COST-EFFECTIVENESS COMPARISON OF RISANKIZUMAB AND USTEKINUMAB FOR THE TREATMENT OF SEVERE PSORIASIS

Dzik M[1], Nadzieja-Kozioł A[1], Owczarek W[2]
[1]MAHTA, Warsaw, Poland , [2]Military Institute of Medicine, Warsaw, Poland

BACKGROUND

Psoriasis is a chronic inflammatory skin disease that requires continuous skin care and is associated with psychological and social problems. It worsens well-being of affected patients and their cohabitants[1]. Current guidelines recommend biologic therapy in patients with moderate-to-severe psoriasis if standard systemic therapy has failed, is not tolerated or contraindicated [2].
In Poland biologic therapy for plaque psoriasis is used in approx. 1000 patients. Most common drugs are adalimumab and ustekinumab (UST) which constitute nearly two-thirds of the market. Only cases of severe psoriasis are eligible for the treatment with these drugs. All patients receive biologics as an intermittent regiment with fixed cycle length and retreatment as needed.
Risankizumab (RIS) is an innovative drug registered by EMA in 2019 for the treatment of moderate-to-severe psoriasis. In UltIMMA-1 and UltIMMA-2 trials RIS has demonstrated high efficacy with a PASI 90 response rate of 75% and met primary endpoint of superiority versus UST[3].

OBJECTIVES

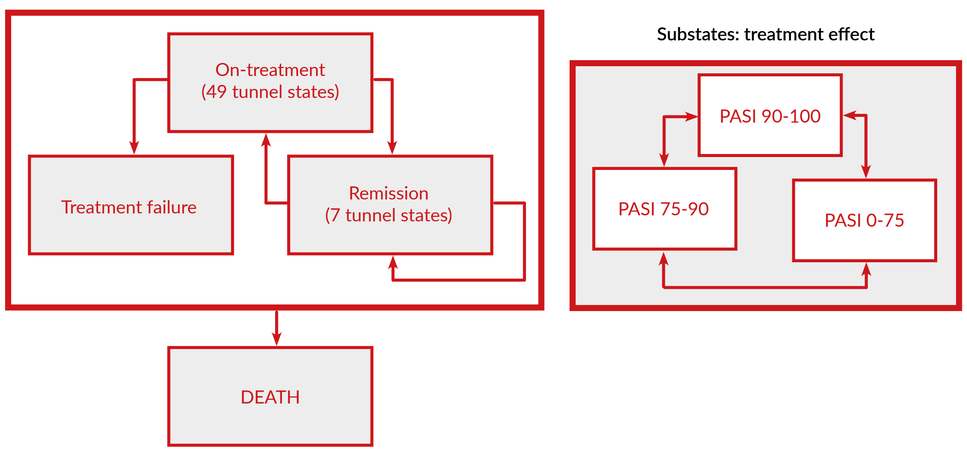
The purpose of this analysis was to explore cost-effectiveness of RIS in comparison with UST in the treatment of severe psoriasis from the perspective of public payer in the Polish setting.

METHODS

ECONOMIC MODEL

Cost-effectiveness analysis utilizes a Markov model with 3 main states that represent patient in the health care system and death state. Tunnel states are used both to address the differences in treatment regimens of biologic therapies and change of transition probabilities over time. Each of the main states is divided into 3 sub-states which represent patients' response to the treatment.

