Learning from Real Life Data – highlights of the national ABCD programme

Dr Bob Ryder,
Clinical lead, ABCD nationwide audits of new diabetes therapies and devices
29 October, 2019
ABCD nationwide and worldwide audit programme

- New diabetes medications and devices as they start being used in real clinical practice (as opposed to research)
The New England Journal of Medicine

Volume 329, September 30, 1993
Number 14

THE EFFECT OF INTENSIVE TREATMENT OF DIABETES ON THE DEVELOPMENT AND PROGRESSION OF LONG-TERM COMPLICATIONS IN INSULIN-DEPENDENT DIABETES MELLITUS

The Diabetes Control and Complications Trial Research Group

Abstract Background Long-term microvascular and neuropathic complications cause major morbidity and mortality in patients with insulin-dependent diabetes mellitus (IDDM). We examined whether intensive treatment with the goal of maintaining blood glucose concentrations closer to the normal range would decrease the frequency and severity of these complications.

Methods A total of 1441 patients with IDDM—726 with prior (primary-episode) retinopathy and 716 without retinopathy—were randomly assigned to intensive therapy, administered either with an insulin pump or by three or more daily insulin injections and guided to frequent blood-glucose monitoring in conventional therapy with one to two daily insulin injections. The patients were followed for a mean of 6.5 years, and the appearance and progression of retinopathy and other complicating microvascular and neuropathic complications were monitored.

Results In the primary prevention cohort, intensive therapy reduced the adjusted mean rate for the development of retinopathy by 43% (95% confidence interval, 30 to 56%), as compared with conventional therapy. In the secondary prevention cohort, intensive therapy slowed the progression of retinopathy by 14% (95% confidence interval, 3 to 25%) and reduced the development of proliferative or severe nonproliferative retinopathy by 47% (95% confidence interval, 14 to 57%). In the two cohorts combined, intensive therapy reduced the occurrence of new or worsening retinopathy by 39% (95% confidence interval, 32 to 45%) and reduced the incidence of new clinical maculopathy by 57% (95% confidence interval, 28 to 74%). The overall adverse-event association with intensive therapy was a two-fold increased incidence of severe hypoglycemia, which was effectively treated. The benefit and the slowing of the progression of diabetic retinopathy, nephropathy, and neuropathy in patients with IDDM.

NEUROLOGY-painful diabetic neuropathy (IDSN) is accompanied by long-term microvascular, neurologic, and macrovascular complications. Although the daily management of EDOM is hardcover and its counterpart of metabolic decompensation, long-term complications, including retinopathy, nephropathy, neuropathy, and cardiovascular disease, have caused the adult morbidity and mortality since the introduction of insulin therapy. The prevention and amelioration of these complications have been the goal of research and clinical trials. Although studies in several models of diabetes and neurotoxicity under various experimental hyperglycemia in the pathogenesis of long-term complications, provision of clinical trials have demonstrated a consistent or extending beneficial effect of intensive therapy on these complications. A meta-analysis published from the Recklinghun Diabetes Intervention Study demonstrated a more uniform benefit of intensive therapy in patients with multifocal complications, despite the apparent absence of end-organ cardiovascular mortality in patients with diabetes during the trial. The Diabetes Control and Complications Trial was a multinational, randomized clinical trial designed to test the hypothesis that intensive therapy with frequent blood-glucose monitoring and insulin administration is associated with reduced microvascular and neuropathic complications in patients with IDDM. The intensive therapy regimen was designed to achieve blood-glucose values as close to the normal range as possible, with three or more daily insulin injections or with an insulin-pump. Conventional therapy consisted of one or two injections of insulin daily. Two groups of patients were studied to assess two different, but related, questions: Will intensive therapy delay the development of diabetic retinopathy in patients with no retinopathy (primary prevention), and will intensive...
UKPDS – EASD – Barcelona - 1998

The Lancet

Treating type 2 diabetes

The Lancet
Other great moments in the history of diabetes
My favourite moment – satellite symposium, DUK Glasgow, 2007
Development of Exenatide: An Incretin Mimetic

Exenatide (Exendin-4)
- Synthetic version of salivary protein found in the Gila monster
- Approximately 50% identity with human GLP-1
  - Binds to known human GLP-1 receptors on β cells \textit{in vitro}
  - Resistant to DPP-IV inactivation

Site of DPP-IV Inactivation
Using insulin in type 2 diabetes (HbA1c down but weight up)

Using insulin in type 2 diabetes (HbA1c down but weight up)

Exenatide – coming off insulin, improving control, and losing weight

- June 2008
  - Wt = 87 kg
  - BMI = 35.3
  - A1c = 9.0%
  - Insulin 82 units, Repaglinide 4mg tds, Metformin 1gm BD

- April 2011
  - Wt = 65 kg
  - BMI = 26.7
  - A1c = 7.2%
  - Exenatide 10ug BD, Metformin 1gm BD
ABCD nationwide and worldwide audit programme

• ABCD exenatide audit – launched December 2008
Top contributors > 100 patients

<table>
<thead>
<tr>
<th>Rank</th>
<th>Name and Affiliation</th>
<th>Hospital or Area of Service</th>
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<td>1.</td>
<td>B.M. Singh, U. A. Nayak, J. Govindan, D.N.Kalupahana</td>
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<td>Jackie Elliott et al</td>
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<td>Mark Edwards, Helen Doolittle et al</td>
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<td>Keith Sands, Lincoln County Hospital</td>
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<td>Julie Mehaffy Jean MacLeod et al</td>
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<td>Jeffrey W Stephens et al</td>
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<td>Richard Paisey et al</td>
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<td>Patrick English et al</td>
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<td>Phil Coates, Peter Daggett, Gill Green et al</td>
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</table>
ABCD nationwide and worldwide audit programme

• ABCD exenatide audit – launched December 2008
• ABCD liraglutide audit – launched Autumn 2009
Liraglutide – coming off insulin, improving control, losing weight and “never felt so good”

- September 2009
  - Wt = 93.9 kg
  - BMI = 36.7
  - A1c = 9.3%
  - Insulin 60 units, Metformin 1gm BD

- February 2012
  - Wt = 70 kg
  - BMI = 26.3
  - A1c = 7.2%
  - Liraglutide 1.2mg daily, Metformin 1gm BD
ABCD nationwide exenatide and liraglutide audits

Dr Bob Ryder,
Clinical lead, ABCD nationwide audits of new diabetes therapies and devices
29 October, 2019
ABCD nationwide exenatide and liraglutide audits

- Real-life data
  - >13000 patients from
  - >150 centres
  - >500 contributors

- There had been (by 2019)
  - 12 published papers
  - 24 abstracts
  - 13 oral presentations

http://www.diabetologists-abcd.org.uk/GLP1_Audits/PresentationsPostersAbstractsExenatide.htm
http://www.diabetologists-abcd.org.uk/GLP1_Audits/PresentationsPostersAbstractsLiraglutide.htm
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Guildford:
Edinburgh:
S, Jones G, Wilkinson R.

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Acknowledgment

The Abbreviation of exenatide audit contributors is an independent audit supported by an unrestricted grant from Eli Lilly Ltd.
ABCD nationwide exenatide and liraglutide audits

- Real-life data
  - >13000 patients from
  - >150 centres
  - >500 contributors

- There had been (by 2019)
  - 12 published papers
  - 24 abstracts
  - 13 oral presentations

http://www.diabetologists-abcd.org.uk/GLP1_Audits/PresentationsPostersAbstractsExenatide.htm
http://www.diabetologists-abcd.org.uk/GLP1_Audits/PresentationsPostersAbstractsLiraglutide.htm
What did we learn from these audits?
ABCD GLP1-RA audits v clinical trials

- The patients treated with GLP1-RAs in real clinical practice are much heavier and with much poorer glycaemic control than in clinical trials of these agents
- Nevertheless the agents have proven to be very effective

<table>
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<tr>
<th>Clinical trials combined</th>
<th>Real clinical use in UK (ABCD audit)</th>
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<td>Baseline HbA1c (%)</td>
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<td>Baseline BMI (kg/m²)</td>
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<td>Exenatide</td>
<td>32.72</td>
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<td>Liraglutide</td>
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Difference in HbA1c and weight responses – exenatide v liraglutide audits

- Patients appear to achieve greater HbA1c reduction but lesser weight reduction in the liraglutide audit as compared with the exenatide audit
- However, there was much less insulin and TZD discontinuation in the liraglutide audit
- Contributors may have learnt from the previous use of exenatide (2007-2009) to avoid over-reduction of diabetes treatment when initiating liraglutide (2009-2011)

Exenatide and liraglutide used outside NICE guidelines in substantial numbers of patients

Proven effective in outside NICE guidelines

In particular used with insulin (40% in the nationwide liraglutide audit) with good effect in many patients

