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Cost-effectiveness of combined treatment with alteplase (rt-PA) and Cerebrolysin in acute ischemic hemispheric stroke in Austria

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Objectives

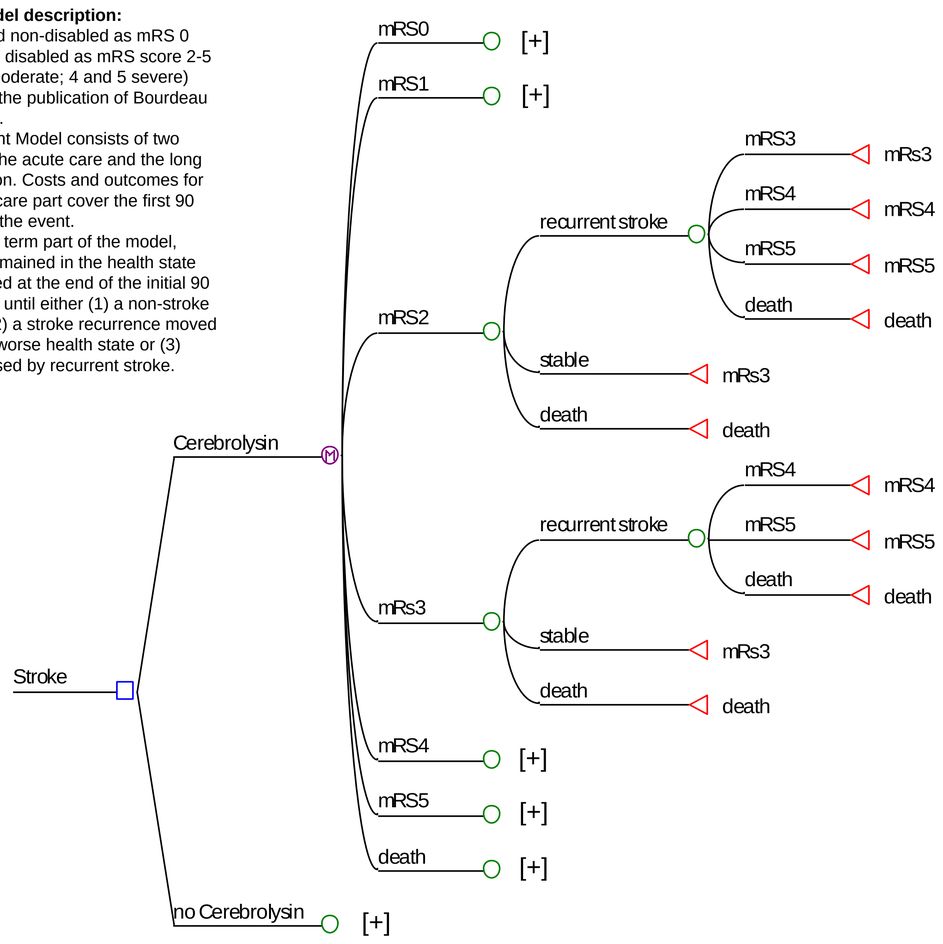
Worldwide, stroke is the third most common cause of death in developed countries with declining death rates. In Austria the incidence rate of stroke is 2.1 – 2.3 per thousand annually. Cerebrolysin prevents acute neuronal damage and accelerates recovery after stroke. The purpose of this analysis was to determine costs of stroke for Austria in general and to estimate the cost-effectiveness of Cerebrolysin in combination with alteplase compared to alteplase alone. The analysis should assess health economic advantages in the acute care due to a faster improvement in neurological impairment and for rehabilitation in early post-acute phase and quantify the correlated reduced resource use in the health care and social system.

Methods

A Markov-model was developed based on the mRS states 90 days after stroke to simulate consequences over a 10-year time-horizon. Consequences include recurrent stoke, deteriorated mRS, death due to recurrent stroke or other reasons. Health benefits were measured in quality-adjusted life years (QALYs) and life years (LYs). Monte-Carlo-simulation accounted for uncertainty. Probabilities were derived from RCTs and open-label studies; direct costs (2014) were derived from published sources from the payer's perspective. QALYs, life years and costs were projected over a 10-year time-horizon. Costs and outcomes were discounted according to the national guidelines with 5%.

