Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

Name of company: Boehringer Ingelheim		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Not applicable		**EudraCT No.:** 2008-007938-21	
Name of active ingredient: Empagliflozin (BI 10773)		**Page:** 1 of 8	**Synopsis No.:**
Module:		**Volume:** {hyperlink }	
Report date: 11 JUL 2012	**Trial No. / U No.:** 1245.24 / U12-1213-01	**Dates of trial:** 30 MAR 2009 – 13 MAY 2011	**Date of revision:** Not applicable

Title of trial:	A 78 week open label extension to trials assessing the safety and efficacy of BI 10773 as monotherapy or in combination with metformin in type 2 diabetic patients
Coordinating Investigator:	[redacted]
Trial sites:	Multi-centre trial: 132 sites in 21 countries (Austria, Czech Republic, Germany, Spain, Estonia, France, Hungary, Italy, Croatia, Lithuania, Latvia, Norway, Taiwan, Korea, Romania, Russia, Sweden, Finland, Slovakia, Ukraine, and USA)
Publication (reference):	Data from this trial have not been published
Clinical phase:	IIb
Objectives:	The primary objective was to investigate the safety of empagliflozin (BI 10773) during open label, long-term treatment. The secondary objective was to assess the efficacy of empagliflozin as monotherapy and as add-on therapy to metformin in the treatment of type 2 diabetes mellitus (T2DM)
Methodology:	This was an open label extension trial of the blinded 12-week dose-finding studies 1245.9 and 1245.10. Patients from the preceding empagliflozin 10 and 25 mg treatment groups (with or without metformin background) continued to take the same doses. Patients on placebo and other empagliflozin doses (with or without metformin background) in the preceding trials were re-randomised to one of the empagliflozin treatments (10 or 25 mg). Patients on metformin monotherapy or sitagliptin added-on to metformin in the preceding trials continued their open label treatments.
No. of subjects:	
planned:	entered: 860

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actual:	enrolled: 660 Empagliflozin 10 mg: entered: 107 treated: 106 analysed (for primary endpoint): 106 Empagliflozin 25 mg: entered: 109 treated: 109 analysed (for primary endpoint): 109 Metformin 1000-2000 mg daily: entered: 56 treated: 56 analysed (for primary endpoint): 56 Empagliflozin 10 mg added to metformin background: entered: 166 treated: 166 analysed (for primary endpoint): 166 Empagliflozin 25 mg added to metformin background: entered: 166 treated: 166 analysed (for primary endpoint): 166 Sitagliptin 100 mg added to metformin background: entered: 56 treated: 56 analysed (for primary endpoint): 56
Diagnosis and main criteria for inclusion:	Patients with type 2 diabetes mellitus who had completed the entire treatment period of the blinded studies 1245.9 or 1245.10
Test product:	Empagliflozin tablets 5 mg or 25 mg
dose:	10 mg (co-administered as two 5 mg tablets) or 25 mg once daily as monotherapy or added to metformin background
mode of admin.:	Oral
batch no.:	5 mg: B073000781, B073000791, B083000717, B083001194, B093000189 25 mg: B073000869, B083000719, B093000196**,** B093000531
Reference therapy:	Metformin immediate release (IR) tablet 500 mg or sitagliptin tablet 100 mg
dose:	Metformin total daily dose between 1000 and 2000 mg as monotherapy; sitagliptin 100 mg once daily added to metformin background
mode of admin.:	Oral
batch no.:	Metformin 500 mg: B093000244, B093000925 Sitagliptin 100 mg: B093000240 (US), B093000877 (US), B093000242 (EU), B093000926 (EU)

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Duration of treatment: 78 weeks

Criteria for evaluation:

Efficacy: No primary efficacy endpoint was defined for this open label extension trial, but the following secondary efficacy endpoints were evaluated: changes in HbA_{1c} and fasting plasma glucose (FPG) from baseline over time to Week 78 of the current trial, the occurrence of a treat-to-target response (HbA_{1c}<7.0% and <6.5%) and a relative efficacy response (lowering of HbA_{1c} by ≥0.5%) over time. Additionally, changes from baseline over time to Week 78 of the current trial in body weight, waist circumference, blood pressure (BP), as well as the use of rescue therapy were also assessed as efficacy endpoints.

Safety: Incidence of adverse events (AEs) and hypoglycaemic events, changes from baseline in laboratory parameters (including lipid parameters) electrocardiograms, physical examinations, and vital signs.

Statistical methods: For the evaluation of safety and efficacy, empagliflozin monotherapy (10 or 25 mg) was compared with metformin monotherapy, and empagliflozin (10 or 25 mg) as add-on therapy to metformin was compared with sitagliptin as add-on therapy to metformin. All analyses were descriptive and based on the treated set, which included all patients treated with at least 1 dose of study drug. For efficacy evaluation, the baseline was defined as the last observed measurement before the first intake of active treatment (in the preceding trial or in the current extension trial). In addition, exploratory analyses on efficacy were performed using an analysis of covariance (ANCOVA) model.

SUMMARY – CONCLUSIONS:

Efficacy results: Of the patients who completed either of the preceding trials (1245.9 or 1245.10), 660 were enrolled and entered in this extension trial. All but 1 were treated with at least 1 dose of study medication. Of the 659 treated patients, 52 (7.9%) discontinued treatment prematurely with the most common reasons being adverse events (3.5%) and refusal to continue with study medication (1.8%).

In general, the demographics and baseline characteristics were balanced among the treatment groups within the monotherapy groups (empagliflozin 10 and 25 mg, metformin) and within the add-on to metformin IR groups (empagliflozin

10 and 25 mg, sitagliptin). The proportion of male patients was 50.7%. Most patients were White (89.5%), 8.8% were Asian. Overall, 83.5% of the patients had been diagnosed with T2DM for more than one year. Mean (standard deviation; SD) age was 58.6 (8.8) years, body mass index 30.0 (4.5) kg/m^2, baseline HbA_{1c} 7.95% (0.83%), FPG 177.6 (41.6) mg/dL, body weight 87.27 (16.28) kg, systolic BP 133.32 (14.05) mmHg, and diastolic BP 80.33 (8.77) mmHg.

Compared with the values before the administration of active treatment, all groups treated with empagliflozin (10 or 25 mg, monotherapy or added-on to metformin) showed reductions in HbA_{1c}, FPG, body weight, and waist circumference at all visits over the 78 weeks of the extension trial. The reductions were generally stable over time. However, a reduction from baseline in both systolic and diastolic blood pressure was only seen with the empagliflozin added-on to metformin groups (10 and 25 mg) over the 78 weeks of the extension trial, with some fluctuations.

