IMPACT of PD-1/PD-L1 Inhibitors on Health Outcomes for Patients with Cancer in South Korea

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ABSTRACT

OBJECTIVE: To estimate the health impact of the programmed cell death protein 1 (PD-1) / programmed death-ligand 1 (PD-L1) inhibitor class to cancer treatment in real-world situations.

METHODS: A model was developed to estimate the impact of PD-1/PD-L1 inhibitors on outcomes in situations where both anti-PD-1/PD-L1s and standard of care (SOC) were available vs. counterfactual situations with the SOC alone. A partitioned survival model was adopted to estimate the impact of introducing anti-PD-1/PD-L1s on outcomes, including life years gained, quality-adjusted life years gained, progression-free survival years obtained, and grade 3+ adverse events avoided for six indications over 5 years. An exponential distribution was fitted to the survival function of the SOC based on visual inspection. For anti-PD-1/PD-L1s, piecewise modeling approach with Kaplan–Meier analysis followed by best-fitting survival analysis was employed. The incident number of patients and market share of anti–PD-1/PD-L1s during 2020-2024 were projected using published literature and Korean market survey data. Sensitivity analysis was conducted with patients who had entered the cohort in 2020 only, thereby could be assessed for the outcomes over a full 5-year period (2020–2024).

RESULTS: The introducing anti–PD-1/PD-L1 class was predicted to increase health gains by 22,001 life years (+31%), 19,073 quality adjusted life years (+38%), and 22,893 progression-free life years (+82%), and reduce 3,610 (11%) of the adverse events. Most of the adverse events from anti–PD-1/PD-L1s was attributed to the combination product with chemotherapy (91%). In the sensitivity analysis, each patient in the 2020 cohort who received anti-PD-1/PD-L1 therapy was expected to gain an additional 0.72 life years and 0.58 quality adjusted life years over the 5-year period compared with those patients treated with the SOC alone.

BACKGROUND

- To complement conventional chemotherapy, safer and more effective immuno-oncology therapies have been developed.
- The PD-1/PD-L1 class offers new opportunities to treat cancer effectively by prolonging survival with more increased tolerability.[1]
- Given the new treatment options for different cancer types at different stages, no assessments have been performed on the overall health outcomes associated with anti-PD-1/PD-L1 treatment.

OBJECTIVE

- To obtain high-level estimates of the impact of treatment with the anti-PD-1/PD-L1s on key health outcomes of cancer patients in South Korea and to quantify the impact of lead time for the reimbursement of anti-PD-1/PD-L1s.

METHODS

Model Structure

- Key health outcomes obtained in a world where patients are treated with standard of care were compared to those obtained in a world where patients are treated with a mix of SOC and anti–PD-1/PD-L1 treatments.
- A partitioned survival model was utilized to estimate the survival function of the study outcomes.

Data Fitting Models

- Based on visual inspection, the survival function of the exponential distribution was fitted to the SOC survival curve and used to extrapolate to a 5-year time horizon.
- For the anti-PD-1/PD-L1, a parametric piecewise modeling approach was applied. [2]

Clinical Input Parameters

- Survival outcomes associated with the anti-PD-1/PD-L1s were assumed to represent the entire anti-PD-1/PD-L1 class.
- The most conservative trials that showed the smallest differences in time to progression of the anti-PD-1/PD-L1 class vs. the SOC were selected.

Market Dynamic Input Parameters

- To estimate the number of patients, incidence rate by disease classification and stage, and the probability of transitioning to a different stage were retrieved from published studies.
- The market share of anti-PD-1/PD-L1s for each indication was estimated by the market penetration of anti-PD-1/PD-L1 in South Korea.

Sensitivity Analysis

- Sensitivity analysis was conducted with patients who had entered the cohort in 2020 only, who could be assessed for the outcomes over a full 5-year period (2020–2024); per-patient outcomes were also calculated for each indication.

