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Financial impact of oral chemotherapy wastage on society and the patient

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Abstract

Background: targeted oral agents are now increasingly being utilized in cancer treatment, but are expensive. Changing the dose of these medications due to toxicity or discontinuation secondary to disease progression or death causes waste from unused medication. Limiting waste is an important goal, as waste has a substantial financial impact on patients and insurance companies.

Methods: Patients started on oral targeted agents' sunitinib, everolimus, axitinib, or vemurafenib between January 2012 and February 2015 who obtained their medications at Holden Comprehensive Cancer Center specialty pharmacy were included in the analysis. We acquired dispensing data retrospectively for each of the agents and reviewed patient charts. Wasted tablets/capsules were calculated from their last fill to the dates of stoppage or dose adjustment. The amount associated with the wastage was calculated using the average wholesale price. Repository drug usage data during the same time period was obtained.

Results: Eighty-eight patients had their prescriptions filled at Holden Comprehensive Cancer Center during the study time period. Waste occurred in 41% of all patients with primary reasons attributed to cancer progression in 25 patients, death in five patients, toxicity in five patients and increase in dosage of targeted therapy in two patients. A total of 1179 tablets or capsules were wasted from all causes, priced at a total of \$248,595.69.

Conclusion: Oral chemotherapy medications are associated with wastage, which is a significant financial burden to society. Progression of disease emerged as the single most important factor accounting for wastage. Novel ideas are needed to prevent wastage, thereby reducing healthcare costs.

Keywords

Financial toxicity; targeted therapy; wastage

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Background

Cancer drugs make up the single largest category of specialty drug spending, and protein kinase inhibitors are a growing class of cancer drugs.¹ Unused oral targeted agents create an expensive loss for society. Apart from the question of whether the high cost of oral cancer therapy in the US is justifiable, medication that cannot be used is a waste. Whether the cost is a loss to the individual patient or to the insurer who has to pass on costs to policyholders, limiting waste is an important goal.

Reasons for wastage vary. A patient starting an oral agent and needing a lower dose due to toxicity may have no use for the remaining doses of their prescription. If the patient's cancer progresses while on therapy and the treatment is changed, any remaining drug at the time of the change is a loss. Noncompliance is also a waste if the medication goes unused due to patient-related factors. Many oral antineoplastic agent refills are being mailed to the patients in advance. These refills could be wasted if the time of delivery and time of evaluation do not coincide. Examples could include discovery of disease progression or diagnostic test that reveal adverse events requiring dose modification or discontinuation, such as drug-induced organ dysfunction or QT prolongation detected by ECG. The cost of wasted chemotherapy agents for any individual patient depends upon the patient's copayment structure for filling a prescription, the yearly deductible, and the number of times the patient has to refill the prescription. A prescription written for a shorter time interval would reduce potential wastage due to dosage adjustments for toxicity, but, if the patient has a copayment with each prescription, the cost to the patient would be increased. For the drug manufacturer, drug wasted would imply generation of more revenue. Potential costs for safe disposal of oral chemotherapies and its impact on the environment also add cost to the society. We retrospectively evaluated the reasons for wastage of oral targeted therapeutic agents, the cost to the insurance company thereby an indirect cost to the society and the direct costs to the patient resulting from this wastage and evaluated potential means of reducing wastage.

Methods

Holden Comprehensive Cancer Center (HCCC) pharmacy is a designated specialty pharmacy permitted to dispense oral chemotherapy agents. The chemotherapeutic agents were selected based on their high cost and packaging (e.g. everolimus is dispensed in blister packaging versus others in sealed bottles). Dispensing data for patients filling their sunitinib² (metastatic renal cancer, gastrointestinal stromal tumor, pancreatic neuroendocrine cancer, alveolar soft part sarcoma, desmoplastic small round cell tumor), vemurafenib³ (metastatic melanoma), everolimus⁴ (metastatic renal cancer, pancreatic neuroendocrine tumor, hormone receptor positive metastatic breast cancer, relapsed Hodgkin's lymphoma, and esthesioneuroblastoma) and axitinib⁵ (metastatic renal cancer) oral chemotherapy prescriptions at HCCC pharmacy between January 2012 and February 2015 was obtained after institutional review board approval. Data included the patients' primary insurance and any supplementary insurance plan, the strength and quantity of each chemotherapy dispensed, package size, and patient copayments. Patient charts were retrospectively reviewed to obtain information regarding indication of therapy, dose adjustment, and discontinuation reasons, which could include progression of disease, toxicity, and/or death.

