COST-EFFECTIVENESS ANALYSIS OF SECUKINUMAB COMPARED TO USTEKINUMAB IN THE TREATMENT OF MODERATE TO SEVERE PLAQUE PSORIASIS IN THE CZECH REPUBLIC

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BACKGROUND

In recent years, treatment of plaque psoriasis (PSO) has evolved due to the launch of biologic drugs, anti-tumor necrosis factor (anti-TNF) drugs, and anti-interleukin (IL)-12/23 inhibitor (ustekinumab [UST]).Thus, the treatment goal has shifted from Psoriasis Area Severity Index (PASI) 50 response to PASI 75 response, as mentioned in the current European and Czech clinical guidelines [1,2]. New biologic drugs have been studied for treatment of moderate to severe plaque PSO, namely IL-17 inhibitors and IL-17 receptor antagonist. Introduction of these highly potent molecules has resulted in discussion of a new treatment goal of PASI 90 response or PASI 100 response [3,4], which refer to almost clear skin and clear skin, respectively.

In January 2015, secukinumab (SEC) became the first IL-17A antibody approved by the European Medicines Agency for moderate-to-severe plaque PSO. SEC 300 mg (SEC300) was approved via a clinical program including placebo and active control (etanercept) phase 3 studies (ERASURE, FIXTURE [5], FEATURE [6], and JUNCTURE [7]). Moreover, SEC has been studied in phase 3b head-to-head trial comparing SEC300 with UST45/90 mg (UST45/90) (CLEAR study) [8].

OBJECTIVES

In the Czech Republic, anti-TNF drugs and UST are reimbursed for treatment of PSO in patients with a previous failure to respond to conventional systemic therapy (i.e., methotrexate, Cyclosporin A, retinoids) and/ or phototherapy. UST was considered the most potent subcutaneous PSO biologic therapy before SEC approval. UST (same as anti-TNF drugs) is reimbursed in the Czech Republic under the condition of ≥ PASI 50 response at week 16.

Our aim was to investigate the effect of a higher treatment goal for SEC (PASI 75 response) compared with UST (PASI 50 response) in terms of quality of life (QOL) gain and cost.

Using efficacy data obtained from the CLEAR study up to week 16, we estimated the cost-effectiveness of SEC300 compared with UST45/90 based on different PASI response (discontinuation/continuation) criteria (PASI ≥ 75 for SEC300 and PASI ≥ 50 for UST45/90).

METHODS

A decision-analytic model was developed with a decision tree reflecting response to treatment for the first 52 weeks (PASI change < 50, 50-74 75-89, 90-99, 100). After 1 year, cost and outcomes are predicted by a long-term Markov model with health states related to treatment continuation, dropout, and death. Responders at week 16 (defined as PASI ≥ 75 response for SEC300, PASI ≥ 50 response for UST45/90) continued on biologic treatment. Nonresponders and dropouts were switched to standard of care (SOC) (e.g., methotrexate, Cyclosporin A, phototherapy, emollients) (*Figure 1* and *Figure 2*). Analyses were conducted from health care system perspective with a 3% discount rate for costs and outcomes in a 10-year time horizon. The modelled outcomes were QALY (quality-adjusted life-year) and time (years) spent in PASI ≥ 90 response (clear or almost clear skin).

Figure 1 • Structure of the Model – Decision Analysis up to 52 Weeks
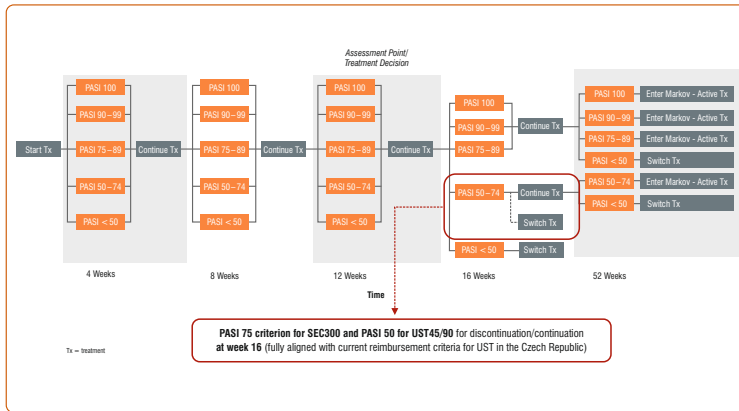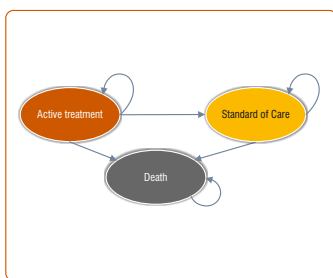

