Conclusions Optimization of the deployment of BCMA in the Geriatric units of Toulouse CHU allows us to plan the development of this practise over a large number of clinical departments at a later date.

No conflict of interest.

PHC-008 DEVELOPMENT AND APPLICATION OF A SIMPLE LC-MS METHOD FOR THE DETERMINATION OF PLASMA RILPIVIRINE CONCENTRATIONS

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[1]M Shibata, [1]M Takahashi, [1]N Fukushima, [1]F Yamaguchi, [1]T Nomura, [2]Y Yokomaku, [2]W Sugiura. *[1]National Hospital Organization Nagoya Medical Center, Pharmacy, Nagoya, Japan; [2]National Hospital Organization Nagoya Medical Center, Clinical Research Center, Nagoya, Japan*

Background Rilpivirine is a second-generation non-nucleoside reverse transcriptase inhibitor that is highly potent against both wild-type and drug-resistant HIV-1 strains. The quantification of rilpivirine in human plasma is important to support clinical studies.

Purpose Rilpivirine was just approved in May 2012 in Japan. Therefore, pharmacokinetic studies of rilpivirine have still not been completed in Japanese patients. We intended to develop a conventional method for determining plasma rilpivirine concentrations and compare plasma rilpivirine concentrations of Japanese HIV-1 infected patients with those of foreign healthy volunteers.

Materials and Methods We used a Waters Alliance 2695 HPLC and a Micromass ZQ-2000 MS, controlled with MassLynx version 4.0 software. Our method involves rapid liquid-liquid drug extraction from plasma and use of gradient elution on a reversed-phase C18 column. We recruited 34 Japanese HIV-1 infected patients who were treated with a rilpivirine-containing regimen at the National Hospital Organization Nagoya Medical Center, Japan. All patients had been given 75 mg rilpivirine once daily in combination with other antiretrovirals.

Results The LC-MS method established was validated by estimating the precision and accuracy for inter- and intraday analysis in the concentration range of 18–715 ng/ml. The calibration curve was linear in this range. Average accuracy ranged from 100.0 to 100.6%. Relative standard deviations of both inter- and intraday assays were less than 3.3%. In this study, mean rilpivirine plasma concentration for Japanese patients at trough was 58 ng/ml (n = 18). Mean rilpivirine concentration at peak was 126 ng/ml (n = 6). These levels were higher than rilpivirine concentrations seen in trials with healthy foreign volunteers.

Conclusions Our LC-MS method provides a conventional, accurate and precise way of determining rilpivirine in human plasma. In clinical practise, AUC of rilpivirine for Japanese HIV-1 infected patients is larger in comparison with foreign data. We think that this was caused by the poor build of Japanese HIV-1 infected patients.

No conflict of interest.

PHC-009 DRUG DOSE ADJUSTMENT IN RENAL FAILURE

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AM Rizo Cerdá, P Selvi-Sabater, MC Sanchez-Mulero, A Boso-Ribelles, B Arribas-Diaz, A Morego-Soler, N Manresa-Ramon, I Sanchez-Martinez, MD Najera-Perez, I Sanchez-Quilez. *Hospital Morales Meseguer, Pharmacy, Murcia, Spain*

Background In renal failure, alteration in the pharmacokinetics increases the frequency of overdoses.

Purpose To evaluate pharmaceutical care using a computer programme for drug dose adjustment in renal failure.

Materials and Methods The study period lasted from September 2011 to January 2012 (inclusive), in a 420-bed hospital. Every day creatinine values over 130 mmol/l were filtered. Treatment was reviewed and we obtained creatinine clearance values (Crockcoft & Gault) of selected patients. After consulting the drug dose adjustment on the sheet and in Micromedex, a report was sent with the pharmaceutical recommendation.

Results There were 68 interventions for the 2147 patients studied: Internal Medicine (34) Cardiology (1), Short Stay Unit (5), Orthopaedics (7), Urology (5), Haematology (7) Surgery (5), Neurology (1), Intensive Care Unit (ICU) (2) Oncology (1). 55.9% of notifications were for changes in the dose of enoxaparin (38), 11.8% of amoxicillin-clavulanic acid (8), piperacillin-tazobactam 14.7% (10), 8.8% levofloxacin (6), 2.9% meropenem (2), 2.9% ciprofloxacin (2), 1.5% imipenem (1) and 1.5% aztreonam (1). The proportion of suggested changes accepted was 58.8% (40). 5.9% (4) discontinued treatment, 5.9% (4) were discharged and 29.4% (20) not changed. Of the latter, five were for changes in the pattern of enoxaparin in trauma patients, another 5 from Internal Medicine and 2 more from Haematology and ICU. The rest of them were changes in the pattern of antibiotics (imipenem 1, 2 levofloxacin, 1 meropenem, 1 ciprofloxacin, piperacillin-tazobactam 3) that were given out in the different services.

