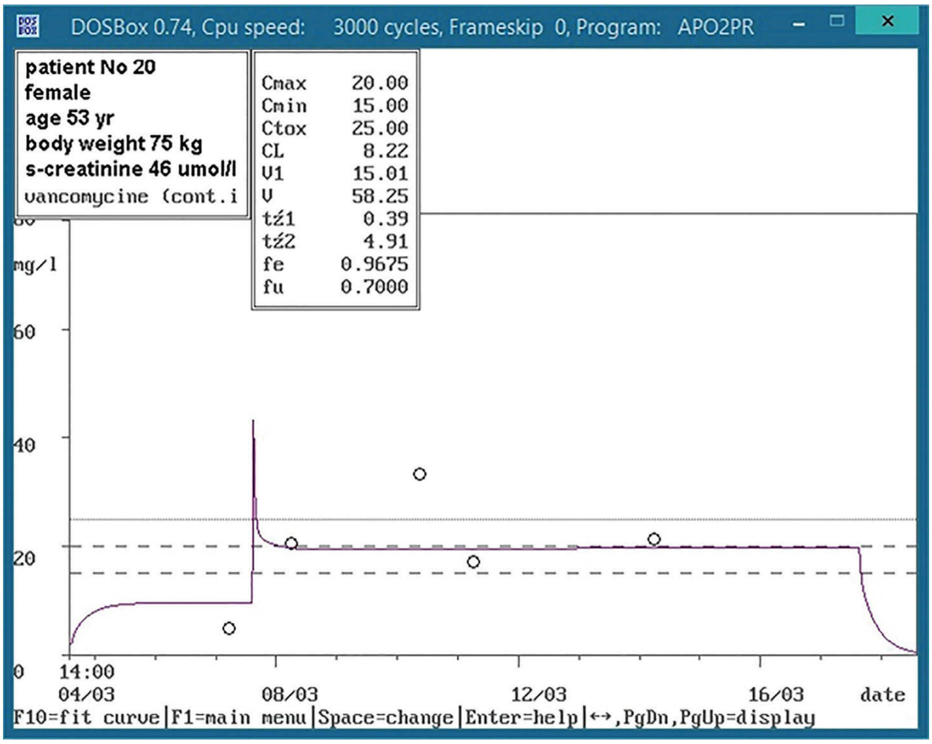
**Add Fig. 1.** *Graphical output of DOS1 model*

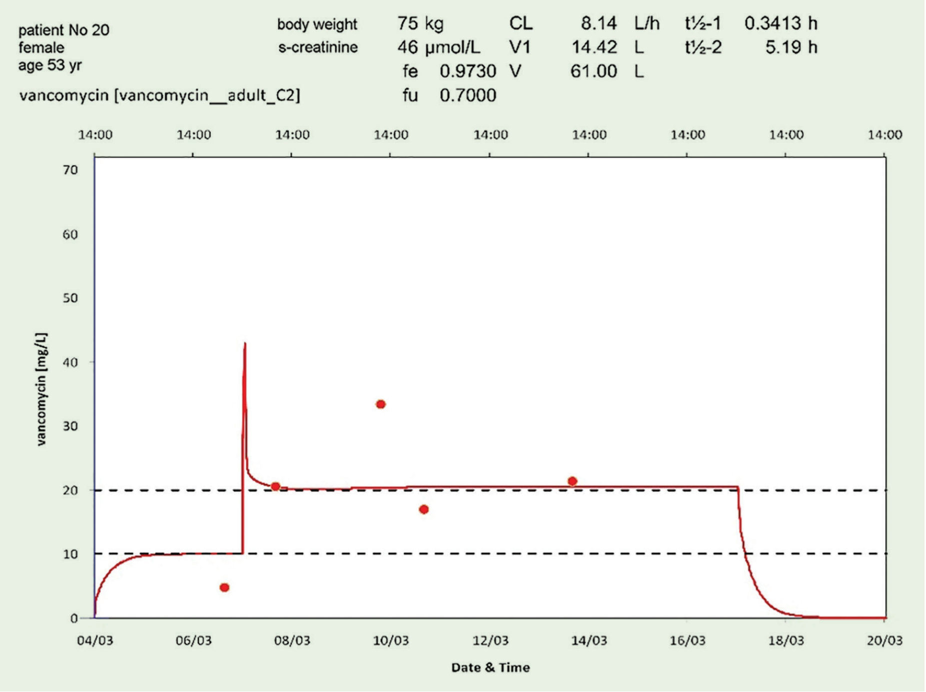


```
patient No 20
female
age 53 yr
body weight 75 kg
s-creatinine 46 umol/l
vancomycine (cont.i

Cmax     20.00
Cmin     15.00
Ctox     25.00
CL        8.22
V1       15.01
V        58.25
t½1       0.39
t½2       4.91
fe      0.9675
fu      0.7000

F10=fit curve|F1=main menu|Space=change|Enter=help|↔,PgDn,PgUp=display
```

