Predicting true time to recovery from insulin-induced hypoglycemia with dasiglucagon

Tadej Battelino,1 Timothy Bailey,2 Ramin Tehranchi,3 Leslie Klaff,4 Thomas R Pieber,5 Ulrike Hövelmann,6 Leona Plum-Mörschel,6,7 Anita E Melgaard,3 Ronnie Aronson,8 Linda A DiMeglio,9 Thomas Danne,10 and Anne Peters11

University Medical Center Ljubljana and University of Ljubljana, Ljubljana, Slovenia; AMCR Institute, Escondido, CA, USA; Zealand Pharma A/S, Søborg, Denmark; Rainer Clinical Research Center, Renton, WA, USA; Medical University of Graz, Graz, Austria; Profil, Neuss, Germany; Profil, Mainz, Germany; Children’s Hospital AUF DER BULT, Hannover, Germany; Thomas Jefferson School of Medicine, Los Angeles, CA, USA.

OBJECTIVES

• Dasiglucagon has undergone an extensive clinical development program and is approved by the US Food and Drug Administration (FDA) for use in severe hypoglycemia (SH) in both children and adults with diabetes aged ≥6 years old.

• The objective of this study was to use linear interpolation to estimate the true but unmeasured time to individual plasma glucose (PG) recovery following dasiglucagon treatment in phase 2 and phase 3 trials.

RESULTS

• Dasiglucagon is a novel, ready-to-use glucagon analog approved by the FDA for use in SH that has been investigated in a comprehensive clinical development program including one phase 2 trial and three phase 3 registration trials.

• Primary and secondary end points in phase 2 and phase 3 trials included time to PG recovery from insulin-induced hypoglycemia, defined as first PG increase ≥20 mg/dL after treatment initiation without the need for rescue glucose.

• In the trials included in this study, linear interpolation estimated a 20-mg/dL PG increase to occur earlier than the observed time to PG recovery. Using interpolated values, the median estimated true time to recovery for dasiglucagon across the comprehensive clinical development program ranged from 8.7–9.3 minutes in phase 2 and phase 3 trials.

CONCLUSIONS

• These results confirm the consistent efficacy of dasiglucagon for the treatment of hypoglycemia.

• Estimating true time to recovery enables better comparison between trials observed versus observed time to PG recovery only.

ABSTRACT

Background: The efficacy of dasiglucagon 0.6 mg has been investigated in multiple trials in individuals with type 1 diabetes mellitus. The primary endpoint was time to plasma glucose (PG) recovery from insulin-induced hypoglycemia, defined as first PG increase ≥20 mg/dL after treatment initiation without the need for rescue glucose. Different sampling schemes were used in phase 2 (5-min intervals) vs phase 3 trials (more frequent sampling to quantify PG increase). Using linear interpolation to estimate the actual time to PG recovery for individuals receiving dasiglucagon enables better comparison between trials compared to observed time to PG recovery only.

Objective: The objective of this study was to use linear interpolation to estimate the true but unmeasured time to individual PG recovery following dasiglucagon treatment in phase 2 and phase 3 trials.

Methods: The true time was calculated using linear interpolation between the time points before and after PG recovery occurred, assuming a linear PG increase in the limited time interval between 2 consecutive sampling time points.

Results: In the trials included in this study, linear interpolation estimated a 20-mg/dL PG increase to occur earlier (9 minutes on average) than the observed time to PG recovery. Using interpolated values, the median estimated true time to recovery for dasiglucagon was 8.7 minutes in the phase 2 trial and ranged from 9.0 to 9.3 minutes in phase 3 trials.

Conclusions: These data provide further insight into the true but unmeasured time to PG recovery and confirm the consistent efficacy of dasiglucagon in the treatment of hypoglycemia.

METHOD

• Linear interpolation between the two time points before and after PG recovery occurred was calculated.

• This interpolation assumed PG increased linearly in the limited time interval between 2 consecutive time points.

RESULTS

• In a representative patient, a PG sample taken at 10 minutes was the first sample showing an increase of at least 20 mg/dL from the pre-dose level.

• Linear interpolation estimated that the increase of 20 mg/dL occurred at 9 minutes.

• Linear interpolation estimates that PG recovery occurs earlier than the predetermined time point in patients treated with dasiglucagon.

• Observed time to PG recovery is a discrete measure dependent on the predetermined time point in patients treated with dasiglucagon.

• Linear interpolation of PG recovery estimates the true time to recovery on a continuous time scale.

• Median estimated true time to recovery with dasiglucagon ranges from 8.7 to 9.3 minutes across trials.

CONCLUSIONS

• Using interpolated values, median estimated true times to PG recovery ranged from 8.7–9.3 minutes in phase 2 and phase 3 trials.

• These results confirm the consistent efficacy of dasiglucagon for the treatment of hypoglycemia.

• Estimating true time to recovery enables better comparison between trials observed versus observed time to PG recovery only.

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