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1.1.1 Adverse events

Table 1.1.1 Frequencies and proportions of patients with any adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	34	64.2	52	40	76.9	0.2036	1.20	(0.93,1.60) (0.93,1.54)	1.86	(0.79, 4.47)	0.13	(-0.05,0.30)	
Sex														0.1035
Male	19	15	78.9	19	14	73.7	0.8107	0.93	(0.60,1.43) (0.65,1.33)	0.75	(0.15, 3.57)	-0.05	(-0.33,0.23)	
Female	34	19	55.9	33	26	78.8	0.0519	1.41	(0.99,2.12) (1.00,2.00)	2.93	(0.99, 8.94)	0.23	(0.00,0.44)	
Age														0.8656
<15	26	16	61.5	25	18	72.0	0.5454	1.17	(0.76,1.85) (0.79,1.73)	1.61	(0.48, 5.43)	0.10	(-0.16,0.36)	
>=15 to <18	27	18	66.7	27	22	81.5	0.2355	1.22	(0.87,1.83) (0.89,1.69)	2.20	(0.61, 8.32)	0.15	(-0.10,0.38)	
Region														0.8040
US	33	22	66.7	36	28	77.8	0.4933	1.17	(0.86,1.66) (0.87,1.57)	1.75	(0.59, 5.26)	0.11	(-0.11,0.33)	
Non-US	20	12	60.0	16	12	75.0	0.4429	1.25	(0.73,2.17) (0.79,1.97)	2.00	(0.46, 9.32)	0.15	(-0.18,0.45)	
BMI [kg/m2] at baseline														0.5267
< median	27	17	63.0	26	18	69.2	0.7213	1.10	(0.71,1.69) (0.75,1.62)	1.32	(0.41, 4.28)	0.06	(-0.20,0.32)	
>= median	26	17	65.4	26	22	84.6	0.1264	1.29	(0.93,1.93) (0.94,1.79)	2.91	(0.76,12.30)	0.19	(-0.06,0.43)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). inf=infinity.

Table 1.1.1 Frequencies and proportions of patients with any adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
BMI Z-Score														0.4750
<=2 (Underweight, normal or overweight)	9	6	66.7	5	5	100.0	0.2005	1.50	(0.67,3.34)	inf	(0.52,inf)	0.33	(-0.23,0.72)	
>2 to <=3 (Class 1 obesity)	17	10	58.8	21	12	57.1	1.0000	0.97	(0.95,2.38) (0.54,1.89) (0.56,1.67)	0.93	(0.24, 3.52)	-0.02	(-0.33,0.30)	
>3 (Class 2 or 3 obesity)	27	18	66.7	26	23	88.5	0.0664	1.33	(0.98,2.00) (0.98,1.79)	3.83	(0.91,19.32)	0.22	(-0.01,0.44)	
HbA1c [%] at baseline														0.6356
<8.0	29	21	72.4	28	22	78.6	0.7007	1.09	(0.78,1.55) (0.81,1.46)	1.40	(0.40, 4.97)	0.06	(-0.17,0.29)	
8.0 to 9.0	12	7	58.3	12	10	83.3	0.2283	1.43	(0.78,3.01) (0.83,2.45)	3.57	(0.51,31.46)	0.25	(-0.14,0.59)	
>9.0	12	6	50.0	12	8	66.7	0.5249	1.33	(0.62,3.08) (0.67,2.67)	2.00	(0.36,11.29)	0.17	(-0.25,0.54)	
FPG [mg/dl] at baseline														0.3967
<126	13	9	69.2	19	14	73.7	0.8991	1.06	(0.66,2.07) (0.68,1.67)	1.24	(0.24, 6.24)	0.04	(-0.28,0.38)	
>=126	39	24	61.5	29	24	82.8	0.0642	1.34	(0.97,1.91) (1.00,1.81)	3.00	(0.94,10.37)	0.21	(-0.01,0.41)	
eGFR (Zappitelli) at baseline														0.9500
<120	24	15	62.5	21	16	76.2	0.4762	1.22	(0.77,1.95) (0.82,1.80)	1.92	(0.51, 7.55)	0.14	(-0.15,0.40)	
120 to <150	23	15	65.2	19	14	73.7	0.6385	1.13	(0.71,1.78) (0.76,1.69)	1.49	(0.38, 6.08)	0.08	(-0.21,0.37)	
>=150	6	4	66.7	12	10	83.3	0.4982	1.25	(0.69,5.60) (0.67,2.32)	2.50	(0.19,29.87)	0.17	(-0.26,0.64)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). inf=infinity.

Table 1.1.1 Frequencies and proportions of patients with any adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Backg. Antidiabetic Med. at baseline														
Metformin only	28	20	71.4	26	19	73.1								
Insulin only	2	1	50.0	3	2	66.7								
Metformin and Insulin	19	11	57.9	22	19	86.4								
None	4	2	50.0	1	0	0								
Time since diagnosis of T2DM														0.8783
<1 year	18	12	66.7	17	13	76.5	0.6444	1.15	(0.71,1.94) (0.75,1.75)	1.63	(0.35, 7.91)	0.10	(-0.21,0.40)	
1 year - 3 years	24	15	62.5	21	17	81.0	0.1970	1.30	(0.86,2.07) (0.89,1.88)	2.55	(0.64,11.07)	0.18	(-0.09,0.44)	
>3 years	11	7	63.6	14	10	71.4	0.7440	1.12	(0.60,2.38) (0.64,1.96)	1.43	(0.24, 8.39)	0.08	(-0.32,0.46)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). inf=infinity.

Table 1.1.2 Frequencies and proportions of patients with serious adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	2	3.8	52	2	3.8	1.0000	1.02	(0.07,15.13) (0.15, 6.97)	1.02	(0.10,10.11)	0.00	(-0.10,0.10)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.1.3 Frequencies and proportions of patients with adverse events with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	2	3.8	52	1	1.9	0.6927	0.51	(0.02,5.59) (0.05,5.45)	0.50	(0.02,6.79)	-0.02	(-0.11,0.07)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
Maximum intensity: If a patient has more than one AE only the worst is recorded.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.1.4 Frequencies and proportions of patients with adverse events leading to treatment discontinuation overall and by subgroup up to week 26 - TS (TG1)

Subgroup Category	Placebo			E pooled		
	N	n	%	N	n	%
Overall	53	2	3.8	52	0	0

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
N is the number of patients, n the number of patients with at least one event
MedDRA version: 25.0.

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1.1.2 Adverse events excluding disease-specific adverse events

Table 1.2.1 Frequencies and proportions of patients with any adverse events excluding disease-specific adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	33	62.3	52	40	76.9	0.1257	1.24	(0.95,1.64) (0.96,1.60)	2.02	(0.86, 4.82)	0.15	(-0.04,0.32)	
Sex														0.1909
Male	19	14	73.7	19	14	73.7	NC.	1.00	(0.64,1.55) (0.68,1.46)	1.00	(0.22, 4.52)	0.00	(-0.29,0.29)	
Female	34	19	55.9	33	26	78.8	0.0519	1.41	(0.99,2.12) (1.00,2.00)	2.93	(0.99, 8.94)	0.23	(0.00,0.44)	
Age														0.7027
<15	26	16	61.5	25	18	72.0	0.5454	1.17	(0.76,1.85) (0.79,1.73)	1.61	(0.48, 5.43)	0.10	(-0.16,0.36)	
>=15 to <18	27	17	63.0	27	22	81.5	0.1466	1.29	(0.92,1.93) (0.92,1.82)	2.59	(0.73, 9.66)	0.19	(-0.06,0.42)	
Region														0.5922
US	33	22	66.7	36	28	77.8	0.4933	1.17	(0.86,1.66) (0.87,1.57)	1.75	(0.59, 5.26)	0.11	(-0.11,0.33)	
Non-US	20	11	55.0	16	12	75.0	0.2699	1.36	(0.81,2.45) (0.84,2.22)	2.45	(0.57,11.30)	0.20	(-0.14,0.50)	
BMI [kg/m2] at baseline														0.6988
< median	27	16	59.3	26	18	69.2	0.5449	1.17	(0.75,1.87) (0.78,1.75)	1.55	(0.49, 4.96)	0.10	(-0.16,0.36)	
>= median	26	17	65.4	26	22	84.6	0.1264	1.29	(0.93,1.93) (0.94,1.79)	2.91	(0.76,12.30)	0.19	(-0.06,0.43)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). inf=infinity. NC.=Not calculated.

Table 1.2.1 Frequencies and proportions of patients with any adverse events excluding disease-specific adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
BMI Z-Score														0.6856
<=2 (Underweight, normal or overweight)	9	6	66.7	5	5	100.0	0.2005	1.50	(0.67,3.34)	inf	(0.52,inf)	0.33	(-0.23,0.72)	
>2 to <=3 (Class 1 obesity)	17	9	52.9	21	12	57.1	0.8518	1.08	(0.95,2.38) (0.57,2.31) (0.60,1.93)	1.19	(0.32, 4.43)	0.04	(-0.28,0.36)	
>3 (Class 2 or 3 obesity)	27	18	66.7	26	23	88.5	0.0664	1.33	(0.98,2.00) (0.98,1.79)	3.83	(0.91,19.32)	0.22	(-0.01,0.44)	
HbA1c [%] at baseline														0.7500
<8.0	29	20	69.0	28	22	78.6	0.5414	1.14	(0.81,1.62) (0.83,1.56)	1.65	(0.49, 5.77)	0.10	(-0.15,0.33)	
8.0 to 9.0	12	7	58.3	12	10	83.3	0.2283	1.43	(0.78,3.01) (0.83,2.45)	3.57	(0.51,31.46)	0.25	(-0.14,0.59)	
>9.0	12	6	50.0	12	8	66.7	0.5249	1.33	(0.62,3.08) (0.67,2.67)	2.00	(0.36,11.29)	0.17	(-0.25,0.54)	
FPG [mg/dl] at baseline														0.3222
<126	13	9	69.2	19	14	73.7	0.8991	1.06	(0.66,2.07) (0.68,1.67)	1.24	(0.24, 6.24)	0.04	(-0.28,0.38)	
>=126	39	23	59.0	29	24	82.8	0.0481	1.40	(1.01,2.02) (1.03,1.91)	3.34	(1.06,11.48)	0.24	(0.00,0.44)	
eGFR (Zappitelli) at baseline														0.8823
<120	24	14	58.3	21	16	76.2	0.2846	1.31	(0.82,2.16) (0.86,1.98)	2.29	(0.62, 8.89)	0.18	(-0.12,0.45)	
120 to <150	23	15	65.2	19	14	73.7	0.6385	1.13	(0.71,1.78) (0.76,1.69)	1.49	(0.38, 6.08)	0.08	(-0.21,0.37)	
>=150	6	4	66.7	12	10	83.3	0.4982	1.25	(0.69,5.60) (0.67,2.32)	2.50	(0.19,29.87)	0.17	(-0.26,0.64)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). inf=infinity. NC.=Not calculated.

Table 1.2.1 Frequencies and proportions of patients with any adverse events excluding disease-specific adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Backg. Antidiabetic Med. at baseline														
Metformin only	28	19	67.9	26	19	73.1								
Insulin only	2	1	50.0	3	2	66.7								
Metformin and Insulin	19	11	57.9	22	19	86.4								
None	4	2	50.0	1	0	0								
Time since diagnosis of T2DM														0.9154
<1 year	18	11	61.1	17	13	76.5	0.5487	1.25	(0.75,2.16) (0.80,1.97)	2.07	(0.46, 9.84)	0.15	(-0.17,0.45)	
1 year - 3 years	24	15	62.5	21	17	81.0	0.1970	1.30	(0.86,2.07) (0.89,1.88)	2.55	(0.64,11.07)	0.18	(-0.09,0.44)	
>3 years	11	7	63.6	14	10	71.4	0.7440	1.12	(0.60,2.38) (0.64,1.96)	1.43	(0.24, 8.39)	0.08	(-0.32,0.46)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). inf=infinity. NC.=Not calculated.

Table 1.2.2 Frequencies and proportions of patients with serious adverse events excluding disease-specific adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	2	3.8	0.6702	2.04	(0.19,55.36) (0.19,21.80)	2.08	(0.15,62.46)	0.02	(-0.07,0.11)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.2.3 Frequencies and proportions of patients with adverse events with severe maximum intensity excluding disease-specific adverse events overall and by subgroup up to week 26 - TS (TG1)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	2	3.8	52	1	1.9	0.6927	0.51	(0.02,5.59) (0.05,5.45)	0.50	(0.02,6.79)	-0.02	(-0.11,0.07)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
Maximum intensity: If a patient has more than one AE only the worst is recorded.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Appendix 1, 1.3

1.1.3 Adverse events of special interest

Table 1.3.1 Frequencies and proportions of patients with adverse events of special interest overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Hypersensitivity reactions (narrow SMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	4	7.7	0.2345	4.08	(0.57,103.04) (0.47, 35.27)	4.33	(0.52,109.12)	0.06	(-0.04,0.17)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.1 Frequencies and proportions of patients with adverse events of special interest overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Skin lesion (narrow SMQ)

There is no data to be displayed.

Table 1.3.1 Frequencies and proportions of patients with adverse events of special interest overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Pancreatitis (narrow SMQ, PT)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00, 14.86) NC.	0.00	(0.00, 9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.1 Frequencies and proportions of patients with adverse events of special interest overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Pancreatic cancer (narrow BIcMQ)

There is no data to be displayed.

Table 1.3.1 Frequencies and proportions of patients with adverse events of special interest overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Hepatic injury (narrow sub SMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI) p-value **
Overall	53	1	1.9	52	2	3.8	0.6702	2.04	(0.19, 55.36) (0.19, 21.80)	2.08	(0.15, 62.46)	0.02	(-0.07,0.11)

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.1 Frequencies and proportions of patients with adverse events of special interest overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Decreased renal function (narrow SMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00, 14.86) NC.	0.00	(0.00, 9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.1 Frequencies and proportions of patients with adverse events of special interest overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Diabetic ketoacidosis (narrow BIcMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI) p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00, 14.86) NC.	0.00	(0.00, 9.17)	-0.02	(-0.10,0.06)

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.1 Frequencies and proportions of patients with adverse events of special interest overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Events leading to lower limb amputation (investigator determined)

There is no data to be displayed.

Table 1.3.2 Frequencies and proportions of patients with serious adverse events of special interest overall and by subgroup up to week 26- TS (TG1)
User-defined AE category: Hypersensitivity reactions (narrow SMQ)

There is no data to be displayed.

Table 1.3.2 Frequencies and proportions of patients with serious adverse events of special interest overall and by subgroup up to week 26- TS (TG1)
User-defined AE category: Skin lesion (narrow SMQ)

There is no data to be displayed.

Table 1.3.2 Frequencies and proportions of patients with serious adverse events of special interest overall and by subgroup up to week 26- TS (TG1)
User-defined AE category: Pancreatitis (narrow SMQ, PT)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00,14.86) NC.	0.00	(0.00,9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.2 Frequencies and proportions of patients with serious adverse events of special interest overall and by subgroup up to week 26- TS (TG1)
User-defined AE category: Pancreatic cancer (narrow BIcMQ)

There is no data to be displayed.

Table 1.3.2 Frequencies and proportions of patients with serious adverse events of special interest overall and by subgroup up to week 26- TS (TG1)
User-defined AE category: Hepatic injury (narrow sub SMQ)

There is no data to be displayed.

Table 1.3.2 Frequencies and proportions of patients with serious adverse events of special interest overall and by subgroup up to week 26- TS (TG1)
User-defined AE category: Decreased renal function (narrow SMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00,14.86) NC.	0.00	(0.00,9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.2 Frequencies and proportions of patients with serious adverse events of special interest overall and by subgroup up to week 26- TS (TG1)
User-defined AE category: Diabetic ketoacidosis (narrow BIcMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00,14.86) NC.	0.00	(0.00,9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.2 Frequencies and proportions of patients with serious adverse events of special interest overall and by subgroup up to week 26- TS (TG1)
User-defined AE category: Events leading to lower limb amputation (investigator determined)

There is no data to be displayed.

Table 1.3.3 Frequencies and proportions of patients with adverse events of special interest with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Hypersensitivity reactions (narrow SMQ)

There is no data to be displayed.

Table 1.3.3 Frequencies and proportions of patients with adverse events of special interest with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Skin lesion (narrow SMQ)

There is no data to be displayed.

Table 1.3.3 Frequencies and proportions of patients with adverse events of special interest with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Pancreatitis (narrow SMQ, PT)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00,14.86) NC.	0.00	(0.00,9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
Maximum intensity: If a patient has more than one AE only the worst is recorded.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.3 Frequencies and proportions of patients with adverse events of special interest with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Pancreatic cancer (narrow BIcMQ)

There is no data to be displayed.

Table 1.3.3 Frequencies and proportions of patients with adverse events of special interest with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Hepatic injury (narrow sub SMQ)

There is no data to be displayed.

Table 1.3.3 Frequencies and proportions of patients with adverse events of special interest with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Decreased renal function (narrow SMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00,14.86) NC.	0.00	(0.00,9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
Maximum intensity: If a patient has more than one AE only the worst is recorded.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.3 Frequencies and proportions of patients with adverse events of special interest with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Diabetic ketoacidosis (narrow BIcMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00,14.86) NC.	0.00	(0.00,9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
Maximum intensity: If a patient has more than one AE only the worst is recorded.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.3.3 Frequencies and proportions of patients with adverse events of special interest with severe maximum intensity overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Events leading to lower limb amputation (investigator determined)

There is no data to be displayed.

