Research Article

Utilization Trends and Management and Prescription of Oral Anticancer Medicines Using Nationwide Pharmacy Databases and a Questionnaire Survey of Community Pharmacies in Japan

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ABSTRACT

Background: Introduction of oral anticancer medicines (OAMs) and transitions from in-hospital care to outpatient care and from in-hospital prescriptions to external prescriptions at community pharmacies may substantially influence cancer care in Japan. **Objectives:** To describe practices related to the prescription of oral anticancer medicines in community pharmacies in Japan. **Methods:** We initially performed a cross-sectional drug utilization study using administrative databases of dispensations at 489 community pharmacies nationwide in Japan. Practices related to OAMs in community pharmacies in databases were surveyed using questionnaires that consisted of 29 items. **Results:** Database analysis revealed the number of patients who received hormone therapy (n=19899, 62.9%), anti-metabolic drugs (n=9002, 28.5%), molecularly-targeted drugs (n=1716, 5.4%). Among 489 community pharmacies, 394 (80.6%) responded to the questionnaires. The main prescribers were doctors in hospitals (66.7%) rather than in clinics (33.3%). Of the pharmacists, 59.9% received training on OAMs voluntarily. Topics of counseling included adverse drug reactions, usage and dosage, and unused OAMs. In counseling patients, 45.9% did not use any prepared materials. The major topics for queries to medical facilities were usage and dosage inconsistent with the package insert. Most of the pharmacies did not collect information on laboratory measurements from patients or medical facilities. With regard to generic OAMs, 50% were concerned about their efficacy, safety, and steady supply. **Conclusions:** About 90% of OAMs dispensed at pharmacies in Japan were drugs for hormone therapy and anti-metabolic drugs. Our study suggests the importance of pharmacy and clinic cooperation including sharing medical records and information.

INTRODUCTION

Intravenous (IV) chemotherapy has played a central role in cancer treatment but recently oral anticancer medicines (OAM) such as capecitabine, gefitinib, and S-1, which are generally easier to administer than IV chemotherapy, were introduced as efficacious alternatives (1, 2). OAMs have brought about several changes in practice settings for chemotherapy (3). First, they make it possible to treat patients in outpatient settings rather than in hospital. Second, as outpatient prescriptions increased, the role of pharmacists in community pharmacies became more important in cancer care (4-7). A previous survey in the US suggested that community pharmacists' knowledge about OAMs was useful in several areas with regard to counseling patients on medications(6). Third, several generic (GEs) OAMs have been introduced in Japan as well as in Western countries(8). Manufacturers of GEs are expected to contribute information and assistance in the proper use of OAM GEs, which are more toxic than other GEs.

Clinical guidelines for the management of OAMs have contributed to the proper use of OAMs in Western countries (9-11). The management of OAMs particularly requires training of medical staff, medication counseling, distribution, supply chains for medical facilities, informative packaging, inventory control, and communication with patients to enhance the proper use of OAMs (12-14). However, there are no guidelines for the management of OAMs, and practices regarding their use in community pharmacies in Japan remain unknown.

This study aims to describe trends in the use of OAMs and practices related to their use in community pharmacies in Japan through a drug utilization study and a questionnaire survey of community pharmacies.

MATERIALS AND METHODS

Databases for the drug utilization study

We initially performed a cross-sectional drug utilization study of OAMs using administrative databases of dispensation records of the largest and third largest pharmacy chains in Japan. We examined records of 489 pharmacies that dispensed OAMs between June 1, 2011 and May 31, 2012 and had contracts with the pharmacy chains (Ain Pharmaciez Inc. and Kraft Inc.). The databases analyzed included age and gender of patients, identifier of each pharmacy, and OAMs

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dispensed (HOT reference code [standard master for pharmaceutical products], brand name, specifications, usage, dosage, and length of dispensing days). We used 35 indications for hormone therapy drugs, anti-metabolic drugs, molecularly-targeted drugs, alkylating compound drugs, microtubule inhibitors, and immune-suppressing drugs as the therapeutic categories of OAMs.

