

An Empirical Analysis of Anti-Cancer Drug Lags in South Korea

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Abstract

This study attempts to examine how cancer drug lags in South Korea, along with submission-to-approval and approval-to-reimbursement decision time spans, have evolved over the last decade, from 2013 to 2022. For the same set of cancer drugs, the drug lags observed in South Korea were compared with those of United States, European Union, and Japan. Multivariate linear regression and multivariate Cox regression analyses were performed to conduct quantitative analyses. Compared with the 3 other advanced medicine agencies, South Korea (Ministry of Food and Drug Safety [MFDS]) displays an average delay of 1 to 2 years in submission and approval over the sample period. However, the average review processing time is much shorter than the submission and approval lags, and the MFDS fares even better than the European Union (European Medicines Agency [EMA]) in terms of reviewing efficiency. Notable progress has been made in addressing delays in the reimbursement decision process, roughly cut in half over the period, whereas other lags are rather elongated. The multivariate regression results confirm that the variations in approval delays in South Korea are largely associated with submission delays. The fact that South Korea fares poorly in submission and ensuing approval lags compared to other nations and regions with advanced medicine agencies mirrors the reality that South Korea is still not yet being considered as one of the most preferred testing grounds for innovative cancer drugs. The findings highlight that the goal of regulators should be geared towards ensuring more equitable access to oncology drugs in a timely manner for the Korean population.

Keywords

cancer drug, drug lags, drug approval, drug accessibility, drug affordability

Introduction

Devising innovative therapeutics for once-formidable chronic and rare diseases—most notably, cancer—and regulations that promote equitable access has taken the spotlight worldwide. While the United States (US) market has been recognized as the most accessible for decades, its consumers pay 2 to 3 times more for the same drugs than those in other Organization for Economic Co-operation and Development (OECD) member countries.¹ In light of this affordability issue, the US has announced a series of follow-up measures following the initial Inflation Reduction Act (IRA), which primarily focuses on ensuring equitable access by lowering prescription drug costs, especially targeted for Medicare which primarily serves older people.²

Meanwhile, continuing to advance the frontier of oncology research, the US has pushed the Cancer Moonshot, which subsidizes oncology R&D projects, with its core agenda set to halve cancer deaths over the next 25 years.³ The Food and Drug Administration (FDA) Oncology Center of Excellence (OCE) launched the Real-Time Oncology Review (RTOR) in 2018 to ensure the efficiency and rigor of the oncology drug review process; the OCE has also been

running Project Orbis since May 2019, which grants earlier access to drugs that are approved in other countries but have not yet been processed by the FDA.

Similarly, the South Korean government has implemented a suite of policies geared toward equitable and timely access to newly launched innovative drugs. In September 2022, the Ministry of Food and Drug Safety (MFDS) launched the Global Innovative Products on Fast Track (GIFT) program to expedite the review process of innovative pipelines and announced its intention to apply globally harmonized regulations that have not yet been introduced in South Korea with no lags.⁴ In June 2023, the

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MFDS announced policy measures that integrate expedited review and orphan drug designation processes, and that firms that are designated as innovative pharmaceutical firms will be given priority in processing expedited review.⁵

A full scope of anti-cancer drugs approved in South Korea so far can be found in the report of the MFDS.⁶ In South Korea, the regulatory approval of new drugs is overseen by MFDS. The MFDS evaluates the safety, efficacy, and quality of pharmaceutical products before granting marketing authorization. Cancer drugs can be qualified for expedited review and conditional approvals along with other life-threatening diseases; Expedited review process and conditional approvals also can be initiated in the absence of other alternative treatments.⁷⁻⁹ Once regulatory approval is obtained, drugs must go through a separate reimbursement and pricing process managed by the Health Insurance Review and Assessment Service (HIRA) and the National Health Insurance Service (NHIS). HIRA assesses the drug's clinical usefulness and cost-effectiveness, while NHIS negotiates pricing and determines reimbursement eligibility. Only after this process can the drug be listed for coverage under the national health insurance system. To enhance access to cancer therapies, South Korea has implemented various pricing and reimbursement mechanisms, including waivers of pharmacoeconomic evaluations, flexible Incremental Cost-Effectiveness Ratio (ICER) thresholds, and Risk-Sharing Agreements (RSA).^{10,11}

A substantial body of prior research has examined the impact of national regulatory reform initiatives on drug lag, with particular emphasis on comparative analyses involving leading regulatory authorities such as the FDA and the European Medicines Agency (EMA).

