Combination BRAF and MEK inhibitor therapy for redifferentiation of radioiodine refractory BRAF mutated papillary thyroid cancer: a Case Study

Case Description:

69-year-old male with metastatic papillary thyroid cancer bearing $BRAF^{V600E}$ mutation, with involvement of the lungs and cervical lymph nodes (Stage IV). He had undergone a thyroidectomy four years prior, and two subsequent I^{131} therapies with a cumulative administered activity of 9971.5MBq (269.5mCi). Follow-up I^{131} and F^{18}-FDG imaging show non-Iodine avid/FDG-avid lesions, increasing in size and number in the last 12 months. Rising serum thyroglobulin levels and histopathology supported papillary thyroid cancer.

Procedures Performed:

The patient underwent BRAF-inhibitor (dabrafenib) and MEK-inhibitor (trametinib) therapy for four weeks, whilst simultaneously undergoing thyroid stimulating hormone (TSH) stimulation by thyroxine withdrawal. This was followed by F^{18}-FDG imaging, and I^{124} imaging at 48 and 72hours to confirm restoration of iodine-avidity and assist with dosimetry calculations.

Findings:

Patient tolerated BRAF/MEK-inhibitor therapy well, with side-effects being a low-grade fever and rigor for two days in the second week of treatment and was able to resume treatment once resolved.

I^{124} imaging showed intense iodine-uptake in the lung nodules, hilar lymph nodes, right thyroid bed, and some other nodal activity. Conversely, FDG imaging showed a decrease in the number and avidity of lesions. All sites of FDG-avid disease were concordant with iodine-avid disease.

The patient went on to have 4995MBq (135mCi) of I^{131} the following day whilst still following preparation instructions.

Outcome:

Redifferentiation therapy successfully converted the iodine-negative papillary thyroid cancer lesions to iodine-avid disease with subsequent sufficient I^{131} retention on post-therapy scan. I^{131} therapy resulted in a significant response, with stabilisation of disease seen on follow-up scans, and a 30% decrease in thyroglobulin.

Discussion:

This study is an example of how the use of BRAF-inhibitor and MEK-inhibitor therapy leads to redifferentiation of the BRAF mutation bearing thyroid cancer cells. By targeting the mutations such as $BRAF^{V600E}$, iodine-avidity can be restored in patients with previously iodine-refractory metastatic disease, allowing successful I^{131} therapy.