

- The use of materials meeting Good Laboratory Practice (GLP) standards is adequate for Phase 0 clinical trials. Namely, the process of labeling the drug takes place in a controlled environment adhering to Good Manufacturing Practice (GMP) standards, making it fit for in-human use
- For imaging and therapy, the effective dose is often already a microdose or lower
- It is a current prerogative in the radiopharmaceutical area that the tracer should not have pharmacological activity when it binds to the receptor, instead, it should work only as a vector.

Conclusion

In conclusion, the introduction of Phase 0 imaging studies with radiopharmaceuticals marks a significant advancement in translational clinical research, bridging the gap between preclinical evaluations and traditional Phase I trials. These exploratory investigational studies offer a unique opportunity to assess the Pharmacokinetics and Pharmacodynamics of potential drug candidates in a small cohort of patients. This enables early go/no-go decisions in drug development while minimizing costs and time.

However, it's imperative to recognize that Phase 0 studies primarily focus on early human data acquisition and do not replace the necessity of subsequent phases for toxicity assessment and dose establishment. Still, the early data can accelerate Phase I and II trials and help drug developers to have much smarter study designs (e.g., less participants).

As the field of radiopharmaceuticals continues to evolve, Phase 0 imaging studies can contribute to the success of radiopharmaceutical development. The chances of getting new drugs to the right patients can be increased simply by careful consideration of study design, and of course, adherence to regulatory standards.

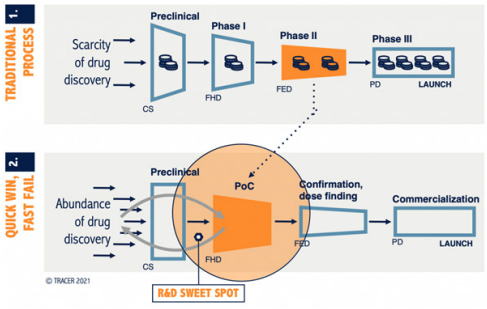


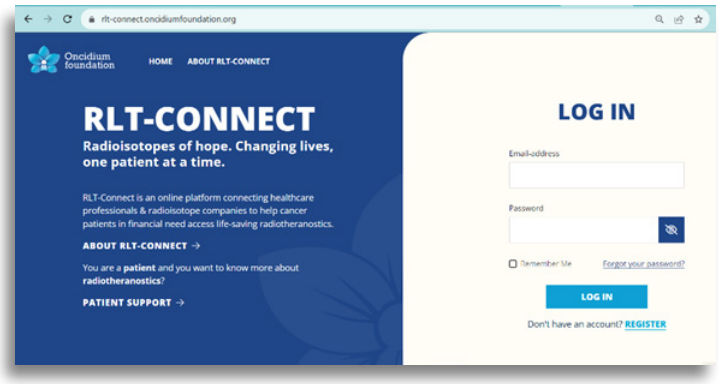
Figure 1 – A comparison of drug development processes adapted from Paul et al., 2010

The Launch of Global 'RLT-Connect' Platform to Enhance Radioligand Therapy Access for Cancer Patients in Need

An Oncidium foundation initiative

More and more radioligand therapies (RLT) are under development, and their adoption is steadily increasing as ongoing research continues to demonstrate their potential benefits in improving patient outcomes. Unfortunately, access to radioligand therapies is deeply unequal around the world, and it is dependent on where the patient lives; for example, in most low-and middle-income new radiopharmaceuticals are paid out-of-pocket; therefore this treatment is available only to a small number of people living with cancer.

In this context, the Oncidium foundation has initiated a significant effort to ensure that more patients have the opportunity to receive the adequate care they require by launching RLT-Connect, an online platform designed to facilitate collaboration between healthcare professionals seeking radioligand therapy for their patients who cannot afford it, and radioisotope suppliers willing to donate doses to make this life-saving treatment accessible to those in need.



As a collaborative platform each stakeholder will have an important role:

Isotope supplier

- Definition of number of doses to be donated each year
- Establishment of donation schedule
- Shipment process

Local Radiopharmacy

- Importation process: documents preparation, customs clearance, inland transportation.
- Labelling and quality control
- Delivery at clinical site

Clinical Facility

- Selection of patients and creation of paperwork for treatment access: early access, compassionate use, expanded access, etc.
- Submission of cases on the RLT-Connect platform
- Feedback on treatment outcomes by filling a Case Report File (CRF)

"In establishing 'RLT-Connect,' Oncidium foundation has forged a comprehensive ecosystem—a true chain of solidarity extending from therapy centers to radiopharmacies, and radioisotope suppliers—all united in pursuit of a common mission to ensure that every cancer patient has an equal opportunity to access a potentially life-saving technology, whoever and wherever they are."

