

UKINETS website information - JW Valle 10.08.2016 (updated 03.10.2016)

The UK, through the National Cancer Research Institute (NCRI) Neuroendocrine Subgroup, is able to offer access to clinical trials to patients diagnosed with neuroendocrine tumours. It is important to note that the term “neuroendocrine tumours” refers to many types of NETs and clinical trials are tailored to address a specific scientific question within a particular type, stage and activity of NET. Therefore an individual patient may be eligible for one or more trials at a time, or none.

If you wish to see the portfolio map of clinical trials in NETs, please follow the NCRI link: <http://csg.ncri.org.uk/portfolio/portfolio-maps/> and select “Upper gastro-intestinal cancer” where you will find “Map B - Neuroendocrine”

Follow the NCRI link given for each study for more details of the clinical trial (including inclusion and exclusion criteria) and contact details. Where available, links to the clinical-trials.gov database are also provided.

Open studies (in alphabetical order)

ADUIVO | UK PI Wiebke Arlt [[NCRI link](#)][[NCT00777244](#)]

Efficacy of Adjuvant Mitotane Treatment in Prolonging Recurrence-free Survival in Patients With Adrenocortical Carcinoma at Low-intermediate Risk of Recurrence

This is an international study involving the USA, Canada, France, Germany, Italy, Netherlands and the UK. It is evaluating the effectiveness of a chemotherapy drug called mitotane in reducing the chances of disease relapse after patients have had potentially-curative surgery of adrenal cancer (adrenocortical carcinoma).

Recruiting UK site: Queen Elizabeth Medical Centre, Birmingham

CLARINET-Forte | UK PI Christos Toumpanakis [[NCRI link](#)][[NCT02651987](#)]

Efficacy and safety of Lanreotide Autogel 120 mg administered every 14 days in well-differentiated, metastatic or locally-advanced, unresectable pancreatic or midgut neuroendocrine tumours, having progressed radiologically while previously treated with Lanreotide Autogel 120 mg administered every 28 days

A previous study (CLARINET) has shown that lanreotide, given every 4 weeks, delays the growth of neuroendocrine tumours of the pancreas or mid-gut. In time, the tumours will get larger; this study is evaluating how effective lanreotide is when the injection interval is then reduced to 2-weekly (i.e. two injections per month, instead on once a month) in such patients.

Recruiting UK sites: Queen Elizabeth Medical Centre, Birmingham; Royal Free Hospital, London; and The Christie, Manchester

REMINET | UK PI Juan Valle [[NCRI link](#)][[NCT02288377](#)]

A European, multicentre, phase II/III randomised double-blind, placebo controlled study evaluating Lanreotide as maintenance therapy in patients with non-resectable duodeno-pancreatic neuroendocrine tumours after first-line treatment

This is an academic study led by colleagues in France assessing the effectiveness of lanreotide injections as a holding treatment (“maintenance”) following initial treatment (which may be either chemotherapy or a targeted-therapy, such as everolimus or sunitinib) in patients with well-differentiated neuroendocrine tumours of the pancreas or duodenum. Patients are randomised to receive either lanreotide or placebo.

Recruiting UK sites: Royal Free, London & The Christie, Manchester

SEQTOR | UK PI Tim Meyer [[NCRI link](#)][[NCT02246127](#)]

Randomized phase III open label cross-over study to compare the efficacy and safety of everolimus followed by chemotherapy with STZ-5FU upon progression or the reverse sequence, chemotherapy with STZ-5FU followed by everolimus upon progression, in advanced progressive pNETs.

