

## Personalized targeted glioblastoma therapies by *ex vivo* drug screening: Advanced brain tumor therapy clinical trial (ATTRACT).

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**Background:** Targeted therapies used in a personalized treatment concept have revolutionized the management of several solid cancers. So far, various clinical trials aiming to introduce the concept of personalized targeted therapies in glioblastoma have failed, as no clinically meaningful responses were observed. Importantly, most clinical trials investigating molecular targeted therapies included all-comers and concentrated on genetic biomarkers to predict treatment response. Given the biological complexity of glioblastoma, genetic biomarkers might give only an insufficient insight into the response of a given patient, and more personalized approaches are warranted. As novel approaches to guide personalized treatment in glioblastoma are urgently needed, we designed a prospective clinical trial to investigate the novel approach of cultivated patient-derived tumor cells (PDCs) for *ex vivo* drug screening. **Methods:** In this randomized phase 2 study, we are testing the ability of PDC-based *ex vivo* drug screening to formulate a personalized recommendation for maintenance treatment in patients with newly diagnosed glioblastoma with unmethylated MGMT promoter after neurosurgical resection followed by combined radio-chemotherapy. Based on overall survival as the primary endpoint, we plan to include 240 patients (120 per group) to show with a power of 80% that we can increase the median survival from 12 to 17 months (hazard ratio 0.7). Patients are randomized 1:1 to either the standard group (no drug screening) or the intervention group (drug screening and personalized recommendation for maintenance treatment). In the intervention group, automated drug screening is performed on PDCs with 28 drugs used for treatment of solid tumors and hematological malignancies. Based on the cytotoxic/cytostatic activity of these drugs, as quantified by relative viability based on adenosine triphosphate levels, a molecular tumor board recommends a personalized treatment regimen. The first patient was enrolled in July 2024. Interim analysis of the ATTRACT study (NCT06512311) is expected in late 2027, and final results in 2030. Moreover, the clinical trial is accompanied by a comprehensive translational research program to gain insights into the biological underpinnings of treatment response in glioblastoma. Clinical trial information: NCT06512311. Research Sponsor: Ludwig Boltzmann Society.