ejpmr, 2021,8(10), 78-83

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

EVALUATION OF THE ECONOMIC IMPACT OF THE LOSS OF EXPENSIVE DRUGS IN THE RETROCESSION UNIT OF THE HMIMV OF RABAT

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Article Received on 10/08/2021 **Article Revised on 31/08/2021** **Article Accepted on 21/09/2021**

ABSTRACT

Introduction: The unit of retrocession of anticancer drugs at the Military Hospital of Instruction Mohammed V (HMIMV) Rabat ensures the dispensation of anticancer chemotherapy drugs to patients. The objective of this study is to quantify the losses of leftovers generated by the current mode of preparation of anticancer chemotherapies for our hospital establishment. **Materials and Methods:** This is a retrospective study that was conducted at the cancer drug retrocession unit of HMIMV in Rabat, Morocco between January and October 2020. The main analysis compared the actual cost of leftover preparations with the theoretical costs of leftover preparations if they were made in the care units. This analysis covered a set of 3000 chemotherapy preparations prescribed in the prescriptions. **Results:** During the 10 months of the study, 4,511 vials of the different molecules in the study were dispensed to patients, corresponding to a total of €480,518.07. From this number of vials used, we can save 1,779 vials per medical prescription, which represents an average of potential savings of around €**56,572.50** (total cost of the remaining vials for 10 months*100/total amount of the expenses) This amount corresponds to **11.77**% of the total amount of care granted to patients. The total cost of the remainders for 10 months is 56,572.50 euros, which corresponds to a total annual cost of 67,887.00 euros. TRASTUSUMAB, BEVACIZUMAB, BOTEZOMIB, AZACITIDINE, CETUXIMAB and PEMETREXED are the six molecules that represent the most losses among all our molecules studied. **Conclusion:** According to the financial elements found in our study, it is imperative to set up a centralized cytotoxic reconstitution unit (CCRU). The management of leftovers in this unit can generate significant savings depending on the molecules. Centralizing the preparation of anti-cancer drugs is of economic interest, by optimizing the management of leftovers. Our perspective is to be able to participate in this new setting up of the UCRC and to compare our results with those of the new installation.

KEYWORDS: Retrocession, anti-cancer drugs, expensive drugs, loss, leftovers.

INTRODUCTION

The management of cancer patients is a major public health issue due to its frequency, which is increasing year after year, its severity and the cost of its management. Therapeutic innovations are constantly appearing, bringing many hopes for patients, but are generally accompanied by high prices. This is why it is essential to find solutions to finance these innovations or limit expenses.

The unit of retrocession of anticancer drugs at the Military Hospital of Instruction Mohammed V Rabat (HMIMV) ensures the dispensation of anticancer chemotherapy drugs to patients, however the cost of the bottles of anticancer drugs is high and any loss of substance can lead to a significant additional cost of the therapeutic management of the patient.

The objective of this study is to quantify the losses of leftovers generated by the current mode of preparation of anticancer chemotherapy for our hospital establishment.

MATERIALS AND METHODS

This is a retrospective study that was conducted at the retrocession unit of anticancer drugs of the HMIMV of Rabat in Morocco between January and October 2020. All prescriptions that involved preparations were collected and analyzed using a collection grid.

The main analysis compared the actual cost of leftover preparations with the theoretical costs of leftover preparations if they were made in a centralized cytotoxic reconstitution unit (CCRU).This analysis covered a set of 3000 chemotherapy preparations prescribed in the orders.

1. The context of the retrocession unit of anti-cancer drugs of the HMIMV of Rabat

Since the amendment of Article 44 of Law 65-00 on the code of basic medical coverage (7/7/2011), as of December 31, 2012, it was prohibited for managing organizations to combine the function of health insurance manager and producer of care including the acquisition and management of drugs.

Thus since 2014 the Pharmacy division has a retrocession unit for anticancer drugs, biotherapy, antivirals, immunosuppressants, products for the prevention of graft rejection; hormone therapy, hemophilia and multiple sclerosis.