Recipients of questionnaire survey

Second, we conducted a questionnaire survey about OAMs. Selection criteria of recipients included employment in community pharmacies that had records of OAMs dispensed in their databases of the drug utilization study and experience in dispensing OAMs between October 1, 2011 and September 30, 2012. One pharmacist per pharmacy received the questionnaire. We sent and collected questionnaires by post between January 4 and March 30, 2013.

Questionnaires

Questionnaire items were based on results of previous questionnaire study about the background of pharmacies, education and training of pharmacists, medication counseling of patients, required elements, risk management of community pharmacies (6, 7, 15, 16), educational materials and interviews with pharmacists specializing in OAMs. The questionnaire used in this study consisted of 29 items that covered background of pharmacies, training of pharmacists, patient medication counseling, and communication with prescribers, and opinions about generic OAMs. The items included both closed-ended questions (number, single answer, multiple answers, ordered answer) and open-ended (free) questions.

Statistical analysis

All continuous data are presented as mean±SD and qualitative data as the percentage of frequency. Subgroup analysis about content of patient medication counseling and content of inquiries to medical facilities according to dispensing volume of anti-metabolic drugs, molecularly-targeted drugs were also performed. All statistical analyses were conducted using SPSS for Windows ver.19 (IBM Corporation, Tokyo, Japan).

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Ethical approval

The drug utilization study and the questionnaire survey were conducted in accordance with the Ethical Guidelines for Epidemiological Research in Japan. This study was exempt from informed consent by individual patients because the databases were de-identified before provision.

RESULTS

Characteristics of pharmacies

The examined databases included those of 489 community pharmacies in Japan. From these pharmacies, 156904 prescriptions of OAMs were dispensed to a total of 31628 patients, and 1192 medical facilities were prescribers of the OAMs.

Most frequently dispensed therapeutic classification was hormone therapy drugs such as bicalutamide (antiandrogens) and anastrozole (nonsteroidal aromatase inhibitors) (N=19899, 62.8%), followed by anti-metabolic drugs such as S-1 (tegafur-oxonate combination), UFT (tegafur-uracil combination), and capecitabine (N=9002, 28.5%), molecularly-targeted drugs (N=1716, 5.4%) such as gefitinib and imatinib, alkylating compound drugs (N=839, 2.7%), microtubule inhibitors (N=148, 0.5%), and immune-suppressing drugs (N=24, 0.1%). Average prescribed duration for a dispensed drug was 40.7 days in total, 52.3 days for hormone therapy drugs, 20.1 days for anti-metabolic drugs, and 27.1 days for molecularly-targeted drugs.

Of the 489 pharmacies, 394 responded (response rate 80.6%) to the questionnaire survey. Table 1 describes background characteristics and practices of the 394 responding pharmacies. There was little practical difference between all pharmacies surveyed (489) and the responding pharmacies (394); therefore we assumed that the results indicate no bias. Among hormone therapy drugs dispensed, which included both branded (patent off) drugs and GEs, of GEs dispensations numbered 23898 (26.8%).

Those responding pharmacies dispensed an average of 1848.8 prescriptions daily and employed an average of 3 full-time pharmacists. Of the 394 pharmacies, 90.9% were community pharmacies in the immediate area of a specific hospital and 65.5% answered that their main prescribers were hospitals. More than half of the pharmacists received training in OAMs on an

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individual basis (59.9%) and some used seminars offered by manufacturers and phamacists' associations.

With regard to measures to acquire information on OAMs, 82.0% obtained information from sales persons termed medical representatives (MR), OAM specialists employed by drug manufacturers, followed by homepages of manufacturers, Pharmaceuticals and Medical Devices Agency and other organizations (around 50%), seminars by manufacturers, academic societies and community pharmacists (around 30%) and academic journals and treatises (20 to 30%).

In medication counseling of patients about OAMs, 45.9% did not use any materials, followed by a fact sheet (not fill-able form) (40.9%) and a medicine pocketbook (fill-able form) (28.4%). Electronic devices such as smart phones and tablets were not frequently used. The pharmacists spent a mean of 6.5 and 3.6 minutes for each patient in medication counseling for the first and second dispensations of OAMs, respectively. Less than half of the pharmacists answered that they spent more time for medication counseling on OAMs than for other drug categories (45.9%).

