PND47

COST-EFFECTIVENESS ANALYSIS OF GINKGO BILOBA EXTRACT (EGb 761®) FOR THE TREATMENT OF DEMENTIA IN THE CZECH REPUBLIC

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BACKGROUND

EGb 761® belongs among effective therapies for dementia[1,2]. However, this therapy lost reimbursement from payers (public health insurance) in the middle of 2012 in the Czech Republic and is thereby currently available only through full participation of patients which represents a significant burden particularly to the low income population (e.g. seniors). Consequently, this makes the EGb 761® therapy unavailable to numerous patients. In order to regain the reimbursement, the cost-effectiveness analysis was conducted.

OBJECTIVE

The aim of this study was to assess the cost-effectiveness of EGb 761® for the treatment of mild dementia due to Alzheimer's disease (AD) and vascular dementia (VaD) in the Czech Republic in comparison to no treatment or acetylcholinesterase inhibitor (AChEI – donepezil; only in the treatment of AD).

Table 1. Treatment scheme for AD/VaD

Health state	Intervention – EGb 761®	Comparator – placebo	Comparator – donepezil
no & minimal dementia	placebo/placebo	placebo/placebo	placebo/–
mild dementia	EGb 761®*/EGb 761®*	placebo/placebo	donepezil*/–
moderate dementia	donepezil/placebo	donepezil/placebo	donepezil/–
moderately severe dementia	memantin/placebo	memantin/placebo	memantin/–
severe dementia	memantin/placebo	memantin/placebo	memantin/–
death	–	–	–

* Probability of drop-out is 15%[3,12], drop-out patients are switched to placebo.

METHODS

Developed a ten-year Markov cohort model with half-year cycle length projects outcomes (Quality-Adjusted Life-Years, QALYs; Life-Years Gained, LYGs) and costs of treatment for patients with AD and VaD aged 65 years from payers' perspective.

The model was developed with six health states, which are defined by the severity of dementia according to Mini-Mental State Examination (MMSE), i.e. no/minimal, mild, moderate, moderately severe and severe dementia, and by death (**Figure 1**). Patients enter into the model in the state no/minimal dementia and they do not take any pharmacotherapy of dementia. The therapy is then initiated and escalated depending on disease severity and assessed interventions (**Table 1**).

Transition probabilities between states of dementia severity (**Table 2**) were taken from Stewart et al.[3] (no&minimal/mild/moderate dementia – donepezil, placebo; moderately severe/severe dementia – placebo) and Jönsson et al.[4] (moderately severe/severe dementia – donepezil). Transition probabilities for EGb 761® were then derived using direct comparison of donepezil and EGb 761®[5] according to which donepezil is slightly but insignificantly more effective (achievement of clinically significant response ~ preservation of cognitive functions; $RR_{donepezil:\ EGb\ 761®}$ 1.06). Dementia increases the risk of death of the general population (Czech statistical office[6]); moreover, the risk also increases with disease severity (Villarejo et al.[7]).

Patients' quality of life depends on the health state which is influenced by cognitive function damage and the dementia progression; corresponding utilities were taken from Andersen et al.[8] (**Table 3**).

Annual drug acquisition costs (EGb 761® €62.8/half-year, donepezil €93.5/half-year, menantin €289.7/half-year) were calculated in accordance with SmPC drug dosing scheme and a price of particular drug[9,10]. Costs of dementia by disease severity (**Table 3**) were calculated based on statement of KOLs and reimbursed lists[9,11].

Costs and outcomes were discounted by 3%.

Probability sensitivity analysis (PSA; 3,000 iteration) was performed with willingness-to-pay (WTP) threshold of 3 times GDP per capita in the Czech Republic (i.e. €44,000). **Table 4** summarizes setting of PSA.

