Optimizing docetaxel scheduling to delay progression in metastatic prostate cancer patients receiving hormone therapy

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Continuous androgen deprivation therapy (ADT) has been the standard of care for patients with advanced prostate cancer since the 1940s. Treating concurrently with docetaxel chemotherapy has shown to significantly improve median overall survival from 71 months with ADT alone to 81 months with concurrent treatment ($p = 0.006$) [1]. We developed a mathematical model of prostate cancer stem and non-stem cell dynamics, serum prostate specific antigen levels and docetaxel during concurrent treatment. We generate highly accurate fits to the longitudinal data of 100 patients receiving ADT treatment with docetaxel either given at the initiation of ADT treatment (50 patients, 6 cycles) or after the development of castration resistant prostate cancer (50 patients, 10 cycles) ($R^2 = 0.79$). As androgen-independent prostate cancer stem cells are sensitive to docetaxel, simulations show that early administration of chemotherapy results in sufficient reduction of the prostate cancer stem cell population. In contrast, late administration is unable to efficiently combat the large stem cell population that has developed during androgen deprivation, thereby resulting in resistance earlier. We use the dynamic model to optimize concurrent docetaxel and ADT, administered both continuously and intermittently and use patient-specific parameters to identify patients who may benefit from alternative treatment schedules.

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References

[1] James ND, Sydes MR, Clarke NW, Mason MD, Dearnaley DP, Spears MR, et al. *Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial.* The Lancet 2016; 387 (10024): 1163-77.