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## **Evaluation of the antitumor effect of PCV chemotherapy on diffuse low-grade gliomas with a longitudinal tumor growth inhibition model**

**Objective:** To develop a tumor growth inhibition (TGI) model able to describe the evolution of diffuse low-grade gliomas (LGGs) growth dynamics after first-line PCV chemotherapy and to use this model as a theoretical tool to suggest potential improvements of the PCV chemotherapy regimen.

**Methods:** The model was formulated as systems of ordinary differential equations distinguishing between two cell populations: one proliferative treatment-sensitive cell population and one quiescent treatment-resistant cell population that spontaneously undergoes apoptosis. Model evaluation was performed in a series of 21 patients treated with first-line PCV chemotherapy in which the evolution of the mean tumor diameter had been previously assessed.

**Results:** Consistent with LGGs biology, the model estimated that LGGs consist mostly of quiescent cells. Despite large inter-individual variability the model correctly predicted individual tumor response profiles in the 21 patients. Unexpectedly, model simulations suggested that the 6 weeks interval between PCV cycles might be suboptimal and that lengthening the time interval between cycles might significantly improve treatment efficacy.

**Interpretation:** Based on the hypothesis that LGGs consist of proliferative treatment-sensitive cells and quiescent treatment-resistant cells that spontaneously undergo apoptosis we propose a mixed-effect model that accurately describes the evolution of these tumors during and after PCV chemotherapy. Model simulations of different PCV schedules illustrate how this approach could possibly help designing more effective chemotherapy regimens for LGGs.