

Cost effectiveness of Apomorphine infusion in the treatment of advanced Parkinson Disease in the UK

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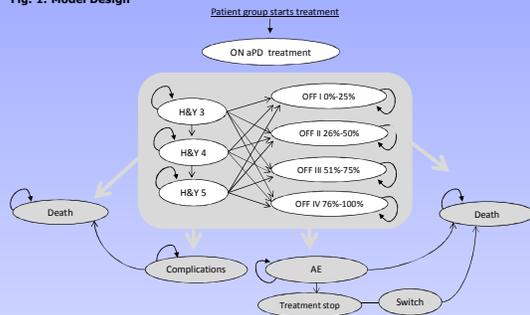
Objectives

Parkinson Disease (PD) is the second commonest cause of neurological disability and affects 100-180 people per 100,000 of the population and increases with age. Continuous subcutaneous apomorphine represents an alternative treatment option of advanced PD with motor fluctuation. The purpose of this analysis was to estimate the cost-effectiveness of continuous s.c. Apomorphine infusion (CSAI) compared with Levodopa/carbidopa intestinal gel (LCIG), Deep-Brain-Stimulation (DBS) and Standard-of-care (SOC).

Methods

We developed a Markov-Model to simulate the long-term consequences, disease progression (Hoehn&Yahr-stages 3-5, percentage of waking-time in the OFF-state), complications and adverse-events. The model is adopted based on models which have been published for the UK and Sweden. Complications are different for the alternatives (e.g. pump problems in case of LCIG, temporary/permanent complications in case of DBS). Moderate and severe adverse-events (e.g. motor fluctuation, dyskinesia, nausea, dizziness, hallucination, skin problems, depression, anxiety) and death were included. Including 25 health-states, the model comprises moderate and severe health conditions. Probabilities derived from RCT and open-label studies; direct costs (2012 £) from published sources from the payer's perspective.

Fig. 1: Model Design



Source: developed by IPF

Cohort definition

The model cohort comprises PD patients aged 50 years or older with Hoehn&Yahr (H&Y) stages 3, 4 or 5 experiencing more than 50% of waking-time (14 hour) in the OFF state at treatment initiation. After treatment initiation with CSAI, LCIG or DBS an improvement in health states in the following cycle may arise; or patients continue SOC. During different therapeutic alternatives adverse events or complications may arise. Due to intolerable adverse events, patients have the opportunity to switch to an alternative treatment. Patients receiving first-line CSAI or LCIG switch to DBS and patients after a DBS either start or increase SOC medication.

Results

Over a life-time horizon, costs associated with CSAI amounts to 70,258.28 £ and 2.85 QALYs (6.28 LYs). Costs associated with LCIG are 117,121.48 £ and 3.06 QALYs (6.93 LYs). The cost-saving amounts to 46,863.20 £ per patient and the incremental-cost per QALY gained (ICER) was 223,051.88 £. Costs associated with DBS are 88,361.61 £ and 2.75 QALYs (6.38 LYs). CSAI dominates DBS. SOC associated total-cost are 68,082.92 £ and 2.62 QALYs (5.76 LYs). The ICER of CSAI versus SOC amounts to 9,296.41 £.

Tab. 1: Results of costs QALYs and LYs

Strategy	Costs C	Diff. AC	QALYs E	Diff. QALYs ΔE	ICER
CSAI	70,258.28 £		2.85		9,296.41 vs. SOC
LCIG	117,121.48 £	46,863.20 £	3.06	0.21	223,051.88 vs. CSAI
DBS	88,361.61 £	18,103.33 £	2.75	-0.10	(Dominated by CSAI)
SOC	68,082.92 £	-2,175.36 £	2.62	-0.23	
Strategy	Costs C	Diff. AC	LYs E	Diff. LYs ΔE	C per LYs gained
CSAI	70,258.28 £		6.28		4,225.64 vs. SOC
LCIG	117,121.48 £	46,863.20 £	6.93	0.65	72,075.05 vs. CSAI
DBS	88,361.61 £	18,103.33 £	6.38	0.11	170,144.08 vs. CSAI
SOC	68,082.92 £	-2,175.36 £	5.76	-0.51	

