



INNOVATIONS IN THYROID CANCER MANAGEMENT: MOLECULAR DIAGNOSTICS AND TARGETED THERAPIES

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Abstract:

Thyroid cancer, the most common endocrine malignancy, has experienced significant advancements in its diagnosis and treatment, driven by a deeper understanding of molecular biology. This review explores the transformative role of molecular diagnostics and targeted therapies in improving outcomes for patients with thyroid cancer. Genetic profiling has enabled the identification of key mutations, such as BRAF, RAS, and RET/PTC, facilitating more accurate risk stratification and personalized treatment planning. Targeted therapies, including tyrosine kinase inhibitors and immune checkpoint inhibitors, have emerged as promising alternatives for advanced or refractory cases, offering enhanced efficacy with reduced systemic toxicity. Additionally, liquid biopsy and next-generation sequencing are revolutionizing monitoring and therapeutic decision-making. Despite these advances, challenges remain in overcoming resistance mechanisms and optimizing integration into clinical practice. This study underscores the need



for multidisciplinary collaboration and further research to refine and expand the application of these innovations, ultimately aiming to improve patient survival and quality of life.

Keywords: thyroid cancer, oncogenes, gene mutations, DNA methylation, histone modification, non-coding RNA;

Introduction:

Thyroid cancer, the most prevalent malignancy of the endocrine system, has seen a consistent rise in incidence over recent decades. Advances in high-throughput sequencing technologies have facilitated comprehensive analysis of the thyroid cancer genome, revealing critical genetic lesions and epigenetic modifications that contribute to tumor initiation, progression, dedifferentiation, and metastasis. Studies have identified driver mutations, including those affecting genes such as **BRAF**, **RAS**, and **RET/PTC**, alongside novel molecular pathways involved in tumorigenesis. Integrated genomic approaches have also elucidated the complex interplay between these mutations and tumor behavior, enhancing our ability to stratify risk and predict outcomes.

Epigenomic studies have further expanded our understanding of thyroid cancer biology by identifying alterations in DNA methylation, histone modifications, and non-coding RNAs that regulate gene expression and cellular malignancy. Such changes are particularly prominent in aggressive forms of the disease, such as poorly differentiated thyroid carcinoma (PDTC) and anaplastic thyroid carcinoma (ATC). These aggressive subtypes are characterized by high proliferation rates, extensive mutational burdens, and a propensity for local invasion and distant metastases. Unlike well-differentiated types, such as papillary thyroid carcinoma (PTC), which constitutes approximately 80% of cases, and follicular thyroid carcinoma (FTC), comprising 10–15% of cases, PDTC and ATC are associated with significantly poorer outcomes, with median survival rates of 3.2 years and less than 6 months, respectively.

The classical model of thyroid cancer pathogenesis posits a stepwise accumulation of genetic mutations leading to progressive dedifferentiation. However, recent



genomic and epigenomic studies have redefined this view, highlighting the dynamic nature of thyroid cancer progression. Landmark research, such as the 2014 integrative analysis by The Cancer Genome Atlas (TCGA), analyzed nearly 500 PTC cases and provided a comprehensive genomic and transcriptomic profile of this subtype. Subsequent studies have extended these findings to PDTC and ATC, uncovering aberrations in both tumor DNA and RNA relative to normal thyroid tissue and identifying novel mechanisms underlying tumorigenesis.

In addition to genomic alterations, functional studies utilizing cell and animal models have clarified the roles of key oncogenic pathways, such as the MAPK and PI3K-AKT pathways, in driving tumor progression. These advances have resulted in a refined classification system for thyroid tumors, enabling more precise characterization of tumor subtypes and their associated prognostic and therapeutic implications.

Clinically, these discoveries have catalyzed the development of targeted therapies, such as tyrosine kinase inhibitors (TKIs), and diagnostic tools, including molecular tests for mutation detection and risk stratification. Despite these advancements, challenges remain, particularly in addressing treatment resistance and improving outcomes for refractory and aggressive cases. Continued research efforts are critical to translating these genomic insights into effective therapeutic strategies and improving long-term survival rates for all thyroid cancer patients.

