

Prospective Analysis of Cancer Stem Cell Drug Response Assay for Glioblastoma Patients

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Background: Over the past 20 years even with the aggressive standard of care (SoC) Stupp treatment protocol the prognosis of glioblastoma (GBM) has only minimally improved from 12 to 14 months. This is due in large part to the presence of chemo- and radiation-resistant GBM cancer stem cells (CSCs) that contribute to tumor propagation, maintenance, and treatment resistance. We are using ChemOID, a CLIA certified and CAP accredited drug response assay to identify the most effective chemotherapy treatment against CSCs and bulk of tumor cells from of a panel of chemotherapies, offering great promise for individualized cancer management. A prospective study was conducted evaluating the use of the ChemOID drug response assay in glioblastoma patients.

Methods: Fresh tissue samples were collected for drug sensitivity testing from 61 glioblastoma patients enrolled in IRB approved protocol. Patients were prospectively monitored for tumor response, time to recurrence, progression-free survival (PFS), and overall survival (OS). Odds Ratio (OR) associations of 12-month recurrence, PFS, and OS outcomes were estimated for CSCs, bulk tumor and combined assay responses to treatment; sensitivities/specificities, areas under the curve (AUC) were examined.

Results: The data suggests that ChemOID guided treatment significantly enhanced tumor response. For every 5% increase in cell kill of CSCs by assay-guided chemotherapy, 12-month patient response (non-recurrence of cancer) increased 2.5-fold, OR = 2.3 ($P = 0.01$). Bulk of tumor assay was found not statistically significant. Median recurrence time was 20 months for patients with a positive (> 40% cell kill) CSCs test versus only 3 months with a negative CSCs test, whereas median recurrence time was 13 months versus 4 months for patients with a positive (>55% cell kill) bulk test versus negative. Similar favorable results for the CSC test were observed for PFS and OS outcomes.

Conclusions: The ChemOID CSCs drug response assay has the potential to increase the accuracy of bulk tumor assays to help guide individualized chemotherapy choices. Glioblastoma cancer recurrence may occur quickly if the CSC test has a low cell kill rate, even if the bulk tumor test cell kill rate is high.

Keywords: Cancer stem cells, Glioblastoma, Chemosensitivity.

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