

## Poster 23 High-throughput patient-derived tumor (HPDT)-drug screening platform for gastro-enteropancreatic neuroendocrine tumors

---

Katharina Wang <sup>1</sup>, Kathrin Zitzmann <sup>1</sup>, Maximilian P Hungbauer <sup>2,3</sup>, Katharina Schilbach <sup>1</sup>, Thomas Knösel <sup>3,4</sup>, Diana Vetter <sup>6</sup>, Constanze Hantel <sup>5</sup>, Martin Reincke <sup>1</sup>, Felix Beuschlein <sup>1,5,7</sup>, Christoph J Auernhammer <sup>1,3\*</sup> and Svenja Nölting <sup>1,5\*</sup>

<sup>1</sup>Department of Internal Medicine IV, LMU University Hospital Munich, Germany

<sup>2</sup>Interdisciplinary Center of Neuroendocrine Tumors of the GastroEnteroPancreatic System (GEPNET-KUM, ENETS Centre of Excellence), LMU University Hospital Munich, Germany

<sup>3</sup>Interdisciplinary Center of Neuroendocrine Tumors of the GastroEnteroPancreatic System (GEPNET-KUM, ENETS Centre of Excellence), LMU University Hospital Munich, Germany

<sup>4</sup>Institute of Pathology, Faculty of Medicine, LMU Munich, Germany

<sup>5</sup>Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich, Switzerland

<sup>6</sup> Department of Visceral and Transplantation Surgery, University Hospital Zurich and University of Zurich, Switzerland

<sup>7</sup>The LOOP Zurich - Medical Research Center, Switzerland

\*Both senior authors contributed equally

There is still a medical need for further innovative systemic therapies for metastatic gastro-enteropancreatic neuroendocrine tumours (GEP-NETs).

In order to evaluate the anti-tumor effects of novel therapeutic options in personalized settings, we have established a high-throughput patient-derived tumor (HPDT)-drug screening platform for GEP-NET primary cultures at 2 centres (n=24; University Hospitals Munich [n=19] and Zurich [n=5]) within NeoExNET in cooperation with HTCR. These included 11/24 pancreatic NETs and 13/24 small intestinal NETs (biochemically active tumors: n=1 insulinoma, n=1 glucagonoma, n=2 carcinoid syndromes); 17/24 tumors were metastatic.

Systematic drug testing of more than 40 different drugs was performed in human primary tumor cultures, including targeted therapies (e.g., the SSTR2 agonist paltusotine, multi-tyrosine kinase inhibitors cabozantinib and sunitinib, mTOR inhibitor everolimus, Akt inhibitor capivasertib, PI3K inhibitor alpelisib, GSK3 inhibitor AR-A014418), chemotherapeutics (e.g., temozolomide, 5-fluorouracil), cannabinoids (e.g., CBD, THC), sex hormones, and substances aiming for drug-repurposing (e.g., metformin, semaglutide, zoledronic acid).

Overall, we provide novel data on the efficacy of both putative and established therapies in patient-derived GEP-NET primary cultures. Our HPDT-drug screening for GEP-NET primary cultures provides a translational research platform to predict potential personalized treatment options in this orphan disease. This ongoing project (with a continuously increasing drug panel) will also enable us to correlate the *in vitro* data with individual tumor biology as well as patient-specific therapy response and outcomes.