Drugs that require special management to compensate for national and international shortages and ensure permanent availability in order to avoid "therapeutic voids" that compromise the success of treatment protocols while avoiding losses due to expiration or the holding of "dead" stocks; requiring special vigilance during handling and storage; some are subject to a risk management plan (e.g. thalidomide, lenalidomide); significant adverse effects, hence the need for therapeutic education of the patient.

2. Context of cytotoxic preparation units at the patient's bed

The handling of cytotoxic substances by health professionals is sometimes carried out by personnel who are not trained for this type of procedure and are unaware of the danger involved in the use of these drugs in the absence of the necessary precautions, in addition to the conditions of execution that do not always offer sufficient safety, puts the nursing staff who prepare and administer anti-cancer treatments, the environment and the patient at risk.

3. Economic analysis

The economic analysis concerned the evaluation of the quantities of anticancer drugs inherent in two modes of organization: preparation circuit in a centralized system (simulation mode) and decentralized.

The main analysis compared the actual cost of anticancer drugs for preparations in a centralized system with the theoretical costs of the same preparations performed in the care units. It covered all the prescriptions made between January and October 2020, including the following molecules (trastusumab, bevacizumab, carboplatin, cyclophosphamide, docetaxel, oxaliplatin, cetuximab, dacarbazine, gemcitabine, epirubicin, paclitaxel, etoposide, irinotecan, pemetrexed, vinorelbine, cisplatin, botezomib, azacitidine, and rituximab)

Decentralized system

Each preparation is carried out taking into account the different packaging of the drug available on the market. The estimate is made "to the nearest vial" per preparation, considering that the rest of the unused vial is disposed of after each preparation.

Centralized system (simulation mode)

Over the period studied, the quantities of active ingredient (API) observed on the prescriptions include : the exact dose prepared (mg, IU);

Cost estimate

The valuation is based on hospital prices for the year 2020. It concerns only anticancer drugs. It therefore excludes diluting solutions and sterile medical devices, on the assumption that they do not vary regardless of the place and type of preparation. Similarly, structural and personnel costs are not taken into account.

RESULTS

During the 10 months of the study, 4,511 vials of the different study molecules were dispensed to patients, corresponding to an amount of €480,518.07; of this number of vials used, 1,779 vials can be saved per medical prescription, which represents an average of potential savings of around €56,572.50 (total cost of the remaining vials for 10 months*100/total amount of the ECP) This amount corresponds to 11.77% of the total amount of care granted to patients (Table 1).

Table 1: Overall table of results obtained for the study molecules.

Designation	Dosage per ur	Total amount of pec (€)	Cost of the remainder/molecule (€)	Share of cost per molecule (%)	Number of fls used (n=4511)	Nombre de flacons de reliquats (n=1779)	Dose of residue in mg
TRASTUSUMAB	150 440	227999,74	31329,93	55,38	642	409	28932
BEVACIZUMAB	100 400	77492,76	7415,27	13,11	371	164	8285
CARBOPLATINE	150 450	5662,09	760,06	1,34	340	164	12062
CYCLOPHOSPHAMIDE	1000 200	1205,42	90,49	0,16	486	176	17392
DOCETAXEL	80 20	13376,64	769,06	1,36	405	125	1105
OXALIPLATINE	100	5587,29	718,61	1,27	397	169	4532