Drug lags are conventionally defined as the gap between the first global submission or approval date of a particular drug and the corresponding date of availability in the country of interest. It refers to the delay in the approval, availability, or market access to new drugs in 1 country compared to another—typically when comparing to the United States, the European Union, or Japan.^{12,13}

Even though there have been steady increments in cases where drugs receive their first approvals in countries other than the US, the latest report covering newly launched drugs from 2005 to 2021 illustrates that approximately 65% of new medicines are launched first in the US, 23% in the European Union (EU), and 8% in Japan.¹⁴ On average, the US has a delay of approximately 4 months in the release of new drugs, G20 countries have a delay of 27 months, and South Korea has a delay of 28 months.¹⁴ As for the time it takes from global first approvals to public reimbursement, the US ranks first with an average of 4 months, which is split into 4 months for local launches and zero months for the public reimbursement decision process; South Korea records an average of 46 months, with an average of 28 months spent for local launches and 18 months for the public reimbursement decision process.¹⁴

As expected, most of the literature on drug lags has focused on delays in domestic markets compared to the cases of the US and/or EU. Most recently, Wei et al¹⁵ followed up drug submission and approval timings in China, focusing on cancer drug indications that were approved by the FDA between 2001 and 2020. Submission lags in China still constitute a major part accounting for anti-cancer drug approval delays, even though China has witnessed a conspicuous drop in drug lags around 2015, largely due to its accession to the International Council for Harmonization (ICH) and the enactment of a series of regulatory reforms.¹⁶ Government-initiated expedited pathways, such as priority review (PR) and accelerated approval for urgently needed overseas drugs (UNOD), can be credited for the recent progress in drug lags observed in China from 2011 to 2021.¹⁷ Further, Tachibana and Narukawa compared the approval dates of anti-cancer drugs between the US and Japan using data from 2011 to 2022, and found that drug lags increased during the second half of the sample period. They argued that greater participation by Japan in global clinical trials and international drug development could facilitate earlier approvals, as it would reduce the need to repeat clinical trials domestically and thereby shorten the overall review timeline.¹⁸

There are a few studies that delve into drug delays in the context of South Korea, but none of them have focused on cancer drugs. Cho and Han¹⁹ analyzed 424 new drugs approved by the MFDS from 2000 to 2019 and found that longer drug delays were associated with orphan drug designations and marketing authorization holders based in South Korea. However, drugs approved after 2015 showed improvements with respect to drug delays. Choi and Lee²⁰ examined newly approved drugs during the period 2011 to 2017 and found that review lags, defined as the gap between submission to the MFDS and approval by the MFDS, and submission and approval gaps, defined as the difference between global first dates and dates processed by the MFDS, did not necessarily decrease over this period. Choi et al²¹ also investigated new drug submissions, approval lags, and review durations over the period 2011 to 2020 and pointed out that there are significant submission and approval gaps between the MFDS, FDA, and EMA.

In line with the aforementioned literature, this study attempts to examine how cancer drug lags in South Korea, along with submission-to-approval and approval-to-reimbursement decision time spans, have evolved over the last decade, from 2013 to 2022, and delves into potential factors that are associated with the variation of drug lags. We attempt to assess the interplay of the elements of drug characteristics, such as orphan designation, modality, indication, and policy environment, with drug lags over the sample period. In other words, we split the discussion into the components of submission and approval lags and submission-to-approval (review) and approval-to-reimbursement decision process spans, and pinpoint potential factors that can explain the variations in drug lag variables.

Methods

This study is a retrospective, cross-national, quantitative analysis based on secondary data. It employs multivariate linear and Cox regression methods to examine the anti-cancer drug lags.

Data Collection

We define submission/approval lag as the gap between the first submission/approval date to/by any of the 4 medicine agencies (FDA, EMA, PMDA, and MFDS) and the submission/approval date to/by the MFDS.

