

Age-related neoplastic risk profiles and penetrance estimations in multiple endocrine neoplasia type 2A caused by germ line RET Cys634Trp (TGC>TGG) mutation

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RET testing in multiple endocrine neoplasia type 2 for molecular diagnosis is the paradigm for the practice of clinical cancer genetics. However, precise data for distinct mutation-based risk profiles are not available. Here, we survey the clinical profile for one specific genotype as a model, TGC to TGG in codon 634 (C634W). By international efforts, we ascertained all available carriers of the RETC634W mutation. Age at diagnosis, penetrance, and clinical complications were analyzed for medullary thyroid carcinoma (MTC), pheochromocytoma, and hyperparathyroidism (HPT), as well as overall survival. Our series comprises 92 carriers from 20 unrelated families worldwide. Sixty-eight subjects had MTC diagnosed at age 3-72 years (mean 29). Lymph node metastases were observed

in 16 subjects aged 20-72 and distant metastases in 4 subjects aged 28-69. Forty-one subjects had pheochromocytoma detected at age 18-67 (mean 36). Amongst the 28 subjects with MTC and pheochromocytoma, six developed ph