	50						
CETUXIMAB	100	28454,03	1762,31	3,12	155	19	960
DACARBAZINE	100	540,89	38,09	0,07	71	10	500
GEMCITABINE	1000 200	2896,97	174,79	0,31	419	100	10090
EPIRUBICINE	50 10	312,30	25,55	0,05	31	7	102
PACLITAXEL	100 30	9348,63	501,14	0,89	390	105	1316
ETOPOSIDE	100 200	567,97	121,87	0,22	74	74	3129
IRINOTECAN	100 40	1856,98	124,71	0,22	194	54	962
PEMETREXED	500 100	56942,32	3125,57	5,52	126	28	1370
VINORELBINE	10 50	1537,87	167,71	0,30	50	26	133
CISPLATINE	50 10	372,50	19,60	0,03	132	31	161
BOTEZOMIB	1 3.5	28839,37	7093,56	12,54	110	76	58
AZACITIDINE	100	5049,00	1539,33	2,72	41	21	1250
RITUXIMAB	100 500	12475,30	794,85	1,41	77	21	995
Total amount of CEP LF (€) for 10 months		480 518,07	Contract amount 2020 (€)		3 003 404,54		
total cost of backlog for 10 months (€)		56 572,50	annual estimate of the total cost of the backlog (€)		67 887,00		
Remaining balances/total CEP		11,77	Estimated % backlog/total market2020		2,26%		

DESIGNATION: international common designation of the 19 molecules included in the study.
DOSAGE PER REGULATORY UNIT: this is the dosage of the molecule in mg.
GLOBAL AMOUNT OF CEP: corresponds to the global amount of the molecules granted to
price of the molecule x number of vials dispensed to the patient
RELIQUATE DOSE IN MG: sum of the residual doses collected by molecule = dose in relation to the regulatory unit of the product - the dose on the prescription in mg
COST OF REMAINDER PER MOLECULE = sum of the prices of the doses of collected remnants = dose of remnant in mg x overall amount of CEP /dose in relation to the UR of the product.
SHARE OF COST PER MOLECULE IN % = cost of residue dose per molecule x100/ total CEP amount.
NUMBER OF BOTTLES USED: total number of bottles dispensed to patients of the different molecules (N=4511).
-NUMBER OF BOTTLES OF RELIEF: number of bottles to be saved per medical prescription (N=1779) out of the 4511 bottles used.
NB: 1 euro(€)=10.83 Moroccan Dirham (DHS).

Economic aspect: Our study shows that the total cost of residuals for 10 months is 56 572,50 € which corresponds to a total annual cost of 67 887,00 €.

TRASTUSUMAB, BEVACIZUMAB, BOTEZOMIB, AZACITIDINE, CETUXIMAB and PEMETREXED were the six molecules that represent the most losses among all our studied molecules (Table 2, Figure 1 and 2).

Table 2 : Cost of the residue dose per product and estimated financial losses in euro.

DESIGNATION	Cost of the dose of the residue by product (€)
CISPLATINE	19,6
EPIRUBICINE	25,55
DACARBAZINE	38,09
CYCLOPHOSPHAMIDE	90,49
ETOPOSIDE	121,87
IRINOTECAN	124,71
VINORELBINE	167,71
GEMCITABINE	174,79

PACLITAXEL	501,14
OXALIPLATINE	718,61
CARBOPLATINE	760,06
DOCETAXEL	769,06
RITUXIMAB	794,85
AZACITIDINE	1539,33
CETUXIMAB	1762,31
PEMETREXED	3125,57
BOTEZOMIB	7093,56
BEVACIZUMAB INJ	7415,27
TRASTUSUMAB INJ	31329,93
total cost of balances for 10 months (euro)	**56 572,50**
annual estimate of the total cost of leftovers (euro)	**67 887,00**

