

Accelerating and Improving the Consistency of Rapid-Acting Analog Insulin Absorption and Action for Both Subcutaneous Injection and Continuous Subcutaneous Infusion Using Recombinant Human Hyaluronidase

Douglas B. Muchmore, M.D., and Daniel E. Vaughn, Ph.D.

Abstract

Rapid-acting insulin analogs were introduced to the market in the 1990s, and these products have improved treatment of diabetes by shortening the optimum delay time between injections and meals. Compared with regular human insulin, rapid-acting insulin formulations also reduce postprandial glycemic excursions while decreasing risk of hypoglycemia. However, the current prandial products are not fast enough for optimum convenience or control.

Recombinant human hyaluronidase (rHuPH20) has been used to increase the dispersion and absorption of other injected drugs, and in the case of prandial insulin analogs, it confers both ultrafast absorption and action profiles. Animal toxicology studies have demonstrated excellent tolerability of rHuPH20, and human studies, involving over 60,000 injections of prandial insulin + rHuPH20 to date, have similarly shown excellent safety and tolerability. Studies using rapid-acting analog insulin with rHuPH20 have included clinic-based pharmacokinetic and glucodynamic euglycemic glucose clamp studies, test meal studies, and take-home treatment studies. Administration methods have included subcutaneous injection of coformulations of rapid-acting insulin + rHuPH20 as well as continuous subcutaneous infusion of coformulations or use of pretreatment of newly inserted infusion sets with rHuPH20 followed by standard continuous subcutaneous insulin infusion therapy.

These studies have demonstrated acceleration of insulin absorption and action along with improvement in postprandial glycemic excursions and reduction in hypoglycemia risks. Further, rHuPH20 reduces intrasubject variability of insulin absorption and action and provides greater consistency in absorption and action profiles over wear time of an infusion set. Further studies of rHuPH20 in the take-home treatment setting are underway.

J Diabetes Sci Technol 2012;6(4):764-772

Author Affiliation: Halozyme Therapeutics Inc., San Diego, California

Abbreviations: (AUC) area under the curve, (CSII) continuous subcutaneous insulin infusion, (FDA) Food and Drug Administration, (rHuPH20) recombinant human hyaluronidase

Keywords: hyaluronidase, recombinant human hyaluronidase, ultrafast insulin

Corresponding Author: Douglas B. Muchmore, M.D., Halozyme Therapeutics Inc., 11388 Sorrento Valley Rd., San Diego, CA 92121; email address dmuchmore@halozyme.com