An exploratory analysis to assess the change of HbA_{1c}, FPG, body weight, waist circumference, systolic blood pressure (SBP), and diastolic blood pressure (DBP) from baseline to Week 78 of the extension trial was performed using an ANCOVA model, based on the full analysis set (FAS) and the 'last observation carried forward' (LOCF) imputation method. For this analysis, patients who had been randomised to empagliflozin in the preceding trials (any dose; 'old empagliflozin') and those randomised to placebo in the preceding trials (who were re-randomised to empagliflozin in the current trial; 'new empagliflozin') were evaluated separately. The results from the comparator groups (metformin and sitagliptin) and from the 'old empagliflozin' groups are presented in the table below.

The numbers of the patients in the 'new empagliflozin' groups (who switched from placebo in the 12-week preceding trials to empagliflozin in the 78-week extension trial) were relatively low (below 30 for each group); these groups also showed decreased HbA_{1c}, FPG, and body weight at Week 78 of the extension trial, based on FAS LOCF. However, decreased waist circumference and blood pressure (systolic and diastolic) could only be observed in the added-on to metformin groups.

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Change in efficacy endpoints from baseline at Week 78 of the extension trial – FAS LOCF

Change from baseline, adjusted mean (95% CI)	Comparator	Empagliflozin 'old' 10 mg	Empagliflozin 'old' 25 mg
HbA_{1c} (%)			
Monotherapy, metformin as comparator	-0.56 (-0.79, -0.33)	-0.34 (-0.54, -0.14)	-0.47 (-0.66, -0.27)
Add-on to metformin, sitagliptin as comparator	-0.40 (-0.60, -0.20)	-0.34 (-0.47, -0.21)	-0.63 (-0.76, -0.50)
FPG (mg/dL)			
Monotherapy, metformin as comparator	-26.0 (-33.5, -18.4)	-30.4 (-37.1, -23.7)	-27.8 (-34.3, -21.3)
Add-on to metformin, sitagliptin as comparator	-15.6 (-23.6, -7.62)	-21.3 (-26.4, -16.2)	-31.8 (-36.8, -26.7)
Body weight (kg)			
Monotherapy, metformin as comparator	-1.28 (-2.30, -0.26)	-2.24 (-3.12, -1.36)	-2.61 (-3.46, -1.77)
Add-on to metformin, sitagliptin as comparator	-0.41 (-1.49, 0.67)	-3.14 (-3.89, -2.38)	-4.03 (-4.77, -3.29)
Waist circumference (cm)			
Monotherapy, metformin as comparator	-0.16 (-2.77, 2.45)	-3.03 (-5.32, -0.74)	-2.22 (-4.45, 0.01)
Add-on to metformin, sitagliptin as comparator	0.04 (-2.47, 2.54)	-1.86 (-3.57, -0.14)	-2.42 (-4.09, -0.75)
Systolic blood pressure (mmHg)			
Monotherapy, metformin as comparator	1.96 (-1.77, 5.70)	0.12 (-3.18, 3.42)	-1.66 (-4.87, 1.56)
Add-on to metformin, sitagliptin as comparator	1.83 (-1.50, 5.15)	-3.28 (-5.66, -0.91)	-2.97 (-5.30, -0.64)
Diastolic blood pressure (mmHg)			
Monotherapy, metformin as comparator	-0.58 (-2.67, 1.50)	-1.63 (-3.38, 0.11)	-2.21 (-3.87, -0.54)
Add-on to metformin, sitagliptin as comparator	1.19 (-0.92, 3.30)	-0.88 (-2.39, 0.63)	-1.97 (-3.46, -0.49)

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Responder rates for HbA_{1c} below 7.0% were relatively constant over the 78 weeks of the extension trial for all treatments. At Week 78 of the extension trial, the proportions of patients in the monotherapy groups who showed response were 31.9% for empagliflozin 10 mg, 32.1% for empagliflozin 25 mg, and 31.0% for metformin; the proportions of responders in the add-on therapy groups were 27.0% for empagliflozin 10 mg, 44.6% for empagliflozin 25 mg, and 36.8% for sitagliptin. The trend was similar for the proportion of patients with HbA_{1c} below 6.5% or HbA_{1c} lowered by at least 0.5% compared with the value before the administration of active treatment.

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Safety results:

The median exposure to study drug ranged from 545 to 546 days for all groups and the mean was comparable for all groups. Mean daily dose of metformin IR as monotherapy in this trial (1749.5 mg, SD: 380.9 mg) was comparable to the preceding trial (trial 1245.9; 1566.7 mg, SD: 405.3 mg).

Overall AE rate for the 4 empagliflozin groups was 63.2% to 74.1% with most events being mild or moderate in intensity; AE frequency was 69.6% for both metformin and sitagliptin added-on to metformin. The occurrence of serious AE (SAE) was 6.0% to 9.4% for empagliflozin with none considered empagliflozin related and no pattern could be observed; SAE frequency was 5.4% for metformin and 16.1% for sitagliptin added-on to metformin.

The incidence of Clinical Event Committee-confirmed cardiovascular death, myocardial infarction, stroke or unstable angina in the empagliflozin treatment groups (all 4 groups combined) was 1.3% (7 patients in total), and in the comparator groups (metformin and sitagliptin combined) was 3.6% (4 patients in total). Two patients died during the trial: one in the empagliflozin 10 mg monotherapy group and the other in the metformin monotherapy group; both deaths were adjudicated to be sudden cardiovascular death.

Incidence of investigator-reported hypoglycaemic events was lower in the empagliflozin-treated groups (0.9% to 3.6%) than the comparators (7.1% for metformin and 5.4% for sitagliptin added-on to metformin) and none caused treatment discontinuation.

AEs related to urinary tract infection occurred at a similar frequency for empagliflozin (3.8% to 12.7%) and comparator groups (3.6% for metformin and 12.5% for sitagliptin added-on to metformin) and none led to treatment discontinuation. AEs related to genital infection were more frequent with the empagliflozin treatments (3.0% to 5.5%; 1.8% for metformin and none for sitagliptin added-on to metformin). However most events were mild and resolved after therapy; 4 of the 22 empagliflozin-treated patients with genital infection discontinued the study drug.

The frequency of the system organ class “neoplasms benign, malignant and unspecified (including cysts and polyps)” for the empagliflozin groups (all 4 groups combined) was 1.1% (6 patients in total), and for the comparators (metformin and sitagliptin combined) was 3.6% (4 patients in total).

