Project title: Developing anti-cancer immunotherapy in high-grade neuroendocrine carcinoma (HG-NEC): the PELICAN phase II study.

Project Summary:

Platinum-based chemotherapy is the mainstay of treatment in metastatic high-grade NECs. Despite initial response, patients with HG-NECs will inevitably relapse and survival in these patients is generally <1 year. Because HG-NECs rely on the PD-1/PD-L1 immune checkpoint as a mechanism of immune escape, targeted inhibition of this pathway is expected to synergise with chemotherapy and induce deeper and more durable anti-tumour responses.
PELICAN is an open label, single-arm phase II study that will evaluate anti-tumour activity and safety of carboplatin and etoposide + pembrolizumab followed by pembrolizumab + lenvatinib maintenance in 20 patients with treatment-naive HG-NECs. The study will generate a biorepository of pre and post-treatment tissue, blood samples (PBMCs, plasma), urine and stool samples to broadly explore mechanism of efficacy of experimental therapy.
The clinical aim of the study is to assess the preliminary efficacy of the chemo-immunotherapy combination in HG-NECs by determining objective response and progression free survival rates.

The translational aims of the study are based on the identification of mechanisms underlying the relationship between reversal of T-cell exhaustion and response to treatment:
1. To evaluate differences in phenotype of tumour infiltrating lymphocytes collected prior to and on treatment using multiplex immunohistochemistry and targeted bulk and single-cell transcriptomics.
2. To detect dynamic changes in relative abundance, functional phenotype and clonality of circulating immune cells collected prior to and during treatment using multi-parameter mass cytometry and T-cell receptor sequencing.
3. To explore the role of gut bacterial diversity as a determinant of T-cell exhaustion and response to ICI by sequencing hypervariable V1-V4 regions of 16S rRNA gene from stool DNA collected at baseline and during treatment.

The candidate will be based in the Developmental Therapeutics Unit led by Dr Pinato, at the Hammersmith Hospital and will have the opportunity to develop clinical, dry and wet lab skills.

Supervisory Team:
Prof. David James Pinato, Imperial College London, UK
Prof. Julian Marchesi, Imperial College London, UK

Clinical Specialities:

Medical Oncology, Clinical Oncology, Surgery, Histopathology, Hepatology/Gastroenterology.