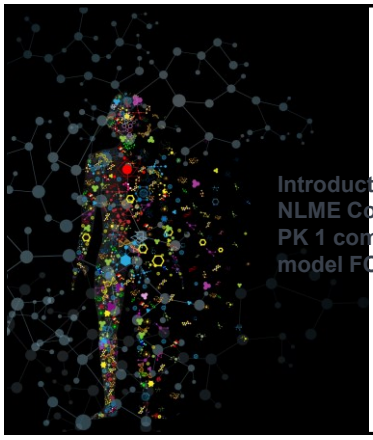
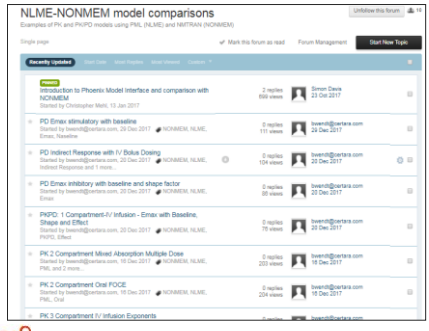


Introduction to NONMEM - NLME Comparions: PK 1 compartment IV Bolus model FOCE

NONMEM-NLME Copmarisons: On the Forum

https://support.certara.com/forums/forum/35-nlme-nonmem-model-comparisons/



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New Series: NONMEM- NLME Comparisons

Introduction to NONMEM-NLME Comparisons
PK 1-compartment IV bolus model FOCE
February 8, 2018 | 10am EST
Presenter: Bernd Wendt

NONMEM-2-NLME
PK 2-compartment multiple dose-IV bolus Plasma and Urine QRPEM/IMP
February 22, 2018 | 10am EST
Presenter: Bernd Wendt

NONMEM-2-NLME
PK 2-compartment oral with Disease State covariate on V and CL
March 8, 2018 | 10am EST
Presenter: Venkateswari Muthukrishnan

TMDD Model Translated from NONMEM (NM-TRAN) to Phoenix NLME (PML)
March 22, 2018 | 10am EST
Presenter: Loan Pham, Camargo

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Agenda

- Model Description
- Exploratory Data Analysis
- Input Data
- Model in NM-TRAN and PML Code
- Demo
- Summary
- Q&A

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NONMEM to NLME: 1c_iv_bolus_foce

- Model Description
  - Structural Model
    - One compartment model, single IV Bolus of 100 units, first order kinetics
      - Parametrization: Cl and V
  - Error model
    - Multiplicative: 10% CV
  - Structural Parameters
    - V: Lognormal
    - Cl: Lognormal
  - Fixed Effects
    - tvV: 1
    - tvCl:1
  - Random Effects
    - Variances all 0.1 (~30% population variability)
  - Engine
    - FOCE ELS

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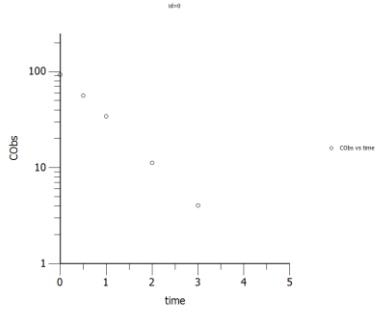
1c_iv_bolus_foce: Plot First Patient



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1c_iv_bolus_foce: Input Data

NONMEM

	CID	TIME	DV	MDV	AMT
1	0	0	93.1026	1	100
2	0	0.5	56.3592	0	.
3	0	1	34.2869	0	.
4	0	2	11.2408	0	.
5	0	3	4.04057	0	.
6	0	5	0.577354	0	.
7	1	0	94.7754	1	100
8	1	0.5	60.9031	0	.
9	1	1	44.78	0	.
10	1	2	22.824	0	.
11	1	3	9.86758	0	.
12	1	5	2.61519	0	.
13	2	0	124.589	1	100
14	2	0.5	72.2567	0	.
15	2	1	36.7722	0	.