Conclusions A high percentage of doctors followed the recommendations. Part of the unaccepted tally corresponds to trauma patients whose prophylactic regimen of enoxaparin (40 mg/24 h) was not modified due to the service criteria. Some of the antibiotic prescriptions were not changed because of the severity of the patient's illness (1 levofloxacin and 1 Internal Medicine Meropenem Imipenem Oncology and 1). The rest were rejected without explanation.

No conflict of interest.

PHC-010 DRUG INTERACTION: A CASE REPORT

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E Fernández López, E Tevar Alfonso, MA Ocaña Gomez, JA De León Gil, I Plasencia García, J Merino Alonso, R Jurado López, E Marqués Guell. *Hospital Nuestra Señora de Candelaria, Farmacia Hospitalaria, Santa Cruz de Tenerife, Spain*

Background The serum concentration of valproic acid (VPA) in epilepsy patients is reduced to sub-therapeutic by the administration of carbapenems antibiotics.

Purpose Description of the interaction and communication to the Pharmacovigilance Center with yellow cards.

Materials and Methods A 66-year-old was admitted to the resuscitation unit after being operated on for perforation peritonitis secondary to cytomegalovirus. Treatment was with imipenem because the suspicion of extended-spectrum beta-lactamases (ESLB) organisms was confirmed. Concomitant treatment was with VPA 400mg–400mg–400mg due to an underlying disease, epilepsy. The pharmacy department was asked to cheque the VPA blood level: initially levels were within the therapeutic interval (TI), but at 24 hours after starting treatment with imipenem it decreased by 70% to below the TI. In addition, because of the proconvulsive properties of imipenem, the patient started to have convulsions.

After reporting the suspected interaction, the doctor decided to change the antibiotic to meropenem 1g/8h and so eliminate at least the pharmacodynamic component of the interaction. After 24 hours of the change VPA levels continued to fall and at 48 hours were almost undetectable (≤3 mcg/mL). VPA dose was increased, 1000 mg-1200 mg-1000 mg, without the situation reversimg. After 30 days meropenem was suspended and VPA levels did not return to the TI until after approximately 120 h.

Results Although the exact mechanism is unknown, it is suspected to be of the pharmacokinetic kind and at several levels:

intestinal absorption, enterohepatic cycling, distribution and hepatic conjugation. This would explain the rapid and of intense decline in levels, in spite of the high dose of antiepileptic, and the difficulty reversing the situation.

Conclusions Given the magnitude of the reduction in plasma levels, the speed with which it appears and the difficulty of getting it back at TI, we think that monitoring and dose adjustments are not useful to manage this interaction. A change of anticonvulsivant or antibiotic treatment should be considered.

No conflict of interest.

PHC-011 DUAL ABSORPTION IN INTRANASAL ADMINISTRATION: A NEW PHARMACOKINETIC MODEL

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[1]C Neef, [1]N Veldhorst-Janssen, [2]N Punt, [3]PHM Van der Kuy, [4]M Marcus. *[1]Maastricht University Medical Center, Clinical Pharmacy & Toxicology, Maastricht, The Netherlands; [2]Maastricht University, Toxicology, Maastricht, The Netherlands; [3]Orbis Medical Center, Pharmacy, Sittard-Geleen, The Netherlands; [4]Maastricht University Medical Center, Anaesthesiology, Maastricht, The Netherlands*

Background The role of pharmacokinetic modelling is important in the development of new formulations. Some of these models are related to a particular dosage form, others are similar to models that have already been developed. Intranasal (IN) administration can be an example of a dosage form with a specific pharmacokinetic model, especially when it is applied to create a systemic effect.

Purpose To design a pharmacokinetic model that adequately describes a dual absorption profile of the concentration-time curve for intranasal administration.

Materials and Methods A strategy to predict dual absorption was developed to describe the pharmacokinetics of an intranasal administration (model1 and model2). A programme for fitting and simulation was developed (SIMLAB). Midazolam nasal spray was used as an example for this model. To validate the final pharmacokinetic model, Monte Carlo simulations were performed.

