Insulin glargine biosimilar (GP40061) shows no difference of immunogenicity as compared to the reference drug

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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);
- hyperinsulinemic euglycaemic clamp study.

OOO GEROPHARM has conducted all the above mentioned studies in accordance with international regulatory guidelines.

A comparative safety (immunogenicity) study of insulin biosimilar and reference drug is the last stage of the development program. Its results for GP40061 are performed here.

Aim

To confirm similar immunogenicity of GP40061 and reference insulin glargine (Lantus SoloStar).

Methods

An open-label, randomized, parallel 26-week trial; 180 adult patients with T1DM for at least 12 months before screening treated with stable daily insulin doses in basal-bolus regimen for at least 30 days before screening, with HbA1c level 6.5–12.0% were enrolled 1:1. No changes in insulin INN were allowed after randomization.

The primary endpoint

- frequency of immune response development at 26th week of treatment.

Secondary endpoints

- change of anti-insulin antibody (AIA) concentration at weeks 12 and 26 from baseline,
- percentage of participants with neutralizing AIA formation.

AIA concentration was assessed via enzyme-linked immunosorbent assay. Neutralizing activity was established via binding of insulin alfa-chain and CD220 receptor.

Results

	GP40061	Lantus SoloStar	p-value
No. of patients with criteria of immune response			
• at week 12	1 (1.1 %)	1 (1.1 %)	1.000
• at week 26	1 (1.1 %)	1 (1.1 %)	
Total No. of patients with immune response by week 26	2 (2.2 %)	2 (2.2 %)	1.000
Change of AIA concentration from baseline, IU/mL			
• at week 12	-0.19 ± 2.49	1.38 ± 10.98	0.399
• at week 26	-0.02 ± 2.85	0.30 ± 4.07	0.167
No. of patients			
• with neutralizing AIA at screening	23 (25.6 %)	24 (26.7 %)	1.000
• developed neutralizing AIA during study period	17 (18.9 %)	15 (16.7 %)	
• had neutralizing AIA disappeared by week 26	18 (20.0 %)	18 (20.0 %)	
• had neutralizing AIA both at screening and week 26	6 (6.7 %)	9 (10.0 %)	
• did not develop neutralizing AIA during study period	47 (52.2 %)	48 (53.3 %)	

Conclusions

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

Considering the whole development program, including clamp study, the biosimilarity of GP40061 to reference insulin glargine was proved.

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