Prostate

Prostate-specific antigen dynamics predict individual responses to intermittent androgen deprivation

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Abstract

Intermittent androgen deprivation therapy (IADT) is an attractive treatment for biochemically recurrent prostate cancer (PCa), whereby cycling treatment on and off can reduce cumulative dose and limit toxicities. We simulate prostate-specific antigen (PSA) dynamics, with enrichment of PCa stem-like cell (PCaSC) during treatment as a plausible mechanism of resistance evolution. Simulated PCaSC proliferation patterns correlate with longitudinal serum PSA measurements in 70 PCa patients. Learning dynamics from each treatment cycle in a leave-one-out study, model simulations predict patient-specific evolution of resistance with an overall accuracy of 89% (sensitivity = 73%, specificity = 91%). Previous studies have shown a benefit of concurrent therapies with ADT in both low- and high-volume metastatic hormone-sensitive PCa. Model simulations based on response dynamics from the first IADT cycle identify patients who would benefit from concurrent docetaxel, demonstrating the feasibility and potential value of adaptive clinical trials guided by patient-specific mathematical models of intratumoural evolutionary dynamics.