In accordance with the Iowa Drug Repository law,⁶ some patients meeting specific eligibility criteria are able to obtain donated medication from the repository program at no cost. That data were requested from the medication assistance center at University of Iowa Hospitals and Clinics.

The amount of wasted medication was calculated from the last prescription fill date of each oral chemotherapy agent and the date of discontinuation or dose adjustment of that agent or the date of the patient's death. The cost of obtaining each chemotherapeutic agent by the specialty pharmacy from the drug manufacturers is dependent on several contractual factors. That amount together with the dispensing fee is billed to the insurance and an amount deemed appropriate by the insurer is paid to the pharmacy. For the purpose of this study, a standard average wholesale price (AWP) for each chemotherapeutic agent and its respective strengths were obtained from a reputable online source⁷ (Supplementary Table 4). To calculate the average cost to the patient of wasted medication, we added each patient's total copayments and divided it by quantity dispensed during the duration of therapy.

Results

A total of 88 patients whose dispensing and insurance data were available during the studied time period filled their prescriptions for any of the studied drugs at least once at the HCCC specialty pharmacy. Eighteen patients had ongoing treatment beyond the study interval and 13 patients eventually transferred pharmacies during our study interval, resulting in 57 total patients who completed their treatment while filling their prescriptions at HCCC. Dose adjustments due to drug toxicity triggered a new prescription in 6 of 88 patients. Drug discontinuations occurred in 40 patients due to progressive disease and in nine patients secondary to death.

Progression of disease was the most frequent reason for drug waste (25 of 88 patients). Drug toxicity and death equally contributed towards wasted medication (5 of 88). Interestingly, dose escalation in two patients receiving axitinib resulted in drug waste (Table 1).

In January 2014, a clinical pharmacist was assigned to the outpatient oncology clinic at our institution. From 2012 to 2013, 14 of 33 patients (42%) experienced medication waste. From 2014 to 2015, 20 of 55 patients (36%) experienced medication waste.

Collectively 1179 tablets/capsules potentially worth \$248,595.69 (as calculated using AWP pricing) were wasted. The wasted medication led to \$2514.21 in patient copayments (Table 2).

During the study time period, a total of 450 tablets (sunitinib—none, one hundred and twenty 5 mg axitinib tablets, one hundred and eighty 1 mg axitinib tablets, one hundred and twenty vemurafenib tablets, and thirty 10 mg everolimus tablets) were requested from the Iowa Drug Repository program and used by three patients (Table 3).

Patients have different prescription coverage through their insurances. We examined the most frequently utilized insurance plans billed for prescriptions through our specialty pharmacy. Private health insurance accounted for 62% of the health care coverage for these

medications, followed by Medicare D plans (16%), state Medicaid (16%), and a medication discount program (6%).

Discussion

In our retrospective observational study, we examined four oral targeted chemotherapy drugs used for various indications and calculated the total amount of wasted medication.

Progression of disease was found to be the primary reason for wastage (28.4%), resulting in an increase cost to society. Drug toxicity and death were other reasons that lead to wastage (Figure 1). We assumed the medication wasted was not returned or reused. In several cases, patients received 30-day supplies a few days prior to imaging for assessment. In these cases, imaging tests showed progression of disease, prompting a change in therapy and resulting in wasted medication. This emphasizes the importance of coordinating the dispensing date with disease assessment testing.

Pharmaceutical manufacturers determine the strength of the drug in each dosing unit, and optimal dosing is determined in clinical trials. In an attempt to dose reduce a drug secondary to toxicity, the prescriber may try to use the available strengths to minimize waste. However, this is not always feasible. For example, an evaluated patient with a pancreatic neuroendocrine tumor was prescribed sunitinib malate at the recommended dose of one 37.5 mg capsule daily. As per the prescribing instructions, a decrement of 12.5 mg was recommended which required a new prescription for 25 mg capsules, resulting in wastage of the remaining 37.5 mg capsules. An alternative dosing strategy could have been to prescribe three 12.5 mg capsules to make the 37.5 mg dose, for which a 30-day supply would cost the same amount (30 capsules of 37.5 mg sunitinib at AWP of \$442.51 = \$13,275.30; 90 capsules of 12.5 mg sunitinib at AWP of \$147.50 = \$13,275.00) for both the patient and the insurance company (assuming patient copayments are based on a percentage of total cost or flat amount per prescription), but would increase the “pill burden” for the patient. In some cases, tablets may be split in order to decrease the dose, which is not a feasible option for sunitinib capsules or other oral chemotherapy agents, as the pharmacokinetics of split tablets have not been studied.

