Systemic Management of MTC

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Medullary thyroid cancer (MTC) is an uncommon tumor, accounting for ~3 to 5% of all thyroid malignancies. Unlike papillary thyroid cancer, there are no accepted adjuvant therapies and only limited options for patients with disseminated disease. MTC stems from calcitonin-producing parafollicular C cells of the thyroid. Among well-differentiated thyroid tumors, it is the most aggressive, with 10-year survival rates of 40% to 50%. Screening of at-risk populations has resulted in finding preclinical disease, leading to early surgical intervention and high cure rates. Unfortunately, 80% of MTC cases are sporadic, and early detection of this form of MTC is difficult. The consequence of an inability to detect the sporadic form of MTC early is more advanced disease present at the time of surgery with metastases involving cervical nodes, lungs, liver and/or bone marrow in 40% to 50% of cases. Current palliative therapy includes repeat surgical exploration, external beam radiation therapy, and chemotherapy, all with limited success.

There has been limited success in the use of systemic chemotherapy to treat patients with metastatic MTC. The chemotherapeutic drug studied most is doxorubicin, whose single-agent activity yields a response rate of 10% to 20%. The use of combination chemotherapy does not appear to improve response rate or survival; however, this has not been studied in large randomized trials. Therefore, chemotherapy is not a particularly attractive option for patients with metastatic MTC.

Recently, there has been major advance in molecular targeted therapy. The small-molecule tyrosine kinase inhibitors share the property of binding to the RET ATP-binding pocket and have overlapping specificities, frequently inhibiting VEGFR2, PDGFR and EGFR to varying degrees as well as RET. Examples of such small molecules under study for MTC include ZD6474, sorafenib, and sunitinib. The ongoing clinical trials on small-molecule tyrosine kinase inhibitors will be discussed. In addition, radinuclide therapy, radioimmunotherapy in particular, presents another systemic treatment option under investigation. Recent results from clinical trials with anti-CEA radioimmunotherapy will be briefly discussed.