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Personalized targeted glioblastoma therapies by ex vivo drug screening: Study protocol of the Advanced brain Tumor TheRApy Clinical Trial (ATTRACT)

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Abstract

Background. Novel approaches to guide personalized treatment in glioblastoma are urgently needed. Given the poor predictive value of genetic biomarkers in glioblastoma, we are conducting 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 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 will be 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 will be performed on PDCs with 28 drugs used for the treatment of solid tumors and hematological malignancies. Based on the cytotoxic activity of these drugs, as quantified by relative viability based on adenosine triphosphate levels, a molecular tumor board will recommend a personalized treatment regimen.

Results. 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.

Trial Registration. The ATTRACT trial is registered under the ID NCT06512311 (https://clinicaltrials.gov/study/NCT06512311).

Key Points

- ATTRACT performs ex vivo drug screening in IDH-wildtype, MGMT unmethylated glioblastoma using patient-derived cells
- 28 approved drugs targeting the major cancer pathways are tested
- Study design: randomized phase 2 trial with overall survival as primary endpoint

Glioblastoma is the most frequent malignant primary tumor of the central nervous system (CNS) in adults with a poor prognosis and a median survival ranging between 12 and 24 months.[1,2] Standard first-line treatment consists of maximum safe resection followed by concomitant radio-chemotherapy with temozolomide and subsequent maintenance treatment

Importance of the Study

In this randomized phase 2 study, we aim to investigate the clinical potential of patient-derived tumor cell (PDC)- based ex vivo drug screening for guiding maintenance treatment in newly diagnosed, *MGMT* promoter-unmethylated glioblastoma. Overall, 240 patients will be included and 1:1 randomized between the control group receiving temozolomide and the intervention group receiving ex vivo drug screening of patient-derived tumor cells followed by optional personalized maintenance treatment based on the result. This is the first clinical study evaluating the clinical value of PDC-based drug screening within a randomized phase 2 trial with overall survival as the primary endpoint. Moreover, the clinical trial is accompanied by a comprehensive translational research program to gain insights into the biological underpinnings of treatment response in glioblastoma.

with temozolomide with or without tumor treating fields.[3,4] Glioblastoma patients without O6-methylguanine methyltransferase (*MGMT*) gene promoter methylation have an inferior prognosis and benefit to a lesser extent from temozolomide treatment.[5–8] In line, recent trials such as CheckMate-498 omitted maintenance temozolomide treatment from the experimental arms in glioblastoma patients lacking *MGMT* promoter methylation.[9] This leaves *MGMT* promoter-unmethylated glioblastoma a highly unaddressed medical need considering both its extremely poor prognosis and lack of efficient treatment approaches that adequately improve patient survival and quality of life.

Genetic insights into driver mutations and the development of molecular targeted therapies have allowed the introduction of precision medicine in various fields of oncology. This has been, thus far, characterized by improved, biology-based treatment decisions resulting in sustained response rates compared to unselective chemotherapy, consequently leading to improved overall patient survival (reviewed in[10–13]). Indeed, extensive molecular analysis of glioblastoma and in-depth sequencing within The Cancer Genome Atlas (TCGA) project and other large-scale efforts revealed numerous driver mutations, such as epidermal growth factor receptor (*EGFR*) mutations, v-raf murine sarcoma viral oncogene homolog B1 (*BRAF)* mutations, neurotrophic tyrosine receptor kinase (*NTRK*) translocations, and fibroblast growth factor receptor (*FGFR*) fusions as potential therapeutic targets.[14] However, despite several trials investigating targeted therapy approaches in glioblastoma over the last decade, only very small patient populations with potential benefit from targeted treatments, such as BRAF/MEK or NTRK inhibitors have been identified, and these therapies are only considered in the recurrent setting based on limited evidence.[15] Reasons for this are manifold and encompass not only tumor heterogeneity but also transcriptional/epigenetic plasticity which complicates anti-tumoral treatment.[16] Therefore, new approaches to guide personalized treatment in glioblastoma are needed.

Several studies established the overall usage and proved the biological validity of patient-derived tumor cells (PDCs).[17–19] However, these studies either follow a single-arm design,[18] do not test the clinical efficacy of targeted anticancer drugs,[19] or did not include clinical follow-up monitoring,[17] thereby limiting the applicability of these findings on PDC-based drug screening in clinical routine. We, therefore, established the current randomized phase 2 performance study ATTRACT (NCT06512311) to explore whether PDC-based ex vivo drug screening can be used for personalized recommendations for the maintenance phase of the first-line treatment of patients with newly diagnosed *IDH*-wildtype glioblastoma, with an unmethylated *MGMT* promoter.