Figure 1. Model scheme

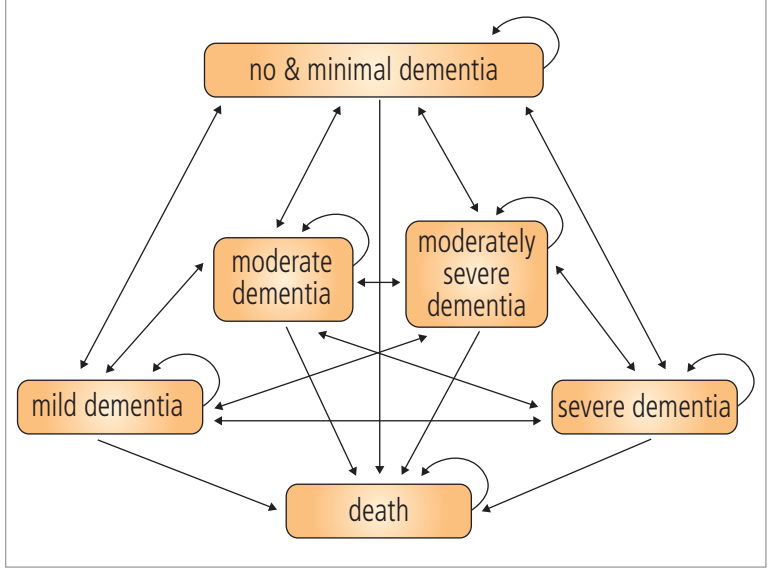

Table 2. Transition probabilities between health states – AD/VaD

		Health state					
Intervention – EGb 761®	Health state	no & minimal dementia	mild dementia	moderate dementia	moderately severe dementia	severe dementia	death
placebo/placebo	no & minimal dementia	0.778[3]/0.778[3]	0.222[3]/0.222[3]	0.000[3]/0.000[3]	0.000[3]/0.000[3]	0.000[3]/0.000[3]	0.017[7]/0.017[7]
EGb 761®/EGb 761®	mild dementia	0.255[3,*]/0.255[3,*]	0.524[3,*]/0.524[3,*]	0.190[3,*]/0.190[3,*]	0.026[3,*]/0.026[3,*]	0.005[3,*]/0.005[3,*]	0.038[7]/0.038[7]
donepezil/placebo	moderate dementia	0.016[3]/0.000[3]	0.190[3]/0.000[3]	0.566[3]/0.885[3]	0.189[3]/0.095[3]	0.040[3]/0.020[3]	0.053[7]/0.053[7]
memantin/placebo	moderately severe dementia	0.000[4]/0.000[3]	0.000[4]/0.000[3]	0.195[4]/0.000[3]	0.585[4]/0.836[3]	0.220[4]/0.164[3]	0.069[7]/0.069[7]
memantin/placebo	severe dementia	0.000[4]/0.000[3]	0.000[4]/0.000[3]	0.000[4]/0.000[3]	0.110[4]/0.000[3]	0.890[4]/1.000[3]	0.084[7]/0.084[7]
Comparator – placebo	Health state	no & minimal dementia	mild dementia	moderate dementia	moderately severe dementia	severe dementia	death
placebo/placebo	no & minimal dementia	0.778[3]/0.778[3]	0.222[3]/0.222[3]	0.000[3]/0.000[3]	0.000[3]/0.000[3]	0.000[3]/0.000[3]	0.017[7]/0.017[7]
placebo/placebo	mild dementia	0.096[3]/0.096[3]	0.580[3]/0.580[3]	0.307[3]/0.307[3]	0.014[3]/0.014[3]	0.003[3]/0.003[3]	0.038[7]/0.038[7]
donepezil/placebo	moderate dementia	0.016[3]/0.000[3]	0.190[3]/0.000[3]	0.566[3]/0.885[3]	0.189[3]/0.095[3]	0.040[3]/0.020[3]	0.053[7]/0.053[7]
memantin/placebo	moderately severe dementia	0.000[4]/0.000[3]	0.000[4]/0.000[3]	0.195[4]/0.000[3]	0.585[4]/0.836[3]	0.220[4]/0.164[3]	0.069[7]/0.069[7]
memantin/placebo	severe dementia	0.000[4]/0.000[3]	0.000[4]/0.000[3]	0.000[4]/0.000[3]	0.110[4]/0.000[3]	0.890[4]/1.000[3]	0.084[7]/0.084[7]
Comparator – donepezil	Health state	no & minimal dementia	mild dementia	moderate dementia	moderately severe dementia	severe dementia	death
placebo/–	no & minimal dementia	0.778[3]/–	0.222[3]/–	0.000[3]/–	0.000[3]/–	0.000[3]/–	0.017[7]/0.017[7]
donepezil/–	mild dementia	0.239[3]/–	0.554[3]/–	0.178[3]/–	0.024[3]/–	0.005[3]/–	0.038[7]/0.038[7]
donepezil/–	moderate dementia	0.016[3]/–	0.190[3]/–	0.566[3]/–	0.189[3]/–	0.040[3]/–	0.053[7]/0.053[7]
memantin/-	moderately severe dementia	0.000[4]/–	0.000[4]/–	0.195[4]/–	0.585[4]/–	0.220[4]/–	0.069[7]/0.069[7]
memantin/–	severe dementia	0.000[4]/–	0.000[4]/–	0.000[4]/–	0.110[4]/–	0.890[4]/–	0.084[7]/0.084[7]

* Transition probability of EGb 761® was derived from transition probability of donepezil with using RR 1.065, which refer on higher effect (achievement of clinically significant response ~ preservation of cognitive functions) of donepezil compared to EGb 761®.

