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Navigating thyroid cancer: a theranostics odyssey “joining the dots to make a line”

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ABSTRACT

Over the past few decades, the incidence of thyroid cancer, which was once a relatively uncommon aspect of oncology, has significantly increased worldwide. This tendency makes opening new horizons and finding new modalities for both its diagnosis and therapy all the more crucial. The concept of theranostics in thyroid cancer has shown potential in individualizing treatments, and tailoring therapies to the specific molecular characteristics of the patient's cancer.

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Introduction

Theranostics in thyroid cancer, particularly differentiated thyroid cancer (DTC), have shown promise in recent years. The approach involves pairing diagnostic procedures with therapeutic interventions that target specific biomarkers expressed in thyroid cancer cells. Thyroid cancer, while a rarity in comparison to other malignancies, poses a considerable problem for oncologists. It occupies a special place as a case study for the effective use of theranostics in the treatment of cancer [1]. A great example of how a good theranostics model could change the way we treat any disease is how thyroid cancer care has changed over time, combining diagnostic and treatment methods. When thyroid cancer is treated using the theranostics model, a customized treatment plan that reflects on the unique parameters of each patient is created. This model helps advance therapeutic nuclear medicine by demonstrating how it personalizes patient care, enhances treatment results, and minimizes unneeded treatments. The model of thyroid cancer treatment not only captures its historical significance but also predicts a brighter future. Theranostics in thyroid cancer is basically a model and an example of how medical science is always getting better and devoted to finding better treatments for patients and practitioners [2].

The Genesis of Theranostics

The early use of radioactive iodine (I-131) as a ground-breaking strategy for treating thyroid illnesses

emerged as a game-changing method (in 1946), and this is where conceptually the origins of theranostics may be found. This clever use involved the oral administration of radioactive iodine, a technique that took advantage of iodine's special ability to accumulate in thyroid tissue. A dual-functionality strategy became possible as a result of this selective accumulation [2-3]. Along with being useful for diagnosis, radioactive iodine also has a surprising property that makes it an effective and focused treatment for thyroid cancer. It ushered in a paradigm shift that led to a personalized and highly effective therapeutic model by administering high (ablative) doses of radiation directly to thyroid cells.

This paradigm change created the essential groundwork for the current theranostic worldview. It was a ground-breaking development that brought together the diagnostic and therapeutic fields, allowing medical professionals to treat thyroid cancer patients with pinpoint accuracy and efficacy while also diagnosing thyroid illnesses with previously unheard-of physiological accuracy. The strength of integration and innovation in the field of nuclear medicine is demonstrated by an early success story of theranostics in the therapy of thyroid disease [2].

Advances in Imaging

The precise and timely implementation of modern imaging technologies is vital for the proper management of cancer. A spectacular convergence of state-of-the-art imaging techniques and the use of radiolabeled tracers has been

observed in the field of thyroid cancer. Hybrid imaging, single-photon emission computed tomography (SPECT/CT), and positron emission tomography (PET/CT), have proven to be a revolutionary development in the study of malignancies. Radiotracers utilized in SPECT encompass technetium-99m and iodine isotopes such as iodine-123, iodine-125, and iodine-131. PET commonly employs tracers such as iodine-124 and 18F-FDG. In addition, [18F] tetrafluoroborate has recently surfaced as a notable iodide analog PET radiotracer displaying promise in NaI symporter imaging [5]. These techniques, strengthened by the addition of radiolabeled tracers, have radically changed our ability to diagnose in numerous important ways.

First and foremost, they have greatly improved our capacity to identify even the smallest thyroid lesions, aiding in the early diagnosis and treatment of disease. These imaging technologies are distinguished by their extraordinary sensitivity, which makes it possible to see small abnormalities that would otherwise elude detection using standard procedures. These techniques enable clinicians to develop treatment plans that are specifically matched to the disease-specific traits of each patient by analyzing the metabolic activity and receptor expression patterns within thyroid cancer cells. Clinicians are equipped to choose the most effective treatment modalities by giving them thorough insights into the scope and localization of metastatic lesions [6].

Targeted Therapies

The advent of targeted medications has transformed the treatment of iodine-refractory thyroid cancer, bringing about a substantial change in how we approach the management of this tumor. This shift is particularly noteworthy when traditional options seem limited or nonsignificant. These treatments offer a ray of hope, particularly when used alongside the identification of targets through molecular and genetic analyses [7].

Precision is one of the distinguishing characteristics of targeted therapy for thyroid cancer. Tyrosine kinase inhibitors (TKIs) provide a highly specialized and individualized approach to treatment by precisely focusing on key chemicals and pathways that fuel tumor development and proliferation.

The capacity to locate particular genetic abnormalities within the tumor through molecular testing forms the basis of this precision. Notably, it has become clear that mutations in genes like BRAF and RET are major stakeholders of thyroid cancer. Oncologists can analyze a patient's cancer's genetic makeup using molecular testing, which gives them important new information about the processes driving cancer growth. With this information at hand, treatment strategies may be created to address the distinctive features of each patient's ailment. The last 10 years have seen the introduction of innovative therapies, including FDA-approved TKIs and small

molecule inhibitors of v-raf murine sarcoma viral oncogene homolog B1 (BRAF), neurotrophic tyrosine receptor kinase (NTRK), vascular endothelial growth factor receptor (VEGFR), rearranged during transfection (RET), mitogen-activated ERK kinase (MEK), as a result of our growing understanding of the molecular underpinnings of thyroid function and carcinogenesis [8].