Methods

ATTRACT aims to establish proof-of-principle for the use of functional PDC-based drug screening as a tool for formulating personalized treatment recommendations in patients with newly diagnosed, *IDH* wildtype *MGMT* promoter-unmethylated glioblastoma. We hypothesize that additional diagnostic work-up using PDC-based drug screening along with the standard diagnostic work-up will improve the overall survival (OS). To this end, we have initiated a prospective, randomized Phase 2 performance study (Figure 1) utilizing the advanced drug screening technology established at CBmed, namely the CBmed Drug Screening Platform. The curated drug panel in use comprises 28 pre-specified drugs used for the treatment of solid tumors and hematological malignancies. All drugs included in the in vitro drug screening are licensed for different indications in the EU and safety was shown. The formulation of a personalized treatment will be the task of a molecular tumor board and will be based on the results of the PDC-based drug screening in the context of clinical characteristics such as comorbidities and potential interactions with other drugs. Patients will have the option to be treated in a named patient program according to Austrian legislation.

Primary and Secondary Objectives

The primary objective (hypothesis) of the study is to demonstrate that the OS is superior in the patients receiving PDC-based drug screening in addition to the standard diagnostic work-up (interventional arm) compared to patients only receiving the standard diagnostic work-up (standard arm).

Secondary objectives (hypotheses) are:

- to assess the feasibility of a PDC-based drug screening approach in a multi-center study throughout Austria
- to compare the quality of life between the interventional and standard arms

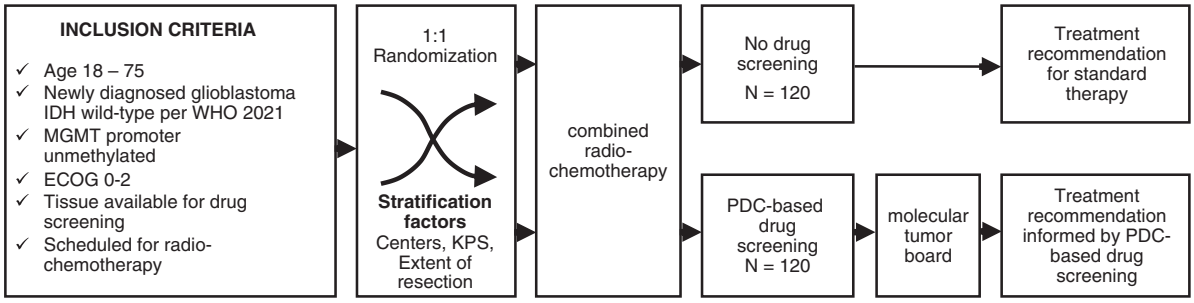

Figure 1. Overall design of the clinical study

- to assess differences in neurocognitive function and neurological function between the interventional and standard arms
- to assess differences in progression-free survival (PFS) between the interventional and standard arms

Study population

In total, 240 patients with newly diagnosed, *IDH* wildtype, *MGMT* promoter-unmethylated glioblastoma, successful PDC establishment after surgery, scheduled for standard first-line treatment consisting of concomitant radio-chemotherapy with temozolomide followed by 6 cycles of maintenance temozolomide chemotherapy will be included from five clinical centers in Vienna, Graz, Linz, Innsbruck and St. Pölten. According to the 1:1 randomization, 120 patients will be included in the intervention group and will receive PDC-based drug screening, and 120 in the standard group.