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Acute pancreatitis	Pancreatitis	0000000005	Narrow	10033625	Pancreatic haemorrhage
				10033635	Pancreatic pseudocyst
				10033636	Pancreatic pseudocyst drainage
				10033645	Pancreatitis
				10033647	Pancreatitis acute
				10033650	Pancreatitis haemorrhagic
				10033654	Pancreatitis necrotising
				10033657	Pancreatitis relapsing
				10048984	Pancreatic abscess
				10052400	Oedematous pancreatitis
				10056277	Pancreatorenal syndrome
				10056975	Pancreatic phlegmon
				10059029	Cullen's sign
				10066127	Ischaemic pancreatitis
				10075426	Grey Turner's sign
				10076058	Haemorrhagic necrotic pancreatitis
				10081762	Pancreatic pseudoaneurysm
				10082531	Pancreatic cyst drainage
				10083072	Immune-mediated pancreatitis
				10083811	Pancreatic pseudocyst rupture
				10083813	Pancreatic pseudocyst haemorrhage
				10084554	Subacute pancreatitis
				10085347	Walled-off pancreatic necrosis
Acute renal failure	Decreased renal function	0000000008	Narrow	10002847	Anuria
				10003885	Azotaemia
				10018875	Haemodialysis
				10029155	Nephropathy toxic
				10030302	Oliguria
				10034660	Peritoneal dialysis
				10038435	Renal failure
				10038447	Renal failure neonatal
				10049776	Renal impairment neonatal
				10049778	Neonatal anuria
				10053090	Haemofiltration
				10061105	Dialysis
				10062237	Renal impairment
				10066338	Continuous haemodiafiltration
				10069339	Acute kidney injury
				10069688	Acute phosphate nephropathy
				10072370	Prerenal failure
				10078987	Foetal renal impairment

MedDRA version: 25.0

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Acute renal failure	Decreased renal function	0000000008	Narrow	10081980	Subacute kidney injury
Cholestasis and jaundice of hepatic origin	Hepatic injury	0000000007	Narrow	10008635	Cholestasis
				10019754	Hepatitis cholestatic
				10021209	Icterus index increased
				10023126	Jaundice
				10023129	Jaundice cholestatic
				10023136	Jaundice hepatocellular
				10048611	Cholaemia
				10058117	Ocular icterus
				10061009	Bilirubin excretion disorder
				10064190	Cholestatic pruritus
				10066758	Mixed liver injury
				10067969	Cholestatic liver injury
				10072268	Drug-induced liver injury
				10074151	Parenteral nutrition associated liver disease
Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions	Hepatic injury	0000000007	Narrow	10000804	Acute hepatic failure
				10003547	Asterixis
				10004659	Biliary cirrhosis
				10004664	Biliary fibrosis
				10010075	Coma hepatic
				10019637	Hepatic atrophy
				10019641	Hepatic cirrhosis
				10019660	Hepatic encephalopathy
				10019663	Hepatic failure
				10019668	Hepatic fibrosis
				10019692	Hepatic necrosis
				10019708	Hepatic steatosis
				10019837	Hepatocellular injury
				10019845	Hepatorenal failure
				10019846	Hepatorenal syndrome
				10019851	Hepatotoxicity
				10024670	Liver disorder
				10024714	Liver transplant
				10025129	Lupoid hepatic cirrhosis
				10029530	Non-alcoholic fatty liver
				10030210	Oesophageal varices haemorrhage
				10036200	Portal hypertension
				10039012	Reye’s syndrome

MedDRA version: 25.0

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions	Hepatic injury	0000000007	Narrow	10050897	Portal hypertensive gastropathy
				10051010	Duodenal varices
				10051012	Gastric varices
				10051081	Nodular regenerative hyperplasia
				10052274	Hepatopulmonary syndrome
				10052279	Renal and liver transplant
				10053244	Hepatocellular foamy cell syndrome
				10056091	Varices oesophageal
				10056956	Subacute hepatic failure
				10057572	Gastric varices haemorrhage
				10057573	Chronic hepatic failure
				10061135	Spontaneous bacterial peritonitis
				10061997	Hepatectomy
				10061998	Hepatic lesion
				10062000	Hepatobiliary disease
				10062040	Liver operation
				10063075	Cryptogenic cirrhosis
				10064668	Hepatic infiltration eosinophilic
				10065274	Hepatic calcification
				10066597	Gastrooesophageal variceal haemorrhage prophylaxis
				10066599	Hepatic encephalopathy prophylaxis
				10067125	Liver injury
				10067281	Portopulmonary hypertension
				10067823	Splenic varices
				10068662	Splenic varices haemorrhage
				10068923	Portal hypertensive enteropathy
				10070815	Acute yellow liver atrophy
				10070953	Reynold's syndrome
				10071265	Diabetic hepatopathy
				10071502	Intestinal varices
				10072284	Varicose veins of abdominal wall
				10072319	Gallbladder varices
				10073209	Portal vein dilatation
				10073215	Peripancreatic varices
				10073979	Portal vein cavernous transformation
				10074726	Portal fibrosis
				10076237	Gastric variceal injection
				10076238	Gastric variceal ligation
				10076640	Liver dialysis
				10077215	Hepatic steato-fibrosis
				10077259	Non-cirrhotic portal hypertension

MedDRA version: 25.0

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions	Hepatic injury	0000000007	Narrow	10077305	Acute on chronic liver failure
				10078058	Intestinal varices haemorrhage
				10079446	Portal hypertensive colopathy
				10080429	Primary biliary cholangitis
				10080679	Regenerative siderotic hepatic nodule
				10080860	Acquired hepatocerebral degeneration
				10082480	Cardiohepatic syndrome
				10083010	Sugiura procedure
				10083406	Immune-mediated cholangitis
				10083521	Immune-mediated hepatic disorder
				10084797	Flood syndrome
				10087030	Omental oedema
Hepatitis, non-infectious	Hepatic injury	0000000007	Narrow	10003827	Autoimmune hepatitis
				10008909	Chronic hepatitis
				10019717	Hepatitis
				10019727	Hepatitis acute
				10019755	Hepatitis chronic active
				10019759	Hepatitis chronic persistent
				10019772	Hepatitis fulminant
				10019795	Hepatitis toxic
				10023025	Ischaemic hepatitis
				10049199	Hepatic cytolysis
				10051015	Radiation hepatitis
				10053219	Non-alcoholic steatohepatitis
				10064676	Graft versus host disease in liver
				10066263	Acute graft versus host disease in liver
				10067737	Lupus hepatitis
				10071198	Allergic hepatitis
				10072160	Chronic graft versus host disease in liver
				10076331	Steatohepatitis
				10078962	Immune-mediated hepatitis
				10080576	Alloimmune hepatitis
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10002198	Anaphylactic reaction
				10002199	Anaphylactic shock
				10002216	Anaphylactoid reaction
				10002222	Anaphylaxis treatment
				10002424	Angioedema
				10003036	Application site dermatitis

MedDRA version: 25.0

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10003054	Application site rash
				10003645	Atopy
				10005149	Blepharitis allergic
				10005589	Blood immunoglobulin E abnormal
				10005591	Blood immunoglobulin E increased
				10006404	Bromoderma
				10006482	Bronchospasm
				10009192	Circulatory collapse
				10010726	Conjunctival oedema
				10010744	Conjunctivitis allergic
				10010836	Contrast media reaction
				10011033	Corneal oedema
				10011411	Cross sensitivity reaction
				10011686	Cutaneous vasculitis
				10012431	Dermatitis
				10012432	Dermatitis acneiform
				10012434	Dermatitis allergic
				10012438	Dermatitis atopic
				10012441	Dermatitis bullous
				10012442	Dermatitis contact
				10012455	Dermatitis exfoliative
				10012456	Dermatitis exfoliative generalised
				10012468	Dermatitis herpetiformis
				10012470	Dermatitis infected
				10013687	Drug eruption
				10013700	Drug hypersensitivity
				10014184	Eczema
				10014198	Eczema infantile
				10014201	Eczema nummular
				10014627	Encephalopathy allergic
				10014989	Epidermolysis bullosa
				10015029	Epiglottic oedema
				10015218	Erythema multiforme
				10015226	Erythema nodosum
				10015907	Eye allergy
				10015967	Eye swelling
				10015993	Eyelid oedema
				10016029	Face oedema
				10016741	Fixed eruption
				10018258	Giant papillary conjunctivitis
				10018291	Gingival swelling
				10019617	Henoch-Schonlein purpura

MedDRA version: 25.0

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10020751	Hypersensitivity
				10020764	Hypersensitivity vasculitis
				10021247	Idiopathic urticaria
				10022056	Injection site dermatitis
				10022071	Injection site hypersensitivity
				10022094	Injection site rash
				10022107	Injection site urticaria
				10023845	Laryngeal oedema
				10023891	Laryngospasm
				10023893	Laryngotracheal oedema
				10024558	Lip oedema
				10024570	Lip swelling
				10028164	Multiple allergies
				10029120	Nephritis allergic
				10029415	Nikolsky's sign
				10030081	Oculomucocutaneous syndrome
				10030110	Oedema mouth
				10031111	Oropharyngeal spasm
				10031118	Oropharyngeal swelling
				10034541	Perioral dermatitis
				10034545	Periorbital oedema
				10034829	Pharyngeal oedema
				10037789	Radioallergosorbent test positive
				10037844	Rash
				10037855	Rash erythematous
				10037857	Rash follicular
				10037867	Rash macular
				10037868	Rash maculo-papular
				10037870	Rash morbilliform
				10037871	Rash neonatal
				10037879	Rash papulosquamous
				10037884	Rash pruritic
				10037888	Rash pustular
				10037890	Rash scarlatiniform
				10037898	Rash vesicular
				10037973	Reaction to azo-dyes
				10037974	Reaction to colouring
				10037977	Reaction to food additive
				10039085	Rhinitis allergic
				10039755	Scrotal oedema
				10040400	Serum sickness
				10040402	Serum sickness-like reaction

MedDRA version: 25.0

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10040560	Shock
				10040581	Shock symptom
				10040893	Skin necrosis
				10040914	Skin reaction
				10040934	Skin test positive
				10041307	Solar urticaria
				10041316	Solvent sensitivity
				10042033	Stevens-Johnson syndrome
				10042682	Swelling face
				10042690	Swelling of eyelid
				10042727	Swollen tongue
				10043967	Tongue oedema
				10044223	Toxic epidermal necrolysis
				10044296	Tracheal oedema
				10045240	Type I hypersensitivity
				10046735	Urticaria
				10046740	Urticaria cholinergic
				10046742	Urticaria contact
				10046750	Urticaria papular
				10046751	Urticaria physical
				10046752	Urticaria pigmentosa
				10046755	Urticaria vesiculosa
				10046943	Vaginal ulceration
				10047111	Vasculitic rash
				10047768	Vulval ulceration
				10048799	Acute generalised exanthematous pustulosis
				10048820	Urticarial vasculitis
				10049153	Allergic sinusitis
				10049305	Gingival oedema
				10050004	Rash maculovesicular
				10050099	Application site eczema
				10050104	Application site urticaria
				10050181	Vulvovaginal ulceration
				10050639	Allergic pharyngitis
				10050894	Anti-neutrophil cytoplasmic antibody positive vasculitis
				10051126	Scleritis allergic
				10051394	Allergic cystitis
				10051792	Infusion related reaction
				10052098	Iodine allergy
				10052139	Eye oedema

MedDRA version: 25.0

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10052250	Circumoral oedema
				10052271	Catheter site rash
				10052272	Catheter site urticaria
				10052568	Urticaria chronic
				10052613	Allergic bronchitis
				10053177	Epidermolysis
				10053613	Type IV hypersensitivity reaction
				10053614	Type III immune complex mediated reaction
				10053779	Allergic cough
				10054000	Type II hypersensitivity
				10055048	Allergy to vaccine
				10055182	Eczema weeping
				10056352	Allergy test positive
				10056387	Encephalitis allergic
				10056647	Periorbital swelling
				10056671	Mucocutaneous rash
				10056872	Palpable purpura
				10056998	Palatal oedema
				10057380	Allergic keratitis
				10057431	Scleral oedema
				10057970	Toxic skin eruption
				10057984	Rash rubelliform
				10058675	Dermatitis psoriasiform
				10058681	Eczema vesicular
				10058898	Hand dermatitis
				10059071	Stoma site rash
				10059284	Epidermal necrosis
				10059447	Allergic colitis
				10059499	Haemorrhagic urticaria
				10059830	Infusion site rash
				10060934	Allergic oedema
				10061430	Arthritis allergic
				10061557	Allergic otitis media
				10062506	Heparin-induced thrombocytopenia
				10062918	Dennie-Morgan fold
				10063119	Anaphylactoid shock
				10063438	Pruritus allergic
				10063527	Allergic respiratory symptom
				10063532	Allergic respiratory disease
				10063683	Application site hypersensitivity
				10063786	Implant site rash

MedDRA version: 25.0

Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10063787	Implant site urticaria
				10063855	Implant site dermatitis
				10063858	Implant site hypersensitivity
				10064059	Antiallergic therapy
				10064579	Exfoliative rash
				10064788	Reaction to preservatives
				10064866	Laryngitis allergic
				10065458	Infusion site dermatitis
				10065471	Infusion site hypersensitivity
				10065490	Infusion site urticaria
				10065514	Antiendomysial antibody positive
				10066042	Eczema vaccinatum
				10066173	Allergic transfusion reaction
				10066221	Injection site eczema
				10066273	Vulval eczema
				10066797	Injection site recall reaction
				10066837	Gleich's syndrome
				10066973	Contrast media allergy
				10067113	Anaphylactic transfusion reaction
				10067142	Immediate post-injection reaction
				10067317	Oculorespiratory syndrome
				10067510	Contact stomatitis
				10067950	Oropharyngeal blistering
				10067972	Interstitial granulomatous dermatitis
				10067995	Injection site vasculitis
				10068355	Oral allergy syndrome
				10068809	Palisaded neutrophilic granulomatous dermatitis
				10068880	Vaccination site hypersensitivity
				10069167	Kounis syndrome
				10069440	Henoch-Schonlein purpura nephritis
				10069477	Vaccination site dermatitis
				10069482	Vaccination site rash
				10069489	Vaccination site exfoliation
				10069622	Vaccination site urticaria
				10069623	Vaccination site vesicles
				10069773	Administration related reaction
				10070492	Limbal swelling
				10070559	Distributive shock
				10070581	Immune tolerance induction
				10071152	Injection related reaction
				10071156	Administration site rash

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Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10071198	Allergic hepatitis
				10071380	Chronic hyperplastic eosinophilic sinusitis
				10071399	Chronic eosinophilic rhinosinusitis
				10071588	Vulvovaginal rash
				10072867	Device allergy
				10073168	Incision site dermatitis
				10073411	Incision site rash
				10073508	Drug reaction with eosinophilia and systemic symptoms
				10073612	Instillation site hypersensitivity
				10073622	Instillation site rash
				10073627	Instillation site urticaria
				10073992	Catheter site dermatitis
				10073995	Catheter site eczema
				10073998	Catheter site hypersensitivity
				10074014	Catheter site vasculitis
				10074079	Allergy to immunoglobulin therapy
				10074332	Pathergy reaction
				10074350	Drug provocation test
				10074403	Palatal swelling
				10074509	Stoma site hypersensitivity
				10074850	Infusion site eczema
				10074851	Infusion site vasculitis
				10075072	Allergic otitis externa
				10075084	Aspirin-exacerbated respiratory disease
				10075096	Administration site dermatitis
				10075099	Administration site eczema
				10075102	Administration site hypersensitivity
				10075109	Administration site urticaria
				10075185	Allergic eosinophilia
				10075203	Mouth swelling
				10075217	Mast cell activation syndrome
				10075308	Allergic gastroenteritis
				10075479	Allergy alert test positive
				10075572	Medical device site dermatitis
				10075575	Medical device site eczema
				10075579	Medical device site hypersensitivity
				10075585	Medical device site rash
				10075588	Medical device site urticaria
				10075807	Nodular rash
				10075964	Administration site recall reaction

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Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10075969	Administration site vasculitis
				10076024	Application site recall reaction
				10076027	Application site vasculitis
				10076085	Infusion site recall reaction
				10076140	Medical device site recall reaction
				10076161	Vaccination site eczema
				10076188	Vaccination site recall reaction
				10076191	Vaccination site vasculitis
				10076229	Intestinal angioedema
				10076470	Documented hypersensitivity to administered product
				10076606	Mast cell degranulation present
				10076665	Dialysis membrane reaction
				10077117	Vessel puncture site rash
				10077279	Allergy to surgical sutures
				10077813	Vessel puncture site vesicles
				10078117	Eosinophilic granulomatosis with polyangiitis
				10078325	Symmetrical drug-related intertriginous and flexural exanthema
				10078682	Anal eczema
				10078783	Oropharyngeal oedema
				10078853	Allergic reaction to excipient
				10079554	Allergic stomatitis
				10079925	Reaction to excipient
				10080783	Vulvovaginitis allergic
				10080894	Procedural shock
				10081000	Vernal keratoconjunctivitis
				10081004	Hypersensitivity myocarditis
				10081035	Acquired C1 inhibitor deficiency
				10081492	Atopic cough
				10081703	Circumoral swelling
				10081988	Hypersensitivity pneumonitis
				10082270	Pharyngeal swelling
				10082290	Urticarial dermatitis
				10082681	Reaction to flavouring
				10082742	Infusion related hypersensitivity reaction
				10083164	SJS-TEN overlap
				10083260	Scrotal dermatitis
				10083809	Bullous haemorrhagic dermatosis
				10083842	Immune thrombocytopenia

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Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Hypersensitivity	Hypersensitivity reactions	0000000003	Narrow	10084049	Nutritional supplement allergy
				10084905	Generalised bullous fixed drug eruption
				10085938	Vascular access site dermatitis
				10085939	Vascular access site eczema
				10086007	Allergic lymphangitis
				10086347	Polymers allergy
				10086454	Reaction to sweetener
				10086476	Dermal filler reaction
				10086737	Vancomycin infusion reaction
				10087203	Periorbital dermatitis
				10087325	Bone cement allergy
Ketoacidosis	Diabetic ketoacidosis	0000000009	Narrow	10012668	Diabetic hyperglycaemic coma
				10012671	Diabetic ketoacidosis
				10012672	Diabetic ketoacidotic hyperglycaemic coma
				10023379	Ketoacidosis
				10080061	Euglycaemic diabetic ketoacidosis
Liver related investigations, signs and symptoms	Hepatic injury	0000000007	Narrow	10001547	Alanine aminotransferase abnormal
				10001551	Alanine aminotransferase increased
				10001942	Ammonia abnormal
				10001946	Ammonia increased
				10003445	Ascites
				10003477	Aspartate aminotransferase abnormal
				10003481	Aspartate aminotransferase increased
				10004685	Bilirubin conjugated increased
				10004792	Biopsy liver abnormal
				10005364	Blood bilirubin increased
				10005370	Blood bilirubin unconjugated increased
				10006408	Bromosulphthalein test abnormal
				10017688	Gamma-glutamyltransferase abnormal
				10017693	Gamma-glutamyltransferase increased
				10019621	Hepaplastin abnormal
				10019622	Hepaplastin decreased
				10019670	Hepatic function abnormal
				10019705	Hepatic pain
				10019842	Hepatomegaly
				10019847	Hepatosplenomegaly
				10020575	Hyperammonaemia

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Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Liver related investigations, signs and symptoms	Hepatic injury	0000000007	Narrow	10020578	Hyperbilirubinaemia
				10023321	Kayser-Fleischer ring
				10024690	Liver function test abnormal
				10024712	Liver tenderness
				10045428	Ultrasound liver abnormal
				10049631	Oedema due to hepatic disease
				10050792	Urine bilirubin increased
				10051333	Guanase increased
				10051343	Bile output decreased
				10051344	Bile output abnormal
				10051924	Hypercholia
				10052550	Liver induration
				10052554	Foetor hepaticus
				10054125	Perihepatic discomfort
				10054889	Transaminases increased
				10056536	X-ray hepatobiliary abnormal
				10057110	Hepatic mass
				10058477	Blood bilirubin abnormal
				10059710	Galactose elimination capacity test abnormal
				10059712	Galactose elimination capacity test decreased
				10060107	Liver-kidney microsomal antibody positive
				10060794	Hepatic enzyme decreased
				10060795	Hepatic enzyme increased
				10061947	Liver scan abnormal
				10062685	Hepatic enzyme abnormal
				10062688	Transaminases abnormal
				10064558	Total bile acids increased
				10064712	Mitochondrial aspartate aminotransferase increased
				10066195	Hepatobiliary scan abnormal
				10066244	Hepatic sequestration
				10066869	Molar ratio of total branched-chain amino acid to tyrosine
				10067338	Retrograde portal vein flow
				10067365	Hepatic hydrothorax
				10067718	Bilirubin conjugated abnormal
				10068237	Hypertransaminasaemia
				10068287	Child-Pugh-Turcotte score increased
				10068358	Hepatic vascular resistance increased

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Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Liver related investigations, signs and symptoms	Hepatic injury	0000000007	Narrow	10068547	Bacterascites
				10068997	Hepatic artery flow decreased
				10074150	Biliary ascites
				10075895	Liver palpable
				10076254	Hepatic hypertrophy
				10077020	Child-Pugh-Turcotte score abnormal
				10077356	Bilirubin urine present
				10077677	Liver function test decreased
				10077692	Liver function test increased
				10078360	Computerised tomogram liver abnormal
				10078438	White nipple sign
				10082443	Magnetic resonance proton density fat fraction measurement
				10082832	AST/ALT ratio abnormal
				10083171	Hepatic venous pressure gradient increased
				10083172	Hepatic venous pressure gradient abnormal
				10084058	Congestive hepatopathy
				10084751	Hepatic hypoperfusion
				10085121	Magnetic resonance imaging hepatobiliary abnormal
				10086006	Acquired factor V deficiency
				10086970	Anti-liver cytosol antibody type 1 positive
Pancreatic neoplasms	Pancreatic cancer	0000000006	Narrow	10004334	Benign neoplasm of islets of Langerhans
				10017852	Gastrinoma
				10018404	Glucagonoma
				10022498	Insulinoma
				10025997	Malignant neoplasm of islets of Langerhans
				10029341	Neurotensinoma
				10033609	Pancreatic carcinoma
				10033610	Pancreatic carcinoma metastatic
				10033613	Pancreatic carcinoma recurrent
				10041329	Somatostatinoma
				10047430	Vipoma
				10051709	Gastrinoma malignant
				10052747	Adenocarcinoma pancreas
				10055006	Pancreatic sarcoma
				10055007	Carcinoid tumour of the pancreas