Figure 1. Model Estimating the Health Impact of Introducing PD-1/PD-L1 Inhibitors

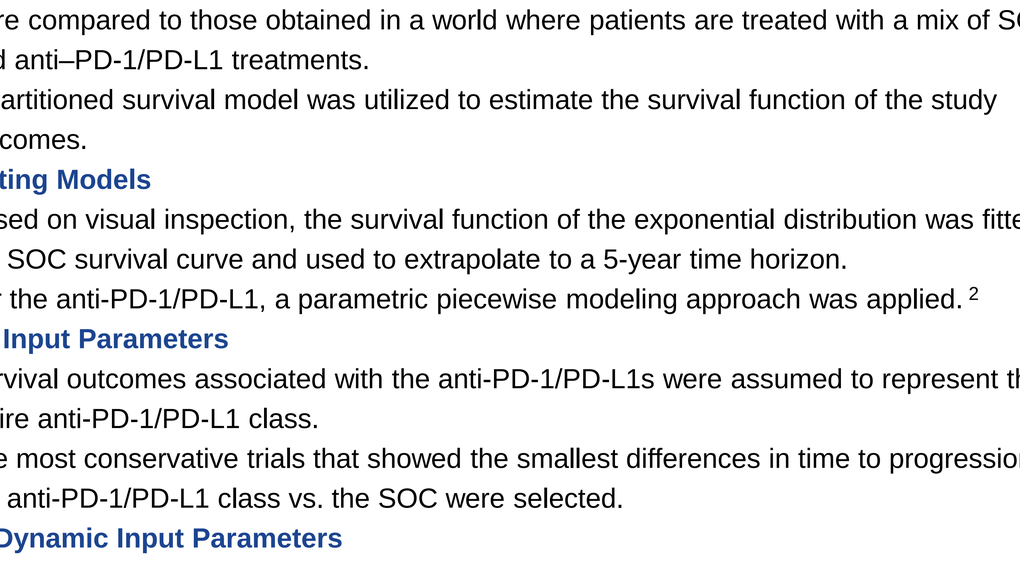

Table 1. Input parameters for clinical survival outcomes in base scenario

Indication	Anti-PD-1/PD-L1	Standard of Care	Clinical Endpoint	Time Period Cut-off Point (Week)	HR in Time Period 1	HR in Time Period 2
Advanced Melanoma [3]	Nivolumab	Dacarbazine	OS	15	0.50	0.45
			PFS	9	0.80	0.53
1L NSQ-NSCLC [4, 5]	Pembrolizumab	Platinum-based CTX	OS	40	0.75	0.60
			PFS	8	1.00	0.50
	Pembrolizumab + CTX	Cisplatin + Pemetrexed	OS	30	0.49	0.83
			PFS	20	0.50	1.23
1L SQ-NSCLC [4, 6]	Pembrolizumab	Platinum-based CTX	OS	40	0.75	0.60
			PFS	8	1.00	0.50
	Pembrolizumab + CTX	Carboplatin + (nab) paclitaxel	OS	31	0.64	1.20
			PFS	15	0.40	1.22
2L NSCLC [7]	Atezolizumab	Docetaxel	OS	21	0.68	0.95
			PFS	12	1.23	0.71
M-TNBC [8]	Atezolizumab + CTX	Nab–paclitaxel	OS	48	0.70	1.15
			PFS	8	0.50	1.09
2L Urothelial carcinoma [9]	Pembrolizumab	Paclitaxel, docetaxel or vinflunine	OS	50	0.80	0.73
			PFS	8	1.30	0.65

Abbreviations: PD-1/PD-L1: programmed cell death protein 1/programmed death-ligand 1, CTX: chemotherapy, 1L: first-line, 2L: second-line, NSQ-NSCLC: non-squamous non-small-cell lung cancer, SQ-NSCLC: squamous non-small-cell lung cancer, M-TNBC: metastatic triple-negative breast cancer, HR: hazard ratio, PFS: progression-free survival, OS: overall survival, nab-paclitaxel: nanoparticle albumin-bound-paclitaxel