Inclusion Criteria

- Age 18–75
- ECOG performance status 0–2
- Newly diagnosed glioblastoma, *IDH* wildtype—according to the 2021 WHO classification of Tumors of the Central Nervous System[20]
- *MGMT* promoter-unmethylated
- successful PDC establishment and PDC available for drug screening
- Scheduled for concomitant radio-chemotherapy with temozolomide and maintenance temozolomide chemotherapy
- Written informed consent

Exclusion Criteria

- Current participation in another therapeutic clinical trial.
- Patients with a concurrent malignancy or malignancy within five years of study enrollment except for carcinoma in situ of the cervix, non-melanoma skin cancer, or stage I uterine cancer within the last 3 years.
- Pregnant or lactating women.
- Current known infection with hepatitis B virus (HBV), or hepatitis C virus (HCV). Patients with past HBV infection or resolved HBV infection (defined as having a negative hepatitis B surface antibody [HBsAg] test and a positive anti-hepatitis B core antibody [HBcAb] test, accompanied by a negative HBV DNA test) are eligible. Patients positive for anti-HCV antibodies are eligible only if polymerase chain reaction (PCR) is negative for HCV RNA.
- Known human immunodeficiency virus (HIV) infection that is not well controlled. All of the following criteria are required to define an HIV infection that is well controlled: undetectable viral RNA, CD4 + count ≥ 350 cells/mm^3, no history of AIDS-defining opportunistic infection within the past 12 months, and stable for at least 4 weeks on the same anti-HIV medications (meaning there are no expected further changes in that time to the number or type of antiretroviral drugs in the regimen). If an HIV infection meets the above criteria, monitoring of viral RNA load and CD4+ count is recommended.

Any of the following comorbidities:

- preexisting severe peripheral neuropathy (> CTCAE grade 2)
- Hepatic impairment (Bilirubin Level > 1.5x–3x ULN)
- Kidney dysfunction (CrCl < 59 mL/min)
- Cardiac dysfunction with left ventricular ejection fraction < 60%
- Any grade of interstitial lung disease
- Ongoing or previous history of rhabdomyolysis
- Acute pancreatitis
- QTcF ≥ 480 msec
- Diabetes mellitus with fasting glucose > 250 mg/dL or 13.9 mmol/L
- Participants who are unable or unwilling to comply with the requirements of the protocol as assessed by the investigator.

Ex Vivo Drug Screening, Reporting, and Molecular Tumor Board

The CBmed Drug Screening Platform, a fully automated high-throughput system, will be used to apply a range of 7

different concentrations (4.9 nM to 20 μM) of drugs to 384 plates with 500 cells per well. The application of drugs is executed by a contactless, acoustic transfer system (Echo 650, Beckman Coulter), and all drug plate and cell culture plate handling will be done by a robotic system. After 7 days of incubation, chemoluminescent ATP quantification measurements as a surrogate for cell viability will be generated by adding CellTiter-Glo 3D reagent (Promega) via an automated dispenser. Negative and positive controls are included to define relative viability in % and to calculate Z factors.

Dose–response curves and the list of area under the curve (AUC) per all investigated drugs will be transferred for further evaluation to the molecular tumor board. The molecular tumor board will consist of at least one clinical investigator per site, a representative for every specialty (medical oncology, neurology, pathology, neurosurgery, radiation oncology, and radiology from the entire investigator team) as well as a representative from CBmed laboratory performing the PDC-based drug screening.

The molecular tumor board will meet within 21 days of receiving the results of the drug screening that will be discussed for each patient separately. A personalized treatment approach will be formulated incorporating the results of the drug screening as well as the patient's clinical characteristics including age, comorbidities, co-medication, and performance status.

The personalized treatment recommendation will be transferred via a written report by the head of the tumor board to the treating physician of the particular patient. The treating physician will communicate the personalized treatment recommendation to the patient and initiate—if wanted by the patient—the named patient program to acquire the experimental medication.

Drug Selection for Ex Vivo Screening

Drug selection was performed from 80 previously established drugs.[21] The panel was curated based on the following criteria using a preliminary data set from a pilot study:

*Quality*In a first step, the technical quality of the screening process per drug was assessed based on a test set of patients ($n = 17$ from a pilot study). Drug screening quality was ranked based on the frequency of statistically adequate drug-response-curve fits. For each patient sample and drug, a 4-parameter-log-logistic function was fit to normalize cell viability readouts. Curve quality was defined as good (successful fit with bounded confidence intervals), bad (successful fit with unbounded confidence intervals), or failed (no model convergence). For each drug, the frequency of good drug-response-curve fits was used to rank drugs from highest to lowest. Drugs with more than 60% good quality curves were included. The remaining drugs were excluded.

ESCAT (European Society for Medical Oncology Scale for Clinical Actionability of molecular Targets)

The drugs passing the first step were reviewed based on the adapted ESCAT guidelines for glioblastoma to ensure that the inclusion of drugs is in line with the ESCAT Tier I or Tier II recommendations.[15] Accordingly, drugs targeting FGFR, MET/Alk, NRTK, and BRAF were included.