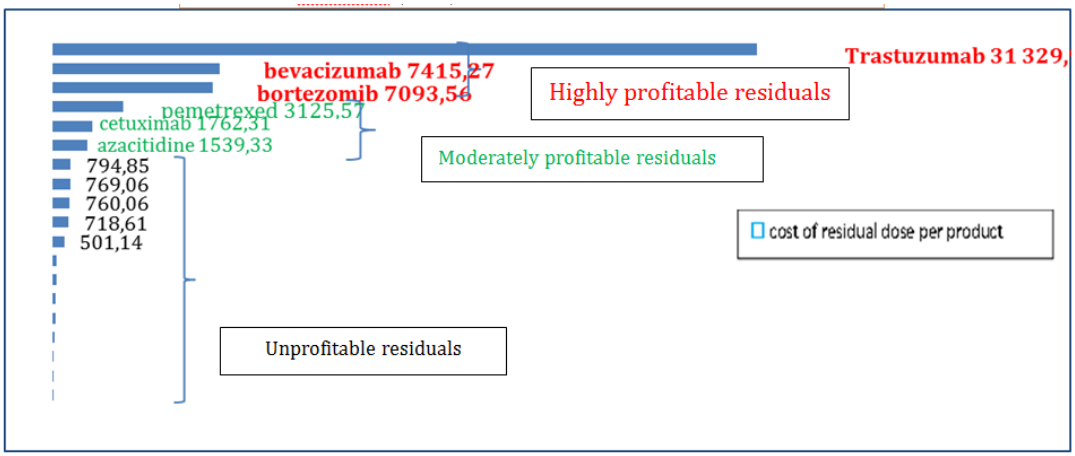

Figure 1: Cost of residual dose by product.

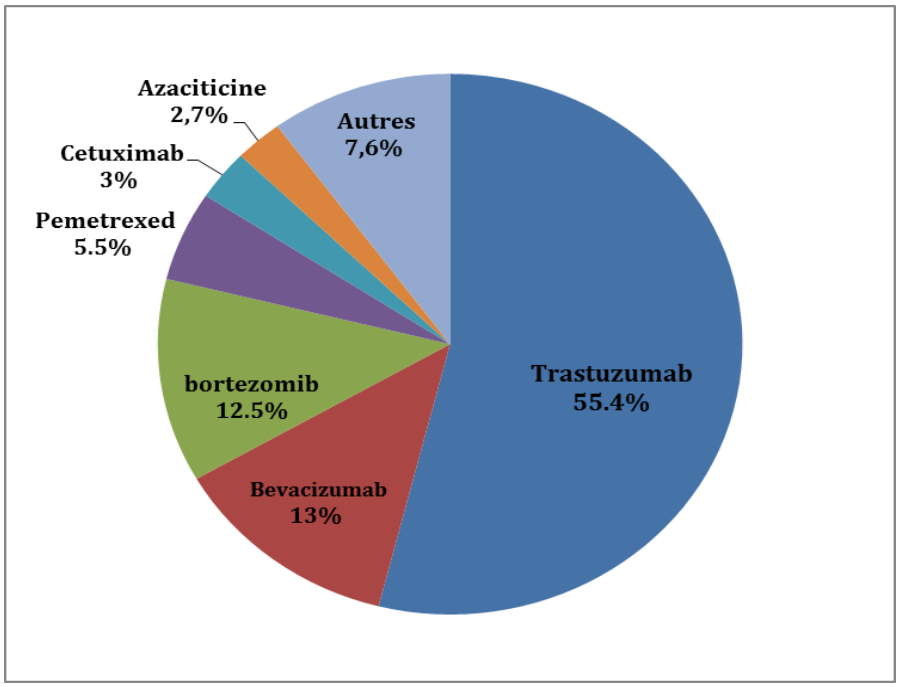

Figure 2: Share of residual cost by product in % - Over 10 months.

DISCUSSION

The financial losses observed during the preparation of anti-cancer chemotherapy were of the order of 56 572.50 € over 10 months or 67 887.00 € per year.

This cost corresponds to a value of 11.77% of loss on the total of care granted to patients and 2.26% of the global budget allocated to the 19 anticancer drugs for the year 2020. These huge losses are mainly due to the mode of

preparation of chemotherapies, notably the absence of UCRC.

It was noted that these losses mainly concerned 06 molecules/19 molecules studied which were classified according to their profitability and physicochemical stability (Figure 3). Thus, the management of the residues of these 6 molecules would be very profitable for our establishment in terms of savings to be made, safety for the nursing staff as well as for the patient and the environment.