Fig. 1: Model Design

Short model description:
We defined non-disabled as mRS 0 and 1, and disabled as mRS score 2-5 (2 and 3 moderate; 4 and 5 severe) according the publication of Bourdeau et al. 2013.
The present Model consists of two modules: the acute care and the long term section. Costs and outcomes for the acute care part cover the first 90 days after the event.
In the long term part of the model, patients remained in the health state experienced at the end of the initial 90 day period until either (1) a non-stroke death or (2) a stroke recurrence moved them to a worse health state or (3) death caused by recurrent stroke.



[+] indicates that the subtree is not completely displayed. The content of the subtrees are the same as in the subtree above.

mRS = modified Ranking scale

Source: own developed

Clinical Data

The model input parameters were drawn from published literature (Table 1). Health states after ischemic stroke were defined by mRS. The distribution of health states after 90 days of Cerebrolysin-treated patients versus non Cerebrolysin (Placebo) were derived from the study of Lang et al. (2013). Transition to a worse disability state took place as a consequence of a recurrent stroke. The Model assumes different recurrence rates over time according to the publication of Chambers et al. (2002). The study has used probabilities over the first 2 years from the second European Stroke Prevention Study (ESPS-2).

Resource Use and Costs

The cost assessment is based on the assignment of costs to the health states. The costs of each health state are determined by the resource utilisation associated with a health state. Resource use and monetary value (prices, tariffs and/or opportunity costs) for each unit of medical goods and services were used to calculate the total direct costs. The following costs were included in the analysis: acute stroke and rehabilitation (first 90 days), nursing and rehabilitation (after 90 days, recurrent stroke and follow-up costs).
Direct medical costs derived from a number of publicly available sources like the DRG catalogue (LKF) and official price lists for the Austrian Health insurances funds, etc. When necessary, prices were adjusted to 2014 prices using the consumer price index.

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Results

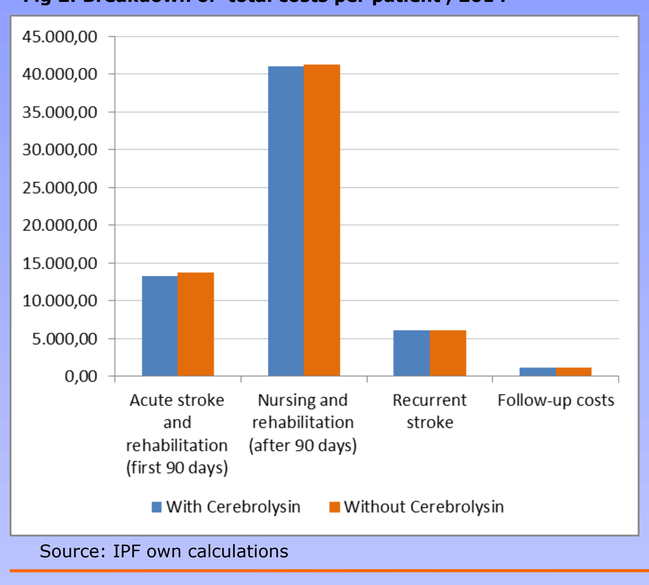
Total costs in the Cerebrolysin group over a 10-year time horizon led to discounted costs of € 61,468.67. Per-patient costs in the comparator group are estimated at € 62,257.88 in Austria. Acute stroke treatment resulted in a discounted quality-adjusted life expectancy of 3.77 years. The corresponding life expectancy without quality adjustment amounts to 6.70 LYs. Acute treatment without Cerebrolysin is associated with 3.75 discounted quality-adjusted life years and 6.70 LYs. The saving potential due to add Cerebrolysin to the acute treatment would reduce costs by € 789.20 and increase QALYs by 0.014 (= 5 days with perfect health) per patient.

Tab. 1: Results, 2014

Strategy	Costs per patient (€)	Cost difference (€)	QALYs per patient	LYs per patient	QALY difference	ICER
With Cerebrolysin	61,468.67		3.7658	6.6954		Dominant
Without Cerebrolysin	62,257.88	789.20	3.7517	6.6999	-0.014	

Source: own calculations

Fig 2: Breakdown of total costs per patient , 2014



Source: IPF own calculations

Assessing the disaggregated costs it becomes apparent that costs savings are due to lower acute stroke costs (€ -493.29) and nursing home costs mainly after first stroke (€ 250.88). Based on the results of the study from Lang et al. (2013) stroke treatment with rt-PA and Cerebrolysin could be able to reduce event costs, mainly due to a shorter LOS and reduced requirement of institutional care after stroke. Long-term savings and favourable long-term outcome effects were not calculated and proven.