*In Vitro Efficacy*From the list of drugs that passed steps 1 and 2, those having at least one sample with an AUC value < 200 were selected.

*Safety and Authorization*The curated drug panel was extensively reviewed and cross-referenced to ensure that the included drugs were approved for use in the European Union and in Austria. By selecting only those drugs that met this criterion, we ensured that only drugs proven to be safe for human use were included. Furthermore, the inclusion of authorized drugs only also ensures overcoming regulatory hurdles and the utilization in the clinical trial.

*Availability*Drugs with limited access (eg, due to cost or unavailability for producers) were excluded.

*Blood–Brain Barrier (BBB)*Drugs that have been conclusively proven to fail crossing the BBB were excluded.

As a result, the drugs listed in Table 1 are all licensed in Austria for use in other malignancies than glioblastoma. This panel is fixed and no other drugs will be added throughout the performance study.

Statistical Considerations

The sample size calculation was based on the primary endpoint OS in a phase 2 design. The sample size was calculated for a two-sample log-rank test using a one-sided significance level of 5%. We assume that the median survival of patients with MGMT promoter-unmethylated glioblastoma is about 12 months based on previous publications.[7,22,23] For the overall study design, we decided to base our sample size calculation on a hazard ratio of 0.7 or the translation of a survival increase from about 12 to 17 months as previous similar studies in MGMT promoter-unmethylated glioblastoma used comparable statistical considerations (eg, HR 0.82 in CheckMate 498[9]). Hence, the inclusion of 240 subjects (120 per group) will result in a power of about 80%—assuming a median survival time of about 12 months for the control arm and a hazard ratio of 0.7 (meaning a median survival time of about 17 months for the interventional arm).

The adaptive group sequential design allows for one interim analysis with stopping for futility in case a negative trend is observed and O'Brien & Fleming type boundaries to stop for efficacy. For this scenario, we assumed an accrual time of 48 months and that the final analysis will be conducted after 210 events. This translates to a time of interim analysis after 38 months after the first patient has been included and the final analysis is expected after 72 months.

Adequate randomization will be implemented with participating centers as strata. A stratified block randomization will be implemented. Established parameters

Table 1. List of the Drugs Used in the Drug Screen

Compound	Trade name	Target	Manufacturer
Abemaciclib	Verzenios	CDK4/6	Eli Lilly Nederland B.V.
Afatinib	Giotrif	HER2/4, EGFR	Boehringer Ingelheim International GmbH
Alectinib	Alecensa	ALK, RET	Roche Registration GmbH
Alpelisib	Piqray	PI3K	Novartis EuroPharm Limited
Avapritinib	Ayvakit	KIT, PDGFRA	Blueprint Medicines B.V.
Axitinib	Inlyta	VEGFR1/2/3	Pfizer Europe M.A. EEIG
Bortezomib	Velcade	Proteasome	Janssen-Cilag International NV
Carfilzomib	Kyprolis	Proteasome	Amgen Europe B.V.
Ceritinib	Zykadia	ALK	Novartis Europharm Limited
Cobimetinib	Cotellic	MEK1, MAP2K1	Roche Registration GmbH
Crizotinib	Xalkori	ALK, HGFR, ROS1, RON	Pfizer Europe M.A. EEIG
Dacomitinib	Vizimpro	HER2/4, EGFR	Pfizer Europe M.A. EEIG
Entrectinib	Rozlytrek	TRKA/B/C, ROS1, ALK	Roche Registration GmbH
Erdafitinib	Balversa	FGFR	Janssen-Cilag International NV
Ibrutinib	Imbruvica	BTK	Janssen-Cilag International NV
Ixazomib	Ninlaro	Proteasome	Takeda Pharma A/S
Lurbinectedin	Zepzelca	DNA	PharmaMar S.A.
Neratinib	Nerlynx	HER1/2/4, EGFR	Pierre Fabre Médicament
Osimertinib	Tagrisso	EGFR	AstraZeneca AB
Panobinostat	Farydak	HDAC	Secura Bio Limited
Ponatinib	Iclusig	BCR-ABL, FGFR, PDGFR, SRC, RET, KIT, VEGFR1	Incyte Biosciences Distribution B.V.
Regorafenib	Stivarga	VEGFR1/2/3, TIE2, KIT, PDGFRA/B, FGFR1/2, RAF-1, BRAF	Bayer A.G..
Ripretinib	Qinlock	KIT, PDGFRA	Deciphera Pharmaceuticals B.V.
Selinexor	Nexpovio	Exportin-1	StemlineTherapeutics B.V
Selumetinib	Koselugo	MEK1/2	AstraZeneca AB
Temozolomide	Temodal	DNA	Merck Sharp & Dohme B.V.
Tucatinib	Tukysa	HER2	Seagen B.V.
Vandetanib	Caprelsa	VEGFR2, EGFR, RET	Genzyme Europe B.V.