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Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Pancreatic neoplasms	Pancreatic cancer	0000000006	Narrow	10059320	Pancreatic carcinoma stage 0
				10059321	Pancreatic carcinoma stage I
				10059322	Pancreatic carcinoma stage II
				10059323	Pancreatic carcinoma stage III
				10059326	Pancreatic carcinoma stage IV
				10061000	Benign pancreatic neoplasm
				10061902	Pancreatic neoplasm
				10065908	Cystadenocarcinoma pancreas
				10067517	Pancreatic neuroendocrine tumour
				10068909	Pancreatic neuroendocrine tumour metastatic
				10069345	Solid pseudopapillary tumour of the pancreas
				10070999	Intraductal papillary mucinous neoplasm
				10073363	Acinar cell carcinoma of pancreas
				10073364	Ductal adenocarcinoma of pancreas
				10073365	Intraductal papillary-mucinous carcinoma of pancreas
				10073367	Pancreatoblastoma
				10075245	Metastatic glucagonoma
				10077559	Gastroenteropancreatic neuroendocrine tumour disease
				10087099	Pancreatic haemangioma
Pancreatitis chronic	Pancreatitis	0000000005		10033649	Pancreatitis chronic
Severe cutaneous adverse reactions	Skin lesions	0000000004	Narrow	10011686	Cutaneous vasculitis
				10012441	Dermatitis bullous
				10012455	Dermatitis exfoliative
				10012456	Dermatitis exfoliative generalised
				10015218	Erythema multiforme
				10030081	Oculomucocutaneous syndrome
				10040893	Skin necrosis
				10042033	Stevens-Johnson syndrome
				10044223	Toxic epidermal necrolysis
				10048799	Acute generalised exanthematous pustulosis
				10057970	Toxic skin eruption
				10059284	Epidermal necrosis
				10064579	Exfoliative rash
				10073508	Drug reaction with eosinophilia and systemic symptoms
				10081998	Target skin lesion

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Listing 1.3.4 Listing of preferred terms that define adverse events of special interest

Source	Group	Group code	Scope	Preferred term code	Preferred term
Severe cutaneous adverse reactions	Skin lesions	0000000004	Narrow	10082985	Erythrodermic atopic dermatitis
				10083164	SJS-TEN overlap
				10083809	Bullous haemorrhagic dermatosis
				10084905	Generalised bullous fixed drug eruption
				10085778	Severe cutaneous adverse reaction

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Appendix 1, 1.4

1.1.4 Specific adverse events

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Hypoglycaemia (reported)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	5	9.4	52	12	23.1	0.0656	2.45	(0.95, 11.59) (0.93, 6.46)	2.88	(0.94, 9.69)	0.14	(-0.01,0.29)	
Sex														0.2547
Male	19	1	5.3	19	6	31.6	0.0486	6.00	(1.01,155.75) (0.80, 45.20)	8.31	(1.01,202.07)	0.26	(0.00,0.52)	
Female	34	4	11.8	33	6	18.2	0.5424	1.55	(0.46, 6.19) (0.48, 4.98)	1.67	(0.41, 7.30)	0.06	(-0.12,0.25)	
Age														0.2601
<15	26	4	15.4	25	6	24.0	0.5454	1.56	(0.49, 5.97) (0.50, 4.88)	1.74	(0.41, 7.85)	0.09	(-0.16,0.32)	
>=15 to <18	27	1	3.7	27	6	22.2	0.0538	6.00	(0.98,153.97) (0.77, 46.55)	7.43	(0.96,178.06)	0.19	(0.00,0.38)	
Region														0.9824
US	33	3	9.1	36	8	22.2	0.2086	2.44	(0.75, 13.63) (0.71, 8.45)	2.86	(0.69, 14.27)	0.13	(-0.05,0.32)	
Non-US	20	2	10.0	16	4	25.0	0.2885	2.50	(0.48, 18.26) (0.52, 11.96)	3.00	(0.45, 25.77)	0.15	(-0.11,0.44)	
BMI [kg/m2] at baseline														0.2596
< median	27	4	14.8	26	6	23.1	0.5449	1.56	(0.48, 5.99) (0.50, 4.89)	1.73	(0.41, 7.76)	0.08	(-0.14,0.31)	
>= median	26	1	3.8	26	6	23.1	0.0533	6.00	(0.98,154.12) (0.78, 46.42)	7.50	(0.97,180.01)	0.19	(0.00,0.40)	
BMI Z-Score														
<=2 (Underweight, normal or overweight)	9	0	0	5	2	40.0								
>2 to <=3 (Class 1 obesity)	17	3	17.6	21	4	19.0								
>3 (Class 2 or 3 obesity)	27	2	7.4	26	6	23.1								

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Hypoglycaemia (reported)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
HbA1c [%] at baseline														
<8.0	29	2	6.9	28	6	21.4								
8.0 to 9.0	12	1	8.3	12	3	25.0								
>9.0	12	2	16.7	12	3	25.0								
FPG [mg/dl] at baseline														0.1894
<126	13	2	15.4	19	3	15.8	1.0000	1.03	(0.18, 10.03) (0.20, 5.31)	1.03	(0.13, 9.89)	0.00	(-0.31,0.28)	
>=126	39	3	7.7	29	9	31.0	0.0147	4.03	(1.17, 19.97) (1.20, 13.60)	5.40	(1.32, 26.52)	0.23	(0.04,0.44)	
eGFR (Zappitelli) at baseline														0.9636
<120	24	1	4.2	21	3	14.3	0.2877	3.43	(0.37, 88.25) (0.39, 30.52)	3.83	(0.37,104.96)	0.10	(-0.09,0.33)	
120 to <150	23	3	13.0	19	9	47.4	0.0168	3.63	(1.18, 17.76) (1.14, 11.55)	6.00	(1.31, 31.41)	0.34	(0.06,0.60)	
>=150	6	1	16.7	12	0	0	0.3018	0.00	(0.00, 7.07) NC.	0.00	(0.00, 4.50)	-0.17	(-0.64,0.14)	
Backg. Antidiabetic Med. at baseline														
Metformin only	28	2	7.1	26	4	15.4								
Insulin only	2	0	0	3	2	66.7								
Metformin and Insulin	19	3	15.8	22	6	27.3								
None	4	0	0	1	0	0								
Time since diagnosis of T2DM														
<1 year	18	2	11.1	17	4	23.5								
1 year - 3 years	24	2	8.3	21	5	23.8								
>3 years	11	1	9.1	14	3	21.4								

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Urinary tract infection (narrow sub BIcMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI) p-value **
Overall	53	1	1.9	52	3	5.8	0.3583	3.06	(0.32, 78.52) (0.33, 28.45)	3.18	(0.32, 85.31)	0.04	(-0.05,0.14)

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Genital infection (narrow sub BIcMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI) p-value **
Overall	53	1	1.9	52	1	1.9	1.0000	1.02	(0.03, 33.97) (0.07, 15.87)	1.02	(0.03, 40.49)	0.00	(-0.08,0.09)

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Acute pyelonephritis (narrow sub BIcMQ) or Urosepsis (PT)

There is no data to be displayed.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Bone fracture (narrow BIcMQ)

There is no data to be displayed.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Arthralgia (HLGT-primary path)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI) p-value **
Overall	53	1	1.9	52	1	1.9	1.0000	1.02	(0.03, 33.97) (0.07, 15.87)	1.02	(0.03, 40.49)	0.00	(-0.08,0.09)

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Pemphigoid in bullous conditions (HLT-primary path)

There is no data to be displayed.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Volume depletion (narrow BIcMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI) p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00, 14.86) NC.	0.00	(0.00, 9.17)	-0.02	(-0.10,0.06)

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.1 Frequencies and proportions of patients with specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Ketone measurements reported as AE (narrow BIcMQ)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	2	3.8	52	2	3.8	1.0000	1.02	(0.07, 15.13) (0.15, 6.97)	1.02	(0.10, 10.11)	0.00	(-0.10,0.10)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Hypoglycaemia (reported)

There is no data to be displayed.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Urinary tract infection (narrow sub BIcMQ)

There is no data to be displayed.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Genital infection (narrow sub BIcMQ)

There is no data to be displayed.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Acute pyelonephritis (narrow sub BIcMQ) or Urosepsis (PT)

There is no data to be displayed.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Bone fracture (narrow BIcMQ)

There is no data to be displayed.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Arthralgia (HLGT-primary path)

There is no data to be displayed.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Pemphigoid in bullous conditions (HLT-primary path)

There is no data to be displayed.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Volume depletion (narrow BIcMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00,14.86) NC.	0.00	(0.00,9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.2 Frequencies and proportions of patients with serious specific adverse events overall and by subgroup up to week 26 - TS (TG1)
User-defined AE category: Ketone measurements reported as AE (narrow BIcMQ)

There is no data to be displayed.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Hypoglycaemia (reported)

There is no data to be displayed.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Urinary tract infection (narrow sub BIcMQ)

There is no data to be displayed.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Genital infection (narrow sub BIcMQ)

There is no data to be displayed.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Acute pyelonephritis (narrow sub BIcMQ) or Urosepsis (PT)

There is no data to be displayed.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Bone fracture (narrow BIcMQ)

There is no data to be displayed.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Arthralgia (HLGT-primary path)

There is no data to be displayed.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Pemphigoid in bullous conditions (HLT-primary path)

There is no data to be displayed.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Volume depletion (narrow BIcMQ)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	1	1.9	52	0	0	0.5361	0.00	(0.00,14.86) NC.	0.00	(0.00,9.17)	-0.02	(-0.10,0.06)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
Maximum intensity: If a patient has more than one AE only the worst is recorded.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 1.4.3 Frequencies and proportions of patients with specific adverse events with severe maximum intensity overall and by subgroup
up to week 26 - TS (TG1)
User-defined AE category: Ketone measurements reported as AE (narrow BIcMQ)

There is no data to be displayed.

Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Bone fractures	Bone fractures	0000000014	Narrow	10000397	Acetabulum fracture
				10002544	Ankle fracture
				10009245	Clavicle fracture
				10009506	Closed fracture manipulation
				10010149	Complicated fracture
				10010214	Compression fracture
				10015741	External fixation of fracture
				10016042	Facial bones fracture
				10016450	Femoral neck fracture
				10016454	Femur fracture
				10016667	Fibula fracture
				10016747	Flail chest
				10016970	Foot fracture
				10016997	Forearm fracture
				10017076	Fracture
				10017081	Fracture delayed union
				10017085	Fracture malunion
				10017088	Fracture nonunion
				10017107	Fracture of clavicle due to birth trauma
				10017296	Fractured maxilla elevation
				10017308	Fractured sacrum
				10017310	Fractured skull depressed
				10018720	Greenstick fracture
				10019114	Hand fracture
				10020100	Hip fracture
				10020462	Humerus fracture
				10021343	Ilium fracture
				10022576	Internal fixation of fracture
				10023149	Jaw fracture
				10028200	Multiple fractures
				10030527	Open fracture
				10030682	Open reduction of fracture
				10030684	Open reduction of spinal fracture
				10031290	Osteoporotic fracture
				10034122	Patella fracture
				10034156	Pathological fracture
				10037802	Radius fracture
				10039117	Rib fracture
				10039579	Scapula fracture
				10040960	Skull fractured base
				10041541	Spinal compression fracture
				10041569	Spinal fracture
				10042015	Sternal fracture

MedDRA version: 25.0

Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Bone fractures	Bone fractures	0000000014	Narrow	10042212	Stress fracture
				10043827	Tibia fracture
				10045375	Ulna fracture
				10048049	Wrist fracture
				10048617	Pseudarthrosis
				10049164	Fractured coccyx
				10049514	Traumatic fracture
				10049946	Cervical vertebral fracture
				10049947	Lumbar vertebral fracture
				10049948	Thoracic vertebral fracture
				10052614	Comminuted fracture
				10053206	Fracture displacement
				10053962	Epiphyseal fracture
				10057147	Fracture debridement
				10057609	Fracture reduction
				10059362	Fractured zygomatic arch elevation
				10061161	Pelvic fracture
				10061365	Skull fracture
				10061394	Upper limb fracture
				10061599	Lower limb fracture
				10061959	Fracture treatment
				10064210	Bone fissure
				10064211	Bone fragmentation
				10066094	Torus fracture
				10066184	Avulsion fracture
				10066386	Impacted fracture
				10069066	Intramedullary rod insertion
				10069135	Periprosthetic fracture
				10069723	Loss of anatomical alignment after fracture reduction
				10070884	Atypical femur fracture
				10072132	Fracture pain
				10072395	Atypical fracture
				10073162	Chance fracture
				10073853	Osteochondral fracture
				10074362	Sacroiliac fracture
				10074551	Limb fracture
				10074807	Spinal fusion fracture
				10077270	Surgical fixation of rib fracture
				10077603	Craniofacial fracture
				10078749	Lisfranc fracture
				10079423	Fracture blisters
				10079667	Metaphyseal corner fracture

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Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Bone fractures	Bone fractures	0000000014	Narrow	10079813	Fracture infection
				10079864	Subchondral insufficiency fracture
				10080550	Osteophyte fracture
				10081343	Maisonneuve fracture
				10081442	Stapes fracture
				10083585	Skull fracture treatment
				10083586	Spinal fracture treatment
				10085543	Neurogenic fracture
				10085774	Microfracture surgery
				10087273	Depressed fracture
Bullous conditions	Pemphigoid in bullous conditions	0000000011	Primary Path	10005191	Blister
				10005372	Blood blister
				10012441	Dermatitis bullous
				10012468	Dermatitis herpetiformis
				10015218	Erythema multiforme
				10019939	Herpes gestationis
				10024515	Linear IgA disease
				10030081	Oculomucocutaneous syndrome
				10034277	Pemphigoid
				10034280	Pemphigus
				10037145	Pseudoporphyria
				10042033	Stevens-Johnson syndrome
				10044223	Toxic epidermal necrolysis
				10053177	Epidermolysis
				10056508	Acquired epidermolysis bullosa
				10057056	Paraneoplastic pemphigus
				10062356	Diabetic bullosis
				10069827	Coma blister
				10073385	Blister rupture
				10079423	Fracture blisters
				10080039	Oedema blister
				10083164	SJS-TEN overlap
				10083809	Bullous haemorrhagic dermatosis
				10083961	Autoimmune blistering disease
				10084905	Generalised bullous fixed drug eruption
				10087064	Mucous membrane pemphigoid
Genital tract infections predisposed by glucosuria	Genital infections	0000000001	Narrow	10004055	Bacterial vaginosis
				10004074	Balanitis candida
				10004078	Balanoposthitis

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Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Genital tract infections predisposed by glucosuria	Genital infections	0000000001	Narrow	10004138	Bartholin's abscess
				10004142	Bartholinitis
				10008323	Cervicitis
				10014791	Endometritis
				10015000	Epididymitis
				10015001	Epididymitis blastomyces
				10018143	Genital candidiasis
				10020497	Hydrocele male infected
				10030345	Oophoritis
				10031064	Orchitis
				10033119	Ovarian abscess
				10033847	Parametritis
				10034236	Pelvic abscess
				10034254	Pelvic inflammatory disease
				10034256	Pelvic inflammatory disease mycoplasmal
				10034294	Penile abscess
				10036934	Prostatic abscess
				10036978	Prostatitis
				10037651	Pyometra
				10039453	Salpingitis
				10039748	Scrotal gangrene
				10039954	Seminal vesiculitis
				10044250	Toxic shock syndrome staphylococcal
				10044251	Toxic shock syndrome streptococcal
				10046470	Urethral stricture post infection
				10046914	Vaginal infection
				10046957	Vaginitis gardnerella
				10047732	Vulval abscess
				10047752	Vulval cellulitis
				10047780	Vulvitis
				10047784	Vulvovaginal candidiasis
				10047794	Vulvovaginitis
				10048461	Genital infection
				10049205	Clitoris abscess
				10049571	Scrotal abscess
				10049573	Vaginal abscess
				10049677	Salpingo-oophoritis
				10050428	Fallopian tube abscess
				10050662	Prostate infection
				10050739	Erosive balanitis
				10051458	Myometritis
				10051483	Prostatovesiculitis

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Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Genital tract infections predisposed by glucosuria	Genital infections	0000000001	Narrow	10052301	Vaginal cellulitis
				10052457	Perineal abscess
				10053043	Epididymitis ureaplasmal
				10054259	Escherichia vaginitis
				10054824	Tubo-ovarian abscess
				10056254	Intrauterine infection
				10056345	Rectovaginal septum abscess
				10056628	Ovarian bacterial infection
				10057001	Seminal vesicular infection
				10058674	Pelvic infection
				10059070	Pelvic sepsis
				10061179	Genital infection bacterial
				10061180	Genital infection fungal
				10061182	Genitourinary tract infection
				10061912	Penile infection
				10061977	Genital infection female
				10062156	Scrotal infection
				10062233	Uterine infection
				10062316	Genital abscess
				10062521	Genital infection male
				10062707	Parametric abscess
				10063012	Uterine abscess
				10064501	Spermatic cord funiculitis
				10064724	Testicular abscess
				10064899	Vulvovaginal mycotic infection
				10064929	Cellulitis of male external genital organ
				10065583	Urogenital infection bacterial
				10066876	Perineal infection
				10067185	Vulvovaginitis streptococcal
				10067236	Cervicitis streptococcal
				10067320	Prostatitis Escherichia coli
				10067741	Balanoposthitis infective
				10068682	Gangrenous balanitis
				10069918	Bacterial prostatitis
				10071209	Candida cervicitis
				10072020	Pyospermia
				10074861	Endometritis bacterial
				10074997	Mycoplasma genitalium infection
				10075062	Cervicitis mycoplasmal
				10075620	Seminal vesicle abscess
				10078662	Bacterial salpingitis

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Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Genital tract infections predisposed by glucosuria	Genital infections	0000000001	Narrow	10079520	Vulvovaginitis staphylococcal
				10079521	Fungal balanitis
				10079528	Bacterial vulvovaginitis
				10081280	Ureaplasmal vulvovaginitis
				10082162	Ureaplasma cervicitis
				10083412	Neovaginal infection
				10084348	Scrotal cellulitis
				10085545	Penile gangrene
Increased ketones excluding acidosis and diabetic ketoacidosis	Ketone measurements reported as AE	0000000015	Narrow	10000410	Acetonaemia
				10012673	Diabetic ketosis
				10023388	Ketonuria
				10023391	Ketosis
				10057594	Blood ketone body increased
				10057597	Urine ketone body present
				10057598	Blood ketone body present
				10058938	Acetonaemic vomiting
Joint disorders	Arthralgia	0000000010	Primary Path	10002556	Ankylosing spondylitis
				10003239	Arthralgia
				10003246	Arthritis
				10003251	Arthritis climacteric
				10003253	Arthritis enteropathic
				10003267	Arthritis reactive
				10003285	Arthropathy
				10003422	Articular calcification
				10003433	Articular disc disorder
				10008690	Chondrocalcinosis pyrophosphate
				10008729	Chondromalacia
				10016386	Felty’s syndrome
				10018634	Gouty arthritis
				10018641	Gouty tophus
				10018829	Haemarthrosis
				10020677	Hypermobility syndrome
				10023198	Joint ankylosis
				10023201	Joint contracture
				10023202	Joint deposit
				10023203	Joint destruction
				10023206	Joint dislocation pathological
				10023215	Joint effusion