Our dataset covers 45 new oncology drugs approved by the MFDS from 2013 to 2022, and details regarding their corresponding submission dates were collected alongside information on equivalent submission and approval dates by the FDA, EMA, and PMDA from each official government agency site.²²⁻²⁶ We excluded cases where new indications were added to already approved drugs. Our analysis focuses solely on newly approved drugs that received their initial marketing authorization in South Korea. Data on reimbursement dates were collected only for cases of the MFDS, owing to limited access to the dataset.²³ Other drug characteristics data, such as orphan designation, cancer type, and modality, were also collected.²²

Statistical Analysis

First, we highlight notable findings primarily based on the analysis of the first moments, mean, and medians of the drug lag variables, where the dataset is split based on key characteristics such as authorization dates, orphan drug designation, modalities, and cancer types. Drug delays were also compared with those of 3 advanced medicine agencies: the FDA, EMA, and PMDA. We then proceeded to a formal statistical testing stage to quantify the statistical significance of the characteristics with regard to drug lags. To determine the attributes associated with and factors that can explain variations in drug delays, multivariate linear regression and multivariate Cox regression analyses were performed. Terms such as oncology drugs, anti-cancer drugs, and cancer drugs are used interchangeably in this paper. Statistical analyses were performed using R 4.3.1.

Results

Between 2013 and 2022, South Korea approved a total of 45 new oncology drugs, which translates into an average of 4.5 oncology drug approvals per year. We classified the characteristics and drug lags of our selected set by segregating them based on authorization dates, orphan drug designation, modality, indication, and cancer type (hematologic/solid and detailed indication; Table 1). The most common modality is targeted therapies that mostly take the form of either

monoclonal antibodies, antibody drug conjugates (ADC), or enzyme- or protein-specific inhibitors, accounting for 28; the rest includes 9 immunotherapies and 4 hormone therapies. The most frequent indications receiving approval in South Korea during the sample period are breast cancer and non-small cell lung cancer, with 9 approvals thus far for each. This matches the most prevalent cancer types of each sex occurring in South Korea, with breast cancer being the main cancer type occurring among women and lung cancer being the primary type among men as of 2020.²⁷ This is followed by leukemia with 5 approvals, and multiple myeloma and prostate cancer with 4 approval cases. Indications could also be grouped into binary types: 33 solid cancers and 12 blood cancers. Of the 45 approved drugs, 6 drugs were approved through the orphan drug pathway. A total 33 of 45 approved drugs have received approval for public reimbursement as of May 2023. On average, the reimbursement decision process (597 days) took longer than the review process (350 days). The average length of the reimbursement decision process almost halved during the recent 5 years compared to the first 5 years, from 760 to 413 days. Non-orphan drugs, on average, have shorter spans of submission and approval lags and review and reimbursement decision processes. The difference in lags between orphan and non-orphan drugs is most pronounced in the submission stage, consequently leading to approval lags. Reimbursed drugs, on average, have shorter spans of submission, review, and approval lags than the averages of the entire dataset. Immunotherapies and targeted therapies took longer to review than hormone therapies, but both took fewer days to go through the reimbursement decision process than hormone therapies. Solid cancers, on average, had shorter submission, review, and approval lags than blood cancers, but blood cancers went through shorter spans of the approval-to-reimbursement process.

To get a glimpse of whether the drug delays in South Korea fare well based on a global comparison, we compared the drug delays across 4 medicine agencies, the FDA, EMA, PMDA, and MFDS, using mean and median values (Figures 1-4). The yearly time series plots can be found in the Supplemental files (Supplemental Figures 1-4). It is noteworthy that the relative gaps between agencies are smaller for review lags than for submission and approval lag cases, which indicates that the timing of market entrance can possibly make a difference to the end results. Regarding submission and approval lags, the US records a median of zero delay, proving to be the most accessible market. The MFDS trails all other medicine agencies in submission and approval lags; on average, the MFDS has a shorter review span than the EMA, but still lags behind the FDA and PMDA.

We used multivariate linear regression and multivariate Cox regression models to check the extent to which the independent variables of our choice, drug characteristics and policy variables, can explain the variation in drug lag variables.

Table I. Characteristics and Drug Lags of the Anti-Cancer Drugs Newly Approved in South Korea (2013-2022).