including center, post-operative performance status (Karnofsky Score ≤ 85 vs > 85), and extent of resection (Gross total resection vs partial resection) will be used as stratification factors.

Primary Endpoint Analysis

The primary analysis will be based on the intention-to-test (ITT) set.

The primary endpoint is OS from diagnosis (date of randomization) of *IDH*-wildtype, *MGMT* promoter-unmethylated glioblastoma. Patients without a survival event will be censored with the date of the last survival follow-up. Survival updates also including data from Statistic Austria will be included in case of lost to follow up. Differences between the two randomized groups will be assessed via a stratified log-rank test at a one-sided level of 5%. The stratification factors used for randomization will be used in all stratified analyses. Thus, the log-rank test will be stratified by the factors used for randomization, ie, by post-operative performance status (Karnofsky Score ≤ 85 vs > 85), the extent of resection (Gross total resection vs partial resection), and center. In the event there are small strata, strata may be combined to ensure a sufficient number of participants and events in each strata.

Furthermore, a stratified Cox proportional hazard model, using the stratification factors applied as randomization will be used to estimate the hazard ratio (HR) and the corresponding one-sided 95% confidence interval. Furthermore, to check the robustness of the estimate, we will use also Cox proportional hazard models adjusting for additional covariates and factors, eg, sex and age (in years).

The survival data will be visualized by Kaplan–Meier survival plots.

Secondary Endpoint Analysis

Secondary endpoints include feasibility, PFS, quality of life (QOL) assessed by the European Organisation for Research and Treatment of Cancer (EORTC) quality of life paper-based questionnaire (QLQ-C30) and the brain cancer-specific questionnaire (QLQ-BN20), neurocognitive

function as well as the Neurological Assessment in Neuro-Oncology (NANO) scale.

For time-to-event endpoints (such as PFS) Kaplan–Meier plots will be provided. The two randomized groups will be compared with stratified log-rank tests as described above. Additionally, similar analyses as for the primary endpoint OS will be performed. Continuous secondary endpoints such as QOL scores and NANO scale will be summarized by the mean, standard deviation (SD), median, first and third quartiles, minimum and maximum for each group and time point separately. Continuous endpoints will be analyzed using either an analysis of covariance (ANCOVA) or a mixed model for repeated measurements (MMRM) depending on whether the endpoint has been measured just once or more frequently after randomization. The MMRM will be adjusted for the stratification factors used for randomization as stated above.

Feasibility will be assessed qualitatively. Feasibility will be considered as achieved if the study can be conducted as planned and the individual screening for the interventional arm can be successfully conducted in the initial time window to provide the sufficient data for the decision making of the tumor board.

Multiple Testing

A hierarchical testing procedure will be employed to enable a confirmatory testing of the primary endpoint OS and the secondary endpoint PFS.

For all the other secondary endpoints (QLQ-C30, QLQ-BN20, neurocognitive function score, and Neuro-Oncology (NANO) scale) p-values and 95%-two-sided confidence intervals will be reported. However, as they are not subject to multiplicity adjustment, these analyses should be considered as descriptive.

Missing Data for Time-to-event Analyses

For time-to-event endpoints (such as OS or PFS), subjects without experiencing an event concerned will be censored at the date of the last follow-up where it is clear that the event is not present.

Criteria for the Termination of the Study

One interim analysis will be performed after 50% of the pre-planned events. To allow for early stopping for efficacy at the interim analysis, an alpha spending function with O´Brien and Fleming (OBF) type boundaries at one-sided alpha of 5% will be used. The interim analysis will use non-binding futility boundaries, ie, stopping in case a negative effect is observed.