Rebecca Lo bue, CEO of the Oncidium foundation

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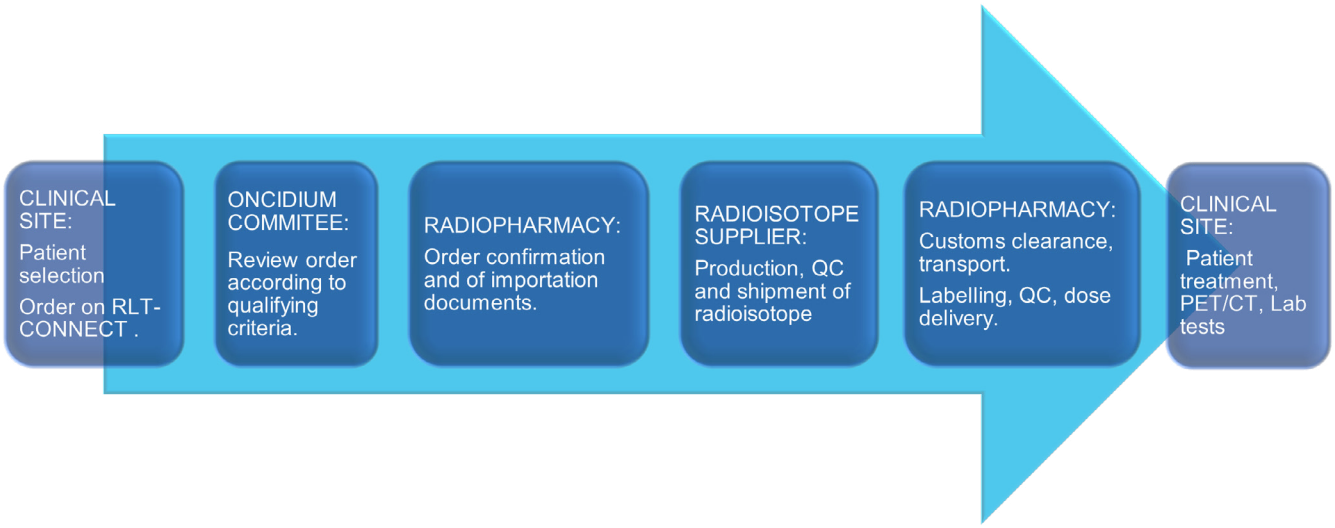
How does the collaboration work ?



"Access to radiotheranostics if often constrained due to limited resources and logistical challenges. This platform will simplify the process, ensuring that we can provide the best care possible; thus, enabling the best of all worlds for everyone involved, and primarily for patients."

Dr. Cecilia Carreras,
Oncidium Ambassador and Head of Nuclear Medicine and PET/CT at Ángeles Lomas Hospital, pilot center of the RLT-Connect Platform.

The platform was tested in 2023 in pilot countries, where the foundation received doses from two generous suppliers, Monrol Nuclear Products Co and Isotopia Molecular Imaging.

isotopia Nuclear Medicine

Keren Eyal-Kotlizky,
VP Business Development at Isotopia Molecular Imaging

"We are proud to partner with the Oncidium foundation in its endeavors to make radiotheranostics available for as many people as possible. We are delighted for the opportunity to contribute in making a difference in the lives of individuals who lack access to vital medical resources."

The foundation has entered into collaboration agreements with other prominent radioisotope suppliers in the market, including ITM Isotope Technologies Munich SE, PanTera, and Telix Pharmaceuticals Ltd., and is actively engaged in ongoing discussions with additional suppliers.

The full-scale launch of the platform will take place during the 7th Theranostics World Congress in Chile. To learn more about this important project access: https://www.oncidiumfoundation.org/rlt-connect/
The success of RLT-Connect also depends on the collective support of individuals and companies. Support the cause and join the mission to impact 365 lives in five years. This brings us one step closer to a future where accessible cancer care knows no bonds.

Learn more about the RLT-Connect and help us build the ecosystem

Gemelli Nuclear Medicine and Radiopharmacies Towards Accreditation for Phase I Studies

By Dr. Salvatore Annunziata

On March 18 at the Gemelli Hospital was inaugurated a Phase 1 research center in Nuclear Medicine and Radiopharmacy. Basic research is growing rapidly at an international level, thanks to the development of new radiopharmaceuticals for personalized diagnostics and therapy.

