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ABSTRACTS COLLECTION

The 46th Annual Meeting of the European Society for Blood and Marrow Transplantation: Pharmacist Committee Poster Session (P711-P718)

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Pharmacology Poster Session

P711.

Clinical Impact of Model Pk guided-cyclosporine Dose Individualization in Children Undergoing Hsct

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Background: The benefits of a pharmacokinetic (PK) model-based therapeutic drug monitoring (TDM) in better achieving a target are known, but few studies showed a real clinical impact, especially in the field of the hematopoietic stem cell transplantation (HSCT). Indeed, management of immunosuppressive therapy is critical as acute graft-versus host disease (aGvHD) remains a major complication. The objective of this study was to evaluate the incidence of severe aGvHD regarding to PK model- or clinical experience-based cyclosporine (CsA) dose adaptation.

Methods: We retrospectively assessed 146 consecutive patients who underwent allo-HSCT between January 2014 and December 2018 in our center. aGvHD prophylaxis consisted in CsA, mainly as a monotherapy, as previously published by our team[1]. Due to lack of human resources, some children benefited from dose adaptation based on physician experience (**non-PK group**), whereas other had Bayesian approach-based dose adaptation (**PK group**). We examined the relationships between severe aGvHD incidence (grade III or IV) and available data (disease and graft characteristics, conditioning regimen, infections, immunosuppressive therapy and method used for dose adaptation) by logistic regression (R software, version 3.3.2). aGvHD was graded according to the Glucksberg et al.[2] criteria.

Results: Among the 146 children, 62.3% were in the PK group. The two groups were balanced for patient's characteristics and allo-HSCT indication and modality. The overall incidence of aGvHD was 67.8% and severe aGvHD (grade III-IV) occurred in 17 patients (11.6%).

Univariate analyses evidenced that: (1) way of proceeding the CsA dose adaptation, (2) unrelated donor HSCT (*versus* matched sibling donor MSD), (3) etoposide-based conditioning, (4) serotherapy-containing GvHD prophylaxis, (5) EBV reactivation and (6) fungal infection were associated with severe aGvHD occurrence (*p-value* < 0.20). In the multivariate analysis, only two predictors were retained for the final model (*p-value* < 0.05): the type of donor (MSD *versus* other) and the method used for CsA dose adaptation. Indeed, probability of developing severe aGvHD was statistically higher with an unrelated donor HSCT (**OR = 1.27**) and if TDM was not based on Bayesian approach (**OR = 0.86**).

In addition to reducing severe aGvHD incidence, TDM has a direct economic impact as it avoided the use of expensive second-line treatments: respectively seven and

two patients from the non-PK group required ruxolutinib and basiliximab therapy whereas no patient required any of these drugs in the PK group.

A similar procedure was applied to analyze determinants of documented infections and hospital length of stay. If no final model was statistically significant, there was a trend to a shorter length of stay (60 ± 27 *versus* 67 ± 37, $p = 0.23$) and less viral and fungal documented infections (60.4% *versus* 98.2%, $p = 0.058$) in patients of the PK group.

Conclusions: These results suggest that a multidisciplinary approach may improve outcomes in children undergoing allo-HSCT. The role of clinical pharmacist, especially with an expertise in PK, must be considered as essential for patient management. A larger prospective comparative study is required to confirm the impact of TDM on clinical and economic outcomes.

Disclosure: Nothing to declare.

P712.

Influence of Cyp2d6 Metabolizer Status on The Control of Chemotherapy Induced Nausea and Vomiting by Ondansetron on Pediatric Patients Undergoing Hematopoietic Stem Cell Transplantation

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Background: A portion of hematopoietic stem cell transplantation (HSCT) recipients have significant emesis despite ondansetron to prevent chemotherapy induced nausea and vomiting (CINV). A possible explanation for differences in response is that ondansetron is metabolized by CYP2D6, an enzyme whose gene harbours function altering variants. Adult patients who are ultrarapid metabolizers (UMs) due to multiple functional copies of *CYP2D6* are at an increased risk for CINV owing to rapid ondansetron clearance. It is unclear whether *CYP2D6* genetic variation also affects how pediatric HSCT patients respond to ondansetron.