The NICE 6 month weight loss (≥3% initial body weight) and HbA1c fall (≥1%) criteria are too restrictive by not taking into account the diversity of patients and their responses which can be much more one criterion than the other
Off licence use with insulin

- Off licence exenatide with insulin safe and effective in real clinical practice
- Reduction in insulin dose frequently occurred
- Weight fell
- 1 in 6 patients came off insulin
An important safety issue uncovered

- Some clinicians attempted to stop insulin when starting exenatide in order to stay within guidelines
- This led to harm to the patient in some instances
- For example there are 11 reported cases of ketosis or diabetic ketoacidosis - 7 of these occurred to patients who stopped insulin at the time of exenatide initiation
- Analysis of audit data allowed us to recommend that when starting a GLP1-RA in an insulin-treated patient not to stop the insulin but rather to tail the insulin off during treatment if response to treatment allowed
Pancreatitis

• Alarm raised (BMJ and Channel 4 Dispatches TV programme) in 2013 that incretin therapies might cause pancreatic damage

• We have been able to contribute by publishing data suggesting that in the ABCD audits there is no evidence of such a side effect:
Rates of acute pancreatitis in people with type 2 diabetes

- Not on GLP-1 based therapy:
  - between 5 and 56 per 10,000 person years
- ABCD nationwide exenatide audit
  - 12 per 10,000 person year
- ABCD nationwide liraglutide audit
  - 10.8 per 10,000 person years

http://www.diabetologists-abcd.org.uk/GLP1_Audits/pancreatitis_incidence_exenatide_audit.pdf
Rates of acute pancreatitis in people with type 2 diabetes

- Rates of acute pancreatitis in the ABCD exenatide and liraglutide audits are at the low end of the rates expected for people with type 2 diabetes in general.

AND

- 75% of the cases of acute pancreatitis in the ABCD exenatide and liraglutide audits had other causes for acute pancreatitis, in particular gall bladder disease.

Otherwise unexplained pancreatitis – is it likely to be due to the GLP-1RA?

- ...it is worth remembering that many cases of acute pancreatitis are “idiopathic” ....
- ...hence exenatide or liraglutide may not be the actual cause even if no other cause is found
GLP1-RAs in professional drivers

• Many patients with a professional drivers licence who would lose their jobs if they went onto insulin, have been able to avoid insulin, and maintain similar glycaemic outcomes and keep their jobs by using exenatide or liraglutide.
Liraglutide in renal impairment

- Liraglutide was safe and effective among patients with moderate renal impairment, which was an exclusion for use at the time.

Thong et al. Practical Diabetes 2013; 30(2): 71-76
Diabetes and NAFLD – impact on ALT

- Liraglutide can reduce ALT when it is elevated – ALT being an index of fat in the liver ....

Liraglutide with different insulin regimes

- Liraglutide was effective with all the common insulin regimes - i.e. with:
  - Basal
  - Basal bolus
  - Biphasic

Sen Gupta et al. Diabetes 2014; 63 (Suppl. 1): 1023-P
Effectiveness in South Asians

- GLP1-RAs may be less effective at improving glycaemic control amongst non-insulin treated South Asians

Thong et al. Abstract Book, 22nd World Diabetes Congress, IDF, Melbourne, Australia, 2-6 December 2013
Liraglutide – predicting treatment response

- Long duration of diabetes and insulin use both predict reduced response
Switching to liraglutide from BD exenatide or from DPP4 inhibitor

- Improvements in HbA1c and weight are seen when switching from exenatide and DPP4 inhibitors to liraglutide

Ryder and Gough. Presentation at IDF Scientific Update Satellite Meeting, Dubai, December 6 2011
Influence of age and non-use of metformin on GI side effects with liraglutide

- Older age and non-metformin use were associated with more significant GISE leading to discontinuation of liraglutide treatment.
- Reasons for these findings are unclear
Safety

In some patients the nausea, vomiting or diarrhoea was so severe that they developed transient acute kidney injury

There have been no other new safety issues uncovered
Conclusion

• We learned a lot from these audits
• Let's do some more audits!
ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutide audit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit
ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutide audit
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- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit
ABCD nationwide dapagliflozin audit

- Launched October 2014
- Findings so far .....
Year 1 Audit Overview – October 2015

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<td>Baseline HbA(_1c) (mmol/mol)</td>
<td>80.2±16.1</td>
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<td>9.5±1.5</td>
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<tr>
<td>Duration of follow up (months)*</td>
<td>6.4 (0–12.3)</td>
<td></td>
</tr>
</tbody>
</table>

Reported as mean±SD or median (IQR)*

Data presented at ABCD autumn meeting, November 2015
Reductions in HbA$_{1c}$: RCT data vs. ABCD audit


Data presented at ABCD autumn meeting, November 2015
Weight loss: RCT data vs. ABCD audit

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Add-on to metformin</th>
<th>Add-on to an SU</th>
<th>Add-on to metformin + an SU</th>
<th>Add-on to a DPP-4 inhibitor ± metformin</th>
<th>Add-on to insulin ± OADs</th>
<th>ABCD Audit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(24 weeks)</td>
<td></td>
<td>(24 weeks)</td>
<td></td>
<td></td>
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<tr>
<td>Adjusted mean change from baseline body weight (kg) at 24 weeks</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Baseline weight (kg)</td>
<td>94.2</td>
<td>86.3</td>
<td>80.6</td>
<td>88.6</td>
<td>91.0</td>
<td>94.5</td>
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<td>0.0</td>
<td>-3.2</td>
<td>-2.9*</td>
<td>-2.26*</td>
<td>-2.7*</td>
<td>-2.1*</td>
<td>-1.6*</td>
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<td>-1.0</td>
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<td>-1.5</td>
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<td>-2.0</td>
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<td>-2.5</td>
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<td>-3.0</td>
<td></td>
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<tr>
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<td></td>
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</tr>
</tbody>
</table>


Data presented at ABCD autumn meeting, November 2015
ALT response to dapagliflozin

Data presented at DUK annual professional conference, Glasgow, March 2016
Dapagliflozin – improvements sustained

Data presented at ADA meeting, New Orleans, June 2016
Data are adjusted mean and estimated difference (ED) were analysed by ANCOVA with baseline HbA1c and eGFR as covariates. DD; diabetes drugs

Data presented at ADA meeting, New Orleans, June 2016
**ABCD dapagliflozin audit**

*Figure 2: Change in HbA1c stratified by duration of diabetes*

Data are adjusted mean analysed by ANCOVA with baseline HbA1c and eGFR as covariates.

---

**ABCD liraglutide audit**

*Figure 2. Mean HbA1c changes after 26 weeks of liraglutide treatment, stratified according to duration of diabetes*

Columns show adjusted mean changes analysed by ANCOVA with baseline HbA1c as a covariate. ED: estimated difference; CI: confidence interval.

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Data presented at ADA meeting, New Orleans, June 2016


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**Thong KY et al.**

Data presented at ADA meeting, New Orleans, June 2016
Similar results between the ABCD canagliflozin and dapagliflozin* audits

*Dapagliflozin audit data presented at ADA meeting, New Orleans, June 2016
Effect of dapagliflozin on HbA1c and weight after its addition to various combinations of other diabetes medications: ABCD nationwide dapagliflozin audit*

Mean HbA1c fall (mmol/mol) from baseline at median of 26 weeks

-15.0
-12.0
-9.0
-6.0
-3.0
0.0

Mean Weight fall (kg) from baseline at median of 26 weeks

-15.0
-12.0
-9.0

Group 1 (Met)
Group 2 (Met+SU)
Group 3 (Met+DPP-4i)
Group 4 (Any Pio)
Group 5 (Any GLP-1)
Group 6 (Any Insulin)

-9.8*
-12.0*
-13.3*
-10.2*
-9.7*
-9.2*

-3.1*
-3.8*
-2.9*
-3.4*
-3.8*
-2.0*

* p<0.001

* EASD 2016 Poster Presentation: M. Yadagiri, P. Sen Gupta, R.E.J. Ryder et al on behalf of all ABCD nationwide dapagliflozin audit contributors
Data presented at ADA meeting, San Diego, June 2017
Conclusion

- Dapagliflozin reduces HbA1c, weight, BMI, systolic BP and ALT by statistically and clinically significant amounts in normal and mild renal impairment.
- In moderate renal impairment, there is a reduction in weight and ALT but has no significant impact on HbA1c or systolic BP.

