Clinical Trials Update

December 2025

Klaire Exarchou

ST8 Upper GI Surgery

Active, not recruiting

Lutetium 177Lu-Edotreotide Versus Best Standard of Care in Well-differentiated Aggressive Grade-2 and Grade-3 GastroEnteroPancreatic NeuroEndocrine Tumors (GEP-NETs) - COMPOSE (COMPOSE)

ClinicalTrials.gov ID NCT04919226

Sponsor ITM Solucin GmbH

Information provided by ITM Solucin GmbH (Responsible Party)

Last Update Posted 2025-09-10

- **Purpose**: The trial is evaluating the efficacy and safety of a targeted radiopharmaceutical, **Lutetium-177 (^{177}Lu)-edotreotide** (PRRT), as a first- or second-line treatment for patients with well-differentiated, aggressive grade 2 and grade 3 gastroenteropancreatic neuroendocrine tumours (GEP-NETs).
- **Comparison**: The experimental treatment is being compared to the best standard of care, which is the investigator's choice of either chemotherapy (CAPTEM or FOLFOX) or everolimus.
- **Primary end-point: PFS (measured 12 weekly during study)**
- **Status**: The study began recruitment in September 2021 and is estimated to be completed by September 2027.
- **Recruitment:** Completed earlier this year, June 2025 enrollment 259pts
- **Study completion date**: Sept 2027
- **Srirajskanthan (King's)**

Not yet recruiting

Trial of Lu-177 DOTATATE (Lutathera®) in Unlicensed Indications

ClinicalTrials.gov ID NCT06121271

Sponsor University College, London

Information provided by University College, London (Responsible Party)

Last Update Posted 2023-12-07

- Contact: Martyn Caplin, Prof.
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- **Purpose**: To prospectively evaluate the safety and efficacy of Lu-177 DOTATATE in neuroendocrine tumors (NETs) with somatostatin receptor expression in indications where it is not yet licensed.

Targeted Indications: The trial is recruiting participants with specific conditions who will be divided into the following subgroups:

Bronchial and Thymic NETs: Participants receive 4 cycles of Lutathera.

Paraganglioma/Phaeochromocytoma: Participants receive 4 cycles of Lutathera.

Medullary Thyroid Carcinoma (among "Others NETs" group): Participants receive 4 cycles of Lutathera.

Repeat PRRT: Participants who have previously had PRRT treatment will receive 2 further cycles

- **Outcome measures:**
- Treatment-related toxicity
- Treatment-related side effects and cancer-related symptoms will be assessed in all participants Questionnaire after every treatment and during the follow-up period.
- Progression Free Survival (PFS) and defined as the time from the date of start of treatment the date of the first documented tumour progression or death due to any cause.
- **Status**: Active.
- **Recruitment: 21 consented – 9 completed, 16 repeat PRRT, 2 PGL, 3 Bronchial NET**
- **Study completion date**: Estimated completion date of November 6, 2027

Recruiting

Lutathera and ASTX727 in Neuroendocrine Tumours (LANTana)

ClinicalTrials.gov ID NCT05178693

Sponsor Imperial College London

Information provided by Imperial College London (Responsible Party)

Last Update Posted 2025-11-24

- Contact: Rohini Sharma, Professor
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- **Purpose:** To test if ASTX727 can "up-regulate" (increase) the SSTR2 receptor on neuroendocrine tumor cells to make them more sensitive to the targeted therapy, lutathera.
- Trial design: Phase Ib
- **Outcome measures:** To determine whether pre-treatment with ASTX727 results in re-expression of SSTR2 in patients with metastatic NETs, using [68Ga]-DOTA-TATE to image epigenetic modification of the SSTR2 locus allowing subsequent treatment with Lutathera.
- **Status**: Active
- **Recruitment: 27**
- **Study completion date**: Sept 2029

Recruiting

A Study of Etoposide-carboplatin in Combination With Pembrolizumab and Lenvatinib Maintenance in HG-NETs (PELICAN)

ClinicalTrials.gov ID NCT06232564

Sponsor Imperial College London

Information provided by Imperial College London (Responsible Party)