Table 3. Utilities and costs of health states – AD/VaD

Health state	Utilities	Costs (€/half year)
no & minimal dementia	0.78[8]	0.0
mild dementia	0.70[8]	192.3
moderate dementia	0.42[8]	318.2
moderately severe dementia*	0.51[8]	1,013.6
severe dementia	0.34[8]	1,799.0

*Utility and costs of moderately severe dementia are given by average of utilities/costs of moderate and severe dementia.

Table 4. Setting of PSA

Parameter	Distribution
costs	gamma
utilities	beta
efficacy – transition probability	Dirichlet
RR efficacy; donepezil vs. EGb 761®	gamma
HR for death	gamma

RESULTS

EGb 761® was dominant compared to no treatment in both mild AD and mild VaD while generating cost savings of €560 and €355 and gaining 0.2150QALYs/0.1287LYGs and 0.1841QALYs/0.11439LYGs over a 10-year horizon (**Table 5**, **Table 6**).

In comparison to active therapy in mild AD, EGb 761® is slightly less effective (loss of 0.0025QALYs/0.0001LYGs), but also cheaper (by €35) than AChEI in a 10-year horizon (**Table 5**).

PSA showed that probability of EGb 761® to be cost-effective varies from 50% to 84% at the WTP threshold (**Figure 2** – **Figure 4**).

Figure 2. Cost-Effectiveness Scatter plot (left) and Cost-effectiveness acceptability curve (right) – AD, EGb 761® vs. placebo

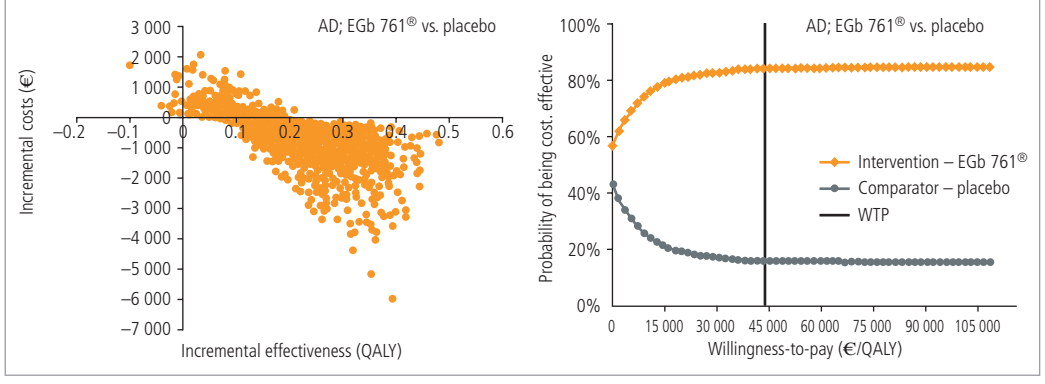

Figure 3. Cost-Effectiveness Scatter plot (left) and Cost-effectiveness acceptability curve (right) – VaD, EGb 761® vs. placebo

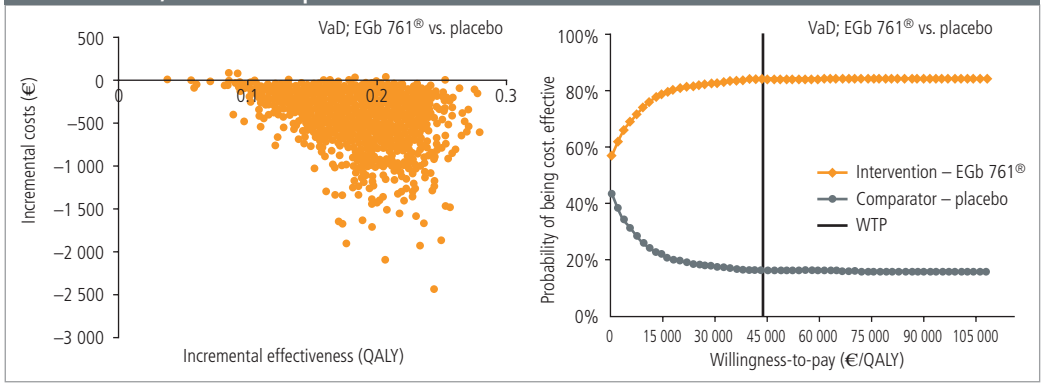

Figure 4. Cost-Effectiveness Scatter plot (left) and Cost-effectiveness acceptability curve (right) – AV, EGb 761® vs. donepezil