Drug lag																			
Characteristic	Authorization date	Approved, N (%)	Reimbursed, N (%)	First submission to MFDS submission				Submission to approval by the MFDS				First approval to MFDS approval				MFDS approval to reimbursement			
				Approved		Reimbursed		Approved		Reimbursed		Approved		Reimbursed		Approved		Reimbursed	
				M	A	M	A	M	A	M	A	M	A	M	A	M	A	M	A
Total		45 (100)	33 (100)	476	786	421	684	333	350	315	324	581	774	530	661	493	597		
Authorization date	First half	22 (48.9)	15 (45.5)	357	507	306	530	273	307	245	279	333	508	327	521	769	760		
	Second half	23 (51.1)	18 (54.5)	798	943	798	787	349	378	329	359	953	1028	841	840	397	413		
Orphan drug	Orphan	6 (13.3)	4 (12.1)	908	1230	979	1065	353	423	379	421	985	1359	1134	1150	522	619		
	Non orphan	39 (86.7)	29 (87.9)	447	678	418	612	331	332	308	305	577	666	396	591	396	442		
Modality	Targeted therapy	28 (62.2)	21 (63.6)	502	788	455	648	333	354	319	332	577	772	469	597	522	614		
	Hormone therapy	4 (8.9)	3 (9.1)	254	639	867	867	272	275	277	277	302	726	938	938	710	710		
	Immunotherapy	9 (20.0)	7 (21.2)	371	441	371	441	368	346	368	346	421	486	421	548	522	595		
	Others	4 (8.9)	2 (6.1)	1767	1767	1405	1405	245	245	245	245	1715	1715	1715	1715	311	311		
Cancer type	Total	12 (26.7)	8 (24.2)	965	1066	976	916	332	401	284	354	850	1065	770	837	396	532		
	Multiple myeloma	4 (8.9)	2 (6.1)	463	793	1767	1767	353	395	245	245	531	775	1020	1020	617	617		
	Leukemia	5 (11.1)	4 (12.1)	1033	871	1043	820	377	411	442	444	1143	886	849	810	350	464		
	Myelofibrosis	2 (4.4)	2 (6.1)	633	633	633	633	258	273	273	273	709	709	709	709	585	585		
	Sézary syndrome	1 (2.2)	0 (0)	3529	3529	N/A	N/A	638	638	N/A	N/A	3828	3828	N/A	N/A	N/A	N/A		
	Total	33 (73.3)	25 (75.8)	442	678	418	611	333	330	323	315	580	668	432	602	522	619		
	Non-small cell lung	9 (20.0)	9 (27.3)	418	385	418	385	306	304	306	304	505	435	505	435	365	343		
	Breast	9 (20.0)	5 (15.2)	677	719	591	591	359	371	351	351	720	766	468	556	842	879		
	Prostate	4 (8.9)	3 (9.1)	549	691	844	859	303	290	334	296	676	807	1050	975	822	747		
	Melanoma	2 (4.4)	2 (6.1)	334	334	334	334	234	234	234	234	278	278	278	278	999	999		
Colorectal	2 (4.4)	1 (3.0)	1029	1029	76	76	425	425	406	406	1181	1181	329	329	1014	1014			
Others*		7 (15.6)	5	1729	1344	1729	1344	315	360	315	360	602	730	729	901	559	599		

Note. *Others include ovarian, stomach, pancreatic, thyroid, renal cell, endometrial, and Merkel cell carcinoma cancers. For comparison, we split the dataset; for the submission lag, the dataset is split into 2 halves: the first half from 2012 to 2016 and the second half from 2017 to 2021. For the approval and review lag, the first half is from 2013 to 2017 and the second half is from 2018 to 2022. For the reimbursement lag, the first half is from 2014 to 2018 and the second half is from 2019 to 2023.

A=average; M=median.

