Model-1 phase 1 trial, a PK-PD model-based adjustment of chemotherapy dose

EPIRUBICIN-DOCETAXEL regimen is a very effective treatment in patients with metastatic breast cancers. Although dose-dense chemotherapy might improve efficacy, it is limited by hematological toxicity (Viens et al.). Iliadis et al. developed a mathematical model able to describe chemotherapy-related hematological toxicity. Simulations suggested feasibility of chemotherapy administrations every 2 weeks, instead of standard every 3 weeks, provided drug doses be individually adjusted at each cycle according to neutrophil toxicity observed during the previous cycle (Iliadis et al., Meille et al.).

A clinical phase Ib trial was performed in 17 patients with metastatic breast cancer to test the safety and feasibility of model-based adjustment of dose and dosing schedule of EPIRUBICIN-DOCETAXEL regimen. During a run-in period, patients were treated with standard chemotherapy regimen and initial PK and PD values were assayed. These data were used to parameterize the model with patients’ data. The model adequately predicted evolution of blood cell counts and guided chemotherapy doses (Figure). This study showed this strategy was feasible and allowed dose-dense chemotherapy in selected patients without exacerbated toxicity.

Figure: Observed vs predicted ANC


