Development of Quantitative Systems Pharmacology Model of Multiple Myeloma

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Objectives: To develop a quantitative systems pharmacology model of multiple myeloma.

Methods: The quantitative systems pharmacology (QSP) model of multiple myeloma (MM) was developed on the basis of Immune Response Template (IRT), first presented at ASCPT 2016 [1]. MM model describes normal B cells, their maturation, migration and differentiation into malignant B cells. Also it describes normal myeloid cells (including neutrophils, platelets, monocytes, MDSC, DC, different subsets of T cells (naïve, Th1, Th2, Th17, Treg); CD4+ and CD8+ T cells, NK cells, different cytokines (IL-2, IL-6, TGFβ, TNFα and other) in 3 physiological compartments - lymph nodes, bone marrow and blood/plasma. Global sensitivity analysis was implemented by calculation of correlation coefficients based on Monte Carlo simulations.

Results: Multiple myeloma model was developed and model parameters were partly taken from IRT and partly estimated on the basis of available literature data. The model is ready for drugs pharmacokinetics and pharmacodynamics implementation. Global sensitivity analysis was performed and the most sensitive parameters were identified.

Conclusions: The approach applied to construct QSP model of multiple myeloma allows to successfully integrate both in vitro and in vivo data and resulting model can be considered as a template for further implementation and exploration of various therapies of the disease.