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COMMENTS:

Differentiated thyroid cancer is a potentially curable disease in majority of cases.TSH control and activation of the sodium iodide symporter (NIS) remains the cornerstone of both adjuvant and salvage treatment. At the same time we also know that it is difficult to destroy all metastatic sites with radio-iodine to an acceptable level even in radioiodine concentrating or the differentiated variety. This has been assumed mainly due to low residence time of radioactive iodine in the thyroid cancer cells resulting in delivery of low radiation doses. Iodine as a base of common medications and its dietary intake are two important causes . Different strategies have been attempted to increase intracellular residency time of radioiodine. On the other hand majority of deaths due to thyroid cancer occurs due to its inability to concentrate radioiodine and de-differentiaton of cancer cells is supposed to be the prime cause for this effect. It has been seen here that thyroid cancer, like many other malignancies is also characterized by genetic alterations resulting in dysregulated cell growth and various attempts and strategies are being put forward for attempting re-differentiation of such thyroid cancer cells. This will be of prime importance in case some of these attempts are translated into actual clinical practice which could re-differentiate the cancer cells putting them under TSH regulation again so that it could further concentrate radioiodine. The aim of any alternative strategy thus should be two fold : firstly there should be an attempt to re-differentiate cancer cells and secondly to increase residence time of radioiodine in the cells. Gene therapy, especially for restoration of iodine uptake in thyroid cancers by re-expression of the NIS and re-differentiating properties of retinoic acid derivatives are the only ones that hold some promise in thyroid cancer. Some other agents which could be a potential adjuvant to increase the effectiveness of radioiodine, based on increasing NIS expression, are histone deacetylase inhibitors, suberoylanilide, hydroxamic acid and demethylating agents. These have been found to

increase radioiodine uptake. However opinion is divided regarding re-differentiating power of these derivatives and different groups have supported as well as rejected this approach. Two retinoid receptors, RARâ and RXRã have been identified which are differentially expressed in thyroid cancer cell lines and application of the amyloid precursor protein ligand generally suppress proliferation in those cell lines that expresses both these isoforms. However no difference in outcomes have been reported with any of these agents. All the same, the best curable cancer, is a treating physicians dilemma as soon as 'escape' phenomenon from radioiodine occurs in the form of de-differentiation in thyroid cancer cells when they no longer have the power of concentrating radioiodine. Most alternative strategies however still fall under the 'promising' category and do not have the potential to benefit clinical management and improve outcome. Unfortunately not much benefit from chemotherapy or radiotherapy has been achieved in thyroid cancer except for some isolated reports in literature about the use of chemotherapeutic agents as a radio sensitizer for radioactive iodine. Recent reports point out that these de-differentiated thyroid cancer cells however retain the potential of glucose metabolism, thus facilitating their detection by positron emission tomography (PET) as ^{18}FDG avid sites. Excision, if feasible, of some of these sites by radioguided surgery with a hand held PET detector may be a viable option in the future to deal with some of these situations.

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