Liquid biopsy is a biomarker analysis, where fluid samples are taken from the patient's body. Such as cerebrospinal fluid, as well as urine and blood. Unlike tissue biopsy, it has the advantage of being minimally invasive. It is much cheaper and more accessible to the patient. It is also worth noting that, like traditional tissue biopsy, this method does not only diagnose cancer, but also allows the doctor to monitor tumor cells and mutations during treatment, since during liquid biopsy the doctor has the opportunity to take a sample multiple times.

Liquid biopsy in oncology is mainly aimed at analyzing and detecting CTCs, circulating tumor nucleic acids, as well as extracellular vesicles of tumor origin and extrachromosomal circular DNA of the tumor.

As for thyroid cancer, its diagnosis is standardly made through cytology and histopathology of thyroid tissue, using a fine needle aspiration. New discoveries in



both genetic and epigenetic aspects of thyroid neoplasms provide improved treatment management.

In thyroid cancer, certain genetic alterations occur, resulting in the activation of metabolic pathways of thyroid tumorigenesis. Such as the mitogen-activated protein kinase pathway, which mediates ERK, JNK and p38, as well as phosphorylation events, during which cell transformation and the formation of tumor cells occur.

Liquid biopsy allows you to determine both genetic and epigenetic changes in the tumor through a simple blood sample. BRAF mutation is a circulating mutation in the blood, for which liquid biopsy is considered a way to detect it early, although this method has not yet been fully implemented in medicine, we encounter certain contradictions.

Future prospects of liquid biopsy in thyroid cancer management: Based on the conducted studies, it is established that timely detection of genetic and epigenetic changes in tumor cells is necessary for timely detection of thyroid cancer, one of the main and simple means of which is liquid biopsy. The new vision of liquid biopsy, together with other scientific achievements, such as genome-wide association studies, as well as epigenome-wide association studies, allows us to perform early diagnosis of tumors, effective treatment, in a minimally invasive way.

Targeted Drug Therapy for Thyroid Cancer:

Standard chemo drugs work by attacking rapidly growing cells. drugs attack specific genes, which release specific protein that changes inside thyroid cancer cells. The types of targeted drugs which are known as kinase inhibitors. Kinases are proteins inside cells that normally relay signals (such as telling the cell to grow, etc.). Blocking certain kinases can help treatment of the some cancers.

Most of these cancers can be treated with surgery and radioactive iodine therapy. But when those treatments aren't effective, targeted drugs can often be helpful.



Multikinase inhibitors

Lenvatinib (Lenvima), sorafenib (Nexavar), and cabozantinib (Cabometyx) are targeted drugs known as *multikinase inhibitors*, because they block several proteins. These drugs work in 2 main ways:

1. They help block tumors from forming new blood vessels, which impact to the tumors need to grow.

2. The specific proteins made by cancer cells that normally help them grow.

Lenvatinib and sorafenib can often help stop cancer growth for a time in people with papillary or follicular thyroid cancer whose radioactive iodine treatment is no longer working. If these drugs are no longer helpful, cabozantinib may be an option. All of these drugs should be taken orally.

Common side effects can include fatigue, rash, loss of appetite, diarrhea, nausea, high blood pressure, and hand foot syndrome (redness, pain, swelling, or blisters on the palms of the hands or soles of the feet). Other more serious side effects, such as severe bleeding and perforations in the intestine, can also occur.

RET inhibitors ----- In some papillary and follicular thyroid cancers, the cells have certain changes in the *RET* gene that cause them to make an abnormal forms, which produce abnormal protein. Selpercatinib (Retevmo) and pralsetinib (Gavreto) are drugs known as *RET inhibitors*.

These drugs are also taken orally, as capsules or pills, typically once or twice a day. Common side effects can include dry mouth, diarrhea, constipation, high blood pressure, fatigue, swelling in the hands or feet, skin rash, high blood sugar levels, low white blood cell or blood platelet counts, and changes in certain other blood tests. Less common but more serious and diagnostic side effects can include liver damage, allergic reactions, changes in heart rhythm, bleeding easily, and problems with wound healing.