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	In general, no clinically relevant change was observed in renal or hepatic function, laboratory evaluation, or vital sign evaluation. Haematocrit value, which was slightly increased in empagliflozin-treated groups in the preceding trials, continued to increase during the extension trial; the mean increase for the whole period of 90 weeks was between 2.1% and 3.4%. Uric acid, which was decreased in empagliflozin-treated groups in the preceding trials, continued to decrease during the extension trial; the mean decrease for the whole period of 90 weeks was between 44 and 51 µmol/L.
Conclusions:	In this open-label extension study (of the preceding 1245.9 and 1245.10 blinded 12-week dose-finding studies), patients with T2DM were treated with 10 or 25 mg empagliflozin with or without metformin background for 78 weeks. Treatment with empagliflozin was generally safe and well tolerated. Hypoglycaemic events occurred less often with empagliflozin treatment than with metformin or sitagliptin. Overall, adverse events related to urinary tract infection did not increase in frequency with empagliflozin treatment. Adverse events related to genital infection were observed more frequently with empagliflozin, although generally manageable, and few led to treatment discontinuation. The efficacy of empagliflozin as expressed in the reduction of HbA_{1c}, FPG, body weight, and waist circumference was generally maintained over 90 weeks, adding the preceding studies (12 weeks) and the extension (78 weeks) together. Taken together, long-term treatment with empagliflozin demonstrated sustained glycaemic control and weight loss while being well tolerated.

Trial Synopsis - Appendix

The appended tables on the following pages supplement the trial results presented in the Trial Synopsis. They complement primary and secondary endpoints of the trial.

Results for	**presented in**
Adverse event overall summary up to 7 days after the last intake of study drug (primary endpoint)	Table 15.3.2: 1
Clinical laboratory evaluation change from baseline in lipid paramaters over 78 weeks (primary endpoint)	Table 15.3.3:1
HbA1c change from baseline over 78 weeks	Table 15.2.2.1.1: 1
Patients with HbA1c <6.5% over time by treatment over 78 weeks (secondary endpoint)	Table 15.2.2.1.2: 2
Patients with lowered HbA1c by at least 0.5% by treatment over 78 weeks (secondary endpoint)	Table 15.2.2.1.3: 1
Fasting plasma glucose (FPG) change from baseline over 78 weeks	Table 15.2.2.2.1: 1
Number of patients with rescue therapy over 78 weeks	Table 15.2.3: 1

Table 15.3.2: 1 Adverse event overall summary - treated set

Treatment analysis: All periods up to 7 days after the last intake of study drug

	Prev trial N (%)	Between N (%)	BI 10 N (%)	BI 25 N (%)	Met N (%)	BI 10+Met N (%)
Number of patients	659 (100.0)	14 (100.0)	106 (100.0)	109 (100.0)	56 (100.0)	166 (100.0)
Patients with any AE	127 (19.3)	0 (0.0)	67 (63.2)	75 (68.8)	39 (69.6)	112 (67.5)
Patients with severe AEs	3 (0.5)	0 (0.0)	7 (6.6)	5 (4.6)	4 (7.1)	4 (2.4)
Patients with investigator defined drug-related AEs	35 (5.3)	0 (0.0)	14 (13.2)	13 (11.9)	4 (7.1)	23 (13.9)
Patients with other significant AEs (according to ICH E3)	1 (0.2)	0 (0.0)	3 (2.8)	2 (1.8)	0 (0.0)	2 (1.2)
Patients with AEs leading to discontinuation of trial drug	1 (0.2)	0 (0.0)	5 (4.7)	1 (0.9)	1 (1.8)	4 (2.4)
Patients with significant AEs (pre-specified events)	4 (0.6)	0 (0.0)	5 (4.7)	4 (3.7)	3 (5.4)	3 (1.8)
Patients with serious AEs	2 (0.3)	0 (0.0)	10 (9.4)	7 (6.4)	3 (5.4)	10 (6.0)
Fatal	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	1 (1.8)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Req.hospitalisation	2 (0.3)	0 (0.0)	9 (8.5)	7 (6.4)	2 (3.6)	9 (5.4)
Prol.hospitalisation	0 (0.0)	0 (0.0)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)	1 (0.6)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 14.0
Ongoing AEs started in the preceding trials 1245.9 and 1245.10.
`Between´: AEs started between the preceding trial (1245.9 or 1245.10) and the 1245.24 trial

Table 15.3.2: 1 Adverse event overall summary - treated set

Treatment analysis: All periods up to 7 days after the last intake of study drug

	BI 25+Met N (%)	Sita+Met N (%)	Post trt N (%)
Number of patients	166 (100.0)	56 (100.0)	629 (100.0)
Patients with any AE	123 (74.1)	39 (69.6)	8 (1.3)
Patients with severe AEs	5 (3.0)	5 (8.9)	2 (0.3)
Patients with investigator defined drug-related AEs	24 (14.5)	5 (8.9)	1 (0.2)
Patients with other significant AEs (according to ICH E3)	7 (4.2)	3 (5.4)	0 (0.0)
Patients with AEs leading to discontinuation of trial drug	9 (5.4)	2 (3.6)	0 (0.0)
Patients with significant AEs (pre-specified events)	5 (3.0)	3 (5.4)	0 (0.0)
Patients with serious AEs	13 (7.8)	9 (16.1)	2 (0.3)
Fatal	0 (0.0)	0 (0.0)	0 (0.0)
Imm life-threatening	0 (0.0)	0 (0.0)	0 (0.0)
Disability/incap.	0 (0.0)	2 (3.6)	0 (0.0)
Req.hospitalisation	13 (7.8)	9 (16.1)	1 (0.2)
Prol.hospitalisation	0 (0.0)	0 (0.0)	0 (0.0)
Congenital anomaly	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	1 (1.8)	1 (0.2)

A patient may be counted in more than one seriousness criterion.
Percentages are calculated using total number of patients per treatment as the denominator.
MedDRA version used for reporting: 14.0
Ongoing AEs started in the preceding trials 1245.9 and 1245.10.
`Between´: AEs started between the preceding trial (1245.9 or 1245.10) and the 1245.24 trial

Table 15.3.3: 1 Descriptive statistics for baseline, last value on treatment, and difference from baseline (normalised) - Treated set

Baseline source: before first intake of active treatment (preceding trial or OLE)
Treatment analysis: All periods, +3 days

