

The eGFR was calculated by CKD-EPI, MDRD4-IDMS and Cockcroft-Gault. Patients with serum creatinine below 0.4 mg/dl were excluded.

CKD-EPI was used as a reference formula to assess the concordance between the different methods of estimating, classifying patients in 3 eGFR groups according to the IV dexketoprofen SmPC: <50 mL/min/1.73 m², 50–80 mL/min/1.73 m² and >80 mL/min/1.73 m².

Results The study included 1946 patients – 54.3% men, 45.7% women – from a total population of 2052 admissions; mean age of 59.8 years (range 17–103). The mean serum creatinine concentration was 0.84 mg/dL ± 0.43 and mean eGFR, according to CKD-EPI, 83.05 ± 26.17 mL/min/1.73 m².

The following results of non-concordance were found by comparing these formulas to estimate renal function:

- CKD-EPI vs. MDRD4-IDMS: 4.3% in eGFR <50 mL/min/1.73 m² group, 23.2% in the eGFR 50–80 mL/min/1.73 m² and 18.9% in eGFR > 80 mL/min/1.73 m².
- CKD-EPI vs. CG: 2.8% in eGFR <50 mL/min/1.73 m² group, 10.5% in eGFR 50–80 mL/min/1.73 m² and 7.8% in eGFR > 80 mL/min/1.73 m².
- MDRD4-IDMS vs. CG: 4.5% in the group of eGFR < 50 ml/min, 21.4% in group eGFR 50–80 mL/min and 17.1% in the group of eGFR > 80 ml/min.

Conclusions A great difference was found in the estimates of renal function between the three methods used – CKD-EPI, MDRD4-IDMS and CG – in the three eGFR functional categories – <50, 50–80 and >80 mL/min/1.73 m² – ranging between 2.8% and 23.2%.

These results are relevant in clinical practise because the functional category determines the non-use or limited dose of dexketoprofen IV for each patient.

No conflict of interest.

PHC-025 SINGLE NUCLEOTIDE POLYMORPHISMS ASSOCIATED WITH ADVERSE EVENTS IN TAXANE-TREATED BREAST CANCER PATIENTS

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Background Inter-individual differences in drug efficacy and toxicity are linked, in many cases, to single nucleotide polymorphisms (SNPs) in genes coding for drug metabolising enzymes and transporters. Taxanes are active for several tumour types, including breast cancer. But this is limited by adverse events such as neurotoxicity and haematological toxicity.

Purpose To evaluate the associations between a panel of 92 SNPs in 33 genes and adverse events developed by breast cancer patients treated with taxanes.

Materials and Methods Between June 2011 and May 2012 breast cancer patients treated with taxanes who gave informed consent were genotyped for 92 SNPs in 33 genes. Genomic DNA was analysed by a genetic analysis platform (MassArray, Sequenom). Hardy-Weinberg equilibrium was assessed. Clinical data were recorded. The association between genotypes and adverse reactions was assessed with Fisher's exact test and X²-test.

Results Sixty-seven Caucasian women (mean age: 53 years old; 95%CI = 49–56) were genotyped. All genotype frequencies were in Hardy-Weinberg equilibrium. 53.7% (n = 36) of the patients were treated with docetaxel and 46.3% (n = 31) with paclitaxel. Histotypes: 88.1% (n = 59) ductal, 7.5% (n = 5) lobular and 4.5% (n = 3)

other. Significant associations were found between: A) **Overall grade III–IV toxicity**: *TP53 rs1045522* [10.8% (n = 4) GG vs. 43.3% (n = 13) GC/CC, p = 0.004]; DNA repair gene *XPC rs2228001* [8.7% (n = 2) AA vs. 34.1% (n = 15) AC/CC, p = 0.037]. B) **Anaemia grade II–IV**: *ERCC2 rs1799793* [7.1% (n = 2) GG vs. 33.3% (n = 13) GA/AA, p = 0.016]; *XPC rs2228001* [4.3% (n = 1) AA vs. 31.8% (n = 14) AC/CC, p = 0.012]. C) **Neutropenia grade II–IV**: *CYP2C8 rs1341164* [6.5% (n = 2) TT vs. 27.8% (n = 10) TC/CC, p = 0.028]; *TP53 rs1045522* [8.1% (n = 3) GG vs. 30.0% (n = 9) GC/CC, p = 0.027]; *XPC rs2228001* [0.0% AA vs. 27.3% (n = 12) AC/CC, p = 0.006]. D) **Diarrhoea grade II–IV**: *ABCB1 rs1128503* [21.4% (n = 6) TT vs. 2.6% (n = 1) TC/CC, p = 0.018]; *CYP1B1 rs72549389* [20.0% (n = 7) TT vs. 0% TG/GG, p = 0.014]. No associations with neurotoxicity were found.