Table 1. Characteristics and practices of the 394 pharmacies that responded to the survey

Characters		mean±SD or %
Prescriptions per month		1848.8±1308.8
No. full-time employees		3.0 ± 2.1
Type of pharmacy*	In front of medical facilities	90.9%
	Others	9.1%
Types of major prescribers**	Clinics (0 to 19 beds)	33.5%
	General hospitals	32.0%
	National and public hospitals	16.7%
	Privately operated hospitals (≥20 beds)	10.4%
	University hospitals	6.3%
	Others	1.5%

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Number of OAMs as inventoried items		8.3±8.1
Training of pharmacists on OAMs***	On an individual basis	59.9%
	Seminar by manufacturers	51.3%
	Printed materials	32.4%
	Seminar by pharmacists' association	27.7%
	On a store basis	23.8%
	Not implemented by the pharmacy	21.6%
	Conference on a conjoint basis	9.1%
	E-learning	8.1%
	Others	1.7%
Materials for patient counseling on medications***	Not in use	45.9%
	Fact sheet(not fill-able form)	40.9%
	Medicine pocketbook (fill-able form)	28.4%
	Homepage (by the regulatory agency)	8.6%
	Electronic devises (smart phone, tablets)	1.8%
	Others	1.5%
Time (minutes) spent patient medication counseling***	Initial dispensation	6.5±3.6
	Second dispensation	3.6±2.3
Time of patient medication counseling** compared with other medicines	Longer	45.9%
	Shorter	0.8%
	No change	53.3%

*Single answer **Multiple answers ***2 pharmacies did not respond to this item

Tables 2 and 3 describe dispensation of OAMs among the 394 pharmacies according to types of main prescribers. The volume of OAM dispensations and the number of patients receiving OAMs were greater in pharmacies that mostly filled prescriptions from large-scale hospitals

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(university, national and public). The volumes of anti-metabolic drugs and molecularly-targeted drugs dispensed were relatively high in these pharmacies. However, patients' age and the number of days that a pharmacy dispensed OAMs did not differ greatly among prescribers. Average age of patients provided with OAMs was almost 70 years (average age of patients was 66.1 years), and the days that pharmacies dispensed such drugs were almost 40 days among categories of prescribers, indicating little difference among the various types of prescribers.

Table 2. Dispensation of drugs by the 394 pharmacies that responded to the survey

	Types of main prescribers				
	University hospitals	National and public hospitals	General hospitals	Private operation hospitals	Clinics
Numbers of pharmacies*	25	65	126	41	132
No, total prescriptions per pharmacy per year (mean ± SD)	32509.2±26727.6	19201.2±13275.6	23017.2±17370.0	22218.0±125472	20862.0±11706.0
No. dispensations of OAMs per pharmacy per year (mean ± SD)	1226.0 ± 1143.3	506.9 ± 729.0	382.0 ± 461.4	198.8 ± 364.5	40.0 ± 60.9
No. patients dispensed OAMs per pharmacy per year (mean ± SD)	255.7 ± 237.0	107.9 ± 168.9	75.6 ± 91.1	29.8 ± 51.6	8.5 ± 15.7
Age of patients dispensed OAMs (mean ± SD)	63.6 ± 5.6	69.5 ± 9.2	69.0 ± 7.1	71.5 ± 7.3	69.4 ± 11.6
Days dispensing OAMs (mean ± SD)	37.8 ± 7.2	38.9 ± 10.2	38.7 ± 14.8	34.4 ± 12.4	39.4 ± 18.3

