# B-27

## Development of GEP-NEN Patient Derived Organoids for Therapy Screening

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### BACKGROUND

Gastroenteropancreatic Neuroendocrine Neoplasms (GEP-NENs) are a rare subset of cancers which nevertheless are a rising health burden. Development of new therapies suffers from several bottlenecks, including low patient accrual and poor understanding of tumor characteristics. Patient tumor organoids (PTOs) are a novel model capable of improving screening of patient tissue in an accurate, standardized, and high-throughput capacity. In this study, we utilized patient tumors for creation of high-fidelity PTOs from a variety of GEP-NENs.

### METHODS

Tumors from patients undergoing clinically guided surgeries were processed within two hours of resection and dissociated into single-cell suspension. Cells were encapsulated into Matrigel and cultured into two groups. The first group was grown for 10 days and assessed for viability then treated with a panel of clinically approved therapies for treatment sensitivity. The second group was grown for long-term expansion and biobanking, followed by characterization using immunohistochemistry and genetic profiling at passage 2 to ensure tumor cell maintenance.

### RESULTS

From March 2023-June 2023, six patients provided 14 tumors for PTO development. These included small intestine (n=3), pancreatic (n=2), and gastric (n=1) nueroendocrine tumors. Long-term culture (>3 passages) was successful for 11/14 specimens, with an average passage time of ~4 weeks. PTOs maintained immunohistochemical characteristics of the parent tumor types and demonstrated similar genetic profiles, including neuroendocrine tumor cell markers and grade. The early-stage therapeutic screening was performed for four patients, demonstrating dose-dependent effects and showing clinically dose relevant sensitivity towards small molecule inhibitor therapies including cabozantinib and sunitinib in a patient-dependent manner. Finally, a comparison of treatments between multiple resection sites within the same patient demonstrated variance in treatment responses, suggesting tumor heterogeneity.

### CONCLUSIONS

Development of GEP-NEN PTOs is feasible for standard of care therapy testing. Further study will lead to continued understanding of therapeutic testing and the development of new therapy options.

**ABSTRACT ID 23760**