Impact of Exenatide on Medical Costs and Health Utilities in Type 2 Diabetes: Experience from EXSCEL

Duke Clinical Research Institute | FROM THOUGHT LEADERSHIP TO CLINICAL PRACTICE

DIABETES TRIALS UNIT
The Oxford Centre for Diabetes, Endocrinology and Metabolism

Reed SD[1], Li Y[1], Dakin H[2], Becker F[2], Leal J[2], Gustavson SM[3], Kartman B[4], Wittbrodt E[3], Mentz RJ[1], Pagidipati N[1], Bethel MA[5], Gray AM[2], Holman RR[5], Hernandez AF[1]

[1]Duke Clinical Research Institute, Durham, NC, USA; [2]Oxford Health Economics Research Centre, University of Oxford, Oxford, UK; [3]AstraZeneca Research and Development, Gaithersburg, MD, USA; [4]AstraZeneca, Mölndal, Sweden; [5]Diabetes Trials Unit, University of Oxford, Oxford, UK

BACKGROUND AND AIMS

- EXSCEL (Exenatide Study of Cardiovascular Event Lowering) trial randomized 14,752 intention-to-treat (ITT) patients with type 2 diabetes (T2D), with or without previous cardiovascular disease to exenatide once-weekly 2mg (EQW) or placebo added to usual care.
- EXSCEL demonstrated a numerical reduction in major adverse cardiovascular composite outcome (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke) and a nominally significant improvement in all-cause mortality.
- Our objective was to compare the within-trial impact of exenatide vs placebo when added to usual care on medical costs and health utilities.

EXSCEL
Exenatide Study of Cardiovascular Event Lowering

METHODS

- A prespecified detailed Costing and Data Analysis Plan guided the analyses.
- Medical resource use data included hospitalisations, major procedures, study visits, outpatient visits to usual diabetes care providers and other providers, concomitant cardiovascular and diabetic medications, and study medications.
- Medical resources were valued from UK and US perspectives using:
  - English National Schedule of Reference Costs and Prescription Cost Analysis database for the UK analysis, and
  - Medicare payments and wholesale acquisition costs for concomitant medications with a 23.1% discount for branded EQW in the US analysis.
- EQ-5D-5L and EQ-5D-3L (EuroQol 5 Dimension: 5-level version and 3-level version) responses were valued using both UK and US tariffs.

STATISTICAL ANALYSES

- Hierarchical generalised linear models were applied to compare medical costs and health utilities between treatment arms.

Medical resource use and cost models

- Countries were modelled as random intercepts.
- Treatment assignment was modelled as a fixed-effect.
- Log-transformed follow-up duration was included as an offset variable.
- Models were fitted with negative binomial (counts) or gamma (costs) error distributions and log links.

EQ-5D health utility models

- Countries and patients were modelled as random intercepts.
- Models were specified with normal error distributions.
- Independent variables included treatment assignment, baseline health utilities, time since baseline, and interaction term between treatment and time.

RESULTS

- Mean follow-up: 3.3 years; median (IQR) follow-up: 3.2 (2.2– 4.4) years.
- Mean number of hospitalisations per patient and annual hospitalisation rates were similar in both groups (Table 1, Figure 1), although the total number of inpatient days over the course of the trial was reduced for the EQW group.
- Inpatient and outpatient costs were similar between treatment groups when UK or US costs were assigned (Table 2).
- In the UK analyses, mean total costs for medical resources, exclusive of exenatide, were significantly lower for the EQW group at £8,790 vs £9,204 for the placebo group. When including mean costs for exenatide of £2,084, total mean costs for the EQW group increased to £10,874, which were £1,670 higher than the placebo group.

Table 1. Medical resource use

	Exenatide (N=7,356)	Placebo (N=7,396)	Relative rate (95% CI)	P-value*
All-cause hospitalisations	0.83 (1.68)	0.84 (1.62)	0.97 (0.91 to 1.03)	0.31
Inpatient days	7.05 (18.24)	7.46 (19.32)	0.91 (0.83 to 1.00)	0.05
Outpatient care visits	21.07 (23.26)	20.92 (23.55)	0.99 (0.97 to 1.02)	0.66

* P-value from SAS GLIMMIX procedure.

