REAL-WORLD PERSISTENCE WITH DOLUTEGRAVIR/ TENOFOVIR ALAFENAMIDE AMONG HUMAN IMMUNODEFICIENCY VIRUS PATIENTS

Background and Importance Persistence can provide information on the comparative effectiveness, durability and tolerability in real-world patient populations.

Little is known about comparative persistence of dolutegavir/ lamivudine (DTG/3TC) and bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF), two preferred antiretroviral treatments in our country.

Aim and Objectives To compare persistence between two preferred antiretroviral therapies and analyse reasons for discontinuation.

Material and Methods We conducted a retrospective, non-interventional, longitudinal study. All HIV patients over 18 years treated with DTG/3TC or BIC/FTC/TAF in our centre were included.

Persistence was defined as the duration of time from initiation to discontinuation of therapy (last dispensing or end of treatment). TWI, as well as the role of pharmaceutical intervention (PI) in preventing possible adverse events due to this DDI.

Potential nephrotoxic groups of drugs: Non-steroidal anti-inflammatory drugs (NSAIDs), diuretics and ACE inhibitors/angiotensin receptor blockers (ARB).

Aim and Objectives To evaluate clinical significance of the TWI, as well as the role of pharmaceutical intervention (PI) in preventing possible adverse events due to this DDI.

Results

Overall, mean persistence duration was 1.189 days (CI 95% 1.163-1.215). Persistence with DTG/3TC was 1.231 days (CI 95% 1.206-1.255) and persistence with BIC/FTC/TAF was 980 days (CI 95% 944-1.0166); p=0.001. However Cox-model adjusted HR was 2.5 (IC95% 0.5-12; p=0.26).

The main reasons for discontinuation for BIC/FTC/TAF were tolerability/toxicity (n=9) and death (n=3). Only two patients withdrew DTG/3TC, due to toxicity (n=1) and death (n=1).

Conclusion and Relevance In our study, more patients on DTG/3TC were persistent after the first year compared to BIC/FTC/TAF. However, there were no differences in overall persistence in covariate-adjusted analysis. Main reason for BIC/ FTC/TAF discontinuation was tolerability/toxicity.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest

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Conclusion and Relevance The TWI can participate in acute kidney injury, particularly in high risk patients. Clinical pharmacists play an important role detecting patients at increased risk of AKI, preventing adverse events due to TW interaction, monitoring AKI biomarkers and recommending deprescription of possible nephrotoxic drugs.

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Background and Importance Proton pump inhibitors (PPIs) are hepatically metabolised primarily by the cytochrome P 450 2C19 enzyme. PPIs are generally considered effective, however CYP2C19 genetic polymorphisms may result in patients not responding appropriately to treatment. CYP2C19 genotyping and interpretation of results may be a contribution by pharmacists towards personalised PPI therapy.

Aim and Objectives The aim was to determine the prevalence of CYP2C19 genetic polymorphisms in a cohort of patients showing PPI therapy resistance.

Material and Methods Patients diagnosed with gastro-oesophageal reflux disease or peptic ulcer disease and with documented PPI therapy resistance were identified using ambulatory reflux monitoring and endoscopy databases. An EDTA blood sample was collected from each patient, followed by genomic DNA extraction with the QIAcube (Qiagen). CYP2C19 genotyping was performed with real-time polymerase chain reaction on the GeneAmp PCR System 9700 thermal cycler and reverse hybridisation using the TwinCubator with the PGX-CYP2C19 StripAssay® (ViennaLab). Genotypes (phenotypes) were classified as: *1*1 (normal metabolisers, NMs), *1*17 (rapid metabolisers, RMs), *1*2 or *2*17 (intermediate metabolisers, IMs), or *2*2 (poor metabolisers, PMs). The 2021 Clinical Pharmacogenetics Implementation Consortium (CPCi) guideline was used for genotype-based dosing recommendations, which suggests that NMs may be at increased risk of therapeutic failure compared to IMs/PMs, RMs are at increased risk of therapeutic failure, while IMs/PMs have increased chance of efficacy but risk potential toxicity.

Results Thirty-eight patients were recruited; all Caucasian; 20 female, mode 50-59 years (n=11). Most patients (n=17) experienced reflux hypersensitivity, followed by persistent oesophagitis despite PPI treatment (n=10). PPI therapy included esomeprazole (n=20), omeprazole (n=16) or lansoprazole (n=2). The majority of patients (n=20) were genotyped as *1*1 (NM), followed by *1*17 (n=7, RM), *2*17 (n=6, IM), *1*2 (n=4, IM) and *2*2 (n=1, PM).

Conclusion and Relevance The majority of patients in this study may be (53% NMs) or are (18% RMs) at risk of therapeutic failure, and the guideline recommends considering a dose increase and monitoring for efficacy in these patients. In patients at risk of side-effects (29% IMs, PMs), the guideline suggests reduction in dose and continued monitoring for efficacy. Pharmacist-led CYP2C19 pharmacogenetic testing can be used to guide dosing and monitoring in patients taking PPIs.

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4CPS-163 CYTOCHROME P450 2C19 GENOTYPING FOR PERSONALISATION OF PROTON PUMP INHIBITOR THERAPY
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4CPS-164 ADEQUACY REVIEW IN THE USE OF DAPAFLIFLOZIN FOR THE TREATMENT OF HEART FAILURE
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