4CPS-031 THERAPEUTIC DRUG MONITORING OF CEFTAZIDIME/AVIBACTAM ADMINISTERED BY CONTINUOUS INFUSION: PK/PD TARGET ACHIEVEMENT AND CLINICAL OUTCOMES

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Background and Importance Ceftazidime/avibactam (CAZ/AVI) is a novel betalactam antibiotic utilised for multi-drug resistant (MDR) gram-negative bacteria. Therapeutic drug monitoring (TDM) ensures that CAZ/AVI levels achieve the pharmacokinetic/pharmacodynamic (PK/PD) target. Continuous infusion (CI) has been used to optimise CAZ/AVI pharmacodynamics.
Aim and Objectives To analyse the correlation between PK/PD target attainment of CAZ/AVI administered by CI, clinical outcomes and toxicity.
Material and Methods Patients treated with CAZ/AVI administered by CI and undergoing TDM of the CAZ plasma concentrations were included. Definitions:
CAZ/AVI PK/PD target:

- time that CAZ free concentrations remain 4 times above the minimum inhibitory concentration (MIC) of the causative pathogen (%*f*T>4xMIC).
- Overexposure:%*f*T>10xMIC.
- Clinical cure: disappearance of all signs and symptoms related to the infection and no requirement for additional antibiotic treatment initiation (except as part of de-escalation strategy) for the disease to be investigated within 48h after completion of the study drug.
- Thirty-day all-cause mortality: death from any cause during the 30 days following the end of treatment.

When real MIC was not available, a MIC of 8 mg/L was assumed.
Results Thirty-one patients (28 males, median (range) age of 64 (37-78) years) infected with extensively drug-resistant *Pseudomonas aeruginosa* and extended-spectrum betalactamase-producing *Klebsiella pneumoniae* were included (26 directed treatments and 5 empirical).

Twenty-six (83.9%) achieved the PK/PD target, 15 of which presented overexposure. Only 4 (26.6%) overexposed patients presented adverse reactions (3 increased liver enzymes and 1 thrombocytopenia).

Twenty-one (67.7%) patients achieved clinical cure, 18 (85.7%) of which achieved the PK/PD target. There was a higher frequency of patients with a%*f*T>4xMIC that achieved clinical cure (18/26 (69.2%) in patients with clinical cure *vs* 2/5 (40%) with clinical failure, p= 0.686).

The 30-day all-cause mortality was 19.4% (6 patients). A lower mortality rate was observed in patients that did achieve a%*f*T>4xMIC (14.8%) in patients who survived vs 50% in those who died, p=0.096.
Conclusion and Relevance CI seems a useful strategy to reach the PK/PD target of CAZ/AVI. Few patients with overexposure presented adverse events. There seems to be a correlation between PK/PD target attainment, clinical cure and 30-day all-cause mortality but larger studies with bigger samples are needed.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest

4CPS-034 ANALYSIS OF THE EFFECTIVENESS OF SOTROVIMAB IN PATIENTS DIAGNOSED WITH COVID-19

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Background and Importance Sotrovimab is indicated in treatment of COVID19 in adults and adolescents who do not require supplemental oxygen and who are at increased risk of progressing to COVID-severe. The drug is administered according to prioritisation criteria published by the Spanish Agency of Medicines and Health Products (AEMPS)1.
Aim and Objectives To analyse the effectiveness of sotrovimab and to know the profile of patients.
Material and Methods Observational, retrospective and descriptive study in a tertiary level hospital. Patients who had received sotrovimab from January/2022-May/2022 were included. Variables: sex, age, mild-moderate/severe disease, vaccination-COVID, risk factors, hospitalisation/death at 29 day. Effectiveness was measured as rate of patients without progression to COVID-severe (defined as hospitalisation/death at 29 days). Variables were collected from digital medical records and in-hospital electronic prescribing.
Results Thirty-seven patients were included, mean age=61 years (21-82), 20 women (54.05%). Twenty-nine patients (78.38%) had mild-moderate COVID. 29 patients (78.38%) had received a complete vaccination regimen (3 doses), 6 patients (16.22%) two doses and 2 patients (5.41%) not vaccinated. Risk factors: 23 hypertension (62.16%), 13 diabetes (35.14%), 5 obesity (13.51%) and 4 asthma (10.81%). All patients were immunosuppressed. 17 patients (45.94%) with 2 risk factors, 9 with 3 risk factors (24.32%), 7 with 1 risk factor (18.91%) and 2 patients (5.40%) with 4 risk factors. According to the AEMPS prioritisation criteria, all belonged to the group of 'Immunocompromised persons and high-risk conditions, regardless of vaccination status'. The high-risk conditions were: 23 patients (62.16%) had received solid organ transplantation with immunosuppressive treatment, 13 patients (35.14%) had received immunosuppressive treatment with antiCD20 in the previous 6 months (100% rituximab) and 1 patient (2.7%) was receiving active treatment with myelotoxic chemotherapy (inotuzumab) for acute lymphocytic leukaemia. 7 patients (18.9%) were hospitalised/dead at 29 days (3 exitus). All these patients had received rituximab. 30 patients (81.1%) did not progress to severe COVID. During the study period, 6 patients attended the emergency department, without admission.
Conclusion and Relevance Most patients presented good response and tolerance to treatment. This result was independent of previous treatments or risk factors. Previous treatment with anti-CD20 seems to show a tendency to progression to severe COVID. Long-term studies are needed to confirm results