TRK inhibitors ----- A small number of thyroid cancers have changes in one of the *NTRK* genes. Larotrectinib (Vitrakvi), and entrectinib (Rozlytrek), and repotrectinib (Augtyro) target and disable the abnormal TRK proteins made by the *NTRK* genes. These drugs are taken as pills or capsules, once or twice a day. Common side effects of these drugs can include dizziness, fatigue, nausea, vomiting, constipation, weight gain, and diarrhea. Less common but more serious



side effects can include liver damage, heart problems, confusion, and other nervous system problems.

Multikinase inhibitors ----- Vandetanib (Caprelsa) and cabozantinib (Cometriq) are multikinase inhibitors (drugs that target several different kinase proteins). They can affect both cancer cells themselves and the growth of new blood vessels (which tumors need to grow). These drugs are taken as pills, typically once a day. Common side effects of vandetanib include diarrhea, rash, nausea, high blood pressure, headache, fatigue, decreased appetite, and belly (abdominal) pain. Rarely, it can also cause serious or even life-threatening heart rhythm problems or infections. Because of its potential side effects, doctors must get special training before they are allowed to prescribe this drug. Common side effects of cabozantinib include diarrhea, constipation, belly pain, mouth sores, decreased appetite, nausea, weight loss, fatigue, high blood pressure, loss of hair color, and hand-foot syndrome (redness, pain, and swelling of the hands and feet). Rarely, this drug can also cause serious side effects such as severe bleeding and holes in the intestine.

Molecular testing of thyroid nodules and thyroid cancer has improved the diagnostic accuracy of indeterminate thyroid nodules. Additionally, identifiable molecular variants and fusions provide information about eligibility for targeted systemic therapies for thyroid cancer patients with metastatic, progressive, radio-iodine refractory disease. [2]

Even today Cytologically indeterminate thyroid nodules are a diagnostic, as well as, clinical challenge, molecular testing has been advanced as a diagnostic attribute to help guide treatment, but it should be noted that data demonstrating meaningful clinical impact and supporting their routine use is still limited. Although most thyroid nodules (80–90%) harbor benign pathology, the ability to detect malignancy and determine the appropriate course of treatment is very important. The malignancy potential of a thyroid nodule is studied thoughtfully, which includes clinical history, physical examination, radiographic assessments, and fine needle aspiration (FNA) biopsies.

Molecular testing is recommended only for “indeterminate or suspicious” nodules classified as “atypia of undetermined significance or follicular lesion of



undetermined significance (AUS-FLUS),” “follicular neoplasm or suspicious for a follicular neoplasm (FN-SFN),” or “Suspicious for Malignancy (SFM)” categories. These classifications carry malignancy risk between 5 and 40%, and the primary utilization of molecular testing has centered around obtaining a more definite assessment of this risk performance of Afirma-GEC. [1]

Molecular testing has become a more commonly utilized tool in the clinical setting to help provide additional risk information for ITN. Ideally, the results of the molecular test shift the risk of malignancy (ROM) from ~25% with ITN cytology to risks that help determine which patients will benefit from conservative surveillance versus definitive surgical intervention.

Molecular genetic testing is a valuable tool in understanding patients’ prognosis based on specific mutations detected in thyroid cancer. The main known genetic causes of thyroid cancer include point mutations in the BRAF, RAS, TERT promoter, RET, and TP53 genes and the fusion genes RET/PTC, PAX8/PPAR γ , and NTRK. Molecular genetic testing of thyroid tissue in the preoperative and/or postoperative period is becoming more common, it can also help to determine the extent of surgical treatment and the use of systemic targeted therapy.

