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COST-EFFECTIVENESS ANALYSIS OF SULODEXIDE IN PATIENTS WITH NON-PROLIPHERATIVE DIABETIC RETINOPATHY IN THE CZECH REPUBLIC

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BACKGROUND

Sulodexide is commonly used for the prophylaxis and treatment of thromboembolic diseases. However, recent research (DRESS, *Song et al.*[1]) has also demonstrated the beneficial effects of sulodexide in the treatment of diabetic retinopathy in which it leads to significant reduction in formatted hard exudates (HE, i.e. deposits of serum proteins and lipids in the retina/macula), which cause vision impairment.

OBJECTIVE

The objective of this study was to assess the cost-effectiveness of sulodexide in the treatment of macular HE in patients with mild-to-moderate non-prolipherative diabetic retinopathy (NPDR) in comparison to standard of care (i.e. no treatment; SoC) in the Czech Republic.

METHODS

A developed five-year Markov cohort model with one-year cycle length projects Quality-Adjusted Life-Years (QALYs) and costs HE treatment in NPDR patients aged 59 years from healthcare payers' perspective.

Model health states are defined by HE severity (grade 0-5) and death. Moreover, every HE health state is divided into three sub-states according to the level of visual acuity (VA) defined by read number of letters on ETDRS chart (VA1: ≥ 85 letters, VA2: 70-84 letters, VA3: < 70 letters), which is a key determinant of utility. **Figure 1** shows the model scheme.

Patients enter the model with varying grade of HE (DRESS[1]; **Table 1**) and level of VA (ETDRS Report 22, *Chew et al.*[2]; **Table 2**).

Transition probabilities between HE and VA health states were provided by DRESS[1] (**Table 3**) and ETDRS Report 22[2] (**Table 4**).

Treatment discontinuation rate was taken from DRESS[1] in which 82.6% of sulodexide patients discontinued therapy prematurely.

Mortality rate was sourced from Czech mortality tables (*ČSÚ*[3]) and was adjusted to mortality of diabetic patients by SMR (*Gnavi et al.*[4]; $male_{DM1I2}$: 1.976l1.428, $female_{DM1I2}$: 3.360l1.434) and to mortality of mild-to-moderate non-proliferative diabetic retinopathy patients by HR (ETDRS Report 27, *Cusick et al.*[5]; DM1: 0.880, DM2: 1.270).

Quality of life of patients with ophthalmological disease depends mainly on the level of visual acuity; corresponding utilities were taken from *Czoski-Murray C et al.*[6] (**Table 5**).

Annual sulodexide acquisition costs (€365) were calculated in accordance with dosing scheme in DRESS[1] and reimbursement price of drug (*SÚKL*[7]). Monitoring costs associated with the level of VA in NPRD patients were derived based on the statement of *KOLs*[8] and reimbursed lists (SÚKL[7], VZP[9]) (**Table 5**).

Costs and outcomes were discounted by 3%.

One-way sensitivity analysis (OWSA) accompanied by scenario analysis (SA) were developed, inputs into these analysis are presented in **Figure 3**.

Probabilistic sensitivity analysis (PSA; 1,000 iteration) was performed with willingness-to-pay (WTP) threshold of 3-times GDP per capita in the Czech Republic (i.e. €47,000). **Table 7** summarizes the PSA setting.

