revision of antimicrobial therapies and surveillance of antibiotic consumption.

Purpose The aim of the study was to analyse antibiotic use and microbiological data in the ward between 2010 and 2017.

Material and methods Data was collected on systemic antibiotics dispensed from the pharmacy's database. Both WHO defined daily dose (DDD) and prescribed daily dose (PDD) methods were used to analyse the antibiotic consumption, standardised to 100 patient days. PDDs were defined according to therapeutic guidelines and revised by infectologists. Microbiological data were collected from the Microbiology Department's database.

Results The cost of antibiotics accounts for 65% of all pharmaceutical expenses between 2010 and 2017. Twenty-eight antibacterial agents were used in 2017, 30 in 2013 and 2010. In 2017, 11 agents were responsible for the DU90% segment of the consumption. Most extensively used agents were amoxicillin-clavulanic-acid, cefuroxime and ciprofloxacin. There was a significant difference between the results of DDD-PDD analyses. The utilisation of clindamycin (14.48 DDD/100 patient days in 2013 vs. 2.99 in 2017 – the same in PDDs) and ceftriaxone (3.61 vs. 0.31 DDD/100 patient days – the same in PDDs) decreased notably, while the use of narrow-spectrum beta-lactams increased in the past 3 years (from 2.93 to 7.84 DDD/100 patient days – 1.12 vs. 4.13 PDD/100 patient days), which was an initial goal of the pharmacists' interventions. Microbiological data showed an increased rate of multiresistant pathogens, especially Vancomycin-resistant *E. faecium* (0 in 2010, two in 2013 and 14 in 2017), resulting in increased consumption of reserve antibiotics such as linezolid (no use until 2015, 0.23 DDD/100 patient days in 2017) and tigecycline (no use until 2013, 0.28 DDD/100 patient days in 2017).

Conclusion Monitoring the use of antibiotics and comparing results with microbiological data provides a range of local resistance conditions, which are fundamental to antimicrobial guideline development. The data highlights desirable trends and critical points, allowing pharmacists to feedback to prescribers and emphasise the value of their interventions. Interpretation of results must account for the fact that the generally accepted DDD method can be incorrect due to differences in antibiotic dosing.

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No conflict of interest.

4CPS-057

HOW WELL IS THE TARGET CONCENTRATION OF VANCOMYCIN ACHIEVED IN INTENSIVE CARE UNIT PATIENTS?

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Background The recommended serum trough concentration of vancomycin is 15–20 mg/L.¹ Concentrations outside this interval increase the risk of adverse effects, therapeutic failure and resistance development. To achieve the target trough concentration more rapidly, it is recommended to start with a loading dose of 25–30 mg/kg in critically ill patients. Thereafter,

the continuous dosing regimen is 1000 mg every 8th or 12th hour, but under severe infections a dose of 15–20 mg/kg every 8–12 hours can be considered.

Purpose To determine to what extent trough concentrations of vancomycin are within the recommended range, in patients in intensive care units (ICUs).

Material and methods A retrospective observational study was performed at Uppsala University Hospital, Sweden. Data on vancomycin dose regimen, treatment duration, serum concentration, type of infection and demographic information were extracted from two electronic medical record systems: MetaVision and Cosmic. One-hundred and sixty-four patients treated with intravenous vancomycin at any of the four ICUs: Central Intensive Care Unit (CICU), Thorax Intensive Care Unit (TICU), Burn Injury Intensive Care Unit (BIICU) and Neurologic Intensive Care Unit (NICU) were included.

Results In total, 922 vancomycin concentrations were registered in 185 treatment episodes in 164 patients. More than half (54.7%) of all the trough concentrations were outside of target range, 21.8% were subtherapeutic and 32.9% supratherapeutic. A trend was seen that patients in the CICU and TICU more frequently had supratherapeutic concentrations and patients treated in the BIICU and NICU more often had subtherapeutic concentrations. Out of the 185 treatment episodes, 147 were initiated at an ICU and 61.2% of these started with a loading dose. A majority of cases (74%) had >1 trough concentration outside of target range and 55% of these non-therapeutic concentrations led to a change in dose regimen.

Conclusion More than half of the measured vancomycin concentrations were outside the recommended target range. Dosing and monitoring of vancomycin in patients treated in an ICU should be improved.

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No conflict of interest.

4CPS-058

AVOID SIMULTANEOUS PRESCRIPTION BETWEEN LINEZOLID AND VORICONAZOLE: PHARMACOKINETIC STUDY

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Background Taking linezolid (LIN) and voriconazole (VCZ) at the same time is common in routine clinical practice. Voriconazole is eliminated by hepatic metabolism mainly by CYP2C19 isoform and less by CYP3A4 and CYP2C9. Linezolid is 65% metabolised in two metabolites and the main metabolite is independent of cytochrome P450-isoenzymes.

Purpose The aim of the study was to analyse the potential interaction between LIN and VCZ in patients diagnosed with fungal and active bacterial infection who require both anti-infective drugs simultaneously.

Material and methods Single-centre retrospective observational study was carried out in patients under simultaneous treatment with LIN and VCZ between March 2009 and December 2015. VCZ serum baseline concentrations before treatment

with LIN and after at least 3 days of combined therapy were analysed by liquid chromatography (HPLC). Oral VCZ clearance (CL/F in L/h) was estimated before (CL/Fb) and during treatment with LIN (CL/Fd LIN). It was assumed as VCZ therapeutic range 1.5–4.5 mcg/mL in *Candida* spp. infections and 2–4.5 mcg/mL in *Aspergillus* spp. Demographic variables (age, sex), treatment (dosing schedule, date and time of each administration), clinics (diagnosis, microbiological information, etc.) and kinetics (date and time of each sample extraction) were collected.