A unique situation we encountered was a patient with metastatic renal cell carcinoma prescribed 7 mg of axitinib (one 5 mg tablet plus two 1 mg tablets). The patient tolerated the dose well, so it was increased to 10 mg daily dose (two 5 mg tablets), resulting in wastage of the 1 mg tablets. In the case of axitinib, utilizing 1 mg strength tablets to make up a 30-day supply of a 5 mg daily dose would cost insurance company more money while also increasing the pill burden to the patient (30 tablets of 5 mg axitinib at AWP of \$204.19 = \$6125.70; 150 tablets of 1 mg axitinib at AWP of \$68.06 = \$10,209.00). This could also result in a higher cost to the patient if their copayment was determined based on the percentage of total cost. These two examples emphasize the issue of the inability to make up a dose with the available strengths without resulting in wastage.

The Iowa Prescription Drug Donation Repository Program (IPDDRP) is a statewide drug donation program developed and administered by the Iowa Department of Public Health and the Iowa Prescription Drug Corporation that allows medication to be reused at no cost to the

patient. However, as Iowa law stands, only medications in blister packages or in the original manufacturer-sealed bottles are eligible to be returned. Upon receipt of the donation, the patient and the accepting pharmacist must certify the medication was stored under proper conditions and the integrity of the medication is not compromised. In addition, the patient does not receive compensation for the returned medications and the drug must be forwarded to the IPDDRP. Any pharmacy or medical facility with authorization to dispense per Iowa administrative rules may re-dispense medications from the IPDDRP to fulfill prescriptions for qualifying underinsured patients at no cost to the patient. Iowa is one of 20 states with laws regarding the operation of repository programs. There is also a recently enacted program through IPRRDP specifically for cancer medications, which 13 other states already have in place. The Cancer Take-Away Program puts receptacles for high-cost oral chemotherapy agents in any clinical cancer centers and pharmacies that request one. This has increased program awareness and made the return of unused medications much easier.

A major factor inhibiting this program is the portion of the rule deeming only blister-packaged and original manufacturer-sealed bottles eligible for return. If manufacturers were required to produce high-cost medications in blister packages or pharmacies were required to dispense high-cost medications in blister or sealed packages, all unused dosages would have the potential to be returned and reused, saving society a significant amount of money. Adopting these rules would require less medication to be purchased from manufacturers, decreasing their profits. Blister-packaging medications require more equipment and time for pharmacies and may cause safety issues or difficulty for patients with low dexterity.^{8–10} Repacking medication also decreases the expiration date to one year from the date of packaging or sooner, which could cause more wastage. Some pharmacies in Iowa have started dispensing all oral chemotherapy agents in blister packages since the Cancer Take-Away Program started, aiding in the significant increase in returned and reused cancer medications this year.

Waste due to death occurred in 9.7% of studied patients. Given the ease of administration of oral medications as compared to intravenous therapy, for which patients need to be functional enough to report to an infusion center for administration, more patients are likely to continue oral targeted therapy at home near the end of their life, which is likely to result in drug wastage. In fact, the approval of drug erlotinib is based on a clinical trial in which patients with performance status up to ECOG 3 were tested against a population receiving best supportive care.¹¹

It was not surprising to see drug toxicity-related wastage was the least contributory factor, as the oncologists and clinical pharmacists have acquired more experience in anticipating and managing toxicity profiles of oral targeted therapy, thereby preventing waste. For example, the initial prescribing daily dose of vemurafenib is 960 mg (four 240 mg tablets). Toxicity resulting from this dosage can be easily managed by reducing the dose to 720 mg per day, comprising of three 240 mg tablets, which avoids waste.

In current practice, split filling a prescription is allowed but may result in two separate copayments for the patient. Rather than fill a month supply, one could fill a two-week supply, and if tolerated, then fill the next two weeks. For example, if a patient is due to refill

a prescription and his disease assessment with imaging and corresponding clinic visit is scheduled one week later, a quantity of medication to cover the one week could be considered. On the day of clinic visit, if the prescriber determines therapy should be continued, the remaining quantity of the prescription could be filled and dispensed to the patient (“split filling”). However, this may result in the patient paying two separate copayments for a complete 30-day supply, thus driving patient-related cost. Split filling may also increase pharmacy-related dispensing costs, due to extra supplies, increased time for personnel, and drug distribution. The effectiveness of a split-fill dispensing program for oral chemotherapy agents has been evaluated in two different studies, which reported significant decrease in cost to society secondary to decreased toxicity.^{12–15} The financial impact of a split fill program to the patient or to the pharmacy was not reported in either study. It is interesting to note in the Khandelwal et al.’s study, patient death was the most commonly reported discontinuation reason leading to wastage. However, physician decision, ineffective therapy, and medication switch, which if combined together can be assumed to be secondary to disease progression, account for a percentage higher than death. Our findings were similar.

