IMPLEMENTATION OF RISK-SHARING AGREEMENT IN PATIENTS WITH LUNG CANCER TREATED WITH IMMUNOTHERAPY BASED ON RWD IN THE CZECH REPUBLIC

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BACKGROUND

Aligning with the recommendations of the Czech Society for Oncology, immunotherapy is gaining prominence in the management of lung cancer.[1] Public health insurance in the Czech Republic covers immunotherapy for defined categories of lung malignancies. Insurance providers cover treatment costs even when treatment is discontinued due to early disease progression, immune-related adverse events, or when the treatment duration and the number of administered cycles are low.

OBJECTIVES

Our study aimed to assess the impact of performance-based risk-sharing agreements (PBRSA) on budget considerations and treatment outcomes for immunotherapy in locally advanced and metastatic non-small cell lung cancer (NSCLC) in the Czech Republic. We looked into scenarios where drug manufacturers could help cover the costs if the anticipated progression-free survival (PFS) outcomes were not achieved as defined by randomized controlled trials (RCTs). This could potentially make the treatment more accessible to patients for various medical conditions.

METHODS

Data Source

In collaboration with the Masaryk Memorial Cancer Institute in Brno, we conducted a retrospective analysis of 127 advanced lung cancer patients treated with checkpoint inhibitors (pembrolizumab, nivolumab, atezolizumab, durvalumab, and nivolumab in combination with ipilimumab) from 2018 to 2022. Data primarily encompassed progression-free survival, treatment duration, treatment cycles, and immune-related adverse event incidence.

Outcome Comparison

Real-world PFS data from patients' medical records were compared to PFS defined in randomized controlled studies for each check-point inhibitor. Patients were classified as either successfully or unsuccessfully treated, determined by their adherence to the PFS threshold established in the comparator arm of the respective randomized controlled study, typically involving placebo or chemotherapy (except for nivolumab, where PFS reached lower values than the comparator). As there were not enough patients in the other subgroups, the outcome comparison involved only two immunotherapeutic agents, pembrolizumab and nivolumab, which accounted for 85 patients.

Hypothetical PBRSA

For patients who did not meet our predefined success level, we calculated the average deviation from the threshold. This calculation determined the potential manufacturer's share in the treatment cost, with a greater deviation corresponding to a higher percentage of the cost the manufacturer covers.

Budget Impact Analysis

Subsequently, we performed a comparative analysis of two budget scenarios. The first scenario reflects a real-world situation where the complete treatment cost is borne by public health insurance. In contrast, the second scenario is hypothetical, exploring the incorporation of risk-sharing agreements, with the manufacturer sharing treatment expenses (for those patients who did not achieve the desired treatment outcomes). Treatment costs were calculated based on the maximum reimbursement rates for each medicine.

RESULTS

Table 1: Findings from RWD, their comparison with registration studies, and a proposal for the percentage of treatment costs - for individual checkpoint inhibitors in reimbursed indications.

The first line treatment of metastatic NSCLC (PD-L1 with TPS ≥ 50 %)[2]

	RWD		RCTs*		PBRSA			
Pembrolizumab	Total number of patients	**PFS (median, months)**	PFS (median, months)	**PFS comparator (median, months)**	Number of patients under threshold	**PFS under threshold (median, months)**	% difference PFS under threshold vs. RCTs comparator	**% PBRSA**
	19	**4,63**	10,30	**6,00**	10	**2,88**	43,43	**56,57**

*registration study for pembrolizumab Keynote-024, comparator = chemotherapy [3]

In combination for the first line treatment of metastatic squamous (PD-L1 with TPS ≤ 50 %) or non-squamous[2]

	RWD		RCTs*		PBRSA			
Pembrolizumab	Total number of patients	**PFS (median, months)**	PFS (median, months)	**PFS comparator (median, months)**	Number of patients under threshold	**PFS under threshold (median, months)**	% difference PFS under threshold vs. RCTs comparator	**% PBRSA**
	24	**4,91**	8,80	**4,90**	12	**1,43**	40,77	**59,23**

*registration study for pembrolizumab Keynote-189, comparator = placebo + chemotherapy[3]

Locally advanced (stage IIIB) or metastatic NSCLC patients who have received prior chemotherapy[4]

	RWD		RCTs*		PBRSA			
Nivolumab	Total number of patients	**PFS (median, months)**	**PFS (median, months)**	PFS comparator (median, months)	Number of patients under threshold	**PFS under threshold (median, months)**	% difference PFS under threshold vs. RCTs PFS	**% PBRSA**
	42	**4,02**	**2,33**	4,21	13	**1,68**	66,09	**33,91**

*registration study for nivolumab CA209057, comparator = docetaxel[5]

Pembrolizumab for 1st line metastatic NSCLC (PD-L1 TPS ≥ 50%):
Real-world PFS data did not meet Keynote registration study standards. A risk-sharing proposal of 56,57 % of the manufacturer's reimbursement (allocated to 10 patients who did not achieve the desired treatment outcomes) could save 113 559 EUR and enable a successful treatment for one additional patient (Table 2).

