Genetic tumour and blood profiling in the randomised controlled phase III COMPOSE trial comparing ^{177}Lu-edotreotide and best standard of care for well-differentiated aggressive grade 2/3 gastroenteropancreatic neuroendocrine tumours

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Background/Aims:

- Deeper comprehension of gastroenteropancreatic neuroendocrine tumour (GEP-NET) characteristics has led to development of therapeutic interventions such as targeted radionuclide therapies (TRT)
  - TRT is set to be broadly available for patients with variable phenotypes
- COMPOSE is a randomised, controlled, open-label Phase III trial
  - Includes patients with well-differentiated aggressive G2/G3 (Ki-67 index 15–55%), somatostatin receptor positive GEP-NETs
- ^{177}Lu-edotreotide TRT will be compared with best standard of care (CAPTEM, FOLFOX or everolimus) (Figure 1)

*Treatment response, tumor progression, survival data, information on further antineoplastic treatments and secondary malignancies

Figure 1: *Summary schedule of treatments and follow-up consultation*

- Therapeutic strategies for high grade GEP-NETs demonstrate variable outcomes
  - There is a lack of tools to predict TRT efficacy and disease progression
- **Genetic profiling analysis is proposed to address this need**
  - Applying a multiomics, integrative, systemic approach, we aim to identify genetic predictive and prognostic markers
  - This is to improve understanding of tumour progression and TRT responses and guide individualised treatment of NETs

Conclusions

- We will develop a bioinformatics pipeline that will *integrate genetic data with structural and functional imaging, histopathology and phenotype information* for implementation into clinical practice
- Data from this study are expected to *contribute to individualised management of GEP-NET patients*

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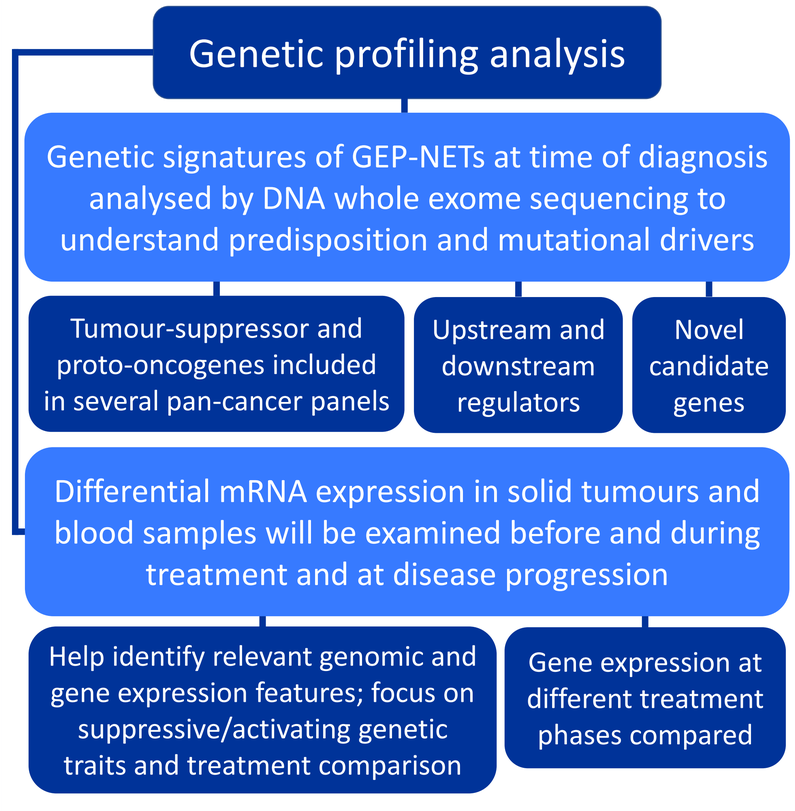
Clinical Phase III Trial COMPOSE
ClinicalTrials.gov NCT04919226
Industry-sponsored study

Methods:

- Genetic profiling analysis will be optional for all trial participants
  - Inclusion or withdrawal will not impact main trial inclusion, disease management or trial procedures
- Samples will be analysed in a central pathology laboratory



Results:

A bioinformatic pipeline will be created integrating the gene expression signatures, correlated with structural and functional imaging, histopathology and patient clinical characteristics, for prediction of TRT efficacy and disease progression