Figure 2 • Structure, the Markov Part of the Model

Baseline patient characteristics and efficacy data for SEC300 and UST45/90 were derived from the CLEAR study, a head-to-head 52-week superiority trial [8]. The efficacy in terms of PASI 50, 75, 90, and100 response at week 16 for SEC300 were 97.0%, 93.1%, 79.0%, and 44.3%, respectively, and for UST45/90 were 92.7%, 82.8%, 57.7%, and 28.4%, respectively. The efficacy data for SOC were derived from the mixed-treatment comparison (MTC), which was performed to address relative efficacy with all biologic drugs. for moderate-to-severe plaque PSO [9]. The efficacy in terms of PASI 50, 75, 90, and100 response at week 16 for SOC was 15.6%, 5.5%, 1.0%, and 0.0%, respectively.

The annual dropout rate was 9.7% for both SEC300 and UST45/90. This rate was assumed based on the proportion of patients who achieved an initial PASI 75 response from induction therapy but then failed to maintain this response to a 52-week follow-up time point. Long-term treatment resistance and dropout were modelled by assuming a 20% annual discontinuation rate, based on previous economic modelling [10].

Utility weights for each health state were calculated from mixed models of EQ-5D responses from SEC phase 3 trials (*Table 1*). A disutility multiplier was applied to patients treated with methotrexate (0.971) and Cyclosporin A (0.912) therapy [11] as part of SOC (approximately 90% of patients on SOC) to reflect the decrement in QOL due to adverse events associated with the two treatments.

Table 1 • Utility and QoL Data Inputs

PASI Response	Mean	Standard Error
< 50	0.753	0.0038
50 – 74	0.838	0.0039
75 – 89	0.868	0.0039
90 – 99	0.907	0.0035
100[a]	0.907	0.0035
Markov model inputs from year 1 onwards		
PASI < 75	0.792	0.0034
PASI ≥ 75	0.890	0.0027

[a] The MTC used for base-case efficacy estimates in this model could not compute PASI 100 response levels due to missing data for some comparators. Thus, utility weights for PASI 100 response were set to those for PASI90-100 response.

Table 2 • Annual Frequency of Serious Adverse Events

Adverse Events	SEC300	UST45/90
Malignancies other than non–melanoma skin cancer	0.004	0.006
Non–melanoma skin cancer	0.004	0.006
Severe infections	0.011	0.010

The frequency of adverse events with SEC300 was obtained from a pooled analysis of phase 3 studies, and the frequency for UST45/90 was derived from product information (i.e., the Summary of Product Characteristics),*Table 2*.

Dosing schedules for first year and maintenance (second and subsequent years) treatment for SEC300 and UST45/90 were taken from the Summary of Product Characteristics: 16.0 doses and 12.0 doses for SEC300 and 6.0 doses and 4.35 doses for UST45/90 per year. For UST, we conservatively calculated costs for the 45 mg dose per administration, regardless of the patient's weight. The 1-year price for maintenance therapy of SEC300 and UST45/90 was set to price parity. The 1-year cost for SOC was derived from a local Czech study [12]. For detailed cost inputs and resources used, see *Table 3*.

All costs were calculated in Czech crowns (CZK) and converted to Euros (exchange rate 1 € = 27.4 CZK).

We assumed that the mortality of all patients with PSO is similar to that of the general mortality in the Czech Republic based on the latest data from the Czech Statistical Office, as of year 2013 [13].

Probabilistic sensitivity analysis with 3,000 iterations was performed for the following parameters: efficacy data (based on CLEAR data using log-normal distribution, according to the Dirichlet), transition probabilities like adverse events and dropout (beta distribution based on mean and standard error), utility weights (beta distribution based on mean and standard error), and costs (gamma distribution).

