インスリン イコデク（遺伝子組換え）

2.7.3.6 付録
3. サブグループ別のデータ（第 3 相試験）

ノボ ノルディスク ファーマ株式会社

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6.3 Subgroup analyses across phase 3a trials

6.3.1 HbA1c (%) at planned end of treatment by age group - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
18<= to <65 years	333	333	6.92	0.07		
65<= to <75 years	134	134	6.94	0.09		
75<= years	25	25	6.97	0.24		
Daily basal insulin						
18<= to <65 years	332	332	7.12	0.06		
65<= to <75 years	144	144	7.09	0.09		
75<= years	16	16	7.39	0.28		
LSMeans, change from baseline						
Insulin icodec						
18<= to <65 years	333	333	-1.56	0.07		
65<= to <75 years	134	134	-1.53	0.09		
75<= years	25	25	-1.50	0.24		
Daily basal insulin						
18<= to <65 years	332	332	-1.35	0.06		
65<= to <75 years	144	144	-1.38	0.09		
75<= years	16	16	-1.09	0.28		
Treatment contrast						
Insulin icodec - Daily basal insulin						
18<= to <65 years			-0.20		[-0.39 ; -0.02]	
65<= to <75 years			-0.15		[-0.41 ; 0.11]	
75<= years			-0.42		[-1.14 ; 0.31]	
Test for treatment by subgroup interaction						0.7590

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.2 HbA1c (%) at planned end of treatment by age group - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
18<= to <65 years	210	210	6.92	0.05		
65<= to <75 years	74	74	6.99	0.09		
75<= years	10	10	7.09	0.24		
Daily basal insulin						
18<= to <65 years	201	201	7.15	0.06		
65<= to <75 years	84	84	7.16	0.09		
75<= years	9	9	7.17	0.26		
LSMeans, change from baseline						
Insulin icodec						
18<= to <65 years	210	210	-1.59	0.05		
65<= to <75 years	74	74	-1.53	0.09		
75<= years	10	10	-1.42	0.24		
Daily basal insulin						
18<= to <65 years	201	201	-1.37	0.06		
65<= to <75 years	84	84	-1.35	0.09		
75<= years	9	9	-1.35	0.26		
Treatment contrast						
Insulin icodec - Daily basal insulin						
18<= to <65 years			-0.23		[-0.38 ; -0.07]	
65<= to <75 years			-0.17		[-0.42 ; 0.07]	
75<= years			-0.08		[-0.76 ; 0.61]	
Test for treatment by subgroup interaction						0.8588

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.3 HbA1c (%) at planned end of treatment by age group - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
18<= to <65 years	359	359	7.28	0.10		
65<= to <75 years	150	150	7.18	0.13		
75<= years	33	33	7.08	0.26		
Daily basal insulin						
18<= to <65 years	363	363	7.56	0.12		
65<= to <75 years	154	153	7.72	0.20		
75<= years	26	26	7.68	0.29		
LSMeans, change from baseline						
Insulin icodec						
18<= to <65 years	359	359	-1.65	0.10		
65<= to <75 years	150	150	-1.74	0.13		
75<= years	33	33	-1.84	0.26		
Daily basal insulin						
18<= to <65 years	363	363	-1.36	0.12		
65<= to <75 years	154	153	-1.20	0.20		
75<= years	26	26	-1.24	0.29		
Treatment contrast						
Insulin icodec - Daily basal insulin						
18<= to <65 years			-0.29		[-0.58 ; 0.00]	
65<= to <75 years			-0.54		[-0.98 ; -0.10]	
75<= years			-0.60		[-1.36 ; 0.15]	
Test for treatment by subgroup interaction						0.3746

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.4 HbA1c (%) at planned end of treatment by age group - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
18<= to <65 years	145	145	7.15	0.07		
65<= to <75 years	99	99	7.25	0.08		
75<= years	19	19	7.35	0.21		
Daily basal insulin						
18<= to <65 years	149	149	7.36	0.06		
65<= to <75 years	99	99	7.54	0.10		
75<= years	15	15	7.32	0.20		
LSMeans, change from baseline						
Insulin icodec						
18<= to <65 years	145	145	-0.99	0.07		
65<= to <75 years	99	99	-0.88	0.08		
75<= years	19	19	-0.78	0.21		
Daily basal insulin						
18<= to <65 years	149	149	-0.77	0.06		
65<= to <75 years	99	99	-0.60	0.10		
75<= years	15	15	-0.81	0.20		
Treatment contrast						
Insulin icodec - Daily basal insulin						
18<= to <65 years			-0.21		[-0.40 ; -0.03]	
65<= to <75 years			-0.29		[-0.54 ; -0.04]	
75<= years			0.03		[-0.54 ; 0.59]	
Test for treatment by subgroup interaction						0.5921

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.5 HbA1c (%) at planned end of treatment by age group - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
18<= to <65 years	189	189	7.12	0.06		
65<= to <75 years	92	92	7.16	0.08		
75<= years	10	10	7.45	0.26		
Daily basal insulin						
18<= to <65 years	184	184	7.18	0.06		
65<= to <75 years	96	96	7.04	0.08		
75<= years	11	11	6.80	0.23		
LSMeans, change from baseline						
Insulin icodec						
18<= to <65 years	189	189	-1.18	0.06		
65<= to <75 years	92	92	-1.14	0.08		
75<= years	10	10	-0.85	0.26		
Daily basal insulin						
18<= to <65 years	184	184	-1.12	0.06		
65<= to <75 years	96	96	-1.26	0.08		
75<= years	11	11	-1.50	0.23		
Treatment contrast						
Insulin icodec - Daily basal insulin						
18<= to <65 years			-0.07		[-0.23 ; 0.10]	
65<= to <75 years			0.12		[-0.11 ; 0.35]	
75<= years			0.65		[-0.03 ; 1.32]	
Test for treatment by subgroup interaction						0.0755

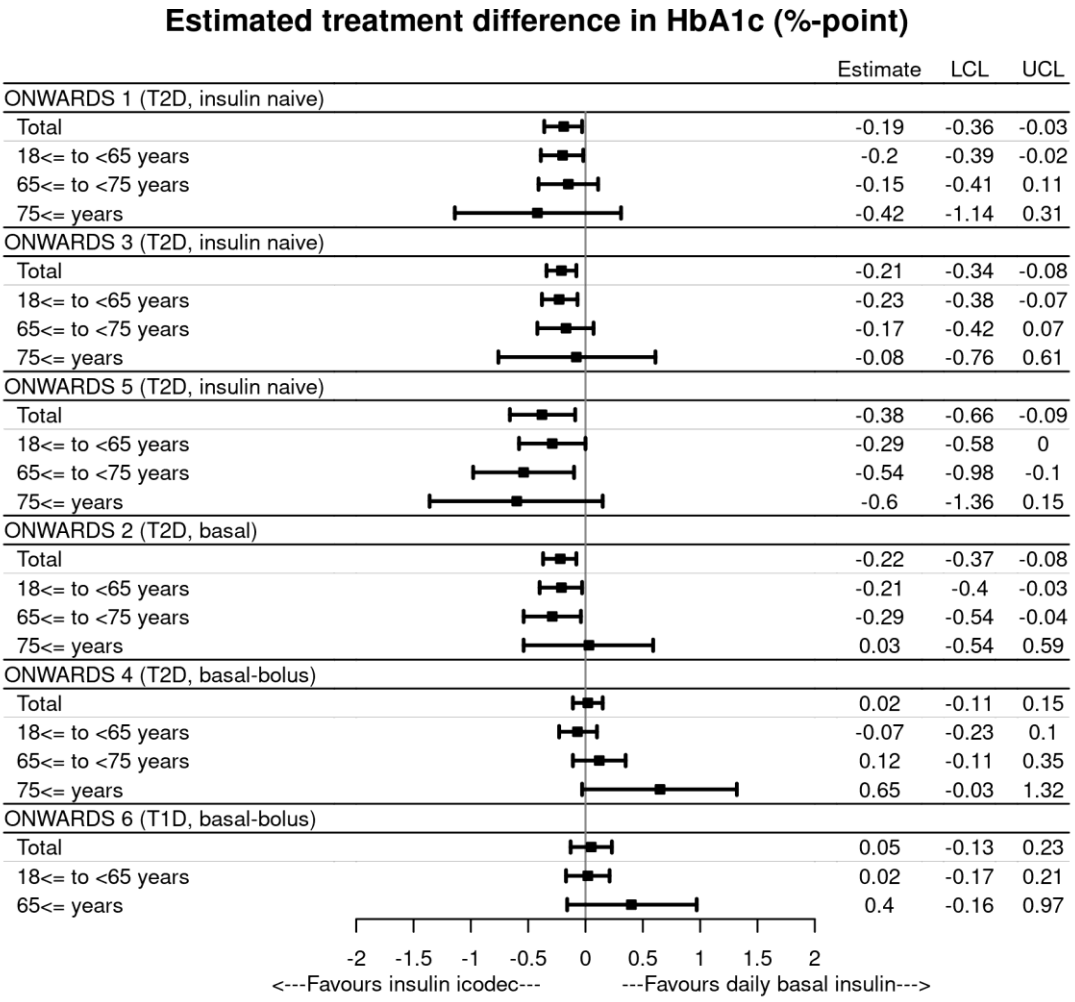
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.6 HbA1c (%) at planned end of treatment by age group - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
18<= to <65 years	267	267	7.12	0.07		
65<= years	23	23	7.52	0.22		
Daily basal insulin						
18<= to <65 years	271	271	7.10	0.07		
65<= years	21	21	7.11	0.18		
LSMeans, change from baseline						
Insulin icodec						
18<= to <65 years	267	267	-0.50	0.07		
65<= years	23	23	-0.10	0.22		
Daily basal insulin						
18<= to <65 years	271	271	-0.51	0.07		
65<= years	21	21	-0.50	0.18		
Treatment contrast						
Insulin icodec - Daily basal insulin						
18<= to <65 years			0.02		[-0.17 ; 0.21]	
65<= years			0.40		[-0.16 ; 0.97]	
Test for treatment by subgroup interaction						0.1954