Data presented at ADA meeting, San Diego, June 2017
ABCD nationwide canagliflozin audit

• Launched January 2016
• Findings so far .....
By first return to clinic at median 14 weeks after starting canagliflozin

- Mean HbA1c fell by 0.8% from 9.1% to 8.3%
- Mean weight fell by 2.6 kg from 100.4 kg to 97.8 kg
- Significant falls in BMI, systolic blood pressure and alanine aminotransferase
Between first return to clinic and second return to clinic continued significant falls in:

- HbA1c
- Weight
- Systolic blood pressure
- Alanine aminotransferase

**EASD 2018 Poster Presentation: A. Puttanna et al, on behalf of all ABCD nationwide canagliflozin audit contributors**
Between first return to clinic and second return to clinic continued significant falls in:

- **HbA1c**
- **Weight**
- **Systolic blood pressure**
- **Alanine aminotransferase**

EASD 2018 Poster Presentation: A. Puttanna et al, on behalf of all ABCD nationwide canagliflozin audit contributors
Between first return to clinic and second return to clinic continued significant falls in:

- HbA1c
- Weight
- Systolic blood pressure
- Alanine aminotransferase
Similar falls in HbA1c when canagliflozin added to:

- One other OHA
- Two other OHAs
- Three other OHAs
- Slightly less when added to insulin+/- OHA
Change in HbA1c at median (IQR) 4.1 (3-6.1) months after starting canagliflozin, stratified by duration of diabetes.

- 0-5 years (n=212): -0.87
- 6-10 years (n=108): -0.88
- >10 years (n=114): -0.86

p=0.99 for effect of duration
Similar results between the ABCD canagliflozin and dapagliflozin* audits

*Dapagliflozin audit data presented at ADA meeting, New Orleans, June 2016
ABCD nationwide Empagliflozin audit

• Launched April 2017
• Findings so far .....
By first return to clinic after starting empagliflozin

- Mean Hba1c fell by 1.35% from 9.41% to 8.06%
- Mean weight fell by 3.6 kg from 99.6 kg to 96.0 kg
The higher baseline HbA1c or weight achieve greater the reduction of HbA1c or weight
Better renal function predicts better HbA1c improvement, but not greater weight loss
ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutide audit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- **ABCD degludec audit**
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit
ABCD nationwide degludec audit – findings so far

http://www.diabetologists-abcd.org.uk/Degludec/Degludec_Audit.htm
Degludec audit - reasons for switching to degludec from another basal insulin

<table>
<thead>
<tr>
<th>RATIONALE FOR STARTING DEGLUDEC? (Please tick all that apply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Problems with hypoglycaemia</td>
</tr>
<tr>
<td>Poor compliance, e.g. need flexible injection timing</td>
</tr>
<tr>
<td>Need of more than 80 IU/day</td>
</tr>
<tr>
<td>Needs OD basal insulin</td>
</tr>
<tr>
<td>Considering going into a pump</td>
</tr>
<tr>
<td>To fit in with variably timed visit by third party to administer (e.g. district nurse, relative...)</td>
</tr>
<tr>
<td>Intra-subject variability of glucometries with current basal insulin</td>
</tr>
</tbody>
</table>

Screenshot from the ABCD degludec nationwide audit on-line form
Effect of insulin degludec on hypoglycaemia

Change in frequency of hypoglycaemia where reason for switching to insulin degludec was hypoglycaemia

<table>
<thead>
<tr>
<th></th>
<th>Reduced</th>
<th>Same</th>
<th>Increased</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T1DM</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>31</td>
<td>16</td>
<td>0</td>
<td>p &lt; .000001</td>
</tr>
<tr>
<td>Severe</td>
<td>16</td>
<td>13</td>
<td>1</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>Nocturnal</td>
<td>22</td>
<td>12</td>
<td>0</td>
<td>P &lt; .00001</td>
</tr>
<tr>
<td><strong>T2DM</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>p &lt; .05</td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>12</td>
<td>0</td>
<td>ns</td>
</tr>
<tr>
<td>Nocturnal</td>
<td>7</td>
<td>12</td>
<td>1</td>
<td>ns</td>
</tr>
</tbody>
</table>
Effect of insulin degludec on hypoglycaemia

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Data presented at EASD meeting, Lisbon, September 2017
Effect of insulin degludec on hypoglycaemia

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<td>1</td>
<td>ns</td>
</tr>
</tbody>
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Data presented at EASD meeting, Lisbon, September 2017
Effect of insulin degludec on HbA1c

Change in HbA1c (mmol/mol) after switching to insulin degludec from another basal insulin

<table>
<thead>
<tr>
<th>Type of diabetes</th>
<th>T1D</th>
<th>T2D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for degludec</td>
<td>Hypoglycaemia</td>
<td>Other</td>
</tr>
<tr>
<td>n</td>
<td>100</td>
<td>41</td>
</tr>
<tr>
<td>HbA1c before degludec</td>
<td>68.2 ± 20.4</td>
<td>87.4 ± 24.4</td>
</tr>
<tr>
<td>HbA1c after degludec</td>
<td>69.5 ± 22.2</td>
<td>80.2 ± 22.5</td>
</tr>
<tr>
<td>Change in HbA1c</td>
<td>+1.0 ± 1.3 (ns)</td>
<td>-7.2 ± 1.9 * (p &lt; .001)</td>
</tr>
</tbody>
</table>

Data presented at EASD meeting, Lisbon, September 2017
Effect of insulin degludec on HbA1c

Change in HbA1c (mmol/mol) after switching to insulin degludec from another basal insulin

<table>
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</tr>
</tbody>
</table>

Data presented at EASD meeting, Lisbon, September 2017
Effect of insulin degludec on weight

Change in weight (kg) after switching to insulin degludec from another basal insulin

<table>
<thead>
<tr>
<th>Type of diabetes</th>
<th>T1D</th>
<th>T2D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for degludec</td>
<td>Hypoglycaemia</td>
<td>Other</td>
</tr>
<tr>
<td>n</td>
<td>83</td>
<td>52</td>
</tr>
<tr>
<td>Weight before degludec</td>
<td>74.5 ± 14.4</td>
<td>79.4 ± 20.5</td>
</tr>
<tr>
<td>Weight after degludec</td>
<td>74.3 ± 14.0</td>
<td>80.5 ± 20.6</td>
</tr>
<tr>
<td>Change in weight</td>
<td>-0.2 ± 0.6 (ns)</td>
<td>+1.1 ± 0.5 * (p &lt; .05)</td>
</tr>
</tbody>
</table>

Data presented at EASD meeting, Lisbon, September 2017
Effect of insulin degludec on weight

Change in weight (kg) after switching to insulin degludec from another basal insulin

<table>
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<tr>
<th>Type of diabetes</th>
<th>T1D</th>
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Effect of insulin degludec on weight

Change in weight (kg) after switching to insulin degludec from another basal insulin

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<tbody>
<tr>
<td>Reason for degludec</td>
<td>Hypoglycaemia</td>
<td>Other</td>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>83</td>
<td>52</td>
<td>37</td>
</tr>
<tr>
<td>Weight before degludec</td>
<td>74.5 ± 14.4</td>
<td>79.4 ± 20.5</td>
<td>87.9 ± 16.3</td>
</tr>
<tr>
<td>Weight after degludec</td>
<td>74.3 ± 14.0</td>
<td>80.5 ± 20.6</td>
<td>85.6 ± 15.1</td>
</tr>
<tr>
<td>Change in weight</td>
<td>-0.2 ± 0.6 <em>(ns)</em></td>
<td>+1.1 ± 0.5 <em>(p &lt; .05)</em></td>
<td>-2.4 ± 1.8 <em>(p &lt; 0.05)</em></td>
</tr>
</tbody>
</table>

Data presented at EASD meeting, Lisbon, September 2017
ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutide audit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
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- ABCD empagliflozin audit
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- **ABCD I DegLira audit**
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit
Treat to Target – IDegLira Vs Glargine

HbA$_{1c}$ over time

ETD = -0.59%
p<0.001

EOT: 7.1%
\(\Delta: -1.13\)

EOT: 6.6%
\(\Delta: -1.81\)
Treat to Target – IDegLira Vs Glargine

Change in body weight over time

IDegLira (n=278)

Glar (n=279)

ETD = -3.20 kg, 
p<0.001

EOT: 89.1 kg
Δ: +1.8

EOT: 86.9 kg
Δ: -1.4

IDegLira is not licensed for weight loss. Change in bodyweight from baseline was a secondary endpoint in DUAL V, a 26 week study.
ABCD nationwide and worldwide audit programme

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Endobarrier – implantable duodenal-jejunal liner

- Fluoropolymer wall
- Nitinol Anchor
- 60 cm impermeable sleeve
- Minimally invasive
EndobARRIER – implantable duodenal-jejunal liner

- Fluoropolymer wall
- Nitinol Anchor
- 60 cm impermeable sleeve
- Minimally invasive
EndobARRIER – implantable duodenal-jejunal liner

- Roux-en-Y gastric bypass surgery
- Fluoropolymer wall
- Nitinol Anchor
- 60 cm impermeable sleeve
- Minimally invasive
851 patients

28 Centres, 8 Countries, 4 Continents
**Background**

Endobard® (G DT Dynamics, Boston, USA), also known as the duodenal jejunal bypass sleeve, is a 60 cm long, inflatable polyurethane sleeve which is implanted by endoscopy into the first part of the small intestine where it remains for about 1 year (Figure 1). It is held in place by a velcro anchor, such that food passes through it in contact with the small intestine, thereby interfering with the normal digestive processes that occur in this region. The endoscopic insertion and removal of Endobard® are day case procedures, performed in less than an hour under general anaesthesia or heavy sedation. This form of reversible bariatric procedure has been shown to reduce weight and improve glycaemic control in patients with diabetes and obesity.

