4CPS-075 A SYSTEMATIC REVIEW OF THE TARGET PHARMACOKINETIC/PHARMACODYNAMIC PARAMETERS OF ANTIBIOTICS TREATING GRAM-NEGATIVE INFECTIONS

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Background and Importance Following the introduction of pharmacokinetic/pharmacodynamic (PK/PD) parameters in preclinical development of antibiotics, the application of PK/PD in guiding doses has been highly encouraged. Previous findings remain controversial and vary greatly, causing difficulties in determining the appropriate PK/PD parameters for individuals in practice.

Aim and Objectives This systematic review aims to identify the PK/PD targets of antibiotics treating gram-negative infections in clinical practice, focusing on multi-drug resistant gram-negative infections.

Material and Methods Database from Cochrane Central, Web of Science, PubMed, Embase and Scopus were searched using defined terms. Studies using PK/PD targets to determine dosing regimens of parenteral antibiotics for patients with gram-negative infections in practice were selected. Studies were excluded if examining the PK/PD targets of antibiotics for healthy participants, virtual patients, and gram-positive infections. Study bias was evaluated using the Cochrane risk of bias tool.

Results A total of 41 studies investigating 21 antibiotics and two combinations involving 799 participants were selected. The majority of eligible studies (21 articles, 51.2%) were case studies, which were evaluated as high risk of bias. Three (5.9%) studies were RCTs and 17 (33.3%) were non-RCTs. Only one RCT was evaluated as at low risk of bias. 58% of the investigated population was treated using predefined PK/PD indices derived from preclinical studies. Yet, among them, more than 60% modified the dosing and the duration of administration to attain a higher target value. Cefiderocol and meropenem were the two antibiotics most prescribed for multi-drug resistant bacteria, usually combined with other antibiotics. Extended infusion of meropenem to at least 30 minutes per administration resulted in the achievement of 100% $fT>MIC$ or 100% $fT>4–6$ MIC instead of 40% $fT>MIC$ while the prescription of Cefiderocol followed the labelled instruction of use. Still, about 79% of these cases targeted a higher value of predefined 77% $fT>MIC$ derived from preclinical data.

Conclusion and Relevance The PK/PD target values of antibiotics treating resistant gram-negative bacteria are variable and divergent from preclinical data. A range of PK/PD targets may be more realistic in practice to optimise dosing regimens for the facilitation of clinical outcomes, and PK/PD targets should be used to inform dosing regimens. Further research with standardised patient outcomes is required.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest.

4CPS-076 EFFECTIVENESS AND SAFETY OF DUPILUMAB AND TRALOKINUMAB IN ATOPIC DERMATITIS IN CLINICAL PRACTICE

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Background and Importance Dupilumab, an IL-4/IL-13 antagonist, and tralokinumab, an IL-13 antagonist, are approved for the treatment of moderate-to-severe atopic dermatitis (AD). Until now, no published studies have compared these treatments in clinical practice.

Aim and Objectives To evaluate and compare the effectiveness and safety of dupilumab and tralokinumab in AD patients in clinical practice.

Material and Methods We conducted a retrospective study in a tertiary hospital. We included AD patients who initiated dupilumab or tralokinumab as the first targeted treatment between 11/2017 and 5/2023.

We collected the following data from electronic medical and pharmacy records: age, sex, Eczema Area and Severity Index (EASI), Peak Pruritus-Numerical Rate Scale (PP-NRS), and adverse effects (AE). Effectiveness endpoints were EASI and PP-NRS at the first follow-up medical visit. Safety endpoints were the number and type of AE during the study period.

Results In total, 78 patients were included in the study. Mean age (±SD) was 40.8 (±17.4) years. Thirty-nine (50.0%) patients were women. Dupilumab group included 61 patients, whereas tralokinumab, 17.

In dupilumab group, mean initial EASI (±SD) was 32.5 (±9.7) and PP-NRS, 8.2 (±1.3). At first follow-up, the mean EASI was 7.1 (±6.0) and PP-NRS 2.7 (±1.8). In the tralokinumab group, mean initial EASI (±SD) was 26.4 (±8.3) and PP-NRS, 7.3 (±1.7). At first follow-up visit, the mean EASI was 2.4 (±4.8) and PP-NRS 1.9 (±2.7). The reduction in EASI and PP-NRS was statistically significant ($p<0.001$) in both groups. At first follow-up visit, tralokinumab was superior to dupilumab in the reduction of EASI ($p=0.005$), but not in PP-NRS. However, comparing the normalised reductions of EASI and PP-NRS, there were no significant differences between dupilumab and tralokinumab groups.

AE were reported in 23 (37.7%) dupilumab-treated patients and 5 (29.4%) tralokinumab-treated patients, which were mostly ophthalmologic (52.2% and 60.0%, respectively). Eight (13.1%) dupilumab-treated patients and 2 (11.8%) tralokinumab had to discontinue the treatment due to AE.

Conclusion and Relevance In our cohort, dupilumab and tralokinumab were effective. Our study shows a significant improvement in EASI and PP-NRS in the first follow-up visit. AE data show that close ophthalmologic monitoring is recommended in these patients. Further studies are warranted to validate the differences found between both treatments.

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