

A prospective study of chemo-predictive assay for targeting cancer stem cells in Glioblastoma patients

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Introduction: Prognosis of glioblastoma (GBM) treated with standard-of-care maximal surgical resection and concurrent adjuvant temozolomide (TMZ)/radiotherapy is still very poor (median survival = 14.2 months). It has been observed that glioblastomas contain a small population of cancer stem cells (CSCs) that contribute to tumor propagation, maintenance, and treatment resistance. Administration of ineffective anticancer therapy is associated with unnecessary toxicity and development of resistant cancer cell clones.

We have developed a drug sensitivity assay (ChemoID) that identifies the most effective chemotherapy management against CSCs and bulk of tumor cells offering great promise for individualized anticancer treatments. A prospective study was conducted evaluating the use of the ChemoID drug sensitivity assay in glioblastoma patients treated with standard-of-care.

Methods: 30 glioblastoma patients, 18-years and older, male/females, eligible for a surgical biopsy, were enrolled in an IRB-approved protocol, and fresh tissue samples were collected for drug sensitivity testing. All patients were treated with standard-of-care TMZ plus radiation with or without maximal surgery, depending on the status of the disease. Each treatment was classified by the assay as: sensitive (S = >60% cell kill), intermediate (I = 30-60% cell kill), or resistant (R = <30% cell kill). Patients were prospectively monitored for tumor response, time to recurrence, progression-free survival (PFS), and overall survival (OS). Associations of assay response for the standard-of-care TMZ selected treatment with tumor response, time to recurrence, PFS, and OS were analyzed.

Results: The median follow-up analysis was 8 months (3-49 months). ChemoID assay on CSCs demonstrated a sensitivity of 100% and a specificity of 95.83%, with a positive predictive value of 80%, and a negative predictive value of 100%. The ChemoID assay on bulk of tumor demonstrated instead a sensitivity of 100% and a specificity of 87.50%, with a positive predictive value of 57.14%, and a negative predictive value of 100%.

Overall, patients treated with assay-sensitive or -intermediate (S+I) TMZ against CSCs demonstrated significantly improved tumor response with increased median and mean time to recurrence, improved median PFS, and prolonged mean OS, when compared to patients treated with assay-resistant TMZ to CSCs or with assay-sensitive or -intermediate TMZ to bulk of tumor cells.

Conclusions: This prospective study compared the sensitivity of patient derived GBM CSCs and bulk of tumor cells to various chemotherapies, demonstrating that GBM patients treated with TMZ whose CSCs were found sensitive (S+I) to TMZ, experienced improved tumor response; extended mean and median time to recurrence; improved median PFS, and prolonged mean OS.

Biography:

Dr. Claudio completed his medical and graduate training at the University "Federico II" in Naples, Italy. He then completed two postdoctoral fellowships in molecular biology and cancer biology at Temple University and at Jefferson University in Philadelphia, USA.

In 2006 he moved at Marshall University in West Virginia where he became tenured Associate Professor in the Department of Biochemistry and Microbiology and director of the Translational Laboratories at the Translational Genomic Research Institute, Edwards Comprehensive Cancer Center. There he developed the ChemoID[®] drug response assay, which compares the sensitivity of cancer stem cells vs. bulk of tumor cells to chemotherapy. Three international patents cover the ChemoID[®] procedure, which is a second-generation functional drug response assay that uses a patient's live tumor cells to indicate which chemotherapy agent (or "combinations") will kill the bulk of the cancer tumor and the cancer stem cells (CSCs) that are known to cause cancer to recur. In 2010 he co-founded Cordgenics, LLC a US company that is focused on cancer stem cells diagnostics and discovery of novel therapeutics.

He moved to the University of Mississippi in 2015 as tenured Professor in the Department of BioMolecular Sciences, National Center for Natural Products Research (NCNPR), and Department of Radiation Oncology, where he became the Director of the Translational Laboratories at the Medical Center Cancer Institute.

Dr. Claudio has authored 143 publications in biomedical journals to date. He has served or serves on numerous grant review panels for NIH, NCI, DOD, and foreign research funding agencies from Italy, Germany, The Netherlands, Eurasia, and the European Commission. He serves as Editor or Associate Editor of a number of biomedical journals, and has served as an advisor to several pharmaceutical and biotechnology companies.