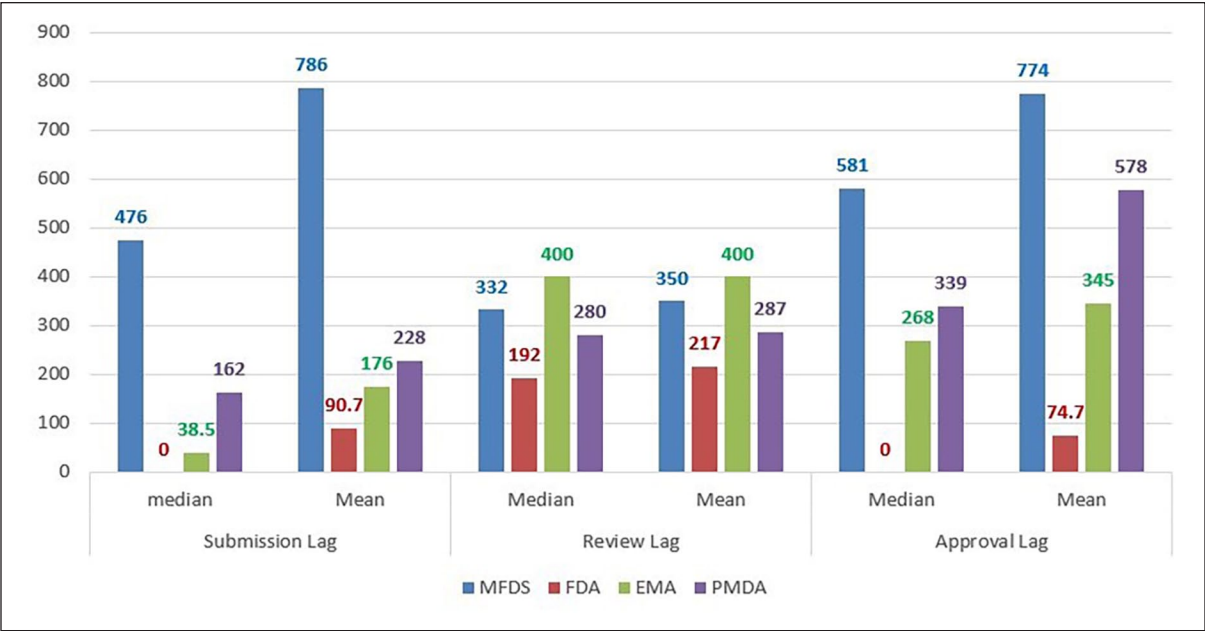


Figure 1. Summary statistics of drug lags across medicine agencies.
Note. Summary statistics are based on a sample set of 45 cancer drugs approved in South Korea between 2013 and 2022.

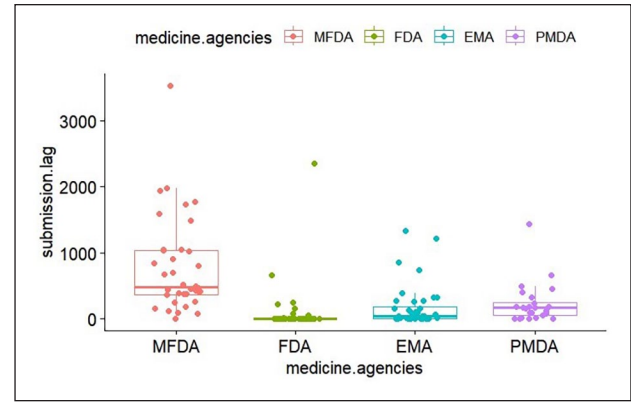


Figure 2. Box plot for submission lags.
Note. The plot traces the authorization dates of 45 cancer drugs approved in South Korea between 2013 and 2022.

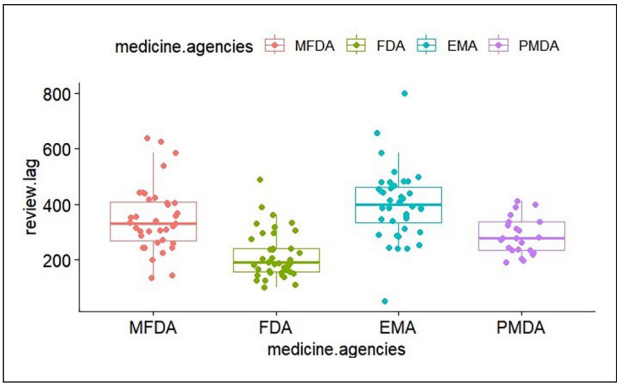


Figure 3. Box plot for review lags.
Note. The plot traces the authorization dates of 45 cancer drugs approved in South Korea between 2013 and 2022.

