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Cost and outcomes of teduglutide in adult patients with short bowel syndrome – is the combination with BSC cost-effective for the society?

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Objectives

The short bowel syndrome with intestinal failure (SBS-IF) describes a rare but devastating medical condition where patients are dependent to parenteral support (PS) due to an absolute loss of bowel length resulting in a variety of medical sequalae and subsequent increased morbidity and mortality. Interdisciplinary treatment may include therapy with the effective, but expensive intestinotrophic peptide teduglutide.

This study aimed at an evaluation of the cost-effectiveness of using teduglutide in adults with SBS-IF from a societal perspective in order to evaluate the socioeconomic impact.

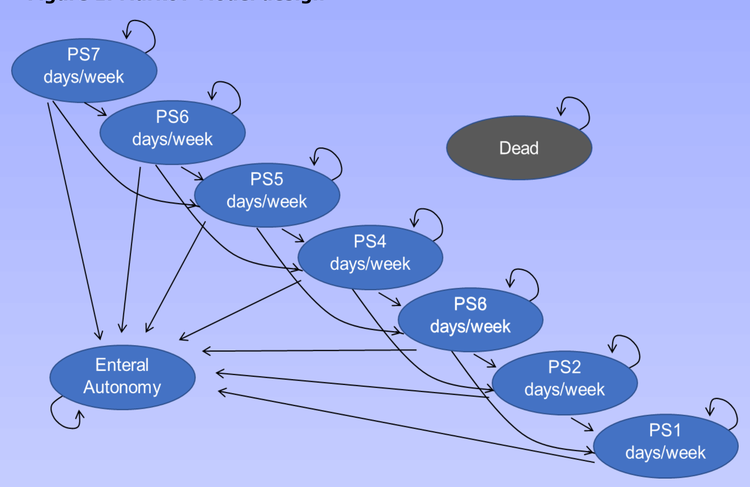
Methods

A time-discrete Markov-model based on published models was developed to simulate the treatment effect (lifetime-costs, quality-adjusted life-years/QALYs and life-years/LYs) of teduglutide plus best supportive care (BSC) compared with BSC alone in SBS-IF patients who are dependent on PS. The health states of the model were structured around the number of days on PS. During each model cycle, patients were either weaned by 1 or 2 days per week or remain in the same PS states or achieve enteral autonomy. Clinical data from three data sets were used:

- an Austrian observational study (base case; Harpain et al 2022)
- 6 pooled observational studies and
- the randomized STEPS study.

Direct costs (2022 €) were derived from published sources. A willingness-to-pay threshold set at 300,000 €/QALY gained was incorporated. One-way and probabilistic sensitivity analysis were performed.

Figure 1: Markov-Model design



- All patients run in the model distributed according to the health states PS3 to PS7.
- During each model cycle, patients were either weaned by 1 or 2 days per week, remain in the same state or achieve enteral autonomy.
- The model allows that patients discontinue therapy with teduglutide at any time, then PS transitions develops according to the BSC alone arm.
- Adverse events are considered in both treatment arms.
- The death health state is an absorbing state and can be entered from any state.

Source: own developed

Tab. 1: Overview of methods applied

Methods	
Type of study	**Cost-utility analysis (CUA) and Cost-effectiveness analysis (CEA)**
Type of the model	**Markov** simulation model
Perspective	**Austrian societal perspective** (direct and indirect costs) Austrian health care systems perspective (payers' perspective; direct costs)
Time horizon Cycle length	**Lifetime** 28 days
Discount rate	**3% for costs & 3% for outcomes**
Population	**Patients with SBS-IF** who are stable following a period of intestinal adaptation after surgery. The population meets the inclusion criteria of the STEPS study. Eligible participants were adults [mean age (range) 50.3 (18-82)] after intestinal resection, mainly due to vascular disease and Crohn's disease.
Intervention	**Teduglutide** plus best supportive care (BSC)
Comparator	**BSC** (Parenteral support [PS])
Direct costs	**Direct costs** comprise teduglutide costs, PN costs plus supplementation, monitoring costs and AE costs.
Indirect costs	**Indirect costs** comprise work absenteeism, caregiver costs, and work absenteeism costs of family members caring patients.
Outcomes	• **Quality-adjusted life-years (QALYs)** based on EQ-5D • **Disutility** per AE was multiplied by the event duration • **Caregiver-disutilities**, as SBS-IF not only affects the patient but also the QoL of carers.
Results	**Incremental cost utility ratio (ICUR) & incremental cost effectiveness ratio (ICER)**
Timing	**2022**

Source: own developed

Clinical Data

The distribution of PS days in the first cycle corresponds to the baseline distribution of average number of days on PS in the STEPS trial. The model uses different weekly PS weaning probabilities up to week 24 and between week 24 and 2.5 years. After that, no improvement was assumed und the distribution remains unchanged.