Functional Group: Substrates

Parameter/ Visit/ Difference from baseline	BI 10 (N= 106) N*	Mean	SD	P25%	Median	P75%	BI 25 (N= 109) N*	Mean	SD	P25%
Glucose [mmol/L]										
Baseline	105	9.1	2.0	7.7	8.8	10.2	109	9.2	2.1	7.7
Last value on treatment	105	7.7	1.1	6.9	7.6	8.5	109	7.9	1.3	7.0
Difference from Baseline	105	-1.4	1.8	-2.2	-1.2	-0.2	109	-1.3	1.8	-2.3
Cholesterol, total [mmol/L]										
Baseline	105	3.33	1.15	2.64	3.29	3.87	109	3.30	0.90	2.57
Last value on treatment	105	3.20	1.04	2.43	3.14	3.71	109	3.40	1.00	2.67
Difference from Baseline	105	-0.13	1.17	-0.51	-0.10	0.31	109	0.09	0.88	-0.30
HDL [mmol/L]										
Baseline	105	1.21	0.16	1.11	1.19	1.29	109	1.22	0.16	1.12
Last value on treatment	105	1.29	0.16	1.18	1.25	1.36	109	1.29	0.18	1.15
Difference from Baseline	105	0.08	0.11	0.01	0.07	0.13	109	0.07	0.10	0.02
LDL [mmol/L]										
Baseline	102	0.61	0.79	0.11	0.61	1.20	108	0.78	0.84	0.10
Last value on treatment	102	0.59	0.89	-0.08	0.57	1.11	108	0.83	0.95	0.22
Difference from Baseline	102	-0.02	0.83	-0.51	-0.02	0.37	108	0.05	0.83	-0.35
Triglyceride [mmol/L]										
Baseline	105	1.6	2.5	0.7	1.2	1.7	109	1.2	0.7	0.7
Last value on treatment	105	1.1	0.8	0.6	0.9	1.5	109	1.2	0.6	0.7
Difference from Baseline	105	-0.5	2.3	-0.5	-0.2	0.1	109	-0.0	0.6	-0.2
Urea [mmol/L]										
Baseline	105	5.6	0.7	5.1	5.5	5.8	109	5.7	0.7	5.3
Last value on treatment	105	5.7	0.6	5.3	5.7	6.1	109	5.9	0.8	5.4
Difference from Baseline	105	0.2	0.7	-0.2	0.2	0.6	109	0.2	0.7	-0.3

N* = Number of patients with non-missing lab values per time-point or visit / summary visit
The selected algorithm for repeat values is WORST.
The selected algorithm for multiple values is WORST.
Trial(s): 1245_0024

Source data: Appendix 16.2.8, Listing 1 labtb001.sas 07OCT2011

Table 15.3.3: 1 Descriptive statistics for baseline, last value on treatment, and difference from baseline (normalised) - Treated set

Baseline source: before first intake of active treatment (preceding trial or OLE)
Treatment analysis: All periods, +3 days

Functional Group: Substrates

Parameter/ Visit/ Difference from baseline	BI 25 (N= 109) Median	BI 25 (N= 109) P75%	Met (N= 56) N*	Met (N= 56) Mean	Met (N= 56) SD	Met (N= 56) P25%	Met (N= 56) Median	Met (N= 56) P75%	BI 10+Met (N= 166) N*	BI 10+Met (N= 166) Mean
Glucose [mmol/L]										
Baseline	9.1	10.0	56	9.0	2.0	7.6	8.6	9.9	164	9.0
Last value on treatment	7.8	8.6	56	7.7	1.3	7.1	7.8	8.5	164	7.9
Difference from Baseline	-1.3	-0.3	56	-1.3	2.0	-2.2	-0.9	-0.0	164	-1.2
Cholesterol, total [mmol/L]										
Baseline	3.25	3.96	56	3.33	1.07	2.59	3.40	3.69	164	2.86
Last value on treatment	3.31	4.02	56	3.09	0.97	2.41	3.02	3.63	164	3.05
Difference from Baseline	0.14	0.49	56	-0.24	0.77	-0.70	-0.27	0.21	164	0.19
HDL [mmol/L]										
Baseline	1.19	1.30	56	1.19	0.15	1.08	1.19	1.27	164	1.20
Last value on treatment	1.27	1.38	56	1.24	0.14	1.13	1.24	1.32	164	1.26
Difference from Baseline	0.07	0.11	56	0.06	0.10	0.01	0.05	0.11	164	0.06
LDL [mmol/L]										
Baseline	0.69	1.36	52	0.61	0.91	0.05	0.71	1.09	161	0.25
Last value on treatment	0.67	1.47	52	0.48	0.96	-0.28	0.54	1.12	161	0.39
Difference from Baseline	0.10	0.53	52	-0.13	0.74	-0.66	-0.05	0.36	161	0.13
Triglyceride [mmol/L]										
Baseline	1.1	1.5	56	1.6	1.4	0.8	1.1	2.0	164	1.2
Last value on treatment	1.0	1.5	56	1.2	0.7	0.7	0.9	1.4	164	1.3
Difference from Baseline	0.0	0.2	56	-0.5	1.2	-0.5	-0.2	0.1	164	0.1
Urea [mmol/L]										
Baseline	5.6	6.1	56	5.8	0.8	5.2	5.7	6.3	164	5.7
Last value on treatment	5.9	6.4	56	5.8	0.8	5.1	5.7	6.1	164	6.0
Difference from Baseline	0.2	0.7	56	-0.0	0.9	-0.5	-0.1	0.5	164	0.3

N* = Number of patients with non-missing lab values per time-point or visit / summary visit
The selected algorithm for repeat values is WORST.
The selected algorithm for multiple values is WORST.
Trial(s): 1245_0024

Source data: Appendix 16.2.8, Listing 1 labtb001.sas 07OCT2011

Table 15.3.3: 1 Descriptive statistics for baseline, last value on treatment, and difference from baseline (normalised) - Treated set

Baseline source: before first intake of active treatment (preceding trial or OLE)
Treatment analysis: All periods, +3 days

Functional Group: Substrates

Parameter/ Visit/ Difference from baseline	BI 10+Met (N= 166)				BI 25+Met (N= 166)					
	SD	P25%	Median	P75%	N*	Mean	SD	P25%	Median	P75%
Glucose [mmol/L]										
Baseline	1.7	7.9	8.7	9.9	163	9.1	1.8	8.0	8.8	10.0
Last value on treatment	1.3	7.1	7.8	8.4	163	7.7	1.4	6.8	7.5	8.3
Difference from Baseline	1.9	-2.1	-1.0	-0.0	163	-1.5	1.8	-2.4	-1.5	-0.2
Cholesterol, total [mmol/L]										
Baseline	0.96	2.24	2.77	3.47	162	2.92	0.99	2.26	2.79	3.55
Last value on treatment	1.02	2.30	2.89	3.67	162	3.05	1.06	2.18	2.98	3.65
Difference from Baseline	0.81	-0.13	0.18	0.51	162	0.13	0.75	-0.19	0.18	0.54
HDL [mmol/L]										
Baseline	0.13	1.12	1.19	1.28	162	1.20	0.12	1.11	1.18	1.26
Last value on treatment	0.16	1.16	1.24	1.35	162	1.27	0.15	1.18	1.26	1.36
Difference from Baseline	0.09	0.01	0.06	0.12	162	0.07	0.10	0.02	0.07	0.12
LDL [mmol/L]										
Baseline	0.87	-0.32	0.14	0.82	159	0.33	0.82	-0.30	0.28	0.81
Last value on treatment	0.91	-0.25	0.22	0.98	159	0.41	0.92	-0.32	0.38	1.00
Difference from Baseline	0.71	-0.17	0.13	0.41	159	0.07	0.69	-0.26	0.07	0.46
Triglyceride [mmol/L]										
Baseline	0.8	0.7	1.0	1.5	162	1.3	1.0	0.7	1.1	1.5
Last value on treatment	0.9	0.7	1.0	1.6	162	1.2	0.7	0.6	1.0	1.4
Difference from Baseline	0.9	-0.2	0.0	0.3	162	-0.1	0.8	-0.3	-0.1	0.2
Urea [mmol/L]										
Baseline	0.7	5.2	5.7	6.1	163	5.7	0.8	5.3	5.6	6.0
Last value on treatment	0.8	5.5	6.0	6.4	163	6.0	0.8	5.4	5.9	6.4
Difference from Baseline	0.8	-0.1	0.3	0.8	163	0.2	0.7	-0.3	0.3	0.8