SN is a calculation of the number of true positives (for this topic, the patient has thyroid cancer, and the molecular test reports a positive finding) divided by all the patients with thyroid cancer (who have true positive plus false negative test results). A low SN indicates thyroid cancers have been missed (called negative or benign) by the molecular marker test. Alternatively, SP is a calculation of the true negatives (the patient does not have thyroid cancer and the test is negative) divided by all the patients without thyroid cancer (true negative plus false positive test results)

The identification of the BRAFV600E mutation in papillary thyroid carcinoma (PTC) in 2003 was one of the earliest identified molecular signatures correlating a molecular variant with final histology. BRAFV600E is a highly specific yet poorly sensitive marker for thyroid cancer, especially in ITN where it is now known that BRAFV600E is present in <10% of molecularly tested ITN aspirates.

Approximately 20-25% of thyroid nodule aspirates result in ITN cytology. The risk of malignancy of BIII and BIV ITN ranges from 6-40% depending on the



institution and the categorization of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) as benign or malignant. [1]

Perhaps the most widely known are the Afirma Gene Expression Classified (GEC, since 2011) and ThyroSeq v2 (since 2014), which evaluates mRNA expression levels of 167 genes, or DNA mutations within a 19 gene panel. Both of these tests have been updated since their initial release to Afirma Genomic Sequencing Classifier (GSC, based on RNA sequencing technology evaluating ~10,000 genes) and ThyroSeq v3 (next generation sequencing of 112 genes) [1]

Thyroseq® has evolved with multiple iterations expanding the number of molecular variants identified from the initial 7 gene panel (targeted variants in 4 genes and 3 gene fusions) to a targeted NGS platform including 12 genes in version 1 to 14 genes analyzed for point mutations and 42 types of gene fusions in version 2.

MPTX screens samples with the ThyGeNEXT NGS panel that include selected DNA mutations in the following genes: ALK, BRAF, GNAS, HRAS, KRAS, NRAS, PIK3CA, PTEN, RET and TERT promoter genes. The following gene fusions are detected by analysis of RNA: ALK, BRAF, NTRK, PPAR γ , RET and THADA. If there is a strong driver mutation detected, the sample is considered positive. If the sample has a weak oncogenic driver mutation or no mutation, it is further risk stratified using the microRNA classifier (ThyraMir). The initial ThyraMir panel included 5 growth-promoting miRNAs (miR-31, -146, -222, -375, -551) and 5 growth-suppressing miRNAs (miR-29, -138, -139, -155, -204).

MPTX results are ultimately reported as one of three categories (negative, moderate, or positive) based on results of the combined ThyGeNEXT mutation panel and ThyraMIR microRNA risk classifier threshold. Finally, MPTX has recently been updated with the addition of miR-21 and an interdependent pairwise microRNA expression analysis (MPTXv2).

The Afirma GSC samples are initially tested for RNA quantity and quality. Sufficient samples are tested against initial classifiers to detect parathyroid tissue, MTC, BRAFV600E variants and RET/PTC1 and RET/PTC3 fusions. Recently, the validation of the MTC classifier of the Afirma GSC showed 100% SN and 100% SP in a cohort of 21 MTC and 190 non-MTC lesions.



TSv3 is a genomic classifier (GC) where a value is assigned to each detected genetic alteration based on the strength of association with malignancy: 0 (no association), 1 (low cancer risk), or 2 (high cancer risk). A GC score calculated for each sample is a sum of individual values of all detected alterations, with GC scores 0 and 1 accepted as test negative (score 1 is commercially reported as “currently negative”) and scores 2 and above as test positive in thyroid nodules with Afirma GSC suspicious results, or thyroid nodules with BV or BVI cytology, Afirma Xpression Atlas (XA) can provide more granular molecular information.

High frequency of oncogenic BRAF mutations has important clinical implications and multiple studies have shown that BRAFV600E correlates with aggressive features of thyroid cancer such as extrathyroidal extensions, vascular invasion, larger thyroid nodule size, advanced staging, lymph node metastasis and recurrence. Conversely, the most aggressive subtypes of thyroid cancer, medullary, poorly differentiated, and anaplastic, have high disease-specific mortality. [2]

Personalized Medicine and Artificial Intelligence in Thyroid Carcinoma:

The rapid advancement of artificial intelligence (AI) and machine learning (ML) has brought unprecedented innovation across multiple sectors, including medicine. Although these technologies have been integrated into healthcare for years, their role in improving medical practices has never been more critical. Following our earlier discussion on thyroid carcinoma therapeutics, we now explore the transformative impact of AI and ML on traditional approaches.

