Periodic treatment in a mathematical model of CAR-T cell therapy for glioblastoma

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In recent years, great progress has been made in the treatment of certain solid tumours with CAR-T (Chimeric Antigen Receptor T) cells. However, their implementation is more complicated than for non-solid tumours where this therapy has been shown to be effective (cf. [1, 2] for leukaemias and lymphomas). Encouraged by the positive results of the treatment, scientists are starting to test this therapy in various solid tumours, including glioblastoma – an aggressive primary brain tumour.

In our work, based on the mathematical model of CAR-T therapy proposed in [3], we study the results of periodic treatment regimen. We show that the model has a tumour-free periodic solution and study its stability. Using linearization and the Floquet theory we find a relationship between the portion of CAR-T cells and the period of application allowing for cure. Interestingly, the cure condition is the same as the condition guaranteeing local stability of the tumour-free steady state in the model with constant treatment.

References

[1] S. L. Maude, T. W. Laetsch, J. Buechner, S. Rives, M. Boyer, H. Bittencourt, et al., Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia, *New England Journal of Medicine*, 378(5):439-448, 2018.

[2] S.J. Schuster, M. R. Bishop, C. S. Tam, E. K. Waller, P. Borchmann, J. P. McGuirk, et al., Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma, *New England Journal of Medicine*, 380(1):45-56, 2019.

[3] O. León-Triana, A. Pérez-Martinez, M. Ramırez-Orellana, V. M. Pérez-Garcia, Dual-Target CAR-Ts with On- and Off-Tumour Activity May Override Immune Suppression in Solid Cancers: A Mathematical Proof of Concept, *Cancers*, 13(4):703, 2021.