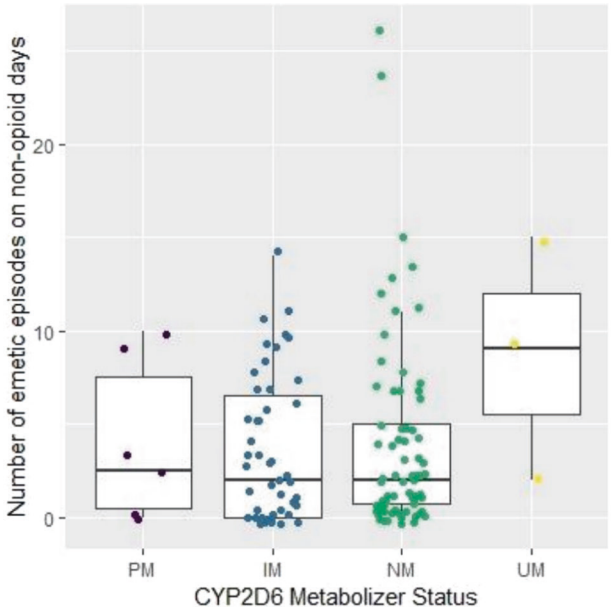
Methods: We performed a retrospective chart review for pediatric HSCT recipients at Cincinnati Children's Hospital who received ondansetron for CINV prevention and had *CYP2D6* genotyping from August 2013- July 2019. The assay used for *CYP2D6* genotyping detected 20 *CYP2D6* alleles via TaqMan™ and long-range PCR was used for duplication detection. Number of emetic episodes for each patient was collected from the start of chemotherapy through seven days after cell infusion. For statistical analyses, the number of emetic episodes was analyzed with a zero-inflated Poisson regression in R.

Results: In our pediatric cohort of 128 HSCT recipients, the mean age was 6.6 years (range: 0.2–16.7). Non-UMs included normal metabolizers (NM, $n = 72$), intermediate metabolizers (IM, $n = 47$), and poor metabolizers (PM, $n = 6$). When comparing median number of total emetic episodes and accounting for chemotherapy emetogenicity, diagnosis, and number of days of ondansetron administration, there was not a statistically significant difference between UMs and non-UMs (11 vs 6, $p = 0.57$). There was not a statistically significant difference between number of emetic episodes per diem between UMs and non-UMs (0.63 vs 0.36, $n = 0.2$). Race, sex, and ondansetron dose were not significantly related to total emetic episodes. Since nausea and vomiting are known side effects of opioids, episodes of emesis on non-opioid days were evaluated separately in an attempt to remove opioids as a confounder. UMs had a statistically significant higher median number of cumulative emetic episodes on non-opioid days compared to non-UMs (9 vs 2, $p = 0.013$). This comparison accounted for number of non-opioid days, chemotherapy emetogenicity, sex, race, diagnosis, and ondansetron dose. UMs also had a statistically significant higher median number of emetic episodes per diem on non-opioid days compared to non-UMs (0.82 vs 0.2, $p < 0.0001$).

Conclusions: Similar to adults, pediatric HSCT recipients who are UMs experience more emesis while receiving ondansetron compared to non-UMs. In pediatric CYP2D6 UMs, CINV may be better controlled with non-CYP2D6 metabolized antiemetics such as granisetron.

	Race		Sex		Diagnosis		Metabolizer Status	
	White	Non-white	Male	Female	Non-malignant	Malignant	UM	Non-UM
n (%)	108 (84.4%)	20 (15.6%)	73 (57%)	55 (43%)	82 (64.1%)	46 (35.9%)	3 (2.3%)	125 (97.7%)
Cumulative emetic episodes, median (range)	6 (0-41)	4.5 (0-33)	6 (0-31)	5 (0-41)	4 (0-33)	10.5 (0-41)	11 (2-22)	6 (0-41)
Per diem emetic episodes, median (range)	0.36 (0-2.73)	0.36 (0-1.65)	0.36 (0-2.50)	0.35 (0-2.73)	0.22 (0-1.69)	0.72 (0-2.73)	0.63 (0.14-1.47)	0.36 (0-2.73)
Cumulative emetic episodes on non-opioid days, median (range)	2 (0-26)	1.5 (0-9)	3 (0-26)	1 (0-15)	2 (0-24)	3 (0-26)	9 (2-15)	2 (0-26)
Per diem emetic episodes on non-opioid days, median (range)	0.22 (0-2.60)	0.16 (0-1.00)	0.21 (0-2.60)	0.18 (0-2.14)	0.15 (0-2.40)	0.50 (0-2.60)	0.82 (0.14-2.14)	0.20 (0-2.60)