AI-Driven Omics Analysis for Patient Stratification and Biomarker Discovery:

Cancer is a multifaceted disease arising from genetic, epigenetic, proteomic, and transcriptomic alterations. AI-powered analysis of multi-omics data—including genomics, proteomics, and transcriptomics—has become pivotal in understanding cancer’s molecular complexities. Using advanced machine learning and deep learning algorithms, researchers can extract valuable insights from large datasets to identify biomarkers, uncover molecular mechanisms, and develop personalized treatments. AI-based tools enable the detection of cancer-driving mutations by



sifting through massive genomic datasets. For instance, in lung cancer, AI has been instrumental in identifying activating mutations in the EGFR gene, such as exon 19 deletions and the L858R mutation, which are critical predictors of targeted therapy response. Similarly, machine learning has been used to classify tumors into distinct subtypes based on genetic patterns, aiding in therapy selection and patient outcome prediction. Proteomics and transcriptomics also benefit significantly from AI. For example, AI-driven analysis of mass spectrometry data can identify cancer-specific protein signatures, such as elevated HE4 and CA125 levels in ovarian cancer. Additionally, AI models can analyze post-translational modifications (PTMs) and protein-protein interactions, uncovering dysregulated pathways like the Wnt signaling pathway in colorectal cancer.

AI in Clinical Decision-Making and Personalized Treatment Plans:

AI is reshaping cancer therapy by providing personalized treatment strategies tailored to individual patients. By analyzing diverse data sources—genomic, proteomic, clinical, and more—AI algorithms can predict treatment responses and identify biomarkers linked to specific tumor characteristics. For instance, in breast cancer, AI models predict responses to neoadjuvant chemotherapy, enabling clinicians to choose the most effective therapies while minimizing side effects. AI also plays a role in optimizing treatment schedules and doses by analyzing patient-specific data to dynamically adjust therapy plans. For example, AI models in lung cancer have been used to predict tumor progression and optimize radiation schedules, improving efficacy while reducing treatment times. Moreover, AI can suggest synergistic drug combinations to combat resistance mechanisms, as demonstrated in melanoma studies involving BRAF and MEK inhibitors. Beyond treatment planning, AI facilitates continuous monitoring of patients during and after therapy by analyzing data from wearable devices, electronic health records, and patient-reported outcomes. In prostate cancer, for instance, AI models predict disease recurrence, aiding in decisions about follow-up care and adjuvant therapy. While promising, integrating AI into healthcare requires rigorous validation, regulatory oversight, and ethical considerations. Collaboration among clinicians, researchers, and AI experts is essential to ensure reliable and effective AI tools.



Progress in Thyroid Cancer Diagnosis and Treatment:

Personalized medicine for thyroid cancer faces unique challenges, including subjective interpretation of ultrasound (US) findings, limitations in cytopathology, and difficulties in distinguishing between benign and malignant neoplasms. AI offers transformative potential in addressing these issues by enhancing diagnostic accuracy and efficiency. AI-based systems, such as the Thyroid Imaging Reporting and Data Systems (TI-RADS), aid in assessing malignancy risk for thyroid nodules based on US features like solid composition, irregular margins, and microcalcifications. Advanced tools like the ThyNet deep-learning algorithm, which integrates models like ResNet and DenseNet, excel in differentiating benign from malignant nodules and identifying additional tumor characteristics, such as lymph node metastases. Emerging AI techniques also analyze tumor texture features from US images, achieving diagnostic accuracies of up to 94.64%. These tools integrate traditional US data with advanced image analysis, narrowing diagnostic discrepancies globally. Fine-needle aspiration (FNA) remains a critical preoperative diagnostic method, and the Bethesda system provides a structured framework for evaluating thyroid nodules. AI-enhanced cytology leverages machine learning to classify tumors based on morphology and genetic profiles, offering reliable differentiation between benign and malignant lesions.