	GROUP AND CATEGORY	RANKING	MOLECULES
PROFITABILITY OF THE RELIQUAT (Cost)	**GROUP 1**	Very profitable residues 81.03%.	**TRASTUZUMAB (55,38 %)** BEVACIZUMAB BORTEZOMIB
	GROUP 2	Moderately profitable residuals 11,36 %	AZACITIDINE CETUXIMAB PEMETREXED
	GROUP 3	Unprofitable residuals 7.61	CISPLATINE EPIRUBICINE DACARBAZINE CYCLOPHOSPHAMIDE ETOPOSIDE IRINOTECAN VINORELBINE GEMCITABINE PACLITAXEL OXALIPLATINE DOCETAXEL CARBOPLATINE RITUXIMAB
PHYSICO-CHEMICAL STABILITY OF THE RESIDUE	**CATEGORY I**	Long-term stability 35D-14D	BORTEZOMIB, BEVACIZUMAB, CETUXIMAB, GEMCITABINE RITUXIMAB CISPLATINE DOCETAXEL EPIRUBICINE ETOPOSIDE IRINOTECAN OXALIPLATINE VINORELBINE CARBOPLATINE PEMETREXED CYCLOPHOSPHAMIDE PACLITAXEL
	CATEGORY II	Short-term stability 1d -2d-5d	AZACITIDINE, TRASTUZUMAB, DACARBAZINE

Figure 3: Classification of molecules according to cost effectiveness and physicochemical properties.

The current model for the preparation of cytotoxics no longer meets the current needs of large hospitals such as our institution. In addition, the very high cost of new targeted therapies is pushing us to review our model. Several studies have shown that we can save up to 46.7% of these losses.[1-11] This investment could be amortized in less than 2.5 years with the savings made if a centralized cytotoxic reconstitution unit (UCRC) is set up at the HMIMV. It would allow these products to be kept in good storage and identification conditions with little or no risk of product contamination.[12] Numerous studies carried out in different hospitals have been published on this subject. They have defined the losses as a consequence of inappropriate disposal, non-use or partial use of drug ampoules, vials or syringes.[13]

In Morocco, our study carried out at the HMIMV in Rabat for the year 2020 estimated a saving to be generated of about 2.26% in relation to the overall budget for anticancer drugs, which is similar to the study carried out in France in 1998, in a hospital center, which showed that there is a saving generated by the centralised system of 3.5% in relation to the overall budget for consumption of cytotoxics. This value takes into account

the reuse of opened vials within the limits of their stability and, secondarily, the use of multidose vials.[1] A second study conducted in another hospital in France in 2000 estimated this saving at 8.1% of the overall budget allocated to these products.[2] In a third study conducted in an Italian hospital, the savings generated were 9.6%. Finally, other studies have demonstrated this reduction in treatment costs from 2.9% to 46.7%, by implementing a UCRC.[3-11]

To minimize waste, four corrective measures are proposed :

- A weekly pathology/drug program, to allow the reuse of leftovers for other patients, while respecting the chemical and microbiological stability of cytotoxics.
- For molecules whose stability is short-lived, a more systematic grouping of courses of treatment on the same day can also be an additional factor of economy. Stability data are physicochemical data with maximum durations subject to preparation under aseptic conditions and to be adapted according to the organization adopted by each establishment, in compliance with Good Manufacturing Practices.
- The choice, as much as possible, of multi-dose vials because they maintain microbial and chemical stability for a period of several weeks.
- Rounding of doses to less than 5% of the calculated dose (dose banding).

CONCLUSION

According to the financial elements found in our study, it is imperative to set up a centralized cytotoxic reconstitution unit (CCRU). The management of leftovers in a CRU can generate significant savings depending on the molecules. Centralizing the preparation of anti-cancer drugs is of economic interest, by optimizing the management of leftovers. Our perspective is to be able to participate in this new UCRC set-up and to compare our results with those of the new facility. Concerning the reduction of financial losses, the UCRC has an important investment cost. Cytotoxics being risky, sensitive and expensive agents, the setting up of the UCRC is a solution which will allow to reduce the financial losses, to guarantee the quality of the reconstitution (for the patient), the protection of the manipulators and the protection of the environment.

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