In this academic, ENETS-approved study, sponsored by the Spanish neuroendocrine group (GETNE) patients with well-differentiated pancreatic neuroendocrine tumours (pNETs) receive treatment with chemotherapy (streptozocin and 5-FU) and everolimus, one after the other. In the trial patients are allocated (at random, by chance) to either receive everolimus first (then chemotherapy) or chemotherapy first (then everolimus). The aim of the study is to evaluate whether there is a difference in outcome depending on the sequence of treatment. **This study is still in set-up.**

SPINET | CI Eric Baudin (Paris) | UK PI Martyn Caplin [[NCRN ID TBC](#)] [[NCT02683941](#)]

Efficacy and Safety of Lanreotide Autogel/ Depot 120 mg vs. Placebo in Subjects With Lung Neuroendocrine Tumors (SPINET)

In this international, randomised study, patients with well-differentiated bronco-pulmonary NETs (typical or atypical carcinoids of the lung) will be allocated to receive either lanreotide or placebo (in a 2:1 ratio). The study aims to assess how effective lanreotide is in controlling the growth of lung NETs.

TALENT | UK PI Juan Valle [[NCRN ID TBC](#)] [[NCT02678780](#)]

Trial to Assess the efficacy of Lenvatinib in metastatic Neuroendocrine Tumours

This is an academic study, sponsored by the Spanish neuroendocrine group (GETNE). All patients in this study will receive oral lenvatinib 24mg/day. Eligible patients are those with well differentiated (grade 1-2) NET of the pancreas (55 patients) or elsewhere in the GI tract (including stomach, small intestine and colorectal origin, also 55 patients) with evidence of progressive disease within 12 months. Patients should have failed a prior targeted therapy (for pancreatic NET patients) or a somatostatin analogue (intestinal NET patients). Lenvatinib is already licensed in thyroid cancer, where a high response rate was observed. The study is opening in Manchester, Glasgow and London (Guy’s and St Thomas’).

TELEPATH | UK PI Martyn Caplin [[NCRI link](#)][[NCT02026063](#)]

A Multicenter, Long-term Extension Study to Further Evaluate the Safety and Tolerability of Telotristat Etiprate (LX1606)

A new compound (telotristat etiprate), aimed at reducing the production of the hormone responsible for carcinoid syndrome (serotonin) has been evaluated in two earlier studies, called TELESTAR and TELECAST. Having completed the initial follow-up phase in either of those two studies, patients may participate in this study to assess the long-term effects of telotristat. Unfortunately, this study is not open to new patients, only those who participated in the earlier studies, detailed above.

FETONET | UK CI Rohini Sharma [[NCRI link](#)]

Evaluation of [¹⁸F]fluoroethyl triazole labelled [Tyr³]Octreotate analogue for the imaging of Neuroendocrine tumours

The use of nuclear imaging is well-established in patients with NETs; octreotide scans and 68-Gallium PET scans are most commonly used. In this study, a novel tracer is being evaluated called [¹⁸F]fluoroethyl triazole labelled [Tyr³]Octreotate analogue ([¹⁸F]-FET-BAG-TOCA, for short). At this stage, this novel tracer does not replace the standard scans.

Recruiting UK sites: Imperial College, London

IMMUNET | UK CI Tim Meyer [[NCRI link](#)]

Systematic Evaluation of the Immune Environment of Neuroendocrine Tumours

This clinical trial is investigating how the immune system responds to neuroendocrine cancers and aims to provide a scientific rationale that will lead to clinical trials of immunotherapy in this group of patients. The study is open for patients with NETs due to commence systemic therapy (either for advanced disease or prior to potential surgery); fresh tissue biopsy and blood samples to characterise the diversity, quantity and quality of the immune cells infiltrating the NET.

Recruiting UK sites: Royal Free Hospital, London; Kings College, London; and The Christie, Manchester

Studies recently closed to accrual | awaiting results

OBLIQUE | UK PI John Ramage [NCRN572]

A Phase IV, Observational study to assess Quality of Life in patients with pNETs receiving treatment with oral 10 mg Everolimus (Afinitor®) o.d.

This prospective, observational, study evaluated quality of life (through the use of patient-reported outcomes) of patients with well-differentiated pancreatic neuroendocrine tumours (pNETs) who were receiving everolimus as part of their standard care. A total of 44 UK patients were recruited.