N* = Number of patients with non-missing lab values per time-point or visit / summary visit
The selected algorithm for repeat values is WORST.
The selected algorithm for multiple values is WORST.
Trial(s): 1245_0024

Source data: Appendix 16.2.8, Listing 1 labtb001.sas 07OCT2011

Table 15.3.3: 1 Descriptive statistics for baseline, last value on treatment, and difference from baseline (normalised) - Treated set

Baseline source: before first intake of active treatment (preceding trial or OLE)
Treatment analysis: All periods, +3 days

Functional Group: Substrates

Parameter/ Visit/ Difference from baseline	Sita+Met (N= 56)					
	N*	Mean	SD	P25%	Median	P75%
Glucose [mmol/L]						
Baseline	56	9.2	1.9	7.8	9.0	10.6
Last value on treatment	56	8.2	1.8	7.0	8.1	9.1
Difference from Baseline	56	-1.1	2.0	-2.0	-0.5	0.0
Cholesterol, total [mmol/L]						
Baseline	56	2.97	0.90	2.33	2.96	3.33
Last value on treatment	56	2.91	1.03	2.19	2.86	3.56
Difference from Baseline	56	-0.05	0.91	-0.56	-0.04	0.40
HDL [mmol/L]						
Baseline	56	1.18	0.11	1.10	1.17	1.25
Last value on treatment	56	1.22	0.11	1.13	1.21	1.30
Difference from Baseline	56	0.03	0.08	-0.03	0.03	0.08
LDL [mmol/L]						
Baseline	55	0.39	0.77	-0.16	0.47	0.91
Last value on treatment	55	0.40	1.02	-0.40	0.31	1.08
Difference from Baseline	55	0.00	0.79	-0.50	0.00	0.40
Triglyceride [mmol/L]						
Baseline	56	1.3	1.4	0.8	1.1	1.3
Last value on treatment	56	1.2	0.9	0.7	0.9	1.2
Difference from Baseline	56	-0.2	0.9	-0.5	-0.2	0.1
Urea [mmol/L]						
Baseline	56	5.5	0.6	5.1	5.4	5.8
Last value on treatment	56	5.8	1.0	5.3	5.6	6.2
Difference from Baseline	56	0.3	0.8	-0.1	0.2	0.7

N* = Number of patients with non-missing lab values per time-point or visit / summary visit
The selected algorithm for repeat values is WORST.
The selected algorithm for multiple values is WORST.
Trial(s): 1245_0024

Source data: Appendix 16.2.8, Listing 1 labtb001.sas 07OCT2011

Table 15.2.2.1.1: 1 Descriptive statistics of HbA1c (%) over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Number of patients	106	109	56	166	166	56
HbA1c [%]						
Baseline						
N	106	109	56	166	166	56
Mean	7.89	8.00	8.15	7.88	7.91	8.03
SD	0.87	0.87	0.95	0.74	0.78	0.89
Min	6.0	6.1	6.9	6.2	6.3	6.5
Median	7.70	7.90	8.00	7.75	7.80	7.95
Max	11.8	9.9	10.7	10.5	10.9	10.5
Week 6						
N	104	108	55	162	163	54
Mean	7.44	7.42	7.12	7.53	7.36	7.29
SD	0.82	0.74	0.73	0.80	0.71	0.74
Min	5.4	5.6	5.7	6.0	5.7	5.9
Median	7.40	7.30	7.00	7.40	7.30	7.20
Max	12.0	10.2	8.8	10.5	9.8	9.1
Change from baseline at Week 6						
N	104	108	55	162	163	54
Mean	-0.40	-0.57	-1.03	-0.36	-0.55	-0.75
SD	0.77	0.81	0.76	0.67	0.60	0.80
Min	-2.5	-2.4	-3.5	-2.2	-2.1	-3.0
Median	-0.40	-0.50	-0.90	-0.35	-0.50	-0.75
Max	2.5	2.6	0.5	1.6	0.8	0.8
Week 18						
N	93	105	53	149	157	48
Mean	7.23	7.27	7.13	7.34	7.19	7.26
SD	0.64	0.68	0.78	0.64	0.63	0.63
Min	5.8	6.0	5.5	5.9	5.5	6.1
Median	7.20	7.20	7.00	7.30	7.10	7.30
Max	9.3	9.2	9.8	9.5	9.3	8.6

Only patients who had values after the intake of study drug
The time points refer to the OLE trial

Source data: Appendix 16.2.6, Listing 1.1 hbatb001.sas 07OCT2011

Table 15.2.2.1.1: 1 Descriptive statistics of HbA1c (%) over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Change from baseline at Week 18						
N	93	105	53	149	157	48
Mean	-0.58	-0.72	-0.92	-0.51	-0.70	-0.79
SD	0.75	0.88	0.91	0.68	0.68	0.84
Min	-2.8	-2.6	-3.3	-2.7	-2.4	-3.0
Median	-0.50	-0.60	-1.00	-0.50	-0.60	-0.70
Max	1.6	1.3	2.5	1.6	0.9	0.9
Week 30						
N	93	99	50	140	151	45
Mean	7.31	7.35	7.14	7.27	7.10	7.36
SD	0.77	0.79	0.75	0.63	0.61	0.66
Min	5.4	5.5	5.8	5.7	5.5	6.0
Median	7.30	7.30	7.05	7.20	7.00	7.20
Max	10.0	9.9	9.5	9.3	9.0	8.9
Change from baseline at Week 30						
N	93	99	50	140	151	45
Mean	-0.47	-0.61	-0.95	-0.58	-0.76	-0.68
SD	0.85	0.90	0.82	0.69	0.70	0.82
Min	-2.9	-2.6	-3.4	-3.0	-3.9	-2.7
Median	-0.50	-0.50	-0.95	-0.60	-0.70	-0.70
Max	2.2	1.8	1.5	1.4	1.5	0.8
Week 42						
N	85	93	46	132	140	44
Mean	7.19	7.16	6.97	7.18	7.04	7.48
SD	0.77	0.68	0.61	0.61	0.69	0.94
Min	5.0	5.7	5.9	6.0	5.4	5.6
Median	7.10	7.10	6.90	7.10	7.00	7.25
Max	9.8	9.2	8.4	9.1	9.3	11.1
Change from baseline at Week 42						
N	85	93	46	132	140	44
Mean	-0.59	-0.74	-1.10	-0.65	-0.79	-0.51
SD	0.87	0.98	0.80	0.72	0.76	1.03
Min	-3.1	-3.4	-3.9	-3.1	-3.8	-2.8
Median	-0.70	-0.60	-1.00	-0.70	-0.80	-0.65
Max	2.3	2.0	0.4	1.1	1.5	3.4