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.7 HbA1c (%) at planned end of treatment by age group - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

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6.3.8 HbA1c (%) at planned end of treatment by sex - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Female	197	197	7.01	0.08		
Male	295	295	6.87	0.07		
Daily basal insulin						
Female	229	229	7.16	0.07		
Male	263	263	7.09	0.07		
LSMeans, change from baseline						
Insulin icodec						
Female	197	197	-1.47	0.08		
Male	295	295	-1.60	0.07		
Daily basal insulin						
Female	229	229	-1.31	0.07		
Male	263	263	-1.39	0.07		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Female			-0.15		[-0.37 ; 0.07]	
Male			-0.21		[-0.41 ; -0.02]	
Test for treatment by subgroup interaction						0.6328

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.9 HbA1c (%) at planned end of treatment by sex - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Female	109	109	7.00	0.08		
Male	185	185	6.92	0.06		
Daily basal insulin						
Female	110	110	7.16	0.08		
Male	184	184	7.15	0.06		
LSMeans, change from baseline						
Insulin icodec						
Female	109	109	-1.52	0.08		
Male	185	185	-1.60	0.06		
Daily basal insulin						
Female	110	110	-1.36	0.08		
Male	184	184	-1.36	0.06		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Female			-0.16		[-0.37 ; 0.05]	
Male			-0.24		[-0.40 ; -0.07]	
Test for treatment by subgroup interaction						0.5782

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.10 HbA1c (%) at planned end of treatment by sex - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Female	233	233	7.24	0.11		
Male	309	309	7.24	0.10		
Daily basal insulin						
Female	230	229	7.67	0.14		
Male	313	313	7.57	0.14		
LSMeans, change from baseline						
Insulin icodec						
Female	233	233	-1.68	0.11		
Male	309	309	-1.69	0.10		
Daily basal insulin						
Female	230	229	-1.25	0.14		
Male	313	313	-1.35	0.14		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Female			-0.43		[-0.77 ; -0.10]	
Male			-0.33		[-0.66 ; -0.01]	
Test for treatment by subgroup interaction						0.5678

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.11 HbA1c (%) at planned end of treatment by sex - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Female	101	101	7.24	0.08		
Male	162	162	7.17	0.07		
Daily basal insulin						
Female	123	123	7.47	0.08		
Male	140	140	7.38	0.07		
LSMeans, change from baseline						
Insulin icodec						
Female	101	101	-0.89	0.08		
Male	162	162	-0.96	0.07		
Daily basal insulin						
Female	123	123	-0.66	0.08		
Male	140	140	-0.75	0.07		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Female			-0.23		[-0.45 ; -0.01]	
Male			-0.21		[-0.39 ; -0.02]	
Test for treatment by subgroup interaction						0.8661

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.12 HbA1c (%) at planned end of treatment by sex - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Female	137	137	7.09	0.07		
Male	154	154	7.19	0.06		
Daily basal insulin						
Female	141	141	7.15	0.07		
Male	150	150	7.10	0.07		
LSMeans, change from baseline						
Insulin icodec						
Female	137	137	-1.21	0.07		
Male	154	154	-1.11	0.06		
Daily basal insulin						
Female	141	141	-1.16	0.07		
Male	150	150	-1.20	0.07		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Female			-0.06		[-0.24 ; 0.13]	
Male			0.09		[-0.09 ; 0.27]	
Test for treatment by subgroup interaction						0.2707

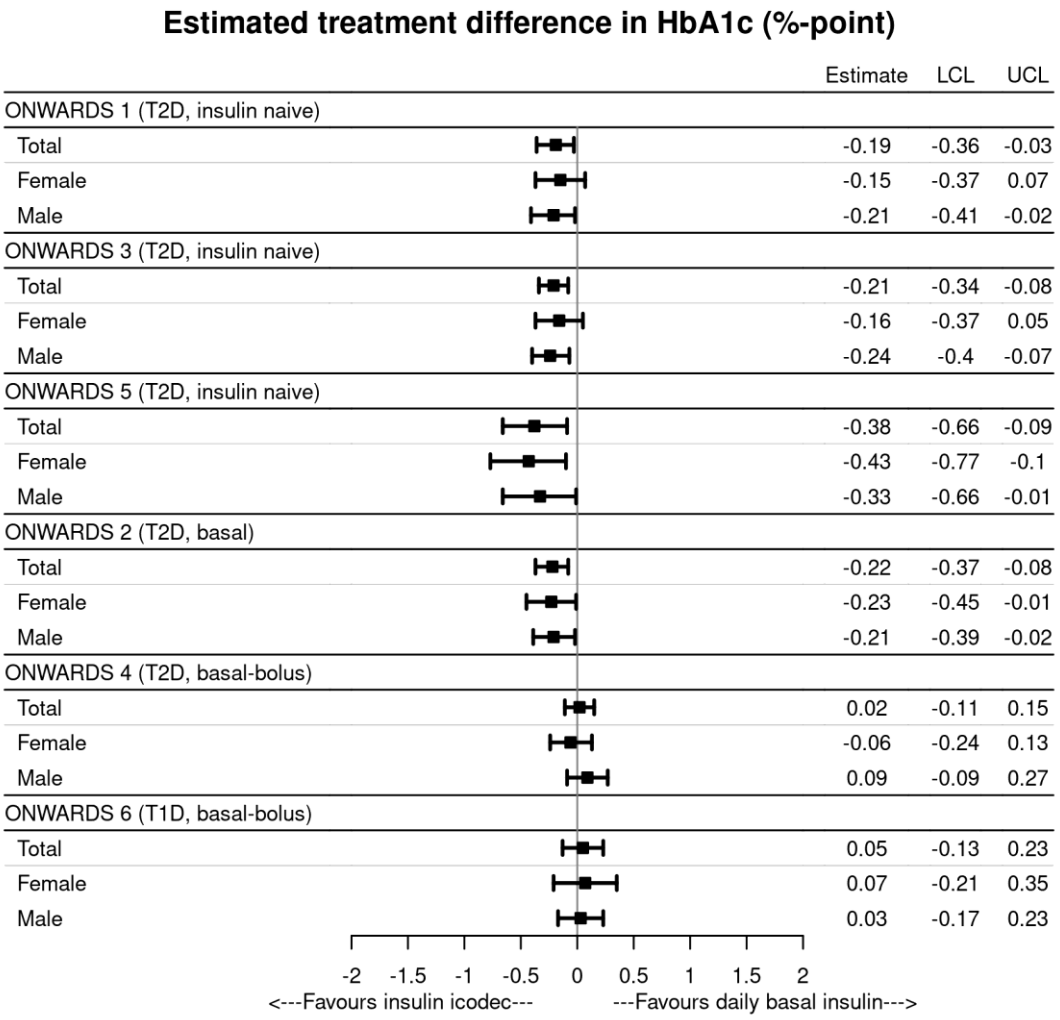
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.13 HbA1c (%) at planned end of treatment by sex - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Female	125	125	7.22	0.11		
Male	165	165	7.09	0.07		
Daily basal insulin						
Female	120	120	7.15	0.09		
Male	172	172	7.07	0.07		
LSMeans, change from baseline						
Insulin icodec						
Female	125	125	-0.39	0.11		
Male	165	165	-0.52	0.07		
Daily basal insulin						
Female	120	120	-0.46	0.09		
Male	172	172	-0.55	0.07		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Female			0.07		[-0.21 ; 0.35]	
Male			0.03		[-0.17 ; 0.23]	
Test for treatment by subgroup interaction						0.7914