Results We had trouble fitting the observations to a single one-compartment dual absorption model. In many cases a flip-flop condition occurred in which the fitted absorption rate was lower than the estimated elimination rate, and the elimination rate showed an unrealistic value. To prevent this flip-flop condition, we used the absorption parameters from the associated observations. We developed the following model: the model superposes two one-compartment absorption models where the dose is split up over the two compartment inputs and the concentration-time curves are separated by using different lag-times (t0). Monte Carlo simulations resulted in a plasma concentration-time profile, indicating the median concentration and the 5th–95th percentile ranges. Biphasic profiles were observed starting at a parameter error of 15%, increasing to 13.6% of biphasic profiles at a parameter error of 50%. When increasing the difference between a parameter in Model 1 and Model 2, the contribution of t0 to creating a local minimum exceeded the contribution of ka. The AUC of the measured and estimated curve was 201.6 μg/L*h and 201.3 μg/L*h, respectively.

Conclusions The model developed is able to fit concentration-time curves showing individual dual absorption curves adequately.

No conflict of interest.

PHC-012 ERLOTINIB IN NON-SMALL CELL LUNG CANCER PATIENTS FROM FERNANDO FONSECA HOSPITAL

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J Fernandes, P Frade, S Teixeira, R Afonso. *Hospital Fernando Fonseca, Pharmacy, Amadora, Portugal*

Background The oral epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) erlotinib is an established second-line treatment for advanced non-small cell lung cancer (NSCLC). Erlotinib delays disease progression and increases survival after first-line chemotherapy in patients with advanced NSCLC as second-line treatment. Maintenance treatment with erlotinib, when compared to placebo, could be associated with a significantly longer progression-free survival and tolerability mainly in EGFR-activating mutation tumours. However second-line treatment with erlotinib is not more effective than chemotherapy (pemetrexed or other). In terms of traditional toxicities associated with chemotherapy, erlotinib seems to have a better safety profile than chemotherapy, with no haematological toxicities. The most common event has been mild to moderate skin rash which is relatively manageable.

Purpose To study erlotinib's efficacy profile in Fernando Fonseca hospital NSCLC patients.

Materials and Methods We followed up 30 NSCLC patients, who had taken erlotinib before and after other approved chemotherapies, during the 14 months starting from June 2011. During this period we collected patient demographics and baseline characteristics and also their EGFR mutational status. To determine erlotinib effectiveness we calculated progression-free survival (PFS) which was defined as the time from starting erlotinib treatment to the date of documented disease progression or death.

Results The median age of our 30 patients was 62.5 years. The most common pathological subtype was adenocarcinoma (66.7%). 46.6% of our patients had received one prior chemotherapy regimen before erlotinib and 36.6% had received two prior chemotherapy regimens before erlotinib. Two patients took erlotinib as a first line treatment. Median PFS for second-line erlotinib patients was 18.7 weeks while for third-line erlotinib patients it was 12.3 weeks. Only 50% of our patients had information available regarding EGFR mutational status; however patients who harboured tumour-associated EGFR activating mutations seemed to have higher response rates to erlotinib. Rash was the most common treatment-related adverse event with erlotinib, as expected.

Conclusions Our results show that maybe there could be a better disease outcome for advanced NSCLC patients if the oral epidermal growth factor receptor tyrosine kinase inhibitor (erlotinib) were administered as a second-line treatment instead of using it as a third-line treatment. As far as EGFR mutational status is concerned it seems that enhanced efficacy is related to EGFR mutation-positive disease.

No conflict of interest.

PHC-013 EXPERIENCE WITH CANNABINOID TREATMENT

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MT Martín, M Gómez, MS Rivero, MR Garrido, LC Fernández. *Hospital San Pedro Alcántara, Pharmacy Service, Caceres, Spain*

Background Since March 2011 cannabinoids have been authorised in Spain for the treatment of spasticity due to multiple sclerosis (MS). The product is composed primarily of two cannabinoids: CBD (cannabidiol) and THC (delta 9 tetrahydrocannabinol) and it is administered as a metered dose oro-mucosal spray. The dose should be individualised after a titration period.

Purpose To describe the use of CBD-THC in our hospital and to evaluate adverse effects and the quality of life of the patients treated.

Materials and Methods Descriptive study of all patients treated with CBD-THC from March 2011 to September 2012.

Patients were monitored from the start of their treatment. We recorded the titration period, maintenance dose and adverse