Results Five patients were analysed with a median age of 67 years (range: 57–73), all of them males. Mean daily dose $\pm$ SD administered were 454.5 ± 157.2 mg (VCZ) and 1,200 mg (LIN). Serum baseline concentration of VCZ before LIN was 2.7 ± 0.8 mcg/mL. CL/Fb and CL/Fd of VCZ were, respectively, 6.3 ± 1.7 L/h and 22.09 ± 11.74 L/h, which represents a large increase of 250%. VCZ and LIN interaction generated infra-therapeutic VCZ concentrations in 80% of patients (n=4). Three patients had to change anti-infective treatment and two patients required increased VCZ dose up to 75% to reach at least the lower limit of the therapeutic range.

Conclusion Adding LIN to VCZ treatment increases VCZ clearance between 250%–700% and serum antifungal concentrations decrease clinically. This translates into a loss of effectiveness in antifungal treatment in 80% of cases. Therefore, the use of this combination is contraindicated and if clinically there is no other alternative, VCZ pharmacokinetic monitoring is recommended to ensure the effectiveness of antifungal treatment.

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No conflict of interest.

4CPS-059 EFFECTIVENESS OF MEROPENEM TREATMENT IN CRITICAL PATIENTS: PHARMACOKINETIC STUDY

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Background Pharmacokinetic/pharmacodynamic efficacy index (PK/PD) for carbapenems, in critical patients, is the maintenance of a free concentration drug, 4–5 times above the minimum inhibitory concentration (MIC) in the isolated germ during 100% of the dosage range. Ensuring this goal is important and requires the use of pharmacokinetic monitoring (TDM).

Purpose Analyse the efficacy of pharmacokinetic optimised meropenem's regimen based on PK/PD criteria and compare it with empirical carbapenem's regimen adjusted by renal function in patients admitted to the intensive care unit.

Material and methods Naturalistic retrospective, observational cohort study, carried out in critically ill patients treated with meropenem from May 2011 to December 2017. Patients were divided into two cohorts: cohort A if they had pharmacokinetic intervention or cohort B if not. In pharmacokinetic analysis two serum samples per patient were extracted (peak and elimination point) to quantify total and free concentration of meropenem. Individual pharmacokinetic parameters were estimated by the Sawchuk–Zaske method to find out what percentage of time, free concentration exceeded four times MIC of isolated germ and dosage regimen was adjusted when

necessary. When CMI was not available, the epidemiological limit of EUCAST_(ECOFF) 2 mcg/mL was used.

Clinical and bacteriological responses were the main goals. Data was analysed using STATA12.0. Propensity score (PS) of each patient was calculated and patients in cohort A were compared and paired one by one with those of cohort B with similar PS.

Results One-hundred and fifty-six patients were included, 78 in each cohort after matching by PS. Main antimicrobial treatments were targeted (71.8% in cohort A and 73% in cohort B). Median duration of meropenem was 11 days (range: 2–31 days). In cohort A, dose adjustment was performed in 65% (n=51) of patients and in up to 88% (n=45) of them it was recommended to reduce dose or extend dosage range. Cohort A was associated with clinical improvement (OR: 1.624, 95% CI: 0.82 to 3.23, p=0.167), bacteriological (OR: 0.636, 95% CI: 0.27 to 1.48, p=0.292), fever resolution (OR: 2.415; 95% CI: 1.04 to 5.61, p=0.040), decreased inflammatory parameters (statistically significant PCR (p=0.0065) and procalcitonin (p=0.0099), lower hospital mortality (OR: 1.184; 95% CI: 0.52–2.68, p=0.685) and early mortality during first 14 days after hospital discharge (OR: 0.7505, 95% CI: 0.1184 to 4.76, p=0.761), against cohort B.

Conclusion Meropenem daily dose was decreased in 56% of critical patients monitored. TDM is important in fighting against antimicrobial resistance, it is a guarantee of safety and it allows a reduction in healthcare cost.

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No conflict of interest.

4CPS-060 PREVALENCE OF VANCOMYCIN-RELATED NEUTROPAENIA, THROMBOCYTOPAENIA AND ACUTE KIDNEY INJURY

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Background Vancomycin is a glycopeptide antibiotic widely used to treat Gram positive related infections. It is well known for its nephrotoxic and ototoxic profile, but neutropenia and thrombocytopenia are not so well described.

Purpose The aim of this study was to describe the prevalence of some relevant vancomycin-related adverse events (AE): neutropenia, thrombocytopenia and acute kidney injury (AKI).

Material and methods This retrospective observational study was conducted in all patients admitted to Donostia University Hospital that received vancomycin during 2016 and 2017 and were monitored by the pharmacy department (PD).

Exclusion criteria: patients with neutropenia, thrombocytopenia or AKI prior to vancomycin therapy.

Collected data: diagnosis, absolute neutrophil count (ANC), absolute platelet count (APT) and creatinine clearance (CrCl, calculated with Cockcroft–Gault formula) prior and during vancomycin therapy. Neutropenia was defined as ANC <1000 cel/microL, thrombocytopenia as APT <100.000 cel/microL and AKI as CrCl <60 ml/min or decrease in CrCl of 25%.