* Main prescribers of 5 pharmacies were other types

Table 3. Use of OAMs by the 394 pharmacies that responded to the survey

Therapeutic classification	Volume of patients		Facility types of main prescribers				
	N	%	University hospitals (%)	National and public hospitals (%)	General hospitals (%)	Privately operated hospitals (%)	Clinics (%)
Hormone therapy drugs	16144	62.8	59.6	64.2	62.0	72.3	76.8
Anti-metabolic drugs	7303	28.4	30.1	26.6	30.2	23.1	16.8
Molecularly-targeted drugs	1471	5.7	6.7	6.4	4.9	2.0	4.0
Alkylating compound drugs	670	2.6	3.0	2.4	2.5	2.4	1.9
Microtubule inhibitors	122	0.4	0.6	0.4	0.4	0.2	0.5

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Dispensing volume and patient medication counseling

Table 4 describes the contents of patient medication counseling in the 394 pharmacies. Adverse drug reactions, usage and dosage, and unused OAMs were addressed by more than 70% of the pharmacies, followed by adherence, combined use with other anticancer agents, and drug-drug interactions. The most infrequently covered topic among the choices given was laboratory measurements (22.0%). There were no differences according to dispensing volume of anti-metabolic drugs or molecularly-targeted drugs.

Table 4. Content of patient medication counseling according to dispensing volume of anti-metabolic drugs or molecularly-targeted drugs

Topics*	Frequency (N=394)	%	Anti-metabolic drugs** (median 3.0, N=388)				Molecularly-targeted drugs** (median 0.0, N=388)			
			Above median (N=193)	%	Below median (N=195)	%	Above median (N=179)	%	Below median (N=209)	%
Adverse drug reactions (e.g. early detection)	366	92.4	182	94.3	176	90.3	170	95.0	188	90.0
Usage and dosage	361	91.2	181	93.8	172	88.2	166	92.7	187	89.5
Unused OAMs	288	72.7	142	73.6	140	71.8	130	72.6	152	72.7
Adherence	240	60.6	123	63.7	112	57.4	110	61.5	125	59.8
Use combined with other anticancer medicines	233	58.8	123	63.7	103	52.8	117	65.4	109	52.2
Response to OAMs	214	54.0	106	54.9	103	52.8	101	56.4	108	51.7
Interaction with other medicines	187	47.2	103	53.4	78	40.0	88	49.2	93	44.5
Indications	156	39.4	77	39.9	75	38.5	70	39.1	82	39.2
Combination use with OTCs or supplements	133	33.6	76	39.4	54	27.7	67	37.4	63	30.1
Laboratory measurements (e.g. renal function)	87	22.0	53	27.5	32	16.4	45	25.1	40	19.1
Others (discontinuation, body weight, diet, family)	3	0.8	3	1.6	0	0.0	3	1.7	0	0.0

*Multiple answers **6 pharmacies were excluded due to non-response to item.

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Priority of inquiries to medical facilities

Table 5 shows topics of inquiries to medical facilities according to frequency. The major reason for inquiries to medical facilities was that usage and dosage prescribed were inconsistent with the package insert. Other reasons included check of unused OAMs, information on in-hospital OAM prescription, and adverse drug reactions but the frequencies were lower than 10%. Most of the pharmacies did not collect information on laboratory measurements from patients or medical facilities. We also asked about communication from pharmacies with medical facilities, but 72.1% of the pharmacies did not provide information about patients to medical facilities.

Table 5. Content of inquiries to medical facilities according to dispensing volume of OAMs

Topics*	Frequency (N=394)	%	Dispensing volume of OAMs			
			Above median (N=200)	%	Below median (N=194)	%
Usage inconsistent with package insert	134	34.0	82	41.0	52	26.8
Dose inconsistent with package insert	117	29.7	64	32.0	53	27.3
Unused OAMs	24	6.1	14	7.0	10	5.2
Others (drug holidays, cancer notification, diversity of prescription, error of date)	22	5.6	8	4.0	14	7.2
Information on in-hospital OAM prescription	15	3.8	7	3.5	8	4.1
Adverse drug reactions	7	1.8	3	1.5	4	2.1
Combined use with other anti-cancer medicines	4	1.0	2	1.0	2	1.0
Information on type of cancer	4	1.0	3	1.5	1	0.5
Particular safety issue	3	0.8	3	1.5	0	0.0
Usage of narcotic drugs	2	0.5	2	1.0	0	0.0
Pharmacotherapy for diseases other than cancer	0	0.0	0	0.0	0	0.0
Laboratory measurements (e.g. renal function)	0	0.0	0	0.0	0	0.0