**Add Fig. 2.** *Graphical output of WIN3 model*



patient No 20
female
age 53 yr
vancomycin [vancomycin__adult_C2]

body weight 75 kg
s-creatinine 46 µmol/L
fe 0.9730
fu 0.7000

CL 8.14 L/h
V1 14.42 L
V 61.00 L

t½-1 0.3413 h
t½-2 5.19 h

The formula is based on the assumptions that CL is related to the CLcr and CLm is linearly related to BSA. CLcr is calculated by Jelliffe II equation (9). BSA is calculated according to Du Bois and Du Bois (10). The *"#vancomycin_adult_k_C2"* model (WIN1) uses renal (kelr) and metabolic (kelm) elimination rate constants instead of fr or Clm, respectively. The parameters were converted by Formula 2 and Formula 3, respectively,

$$fr = kelr * V1 * LBMc * \frac{1000}{60} * \frac{1.73}{BSA} \qquad (2)$$

$$C1m = kelm * V1 * LBMc * \frac{1.85}{BSA} \qquad (3)$$

V1 represents the volume of distribution and LBMc is lean body mass corrected for fat distribution calculated according to Chennavasin (11). The population-based parameters of all the models are given in Table 2.

The Marquardt algorithm was used for extrapolation.

Examples for graphical output of DOS1 and WIN3 models are shown in Add Fig. 1 and Add Fig. 2, respectively.

## Model evaluation

Concentrations predicted by the *"vancomycin (cont.inf.) %ahz"* (DOS1) and *"vancomycin adult"* (DOS2) DOS models and by the *"#vancomycin_adult_k_C2"* (WIN1), *"#vancomycin_adult_C2"* (WIN2), *"vancomycin_adult_C2"* (WIN3), and *"vancomycin_C1"* (WIN4) Windows models were compared with the measured concentration and the concentration predicted by the DOS1 model. All models were two-compartmental, with the exception of WIN4 which is one-compartmental. Predictions by all models were evaluated retrospectively. Percentage prediction error (%PE), RMSE, and Bland-Altman plot were used for prediction precision evaluation. %PE was calculated as the difference between the predicted and the measured value (Formula 4), or as the difference between models (Formula 5). RMSE was calculated according to Formula 6.

$$\%PE = \frac{predicted - measured}{measured} \qquad (4)$$

$$\%PE = \frac{predicted\ (WIN) - predicted\ (DOS1)}{predicted\ (DOS1)} \qquad (5)$$

$$RMSE = \sqrt{\frac{1}{N} \times \Sigma(\%PE)^2} \qquad (6)$$

All values are presented as mean ± standard deviation (SD). Due to normal distribution of values, statistical analysis was performed by using paired Student's t-test. The Prism 5.0 software by GraphPad Software was used for statistical analysis (Pearson's R, Student's t-test, Bland-Altman plot).

## Results

### Best model selection

Vancomycin concentrations predicted by all models are shown in Fig. 1. Mean concentrations predicted by the models were significantly lower than the measured concentrations (Table 3). Mean values of %PE varied from –3.2 in DOS2 to –20.8% in WIN4.