For this reason, the future phase 1 accreditation of Nuclear Medicine and Radiopharmacies represents an important milestone at Gemelli Hospital and Università Cattolica (Rome, Italy), that will allow innovative academic, industrial projects, cutting-edge diagnostic and therapeutic possibilities in Europe.

Gemelli

Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

Research projects

A few months ago we talked about the research projects underway at Gemelli on new experimental diagnostic radiopharmaceuticals, in particular on the possible use of ^{18}F-MC225 in depression, ^{68}Ga-Exendin in diabetes and new tracers of the tumor microenvironment in abdominal-pelvic tumors (^{18}F-FAPI, ^{68}Ga-Pentixafor). But it is only a small preview of what will happen in the next months, thanks to the accreditation of the Nuclear Medicine and Radiopharmacies for phase 1 studies.

“Conducting a Phase 1 study – explains Doctor Salvatore Annunziata, head of the research Radiopharmacy facility – means dealing with research at an earlier stage and carrying out so-called 'first in human' clinical studies on a small number of patients in which new radiopharmaceuticals will be used for the first time in humans for diagnostic or therapeutic purposes".

Applications in diagnostics

"In the coming months – announces Dr. Annunziata – we will begin to produce innovative isotopes such as ^{89}Zr and ^{64}Cu, which are suitable for conjugation with monoclonal antibodies, for the first time in an Italian hospital radiopharmacy.

This is why we talk about 'immuno-PET', a pre-treatment imaging test that would allow us to better identify those patients who express surface antigens, not only at the biopsy site, but in all disease sites. Immuno-PET is a diagnostic tool used experimentally for now only by Northern European countries”.

To be continued page 11

Innovative treatments

“From next year we will try to extend the phase 1 studies also to the therapeutic part; this will allow us to carry out first-in-human studies also with theranostic radiopharmaceuticals. An interesting first-in-human theranostic could be represented by the aforementioned ligands of the tumor microenvironment for abdominal-pelvic tumors (FAPI, Pentixafor), or by the so-called 'alpha-therapy' ('alpha-emitting' radiopharmaceuticals)”.

International network.

Gemelli Hospital and Università Cattolica (Rome, Italy) are well inserted within international research networks. “This is fundamental not only from a collaborative-scientific perspective, but also to obtain research funding at an Italian and European level. Among the tenders already won is EU4Health (CLAUD-IT and SAMIRA consortia), two European network initiatives between nuclear medicine and radiopharmacy departments, to promote the development of diagnostic and therapeutic radiopharmaceuticals in Europe. Gemelli is currently one of the few Italian GMP-like radiopharmacies for research on experimental radiopharmaceuticals, the only one at a hospital and academic level with rooms and staff dedicated to independent research".

Dr. Salvatore Annunziata
Medical Director, UOC Nuclear Medicine, Head of GSTeP Radiopharmacy - TracerGLab

Oncidium Note

Advancing Precision Health Through Patient-Centered Clinical Trials at Gemelli Facility

The Oncidium foundation participated in the opening ceremony of the Gemelli facility, where phase I clinical trials with radiopharmaceuticals will take place.

Phase 1 studies for radionuclide therapies are an important step in medical research, and require specialized centers with expertise, patient access, and the capability for dosimetry and pharmacovigilance. Unfortunately, the expertise in dedicated early phase radiotheranostics remains limited throughout Europe. Hence, the importance of such facilities to fill this major gap.

Being patient-focused, the foundation emphasizes the vital role of patients and patient advocates in clinical trial design, that they are a crucial part of the equation. Patient advocates bring unique vision to trial design and real-world perspectives to the table, helping shape trials in ways that make sense for them, as they are the primary stakeholders in this matter. Patient advocates can contribute to the selection of meaningful endpoints, provide insights to make protocols more patient-friendly, and enhance recruitment and retention strategies. By actively involving patient advocates in the design process, researchers can ensure that clinical trials are not only scientifically robust but also centered around patient needs and experiences.

Oncidium foundation

“As we embark on this journey of innovation and discovery, let’s remember one thing: it’s all about the patients. Let’s keep pushing for care centered around their needs and experiences. That’s how we’ll truly make a difference in healthcare”

Rebecca Lo bue
CEO

Oncidium would like to thank the Gemelli Hospital for including the foundation in this important momentum, for an additional building block to advancing healthcare for all.

