



Author's Reply to Petersen: "Differences in In Vitro Properties of Pancreatin Preparations for Pancreatic Exocrine Insufficiency as Marketed in Russia and CIS"

Igor V. Maev¹ · Yury A. Kucheryavyy¹ · Natalya B. Gubergrits¹ · Ingo Bonnacker¹ · Ekaterina A. Shelest¹ · Gwendolyn P. Janssen-van Solingen¹  · J. Enrique Dominguez-Munoz¹

Accepted: 20 September 2021 / Published online: 23 October 2021
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Referring to the Letter to the Editor by Prof. Dr. Karl-Uwe Petersen [1] regarding our article entitled *Differences in In Vitro Properties of Pancreatin Preparations for Pancreatic Exocrine Insufficiency as Marketed in Russia and CIS* [2], we would like to provide further information and feedback.

Our investigation has indeed focused on Feret max X_{50} as the selected representative parameter for particle size measurements. As explained in the publication, this was used as a representative parameter for the overall particle size diameter (PSD), for which the cumulative distribution Q3 (volume-based) assumes a value of 50%, where X_{50} represents the particle size at which 50% of particles in the material are smaller than this. Within the study, X_{10} and X_{90} have also been determined (data on file). For the X_{90} max assessments, Kreon has the lowest PSD (approximately 2000 μm) compared with all other pancreatin preparations (approximately 3000 μm). Upon evaluation of the X_{10} results, the preparations meeting a particle size smaller than 2000 μm are Kreon 25000, Kreon 40000, and Micrazim 25000 and 40000. All other preparations, including Ermytal (both strengths), Pangrol, and Panzytrat, still do not meet a particle size smaller than 2000 μm . Even when assessing the Feret min X_{50} data, only Kreon and Micrazim preparations are below 1500 μm , with averages of 1121 μm for Kreon and 1389 μm for Micrazim. The authors therefore believe that the choice of X_{50} is justified and supportive of the United European Gastroenterology Diagnosis and Treatment of Chronic Pancreatitis (UEG/HaPanEU) guideline consensus

statement [3] and previously published comparative studies assessing the in vitro properties of different pancreatin preparations.

Prof. Dr. Karl-Uwe Petersen mentions that the conclusion of the abovementioned HaPanEU guideline [3] has been challenged, particularly in his systematic review from March 2021 [4], which succeeds our publication; however, the authors would like to point out that the systematic review is based on publications currently in the public domain and is not reflective of the full dataset for our particular study and the pancreatin preparations available in Russia/Commonwealth of Independent States (CIS). Additionally, contrary to what is being postulated and as mentioned in the publication by Prof. Dr. Karl-Uwe Petersen; the pancreatin preparations assessed, including Kreon, do not have a round shape but rather a more cylindrical shape, where the Feret min diameter represents the diameter of the cylinder and the Feret max represents the maximum size of the particle in any dimension, thereby being indicative of the probability of the particle passing the pylorus together with the chyme.

We also note that Prof. Dr. Karl-Uwe Petersen only addresses the PSD and the max Feret X value in his Letter to the Editor [4], and does not comment on the other differences between the specific pancreatin preparations identified in our in vitro investigation, particularly the differences observed regarding lipase activity (with Micrazim 40000 being a significant outlier at 79% of the declared lipase content) and (associated) dissolution [2] - variables likely having an even greater impact on digestive potency and clinical efficacy.

We therefore re-emphasize the conclusion drawn in our publication - aligned with the HaPanEU guidelines and previous investigations - that pancreatin preparations with a diameter of < 2 mm should be regarded as optimal for the treatment of pancreatic exocrine insufficiency (PEI), combined with clinical efficacy data generated with said

This reply refers to the comment available online at <https://doi.org/10.1007/s40268-021-00366-z>.

✉ Gwendolyn P. Janssen-van Solingen
gwendolyn.janssen@abbott.com

¹ Abbott Product Operations AG, Allschwil, Switzerland

preparations as well as enzyme activity and optimal dissolution characteristics.

Funding The research was supported by Abbott Pharmaceuticals.

Declarations

Conflicts of interest Igor V. Maev, Yury A. Kucheryavyy, and Natalya B. Gubergrits have no conflicts of interest that are directly relevant to the content of the original article or the Reply to the Letter to the Editor. Dr. J. Enrique Domínguez-Muñoz has received research grants from Abbott Pharmaceuticals and Mylan; payment for lectures from Abbott and Mylan; and paid consultancy from Mylan. Ingo Bonnacker, Ekaterina A. Shelest, and Gwendolyn P. Janssen-van Solingen are employed by Abbott Pharmaceuticals.

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References

1. Petersen KU. Comment on: "Differences in in vitro properties of pancreatin preparations for pancreatic exocrine insufficiency as marketed in Russia and CIS". *Drugs RD*. <https://doi.org/10.1007/s40268-021-00366-z>
2. Maev IV, Kucheryavyy YA, Gubergrits NB, Bonnacker I, Shelest EA, Janssen-van Solingen GP, et al. Differences in in vitro properties of pancreatin preparations for pancreatic exocrine insufficiency as marketed in Russia and CIS. *Drugs RD*. 2020;20:369–76. <https://doi.org/10.1007/s40268-020-00326-z>.
3. Löhr JM, Domínguez-Muñoz JE, Rosendahl J, Besselink M, Mayerle J, Lerch MM, et al. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *United Eur Gastroenterol J*. 2017;5:153–99. <https://doi.org/10.1177/2050640616684695>.
4. Petersen K-U, Malfertheiner P, Mössner J. The role of sphere size in the context of pancreatin therapy for exocrine pancreatic insufficiency: a systematic review. *J Gastrointest Liver Dis*. 2021;30(1):132–41. <https://doi.org/10.15403/jgld-2985>.