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Real-world results of immune checkpoint inhibitors from the Taiwan National Health Insurance Registration System

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Abstract. – OBJECTIVE: Immune checkpoint inhibitors (ICIs) are a major advance in cancer treatment, but their payment benefits are unclear, resulting in financial risk. In Taiwan, the National Health Insurance Administration (NHIA) has adapted risk-sharing mechanisms to cover ICIs by collecting and assessing real-world evidence, such as case registration data, to adjust benefit packages for each medication, increase payment benefits of ICIs, and enable national health insurance sustainability.

PATIENTS AND METHODS: This nationwide, multicenter, retrospective cohort study assessed the real-world use, effectiveness, and safety of ICIs reimbursed by the NHIA for treating multiple advanced cancers in Taiwan. We obtained data mainly from the NHIA Immune Checkpoint Inhibitor Registry Database.

RESULTS: Between April 1, 2019, and March 31, 2020, 1644 patients received at least one dose of ICIs. The overall response rate (RR) was 29.1%. The metastatic urothelial carcinoma of patients ineligible for chemotherapy showed the highest RR. The estimated median progression-free survival (PFS) was 2.8 months (95% confidence interval [CI]=2.7-3 months), and renal cell carcinoma showed the longest PFS. The median PFS was reached in patients with most cancers except classic Hodgkin's lymphoma, which had a small sample size. The estimated survival probability was 50%.

CONCLUSIONS: Under the national registration tracking system, Taiwan's high-cost drug policy has enabled access to new medicines and maximized patient benefits.

Key Words:
Immune checkpoint inhibitors, Real-world data, National registration tracking system.

Introduction

Cancer is the leading cause of death in Taiwan[1]. The National Health Insurance Administration (NHIA), Taiwan's single-payer health insurance system, substantially invests in cancer treatment every year. Approximately, 720,000 cancer patients in Taiwan required treatment in 2018[2]. The cost of their medication reached NTD 27 billion, and the total cost of treatment, including examination and hospitalization, was NTD 104.3 billion[2].

Immune checkpoint inhibitors (ICIs) are a major advance in cancer treatment. However, due to the accelerated review of new cancer drugs worldwide, the payment benefits of ICIs are still unclear, resulting in financial risk for most public insurance payers. Major health technology assessment agencies worldwide, including the National Institute for Health and Care Excellence (NICE) in the United Kingdom, the Canadian Agency for Drugs and Technologies in Health in Canada, and the Pharmaceutical Benefits Advisory Committee in Australia, pay for ICIs after vendors present acceptable cost-effectiveness plans. The NHIA also reached several risk-sharing agreements with vendors to enable earlier access to treatment for cancers that have not had a new effective treatment for a long time. Through such agreements, the NHIA began covering pembrolizumab, nivolumab, and atezolizumab for eight types of cancers (i.e., melanoma, non-small-cell lung cancer

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[NSCLC], classic Hodgkin's lymphoma [CHL], urothelial carcinoma [UC], head and neck squamous cell carcinoma [HNSCC], gastric adenocarcinoma [GC], renal cell carcinoma [RCC], and hepatocellular carcinoma [HCC]) in April 2019 and established relevant payment guidelines. Taiwan also implemented a precertification mechanism for reimbursing the costs of these new ICIs whereby physicians upload specific patient information on the precertification page of the NHIA's virtual private network[3].

As the NHIA initially covered drug indications with uncertain clinical and cost benefits, it developed a preliminary review system for cancer immunotherapy applications. This system tracks the funds used and the number of drugs uses and collects real-world data (RWD) on patients using ICIs in order to assess the overall payment benefits of ICIs[3]. Today, the NHIA regularly invites oncologists, pharmacy experts, and methodology experts to examine the RWD of ICI-using patients in Taiwan, the latest developments in international treatment guidelines and clinical trials, and the current situation in health insurance financial controls. Rolling reviews are conducted, and the benefit packages are adjusted accordingly. For instance, the NHIA covers GC and HCC indications that receive approval *via* accelerated review.

