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PK-PD Models for viral kinetics of combination treatments in viral hepatitis

Even in the era of direct anti-viral agents, interferon-based combination treatments are very important. It is well known that serum levels of long-acting interferons can vary considerably and that PK of interferon has an observable influence on viral kinetics also in combination treatment. Therefore, reliable viral kinetic modeling of interferon-based treatments should deal with non-constant treatment efficacies based on PK-PD models.

The first topic of the talk will focus on modeling results which analyze the effect of different PK and treatment schedules of long-acting interferons on the treatment efficacy and the development of resistance. Overall, high or low peak-to-trough levels of the PK of interferon has only minor influence on the development of resistance as long as the overall interferon efficacy is not changed.

Secondly, we will illustrate that modeling PK of direct antivirals can be quite challenging and simple open one-compartment models may be too simplistic to obtain reliable modeling results which fit with observed PK profiles.

Besides some theoretical background and illustration of simulation results, we will also show some clinical data analysis where a full PK-PD approach can give some indications how to optimize treatments.