

## Review of: "[Perspective] Exploring the Synergistic Approach of Dual GLP-1 Agonist with Degludec Basal Insulin for Early Type 1 Diabetes Treatment for Albumin-Insulin Producing Cells Expression"

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The authors present interesting theories regarding potential treatment of type 1 diabetes with GLP-1 receptor antagonists. As the prevalence of diabetes continues to rise, the authors' plans for future research are much needed. However, as a response to the NEJM Letter to the Editor "Semaglutide in Early Type 1 Diabetes" this article seems to diverge with from the intent of the Letter by offering unrelated theories. While a small case series, the initial NEJM letter focuses on potential GLP-1 therapy as a way to reduce anit-GAD antibodies and insulin requirements for patients recently diagnosed with type 1 diabetes. The authors of this response offer three comments and a perspective that reinforce the original article's findings yet seems to focus on some unrelated concepts. The second comment refers to use of hepatic cells as regenerative tissue - this does not seem specific to the article on semaglutide and degludec in type 1 diabetes. The third comment is regarding albumin binding of degludec and strategies to adapt this approach to a GLP-1 administration for longer effects, however, currently semaglutide can be dosed once weekly and it is unclear if the goal is for less frequent dosing than this or how it is specific to the population in question.

I would also encourage discussion of potential adverse effects with any formulation of drug administration in future trial designs shared by the authors.

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