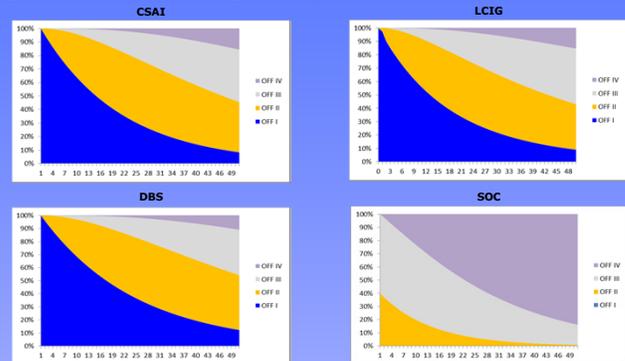
Source: IPF own calculations

ICER = incremental cost effectiveness ratio

The medical resource use and Utilities are based on literature research.

QALYs, life-years and costs are projected over a life-time horizon and discounted at 3.5%. Monte-Carlo-simulation accounted for uncertainty.

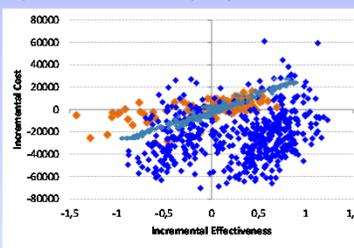
Fig. 2: Distribution of patients according to OFF time per 6 month



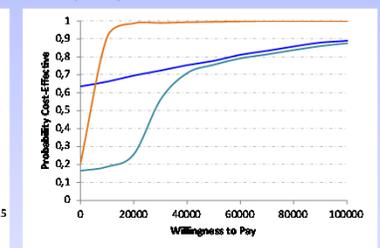
Source: IPF own calculations

CSAI, LCIG and DBS patients spent less time in higher OFF states compared to patients maintained on SOC. Comparison of the graphs illustrates the better prognosis for patients treated with CSAI, who spent 69% of their remaining life-time in OFF I stage, 24% in OFF II, 6% of time in OFF III and 1% in OFF IV. Patients treated with LCIG spent 76% of their life-time after treatment start in OFF I, 20% in OFF II, 3% in OFF III and 1% in OFF IV. DBS shows the following effect: patients spent 78% of time in OFF I state, 19% in OFF II, 2.5% in OFF III and 0.5% in OFF IV. In comparison to that, patients remaining on SOC therapy spend 27% of time in OFF II, 57% in OFF III and 16% in OFF IV stage.

Fig. 3a: Probabilistic Sensitivity Analysis



3b: Acceptability curves



Source: IPF own calculations

Monte Carlo probabilistic sensitivity analysis pools the results of 500 trials plotting incremental cost versus incremental effects. Based on this it creates acceptability curves to assess the likelihood of the comparators being cost-effective over a range of willingness to pay values in the UK setting. Sensitivity analysis revealed that CSAI is cost effective compared to LCIG in more than 69.6% (72.4%) of the simulations with a willingness to pay of 20,000 £ (30,000 £); versus DBS in 25.8% (56.2%) and versus SOC in 98.7% (98.9%) of all simulations (Fig. 3b). One-way sensitivity analysis shows the robustness of model.

Conclusion

Patients with advanced PD who are not eligible for alternate treatments are currently maintained on standard care and show a clear unmet need for alternative effective treatment options. The presented model has found a substantial incremental gain in QALYs for CSAI compared to SOC (0.23 QALYs) and to DBS (0.10 QALYs). CSAI could therefore be considered as cost-effective in the limited cohort of patients for whom it is indicated. The findings of this analysis must be considered in the light of the limitations outlined. CSAI is a cost-effective alternative, reducing OFF-time and improving quality-of-life and is associated with a cost-advantage.

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 Additional Literature with the author

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