Longitudinal Model-Based Meta-Analysis (MBMA) for rheumatoid arthritis with Monolix

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Objectives: Model-based meta-analysis (MBMA) uses published aggregate data from many studies to develop a study-level model. Because in an MBMA approach one considers studies instead of individuals, the formulation of the problem as a mixed effect model differs from the typical PK/PD formulation. Here we present how MBMA models can be implemented, analyzed and used for decision support in Monolix and Simulx. We focus on longitudinal data of the clinical efficacy of drugs for rheumatoid arthritis, following [1]. The goal is to evaluate the efficacy of Canakinumab in comparison to two drugs already on the market.

Methods: We first collected literature data, focusing on the ACR20 as endpoint, the percentage of patients achieving 20% improvement. We then formulated a longitudinal mixed effect model with: (i) an Emax structural model, (ii) between-study variability (BSV) and (iii) between treatment arm variability (BTAV). The variance of the residual error and BTAV terms is weighted by the number of individuals per arm. The model is then used to simulate the true effect of the three drugs, taking into account the uncertainty of the parameter estimates.

Results: The proposed model satisfactorily describe the longitudinal ACR20 data for the three drugs. To compare the true efficacy of the three drugs, we perform a large number of simulations using Simulx, drawing the Emax population value from its uncertainty distribution. The results show that there are only 6% chances that Canakinumab is better than Abatacept and 16% chance that it is better than Adalimumab.

Conclusion: We have shown that chances are low that Canakinumab performs better than the two drugs already on the market. As a consequence of study [1], the development of this drug has been stopped. The MonolixSuite offers a powerful environment for longitudinal MBMA analysis.