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Biometrical statement to the peer-reviewed manuscript "Protective Effects of the Complement Inhibitor Compstatin Cp40 in Hemorrhagic Shock" by van Griensven et al.

Dear editors, dear independent reviewers,

in the course of the peer-review process of the above mentioned paper of van Griensven and colleagues one of the independent reviewers asked for a statement of a statistician that the study design and the statistical analysis is valid and appropriate. Therefore, I will describe my appraisal of the submitted work in the following referring to the statistical issues of the manuscript, and especially with respect to the comments raised by the third reviewer.

Of course, the reviewer is right to remark that the sample size is low in this study. In accordance, in the discussion section (page 17) the authors pointed to this limitation of our study.

Having such a limited number of samples per group (n=4), the reviewer is also correct in critically scrutinizing the normal assumption by means of the D'Agostino-Pearson test which was initially noted in the methods section. It is generally hard to argue on the fulfilled normal assumption in such small samples. In fact, the normal assumption cannot be checked validly by means of a statistical test (either D'Agostino-Pearson, Shapiro-Wilk, or others), since these tests are of poor power due to the small sample size.

The authors should simply assume that the data are normally distributed (and should not try to verify this assumption by means of a formal test). The validity of this assumption can be descriptively confirmed for nearly all analysis parameters by proportioning the reported means and SEMs.

With respect to the design of the study, from a statistical point of view it was well-chosen. The two-group-comparison design along with the comprehensively defined experimental procedure enables valid conclusions on the effect of Cp40. As stated above, the applied analysis methods were appropriate

assuming that the data in principle follow a normal assumption. This circumstance should be mentioned as a limitation within the discussion section.

Concerning the histology data, the data provided in the table followed a one way ANOVA analysis, but as the reviewer suspected, missed to run a post-hoc analysis. The p-values given are correctly displayed for the statistical significance among all groups, but do not necessarily reflect statistical differences between the HS + NaCl and HS + CP40 treatment group. By post-hoc testing with the Student-Newman-Keuls (SNK) method, the statistical significance between the treatment groups cannot be stated given the low sample size and should be changed in n.s.

Kind regards

W. Gaus

Prof. Dr. Wilhelm Gaus