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.14 HbA1c (%) at planned end of treatment by sex - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

6.3.15 HbA1c (%) at planned end of treatment by BMI group - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<25 kg/m^2	87	87	7.05	0.12		
25<= to <30 kg/m^2	164	164	6.90	0.09		
30<= to <35 kg/m^2	162	162	6.84	0.09		
>=35 kg/m^2	79	79	7.02	0.11		
Daily basal insulin						
<25 kg/m^2	80	80	7.31	0.12		
25<= to <30 kg/m^2	171	171	7.17	0.08		
30<= to <35 kg/m^2	146	146	7.06	0.09		
>=35 kg/m^2	95	95	6.98	0.11		
LSMeans, change from baseline						
Insulin icodec						
<25 kg/m^2	87	87	-1.42	0.12		
25<= to <30 kg/m^2	164	164	-1.57	0.09		
30<= to <35 kg/m^2	162	162	-1.64	0.09		
>=35 kg/m^2	79	79	-1.45	0.11		
Daily basal insulin						
<25 kg/m^2	80	80	-1.16	0.12		
25<= to <30 kg/m^2	171	171	-1.31	0.08		
30<= to <35 kg/m^2	146	146	-1.42	0.09		
>=35 kg/m^2	95	95	-1.49	0.11		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<25 kg/m^2			-0.26		[-0.59 ; 0.08]	
25<= to <30 kg/m^2			-0.26		[-0.49 ; -0.04]	
30<= to <35 kg/m^2			-0.22		[-0.48 ; 0.03]	
>=35 kg/m^2			0.04		[-0.27 ; 0.34]	
Test for treatment by subgroup interaction						0.4001

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, BMI: Body mass index, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.16 HbA1c (%) at planned end of treatment by BMI group - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<25 kg/m^2	52	52	6.86	0.11		
25<= to <30 kg/m^2	109	109	6.97	0.08		
30<= to <35 kg/m^2	76	76	6.97	0.09		
>=35 kg/m^2	57	57	6.96	0.10		
Daily basal insulin						
<25 kg/m^2	58	58	7.13	0.11		
25<= to <30 kg/m^2	121	121	7.12	0.07		
30<= to <35 kg/m^2	70	70	7.25	0.10		
>=35 kg/m^2	45	45	7.14	0.11		
LSMeans, change from baseline						
Insulin icodec						
<25 kg/m^2	52	52	-1.66	0.11		
25<= to <30 kg/m^2	109	109	-1.55	0.08		
30<= to <35 kg/m^2	76	76	-1.55	0.09		
>=35 kg/m^2	57	57	-1.56	0.10		
Daily basal insulin						
<25 kg/m^2	58	58	-1.39	0.11		
25<= to <30 kg/m^2	121	121	-1.39	0.07		
30<= to <35 kg/m^2	70	70	-1.27	0.10		
>=35 kg/m^2	45	45	-1.38	0.11		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<25 kg/m^2			-0.27		[-0.57 ; 0.03]	
25<= to <30 kg/m^2			-0.16		[-0.36 ; 0.05]	
30<= to <35 kg/m^2			-0.28		[-0.54 ; -0.02]	
>=35 kg/m^2			-0.18		[-0.48 ; 0.12]	
Test for treatment by subgroup interaction						0.8510

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, BMI: Body mass index, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.17 HbA1c (%) at planned end of treatment by BMI group - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<25 kg/m^2	54	54	7.43	0.21		
25<= to <30 kg/m^2	159	159	7.14	0.12		
30<= to <35 kg/m^2	154	154	7.18	0.14		
>=35 kg/m^2	175	175	7.32	0.12		
Daily basal insulin						
<25 kg/m^2	51	51	7.69	0.22		
25<= to <30 kg/m^2	154	154	7.54	0.14		
30<= to <35 kg/m^2	157	156	7.66	0.15		
>=35 kg/m^2	180	180	7.62	0.17		
LSMeans, change from baseline						
Insulin icodec						
<25 kg/m^2	54	54	-1.49	0.21		
25<= to <30 kg/m^2	159	159	-1.78	0.12		
30<= to <35 kg/m^2	154	154	-1.75	0.14		
>=35 kg/m^2	175	175	-1.61	0.12		
Daily basal insulin						
<25 kg/m^2	51	51	-1.24	0.22		
25<= to <30 kg/m^2	154	154	-1.38	0.14		
30<= to <35 kg/m^2	157	156	-1.27	0.15		
>=35 kg/m^2	180	180	-1.31	0.17		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<25 kg/m^2			-0.25		[-0.83 ; 0.33]	
25<= to <30 kg/m^2			-0.40		[-0.77 ; -0.03]	
30<= to <35 kg/m^2			-0.48		[-0.86 ; -0.10]	
>=35 kg/m^2			-0.30		[-0.71 ; 0.11]	
Test for treatment by subgroup interaction						0.8324

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, BMI: Body mass index, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.18 HbA1c (%) at planned end of treatment by BMI group - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<25 kg/m^2	54	54	7.29	0.11		
25<= to <30 kg/m^2	93	93	7.19	0.09		
30<= to <35 kg/m^2	69	69	7.19	0.10		
>=35 kg/m^2	47	47	7.12	0.11		
Daily basal insulin						
<25 kg/m^2	56	56	7.39	0.13		
25<= to <30 kg/m^2	104	104	7.43	0.08		
30<= to <35 kg/m^2	63	63	7.37	0.10		
>=35 kg/m^2	40	40	7.54	0.13		
LSMeans, change from baseline						
Insulin icodec						
<25 kg/m^2	54	54	-0.84	0.11		
25<= to <30 kg/m^2	93	93	-0.94	0.09		
30<= to <35 kg/m^2	69	69	-0.94	0.10		
>=35 kg/m^2	47	47	-1.01	0.11		
Daily basal insulin						
<25 kg/m^2	56	56	-0.75	0.13		
25<= to <30 kg/m^2	104	104	-0.70	0.08		
30<= to <35 kg/m^2	63	63	-0.76	0.10		
>=35 kg/m^2	40	40	-0.59	0.13		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<25 kg/m^2			-0.09		[-0.40 ; 0.22]	
25<= to <30 kg/m^2			-0.24		[-0.48 ; -0.01]	
30<= to <35 kg/m^2			-0.19		[-0.46 ; 0.08]	
>=35 kg/m^2			-0.42		[-0.75 ; -0.09]	
Test for treatment by subgroup interaction						0.5469