Last Update Posted 2025-01-30

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- Contact: Maria Martinez
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- **Purpose**:To evaluate the efficacy and safety of pembrolizumab in combination with carboplatin and etoposide chemotherapy followed by pembrolizumab and lenvatinib maintenance therapy in patients with HG-NETs who are chemotherapy-naïve for their metastatic disease.
- Trial design: open label, single arm, phase II multicentre study
- **Intervention:**Pembrolizumab in combination with carboplatin and etoposide chemotherapy followed by pembrolizumab and lenvatinib maintenance therapy
- **Outcome measures:** Evaluation of the effects of carboplatin, etoposide and pembrolizumab followed by pembrolizumab and lenvantinib maintenance in treatment naïve HG-NETs as measured by RECIST v1.1 criteria. To evaluate overall response rates (ORR) as measured by RECIST v1.1 criteria.
- **Status**: Active, completed recruitment phase
- **Recruitment:22, 16 still on trial**
- **Study completion date**: Aug 2028

Recruiting

Comparison of Adjuvant Treatment With 177Lu-DOTATATE to Best Supportive Care in Patients After Resection of Neuroendocrine Liver Metastases (NELMAS)

ClinicalTrials.gov ID NCT05987176

Sponsor Imperial College London

Information provided by Imperial College London (Responsible Party)

Last Update Posted 2024-08-09

Not active due to funding being withdrawn.

- Contact: Boehringer Ingelheim
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Recruiting

DAREON™-5: A Study to Test Whether Different Doses of BI 764532 Help People With Small Cell Lung Cancer or Other Neuroendocrine Cancers

ClinicalTrials.gov ID NCT05882058

Sponsor Boehringer Ingelheim

Information provided by Boehringer Ingelheim (Responsible Party)

Last Update Posted 2025-11-12

1.Contact: Boehringer Ingelheim
2.Phone Number: 1-800-243-0127
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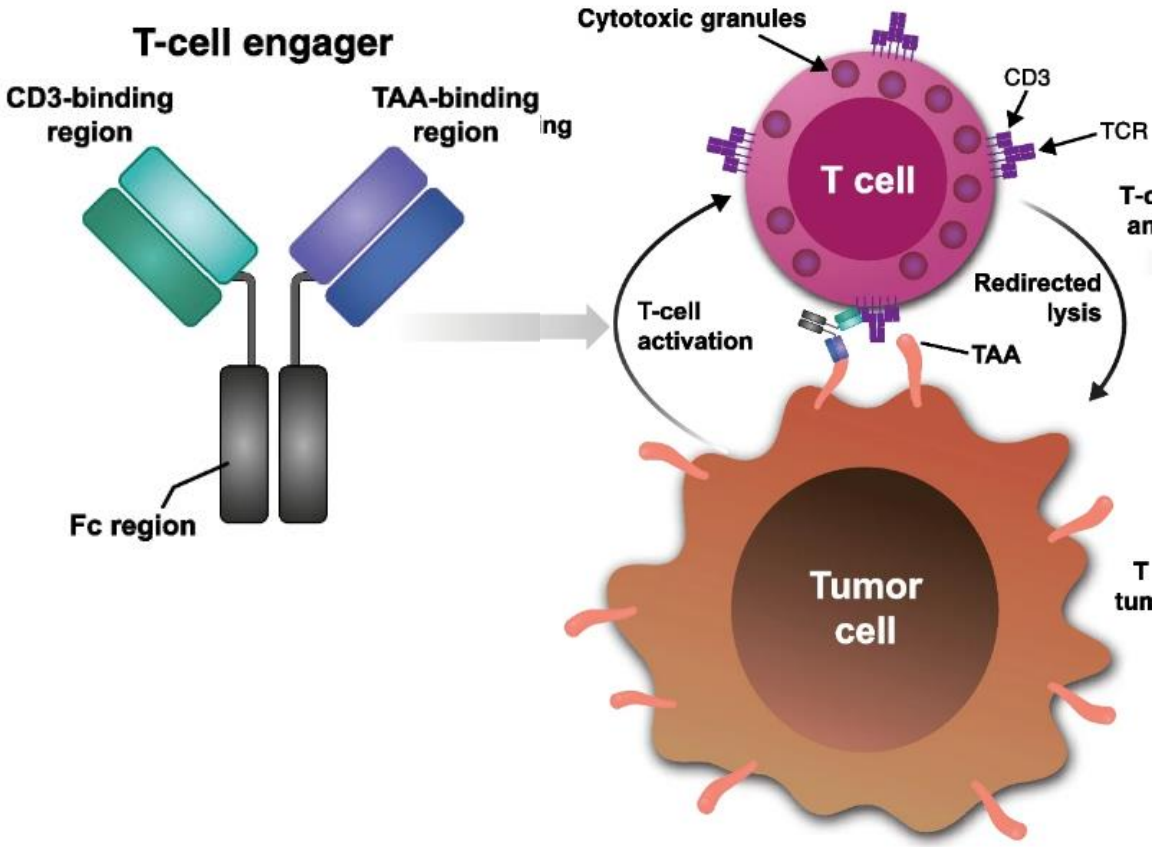
Dareon – 5 trial



