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## **The quantification of growth hormone secretion : application of model-informed drug development in acromegaly**

Growth hormone profiles are pulsatile and highly variable between individuals, limiting the implementation of mathematical models to quantify an individual's secretion. In this thesis, five key topics regarding the quantification of growth hormone (GH) in literature and the application in (future) clinical trials were addressed consecutively: 1. The current standards in reporting clinical trial outcomes in acromegaly patients were assessed and recommendations for future reporting were provided 2. A new deconvolution-informed population pharmacodynamic model was developed and validated for the quantification of drug effects on pulsatile profiles 3. Population pharmacokinetic/pharmacodynamic models were developed to better understand the clinical pharmacological properties of BIM23B065 to support decision making and future clinical trial design 4. A population model for GH secretion based on physiological information, including a GHRH pulse generator, was developed based on data from different experiments to be used for the simulation of pulsatile GH profiles in healthy controls, active acromegaly patients and acromegaly patient after surgery. 5. The impact of different sampling protocols, ranging from a single sample to a 24h GH profile, on the study power and classification of responders in GH research were quantified and implementation of the research methodology in new scenarios was stimulated.

Read the full thesis here (under embargo):

<https://scholarlypublications.universiteitleiden.nl/handle/1887/8131>

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