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, BMI: Body mass index, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.19 HbA1c (%) at planned end of treatment by BMI group - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<25 kg/m^2	42	42	7.36	0.13		
25<= to <30 kg/m^2	95	95	7.15	0.08		
30<= to <35 kg/m^2	93	93	7.04	0.08		
>=35 kg/m^2	61	61	7.13	0.11		
Daily basal insulin						
<25 kg/m^2	49	49	7.16	0.12		
25<= to <30 kg/m^2	96	96	7.23	0.08		
30<= to <35 kg/m^2	99	99	7.05	0.08		
>=35 kg/m^2	47	47	7.02	0.12		
LSMeans, change from baseline						
Insulin icodec						
<25 kg/m^2	42	42	-0.94	0.13		
25<= to <30 kg/m^2	95	95	-1.15	0.08		
30<= to <35 kg/m^2	93	93	-1.26	0.08		
>=35 kg/m^2	61	61	-1.17	0.11		
Daily basal insulin						
<25 kg/m^2	49	49	-1.14	0.12		
25<= to <30 kg/m^2	96	96	-1.07	0.08		
30<= to <35 kg/m^2	99	99	-1.25	0.08		
>=35 kg/m^2	47	47	-1.28	0.12		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<25 kg/m^2			0.20		[-0.12 ; 0.53]	
25<= to <30 kg/m^2			-0.07		[-0.30 ; 0.15]	
30<= to <35 kg/m^2			-0.01		[-0.24 ; 0.22]	
>=35 kg/m^2			0.11		[-0.21 ; 0.42]	
Test for treatment by subgroup interaction						0.5240

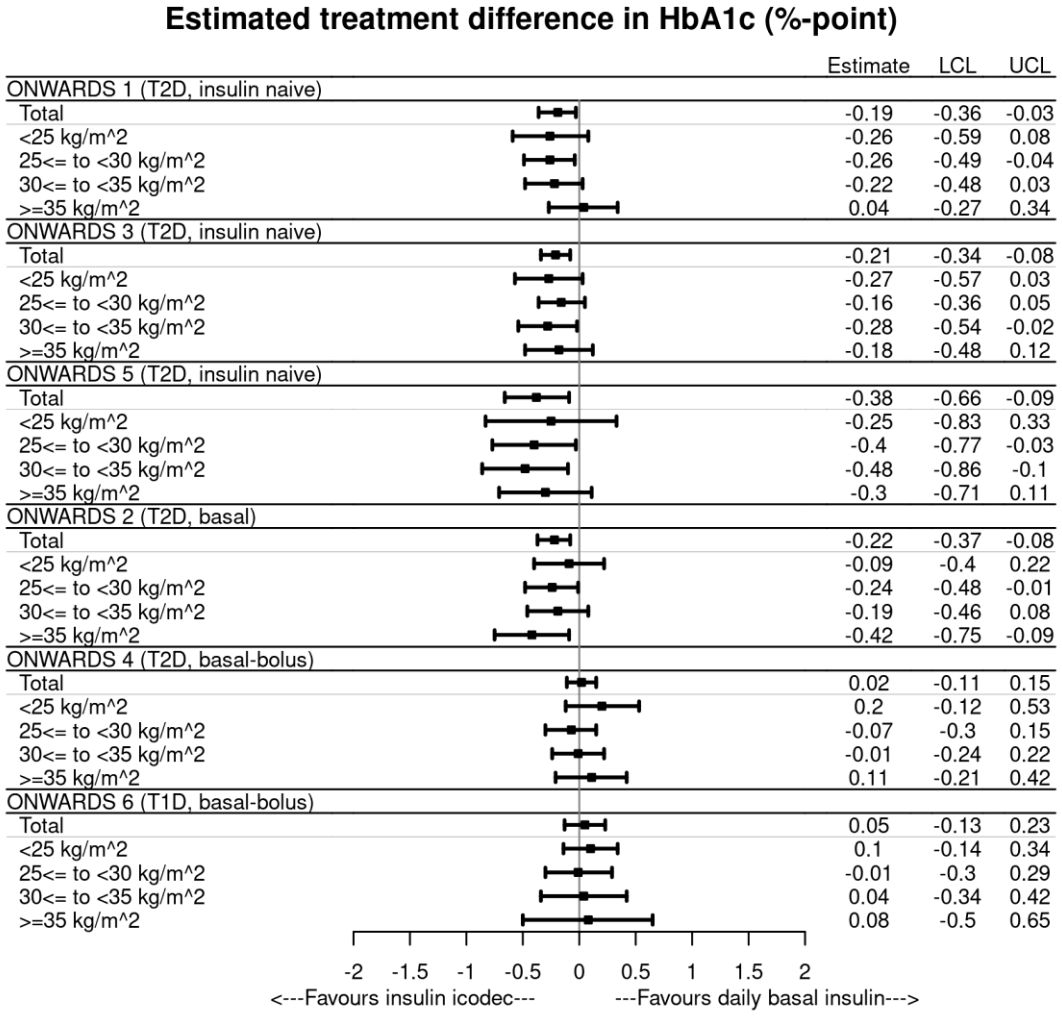
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, BMI: Body mass index, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.20 HbA1c (%) at planned end of treatment by BMI group - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<25 kg/m^2	105	105	7.20	0.10		
25<= to <30 kg/m^2	118	118	7.12	0.11		
30<= to <35 kg/m^2	46	46	7.08	0.12		
>=35 kg/m^2	21	21	7.16	0.20		
Daily basal insulin						
<25 kg/m^2	135	135	7.10	0.08		
25<= to <30 kg/m^2	102	102	7.13	0.11		
30<= to <35 kg/m^2	41	41	7.04	0.15		
>=35 kg/m^2	14	14	7.08	0.22		
LSMeans, change from baseline						
Insulin icodec						
<25 kg/m^2	105	105	-0.41	0.10		
25<= to <30 kg/m^2	118	118	-0.49	0.11		
30<= to <35 kg/m^2	46	46	-0.53	0.12		
>=35 kg/m^2	21	21	-0.46	0.20		
Daily basal insulin						
<25 kg/m^2	135	135	-0.51	0.08		
25<= to <30 kg/m^2	102	102	-0.48	0.11		
30<= to <35 kg/m^2	41	41	-0.57	0.15		
>=35 kg/m^2	14	14	-0.53	0.22		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<25 kg/m^2			0.10		[-0.14 ; 0.34]	
25<= to <30 kg/m^2			-0.01		[-0.30 ; 0.29]	
30<= to <35 kg/m^2			0.04		[-0.34 ; 0.42]	
>=35 kg/m^2			0.08		[-0.50 ; 0.65]	
Test for treatment by subgroup interaction						0.9313

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, BMI: Body mass index, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.21 HbA1c (%) at planned end of treatment by BMI group - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, BMI: Body mass index, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

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6.3.22 HbA1c (%) at planned end of treatment by race - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
White	333	333	6.87	0.08		
Black or African American	10	10	6.92	0.41		
Asian	129	129	7.08	0.16		
Other	20	20	6.80	0.55		
Daily basal insulin						
White	317	317	7.09	0.08		
Black or African American	17	17	7.13	0.30		
Asian	145	145	7.20	0.15		
Other	13	13	7.04	0.45		
LSMeans, change from baseline						
Insulin icodec						
White	333	333	-1.60	0.08		
Black or African American	10	10	-1.55	0.41		
Asian	129	129	-1.39	0.16		
Other	20	20	-1.67	0.55		
Daily basal insulin						
White	317	317	-1.38	0.08		
Black or African American	17	17	-1.34	0.30		
Asian	145	145	-1.28	0.15		
Other	13	13	-1.44	0.45		
Treatment contrast						
Insulin icodec - Daily basal insulin						
White			-0.22		[-0.39 ; -0.05]	
Black or African American			-0.21		[-1.26 ; 0.84]	
Asian			-0.12		[-0.35 ; 0.12]	
Other			-0.23		[-1.29 ; 0.83]	
Test for treatment by subgroup interaction						0.9484