[Pediatric HSCT Recipients (n=128): Demographics and Emetic Episodes]



[CYP2D6 Metabolizer Status vs Number of Emetic Episodes on Non-opioid Days]

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P713.

Estimation of Glomerular Filtration Rate in Adults After Allogeneic Stem Cell Transplantation: Cystatin C Versus Creatinine

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Background: Estimation of glomerular filtration rate (GFR) reflecting patient's renal function is usually based on serum creatinine. As creatinine is a metabolite of the muscle enzyme creatine (crea), GFR is probably overestimated in patients with markedly reduced muscle mass or malnutrition. A more accurate estimation of GFR provides the endogenic protein cystatin C (cysC) that is produced independently of muscle mass and excreted via glomerular filtration. To our knowledge, no data exist about the GFR estimation in patients undergoing an allogeneic haematopoietic stem cell transplantation (allo-HSCT) using cystatin C.

The aim of this study was to systematically analyse the differences of GFR estimation using creatinine (crea-GFR) or cystatine C (cysC-GFR) differ in allo-HSCT patients and the impact on drug dosing.

Methods: According to a local policy cysC-GFR was be determined at least once in adult allo-HSCT patients with reduced muscle mass according to clinical perception and treatment with a drug with a narrow therapeutic index and renal excretion. All patients being discharged between 1.1.2019 and 30.6.2019 from one of the HSCT wards in our center, have been included in this retrospective analysis. Data were analysed anonymously using descriptive statistics and linear regression analysis.

Results: In 54 patients (26 male/28 female) with a median age of 63 years (range 22-77) and a median body mass index of 23,2 kg/m^2 (range: 15,3-40,2) cysC-GFR was determined 141 times (median: 2 measurements/patient; range 1-14). In median, cysC-GFR was 39 ml/min/1.73 m^2 (range: 9-98), while at the same time crea-GFR was 76 ml/min/1.73 m^2 (range: 10–146). The difference in the corresponding 141 measurements accounts for 35 ml/min/1.73 m^2 (range: (−21)−94) in median. With regard to chronic kidney disease classification, 82% of the cysC-GFR values are categorised in GFR stages 3 to 5 (<60 ml/min1.73 m^2) versus 34% of the crea-GFR values. 104/141 (74 %) of the cysC-GFR estimations are graded into a higher GFR stage as the corresponding crea-GFR estimations, while 2 values were stage 3 according to crea-GFR, but stage 2 according to cysC-GFR. Vancomycin with dose adjustment according to therapeutic drug monitoring (TDM) was administered to 14 patients. Median cysC-GFR in this subgroup was 64 ml/min/1.73 m^2 (range: 21-99) vs crea-GFR 87 ml/min/1.73 m^2 (range: 54-103). Those patients within the target vancomycin range and a cysC-GFR <50 ml/min/1.73 m^2 received significantly lower vancomycin doses of 11 mg/kg (range 5-16) as compared to 26 mg/kg (range 22-42) in those patients with a cysC-GFR >50 ml/min/1.73 m^2, with a linear correlation of $R^2 = 0.708$ ($p < 0.0001$), while there was linear correlation between crea-GFR and mg/kg vancomycin dose was much lower ($R^2 = 0.438$, $p = 0{,}01$).

Conclusions: The observed large differences GFR estimation and the subsequent GFR stages confirm the relevance of cysC-GFR determination in our patient cohort with significant impact on drug dosing, as we could show it for vancomycin, a drug that is preliminary excreted by the kidneys via glomerular filtration. In the future, it is reasonable to work out objective factors to identify patient groups who will benefit from regular cysC-GFR determination for optimal drug dosing.

