Reviewer's report

Title: Population pharmacokinetic and pharmacodynamic modeling of transformed binary effect data of triflusal in healthy Korean male volunteers

Version: 3 Date: 7 July 2014

Reviewer: Thorsten Lehr

Reviewer's report:

The manuscript by Park et al describes the pharmacokinetics and pharmacodynamics of triflusal in healthy Korean male using the population modeling approach.

Major Compulsory Revisions

* The assessment of the final PK model is very difficult. In figure 3 the CWRES should be shown with time after dose and not time elapsed from the first dose.

* The authors should discuss their PK findings in relation to other PK studies from trifusal. For example Yun et al (http://www.ncbi.nlm.nih.gov/pubmed/24612881) and Valle et al (http://www.ncbi.nlm.nih.gov/pubmed/15711832) published a PK models for trifusal.

* The authors should discuss also the effect of the kidney more thoroughly. In Line 299 the authors present the relationship. This equation is raising the question of the impact of CrCl on the concentration-time profiles. A simulation may help to answer the question. Further, it may be asked how the increased exposure impacts the pharmacodynamics. In addition, it is unclear (Table 1) which range of CrCl was investigated. Please add the statistic and discuss your population. The authors also select the CrCl based on Baysian estimates. What was the Eta shrinkage? How significant was the covariate effect?

* It is unclear to me, why the PD measurements were discretized. A graphic (e.g. concentration vs. platelet) aggregation may help. Yun et al also modeled the platelet aggregation. Where is the difference between the two models? Did the authors tested the model from Yun et al?

* Please add a c-value or an ROC-curve for the final PD model. Did the authors perform a covariate analysis of the PD model as well?

Minor Essential Revisions

* Please add the RSE of the IIV estimates in table 3

* Please check the order of your tables.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.