

INPLASY PROTOCOL

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Review Stage at time of this submission: Completed but not published.

Difelikefalin in the treatment of chronic kidney disease-associated pruritus: a systematic review

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Review question / Objective: The objective of this study is to evaluate the clinical efficacy and safety as well as to summarize the current knowledge of difelikefalin in treatment of patients with CKD-aP based on the available clinical trials.

Condition being studied: Chronic kidney disease-associated pruritus (CKD-aP), also known as uremic pruritus, is a condition that significantly reduces the quality of life of patients with end-stage renal disease. There were unmet needs in the treatment of this condition. Difelikefalin is a novel opioid agonist with high selectivity for kappa opioid receptors (KOR) that has been shown to be effective in the treatment of this type of chronic pruritus.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 May 2022 and was last updated on 28 May 2022 (registration number INPLASY202250154).

INTRODUCTION

Review question / Objective: The objective of this study is to evaluate the clinical efficacy and safety as well as to summarize the current knowledge of difelikefalin in treatment of patients with CKD-aP based on the available clinical trials.

Rationale: Difelikefalin is the first agent just registered by FDA and EMA for the chronic kidney disease-associated pruritus. The analysis of available data from clinical trials will help clinicians in their daily practice.

Condition being studied: Chronic kidney disease-associated pruritus (CKD-aP), also known as uremic pruritus, is a condition that significantly reduces the quality of life of patients with end-stage renal disease. There were unmet needs in the treatment of this condition. Difelikefalin is a novel opioid agonist with high selectivity for kappa opioid receptors (KOR) that has been shown to be effective in the treatment of this type of chronic pruritus.

METHODS

Search strategy: PubMed, ScienceDirect and Scholar Google databases were searched for relevant articles using the combination of the keywords "difelikefalin" or "CR845" AND "pruritus" or "itch" or "chronic kidney disease" or "hemodialysis".

Participant or population: Patients undergoing hemodialysis treatment.

Intervention: The effect of difelikefalin on chronic pruritus in maintenance hemodialysis patients.

Comparator: NA.

Study designs to be included: PRISMA methodology.

Eligibility criteria: The exclusion criteria included all types of articles except for research works (e.g. re-views, letters) and a language other than Polish or English. Inclusion criteria were full-text original articles on the effects of difelikefalin in dialysis patients with chronic pruritus.

Information sources: The following electronic databases constituted the source for the study: PubMed, ScienceDirect and Scholar Google.

Main outcome(s): Effectiveness of difelikefalin on reduction of intensity of pruritus. The reduction of at least 4 point on Numeral Rating Scale was considered as the primary outcome. The safety profile of the agent was also evaluated.

Quality assessment / Risk of bias analysis: Risk of bias was assessed. We evaluated the bias due to randomisation process, bias due to deviations from intended intervention, bias due to missing outcome data, bias in measurement of the outcome, bias of the selection of reported results.

Strategy of data synthesis: The data were analysed by both authors. The risk of bias was assessed by both authors independently.

Subgroup analysis: No subgroup analysis was performed, as this was not needed for this project.

Sensitivity analysis: NA.

Language: English and Polish.

Country(ies) involved: Poland.

Keywords: chronic kidney disease-associated pruritus, uremic pruritus, difelikefalin.

Dissemination plans: There is a plan to publish this study in international scientific journal.

Contributions of each author:

Author 1 - Kamila Wala - Conceptualization, resources, writing—original draft preparation, writing—review and editing, visualization.

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Author 2 - Jacek Szepietowski - Conceptualization, resources, writing—original draft preparation, review and editing, supervision, funding acquisition.

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Conflicts of interest:

Prof. Szepietowski has served as advisory Board/Consultant: AbbVie, Leo Pharma, Novartis, Sandoz, Sanofi-Genzyme, Trevi, Viofor; as speaker for Speaker: AbbVie, Janssen-Cilag, Eli-Lilly, Leo-Pharma, Sanofi-Genzyme, as an investigator in Clinical trials: AbbVie, Amgen, BMS, Galderma, Galapagos, Incyte, InfraRX, Janssen-Cilag, Menlo Therapeutics, Merck, Novartis, Pfizer, Regeneron, UCB, Trevi.