

GENOTYPE - PHENOTYPE ANALYSIS IN PATIENTS WITH MEDULLARY THYROID CARCINOMA: A SINGLE CENTER EXPERIENCE

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INTRODUCTION

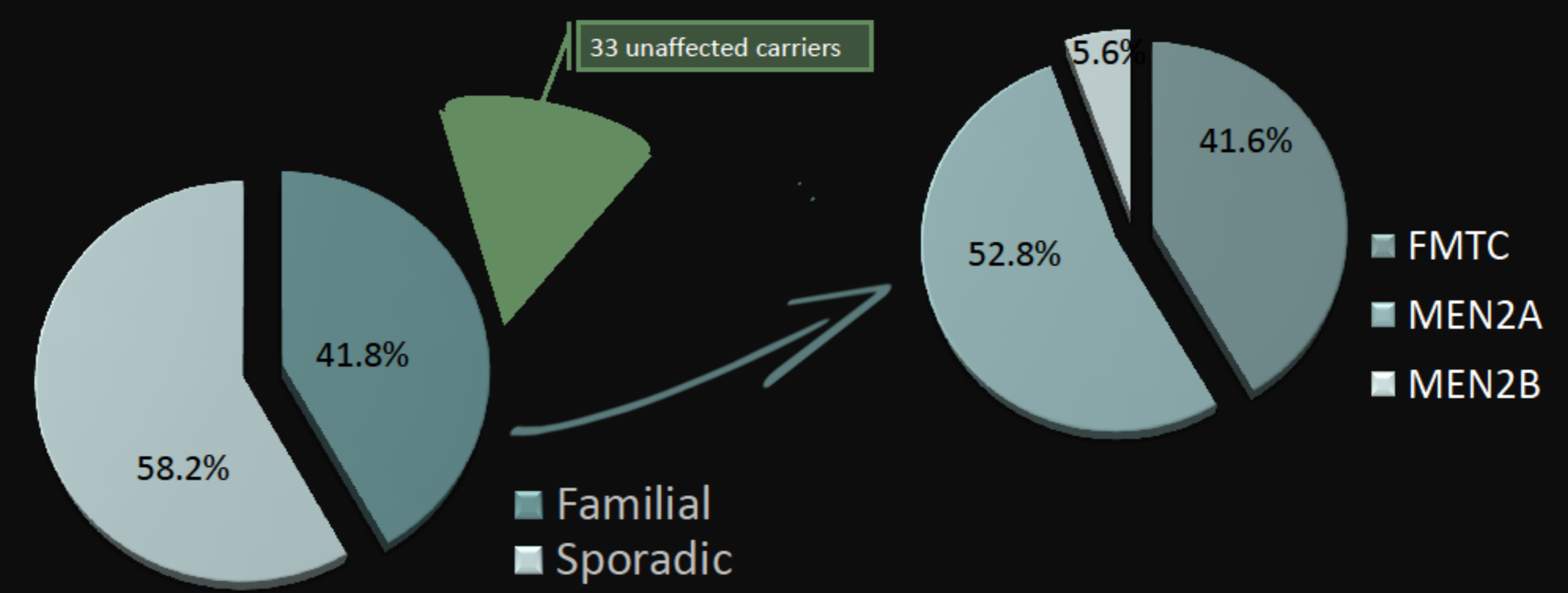
Medullary thyroid carcinoma (MTC) is a malignant neoplasm derived from the parafollicular cells of the thyroid gland. Approximately 25% of them are caused by germline mutations of the *RET* protooncogene, presenting as a part of FMTC, MEN2A or MEN2B syndrome.