Table 2. Medical costs

	Exenatide (N=7,356)	Placebo (N=7,396)	Means ratio (95% CI)	P-value*
Direct medical costs* *(British £, 2016)*				
Inpatient care	5,021 (14,028)	5,204 (13,929)	0.92 (0.83 to 1.04)	0.51
Outpatient care	1,313 (1,231)	1,293 (1,215)	1.01 (0.98 to 1.03)	0.74
Medications	2,457 (2,558)	2,708 (2,913)	0.91 (0.89 to 0.93)	<0.01
Diabetic medications	1,640 (1,618)	1,823 (1,687)	0.89 (0.87 to 0.92)	<0.01
Other medications	817 (1,676)	885 (2,019)	0.96 (0.92 to 0.99)	0.03
Total, excluding exenatide	8,790 (15,024)	9,204 (14,970)	0.93 (0.88 to 0.99)	0.02
Exenatide	2,084 (1,254)	-	-	-
Total Costs	**10,874 (15,136)**	**9,204 (14,970)**	**1.18 (1.12 to 1.24)**	**<0.01**
Direct medical costs‡ *(US$, 2017)*				
Inpatient care	9,654 (25,051)	10,078 (26,016)	0.92 (0.83 to 1.02)	0.10
Outpatient care	2,156 (1,872)	2,139 (1,910)	1.01 (0.98 to 1.04)	0.68
Medications	17,098 (15,992)	18,698 (16,899)	0.91(0.89 to 0.93)	<0.01
Diabetic medications	13,882 (14,592)	15,445 (15,295)	0.89 (0.87 to 0.92)	<0.01
Other medications	3,216 (3,610)	3,252 (3,876)	0.99 (0.96 to 1.02)	0.39
Total, excluding exenatide	28,907 (32,600)	30,914 (34,089)	0.92 (0.89 to 0.96)	<0.01
Exenatide	13,790 (8,374)	-	-	-
Total Costs	**42,697 (34,355)**	**30,914 (34,089)**	**1.39 (1.35 to 1.44)**	**<0.01**

Data are mean (SD) unless otherwise indicated.
*P-value from SAS GLIMMIX procedure with Laplace estimation. **Costs discounted at 3.5% per annum. ‡Costs discounted at 3% per annum.

- In the US cost analyses, mean total costs for medical resources, exclusive of exenatide, were significantly lower in patients on EQW ($28,907 vs $30,914 in the placebo group). When including mean costs for exenatide of $13,790, total costs were $42,697 in the EQW group and $30,914 in the placebo group.
- There were no significant differences observed in UK or US EQ-5D health utilities between the groups over the follow-up period (Figure 2).

Figure 1. Mean cumulative number of hospitalisations over time by treatment group.

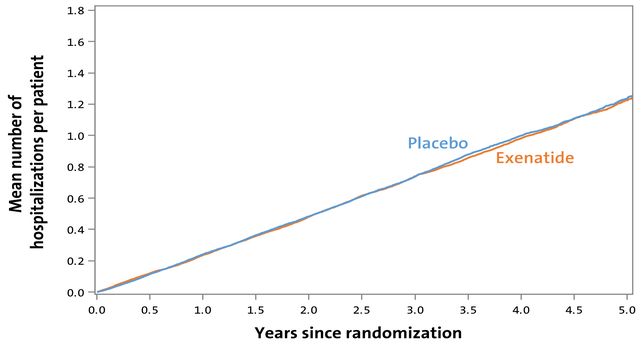
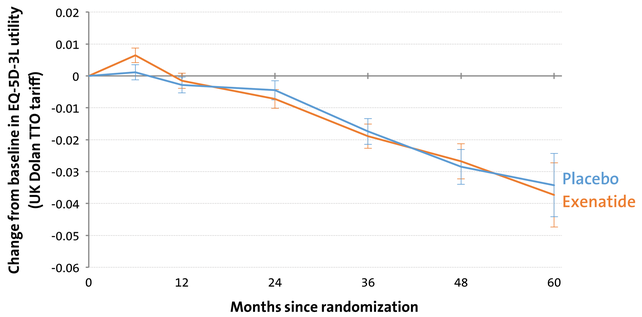


Figure 2. Change from baseline in EQ-5D utility (UK weights).



CONCLUSIONS

- Similar hospitalisation rates and health utilities were reported across time with EQW, compared with placebo. Mean cumulative inpatient days were significantly reduced with EQW, compared with placebo.
- Although EQW-treated patients incurred lower costs for concomitant diabetic and non-diabetic medications, inclusion of EQW costs led to higher total mean costs in the EQW arm.
- Total costs were significantly lower in the EQW group when the cost of study medication was excluded, but were significantly higher when the cost of branded EQW was included in the analysis.
- Estimating the cost-effectiveness of EQW requires lifetime extrapolation of incremental costs and benefits, and will be reported separately.

CONTACT INFORMATION

Shelby D. Reed, PhD.
Shelby.reed@duke.edu
PO Box 17969
Durham, NC 27715
919-668-8991

DISCLOSURES

Dr. Reed's disclosures are available at http://www.dcri.duke.edu/about-us/conflict-of-interest/.

FUNDING

The EXSCEL trial was funded by Amylin Pharmaceuticals, Inc., a wholly owned subsidiary of AstraZeneca.