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Other race includes American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.23 HbA1c (%) at planned end of treatment by race - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
White	179	179	6.89	0.08		
Black or African American	9	9	6.83	0.26		
Asian	80	80	7.12	0.16		
Other	11	11	6.44	0.24		
Daily basal insulin						
White	175	175	7.02	0.08		
Black or African American	6	6	7.61	0.34		
Asian	85	85	7.41	0.15		
Other	12	12	7.21	0.23		
LSMeans, change from baseline						
Insulin icodec						
White	179	179	-1.62	0.08		
Black or African American	9	9	-1.68	0.26		
Asian	80	80	-1.39	0.16		
Other	11	11	-2.07	0.24		
Daily basal insulin						
White	175	175	-1.49	0.08		
Black or African American	6	6	-0.90	0.34		
Asian	85	85	-1.11	0.15		
Other	12	12	-1.30	0.23		
Treatment contrast						
Insulin icodec - Daily basal insulin						
White			-0.13		[-0.29 ; 0.03]	
Black or African American			-0.78		[-1.61 ; 0.06]	
Asian			-0.29		[-0.53 ; -0.04]	
Other			-0.77		[-1.38 ; -0.15]	
Test for treatment by subgroup interaction						0.1047

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Other race includes American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.24 HbA1c (%) at planned end of treatment by race - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
White	478	478	7.24	0.09		
Black or African American	24	24	7.12	0.37		
Asian	28	28	7.42	0.32		
Other	11	11	6.96	0.39		
Daily basal insulin						
White	493	492	7.59	0.12		
Black or African American	28	28	7.75	0.38		
Asian	19	19	7.99	0.49		
Other	3	3	7.59	0.74		
LSMeans, change from baseline						
Insulin icodec						
White	478	478	-1.68	0.09		
Black or African American	24	24	-1.80	0.37		
Asian	28	28	-1.50	0.32		
Other	11	11	-1.96	0.39		
Daily basal insulin						
White	493	492	-1.33	0.12		
Black or African American	28	28	-1.17	0.38		
Asian	19	19	-0.93	0.49		
Other	3	3	-1.33	0.74		
Treatment contrast						
Insulin icodec - Daily basal insulin						
White			-0.35		[-0.61 ; -0.09]	
Black or African American			-0.63		[-1.67 ; 0.41]	
Asian			-0.57		[-1.78 ; 0.64]	
Other			-0.63		[-2.26 ; 1.01]	
Test for treatment by subgroup interaction						0.9027

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Other race includes American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.25 HbA1c (%) at planned end of treatment by race - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
White	161	161	7.19	0.09		
Black or African American	11	11	7.25	0.26		
Asian	86	86	7.23	0.14		
Other	5	5	6.84	0.35		
Daily basal insulin						
White	137	137	7.38	0.10		
Black or African American	12	12	7.48	0.24		
Asian	110	110	7.47	0.13		
Other	4	4	7.39	0.39		
LSMeans, change from baseline						
Insulin icodec						
White	161	161	-0.94	0.09		
Black or African American	11	11	-0.89	0.26		
Asian	86	86	-0.91	0.14		
Other	5	5	-1.29	0.35		
Daily basal insulin						
White	137	137	-0.75	0.10		
Black or African American	12	12	-0.66	0.24		
Asian	110	110	-0.66	0.13		
Other	4	4	-0.74	0.39		
Treatment contrast						
Insulin icodec - Daily basal insulin						
White			-0.19		[-0.39 ; -0.00]	
Black or African American			-0.23		[-0.89 ; 0.43]	
Asian			-0.25		[-0.48 ; -0.02]	
Other			-0.55		[-1.56 ; 0.45]	
Test for treatment by subgroup interaction						0.9100

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Other race includes American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.26 HbA1c (%) at planned end of treatment by race - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
White	183	183	6.99	0.10		
Black or African American	13	13	6.94	0.23		
Asian	95	95	7.47	0.19		
Daily basal insulin						
White	187	187	6.95	0.10		
Black or African American	8	8	7.72	0.33		
Asian	93	93	7.41	0.20		
LSMeans, change from baseline						
Insulin icodec						
White	183	183	-1.32	0.10		
Black or African American	13	13	-1.36	0.23		
Asian	95	95	-0.83	0.19		
Daily basal insulin						
White	187	187	-1.35	0.10		
Black or African American	8	8	-0.58	0.33		
Asian	93	93	-0.89	0.20		
Treatment contrast						
Insulin icodec - Daily basal insulin						
White			0.03		[-0.13 ; 0.20]	
Black or African American			-0.78		[-1.53 ; -0.02]	
Asian			0.07		[-0.16 ; 0.29]	
Test for treatment by subgroup interaction						0.0893

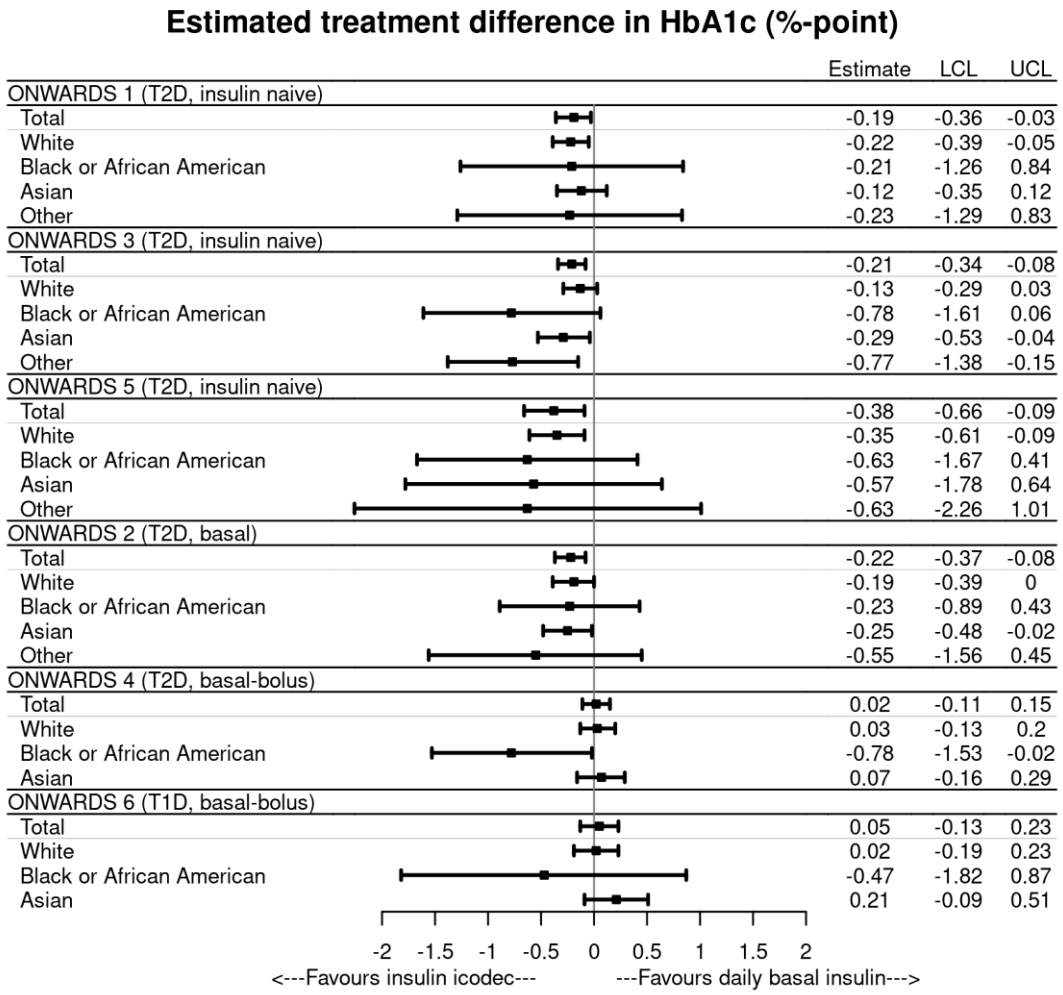
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.27 HbA1c (%) at planned end of treatment by race - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
White	230	230	7.16	0.10		
Black or African American	9	9	6.83	0.38		
Asian	51	51	7.15	0.26		
Daily basal insulin						
White	218	218	7.14	0.10		
Black or African American	2	2	7.30	0.57		
Asian	72	72	6.94	0.25		
LSMeans, change from baseline						
Insulin icodec						
White	230	230	-0.45	0.10		
Black or African American	9	9	-0.79	0.38		
Asian	51	51	-0.46	0.26		
Daily basal insulin						
White	218	218	-0.47	0.10		
Black or African American	2	2	-0.31	0.57		
Asian	72	72	-0.67	0.25		
Treatment contrast						
Insulin icodec - Daily basal insulin						
White			0.02		[-0.19 ; 0.23]	
Black or African American			-0.47		[-1.82 ; 0.87]	
Asian			0.21		[-0.09 ; 0.51]	
Test for treatment by subgroup interaction						0.4230

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.28 HbA1c (%) at planned end of treatment by race - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Other race includes American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander. Missing data are imputed using multiple imputation.