Only patients who had values after the intake of study drug
The time points refer to the OLE trial

Source data: Appendix 16.2.6, Listing 1.1 hbatb001.sas 07OCT2011

Table 15.2.2.1.1: 1 Descriptive statistics of HbA1c (%) over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Week 54						
N	78	85	44	128	136	41
Mean	7.14	7.18	6.93	7.20	7.07	7.23
SD	0.69	0.56	0.64	0.67	0.65	0.56
Min	5.2	5.7	5.7	5.7	5.5	5.9
Median	7.10	7.20	6.90	7.15	7.00	7.10
Max	9.9	9.2	8.3	8.9	9.3	8.2
Change from baseline at Week 54						
N	78	85	44	128	136	41
Mean	-0.66	-0.71	-1.13	-0.62	-0.75	-0.79
SD	0.83	0.87	0.89	0.76	0.73	0.79
Min	-2.9	-3.0	-3.8	-3.1	-3.0	-2.7
Median	-0.60	-0.60	-1.05	-0.60	-0.80	-0.80
Max	2.1	1.4	0.9	1.4	1.0	0.9
Week 66						
N	80	87	43	120	127	39
Mean	7.23	7.20	7.03	7.23	7.06	7.22
SD	0.74	0.62	0.53	0.65	0.65	0.70
Min	5.3	5.9	5.9	5.6	5.2	5.8
Median	7.20	7.20	7.00	7.10	7.00	7.20
Max	10.0	8.7	8.2	9.1	8.9	8.6
Change from baseline at Week 66						
N	80	87	43	120	127	39
Mean	-0.55	-0.71	-1.04	-0.59	-0.73	-0.78
SD	0.80	1.01	0.79	0.79	0.77	0.90
Min	-2.8	-3.1	-3.5	-3.1	-3.4	-3.1
Median	-0.50	-0.60	-0.90	-0.60	-0.70	-0.80
Max	1.8	1.6	0.3	1.7	1.4	1.3
Week 78						
N	72	84	42	115	121	38
Mean	7.22	7.35	7.29	7.27	7.11	7.35
SD	0.62	0.74	0.71	0.69	0.68	0.86
Min	5.3	5.6	5.9	5.0	5.6	5.8
Median	7.20	7.25	7.20	7.20	7.10	7.30
Max	8.9	10.2	8.7	9.3	9.3	9.3

Only patients who had values after the intake of study drug
The time points refer to the OLE trial

Source data: Appendix 16.2.6, Listing 1.1 hbatb001.sas 07OCT2011

Table 15.2.2.1.1: 1 Descriptive statistics of HbA1c (%) over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Change from baseline at Week 78						
N	72	84	42	115	121	38
Mean	-0.50	-0.55	-0.80	-0.56	-0.71	-0.66
SD	0.77	0.90	0.88	0.80	0.81	0.99
Min	-2.7	-2.8	-3.3	-3.3	-3.3	-2.9
Median	-0.45	-0.45	-0.75	-0.60	-0.80	-0.70
Max	1.6	1.5	1.2	1.6	1.9	2.0

Only patients who had values after the intake of study drug
The time points refer to the OLE trial

Source data: Appendix 16.2.6, Listing 1.1 hbatb001.sas 07OCT2011

Table 15.2.2.1.2: 2 Number of patients with HbA1c <6.5% over time by treatment - treated set OC

HbA1c response: <6.5%	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Number of patients	106	109	56	166	166	56
Week 6						
N	104 (100.0)	108 (100.0)	55 (100.0)	162 (100.0)	163 (100.0)	54 (100.0)
Yes	4 (3.8)	12 (11.1)	9 (16.4)	10 (6.2)	11 (6.7)	6 (11.1)
No	100 (96.2)	96 (88.9)	46 (83.6)	152 (93.8)	152 (93.3)	48 (88.9)
Week 18						
N	93 (100.0)	105 (100.0)	53 (100.0)	149 (100.0)	157 (100.0)	48 (100.0)
Yes	11 (11.8)	13 (12.4)	7 (13.2)	7 (4.7)	8 (5.1)	6 (12.5)
No	82 (88.2)	92 (87.6)	46 (86.8)	142 (95.3)	149 (94.9)	42 (87.5)
Week 30						
N	93 (100.0)	99 (100.0)	50 (100.0)	140 (100.0)	151 (100.0)	45 (100.0)
Yes	8 (8.6)	10 (10.1)	7 (14.0)	12 (8.6)	16 (10.6)	2 (4.4)
No	85 (91.4)	89 (89.9)	43 (86.0)	128 (91.4)	135 (89.4)	43 (95.6)
Week 42						
N	85 (100.0)	93 (100.0)	46 (100.0)	132 (100.0)	140 (100.0)	44 (100.0)
Yes	10 (11.8)	10 (10.8)	10 (21.7)	14 (10.6)	30 (21.4)	4 (9.1)
No	75 (88.2)	83 (89.2)	36 (78.3)	118 (89.4)	110 (78.6)	40 (90.9)
Week 54						
N	78 (100.0)	85 (100.0)	44 (100.0)	128 (100.0)	136 (100.0)	41 (100.0)
Yes	9 (11.5)	5 (5.9)	8 (18.2)	14 (10.9)	21 (15.4)	4 (9.8)
No	69 (88.5)	80 (94.1)	36 (81.8)	114 (89.1)	115 (84.6)	37 (90.2)

The time points refer to the OLE trial

Source data: Appendix 16.2.6, Listing 1.4

Table 15.2.2.1.2: 2 Number of patients with HbA1c <6.5% over time by treatment - treated set OC

HbA1c response: <6.5%	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Week 66						
N	80 (100.0)	87 (100.0)	43 (100.0)	120 (100.0)	127 (100.0)	39 (100.0)
Yes	8 (10.0)	10 (11.5)	6 (14.0)	10 (8.3)	16 (12.6)	6 (15.4)
No	72 (90.0)	77 (88.5)	37 (86.0)	110 (91.7)	111 (87.4)	33 (84.6)
Week 78						
N	72 (100.0)	84 (100.0)	42 (100.0)	115 (100.0)	121 (100.0)	38 (100.0)
Yes	5 (6.9)	7 (8.3)	4 (9.5)	12 (10.4)	16 (13.2)	7 (18.4)
No	67 (93.1)	77 (91.7)	38 (90.5)	103 (89.6)	105 (86.8)	31 (81.6)