Conclusions Studying genetic variations can help to identify patients at higher risk of suffering adverse events and provides useful information to individualise therapy.

No conflict of interest.

PHC-026 TACROLIMUS AND IMATINIB INTERACTION. A CASE STUDY

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Background Tacrolimus is a drug metabolised by CYP3A4. Since imatinib increases the plasma concentrations of simvastatin, a CYP3A4 substrate, this indicates that it is an inhibitor of this enzyme and may affect other drugs.

Purpose To describe the possible interaction between imatinib and tacrolimus that result in increased blood levels of Tacrolimus.

Materials and Methods Information was collected through the SAVAC and SELENE computer systems and reviewing patient history. The variables compiled were tacrolimus blood levels, dose and dose regimen.

Results The patient had an allogeneic blood stem cells transplant from an unrelated donor, HLA and ABO compatible, presenting cutaneous sclerodermiform graft versus host disease (GVHD) on tacrolimus (2 mg/12 h) treatment and blood levels around 4 ng/ml for 12 weeks. After starting treatment with imatinib, in the following five tests tacrolimus levels ranged from 5.8 ng/ml to 8.9 ng/ml with no change in the dose of tacrolimus. After 45 days of treatment imatinib was suspended and tacrolimus levels recorded in the following test after discontinuation of imatinib fell to around 4 ng/ml.

Conclusions The increase in tacrolimus blood levels, without changing the dose, supports the possible interaction between imatinib and tacrolimus.

No conflict of interest.

PHC-027 THE PHARMACIST'S ROLE IN IMPROVING VALPROIC ACID PRESCRIPTIONS

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Background Valproic acid (VPA) is 90–95% protein bound to albumin; this binding can be saturated so other parameters that can modify the free fraction of VPA should be taken into account.

Purpose To identify areas for improvement in VPA use and monitoring in a tertiary hospital where the pharmacy service does not routinely send pharmacokinetic dose adjustment recommendations.

Materials and Methods A retrospective study was conducted from February to April 2012. All patients treated with VPA were included and grouped depending on whether VPA was part of their home treatment or not.

Variables collected were: dose, indication, total VPA serum concentration (C), drug interactions classified as $\geq C$ by Lexi-Comp, glomerular filtration rate (GFR), Child-Pugh score, albumin and bilirubin.

Results 30 patients were treated with VPA, 24 of whom were on VPA before admission (15 epilepsy, 9 psychiatric disorders and 1 unknown reason).

Reasons for admission were: 5 convulsions, 12 psychiatric disorders and 13 causes unrelated to VPA. At discharge 27 patients continued on VPA with a mean dose similar to the dose at admission.

C was determined in 14 patients: 5 were within the reference range (50–100 mg/L); 2 above, achieving therapeutic levels before discharge and 7 below. In these latter cases, 3 had an albumin < 4.2 g/dL, but none reached $C > 50$ mg/L after correcting it with the J. Hermida formula which is a theoretical method for normalising C in hypoalbumenic patients. GFR, Child-Pugh score and bilirubin were normal. Mean time between changes in dose and C determinations was 1.5 days (0–5 days).

21 drug interactions were detected in 15 patients, involving a total of 10 drugs. Only 2 interactions were reported: VPA meropenem and VPA lamotrigine.

Conclusions Changes in free fraction of VPA, due to hypoalbuminaemia, liver or kidney disease and hyperbilirubinaemia, must be detected.

C should be measured once a steady state has been achieved (3–5 days).

Drug interactions affecting VPA should be added to the pharmacy service's interaction notification programme.

No conflict of interest.

PHC-028 THERAPEUTIC DRUG MONITORING OF DARUNAVIR IN TWO DIFFERENT TREATMENT MODALITIES

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Background Darunavir (DRV) is a protease inhibitor (PI) that when boosted with ritonavir is effective against both wild-type and PI-resistant HIV. It's relatively long half-life supports once-daily dosing (QD) in treatment-naïve patients. To treat treatment-experienced patients twice-daily dosing (BID) is preferred.