6.3.29 HbA1c (%) at planned end of treatment by ethnicity - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Not Hispanic or Latino	439	439	6.90	0.06		
Hispanic or Latino	53	53	7.14	0.16		
Daily basal insulin						
Not Hispanic or Latino	439	439	7.08	0.06		
Hispanic or Latino	53	53	7.46	0.17		
LSMeans, change from baseline						
Insulin icodec						
Not Hispanic or Latino	439	439	-1.57	0.06		
Hispanic or Latino	53	53	-1.34	0.16		
Daily basal insulin						
Not Hispanic or Latino	439	439	-1.39	0.06		
Hispanic or Latino	53	53	-1.02	0.17		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Not Hispanic or Latino			-0.18		[-0.35 ; -0.02]	
Hispanic or Latino			-0.32		[-0.74 ; 0.10]	
Test for treatment by subgroup interaction						0.5139

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.30 HbA1c (%) at planned end of treatment by ethnicity - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Not Hispanic or Latino	203	203	6.92	0.07		
Hispanic or Latino	76	76	6.99	0.13		
Daily basal insulin						
Not Hispanic or Latino	190	190	7.08	0.07		
Hispanic or Latino	88	88	7.34	0.12		
LSMeans, change from baseline						
Insulin icodec						
Not Hispanic or Latino	203	203	-1.59	0.07		
Hispanic or Latino	76	76	-1.52	0.13		
Daily basal insulin						
Not Hispanic or Latino	190	190	-1.43	0.07		
Hispanic or Latino	88	88	-1.18	0.12		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Not Hispanic or Latino			-0.16		[-0.32 ; -0.00]	
Hispanic or Latino			-0.34		[-0.58 ; -0.10]	
Test for treatment by subgroup interaction						0.2133

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.31 HbA1c (%) at planned end of treatment by ethnicity - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Not Hispanic or Latino	490	490	7.22	0.09		
Hispanic or Latino	51	51	7.45	0.24		
Daily basal insulin						
Not Hispanic or Latino	499	498	7.60	0.13		
Hispanic or Latino	44	44	7.79	0.21		
LSMeans, change from baseline						
Insulin icodec						
Not Hispanic or Latino	490	490	-1.71	0.09		
Hispanic or Latino	51	51	-1.48	0.24		
Daily basal insulin						
Not Hispanic or Latino	499	498	-1.32	0.13		
Hispanic or Latino	44	44	-1.13	0.21		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Not Hispanic or Latino			-0.38		[-0.67 ; -0.09]	
Hispanic or Latino			-0.34		[-0.96 ; 0.28]	
Test for treatment by subgroup interaction						0.9038

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.32 HbA1c (%) at planned end of treatment by ethnicity - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Not Hispanic or Latino	247	247	7.19	0.05		
Hispanic or Latino	16	16	7.40	0.21		
Daily basal insulin						
Not Hispanic or Latino	247	247	7.41	0.06		
Hispanic or Latino	16	16	7.59	0.20		
LSMeans, change from baseline						
Insulin icodec						
Not Hispanic or Latino	247	247	-0.94	0.05		
Hispanic or Latino	16	16	-0.73	0.21		
Daily basal insulin						
Not Hispanic or Latino	247	247	-0.72	0.06		
Hispanic or Latino	16	16	-0.54	0.20		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Not Hispanic or Latino			-0.22		[-0.37 ; -0.07]	
Hispanic or Latino			-0.19		[-0.73 ; 0.35]	
Test for treatment by subgroup interaction						0.9132

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.33 HbA1c (%) at planned end of treatment by ethnicity - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Not Hispanic or Latino	239	239	7.19	0.05		
Hispanic or Latino	52	52	6.94	0.14		
Daily basal insulin						
Not Hispanic or Latino	237	237	7.11	0.06		
Hispanic or Latino	53	53	7.18	0.14		
LSMeans, change from baseline						
Insulin icodec						
Not Hispanic or Latino	239	239	-1.11	0.05		
Hispanic or Latino	52	52	-1.36	0.14		
Daily basal insulin						
Not Hispanic or Latino	237	237	-1.19	0.06		
Hispanic or Latino	53	53	-1.12	0.14		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Not Hispanic or Latino			0.08		[-0.07 ; 0.22]	
Hispanic or Latino			-0.24		[-0.55 ; 0.07]	
Test for treatment by subgroup interaction						0.0721

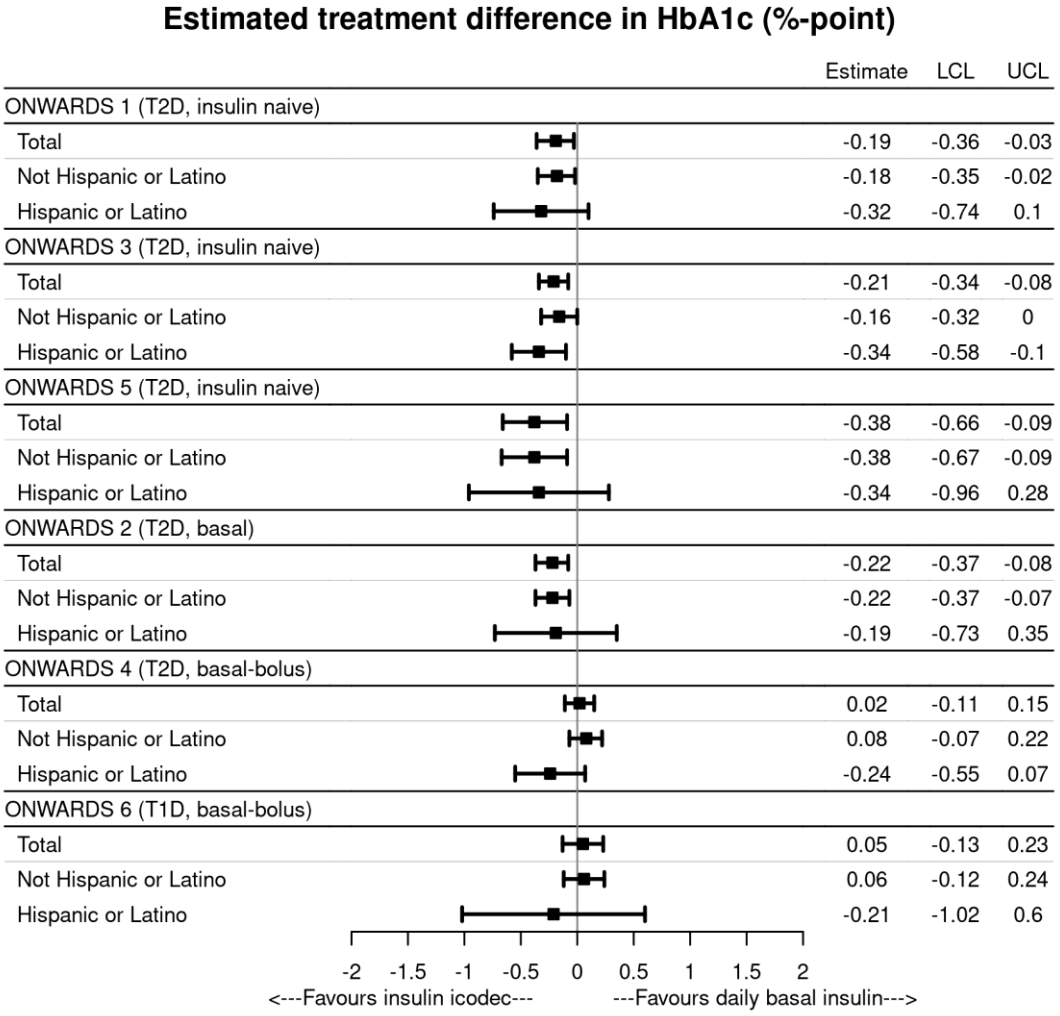
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.34 HbA1c (%) at planned end of treatment by ethnicity - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Not Hispanic or Latino	280	280	7.16	0.07		
Hispanic or Latino	10	10	6.73	0.26		
Daily basal insulin						
Not Hispanic or Latino	282	282	7.11	0.06		
Hispanic or Latino	10	10	6.94	0.33		
LSMeans, change from baseline						
Insulin icodec						
Not Hispanic or Latino	280	280	-0.45	0.07		
Hispanic or Latino	10	10	-0.88	0.26		
Daily basal insulin						
Not Hispanic or Latino	282	282	-0.51	0.06		
Hispanic or Latino	10	10	-0.67	0.33		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Not Hispanic or Latino			0.06		[-0.12 ; 0.24]	
Hispanic or Latino			-0.21		[-1.02 ; 0.60]	
Test for treatment by subgroup interaction						0.5181