RESULTS

With a 10-year time horizon in the base-case analysis (*Table 4*), SEC300 treatment gained 0.049 QALYs and 0.80 years in PASI ≥ 90 response, with €162 cost savings compared with UST45/90, reflecting dominance of SEC300 over UST45/90. The net monetary benefit is €2,298. Probabilistic sensitivity analysis indicated that almost 60% of all iterations are in dominant quadrant IV (lower costs, more QALYs). There was a 100% probability that SEC300 is a more cost-effective approach than UST45/90 in the modelled setting, at the willingness-to-pay threshold of 3 times Gross Domestic Product (GDP)/capita in the Czech Republic (i.e. €43,800 per QALY), *Figure 3*.

Table 4 • Results of the Analysis in Base-Case Settings

	SEC300 --> SOC	UST45/90 --> SOC	Difference (SEC-UST)
Total Costs (€)	58,942	59,104	−162
Drugs (€)	44,728	44,799	−71
Medical (€)	14,21	14,305	−91
QALYs	6.840	6.791	0.049
Years in PASI ≥ 90	2.873	2.077	0.796
Incremental cost-effectiveness ratio (€/ QALY)			Dominates
Net monetary benefit			€ 2,298

Figure 3 • Results of the Probabilistic Sensitivity Analysis: SEC300 vs. UST 45/90
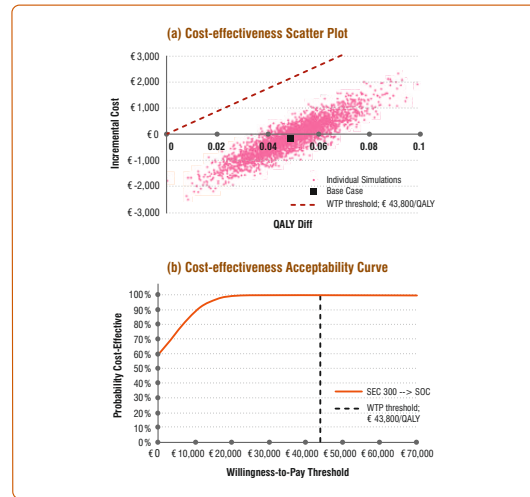
DISCUSSIONS

To our knowledge, this is the first study describing the outcomes (QALYs gained/lost) and costs by applying stricter criteria and a higher treatment goal in PSO compared with the current treatment situation for PSO. From the Czech reimbursement perspective, PASI 75 response was compared with PASI 50 response (which is still the current treatment goal). We believe that this approach also could be suitable for situations where current standard is PASI 75 response, hence stricter criteria/higher treatment goal would be PASI 90 response.

There are potential limitations of our analysis. First, we did not include subsequent lines within biological treatment, mainly because of absence of data for other biologic drugs after failure of previous biologic treatment; another reason was to avoid mixing efficacy data from a head-to-head trial (CLEAR) with that from an MTC. Second, we believe that in terms of QOL gain, we underestimated the benefit of SEC300, as the current model conservatively assumes the same utility for health states PASI 90-100 response and PASI 100 response. The reason was that the model for QOL computation could not compute PASI 100 response levels due to missing data for some comparators. SEC300 provided more PASI 90 and 100 responders than UST45/90.

CONCLUSIONS

Applying stricter criteria for response (i.e., PASI ≥ 75 response instead of PASI ≥ 50 response) for treatment discontinuation/continuation for highly efficacious PSO therapy (SEC300) results in overall greater QALYs gained and cost savings for the health care system. These findings could be also valid for situations where current treatment goal is PASI 75 response, hence the stricter criteria/higher treatment goal would be PASI 90 response.

Table 3 • Cost and Resources Used Inputs

Unit/Item	Cost / Reimbursed Price (€)	Clinician visits, monitoring SEC300, UST45/90	
SEC300/dose	969		
UST 45/90 prefilled syringe/dose	2,676	*0 – 16 weeks*	
Nonbiologic systemic treatments/SOC per year	2,666	Number of screening tests	1
Cost per visit/assessment	12	Number of physician visits	1
Pretreatment/assessment	232	Number of monitoring tests	2
Regular physician visit/monitoring	4		
Skin cancer screening	31	*17 – 52 weeks*	
Cost per inpatient episode		Number of physician visits	3
PSO	370	Number of monitoring tests	3
Sepsis	1,316		
Lymphoma	3,327	*Annual*	
Melanoma/malignancies	12,773	Number of physician visits	4
non–melanoma skin cancer	215	Number of monitoring tests	4

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