*Ordered answers, In order of the frequency of the No1. answer by pharmacies queried

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Opinion on GEs

With regard to GEs, only 14.2% of pharmacies answered "no concerns". The pharmacies selected efficacy, safety, and steady supply of GEs as the major concerns (around 50%), followed by quality and information services. As to merits and demerits of GEs, 48.7% of the pharmacies commented on the economic advantages of GEs such as lower cost, which may improve adherence to chemotherapy and be an incentive to dispense GEs. On the other hand, some pharmacists felt anxious about the use of GEs and suggested the burden of inventorying these agents (buildup of inventory, houseroom, dead stock, non-refundable products).

DISCUSSION

We explored the actual practices of management of OAMs by a drug utilization study of 489 community pharmacies and a questionnaire survey to describe trends in the use of OAMs and of practices in community pharmacies in Japan. Most frequently dispensed OAMs were hormone therapy drugs, anti-metabolic drugs, and molecularly-targeted drugs. The questionnaire survey, with a response rate of 80.6%, demonstrated that more than half of the community pharmacists received training on OAMs on an individual basis, and the content of medication counseling of patients included adverse drug reactions, and usage and dosages inconsistent with information in package inserts. Information on laboratory measurements from patients or medical facilities was not sought by pharmacies.

We used administrative databases of dispensation records of the largest and third largest pharmacy chains in Japan. The pharmacy chains cover about 1% of all pharmacies in Japan (54780 pharmacies in 2014)(17). Common cancers among the Japanese population are colorectal, lung, breast, and prostate cancer (23). The frequent use of hormone therapy drugs, anti-metabolic drugs, and molecularly-targeted drugs would reflect their prevalence in Japan.

Responses to the questionnaire survey suggested the importance of risk management and medication counseling on OAMs. Toxicities of hormone therapy drugs, the most commonly used of the OAMs are not severe compared to other OAMs. On the other hand, anti-metabolic drugs require caution for possible multiple adverse drug reactions, compliance, and interaction with other medicines. For example, hand-foot syndrome, known as a pathognomonic side effect by capecitabine, builds towards a peak two weeks after the start of its administration (3, 18).

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Medication counseling about self-care at home, preventive measures, and topical medicines are necessary for patients in community pharmacies. Molecularly-targeted drugs are also toxic (19). Thus, skills of pharmacists and medication counseling by community pharmacies are key factors to enhance the proper use of anti-metabolic drugs and molecularly-targeted drugs. Furthermore, the NCCN Task Force Report of OAMs noted that inadequate supervision and poor communication with health care providers can lead to non-adherence to OAMs (12). As shown in Table 1, one-third of the main prescribers through community pharmacies were clinics, indicating that pharmacy and clinic communication is necessary for the proper use of OAMs (16), although the number of patients and volume of dispensed OAMs per pharmacy was relatively small. Adverse drug reactions and usage and dosage were routinely covered in medication counseling but other potentially important issues, e.g. interaction with other medicines and information on laboratory measurements, seemed not to be widely recognized as important by pharmacists (Tables 4, 5). As shown in Table 2 older patients were more often treated in clinics and hospitals than in university hospitals. Cancer care for the elderly in outpatient settings is an emerging issue for community pharmacists. For example, it was reported that community pharmacists can simplify daily drug regimens and provide education on medication-related fall risk in the elderly (20).

It was previously shown that information sharing is a major issue for the proper use of OAMs (16). However, the prescription form used in Japan does not include the disease name and, furthermore, it would be difficult for community pharmacists to obtain sufficient information from a cancer patient partially because pharmacists do not know if the patient had been notified about the diagnosis of cancer. Moreover, a previous questionnaire survey showed that more than half of community pharmacists experienced difficulties in contacting prescribers (16). As shown Table 1, about half of community pharmacies in Japan did not use prepared materials to provide information to patients, and the use of fact sheet, medicine pocketbook, homepage, and electronic devices was not common. Recent literature reviews suggested that the introduction of online scheduling of chemotherapy regimens or electronic medical systems could improve the quality of cancer care (21). In fact, a variety of electronic devices, such as iPads (22) and mobile phones (23), are now available for information sharing in cancer care. Such helpful tools had not been introduced in most community pharmacies in Japan.

