

```

1  [PROB]
2  # Population pharmacokinetics of tacrolimus
3  woillard de winter bjcp 2011
4
5  [SET] end=10*12, delta=0.1
6
7  [PARAM] @annotated
8  TVCL : 21.2 : Typical value of clearance (L/h)
9  TVV1 : 486 : Typical central volume of distribution (L)
10 TVQ : 79 : Typical intercomp clearance 1 (L/h)
11 TVV2 : 271 : Typical peripheral volume of distribution 1 (L)
12 TVKTR : 3.34 : Typical transfert rate constant(1/h)
13 HTCL : -1.14 : effect of HT on cl
14 CYPCL : 2.00 : effect of CYP on cl
15 STKTR : 1.53 : effect of study on ktr
16 STV1 : 0.29 : effect of study on v1
17 HT : 70 : hematocrit (perc)
18 ST : 1 : Prograf(1) adv(0)
19 CYP : 0 : expressor (1) non exp(0)
20
21
22 [CMT] @annotated
23 DEPOT : Dosing compartment (mg)
24 TRANS1 : transit compartment 1 (mg)
25 TRANS2 : transit compartment 2 (mg)
26 TRANS3 : transit compartment 3 (mg)
27 CENT : Central comaprtnent (mg)
28 PERI : First peripheral compartment (mg)
29 AUC : AUC cp
30
31
32 [OMEGA] @annotated
33 ETACL : 0.28 : ETA on clearance
34 ETAV1 : 0.31 : ETA on V1
35 ETAQ : 0.54 : ETA on Q
36 ETAV2 : 0.60 : ETA on V2
37 ETAKTR : 0.24 : ETA on KTR
38
39 [MAIN]
40 double CL = TVCL*pow(HT/35,HTCL)*pow(CYPCL,CYP)*exp(ETACL);
41 double V1 = TVV1*pow(STV1,ST)*exp(ETAV1);
42 double Q = TVQ*exp(ETAQ);
43 double V2 = TVV2*exp(ETAV2);
44 double KTR = TVKTR*pow(STKTR,ST)*exp(ETAKTR);
45
46 [SIGMA] @annotated
47 ADD : 0.78 : additive Residual unexplained variability
48 PROP : 0.113: proportionnal Residual unexplained variability
49
50 [ODE]
51 dxdt_DEPOT = -KTR*DEPOT;
52 dxdt_TRANS1 = KTR*DEPOT -KTR*TRANS1;
53 dxdt_TRANS2 = KTR*TRANS1 -KTR*TRANS2;
54 dxdt_TRANS3 = KTR*TRANS2 -KTR*TRANS3;
55 dxdt_CENT = KTR*TRANS3 - (CL+Q)*CENT/V1 + Q*PERI/V2 ;
56 dxdt_PERI = Q*CENT/V1 - Q*PERI/V2 ;
57 dxdt_AUC = CENT/(V1/1000);
58 if(SS_ADVANCE) dxdt_AUC = 0;
59
60 [TABLE]
61 capture CP = (CENT/(V1/1000))*(1+PROP) + ADD;
62

```