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.35 HbA1c (%) at planned end of treatment by ethnicity - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

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6.3.36 HbA1c (%) at planned end of treatment by region- change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Europe	245	245	6.88	0.08		
North America	108	108	6.95	0.11		
Asia	120	120	7.00	0.09		
South America	19	19	6.90	0.26		
Daily basal insulin						
Europe	226	226	7.14	0.07		
North America	112	112	7.17	0.11		
Asia	132	132	7.04	0.09		
South America	22	22	7.21	0.24		
LSMeans, change from baseline						
Insulin icodec						
Europe	245	245	-1.59	0.08		
North America	108	108	-1.52	0.11		
Asia	120	120	-1.47	0.09		
South America	19	19	-1.57	0.26		
Daily basal insulin						
Europe	226	226	-1.34	0.07		
North America	112	112	-1.31	0.11		
Asia	132	132	-1.43	0.09		
South America	22	22	-1.27	0.24		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Europe			-0.26		[-0.47 ; -0.05]	
North America			-0.22		[-0.52 ; 0.09]	
Asia			-0.04		[-0.29 ; 0.21]	
South America			-0.30		[-0.97 ; 0.36]	
Test for treatment by subgroup interaction						0.5740

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.37 HbA1c (%) at planned end of treatment by region - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Europe	71	71	6.95	0.09		
North America	75	75	7.09	0.09		
Asia	72	72	7.00	0.09		
South America	76	76	6.75	0.09		
Daily basal insulin						
Europe	71	71	7.04	0.09		
North America	74	74	7.29	0.10		
Asia	73	73	7.31	0.09		
South America	76	76	6.99	0.09		
LSMeans, change from baseline						
Insulin icodec						
Europe	71	71	-1.56	0.09		
North America	75	75	-1.43	0.09		
Asia	72	72	-1.52	0.09		
South America	76	76	-1.77	0.09		
Daily basal insulin						
Europe	71	71	-1.48	0.09		
North America	74	74	-1.23	0.10		
Asia	73	73	-1.21	0.09		
South America	76	76	-1.53	0.09		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Europe			-0.08		[-0.34 ; 0.17]	
North America			-0.20		[-0.47 ; 0.06]	
Asia			-0.31		[-0.56 ; -0.05]	
South America			-0.24		[-0.49 ; 0.00]	
Test for treatment by subgroup interaction						0.6658

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.38 HbA1c (%) at planned end of treatment by region - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Europe	286	286	7.13	0.09		
North America	256	256	7.35	0.13		
Daily basal insulin						
Europe	271	271	7.40	0.10		
North America	272	271	7.84	0.18		
LSMeans, change from baseline						
Insulin icodec						
Europe	286	286	-1.79	0.09		
North America	256	256	-1.58	0.13		
Daily basal insulin						
Europe	271	271	-1.53	0.10		
North America	272	271	-1.08	0.18		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Europe			-0.26		[-0.52 ; -0.01]	
North America			-0.49		[-0.92 ; -0.07]	
Test for treatment by subgroup interaction						0.2712

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.39 HbA1c (%) at planned end of treatment by region - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Europe	86	86	7.20	0.09		
North America	78	78	7.11	0.09		
Asia	74	74	7.34	0.09		
Africa	25	25	6.99	0.16		
Daily basal insulin						
Europe	81	81	7.30	0.10		
North America	61	61	7.46	0.11		
Asia	96	96	7.54	0.09		
Africa	25	25	7.37	0.15		
LSMeans, change from baseline						
Insulin icodec						
Europe	86	86	-0.93	0.09		
North America	78	78	-1.02	0.09		
Asia	74	74	-0.80	0.09		
Africa	25	25	-1.14	0.16		
Daily basal insulin						
Europe	81	81	-0.83	0.10		
North America	61	61	-0.67	0.11		
Asia	96	96	-0.60	0.09		
Africa	25	25	-0.76	0.15		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Europe			-0.10		[-0.36 ; 0.15]	
North America			-0.35		[-0.63 ; -0.07]	
Asia			-0.20		[-0.45 ; 0.05]	
Africa			-0.38		[-0.81 ; 0.05]	
Test for treatment by subgroup interaction						0.5366

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.40 HbA1c (%) at planned end of treatment by region - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Europe	96	96	7.14	0.08		
North America	74	74	7.25	0.09		
Asia	88	88	7.11	0.08		
South America	33	33	7.02	0.14		
Daily basal insulin						
Europe	109	109	7.03	0.08		
North America	59	59	7.25	0.11		
Asia	90	90	7.04	0.08		
South America	33	33	7.38	0.15		
LSMeans, change from baseline						
Insulin icodec						
Europe	96	96	-1.16	0.08		
North America	74	74	-1.05	0.09		
Asia	88	88	-1.19	0.08		
South America	33	33	-1.28	0.14		
Daily basal insulin						
Europe	109	109	-1.27	0.08		
North America	59	59	-1.05	0.11		
Asia	90	90	-1.26	0.08		
South America	33	33	-0.92	0.15		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Europe			0.12		[-0.10 ; 0.33]	
North America			-0.00		[-0.28 ; 0.27]	
Asia			0.07		[-0.16 ; 0.30]	
South America			-0.37		[-0.76 ; 0.02]	
Test for treatment by subgroup interaction						0.1875