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Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Joint disorders	Arthralgia	0000000010	Primary Path	10023230	Joint stiffness
				10023232	Joint swelling
				10024452	Ligament laxity
				10024829	Loose body in joint
				10029326	Neuropathic arthropathy
				10029469	Nodal osteoarthritis
				10031161	Osteoarthritis
				10031173	Osteoarthropathy
				10033534	Palindromic rheumatism
				10034464	Periarthritis
				10036030	Polyarthritis
				10037162	Psoriatic arthropathy
				10039054	Rheumatic fever
				10039073	Rheumatoid arthritis
				10039227	Rotator cuff syndrome
				10039361	Sacroiliitis
				10040968	SLE arthritis
				10041591	Spinal osteoarthritis
				10042061	Still’s disease
				10042744	Sympathetic posterior cervical syndrome
				10043220	Temporomandibular joint syndrome
				10048694	Rheumatoid nodule
				10048706	Joint range of motion decreased
				10048745	Periarticular disorder
				10049143	Patellofemoral pain syndrome
				10050506	Spinal fusion acquired
				10051265	Spondyloarthropathy
				10054106	Joint warmth
				10054813	Facet joint syndrome
				10055042	Vertebral osteophyte
				10058029	Arthrofibrosis
				10058031	Joint adhesion
				10059176	Juvenile idiopathic arthritis
				10061258	Joint lock
				10061371	Spondylitis
				10061419	Crystal arthropathy
				10061430	Arthritis allergic
				10061761	Chondrocalcinosis
				10062164	Seronegative arthritis
				10062310	Joint hyperextension
				10062686	Carpal collapse
				10063580	Atlantoaxial instability

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Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Joint disorders	Arthralgia	0000000010	Primary Path	10064554	Amyloid arthropathy
				10064931	Joint instability
				10065057	Haemophilic arthropathy
				10065564	Floating patella
				10065568	Lateral patellar compression syndrome
				10066850	Plica syndrome
				10068323	Arthrotoxicity
				10069429	Ulnocarpal abutment syndrome
				10069494	Carcinomatous polyarthritis
				10069498	Knee impingement syndrome
				10069690	Vertebral foraminal stenosis
				10070874	Joint laxity
				10070899	Femoroacetabular impingement
				10071155	Autoimmune arthritis
				10071400	Axial spondyloarthritis
				10071742	Poncet’s disease
				10072120	Ankle impingement
				10072125	Infrapatellar fat pad inflammation
				10073029	Antithyroid arthritis syndrome
				10074327	Joint vibration
				10074329	Joint noise
				10075005	Crowned dens syndrome
				10075201	Rapidly progressive osteoarthritis
				10076549	Enteropathic spondylitis
				10076674	Juvenile psoriatic arthritis
				10076675	Juvenile spondyloarthritis
				10077089	Jaw clicking
				10077507	Paraneoplastic arthritis
				10077666	Joint microhaemorrhage
				10078014	Interspinous osteoarthritis
				10078114	Destructive spondyloarthropathy
				10079555	Scapular dyskinesis
				10079942	Joint space narrowing
				10080059	Diffuse idiopathic skeletal hyperostosis
				10080832	Snapping hip syndrome
				10081395	Spinal segmental dysfunction
				10081448	Scapholunate dissociation
				10081810	Pustulotic arthro-osteitis
				10082100	Oligoarthritis
				10083155	Immune-mediated arthritis
				10083266	Paralytic hip dislocation
				10083338	Atlantoaxial subluxation

MedDRA version: 25.0

Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Joint disorders	Arthralgia	0000000010	Primary Path	10085237	Rotator cuff injury of hip
				10085378	Hydroxyapatite crystal deposition disease
				10085600	Acute aseptic arthritis
				10085753	Peripheral spondyloarthritis
				10086187	Undifferentiated spondyloarthritis
				10086277	Joint fistula
				10086279	Rheumatoid bursitis
				10086355	Rotator cuff tear arthropathy
				10087218	Joint impingement
				10087333	Greater trochanteric pain syndrome
Renal infections predisposed by glucosuria	Acute pyelonephritis or urosepsis	0000000013	Narrow	10023424	Kidney infection
				10034531	Perinephric abscess
				10037584	Pyelitis
				10037596	Pyelonephritis
				10037597	Pyelonephritis acute
				10037601	Pyelonephritis chronic
				10037603	Pyelonephritis mycoplasmal
				10037653	Pyonephrosis
				10038351	Renal abscess
				10049100	Pyelocystitis
				10058596	Renal cyst infection
				10059517	Bacterial pyelonephritis
				10065214	Pyelonephritis fungal
				10068822	Emphysematous pyelonephritis
				10072058	Perinephritis
				10074409	Escherichia pyelonephritis
				10078229	Renal graft infection
				10082040	Nephritis bacterial
				10084121	Infected urinoma
UTI predisposed by glucosuria	Urinary tract infections	0000000002	Narrow	10004056	Bacteriuria
				10004058	Bacteriuria in pregnancy
				10011781	Cystitis
				10011790	Cystitis escherichia
				10011792	Cystitis gonococcal
				10011793	Cystitis haemorrhagic
				10011797	Cystitis klebsiella

MedDRA version: 25.0

Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
UTI predisposed by glucosuria	Urinary tract infections	0000000002	Narrow	10011799	Cystitis pseudomonal
				10017525	Fungal cystitis
				10023424	Kidney infection
				10034531	Perinephric abscess
				10037584	Pyelitis
				10037596	Pyelonephritis
				10037597	Pyelonephritis acute
				10037601	Pyelonephritis chronic
				10037603	Pyelonephritis mycoplasmal
				10037653	Pyonephrosis
				10038351	Renal abscess
				10046424	Urethral abscess
				10046470	Urethral stricture post infection
				10046480	Urethritis
				10046482	Urethritis chlamydial
				10046483	Urethritis gonococcal
				10046489	Urethritis trichomonal
				10046490	Urethritis ureaplasmal
				10046571	Urinary tract infection
				10046572	Urinary tract infection enterococcal
				10046573	Urinary tract infection neonatal
				10046704	Urogenital trichomoniasis
				10048709	Urosepsis
				10049059	Urinary tract infection fungal
				10049100	Pyelocystitis
				10051250	Ureteritis
				10051959	Urinary bladder abscess
				10052238	Escherichia urinary tract infection
				10052299	Urethral carbuncle
				10054088	Urinary tract infection bacterial
				10056351	Emphysematous cystitis
				10056396	Asymptomatic bacteriuria
				10058523	Bladder candidiasis
				10058596	Renal cyst infection
				10059517	Bacterial pyelonephritis
				10061181	Genitourinary tract gonococcal infection
				10061395	Ureter abscess
				10062279	Urinary tract infection pseudomonal
				10062280	Urinary tract infection staphylococcal
				10064850	Cystitis erosive
				10065198	Cystitis bacterial
				10065214	Pyelonephritis fungal

MedDRA version: 25.0

Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
UTI predisposed by glucosuria	Urinary tract infections	0000000002	Narrow	10065582	Urogenital infection fungal
				10065583	Urogenital infection bacterial
				10066757	Urinary tract abscess
				10068822	Emphysematous pyelonephritis
				10070300	Streptococcal urinary tract infection
				10072058	Perinephritis
				10074409	Escherichia pyelonephritis
				10074457	Bladder diverticulitis
				10075063	Urethritis mycoplasmal
				10077375	Funguria
				10078229	Renal graft infection
				10078665	Bacterial urethritis
				10078666	Bacterial ureteritis
				10081163	Fungal urethritis
				10081185	Gonococcal infection
				10081262	Candida urethritis
				10082040	Nephritis bacterial
				10082818	Providencia urinary tract infection
				10083162	Urinary tract candidiasis
				10083524	Campylobacter urinary tract infection
				10084121	Infected urinoma
				10084826	Aerococcus urinae infection
Urosepsis	Acute pyelonephritis or urosepsis	0000000013		10048709	Urosepsis
Volume depletion and hypotension due to dehydration	Volume depletion	0000000012	Narrow	10005731	Blood pressure ambulatory decreased
				10005734	Blood pressure decreased
				10005737	Blood pressure diastolic decreased
				10005758	Blood pressure systolic decreased
				10009192	Circulatory collapse
				10012174	Dehydration
				10021097	Hypotension
				10021137	Hypovolaemia
				10021138	Hypovolaemic shock
				10026983	Mean arterial pressure decreased
				10031127	Orthostatic hypotension
				10036653	Presyncope
				10042772	Syncope
				10053356	Blood pressure orthostatic decreased

MedDRA version: 25.0

Listing 1.4.4 Listing of preferred terms that define specific adverse events

Source	Group	Group code	Scope	Preferred term code	Preferred term
Volume depletion and hypotension due to dehydration	Volume depletion	0000000012	Narrow	10066077	Diastolic hypotension
				10078280	CT hypotension complex
				10083659	Hypotensive crisis
				10084012	Dialysis hypotension

MedDRA version: 25.0

Appendix 1, 1.5

1.1.5 Adverse events on SOC level

Table 1.5.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Infections and infestations

Subgroup	Placebo			E pooled			E pooled vs Placebo							
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)		Risk diff.	(95% CI)	p-value **
Overall	53	13	24.5	52	18	34.6	0.2871	1.41	(0.77, 2.81) (0.77, 2.58)	1.63	(0.69, | 3.86)	0.10	(-0.08, 0.28)	

Overall comparison of treatments is not significant on 5% level.

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.5.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Metabolism and nutrition disorders

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio (95% CI)	Risk diff. (95% CI)	p-value **
Overall	53	12	22.6	52	16	30.8	0.5361	1.36	(0.70, 2.84) (0.71, 2.59)	1.52 (0.63, 3.70)	0.08 (-0.10, 0.25)	

Overall comparison of treatments is not significant on 5% level.

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.5.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Gastrointestinal disorders

Subgroup	Placebo			E pooled			E pooled vs Placebo							
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)		Risk diff.	(95% CI)	p-value **
Overall	53	10	18.9	52	12	23.1	0.6927	1.22	(0.57, 2.85) (0.58, 2.58)	1.29	(0.49, 3.40)		0.04	(-0.12, 0.21)	
Overall comparison of treatments is not significant on 5% level.															

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.5.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Nervous system disorders

Subgroup	Placebo			E pooled			E pooled vs Placebo							
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	11	20.8	52	11	21.2	1.0000	1.02	(0.46, 2.24) (0.48, 2.14)	1.02	(0.39, 2.68)	0.00	(-0.16, 0.17)	

Overall comparison of treatments is not significant on 5% level.

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.5.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Respiratory, thoracic and mediastinal disorders

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI) p-value **
Overall	53	8	15.1	52	2	3.8	0.0583	0.25	(0.03, 1.04) (0.06, 1.14)	0.23	(0.03, 1.05)	-0.11	(-0.24, 0.00)

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.5.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Injury, poisoning and procedural complications

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI) p-value **
Overall	53	7	13.2	52	3	5.8	0.2490	0.44	(0.07, 1.57) (0.12, 1.60)	0.40	(0.08, 1.64)	-0.07	(-0.21, 0.04)

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.5.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Investigations

Subgroup	Placebo			E pooled			E pooled vs Placebo							
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)		Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	7	13.2	52	6	11.5	0.8737	0.87	(0.29, 2.73) (0.31, 2.43)		0.86	(0.25, 2.85)	-0.02	(-0.15, 0.12)	
Overall comparison of treatments is not significant on 5% level.															

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.5.2 Frequencies and proportions of patients with serious adverse events with >=5% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)

There is no data to be displayed.

Table 1.5.3 Frequencies and proportions of patients with adverse events with severe maximum intensity with >=5% occurrence in at least one treatment arm on SOC level overall and by subgroup up to week 26 - TS (TG1)

There is no data to be displayed.

Table 1.5.4 Frequencies and proportions of patients with adverse events leading to treatment discontinuation on SOC level up to week 26 - TS (TG1)
System organ class: Gastrointestinal disorders

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %
Overall	53	1	1.9	52	0	0

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
N is the number of patients, n the number of patients with at least one event
MedDRA version: 25.0.

Table 1.5.4 Frequencies and proportions of patients with adverse events leading to treatment discontinuation on SOC level up to week 26 - TS (TG1)
System organ class: Renal and urinary disorders

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %
Overall	53	1	1.9	52	0	0

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
N is the number of patients, n the number of patients with at least one event
MedDRA version: 25.0.

Table 1.5.4 Frequencies and proportions of patients with adverse events leading to treatment discontinuation on SOC level up to week 26 - TS (TG1)
System organ class: Reproductive system and breast disorders

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %
Overall	53	1	1.9	52	0	0

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
N is the number of patients, n the number of patients with at least one event
MedDRA version: 25.0.

Appendix 1, 1.6

1.1.6 Adverse events on PT level

Table 1.6.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on PT level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Metabolism and nutrition disorders
Preferred term: Hypoglycaemia

Subgroup	Placebo			E pooled			E pooled vs Placebo							
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	5	9.4	52	11	21.2	0.1152	2.24	(0.85, 9.54) (0.84, 6.01)	2.58	(0.83, 8.76)	0.12	(-0.02, 0.26)	

Overall comparison of treatments is not significant on 5% level.

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.6.1 Frequencies and proportions of patients with adverse events with >=10% occurrence in at least one treatment arm on PT level overall and by subgroup up to week 26 - TS (TG1)
System organ class: Nervous system disorders
Preferred term: Headache

Subgroup	Placebo			E pooled			E pooled vs Placebo							
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	7	13.2	52	8	15.4	0.8366	1.16	(0.42, 3.29) (0.46, 2.98)	1.19	(0.39, 3.73)	0.02	(-0.12, 0.17)	

Overall comparison of treatments is not significant on 5% level.

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.6.2 Frequencies and proportions of patients with serious adverse events with >=5% occurrence in at least one treatment arm on PT level overall and by subgroup up to week 26 - TS (TG1)

There is no data to be displayed.

Table 1.6.3 Frequencies and proportions of patients with adverse events with severe maximum intensity with >=5% occurrence in at least one treatment arm on PT level overall and by subgroup up to week 26 - TS (TG1)

There is no data to be displayed.

Table 1.6.4 Frequencies and proportions of patients with adverse events leading to treatment discontinuation on PT level up to week 26 - TS (TG1)
System organ class: Gastrointestinal disorders
Preferred term: Pancreatitis acute

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %
Overall	53	1	1.9	52	0	0

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
N is the number of patients, n the number of patients with at least one event
MedDRA version: 25.0.

Table 1.6.4 Frequencies and proportions of patients with adverse events leading to treatment discontinuation on PT level up to week 26 - TS (TG1)
System organ class: Renal and urinary disorders
Preferred term: Polyuria

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %
Overall	53	1	1.9	52	0	0

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
N is the number of patients, n the number of patients with at least one event
MedDRA version: 25.0.

Table 1.6.4 Frequencies and proportions of patients with adverse events leading to treatment discontinuation on PT level up to week 26 - TS (TG1)
System organ class: Reproductive system and breast disorders
Preferred term: Menstruation irregular

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %
Overall	53	1	1.9	52	0	0

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
N is the number of patients, n the number of patients with at least one event
MedDRA version: 25.0.

Appendix 1, 1.7

1.1.7 Other adverse Events

Table 1.7.1 Frequencies and proportions of patients with reported non-severe hypoglycaemia with symptoms and plasma glucose <54 mg/dl overall and by subgroup up to week 26 - TS (TG1)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	2	3.8	52	6	11.5	0.1532	3.06	(0.68,33.98) (0.65,14.46)	3.33	(0.66,24.70)	0.08	(-0.03,0.20)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.7.2 Frequencies and proportions of patients with reported non-severe hypoglycaemia with symptoms and plasma glucose <=70 mg/dl overall and by subgroup up to week 26 - TS (TG1)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	2	3.8	52	8	15.4	0.0507	4.08	(1.00,33.98) (0.91,18.30)	4.64	(1.00,32.98)	0.12	(0.00,0.25)	

Only treatment emergent AEs are displayed (onset between first dose until treatment stop +7 days).
Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
MedDRA version: 25.0. N: number of patients. n: number of patients with an AE. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity (H0) of risk ratios (treatment by subgroup interaction).

Table 1.7.3 Frequencies and proportions of patients with reported severe hypoglycaemia (requiring the assistance of another person) overall and by subgroup up to week 26 - TS (TG1)

There is no data to be displayed.

Appendix 1, 2

Appendix 1, 2.1

1.2.1 Responder Analyses

Table 2.1.1 Responder analysis for HbA1c [%] <6.5% at week 26 overall and by subgroup - mITT (TG1) (NCF)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	5	9.4	52	11	21.2	0.1152	2.24	(0.85, 9.54) (0.84, 6.01)	2.58	(0.83, 8.76)	0.12	(-0.02,0.26)	
Sex														
Male	19	2	10.5	19	5	26.3								
Female	34	3	8.8	33	6	18.2								
Age														
<15	26	2	7.7	25	5	20.0								
>=15 to <18	27	3	11.1	27	6	22.2								
Region														
US	33	2	6.1	36	5	13.9								
Non-US	20	3	15.0	16	6	37.5								
BMI [kg/m2] at baseline														0.8531
< median	27	3	11.1	26	7	26.9	0.1711	2.42	(0.71,15.25) (0.70, 8.38)	2.95	(0.66,15.38)	0.16	(-0.06,0.38)	
>= median	26	2	7.7	26	4	15.4	0.5291	2.00	(0.37,14.81) (0.40, 9.99)	2.18	(0.35,18.20)	0.08	(-0.12,0.28)	
BMI Z-Score														
<=2 (Underweight, normal or overweight)	9	2	22.2	5	2	40.0								
>2 to <=3 (Class 1 obesity)	17	1	5.9	21	5	23.8								
>3 (Class 2 or 3 obesity)	27	2	7.4	26	4	15.4								
HbA1c [%] at baseline														NC.
<8.0	29	5	17.2	28	9	32.1	0.2491	1.86	(0.70, 5.96) (0.71, 4.88)	2.27	(0.64, 8.51)	0.15	(-0.08,0.39)	
8.0 to 9.0	12	0	0	12	1	8.3	0.5233	NC.	NC. NC.	inf	(0.11,inf)	0.08	(-0.19,0.38)	
>9.0	12	0	0	12	1	8.3	0.5233	NC.	NC. NC.	inf	(0.11,inf)	0.08	(-0.19,0.38)	

Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
N: number of patients. n: number of patients with response. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity of risk ratios (treatment by subgroup interaction). inf=infinity. NC.=Not calculated.

Table 2.1.1 Responder analysis for HbA1c [%] <6.5% at week 26 overall and by subgroup - mITT (TG1) (NCF)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
FPG [mg/dl] at baseline														
<126	13	3	23.1	19	6	31.6								
>=126	39	2	5.1	29	4	13.8								
eGFR (Zappitelli) at baseline														0.7170
<120	24	3	12.5	21	7	33.3	0.1121	2.67	(0.79,16.71) (0.79, 9.02)	3.50	(0.76,18.64)	0.21	(-0.04,0.46)	
120 to <150	23	2	8.7	19	3	15.8	0.6158	1.82	(0.32,17.76) (0.34, 9.77)	1.97	(0.26,17.93)	0.07	(-0.15,0.33)	
>=150	6	0	0	12	1	8.3	0.7821	NC.	NC. NC.	inf	(0.06,inf)	0.08	(-0.37,0.39)	
Backg. Antidiabetic Med. at baseline														
Metformin only	28	4	14.3	26	8	30.8								
Insulin only	2	0	0	3	1	33.3								
Metformin and Insulin	19	1	5.3	22	2	9.1								
None	4	0	0	1	0	0								
Time since diagnosis of T2DM														
<1 year	18	1	5.6	17	2	11.8								
1 year - 3 years	24	2	8.3	21	5	23.8								
>3 years	11	2	18.2	14	4	28.6								

Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
N: number of patients. n: number of patients with response. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity of risk ratios (treatment by subgroup interaction). inf=infinity. NC.=Not calculated.

