

# **ABSTRACT GDR <Statistiques et santé> 5 et 6 octobre 2017**

## **Use of mechanistic models for in Silico trials: Evaluating new strategies design for HAART in HIV infected patients**

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### **Thème privilégié : Statistiques et médecine personnalisée**

An in silico clinical trial is an individualized computer simulation used in the development of a medicinal product, device, or intervention. Expected benefits are to provide a mechanistic understanding, to optimize the strategies of delivery and to improve de clinical trials designs. We propose to present how in silico trials could be used to investigate simplified antiretroviral therapies (HAART) such as therapies based on two antiretroviral treatments (ANRS 163 ETRAL, ANRS 167 LAMIDOL), dose reduction (ANRS 165 DARULIGHT) or short cycle treatment interruption (ANRS 162 4D, BREATHER Study). We propose to model dynamics of viral load and CD4 with a dynamical model based on ordinary differential equations (ODE) with mixed effects models on parameters (NLME). We account for pharmacokinetics and pharmacodynamics properties of HAART by using in vitro indicators and in vivo pre-established properties from phase I trials. Viral escape is modelled by a stochastic process depending on HAART dose level. Model for in silico trials has been defined and parameters estimated using data from previous clinical trials and observational cohort (the Aquitaine cohort). By simulating a phase III in silico trial, we investigate the expected results of on-going studies. We discuss how to simulate an in-silico population which is heterogeneous enough to build reliable confidence bounds. Altogether, we show that such pipeline for in silico trials is a promising tool for investigating novel strategies of treatment and opens the perspective for personalized medicine for HIV.