The role of clinical pharmacists in improving the safety of oral chemotherapy has been well established, particularly in preventing toxicity-related wastage. As identified in Shah et al.’s study,¹⁶ the documented interventions made by the clinical pharmacist included recommending additional drug monitoring, identifying an interacting drug, and dose-adjusting the prescribed oral chemotherapy agent. At our institution, a clinical pharmacist in the outpatient oncology clinic was implemented in January of 2014. A statistically significant difference in preventing drug wastage between the time period prior to and after the implementation of oncology trained pharmacist could not be determined. This may in part be due to the fact that drug toxicity accounted for the least amount of wastage. Future studies should explore potential methods clinical pharmacists can utilize to prevent progression-related wastage.

Potential solutions to minimizing waste need to be thought of and implemented. Discoordination of prescription fills and disease assessment clinic visits accounted for the majority of waste. Every effort should be made between patient and oncologist to coordinate the two. In situations where this cannot occur, a partial fill with accompanying proportionate patient copayments as approved by insurance could be a potential solution to the problem. This would minimize higher patient-related costs. Drug repository or similar donation programs have the potential to significantly reduce wastage if an effort is made by pharmacies or drug manufacturers to make medications eligible to be returned for reuse. Mandated manufacturer preparation of high-cost medications in unit dose packaging could increase the number of medications eligible to be reused, decreasing society- and patient-related cost. However, we recognize this packaging comes with potential safety and accessibility issues, especially in the elderly or patients with poor performance status. During counseling, pharmacists should emphasize the importance of returning unused medication for safe disposal or submission to donation programs. With the capability of self-administering oral targeted therapies in the patient’s home, more cancer patients are likely to continue receiving treatment with these drugs toward the end of their life. Oncologists should consider prescribing smaller quantities of medication and encouraging family

members to return unused medications upon patient's progression of disease or death. In terms of cost to the society, this can be seen as a potential way to put medication back into the system that would otherwise go unused (Table 3).

There are several limitations to our study. Being a single-site study, external validity is limited. Complete dispensing data could not be obtained for some patients, as they transferred their prescriptions to different pharmacies or had ongoing treatment beyond the study interval. The reason for discontinuation or dose reduction was not always readily available. In the patient population where patient death led to wastage, the exact date of stopping medication was unclear in some cases, which would have attributed to more wastage than our estimate if therapy were discontinued before the date of death. Data regarding the return of the four studied drugs from HCCC specialty pharmacy or from the study subjects to IPDDRP could not be obtained, which would have helped us understand whether manufacturer blister-packaged medications (e.g. everolimus) were more likely to be reused. Given the retrospective nature of the study, our calculation of wasted medication could have been affected by several patient-related events, such as non-adherence, inpatient admissions, needing to hold therapy, or the date of dispensing with respect to the date the drug was started. For the purpose of this study, we used the AWP of each drug at a pre-specified time point in an attempt to maintain consistency, which may not be reflective of the drug prices throughout the entire length of the study or the true cost to society. Although we chose only four chemotherapy drugs for our study, the results on wastage can practically be generalized to any oral chemotherapy agent.

Conclusion

Targeted oral chemotherapy agents are associated with large amounts of wastage, which is a significant financial burden to society. Progression of disease emerged as the single most important factor accounting for drug wastage. Potential solutions can be devised in a collaborative effort amongst drug manufacturers, specialty pharmacies, insurance plan policies, pharmacists, prescribers, and patients. Novel ideas are needed to prevent wastage, thereby reducing healthcare costs.

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References

1. IMS Health Study: U.S. drug spending growth reaches 8.5 percent in 2015 In: Constantino T (ed) PARSIPPANY, NJ2016.
2. Chen CCV, Hsu YH, Jayaseema DM, et al. White matter tracts for the trafficking of neural progenitor cells characterized by cellular MRI and immunohistology: the role of CXCL12/CXCR4 signaling. *Brain Struct Func* 2015; 220: 2073–2085.
3. Zelboraf® (package insert). South San Francisco, CA: Genentech USA, Inc.