NLME

	ID	TIME	CObs	MDV	A1
1	0	0	93.1026	1	100
2	0	0.5	56.3592	0	
3	0	1	34.2869	0	
4	0	2	11.2408	0	
5	0	3	4.04057	0	
6	0	5	0.577354	0	
7	1	0	94.7754	1	100
8	1	0.5	60.9031	0	
9	1	1	44.78	0	
10	1	2	22.824	0	
11	1	3	9.86758	0	
12	1	5	2.61519	0	
13	2	0	124.589	1	100
14	2	0.5	72.2567	0	
15	2	1	36.7722	0	

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NONMEM to NLME: 1c_iv_bolus_foce

NONMEM

```
;Model Selection
$SUB ADVAN1 TRANS2
;Structural Parameters
$PK
TVV = THETA(1)
 V = TVV * EXP(ETA(1))


 TVCL = THETA(2)
 CI = TVCL * EXP(ETA(2))
```

NLME

```
# Model Selection
cfMicro(A1, CI / V)
dosepoint(A1)
#Structural Parameters

stparm(V = tvV * exp(nV))


stparm(CI = tvCI * exp(nCI))
```

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Using the PML: 1c_iv_bolus_foce

NONMEM

```
; scale parameter
 S1 = V

; =======setup initial values for
THETA and OMEGA ===
$THETA
 (0, 1, ) ;TVV
 (0, 1, ) ;TVCL

 $OMEGA
 0.1
 0.1
```

NLME

```
 ; scale parameter: Must be
defined explicitly
C = A1 / V
# =======setup initial values for
THETA and OMEGA ===

fixef(tvV = c(, 1, ))
fixef(tvCl = c(, 1, ))

ranef(diag(nV, nCl) = c(0.1, 0.1))
```

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Using the PML: 1c_iv_bolus_foce

NONMEM

```
; specify residual error model
; setup initial estimates for the
variance matrix (SIGMA) of the
residual variability
$SIGMA 0.01

$ERROR
 Y = F*(1 + EPS(1))

; additional output
IVAR = TIME
IPRED = F
IRES = DV - IPRED
```

NLME

```
# specify residual error model
# setup initial estimates for the
variance matrix (SIGMA) of the
residual variability
error(CEps = 0.1)


observe(CObs = C * (1 + CEps))
```

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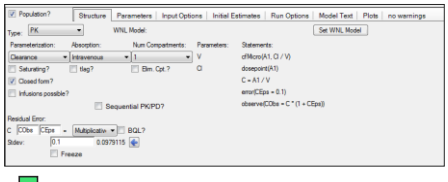
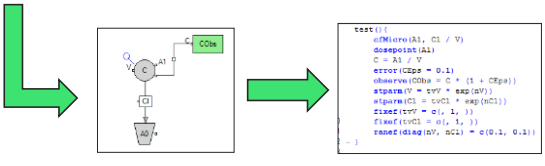
Using the PML: 1c_iv_bolus_foce





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Demo

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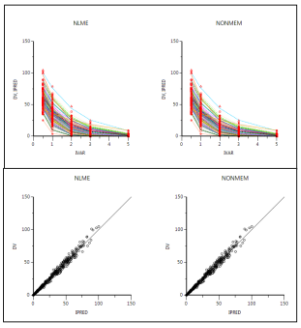
1c_iv_bolus_foce: Results



	Source			
	NLME		NONMEM	
Parameter	Estimate	Stderr	Estimate	Stderr
stdev0	0.098	0.004	0.097	0.028
tvCl	1.044	0.024	1.040	0.024
tvV	0.988	0.027	0.988	0.027

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1c_iv_bolus_foce: Summary

- Setup and Run a NONMEM Model:
  - 1-compartment IV Bolus
- Setup and run the equivalent Model in Phoenix NLME
- Postprocessed the NONMEM results and compared them with the NLME results
  - Only small differences

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Questions?

Certara University

- A wide range of On Demand and Classroom courses are available through Certara University:
  - Introductory, intermediate and advanced instruction in Phoenix WinNonlin, **Population Modeling using NLME**, IVIVC Toolkit
  - Fundamentals of Pharmacokinetics and Pharmacodynamics
  - Noncompartmental data analysis
  - Programming Bootcamp
  - Partner Lectures and Webinar series
- Please visit our Certara University web site for more information

www.certarauniversity.com

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Coming up…

NONMEM-2-NLME
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