Insulin glargine biosimilar (GP40061) shows similar pharmacokinetics and pharmacodynamics as compared to the reference drug

A. Mosikian, I. Makarenko, O. Avdeeva, T. Belikova, I. Lunev, R. Drai

Background

A biosimilar is a biological medicine highly similar to already approved biological reference medicine. Several biosimilars of insulin glargine have been already registered in the EU.
Based on regulatory requirements the proof of biosimilarity of insulin involves a stepwise approach:

- studies of physical and chemical properties (primary, secondary, tertiary and quaternary structure of insulin molecule; related substances);
- *in vitro* pharmacodynamics studies (e.g. binding to insulin receptors A & B, binding to IGF receptor, functional tests of muscle glucose uptake, lipogenesis response, simulated lipolysis inhibition, etc);
- clinical trials.

The program of clinical trials of insulin biosimilars obligatory includes pharmacology studies:

- pharmacokinetics (PK) – concentration-time;
- pharmacodynamics (PD) – glucose infusion rate (GIR)-time.

OOO GEROPHARM has conducted all the above mentioned studies in accordance with international regulatory guidelines and here performs the results of pharmacology studies.

Aim

To test if GP40061 – a biosimilar to reference insulin glargine – has similar PK and PD profiles in a hyperinsulinemic euglycaemic clamp setting in patients with type 1 diabetes mellitus.

Methods

A double-blind, randomized, crossover study
42 adult patients with T1DM

Each patient received a single dose of insulin (0.6 U/kg) subcutaneously.
Regular blood sampling was performed.
The amount of insulin glargine in the samples was determined by enzyme-linked immunosorbent assay.

The primary endpoints

- $AUC_{ins.0-24}$ (PK), 90% CI
- $AUC_{GIR.0-24}$ (PD), 95% CI

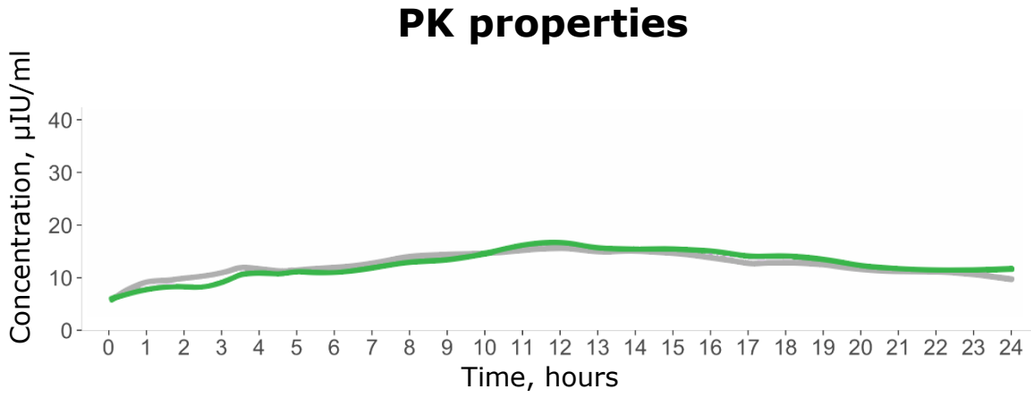
for GP40061/RIG geometric mean ratio.
CI limits of 80%—125% establish similarity.

Secondary endpoints

- $AUC_{ins.0-12}$ (PK), $AUC_{ins.12-24}$ (PK)
- $AUC_{GIR.0-12}$ (PD), $AUC_{GIR.12-24}$ (PD)

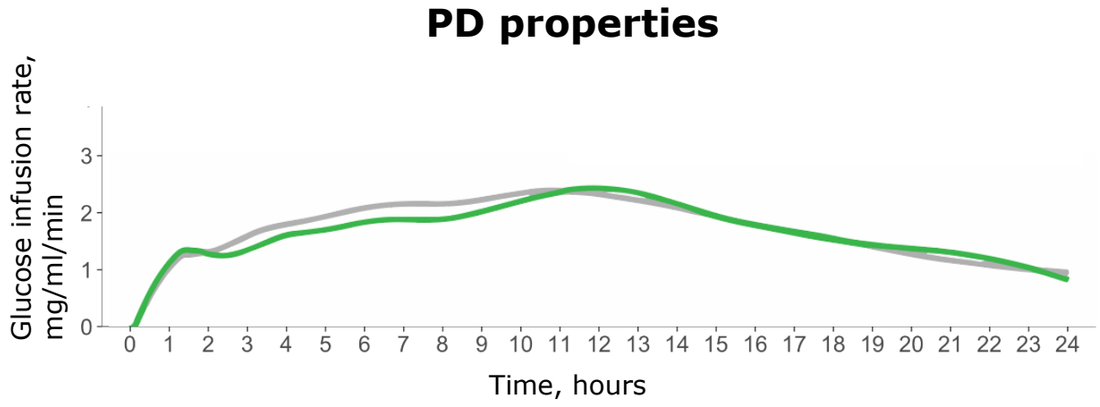
Results

PK properties



Ratio of GP40061/RIG
- $AUC_{ins.0-24}$ – 99% (90% CI: 81.02-120.62%)
- $AUC_{ins.0-12}$ – 95.39%
- $AUC_{ins.12-24}$ – 106.45%

PD properties



Ratio of GP40061/RIG
- $AUC_{GIR.0-24}$ – 99% (95% CI: 85.43-116.64%)
- $AUC_{GIR.0-12}$ – 93.39%
- $AUC_{GIR.12-24}$ – 92.55%

Conclusions

GP40061 demonstrated similar PK and PD profiles to reference insulin glargine in accordance with actual international guidelines (EMA, Eurasian Economic Union).

The study results proved biosimilarity of GP40061 to reference insulin glargine.

The next step to prove biosimilarity is a comparative immunogenicity trial.

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