Considering the relative lack of payment benefits in existing treatments and the failure to reach risk-sharing agreements, the NHIA unprecedentedly suspended new applications in April 2020; however, it still continued payments for patients already using ICIs until their conditions worsened[3]. To ensure that patients could fully benefit from the new medications, the NHIA passed another resolution to extend the total course of medication to a maximum of 2 years for those responding to the medication. It also expanded the conditions for medications effective for UC. Meanwhile, for first-line treatments that are not as effective as expected for melanoma and NSCLC, the NHIA continued to observe real-world evidence (RWE) and adjust benefits accordingly[3].

By adapting risk-sharing mechanisms to cover ICIs and collecting and assessing RWE (e.g., case registration data), the NHIA can adjust benefit packages for each medication, increase the payment benefits of ICIs, and create opportunities for national health insurance (NHI) sustainability[3]. However, coverage and reimbursement decisions for expensive medications should be based on scientific evidence, especially data obtained through value-based pharmaco-economic evaluations. Such decisions should also include stakeholders in the process in order to account for patient and public preferences[4]. Using the RWD collected *via* the NHIA patient registry system[3,5], this study analyzed the effectiveness of current ICI treatments for cancer patients in Taiwan.

Patients and Methods

Study Design

This nationwide, multicenter, retrospective cohort study reported the real-world use, effectiveness, and safety of ICIs reimbursed by the NHIA for treating multiple advanced cancers in Taiwan. The Antai Medical Care Cooperation Antai-Tian-Sheng Memorial Hospital Institutional Review Board (19-044-C) approved the study's protocol. Considering the retrospective nature of this study, informed consent was not required.

Data Sources/Measurement

We used the Immune Checkpoint Inhibitor Registry Database (ICIRD) as our main data source. The NHIA developed the ICIRD to collect baseline and disease characteristics, biomarker profiles, previous surgical and medication histories, and treatment outcomes of patients starting on April 1, 2019, the first date of reimbursement for ICIs[3]. Physicians submitted applications online through the ICIRD for initial and subsequent treatments, with up to 12 weeks of dosage being authorized per application. To continue treatment, the patient had to show a response to the most recent course of ICIs as evidenced *via* imaging reports and verified by independent and competent physicians. Stable patients could be authorized one time for an additional 4-12 weeks dosage. If a response was indicated following reassessment, the patient could continue therapy; otherwise, the subsidized treatment ended. The total duration of any funded treatment per patient was limited to 2 years. Once treatment ended, the physician had 28 days to report the date of treatment discontinuation and reason for the discontinuation[3]. Finally, we also obtained data from the National Health Insurance Research Database (NHIRD) related to prescription claims, inpatient and outpatient visit dates, and mortality prior to June 2020.

Participants and Exposures

All eligible patients who met the listed criteria for ICIs and filed at least one corresponding prescription claim between April 1, 2019, and March 31, 2020, were included in the study. The cutoff date of this study was September 30, 2020, and each patient was followed up for at least 6 months[3].

Three ICIs were reimbursed: nivolumab and pembrolizumab (programmed cell death protein 1 [PD-1] inhibitors) as well as atezolizumab (a programmed cell death ligand 1 [PD-L1] inhibitor). Nivolumab was administered intravenously at 3 mg/kg body weight every 2 weeks. Pembrolizumab was administered intravenously at 2 mg/kg body weight or at a fixed dose of 200 mg every 3 weeks. Atezolizumab was administered intravenously at a fixed dose of 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks. Patients were reimbursed for the individual drugs when they were used as monotherapy, with marketing authorizations across multiple locations for treating the following eight cancer types[3]:

- Unresectable or metastatic melanoma in patients who received at least one systemic therapy;
- NSCLC with no epidermal growth factor receptor, anaplastic large-cell lymphoma kinase, or c-ros oncogene 1 (*ROS-1*) genomic tumor aberrations in adults (i) with advanced squamous cell carcinoma with disease progression on/after platinum-containing chemotherapy, (ii) with advanced adenocarcinoma with disease progression on/after platinum-containing chemotherapy and subsequent taxanes, and (iii) who are ineligible for chemotherapy;
- Relapsed/refractory CHL in adults who previously underwent autologous stem cell transplantation and subsequent brentuximab vedotin;
- UC in adults with disease progression on/after platinum-containing chemotherapy for local disease advance or metastasis and in adults' ineligible for chemotherapy;
- Recurrent/metastatic HNSCC in adults with disease progression on/after platinum-containing chemotherapy;
- Metastatic GC in adults with disease progression on/after two or more prior lines of chemotherapy;
- Advanced clear-cell RCC in adults who received two or more prior lines of target therapy; and
- Advanced HCC in adults previously treated with at least one targeted therapy.

