HG-51. DELTA-24-RDG IN COMBINATION WITH RADIOTHERAPY FOR DIPG: OPENING NEW THERAPEUTIC AVENUES

Naiara Martinez-Velez1, Miguel Marigil1, Pablo Dominguez1, Javier Aristu1, Juan Fueyo2, Cande Gomez-Manzano2, Marie Piere Junier3, Herve Chneiweiss3, Elias A. El-Habr3, Ricardo Diaz-Valle1, Sonia Tejada1, and Marta M. Alonso1; 1Clinica Universidad de Navarra, Pamplona, Navarra, Spain; 2MD Anderson Cancer Center, Houston, TX, USA; 3Institut National de la Santé et de la Recherche Medicale (INSERM), Paris, France

Diffuse intrinsic pontine glioma (DIPG) is one of the most aggressive brain tumors in kids. The standard treatment is radiotherapy which improves the quality of life of these children transitorily however, in a few months the tumor relapse. Despite the advances in the genetic knowledge of these tumors the outcome remains dismal. Delta-24-RGD is an adenovirus that is currently undergoing phase I clinical trial in adult gliomas with promising results. The aim of this work was to evaluate the safety and the antitumor effect of Δ24-RGD alone or combined with radiotherapy in DIPGs. Our results showed that Delta-24-RGD displayed a potent antiglioma effect (IC50 ranging from 5 to 50 MOIs) in DIPG cell lines (n = 4) that was mediated by an effective replication. Addition of radiotherapy improved the antitumor effect of Delta-24-RGD, due to synergistic effect (CI < 1). Viral viability was not affected by the addition of radiotherapy even at high doses (12Gy). Mechanistic studies showed that the virus inhibited key proteins involved in DNA repair that play important roles in the resistance to radiotherapy such as Rad51 or the MNR complex. Intratumoral delivery of Delta-24-RGD in nude mice bearing orthotopic DIPG tumors did not showed any toxicity. In vivo efficacy studies of the virus alone or in combination with radiotherapy are on-going. Our results showed that Delta-24-RGD exerts an effective anti-glioma effect in vitro with no toxicity in vivo. This adenovirus is able to block the DNA damage repair machinery underscoring that combination with radiotherapy could provide a significant therapeutic advantage.