



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Disponible en ligne sur

**ScienceDirect**  
www.sciencedirect.com

Elsevier Masson France

**EM|consulte**  
www.em-consulte.com



## EDITORIAL

## DPP-4 inhibitors and severe course of illness in patients with COVID-19

### Abbreviations

DPP-4 dipeptidyl peptidase-4  
 COVID-19 coronavirus disease 2019  
 MERS Middle East Respiratory Syndrome  
 SARS-CoV2 severe acute respiratory syndrome coronavirus 2

We have a dream: that 2021 will be a better year than 2020 and will provide a reduction of the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Vaccine campaigns are beginning all around the world to protect people with risk factors first. Diabetes seems to be a risk factor of poor prognosis as it worsens the serious clinical events caused by coronavirus disease 2019 (COVID-19). Fortunately, the knowledge of the pandemic in diabetic patients dramatically increases as scientific data are rapidly published (more than 3500 publications on PUBMED in January 2021). Emerging evidence demonstrates that the degree of blood glucose control in patients infected with SARS-CoV-2 is of importance for the viral progression.

In 2020, we reported research data on antidiabetic drugs in this context and the potential influence of dipeptidyl peptidase-4 (DPP-4) inhibitors [1]. DPP-4 inhibitors target the enzymatic activity of DPP-4 and block the breakdown of GLP-1 and GIP leading to increased insulin secretion and reduced hyperglycemia in patients with type 2 diabetes. In addition to its effects on glucose metabolism, DPP-4 is also the T-cell antigen CD26 which is supposed to play a role in T-cell proliferation. Therefore, its inhibition was initially thought to potentially increase the risk of infection. However, other studies suggest that DPP-4 inhibition may have opposite effect. Being a ubiquitously transmembrane glycoprotein found on the surface of many cells with non-specific exopeptidase enzyme activity, human DPP-4 has been identified as a functional receptor for the spike protein of the coronavirus which caused the Middle East Respiratory Syndrome (MERS). The use of antibodies directed against DPP-4 resulted in inhibited MERS-CoV infection. Besides, DPP-4 was also found to increase inflammatory immune responses by modifying the production of several cytokines and chemokines. Another element of complexity is the fact that DPP-4 also exists as a soluble enzyme in the circulation. However, its role as a virus receptor or protector against it is currently totally unclear.

DOI de l'article original : <https://doi.org/10.1016/j.therap.2020.12.015>.

<https://doi.org/10.1016/j.therap.2021.01.051>

0040-5957/© 2021 Société française de pharmacologie et de thérapeutique. Publié par Elsevier Masson SAS. Tous droits réservés.

Whether diabetes treatment with DPP-4 inhibitors in clinical practice influences the course of the infection caused by COVID-19 is currently unknown. In the present issue of Therapies, Kow and Hasan showed the results of a meta-analysis to summarize the overall effect of DPP-4 inhibitors on the clinical outcomes in patients with COVID-19 [2]. Including six observational studies with overall 1,531 patients with COVID-19, neither beneficial nor harmful effect was evidenced when using DPP-4 inhibitors. These preliminary data seem therefore reassuring on that population and, at this time, no conclusive evidence exists to support the discontinuation of DPP4 inhibitors because of COVID-19 in people with diabetes. Nevertheless, the hypothesis that these agents could, by reducing DPP-4 concentrations, provide therapeutic opportunities for treatment of COVID-19 remains unproved. More studies and particularly randomized clinical trials focusing on the links between DPP-4 and coronavirus infection have to be carried on.

## Disclosure of interest

The authors declare that they have no competing interest.

## Références

- [1] Bouhanick B, Cracowski JL, Faillie JL, French Society of Pharmacology Therapeutics (SFPT). Diabetes and COVID-19. *Therapie* 2020;75(4):327–33.

- [2] Kow CS, Hasan SS. A meta-analysis on the preadmission use of DPP-4 inhibitors and risk of a fatal or severe course of illness in patients with COVID-19. *Therapie* 2020, <http://dx.doi.org/10.1016/j.therap.2020.12.015> [S0040-5957(20)30241-9].

Béatrice Bouhanick<sup>a,\*</sup>, Jean-Luc Cracowski<sup>b</sup>,  
Jean-Luc Faillie<sup>c</sup>

<sup>a</sup> Service d'Hypertension Artérielle et  
Thérapeutique PCVM, UMR 1027, Université de  
Toulouse 3, CHU de Rangueil, 1, avenue  
J.-Poulhes, 31059 Toulouse cedex 9, France

<sup>b</sup> INSERM, HP2, Centre Régional de  
Pharmacovigilance et Centre d'Investigation  
Clinique de Grenoble, Université de  
Grenoble-Alpes, 38000 Grenoble, France

<sup>c</sup> Département de Pharmacologie Médicale et  
Toxicologie, Centre Régional de Pharmacovigilance  
Occitanie-Est, Université de Montpellier, CHU de  
Montpellier, 34295 Montpellier, France

\* Corresponding author.

Adresse e-mail :

[duly-bouhanick.b@chu-toulouse.fr](mailto:duly-bouhanick.b@chu-toulouse.fr) (B. Bouhanick)  
Disponible sur Internet le 18 janvier 2021