

SUPPLEMENTARY FILE S2 - The index Δ

The evaluation of the horizontal distance between the PTGC (obtained by the zero-interaction model) and that obtained by the new model in combination regimen is a very interesting measure of the additional amount due to the drug-drug interaction.

As previously, let us consider the perturbed-growth curve in combination regimen under the assumption of no-interaction between drugs effects in order to compute $\tau_{add}(w)$. Observing that $\tau_{add}(w)$ can be obtained from $\tau_{comb}(w)$ imposing $\gamma = 0$ and substituting $\epsilon_1 \mapsto \epsilon_{1add}$ and $\epsilon_2 \mapsto \epsilon_{2add}$ in 8, we have

$$\begin{aligned}\tau_{add}(w) &= \frac{1}{\lambda_1} [w - \epsilon_{1add}(w) - (\tilde{w} - \epsilon_{1add}(\tilde{w})) + \epsilon_{2add}(w)] \\ &\quad + \frac{1}{\lambda_0} [\ln(\tilde{w} - \epsilon_{1add}(\tilde{w})) - \ln(w_0) + k_{2a}AUC_{c_a} + k_{2b}AUC_{c_b}]\end{aligned}$$

Being by definition

$$\begin{aligned}\Delta &= \lim_{w \rightarrow +\infty} (\tau_{comb} - \tau_{add}) \\ &= \frac{1}{\lambda_1} [\epsilon_1(\tilde{w}) - \epsilon_{1add}(\tilde{w}) + \bar{\epsilon}_2 - \bar{\epsilon}_{2add}] + \\ &\quad + \frac{1}{\lambda_0} [\ln(\tilde{w} - \epsilon_1(\tilde{w})) - \ln(\tilde{w} - \epsilon_{1add}(\tilde{w})) + \gamma AUC_{c_a c_b}]\end{aligned}$$

If also $\epsilon_{1add}(\tilde{w}) \simeq 0$, a first order Taylor expansion of the logarithm yields:

$$\Delta \simeq \frac{\bar{\epsilon}_2 - \bar{\epsilon}_{2add} + \epsilon_1(\tilde{w}) - \epsilon_{1add}(\tilde{w})}{\lambda_1} + \frac{1}{\lambda_0} [\gamma AUC_{c_a c_b} - \epsilon_1(\tilde{w})/\tilde{w} + \epsilon_{1add}(\tilde{w})/\tilde{w}]$$

observing that $x_{00}(\tilde{\tau}_{add}) \simeq w(\tilde{\tau}_{add})$ implies $\frac{\bar{\epsilon}_{2add}}{\lambda_1} \simeq 0$, the final approximation is

$$\Delta \simeq \frac{\gamma AUC_{c_a c_b}}{\lambda_0} \quad (10)$$