BI764532 – DLL3 / CD3 IgG like T-cell engager

DLL3 over-expressed in cells with neuroendocrine differentiation e.g. SCLC / NEC

Relapsed/refractory extra-pulmonary NECs or large cell NEC of the lung, after ≥1 prior line of therapy including at least one platinum-based regimen

Currently closed for interim analysis

McNamara (Christie, Manchester) – likely open during 2025

- **Purpose**: Dareon®-5 Part 2 is an expansion cohort of the Dareon®-5 trial enrolling patients with epNEC with DLL3 high expressing tumours who have progression or recurrence following at least one platinum-based regimen. Patients will be treated with the DLL3/CD3 T-cell engager obrixtamig at the selected target dose determined from the dose selection part of the Dareon®-5 trial (Part 1).
- **Part 1 (Dose Selection):** This completed phase evaluated the safety and efficacy of two obrixtamig doses to find the optimal dose.
- **Part 2 (Expansion Cohort):** This ongoing phase focuses on the anti-tumor activity, measured by the **objective response rate** (ORR), of the selected dose in patients with advanced epNEC whose tumors highly express the DLL3 protein.

- Trial design: Interventional Phase II
- **Intervention:** BI764532 – DLL3 / CD3 IgG
- **Outcome measures:** Objective response rate
- **Status**: Active
- **Recruitment:174**
- **Study completion date**: Jul 2027
- Current UK centers: Leicester Royal Infirmary and Freeman Hospital

Recruiting

A Phase 3 Study of Ersodetug in Patients With Tumor Hyperinsulinism (Tumor HI)

ClinicalTrials.gov ID NCT06881992

Sponsor Rezolute

Information provided by Rezolute (Responsible Party)

Last Update Posted 2025-10-21

- Contact: Rezolute Clinical Trial
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- **Purpose**: The objectives of this study are to evaluate the glycemic efficacy, safety, and tolerability of ersodetug as add-on to standard of care (SOC) therapy for treatment of hypoglycemia in patients with Tumor Hyperinsulinism (Tumor HI).
- Trial design: A Phase 3, Single-Arm, Open-label
- **Intervention:** Ersodetug
- **Outcome measures:** Proportion of participants with clinically meaningful reduction in IV glucose infusion rate from baseline. [Time Frame: 8 weeks]
- **Status**: Active
- **Recruitment: 16**
- **Study completion date**: Sept 2027

A Late-stage Rare Disease Company
Treating Life-threatening Hypoglycemia
Due To Hyperinsulinism (HI)

Ersodetug Tumor HI Clinical Program

Real-world Patient Experience in Treating Hypoglycemia with Ersodetug

13 patients have been treated under EAP/ Compassionate use (12 Insulinoma and 1 NICTH)

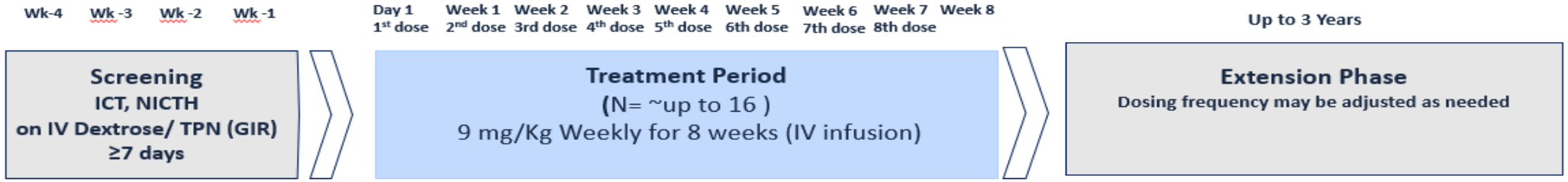
- All patients with severe hypoglycemia refractory to treatment
  - Inadequately controlled with ant-hypoglycemic treatment
  - Received several courses of tumor directed therapies
  - Many were hospitalized with uncontrolled / life-threatening hypoglycemia or hospice-bound condition, required continuous IV dextrose/ TPN (GIR)
  - New tumor-directed therapies (e.g., radiotherapy, chemotherapy) deferred because of hypoglycemia
  - Physician-requested use of ersodetug
- Administration of ersodetug resulted in:
  - Rapid hypoglycemia correction, discontinuation of IV dextrose /TPN resulting in discharge from in-patient to out-patient care
  - Resumption of tumor-directed therapies
  - Improved quality of life
  - No significant drug related side effects/toxicities