Table 2.1.2 Responder analysis for HbA1c [%] <7% at week 26 overall and by subgroup - mITT (TG1) (NCF)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	13	24.5	52	18	34.6	0.2871	1.41	(0.77, 2.81) (0.77, 2.58)	1.63	(0.69, 3.86)	0.10	(-0.08,0.28)	
Sex														0.6157
Male	19	4	21.1	19	7	36.8	0.3201	1.75	(0.60, 7.18) (0.61, 5.01)	2.19	(0.50,10.18)	0.16	(-0.14,0.44)	
Female	34	9	26.5	33	11	33.3	0.6628	1.26	(0.59, 3.07) (0.60, 2.64)	1.39	(0.48, 4.08)	0.07	(-0.16,0.29)	
Age														0.8519
<15	26	7	26.9	25	9	36.0	0.5562	1.34	(0.54, 3.38) (0.59, 3.04)	1.53	(0.45, 5.22)	0.09	(-0.17,0.35)	
>=15 to <18	27	6	22.2	27	9	33.3	0.5269	1.50	(0.62, 4.15) (0.62, 3.63)	1.75	(0.51, 6.18)	0.11	(-0.14,0.35)	
Region														0.9114
US	33	6	18.2	36	10	27.8	0.5353	1.53	(0.61, 4.21) (0.62, 3.74)	1.73	(0.54, 5.77)	0.10	(-0.11,0.30)	
Non-US	20	7	35.0	16	8	50.0	0.5864	1.43	(0.63, 3.80) (0.66, 3.09)	1.86	(0.47, 7.40)	0.15	(-0.18,0.46)	
BMI [kg/m2] at baseline														0.8629
< median	27	7	25.9	26	10	38.5	0.5423	1.48	(0.65, 3.57) (0.67, 3.31)	1.79	(0.54, 5.97)	0.13	(-0.13,0.37)	
>= median	26	6	23.1	26	8	30.8	0.5915	1.33	(0.52, 3.63) (0.54, 3.31)	1.48	(0.42, 5.36)	0.08	(-0.17,0.32)	

Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
N: number of patients. n: number of patients with response. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity of risk ratios (treatment by subgroup interaction). inf=infinity. NC.=Not calculated.

Table 2.1.2 Responder analysis for HbA1c [%] <7% at week 26 overall and by subgroup - mITT (TG1) (NCF)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
BMI Z-Score														0.2861
<=2 (Underweight, normal or overweight)	9	2	22.2	5	3	60.0	0.2083	2.70	(0.55,24.48) (0.66,11.13)	5.25	(0.41,66.09)	0.38	(-0.18,0.80)	
>2 to <=3 (Class 1 obesity)	17	6	35.3	21	6	28.6	0.7035	0.81	(0.26, 2.49) (0.32, 2.06)	0.73	(0.18, 3.06)	-0.07	(-0.37,0.25)	
>3 (Class 2 or 3 obesity)	27	5	18.5	26	9	34.6	0.2491	1.87	(0.71, 5.95) (0.72, 4.84)	2.33	(0.65, 8.84)	0.16	(-0.08,0.40)	
HbA1c [%] at baseline														0.3837
<8.0	29	11	37.9	28	15	53.6	0.2930	1.41	(0.78, 2.82) (0.79, 2.52)	1.89	(0.64, 5.54)	0.16	(-0.12,0.41)	
8.0 to 9.0	12	2	16.7	12	1	8.3	0.6750	0.50	(0.02, 5.08) (0.05, 4.81)	0.45	(0.01, 6.99)	-0.08	(-0.42,0.25)	
>9.0	12	0	0	12	2	16.7	0.2202	NC.	NC. NC.	inf	(0.48,inf)	0.17	(-0.11,0.49)	
FPG [mg/dl] at baseline														0.5263
<126	13	7	53.8	19	11	57.9	0.9235	1.08	(0.56, 2.31) (0.57, 2.02)	1.18	(0.27, 5.09)	0.04	(-0.31,0.39)	
>=126	39	5	12.8	29	6	20.7	0.4207	1.61	(0.50, 5.33) (0.55, 4.78)	1.77	(0.46, 6.96)	0.08	(-0.11,0.29)	
eGFR (Zappitelli) at baseline														0.9285
<120	24	8	33.3	21	11	52.4	0.2431	1.57	(0.77, 3.54) (0.78, 3.16)	2.20	(0.64, 7.57)	0.19	(-0.11,0.47)	
120 to <150	23	4	17.4	19	5	26.3	0.6169	1.51	(0.39, 5.51) (0.47, 4.86)	1.70	(0.36, 8.21)	0.09	(-0.17,0.37)	
>=150	6	1	16.7	12	2	16.7	NC.	1.00	(0.10,27.02) (0.11, 8.95)	1.00	(0.06,35.11)	0.00	(-0.48,0.37)	

Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
N: number of patients. n: number of patients with response. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity of risk ratios (treatment by subgroup interaction). inf=infinity. NC.=Not calculated.

Table 2.1.2 Responder analysis for HbA1c [%] <7% at week 26 overall and by subgroup - mITT (TG1) (NCF)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio (95% CI)	Risk diff. (95% CI)	p-value **
Backg. Antidiabetic Med. at baseline												
Metformin only	28	8	28.6	26	13	50.0						
Insulin only	2	0	0	3	1	33.3						
Metformin and Insulin	19	4	21.1	22	4	18.2						
None	4	1	25.0	1	0	0						
Time since diagnosis of T2DM												0.4067
<1 year	18	6	33.3	17	6	35.3	0.9998	1.06	(0.35, 3.22) (0.42, 2.65)	1.09 (0.26, 4.63)	0.02 (-0.30,0.34)	
1 year - 3 years	24	3	12.5	21	7	33.3	0.1121	2.67	(0.79,16.71) (0.79, 9.02)	3.50 (0.76,18.64)	0.21 (-0.04,0.46)	
>3 years	11	4	36.4	14	5	35.7	1.0000	0.98	(0.28, 3.27) (0.34, 2.81)	0.97 (0.18, 5.54)	-0.01 (-0.39,0.38)	

Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
N: number of patients. n: number of patients with response. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity of risk ratios (treatment by subgroup interaction). inf=infinity. NC.=Not calculated.

Table 2.1.3 Responder analysis of patients who initiate glycaemic rescue therapy up to 26 weeks, overall and by subgroup - mITT (TG1) (OR)

Subgroup	Placebo			E pooled			E pooled vs Placebo						
Category	N	n	%	N	n	%	p-value *	Risk ratio	(exact 95% CI) (asymp 95% CI)	Odds ratio	(95% CI)	Risk diff.	(95% CI)	p-value **
Overall	53	6	11.3	52	5	9.6	0.8575	0.85	(0.25,2.92) (0.28,2.61)	0.83	(0.22,3.05)	-0.02	(-0.15,0.11)	
Sex														
Male	19	4	21.1	19	1	5.3								
Female	34	2	5.9	33	4	12.1								
Age														
<15	26	3	11.5	25	3	12.0								
>=15 to <18	27	3	11.1	27	2	7.4								
Region														
US	33	4	12.1	36	4	11.1								
Non-US	20	2	10.0	16	1	6.3								
BMI [kg/m2] at baseline														
< median	27	2	7.4	26	3	11.5								
>= median	26	4	15.4	26	2	7.7								
BMI Z-Score														
<=2 (Underweight, normal or overweight)	9	0	0	5	0	0								
>2 to <=3 (Class 1 obesity)	17	1	5.9	21	3	14.3								
>3 (Class 2 or 3 obesity)	27	5	18.5	26	2	7.7								
HbA1c [%] at baseline														
<8.0	29	2	6.9	28	1	3.6								
8.0 to 9.0	12	1	8.3	12	3	25.0								
>9.0	12	3	25.0	12	1	8.3								
FPG [mg/dl] at baseline														NC.
<126	13	1	7.7	19	0	0	0.3904	0.00	(0.00,9.81) NC.	0.00	(0.00,6.16)	-0.08	(-0.36,0.11)	
>=126	39	5	12.8	29	5	17.2	0.6594	1.34	(0.39,4.65) (0.43,4.22)	1.42	(0.34,5.79)	0.04	(-0.13,0.24)	

Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
N: number of patients. n: number of patients with response. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Table 2.1.3 Responder analysis of patients who initiate glycaemic rescue therapy up to 26 weeks, overall and by subgroup - mITT (TG1) (OR)

Subgroup Category	Placebo N	Placebo n	Placebo %	E pooled N	E pooled n	E pooled %	E pooled vs Placebo p-value *	Risk ratio (exact 95% CI)	(asymp 95% CI)	Odds ratio (95% CI)	Risk diff. (95% CI)	p-value **
eGFR (Zappitelli) at baseline												
<120	24	5	20.8	21	1	4.8						
120 to <150	23	1	4.3	19	1	5.3						
>=150	6	0	0	12	3	25.0						
Backg. Antidiabetic Med. at baseline												
Metformin only	28	2	7.1	26	2	7.7						
Insulin only	2	0	0	3	1	33.3						
Metformin and Insulin	19	3	15.8	22	2	9.1						
None	4	1	25.0	1	0	0						
Time since diagnosis of T2DM												
<1 year	18	3	16.7	17	1	5.9						
1 year - 3 years	24	2	8.3	21	2	9.5						
>3 years	11	1	9.1	14	2	14.3						

Subgroups will only be analysed if at least 10 patients are in each subgroup category and at least 10 patients with event in at least one subgroup category (both treatments combined).
A ratio less than one or risk difference less than zero indicates less risk for E pooled.
N: number of patients. n: number of patients with response. Risk ratio exact CI estimated by Chan and Zhang, asymptotic CI by Wald. CIs for odds ratios are exact mid-p estimates. Risk diff. exact CI estimated by Chan and Zhang. * 2*one-sided Suissa-Shuster Z-pooled test. ** Q-test for homogeneity of risk ratios (treatment by subgroup interaction). NC.=Not calculated.

Appendix 1, 2.2

1.2.2 Analyses of continuous variables

Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
Overall																
Baseline																
Placebo	53	52	8.07	1.23												
E pooled	52	51	7.95	1.25												
Week 4																
Placebo	53	50	8.17	1.56	0.07	0.08	-0.08	0.22								
E pooled	52	50	7.39	1.05	-0.57	0.08	-0.73	-0.42	-0.65	0.11	-0.86	-0.43	<0.0001	-1.19	-1.59	-0.80
Week 12																
Placebo	53	52	8.40	1.96	0.33	0.18	-0.03	0.69								
E pooled	52	48	7.24	1.50	-0.66	0.18	-1.03	-0.30	-0.99	0.26	-1.50	-0.48	0.0002	-0.77	-1.17	-0.38
Week 26																
Placebo	53	50	8.77	2.41	0.68	0.22	0.23	1.12								
E pooled	52	47	7.58	1.69	-0.32	0.23	-0.78	0.13	-1.00	0.32	-1.63	-0.37	0.0022	-0.63	-1.04	-0.23
Sex																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.5999^			
Week 12													0.7556^			
Week 26													0.3678^			
Male																
Baseline																
Placebo	19	19	8.12	1.42												
E pooled	19	19	7.92	1.26												
Week 4																
Placebo	19	18	8.24	1.80	0.07	0.13	-0.18	0.32								
E pooled	19	19	7.27	0.90	-0.65	0.13	-0.90	-0.40	-0.72	0.18	-1.08	-0.37	<0.0001			
Week 12																
Placebo	19	19	8.17	2.25	0.06	0.30	-0.52	0.65								
E pooled	19	18	6.80	0.78	-1.03	0.30	-1.63	-0.44	-1.10	0.42	-1.93	-0.26	0.0104			
Week 26																
Placebo	19	18	8.64	2.34	0.57	0.37	-0.16	1.31								
E pooled	19	17	6.98	0.94	-0.82	0.38	-1.57	-0.06	-1.39	0.53	-2.44	-0.33	0.0104			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline HBA1C [%] by Visit interaction as fixed effect(s).
Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
Sex																
Female																
Baseline																
Placebo	34	33	8.04	1.13												
E pooled	33	32	7.97	1.27												
Week 4																
Placebo	34	32	8.13	1.44	0.08	0.10	-0.11	0.26								
E pooled	33	31	7.46	1.13	-0.53	0.10	-0.72	-0.33	-0.60	0.14	-0.87	-0.33	<0.0001			
Week 12																
Placebo	34	33	8.52	1.79	0.48	0.22	0.04	0.93								
E pooled	33	30	7.50	1.77	-0.45	0.23	-0.90	0.01	-0.93	0.32	-1.57	-0.29	0.0045			
Week 26																
Placebo	34	32	8.84	2.48	0.74	0.28	0.18	1.29								
E pooled	33	30	7.92	1.92	-0.04	0.29	-0.61	0.53	-0.78	0.40	-1.58	0.01	0.0533			
Age																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.7240^			
Week 12													0.7124^			
Week 26													0.3333^			
<15																
Baseline																
Placebo	26	25	8.12	1.40												
E pooled	25	25	7.98	1.26												
Week 4																
Placebo	26	24	8.22	1.74	0.09	0.11	-0.13	0.30								
E pooled	25	25	7.38	1.02	-0.60	0.11	-0.81	-0.39	-0.69	0.15	-0.99	-0.38	<0.0001			
Week 12																
Placebo	26	25	8.55	2.17	0.44	0.26	-0.07	0.95								
E pooled	25	25	7.33	1.82	-0.66	0.26	-1.16	-0.15	-1.10	0.36	-1.81	-0.38	0.0031			
Week 26																
Placebo	26	25	9.01	2.68	0.90	0.32	0.26	1.53								
E pooled	25	23	7.59	1.92	-0.42	0.33	-1.07	0.23	-1.32	0.46	-2.23	-0.41	0.0047			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline HBA1C [%] by Visit interaction as fixed effect(s).
Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
Age																
>=15 to <18																
Baseline																
Placebo	27	27	8.03	1.08												
E pooled	27	26	7.92	1.26												
Week 4																
Placebo	27	26	8.12	1.41	0.06	0.11	-0.15	0.27								
E pooled	27	25	7.39	1.09	-0.55	0.11	-0.76	-0.34	-0.61	0.15	-0.91	-0.31	<0.0001			
Week 12																
Placebo	27	27	8.25	1.76	0.23	0.25	-0.26	0.72								
E pooled	27	23	7.13	1.10	-0.68	0.26	-1.19	-0.17	-0.91	0.36	-1.62	-0.20	0.0124			
Week 26																
Placebo	27	25	8.53	2.13	0.46	0.31	-0.16	1.09								
E pooled	27	24	7.57	1.47	-0.23	0.32	-0.87	0.41	-0.69	0.45	-1.59	0.20	0.1261			
Region																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.2736^			
Week 12													0.2594^			
Week 26													0.2497^			
US																
Baseline																
Placebo	33	33	8.08	1.16												
E pooled	36	35	7.97	1.25												
Week 4																
Placebo	33	31	8.15	1.43	0.03	0.10	-0.16	0.22								
E pooled	36	34	7.45	1.10	-0.53	0.09	-0.72	-0.35	-0.56	0.13	-0.83	-0.30	<0.0001			
Week 12																
Placebo	33	33	8.38	1.73	0.30	0.23	-0.15	0.75								
E pooled	36	32	7.41	1.74	-0.49	0.22	-0.94	-0.05	-0.79	0.32	-1.42	-0.17	0.0137			
Week 26																
Placebo	33	31	8.89	2.52	0.77	0.28	0.21	1.32								
E pooled	36	31	7.93	1.84	0.01	0.28	-0.54	0.56	-0.76	0.39	-1.54	0.02	0.0566			

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Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
Region																
Non-US																
Baseline																
Placebo	20	19	8.05	1.38												
E pooled	16	16	7.91	1.30												
Week 4																
Placebo	20	19	8.20	1.80	0.15	0.13	-0.10	0.40								
E pooled	16	16	7.25	0.94	-0.66	0.14	-0.93	-0.39	-0.81	0.19	-1.18	-0.45	<0.0001			
Week 12																
Placebo	20	19	8.42	2.35	0.38	0.30	-0.21	0.97								
E pooled	16	16	6.88	0.80	-1.03	0.32	-1.67	-0.39	-1.41	0.44	-2.28	-0.54	0.0017			
Week 26																
Placebo	20	19	8.57	2.26	0.53	0.36	-0.19	1.25								
E pooled	16	16	6.91	1.09	-1.00	0.40	-1.78	-0.22	-1.53	0.54	-2.59	-0.47	0.0051			
BMI [kg/m2] at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.1470^			
Week 12													0.4864^			
Week 26													0.3109^			
< median																
Baseline																
Placebo	27	26	8.25	1.30												
E pooled	26	26	8.11	1.29												
Week 4																
Placebo	27	26	8.37	1.62	0.11	0.11	-0.10	0.32								
E pooled	26	26	7.42	0.98	-0.69	0.11	-0.90	-0.48	-0.80	0.15	-1.09	-0.50	<0.0001			
Week 12																
Placebo	27	26	8.48	2.03	0.23	0.25	-0.28	0.73								
E pooled	26	26	7.17	0.97	-0.94	0.25	-1.44	-0.44	-1.17	0.36	-1.88	-0.45	0.0015			
Week 26																
Placebo	27	26	8.75	2.10	0.50	0.31	-0.12	1.11								
E pooled	26	25	7.32	1.31	-0.80	0.31	-1.41	-0.18	-1.29	0.44	-2.16	-0.42	0.0039			

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Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
BMI [kg/m2] at baseline																
>= median																
Baseline																
Placebo	26	26	7.89	1.15												
E pooled	26	25	7.78	1.22												
Week 4																
Placebo	26	24	7.95	1.50	0.03	0.11	-0.19	0.24								
E pooled	26	24	7.35	1.13	-0.45	0.11	-0.67	-0.24	-0.48	0.15	-0.79	-0.18	0.0022			
Week 12																
Placebo	26	26	8.32	1.91	0.43	0.25	-0.07	0.94								
E pooled	26	22	7.31	1.98	-0.37	0.27	-0.90	0.15	-0.81	0.37	-1.54	-0.08	0.0305			
Week 26																
Placebo	26	24	8.79	2.75	0.86	0.32	0.23	1.48								
E pooled	26	22	7.87	2.03	0.21	0.33	-0.44	0.86	-0.65	0.46	-1.55	0.26	0.1590			
BMI Z-Score																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.0695^			
Week 12													0.0917^			
Week 26													0.8190^			

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Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
BMI Z-Score																
<=2 (Underweight, normal or overweight)																
Baseline																
Placebo	9	9	8.51	1.47												
E pooled	5	5	7.52	1.74												
Week 4																
Placebo	9	9	8.34	1.73	-0.17	0.18	-0.53	0.18								
E pooled	5	5	7.02	1.37	-0.47	0.25	-0.96	0.01	-0.30	0.31	-0.91	0.30	0.3282			
Week 12																
Placebo	9	9	8.08	2.12	-0.43	0.43	-1.28	0.42								
E pooled	5	5	7.22	1.07	-0.31	0.58	-1.46	0.85	0.13	0.73	-1.31	1.56	0.8628			
Week 26																
Placebo	9	9	8.67	2.14	0.16	0.54	-0.91	1.23								
E pooled	5	5	7.20	1.12	-0.32	0.73	-1.77	1.12	-0.48	0.91	-2.28	1.32	0.6009			
>2 to <=3 (Class 1 obesity)																
Baseline																
Placebo	17	16	7.83	1.04												
E pooled	21	21	8.09	1.01												
Week 4																
Placebo	17	16	8.08	1.42	0.26	0.14	-0.01	0.52								
E pooled	21	21	7.37	0.77	-0.72	0.12	-0.96	-0.49	-0.98	0.18	-1.33	-0.62	<0.0001			
Week 12																
Placebo	17	16	8.45	1.95	0.61	0.32	-0.02	1.25								
E pooled	21	20	7.00	0.90	-1.03	0.28	-1.59	-0.47	-1.65	0.43	-2.50	-0.80	0.0002			
Week 26																
Placebo	17	16	8.46	2.16	0.62	0.41	-0.18	1.43								
E pooled	21	21	7.59	1.46	-0.50	0.35	-1.20	0.20	-1.12	0.54	-2.18	-0.05	0.0395			