**Methods**

We invited Endobard® users from centres worldwide to register to enter the before and after data from their Endobard® treated patients into the registry.

**References**


**Table 1**: Baseline demographics of the 873 patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.1 ± 14.5</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>51.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>41.6 ± 9.2</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>84.3</td>
</tr>
</tbody>
</table>

**Table 2**: Changes in weight, HbA1c, systolic BP and cholesterol

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Endobard® Explant</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>852</td>
<td>121.8 ± 28.9</td>
<td>-137.9 ± 8.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>101</td>
<td>5.4 ± 1.4</td>
<td>-1.0 ± 0.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>136</td>
<td>135 ± 18.2</td>
<td>0.0 ± 1.0</td>
<td>0.866</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>20</td>
<td>7.0 ± 2.0</td>
<td>-0.9 ± 0.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Summary and Conclusion**

In this analysis from the worldwide Endobard® registry, the mean weight loss during the period of Endobard® implantation was 13.7 kg with associated improvements in glycaemic control, blood pressure and cholesterol. The BMI increased from the baseline HbA1c, the greater the fall in HbA1c with a mean fall of 3.3% with those with a baseline HbA1c ≥ 10. The rate of serious adverse events was 4.2% with the majority of these (2.5%) being gastrointestinal bleeds.

The rate of early removal for hepatic abscess (1.1%) was significantly less than that the 3.3% rate found in the US pivotal trial. All patients with a serious adverse event made a full recovery and most experienced considerable benefit from the treatment despite the adverse event. The effects of Endobard® therapy on glycaemic control, weight and blood pressure are likely to reduce the complications of diabetes. This international data from the Endobard® worldwide registry suggests that the likely benefits of Endobard® treatment, outweigh the risks.
Table 1: Baseline demographics of the 871 patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n=871</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.1±10.5</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>53.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>41.6±9.2</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>84.2</td>
</tr>
</tbody>
</table>

Table 2: Changes in weight, HbA1c, systolic BP and cholesterol

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>Baseline</th>
<th>EndoBarrier Explant</th>
<th>Difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>662</td>
<td>121.6±25.8</td>
<td>107.9±2644</td>
<td>-13.7±9.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>501</td>
<td>8.2±1.8</td>
<td>7.0±1.2</td>
<td>-1.2±1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>298</td>
<td>137.9±18.2</td>
<td>130.5±16.8</td>
<td>-7.4±20.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>332</td>
<td>4.8±1.2</td>
<td>4.3±1.0</td>
<td>0.55±0.98</td>
<td>&lt;0.001</td>
</tr>
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</table>

EASD 2019 Poster Presentation: K. Laubner et al,
Table 1. Impact of EndoBarrier on HbA1c depending on baseline HbA1c.
Conclusion – the higher the baseline HbA1c the greater the impact. Values are mean±SD

<table>
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<tr>
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<th>At removal</th>
<th>Difference</th>
<th>P value</th>
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<tr>
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<tr>
<td>≥ 7</td>
<td>377</td>
<td>8.9±1.5 to</td>
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<td>1.6±1.5</td>
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<tr>
<td>≥ 8</td>
<td>262</td>
<td>9.6±1.4</td>
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<tr>
<td>≥ 9</td>
<td>143</td>
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<tr>
<td>≥ 10</td>
<td>86</td>
<td>11.2±1.0</td>
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<tr>
<td>HbA1c (%)</td>
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FDA puts hold on pivotal GI Dynamics trial for obesity device due to bacterial infection

by Stacy Lawrence | Mar 6, 2015 10:27am

The U.S. Food and Drug Administration has placed a hold on enrollment in the ongoing U.S. pivotal trial for the EndoBarrier. The device is a gastric liner from GI Dynamics that is intended to inhibit the absorption of nutrients, thereby providing weight loss and addressing obesity and Type 2 diabetes.

The FDA hold was due to four cases of bacterial infection of the liver, or hepatic abscesses, in the 325 trial subject population. This is a known adverse event related to use of the EndoBarrier—but it presented at higher rates than expected in the trial. The company had set relative thresholds for an anticipated incident rate of hepatic abscesses in the trial; the incident with the fourth patient exceeded that and triggered an analysis.

On a conference call, GI Dynamics’ President and CEO Michael Dale said the infections are “likely related to the anchoring system interacting with the duodenum.”

The EndoBarrier is a flexible, tube-shaped liner that is inserted endoscopically and placed at the beginning of the small intestine for up to one year. After that, it’s removed during another endoscopic procedure.

Of the more than 2,900 commercial EndoBarrier units shipped outside the U.S. since 2009, about 1% of these have been implicated in hepatic abscesses cases. Enrolled patients in the trial will continue to be the subject of data collection in the trial that’s been put on hold. Patients presenting with bacterial infection due to the EndoBarrier typically have the device removed and are treated with antibiotics to resolve the infection.

The company said it has implemented “several risk mitigation strategies” in the pivotal trial and is working with the FDA to resume enrollment.

Dale said the company is “expeditiously working to submit additional risk/benefit information as requested by the FDA to resume the trial as quickly as possible.”

Already a penny stock, GI Dynamics shares were cut in half on the trial hold news to 30.15.

- here is the release

March 2015

Hepatic abscess rate 3.5%
Table 1: Serious adverse events in 871 EndoBarrier treated patients (GI = gastrointestinal).

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<tr>
<th>Serous Adverse Event</th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td>Early removal because of GI bleed</td>
<td>22</td>
<td>2.5</td>
</tr>
<tr>
<td>Liver abscess (early removal = 7/10; found at time of routine explant = 3/10)</td>
<td>10</td>
<td>1.1</td>
</tr>
<tr>
<td>Early removal because of pancreatitis</td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>Early removal because of cholecystitis</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Abdominal abscess due to small perforation of bowel in relation to EndobARRIER</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Liver abscess after prolonged implant (nearly 2 years EndoBarrier treatment; lost 37 kg)</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>37</td>
<td>4.2</td>
</tr>
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</tr>
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<tr>
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<td>33</td>
<td>3.8</td>
</tr>
<tr>
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<td>31</td>
<td>3.6</td>
</tr>
<tr>
<td>Early removal because of GI symptoms - EndobARRIER had migrated</td>
<td>18</td>
<td>2.1</td>
</tr>
<tr>
<td>Early removal because of liner obstruction</td>
<td>7</td>
<td>0.8</td>
</tr>
<tr>
<td>Minor GI bleeding. EndobARRIER not removed</td>
<td>5</td>
<td>0.6</td>
</tr>
<tr>
<td>Precautionary hospitalisation because of transient GI problems at time of removal</td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td>Hospitalisation because difficult removal - needed two attempts</td>
<td>3</td>
<td>0.3</td>
</tr>
<tr>
<td>Transient obstruction of device cleared at endoscopy - device not removed</td>
<td>3</td>
<td>0.3</td>
</tr>
<tr>
<td>Precautionary early removal because of asymptomatic EndobARRIER migration</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>105</td>
<td>12.5</td>
</tr>
<tr>
<td>Serous Adverse Event</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------------</td>
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GI Dynamics wins FDA nod for pivotal US EndoBarrier trial

AUGUST 13, 2018 BY FIONA OEDSFORD — LEAVE A COMMENT

GI Dynamics (ASX:GDI) said today it won FDA investigational device exemption approval to launch a pivotal trial of its EndoBarrier device designed for treating patients with type 2 diabetes and obesity, pending Institutional Review Board approval.

The EndoBarrier device is a plastic gut sleeve designed to prevent the absorption of nutrients from food as it exits the stomach and enters the intestinal tract to treat type 2 diabetes and obesity, the Lexington, Mass.-based company said.

The approval is a boon for the company, which has faced a number of hurdles with its device over the past few years, including shutting down an initial FDA approved study, being pulled off the shelves in Australia and losing its CE Mark approval in the European Union.

"It’s the first good news and a positive sign of all the hard work the team has been putting in over the last two years. This is the first sign that the results are starting to turn around, so we’re very excited about it," CEO Scott Schoener, who took over the company in March 2015, told MassDevice.com in an interview.

