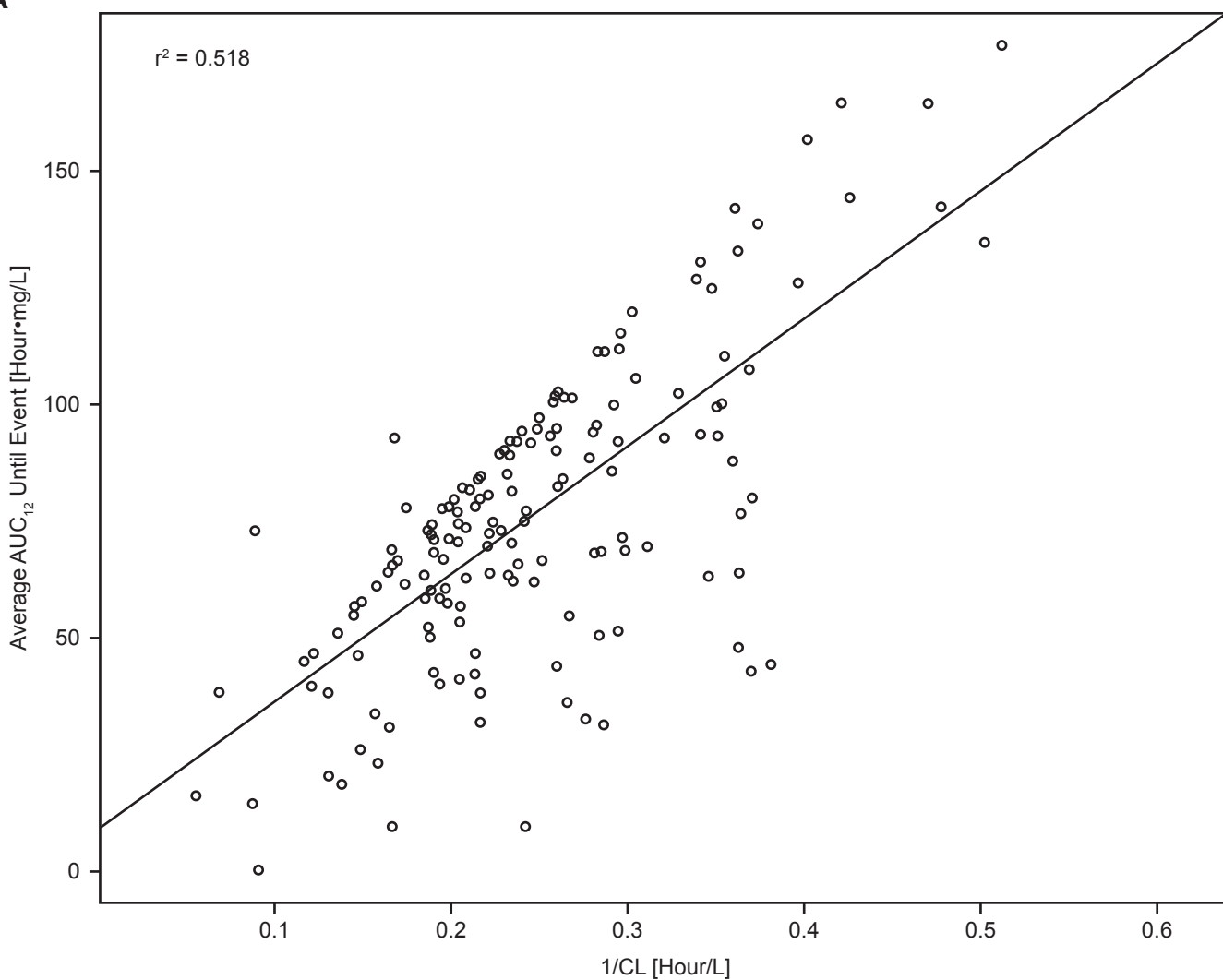


Figure S5. (A) Correlation between the average sofaremb exposure over the 12-hour dosing interval during the entire treatment period (AUC_{12AV}) and the estimated individual clearance normalized to a unity dose. The AUC_{12AV} covariate is the average AUC_{12} over the time up to the occurrence of an event. While this parameter, as such, contains information about the time of the event it is also clear that it remains well related to PK parameters known only at start of treatment. It should be noted that the strength of the signal is not entirely well captured by the Pearson's correlation coefficient since the data is not normally distributed about its major trend. **(B)** General trend of the average AUC_{12} in each cycle (mean_ AUC_{12}) over time. A downward trend over time is observed, which is unsurprising since the patients are unlikely to be up titrated beyond their starting dose; thus, any movement is likely to be downward. Also, while a downward trend exists it is not very large, and the correlation is low considering the Pearson's correlation coefficient of 0.180.

A



B