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Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
BMI Z-Score																
>3 (Class 2 or 3 obesity)																
Baseline																
Placebo	27	27	8.06	1.26												
E pooled	26	25	7.92	1.36												
Week 4																
Placebo	27	25	8.16	1.65	0.04	0.11	-0.17	0.25								
E pooled	26	24	7.48	1.20	-0.46	0.11	-0.68	-0.24	-0.51	0.15	-0.81	-0.20	0.0013			
Week 12																
Placebo	27	27	8.47	1.98	0.41	0.25	-0.08	0.90								
E pooled	26	23	7.45	1.95	-0.41	0.26	-0.94	0.11	-0.82	0.36	-1.54	-0.11	0.0247			
Week 26																
Placebo	27	25	9.01	2.70	0.89	0.32	0.26	1.52								
E pooled	26	21	7.66	2.03	-0.18	0.34	-0.86	0.49	-1.07	0.47	-2.00	-0.15	0.0234			
HbA1c [%] at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													<0.0001^			
Week 12													0.0004^			
Week 26													0.0080^			
<8.0																
Baseline																
Placebo	29	28	7.15	0.48												
E pooled	28	28	7.01	0.51												
Week 4																
Placebo	29	26	7.02	0.66	-0.11	0.10	-0.30	0.09								
E pooled	28	27	6.73	0.71	-0.28	0.10	-0.47	-0.08	-0.17	0.14	-0.44	0.10	0.2162			
Week 12																
Placebo	29	28	7.26	1.08	0.11	0.23	-0.35	0.57								
E pooled	28	27	6.96	1.76	-0.02	0.24	-0.49	0.44	-0.13	0.33	-0.79	0.52	0.6913			
Week 26																
Placebo	29	27	7.70	2.18	0.52	0.30	-0.07	1.11								
E pooled	28	26	7.19	1.84	0.24	0.30	-0.36	0.83	-0.28	0.42	-1.12	0.55	0.5035			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
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Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
HbA1c [%] at baseline																
8.0 to 9.0																
Baseline																
Placebo	12	12	8.36	0.29												
E pooled	12	12	8.38	0.32												
Week 4																
Placebo	12	12	8.53	0.48	0.18	0.14	-0.11	0.46								
E pooled	12	12	7.55	0.42	-0.83	0.14	-1.12	-0.54	-1.01	0.20	-1.41	-0.60	<0.0001	-2.01	-2.82	-1.20
Week 12																
Placebo	12	12	8.62	1.28	0.26	0.36	-0.45	0.97								
E pooled	12	11	7.05	0.61	-1.23	0.36	-1.94	-0.51	-1.49	0.51	-2.49	-0.48	0.0040	-1.22	-2.04	-0.40
Week 26																
Placebo	12	11	8.80	1.61	0.47	0.46	-0.44	1.39								
E pooled	12	12	7.83	1.41	-0.55	0.45	-1.44	0.35	-1.02	0.65	-2.30	0.26	0.1169			
>9.0																
Baseline																
Placebo	12	12	9.92	0.67												
E pooled	12	11	9.86	0.54												
Week 4																
Placebo	12	12	10.28	1.23	0.36	0.14	0.08	0.65								
E pooled	12	11	8.83	0.61	-1.04	0.15	-1.34	-0.74	-1.40	0.21	-1.82	-0.99	<0.0001	-2.79	-3.62	-1.97
Week 12																
Placebo	12	12	10.83	1.87	0.91	0.36	0.20	1.61								
E pooled	12	10	8.17	1.09	-1.64	0.38	-2.40	-0.89	-2.55	0.52	-3.58	-1.52	<0.0001	-2.08	-2.93	-1.24
Week 26																
Placebo	12	12	11.14	1.83	1.22	0.45	0.33	2.12								
E pooled	12	9	8.37	1.33	-1.59	0.51	-2.59	-0.59	-2.82	0.68	-4.16	-1.47	<0.0001	-1.82	-2.69	-0.95
FPG [mg/dl] at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.0529^			
Week 12													0.0359^			
Week 26													0.0433^			

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Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
FPG [mg/dl] at baseline																
<126																
Baseline																
Placebo	13	12	7.38	1.33												
E pooled	19	19	7.11	0.70												
Week 4																
Placebo	13	11	7.41	1.78	-0.01	0.16	-0.33	0.30								
E pooled	19	18	6.76	0.80	-0.34	0.13	-0.59	-0.09	-0.32	0.20	-0.73	0.08	0.1135			
Week 12																
Placebo	13	12	7.37	2.40	-0.03	0.37	-0.76	0.70								
E pooled	19	18	6.91	2.11	-0.17	0.30	-0.76	0.42	-0.14	0.47	-1.08	0.80	0.7674			
Week 26																
Placebo	13	11	7.74	2.77	0.26	0.47	-0.66	1.18								
E pooled	19	18	7.34	2.27	0.24	0.37	-0.49	0.96	-0.02	0.59	-1.20	1.15	0.9699			
>=126																
Baseline																
Placebo	39	39	8.28	1.15												
E pooled	29	29	8.49	1.19												
Week 4																
Placebo	39	38	8.39	1.47	0.10	0.09	-0.07	0.27								
E pooled	29	29	7.79	0.99	-0.70	0.10	-0.90	-0.50	-0.80	0.13	-1.06	-0.54	<0.0001			
Week 12																
Placebo	39	39	8.72	1.74	0.44	0.21	0.04	0.85								
E pooled	29	27	7.50	0.98	-0.91	0.24	-1.38	-0.43	-1.35	0.32	-1.98	-0.73	<0.0001	-1.07	-1.56	-0.57
Week 26																
Placebo	39	38	9.12	2.25	0.85	0.25	0.35	1.35								
E pooled	29	27	7.79	1.22	-0.63	0.30	-1.22	-0.03	-1.48	0.39	-2.26	-0.70	0.0003	-0.94	-1.44	-0.45
eGFR (Zappitelli) at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.2813^			
Week 12													0.7244^			
Week 26													0.7903^			

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eGFR (Zappitelli) at baseline																
<120																
Baseline																
Placebo	24	23	7.71	1.32												
E pooled	21	21	7.44	1.13												
Week 4																
Placebo	24	22	7.75	1.73	0.01	0.12	-0.22	0.24								
E pooled	21	20	6.99	0.92	-0.45	0.12	-0.69	-0.21	-0.46	0.17	-0.79	-0.12	0.0074			
Week 12																
Placebo	24	23	7.89	2.10	0.18	0.27	-0.36	0.73								
E pooled	21	20	6.77	0.88	-0.65	0.29	-1.22	-0.08	-0.83	0.40	-1.62	-0.04	0.0385			
Week 26																
Placebo	24	21	8.03	2.23	0.32	0.34	-0.36	0.99								
E pooled	21	19	6.94	1.30	-0.42	0.36	-1.13	0.29	-0.73	0.50	-1.71	0.25	0.1414			
120 to <150																
Baseline																
Placebo	23	23	8.27	0.99												
E pooled	19	19	7.99	0.98												
Week 4																
Placebo	23	22	8.39	1.31	0.11	0.12	-0.12	0.33								
E pooled	19	19	7.39	0.87	-0.59	0.13	-0.84	-0.35	-0.70	0.17	-1.04	-0.36	<0.0001			
Week 12																
Placebo	23	23	8.73	1.87	0.47	0.27	-0.07	1.01								
E pooled	19	19	7.55	2.02	-0.44	0.30	-1.04	0.15	-0.91	0.41	-1.72	-0.11	0.0264			
Week 26																
Placebo	23	23	9.30	2.58	1.04	0.33	0.38	1.70								
E pooled	19	19	7.97	2.05	-0.03	0.37	-0.75	0.70	-1.07	0.50	-2.05	-0.09	0.0329			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline HBA1C [%] by Visit interaction as fixed effect(s).
Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
eGFR (Zappitelli) at baseline																
>=150																
Baseline																
Placebo	6	6	8.68	1.53												
E pooled	12	11	8.85	1.46												
Week 4																
Placebo	6	6	8.88	1.58	0.20	0.22	-0.25	0.64								
E pooled	12	11	8.09	1.24	-0.76	0.17	-1.08	-0.43	-0.95	0.28	-1.50	-0.40	0.0008			
Week 12																
Placebo	6	6	9.08	1.42	0.38	0.54	-0.68	1.44								
E pooled	12	9	7.61	1.16	-1.08	0.41	-1.89	-0.26	-1.46	0.68	-2.79	-0.12	0.0329			
Week 26																
Placebo	6	6	9.35	1.92	0.64	0.65	-0.65	1.94								
E pooled	12	9	8.12	1.19	-0.70	0.52	-1.73	0.32	-1.35	0.83	-2.99	0.30	0.1084			
Backg. Antidiabetic Med. at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4																
Week 12																
Week 26																

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline HBA1C [%] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	95% CI Lower	95% CI Upper	p-value	Hedges' g	95% CI Lower	95% CI Upper
Backg. Antidiabetic Med. at baseline																
Metformin only																
Baseline																
Placebo	28	0														
E pooled	26	0														
Week 4																
Placebo	28	0														
E pooled	26	0														
Week 12																
Placebo	28	0														
E pooled	26	0														
Week 26																
Placebo	28	0														
E pooled	26	0														
Insulin only																
Baseline																
Placebo	2	0														
E pooled	3	0														
Week 4																
Placebo	2	0														
E pooled	3	0														
Week 12																
Placebo	2	0														
E pooled	3	0														
Week 26																
Placebo	2	0														
E pooled	3	0														

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline HBA1C [%] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	95% CI Lower	95% CI Upper	p-value	Hedges' g	95% CI Lower	95% CI Upper
Backg. Antidiabetic Med. at baseline																
Metformin and Insulin																
Baseline																
Placebo	19	0														
E pooled	22	0														
Week 4																
Placebo	19	0														
E pooled	22	0														
Week 12																
Placebo	19	0														
E pooled	22	0														
Week 26																
Placebo	19	0														
E pooled	22	0														
None																
Baseline																
Placebo	4	0														
E pooled	1	0														
Week 4																
Placebo	4	0														
E pooled	1	0														
Week 12																
Placebo	4	0														
E pooled	1	0														
Week 26																
Placebo	4	0														
E pooled	1	0														

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline HBA1C [%] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	SE	95% CI Lower	95% CI Upper	p-value	Hedges' g	95% CI Lower	95% CI Upper
Time since diagnosis of T2DM																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.3933^			
Week 12													0.3210^			
Week 26													0.3793^			
<1 year																
Baseline																
Placebo	18	18	8.28	1.56												
E pooled	17	17	7.61	1.22												
Week 4																
Placebo	18	17	8.44	1.89	0.05	0.13	-0.22	0.31								
E pooled	17	17	7.22	1.08	-0.40	0.13	-0.66	-0.13	-0.44	0.19	-0.82	-0.07	0.0194			
Week 12																
Placebo	18	18	8.69	2.38	0.39	0.30	-0.21	0.99								
E pooled	17	17	7.51	2.11	-0.12	0.31	-0.73	0.50	-0.51	0.44	-1.37	0.35	0.2468			
Week 26																
Placebo	18	18	8.90	2.30	0.60	0.38	-0.15	1.34								
E pooled	17	15	7.62	2.14	0.03	0.40	-0.76	0.82	-0.57	0.55	-1.66	0.52	0.3032			
1 year - 3 years																
Baseline																
Placebo	24	24	7.99	1.13												
E pooled	21	21	8.06	1.20												
Week 4																
Placebo	24	23	8.13	1.50	0.15	0.12	-0.08	0.38								
E pooled	21	20	7.46	1.02	-0.64	0.12	-0.88	-0.40	-0.79	0.17	-1.13	-0.46	<0.0001			
Week 12																
Placebo	24	24	8.43	1.84	0.46	0.26	-0.06	0.97								
E pooled	21	20	7.15	1.12	-0.92	0.28	-1.48	-0.36	-1.38	0.38	-2.14	-0.62	0.0005			
Week 26																
Placebo	24	23	9.15	2.66	1.10	0.33	0.46	1.75								
E pooled	21	20	7.73	1.46	-0.35	0.35	-1.04	0.34	-1.45	0.48	-2.40	-0.50	0.0030			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline HBA1C [%] by Visit interaction as fixed effect(s).
Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.1 HbA1c [%] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Hedges' g	Hedges' g: 95% CI Lower	Hedges' g: 95% CI Upper
Time since diagnosis of T2DM																
>3 years																
Baseline																
Placebo	11	10	7.88	0.77												
E pooled	14	13	8.22	1.37												
Week 4																
Placebo	11	10	7.81	1.08	-0.06	0.17	-0.41	0.28								
E pooled	14	13	7.49	1.11	-0.70	0.16	-1.00	-0.39	-0.63	0.23	-1.09	-0.17	0.0077			
Week 12																
Placebo	11	10	7.79	1.34	-0.09	0.40	-0.89	0.71								
E pooled	14	11	6.97	0.96	-0.97	0.37	-1.69	-0.24	-0.87	0.55	-1.95	0.21	0.1117			
Week 26																
Placebo	11	9	7.53	1.63	-0.23	0.52	-1.25	0.79								
E pooled	14	12	7.29	1.50	-0.75	0.46	-1.65	0.15	-0.52	0.69	-1.88	0.84	0.4517			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline HBA1C [%] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Appendix 1, Figure 2.2.2

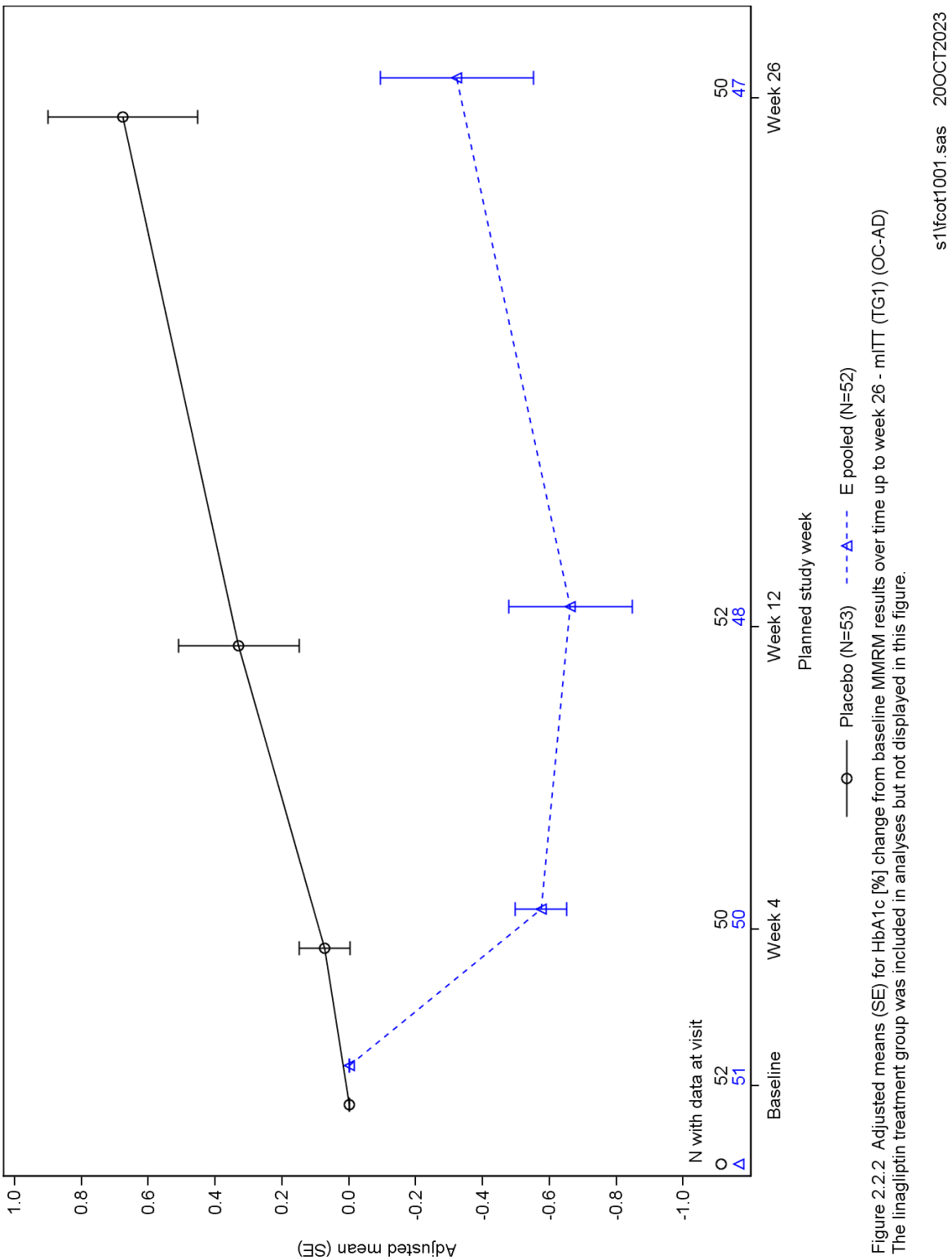

Figure 2.2.2 Adjusted means (SE) for HbA1c [%] change from baseline MMRM results over time up to week 26 - mITT (TG1) (OC-AD)
The linagliptin treatment group was included in analyses but not displayed in this figure.