August 2018

GI Dynamics’ 2nd Chance at an EndoBarrier Pivotal Trial

The company has had significant struggles with the EndoBarrier in the past, but a nod from FDA and the IRB to begin a new pivotal trial might be step back in the right direction for the technology.

By Omar Ford
February 14, 2019 in Regulatory and Compliance

GI Dynamics’ fortunes might be changing, as the embattled device maker has crossed the last hurdle in its bid for the approval of a new pivotal trial to evaluate its obesity and diabetes treatment device, the EndoBarrier.

The company recently announced it had received Institutional Review Board approval to launch a pivotal trial of the EndoBarrier. GI Dynamics has struggled significantly with the device in the past (more on that later), but until recently it has had some success.

In August of 2018, FDA gave a nod to the EndoBarrier’s pivotal trial. The last step was for the IRB to...
ABCD nationwide and worldwide audit programme

- ABCD exenatide audit
- ABCD liraglutide audit
- ABCD exenatide QW audit
- ABCD dapagliflozin audit
- ABCD canagliflozin audit
- ABCD empagliflozin audit
- ABCD degludec audit
- ABCD IDegLira audit
- Endobarrier worldwide registry
- ABCD FreeStyle Libre audit
- ABCD semaglutide audit
- ABCD testosterone in men with type 2 diabetes audit
ABCD FreeStyle Libre Audit
ABCD FreeStyle Libre Audit

The ABCD FSL Audit aims to explore the impact of the FSL on:

• HbA1c
• Hypoglycaemia awareness
• Resource utilisation: hospital admissions
• User satisfaction
• Diabetes related distress
• Discontinuation rate and causes
As of May 29, 2019 there are 296 users registered to the audit at 156 sites in 114 centres contributing data on 6644 patients.
ABCD FreeStyle Libre Audit

- **Hypoglycaemia**
  - Mean GOLD score reduced from 2.85 to 2.46 (P<0.0001)
  - FSL use was associated with reversal of impaired awareness of hypoglycaemia (IAH):
    - 33% had IAH at baseline; 23% at follow up
    - Hypoglycaemia related admissions reduced from 2.71% to 0.5%
  - 79% (966/1234) reported that with use of FSL they were able to reduce the proportion of time in hypoglycaemia
    - 31% (372/1200) reported a reduced rate of hypoglycaemia
    - 39% (380/968) reported reduced nocturnal hypoglycaemia
ABCD FreeStyle Libre Audit

• **Diabetes Distress**
  – Diabetes Distress Scores improved from 3 (2-4) at baseline to 2 (1-3) at follow-up
  P<0.0001

• **HbA1c**
  – Change in HbA1c: -0.6% (6 mmol/mol) (P<0.0001)

*The audit continues in particular to gather longer term results*
ABCD nationwide and worldwide audit programme

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ABCD NATIONWIDE AUDIT OF TESTOSTERONE DEFICIENCY IN MEN WITH TYPE 2 DIABETES

Questionnaire developed – audit tool being built
Lead – Professor Hugh Jones, Barnsley
TESTOSTERONE DEFICIENCY IN MEN WITH TYPE 2 DIABETES

• Asking about erectile dysfunction should be part of routine annual review in all men with diabetes
• If present should measure testosterone and, if low, repeat with SHBG, LH, FSH
TESTOSTERONE DEFICIENCY IN MEN WITH TYPE 2 DIABETES

• High prevalence - 40% of men with type 2 diabetes have symptomatic testosterone deficiency
• Testosterone deficiency is associated with an adverse effect on cardiovascular risk factors, osteoporosis, reduced muscular strength (including frailty), anaemia and psychological well-being
• Testosterone deficiency is also associated with an increased mortality in type 2 diabetes and independently in cardiovascular disease
• Testosterone replacement has been shown to improve insulin resistance, lower HbA1c and cholesterol as well as reduce body weight and mortality
New ABCD audit imminent

The ABCD Nationwide Testosterone Deficiency audit is an independent audit supported by an unrestricted grant from Besins Healthcare.

ABCDF NationWide Audit of Testosterone Deficiency in Men with Type 2 Diabetes

FIRST VISIT DATA COLLECTION FORM

Date: /

Clinician: ___________________________ Clinician’s email: ___________________________ Centre ID: ___________________________

PATIENT IDENTIFICATION

AFFIX PATIENT LABEL

FORENAME: ___________________________
SURNAME: ___________________________
DoB: / / [dd/mm/yyyy]
NHS Number: ___________________________

Ethnicity
- Afro-Caribbean
- Asian
- Oriental
- White

Marital Status
- Married/Civil
- Single
- Separated/Divorced
- Widowed

DIAGNOSIS OF HYPOGONADISM MUST COMPRIZE BOTH SYMPTOMS AND LOW TESTOSTERONE
Testosterone replacement therapy is being used more commonly in men with hypogonadism and T2D

- TO DETERMINE THE CLINICAL BENEFITS OF TESTOSTERONE REPLACEMENT THERAPY
  Effect on symptoms of testosterone deficiency
  (a) Sexual  (b) Physical (c) Psychological
  Glycaemic control, Lipid profile, body weight and change in diabetes medication.
  Effect of Testosterone therapy on Diabetes Distress and to assess normalisation of testosterone levels on treatment
PURPOSE OF THE AUDIT - 2

• TO DETERMINE THE SAFETY OF TESTOSTERONE REPLACEMENT THERAPY
  – To determine how frequently hypoglycaemia is reported after initiation of testosterone therapy
  – Secondary polycythaemia – haematocrit >0.54
  – Cardiovascular events
  – Rate and cause of hospitalisation
An audit that is not yet on the list
ABCD Nationwide Audit of Open Artificial Pancreas Systems

ABCD research fellow – Dr Tom Crabtree
Dr Emma Wilmot lead - Derby
Please be active in the current ABCD audits

Especially:

• FreeStyle Libre
• Semaglutide
• Testosterone – when it starts
• Open APS – start making a note of your patients ready to contact them – they are very enthusiastic and want to help!
Using insulin in type 2 diabetes (HbA1c down but weight up)

ABCD nationwide and worldwide audit programme

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GLP-1 receptor agonists
ABCD nationwide and worldwide audit programme

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- ABCD FreeStyle Libre audit
- **ABCD semaglutide audit**
- ABCD testosterone in men with type 2 diabetes audit
ABCD Nationwide Semaglutide Audit

Dr Bob Ryder
ABCD-DPC, London
October 29, 2019
Semaglutide

- **Semaglutide** now accepted onto most formularies and can be readily prescribed.
- **Semaglutide** is considerably more effective at reducing HbA1c and Weight than other GLP1-receptor agonists. **It is the same price or cheaper**
## Previous ABCD GLP1 RA Nationwide Audits

- Combined trials v real world

<table>
<thead>
<tr>
<th></th>
<th>Clinical trials combined</th>
<th>Real clinical use in UK (ABCD audit)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Baseline HbA$_{1c}$ (%)</td>
</tr>
<tr>
<td>Exenatide</td>
<td>8.37</td>
<td>9.47</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>8.5</td>
<td>9.40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Baseline BMI (kg/m$^2$)</td>
</tr>
<tr>
<td>Exenatide</td>
<td>32.72</td>
<td>39.8</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>31</td>
<td>39.0</td>
</tr>
</tbody>
</table>
**HbA$_1$c changes in SUSTAIN 1–5 and 7**

