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Horizon Scanning of Oncology Drugs in Iran in 2015

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ABSTRACT

Background: Healthcare horizon scanning systems, have become one of the main components of health technology assessment. We conducted a horizon scanning exercise to identify new oncology drugs that may have a high impact on cancer patients and the health system in Iran.

Methods:We reviewed existing health technology horizon scanning systems, and selected and weighted criteria for prioritizing oncology drugs, including 1) clinical efficiency and effectiveness, 2) incidence and prevalence of cancer types, 3) potential costs, 4) availability of alternative treatment, 5) having variable indications, 6) quality of evidence, and 7) being a first, second or third line drug. We reviewed horizon scanning reports in other countries and prepared a list of new oncology drugs to be ranked. We summarized clinical and epidemiological information about the drugs and presented them to a member of our expert panel who ranked them based on a structured checklist. Eventually, the drugs were categorized into four groups from low to high impact, based on their effect on patients and the health system of Iran in the future

Results: We identified 158 new oncology drugs, most of which were in their phase III clinical trials, and had been approved by the US Food and Drug Administration (FDA). Finally, we selected 18 medicines as having the highest impact on patients and the health system of Iran.

Conclusion: The results of this study can be used for several purposes, including research and drug development. These results suggest the need for periodical horizon scanning in Iran and other low and middle income countries.

Keywords: Horizon Scanning, Cancer, Oncology Drugs, Iran

INTRODUCTION:

In recent years, the incidence and prevalence of cancer in many low and middle-income countries, including Iran, has had an upward trend[1, 2]. Along with the increasing incidence and prevalence of cancer, the introduction of new and expensive treatments has led to significant increases in cancer treatment costs in these countries[3]. Cancer drugs are a major contributor to overall cancer care costs, and their share of total cancer care costs is rising as a result of their increasing price and quantity[4, 5]. A national study estimated that more than 20 percent of the cost of cancer treatment in Iran is related to chemotherapy drugs. In the last decade, the cost of cancer drugs has almost doubled in Iran, reaching US$350 million in 2014[3]. Cancer drugs impose high financial costs on patients, their families, and health systems. Nowadays, managing the rise of cancer drug costs is one of the main challenges of health systems, even in high-income countries[5- 7].

Many countries in the world -especially high-income countries- have used health technology assessment (HTA) to prioritize resource allocation and control the rising cost of cancer care[8]. In recent years, healthcare horizon scanning systems (HSS), also known as early awareness and alert systems or early warning systems, have become one of the main components of health technology assessment[9]. The aim of horizon scanning systems is to "identify, filter and prioritize new and emerging health technologies (including drugs, devices, diagnostics, procedures, programmes, and settings); to assess or predict their impact on health, costs, society, and the healthcare system; and to inform decision-makers and research planners"[10]. Horizon scanning consists of two principal parts; including identifying new and emerging technologies and assessing the potential impact of technology on patients, health systems, costs, and the community. Suitable technologies for horizon scanning are those that are still in the early stages of development and have not yet become a part of established healthcare practice[11].

Throughout the world, both public and private organizations (such as governments, health systems, manufacturers of new technologies) run health technology horizon scanning programs formally or informally. These organizations use horizon scanning to aid in business planning, prioritizing health services research, financial or operational planning, controlling the introduction of new technologies to the market, and providing relevant information to policy makers, health care providers and purchasers[11]. Currently, there are several official health technologies horizon scanning systems in the world. Some of the most important horizon scanning systems in the world include the International Information Network on New and Emerging Health Technologies (the EuroScan International Network) and the Agency for Healthcare Research and Quality (AHRQ) Healthcare Horizon Scanning System[9, 11]. The EuroScan is an international collaboration of more than 20 publicly funded health technology horizon scanning systems. Most of the EuroScan members are based in European countries[9].

Although most horizon scanning systems across the world have the same goals and methods, they are designed based on the needs of their own specific countries, therefore the results of these systems will not be able to fully respond to the needs of policy-makers, planners, providers, and other stakeholders in other countries[11].

Despite the many benefits of the healthcare technology horizon scanning system, this system has not been officially launched in Iran. The aim of this study was to conduct horizon scanning for oncology drugs and identify the drugs with potential

high-impact on cancer patients and the health system in Iran.

METHODS:

In this study, we conducted a horizon scanning exercise to identify and prioritize new and emerging anti-cancer drugs, most of which were in their phase II or III clinical trials. The study was conducted in four stages. First, we review the process of horizon scanning in the most important health care horizon scanning systems in the world, including the EuroScan International Network and the AHRQ Healthcare Horizon Scanning System, and then extracting the criteria used by these systems to prioritize health technologies.

