THE PROBLEM OF GENERALIZING A MATHEMATICAL PHARMACOKINETICS-PHARMACODYNAMICS MODEL FOR ANTI-PD-1 DRUGS.

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Immunotherapy with aPD-1/a-PD-L1 checkpoint inhibitors is effective for tumors resistant to other treatments. Blocking the interaction of PD-1 with PD-L1 avoids immunosuppressive responses in T cells. The use of generalized mathematical models is a good tool for selecting the minimum effective dose in the early stages of clinical trials.

The mathematical model is a system of ordinary differential equations. The model includes 5 compartments: peripheral, central, vessels, endosomal space, interstitial space. The aPD-1 antibody binds to its ligand PD-L1 in the central compartment and in the interstitial space of the tumor. For the summarized drug (Nivolumab), the binding parameters were taken from the literature [1]. The other parameters were determined using the concentration profile of Nivolumab.

The mathematical model of Lindauer et al [2] for aPD-1 antibody (Pembrolizumab) was chosen as a generalization model. The model describes experimental data of aPD-1 (Nivolumab) occupied receptors in plasma.

The model was used to analyze the dependence of Kd on RO. Even on a small amount of data, the curve can be characterized as a linear dependence.

The mathematical model of Lindauer et al [2] aPD-1 antibody is summarized. This model describes the RO in plasma of Nivolumab and can be applied to other aPD-1 antibodies.

References

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2. Lindauer A. et al. Translational pharmacokinetic/pharmacodynamic modeling of tumor growth inhibition supports dose-range selection of the anti–PD-1 antibody pembrolizumab //*CPT: pharmacometrics & systems pharmacology*. **Vol. 6**. No. 1. 2017. Pp. 11-20.