New PK-PD model for combination therapy by considering contributions from individual drugs

Drug A (Dox, iv)

Drug exposure C(t) from PK model

Proliferating cells

\[ \alpha \cdot k_{2A} \cdot C_A + \beta \cdot k_{2B} \cdot C_B \]

Drug B (Sor, po)

Non-proliferating and damaged cells

The new model 1) offers one definitive prediction of the responses to drug combinations, and 2) discloses a much greater contribution from sorafenib (Sor) to tumor growth inhibition than co-administered doxorubicin (Dox).

Combination Index (CI) Method is integrated into the predictive PK-PD model to critically define in vivo pharmacologic synergism.

- CI > 1, antagonism
- CI = 1, addition
- CI < 1, synergism

\[ \alpha = 0.644 \quad \beta = 1.62 \]