Table 2.2.3 FPG [mg/dL] change from baseline ANCOVA results at week 26 overall and by subgroup - mITT (TG1) (OC-AD-BOCF)

Subgroup Category Treatment	N	n	Baseline[1] Mean	Baseline[1] SD	Week 26[1] Mean	Week 26[1] SD	Change from Baseline at Week 26[1] Mean	Change from Baseline at Week 26[1] SD	95% CI Lower	95% CI Upper
Overall										
Placebo	53	52	158.62	53.80	174.34	79.49	15.73	67.73	-3.13	34.58
E pooled	52	48	154.43	57.78	136.91	55.03	-17.52	67.45	-37.11	2.06
Sex										
Male										
Placebo	19	19	155.28	56.29	174.61	56.59	19.34	55.44	-7.38	46.06
E pooled	19	18	151.47	50.07	130.86	35.37	-20.61	32.02	-36.54	-4.69
Female										
Placebo	34	33	160.54	53.11	174.19	90.93	13.65	74.64	-12.82	40.11
E pooled	33	30	156.20	62.70	140.54	64.33	-15.67	82.23	-46.37	15.04
Age										
<15										
Placebo	26	25	152.37	67.00	170.10	89.21	17.73	82.88	-16.48	51.94
E pooled	25	23	151.30	50.08	123.95	28.25	-27.34	44.37	-46.53	-8.15
>=15 to <18										
Placebo	27	27	164.40	38.23	178.27	70.80	13.87	51.48	-6.50	34.23
E pooled	27	25	157.31	64.97	148.82	69.93	-8.48	83.22	-42.84	25.87
Region										
US										
Placebo	33	32	151.47	41.89	178.91	73.05	27.44	63.05	4.71	50.17
E pooled	36	34	147.50	53.20	140.28	62.14	-7.22	66.79	-30.53	16.08
Non-US										
Placebo	20	20	170.06	68.43	167.04	90.34	-3.02	72.29	-36.85	30.82
E pooled	16	14	171.25	66.73	128.73	32.33	-42.53	64.59	-79.82	-5.23

N: Number of patients in analysis set, n: Number of patients analysed at visit, [1]Absolute (unadjusted) values, [2]Test for treatment difference at the visit, ^: Interaction p-value.
[3] Model includes Baseline FPG [mg/dL] as linear covariate(s) and Age (2 cat.), Treatment, subgroup, Treatment by subgroup interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The overall model does not include subgroup or treatment by subgroup interaction.
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.3 FPG [mg/dL] change from baseline ANCOVA results at week 26 overall and by subgroup - mITT (TG1) (OC-AD-BOCF)

Subgroup Category Treatment	Change from Baseline at Week 26[3]				Comparison vs Placebo[3]					Hedges' g		
	Adjusted mean	SE	95% CI Lower	95% CI Upper	Adjusted mean	SE	95% CI Lower	95% CI Upper	p-value[2]	Hedges' g	95% CI Lower	95% CI Upper
Overall												
Placebo	15.70	8.21	-0.53	31.93								
E pooled	-19.48	8.56	-36.39	-2.57	-35.18	11.86	-58.61	-11.74	0.0035	-0.59	-0.99	-0.20
Sex									0.6938^			
Male												
Placebo	21.33	13.72	-5.79	48.45								
E pooled	-19.97	14.10	-47.84	7.91	-41.30	19.69	-80.23	-2.37	0.0377			
Female												
Placebo	12.21	10.41	-8.36	32.79								
E pooled	-19.28	10.94	-40.90	2.34	-31.50	15.09	-61.33	-1.66	0.0387			
Age									0.4022^			
<15												
Placebo	15.83	11.84	-7.58	39.23								
E pooled	-29.75	12.35	-54.16	-5.34	-45.57	17.10	-79.37	-11.77	0.0086			
>=15 to <18												
Placebo	15.57	11.40	-6.95	38.10								
E pooled	-10.07	11.84	-33.48	13.33	-25.65	16.44	-58.14	6.85	0.1210			
Region									0.9030^			
US												
Placebo	25.30	10.46	4.63	45.98								
E pooled	-10.93	10.16	-31.02	9.15	-36.24	14.57	-65.03	-7.44	0.0140			
Non-US												
Placebo	-0.08	13.24	-26.26	26.09								
E pooled	-39.40	15.81	-70.65	-8.15	-39.32	20.62	-80.08	1.44	0.0585			

N: Number of patients in analysis set, n: Number of patients analysed at visit, [1]Absolute (unadjusted) values, [2]Test for treatment difference at the visit, ^: Interaction p-value.
[3] Model includes Baseline FPG [mg/dL] as linear covariate(s) and Age (2 cat.), Treatment, subgroup, Treatment by subgroup interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The overall model does not include subgroup or treatment by subgroup interaction.
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.3 FPG [mg/dL] change from baseline ANCOVA results at week 26 overall and by subgroup - mITT (TG1) (OC-AD-BOCF)

Subgroup Category / Treatment	N	n	Baseline[1] Mean	Baseline[1] SD	Week 26[1] Mean	Week 26[1] SD	Change from Baseline at Week 26[1] Mean	Change from Baseline at Week 26[1] SD	95% CI Lower	95% CI Upper
BMI [kg/m2] at baseline										
< median										
Placebo	27	26	165.78	62.08	175.61	86.85	9.83	70.37	-18.60	38.25
E pooled	26	26	163.41	56.29	127.94	31.14	-35.47	52.88	-56.83	-14.11
>= median										
Placebo	26	26	151.46	44.09	173.08	73.10	21.62	65.83	-4.97	48.21
E pooled	26	22	143.82	59.00	147.51	73.53	3.69	77.34	-30.60	37.99
BMI Z-Score										
<=2 (Underweight, normal or overweight)										
Placebo	9	9	162.84	53.87	178.50	67.89	15.66	67.06	-35.89	67.20
E pooled	5	5	164.38	43.18	147.01	22.50	-17.37	33.89	-59.45	24.70
>2 to <=3 (Class 1 obesity)										
Placebo	17	16	161.85	60.72	176.26	99.92	14.40	66.26	-20.90	49.71
E pooled	21	21	167.36	61.89	137.83	68.07	-29.54	93.36	-72.03	12.96
>3 (Class 2 or 3 obesity)										
Placebo	27	27	155.29	51.32	171.82	72.12	16.53	71.28	-11.66	44.73
E pooled	26	22	139.82	55.26	133.73	47.26	-6.09	37.15	-22.56	10.39
HbA1c [%] at baseline										
<8.0										
Placebo	29	29	136.69	34.15	149.08	67.38	12.38	65.31	-12.46	37.23
E pooled	28	26	122.47	38.82	131.97	63.18	9.50	68.37	-18.12	37.11
8.0 to 9.0										
Placebo	12	11	167.60	48.30	194.55	78.90	26.95	55.48	-10.33	64.22
E pooled	12	12	170.21	46.59	130.53	29.84	-39.69	27.09	-56.90	-22.48
>9.0										
Placebo	12	12	203.37	69.26	216.89	89.50	13.52	86.33	-41.34	68.37
E pooled	12	10	218.56	52.37	157.40	55.22	-61.16	70.68	-111.72	-10.60

N: Number of patients in analysis set, n: Number of patients analysed at visit, [1]Absolute (unadjusted) values, [2]Test for treatment difference at the visit, ^: Interaction p-value.
[3] Model includes Baseline FPG [mg/dL] as linear covariate(s) and Age (2 cat.), Treatment, subgroup, Treatment by subgroup interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The overall model does not include subgroup or treatment by subgroup interaction.
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.3 FPG [mg/dL] change from baseline ANCOVA results at week 26 overall and by subgroup - mITT (TG1) (OC-AD-BOCF)

Subgroup Category Treatment	Change from Baseline at Week 26[3] Adjusted mean	SE	95% CI Lower	95% CI Upper	Comparison vs Placebo[3] Adjusted mean	SE	95% CI Lower	95% CI Upper	p-value[2]	Hedges' g Hedges' g	95% CI Lower	95% CI Upper
BMI [kg/m2] at baseline									0.2819^			
< median												
Placebo	10.21	11.64	-12.81	33.22								
E pooled	-36.50	11.61	-59.44	-13.56	-46.70	16.45	-79.22	-14.19	0.0052			
>= median												
Placebo	21.23	11.64	-1.77	44.24								
E pooled	0.28	12.63	-24.70	25.25	-20.96	17.19	-54.93	13.02	0.2247			
BMI Z-Score									0.8765^			
<=2 (Underweight, normal or overweight)												
Placebo	13.67	19.94	-25.74	53.08								
E pooled	-20.72	26.86	-73.83	32.38	-34.40	33.51	-100.65	31.86	0.3065			
>2 to <=3 (Class 1 obesity)												
Placebo	12.23	14.94	-17.32	41.77								
E pooled	-29.90	13.07	-55.75	-4.06	-42.13	19.87	-81.41	-2.85	0.0357			
>3 (Class 2 or 3 obesity)												
Placebo	18.53	11.51	-4.23	41.28								
E pooled	-10.01	12.87	-35.45	15.44	-28.53	17.32	-62.77	5.70	0.1017			
HbA1c [%] at baseline									0.0680^			
<8.0												
Placebo	16.16	10.93	-5.45	37.77								
E pooled	5.84	11.54	-16.98	28.66	-10.32	15.93	-41.82	21.18	0.5181			
8.0 to 9.0												
Placebo	22.62	17.76	-12.49	57.73								
E pooled	-42.42	16.97	-75.97	-8.87	-65.04	24.51	-113.51	-16.58	0.0089			
>9.0												
Placebo	9.54	17.00	-24.08	43.15								
E pooled	-57.46	18.58	-94.20	-20.72	-67.00	25.20	-116.82	-17.17	0.0088			

N: Number of patients in analysis set, n: Number of patients analysed at visit, [1]Absolute (unadjusted) values, [2]Test for treatment difference at the visit, ^: Interaction p-value.
[3] Model includes Baseline FPG [mg/dL] as linear covariate(s) and Age (2 cat.), Treatment, subgroup, Treatment by subgroup interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The overall model does not include subgroup or treatment by subgroup interaction.
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.3 FPG [mg/dL] change from baseline ANCOVA results at week 26 overall and by subgroup - mITT (TG1) (OC-AD-BOCF)

Subgroup Category / Treatment	N	n	Baseline[1] Mean	Baseline[1] SD	Week 26[1] Mean	Week 26[1] SD	Change from Baseline at Week 26[1] Mean	Change from Baseline at Week 26[1] SD	95% CI Lower	95% CI Upper
FPG [mg/dl] at baseline										
<126										
Placebo	13	13	99.04	18.51	111.52	27.66	12.48	28.65	-4.84	29.79
E pooled	19	19	102.38	18.37	123.58	70.96	21.20	73.29	-14.13	56.52
>=126										
Placebo	39	39	178.48	46.45	195.29	80.23	16.81	76.77	-8.08	41.69
E pooled	29	29	188.53	48.42	145.64	40.59	-42.89	50.00	-61.91	-23.87
eGFR (Zappitelli) at baseline										
<120										
Placebo	24	24	141.55	53.75	139.60	50.04	-1.95	43.03	-20.12	16.22
E pooled	21	20	126.27	33.34	138.30	72.76	12.04	75.37	-23.24	47.31
120 to <150										
Placebo	23	22	168.59	37.86	197.93	89.58	29.34	84.49	-8.12	66.80
E pooled	19	19	161.67	65.38	121.67	22.23	-39.99	62.03	-69.89	-10.10
>=150										
Placebo	6	6	190.32	84.69	226.84	87.64	36.52	73.90	-41.04	114.08
E pooled	12	9	201.72	52.26	165.96	51.02	-35.76	28.63	-57.76	-13.76

N: Number of patients in analysis set, n: Number of patients analysed at visit, [1]Absolute (unadjusted) values, [2]Test for treatment difference at the visit, ^: Interaction p-value.
[3] Model includes Baseline FPG [mg/dL] as linear covariate(s) and Age (2 cat.), Treatment, subgroup, Treatment by subgroup interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The overall model does not include subgroup or treatment by subgroup interaction.
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.3 FPG [mg/dL] change from baseline ANCOVA results at week 26 overall and by subgroup - mITT (TG1) (OC-AD-BOCF)

Subgroup / Category / Treatment	Change from Baseline at Week 26³				Comparison vs Placebo³					Hedges' g		
	Adjusted mean	SE	95% CI Lower	95% CI Upper	Adjusted mean	SE	95% CI Lower	95% CI Upper	p-value²	Hedges' g	95% CI Lower	95% CI Upper
FPG [mg/dl] at baseline									0.0137^			
<126												
Placebo	12.68	17.43	-21.77	47.13								
E pooled	21.19	14.30	-7.07	49.46	8.52	22.55	-36.05	53.08	0.7062			
>=126												
Placebo	16.75	10.00	-3.03	36.52								
E pooled	-42.88	11.57	-65.76	-20.00	-59.63	15.30	-89.87	-29.38	0.0001	-0.96	-1.44	-0.47
eGFR (Zappitelli) at baseline									0.0044^			
<120												
Placebo	-1.18	11.65	-24.21	21.86								
E pooled	5.10	12.82	-20.26	30.45	6.27	17.34	-28.01	40.55	0.7180			
120 to <150												
Placebo	33.46	12.19	9.35	57.56								
E pooled	-39.06	13.10	-64.96	-13.16	-72.52	17.90	-107.90	-37.14	<0.0001	-1.27	-1.89	-0.65
>=150												
Placebo	32.03	23.38	-14.20	78.26								
E pooled	-36.26	19.07	-73.96	1.44	-68.29	30.25	-128.10	-8.48	0.0255	-1.19	-2.24	-0.15

N: Number of patients in analysis set, n: Number of patients analysed at visit, ¹Absolute (unadjusted) values, ²Test for treatment difference at the visit, ^: Interaction p-value.
³ Model includes Baseline FPG [mg/dL] as linear covariate(s) and Age (2 cat.), Treatment, subgroup, Treatment by subgroup interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The overall model does not include subgroup or treatment by subgroup interaction.
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.3 FPG [mg/dL] change from baseline ANCOVA results at week 26 overall and by subgroup - mITT (TG1) (OC-AD-BOCF)

Subgroup Category Treatment	N	n	Baseline[1] Mean	Baseline[1] SD	Week 26[1] Mean	Week 26[1] SD	Change from Baseline at Week 26[1] Mean	Change from Baseline at Week 26[1] SD	95% CI Lower	95% CI Upper
Backg. Antidiabetic Med. at baseline										
Metformin only										
Placebo	28	0								
E pooled	26	0								
Insulin only										
Placebo	2	0								
E pooled	3	0								
Metformin and Insulin										
Placebo	19	0								
E pooled	22	0								
None										
Placebo	4	0								
E pooled	1	0								
Time since diagnosis of T2DM										
<1 year										
Placebo	18	17	164.15	67.27	164.05	60.33	-0.11	67.83	-34.98	34.77
E pooled	17	15	141.01	47.93	131.86	26.61	-9.15	46.12	-34.69	16.38
1 year - 3 years										
Placebo	24	24	166.76	48.55	194.69	86.64	27.93	68.86	-1.14	57.01
E pooled	21	20	159.95	64.47	141.80	76.47	-18.15	93.46	-61.89	25.60
>3 years										
Placebo	11	11	132.30	33.60	145.86	84.08	13.56	65.89	-30.70	57.83
E pooled	14	13	161.42	59.05	135.21	41.27	-26.21	36.54	-48.29	-4.13

N: Number of patients in analysis set, n: Number of patients analysed at visit, [1]Absolute (unadjusted) values, [2]Test for treatment difference at the visit, ^: Interaction p-value.
[3] Model includes Baseline FPG [mg/dL] as linear covariate(s) and Age (2 cat.), Treatment, subgroup, Treatment by subgroup interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The overall model does not include subgroup or treatment by subgroup interaction.
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.3 FPG [mg/dL] change from baseline ANCOVA results at week 26 overall and by subgroup - mITT (TG1) (OC-AD-BOCF)

Subgroup Category Treatment	Change from Baseline at Week 26[3] Adjusted mean	SE	95% CI Lower	95% CI Upper	Comparison vs Placebo[3] Adjusted mean	SE	95% CI Lower	95% CI Upper	p-value[2]	Hedges' g Hedges' g	95% CI Lower	95% CI Upper
Backg. Antidiabetic Med. at baseline												
Metformin only												
Placebo												
E pooled												
Insulin only												
Placebo												
E pooled												
Metformin and Insulin												
Placebo												
E pooled												
None												
Placebo												
E pooled												
Time since diagnosis of T2DM									0.5779^			
<1 year												
Placebo	6.43	14.74	-22.71	35.58								
E pooled	-13.42	15.58	-44.23	17.39	-19.86	21.09	-61.56	21.85	0.3482			
1 year - 3 years												
Placebo	29.32	12.35	4.90	53.74								
E pooled	-18.86	13.27	-45.10	7.38	-48.18	18.24	-84.25	-12.11	0.0092			
>3 years												
Placebo	0.54	18.07	-35.18	36.26								
E pooled	-27.41	17.00	-61.01	6.19	-27.95	24.94	-77.26	21.36	0.2644			

N: Number of patients in analysis set, n: Number of patients analysed at visit, [1]Absolute (unadjusted) values, [2]Test for treatment difference at the visit, ^: Interaction p-value.
[3] Model includes Baseline FPG [mg/dL] as linear covariate(s) and Age (2 cat.), Treatment, subgroup, Treatment by subgroup interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The overall model does not include subgroup or treatment by subgroup interaction.
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	SE	95% CI Lower	95% CI Upper	p-value	Hedges' g	95% CI Lower	95% CI Upper
Overall																
Baseline																
Placebo	53	52	98.87	29.62												
E pooled	52	52	98.66	24.35												
Week 4																
Placebo	53	50	97.99	29.50	0.05	0.27	-0.48	0.58								
E pooled	52	49	96.41	23.84	-0.84	0.27	-1.37	-0.30	-0.88	0.38	-1.64	-0.13	0.0216	-0.47	-0.86	-0.07
Week 12																
Placebo	53	52	99.14	29.52	0.27	0.46	-0.65	1.18								
E pooled	52	48	96.78	24.42	-1.14	0.47	-2.06	-0.21	-1.40	0.66	-2.70	-0.10	0.0351	-0.43	-0.82	-0.03
Week 26																
Placebo	53	50	98.54	28.85	-0.04	0.69	-1.40	1.32								
E pooled	52	48	97.38	24.99	-0.79	0.70	-2.17	0.59	-0.75	0.98	-2.68	1.19	0.4476			
Sex																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.7108^			
Week 12													0.7212^			
Week 26													0.6671^			
Male																
Baseline																
Placebo	19	19	105.04	22.12												
E pooled	19	19	111.18	24.15												
Week 4																
Placebo	19	18	104.46	22.36	0.37	0.45	-0.52	1.25								
E pooled	19	17	108.58	24.14	-0.71	0.45	-1.61	0.19	-1.07	0.64	-2.34	0.19	0.0953			
Week 12																
Placebo	19	19	106.15	21.99	1.08	0.77	-0.44	2.59								
E pooled	19	18	108.66	24.59	-0.63	0.77	-2.16	0.90	-1.71	1.09	-3.86	0.45	0.1192			
Week 26																
Placebo	19	18	106.60	22.47	1.73	1.12	-0.49	3.95								
E pooled	19	17	110.95	25.20	0.43	1.14	-1.83	2.70	-1.30	1.60	-4.47	1.87	0.4204			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline body weight [kg] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	SD	Change from baseline: Adj. mean	SE	95% CI Lower	95% CI Upper	Comparison vs Placebo*: Adj. mean	SE	95% CI Lower	95% CI Upper	p-value	Hedges' g	95% CI Lower	95% CI Upper
Sex																
Female																
Baseline																
Placebo	34	33	95.32	32.98												
E pooled	33	33	91.44	21.69												
Week 4																
Placebo	34	32	94.35	32.61	-0.14	0.34	-0.81	0.53								
E pooled	33	32	89.94	21.33	-0.92	0.34	-1.59	-0.24	-0.78	0.48	-1.72	0.17	0.1080			
Week 12																
Placebo	34	33	95.11	32.73	-0.21	0.58	-1.36	0.94								
E pooled	33	30	89.65	21.72	-1.43	0.59	-2.60	-0.26	-1.22	0.83	-2.86	0.42	0.1437			
Week 26																
Placebo	34	32	94.00	31.31	-1.07	0.85	-2.74	0.60								
E pooled	33	31	89.95	21.87	-1.50	0.86	-3.19	0.20	-0.43	1.21	-2.81	1.95	0.7222			
Age																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.5749^			
Week 12													0.6988^			
Week 26													0.6186^			
<15																
Baseline																
Placebo	26	25	87.73	26.84												
E pooled	25	25	99.91	24.40												
Week 4																
Placebo	26	24	86.59	26.35	0.20	0.39	-0.57	0.97								
E pooled	25	23	97.03	23.63	-0.45	0.39	-1.23	0.33	-0.65	0.56	-1.75	0.45	0.2442			
Week 12																
Placebo	26	25	88.05	27.46	0.27	0.67	-1.06	1.60								
E pooled	25	25	99.02	25.19	-0.84	0.67	-2.17	0.49	-1.11	0.96	-3.00	0.78	0.2478			
Week 26																
Placebo	26	25	88.26	27.35	0.36	1.00	-1.61	2.33								
E pooled	25	23	100.63	26.42	0.16	1.01	-1.84	2.15	-0.20	1.42	-3.02	2.61	0.8868			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline body weight [kg] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
Age																
>=15 to <18																
Baseline																
Placebo	27	27	109.18	28.75												
E pooled	27	27	97.49	24.72												
Week 4																
Placebo	27	26	108.52	28.75	-0.11	0.37	-0.85	0.64								
E pooled	27	26	95.85	24.48	-1.19	0.38	-1.94	-0.45	-1.09	0.53	-2.15	-0.03	0.0435			
Week 12																
Placebo	27	27	109.41	28.03	0.26	0.65	-1.02	1.54								
E pooled	27	23	94.35	23.87	-1.38	0.67	-2.70	-0.05	-1.63	0.94	-3.48	0.21	0.0828			
Week 26																
Placebo	27	25	108.81	27.05	-0.45	0.97	-2.37	1.46								
E pooled	27	25	94.40	23.74	-1.66	0.99	-3.61	0.30	-1.21	1.39	-3.95	1.54	0.3870			
Region																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.2849^			
Week 12													0.3487^			
Week 26													0.3702^			
US																
Baseline																
Placebo	33	33	108.05	24.97												
E pooled	36	36	101.96	23.51												
Week 4																
Placebo	33	31	106.99	24.60	-0.11	0.34	-0.77	0.56								
E pooled	36	33	99.50	23.68	-0.71	0.33	-1.35	-0.07	-0.60	0.47	-1.53	0.32	0.2010			
Week 12																
Placebo	33	33	108.11	24.43	0.09	0.58	-1.05	1.24								
E pooled	36	32	100.44	24.35	-0.88	0.57	-2.00	0.25	-0.97	0.82	-2.58	0.64	0.2358			
Week 26																
Placebo	33	31	107.30	24.58	-0.74	0.87	-2.47	0.98								
E pooled	36	32	100.91	24.97	-0.83	0.85	-2.51	0.86	-0.08	1.22	-2.50	2.33	0.9449			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline body weight [kg] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit Mean	Value at visit SD	Change from baseline Adj. mean	Change from baseline SE	Change from baseline 95% CI Lower	Change from baseline 95% CI Upper	Comparison vs Placebo* Adj. mean	Comparison vs Placebo* SE	Comparison vs Placebo* 95% CI Lower	Comparison vs Placebo* 95% CI Upper	Comparison vs Placebo* p-value	Comparison vs Placebo* Hedges' g	Comparison vs Placebo* 95% CI Lower	Comparison vs Placebo* 95% CI Upper
Region																
Non-US																
Baseline																
Placebo	20	19	82.92	30.91												
E pooled	16	16	91.22	25.34												
Week 4																
Placebo	20	19	83.30	31.51	0.31	0.44	-0.56	1.17								
E pooled	16	16	90.03	23.64	-1.16	0.48	-2.10	-0.22	-1.46	0.65	-2.74	-0.18	0.0254			
Week 12																
Placebo	20	19	83.56	31.70	0.56	0.77	-0.96	2.08								
E pooled	16	16	89.46	23.61	-1.73	0.83	-3.38	-0.08	-2.29	1.14	-4.53	-0.05	0.0456			
Week 26																
Placebo	20	19	84.25	30.20	1.15	1.14	-1.11	3.40								
E pooled	16	16	90.34	24.25	-0.81	1.24	-3.26	1.64	-1.96	1.69	-5.30	1.37	0.2462			
BMI [kg/m2] at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.4824^			
Week 12													0.5533^			
Week 26													0.7710^			
< median																
Baseline																
Placebo	27	26	78.20	16.43												
E pooled	26	26	83.95	16.02												
Week 4																
Placebo	27	26	78.38	16.53	0.11	0.38	-0.64	0.86								
E pooled	26	26	83.42	15.90	-0.51	0.38	-1.26	0.24	-0.62	0.54	-1.68	0.44	0.2513			
Week 12																
Placebo	27	26	78.27	16.64	-0.04	0.66	-1.35	1.27								
E pooled	26	26	82.89	15.35	-1.02	0.66	-2.32	0.28	-0.98	0.93	-2.83	0.86	0.2941			
Week 26																
Placebo	27	26	78.90	16.73	0.53	0.98	-1.41	2.47								
E pooled	26	25	82.99	16.91	-0.46	0.98	-2.41	1.48	-0.99	1.39	-3.74	1.76	0.4776			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline body weight [kg] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
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Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
BMI [kg/m2] at baseline																
>= median																
Baseline																
Placebo	26	26	119.53	25.15												
E pooled	26	26	113.36	22.43												
Week 4																
Placebo	26	24	119.23	25.53	-0.04	0.39	-0.80	0.73								
E pooled	26	23	111.09	22.99	-1.20	0.39	-1.98	-0.42	-1.17	0.55	-2.26	-0.07	0.0365			
Week 12																
Placebo	26	26	120.01	24.40	0.55	0.66	-0.75	1.85								
E pooled	26	22	113.20	23.08	-1.23	0.68	-2.58	0.12	-1.78	0.95	-3.66	0.10	0.0630			
Week 26																
Placebo	26	24	119.82	23.68	-0.68	0.99	-2.65	1.28								
E pooled	26	23	113.03	23.03	-1.09	1.02	-3.10	0.91	-0.41	1.42	-3.22	2.40	0.7746			
BMI Z-Score																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.8300^			
Week 12													0.8294^			
Week 26													0.6440^			