LUNA | UK PI Tim Meyer [NCRN574][[NCT01563354](#)]

Multicenter 3-arm trial to evaluate the efficacy and safety of Pasireotide LAR or Everolimus alone or in combination in patients with well differentiated neuroendocrine carcinoma of the lung and thymus

This study closed to accrual having recruited ahead of target; 20 patients were recruited in the UK. Results of the study are expected in late 2016/early 2017.

CLOSED (archived) studies | publications

New abstracts/publications in blue

TELESTAR UK PI Martyn Caplin [NCRN502]	Abstract: Telotristat etiprate is effective in treating patients with carcinoid syndrome that is inadequately controlled by somatostatin analog therapy (the phase 3 TELESTAR clinical trial). Kulke et al, European Cancer Congress 2015; 37LBA (29/09/2015) Publication:
NETTER-1 UK PI Ashley Grossman [NCRN328]	Abstract: ¹⁷⁷ Lu-Dotatate significantly improves progression-free survival in patients with midgut neuroendocrine tumours: Results of the phase III NETTER-1 trial. Strosberg, J et al. The European Cancer Congress 2015; abstr 6LBA (27/09/2015) Publication:
RADIANT-4 UK PI Juan Valle [NCRN333]	Abstract: Everolimus in advanced non-functional neuroendocrine tumors (NET) of lung or gastrointestinal (GI) origin: Efficacy and safety results from the placebo-controlled, double-blind, multicenter, Phase 3 RADIANT-4 study. Yao, J et al. European Cancer Congress 2015; abstr 5LBA Publication: Yao JC, Fazio N, Singh S, Buzzoni R, Carnaghi C, Wolin E, Tomasek J, Raderer M, Lahner H, Voi M, Pacaud LB, Rouyrre N, Sachs C, Valle JW, Fave GD, Van Cutsem E, Tesselaar M, Shimada Y, Oh DY, Strosberg J, Kulke MH, Pavel ME; RAD001 in Advanced Neuroendocrine Tumours, Fourth Trial (RADIANT-4) Study Group. Everolimus for the treatment of advanced, non-functional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study. <i>Lancet</i> . 2016 Mar 5;387(10022):968-77.
BEZ235-Z2401 UK PI Juan Valle [NCRN379]	Abstract: Phase II studies of BEZ235 in patients with advanced pancreatic neuroendocrine tumors (pNET). Salazar et al <i>J Clin Oncol (Meeting Abstracts)</i> May 2015 vol. 33 no. 15_ - suppl 4102 Publication: Fazio N, Buzzoni R, Baudin E, Antonuzzo L, Hubner RA, Lahner H, DE Herder WW, Raderer M, Teulé A, Capdevila J, Libutti SK, Kulke MH, Shah M, Dey D, Turri S, Aimore P, Massacesi C, Verslype C. A phase II study of BEZ235 in patients with Everolimus-resistant, advanced pancreatic neuroendocrine tumours. <i>Anticancer Res</i> . 2016 Feb;36(2): 713-9.

BEZ235-F2201 **Abstract:** Phase II studies of BEZ235 in patients with advanced pancreatic neuroendocrine tumors (pNET). Salazar et al J Clin Oncol (Meeting Abstracts) May 2015 vol. 33 no. 15_ - suppl 4102

UK PI Nick
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[NCRN 12919] **Publication:** Fazio N, Buzzoni R, Baudin E et al. A Phase II Study of BEZ235 in Patients with Everolimus-resistant, Advanced Pancreatic Neuroendocrine Tumours. *Anticancer Res* 2016; 36: 713-719.

COOPERATE-2 **Abstract:** Kulke MH, Ruzniewski P, Van Cutsem E, Valle JW, De Herder W, Pavel M, Degt-yarev E, Lam DH, Salazar R, Borbath I, Fazio N, Lombard-Bohas C and Yao JC. A Random-ized Open-label Phase II Study of Everolimus Alone or in Combination with Pasireotide LAR in Advanced, Progressive Pancreatic Neuroendocrine Tumors: COOPERATE-2 Trial. Presented at ENETS 2015

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[NCRN239] **Publication:**