Tab. 2: Transition probabilities (base case; Harpain et al 2022)

Helath state	up to week 24 (per cycle)	week 24 to 2.5 years (per cycle)
by 1 d of PS	2.54%	0.03%
by 2+ d of PS	1.52%	0.23%
without improvement	78.11%	89.61%
PS independence	17.84%	10.14%

Source: calculated from Harpain et al. 2022

Adverse Events

Adverse events (AE) experienced by at least 5% were included in our model according to the STEPS trial. CLABSIs are only attributed to those patients who receive PS. It was assumed that the probability for CLABSIs decreases with a reduction in PS days.

Survival

Survival was modelled using the published 10-year observational data of 268 non-malignant SBS patients from Lam et al. (2018). Patient characteristics compared to the STEPS trial are similar.

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Direct costs

The model includes teduglutide costs, PN costs plus supplementation, monitoring costs and AE costs. Costs were presented from the payer perspective.

- Teduglutide (Revestive®), PN and supplementation costs were evaluated based on the reimbursement price and were extracted from the official Austrian classified index of goods.
- The average administered PS volume from the STEPS study.
- Monitoring costs were considered. Treatment specific resource use data were obtained from relevant product information and the literature.

Indirect costs

Since the average age of the study population is 50.3 (range: 18-82) years, the majority is of working age. For this reason, it was considered relevant to include indirect costs in the analysis. Indirect costs comprise work absenteeism of patients, caregiver costs, and work absenteeism costs of family members caring patients. The lost productivity is calculated based on the average median income using the human capital approach.

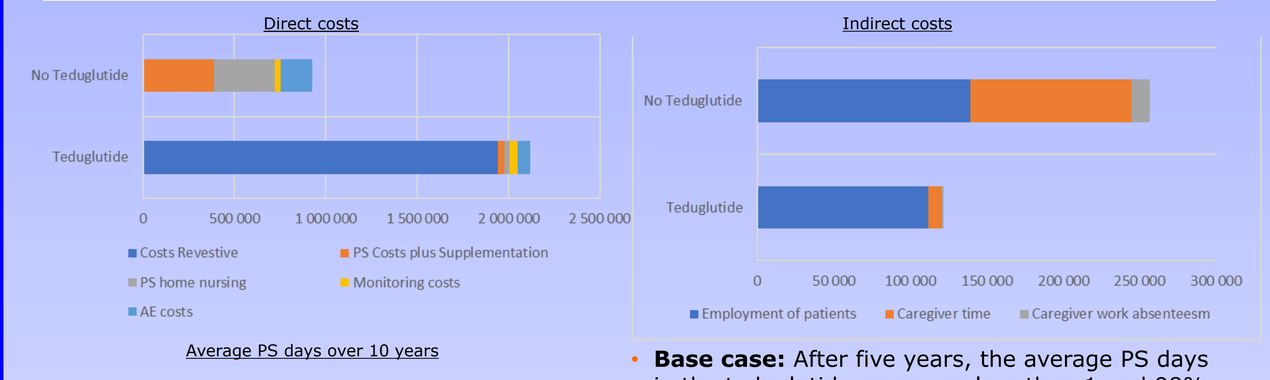
Results

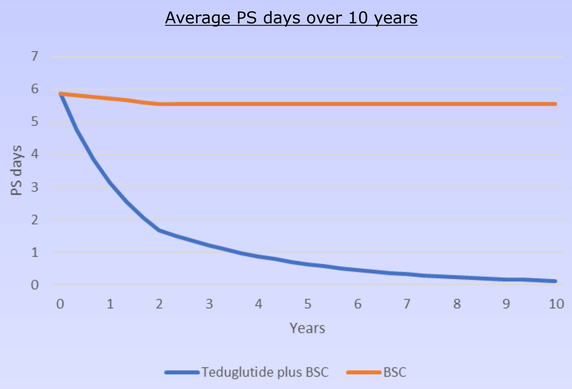
Under the base case assumption teduglutide is associated with costs of 2,238,808.66 € per patient and 10.501 QALYs (13.385 LYs) over a life-time-horizon. No teduglutide accounted for 1,182,698.95 € and 2.133 QALYs (8.181 LYs). the ICUR amounts to 126,610.04 €.

