NCT05376800: Phase 0/i non-randomized, open-label, single-arm trial to measure BI 907828 concentrations in brain tissue of patients with newly diagnosed GBM (Phase 0), and determine the MTD and tolerability of BI 907828 in combination with radiotherapy in patients with GBM (Phase Ia).

Phase 0: The starting dose will be 30 mg; the next dose level to be tested will be 45 mg.

Phase Ia: The starting dose of BI 907828 will be 30 mg q3w; treatment will be continued until criteria for discontinuation are met.

**TRIAL DESIGN**

**OBJECTIVES**

Primary

- Determine total concentration of BI 907828 in brain tumor tissue and calculate unbound concentration of BI 907828 in brain tumors (Phase 0)
- Determine MTD and/or RDE, and safety profile of combined radiotherapy and BI 907828 (Phase Ia)

Secondary

- Determine pharmacodynamic modulation and dose-dependence in brain tumors (Phase 0)
- Determine plasma PK profile (Phase Ia)

**TRIAL RATIONALE**

- Glioblastoma (GBM) is associated with a median survival of less than 1 year after initial diagnosis, if left untreated.
- Current standard therapies such as surgical resection, radiotherapy, and chemotherapy with temozolomide can prolong survival; however, patient outcomes remain poor.
- As the blood-brain barrier often limits drug distribution to the CNS, it is challenging to rely on PK/PD data from patients with non-CNS cancers to predict effects in the brain. The Phase 0 trial will enable accurate assessment of the pharmacologic effects of BI 907828 in brain tissue.

**ENDPOINTS**

Primary

- Measured total concentrations and calculated unbound concentrations of BI 907828 in brain tumors (Phase 0)
- Occurrence of dose-limiting toxicity during MTD evaluation period (Phase Ia)
- Occurrence of adverse events (Phase Ia)

Secondary

- Dose-dependent changes in expression levels of TP53 target genes in brain tumors (Phase 0)
- Progression-free survival (Phase Ia)
- Plasma PK of BI 907828 at cycle 1 (Phase Ia)

AEs, adverse events; GBM, glioblastoma; IDH, isocitrate dehydrogenase; MGMT, O6-methylguanine-DNA methyltransferase; MTD, maximum tolerated dose; PD, pharmacodynamics; PK, pharmacokinetics; pts, patients; q3w, every 3 weeks; RDE, recommended dose for expansion; TP53, tumor suppressor protein p53; wt, wild-type.

**ELIGIBILITY CRITERIA**

Inclusion: Phase 0

- Adult patients with histologically or radiologically diagnosed GBM
- Eligible for neurological tumor resection
- ECOG performance status of 0/1
- Adequate organ function
- Life expectancy ≥3 months at the start of treatment

Exclusion: Phase 0

- Known TP53 mutant GBM
- Known IDH mutant grade 4 astrocytoma
- Pacemakers or other metallic implants
- Inability to undergo contrast-enhanced MRI (GFR <30 mL/min)
- Use of restricted medications or drugs likely to interfere with safe conduct of the trial

Inclusion: Phase Ia

- Adult patients with histologically diagnosed TP53 wild-type GBM harboring unmethylated MGMT promoters and IDH wild-type
- Undergone neurosurgical tumor resection and eligible for standard radiotherapy
- Formalin-fixed paraffin-embedded tumor block or representative H&E slides available for retrospective review
- ECOG performance status 0/1
- Life expectancy ≥3 months at the start of treatment

Exclusion: Phase Ia

- Previous systemic therapy (other than participation in Phase 0) or radiotherapy for GBM
- Pacemakers or other metallic implants
- Inability to undergo contrast-enhanced MRI (GFR <30 mL/min)
- Use of restricted medications or drugs likely to interfere with safe conduct of the trial

**REFERENCES**


This study was funded by Boehringer Ingelheim. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version.

The authors did not receive payment related to the development of the poster. Medical writing support for the development of the poster, under the direction of the authors, was provided by Lauren Main, of Ashfield MedComms, an Insys Company, and funded by Boehringer Ingelheim.