**CHANGE FROM BASELINE IN HbA$_1$c**

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Add-on to OAD</th>
<th>Vs./add-on to basal insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline HbA$_1$c (%)</strong>:</td>
<td><strong>SUSTAIN 1$^1$</strong></td>
<td><strong>SUSTAIN 2$^2$</strong></td>
</tr>
<tr>
<td></td>
<td>8.1</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>128</td>
<td>309</td>
</tr>
<tr>
<td>n=</td>
<td>130</td>
<td>409</td>
</tr>
<tr>
<td></td>
<td>129</td>
<td>407</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Change from baseline in HbA$_1$c (%)</th>
<th>0</th>
<th>-0.2</th>
<th>-0.4</th>
<th>-0.6</th>
<th>-0.8</th>
<th>-1.0</th>
<th>-1.2</th>
<th>-1.4</th>
<th>-1.6</th>
<th>-1.8</th>
<th>-2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Semaglutide 0.5 mg</strong></td>
<td>*</td>
<td>-1.5</td>
<td>*</td>
<td>-1.5</td>
<td>-1.8</td>
<td>*</td>
<td>-1.8</td>
<td>*</td>
<td>-1.8</td>
<td>*</td>
<td>-1.8</td>
</tr>
<tr>
<td><strong>Semaglutide 1.0 mg</strong></td>
<td>*</td>
<td>-1.6</td>
<td>*</td>
<td>-1.6</td>
<td>-1.2</td>
<td>*</td>
<td>-1.2</td>
<td>*</td>
<td>-1.2</td>
<td>*</td>
<td>-1.2</td>
</tr>
<tr>
<td><strong>Exenatide OW 2.0 mg</strong></td>
<td>*</td>
<td>-1.3</td>
<td>*</td>
<td>-1.3</td>
<td>-1.1</td>
<td>*</td>
<td>-1.1</td>
<td>*</td>
<td>-1.1</td>
<td>*</td>
<td>-1.1</td>
</tr>
<tr>
<td><strong>Dulaglutide 0.75 mg</strong></td>
<td>*</td>
<td>-1.6</td>
<td>*</td>
<td>-0.9</td>
<td>-0.5</td>
<td>*</td>
<td>-0.5</td>
<td>*</td>
<td>-0.5</td>
<td>*</td>
<td>-0.5</td>
</tr>
<tr>
<td><strong>Dulaglutide 1.5 mg</strong></td>
<td>*</td>
<td>-1.5</td>
<td>*</td>
<td>-1.5</td>
<td>-1.1</td>
<td>*</td>
<td>-1.1</td>
<td>*</td>
<td>-1.1</td>
<td>*</td>
<td>-1.1</td>
</tr>
<tr>
<td><strong>Placebo</strong></td>
<td>*</td>
<td>-0.4</td>
<td>*</td>
<td>-0.4</td>
<td>-0.9</td>
<td>*</td>
<td>-0.9</td>
<td>*</td>
<td>-0.9</td>
<td>*</td>
<td>-0.9</td>
</tr>
<tr>
<td><strong>Sitagliptin 100 mg</strong></td>
<td>*</td>
<td>-1.2</td>
<td>*</td>
<td>-1.2</td>
<td>-0.8</td>
<td>*</td>
<td>-0.8</td>
<td>*</td>
<td>-0.8</td>
<td>*</td>
<td>-0.8</td>
</tr>
<tr>
<td><strong>IGlar</strong></td>
<td>*</td>
<td>-1.4</td>
<td>*</td>
<td>-1.4</td>
<td>-0.1</td>
<td>*</td>
<td>-0.1</td>
<td>*</td>
<td>-0.1</td>
<td>*</td>
<td>-0.1</td>
</tr>
</tbody>
</table>

*p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly*

**HbA<sub>1c</sub> changes in SUSTAIN 1–5 and 7**

**CHANGE FROM BASELINE IN HbA<sub>1c**

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline HbA&lt;sub&gt;1c&lt;/sub&gt; (%)</th>
<th>n=</th>
<th>Change from baseline in HbA&lt;sub&gt;1c&lt;/sub&gt; (%)</th>
<th>Change from baseline in HbA&lt;sub&gt;1c&lt;/sub&gt; (mmol/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SUSTAIN 1&lt;sup&gt;1&lt;/sup&gt;</td>
<td>8.1</td>
<td>128</td>
<td>-1.5</td>
<td>-0.4</td>
</tr>
<tr>
<td>SUSTAIN 2&lt;sup&gt;2&lt;/sup&gt;</td>
<td>8.1</td>
<td>130</td>
<td>-1.6</td>
<td>-0.4</td>
</tr>
<tr>
<td>SUSTAIN 3&lt;sup&gt;3&lt;/sup&gt;</td>
<td>8.3</td>
<td>129</td>
<td>-1.5</td>
<td>-0.4</td>
</tr>
<tr>
<td>SUSTAIN 7&lt;sup&gt;4&lt;/sup&gt;</td>
<td>8.2</td>
<td>301</td>
<td>-1.5</td>
<td>-0.4</td>
</tr>
<tr>
<td>SUSTAIN 4&lt;sup&gt;5&lt;/sup&gt;</td>
<td>8.2</td>
<td>300</td>
<td>-1.4</td>
<td>-0.4</td>
</tr>
<tr>
<td>SUSTAIN 5&lt;sup&gt;6&lt;/sup&gt;</td>
<td>8.4</td>
<td>299</td>
<td>-1.6</td>
<td>-0.4</td>
</tr>
</tbody>
</table>

*<sup>p</sup><0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly*

ABCD liraglutide audit – the higher the baseline HbA1c the bigger the fall

Table 3 Median HbA1c change, proportion of patients achieving HbA1c reduction of ≥1% and proportion of patients achieving target HbA1c of 7% among patients treated with liraglutide in the ABCD audit; results stratified by baseline HbA1c and use of insulin.

<table>
<thead>
<tr>
<th></th>
<th>7.0-7.9</th>
<th>8.0-8.9</th>
<th>9.0-9.9</th>
<th>10.0-10.9</th>
<th>11.0-11.9</th>
<th>12.0-12.9</th>
<th>13.0-13.9</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-insulin-treated</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>91</td>
<td>158</td>
<td>161</td>
<td>106</td>
<td>60</td>
<td>35</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Median HbA1c change, (%)</td>
<td>-0.7</td>
<td>-1.1</td>
<td>-1.4</td>
<td>-1.9</td>
<td>-2.6</td>
<td>-3.1</td>
<td>-2.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Proportion achieving ≥1% reduction, n(%)</td>
<td>30 (33.0)</td>
<td>95 (60.1)</td>
<td>103 (64.0)</td>
<td>77 (72.6)</td>
<td>51 (85.0)</td>
<td>28 (80.0)</td>
<td>8 (72.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Proportion achieving HbA1c of 7%, n(%)</td>
<td>50 (55.0)</td>
<td>58 (36.7)</td>
<td>35 (21.7)</td>
<td>25 (23.6)</td>
<td>11 (18.3)</td>
<td>4 (11.4)</td>
<td>1 (9.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Insulin-treated</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>73</td>
<td>124</td>
<td>156</td>
<td>98</td>
<td>61</td>
<td>35</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Median HbA1c change, (%)</td>
<td>-0.2</td>
<td>-0.5</td>
<td>-1.1</td>
<td>-1.3</td>
<td>-1.3</td>
<td>-1.8</td>
<td>-3.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Proportion achieving ≥1% reduction, n(%)</td>
<td>11 (15.1)</td>
<td>41 (31.3)</td>
<td>82 (52.6)</td>
<td>61 (62.2)</td>
<td>36 (59.0)</td>
<td>24 (68.6)</td>
<td>9 (90.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Proportion achieving HbA1c of 7%, n(%)</td>
<td>28 (38.4)</td>
<td>18 (14.5)</td>
<td>21 (13.5)</td>
<td>8 (8.2)</td>
<td>3 (4.9)</td>
<td>1 (2.9)</td>
<td>2 (20.0)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Median HbA1c change results are shown as median [interquartile range].

Results show patients are more likely to achieve ≥1% HbA1c reduction when baseline HbA1c is higher and conversely more likely to achieve target HbA1c of 7% if baseline HbA1c is lower.
HbA$_{1c}$ changes in SUSTAIN 1–5 and 7

**CHANGE FROM BASELINE IN HbA$_{1c}$**

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Add-on to OAD</th>
<th>Vs./add-on to basal insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUSTAIN 1</strong></td>
<td><strong>SUSTAIN 2</strong></td>
<td><strong>SUSTAIN 3</strong></td>
</tr>
<tr>
<td>Baseline HbA$_{1c}$ (%)</td>
<td>8.1</td>
<td>8.1</td>
</tr>
<tr>
<td>n=</td>
<td>128</td>
<td>130</td>
</tr>
</tbody>
</table>

Fall in HbA1c of 1.65% from baseline of 8.2% in the clinical trials
- Will the fall be more from higher HbA1c in the real world?
- How much greater will it be?
- The audit will tell us!