RESULTS

Table 2. Input Utility Values for the Partitioned Survival Model

Indication	Treatment	Utility Weight		Instrument
		Progression-Free	Progressed Disease	
Advanced melanoma	Anti-PD-1/PD-L1s	0.810	0.710	EQ-5D
	Standard of care	0.770	0.680	
1L NSQ-NSCLC	Anti-PD-1/PD-L1s	0.768	0.710	EQ-5D, EORTC-QLQ-C30, and QLQ-LC13
	Standard of care	0.757	0.645	
1L SQ-NSCLC	Anti-PD-1/PD-L1s	0.808	0.737	EQ-5D, EORTC-QLQ-C30, and QLQ-LC13
	Standard of care	0.757	0.687	
2L NSCLC	Anti-PD-1/PD-L1s	0.770	0.660	EQ-5D, EORTC-QLQ-C30, and QLQ-LC13
	Standard of care	0.740	0.670	
M-TNBC	Anti-PD-1/PD-L1s	0.741	0.653	EQ-5D and EORTC-QLQ-C30
	Standard of care	0.710	0.653	
2L Urothelial carcinoma	Anti-PD-1/PD-L1s	0.857	0.828	EQ-5D
	Standard of care	0.821	0.764	

Table 3. Changes in Health Outcomes Between World With vs. Without Anti-PD-1/PD-L1s Over 5 Years (2020-2024)

		Life Years			Quality-Adjusted Life Years			Progression-Free Survival Years		
	Number of Patients	With Anti-PD-1/PD-L1s	Without Anti-PD-1/PD-L1s	Incremental Outcome (%)	With Anti-PD-1/PD-L1s	Without Anti-PD-1/PD-L1s	Incremental Outcome (%)	With Anti-PD-1/PD-L1s	Without Anti-PD-1/PD-L1s	Incremental Outcome (%)
All indications	77,244	92,848	70,847	22,001 (+31%)	69,038	49,964	19,073 (+38%)	55,129	30,273	22,893 (+82%)
Advanced melanoma	1,050	1,677	846	831 (+98%)	1,289	601	688 (+114%)	1,017	289	728 (+252%)
1L NSQ-NSCLC	25,495	34,028	25,260	8,768 (+35%)	25,217	17,516	7,701 (+44%)	22,898	10,925	11,973(+110%)
1L SQ-NSCLC	21,012	25,788	20,833	4,955 (+24%)	19,945	14,931	5,014 (+34%)	17,565	8,832	8,733 (+99%)
2L NSCLC	24,499	26,229	20,186	6,043 (+30%)	18,480	14,083	4,396 (+31%)	11,257	8,641	2,616 (+30%)
M-TNBC	880	1,075	984	91 (+9%)	740	667	73 (+11%)	483	424	59 (+14%)
2L Urothelial carcinoma	4,308	4,051	2,738	1,312 (+48%)	3,367	2,166	1,201 (+55%)	1,909	1,162	747 (+64%)

Table 4. Grade 3-5 Adverse Events Avoided by Introducing Anti-PD-1/PD-L1s Over 5 Years (2020 Through 2024)

Indications	Treatment Pattern	With anti-PD-1/PD-L1s		Without anti-PD-1/PD-L1s		Changes (%)
		Patients n	Grade 3-5 Adverse Events n (%)	Patients n	Grade 3-5 Adverse Events n (%)	
All indications	All	77,244	28,321 (36.7%)	77,244	31,931 (41.3%)	-3,610 (-11%)
Advanced melanoma	All	1,050	58 (5.5%)	1,050	115 (11.0%)	-57 (-50%)
1L NSQ-NSCLC	All	25,495	14,911 (58.5%)	25,495	12,744 (50.0%)	2,167 (+17%)
	Pembrolizumab monotherapy	5,245	1,093 (20.8%)			
	Pembrolizumab/Atezolizumab+CTX	14,169	10,762 (76.0%)			
	Standard of care	6,080	3,056 (50.3%)	25,495	12,744 (50.0%)	
1L SQ-NSCLC	All	21,012	9,432 (44.9%)	21,012	7,686 (36.6%)	1,746 (+23%)
	Pembrolizumab monotherapy	4,152	643 (15.5%)			
	Pembrolizumab+CTX	11,399	6,768 (59.4%)			
	Standard of care	5,462	2,021 (37.0%)	21,012	7,686 (36.6%)	
2L NSCLC	All	24,499	3,118 (12.7%)	24,499	9,781 (39.9%)	-6,663 (-68%)
M-TNBC	All	880	316 (35.9%)	880	274 (31.1%)	42 (+15%)
2L Urothelial carcinoma	All	4,308	486 (11.3%)	4,308	1,331 (30.9%)	-845 (-63%)

Table 5. Sensitivity analysis. Comparison of health outcomes between worlds with and without anti-PD-1/PD-L1s during 5 years (2020-2024) in patients belonging to 2020 cohort (n=16,212)

Outcomes		Life Years				Quality-Adjusted Life Years			
Indications	Number of Patients	With Anti-PD-1/PD-L1s	Without Anti-PD-1/PD-L1s	Incremental Outcome (%)	Incremental Outcome per patient	With Anti-PD-1/PD-L1s	Without Anti-PD-1/PD-L1s	Incremental Outcome (%)	Incremental Outcome per patient
All indications	16,212	25,551	18,598	6,953(+37%)	0.72	18,620	13,023	5,597 (+43%)	0.58
Advanced melanoma	195	507	195	312 (+160)	1.84	391	138	253 (+183%)	1.49
1L NSQ-NSCLC	4,720	8,702	6,081	2,621 (+43%)	1.01	6,374	4,180	2,193 (+52%)	0.85
1L SQ-NSCLC	3,890	5,806	5,026	780 (+16%)	0.78	4,308	3,583	725 (+20%)	0.73
2L NSCLC	6,494	9,253	6,484	2,768 (+43%)	0.52	6,517	4,508	2,008 (+45%)	0.38
M-TNBC	153	234	234	0 (+0%)	N/A	157	157	0 (0%)	N/A
2L Urothelial carcinoma	760	1,050	578	472 (+82%)	0.80	874	456	418 (+92%)	0.70

CONCLUSIONS

- The anti–PD-1/PD-L1s treatment is expected to provide substantial health impact for patients with cancers prevalent in South Korea.
- Anti-PD-1/PD-L1s treatment is predicted to increases life years by 31% and quality adjusted life years by 37%, while reducing grade 3+ adverse events by 11%, compared with SOC treatment over 5 years.
- This study provided a realistic depiction of the magnitude of the population-level health improvement that would be obtained with the introduction of PD-1/PD-L1 inhibitors.

REFERENCES

1. Schirrmacher V: From chemotherapy to biological therapy: A review of novel concepts to reduce the side effects of systemic cancer treatment (Review). Int J Oncol 2019, 54(2):407-419: doi:10.3892/ijo.2018.4661.
2. Harris SJ, Brown J, Lopez J, Yap TA: Immuno-oncology combinations: raising the tail of the survival curve. Cancer biology & medicine 2016, 13(2):171
3. Robert C, Long GV, Brady B, Dutriaux C, Maio M, Mortier L *et al*: Nivolumab in previously untreated melanoma without BRAF mutation. N Engl J Med 2015, 372(4):320-330
4. Reck M, Rodríguez-Abreu D, Robinson AG, Hui R, Csőszi T, Fülöp A *et al*: Pembrolizumab versus chemotherapy for PD-L1–positive non–small-cell lung cancer. N Engl J Med 2016, 375(19):1823-1833
5. Gandhi L, Rodríguez-Abreu D, Gadgeel S, Esteban E, Felip E, De Angelis F et al: Pembrolizumab plus chemotherapy in metastatic non–small-cell lung cancer. N Engl J Med 2018, 378(22):2078-2092
6. Paz-Ares L, Luft A, Vicente D, Tafreshi A, Gümüş M, Mazières J et al: Pembrolizumab plus chemotherapy for squamous non–small-cell lung cancer. N Engl J Med 2018, 379(21):2040-2051
7. Rittmeyer A, Barlesi F, Waterkamp D, Park K, Ciardiello F, Von Pawel J et al: Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. Lancet Oncol 2017, 389(10066):255-265
8. Schmid P, Adams S, Rugo HS, Schneeweiss A, Barrios CH, Iwata H et al: Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. N Engl J Med 2018, 379(22):2108-2121
9. Bellmunt J, de Wit R, Vaughn DJ, Fradet Y, Lee JL, Fong L et al: Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma. N Engl J Med 2017, 376(11):1015-1026: doi:10.1056/NEJMoa1613683.

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