

# A Mathematical Cancer Model with BCG Immunotherapy Combined with Immune Checkpoints Inhibitors: an Optimal Control Approach

Evren Hincal<sup>1</sup>, Farouk Tijjani Saad<sup>2</sup>, Isa Abdullahi Baba<sup>3</sup>

<sup>1</sup> *Department of Mathematics, Near East University, Mersin 10, TRNC.*

*evrenhincal@yahoo.co.uk*

<sup>2</sup> *Department of Mathematics, Near East University, Mersin 10, TRNC.*

*farouksaad@yahoo.co.uk*

<sup>3</sup> *Department of Mathematics, Near East University, Mersin 10, TRNC.*

*isababa7@yahoo.com*

**Abstract:** We present a mathematical model of cancer growth in the bladder that includes the immune cells, BCG, immune checkpoints and drug therapy (checkpoint inhibitor) in the form of a control function. The control function blocks the action of immune checkpoints on the immune system. Our aim here is to apply optimal control theory to find a control strategy that will minimize the number of cancer cells in the bladder and cost of control. Existence of the optimal control is stated and Pontryagin's maximum principle is used to characterize the nature of the control function. The optimality system obtained gives a two-point boundary value problem; hence, we use the forward-backward sweep method to present the numerical solutions of the system. The optimality conditions and characterization of the control are discussed.

**Keywords:** Optimal control, mathematical model, Hamiltonian, cancer, immune checkpoint, Pontryagin's principle, forward-backward sweep method.

**2010 Mathematics Subject Classification:** 35J05, 35J08, 35J25

## REFERENCES

- [1] Saad F. T., E. Hincal, and B. Kaymakamzade, Dynamics of immune checkpoints, immune system, and BCG in the treatment of Superficial bladder cancer, *Computational and Mathematical Methods in Medicine*, Volume 2017 (2017), Article ID 3573082, 9 pages.
- [2] W. H. Fleming and R.W. Rishel, *Deterministic and Stochastic Optimal Control*, Springer Verlag, New York, 1975
- [3] Thalya et al, Optimal control applied to immunotherapy, *Discrete and continuous dynamical systems B*, Volume 4, Number 1, February 2004. Pp 135-146.
- [4] A. Ghaffari, N. Naserifar, Optimal therapeutic protocols in cancer immunotherapy, *Computers in Biology and Medicine* 40 (2010) 261-270.