Advances in Thyroid Cancer Research:

Researchers conducted by the NCI are attempting to improve the knowledge of thyroid cancer treatment. Papillary, follicular, medullary, and anaplastic thyroid cancer are the four primary types of thyroid cancer. The majority of thyroid malignancies are detected early and they respond well to treatment. In order to reduce the side effects, researchers are currently trying to determine which thyroid cancer patients can be safely selected for less treatment. Additionally, research is required to develop new therapies for more aggressive and uncommon forms of thyroid cancer.

Diagnosis-overdiagnosis or detecting tiny, slowly developing thyroid tumors that would never result in a medical issue have been a significant worry for the past 20 years. During screening, these tumors, also known as nodules, are found by



ultrasound or by feeling the neck. To determine whether a suspicious nodule on a person's thyroid is malignant, a tiny needle biopsy is frequently performed. But in as many as one-third of cases pathologists are unable to identify whether a nodule is malignant just based on the appearance of the cells.

In the past, the half of the thyroid (called a lobe) that contained the suspicious lump would have needed to be removed for patients with unclear biopsy results. Since there was no malignancy in the bulk, this turned out to be overtreatment. However, over the past several years, scientists supported by the NCI have created genomic tests that can assist in determining if such ambiguous nodules are malignant and if there is a necessity for surgery. Many people may be able to avoid needless surgery thanks to these diagnostics. In the future, the testing could potentially be used to decide how much thyroid tissue should be removed and to choose treatments that match the genetic traits of specific malignancies.

Papillary and Follicular Thyroid Cancer Treatment- Both follicular and papillary thyroid cancers grow slowly and, typically, don't spread to other parts of the body. Thyroid follicular cancer is less frequent. Surgery to remove the entire thyroid usually cures papillary thyroid cancer, which accounts for the majority of thyroid cancer diagnoses. Patients may also be treated with radioactive iodine if their papillary thyroid cancer has progressed. Researchers have been examining whether certain individuals might safely undergo less invasive surgery due to the good prognosis for early-stage papillary thyroid carcinoma. This would spare them the need to take thyroid replacement hormones for the rest of their lives. Possible types of treatment include:

- **Lobectomy-** In a lobectomy, half of the thyroid is removed, leaving the other half intact so it can continue to generate hormones. People with tiny papillary malignancies already undergo this kind of surgery. According to research, some patients may also choose this procedure if their malignancies are between 1 and 4 cm in size and have not migrated to their lymph nodes. The possibility that more patients with papillary thyroid cancer might decide without having their entire thyroid removed surgically is still being investigated.



- Deferring surgery- According to other studies, the majority of patients with papillary thyroid tumors that are smaller than 1cm in size do not require surgery right away. They can be safely monitored with periodic ultrasound imaging and have surgery only if their cancer starts to grow.
- Undergoing radiofrequency ablation- This therapy involves inserting a needle into the tumor utilizing ultrasound imaging. Heat is then applied through the needle to eliminate the tumor tissue. Researchers are assessing the safety and effectiveness of this approach in individuals with small thyroid cancers that are at a low risk of spreading to other parts of the body.

Aggressive forms of papillary and follicular thyroid cancer- in uncommon instances, papillary or follicular thyroid cancer can be aggressive and may grow and spread despite surgery and radioactive iodine therapy. The Food and Drug Administration (FDA) has approved two targeted medications for such cancers: sorafenib tosylate (Nexavar) and lenvatinib (Lenvima). Both medications inhibit the function of several different abnormal proteins that encourage the growth of cancer cells. Another targeted medication, named cabozantinib (Cabometyx), is approved for cancers that continue to progress after treatment with sorafenib or lenvatinib.