TKIs are systemic medications that are specifically intended to target particular proteins that are involved in the PI3K, MAPK, and/or upstream RTK pathways. These medications are divided into two groups: BRAF inhibitors and multitarget TKIs targeting VEGFR 1-3, platelet-derived growth factor, RET, KIT protooncogene (c-KIT), and BRAF. Sorafenib is a TKI authorized by the FDA. When compared to the placebo group, it demonstrated a noticeably longer progression-free survival at about 11 months.

Lenvatinib is an additional FDA-approved multitarget TKI that targets c-KIT, PDGF, FGFR1-4, VEGFR1-3, and RET. Those on lenvatinib had a median progression-free survival of around 18 months, while those on placebo had a median progression-free survival of about 4 months. Nevertheless, once patients cease taking the drugs, the effect is rarely long-lasting, and long-term usage of TKIs, particularly sorafenib, has been linked to resistance.

TKIs such as sunitinib, pazopanib, axitinib, anlotinib, cabozantinib, donafenib, and dovitinib are approved by the FDA to treat iodine-refractory thyroid cancer (DTC). In phase I or phase II clinical trials, these drugs have demonstrated efficacy against DTC. Patients may not be able to tolerate one treatment but may be able to tolerate another, as the adverse effect profile of all the medicines is comparable.

We are poised to make even more strides in the treatment of thyroid cancer as we further our knowledge of the disease's molecular complexities and create more exact medicines, establishing the theranostic strategy as a pillar of contemporary oncology [8]. Moreover, in specific cases, the optimal strategy may involve a combination of multiple treatment approaches for thyroid cancer patients.

Theranostics in the Future

Although theranostics has already made significant strides in the field of managing thyroid cancer, its potential goes much beyond our current successes. As we investigate cutting-edge technology and creative strategies that promise to further enhance the theranostic approach across all elements of oncology, the vista of possibilities is broadening.

Iodine-avid thyroid cancer has a better prognosis than iodine-resistant disease, especially in distant metastasis cases. Resensitization to iodine has been explored through various approaches, including retinoids and anti-diabetic drugs. However, targeted therapies such as BRAF, NTRK, and MEK inhibitors have shown promising results in increasing iodine uptake in previously refractory illnesses.

Mutations that activate MAPK and/or PI3K pathways, such as BRAF V600E, block transcription factors crucial for the synthesis of NIS. Inhibitory compounds have the potential to increase NIS expression at the plasma membrane and accelerate the active transport of iodine into thyrocytes. Research has demonstrated that BRAF V600E mutations can increase iodine awareness, cause partial reactions, and result in a stable illness. However, multikinase inhibitors levatinib and sorafenib do not seem to increase iodine avidity, possibly due to their main targets being further upstream of molecules that regulate NIS expression.

Peptide receptor radionuclide treatment (PRRT) is a potential new field. This state-of-the-art therapeutic approach has the potential to completely alter how many cancers are treated. PRRT provides a highly focused and individualized therapy approach by utilizing the preferential binding of radiolabeled peptides to particular receptors on cancer cells. Even though its initial achievements have been shown in neuroendocrine tumors, ongoing research indicates that its applicability may be able to be applied to a wider variety of cancers, such as thyroid cancer. This is a prime example of theranostics' adaptability and versatility as it looks into new therapy options [9]. Somatostatin receptor, prostate-specific membrane antigen, and fibroblast activation protein targeting tracers have sparked considerable interest in the management of radioactive iodine-resistant DTCs. However, their precise roles and the extent of their efficacy in radioactive iodine-resistant DTC patients are not fully understood yet. There is a need for well-designed studies, including clinical trials, to thoroughly assess these tracers' potential in diagnosing and treating radioactive iodine-resistant DTC [10].

Furthermore, theranostic method advancement continues to benefit greatly from the development of novel radiopharmaceuticals. Researchers are always working to develop radiolabeled substances with better therapeutic efficacy, increased targeting, and fewer side effects. These innovative radiopharmaceuticals possess the potential to expand and improve the theranostic toolset, ultimately assisting a wider range of cancer patients, as they go through rigorous testing and refinement.

Theranostics has already been shown to be a ground-breaking strategy for treating thyroid cancer, but its path is far from complete. Theranostics' next frontier is being defined by the development of new technologies such as PRRT, novel radiopharmaceuticals, and the combination of artificial intelligence and machine learning [11]. Theranostic concept remains a driving force in our pursuit of more efficient, individualized, and accurate cancer care as we continue to research and create. It has limitless potential, and its future effects on oncology are expected to be revolutionary.

Conclusion

In conclusion, the development of theranostics in the treatment of thyroid cancer offers both doctors and patients a ray of hope. We have entered a new era of personalized medicine that has the potential to completely alter the way cancer care is delivered thanks, to the seamless integration of diagnostics and medicines. To fully realize the promise of this extraordinary method, it is crucial that we continue to be dedicated to research, innovation, and collaboration as we expand the horizons of theranostics. The Pakistan Journal of Nuclear Medicine is committed to supporting such initiatives and providing a forum for the exchange of information and concepts in this fast-paced industry.

The advances we have made in theranostics, using thyroid cancer as our model disease, demonstrate the power of integration, teamwork, and innovation in healthcare. Let us be steadfast in our dedication to enhancing patient outcomes and pushing the boundaries of medical knowledge as we continue to explore new areas of nuclear medicine.

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