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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Potential competing interests: No potential competing interests to declare.

Thank you for the opportunity to review the manuscript titled: [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. This article explores a novel treatment approach for early type 1 diabetes. It focuses on combining two therapies: a dual GLP-1 agonist and degludec basal insulin. The article begins by highlighting the destruction of beta cells in early type 1 diabetes and how GLP-1 agonists have emerged as a promising treatment for obesity and type 2 diabetes. The authors discuss a retrospective analysis of semaglutide, a GLP-1 agonist, in newly diagnosed early type 1 diabetes patients, showing promising results in reducing the need for insulin and improving glycemic control. The interpretation section of the article discusses the potential of GLP-1 agonists in protecting remaining beta cells, stimulating cell proliferation, and even reprogramming liver cells into insulin-producing cells. It also explores the benefits of modifying GLP-1 agonists with albumin ligands to extend their effectiveness.

The perspective section provides a holistic view of this combined treatment approach, considering the pharmacokinetics of degludec, the plasticity of adult human hepatic tissue, and the advantages of modified GLP-1 derivatives. The conclusion emphasizes the need for further research to fully understand and unlock the potential of this approach in treating early type 1 diabetes. By integrating the autoimmune hypothesis, the ability of GLP-1 to stimulate cell proliferation, and the use of modified GLP-1 derivatives, the authors aim to restore beta cell mass and function, ultimately improving the lives of individuals with type 1 diabetes. This treatment approach is planned to undergo clinical trials in 2024.

However, there are several areas where the text could be improved. Please find my detailed comments below:

1. Title and Abstract:

- In the abstract, it's beneficial to specify what GLP-1 stands for (Glucagon-like peptide 1) to ensure clarity for all readers.

2. Background:

- The term "prolonged and stable effects of degludec" could be enhanced with a brief description of what degludec is and how it functions, providing more context for the reader.

- When mentioning the "mechanism of action involving binding to albumin," consider briefly explaining how this mechanism contributes to the stability and extended duration of effects.

3. Interpretation and Commentary:

- In Comment 1, it's crucial to expand on the significance of measuring anti-GAD (glutamic acid decarboxylase) and anti-IA2 (islet antigen-2) antibodies and how these measurements relate to the autoimmune response.

- In Comment 2, while discussing the plasticity of adult human hepatic tissue, include examples or references to experimental studies to support these claims.

- In Comment 3, specify what "Rhein-C12" is and how it enhances glucose tolerance and provides hypoglycemic effects. Adding references to studies where these effects were observed would strengthen this argument.

4. Conclusion:

- In the conclusion, it's helpful to summarize the main points of the perspective provided in this article more concisely. Ensure that it highlights the significance of the proposed theory for the treatment of early type 1 diabetes.

- When mentioning "modifications using albumin ligands," explain the practical benefits or applications of these modifications more explicitly. How do these modifications help in real-world scenarios for diabetes management?

- The text could benefit from a smooth transition between the discussion of the autoimmune hypothesis and the role of GLP-1 in beta cell replication. Make sure these topics flow logically.

5. Grammar and Style:

- Throughout the article, be consistent with capitalization. For example, "GAD" and "GLP-1" should be consistently capitalized for clarity.

- Pay close attention to verb tenses. In some places, past and present tenses are mixed, which can make the text less clear.

6. Clinical Trials:

- In the final paragraph, clarify the significance of ClinicalTrials.gov Identifier NCT06057077. Readers might not be familiar with this code, so a brief explanation would be helpful.

7. Use of Abbreviations:

- When using abbreviations such as GLP-1, it's good practice to define them the first time they appear in the text. Subsequently, you can use the abbreviation.