Figure 1. Model diagram

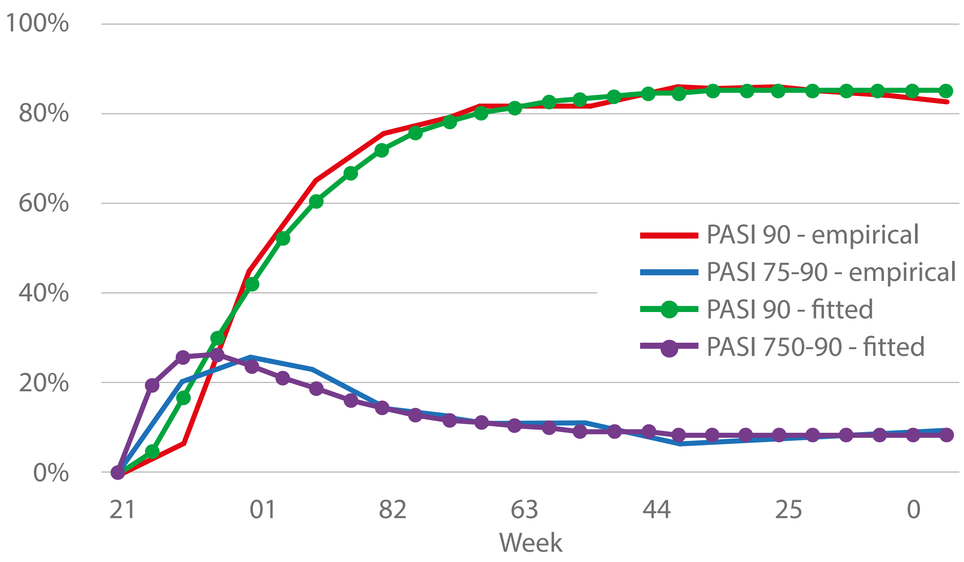


Treatment regimen for a biologic drug is defined by two fixed timepoints. When the first timepoint is reached, treatment response is assessed and all patients who do not have at least PASI 75 are excluded from the treatment. These patients will receive best-supportive care (BSC). When the second timepoint is reached, administration of the biologic drug is terminated, and patients receive BSC until relapse and need of retreatment. For UST, the efficacy assessment and treatment termination are currently set at week 28 and 48, respectively. For RIS, which is currently not reimbursed in Poland, a treatment regimen was based on analogy with ixekizumab treatment regimen, with the efficacy assessment at week 16 and maximum treatment length of 96 weeks.
Analysis has been carried out over a 5-year time horizon, which corresponds to 130 biweekly modeling cycles.

EFFICACY

Efficacy evaluation was based on the data from the pivotal trials UltIMMA-1 and UltIMMA-2[3]. Firstly, graphs representing the percentage of patients with PASI 90 and PASI 75 in the study were digitized. Next, transition matrices for the treatment effect were fitted independently to the data for RIS, UST and PLC using maximum likelihood estimator. Markov process was assumed to be homogenous. Transition matrices showed very good fit to the data.

Figure 1. Empirical and fitted response rates for RIS arm



The rest of parametrization was done with data derived from scientific literature.

Table 1. Model parametrization

PARAMETER	VALUE
Risk of relapse (weeks 1-11 in remission)	0.60% per cycle*
Risk of relapse (weeks 12+ in remission)	10.29% per cycle*
Risk of AE for RIS at weeks 1-16	0.08% per cycle**
Risk of AE for RIS at weeks 17+	0.04% per cycle**
Risk of AE for UST at weeks 1-16	0.25% per cycle**
Risk of AE for RIS at weeks 17+	0.03% per cycle**

**estimated based on Chiu et al.[4], **Gordon et al.[3], SD – standard deviation, AE – adverse events*

COSTS

Calculations included cost of biologic drugs, best supportive care, cost of administration, monitoring and cost of adverse events. Cost of RIS was estimated based on a British price published by NHS[5]. Other costs were estimated based on the data from the National Health Fund and the Ministry of Health.

UTILITIES

In order to find utility values of different health states, a systematic review was carried out in the Medline database. Eight studies or economic analyses reporting utility increments associated with a percentage change of PASI were found.

Table 2. Utility increments associated with change of PASI

PUBLICATION	PASI 0-50	PASI 50-74	PASI 75-89	PASI 90-99	PASI 100
Pickard et al.[6]	0.027	0.102	0.151	0.141	0,200
Johanson et al. A[7]	0.012	0.100	0.131	0.144	0,153
Johanson et al. B[8]	0.030	0.105	0.144	0.153	0,159
Knight et al.[9]	0.101	0.201	0.232	0.232	
Hendrix et al.[10]	0.000	0.084	0.117	0.155	
Woolacott et al.[11]	0.050	0.170	0.190	0.210	
Anis et al.[12]	0.040	0.120	0.120	0.210	
Pan et al.[13]	0.063	0.178	0.178	0.308	

Utilities form the Pickard et al. study were used in the base analysis. For PASI 90+ and PASI 75- pooled utilities were calculated taking into account different distribution of treatment effects of respective therapies.
The model also incorporated disutility for each health state in the base case associated with occurrence of adverse events (Table 2.) Disutility was based on Tolley et al.study[7]. In case of death the analysis assumed a quality of life value of zero.

