

anaplastic large-cell lymphoma in adults. It is currently awaiting conditional marketing authorization for adults in Europe. A Phase I/II study in paediatrics is at the moment recruiting. Brentuximab vedotin is administered every three weeks at 1.8 mg/kg (half-life ranges from 4 to 6 days and steady-state was achieved in 21 days for the ADC). Administration is possible in France, after the ANSM granted it temporary authorization on a named patient basis.

An 8-year-old male child, with a diagnosis of anaplastic large-cell lymphoma, was treated according to the ALCL99 protocol. Two months after diagnosis the tumour grew under this first-line chemotherapy. A multidisciplinary group decided to start brentuximab vedotin treatment. A total of 5 courses spaced 3-weekly were scheduled combined with chemotherapy. Signs of the tumour disappeared, thorax imaging normalised, fever and pulmonary and mediastinum adenopathies decreased.

**Conclusions** After the 4th dose of brentuximab vedotin, the treatment was well tolerated by the patient and the tumour regressed. Among adults, the median response is about 12 months. Thus, confirmation of efficacy still has to be evaluated. Further studies are required to establish the efficacy and safety profile in the paediatric population.

No conflict of interest.

#### DOI-079 VALPROIC ACID AND BEHAVIOUR DISORDERS: OBSERVATION OF EFFICIENCY AND TOXICITY IN A COGNITIVE-BEHAVIORAL UNIT

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**Background** In order to limit neuroleptic use in the elderly, because of cardiovascular events, specialists in charge of behaviour disorders don't have many therapeutic options in cognitive-behavioural units (CBU).

**Purpose** Valproic acid (VPA) is an anticonvulsant and/or a mood stabiliser that can be used in a behavioural way in CBU. One side effect of VPA is hyperammonaemia, which can lead to sedation and changes in behaviour or personality.

**Materials and Methods** Inclusion criteria were opposition, agitation, aggressiveness or impulsiveness. Ammonia levels were assessed before starting the VPA, between 2 and 4 days and after 5 days with VPA. For each person included, Cockcroft's creatinine clearance, medical background and neuroleptic co-prescriptions were identified. Results are presented with mean  $\pm$  SEM.

**Results** The population was defined by an average age of 79.3 y  $\pm$  1.74, a sex ratio of 15 men for 6 women; a creatinine clearance of 65.4 mL/min  $\pm$  8.9, no patients had liver troubles or a history of epilepsy. 21 patients received VPA in the CBU, for at least one of the following indications: opposition (n = 9), agitation (n = 13), aggressiveness (n = 16) or impulsiveness (n = 6). 9/21 patients came out of the CBU with VPA (42.85%), 13/21 without VPA (61.9%), 5/21 with a neuroleptic (23.8%) and 8/21 without VPA or a neuroleptic (38.1%). Ammonia rates at D-1, between D2 and D4 and after D5 were respectively 47.47  $\mu$ M  $\pm$  3.71, 51.4  $\mu$ M  $\pm$  6.43 and 63.76  $\mu$ M  $\pm$  4.95. Response rate to VPA was 55% (5/9 patients) for opposition, 37.5% (6/16) for aggressiveness, 38% (5/13) for agitation and 66.6% (4/6) for impulsiveness.

**Conclusions** Those results show that only one of every two patients with VPA were responders, and average ammonia increases during treatment. However, 100% of patients going out with VPA didn't have any neuroleptics and for 33%, VPA contributed to stopping neuroleptics.

No conflict of interest.

## Pharmacotherapy: pharmacokinetics and pharmacodynamics (including: ADE, TDM, DUE)

### PHC-001 AMIKACIN DOSING TO TREAT RESPIRATORY TRACT INFECTIONS ACCORDING TO PATIENT'S BODY MASS INDEX

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**Background** Body mass index (BMI) is a factor related to the disposition of aminoglycosides (AMG). Dosage is based on total body weight (TBW) or adjusted body weight (ABW) according to patients' BMI.

**Purpose** To assess if the amikacin dosage prescribed to patients matches with the dosage based on BMI.

To calculate the optimal cut-off point of BMI that predicts a 10% discrepancy between dosage based on TBW or ABW.

