PROTOCOL OF A RANDOMIZED PILOT STUDY ON SURVIVAL IN NEWLY DIAGNOSED GLIOBLASTOMA PATIENTS UNDERGOING CHEMORADIATION VERSUS COMBINED CHEMORADIATION WITH INTRANASAL PERILLYL ALCOHOL

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A B S T R A C T

Introduction/Justification: Glioblastoma multiforme (GBM) is a highly aggressive type of brain tumor and remains one of the most challenging cancers to treat. This tumor is characterized by rapid progression and unfavorable prognosis. After undergoing surgery, radiotherapy (RT), and chemotherapy (CT) with temozolomide (TMZ), patients generally exhibit low survival rates. Perillyl alcohol (POH) is a hydroxylated monoterpene with antitumor, anti-angiogenic, and pro-apoptotic properties, inhibiting RAS oncogene-mediated signaling. In vitro and in vivo studies showed POH's cytotoxicity to both TMZ-resistant and sensitive cells, and its effectiveness as a radiosensitizer in malignant glioma cell lines. In phase I/II trials with oral POH in advanced, refractory cancer patients, nausea and other gastrointestinal toxicities led to study discontinuation. Currently, POH is being studied as an inhaled anticancer agent, showing no toxicity and promising activity with increased survival in patients with recurrent gliomas, however, these studies were not randomized, and to date, these investigations have been conducted exclusively in patients with recurrent gliomas. **Objectives:** This study presents a protocol from the University of Campinas, developed by experts across multiple fields, to evaluate the effects of intranasal POH in GBM patients. **Materials and Methods:** Patient's will be recruited from the Oncology Service at the General Hospital of the University of Campinas (UNICAMP) after tumor resection, with a total of 40 participants. Adult individuals of any gender will be included. Through randomization, participants will be randomly assigned to two groups: the control group (RT+CT) and the intervention group (RT+CT + POH inhalations). Block randomization of four patients will ensure balance between groups during recruitment. The randomization sequence was generated at www.randomization.com. The control group will undergo RT and CT with TMZ: 75 mg/m^2 of TMZ daily for 6 weeks during RT (2 Gy/day for 5 days a week, totaling 60 Gy), followed by 150 or 200 mg/m^2 of TMZ for 5 days per cycle in 28-day cycles for 6 cycles. The participants in the intervention group will receive the same treatment plus 0.3% POH inhalations (55 mg in 3 mL of water, 4 times daily, with 6-hour intervals). They will undergo 6 weeks of RT + TMZ + POH, followed by 6 cycles of TMZ + POH (5 days of TMZ + POH, followed by 23 days of POH only). Cranial MRIs will be analyzed by an expert neuroradiologist using T2/FLAIR signal intensity with perfusion, without knowledge of patient group allocation. MRIs are part of routine treatment, performed every 3-4 months in the first year, and response will be assessed using MacDonald and RANO criteria for high-grade gliomas. Toxicity assessment of standard treatment with POH will follow the NCI Common Terminology Criteria, version 5.0. Progression-free survival will be compared between patients receiving only RT and CT and those also undergoing POH inhalation, with survival curves calculated using the Kaplan-Meier method. **Results:** *Perspectives:* Patients in the intervention group are expected to have higher survival rates, indicating a benefit of intranasal POH with standard treatment. **Conclusion:** *Acknowledgement:* The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Keywords: Glioblastoma, Perillyl alcohol, Protocol.

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ANTIPROLIFERATIVE ACTIVITIES IN VITRO OVER SQUAMOUS CELL CARCINOMAS OF A PALLADIUM(II) COMPLEX WITH AMANTADINE

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A B S T R A C T

Introduction/Justification: Metal-based drugs have been used in diagnosis and treatment of different types of cancer since the discovery of cisplatin's antineoplastic properties in the 1960's. Second-generation drugs based on the platinum(II) complex cisplatin, such as carboplatin and oxaliplatin, were developed and used for cancer treatment worldwide. However, platinum(II) drugs typically cause side effects, such as nephrotoxicity, neurotoxicity and myelosuppression, which motivates the search for new drug candidates. Since the platinum(II) and palladium(II) ions have similar characteristics and form analogous compounds, palladium(II) complexes have been also studied as potential anticancer agents. Recently, a new palladium(II) drug named padeliporfin (Tookad® Soluble) has entered the clinic for the treatment of low-risk prostate cancer, which further motivates the investigation of palladium(II) complexes as potential antineoplastic drugs. Adamantanes are a class of organic compounds that consist of a single diamond-like carbon cage. The functionalization of adamantane with an amine group lead to amantadine, which has been used in the clinic as an antiviral and