* $p<0.0001$ vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

Switching to semaglutide from another GLP-1RA
**HbA<sub>1c</sub> changes in SUSTAIN 1–5 and 7**

**CHANGE FROM BASELINE IN HbA<sub>1c</sub>**

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Add-on to OAD</th>
<th>Vs./add-on to basal insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline HbA&lt;sub&gt;1c&lt;/sub&gt; (%):</strong> 8.1</td>
<td><strong>SUSTAIN 2</strong> 8.1</td>
<td><strong>SUSTAIN 4</strong> 8.2</td>
</tr>
<tr>
<td><strong>n=</strong> 128</td>
<td>409</td>
<td>409</td>
</tr>
<tr>
<td><strong>n=</strong> 130</td>
<td>409</td>
<td>360</td>
</tr>
<tr>
<td><strong>n=</strong> 129</td>
<td>407</td>
<td>360</td>
</tr>
<tr>
<td><strong>Change from baseline in HbA&lt;sub&gt;1c&lt;/sub&gt; (%)</strong></td>
<td><strong>Change from baseline in HbA&lt;sub&gt;1c&lt;/sub&gt; (%)</strong></td>
<td><strong>Change from baseline in HbA&lt;sub&gt;1c&lt;/sub&gt; (mmol/mol)</strong></td>
</tr>
<tr>
<td>-1.5</td>
<td>-0.5</td>
<td>-0.8</td>
</tr>
<tr>
<td>-1.6</td>
<td>-1.5</td>
<td>-0.5</td>
</tr>
<tr>
<td>-1.6</td>
<td>-1.8</td>
<td>-1.2</td>
</tr>
<tr>
<td>-1.6</td>
<td>-1.4</td>
<td>-1.4</td>
</tr>
</tbody>
</table>

*<p><i>p<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly</i>
HbA$_{1c}$ changes in SUSTAIN 1–5 and 7

**CHANGE FROM BASELINE IN HbA$_{1c}$**

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Add-on to OAD</th>
<th>Vs./add-on to basal insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline HbA$_{1c}$ (%):</strong></td>
<td><strong>Baseline HbA$_{1c}$ (%):</strong></td>
<td><strong>Baseline HbA$_{1c}$ (%):</strong></td>
</tr>
<tr>
<td>SUSTAIN 1$^1$</td>
<td>SUSTAIN 2$^2$</td>
<td>SUSTAIN 3$^3$</td>
</tr>
<tr>
<td>8.1</td>
<td>8.1</td>
<td>8.3</td>
</tr>
<tr>
<td>128</td>
<td>409</td>
<td>404</td>
</tr>
<tr>
<td>130</td>
<td>409</td>
<td>405</td>
</tr>
<tr>
<td>129</td>
<td>407</td>
<td>301</td>
</tr>
<tr>
<td>*</td>
<td>*</td>
<td>299</td>
</tr>
<tr>
<td>*</td>
<td>*</td>
<td>300</td>
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<td>*</td>
<td>*</td>
<td>299</td>
</tr>
<tr>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>n=</td>
<td></td>
<td></td>
</tr>
<tr>
<td>128</td>
<td></td>
<td></td>
</tr>
<tr>
<td>130</td>
<td></td>
<td></td>
</tr>
<tr>
<td>129</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Change from baseline in HbA$_{1c}$ (%)**

- Exenatide OW 2.0 mg
- Dulaglutide 0.75 mg
- Dulaglutide 1.5 mg
- Sitagliptin 100 mg
- IGlar
- Semaglutide 0.5 mg
- Semaglutide 1.0 mg
- Placebo

If we switch from Exenatide QW 2mg to Semaglutide 1mg, will we get an extra 0.6% reduction in HbA1c?

*p*<0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

HbA₁c changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA₁c

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>Add-on to OAD</th>
<th>Vs./add-on to basal insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline HbA₁c (%):</strong> 8.1</td>
<td>8.1</td>
<td><strong>8.2</strong></td>
</tr>
<tr>
<td><strong>n=</strong> 128 130 129</td>
<td>409 409 407</td>
<td>362 360 360</td>
</tr>
<tr>
<td><strong>Change from baseline (%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SUSTAIN 1¹</strong></td>
<td><strong>SUSTAIN 2²</strong></td>
<td><strong>SUSTAIN 3³</strong></td>
</tr>
<tr>
<td>-1.5</td>
<td>-1.6</td>
<td>-1.3</td>
</tr>
<tr>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>-1.6</td>
<td>-1.6</td>
<td>-1.5</td>
</tr>
<tr>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td><strong>change from baseline in HbA₁c (mmol/mol):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>-2</strong></td>
<td><strong>-1.6</strong></td>
<td><strong>-0.9</strong></td>
</tr>
<tr>
<td><strong>-1.2</strong></td>
<td><strong>-1.5</strong></td>
<td><strong>-1.5</strong></td>
</tr>
<tr>
<td><strong>-0.8</strong></td>
<td><strong>-0.5</strong></td>
<td><strong>-0.9</strong></td>
</tr>
<tr>
<td><strong>0</strong></td>
<td><strong>-0.1</strong></td>
<td><strong>-0.1</strong></td>
</tr>
</tbody>
</table>

*If we switch from Dulaglutide 1.5mg to Semaglutide 1mg, will we get an extra 0.4% reduction in HbA1c?*

---

**Notes:**
- *p<0.0001 vs. comparator.
- IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly.

HbA1c changes in SUSTAIN 1–5 and 7

CHANGE FROM BASELINE IN HbA1c

**Monotherapy**

- **SUSTAIN 1**: Baseline HbA1c (%) = 8.1, n=128
- **SUSTAIN 2**: Baseline HbA1c (%) = 8.1, n=130
- **SUSTAIN 3**: Baseline HbA1c (%) = 8.3, n=129
- **SUSTAIN 4**: Baseline HbA1c (%) = 8.2, n=301
- **SUSTAIN 5**: Baseline HbA1c (%) = 8.4, n=362
- **SUSTAIN 7**: Baseline HbA1c (%) = 8.2, n=300

**Add-on to OAD**

- **SUSTAIN 1**: Change from baseline in HbA1c (%) = -0.5
- **SUSTAIN 2**: Change from baseline in HbA1c (%) = -0.4
- **SUSTAIN 3**: Change from baseline in HbA1c (%) = -1.1
- **SUSTAIN 4**: Change from baseline in HbA1c (%) = -1.4
- **SUSTAIN 5**: Change from baseline in HbA1c (%) = -1.8
- **SUSTAIN 7**: Change from baseline in HbA1c (%) = -1.8

**Vs./add-on to basal insulin**

- **SUSTAIN 1**: Change from baseline in HbA1c (%) = -0.1
- **SUSTAIN 2**: Change from baseline in HbA1c (%) = -0.1
- **SUSTAIN 3**: Change from baseline in HbA1c (%) = -0.1
- **SUSTAIN 4**: Change from baseline in HbA1c (%) = -1.5
- **SUSTAIN 5**: Change from baseline in HbA1c (%) = -1.7
- **SUSTAIN 7**: Change from baseline in HbA1c (%) = -1.7

**Change from baseline (mmol/mol)**

- **SUSTAIN 1**: Change from baseline in HbA1c = -4.4
- **SUSTAIN 2**: Change from baseline in HbA1c = -8.7
- **SUSTAIN 3**: Change from baseline in HbA1c = -13.1
- **SUSTAIN 4**: Change from baseline in HbA1c = -21.9
- **SUSTAIN 5**: Change from baseline in HbA1c = -17.5
- **SUSTAIN 7**: Change from baseline in HbA1c = -17.5

---

If we switch from Dulaglutide 1.5mg to Semaglutide 1mg, will we get an extra 0.4% reduction in HbA1c?

*If we switch from Dulaglutide 1.5mg to Semaglutide 1mg, will we get an extra 0.4% reduction in HbA1c?*

It’s complicated: This patient with HbA1c fall of 1.4% from 8.2% has HbA1c of 6.8% - so you are not going to switch.

---

HbA<sub>1c</sub> changes in SUSTAIN 1–5 and 7

**CHANGE FROM BASELINE IN HbA<sub>1c</sub>**

### Monotherapy

<table>
<thead>
<tr>
<th>Baseline HbA&lt;sub&gt;1c&lt;/sub&gt; (%)</th>
<th>SUSTAIN 1&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Add-on to OAD</th>
<th>Vs./add-on to basal insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1</td>
<td>8.1</td>
<td>8.3</td>
<td>8.2</td>
</tr>
<tr>
<td>n=</td>
<td>128</td>
<td>409</td>
<td>362</td>
</tr>
</tbody>
</table>

### Add-on to OAD

<table>
<thead>
<tr>
<th>SUSTAIN 2&lt;sup&gt;2&lt;/sup&gt;</th>
<th>SUSTAIN 3&lt;sup&gt;3&lt;/sup&gt;</th>
<th>SUSTAIN 4&lt;sup&gt;5&lt;/sup&gt;</th>
<th>SUSTAIN 5&lt;sup&gt;6&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>409 409 407</td>
<td>404 405</td>
<td>301 299 300 299</td>
<td>362 360 360 132 131 133</td>
</tr>
</tbody>
</table>

### Change from baseline

- **HbA<sub>1c</sub> (%)**
  - SUSTAIN 1: 8.1
  - SUSTAIN 2: 8.1
  - SUSTAIN 3: 8.3
  - SUSTAIN 4: 8.2
  - SUSTAIN 5: 8.4

### Which patient on another GLP-1RA might you switch to Semaglutide:

- HbA1c still high despite other GLP-1RA
- Will the HbA1c fall then be much more from the switch – or not?
- The audit will tell us!