DESIGN OF THE STUDY

We analyzed 213 consecutive patients with MTC (142 females, 71 males, age 6-78, mean 45 years), treated in a single centre from 2004-2014. Direct DNA sequencing for detection of mutation in coding region of *RET* exons 5, 8, 10, 11, and 13-16, was performed in all patients

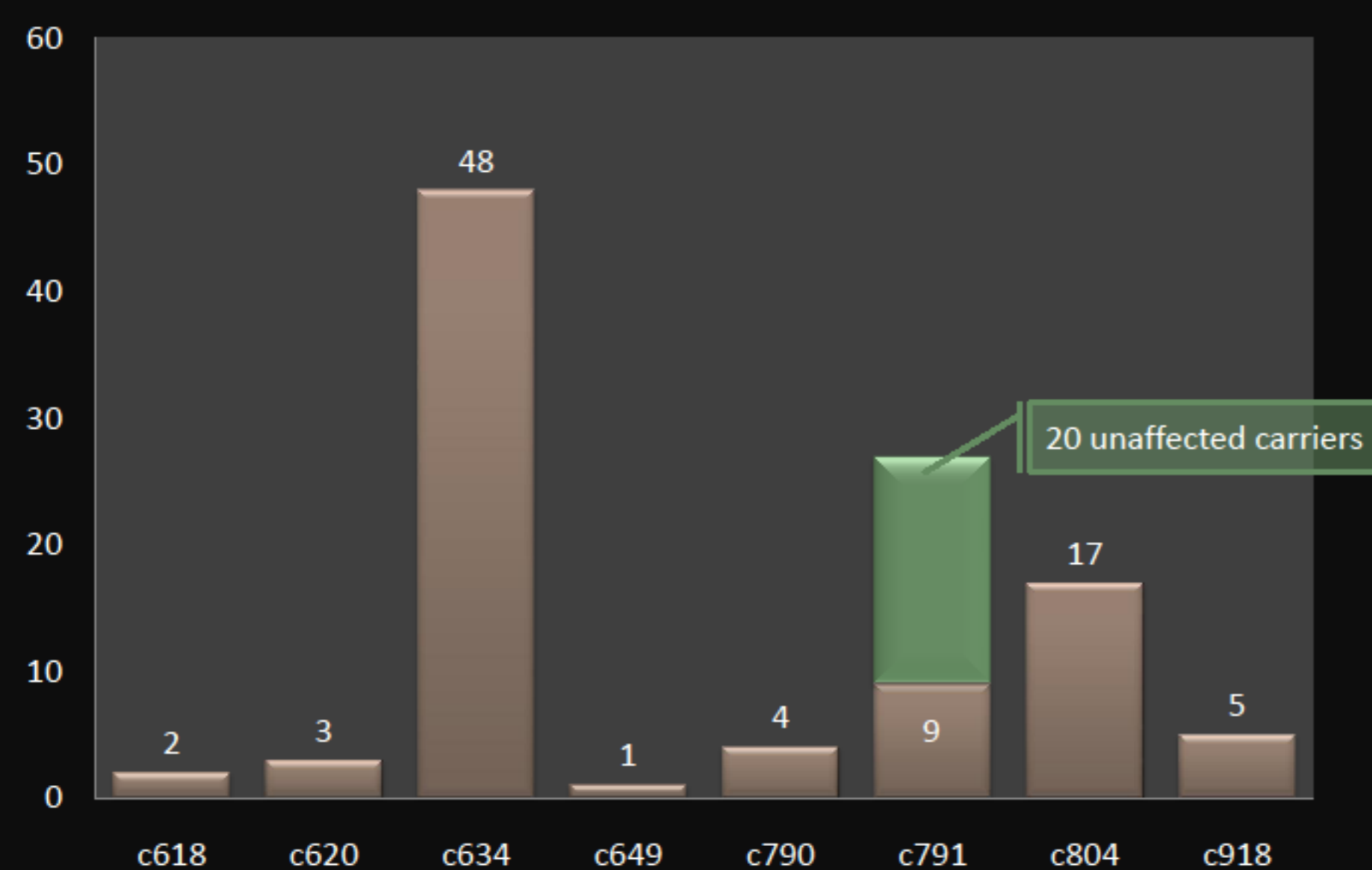
RESULTS

Mutations in *RET* protooncogene were found in 89 (41.8%) MTC patients (age 3 - 72, mean 37.7 years) and their 33 unaffected relatives (age 10 - 70, mean 40 years), comprising 38 different families. FMTC was diagnosed in 37 (41.6%), MEN2A in 47 (52.8%), MEN2B in 5 (5.6%) of MTC patients. (Graph 1)

