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Title

A PHASE I CLINICAL TRIAL TO EVALUATE MTD OF PERAMPANEL AND MEMANTINE IN COMBINATION WITH STANDARD CHEMORADIOOTHERAPY FOR THE TREATMENT OF PATIENTS WITH NEWLY DIAGNOSED GBM -A STUDY DESIGN

Permalink

<https://escholarship.org/uc/item/1j60q07z>

Journal

NEURO-ONCOLOGY, 22

ISSN

1522-8517

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Publication Date

2020

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Peer reviewed

RTID-07. HUMAN PLACENTAL HEMATOPOIETIC STEM CELL DERIVED NATURAL KILLER CELLS (CYNK-001) FOR TREATMENT OF RECURRENT GLIOBLASTOMA

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Glioblastoma (GBM) is the most aggressive primary brain tumor with dismal prognosis. Recent advances of immunotherapy in cancer have sparked interest in the use of cell therapy for treatment of GBM. Active transfer of Natural Killer (NK) cells is of particular interest in GBM because NK cells are capable of exerting anti-tumor cytotoxicity without the need for antigen presentation and sensitization, processes that are impaired in GBM. CYNK-001 is an allogeneic, off-the-shelf product enriched for CD56+/CD3- NK cells expanded from placental CD34+ cells manufactured by Celularity. Here, we demonstrate in vitro cytotoxicity of CYNK-001 against several GBM lines and its in vivo anti-tumor activity in a U87MG orthotopic mouse model via intracranial administration resulting in 94.5% maximum reduction in tumor volume. We have developed a phase I window-of-opportunity trial of CYNK-001 in recurrent GBM via intravenous (IV) and intratumoral (IT) routes. In the IV cohort, subjects receive cyclophosphamide for and 3.4% (P=0.001) for 10 and 20 Gy respectively) compared to control (12.7%). The reduction in the proliferating NSC population subsequently translated to a reduced population of NeuN-labeled mature neurons 70 days post-irradiation. The loss of proliferating NSCs and subsequent reduction in mature neurons demonstrates the long-term effects of radiation. Our initial results indicate COs will be a valuable model to study the effects of radiation therapy on normal and diseased human tissue.