THE IMPACT OF RE-PRICING POLICY ON THE PRICE OF ANTI-CANCER DRUGS FROM 2007 TO 2019 IN SOUTH KOREA – A RETROSPECTIVE STUDY

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Background & Objectives

- **Background:** Pricing strategy and reimbursement policy for drugs basically consider affordable access to medicines and rational use, especially for costly medicines on the cutting edge (1, 2). Value-based pricing has developed based on additional value for patients including affordability and innovation of the drugs (3, 4). List price of drugs should reflect its value on, a price change also needs to reflect their value change because the reimbursement price often functions as the de facto market price. Value considerations have become increasingly important in an era of rapid expansion of new, expensive cancer medicines within cost-constrained health care systems (5, 6). Listing new anti-cancer drugs leads to financial toxicity to both patients and payer (7) but have uncertainty in clinical usefulness or cost-effectiveness. Therefore, the anti-cancer drug has strictly been managed as separate lists by the government due to the disease severity and high-cost in many countries(8, 9). In South Korea, the pharmaceutical cost-containment policy has focused on price control, specifically price reduction (10). A descriptive study in South Korea reported frequency and amount of price-cut through analyzing drug price adjustments of total 13,606 drugs, but it did not investigate factors affecting price-cut (11). However, there is no study analyzing drug price adjustments and factors in anti-cancer drugs.
- **Objectives:** To investigate the impact on price reduction across re-pricing mechanisms in South Korea for over 12 years in anti-cancer drugs

Methods

- The data was built based on the price log of listing drugs spanning from January 2007 to 2019 H1 by Health Insurance Review & Assessment Service (HIRA). Trace of drugs' price for 78 anti-cancer substances, and 439 drugs that were listed from January 2007 to December 2017 were identified and followed up for at least one and half year after a listing date.
- Event of interest was defined as a price change, especially reduction of price

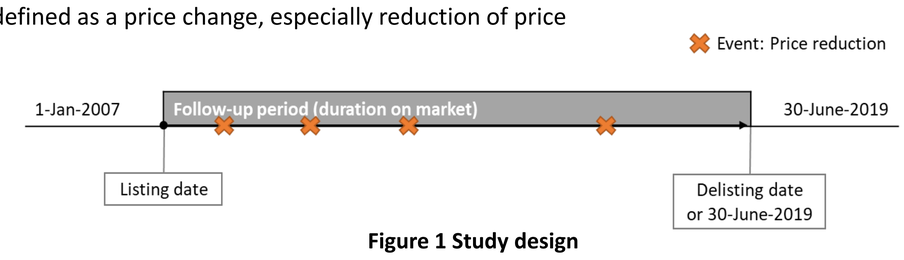

Figure 1 Study design

- All events were categorized into seven repricing mechanisms based on various sources:
  - Intrinsic factor-driven mechanism: Actual transaction pricing, per request from a manufacturer, price-volume agreement, and indication expansion
  - Extrinsic factor-driven mechanism: Price-cut at generic entry or 1 year after, price-cut in April 2012, re-evaluation
  - Unknown
- Differences in baseline characteristics between the price-reduced group and the price-maintained group were evaluated using the Student's t-test and chi-square test.
- Incidence rate was adopted to adjust positive association between number of reduction and duration on market.

$$\text{Incidence rate of price redution} = \frac{The\ number\ of\ price\ reductions}{\sum product\ time\ at\ risk\ (product-year, PY)}$$

- Poisson regression model was used to estimate the characteristics-adjusted IRR of reduction.
- Data analysis was performed using R 3.5.1 (Vienna, Austria; http://www.R-project.org/) with the package, 'fmbs.'

Result

- Total 439 anti-cancer drugs was newly listed, and 271 drugs (67.1%) have at least on price-reduction of for 5.7 years (SD2.7). Average reduction per a product is 1.8 (SD 1.0), and the average reduction rate was 16.3% (SD: 13.3%)
- There are significant differences in the duration on the market (P<0.001), percentages of the route of administration (P <0.001), targeted therapy (P=0.006), and orphan drugs (P=0.046) between the price-reduced group and the price-maintained group since the reimbursement (Table 1).
- In Figure 2, the number of events from intrinsic mechanism (n=196, 61.8%) is higher than that from the extrinsic factor-driven mechanism (n=150, 30.0%). ATP is the most frequent mechanism of repricing (n=196; 39.2%) among intrinsic factor-driven mechanisms, followed by voluntary reductions (10.2 %), while price cut due to generic entries and the lumped price-cut happen the most frequently among extrinsic factor-driven mechanisms with 96 times (19.2%) and 49 times (9.8%), respectively.
- Total 500 price reductions happen during the study period and the IR per 100 PY is 23. The IR of drugs with over 1.34 million USD annual sales is greater than drugs with sales of less 1.34 million USD (IRR 1.40, 95% CI 1.14-1.78). The originator has a higher incidence rate than the generic (IRR 1.32, 95%CI 1.08-1.62). There are significant differences in route of administration, targeted therapy, orphan drug, and listing year (Table 2).
- With the Poisson model (Table 3), listing in 2013-2017 was the highest risk for incidence of price-reduction (IRR 1.80, 95%CI 1.33-2.44). Orphan drug has less risk of reduction (IRR 0.50, 95%CI 0.31-0.76).