Supplemental Table 1 reports a selected set of multivariate regression results with the highest adjusted *R*-squared values. The multivariate Cox regression results illustrate the probabilities of an event occurring in a multivariate context (Table 2). The factors identified as significant in the Cox regression analyses were generally consistent with those found in the multivariate regression models, both in terms of their association with the outcome variables and the direction of effects. According to the hazard ratio estimates, on average, drugs were .202 times (20.2%) less likely to be submitted to the MFDS during the second half period (2017–2021), orphan drugs were .31 times less likely to be submitted, and drugs classified as others in the modality

were .018 less likely to be submitted compared to the rest of the cases. However, when the drugs were first submitted to the FDA, then they were 2.95 times more likely to be submitted. If the drugs were submitted first either to the FDA or MFDS, then they were 5.896 or 315.977 times more likely to get reviews done, respectively. During the second half period (2018–2022), compared to the first half period (2013–2017), drugs were .265 times less likely to have reviews completed. If submission lags increased, then drugs were .99 times less likely to be approved, and during the second half period (2018–2022), drugs were 8.834 times more likely to have the reimbursement decision process completed, compared to the first half period (2014–2018).

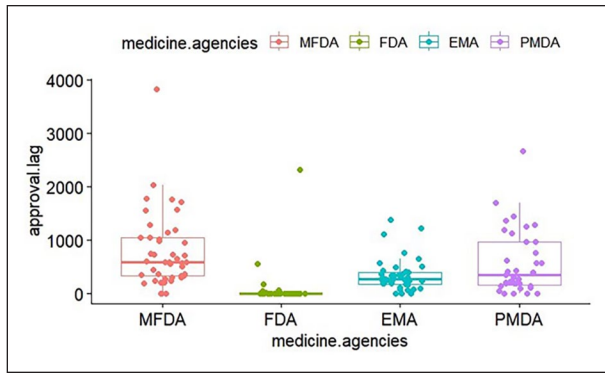


Figure 4. Box plot for approval lags.

Note. The plot traces the authorization dates of 45 cancer drugs approved in South Korea between 2013 and 2022.

Discussion

South Korea, on average, has delays of over 1 to 2 years in submission, which translates into an average of approximately 2 years in approval lags. Accordingly, the main regulatory initiatives, especially in the market for addressing chronic and rare diseases, have focused on ensuring prompt access to innovative drugs while adhering to safety standards. With the emergence of novel therapeutic modalities in recent decades, accelerated approval pathways have been increasingly recognized as critical regulatory mechanisms for facilitating timely access to treatments for life-threatening diseases, particularly cancer.²⁸ In this context, the literature on drug lags has scrutinized how regulations have been harmonized worldwide to secure more equitable and prompt access to innovative drugs, with the regulations and examples of the FDA and EMA set aside as primary references most of the time.^{16,18-20}

However, recently, concerns have been raised that the introduction of expedited and eased regulatory pathways has not necessarily translated into better clinical results.^{25,29,30} The main criticisms are that surrogate endpoint results upon which conditional approvals are based are not necessarily linked to positive confirmatory endpoint results and that the FDA's post-marketing follow-ups are not sufficiently rigorous, leaving scores of conditional approval cases in the market unregulated.³¹ That is, there is a need to be mindful that these systems are indeed sometimes negatively impacting both low-income countries and developed countries such as those in Europe and Japan. This has resulted in the opinion that the EMA has more concrete clinical data, establishing its renown as not giving out hasty false positives as frequently as the FDA, while the US has otherwise always been ranked first in terms of drug accessibility. Therefore, regulators should bear in mind that there is a lack of evidence linking expedited regulatory review processes with higher clinical benefits.³²

Meanwhile, the fact that the US is the first testing ground for innovative drugs most of the time, ironically, has resulted

in financially suboptimal outcomes for patients, with the first-set US pricing mostly regarded as exorbitant according to other countries' standards, referred to as the reference prices, and consequently passed down to other countries.³³

However, with a few multinational initiatives to harmonize pricing and reimbursement mechanisms and the IRA in the making, the landscape of pricing and reimbursement mechanisms in oncology is expected to evolve, hopefully resulting in a more equitable mechanism equipped with a process that weighs the various perspectives of stakeholders in the longer term.^{34,35}

As explained in the previous section, the pharmaceutical market in South Korea lags behind other advanced markets such as those in the US and EU in terms of newly launched cancer drug accessibility. Compared to the FDA, EMA, and PMDA, the MFDS displayed an average delay of 1 to 2 years in submission and approval over the sample period. The multivariate regression results confirm that the variations in approval delays in South Korea are largely associated with submission delays. Drugs that were submitted first either to the FDA or the MFDS displayed shorter average submission and review lags, while those submitted to the PMDA first had longer submission and review lags.