Second, in order to determine appropriate criteria for prioritization of drugs in our study, in addition to the information obtained during the first stage, we used the results of a systematic review that was conducted to identify the criteria used to prioritize health interventions in other countries[12]. In the systematic review study, the most relevant medical databases, including the Cochrane Library, PubMed and Scopus were searched for all papers published in the English language up until March 2015 using MESH and free text. The inclusion criteria of the study were as follows: 1) studies with specific criteria; 2) articles written in English; 3) articles conducted in compliance with priority setting of health technologies[12].

After extracting criteria from different studies, interviews were conducted with 10 experts from various disciplines (including oncologists, pharmaceutical, epidemiologists and health economists) to select appropriate criteria for the prioritization of oncology drugs, and the importance (weight) of each criterion was determined by a checklist. Then, based on the selected criteria, an appropriate tool was designed to assign scores to cancer drugs.

Third, we prepared a list of cancer drugs which were in phase II or III clinical trials and had been identified and were being followed by prestigious horizon scanning systems of the world, at the time of this study, or drugs mentioned in horizon scanning reports had already been published, including reports by the AHRQ horizon scanning system and the EuroScan. Moreover, we summarized clinical and epidemiological information on these medications, in order to help in the process of judging and scoring. Some of these data include indications of use, the status of the medication in terms of research and development, alternative therapies, clinical effectiveness and efficiency, the burden of disease related to the medication, and costs of the medication. Most of this information was extracted from horizon scanning reports which were published by horizon scanning systems. However, some information, such as the burden of disease related to the medications (including the incidence and prevalence) was estimated based on cancer data in Iran. It is worth mentioning that since the majority of these drugs were in phase II or III clinical trials, and had not yet entered the market, there was little published information about their clinical effectiveness and price.

Finally, we ranked the drugs based on our selected criteria, and the information collected in the previous steps. In this regard, the list of medications and their relevant information– which had been prepared in the previous step- , was submitted to 6 medical oncologists, alongside a checklist that had been prepared for drug scoring in the second step. These oncologists - who had already been informed about the goals of the study- were required to score each medication based on the available information. After completion of checklists by the oncologists, various specialists assign scored to each drug, and afterwards the average score for each drug was calculated. Due to disparity among the oncologists regarding the score of some drugs, a meeting was arranged with the experts who had

participated in the study, to discuss those drugs, and correct their scores if necessary. Eventually, the drugs were categorized into four groups based on their average score, with Group 1: having the highest potential impact and Group 4: having the lowest potential impact on cancer patients and the health system in Iran.

RESULTS:

Following the literature review, more than 30 criteria were found which had been used for prioritizing health technologies. After elimination of overlapping criteria, as well as those not suited for this study, we selected 7 criteria for prioritizing the medications, namely: clinical efficiency and effectiveness, the size of the affected population, costs, availability and accessibility to alternative therapies, variety of indications, quality of evidence and line of treatment. The definition of the selected criteria and their importance (weight) is presented in **Table 1**.

Table 2 presents the designed checklist for drug scoring by oncologists. The checklist has 7 ques-

Table 1. Selected criteria for prioritizing anticancer drugs and their definition and weights

No.	Criteria	Definition of criteria	importance (weight)
1	Clinical efficiency and effectiveness	The drug's capability which makes useful and beneficial changes in signs, symptoms and disease conditions more than that caused by alternative interventions and treatments, based on available efficiency and effectiveness data. The drug's ability to reduce the consequences of adverse effects compared to alternative interventions.	0.2
2	The size of the affected population	The number of people affected by the disease (The number of people the drug is produced for) Or the incidence and prevalence of disease in the population (The number of patients needing medicine).	0.16
3	Drug costs	The total costs associated with use of medication in society and other consumable equipment(estimations are based on the offered price or the price of alternative medicines, if there is no specified price for the medicine)	0.1
4	The availability and accessibility of alternative treatments	The number of alternative interventions which are currently or will soon be available. The accessibility and the ability to take advantages of alternative interventions in terms of economic, cultural, etc.	0.14
5	Variable indications	Using medicine in various clinical conditions and diseases (The number of different cancers which the medicine has an effect on)	0.1
6	Quality of evidence	Completeness of evidence related to the medicine (according to international standards reporting of clinical evidence) and the compliance of evidence with references. The validity of evidence according to international standards such as the type of study, study design, sample size, etc.	0.2
7	Treatment line	The line of treatment in which the medicine will be used. (First line, second line or third line and more)	0.1

tions, which are based on the criteria in **Table 1**. **Table 2** presents the designed checklist for drug scoring by oncologists. The checklist has 7 questions, which are based on the criteria in **Table 1**. Except for the first question which has three options, the remaining questions each have 4 options. The oncologists were asked to complete this checklist for each drug. As we stated in the method section, required information to answer these questions about each drug, such as the drugs clinical trials information (number of trials, their sample size, and their initial or final results), drug prices, and etc. was provided to the oncologists as much as possible.