What's up Oncidium foundation?
Keeping patients front and center

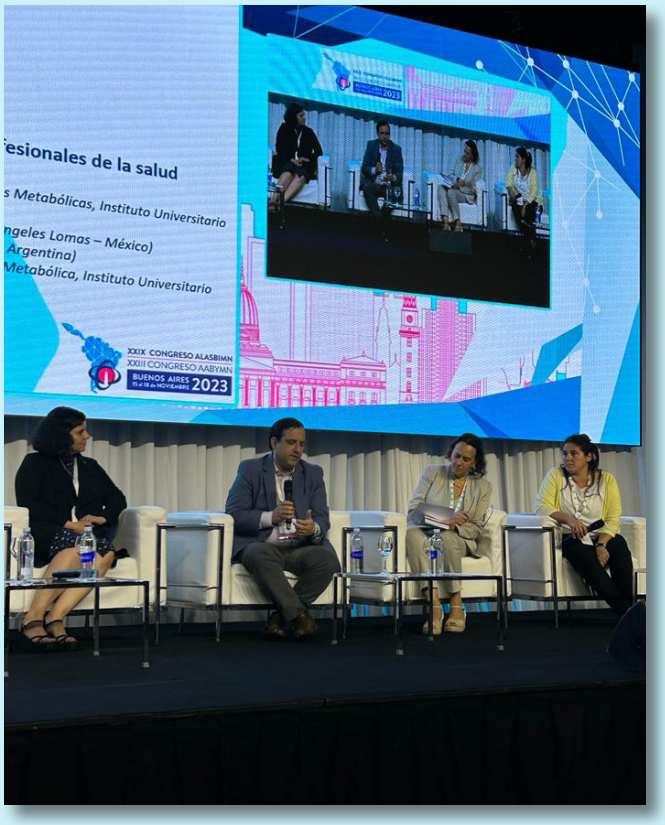
Watch out for the Oncidium foundation during the month of March: see you at the 7th Theranostics World Congress!

Busy month of March for the Oncidium foundation, highlighted by the upcoming official global launch of the "RLT-Connect platform", an initiative connecting healthcare professionals and radioisotope suppliers from all over the world to provide radioligand therapy (RLT) for cancer patients in financial need.

The full deployment will coincide with Theranostics World Congress, during which the Oncidium foundation will be hosting, together with the ICPO foundation, **a patient session titled "Building Hope: Navigating through the Challenges and Barriers"**. This session, moderated by Oncidium foundation Scientific Advisor, Cristiana Gameiro, will feature patients from different countries and with different stories who will be sharing their experiences focusing on:

- Patient education and bringing forward RLT as an option
- Treatment access and navigating through complex healthcare systems
- Treatment journeys, offering perspectives and insights from people living with cancer

Thanks to the organizers of the Theranostics World Congress, patient panelists with their voices will remind us to keep pushing for and prioritizing patient-centered care, urging us to continually strive for advancements in healthcare that address their needs and experiences, and ultimately, to enhance healthcare for all.



Zoom on our previous patient session during the ALASBIMN - November 2023, Argentina

What's up Oncidium foundation?

Growing needs, growing team

As we reflect on our journey, we are proud of the accomplishments checked off on our checklist. However, we also acknowledge the ever-growing to-do list at the Oncidium foundation to reach our ambitious goals.

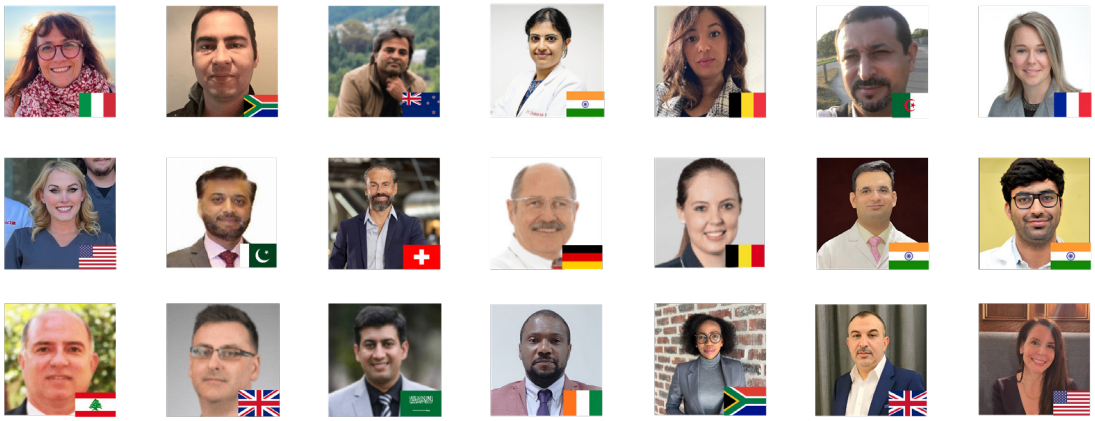
With each new project and initiative, our operational and Ambassador teams continue to expand, a testament to our commitment to advancing radiotheranostics access for people living with cancer.

