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Ramon Sebastian Leon-Zetina et al., J Cancer Sci Ther 2019, Volume 11
DOI: 10.4172/1948-5956-C1-160

32nd Euro Congress on

Cancer Science & Therapy

March 07-08, 2019 | Barcelona, Spain

Preclinical pharmacological safety tests of the combination of Temozolomide and Mifepristone for the treatment of glioblastoma

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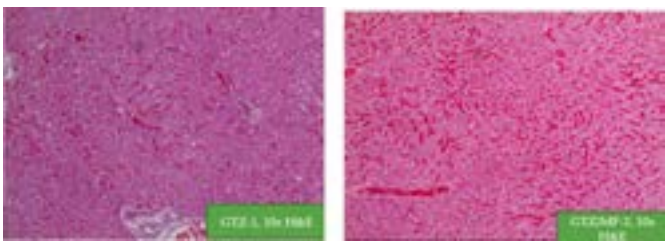
Glioblastoma multiforme is the most aggressive malignant central nervous system neoplasm and is classified as grade IV in the WHO most recent neuropathological classification schemes. Treatment is composed by combination of radiotherapy and chemotherapy, however, even with treatment, survival time is low (12-16 months) besides that glioblastoma has chemoresistance to Temozolomide (Tz). Recent research has showed that Mifepristone (Mf) increase cytotoxicity of several antineoplastic agents, including Tz during Glioblastoma treatment, nevertheless there is no preclinical safety (toxicity) studies including a combination of both drugs; therefore, the objective of this project is to evaluate the toxicity preclinically which is necessary for its use in clinic. Acute toxicity and local tissue damage test were done in male Wistar rats, Specific Pathogen Free (SPF) divided in three groups: 1) Tz, 2) Tz-Mf and 3) control group. The rats were administered by 21 days. During the chemotherapy administration, three blood sampling where obtained for cell blood count (CBC) and biochemistry. After 21 days, animal postmortem study was done as well as histopathological evaluation focusing on organs with toxicological importance. Also, genotoxicity evaluation was carried out using in-vivo model (micronucleus essay) in which ICR SPF mice were used and divided in three groups: 1) Cyclophosphamide, 2) Tz-Mf, 3) negative control. Blood sampling were done at 36 and 72 hours after drug administration. Results in both studies suggest no evidence of toxicity in Tz and Mf combination that prevents its use for Glioblastoma treatment.



Recent Publication

1. Fusocelular Sarcoma and thoracic metastasis, REMEVET, Small animal oncology special edition, #30, year 8, 2017 ISNN2017-3933.

Biography

Ramón Sebastián Leon-Zetina is a Doctor in Veterinary Medicine and Pathologic Diagnostic Specialist. Currently, he is pursuing his Master's at Universidad Nacional Autónoma de México, Instituto Nacional de Cancerología Mexico City, Mexico. He has 4 years of experience in laboratory animal pathology in diagnostic and research fields (toxicity and animal model studies) and has worked in Glioblastoma research for two years.

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