PMT3-A-1 — PMT3 (PROSPECTIVE MONOAMINE-PRODUCING TUMOUR) STUDY OVERVIEW

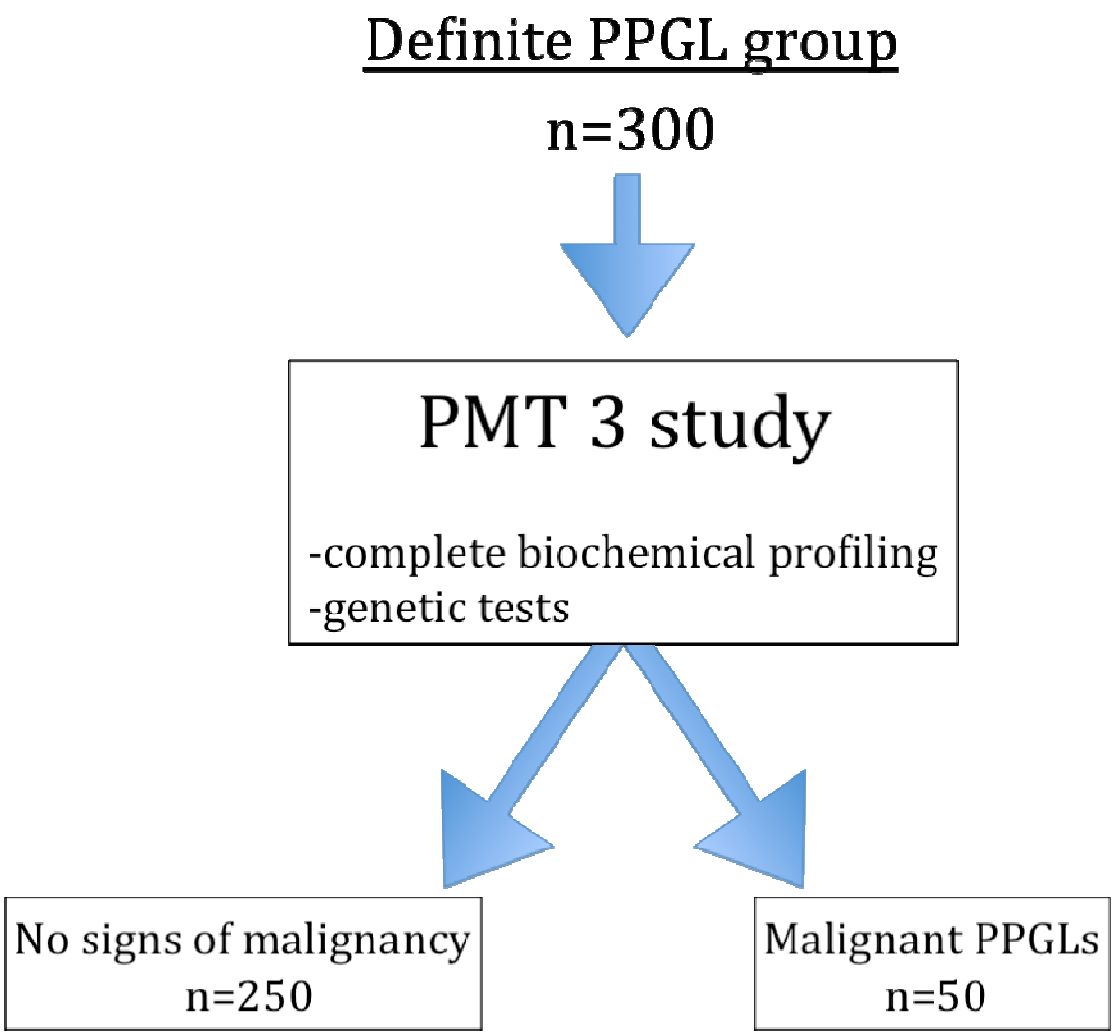
This is an international multicentre prospective study (conceived by Professors Graeme Eisenhofer, Dresden and Jacques Lenders, Nijmegen) directed at elucidating the catecholamine metabolomic profiles of monoamine-producing tumors — primarily pheochromocytomas and paragangliomas (PPGLs) —and the utility of catecholamine-related biomarkers for prediction of malignancy and germ-line mutations. The study combines liquid chromatographic electrochemical and mass spectrometric measurements of catecholamines and metabolites with comprehensive clinical examinations of patients diagnosed with definite PPGLs. The study is coordinated from the University Hospital of Dresden, where diagnostic specimens are received from participating centres.

The study follows from retrospective work indicating that measurements of the O-methylated metabolites of catecholamines (methoxytyramine normetanephrine, metanephrine) are not only useful for initial diagnosis of PPGLs, but also provide potentially useful predictive information about underlying disease-causing mutations and the presence of metastases. The **long-range goal** is to develop new and improved approaches for diagnosis, prediction, management and treatment of patients with malignant PPGLs and those with germ-line mutations. As a step towards reaching this goal, the **primary objective** is to identify new and improved disease biomarkers and establish the biochemical and molecular basis for variations in the clinical presentation of the tumours. A **central hypothesis** is that the varied course of clinical manifestations and complications of PPGLs reflect underlying differences in biochemical phenotypes, which in turn depend on the specific tumour cell types and the underlying mutations responsible for PPGLs. The **rationale** underlying the project is that elucidation of the relationships between biochemical phenotypes, genotypes and the natural history of the disease will lead to improved understanding of tumour biology and development of new and improved approaches for diagnosis, management and treatment of PPGLs.

The study is opened not only for the several ENS@T involved centers, but also for the other members of ENS@T. The study targets patients diagnosed with definite PPGLs. This study is a prospective study, which aims to evaluate biomarkers for prediction of malignancy and underlying germ-line mutations in patients of PPGLs, recruiting at least 300 patients over three years. Patient data, collected under established standard operating procedures, are entered into electronic case report forms at the ENS@T virtual research environment. The protocol also allows for banking of patient specimens (urine, plasma, germlineDNA,) at the central Dresden laboratory or at each the participating centres.

Data collected from the study can be automatically entered into other ENS@T registries (e.g., the pheochromocytoma and paraganglioma registry) or studies (e.g., EURINE-ACT) at the discretion of individual participating coinvestigators, and as dependent on the appropriate local permissions and patient consents.

Every center is required for ENS@T protocol approval, and should obtain written informed consent from a potential study subject according to the protocol before any study-specific procedures are undertaken.



Inclusion: three years
Follow time: open