Clinical Trial Registry: not applicable

Disclosure: Nothing to declare.

P714.

Use of Sublingual Tacrolimus in Pediatric Hematopoietic Stem Cell Transplant Recipients with History of Anaphylaxis to Intravenous Cyclosporine

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Background: Anaphylaxis, though rare, is a known adverse effect of Intravenous (IV) cyclosporine, reported in 0.1% of patients. Parenteral formulation of cyclosporine contains polyoxyethylated castor oil, a solubilizing agent, which has been blamed for hypersensitivity reactions. Oral form of cyclosporine or tacrolimus have been successfully used in such circumstances. There is paucity of literature regarding use of sublingual tacrolimus in HSCT patients in such scenario.

Methods: Case 1

An 11-year-old male, a case of transfusion dependent thalassemia (TDT) with 10/10 HLA-matched mother was admitted for hematopoietic stem cell transplant. He received conditioning with Fludarabine, Thiotepa, Treosulfan and Anti-Thymocyte Globulin (FTTA). On day -3 of conditioning, within five minutes of starting IV cyclosporine infusion, he developed anaphylaxis in form of angioedema and hypotensive shock. IV cyclosporine was stopped immediately, and IV adrenaline, hydrocortisone and fluids were administered, besides other supportive care. Further, oral tacrolimus (0.06 mg/kg/dose twice a day) and IV methotrexate was administered as GVHD prophylaxis. Neutrophils and platelets engrafted on day +13 and +17 respectively. On day +35, patient developed stage III gut GVHD. As IV tacrolimus is not available in our country, we started him on sublingual tacrolimus, 2/3rd of oral dose. This was achieved by placing the contents of tacrolimus capsule under the patient's tongue. Whole Blood tacrolimus levels were monitored by chemiluminescent microparticle immunoassay (CMIA) twice a week. Dose was adjusted to maintain the levels between 5 & 15 ng/ml. However, unfortunately, patient developed steroid refractory stage IV Gut GVHD. This was successfully managed with addition of etanercept and ruxolitinib. Patient was later shifted to oral tacrolimus and is currently doing well on tapering doses.

Case 2

A 7-year-old male, another case of TDT, was planned for 10/10 HLA-matched sibling donor peripheral blood stem cell transplant (PBSCT) at our centre. On day −3 of conditioning (FTTA protocol), patient was started on IV cyclosporine. Ten minutes into the infusion, patient developed sensation of choking and respiratory distress. Cyclosporine infusion was stopped, and patient was successfully managed with adrenaline, hydrocortisone and IV Fluids, besides other supportive care. GVHD prophylaxis was given with oral tacrolimus and IV methotrexate post stem cell transplantation. He developed grade 1 oral mucositis on day +4, which progressed to grade 3. Child developed diarrhoea on day +7. In view of significant mucositis, tacrolimus administration was changed from oral to sublingual, 2/3rd of oral dose. With regular monitoring and dose adjustment, we were able to achieve and maintain therapeutic tacrolimus levels. It was shifted to oral administration once mucositis subsided on day 15. Patient had successful neutrophil and platelet engraftment. He is doing well 3 months post stem cell transplant.

Results: Whole blood Tacrolimus level was successfully achieved (5–15 ng/ml) with minimal dose adjustment during episode of steroid refractory gut GVHD or severe oral mucositis and diarrhoea.

Conclusions: Sublingual tacrolimus should be considered as safe and reliable alternative to IV tacrolimus in cases where oral form cannot be used. It can also become an option to oral or parenteral form of cyclosporine.

Disclosure: Nothing to declare.

P715.

Oral Clonazepam for Seizure Prophylaxis in Adult Patients Treated with High Dose Busulfan

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Background: The incidence of seizures due to high-dose busulfan is about 10% in patients with no prophylaxis, and decreased to 0.5–5% after the introduction of phenytoin prophylaxis. Seizures have been described during busulfan administration, or within 24 hours after the last dose. Due to their favourable toxicity profile and lack of interactions, benzodiazepines have been proposed as prophylaxis of busulfan induced seizures. Although they

are broadly used in pediatric patients, the experience in adults is limited. The objective of this study is to describe the safety and effectivity of a fixed dose of oral clonazepam (1 mg every 8 h, [q8h]) in adult patients receiving intravenous high dose busulfan (IVBU), as part of a hematopoietic cell transplant conditioning regimen.

Methods: This prospective, observational study, was performed from May 2014 to July 2019. Inclusion criteria included: age over 18 years, patients that had received IV high dose busulfan (at least 3,2mg/kg/day for 2 days), and prophylaxis with oral clonazepam 1 mg q8h starting 12 h before IVBU, until 24 h after the last dose of IVBU. The primary endpoints were the occurrence of seizures until 72 h after finishing busulfan administration, and adverse events associated with the use of clonazepam.

The following covariates were recorded: age, sex, diagnosis, type of transplant and conditioning regimen used.

Ethical approval for this study was obtained from the Institutional Review Board.

Written informed consent was obtained from all participants.

Results: Forty patients, 15 female and 25 male, median age 49,5 years [range 25-69], were included. Most frequent diagnosis was acute myeloid leukemia (21 patients), followed by myelodysplastic syndrome (6), multiple myeloma (4), diffuse large B cell lymphoma (2), mantle cell lymphoma (2), follicular lymphoma (1), acute promyelocytic leukemia (1), acute lymphocytic leukemia (1), chronic myeloid leukemia (1) and myelofibrosis (1).

Autologous transplant was performed in 10 patients, and allogeneic transplant in 30 (9 related donor, 7 unrelated donor, 14 haploidentical). Busulfan dose was 3.2 mg/kg every 24 h with a variable duration of 2-4 days. The drugs which were most frequently associated with IVBU in the conditioning regimen were: fludarabine (12 patients, two of them associated to radiotherapy), fludarabine with thymoglobulin (7), fludarabine with thiotepa (7), etoposide with cytarabine (5), melphalan (4), fludarabine with cyclophosphamide (3, one of them associated to radiotherapy) and cyclophosphamide (2).

No seizures were recorded.

The drug was well tolerated. The adverse effects probably associated with clonazepam were somnolence (32.5%), instability/dizziness (25%), disorientation (2.5%) and cognitive disturbances (2.5%); all of them were mild and resolved without intervention.

Conclusions: Clonazepam at an oral fixed dose of 1 mg q8h is easily administered and very effective for the prevention of high dose busulfan induced seizures in adult patients. The toxicity associated with the drug was mild and transient, mainly somnolence and instability/dizziness.

Disclosure: Nothing to declare.

P716.

Dissolution Time for Conventional and Lyophilized Cyclophosphamide: A Single Center Study

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Background: Many formulations of cyclophosphamide for parenteral use are inconvenient to use, due to the prolonged time required for their dissolution[1]. The new lyophilized form of cyclophosphamide has been reported to be easier to prepare than the conventional form of the drug, an advantage which reduces the time needed to prepare the drug for injection (Kjrer & Bjeldbak; unpublished report). The present study was undertaken with the aim of comparing the dissolution time for different preparations of cyclophosphamide available in the Asian countries.

Methods: In a resource constrained country like Pakistan we were using conventional cyclophosphamide till 2017. In subsequent years of 2018 and 2019, the lyophilised drug was available. The study period was December 2017 to November 2019. In this study the different brands used were Cyclphosphamide, cyclo and Endoxan in conventional group and Endoxan N, Zycram, Uniphos, Cyphos were in lyophilized cyclophosphamide group. The strength used were 500 mg 1000 mg. Total 101 vials of drug were tested, which consist on fifty-six conventional vials and forty-five lyophilized vials. In all experiments, different vials of 500 mg and 1000 mg were used. To each vial of 1000mg was added 50 ml of distilled water, while 500mg vial dissolved in 25ml of DW. The vials were hand shaken. The vials were shaken in a vertical direction. Ion of the amount of dissolved drug by means of visual examination.