**Materials and Methods** Retrospective study January 2003–December 2010 performed in a 450-bed tertiary hospital.

Dosage of 15 mg/TBW was considered except for patients with TBW > 30% over ideal body weight (IBW). That dose was calculated according to ABW:  $ABW(kg) = IBW + 0.4(TBW - IBW)$  as recommended.

Patients included: intravenous amikacin treatment of respiratory tract infections in an extended-interval dosing regimen with therapeutic drug monitoring of amikacin.

Patients excluded: <18 years, ClCr < 60 mL/min, sepsis, lack of data.

Data collected: demographics, TBW, height, BMI, renal function. Amikacin levels: fluorescence polarisation immunoassay (TDX, Abbott Lab)

Pharmacokinetic analysis: Bayesian estimation compartmental model (PKS programme)

Statistical analysis: ROC curve.

**Results** 133 patients (79.70% men). Mean ( $\pm$ SD): age: 62.12 years ( $\pm$ 15.48); TBW: 65.52kg ( $\pm$ 13.43); height: 166.89 cm ( $\pm$ 7.44); serum creatinine baseline: 0.68 ( $\pm$ 0.19) and CrCl: 97.32 mL/min ( $\pm$ 34.67).

Difference between TBW dose vs. ABW dose (mg)(%): BMI[<16]:16.45 vs. 16.45(0%); BMI[16–18.49]:16.57 vs. 16.57(0%); BMI[18.5–24.9]:15.28 vs. 15.61(2.2%); BMI[25–29.9]:12.70 vs. 14.30(11.2%); BMI[30–34.9]:11.56 vs. 14.34(19.3%); BMI[35–39.9] and [>40]: 1 patient.

A ROC curve was built to determine the best cut off point of BMI: 26 mg/m<sup>2</sup>

Difference between recommended dosage and prescribed dosage (mg): BMI[<16]: +1.45; BMI 16–18.49: +1.58; BMI[18.5–24.9]: +0.64; BMI[25–29.9]: –0.70; BMI[30–34.9]: –0.66; BMI[35–39.9] and [>40]: 1 patient.

**Conclusions** Considerable variation between the dosage of amikacin based on TBW and ABW was observed with a reduction of recommended dose in patients with BMI  $\geq$  25 kg/m<sup>2</sup> and an overdose in patients with BMI < 24.9 kg/m<sup>2</sup>.

A reduction of 10% or more of the adjusted calculated dose of amikacin was observed in patients with BMI  $\geq$  26 kg/m<sup>2</sup>.

No conflict of interest.

### PHC-002 ANALYSIS OF THE INCIDENCE OF POTENTIAL DRUG INTERACTIONS IN HOSPITALISED PATIENTS

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**Background** Prescriptions with more than one drug increase the risk of drug-drug interactions, treatment failure, large pharmacological effects and adverse events.

**Purpose** To estimate the frequency of potential drug-drug interactions in prescriptions for hospitalised patients, and to identify the factors associated with these prescriptions.

**Materials and Methods** The work was in part sited in the Specialty Hospital in Rybnik (Poland) with the pharmacotherapy team. One of the tasks of the Team was to assess on the basis of documentation, the frequency of random combinations of drugs prescribed and the risk of adverse interactions. Analyses of prescriptions for medicines were made on randomly selected days. The analysis included 760 patients on the fourteen different wards of the hospital. Age, gender and administration of the drugs were noted. The potential D-DIs were identified and recorded.

**Results** Generally 59.42% of the patients received drugs identified as potentially causing D-DIs (52% of the patients were women, 48% were men). 59% of patients older than 65 years of age received a prescription including one potential D-DI. The average number of medicines taken by one patient was 3.29. The highest numbers of medicines were taken by a cardiology patient (8) and an internal patient (5). The greatest risk of occurrence of drug interactions was in patients in the cardiology department medical care facility (84.3%) and internal medicine department (69.9–80%). The lowest was observed in patients in the laryngological, ophthalmic and rehabilitation departments.

The potentially dangerous pairs of drugs most frequently prescribed were: furosemide-angiotensin converting enzyme inhibitors, non-steroidal anti-inflammatory drugs/angiotensin converting enzyme inhibitors, non-steroidal anti-inflammatory drugs/warfarin, spironolactone/potassium and proton pump inhibitors/simvastatin. Gender and the number of drugs received were factors associated with the potential D-DI.