"One in two patients can now witness a reduction or cure of their cancer. However, this isn't sufficient! Radiotherapeutics stands as a crucial and essential option to save the lives of cancer patients. I am privileged to be involved in this journey and I am enthusiastic about contributing to the accomplishment of Oncidium's mission."

Jérôme Majoie,
CEO of the Fournier-Majoie Foundation has joined the Oncidium foundation Board of Directors

Continuous work beyond borders with the growing network of Oncidium foundation Ambassadors

Introducing our newest Ambassadors recruits, who have volunteered to increase our already well-established network in leading the foundation's mission locally and internationally. With almost 70 ambassadors representing 36 countries, this year promises even greater interactions, shared knowledge, and Ambassador-led Oncidium initiatives and projects. Join us in making a difference.



Working Beyond Borders

Chiara Maria Grana, Frikkie Van Deventer, Madhusudan Vyas, Sugandha Dureja, Zena Wimana, Abdelkader Medjahedi, Alexia Daoust, Taylor Kirk, Muhammad Numair Younis, Reno Löffler, Udo Blaseg, Janke Kleynhans, Dharmender Malik, Ritesh R. Suthar, Mohammad B. Haidar, Sean L. Kitson, Arslan Ahmed, Jean Eric Granger, Tebatso Tebeila, Moez Trabelsi,Jess Guarmaschelli

New year, new colleagues

Camille Chapalain
Partnership Manager

Dorian Buekenhoudt
Communication Associate

Thais Rocha Ruda
Communication Manager

What's up Oncidium foundation?
Global perspective, local actions

2023 & 2024 highlights

Tackle Cancer Challenge 2nd edition
May 2023, Global (picture taken in Egypt, collaborative event with Misr Radiology MRC)

IBA Learn and Talk "Enhancing Access to Radiotheranostics for Cancer Care, Worldwide"
June 2023, USA and September 2023, Austria

Ambassador Meeting
September 2023, Austria

PSMA Conference -
January 2024, USA

Joint Framatome Webinar "The growing role of radiotheranostics in cancer care",
February 2024, Global

Virtual Ambassador Meeting (VAM)
February 2024, Global

Meet us soon !

Have you met Mister Bind and his companions ?

The first two videos on "What are radiotheranostics for cancer care?" and "Doctor, will radiotheranostics make me radioactive?", left our network wanting for more and inspired the first Oncidium foundation comic book to follow the adventures of the **"Life-saving mission of Mister Bind and his companions"**. Contact us, If you would like to translate our comic for better patient information access or would like to submit the next adventures for better radiotheranostics awareness and reach.

Supporters of the Oncidium foundation

Telix · ZERO Biotech · WARMTH World Association of Radiopharmaceutical and Molecular Therapy · SPARC Europe · sck cen

monrol · POINT Biopharma · King Baudouin Foundation · isotopia Nuclear Medicine · R2 IBF

MEDraysintell · itm Passion for Precision · framatome · iREElit Radiopharma · ICPO

iba · The Health Policy Partnership [research, people, action] · Global Morpho Pharma GMP for life · Cyclotek PET Radiopharmaceuticals Molecular Imaging · COMECER an ATS company

Chrysalium Consulting · Pantera A better fight for life

Support the foundation and join the fight against cancer

Supporting the foundation will allow to finance research and development of new radiotheranostics, but also to reach patients directly thanks to contributions that will help finance treatments using radiotherapeutics technology.

We know that this path is not easy. We know the importance of finding the right and nearest doctor, understanding the diagnosis and evaluating treatment options. Thus, it is our mission to educate, raise awareness, and support people living with cancer and their loved ones in this daily battle.

Your contribution will help support key areas related to the organization's work: education, R&D, enhanced access to treatments and clinical trials, advocacy, outreach etc.

For more information about our Support Levels: **contact us** **or donate**

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