Notably, the average span of the reimbursement decision process in South Korea was almost halved during the second-half period of 2019 and 2023 compared to the first-half period of 2014 and 2018, while all averages of the submission, review, and approval lags increased, suggesting that further regulatory reforms need to be carried out in the submission-to-approval stage. Non-orphan drugs, on average, had shorter submission and approval lags and shorter spans of review and reimbursement decision processes, largely because of differences in marketability, pricing, and reimbursement mechanisms across markets and the requirement of bridging trials. It suggests that more government support should be followed upon given the relatively high upfront R&D investment required and a smaller patients pool. Ex-post reimbursed drugs, on average, involved shorter processes than those that had not yet made it through the reimbursement decision process, possibly reflecting the value of such anti-cancer therapies.

For the Korean market to advance in the realm of market attractiveness, regulatory harmonization will need to be smoothed ahead of emerging market needs. Specifically, systemization of single-arm and adaptive trials needs to be thought out thoroughly, by taking into account accompanying statistical compromises.^{36,37} It is also critical that the details on post-marketing clinical trials, expedited approvals, rare disease designation, and multinational trials are aligned to the level of international standards. Furthermore, in the era of digital clinical trials, regulations on decentralized trials such as remote clinical trials need to be planned out accordingly.³⁸ In return, such government-led initiatives that will encourage R&D development and innovative drug launches are expected to mitigate the submission lags that we have

Table 2. Multivariate Cox Regression Results on Drug Lags.

Predictor		Submission lag (1)	Review lag (2)	Approval lag (3)	Approval-to-reimbursement (4)
Regressor					
Period indication	First half—reference variable				
	Second half	0.202 [0.078, 0.521] (0.000***)	0.265 [0.123, 0.569] (0.000***)	0.389 [0.109, 1.385] (0.145)	8.834 [2.569, 30.372] (0.000***)
Where It was First Submitted	FDA	2.947 [0.822, 10.569] (0.097*)	5.896 [2.347, 14.812] (0.000***)	0.480 [0.108, 2.141] (0.336)	-
	MFDA	✓	315.977 [28.645, 3485.510] (0.000***)	✓	-
	PMDA	0.000 [0.000, Inf] (0.998)	0.000 [0.000, Inf] (0.992)	0.101 [0.000, Inf] (1.000)	-
	EMA – Reference Variable				
Where It was First Approved	FDA	-	-	-	1.363 [0.115, 16.081] (0.806)
	MFDA	-	-	-	9.216 [0.518, 164.079] (0.131)
	PMDA	-	-	-	1.316 [0.051, 33.887] (0.868)
Submission Lag	EMA – Reference Variable				
	X		1.01 [1.000, 1.002] (0.002***)	0.990 [0.987, 0.994] (0.000***)	-
Orphan Designation	Orphan	0.310 [0.092, 1.046] (0.059*)	0.597 [0.220, 1.623] (0.312)	0.893 [0.206, 3.874] (0.880)	0.7143 [0.088, 5.831] (0.753)
	Non-Orphan – Reference Variable				
Blood or Solid Cancer	Blood – Reference Variable				
	Solid	0.542 [0.175, 1.675] (0.287)	0.889 [0.352, 2.247] (0.804)	1.323 [0.240, 7.298] (0.748)	0.535 [0.141, 2.029] (0.357)
Yearly Expenditure Modality	-	-	-	-	-
	Targeted	1.320 [0.338, 5.1556] (0.690)	0.948 [0.423, 2.123] (0.896)	1.387 [0.253, 7.606] (0.706)	1.999 [0.478, 8.368] (0.343)
	Immunotherapy	2.924 [0.503, 17.000] (0.232)	0.463 [0.144, 1.494] (0.198)	0.756 [0.098, 5.828] (0.788)	1.924 [0.418, 8.860] (0.401)
	Hormone – Reference Variable				
Overall Test	Others	0.018 [0.000, 0.527] (0.020**)	0.514 [0.061, 4.352] (0.541)	7.868 [0.139, 445.394] (0.317)	28.9018 [1.438, 581.070] (0.028**)
	Likelihood Ratio Test	0.00005	0.003	0.000	0.02
	Wald Test	0.04	0.0000002	0.8	0.07
	Score Test	0.00000001	0.002	0.000	0.02