**Conclusions** The high percentage of prescriptions with potential drug-drug interactions makes it necessary to adopt alerting strategies that include warning about any associated factors identified and to implement educational programmes. This action may improve the quality of prescribing and reduce the risks for hospitalised patients.

No conflict of interest.

#### PHC-003 ASSESSMENT OF THE IMPACT OF PHARMACOKINETICS MONITORING RECOMMENDATIONS

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**Background** In our general hospital, with 450 beds, the Pharmacy department (PD) has a pharmacokinetics area in which vancomycin and aminoglycosides are monitored in non-critical adult patients.

The monitoring starts when:

- There is a medical request (MR).
- Or a pharmaceutical proposal (PP) is made followed by medical acceptance (MA)

**Purpose** To determine and quantify the acceptance of monitoring recommendations made by the PD, to assess the recommendations and describe PP monitoring.

**Materials and Methods** Prospective and descriptive study. We collected patients treated with vancomycin or aminoglycosides over a 3-month period (March-June/2012), excluding those for whom there was an MR. Patients included in our study were divided into two categories: monitoring was recommended and not recommended.

Criteria for recommended monitoring: GFR < 60 ml/min, >5 days' treatment, geriatric, obese or concomitant nephrotoxic drugs.

Recommendation was made through the electronic prescription programme with the appropriate justification. If a positive answer was not obtained in two days, it was considered as 'not accepted'.

Patients requiring dose adjustments and the mean number of dose adjustments necessary to achieve appropriate plasma concentrations were also recorded.

**Results** View table.

Due to pharmaceutical intervention, 19.6% patients were monitored, the majority of them with vancomycin (13.3%).

**Conclusions** Pharmacy recommendation is an instrument to strengthen monitoring of certain drugs in some situations. Because gentamicin is used mainly in surgical prophylaxis, the number of patients who might need monitoring was low. Out of range initial concentrations with vancomycin and amikacin, might indicate an inappropriate dosage. The low number of adjustments per patient showed that the correct pharmacokinetic calculations had been made by the PD.

Abstract PHC-003 Table 1

Antibiotic	N*	PP	MA	Relevant recommendation	N° adjustments/patient
Vancomycin	112	53(47.3%)	32(60.4%)	19(60.8%)	1.5
Amikacin	25	10(40.0%)	7(70.0%)	3(42.9%)	1
Tobramycin	8	2(25.0%)	1(50.0%)	1(50.0%)	2
Gentamicin	95	18(18.9%)	7(38.9%)	1(14.3%)	1
TOTAL	240				

\* Patients treated with the antibiotics in question minus patients for whom there was already an MR

No conflict of interest.

#### PHC-004 BAYESIAN APPROACH IN THE DOSING OF VANCOMYCIN IN THE TREATMENT OF STAPHYLOCOCCAL INFECTIONS

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**Background** Vancomycin is primarily effective against Gram-positive cocci. However, as it can only penetrate the tissue superficially, it is uncertain if it is really able to achieve concentrations of therapeutic benefit at the site of infection. Suboptimal concentrations have been associated with lack of clinical response and increased resistance. There are no clear criteria on pharmacokinetic parameters associated with a good response, although the most conservative proposals consider an AUC/MIC > 400, in pathological conditions such as pneumonia and meningitis. Some authors have described the failure to achieve these values with the usual doses when the MIC > 2.

**Purpose** Our work evaluates the pharmacokinetic data of vancomycin in a group of 30 inpatients, and individual Bayesian estimates of the dose needed to overcome the described value of AUC/MIC > 400.

**Materials and Methods** We estimated the kinetic parameters of a population of 30 patients with a staphylococcal infection through a Bayesian model with application v.1.0 Abbotbase Pharmacokinetic Systems. From each patient we obtained the MIC, and the dose required to obtain an AUC/MIC > 400. We calculated the percentage of patients who reached target values for AUC/MIC with a standard dose of 1 g/12 h and those receiving an individualised dose according to the kinetic parameters obtained by Bayesian setting. Maximum doses of 4 grammes/day were considered.

**Results** Mean clearance (CI 95%) obtained through Bayesian estimation was 3.91 l/h (3.2–4.6). Median MIC value was 1 mcg/ml. According to these data, 57% of patients would reach therapeutic AUC values with conventional dose. However, if the dose is set individually 90% of patients would reach the target value, with a mean calculated dose of 2300 mg (CI95%: 1550–3000).