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The questionnaire survey also clarified the diverse opinions of pharmacists about OAM GEs. The Japanese government considers that enhancing the use GEs would be an effective policy to reduce the burden of medical costs; however, the share of GEs in Japan is still lower than in Western countries (24). Indeed, in the drug utilization study dispensing of GEs accounted for 26.8% among hormone therapy drugs for which both branded (patent off) drugs and GEs are available. It is said that a major reason for the underuse of GEs is concern about their efficacy and safety (25). In this questionnaire survey, only 14.2% of pharmacies selected "no-concern for GE use". Other concerns included lack of a steady supply and the burden of outdated stock. GE manufacturers in Japan tend to minimize stocks to reduce distribution costs but they are responsible for a steady supply as well as the proper use of GEs and quality of the drugs.

This study had several limitations. The first is generalizability of study findings. Results from the questionnaire survey would reflect policies of the pharmacy chains (Ain Pharmaciez Inc. and Kraft Inc.), which are not necessarily representative. Pharmacies in Japan may have different policies on the use of GEs, steady supply, and dead stock. Secondly, the questionnaire survey was based on community pharmacies, because all selected answers were about all categories of OAMs. If they restrict the scope on anti-metabolic drugs and molecularly-targeted drugs needed proper usage and management, more high frequencies may demonstrate about management.

CONCLUSION

This study aims to describe utilization trends of OAMs and practices of pharmacists at community pharmacies in Japan. About 90% of OAMs dispensed at pharmacies in Japan were hormone therapy and anti-metabolic drugs. Our study suggests the importance of pharmacy and clinic cooperation on the basis of information sharing in addition to medication counseling and counseling about contents of package inserts and adverse effects to enhance proper management in prescribing OAMs.

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CONFLICT OF INTEREST

None

REFERENCES

1. Muro K, Boku N, Shimada Y, Tsuji A, Sameshima S, Baba H, et al. Irinotecan plus S-1 (IRIS) versus fluorouracil and folinic acid plus irinotecan (FOLFIRI) as second-line chemotherapy for metastatic colorectal cancer: a randomised phase 2/3 non-inferiority study (FIRIS study). Lancet Oncol. 2010;11(9):853-60.

2. Aisner J. Overview of the changing paradigm in cancer treatment: oral chemotherapy. Am J Health Syst Pharm. 2007;64(9 Suppl 5):S4-7.

3.   Amari M, Ishida T, Takeda M, Ohuchi N. Capecitabine monotherapy is efficient and safe in all line settings in patients with metastatic and advanced breast cancer. Jpn J Clin Oncol. 2010;40(3):188-93.

4. Weingart SN, Spencer J, Buia S, Duncombe D, Singh P, Gadkari M, et al. Medication safety of five oral chemotherapies: a proactive risk assessment. J Oncol Pract. 2011;7(1):2-6.

5. Weingart SN, Toro J, Spencer J, Duncombe D, Gross A, Bartel S, et al. Medication errors involving oral chemotherapy. Cancer. 2010;116(10):2455-64.

6. O'Bryant CL, Crandell BC. Community pharmacists' knowledge of and attitudes toward oral chemotherapy. J Am Pharm Assoc (2003). 2008;48(5):632-9.

7. Rick Abbott B, Scott Edwards P, Jonathan Edwards B, George Dranitsaris M, FSCHP, Joy McCarthy M, FRCP(C). Oral anti-cancer agents in the community setting: A survey of pharmacists in Newfoundland and Labrador. Can Pharm J. 2011;144:220-6.

