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Computational modeling of pharmacokinetics and tumor dynamics to guide anti-cancer treatment

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STELLINGEN

behorend bij het proefschrift

Computational modeling of pharmacokinetics and tumor dynamics to guide anti-cancer treatment

1. Applying different model structures to characterize tumor dynamics and evolution of treatment resistance requires different data input and knowledge and can achieve different objectives. *[This thesis, chapter 2]*
2. Intermittent and adaptive schedules were predicted to better suppress the evolving cancer resistance and improve the clinical outcome compared to a conventional continuous anti-cancer treatment schedule. *[This thesis, chapter 3]*
3. The benefits of applying model-informed precision dosing in anti-cancer treatment, including guiding dose selection and adaptation, have been demonstrated in many research studies and clinical trials. *[This thesis, chapter 5]*
4. Determining the starting dose using the developed model is most beneficial in terms of shortening the time to reach the therapeutic target and limiting the risk of toxicity. *[This thesis, chapter 6]*
5. Addressing the biological and pharmacological complexities of evolution of drug resistance, extrapolating the mechanisms, and including them in a tumor growth inhibition model in a simplified manner paves the way for developing new, convincing models of tumor dynamics and new treatment paradigms. *[Terranova N. et al. CPT Pharmacometrics Syst Pharmacol, 2015. 4(6): p. 320-323]*
6. Including evolutionary dynamics into treatment protocols, when cure is not achievable, can prolong the duration of disease control with existing drugs substantially. *[Gatenby R.A. et al. Nature Reviews Clinical Oncology, 2020. 17, 675-686]*
7. Liquid biopsies have demonstrated utility across a range of applications and are beginning to be used for patient benefit. *[Wan J.C.M. et al. Nat Rev Cancer, 2017. 17(4): p. 223-238]*
8. Dose optimization is essential to ensure that patients receive therapies which not only maximize efficacy but also minimize toxicity. *[Fourie Zirkelbach J. et al. J Clin Oncol, 2022. 40(30): p. 3489-3500]*
9. 工欲善其事，必先利其器 [*《论语·卫灵公》前475 - 前221*] (You must first sharpen your tools if you want to do your job well *[Analects, 475 BC - 221 BC]*)
10. It is the effective communication of modeling results and their implications to support decision making milestones that makes the significant effort and cost of population modeling worthwhile. *[Joel S. Owen, Jill Fiedler-Kelly. Introduction to population pharmacokinetic/pharmacodynamic analysis with nonlinear mixed effects models. 2014. Preface]*