4. Carlson BL, Pokorny JL, Schroeder MA, et al. Establishment, maintenance and in vitro and in vivo applications of primary human glioblastoma multiforme (GBM) xenograft models for translational biology studies and drug discovery. *Curr Protocol Pharmacol* 2011; 52: 1–14.
5. Inlyta® (package insert) New York, NY.
6. Cauchi R and Hanson C. State prescription drug return, reuse and recycling laws. 2016.
7. Redbook Online Greenwood Village, CO2016.
8. Philbert D, Notenboom K, Bouvy ML, et al. Problems experienced by older people when opening medicine packaging. *Int J Pharm Pract* 2014; 22: 200–204. [PubMed: 24025086]
9. van Geffen EC, Meuwese E, Philbert D, et al. Problems with medicine packages: experiences reported to a Dutch medicine reporting system. *Ann Pharmacother* 2010; 44: 1104–1109. [PubMed: 20442349]
10. Al-Ramahi G, Mohamed M, Kennedy K, et al. Obstruction and perforation of the small bowel caused by inadvertent ingestion of a blister pill pack in an elderly patient. *BMJ Case Reports* 2015; 2015.
11. Shepherd FA, Rodrigues PJ, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer. *N Engl J Med* 2005; 353: 123–132. [PubMed: 16014882]
12. Khandelwal N, Duncan I, Ahmed T, et al. Impact of clinical oral chemotherapy program on wastage and hospitalizations. *J Oncol Pract* 2011; 7: e25s–e29s. [PubMed: 21886508]
13. Khandelwal N, Duncan I, Ahmed T, et al. Impact of clinical oral chemotherapy program on wastage and hospitalizations. *The American journal of managed care* 2011; 17: e169–73. [PubMed: 21711067]
14. Khandelwal N, Duncan I, Ahmed T, et al. Oral chemotherapy program improves adherence and reduces medication wastage and hospital admissions. *J Natl Compr Canc Netw JNCCN* 2012; 10: 618–625. [PubMed: 22570292]
15. Sharda YP, Megan Z and Shuko L. Evaluating the effects of a 14-day oral chemotherapy dispensing protocol on adherence, toxicity, and cost. *J Hematol Oncol Pharm* 2015; 5: 62–68.
16. Shah NN, Casella E, Capozzi D, et al. Improving the safety of oral chemotherapy at an Academic Medical Center. *J Oncol Pract* 2016; 12: e71–6. [PubMed: 26733627]

Figure 1.

Ways by which toxicity, death, and progression attribute to wastage taking everolimus as an example. AWP: average wholesale price.

Table 1.

Number and percent of patients with wastage by attributing reason.

Drug	Toxicity	Progression	Dose increase	Death	Total
Axitinib	2	5	2	0	9
Everolimus	3	14	0	1	18
Sunitinib malate	0	3	0	0	3
Vemurafenib	0	3	0	4	7
Total	5	25 ^a	2 ^a	5	36
Percent of total patients (88)	5.7%	28.4%	2.3%	5.7%	41%

^aOne of the patient experienced drug wastage from dose increase as well as progression.

Table 2.

Total medication wasted with corresponding wastage to society and to patients in terms of cost.

Drug	Number of tablets or capsules wasted	Amount wasted to society	Amount wasted to patients
Axitinib	468	\$86,032.00	\$160.00
Everolimus	283	\$116,293.19	\$1715.39
Sunitinib malate	74	\$14,154.50	\$11.39
Vemurafenib	354	\$32,116.00	\$627.43
Total	1179	\$248,595.69	\$2514.21

Table 3.

Quantity of drug received by HCCC pharmacy from the repository drug program during the evaluated time period.

Drug	Strength	Quantity received (tablets)	Money saved
Axitinib	1 mg tablets	180	\$12,254.40
	5 mg tablets	120	\$24,502.80
Everolimus	10 mg tablets	30	\$12,327.90
Sunitinib malate	None	None	\$0
Vemurafenib	240 mg tablets	120	\$6510.00
Total		450	\$55,595.10

HCCC: Holden Comprehensive Cancer Center.

Table 4.

Average wholesale prices (AWP) as reported in Redbook accessed in December 2014.

Drug	Strength	AWP (\$)
Sutent (sunitinib)	12.5 mg	147.50
	25 mg	295.01
	37.5 mg	442.51
	50mg	513.57
Zelboraf (vemurafinib)	240 mg	54.25
Inlyta (axitinib)	1 mg	68.06
	5 mg	204.19
Afinitor (everolimus)	2.5 mg	392.86
	5 mg	410.93
	7.5 mg	410.93
	10 mg	410.93