Sensitivity Analysis (SA)

In the probabilistic SA costs were varied assuming a Beta distribution and utilities with a Gamma distribution. Monte Carlo probabilistic SA, results of 500 patient's incremental cost versus incremental effects revealed that Cerebrolysin is cost-effective against no Cerebrolysin in more than 83.2% of simulations with a willingness-to-pay-value up to € 20,000; (Fig. 3a).
When performing the deterministic one-way SA we vary first stroke costs, nursing or rehabilitation facility costs, recurrent stoke costs, mortality rate, utilities and the discount rate. Among inputs considered the nursing and rehabilitation costs and first stroke costs exhibit the greatest influence (Fig. 3b).

Fig. 3a: Probabilistic sensitivity analysis

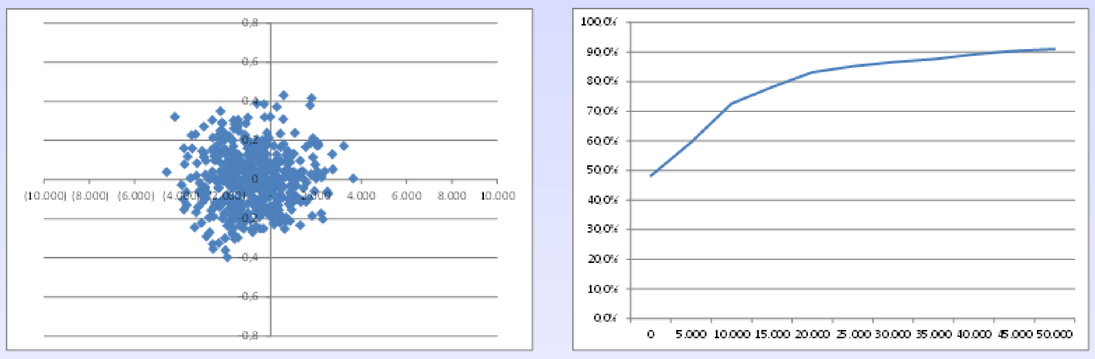
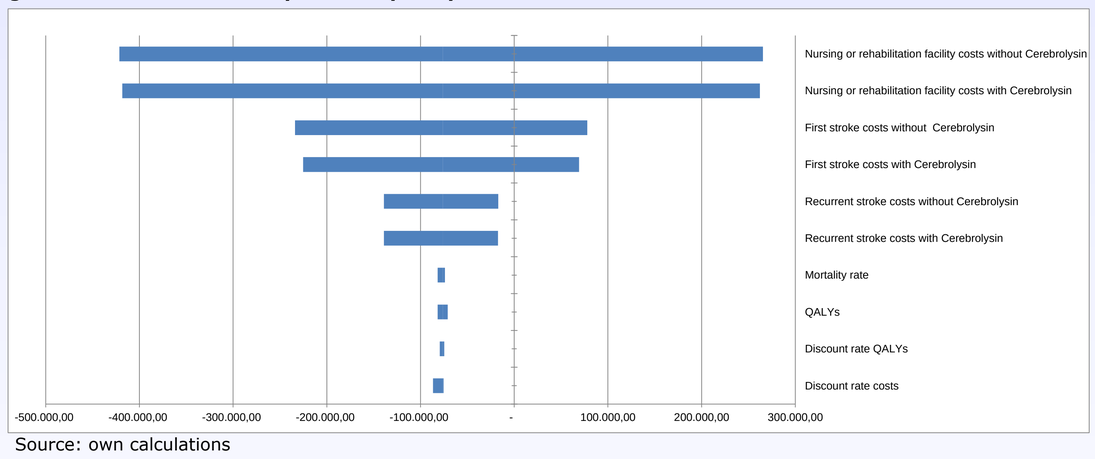


Fig. 3b: Deterministic one-way sensitivity analysis



Source: own calculations

Conclusion

From a health economic perspective, Cerebrolysin is a cost-effective therapy; it mainly reduces event costs due to early remobilization and, in addition, rehabilitation and nursing-home cost.

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Additional Literature with the author

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