- Ersodetug: Humanized IgG2 mAb, an insulin receptor modulator Administered by IV infusion: ≥30 min
- Dose: 9 mg/kg weekly for initial ~8 weeks followed by 9 mg/kg every 2-4 weeks (per physician's discretion)

EAP: Expanded Access Program. Sources: n engl j med 389;8 Aug24, 2023 - https://www.nejm.org/doi/full/10.1056/NEJMc2307576?query=TOC&cid=NEJM+eToc%2C+August+24%2C+2023+DM2279684_NEJM_Non_Subscriber&bid=1754093795

Open-label, Phase 3 Study: upLIFT

A Phase 3, Single-Arm, Open-label, Pivotal Study to Evaluate the Efficacy and Safety of Ersodetug Compared to Baseline in Patients with Inadequately Controlled Hypoglycemia Due to Tumor-Associated Hyperinsulinism [EU CT Number: 2024-515447-36-00]



N= ~16

Inclusion

- ✓ Clinical diagnosis of tumor induced hypoglycemia with biochemical evidence of tumorHI who failed to manage hypoglycemia with usual SOC anti-hypoglycemic therapies, per investigator judgement
- ✓ Receiving IV dextrose and or parenteral nutrition for ≥7 days (prior to the 1st dose of ersodetug)

Exctusion

- ✓ Evidence of active infection including HIV, hepatitis B or C (excluding immunization patterns).
- ✓ H/o investigational therapy within 30 days or 5 half-lives (may qualify if considered safe by the PI)
- ✓ Estimated life expectancy (additional lifespan) due to underlying disease (tumor) is <8 weeks.

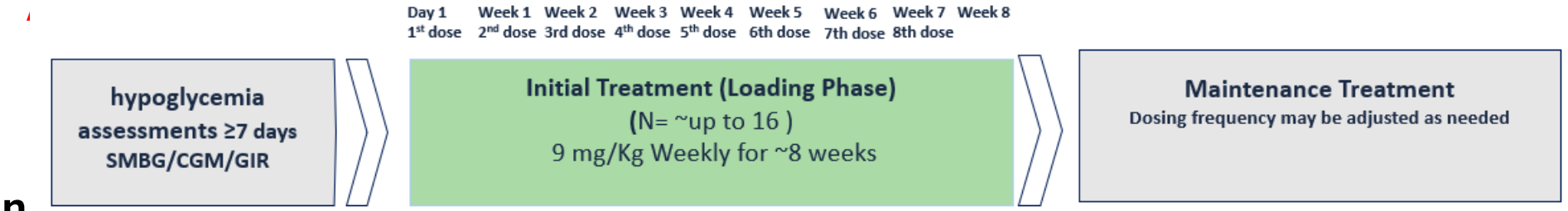
Endpoints:

- Clinically meaningful reduction (≥50%) in glucose infusion rate from baseline
- Hypoglycemia assessments via SMBG and CGM; QOL, overall survival

Emergency Access / Compassionate Use with Ersodetug (EAP)

EAP for Ersodetug in Patients with Refractory Hypoglycemia Due to Tumor-Associated Hyperinsulinism (Tumor HI) Who are Unable to Participate in a Clinical Trial

Can be initiated by any Treating Physician if approved by the local Regulatory



Inclusion

- ✓ Uncontrolled hypoglycemia due to documented tumor HI not adequately managed with available SoC anti-hypoglycemic therapies (per Treating Physician's judgement)
- ✓ Inability to participate in any ersodetug clinical trial

Exclusion

- ✓ Evidence of active infection including HIV, hepatitis B or C (excluding immunization patterns).
- ✓ H/o investigational therapy within 30 days or 5 half-lives (may qualify if considered safe by the PI)

Endpoints: Data entry in EDC is required

- Data will be captured in EDC to evaluate changes in GIR, assess hypoglycemia via SMBG/CGM, QOL, OS

Recruiting

Carcinoid Syndrome Efficacy Study Featuring an Oral Daily Paltusotine Regimen (CAREFNDR)

ClinicalTrials.gov ID NCT07087054

Sponsor Crinetics Pharmaceuticals Inc.