*<sup>p</sup> < 0.0001 vs. comparator. IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly

Duration of diabetes
ABCD liraglutide audit - HbA1c changes according to duration of diabetes

Figure 2. Mean HbA1c changes after 26 weeks of liraglutide treatment, stratified according to duration of diabetes

Columns show adjusted mean changes analysed by ANCOVA with baseline HbA1c as a covariate. ED: estimated difference; CI: confidence interval.

Differences in glycaemic control by baseline diabetes duration

SUSTAIN 1–5 and 7

<table>
<thead>
<tr>
<th>Baseline Diabetes Duration</th>
<th>Change in HbA(_1c) from Baseline (mmol/mol)</th>
<th>Percentage of Patients Achieving HbA(_1c) &lt;7.0% (53 mmol/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5 years</td>
<td>Semaglutide 0.5 mg: -1.4</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>Semaglutide 1.0 mg: -1.7</td>
<td>80</td>
</tr>
<tr>
<td>&gt;5 to ≤10 years</td>
<td>Semaglutide 0.5 mg: -1.4</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Semaglutide 1.0 mg: -1.8</td>
<td>79</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>Semaglutide 0.5 mg: -1.5</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Semaglutide 1.0 mg: -1.7</td>
<td>74</td>
</tr>
</tbody>
</table>

Data presented are estimated change from baseline to week 30 or week 40 based on a meta-analysis of data from the six trials. n, number of subjects in the full analysis set. Adapted from: Rosenstock et al. Diabetes 2018; 67(Suppl. 1):A287 (abstract and poster 1081-P)
Differences in glycaemic control by baseline diabetes duration

SUSTAIN 1–5 and 7

Change in HbA1c from baseline

<table>
<thead>
<tr>
<th></th>
<th>n=</th>
<th>533</th>
<th>641</th>
<th>423</th>
<th>565</th>
<th>376</th>
<th>528</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5 years</td>
<td>-1.4</td>
<td>-1.4</td>
<td>-1.7</td>
<td>-1.8</td>
<td>-1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 to ≤10 years</td>
<td>-1.7</td>
<td>-1.7</td>
<td></td>
<td>-1.5</td>
<td>-1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>-1.2</td>
<td>-0.8</td>
<td>-0.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Change from baseline (%)

- 533
- 641
- 423
- 565
- 376
- 528

n= Semaglutide 0.5 mg  Semaglutide 1.0 mg

Figure 2. Mean HbA1c changes after 26 weeks of liraglutide treatment, stratified according to duration of diabetes

Columns show adjusted mean changes analysed by ANCOVA with baseline HbA1c as a covariate. ED: estimated difference; CI: confidence interval.
Differences in glycaemic control by baseline diabetes duration

SUSTAIN 1–5 and ABCD audit

<table>
<thead>
<tr>
<th>Change in HbA1c from baseline</th>
<th>n</th>
<th>≤5 years</th>
<th>&gt;5 to ≤10 years</th>
<th>&gt;10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change from baseline (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>533</td>
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</tr>
<tr>
<td></td>
<td>528</td>
<td>-1.7</td>
<td>-1.8</td>
<td>-1.7</td>
</tr>
</tbody>
</table>

Change from baseline (mmol/mol) for Semaglutide 0.5 mg and 1.0 mg

- Semaglutide 0.5 mg: -1.4, -1.7, -1.8, -1.7, -1.7
- Semaglutide 1.0 mg: -1.4, -1.7, -1.8, -1.7, -1.7

Liraglutide in ABCD audit

Figure 2. Mean HbA1c changes after 26 weeks of liraglutide treatment, stratified according to duration of diabetes

Columns show adjusted mean changes analysed by ANCOVA with baseline HbA1c as a covariate. ED: estimated difference; CI: confidence interval

Fall from much higher baseline in audit compared to trial
Differences in glycaemic control by baseline diabetes duration

SUSTAIN 1–5 and SUSTAIN 6

Change in HbA₁c from baseline

<table>
<thead>
<tr>
<th>Duration</th>
<th>Semaglutide 0.5 mg</th>
<th>Semaglutide 1.0 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5 years</td>
<td>-1.4</td>
<td>-1.7</td>
</tr>
<tr>
<td>&gt;5 to ≤10 years</td>
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<td>-1.8</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>-1.5</td>
<td>-1.7</td>
</tr>
</tbody>
</table>

Figure 2. Mean HbA₁c changes after 26 weeks of liraglutide treatment, stratified according to duration of diabetes.

Columns show adjusted mean changes analysed by ANCOVA with baseline HbA₁c as a covariate. ED: estimated difference; CI: confidence interval.

What will ABCD semaglutide audit show with regard to duration of diabetes?
What about weight?
**Body weight in SUSTAIN 1–5 and 7**

**CHANGE FROM BASELINE IN BODY WEIGHT**

<table>
<thead>
<tr>
<th>Monotherapy SUSTAIN 1&lt;sup&gt;1&lt;/sup&gt;</th>
<th>SUSTAIN 2&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Add-on to OAD SUSTAIN 3&lt;sup&gt;3&lt;/sup&gt;</th>
<th>SUSTAIN 7&lt;sup&gt;4&lt;/sup&gt;</th>
<th>Vs./add-on to basal insulin SUSTAIN 4&lt;sup&gt;5&lt;/sup&gt;</th>
<th>SUSTAIN 5&lt;sup&gt;6&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline BW (kg): 91.9</td>
<td>89.5</td>
<td>95.8</td>
<td>95.2</td>
<td>93.5</td>
<td>91.7</td>
</tr>
<tr>
<td>n= 128 130 129</td>
<td>409 409 407</td>
<td>404 405 301 299 300 299</td>
<td>362 360 360</td>
<td>132 131 133</td>
<td></td>
</tr>
</tbody>
</table>

**Change from baseline**

-7.0  -6.4  -6.2  -6.0  -5.8  -5.6  -5.4  -5.2  -5.0  -4.8  -4.6  -4.4  -4.2  -4.0  -3.8  -3.6  -3.4  -3.2  -3.0  -2.8  -2.6  -2.4  -2.2  -2.0  -1.8  -1.6  -1.4  -1.2  -1.0  -0.8  -0.6  -0.4  -0.2  0.0  0.2  0.4  0.6  0.8  1.0

**Compounds**

- Semaglutide 0.5 mg
- Semaglutide 1.0 mg
- Placebo
- Dulaglutide 0.75 mg
- Dulaglutide 1.5 mg
- Sitagliptin 100 mg
- Exenatide OW 2.0 mg
- IGlar

*<sup>p</sup><0.0001 vs. comparator. Change from baseline in BW was a secondary endpoint. BW, body weight; IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly.*

All comments about what we might find from ABCD audit re HbA1c also apply to weight – indeed even more so – what weight loss might we see in the much more obese patients we see in our clinics?

*^p<0.0001 vs. comparator. Change from baseline in BW was a secondary endpoint. BW, body weight; IGlar, insulin glargine; OAD, oral antidiabetic drug; OW, once weekly.

Losing weight AND HbA1c
Percentage of subjects achieving fall in HbA$_{1c}$ and weight loss

- Liraglutide 1.8 mg (78%)
- Liraglutide 1.2 mg
- Exenatide 10 µg BID
- Glimepiride 4 mg
- Glargine 24 IU
- Rosiglitazone 4 mg (15%)

Data on file, Novo Nordisk
Patients improving weight AND HbA1c in previous audits

Percentage of subjects achieving fall in HbA1c and weight loss

Exenatide and liraglutide in real clinical use for 6 months

- 60% for Exenatide and liraglutide
- 59% for Exenatide 10 μg BID
- 78% for Liraglutide 1.8 mg
- 72% for Liraglutide 1.2 mg

- 72% for Glimepiride 4 mg
- 32% for Glargine 24 IU
- 25% for Rosiglitazone 4 mg

Data on file, Novo Nordisk
Changes in $\text{HbA}_{1c}$ vs body weight by baseline diabetes duration

Data presented are based on observed on-treatment without rescue medication data, with MMRM predictions for missing $\text{HbA}_{1c}$ and body weight values, from the six trials. MMRM, Mixed Model Repeat Measurements.

Changes in HbA$_{1c}$ vs body weight by baseline diabetes duration

Data presented are based on observed on-treatment without rescue medication data, with MMRM predictions for missing HbA$_{1c}$ and body weight values, from the six trials. MMRM, Mixed Model Repeat Measurements.


What percentage will lose both weight and HbA1c in the semaglutide audit?
ABCD Nationwide Semaglutide Audit

- As you start to use semaglutide please enter ALL your patients into the nationwide audit
- The audit tool allows you easily to analyse your own data – good audit exercise for SpR, CMT or medical student
- All contributors listed in publications – top contributors co-authors

http://www.diabetologists-abcd.org.uk/GLP1_Audits/Semaglutide_Audit.htm