ONLINE APPENDIX

The Role of Adjunctive Exenatide Therapy in Pediatric Type 1 Diabetes

Supplemental Material

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Pharmacokinetic Sampling:
Patients received 1.25 and 2.5 micrograms of exenatide administered subcutaneously with a minimum 3- week wash out period between studies. Blood samples were collected to determine plasma exenatide concentrations pre-dose, and at 10, 20, 40, 60, 120, 180, 240 and 300 minutes post dosing. Human plasma samples were analyzed for exenatide (synthetic exendin-4) concentrations utilizing a validated Enzyme-Linked Immunosorbent Assay (ELISA).The lower limit of quantification (LLQ) for the assay was 10 pg/ml.

Pharmacokinetic Analysis:
Non-compartmental exenatide pharmacokinetic parameters were estimated. The area under the concentration versus time curve (AUC_{0-t}) was calculated using the linear trapezoidal rule. . The apparent terminal elimination half-life ($t_{1/2}$) was calculated by $0.693/k_{el}$ where k_{el} is the apparent terminal elimination rate constant in patient with terminal concentrations above the LLQ. The clearance (CL) was calculated by dose/AUC. The maximum concentration (C_{max}) and time to maximum concentration (T_{max}) were obtained directly from the experimental data without interpolation. Plasma pharmacokinetic results are descriptive. For samples below the LLQ, a value of e-99 was used for pharmacokinetic calculations.

Results for Pharmacokinetic Analysis
For the 1.25 mcg and 2.5 mcg doses the AUC_{5h} were 8321±1561 and 12801±4927 pg-min/ml (mean $\pm$ SD), respectively. The mean half-life ($t_{1/2}$) and T_{max} did not appear to be significantly affected by dose with mean ranges of 85-91 and 98-112 minutes respectively. There was a dose response seen in C_{max} and AUC.