

Review of the Mechanism of Action and Clinical Efficacy of Recombinant Human Hyaluronidase Coadministration with Current Prandial Insulin Formulations

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

Abstract

For patients with type 1 or type 2 diabetes, achieving good glycemic control is critical for successful treatment outcomes. As many patients remain unable to reach glycemic goals with currently available rapid-acting analog insulins, ultrafast insulin products are being developed that provide an even faster pharmacokinetic profile compared with current rapid prandial insulin products. The overall strategy of these ultrafast insulin products is to better mimic the normal physiologic response to insulin that occurs in healthy individuals to further improve glycemic control. Recombinant human hyaluronidase (rHuPH20) is a genetically engineered soluble hyaluronidase approved by the U.S. Food and Drug Administration as an adjuvant to increase the absorption and dispersion of other injected drugs; mammalian hyaluronidases as a class have over 6 decades of clinical use supporting the safety and/or efficacy of hyaluronidase coadministration. Clinical findings have demonstrated that coadministration of rHuPH20 with insulin or an insulin analog achieved faster systemic absorption, reduced inter- and inpatient variability of insulin absorption, and achieved faster metabolic effects compared with injection of either insulin formulation alone. The magnitude of this acceleration is similar to the incrementally faster absorption of prandial insulin analogs as compared with regular insulin. In addition, coadministration of rHuPH20 with regular insulin or insulin analog also improved the achievement of prandial glycemic targets. Thus, rHuPH20 coadministration shows promise as a method of establishing a more rapid insulin profile to prandial insulin in patients with diabetes and has the potential to yield substantial improvements in postprandial glycemic excursion.

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

Abbreviations: (A1C) derived average glucose, (C_{max}) peak plasma concentration, (PK) pharmacokinetics, (PPG) postprandial plasma glucose, (rHuPH20) recombinant human hyaluronidase, (SC) subcutaneous, (t_{max}) time to peak plasma concentration

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