Purpose To analyse the need for therapeutic drug monitoring (TDM)-guided interventions for darunavir and their results in patients receiving darunavir/ritonavir both in BID and QD modalities.

Materials and Methods A prospective study that included 38 patients was performed: 21 (55.3%) in the BID group and 17 (44.7%) in the QD group. Plasma darunavir levels were determined using an HPLC method and viral loads (VL) were measured. Assessments were performed at inclusion and whenever VL was detectable. Patients with detectable VL load were subjected to intervention (change in dose and/or adherence reinforcement) and another plasma drug determination was scheduled. Interventions were considered successful if VL became undetectable.

Results Abnormal plasma drug levels (outside a 1000–8000 ng/ml range) were found in 13/83 (15.6%) determinations which correspond to 9 patients and in all cases detectable VL were also found. Among measures yielding normal levels the proportion of cases

with detectable VL was 49/83 (59%). TDM-guided interventions were performed in 22/38 (58%) patients and were successful in 11 of them (7 BID and 4 QD).

Mean plasma levels in the BID group were greater than in the QD group: 3715 ng/ml (SD: ± 1679) and 2830 ng/ml (SD: ± 1030) respectively ($p < 0.02$). In the BID group cases with undetectable VL had mean plasma levels superior to those of cases with detectable VL: 4524 ng/ml (SD: ± 1679) versus 3375 (SD: ± 1679), $p < 0.05$.

Conclusions TDM-guided interventions could be useful in patients receiving darunavir/ritonavir and experiencing viral failure, especially if the BID dosing modality is used.

No conflict of interest.

PHC-029 VANCOMYCIN PHARMACOKINETICS IN ALCOHOL AND INTRAVENOUS DRUG ABUSERS

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Background Elimination of vancomycin is primarily by glomerular filtration (80–90%), but the liver may also be involved to a small extent. Chronic consumption of ethanol induces hepatic enzymes and can lead to hepatic damage. Both factors could affect vancomycin elimination. Moreover, the use of drugs of abuse could also affect vancomycin clearance.

Purpose To characterise vancomycin pharmacokinetic parameters in non-cirrhotic alcoholics, patients with alcohol-induced cirrhosis and intravenous drug abusers (IVDAs).

Materials and Methods Retrospective study in the aforementioned patients treated with vancomycin in whom therapeutic drug monitoring (TDM) was performed, between 2009–2012, in a tertiary University Hospital. Clinical and pharmacokinetic reports from TDM (PKS Abbot) were reviewed to obtain demographic characteristics, hepatic/renal surrogates, initial/recommended dosage, steady state (SS) distribution volume (V_{dSS}), clearance (CL), CSS_{min} and CSS_{max}. The therapeutic target was 7–12 mg/L for CSS_{min}. Patients with renal failure ($CL_{Cr} < 60$ mL/min) were excluded. Results are shown as a mean \pm SD (T-test for comparisons with controls).

Results Sixty-five patients were included. Demographic data were similar between the groups. 87.7% were men. Pharmacokinetic data is shown in table 1. As regards pharmacokinetic parameters, significant differences were only observed in CL in cirrhotic patients ($\#p = 0.02$).

Conclusions Vancomycin CL is significantly decreased in cirrhotic patients, probably due to hepatorenal syndrome. Initial dose reduction might be considered. Vancomycin CL tends to be higher in alcoholics and IVDAs. Higher doses could be needed to obtain therapeutic concentrations. Therefore, vancomycin TDM is highly advisable in all these groups of patients.

Abstract PHC-029 Table 1

	Control	Non-cirrhotic alcoholics	Cirrhosis	IVDA
Number of patients	20	18	18	9
CL (L/h)	5.27 \pm 1.47 [#]	6.40 \pm 2.16	4.27 \pm 1.18 [#]	6.53 \pm 1.91
Vd ^{SS} (L/Kg)	0.75 \pm 0.33	0.64 \pm 0.16	0.68 \pm 0.10	0.59 \pm 0.09
Initial dosage (mg/kg/day)	29.23 \pm 5.75*	26.55 \pm 7.35*	27.28 \pm 9.01*	28.05 \pm 6.12*
C ^{SS} _{min} (mg/L)	9.76 \pm 3.49	7.91 \pm 4.26	10.37 \pm 4.51	5.30 \pm 3.04

* $p > 0.05$; [#] $p = 0.02$

No conflict of interest.