The time points refer to the OLE trial

Source data: Appendix 16.2.6, Listing 1.4 hbatb002.sas 07OCT2011

Table 15.2.2.1.3: 1 Number of patients with lowered HbA1c by at least 0.5% over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

HbA1c reduction: >=0.5%	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Number of patients	106	109	56	166	166	56
Week 6						
N	104 (100.0)	108 (100.0)	55 (100.0)	162 (100.0)	163 (100.0)	54 (100.0)
Yes	44 (42.3)	55 (50.9)	44 (80.0)	67 (41.4)	92 (56.4)	34 (63.0)
No	60 (57.7)	53 (49.1)	11 (20.0)	95 (58.6)	71 (43.6)	20 (37.0)
Week 18						
N	93 (100.0)	105 (100.0)	53 (100.0)	149 (100.0)	157 (100.0)	48 (100.0)
Yes	48 (51.6)	65 (61.9)	41 (77.4)	80 (53.7)	97 (61.8)	32 (66.7)
No	45 (48.4)	40 (38.1)	12 (22.6)	69 (46.3)	60 (38.2)	16 (33.3)
Week 30						
N	93 (100.0)	99 (100.0)	50 (100.0)	140 (100.0)	151 (100.0)	45 (100.0)
Yes	47 (50.5)	55 (55.6)	39 (78.0)	77 (55.0)	96 (63.6)	31 (68.9)
No	46 (49.5)	44 (44.4)	11 (22.0)	63 (45.0)	55 (36.4)	14 (31.1)
Week 42						
N	85 (100.0)	93 (100.0)	46 (100.0)	132 (100.0)	140 (100.0)	44 (100.0)
Yes	50 (58.8)	56 (60.2)	38 (82.6)	82 (62.1)	93 (66.4)	24 (54.5)
No	35 (41.2)	37 (39.8)	8 (17.4)	50 (37.9)	47 (33.6)	20 (45.5)
Week 54						
N	78 (100.0)	85 (100.0)	44 (100.0)	128 (100.0)	136 (100.0)	41 (100.0)
Yes	49 (62.8)	50 (58.8)	36 (81.8)	76 (59.4)	89 (65.4)	24 (58.5)
No	29 (37.2)	35 (41.2)	8 (18.2)	52 (40.6)	47 (34.6)	17 (41.5)

The time points refer to the OLE trial

Source data: Appendix 16.2.6, Listing 1.5

Table 15.2.2.1.3: 1 Number of patients with lowered HbA1c by at least 0.5% over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

HbA1c reduction: >=0.5%	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Week 66						
N	80 (100.0)	87 (100.0)	43 (100.0)	120 (100.0)	127 (100.0)	39 (100.0)
Yes	43 (53.8)	49 (56.3)	33 (76.7)	66 (55.0)	82 (64.6)	26 (66.7)
No	37 (46.3)	38 (43.7)	10 (23.3)	54 (45.0)	45 (35.4)	13 (33.3)
Week 78						
N	72 (100.0)	84 (100.0)	42 (100.0)	115 (100.0)	121 (100.0)	38 (100.0)
Yes	36 (50.0)	42 (50.0)	28 (66.7)	65 (56.5)	78 (64.5)	23 (60.5)
No	36 (50.0)	42 (50.0)	14 (33.3)	50 (43.5)	43 (35.5)	15 (39.5)

The time points refer to the OLE trial

Source data: Appendix 16.2.6, Listing 1.5 hbatb002.sas 07OCT2011

Table 15.2.2.2.1: 1 Descriptive statistics of FPG (mg/dL) over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Number of patients	106	109	56	166	166	56
Plasma glucose level [mg/dL]						
Baseline						
N	105	108	56	161	164	54
Mean	179.0	178.1	175.5	175.9	178.3	179.4
SD	47.0	44.5	43.0	37.7	39.2	42.9
Min	95	85	110	99	85	95
Median	175.0	173.0	167.5	167.0	174.0	170.0
Max	375	378	353	297	299	308
Week 6						
N	103	109	55	160	162	54
Mean	145.5	142.3	144.6	150.3	141.5	146.9
SD	35.0	26.9	29.0	28.5	25.2	30.9
Min	88	90	94	86	79	90
Median	140.0	139.0	142.0	146.0	139.5	148.5
Max	398	270	241	245	214	223
Change from baseline at Week 6						
N	102	108	55	156	160	53
Mean	-30.6	-35.8	-29.9	-25.7	-36.7	-32.6
SD	42.5	39.6	40.0	35.2	36.3	42.4
Min	-144	-227	-180	-126	-171	-198
Median	-29.5	-34.0	-25.0	-24.0	-33.0	-23.0
Max	234	50	77	121	84	65
Week 18						
N	95	104	51	149	155	47
Mean	138.7	143.7	139.9	143.8	139.3	157.3
SD	21.3	30.1	29.4	25.3	24.5	34.8
Min	79	67	85	92	88	101
Median	140.0	139.0	139.0	140.0	135.0	157.0
Max	193	261	274	220	232	232

Only patients who had values after the intake of study drug
The timepoints refer to the OLE trial

Source data: Appendix 16.2.6, Listing 2.1 fpgtb001.sas 07OCT2011

Table 15.2.2.2.1: 1 Descriptive statistics of FPG (mg/dL) over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Change from baseline at Week 18						
N	94	103	51	144	153	45
Mean	-35.5	-33.7	-30.4	-30.6	-37.6	-16.7
SD	37.9	42.0	40.3	31.6	35.8	44.0
Min	-227	-238	-128	-144	-171	-151
Median	-31.5	-29.0	-27.0	-25.0	-36.0	-16.0
Max	69	79	119	60	48	74
Week 30						
N	93	101	51	138	149	45
Mean	141.9	141.5	142.7	143.7	138.4	153.2
SD	26.5	27.1	28.1	28.7	27.1	32.1
Min	85	81	90	95	79	104
Median	144.0	140.0	140.0	139.5	137.0	153.0
Max	236	274	198	288	254	285
Change from baseline at Week 30						
N	92	101	51	133	147	43
Mean	-32.3	-35.0	-28.5	-29.9	-37.9	-25.6
SD	41.4	39.6	28.9	34.9	38.6	38.6
Min	-215	-212	-98	-139	-172	-148
Median	-24.5	-33.0	-27.0	-27.0	-36.0	-20.0
Max	93	57	46	128	142	29
Week 42						
N	85	93	46	131	142	44
Mean	139.2	141.4	138.8	141.9	137.6	157.1
SD	20.9	23.8	21.9	25.5	24.6	33.8
Min	101	97	99	88	85	90
Median	137.0	137.0	142.0	140.0	135.0	156.0
Max	202	209	196	222	222	238
Change from baseline at Week 42						
N	85	93	46	126	140	42
Mean	-35.8	-31.3	-31.0	-30.8	-36.8	-18.5
SD	39.1	41.4	35.6	36.4	34.1	43.1
Min	-179	-229	-166	-176	-146	-115
Median	-27.0	-28.0	-21.0	-27.0	-31.5	-16.0
Max	83	88	29	112	50	76