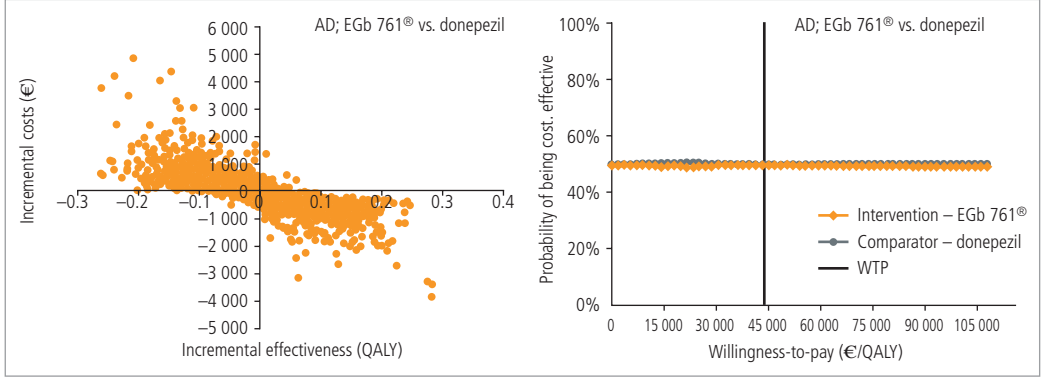

Table 5. Results of deterministic analysis – AD

	Intervention – EGb 761®	Comparator – placebo	Comparator – donepezil	Difference EGb 761® – placebo	Difference EGb 761® – donepezil
Costs, total (€)	**4,881**	**4,915**	**5,441**	**–560**	**–35**
Costs of drug	869	921	888	–19	–51
– EGb 761®	108	0	0	108	108
– donepezil	177	342	216	–39	–165
– memantin	584	579	672	–88	6
Disease management	4,011	3,995	4,553	–541	17
QALY	4.2373	4.2398	4.0224	**0.2150**	**–0.0025**
LYG	6.4577	6.4577	6.3290	**0.1287**	**–0.0001**
ICER (€/QALY)	–	–	–	**dominant*** (–2,605)	**13,814**
ICER (€/LYG)	–	–	–	**dominant*** (–4,351)	**621,992**

* dominant = more effective and less costly

Table 6. Results of deterministic analysis – VaD

	Intervention – EGb 761®	Comparator – placebo	Difference EGb 761® – placebo
Costs, total (€)	**4,607**	**4,962**	**–355**
Costs of drug	67	0	67
– EGb 761®	67	0	67
Disease management	4,540	4,962	–423
QALY	4.0086	3.8245	**0.1841**
LYG	6.3674	6.2535	**0.1139**
ICER (€/QALY)	–	–	**dominant*** (–1,931)
ICER (€/LYG)	–	–	**dominant*** (–3,119)

* dominant = more effective and less costly

CONCLUSIONS

EGb 761® represents a cost-saving intervention with more QALY/LYG gained, i.e. dominant therapy compared to no pharmacotherapy in the treatment of mild dementia in a 10-year horizon. EGb 761® shows very similar results (slightly cheaper and less effective) in comparison to iAchE (e.g. donepezil).

REFERENCES

1 Gauthier S et al. Clin Interv Aging. 2014 Nov 28;9:2065-77 • 2 Tan MS et al. J Alzheimers Dis. 2015;43(2):589-603. • 3 Stewart A et al. 1998 Jul;13(7):445-53 • 4 Jönsson L. Am J Geriatr Pharmacother. 2005 Jun;3(2):77-86 • 5 Yancheva S et al. Aging Ment Health. 2009 Mar;13(2):183-90 • 6 Czech statistical office. Life table for the Czech Republic since 1920. 2015 • 7 Villarejo A et al. J Alzheimers Dis. 2011;26(3):543-51 • 8 Andersen CK et al. 2004 Sep 21;2:52 • 9 State Institute of Drug Control. Medicinal products database. 2015 • 10 IPSEN PHARMA. 2015 • 11 General Health Insurance Company of the Czech Republic. List of medical services. 2015 • 12 Bond M et al. Health Technol Assess. 2012;16(21):1-470

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