One of the proteins that sorafenib inhibits is generated by the BRAF gene. In certain individuals, a mutated form of this gene facilitates the development of aggressive papillary thyroid cancer. Additional medications that target mutant forms of the B-Raf protein are being evaluated in patients whose papillary thyroid cancer has returned or advanced despite treatment. NCI researchers are also examining how the B-Raf protein interacts with other proteins to promote tumor growth, aiming to discover new drugs that target these interactions.

Furthermore, researchers are identifying other genetic alterations in papillary or follicular thyroid cancer that could be targeted with novel treatments. Recent approvals for drugs include:

Selpercatinib (Retevmo) and pralsetinib (Gavreto) are medications that target mutations in a gene known as RET, intended for individuals with advanced or metastatic papillary thyroid cancer that harbors a RET mutation and is resistant to radioactive iodine therapy. Entrectinib (Rozlytrek) and larotrectinib (Vitrakvi) are



used to treat cancers that have a specific genetic alteration referred to as an NTRK gene fusion. A form of thyroid cancer named Hurthle cell thyroid cancer was previously regarded as a subtype of follicular thyroid cancer. It is now recognized as a distinct type of tumor. Ongoing research aims to gain insights into the genetic factors driving Hurthle cell thyroid cancer and to identify potential drugs that could target those genes.

Medullary Thyroid Cancer Treatment- A rare variant of thyroid cancer, known as medullary thyroid cancer, originates in the thyroid cells responsible for producing a hormone called calcitonin. Treatment with radioactive iodine is not effective for these cancers. Targeted therapies such as selipergatinib (Retevmo), vandetanib (Caprelsa), and cabozantinib (Cometriq) may be considered if the disease recurs post-surgery or has metastasized. According to findings from a 2023 study, the majority of patients diagnosed with this type of thyroid cancer are likely to receive selipergatinib as the first line of treatment, prior to attempting other medications.

Researchers are looking for better drugs for the treatment of medullary thyroid cancer: The NCI's My Pediatric and Adult Rare Tumor (MyPART) network operates a rare tumor clinic dedicated to individuals with medullary thyroid cancer that fails to respond to standard treatments or recurs after therapy. Researchers will analyze tissue samples obtained from clinic participants to better understand how these cancers differ genetically from those for which existing treatments are effective.

Research conducted by scientists at the NCI responsible for the MyPART clinic indicated that vandetanib can effectively slow down tumor development in children and young adults with hereditary syndromes associated with medullary thyroid cancer. Investigators have discovered that small clusters of medullary thyroid cancer cells can be identified on PET scans using a radioactive tracer known as gallium Ga 68-Dotatate, which attaches to those cells. Researchers are now exploring whether a similar medication, referred to as lutetium Lu 177-Dotatate (Lutathera), could serve as a treatment for medullary thyroid cancer. This medication might be able to deliver radiation directly to medullary thyroid cancer cells.



Anaplastic Thyroid Cancer Treatment- Anaplastic thyroid cancer is uncommon. Nonetheless, it is the most aggressive form of thyroid cancer and ranks among the most aggressive cancer types overall. Traditionally, very few individuals diagnosed with this condition survive beyond one year. The disease has shown resistance to all available therapies. However, in 2018, the FDA approved the combination of two targeted therapies, dabrafenib mesylate (Tafinlar) and trametinib (Mekinist), for anaplastic thyroid cancers that have a specific mutation in the BRAF gene. Approximately 25% of anaplastic thyroid cancers carry this mutation.

Conclusion:

The integration of molecular diagnostics and targeted therapies has marked a paradigm shift in the management of thyroid cancer. By enabling precise tumor characterization and personalized treatment approaches, these innovations have improved prognostic accuracy and therapeutic outcomes, particularly for patients with advanced or refractory disease. However, challenges such as treatment resistance, accessibility to advanced diagnostic tools, and the need for long-term clinical data remain critical areas for ongoing research. Future efforts should focus on refining these technologies, developing combination therapies, and ensuring equitable access to these advancements. With continued multidisciplinary collaboration and innovation, these strategies have the potential to further enhance survival rates and the quality of life for thyroid cancer patients worldwide.

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