8. Fujimura S, Watanabe A. Generic antibiotics in Japan. J Infect Chemother. 2012;18(4):421-7.

9. Goodin S, Griffith N, Chen B, Chuk K, Daouphars M, Doreau C, et al. Safe Handling of Oral Chemotherapeutic Agents in Clinical Practice: Recommendations From an International Pharmacy Panel. J Oncol Pract. 2011;7(1):7-12.

10. Occupational Safety and Health Administration (OSHA) DpoL. Updating OSHA standards based on national consensus standards. final rule; confirmation of effective date. Fed Regist. 2008;73(51):13753-4.

11. Bardin C, Astier A, Vulto A, Sewell G, Vigneron J, Trittler R, et al. Guidelines for the practical stability studies of anticancer drugs: a European consensus conference. Ann Pharm Fr. 2011;69(4):221-31.

12. Weingart SN, Brown E, Bach PB, Eng K, Johnson SA, Kuzel TM, et al. NCCN Task Force Report: Oral chemotherapy. J Natl Compr Canc Netw. 2008;6 Suppl 3:S1-14.

13. Simchowitz B, Shiman L, Spencer J, Brouillard D, Gross A, Connor M, et al. Perceptions and experiences of patients receiving oral chemotherapy. Clin J Oncol Nurs. 2010;14(4):447-53.

14. Weingart SN, Flug J, Brouillard D, Morway L, Partridge A, Bartel S, et al. Oral chemotherapy safety practices at US cancer centres: questionnaire survey. BMJ. 2007;334(7590):407.

15. Chan A, Leow YC, Sim MH. Patients' perspectives and safe handling of oral anticancer drugs at an Asian cancer center. J Oncol Pharm Pract. 2009;15(3):161-5.

16. Hammond L, Marsden E, O'Hanlon N, King F, Henman MC, Keane C. Identification of risks associated with the prescribing and dispensing of oral anticancer medicines in Ireland. Int J Clin Pharm. 2012;34(6):893-901.

17. Communications MoIAa. Medical care institution and pharmacies by prefecture: Ministry of Internal Affairs and Communications; [cited 2015 2 July]. Available from: http://www.stat.go.jp/english/index.htm.

18. Norman G, Soares M, Peura P, Rice S, Suh D, Wright K, et al. Capecitabine for the treatment of advanced gastric cancer. Health Technol Assess. 2010;14(Suppl. 2):11-7.

19. Klein Hesselink EN, Steenvoorden D, Kapiteijn E, Corssmit EP, van der Horst-Schrivers AN, Lefrandt JD, et al. Therapy of endocrine disease: response and toxicity of small-molecule tyrosine kinase inhibitors in patients with thyroid carcinoma: a systematic review and meta-analysis. Eur J Endocrinol. 2015;172(5):R215-25.

20. Bartlett D, Pang N, Massey C, Evans P. Pharmacist consultations: simplifying daily drug regimens and providing

Citation: Koji Kawakami et al. Ijppr.Human, 2015; Vol. 4 (3): 150-163.

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education on fall risk for older adults. Consult Pharm. 2015;30(3):141-52.

21. Collins CM, Elsaid KA. Using an enhanced oral chemotherapy computerized provider order entry system to reduce prescribing errors and improve safety. Int J Qual Health Care. 2011;23(1):36-43.

22. DiVall MV, Zgarrick DP. Perceptions and use of iPad technology by pharmacy practice faculty members. Am J Pharm Educ. 2014;78(3):52.

23. Agboola S, Flanagan C, Searl M, Elfiky A, Kvedar J, Jethwani K. Improving outcomes in cancer patients on oral anti-cancer medications using a novel mobile phone-based intervention: study design of a randomized controlled trial. JMIR Res Protoc. 2014;3(4):e79.

24. Osamu Takizawa HU, Shiro Tanaka, Koji Kawakami. Price difference as a predictor of the selection between brandname and generic statins in Japan. Health Policy. 2015;119:612–9.

25. Iizuka T, Kubo K. The generic drug market in Japan: will it finally take off? Health Econ Policy Law. 2011;6(3):369-89.

Citation: Koji Kawakami et al. Ijppr.Human, 2015; Vol. 4 (3): 150-163.

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