In case the pooled clinical data set the ICUR improves to 192,750.68 €. If clinical data based on the STEPS studies were used the ICUR increased to 245,958.52 €.

Tab. 3: Base case Results

Costs	Teduglutide plus BSC	BSC	Incremental
Direct:	**2,117,074.42 €**	**926,180.07 €**	**1,190,894.35 €**
Indirect:	**121,734.24 €**	**256,518.89 €**	**-13478,4.64 €**
TOTAL COSTS	**2,238,808.66 €**	**1,182,698.95 €**	**1,056,109.70 €**
Outcomes			
QALYs	10.501	2.133	8.368
ICUR		**126,210.04 €**	
LYs	13.385	8.181	5.204
ICER		**228,860.33 €**	





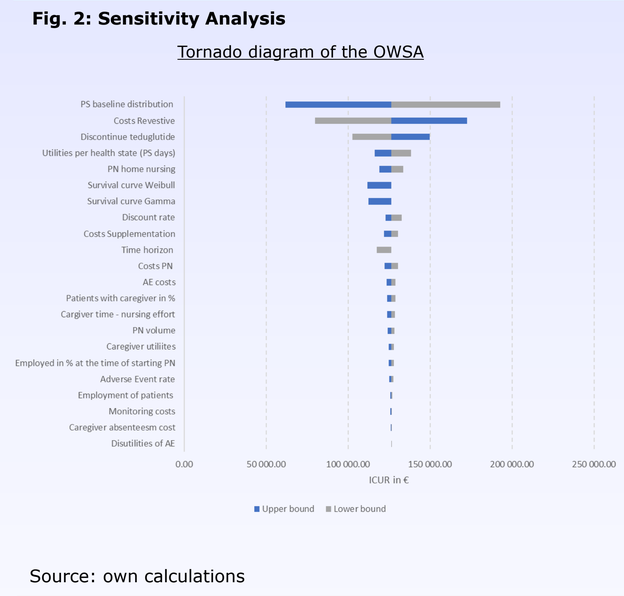
Source: own calculations

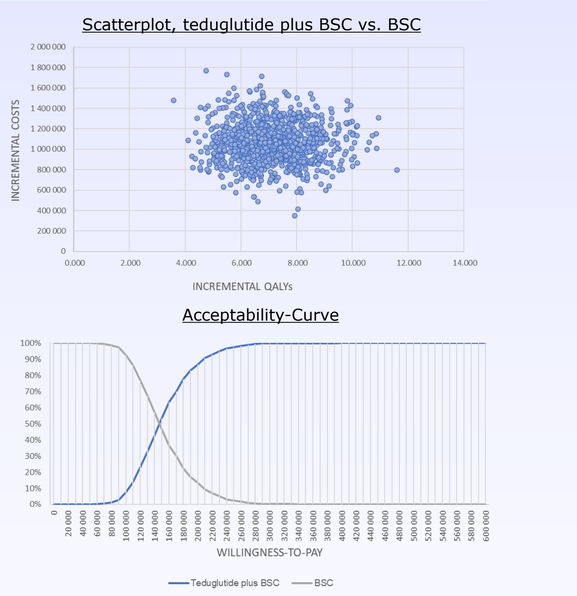
- **Base case:** After five years, the average PS days in the teduglutide group are less than 1 and 98% of patients reach enteral autonomy; in the group without teduglutide average PS days are 5.55 and 0.2% with enteral autonomy.
- Using probabilities derived from the **pooled 6 observational studies**, 6.812 QALYs (11.234 LYs) was determined. The average PS requirement after 5 years was 1.76 days per week and 57.9% of patients reach enteral autonomy.
- With **data from STEPS** 4.400 QALYs (9.786 LYs) was calculated. The average PS days after 5 years are 3.36 days and 30.6% of patients reach enteral autonomy.

Sensitivity Analysis

Probabilistic sensitivity analysis (PSA) and deterministic one-way sensitivity analysis (OWSA) were carried out to examine the robustness of the model.

Fig. 2: Sensitivity Analysis





Source: own calculations

The Monte-Carlo PSA results of 1,000 second-order simulations plotting incremental costs versus incremental effects. At a willingness-to-pay threshold of 300,000 €, 99% of simulation are in the cost-effective range.
OWSA confirms probabilistic results. Variations in the inputs monitoring costs, caregiver absenteeism costs and disutilities due to AE have biggest influence on the result.

Conclusion

In adult patients with SBS-IF, the use of teduglutide plus BSC is cost-effective and improves the quality-of-life significantly.

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Additional literature with the author