After reviewing the horizon scanning systems reports, and removing duplicate anti-cancer medicines or compounds as well as those whose developing process had been stopped for any reason, we identified 158 oncology drugs which had been followed by these systems at the time of this study. The majority of these medications were in phase III of clinical trials, and almost one third had been approved by the US food and drug administration

Table 2. Checklist for scoring of drugs based on different criteria

Please answer the following questions about the drug:		
1	This drug is used for which line of treatment?	1. The first line 2. The second line 3. The third line and more
2	What is the potential impact of this drug on disease outcome (Improving efficiency and clinical effectiveness and reducing severe side effects)?	1. None 2. Small 3. Moderate 4. Large
3	The size of the population affected by the drug in Iran?	1. None 2. Small 3. Moderate 4. Large
4	What is the state of availability and access to alternative therapies of this medicine in Iran?	1. None 2. Small 3. Moderate 4. Large
5	What is the usage of this drug in treating other cancers?	1. None 2. Small 3. Moderate 4. Large
6	What is the potential impact of the drug on the rising costs of disease?	1. None 2. Small 3. Moderate 4. Large
7	How much is the quality of the available scientific evidence about this drug?	1. None 2. Small 3. Moderate 4. Large

Table 3. The list of oncology drugs that were identified with potentially high impact on cancer patients and the health system in Iran

ID	Drug Name	Company name	Indications
1	Ipilimumab (Yervoy)	Bristol-Myers Squibb	Malignant melanoma, Non-small cell lung cancer (NSCLC), Prostate cancer
2	Crizotinib (Xalkori)	Pfizer	Non-small cell lung cancer (NSCLC)
3	Pertuzumab (Perjeta)	Roche	Breast cancer, Gastric cancer
4	Nivolumab (Opdivo)	Bristol-Myers Squibb	Malignant melanoma, Non-small cell lung cancer (NSCLC), Renal cell carcinoma, Hodgkin lymphoma after failure of ASCT - Head, and neck (or upper airways tract) cancers, Metastatic and/or unresectable bladder cancer
5	Enzalutamide (Xtandi)	Medivation, Astellas	Prostate cancer,
6	Brentuximab vedotin (Adcetris)	Millennium Pharmaceuticals, Takeda	Anaplastic large cell lymphoma, Cutaneous T-cell lymphoma, Hodgkin lymphoma, Peripheral T-cell lymphoma
7	Ibrutinib (Imbruvica)	Janssen	Mantle cell lymphoma (MCL), Waldenström's macroglobulinemia (WM), Chronic lymphocytic leukemia (CLL), Diffuse large B-cell lymphoma (DLBCL), Non-Hodgkin lymphoma (NHL), Follicular indolent non-Hodgkin lymphoma (NHL)
8	Idelalisib (Zydelig)	Gilead Sciences	Non-Hodgkin lymphoma (NHL), Chronic lymphocytic leukemia (CLL)
9	Pembrolizumab (Keytruda)	Merck Sharp & Dohme (MSD)	Malignant melanoma, Non-small cell lung cancer (NSCLC), Head and neck (or upper airways tract) cancers, Urothelial cancer, Bladder cancer, Breast cancer, Gastric cancer, Multiple myelomas
10	Palbociclib (Ibrance)	Pfizer	Breast cancer,

(FDA). The list of selected oncology drugs is presented in appendix No.1.

After drug scoring by the oncologists, drugs were divided into four groups based on their average scores. The number of drugs in each of the four groups (1 to 4) was 18, 25, 48 and 67, respectively. The drugs which were in the first group, had the highest potential impact on cancer patients and the health system in Iran. Therefore they should be given the highest priority in conducting research and development in the country (**Table 3**). The second group were the next priority. However, the medicines in the fourth group were not deemed appropriate for investment and development.

DISCUSSION:

In this study, we conducted a horizon scanning ex-

Table 3. Continued

ID	Drug Name	Company name	Indications
11	Vemurafenib (Zelboraf)	Roche	Malignant melanoma
12	Abiraterone (Zytiga)	Centocor Ortho Biotech	Prostate cancer
13	Abraxane	Celgene	Pancreatic cancer, Non-small cell lung cancer (NSCLC), Breast cancer
14	Cabozantinib	Exelixis	Advanced renal cell carcinoma, medullary thyroid cancer, Hepatocellular carcinoma (HCC)
15	Everolimus (Afinitor)	Novartis	Neuroendocrine tumours, gastrointestinal and lung, Diffuse large B-cell lymphoma (DLBCL), breast cancer, Advanced renal cell carcinoma
16	Ramucirumab (Cyramza)	Eli Lilly	Hepatocellular carcinoma (HCC), Non-small cell lung cancer (NSCLC), Colorectal cancer, Gastric cancer, Bladder cancer
17	Ruxolitinib (Jakafi)	Incyte, Novartis	Polycythemia vera, Myelofibrosis,
18	Ado-trastuzumab emtansine (Kadcyla)	Roche	Breast cancer