Patients were assigned an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1 and had adequate cardiac, pulmonary, liver, and renal function. For specified indications, including NSCLC, UC, HNSCC, and GC, high PD-L1 expression was required in tumors, and patients had to be tested with corresponding approved class III in vitro diagnostics to determine specific levels for individual drugs[3].

Outcomes

Tumor response was measured *via* imaging reports according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) in HCC and the immune-related Response Evaluation Criteria in Solid Tumors (iRECIST) in others. The effectiveness endpoints included the following factors:

- Best overall response: the best response recorded during the study period.
- Objective response rate (ORR): the proportion of patients who achieved a complete response (CR) or a partial response (PR).
- Disease control rate (DCR): the proportion of patients who achieved a CR, PR, or stable disease status.
- Progression-free survival (PFS): the PFS is defined as the time from the first prescription claim for ICIs to the date of disease progression or death from any cause, whichever occurs earlier. If there is no documented disease progression or death, the PFS is censored at the date of the last adequate tumor assessment. In this study, the PFS was defined as the last submitted date of tumor assessment that an independent physician in charge of the competent review subsequently verified as having been without disease progression.
- Overall survival (OS): the time from the first prescription claim for ICIs to death from any cause. Patients without a documented death date in the NHIRD were censored at the last point in time at which they were known to be alive.

Physicians in charge of patient care reported and graded adverse events (AEs) using the National Cancer Institute's Common Terminology Criteria for Adverse Events version 4.0. Considering reporting burdens, only grade 3 or worse AEs and immune-related adverse events (irAEs) were collected in the ICIRD at the time of applying for subsequent treatment and reporting treatment discontinuation.

Statistical Analysis

We conducted descriptive statistical analyses. Categorical variables were presented as num-

bers and percentages. We used the Kaplan-Meier method to estimate continuous variables as the mean ± standard deviation or the median (interquartile range [IQR]). Finally, we estimated the OS, PFS, and treatment duration. All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patients and Treatment

Between April 1, 2019, and March 31, 2020, 1644 patients received at least one ICI dose (Figure 1). Their median age was 63.6 years, and 74.9% were male (Table I). Regarding the treatment, 925 (56.3%), 648 (39.4%), and 71 (4.3%) received nivolumab, pembrolizumab, and atezolizumab, respectively. Approximately 25% were diagnosed with HCC and treated with the only reimbursed drug (i.e., nivolumab). The median follow-up duration was 7.1 months to death or the study's cutoff date (September 30, 2020).

Effectiveness

The overall RR to ICIs was 29.1% (Table II). The highest RR was observed in patients with metastatic UC who were not eligible for chemotherapy. The estimated median PFS was 2.8 months (95% confidence interval [CI]=2.7-3 months; Table II). The longest PFS was observed in RCC. The estimated survival probability reached 50%, and the median PFS was reached in most cancers except CHL, which had a small sample size.

The most common late-stage cancers were HCC and NSCLC (treated with first-, second-, or third-line therapy), each accounting for approximately 25% of patients, followed by recurrent or metastatic HNSCC (approximately 14%). Ultimately, nearly 30% of patients showed an objective response (CR=approximately 4%).

