Disease Progression Model To Describe Longitudinal Change In Hemoglobin A1C In Response To Gliclazide Therapy In Type2 Diabetic Patients

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Abstract

Diabetes is a global health issue that affects more than 425 million people and is expected to affect over 690 million people by 2045.

The objectives of the present project are:

1) To quantify longitudinal glycemic response to Gliclazide (GLC) therapy in type 2 diabetic patients using population pharmacodynamic modeling.

2) To identify patients characterize associated with glycemic response to GLC.

This analysis is a secondary analysis for the result of clinical study number GSK-BRL49653/231 sponsored by GlaxoSmithKline. We conducted a population pharmacodynamic analysis with covariate screening analysis. Nonlinear mixed effects modeling approach was implemented. First, we described the longitudinal change in hemoglobin A1c (HbA1c) and Fasting Plasma Glucose (FPG) without including patients'

characteristics as covariates. This was followed by multiple linear regression between individual E_{max} values and various covariates. Finally, significant covariates identified with multiple linear regression were included in the final pharmacodynamic model using backward deletion approach.

We quantified longitudinal change in HbA1c and FPG levels in response to GLC therapy in type 2 diabetic patients using population pharmacodynamic modeling. We also identified patients characteristics associated with glycemic response to GLC. Baseline FPG and lymphocyte count were identified as significant covariates that affect glycemic response to GLC.

Longitudinal change in HbA1c and FPG following GLC therapy was described using a mechanistic pharmacodynamic model. Having a higher baseline FPG was associated with increased magnitude of reduction in HbA1c overtime resulting from GLC therapy. Having a higher baseline lymphocytes was associated with smaller reduction in HbA1c.