Pembrolizumab for metastatic squamous (PD-L1 with TPS ≤ 50 %) or non-squamous NSCLC:
Real-world PFS data also failed to meet the Keynote registration study criteria. A proposed risk-sharing model, distributing 59,23 % of the manufacturer's reimbursement to 12 patients not meeting the desired treatment outcomes, showed potential cost savings of nearly 62 000 EUR. This cost-effective approach might facilitate treatment for an additional patient.

Nivolumab for locally advanced or metastatic NSCLC post-chemotherapy:
Real-world PFS data were compared with the PFS of nivolumab itself, as the RCT values were lower than the values of the comparator. A proposed risk-sharing model of 33,91 % of the manufacturer's reimbursement for 13 patients with undesired treatment outcomes could save nearly 41 000 EUR. This approach may successfully treat one more patient.

Table 2: Comparison of pembrolizumab and nivolumab: 100% health insurance coverage vs. manufacturer contribution based on PFS achievement.

	Pembrolizumab — The first line treatment of metastatic NSCLC (PD-L1 with TPS ≥ 50 %)[2]				Pembrolizumab — In combination for the first line treatment of metastatic squamous (PD-L1 with TPS ≤ 50 %) or non-squamous NSCLC[2]				Nivolumab — Locally advanced (stage IIIB) or metastatic NSCLC patients who have received prior chemotherapy[4]			
	Scenario AS IS		Scenario with PBRSA		Scenario AS IS		Scenario with PBRSA		Scenario AS IS		Scenario with PBRSA	
	↓ threshold (unsuccessful)	↑ threshold (successful)	↓ threshold (unsuccessful)	↑ threshold (successful)	↓ threshold (unsuccessful)	↑ threshold (successful)	↓ threshold (unsuccessful)	↑ threshold (successful)	↓ threshold (unsuccessful)	↑ threshold (successful)	↓ threshold (unsuccessful)	↑ threshold (successful)
Number of patients	10	9	10	9	12	12	12	12	13	29	13	29
Treatment duration (median, months)	2,87	13,34	2,87	13,34	1,25	7,16	1,25	7,16	1,72	5,52	1,72	5,52
Treatment cost/cycle/patient [2,4]	4 818 EUR	4 818 EUR	4 818 EUR	4 818 EUR	4 818 EUR	4 818 EUR	4 818 EUR	4 818 EUR	2 480 EUR	2 480 EUR	2 480 EUR	2 480 EUR
Treatment cost/month/patient	6 983 EUR	6 983 EUR	6 983 EUR	6 983 EUR	6 983 EUR	6 983 EUR	6 983 EUR	6 983 EUR	5 392 EUR	5 392 EUR	5 392 EUR	5 392 EUR
Treatment cost/month/all patients	69 832 EUR	62 849 EUR	69 832 EUR	62 849 EUR	83 798 EUR	83 798 EUR	83 798 EUR	83 798 EUR	70 098 EUR	156 372 EUR	70 098 EUR	156 372 EUR
Treatment cost/treatment duration/patient	**20 075 EUR**	**93 149 EUR**	**20 075 EUR**	**93 149 EUR**	**8 721 EUR**	**50 012 EUR**	**8 721 EUR**	**50 012 EUR**	**9 301 EUR**	**29 763 EUR**	**9 301 EUR**	**29 763 EUR**
Treatment cost/treatment duration/all patients	**200 753 EUR**	**838 344 EUR**	**200 753 EUR**	**838 344 EUR**	**104 648 EUR**	**600 139 EUR**	**104 648 EUR**	**600 139 EUR**	**120 911 EUR**	**863 117 EUR**	**120 911 EUR**	**863 117 EUR**
% Health insurance reimbursement (reached PFS)	**100,00%**	**100,00%**	**43,43%**	**100,00%**	**100,00%**	**100,00%**	**40,77%**	**100,00%**	**100,00%**	**100,00%**	**66,09%**	**100,00%**
Health insurance nominal reimbursement	**200 753 EUR**	**838 344 EUR**	**87 194 EUR**	**838 344 EUR**	**104 648 EUR**	**600 139 EUR**	**42 660 EUR**	**600 139 EUR**	**120 911 EUR**	**863 117 EUR**	**79 915 EUR**	**863 117 EUR**
% Manufacturer reimbursement	**0,00%**	**0,00%**	**56,57%**	**0,00%**	**0,00%**	**0,00%**	**59,23%**	**0,00%**	**0,00%**	**0,00%**	**33,91%**	**0,00%**
Manufacturer nominal reimbursement	**0,00 EUR**	**0,00 EUR**	**113 559 EUR**	**0,00 EUR**	**0 EUR**	**0 EUR**	**61 988 EUR**	**0 EUR**	**0 EUR**	**0 EUR**	**40 995 EUR**	**0 EUR**
Number of extra treated patients for savings	**-**	**-**	**1**	**-**	**-**	**-**	**1**	**-**	**-**	**-**	**1**	**-**

CONCLUSIONS

The findings reveal that over five years, the insurance company bore costs exceeding 2 727 900 EUR for pembrolizumab and nivolumab (monotherapy) treatments, with 426 300 EUR allocated to patients classified as "unsuccessful" (35 out of 85 patients). Implementing risk-sharing agreements allows the manufacturers to cover up to 60 % of the treatment costs for these patients – approximately 216 500 EUR. This approach leads to substantial savings for insurance companies and opens the door to treating at least three additional patients.

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