Safety

Of the 1644 patients, 1365 (83%) registered for discontinuation, and 46 (2.8%) discontinued ICIs due to AEs, which occurred more frequently in NSCLC patients (4.4%–7.8%). Of these 1365 patients, 119 (8.7%) experienced irAEs of any grade, and 6 (0.4%) had multiple irAEs (Table III). Grade 3 or worse irAEs were reported in 59 (4.3%) patients (Table IV). The most commonly reported irAEs were skin reactions (2.6%), pneumonitis (2.5%), and hepatitis (1.1%). The irAE reporting rate was higher among NSCLC and HCC patients,

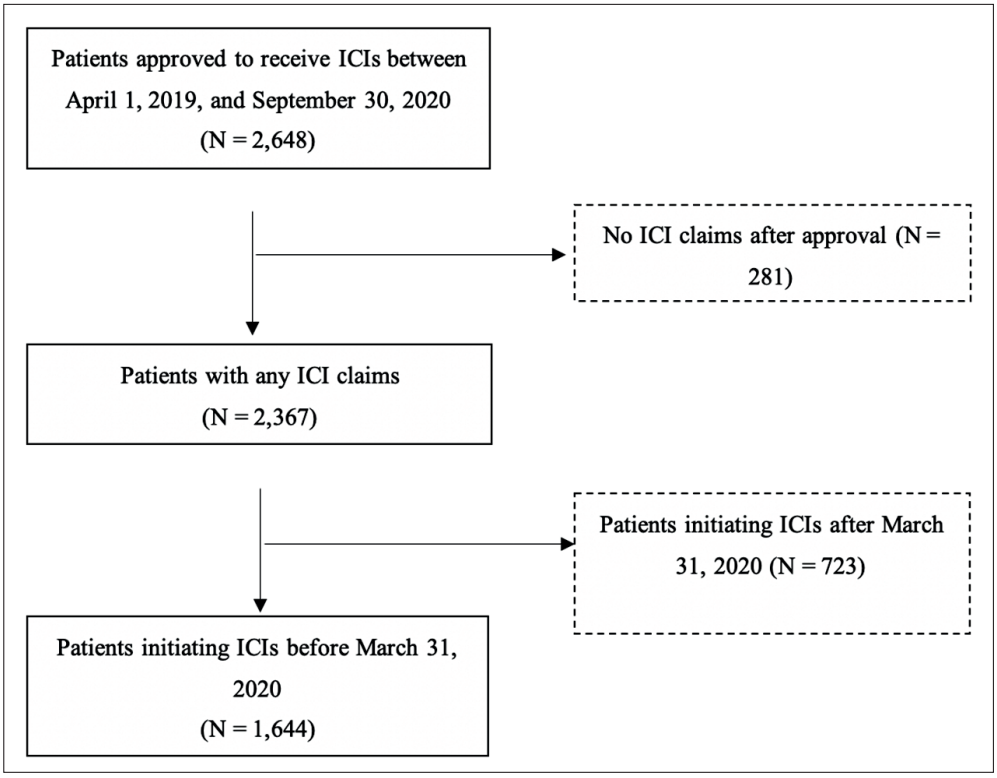

Figure 1. Cohort selection diagram. ICI, immune checkpoint inhibitor.

Table I. Baseline characteristics of the study cohort.

	Cohort (N = 1,644)	
Age-years		
Median (IQR)	63.6	(55.9 to 70.9)
< 65	884	(53.8%)
≥ 65	760	(46.2%)
Sex-number (%)		
Male	1232	(74.9%)
Female	412	(25.1%)
ECOG performance status score-number (%)		
0	758	(46.1%)
1	885	(53.8%)
Unknown	1	(0.1%)
Immune checkpoint inhibitors-number (%)		
Pembrolizumab	648	(39.4%)
Nivolumab	925	(56.3%)
Atezolizumab	71	(4.3%)
Indication-number (%)		
Melanoma	138	(8.4%)
Advanced squamous NSCLC (2-line)	109	(6.6%)
Advanced lung adenocarcinoma (3-line)	137	(8.3%)
Metastatic NSCLC (1-line)	154	(9.4%)
Classic Hodgkin's lymphoma	10	(0.6%)
Advanced urothelial carcinoma (2-line)	112	(6.8%)
Metastatic urothelial carcinoma (1-line)	33	(2.0%)
Head and neck squamous cell cancer	222	(13.5%)
Gastric cancer	213	(13.0%)
Renal cell carcinoma	108	(6.6%)
Hepatocellular carcinoma	408	(24.8%)

IQR, interquartile range; ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small-cell lung cancer.

and the highest irAE reporting rate (13.1%) occurred in metastatic NSCLC patient's ineligible for chemotherapy. No new safety issues were detected.

Table II. Best response and PFS.

Indications	Patients (n)	Best response					Progression-free survival	
		CR	PR	Stable disease	ORR	DCR	Median (95% CI)	Event rate
Melanoma	138	4	35	25	28.3%	46.4%	3.5 (2.8 to 4.7)	73.2%
NSCLC_SQ (2-line)	109	1	34	19	32.1%	49.5%	3.1 (2.6 to 4.7)	70.6%
NSCLC_Adeno (3-line)	137	0	49	15	35.8%	46.7%	3.2 (2.4 to 4.9)	73.0%
NSCLC (1-line)	154	2	58	15	39.0%	48.7%	3.3 (2.5 to 5.7)	64.9%
CHL	10	0	4	3	40.0%	70.0%	NR (2.1 to NR)	30.0%
UC (2-line)	112	11	34	14	40.2%	52.7%	3.8 (2.9 to 5.7)	59.8%
UC (1-line)	33	4	10	3	42.4%	51.5%	2.7 (2.1 to 8.3)	72.7%
HNSCC	222	13	55	19	30.6%	39.2%	2.5 (2.2 to 3)	75.2%
GC	213	5	19	11	11.3%	16.4%	2.0 (1.8 to 2.1)	93.0%
RCC	108	9	34	13	39.8%	51.9%	5.1 (2.8 to 9)	57.4%
HCC	408	20	78	58	24.0%	38.2%	2.9 (2.6 to 3.2)	76.2%
Total	1644	69	410	195	29.1%	41.0%	2.8 (2.7 to 3.0)	72.8%

PFS, progression-free survival; CR, complete response; PR, partial response; ORR, objective response rate; DCR, disease control rate; CI, confidence interval; NSCLC, non-small-cell lung cancer; CHL, classic Hodgkin's lymphoma; UC, urothelial carcinoma; HNSCC, head and neck squamous cell carcinoma; GC, gastric adenocarcinoma; RCC, renal cell carcinoma; HCC, hepatocellular carcinoma.

Table III. AEs.

Indications	irAEs			Discontinuation due to AEs		
	Patients registered for discontinuation (n)	Patients n (%)		Patients n (%)	Patients n (%)	
Melanoma	119	6	(5.0%)	138	0	(0%)
NSCLC_SQ (2-line)	89	10	(11.2%)	109	5	(4.6%)
NSCLC_Adeno (3-line)	111	13	(11.7%)	137	6	(4.4%)
NSCLC (1-line)	122	16	(13.1%)	154	12	(7.8%)
CHL	6	0	(0%)	10	0	(0%)
UC (2-line)	80	7	(8.8%)	112	1	(0.9%)
UC (1-line)	26	3	(11.5%)	33	0	(0%)
HNSCC	175	9	(5.1%)	222	1	(0.5%)
GC	203	9	(4.4%)	213	2	(0.9%)
RCC	81	5	(6.2%)	08	2	(1.9%)
HCC	353	41	(11.6%)	408	17	(4.2%)
Total	1,365	119	(8.7%)	1,644	46	(2.8%)

AE, adverse event; irAE, immune-related adverse event; NSCLC, non-small-cell lung cancer; CHL, classic Hodgkin's lymphoma; UC, urothelial carcinoma; HNSCC, head and neck squamous cell carcinoma; GC, gastric adenocarcinoma; RCC, renal cell carcinoma; HCC, hepatocellular carcinoma.

Discussion

Between April 1, 2019, when the NHIA first started covering ICIs, and March 31, 2020, more than 1000 late-stage cancer patients underwent treatment and received follow-up care for at least 6 months. Considering the individual cancers, the ORRs and PFS of most patients were consistent with the clinical trial data. According to the RWD, the curative effects and responses involving first-line therapy for melanoma and NSCLC were poorer whereas those for UC and RCC were better than the clinical trial data. For patients with GC and HCC indications who received approval *via* accelerated review, the ORRs and PFS were close to the clinical trial data and their treatments had poorer payment benefits compared with existing treatments.