Table 1 Characteristics of target anti-cancer drugs

	Reduction (N=271)	No reduction (N=168)	P-value[2)]
Duration on market (year), mean ± SD	5.7 ± 2.7	2.9 ± 1.8	<0.001
Number of reductions, n	1.8 ± 1.0	-	
Total cumulative reduction (%), mean ± SD	-16.3 ± 13.3	-	
Time to first event (year), mean ± SD	2.3 ± 1.9		
Original drug	58 (21.4%)	27 (16.1%)	0.211
Root of administration: oral agent	124 (45.8%)	44 (26.2%)	<0.001
Targeted therapy	96 (35.4%)	38 (22.6%)	0.006
Orphan drug	20 (7.4%)	23 (13.7%)	0.046
Drugs listed with a risk-sharing agreement[1)]	13 (4.8%)	9 (5.4%)	0.971
CEA* waiver drugs[1)]	3 (1.1%)	4 (2.4%)	0.520
Listing year			0.320
2007-2012	121 (44.6%)	84 (50.0%)	
2013-2017	150 (55.4%)	84 (50.0%)	
Annual sales (USD)			<0.001
< 1.34 million	169 (62.4%)	57 (33.9%)	
≥ 1.34 million	41 (15.1%)	6 (3.6%)	
Unknown	61 (22.5%)	105 (62.5%)	
Increase utilization			<0.001
< 60%	29 (10.7%)	14 (8.3%)	
≥ 60%	157 (57.9%)	38 (22.6%)	
Unknown	85 (31.4%)	116 (69.0%)	

1) Only originator
2) Reduction vs. No reduction: P-value was calculated using the chi-square test for categorical variables and t-test for continuous variables.
CEA: cost-effectiveness analysis

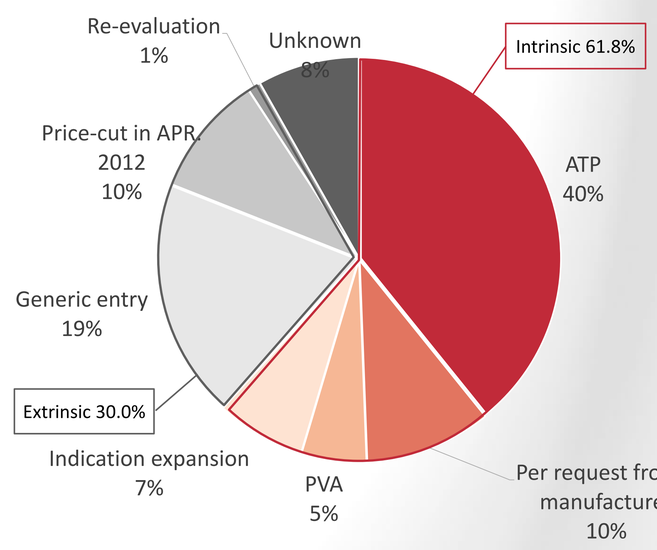

Figure 2 The frequency of events resulting from repricing mechanism

Table 2 The incidence rate ratio across subgroup

	Event	Product	Duration of follow-up	IR per 100 PY	IRR	95% CI
Total	500	439	2,052	23		
Generic drug or originator						
Originator	128	85	444	29	1.32	1.08-1.62
Generic drug	372	354	1,707	23		
Route of administration						
Oral	220	168	839	28	1.23	1.03- 1.47
Injection	280	271	1,312	22		
Targeted therapy						
Yes	167	134	666	28	1.28	1.06-1.54
No	333	305	1,546	22		
Orphan drug						
Yes	24	43	162	15	0.62	0.41-0.93
No	476	396	1,990	24		
RSA[1)]						
Yes	25	22	78	32	1.02	0.74-1.77
No	103	63	367	28		
CEA waiver drug[1)]						
Yes	5	7	21	23	0.80	0.33-1.96
No	123	78	423	29		
Listing year						
2013-2017	242	234	867	28	1.39	1.17-1.66
2007-2012	258	205	1,285	20		
Annual sales (USD)						
≥ 1.34 million	102	47	296	34	1.42)	1.14-1.78
< 1.34 million	314	226	1,294	24		
Unknown	84	166	562	15		
Increase utilization						
≥ 60%	326	195	1,236	26	1.26[2)]	0.94-1.68
< 60%	54	43	257	21		
Unknown	120	201	658	18		

1) Only originator
2) Unknown was not considered
CEA: Cost-effectiveness analysis IR: incidence rate; IRR: incidence rate ratio, PY: product year

Table 3 Adjusted incidence rate ratio

Risk factors	IRR	P-value
Listing year: 2013-2017	1.8 (1.3-2.4)	0.000
Annual sales > USD 1.34 millions	1.6 (1.1-2.3)	0.007
Increased utilization > 60%	1.3 (1.0-1.7)	0.099
Originator (reference: generics)	1.0 (0.7-1.5)	0.866
Duration on market (year)	1.1 (1.0-1.1)	0.067
Oral agent (reference: injection)	1.0 (0.8-1.3)	0.976
Targeted therapy	0.9 (0.7-1.2)	0.409
Listed with a risk-sharing agreement	1.0 (0.6-1.6)	0.949
Orphan drug	0.50 (0.3-0.8)	0.002

Unknown of annual sales and increased utilization included in analysis but were not presented in the table
IRR: incidence rate ratio, HR: hazard ratio

Conclusion

- This study is the first empirical study to analyze the incidence of price reduction associated with factors and a focus on mechanisms.
- The incidence increased gradually, and the repricing mechanism affected the price of anti-cancer drugs in a variety of ways.
- The most critical factor in reduction was the time of listing.
- This would require the establishment of a repricing policy that could comprehensively reflect the change in value throughout the whole drug life cycle.

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