Figure 1. Model scheme

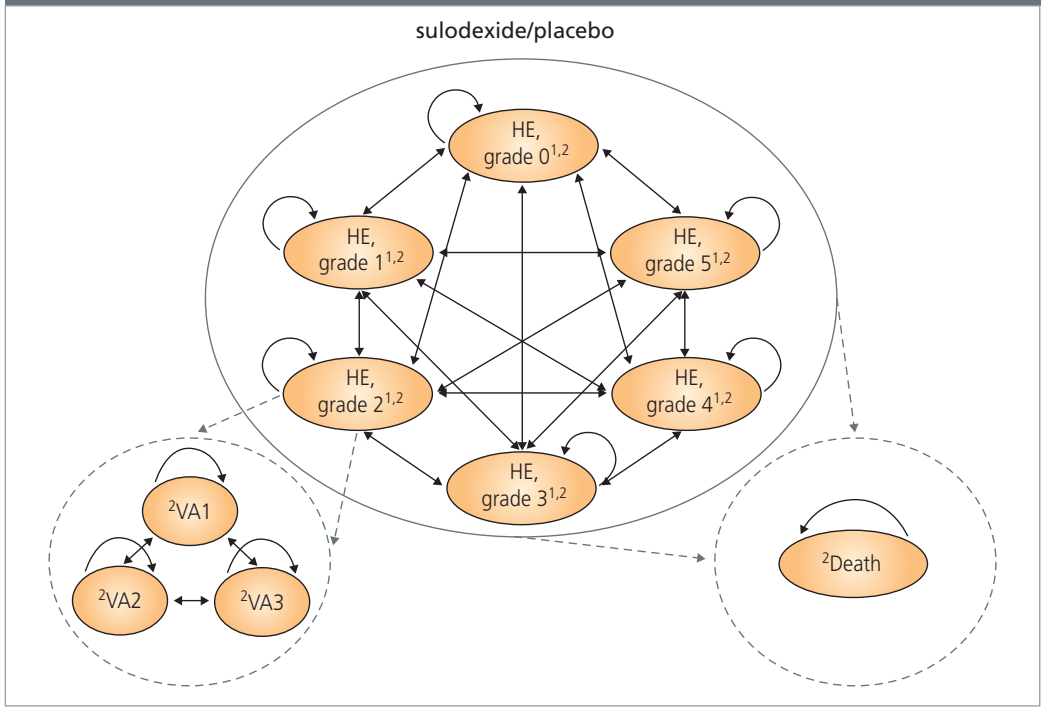

Table 1. Baseline distribution of patients according to grade of HE

	Proportion of patients
HE, grade 0	0.0%[1]
HE, grade 1	0.0%[1]
HE, grade 2	20.0%[1]
HE, grade 3	19.4%[1]
HE, grade 4	58.8%[1]
HE, grade 5	1.8%[1]

Table 2. Baseline distribution of patients according to level of VA and grade of HE

	Proportion of patients		
	VA1	VA2	VA3
HE, grade 0	72.8%[2]–> 0.0%	25.9%[2]–> 0.0%	1.3%[2]–> 0.0%
HE, grade 1	62.0%[2]–> 0.0%	35.9%[2]–> 0.0%	2.1%[2]–> 0.0%
HE, grade 2	60.6%[2]	35.6%[2]	3.8%[2]
HE, grade 3	54.3%[2]	39.7%[2]	6.0%[2]
HE, grade 4	34.5%[2]	48.8%[2]	16.7%[2]
HE, grade 5	18.8%[2]	42.3%[2]	38.9%[2]

Table 3. Transition matrix – changes in grading of HE

	from/to		Proportion of patients after 12 months					
			HE, grade 0	HE, grade 1	HE, grade 2	HE, grade 3	HE, grade 4	HE, grade 5
Sulodexide	Proportion of patients at baseline	HE, grade 0	100.0%[1,*]	0.0%[1]	0.0%[1]	0.0%[1]	0.0%[1]	0.0%[1]
		HE, grade 1	0.0%[1]	100.0%[1,*]	0.0%[1]	0.0%[1]	0.0%[1]	0.0%[1]
		HE, grade 2	0.0%[1]	0.0%[1]	81.8%[1]	18.2%[1]	0.0%[1]	0.0%[1]
		HE, grade 3	0.0%[1]	12.5%[1]	25.0%[1]	25.0%[1]	37.5%[1]	0.0%[1]
		HE, grade 4	0.0%[1]	1.9%[1]	24.5%[1]	18.9%[1]	52.8%[1]	1.9%[1]
		HE, grade 5	0.0%[1]	0.0%[1]	0.0%[1]	0.0%[1]	50.0%[1]	50.0%[1]
Placebo	from/to		Proportion of patients after 12 months					
			HE, grade 0	HE, grade 1	HE, grade 2	HE, grade 3	HE, grade 4	HE, grade 5
	Proportion of patients at baseline	HE, grade 0	100.0%[1,*]	0.0%[1]	0.0%[1]	0.0%[1]	0.0%[1]	0.0%[1]
		HE, grade 1	0.0%[1]	100.0%[1,*]	0.0%[1]	0.0%[1]	0.0%[1]	0.0%[1]
		HE, grade 2	0.0%[1]	18.2%[1]	59.1%[1]	22.7%[1]	0.0%[1]	0.0%[1]
		HE, grade 3	0.0%[1]	18.8%[1]	31.3%[1]	31.3%[1]	18.8%[1]	0.0%[1]
		HE, grade 4	0.0%[1]	0.0%[1]	9.1%[1]	11.4%[1]	75.0%[1]	4.5%[1]
		HE, grade 5	0.0%[1]	0.0%[1]	0.0%[1]	0.0%[1]	100.0%[1]	0.0%[1]

