Application of A Physiologically-Based Subcutaneous Absorption Model to Estimate Bioavailability of Monoclonal Antibodies Using Subcutaneous Data Only

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Objective. To estimate the subcutaneous (SC) bioavailability of therapeutic monoclonal antibodies (mAbs) using a physiologically-based SC absorption model.

Methods. A physiologically-based mathematical model has been previously developed to describe the SC absorption of mAbs [1]. One implication of this model, though not explicitly stated in the original report, is that SC bioavailability (F) of a mAb can be estimated with the model using SC data only. This hypothesis was examined by applying the model to golimumab, ustekinumab, sirukumab and guselkumab using Phase 1, 2 or 3 clinical study data following single or multiple SC administrations of those mAbs. The F values estimated using the model were compared with those obtained from the traditional non-compartmental analyses (NCA) with both intravenous (IV) and SC data. The physiologically based SC absorption model was developed using Monolix 4.3.

Results. The physiologically based SC absorption models were successfully developed for golimumab, ustekinumab, sirukumab and guselkumab with SC data only. The model estimated F values were in good agreement with those obtained from NCA with both IV and SC data. Mena F values obtained from the model vs. NCA were 0.44 vs. 0.51 for golimumab, 0.58 vs. 0.57 for ustekinumab, 0.60 vs. 0.59-0.87 for sirukumab and 0.50 vs. 0.50 for guselkumab.

Conclusions. The results provided evidence to support the application of the physiologically-based SC absorption model to estimate the F values of mAb using SC data only.

Reference: