MEDICINE SUPPLY CHAIN OF A CENTRAL PHARMACY : RISK MAPPING OF SHORTAGE

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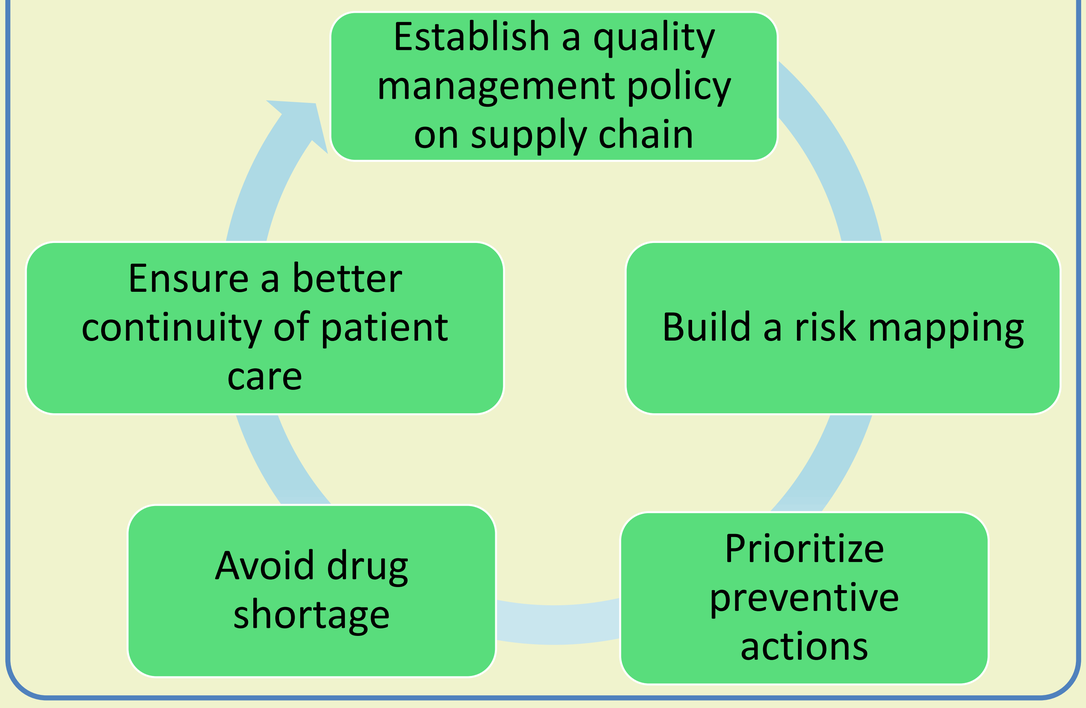
Objectives

The **purpose** of this work is to build a risk mapping of shortage to ensure a better continuity in patient care



Methods

Failure modes and effects analysis methods

- Working group created :
  2 Pharmacists - 1 Pharmacy student - 1 Logistics engineer - Pharmacy technicians
- Supply chain analysis :
  All steps from order to storage process
- Potential failures analysis :
  5 causes of failures : Material – Milieu – Methods – Machine – Man power
- Criticality of potential failures rated :
  Severity (sev) and frequency (frq) rates to determinate the gross criticality (gc)
  Mastered level (ml) of control to determinate the net criticality (nc)
- Priority actions identified :
  Each cause rated over 100 on gross criticality

Frequency : based on error history analysis	
1	Once a year or less
3	Several times a year
5	Several times a month
10	Several times a week

Severity : based on patient's issues	
1	Acceptable
5	To monitor
10	Unacceptable

Master level of control	
1	Knowledge of a written procedure, applied and regularly assessed
3	Application of written procedure
5	Non-existent or not applied procedure, depends on the operator, note secured
10	Non-existent procedure

Results

We identified 15 risks and 28 causes, 5 causes were prioritized

Activity	Step	Risk	Cause	Risk effect on activity	Sev	Frq	GC	Mastering device	ML	NC
Order	Order tracking	Lack of reminder	Non executed reminder on supplier for order not received after 5 days	Delay in supply until stock out	10	10	100	Daily check of order in progress	10	1000
	Order picking	Lack of ordering	Missed order due to poor estimation of drug consumption	Stock out	10	3	30	Drug information in the order software	10	300
		Ordering error	Insufficient quantity ordered due to lack of consumption information (ex : new drug)	Not enough stock before next order	10	3	30	Master our order data in our warehouse management system	10	300
		Lack of ordering	Missed order due to stock issues	Drug on security stock not ordered : stock out	10	3	30	Inventory Analysis of missing	5	150
Reception	Verification of drug supply	Reception error	Wrong quantity received	Stock out or problem of storage area	10	3	30	Process of order reception	5	150

Discussion - Conclusions

The weak points identified on our supply chain lead to review order process and training to improve patient care.
The next step will be to extend it to the delivery of the pharmacy of the 5 hospital sites supplied and considerate financial and juridical aspects of each risk.

CONTAMINATION WITH CYTOTOXIC DRUGS IN THE WORKPLACE
ESOP PILOT STUDY

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BACKGROUND

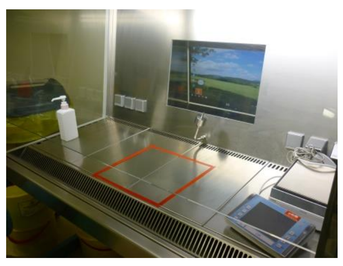
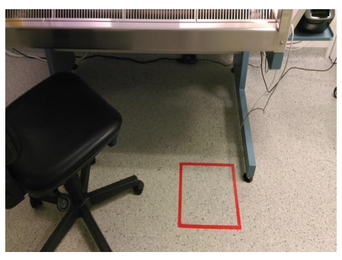
Evaluation of environmental contaminations with cytotoxic drugs in the hospital is one of the fundamental requirements to ensure the safety of all healthcare professionals. Several reports and publications on surface contaminations in pharmacies and hospitals have been reported in the last years. However, knowledge levels on surface contamination with anti-neoplastic drugs in European hospitals in the areas where these drugs are handled, is still limited. No multicentre, non-commercial studies in different European hospitals have been conducted so far.

OBJECTIVES

- To obtain an overview of the current contamination levels of cytotoxic drugs in the workplace in European hospitals (**PART I**)
- To measure the level of environmental contamination with cytotoxic drugs circulating within a facility, known as the hospital medication system - process flow of drug (**PART II**)
- To evaluate the impact of changes to practice designed to protect those who work in the areas where the cytotoxic drugs are handled (**PART III**)

MATERIALS AND METHODS

An evaluation of surface contamination in preparation and administration areas (PART I), and after implementation of cleaning recommendations (PART II). Wipe samples were taken from 10 comparable surfaces (5 in preparation areas and 5 in administration areas), in each of the participating hospitals. Each sample was analyzed for the presence of following 12 cytotoxic drugs using LC-MS/MS: *5-fluorouracil, cyclophosphamide, ifosfamide, gemcitabin, etoposide, methotrexate, paclitaxel, docetaxel, topotecan, irinotecan, doxorubicin and epirubicin*.

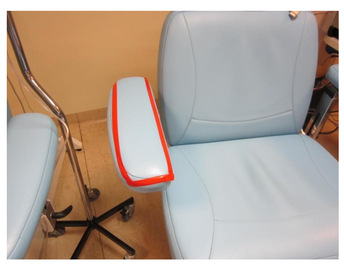
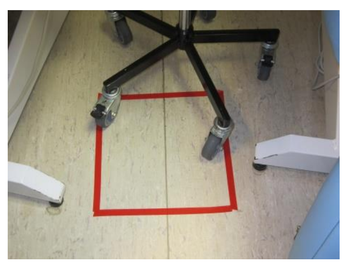




Wipe sampling surfaces in the **PHARMACY**: *work surface of BSC/Isolator, floor under the BSC/Isolator, checking counter (clean area), checking counter (storage area), refrigerator door*

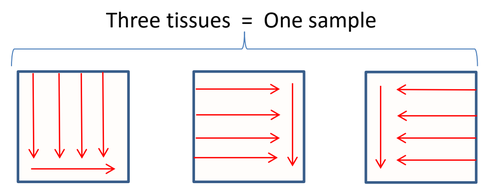
Wipe samples were taken at the end of a working day, before general cleaning.

In each hospital, the investigated surface was wiped by designated pharmacist, according to established procedures.




Wipe sampling surfaces on the **WARD:** *checking counter (nurse station), lid of cytotoxic waste container, armrest of patient chair, floor around the infusion stand, phone*

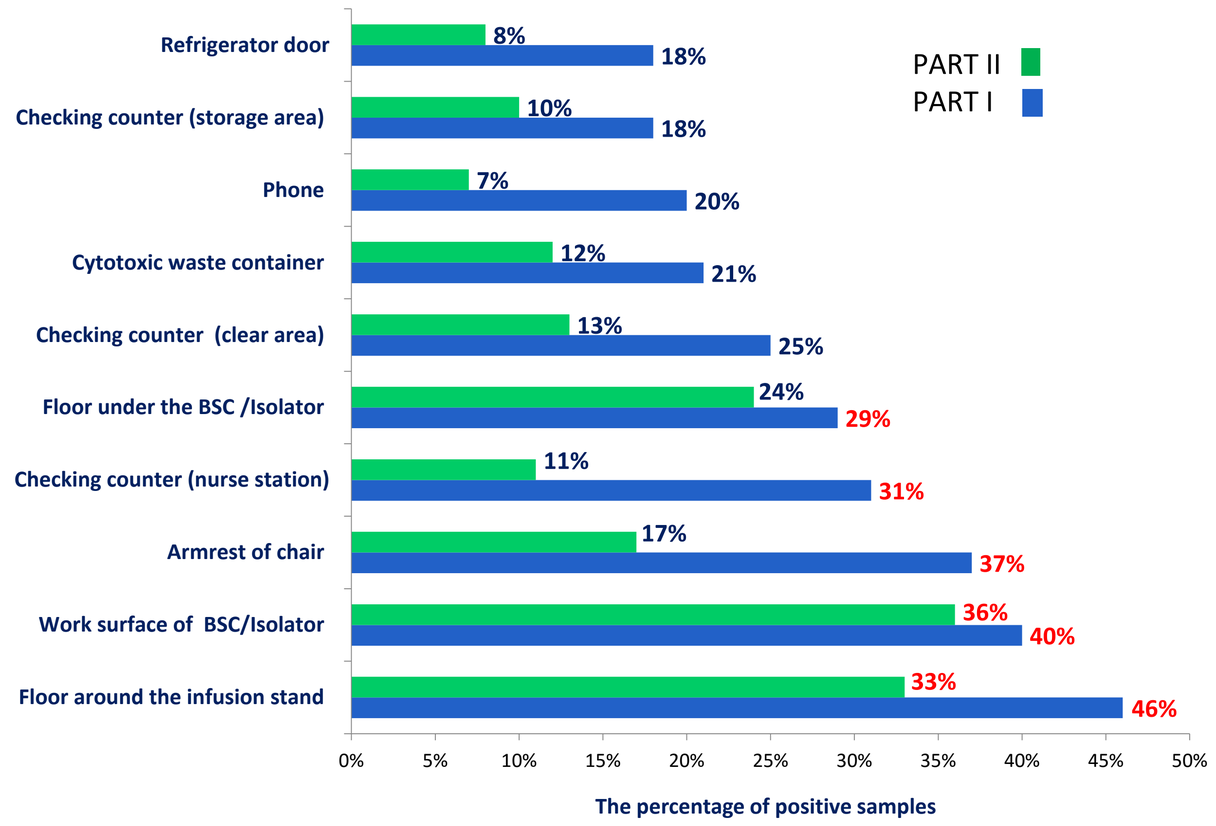


Tuerk J et al. *Int J Environ Anal Chem* **2011**, 91: 1178 - 1190

Evaluation criteria:
90th percentile of load situation
Derived reference value: **0.1 ng/cm²**

RESULTS

The database includes results collected from 15 European hospitals. Out of the 1764 results analyzed in PART I, 505 were positive (29%). In 11 out of 15 hospitals (73%), substances were detected which were not prepared or administrated during the sampling day. After the implementation of the ESOP cleaning recommendations, only 17% of samples were positive (274/1584). Measurable amounts of at least one agent were detected on sampled surfaces in each hospital. Contamination was detected mostly on the work surfaces of BSCs/Isolators, floors (in pharmacies and wards) and the armrests of patient's chairs. The highest number of positive results were recorded for gemcitabin, 5-fluorouracil, cyclophosphamide and paclitaxel. The highest value was recorded for gemcitabin (171 ng/cm²) and 5-fluorouracil (37 ng/cm²) in PART I and PART II, respectively. There was no correlation between contamination and the amounts of prepared drugs.



Range [ng/cm²]	PHARMACY		WARD	
	PART I n = 888	PART II n = 814	PART I n = 876	PART II n = 770
< LOD	655	666	604	644
LOD < 0.1	183	103	208	92
0.1 - 1	32	31	46	30
1.0 - 10.0	14	11	18	4
> 10	4	3	0	0

Fig. 1. Number of analyzed results for all substances in different ranges (PART I and PART II)

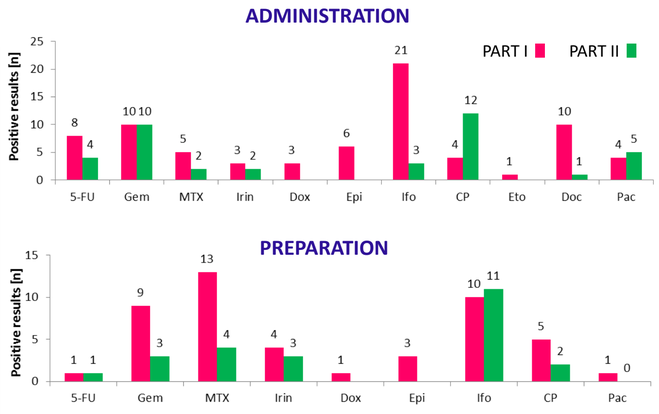


Fig. 2. Number of positive results for substances which were not prepared or administrated in the wipe sampling day (PART I and PART II)

PART I (Pharmacy & Ward)

Min = LOD	5 FU	Gem	MTX	Top	Irino	Dox	Epi	Ifo	CP	Eto	Doc	Pac	All
n	147	147	147	147	147	147	147	147	147	147	147	147	**1764**
Median	0.007	0.003	0	0	0	0	0	0	0	0	0	0	**0**
75th Percentile	0.063	0.024	0	0	0	0	0	0.001	0.020	0	0.002	0.006	**0.001**
90th Percentile	0.284	0.137	0.185	0	0.003	0	0	0.019	0.184	0	0.020	0.038	**0.030**
Max	4.066	170.500	7.458	0.014	14.383	0.036	0.022	6.991	73.162	0.301	1.650	5.775	**170.500**

PART II (Pharmacy & Ward)

Min = LOD	5 FU	Gem	MTX	Top	Irino	Dox	Epi	Ifo	CP	Eto*	Doc	Pac	All
n	144	144	144	144	144	144	144	144	144	n/a	144	144	**1584**
Median	0	0	0	0	0	0	0	0	0	n/a	0	0	**0**
75th Percentile	0.018	0.009	0	0	0	0	0	0	0.026	n/a	0	0	**0**
90th Percentile	0.133	0.072	0	0	0	0	0	0.012	0.131	n/a	0.009	0.066	**0.021**
Max	36.924	11.359	0.046	4.931	0.677	0.082	0.111	14.993	6.932	n/a	0.907	5.122	**36.924**

** n/a: not applicable, because of stability problems during sample storage of some the samples.*

CONCLUSION

The ESOP pilot study provided a brief overview of the local procedures for safe handling of cytotoxic drugs in European hospitals. In PART II of the study, improvements could be seen by the reduction of positive samples, the amount of surface concentration detected and the reduction of the 90th percentile from 0.030 ng/cm² to 0.021 ng/cm². A wipe sampling strategy, together with a clear set of ESOP recommendations based on the results of this pilot study, will be used in the next phase of the ESOP project (PART III).

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PP-001

DOUBLE CHECKING MANIPULATIONS FOR COMPLEX AND/OR HIGH RISK PREPARATIONS

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Background

On a daily basis, hospital pharmacists are confronted with multiple tasks that may compromise, for safety reasons, a positive outcome for the patient. Traditionally, those tasks are focused at the following areas: sterile and non-sterile products preparation and mainly, due to its potential to cause harm, cytotoxic drug preparations.

The implementation of a double verification at the critical points of any preparation process is a national standard. However, most of the times this collides with our reality, due to the scarcity of human resources.

Objective

The main objective of this project is the development of an informatics tool that enables the double verification process and simultaneously eliminates the need for a second element inside the cleanroom, improving quality control and patient's safety .

Methods

Process

An ocular device with a high-definition camera was used to capture images on a preparation environment (Pict.1)

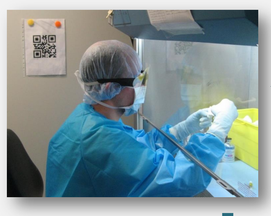
The operators are able to mark predefined critical points through the visualization of a QR * code (Pict.2).

Before liberation to the ward, the pharmacist check the critical points marked by the operator through a specific software designed by vision4lab and, in case of any doubts, he can visualize a part or the entire shooting (Pict.3).

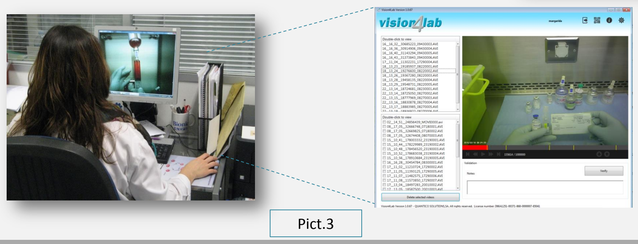
If all critical points are according to the prescription, the treatments are sent to the oncology day unit.

*Quick response

Pict.1



Pict.2

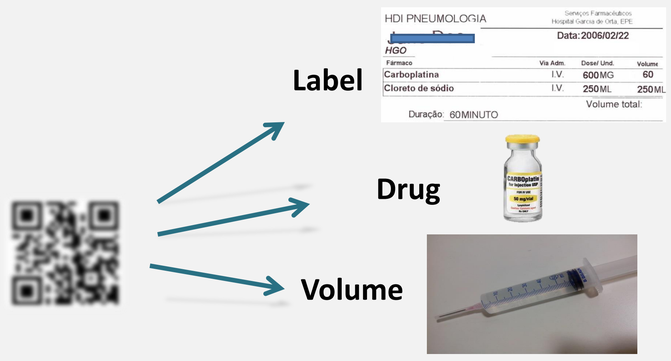


Pict.3

Critical Points

Managing critical points was a big issue and all the onco team (technicians and pharmacists) gave theirs suggestions.

Together they determine that is mandatory to check the labels, drugs and volumes, and get the registry of the operator as well as pharmacist validation of prescriptions and preparations.



Results

Phase 1

Phase one major goal was to test the image capture during the daily environment of manipulation and work on a visualization software that allow drugs identification, constituting solutions and their respective volumes, as well as the preparation labels registry.

After the validation of 3 hours of film (table 1), it was established that, when the validation occurs through the ocular device, it represented a time reduction of 76%, of the time regarding the second element presence.

Total Validation Time				Average Time Reduction	Number of Preparations
Presential		Device			
3 hours	12 min	44 min	19 sec	76 %	44

Table 1. Results from double validation, without marking the critical events.

Phase 2

The goal of the second phase was to implement the marking of the critical points. As referred in the methods this was accomplished through the visualization of the QR code. Our goal was to get a better reduction. Table 2 represents real work data of one day of manipulation (6h) and table 3 shows the direct costs reduction.

Total Validation Time				Average Time Reduction	Number of Preparations
Presential		Device			
6 hours	12 min	25 min	30 sec	92,9 %	75

Table 2. Results from double validation, marking the critical events.

Daily Cost Analysis Materials/Staff	Presential 2 persons	Costs	Device 1 person	Costs
Sterile Gloves	20	6.60 €	8	2.64 €
Gowns	4	14.76 €	2	7.38 €
Boots	8	0.64 €	4	0.32 €
Protection masks	8	5.36 €	4	2.68 €
Caps	8	0.32 €	4	0.16 €
Gloves	8	1.28 €	4	0.64 €
Technicians	2	151.44€	1	75.72 €
	Total	180.40 €		89.54 €

Table 3. Direct daily costs on preparation team.

Conclusion

Since this project represents the implementation of a new routine, it is expected to be a gradual adaptation process. Furthermore, the results here presented in the second phase are extremely positive since they show a potential of a striking reduction.

The implementation of this project will generate a significant reduction in the time cargo associated with this task, the equipment required to enter into the cleanroom and the occupational exposure to carcinogenic substances, allowing operating in accordance with the national good practice.

Additionally this process improves the traceability of the manipulation and validation of every treatment. This gives confidence to all health professionals in the quality and safety of the treatments administrated to our patients and we are fully committed to continue to develop the system and prove is applicability in other areas like sterile and non sterile preparations and to students training or professionals retraining.

References

[1] Conselho do Colégio da Especialidade da Farmácia Hospitalar da Ordem dos Farmacêuticos. Manual de Preparação de Citotóxicos; 2013;

[2] ASHP Guidelines on Handling Cytotoxic and Hazardous Drugs, Am J H Syst Pharm 63 Jun 2006;

[3] Quality Standards for The Oncology Pharmacy Service (QUAPOS 2000).

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Hospital Pharmacists taking the lead – partnerships and technologies

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GANADOR del VII Premio a la Excelencia y Calidad del Servicio Público en Comunidad de Madrid
EXCELENCIA

Abstract Number: CP-085

THE IMPACT OF PHARMACIST INTERVENTIONS ON SAFETY AND COST SAVINGS

Ibáñez-García S, Rodríguez-González C, Martín-Barbero ML, Herranz Alonso A, Tovar-Pozo M, Sanjurjo Sáez M.

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OBJECTIVES

Background: Prescribing errors (PE) are frequent, cause significant harm and prove costly. Pharmacists are a key element for safe prescription of drugs through the interception of PE during the validation process.

Objective: To characterize the severity and cost of the potential outcome of PE and to develop an economic analysis.

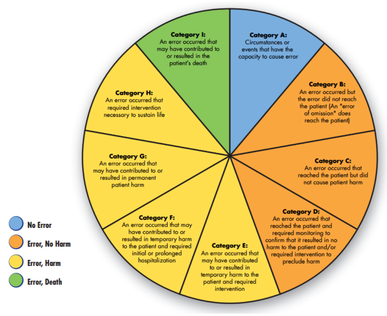
METHODS

Design: A prospective observational study of all prescriptions made during 6 months in a 1,300-bed tertiary teaching hospital provided with a Computerized Physician Order Entry(CPOE) tool combined with a basic Clinical Decision Support System(CDSS).

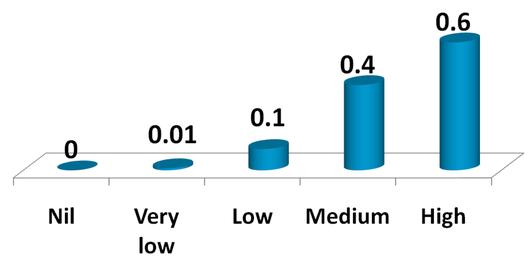
1 

analyzed PE intercepted → through pharmacist validation

Severity (categorized using NCC-MERP Index)



PAE (Probability to cause an Adverse drug Event)



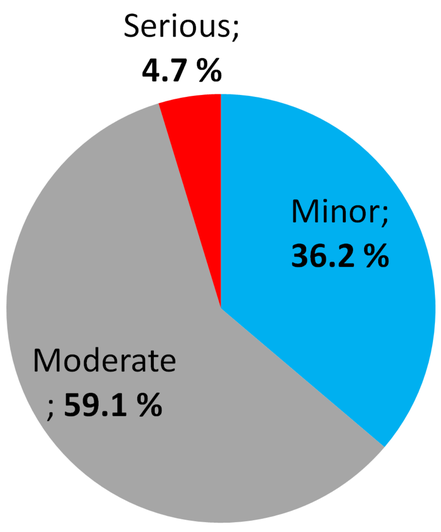
2 **Cost avoidance =** n x PAE x Cost of an adverse drug event (€6,857:standarized by the Spanish Ministry of Health)

3 **Economic analysis** → using the salary of a pharmacist and the cost avoidance estimated

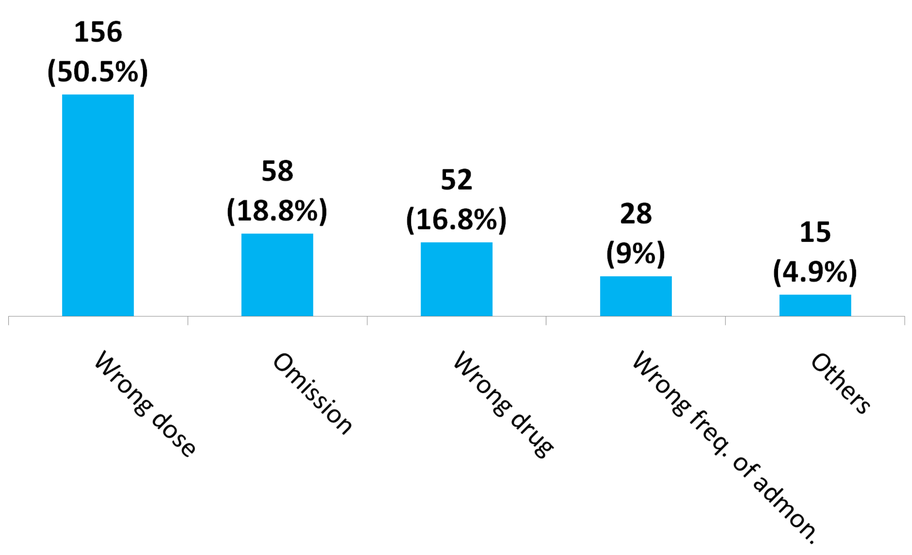
RESULTS

484 PE were intercepted

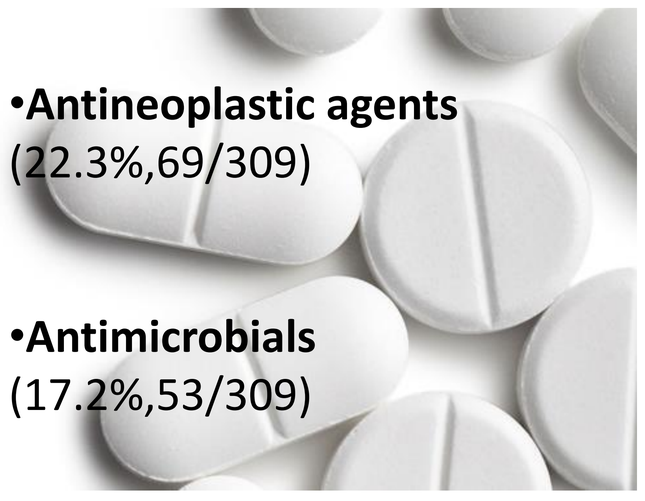
Graph 1. Severity of PE intercepted



Graph 2. Types of moderate-serious PE



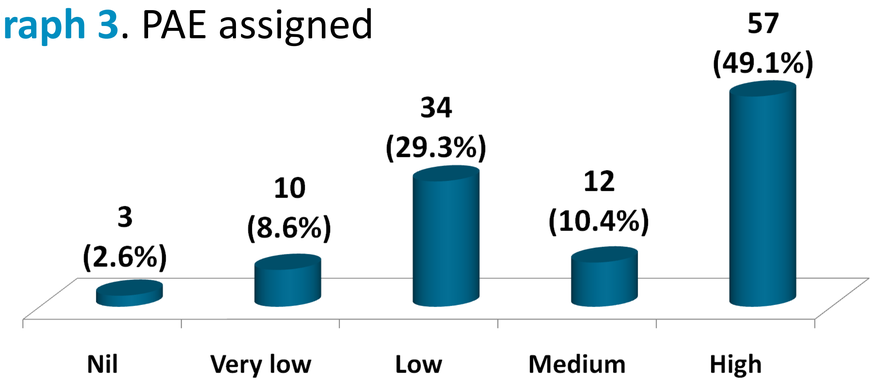
Families of drugs involved in moderate-serious PE:



- **Antineoplastic agents** (22.3%,69/309)
- **Antimicrobials** (17.2%,53/309)

To avoid a possible overestimation of the cost avoidance, we used only those errors with a severity of F-I (116 PE).

Graph 3. PAE assigned



Cost avoidance = € 291,422

Table 1. Economic analysis

Item	
Cost avoidance (€)	291,422
Total profit (€)	291,422
Net profit * (€)	122,312
Profit/cost ratio [1]	1.7

*Taking into account the cost per year of a clinical staff pharmacist: €56,369 (€28,185 during the study period). Six pharmacists were involved in the study: €28,185 × 6 = €169,110. Net profit = 291,422– 169,110. [1]Profit/cost ratio = 291,422/169,110.

Return on investment = 1.7

The overall inter-rater agreement was moderate for the severity (κ =0.57;p<0.005) and strong for the PAE (κ =0.77;p<0.005).

CONCLUSIONS

PE persist despite the implementation of a CPOE system combined with a CDSS.
Pharmacists add important value in preventing PE, and their interventions are financially beneficial for the institution.

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EFFECTIVENESS AND SAFETY OF SWITCHING TO DUAL ANTIRETROVIRAL THERAPY IN A TREATMENT EXPERIENCED HIV COHORT

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BACKGROUND AND OBJECTIVE

Long-term adverse effects, expense, and difficulty of adherence to antiretroviral therapy (ART) have led to study simpler maintenance therapies. Switching from a triple therapy to a dual therapy seems to be effective and safe, but few data exist in clinical practice.

Objective: To assess the effectiveness and safety of simplification to a dual therapy in experienced HIV patients.

MATERIAL AND METHODS

Design: retrospective study. **Inclusion criteria**: experienced HIV patients switching from triple to dual therapy between August 2009 and January 2015. Demographic and clinical characteristics, viral load (VL), CD4+ T-cell count, CD4/CD8 ratio, fasting lipid profile, liver and renal function were recorded when dual therapy was started and at week 24. Previous ARTs, reason for change to dual therapy and adverse events leading to discontinuation of the new regimen were also evaluated.

RESULTS

Previous ART:

- 2 Nucleoside reverse transcriptase inhibitor(NRTI) + ritonavir-boosted Protease Inhibitor (rPI): 55.1%
- 2 NRTI + Non-nucleoside RTI: 18.8%
- 2 NRTI + Integrase inhibitor: 7.2 %

Dual therapy prescription profile:

- rPI + Maraviroc: 41.8%
- rPI + Lamivudine: 35.8%
- rPI + Raltegravir: 13.4%
- Dolutegravir with rilpivirine: 5.9%

Reasons for switching to dual therapy:

- Presence of adverse events (44.8%)
- Treatment simplification (26.9%)
- Virological failure (14.9%)
- Immunological failure (3%)
- Others reasons (10.4%)

✓Bone toxicity: 14 (46.6%)
✓ Nephrotoxicity: 12 (40.0%)
✓ Metabolic disorders: 3 (10.0%)
✓ Gastrointestinal disorders: 1 (3.3%)

Table 1. EFFECTIVENESS AND SAFETY RESULTS

All values are expressed as median (IQR), unless otherwise indicated.

	Baseline (N = 67)	**At week 24 (N = 67)**
VL < 37 copies/ml (% of patients)	55(82.1%)	63(94%) No virological failures was detected during treatment
CD4 cell count (cel/mcL)	569 (418-743)	581(364-785)
CD4/CD8 ratio	0.61(0.39-0.92)	0.57(0.39-0.84)
Cholesterol(mg/dl) LDL(mg/dl) HDL(mg/dl) Triglycerides(mg/dl) Atherogenic Index	189(154-218) 107(86-121) 50(40-64) 120(92-161) 3.7(3.1-4.4)	191(170-229)* 107(86-136) 47(40-64) 129(96-197) 4.1(3.2-5)
ALT(U/L) AST(U/L) GGT(U/L) Alkaline phosphatase(U/L)	22(16-29) 23(17-31) 29(18-68) 80(70-96)	20 (15-26)* 16(15-21)* 25(16-53)* 78(61-94)*
Creatinine(mg/dl) Phosphate(mg/dl) GFR <60 ml/min(% of patients)	0.91(0.8-1.03) 3.2(2.8-3.6) 92.5%	0.91(0.77-1.01) 3.3(2.9-3.9) 92.5%

* p < 0,05

Eighteen patients (26.9%) interrupted the dual therapy: 4 patients (6.0%) switched to a triple therapy. Fourteen patients (21.0%) switched to a different dual therapy due to: toxicity (42.9%), drug interactions (28,6%) simplification (21,4%), and failure to achieved an undetectable VL (7.1%).

CONCLUSIONS

Switching to dual therapy for maintenance treatment is effective, safe and non-inferior to triple therapy in treatment experienced HIV patients.

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20th EAHP Congress – Vienna March 2016
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DD-027

IMPLEMENTATION AND EVALUATION OF AN APPOINTMENT BASED MODEL FOR OUTPATIENTS ATTENDED IN A HOSPITAL PHARMACY.

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Objective

To implement and evaluate the results of changing from a queuing model (QM) to an appointment-based pharmacy care model (ABM) for outpatients attended at a tertiary hospital pharmacy.

Materials and methods

- The study included all outpatients attended at the pharmaceutical care since inclusion of the ABM in hospital in May 2015 to September 2015.
- A retrospective data collection analysis through the records of the dating and dispensing software was performed.

Results and Discussion

✓ Pharmacy workflow was completely redesigned, staff was trained, and patients were informed about the new ABM model. It is shown in Figure 1 below.

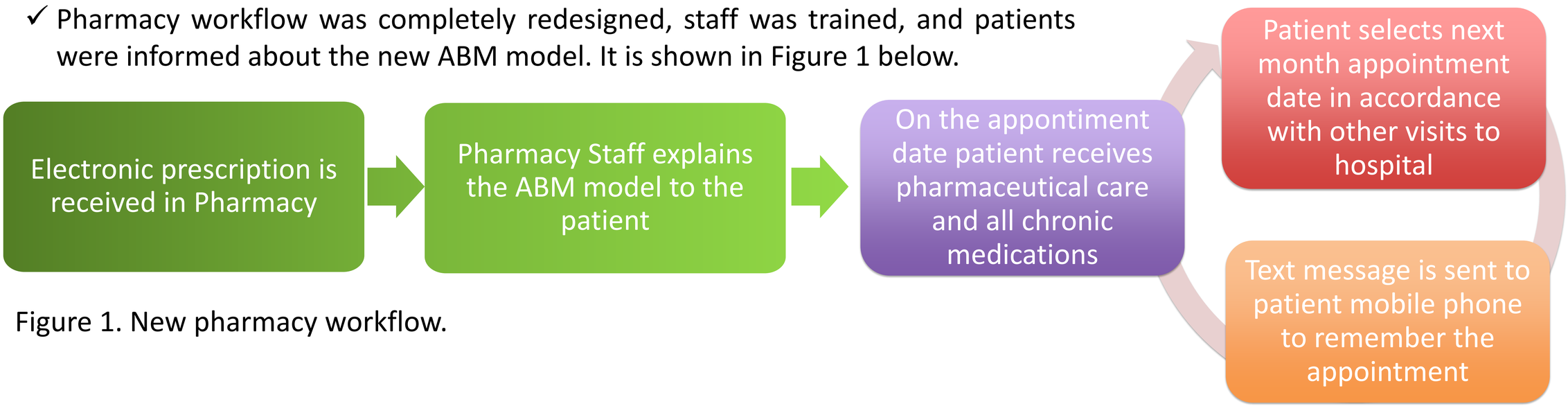


Figure 1. New pharmacy workflow.

✓ As can be seen in figure 2, a mean of 703 outpatients come to collect their medications to the hospital pharmacy weekly (monthly: 2956).

✓ There is an increase in the number of patients attended by the ABM with a reduction in patients remaining QM. Although each month the increase is lower, it has not yet reached a flat line.

✓ The mean percentage of patients coming by the ABM during the first five months post implantation (figure 3) was 21, 47, 63, 75 and 81% of total attended patients.

✓ A 14% of the patients who had and appointment didn't come on their scheduled date and this value is constant along all time the study last.

Figure 2

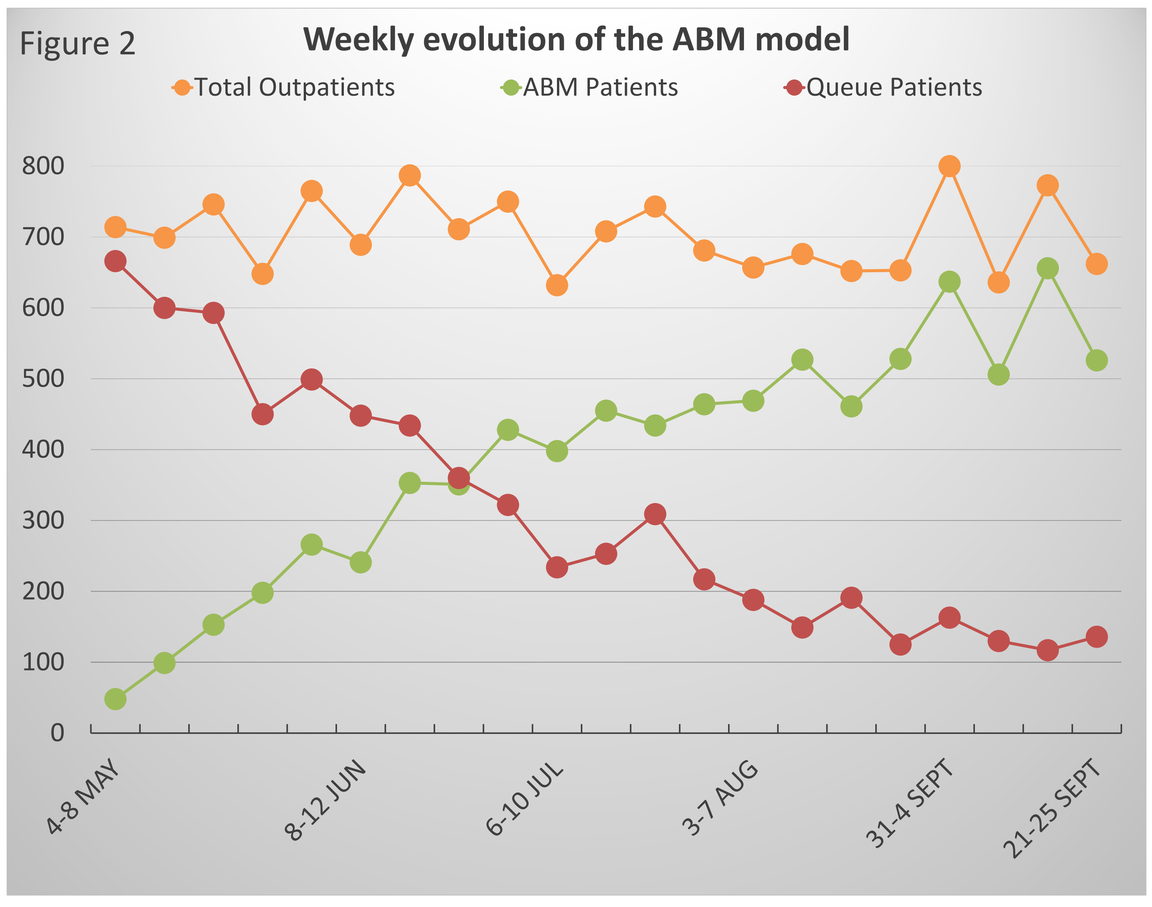
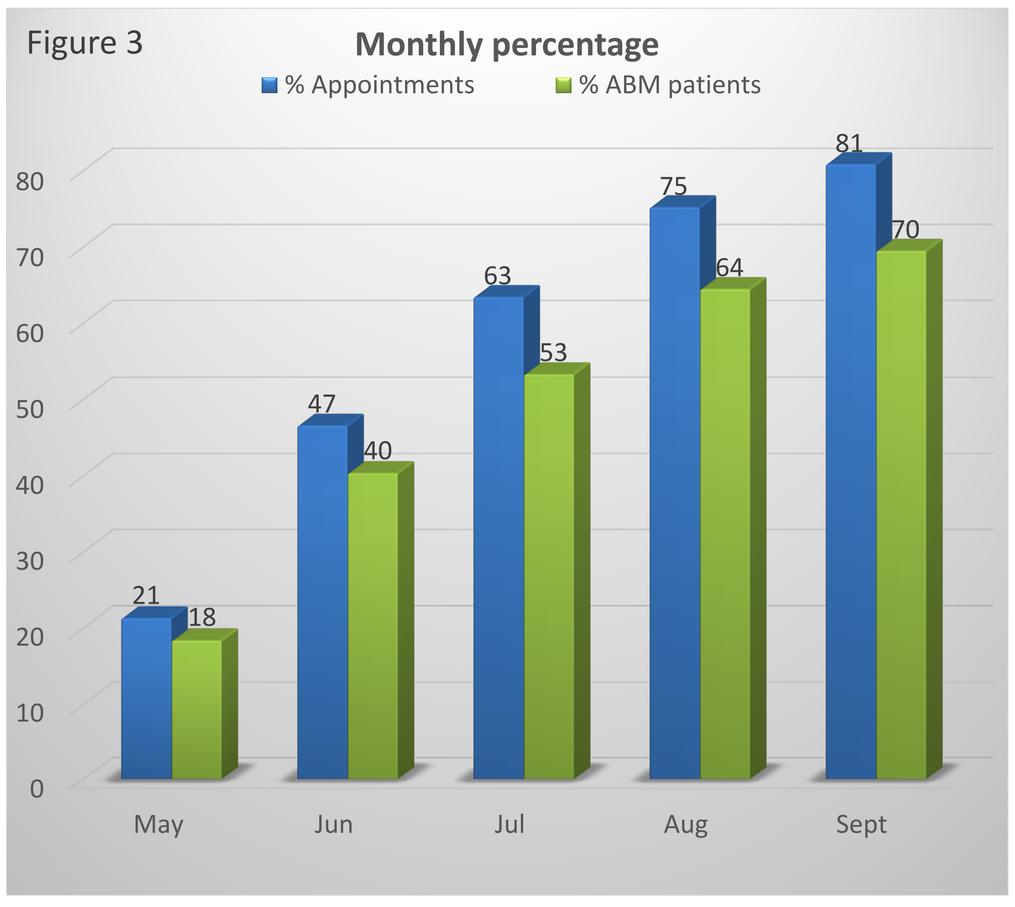