ercise to identify new and emerging oncology drugs and prioritized them. After a review study and interviewing a number of specialists, we selected seven criteria for prioritizing drugs, including clinical efficiency and effectiveness, the size of the affected population, costs, availability and accessibility to alternative therapies, variety of indications, quality of evidence and line of treatment. We identified 158 new oncology drugs or compounds which had been followed by horizon scanning systems in other countries. After scoring and prioritizing the medications by oncologists, 18 medicines were recognized as having the highest potential impact on cancer patients and the health system in Iran. Therefore they should have the highest priority in conducting research and development in Iran.

In recent years, many health systems around the world have established official horizon scanning systems. However, most of these systems have been launched in high-income countries[11]. These systems provide decision-makers and policymakers with the necessary information to make informed decisions on investment in research and development as well as financial coverage of new health services[9]. The horizon scanning systems enable the health systems to effectively manage the introduction of new and emerging health technologies[13].

Identification of new and emerging technologies is the first step of the horizon scanning process[10, 14, 15]. Identification of emerging health technologies can be done by using either active or passive approaches, or both. In active approaches, depending on the field of interest, a broad spectrum of sources is selected and searched for information on target technologies. Whereas in passive approaches the stakeholders, health professionals, and consumers inform the horizon scanning entity about target technologies. Although the inactive method requires fewer resources than the active approach,

it is less comprehensive[11, 14, 15]. Currently, most horizon scanning systems use a combination of both approaches[9, 11].

In this study, we were unable to search all sources related to oncology drugs. As an alternative approach, we searched and reviewed the horizon scanning system reports in other countries to identify new oncology drugs. The horizon scanning systems in the high-income countries search for a wide range of sources to identify new technologies, and therefore identify a large percentage of new technologies[16]. Due to financial and infrastructure constraints, horizon scanning systems in low and middle-income countries (LMICs) including Iran, may not be able to regularly search a wide range of sources to identify new technologies. Since the identification step is almost identical in all horizon scanning systems, the approach for identification of new oncology drugs in this study could be an appropriate approach for identification of new technologies in horizon scanning systems in LMICs.

A large number of new and emerging technologies are usually identified in the first step of horizon scanning, and due to resource constraints, it is not possible for a horizon scanning program to assess all identified target technologies. Therefore, the next step in the horizon scanning process is to prioritize technologies. The aim of priority setting is to define the most potentially important new technologies in which to invest scarce assessment resources[11, 14]. Explicit prioritization of new technologies requires the use of certain prioritization criteria. All horizon scanning systems use explicit or implicit criteria for prioritization. However, due to differences in values, disease burden, cultures, and health care priorities in different countries, the criteria may differ significantly across these countries[11]. In this study, similar to the horizon scanning program in other countries, we selected some criteria for prioritization of oncology drugs. The prioritization criteria were selected based on previous studies and the opinions of our experts. However, the selected criteria were, to some extent, similar to those used in other countries[10, 11, 17].

In our horizon scanning exercise, we identified 18 new oncology drugs which were expected to have a potentially high-impact on cancer patients and the health system in Iran. Most of these drugs are indicated for common cancers, including breast, lung, lymphoma, and prostate cancers. However, some of these drugs are used for cancers that are not very common in Iran, including malignant melanoma. This results from the use of comprehensive criteria, with the drug receiving high scores from other criteria and masking its smaller disease burden. Although further assessment of these drugs may be needed, they can be the first priority for research and drug development in Iran. In addition, the health system of Iran needs to be prepared for introduction of some of these drugs into its market in the near future.

To the best of our knowledge, this study was the first attempt to conduct health technology horizon scanning in Iran. We reviewed horizon scanning systems method and reports in other countries and tried to use similar methods for horizon scanning of oncology drugs in Iran. However, our study had some limitations. As we mentioned earlier, due to some limitations, in order to identify new oncology drugs, we were unable to search all related sources. Furthermore, horizon scanning is a continuous process while our study was limited to a predetermined period.

In conclusion, nowadays, as a result of the rapid growth of health technologies and increased health care costs, most high-income countries have

launched health technology horizon scanning systems to identify novel and emerging health technologies and contribute to a proper and timely reaction of the health system to these technologies. Considering the many benefits of these systems, it is essential to implement them systematically in Iran with support from the Ministry of Health. Although due to financial and infrastructural constraints, establishing a comprehensive horizon scanning system may not be possible in Iran in the near future, using the results of horizon scanning systems in other countries and conducting horizon scanning program can aid in some priority areas such as non-communicable diseases including cardiovascular diseases, diabetes, respiratory diseases, etc. This study can be a trigger to conduct further horizon scanning exercises in other health care fields in Iran.

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