RESULTS

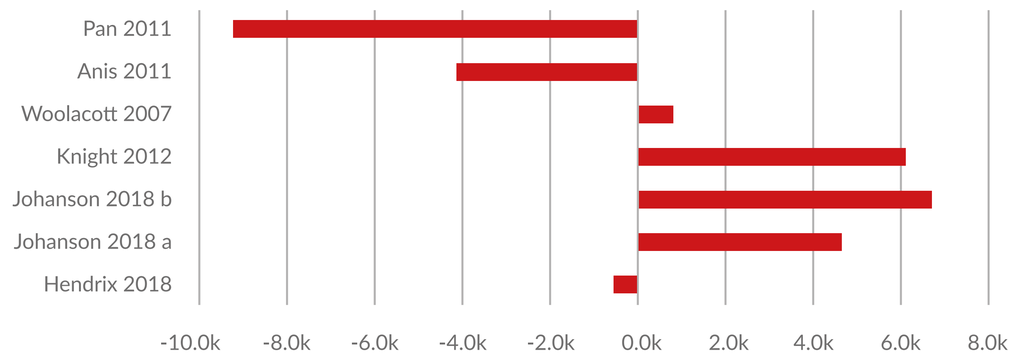
Results of simulation show that RIS in comparison with BSC increases the number of quality-adjusted life years (QALY) by 0.14 and the number of life years without the symptoms of the disease (PASI 100 LY) by 0.91 in the 5-year horizon. The total cost of treatment of psoriasis in the RIS arm amounted to approximately 58.9k EUR, while in the UST arm the cost amounted to 28.6k EUR.
Incremental cost-effectiveness ratio (ICER) was 211.8k EUR/QALY, however the incremental cost for an additional life year without the symptoms of the disease was only 33.3k EUR.

Table 3. Cost-effectiveness analysis results

RESULT	UST	RIS	RIS vs UST
QALY	3.37	3.52	0.14
PASI 100 LY	0.45	1.36	0.91
Total cost (EUR)	28.6k	58.9k	30.3k
ICER (EUR/QALY)	N/A	N/A	211.8k
ICER (EUR / PASI 100 LY)	N/A	N/A	33.3k

Utility values were a significant source of uncertainty in the analysis. Percentage change of ICER compared to the base scenario was between -44% to +32% depending on the source of utilities used in the analysis.

Figure 2. Absolute change of ICER for alternative utility sets



CONCLUSIONS

The economic model shows that ICER for RIS is significantly higher than cost-effectiveness threshold for reimbursement in Poland i.e. 32.7k EUR. Even with the most favourable utility set being used, the technology does not meet administrative cost-effectiveness threshold. It is not very different, however, from ICERs demonstrated by other biologic therapies reimbursed in Poland given their list price: 50-106k EUR for iksekizumab and 58-280k for sekukinumab compared to other therapies[15, 16].
The fact that, arguably, the most effective therapy for psoriasis is unable to demonstrate cost-effectiveness raise a question what might be the reasons for this outcome. Despite RIS offering over 0.9 additional life year with PASI 100 compared to UST the incremental QALY does not show much improvement. Pickard et al. argues that standard instrument for measuring health related quality of life (i.e. EQ-5D) is not responsive enough to capture improvements associated with PASI 100. In fact even the utilities obtained by Pickard et al. with a tailored instrument did not sway the results in favor of RIS. This leads to a conclusion that using QALYs as a measure of treatment effect for the state-of-the-art technologies for psoriasis may not represent full benefits of the therapies. An additional measure, such as PASI 100 LY may be useful in terms of translating the treatment effects to decisionmakers.

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Mahta Ltd. 17/5 Rejtana St, 02-516 Warsaw, Poland
Tel. +48 533 399 146, E-mail: biuro@mahta.pl