Information provided by Crinetics Pharmaceuticals Inc. (Responsible Party)

Last Update Posted 2025-11-28

1.Contact: Crinetics Clinical Trials
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- **Purpose**: The purpose of the clinical trial identified by the code **NCT07087054**, also known as the **CAREFNDR** study, is to evaluate the **efficacy and safety of an oral, once-daily drug called paltusotine** in adults with carcinoid syndrome caused by well-differentiated neuroendocrine tumors (NETs).
- Trial design:A Phase 3, randomized, double-blinded, placebo-controlled study
- **Intervention: Paltusotine vs placebo**
- **Outcome measures:**Participants will record the number of flushing per day in a daily diary to assess the efficacy of paltusotine vs placebo in reducing flushing episodes. [Time Frame: Measured at Week 12]
- Treatment group difference of change from baseline to Week 12 in flushing episodes/day averaged over the 14 days prior to Week 12

- **Status**: Active
- **Recruitment: 141**
- **Study completion date**: 01/2030

Genomic Analyses of Endocrine and Neuroendocrine tumours

James MacFarlane
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Ruth Casey
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- Sponsor: Cambridge University Hospitals NHS Foundation Trust
- CMPD ID: 39995
- Funded by: Association for Multiple Endocrine Neoplasia Disorders
- Purpose: The study involves the genomic analysis of endocrine and neuroendocrine tumours.
- Study design: Observational
- Recruitment: Ongoing due to be completed end 2026, 92/200

Recruiting

Tumour Characterisation to Guide Experimental Targeted Therapy - National

ClinicalTrials.gov ID NCT04723316

Sponsor The Christie NHS Foundation Trust

Information provided by The Christie NHS Foundation Trust (Responsible Party)

Last Update Posted 2024-02-07

- Contact: Matthew Krebs
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- **Purpose:** To determine the number of patients matched to a trial of an experimental therapeutic agent based on molecular findings from ctDNA or tumour
- Trial design: Observational
- **Outcome measures:** The primary aim of TARGET National is to establish a national framework to offer molecular profiling of circulating tumour DNA and/or tumour tissue (optional) to patients with advanced solid cancers referred to any of the Experimental Cancer Medicine Centres (ECMCs) across the UK, in order to help decision making for allocation to molecularly targeted experimental cancer treatments. Patients will be allocated treatment using a national Molecular Tumour Board to find the most suited therapies based on their molecular profiling results.
- **Status**: Active
- **Recruitment: Estimated 6000, currently over 3000**
- **Study completion date**: Jan 2028

Current clinical trial landscape of gastroenteropancreatic neuroendocrine neoplasms.

Trial ID	Drug	Cancer Type	Phase	Status
NCT05477576	[225Ac]DOTATATE (RYZ101) [47]	Advanced, well-differentiated GEP-NETs	III	Active
NCT05153772	[212Pb]DOTAMTATE [49]	unresectable or metastatic somatostatin receptor-expressing GEP-NETs	II	Active
NCT05773274	Lutetium (Lu-177) Dotatate [50]	Advanced, well-differentiated GEP-NETs	II	Active
NCT03049189	Lu-Edotreotide [51]	SSTR+- G1/G2 advanced/metastatic GEP-NETs	III	Active
NCT04919226	Lu-Edotreotide [52]	G2/G3 advanced/metastaticGEP-NETs	III	Active
NCT05724108	triapine plus [177]Lu DOTATATE [54]	SSTR-GEP-NETs	II	Active
NCT04086485	Olaparib [55]	GEP-NETs	I/II	Active
NCT04525638	Nivolumab [56]	NET and Neuroendocrine carcinomas	II	Unknown
NCT06041516	Antibody Drug conjugate ADCT-701 [57]	NET and Neuroendocrine carcinomas	I	Active
NCT06943755	Zanzalintinib	Advanced or Metastatic NETs	II/III	Actice
NCT05040360	Capecitabine and Temozolomide	High-risk pNET	II	Active

Peshin, S., Modi, S., Babakhanlou, R., & Arshad, J. (2025). Current Clinical Trial Landscape of Gastroenteropancreatic Neuroendocrine Tumors: A New Era of Landmark Trials. Journal of Clinical Medicine, 14(18), 6522.