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4CPS-037 INDIRECT COMPARISONS OF BIOLOGICAL TREATMENTS IN PSORIATIC ARTHRITIS

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Background and Importance Psoriatic arthritis (PA) is a complex inflammatory musculoskeletal and skin disease. Nowadays, there are several therapeutic options to treat this disease.
Aim and Objectives To conduct indirect comparisons (ICs) between abatacept, brodalumab, guselkumab, ixekizumab, risankizumab, secukinumab and ustekinumab using a common comparator in patients diagnosed with PA.
Material and Methods A review in PubMed and European Medicines Agency databases was performed. Inclusion criteria: phase III randomised clinical trials (RCTs) of treatments cited with a double-blind and placebo-controlled design, which included patients previously treated with anti-tumour necrosis factor agents. Exclusion criteria: RCT without a comparator common to alternatives considered and recruiting treatment-naive patients. American College of Rheumatology 50% improvement criteria (ACR50) at 24 weeks in RCTs were selected as endpoint to estimate absolute risk reduction (ARR) for each drug. We conducted adjusted ICs using Bucher method. The therapeutic alternative with the greatest magnitude of effect in RCTs was selected as reference therapy. The maximum difference without clinical relevance (Δ) was defined as ± 16% according to previous published literature.
Results
Seven studies were included All treatments –except abatacept– showed benefit over placebo. Regarding ixekizumab 80 mg monthly (reference therapy), ARRs were: -4.2% [95% confidence interval (CI), -15.43 to 7.03] vs brodalumab 210 mg biweekly; -9.20% [95% CI, -22.53 to 4.13] vs guselkumab 100 mg every 8 weeks; -12.20% [95% CI, -32.37 to 7.97] vs secukinumab 300 mg monthly; -13.60% [95% CI, -25.25 to -1.95] vs risankizumab 150 mg every 12 weeks; -19.5% [95% CI, -32.30 to -6.70] vs ustekinumab 45 mg every 12 weeks; and -25.50% [95% CI -37.87 to -13.13] vs abatacept 125 mg weekly. Ixekizumab showed statistically significant benefit compared to risankizumab, ustekinumab and abatacept. Nevertheless, no statistical difference was found compared to brodalumab, guselkumab and secukinumab. Ixekizumab only demonstrated a clinically relevant benefit versus ustekinumab and abatacept.
Conclusion and Relevance Our ICs provide comparative efficacy data between current therapeutic alternatives for PA in terms of ACR50. No statistically significant benefit was observed between ixekizumab, brodalumab, guselkumab and secukinumab. Ixekizumab did not show relevant clinical superiority over brodalumab, guselkumab, secukinumab and risankizumab. These results could promote price competition between these drugs and improve the efficiency of PA treatments.

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4CPS-038 CHALLENGES RELATED TO TRANSITIONING FROM HOSPITAL TO TEMPORARY CARE AT A SKILLED NURSING FACILITY

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Background and Importance With decreasing number of hospital beds, more patients are discharged from hospitals to temporary care at skilled nursing facilities requiring handling of more complex and frail citizens in a non-hospital setting.
Aim and Objectives We aimed to systematically map challenges related to the transition of patients from hospital to temporary care at a skilled nursing facility in relation to (i) medication management, (ii) responsibility of the medical treatment, and (iii) communication.
Material and Methods This descriptive study included medical or surgical patients admitted to hospital and discharged to temporary care at a skilled nursing facility from May-December 2022.
Results Preliminary results are available for 67 patients (52% women and mean age 77 years). A nurse from the skilled nursing facility used in average a ten minute phone call to coordinate with a nurse from the hospital before discharge. In 100% (n=67) of the patients the medication to the first day sent from the hospital was used, even if there in 30% (20 of 67) was problems due to missing update of the Shared Medication Record, changed strength, missing or unidentified medication, or other discrepancies. Only 58% (n=39) received all needed medication during the first day needed for further medication dispensing. The nurses made in average three (range 0-10) calls and sent three electronically correspondences per patient about medication within the first five days. In 36 of 60 (60%) patients did the discrepancy between the discharge notice from the nurses and the discharge letter, not result in any further action from the skilled nursing facility. However in 38% (n=9) of the 24 patient records that required extra action from the skilled nursing facility, the action could have been avoided if the nurses from the skilled nursing facility had had the discharge letter. Full results for an expected 200 patients will be available and presented at the EAHP conference.
Conclusion and Relevance We identified challenges related to, in particular, lack of needed medication and communication. A third of the actions related to medication management were considered avoidable with improved practices around communication.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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