Results: The dissolution variability is expressed as range. The conventional drug range was 34 to 12 min irrespective of the amount of drug in the vials. In contrast. the lyophilized preparations were completely dissolved quickly. The range of dissolution was 8.22 to 1.44. Visual inspection showed the lyophilized preparations clear within one minute. Soaking time was given to conventional drug while immediate reconstitution of drug happened in new drugs, no soaking time was required. in conventional cyclophosphamide the room temperature vials were dissolved in longer time as compared to the vials which were stored in refrigerators. Eighty-eight vials were of room temperature while thirteen vials were dissolved at fridge temperature. There was a significant difference in both the dissolution timings. The low temperature vials dissolved in about half of the time of room temperature conventional cyclophosphamide. Normally, a drug is

considered to be dissolved when the solution looks clear. The dissolution time was very variable within each batch of the conventional brands of cyclophosphamide, which contrasts the dissolution studies with new lyophile brands. These results are in agreement with previous observations as shown in E. Nyhammar & S. Eksborg (1991).

Conclusions: The results in the present study verify that the lyophilized preparation of cyclophosphamide. is more convenient to prepare than the conventional preparations of the drug. The lyophilization industry increased the overall efficiency of clinical set up and especially the haematology oncology patient care. The decreased cyclophosphamide chemotherapy preparation time increases the time for the patient care.

Clinical Trial Registry: NOT APPLICABLE

Disclosure: No conflict of interest and no funding required

P717.

Outcomes of Ebv Viremia and Ptld After Rituximab: A phamraco-cost Analysis

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Background: Epstein-Barr virus (EBV)-related post-transplantation lymphoproliferative disorders (EBV-PTLDs) are rare but potentially fatal complications of allogeneic hematopoietic cell transplantation (HCT). The most common risk factors include T cell depletion of graft, HLA mismatch, severe graft-versus-host disease (GVHD), and EBV sero-omismatch (recipient-negative/donor-positive). The current treatment strategies for probable and proven EBV-PTLDs include reduction of immunosuppression (RI), rituximab, adoptive cell therapy (unselected donor lymphocyte infusion (DLI), and EBV-specific cytotoxic T lymphocyte (EBV-CTLs) infusion and chemotherapy, among which RI and rituximab are the mainstay. Rituximab- based pre-emptive treatment can prevent EBV-viremia from developing into EBV-PTLDs. After October 2018 our institute initiated the pre-emptive treatment for EBV viremia and used 300,000 IU/mL EBV viremia as treatment threshold.

Our aims are to determine the outcome before and after initiation of pre-emptive treatment of EBV-viremia and the cost associated with hospitalized vs out-patient therapy.

Methods: Retrospective analysis of all allo-HCT performed between February 2014 to December 2018 at Princess Margaret cancer center. Pharmacy and Transplant Registry database were used to identified all the patients who received rituximab for EBV-viremia or EBV-PTLD after allo-HCT. Data abstraction was specific for EBV-PCR titer, clinical, PET/CT evident PTLD and/or pathology prior to treatment initiation. Post treatment resolution or recurrence was analyzed. The Finance Department provided cost estimates for hospitalized and out-patient treatment costs.

Results: There were 713 allo-HCT performed during this period and 42 (5.9%) received rituximab for EBV related indication. Their median age of these 42 patients was 57 (range 23–75) with 24 males. Myeloablative conditioning was administered to 17.5% of patients while 82.5% received reduced intensity conditioning. In vivo T-cell depletion was given to 95% of patients, either ATG or alemtuzumab in 33 and 5 patients respectively. Donors were matched related in 15%, unrelated in 72.5% and haploidentical in 12.5%. One patient was excluded because he received rituximab for another reason. Table 1 showed the distribution of the patients for EBV- viremia and EBV-PTLD before after and after pre-emptive treatment and the outcome.

In 18 patients (44%), rituximab was initiated as in-patient and entire course was completed in hospital, while in 5 (12%) patients it was given on out-patient basis. In the rest 18 (44%) patients treatment began in the out-patient but was completed as in-patient. The average cost per cycle treatment of resources including total nursing, supplies and cost of bed or cost of chair for in-patient and ambulatory chair was $1,450 and $100 respectively. The cost of rituximab is not factored in here for the overall cost per cycle treatment.

