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Simulation-Based Assessment of the Impact of Non-Adherence on Endoxifen Target Attainment in Different Tamoxifen Dosing Strategies

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Tamoxifen is widely used in breast cancer treatment and minimum steady-state concentrations of its active metabolite endoxifen (C) above 5.97 ng/mL have been associated with favourable disease outcome. Yet, about 20% of patients do not reach target C applying conventional tamoxifen dosing. Moreover, 4-75% of patients are non-adherent, resulting in worse disease outcomes. Assuming complete adherence, we previously showed model-informed precision dosing (MIPD) to be superior to conventional and -guided dosing in minimising the proportion of patients with subtarget C. Given the high non-adherence rate in long-term tamoxifen therapy, this study investigated the impact of non-adherence on C target attainment in different dosing strategies. We show that MIPD allows to account for the expected level of non-adherence (here: up to 2 missed doses/week): increasing the MIPD target threshold from 5.97 ng/mL to 9 ng/mL (the lowest reported C in normal metabolisers) as a safeguard resulted in the lowest interindividual variability and proportion of patients with subtarget C even in non-adherent patients. This is a significant improvement to conventional and -guided dosing. Adding a fixed increment to the originally selected dose is not recommended, since it inflates interindividual variability.

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