

JEAN-EMMANUEL KOUADIO and QING WANG, Dept. of Computer Sciences, Mathematics and Engineering, Shepherd University, Shepherdstown, WV, 25443. Modeling the effect of a combinatorial anti-CTLA antibody and radiation therapy on metastatic lung cancer.

Cytotoxic T-lymphocyte antigen 4 (CTLA-4) is an inhibitory receptor that is upregulated after T-cell activation, and transmits signals that suppress T-cell activation and proliferation through the depletion of CD8+ T cells. Antibodies targeting CTLA-4 can selectively deplete regulatory T cells by antibody-mediated cellular cytotoxicity mechanisms. However, anti-CTLA-4 antibody therapy as a single treatment is limited on effectiveness to fight against immunogenic diseases like metastatic cancers. Radiation therapy (RT) on the other hand is a longstanding pillar of cancer treatment, historically utilized to treat a discrete target and provide local tumor control. Recent preclinical studies demonstrated that RT is synergistic with anti-CTLA antibody and induces systemic anti-tumor responses. In order to better understand the effect of the combination therapy on metastatic lung cancer, we developed a mathematical model using a system of impulsive differential equations. The objective of this study was to develop a predictive simulation platform to improve cancer management by manipulating dose and fractionation schedule of RT and dose and timing for the anti-CTLA-4 antibody therapy. This study is supported by NIH Grant P20GM103434 to the West Virginia IDeA Network for Biomedical Research Excellence.