Only patients who had values after the intake of study drug
The timepoints refer to the OLE trial

Source data: Appendix 16.2.6, Listing 2.1 fpgtb001.sas 07OCT2011

Table 15.2.2.2.1: 1 Descriptive statistics of FPG (mg/dL) over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Week 54						
N	80	88	44	129	136	41
Mean	144.1	142.1	137.7	144.0	136.7	146.3
SD	24.3	20.2	25.0	25.6	22.8	28.4
Min	85	97	90	95	81	99
Median	142.0	139.0	137.0	142.0	135.0	148.0
Max	222	196	187	231	198	234
Change from baseline at Week 54						
N	80	88	44	124	134	39
Mean	-32.1	-31.0	-31.8	-28.2	-36.8	-29.4
SD	37.2	37.8	35.9	33.7	32.5	35.4
Min	-191	-227	-146	-118	-152	-127
Median	-26.5	-27.0	-29.5	-25.5	-33.5	-25.0
Max	89	70	27	44	36	25
Week 66						
N	80	86	43	121	127	40
Mean	148.2	143.7	142.9	148.7	143.9	142.3
SD	27.9	22.2	25.1	27.3	23.1	36.6
Min	95	99	81	99	86	70
Median	142.0	142.0	146.0	146.0	146.0	135.0
Max	270	195	195	254	216	238
Change from baseline at Week 66						
N	80	86	43	116	125	38
Mean	-28.0	-28.6	-26.4	-21.7	-29.6	-32.5
SD	41.4	42.6	35.7	36.2	36.4	46.9
Min	-197	-250	-143	-151	-164	-166
Median	-25.0	-24.5	-14.0	-19.5	-29.0	-22.0
Max	108	56	21	70	58	34
Week 78						
N	72	84	43	117	123	38
Mean	145.0	147.2	146.4	146.0	141.7	148.3
SD	25.0	23.6	27.4	28.7	22.8	33.2
Min	99	90	88	42	88	59
Median	142.0	146.0	148.0	144.0	142.0	142.0
Max	211	214	211	256	207	232

Only patients who had values after the intake of study drug
The timepoints refer to the OLE trial

Source data: Appendix 16.2.6, Listing 2.1 fpgtb001.sas 07OCT2011

Table 15.2.2.2.1: 1 Descriptive statistics of FPG (mg/dL) over time by treatment - treated set OC
Baseline source: before first intake of active treatment (preceding trial or OLE)

	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Change from baseline at Week 78						
N	72	84	43	112	121	36
Mean	-27.9	-25.4	-22.9	-24.7	-31.9	-25.7
SD	33.1	40.9	39.7	41.5	36.5	48.9
Min	-153	-232	-137	-155	-175	-160
Median	-27.0	-24.0	-18.0	-23.5	-32.0	-7.0
Max	60	90	54	139	88	54

Only patients who had values after the intake of study drug
The timepoints refer to the OLE trial

Source data: Appendix 16.2.6, Listing 2.1 fpgtb001.sas 07OCT2011

Table 15.2.3: 1 Number of patients with rescue therapy over time - treated set

No transformation	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Number of patients	106	109	56	166	166	56
Week 6						
N	105 (100.0)	109 (100.0)	56 (100.0)	165 (100.0)	163 (100.0)	56 (100.0)
Yes	5 (4.8)	3 (2.8)	3 (5.4)	10 (6.1)	5 (3.1)	3 (5.4)
No	100 (95.2)	106 (97.2)	53 (94.6)	155 (93.9)	158 (96.9)	53 (94.6)
Week 18						
N	101 (100.0)	109 (100.0)	56 (100.0)	162 (100.0)	163 (100.0)	53 (100.0)
Yes	8 (7.9)	6 (5.5)	4 (7.1)	19 (11.7)	11 (6.7)	8 (15.1)
No	93 (92.1)	103 (94.5)	52 (92.9)	143 (88.3)	152 (93.3)	45 (84.9)
Week 30						
N	101 (100.0)	108 (100.0)	56 (100.0)	161 (100.0)	162 (100.0)	53 (100.0)
Yes	13 (12.9)	13 (12.0)	7 (12.5)	25 (15.5)	14 (8.6)	8 (15.1)
No	88 (87.1)	95 (88.0)	49 (87.5)	136 (84.5)	148 (91.4)	45 (84.9)
Week 42						
N	98 (100.0)	107 (100.0)	53 (100.0)	160 (100.0)	159 (100.0)	53 (100.0)
Yes	17 (17.3)	16 (15.0)	8 (15.1)	30 (18.8)	20 (12.6)	10 (18.9)
No	81 (82.7)	91 (85.0)	45 (84.9)	130 (81.3)	139 (87.4)	43 (81.1)
Week 54						
N	95 (100.0)	105 (100.0)	52 (100.0)	159 (100.0)	157 (100.0)	52 (100.0)
Yes	15 (15.8)	18 (17.1)	8 (15.4)	36 (22.6)	25 (15.9)	12 (23.1)
No	80 (84.2)	87 (82.9)	44 (84.6)	123 (77.4)	132 (84.1)	40 (76.9)

The time points refer to the OLE trial
Source data: Appendix 16.2.6, Listing 3.1

Table 15.2.3: 1 Number of patients with rescue therapy over time - treated set

No transformation	BI 10	BI 25	Met	BI 10+Met	BI 25+Met	Sita+Met
Week 66						
N	95 (100.0)	106 (100.0)	51 (100.0)	157 (100.0)	154 (100.0)	52 (100.0)
Yes	18 (18.9)	20 (18.9)	8 (15.7)	38 (24.2)	27 (17.5)	12 (23.1)
No	77 (81.1)	86 (81.1)	43 (84.3)	119 (75.8)	127 (82.5)	40 (76.9)
Week 78						
N	93 (100.0)	104 (100.0)	51 (100.0)	157 (100.0)	152 (100.0)	51 (100.0)
Yes	25 (26.9)	26 (25.0)	12 (23.5)	39 (24.8)	28 (18.4)	12 (23.5)
No	68 (73.1)	78 (75.0)	39 (76.5)	118 (75.2)	124 (81.6)	39 (76.5)

The time points refer to the OLE trial
Source data: Appendix 16.2.6, Listing 3.1