Novel Radioligand Agents

- (225Ac)DOTATATE (RYZ101)- ACTION-1 trial (NCT05477576), which is a phase Ib/III study comparing RYZ101 to standard-of-care therapies in patients with SSTR2 positive advanced GEP-NETs refractory to (177Lu)Lu-DOTATATE therapy
- (212Pb)DOTAMTATE-**ALPHAMEDIX02 (**NCT05153772) phase II, open-label, multicenter study evaluating the safety, tolerability and efficacy of ^{212}Pb-DOTAMTATE in PRRT-naïve (Cohort 1, N = 36) and PRRT-refractory (Cohort 2, Target N = 30)

Comparative Trials

- NETRetreat trial. This phase II trial compares the effect of retreatment with two additional cycles of (177)Lu-DOTATATE PRRT to the usual approach of treatment with everolimus in patients who have previously received (177)Lu-DOTATATE for metastatic and unresectable midgut neuroendocrine tumors. (NCT05773274).
- ComPareNET trial.The efficacy of capecitabine plus temozolomide is directly compared to Lu-177 Dotatate in advanced or metastatic *pNET* (NCT01824875).
- COMPETE is a prospective, randomized, controlled, open label, phase III study to evaluate the efficacy and safety of Lu-177 Edotreotide in comparison to everolimus in patients with advanced/metastatic SSTR(+) GEP-NETs(NCT03049189).

Radioligand Combination Trials
DNA repair enzyme inhibitors

- **Peposertib** is a deoxyribonucleic acid protein kinase (DNA-PK) inhibitor which can enhance the DNA damage caused by (177)Lu-DOTATATE. The combination of peposertib and (177)Lu-DOTATATE is currently being studied in an investigator initiated, multi-center phase I clinical trial in patients with well differentiated GEP-NETs after failure of at least one prior line of systemic treatment. (ETCTN10450)
- Combining Lu-177 Dotatate with **triapine** will enhance the double stranded DNA breaks leading to better efficacy. This novel combination is currently being studied in an investigator initiated, multi-center phase one clinical trial in patients with well differentiated GEP-NETs after failure of at least one prior line of systemic treatment. Patients with prior RLT will be excluded. (NCT04234568)
- **Olaparib** is a selective and potent inhibitor of poly(adenosine diphosphate-ribose) polymerase (PARP) enzymes, PARP-1 and PARP-2 causing the inhibition of DNA repair mechanisms. Combining with (177)Lu-Dotatate will lead to possible synergism with double stranded DNA breaks with radiation leading to increased potential efficacy in patients with advanced/inoperable GEP-NETs(NCT04086485).

Radioligand Combination Trials

- Immune checkpoint inhibiotors

A phase II trial evaluates the combination of 177-Lu DOTATE with **nivolumab** (anti-PD1) in adult patients with grade 3 advanced neuroendocrine tumors and neuroendocrine carcinomas. The trial is ongoing, and no results are available (NCT04525638)

TKIs

- **Zanzalintinib** (XL092) is a next-generation, oral multi-targeted TKI that inhibits VEGFR, MET, AXL, and MER kinases. It is currently being evaluated in multiple tumor types, including GEP-NETs, for its potential to block tumor angiogenesis and growth while minimizing off-target toxicity. STELLAR-311 is a planned global, randomized, open-label Phase III pivotal trial evaluating zanzalintinib (XL092) versus everolimus as a firstline oral therapy in patients with advanced neuroendocrine tumors (NETs), regardless of site of origin (including gastroenteropancreatic NETs) (NCT06943755).

Chemotherapy

- The S2104 trial (NCT05040360) is a randomized phase II study comparing CAPTEM versus observation in patients with resected, well-differentiated grade 2 or 3 pNETs (Ki-67 ≥ 3%–≤55%) and a Zaidi score ≥ 3. Patients who underwent resection or ablation of up to five liver metastases were also included, provided they achieved no evidence of disease before enrollment. The trial aims to assess the potential role of CAPTEM in the adjuvant setting.