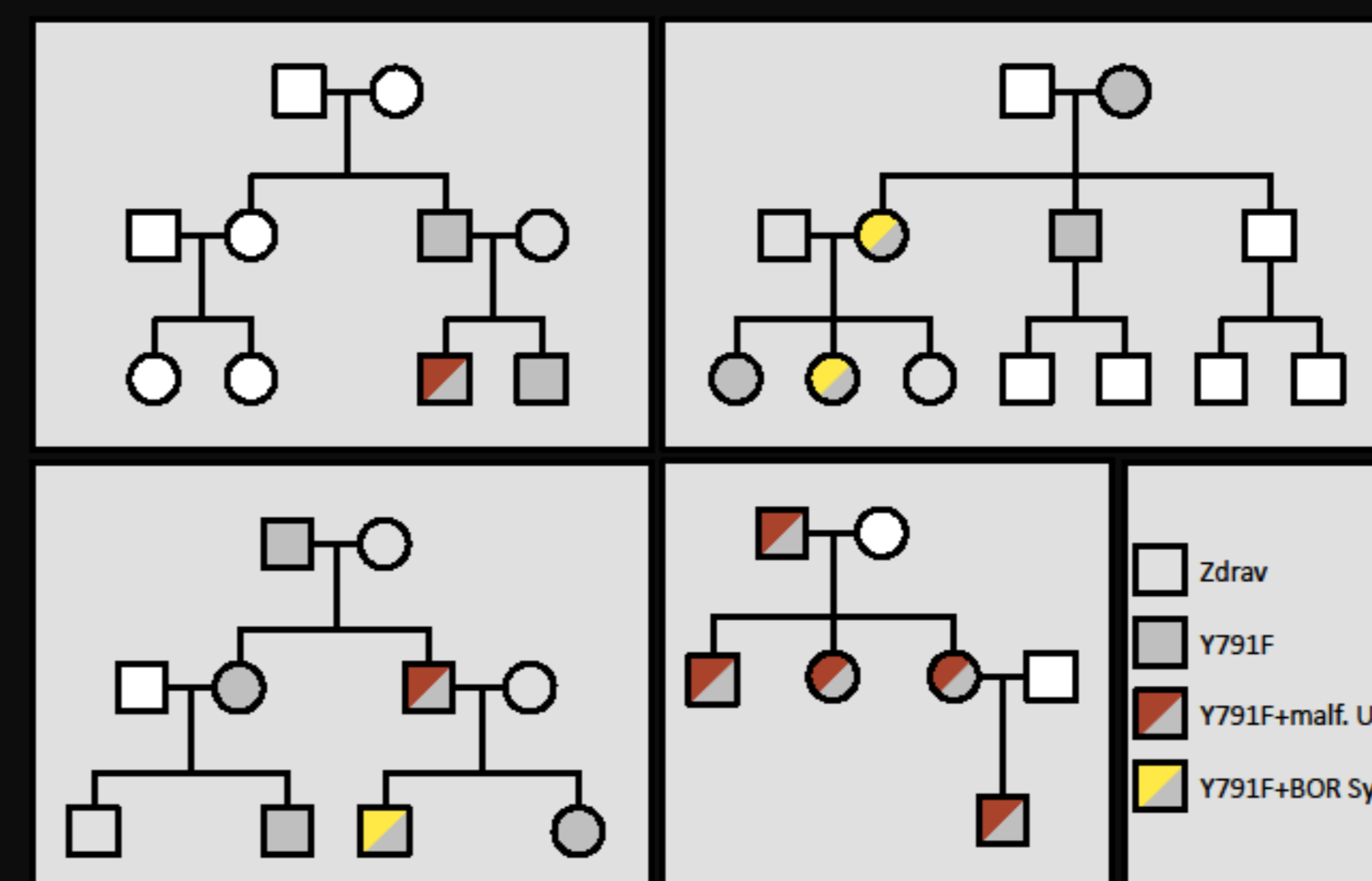


Graph 1: Familial and sporadic MTC

A total of 15 different mutations were found. Cys634Phe, Cys634Arg and Val804Met were the most frequent mutations in MTC patients (21.3%, 20%, and 19.1%, respectively), but the most predominant one among all analyzed patients was Tyr791Phe (29/122 patients, 23%). (Graph 2) However, only 9 (31%) of these patients were diagnosed with MTC. The rest of the patients were asymptomatic, or with different renal and auditory abnormalities. (Graph 3)



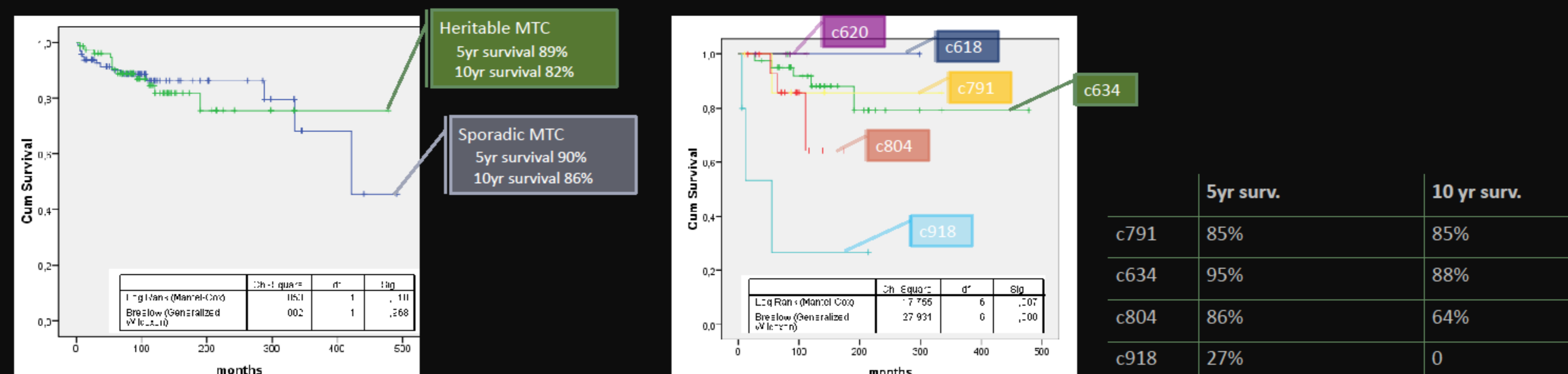
Graph 2: Codon frequencies



Graph 3: Diversity of clinical presentation in patients with Tyr791Phe and no MTC

Polymorphisms of the *RET* protooncogene were found in 101 (47.4%) of MTC patients. The type or the number of detected polymorphisms did not influence clinical presentation, calcitonin level, or the outcome of the disease.

Overall survival among heritable and sporadic MTC did not differ. Patients with MEN2B i.e. mutation in c918, had the lowest survival rate, followed by the patient with the mutation in c804. (Graph 4)



Graph 4: Survival rates

CONCLUSION

A higher prevalence of inherited MTC was found in our group of patients than in other studies. The prevalence of different types of mutations among MTC patients is similar as previously reported. However, in contrast to other European studies, an unusually high prevalence of Tyr791Phe mutation was found among our carriers.