Results

The first patient was enrolled into ATTRACT in July 2024 and accrual is ongoing. Interim analysis of the ATTRACT study is expected in late 2027, and final results in 2030.

Discussion

To our knowledge, ATTRACT is the first randomized phase 2 trial assessing the efficacy and feasibility of a PDC-based ex vivo drug screening approach in *IDH*-wildtype, *MGMT* promoter-unmethylated glioblastoma. The clinical study is embedded into a unique biobanking program, aiming to collect biological samples together with comprehensive clinical annotation and radiological imaging.

Here, we decided to design a study with OS as the primary endpoint, given that this is currently the clinically most meaningful and statistically most robust endpoint in neuro-oncology. Although other phase 2 studies concentrate on different clinical endpoints like PFS or PFS6, we decided to analyze OS although we acknowledge that follow-up treatment could have a potential impact. Importantly, cross over between the groups is not possible as per the protocol and due to regulatory reasons, as drug screening in the standard arm will not be performed. In this regard, we deemed it inappropriate to perform a test without providing the possibility for the patient to use the results thereof. In line with the involved ethics committees, we therefore excluded the possibility of drug screening prospectively in the standard group and only retrospective testing after finalization of the study is possible (and will be performed within the scope of the entire ATTRACT project). However, patients in the interventional group do have the possibility to receive several experimental treatments on the basis of the PDC-based drug screening. Therefore, we postulate that the impact of follow-up treatments will be smaller.

The inclusion of a prespecified and diverse panel consisting of 28 drugs that are approved for the treatment of other malignancies, allows us to gain insights into the biological significance of various pathways in glioblastoma. Here, the potential of drugs to cross the BBB was part of the decision process. In addition, a side project will concentrate on the BBB crossing potential of the drugs in correspondence to the clinical efficacy. To ensure comparability between patients and due to the regulatory setup of the drug screening platform as an in vitro diagnostic test, we decided against an open drug panel including new drugs with emerging evidence, but rather concentrate on the given drug panel representing drugs targeting all major molecular pathways. The implementation of an interdisciplinary molecular tumor board ensures that not only the ex vivo efficacy of drugs but also patient-specific factors such as comorbidities and concomitant medications are considered when formulating personalized treatment recommendations. A standard operation procedure (SOP) describing the discussion of individual patients during the molecular tumor board has been implemented. This SOP ensures the harmonization of the decision-making process for all patients in the experimental arm from drug screening results, through molecular characteristics of the tumor to patient characteristics.

Although the ATTRACT trial is the first randomized trial to address the clinical efficacy of PDC-based drug screening, some limitations of the experimental setup must be addressed. Firstly, only patient with available PDCs will be

included as per our inclusion criteria. During our previous experiments within a pilot study, we experienced that adequate sampling (at least 1 g of material from the contrast-enhancing area) leads to a successful PDC-establishment rate of approximately 95%. Nevertheless, in the course of translational projects, we are currently characterizing other factors influencing the quality of the established PDC cultures. Secondly, important pathophysiological principles like invasion, angiogenesis, or immunosuppression are not acknowledged with the primary readout being ATP levels of tumor cells. Therefore, the tumor microenvironment is not recapitulated in our assay. Importantly, other PDC-based approaches utilize the technique "Pharmacoscopy," a high-content imaging platform incorporating the impact of inflammatory cells as well.[24,25] Notwithstanding, as we were aiming to design a study applicable and feasible for clinical routine, we decided to use the objective and robust ATP measurements as a readout. Nevertheless, the drug screening platform used in the ATTRACT study certainly calls for future improvements in terms of incorporating the impact of the microenvironment.

In conclusion, ATTRACT allows us to investigate a truly personalized approach in the treatment of glioblastoma. Moving forward, ATTRACT opens unparalleled opportunities for further translational research aiming at the identification of novel treatment options in this patient cohort with unmet clinical needs.

Ethical and Regulatory Considerations

PDC establishment is a part of biobanking effort and is covered by local positive ethics committee votes (EK no. (a) Medical University of Graz: 36-253 ex 23/24; (b) Medical University of Vienna: 2186/2023; (c) Karl Landsteiner University of Health Sciences: GS3-EK-1/211-2024; (d) Johannes Kepler University Linz: 1002/2024; and (e) Medical University of Innsbruck 1095/2024). The drug screening process is covered by an ethics vote from the lead-ethics committee at the Medical University of Graz (36-136 ex 23/24) and is authorized by the Austrian Federal Office for Safety in Health Care (ref. no. 103033083).