For patients with melanoma, the real-world median ORR and PFS in Taiwan were 28.3% and 3.5 months, respectively. The median ORR and PFS after first-line nivolumab treatment in CheckMate-066 and CheckMate-067 trials reached 43%-44% and 5-7 months, respectively, whereas those after pembrolizumab treatment in the KEYNOTE-006 trial reached 36%-37% and 8.4 months, respectively[6]. Possible reasons for such differences include differing lines of treatment, trials involving patients who never or mostly never received previous treatment, and poorer prognoses in

Table IV. irAEs†.

	Any grade		Grade 1		Grade 2		Grade 3		Grade 4		Grade 5	
No. of events (%)												
Any adverse event	125	9.2%	20	1.5%	46	3.4%	33	2.4%	22	1.6%	4	0.3%
Skin reaction	36	2.6%	9	0.7%	18	1.3%	5	0.4%	3	0.2%	1	0.1%
Pneumonitis	34	2.5%	1	0.1%	9	0.7%	16	1.2%	6	0.4%	2	0.1%
Hepatitis	15	1.1%	1	0.1%	5	0.4%	4	0.3%	4	0.3%	1	0.1%
Hypothyroidism	7	0.5%	2	0.1%	4	0.3%	1	0.1%	0	0.0%	0	0.0%
Colitis	7	0.5%	3	0.2%	1	0.1%	3	0.2%	0	0.0%	0	0.0%
Infusion reaction	3	0.2%	1	0.1%	2	0.1%	0	0.0%	0	0.0%	0	0.0%
Myositis	2	0.1%	1	0.1%	1	0.1%	0	0.0%	0	0.0%	0	0.0%
Hyperthyroiditis	2	0.1%	0	0.0%	2	0.1%	0	0.0%	0	0.0%	0	0.0%

irAE, immune-related adverse event. †Listed AEs that were reported in at least 2 patients.

Asian patients due to different predilections than Westerners.

After first-line therapy for NSCLC, the real-world ORR (39%) was close to that in KEYNOTE-024 and KEYNOTE-042 trials (39%–45% in highly PD-L1-expressing subgroup)[7,8]; however, the PFS (3.3 months) was poorer compared to clinical trials (7-10 months). One reason for this difference may be budget considerations, such as the NHI limiting payments to patients who could not undergo chemotherapy. Clinical trial subjects do not face such limitation, resulting in poorer RWD among the former patients compared to patients in clinical trials.

The administration of ICIs to real-world UC and late-stage RCC patients produced better curative effects and outcomes than patients in clinical trials. The median ORR and PFS after first-line therapy for UC were 42.4% and 2.7 months, respectively, which were higher than those in IMvigor 210 and KEYNOTE-052 trials (28%–39% in highly PD-L1-expressing subgroup and 2–3 months in total population, respectively). The median ORR and PFS after second-line therapy for UC were 40.2% and 3.8 months, respectively, which were higher than those in IMvigor 211[9], CheckMate-275, and KEYNOTE-045[10] trials (22%–28% in highly PD-L1-expressing subgroup and 2 months in total population, respectively). The median ORR and PFS of late-stage RCC patients were 39.8% and 5.1 months, respectively, which were higher than those in the CheckMate-025[11] trial (25% and 4.6 months, respectively). Such differences may stem from aristolochic acid exposure or the higher UC incidence in Taiwan. Microsatellite instability and hypermethylation are considered common in UC, although this has yet to be confirmed.

Metastatic GC is a leading cause of cancer-related deaths in Taiwan. Nivolumab improved the OS by approximately 1 month, compared to the use of a placebo, in the ATTRACTION-2 trial[12]. Pembrolizumab obtained marketing authorization through phase II single-arm trials and accelerated approval; however, the vendors did not perform confirmatory trials for the same clinical status. KEYNOTE-061 and KEYNOTE-063 trials comparing paclitaxel and pembrolizumab as second-line systematic therapy for late-stage GC did not show statistically significant preliminary results for the OS – the primary curative effect indices[13]. Despite poor or uncertain results with regard to curative effects in clinical trials, the NHIA initially still included these two drugs in insurance coverage to offer a new opportunity to GC patients, who had not had any new or effective medications for a long time. The NHIA will continue to review and adjust their benefits based on patient RWD.