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The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
BMI Z-Score																
<=2 (Underweight, normal or overweight)																
Baseline																
Placebo	9	9	67.37	13.39												
E pooled	5	5	63.52	15.40												
Week 4																
Placebo	9	9	67.79	13.20	0.42	0.65	-0.86	1.70								
E pooled	5	5	62.88	15.18	-0.59	0.87	-2.31	1.14	-1.01	1.09	-3.16	1.15	0.3567			
Week 12																
Placebo	9	9	68.02	12.97	0.65	1.13	-1.58	2.89								
E pooled	5	5	63.78	14.73	0.31	1.52	-2.70	3.32	-0.34	1.90	-4.09	3.41	0.8574			
Week 26																
Placebo	9	9	68.92	12.24	1.60	1.66	-1.68	4.88								
E pooled	5	5	61.98	14.96	-1.55	2.23	-5.97	2.86	-3.15	2.78	-8.66	2.35	0.2591			
>2 to <=3 (Class 1 obesity)																
Baseline																
Placebo	17	16	83.11	15.03												
E pooled	21	21	88.75	11.94												
Week 4																
Placebo	17	16	83.26	15.40	0.10	0.49	-0.86	1.06								
E pooled	21	21	88.21	11.68	-0.49	0.42	-1.33	0.35	-0.59	0.65	-1.87	0.69	0.3617			
Week 12																
Placebo	17	16	83.23	16.13	0.06	0.85	-1.62	1.74								
E pooled	21	20	87.69	11.88	-1.22	0.75	-2.70	0.25	-1.29	1.13	-3.52	0.95	0.2582			
Week 26																
Placebo	17	16	83.71	16.90	0.43	1.25	-2.04	2.90								
E pooled	21	21	88.46	12.70	-0.20	1.09	-2.35	1.96	-0.62	1.66	-3.90	2.66	0.7082			

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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
BMI Z-Score																
>3 (Class 2 or 3 obesity)																
Baseline																
Placebo	27	27	118.70	25.12												
E pooled	26	26	113.41	22.41												
Week 4																
Placebo	27	25	118.29	25.59	-0.10	0.38	-0.85	0.65								
E pooled	26	23	111.17	22.96	-1.20	0.40	-1.99	-0.42	-1.10	0.55	-2.19	-0.02	0.0468			
Week 12																
Placebo	27	27	118.94	24.68	0.27	0.65	-1.02	1.56								
E pooled	26	23	111.87	23.49	-1.36	0.69	-2.72	-0.01	-1.63	0.95	-3.51	0.24	0.0871			
Week 26																
Placebo	27	25	118.69	23.93	-0.86	0.97	-2.79	1.06								
E pooled	26	22	113.95	23.15	-1.10	1.02	-3.13	0.92	-0.24	1.41	-3.03	2.56	0.8659			
HbA1c [%] at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.5463^			
Week 12													0.2914^			
Week 26													0.4566^			
<8.0																
Baseline																
Placebo	29	28	105.49	30.86												
E pooled	28	28	103.26	27.48												
Week 4																
Placebo	29	26	104.16	31.00	-0.05	0.36	-0.77	0.67								
E pooled	28	25	99.69	27.48	-1.32	0.37	-2.05	-0.59	-1.27	0.52	-2.30	-0.25	0.0154			
Week 12																
Placebo	29	28	106.02	30.27	0.54	0.62	-0.69	1.76								
E pooled	28	27	101.20	28.04	-1.81	0.62	-3.05	-0.58	-2.35	0.88	-4.09	-0.61	0.0084			
Week 26																
Placebo	29	27	105.67	29.38	0.06	0.95	-1.82	1.94								
E pooled	28	27	102.09	28.69	-1.48	0.95	-3.36	0.40	-1.54	1.34	-4.20	1.12	0.2539			

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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
HbA1c [%] at baseline																
8.0 to 9.0																
Baseline																
Placebo	12	12	93.39	24.80												
E pooled	12	12	93.87	15.76												
Week 4																
Placebo	12	12	93.70	24.39	0.29	0.55	-0.79	1.37								
E pooled	12	12	93.74	16.15	-0.14	0.55	-1.22	0.94	-0.43	0.77	-1.96	1.10	0.5780			
Week 12																
Placebo	12	12	93.98	24.54	0.58	0.95	-1.30	2.45								
E pooled	12	11	94.90	18.34	0.16	0.96	-1.73	2.06	-0.41	1.35	-3.07	2.25	0.7587			
Week 26																
Placebo	12	11	92.27	24.06	0.32	1.47	-2.58	3.22								
E pooled	12	12	93.37	17.39	-0.62	1.44	-3.48	2.24	-0.94	2.06	-5.00	3.12	0.6481			
>9.0																
Baseline																
Placebo	12	12	88.90	29.39												
E pooled	12	12	92.70	23.04												
Week 4																
Placebo	12	12	88.92	29.95	0.00	0.55	-1.08	1.08								
E pooled	12	12	92.23	22.83	-0.45	0.55	-1.53	0.63	-0.45	0.77	-1.98	1.08	0.5596			
Week 12																
Placebo	12	12	88.25	30.18	-0.66	0.95	-2.54	1.21								
E pooled	12	10	86.92	17.25	-0.85	0.99	-2.80	1.11	-0.18	1.37	-2.89	2.52	0.8940			
Week 26																
Placebo	12	12	88.24	29.37	-0.67	1.44	-3.52	2.18								
E pooled	12	9	88.61	19.81	0.94	1.57	-2.17	4.04	1.61	2.13	-2.60	5.82	0.4516			
FPG [mg/dl] at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.0593^			
Week 12													0.2257^			
Week 26													0.4774^			

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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
FPG [mg/dl] at baseline																
<126																
Baseline																
Placebo	13	12	99.53	25.58												
E pooled	19	19	104.83	21.88												
Week 4																
Placebo	13	11	98.02	26.07	0.50	0.57	-0.62	1.63								
E pooled	19	17	100.59	20.29	-1.52	0.45	-2.42	-0.62	-2.02	0.73	-3.46	-0.58	0.0062			
Week 12																
Placebo	13	12	99.98	26.47	0.36	0.97	-1.57	2.28								
E pooled	19	18	102.33	22.96	-2.21	0.78	-3.75	-0.67	-2.56	1.25	-5.03	-0.10	0.0418			
Week 26																
Placebo	13	11	100.10	28.27	0.58	1.47	-2.33	3.50								
E pooled	19	18	104.01	24.22	-1.29	1.16	-3.59	1.00	-1.88	1.88	-5.58	1.83	0.3188			
>=126																
Baseline																
Placebo	39	39	99.03	31.35												
E pooled	29	29	93.83	25.77												
Week 4																
Placebo	39	38	98.37	31.03	-0.05	0.31	-0.66	0.57								
E pooled	29	28	92.87	26.21	-0.41	0.36	-1.12	0.30	-0.37	0.47	-1.30	0.57	0.4414			
Week 12																
Placebo	39	39	99.28	30.99	0.28	0.54	-0.79	1.34								
E pooled	29	27	91.86	25.25	-0.46	0.63	-1.71	0.80	-0.73	0.83	-2.38	0.91	0.3800			
Week 26																
Placebo	39	38	98.46	29.67	-0.20	0.81	-1.79	1.39								
E pooled	29	28	91.69	24.87	-0.47	0.95	-2.34	1.40	-0.27	1.24	-2.73	2.19	0.8283			
eGFR (Zappitelli) at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.1227^			
Week 12													0.2918^			
Week 26													0.7668^			

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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
eGFR (Zappitelli) at baseline																
<120																
Baseline																
Placebo	24	23	107.13	26.40												
E pooled	21	21	105.10	28.32												
Week 4																
Placebo	24	22	106.69	26.72	0.26	0.40	-0.54	1.06								
E pooled	21	19	101.41	27.90	-1.35	0.43	-2.20	-0.49	-1.61	0.59	-2.77	-0.44	0.0073			
Week 12																
Placebo	24	23	107.91	26.46	0.79	0.69	-0.57	2.15								
E pooled	21	20	103.25	29.08	-1.62	0.73	-3.06	-0.19	-2.42	1.00	-4.39	-0.44	0.0169			
Week 26																
Placebo	24	21	107.91	26.11	0.62	1.06	-1.48	2.71								
E pooled	21	20	104.90	29.68	-0.80	1.10	-2.98	1.37	-1.42	1.52	-4.43	1.59	0.3534			
120 to <150																
Baseline																
Placebo	23	23	97.82	31.50												
E pooled	19	19	94.72	19.64												
Week 4																
Placebo	23	22	96.31	31.28	-0.42	0.40	-1.22	0.38								
E pooled	19	18	93.47	20.13	-0.41	0.44	-1.29	0.47	0.01	0.60	-1.18	1.20	0.9863			
Week 12																
Placebo	23	23	97.33	31.36	-0.49	0.69	-1.85	0.87								
E pooled	19	19	93.99	20.82	-0.74	0.76	-2.23	0.76	-0.25	1.02	-2.27	1.78	0.8107			
Week 26																
Placebo	23	23	96.64	30.35	-1.13	1.04	-3.19	0.92								
E pooled	19	19	93.67	20.51	-1.10	1.14	-3.36	1.16	0.04	1.55	-3.02	3.09	0.9811			

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Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
eGFR (Zappitelli) at baseline																
>=150																
Baseline																
Placebo	6	6	71.18	16.76												
E pooled	12	12	93.60	22.93												
Week 4																
Placebo	6	6	72.25	16.74	0.96	0.79	-0.59	2.52								
E pooled	12	12	92.88	22.58	-0.64	0.56	-1.74	0.45	-1.61	0.97	-3.52	0.31	0.0999			
Week 12																
Placebo	6	6	72.45	16.04	1.23	1.35	-1.45	3.91								
E pooled	12	9	88.29	17.75	-0.90	1.01	-2.90	1.10	-2.13	1.70	-5.49	1.22	0.2114			
Week 26																
Placebo	6	6	73.00	14.51	1.40	2.05	-2.65	5.45								
E pooled	12	9	88.51	19.16	-0.11	1.57	-3.21	2.99	-1.51	2.59	-6.63	3.61	0.5607			
Backg. Antidiabetic Med. at baseline																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4																
Week 12																
Week 26																

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* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline body weight [kg] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
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Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	95% CI Lower	95% CI Upper	p-value	Hedges' g	95% CI Lower	95% CI Upper
Backg. Antidiabetic Med. at baseline																
Metformin only																
Baseline																
Placebo	28	0														
E pooled	26	0														
Week 4																
Placebo	28	0														
E pooled	26	0														
Week 12																
Placebo	28	0														
E pooled	26	0														
Week 26																
Placebo	28	0														
E pooled	26	0														
Insulin only																
Baseline																
Placebo	2	0														
E pooled	3	0														
Week 4																
Placebo	2	0														
E pooled	3	0														
Week 12																
Placebo	2	0														
E pooled	3	0														
Week 26																
Placebo	2	0														
E pooled	3	0														

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
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Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	95% CI Lower	95% CI Upper	p-value	Hedges' g	95% CI Lower	95% CI Upper
Backg. Antidiabetic Med. at baseline																
Metformin and Insulin																
Baseline																
Placebo	19	0														
E pooled	22	0														
Week 4																
Placebo	19	0														
E pooled	22	0														
Week 12																
Placebo	19	0														
E pooled	22	0														
Week 26																
Placebo	19	0														
E pooled	22	0														
None																
Baseline																
Placebo	4	0														
E pooled	1	0														
Week 4																
Placebo	4	0														
E pooled	1	0														
Week 12																
Placebo	4	0														
E pooled	1	0														
Week 26																
Placebo	4	0														
E pooled	1	0														

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline body weight [kg] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
Time since diagnosis of T2DM																
Test for homogeneity (H0) of subgroup categories per visit																
Week 4													0.9650^			
Week 12													0.8732^			
Week 26													0.4845^			
<1 year																
Baseline																
Placebo	18	18	92.12	34.59												
E pooled	17	17	100.19	31.09												
Week 4																
Placebo	18	17	90.52	34.33	0.06	0.48	-0.88	1.00								
E pooled	17	16	98.59	32.26	-1.00	0.48	-1.96	-0.05	-1.06	0.67	-2.38	0.26	0.1133			
Week 12																
Placebo	18	18	92.67	34.88	0.41	0.79	-1.15	1.98								
E pooled	17	17	99.01	31.60	-1.22	0.81	-2.82	0.38	-1.63	1.13	-3.86	0.60	0.1501			
Week 26																
Placebo	18	18	93.03	34.20	0.67	1.17	-1.65	2.99								
E pooled	17	16	99.71	33.53	-1.18	1.22	-3.59	1.22	-1.85	1.69	-5.19	1.48	0.2735			
1 year - 3 years																
Baseline																
Placebo	24	24	104.28	29.23												
E pooled	21	21	101.49	22.27												
Week 4																
Placebo	24	23	103.31	29.19	-0.15	0.41	-0.96	0.67								
E pooled	21	19	97.73	20.15	-1.07	0.44	-1.93	-0.21	-0.92	0.60	-2.12	0.27	0.1286			
Week 12																
Placebo	24	24	104.31	28.61	0.11	0.68	-1.24	1.46								
E pooled	21	20	100.20	22.69	-0.94	0.73	-2.39	0.50	-1.05	1.00	-3.04	0.93	0.2967			
Week 26																
Placebo	24	23	103.70	27.53	-0.56	1.02	-2.58	1.46								
E pooled	21	20	101.97	22.31	0.07	1.09	-2.08	2.22	0.63	1.50	-2.32	3.59	0.6726			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline body weight [kg] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.

Table 2.2.4 Body weight [kg] change from baseline MMRM results over time up to week 26 overall and by subgroup - mITT (TG1) (OC-AD)

Subgroup / Category / Visit / Treatment	N	n	Value at visit: Mean	Value at visit: SD	Change from baseline: Adj. mean	Change from baseline: SE	Change from baseline: 95% CI Lower	Change from baseline: 95% CI Upper	Comparison vs Placebo*: Adj. mean	Comparison vs Placebo*: SE	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper	Comparison vs Placebo*: p-value	Comparison vs Placebo*: Hedges' g	Comparison vs Placebo*: 95% CI Lower	Comparison vs Placebo*: 95% CI Upper
Time since diagnosis of T2DM																
>3 years																
Baseline																
Placebo	11	10	98.01	18.96												
E pooled	14	14	92.55	17.83												
Week 4																
Placebo	11	10	98.45	19.52	0.44	0.61	-0.77	1.65								
E pooled	14	14	92.11	17.53	-0.35	0.54	-1.42	0.73	-0.79	0.82	-2.41	0.84	0.3402			
Week 12																
Placebo	11	10	98.37	19.81	0.36	1.05	-1.72	2.43								
E pooled	14	11	87.13	9.58	-1.52	0.95	-3.39	0.35	-1.88	1.41	-4.68	0.91	0.1856			
Week 26																
Placebo	11	9	96.34	19.46	-0.20	1.60	-3.35	2.96								
E pooled	14	12	86.64	10.17	-1.85	1.41	-4.63	0.94	-1.65	2.13	-5.85	2.56	0.4400			

N: Number of patients in analysis set, n: Number of patients analysed at visit, ^: Interaction p-value.
* Model includes Visit by Treatment by subgroup interaction, Age (2 cat.), Baseline body weight [kg] by Visit interaction as fixed effect(s). Covariate removed from model if also used as the subgroup. The model for overall analysis includes visit by treatment interaction instead of visit by treatment by subgroup interaction.
The following covariance structure has been used to fit the mixed model: Unstructured
Note: All covariate effects are set equal to their mean values within subgroup for the calculation of adjusted means.
Hedges´g is based on adjusted means and respective pooled standard deviation and will only be presented in case of a significant treatment comparison.

A subgroup (all of the subgroup categories) will not be analysed (n:=0) if in at least one subgroup category N<10.
The linagliptin treatment group was included in analyses but not displayed in this table.