All participants will provide written informed consent. Informed consent procedures including how personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial are regulated by local SOPs according to Good Clinical Practice.

Keywords

ATTRACT | drug screening | glioblastoma | patient-derived tumor cells | personalized medicine.

Lay Summary

Glioblastoma is a fast-growing brain cancer. Nearly all patients receive surgery along with standard chemotherapy and radiation. The authors of this study want to see whether using personalized treatments, based on testing the tumor in the lab, could help patients live longer than using standard chemotherapy. To do this, they have designed a clinical trial to treat 240 patients with glioblastoma. These patients will either receive the standard treatment or have their treatment guided by drug screening using their tumor. In the drug screening group, tumor cells from each patient will be tested against a panel of 28 drugs to find the most effective options before choosing a treatment. The study will track how long patients live. The trial began in July 2024, and the authors expect to have early results in 2027, with final results in 2030.

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Conflict of interest statement. A.S.B. has research support from Daiichi Sankyo, Roche, and honoraria for lectures, consultation, or advisory board participation from Roche, Bristol-Myers Squibb, Merck, Daiichi Sankyo, AstraZeneca, CeCaVa, Seagen, Alexion, and Servier. M.J.M. has received research support from Bristol-Myers Squibb and travel support from Pierre Fabre. Z.S. is a previous employee of Boehringer Ingelheim and Turbine AI and a current employee of CBmed GmbH. C.A.M. declares having no conflict of interest. A.E.H. is a previous employee of CBmed GmbH and has received honoraria for lectures from the following for-profit company Illumina. F.E. has honoraria for lectures and advisory board from Dr. Sennewald Medizintechnik and Servier. J.F. has received honoraria for lectures and consultations from the following for-profit companies: Novartis, Seagen, Sanofi, Servier. F.K. declares having no conflict of interest. A.L. declares having no conflict of interest. M.N. declares having no conflict of interest. S.O. declares having no conflict of interest. B.P. is a current employee of CBmed GmbH. J.P. has received honoraria for lectures, consulting, and for travel support from Telix Pharmaceuticals Ltd and Servier. TRPis the CSO of CBmed GmbH, received research support from AstraZeneca, Novo Nordisk Foundaton, and AstraZeneca, and has received honoraria for consulting and lectures from Novo Nordisk, Sanofi, Eli Lilly, and Arecor. S.S.K. declares having no conflict of interest. T.U.P. has been part of a consultancy team for Abbvie and AOP and received travel support as well as honoraria for lectures from Roche, Novocure, Biogen, Sanofi, and Fresenius and is a current employee of CBmed GmbH. A.W. is a previous employee of CBmed GmbH. G.W. declares having no conflict of interest. M.P. has received honoraria for lectures, consultation, or advisory board participation from the following for-profit companies: Bayer, Bristol-Myers Squibb, Novartis, Gerson Lehrman Group (GLG), CMC Contrast, GlaxoSmithKline, Mundipharma, Roche, BMJ Journals, MedMedia, Astra Zeneca, AbbVie, Lilly, Medahead, Daiichi Sankyo, Sanofi, Merck Sharp & Dome, Tocagen, Adastra, Gan & Lee Pharmaceuticals, Janssen, Servier, Miltenyi, Boehringer-Ingelheim, Telix, Medscape.

Authorship Statement

Protocol development: A.S.B., M.P., M.J.M., J.P., T.P., C.A.M., Z.S.; optimizing the laboratory protocols: A.S.B., T.U.P., B.P., S.S.K., G.W.; acquiring of data: A.S.B., A.L., M.N., T.U.P., S.O., B.P., A.W., A.E.H.;trial coordination: A.S.B., M.P., Z.S.;data management: M.J.M., F.E., Z.S., A.S.B., J.S.F., A.L.; statistician: F.K.; quality control: T.U.P., S.S.K., B.P.; manuscript writing and review: A.S.B., M.P., M.J.M., Z.S., F.E., A.E.H., M.N., J.F.S., F.K., A.L., M.N., S.O., B.P., J.P., T.P., S.S.K., T.U.P., A.W., G.W. All authors read and approved the final manuscript.

ATTRACT study group

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Data Availability

The data generated in the course of this study will be made public after the approval of relevant regulatory authorities.

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