Conclusions: In this retrospective study, pre-emptive therapy of EBV was effective in preventing of EBV-PTLD. Given the high cost of hospitalization, out-patient rituximab infusion appears more cost effective.

EBV-viremia/EBV-PTLD		No. of patients	Rituximab Median doses	Outcome Successful (83%)	Outcome Refractory (12%)	Outcome Intolerance/ unknown (5%)
EBV-PTLD	Before preemptive treatment	24 (58.5%)	4 (1-6)	18	5	1
EBV-PTLD	After preemptive treatment	0	0	0	0	0
EBV-viremia	Before preemptive treatment	14 (34%)	2 (1-4)	13	0	1
EBV-viremia	After preemptive treatment	3 (7%)	1 (1-2)	3	0	0

[Patients distribution for EBV- viremia and EBV-PTLD before after and after pre-emptive treatment and the outcome]

Disclosure: Nothing to declare.

P718.

Pharmacological Interactions in the post-transplant Phase of Hematopoyetic Progenitors Transplantation

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Background: Patients undergoing hematopoietic progenitor transplantation (HPT) have a high risk of suffering multiple pharmacological interactions (PI), due to the numerous drugs they are exposed in the post-transplant phase. There is little information published about its prevalence and severity. The knowledge and proper management of these PIs can contribute to improving the quality, safety and effectiveness of the treatments administered to patients.

The objectives of this study were to determine the prevalence of major and contraindicated potential PIs in the immediate post-transplant phase, in patients undergoing hematopoietic progenitor transplantation, as well as to know the profile of the most frequent PIs.

Methods: Observational, retrospective and descriptive study, during the post-transplant phase, including all patients undergoing HPT in a third level hospital, during a period of 2 years (2017-2018). The analysis was performed using the Micromedex® database, recording the contraindicated and major PIs.

Results: 140 patients (78 men and 62 women), median age of 57 years (16-73), were included.

A total of 3622 drugs were prescribed: 1893 supportive drugs, 105 drugs for the prophylaxis of graft versus host disease (GvHD) and 1624 of the other drugs. The median of the total drugs used per patient was 24.5 (14-46). The most frequently prescribed drugs were: ondansetron (139 patients), ursodeoxycholic acid (139), acyclovir (138), potassium chloride (134), meropenem (133), omeprazole (133), fluconazole (131), furosemide (127) and paracetamol (124).

A total of 1953 interactions were found, grouped into 413 drug pairs, with a median of 12 (1-69) potential PIs per patient. The prevalence of PI by the Micromedex® database was 100%; being 95.7% for contraindicated PIs and 99.3% for major PIs.

Based on the severity level, 250 PIs (24 couples) were contraindicated (12.8%) and 1703 (389 couples) were major (87.2%).

The most frequent contraindicated PIs affected the risk of increased QT interval and were caused by the association of fluconazole and: ondansetron (129 patients), tacrolimus (29), escitalopram (5), haloperidol (3), salmeterol (2), quetiapine (1), solifenacin (1) and trazodone (1), and by the association of posaconazole and ondansetron (3); concurrent use of metoclopramide and antipsychotics/antidepressants was associated with the risk of extrapyramidal reactions and neuroleptic malignant syndrome (NMS): with chlorpromazine (31), amitriptyline (10), sertraline (8), escitalopram (5), haloperidol (4), duloxetine (4), venlafaxine (2), olanzapine (1), risperidone (1) and sulpiride (1).

The most frequent major PIs increased the risk of depression of the central nervous system, involving the association of metoclopramide and: lorazepam (83), morphine (46) and codeine (26); and concomitant use of morphine with lorazepam (52). Attention also should be paid to the interactions at risk of producing serotonergic syndrome, which involved the association of ondansetron with morphine (66) and codeine (40).

Conclusions: The prevalence of major and contraindicated potential PIs is very high in patients undergoing HPT. The most frequent contraindicated PIs involve an increased risk of prolongation of the QT interval and the appearance of extrapyramidal reactions and NMS. The drugs most frequently implicated in these PIs are fluconazole, ondansetron and metoclopramide.

Disclosure: Nothing to declare.