Figure 3



Conclusions

✓ Pharmacy workflow redesign allows to implement an ABM for outpatients in a hospital pharmacy.

✓ Five months after its implementation 81% of the patients come to the pharmacy care by ABM.

Aknowledgments

The authors want to thank all personnel in the Pharmacy and patients who voluntary participated in this study.

PKP-031

CLINICAL PHARMACOKINETICS OF EVEROLIMUS IN LUNG TRANSPLANTATION: STRATEGIES OF MONITORING

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BACKGROUND

Therapeutic monitoring of everolimus is necessary to determine an optimal dosage regimen in lung transplantation patiens to prevent graft rejection due to the narrow therapeutic window. The area under the concentration-time curve (AUC0-12) is the best strategy for the pharmacokinetic study because reflects the total drug exposure in the body, especially in cystic fibrosis (CF) patients, who have abnormalities of the gastrointestinal system.

PURPOSE

To evaluate the absorption profile of everolimus in patients with CF after lung transplantation in order to optimize the immunosupresive therapy.

MATERIAL AND METHODS

Pharmacokynetic, descriptive and cross-sectional study was conducted in lung transplantation patients with a determination of AUC0-12 of everolimus at less than four months post-transplantation. After seven days minimum of receiving the same dose, nine blood samples were collected at predose, 0.5, 1, 2, 3, 4, 6, 8 and 12 hours post-morning dose. The target trough levels were 3-8 ng/mL. Everolimus exposure was evaluated according to the dosage. Everolimus serum concentration was measured by QMS Immunoassay.

Table 1. Characteristics of the patients

Patient	Age (Years)	Weight (kg)	Treatment
1	17	46	EVE 1,25/1,25 mg + TAC 4/4 mg
2	29	44	EVE 1,5/0,75/1,5 mg + TAC 3/3/3 mg
3	26	54	EVE 1,5/1mg + MPA 360/360 mg
4	18	47	EVE 1,75/1,75 mg + TAC 5/5 mg
5	40	56	EVE 1,25/1,25 mg + TAC 2,5/2,5 mg
6	13	28	EVE 1,5/1,5 mg + TAC 2,5/2,5 mg
7	29	67	EVE 1,75/1,75 mg + TAC 3/3 mg
Median	26	47	
Range	13-40	28-67	

EVE: everolimus; TAC: tacrolimus; MPA: mycophenolate sodium

RESULTS

Seven full pharmacokynetics analyses were performed in bilateral lung transplant patients (Table 1). All of them were women. Two patients showed a normal absorption profile of everolimus and five patients showed a low overall exposure to everolimus because the value Cmin and AUC0-12 is below the normal range (Table 2). All this patients underwernt dose/interval modification of everolimus after results. Following the adjustment, all patients reached levels within therapeutic range.

Table 2: Pharmacokinetics parameters

Patient	Cmin (ng/mL)	Cmax (ng/mL)	Tmax (h)	Css (ng/mL)	AUC0-12 (ng·h/mL)
1	1.62	6.40	1	2.57	30.81
2	2.00	7.70	6	6.63	53.10
3	3.45	5.74	2	4.18	50.21
4	1.86	5.64	2	2.85	34.30
5	1.97	6.38	2	4.50	54.02
6*	4.58	16.30	1	9.44	113.31
7*	4.51	18.51	1	7.02	84.28
Median	2.00	6.40	2	4.50	53.10
Range	1.62-4.58	5.6-18.5	1-6	2.57-9.44	30.8-113.3

Cmin: trough concentration; Cmax: peak exposure; Tmax; time to reach peak exposure; Css: steady-state concentration; AUC: area under the curve
(*): Patients who showed normal absorption profile of everolimus

CONCLUSIONS

The pharmacokynetics variability of everolimus is very high. Monitoring of everolimus levels could optimize immunosupresive therapy. The AUC0-12 will be calculated at any CF patients regardless time after transplantation as long as they are not trough levels in the therapeutic range.

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