*value is set up on 1, because patients with presence of hard exudates within grade 0 and 1 wasn't included in DRESS – not changes in grading of HE was observed

Table 4. Changes in level of VA due to active therapy

	Proportion of patients after 5 years
	improvement of VA*
HE, grade 0	14.9%[2]
HE, grade 1	17.6%[2]
HE, grade 2	18.5%[2]
HE, grade 3	24.7%[2]
HE, grade 4	37.5%[2]
HE, grade 5	46.7%[2]

*VA3–> VA2; VA2–> VA1

Table 5. Utility and annual cost of VA health states

	Utility	Annual cost
VA1	0.8502[6]	€81[8–7]
VA2	0.7214[6]	
VA3	0.4270[6]	

Table 6. Base-case results of cost-effectiveness analysis

	Sulodexide	On sulodexide	Off sulodexide	Placebo	Difference
Total costs (€)	**1,436**	1,313	123	**361**	**1,075**
Costs of drug (€)	1,075	1,075	0	0	1,075
Monitoring costs according to VA (€)	361	238	123	361	0
QALY	**3.6143**	2.3602	1.2541	**3.5562**	**0.0582**
ICER (€/QALY)	–	–	–	–	**18,489**
NMB (€)	**168,888**			**167,223**	**1,666** $NMB_{sulodexide} > NMB_{placebo}$

RESULTS

Sulodexide brings additional 0.0582 QALYs (3.6143 vs. 3.5562) at additional total cost of €1,075 (€1,435 vs. €361) compared with SoC over a 5-year horizon; the incremental cost-effectiveness ratio (ICER) is then equal to €18,480/QALY gained (**Table 6**).

Treatment with sulodexide leads to the highest net monetary benefits when compared to SoC (€168,888 vs. €167,223; **Table 6**).

PSA showed that probability of sulodexide being cost-effective is nearly 100% at the selected WTP threshold (**Figure 2**).

OWSA and SA confirmed the robustness of the base-case deterministic result (**Figure 3**). Moreover none of the presented scenarios meant an increase of the ICER above the WTP threshold.

Figure 2. Cost-effectiveness scatter plot (left) and cost-effectiveness acceptability curve (right)