After a year of data collection and analysis, the real-world ORR and PFS in Taiwan were 11.3% and 2.0 months, respectively. After payment evaluation, experts agreed that payment benefits were significantly lower compared to current chemotherapy treatment (trifluridine+tipiracil). As of March 2020, no health technology assessment (HTA) agency in Canada, Scotland, or the United Kingdom had approved pembrolizumab and nivolumab for metastatic GC. The National Comprehensive Cancer Network guidelines suggest using pembrolizumab to treat metastatic GC. In 2018, the Pan-Asian-adapted European Society for Medical Oncology (ESMO) Clinical Practice Guidelines suggested using pembrolizumab and nivolumab to treat patients with microsatellite instability-high (MSI-H). Thus, the experts recommended canceling the coverage or reaching more cost-effective agreements.

Nivolumab administration to late-stage HCC patients who previously underwent sorafenib treatment received marketing authorization in Taiwan *via* an accelerated review. However, the vendors did not perform confirmatory trials on nivolumab for this clinical status. The CheckMate 459 trial comparing sorafenib and nivolumab as first-line systematic therapy for late-stage HCC indicated no statistically significant preliminary results for the OS – the primary curative effect index[14]. Yet the NHIA initially still included both of these drugs in its coverage, as HCC is also a leading cause of cancer-related death in Taiwan. The NHIA will continue to review and adjust the benefit package based on patient RWD.

Following a year of data collection and analysis, the real-world ORR and PFS in Taiwan were 24.0% and 2.9 months, respectively. Experts agreed that, compared to regorafenib, payment benefits were limited while producing the same clinical status. As of March 2020, no HTA agencies in Canada, Australia, Scotland, or the United Kingdom had approved or paid for the use of nivolumab for late-stage HCC. Even Japan, nivolumab's country of origin, had not yet approved it for late-stage HCC. Furthermore, following a September 23, 2019, update, the ESMO Clinical Practice Guidelines no longer recommend using nivolumab for late-stage HCC. Other drugs, such as ramucirumab and cabozantinib, received marketing authorization.

However, for both metastatic GC and late-stage HCC, payment agreements with improved cost-effectiveness could not be reached with vendors. Consequently, the NHIA suspended payments for new metastatic GC cases and second-line therapy for new late-stage HCC cases in April 2020, although it continued payments for patients who had already received approval until their condition worsened.

Despite these findings, this study had a few limitations:

- The data source was the preliminary review system for cancer immunotherapy applications; therefore, non-essential review item data may be incomplete and not fully present the patients' RWD or RWE.
- The medications used at the patients' own expense are non-essential review items, so medication data, including treatment drugs used in the past or in conjunction with ICIs, may be incomplete.
- When interpreting safety data, it is important to consider whether the information involving AEs relies on voluntary reports, which could result in an underestimation and lack of representation of the actual AEs among patients using the medication.

Conclusions

The NHID RWD indicate some differences in the effectiveness of ICIs for cancer patients in Taiwan versus Europe/the United States. To monitor trends in precision medicine for cancer, the NHIA collects and evaluates RWE, such as registered case data, which serves as a frame of reference for adjustment decisions on the benefits of such medications. New technologies should be used to identify suitable patients for medication to enhance ICIs' payment benefits. Moreover, given the rapid increase in healthcare expenditures in many countries, the challenges associated with the high costs of medicines, and the uncertainty of their effectiveness, Taiwan has implemented a policy for high-cost medicines. It also uses MEAs to establish a national registry for immunotherapy. However, HTA should be used to support sustainable healthcare.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

Szu-Ting Hsieh, Hsiao-Feng Ho, Hsueh-Yung Tai, Ling-Chen Chien, Hui-Ru Chang, Hui-Ping Chang, Yu-Wen Huang, Jau-Jie Huang, Heng-Jung Lien, Li-Ying Huang, and Po-Chang Lee contributed to the design and implementation of the research, the analysis of the results, and the writing of the manuscript.

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