Note. Period indication is a dummy variable that codes the data either into the first half period or second half period; for the submission lag, the dataset is split into 2 halves: the first half from 2012 to 2016 and the second half from 2017 to 2021. For the approval and review lag, the first half is from 2013 to 2017 and the second half is from 2018 to 2022. For the reimbursement lag, the first half is from 2014 to 2018 and the second half is from 2019 to 2023. Inputs are hazard ratio estimates and exponentiated coefficients, paired numbers in square brackets are corresponding confidence intervals, and numbers in parentheses are P-values. All numbers are rounded to 3 decimal places. ✓ refers to the cases when the corresponding estimates are unavailable because of missing observations and—refers to the cases when such regressors are dropped either because the VIF scores are higher than or close to 5, the adjusted R-squared value is higher without the regressors, or regressions without the variable entail less missing observations.

***Denotes that the corresponding coefficient is statistically significant at a significance level (α) of 1%.

**For the case of $\alpha = 5\%$.

*For the case of $\alpha = 10\%$.

documented in this article. Participating in multinational initiatives to collectively determine pricing, reimbursement mechanisms, and decisions is expected to ease drug lags. Overall, the goal of regulators should be to ensure equitable access to oncology drugs in a timely manner, especially by prioritizing a list of oncology indications that are more relevant for the Korean population.

As for the limitations of our dataset, our study presents a rather skewed description that covers only 45 oncology drugs that were approved in South Korea during the sample period between 2013 and 2022, and did not consider the entire set of cancer drugs that were newly launched elsewhere over the same period but have not yet entered the Korean market. Thus, our analysis of drug lags can be downward biased, given that South Korea trails in drug access in comparison with other advanced pharmaceutical markets. Our analysis can be made more robust if we include drugs that were newly launched elsewhere, but did not manage to enter the Korean market during the sample period. In addition, there are some missing observations with regard to submission and reimbursement dates, while all entries of official approval dates could be searched in repositories hosted by the MFDS.

Finally, with regard to statistical choices and study coverage, while a recent study set lags in drug indication approvals as the outcome variable, in this study, we used drug lags as our outcome variable¹⁵; setting different outcome variables can invoke a systematic bias arising from measurement bias. In addition, it will be interesting to evaluate how these newly implemented regulation reforms, such as GIFT-approved drugs, have influenced overall drug accessibility in South Korea and once enough observations are stacked; its associated clinical benefits can be confirmed in the context of retrospective studies. The addition of clinical benefit variables to test the statistical association between drug accessibility and clinical benefits can also provide important insights.¹⁵

Conclusions

Compared with the FDA, EMA, and PMDA, the MFDA displayed an average delay of 1 to 2 years in submission and approval over the sample period between 2013 and 2022. The multivariate regression results confirm that the variations in approval delays in South Korea are largely associated with submission delays. These empirical findings indicated that South Korea is still not yet being considered as an advanced testing ground for innovative cancer drugs. On the bright side, the average amount of time taken for the reimbursement decision process almost halved over the same sample period.

Overall, the goal of regulators should be geared towards ensuring both timely and equitable access to oncology drugs as well as advancing patients' clinical benefits, particularly by prioritizing a list of oncology indications that are more relevant for the Korean population. Such regulatory

initiatives will in turn encourage more R&D and business opportunities in the South Korean market, ultimately enriching the underlying ecosystem of the pharmaceutical market.

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Ethical Considerations

Not applicable.

Consent to Participate

Not applicable.

Author Contributions

SK Lee: Conceptualization, data curation, formal analysis, investigation, methodology, and writing-original draft/review and editing under the guidance of JH Lee. JH Lee: Supervision of the entire study, from study conceptualization, data curation, formal analysis, methodology, and manuscript editing to manuscript submission. All the authors have read and approved the final version of the manuscript.

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Data Availability Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Supplemental Material

Supplemental material for this article is available online.

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