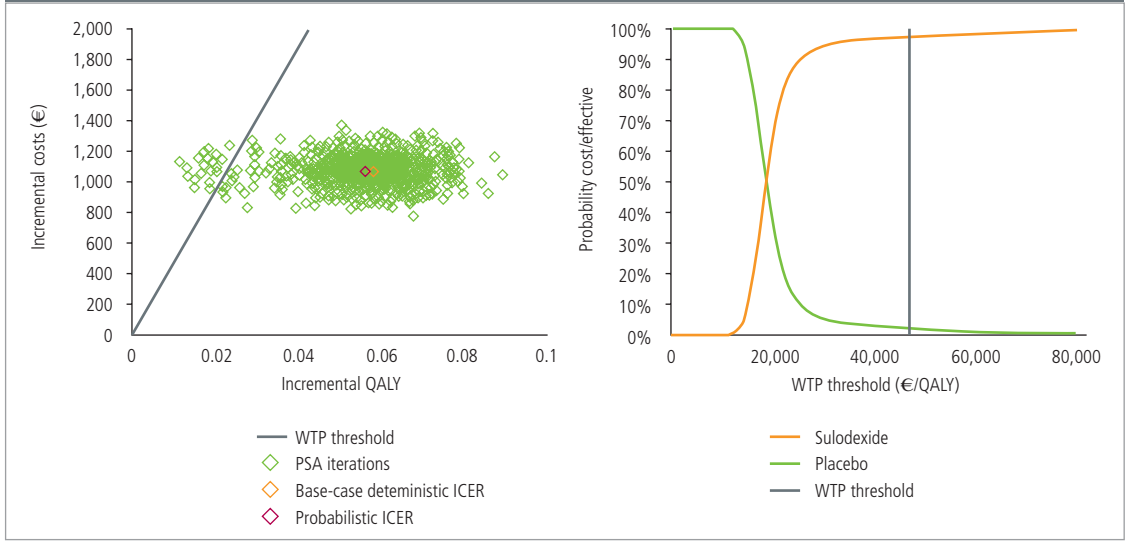

Figure 3. Tornado diagram – one-way sensitivity analysis & scenario analysis

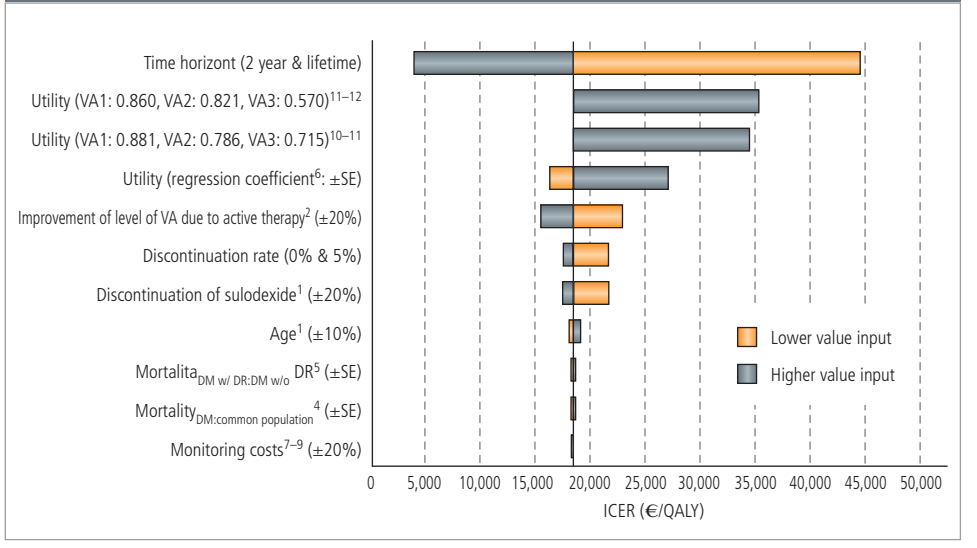

Table 7. Setting of PSA

Parameter	Distribution
Demographic characteristics[1], utility base regression[6]	Normal
Baseline HE distribution[1], treatment effect on HE[1]	Dirichlet
Treatment effect on VA[2], discontinuation of treatment[1]	Beta
Mortality[4,5]	Log-normal
Costs[1,8-7]	Gamma

CONCLUSIONS

Sulodexide is a cost-effective treatment option of HE in patients with mild-to-moderate NPDR, providing improvement of vision.

As sulodexide result in the highest net monetary benefit, this is rank as the most cost-effective strategy in the treatment of HE in patients with mild-to-moderate NPDR.

To our knowledge, this is the first cost-effectiveness analysis of sulodexide in NPDR patients.

REFERENCES

1 Song JH et al. Graefes Arch Clin Exp Ophthalmol. 2015 Jun;253(6):829-37. • 2 Chew EY et al. Arch Ophthalmol. 1996 Sep;114(9):1079-84. • 3 Czech statistical office. Life table for the Czech Republic since 1920. 2015. • 4 Gnavi R et al. Int J Epidemiol. 2004 Aug;33(4):864-71. • 5 Cusick M et al. Diabetes Care. 2005 Mar;28(3):617-25. • 6 Czoski-Murray C et al. Value Health. 2009 Jul-Aug; 12(5):793-9. • 7 State Institute for Drug Control. Medicinal products database. 2016. • 8 Expert panel 2016. • 9 General Health Insurance Company of the Czech Republic. List of medical services. 2016. • 10 Sharma S et al. Br J Ophthalmol. 2003 Mar;87(3):259-61 • 11 Poku E et al. BMC Ophthalmol. 2013 Dec 4;13:74 • 12 Brown MM et al. Arch Ophthalmol. 2002 Apr;120(4):481-4

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