

PEAR-GLIO: Clinical evaluation of an AI-driven functional precision medicine platform for therapeutic efficacy in gliomas.

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Background: Gliomas and other primary brain tumors remain a leading cause of cancer-related mortality, with limited predictive biomarkers to guide therapy selection. The PEAR-GLIO trial investigates the use of Pear Bio's AI-driven ex vivo platform to assess the therapeutic sensitivity of FDA-approved and experimental treatments on patient-derived 3D immune-microtumors. This observational study seeks to validate whether this platform can provide actionable insights for patient stratification and treatment optimization in subsequent trials. The trial also incorporates patient and public involvement and engagement (PPIE) to understand perspectives and enhance study design and accessibility. **Methods:** PEAR-GLIO (NCT06038760) is a UK-based, observational study enrolling 50 patients diagnosed with operable primary brain tumors, including grades 2–4 gliomas. Inclusion criteria require histologically confirmed malignancy, the ability to provide ≥ 0.4 g of tumor tissue and 40mL of whole blood, and consent for data and sample use. Exclusion criteria include pre-surgical chemotherapy or radiotherapy within 30 days and inoperable disease. Tumour-extracted and immune patient cells are cultured as physiologically-relevant 3D immune-microtumors and exposed to FDA-approved and experimental treatments. Phenotypic and molecular responses, including changes in tumour viability, cell death, migration, immune cell infiltration are assessed using live imaging and computer vision. The study uniquely integrates real-time confocal imaging and omics analyses to evaluate drug mechanisms of action. This includes correlation of ex vivo responses with biomarkers such as MGMT methylation, IDH mutation, and 1p/19q co-deletion, alongside exploratory analysis of experimental therapies. Recruitment began in October 2023, with 12 patients of the target 50 enrolled thus far. Data from the first cohort will inform platform optimization and scalability. All biological samples are anonymized, with outcomes tracked per RANO guidelines. Even at this early stage, PPIE has helped improve trial design. We are concurrently validating the platform in other high-unmet-need indications including early-stage breast cancer (NCT05435352), metastatic breast cancer (NCT06182306) and metastatic kidney cancer (NCT06264479) hoping to shift the paradigm in precision treatment selection. Clinical trial information: NCT06038760. Research Sponsor: Ourotech (t/a Pear Bio).