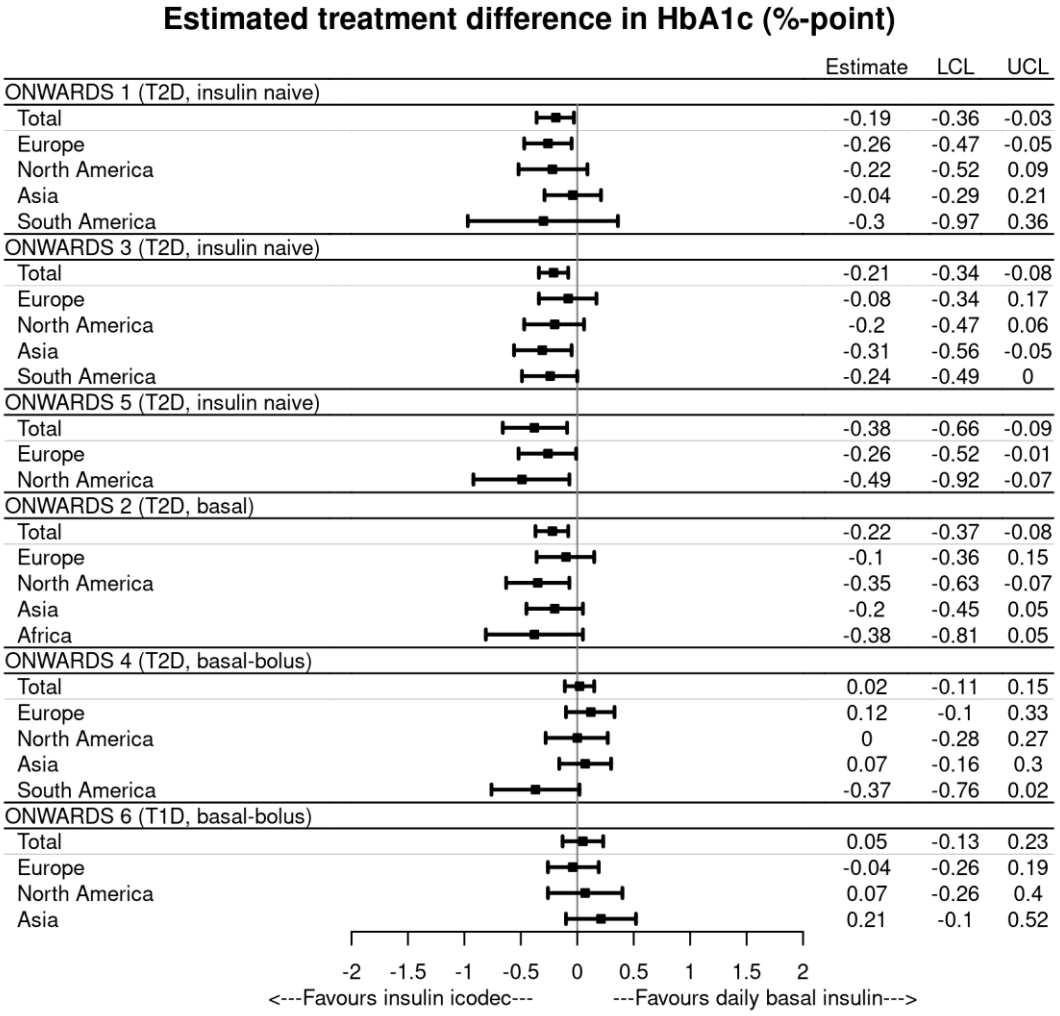
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.41 HbA1c (%) at planned end of treatment by region - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Europe	136	136	7.03	0.08		
North America	106	106	7.24	0.12		
Asia	48	48	7.30	0.13		
Daily basal insulin						
Europe	139	139	7.06	0.08		
North America	85	85	7.16	0.13		
Asia	68	68	7.09	0.10		
LSMeans, change from baseline						
Insulin icodec						
Europe	136	136	-0.59	0.08		
North America	106	106	-0.37	0.12		
Asia	48	48	-0.32	0.13		
Daily basal insulin						
Europe	139	139	-0.55	0.08		
North America	85	85	-0.45	0.13		
Asia	68	68	-0.53	0.10		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Europe			-0.04		[-0.26 ; 0.19]	
North America			0.07		[-0.26 ; 0.40]	
Asia			0.21		[-0.10 ; 0.52]	
Test for treatment by subgroup interaction						0.4911

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.42 HbA1c (%) at planned end of treatment by region - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

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6.3.43 HbA1c (%) at planned end of treatment by baseline HbA1c group - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<8% (<64 mmol/mol)	170	170	6.96	0.09		
>=8% (>=64 mmol/mol)	322	322	6.91	0.08		
Daily basal insulin						
<8% (<64 mmol/mol)	188	188	7.09	0.08		
>=8% (>=64 mmol/mol)	304	304	7.14	0.08		
LSMeans, change from baseline						
Insulin icodec						
<8% (<64 mmol/mol)	170	170	-1.52	0.09		
>=8% (>=64 mmol/mol)	322	322	-1.56	0.08		
Daily basal insulin						
<8% (<64 mmol/mol)	188	188	-1.38	0.08		
>=8% (>=64 mmol/mol)	304	304	-1.33	0.08		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<8% (<64 mmol/mol)			-0.14		[-0.34 ; 0.07]	
>=8% (>=64 mmol/mol)			-0.23		[-0.44 ; -0.01]	
Test for treatment by subgroup interaction						0.5129

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.44 HbA1c (%) at planned end of treatment by baseline HbA1c group - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<8% (<64 mmol/mol)	111	111	6.91	0.09		
>=8% (>=64 mmol/mol)	183	183	6.97	0.07		
Daily basal insulin						
<8% (<64 mmol/mol)	106	106	6.99	0.09		
>=8% (>=64 mmol/mol)	188	188	7.25	0.06		
LSMeans, change from baseline						
Insulin icodec						
<8% (<64 mmol/mol)	111	111	-1.61	0.09		
>=8% (>=64 mmol/mol)	183	183	-1.55	0.07		
Daily basal insulin						
<8% (<64 mmol/mol)	106	106	-1.52	0.09		
>=8% (>=64 mmol/mol)	188	188	-1.27	0.06		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<8% (<64 mmol/mol)			-0.08		[-0.29 ; 0.12]	
>=8% (>=64 mmol/mol)			-0.28		[-0.44 ; -0.11]	
Test for treatment by subgroup interaction						0.1499

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.45 HbA1c (%) at planned end of treatment by baseline HbA1c group - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<8% (<64 mmol/mol)	175	175	7.19	0.13		
>=8% (>=64 mmol/mol)	367	367	7.26	0.10		
Daily basal insulin						
<8% (<64 mmol/mol)	171	171	7.54	0.15		
>=8% (>=64 mmol/mol)	371	371	7.65	0.14		
LSMeans, change from baseline						
Insulin icodec						
<8% (<64 mmol/mol)	175	175	-1.73	0.13		
>=8% (>=64 mmol/mol)	367	367	-1.66	0.10		
Daily basal insulin						
<8% (<64 mmol/mol)	171	171	-1.38	0.15		
>=8% (>=64 mmol/mol)	371	371	-1.28	0.14		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<8% (<64 mmol/mol)			-0.35		[-0.70 ; 0.00]	
>=8% (>=64 mmol/mol)			-0.39		[-0.71 ; -0.07]	
Test for treatment by subgroup interaction						0.8357

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.46 HbA1c (%) at planned end of treatment by baseline HbA1c group - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<8% (<64 mmol/mol)	126	126	7.21	0.08		
>=8% (>=64 mmol/mol)	137	137	7.19	0.09		
Daily basal insulin						
<8% (<64 mmol/mol)	125	125	7.30	0.09		
>=8% (>=64 mmol/mol)	138	138	7.53	0.08		
LSMeans, change from baseline						
Insulin icodec						
<8% (<64 mmol/mol)	126	126	-0.92	0.08		
>=8% (>=64 mmol/mol)	137	137	-0.94	0.09		
Daily basal insulin						
<8% (<64 mmol/mol)	125	125	-0.84	0.09		
>=8% (>=64 mmol/mol)	138	138	-0.60	0.08		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<8% (<64 mmol/mol)			-0.08		[-0.28 ; 0.11]	
>=8% (>=64 mmol/mol)			-0.34		[-0.55 ; -0.14]	
Test for treatment by subgroup interaction						0.0631

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.47 HbA1c (%) at planned end of treatment by baseline HbA1c group - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<8% (<64 mmol/mol)	117	117	7.07	0.09		
>=8% (>=64 mmol/mol)	174	174	7.19	0.07		
Daily basal insulin						
<8% (<64 mmol/mol)	120	120	7.12	0.09		
>=8% (>=64 mmol/mol)	171	171	7.13	0.07		
LSMeans, change from baseline						
Insulin icodec						
<8% (<64 mmol/mol)	117	117	-1.23	0.09		
>=8% (>=64 mmol/mol)	174	174	-1.11	0.07		
Daily basal insulin						
<8% (<64 mmol/mol)	120	120	-1.19	0.09		
>=8% (>=64 mmol/mol)	171	171	-1.17	0.07		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<8% (<64 mmol/mol)			-0.04		[-0.25 ; 0.16]	
>=8% (>=64 mmol/mol)			0.06		[-0.11 ; 0.23]	
Test for treatment by subgroup interaction						0.4229

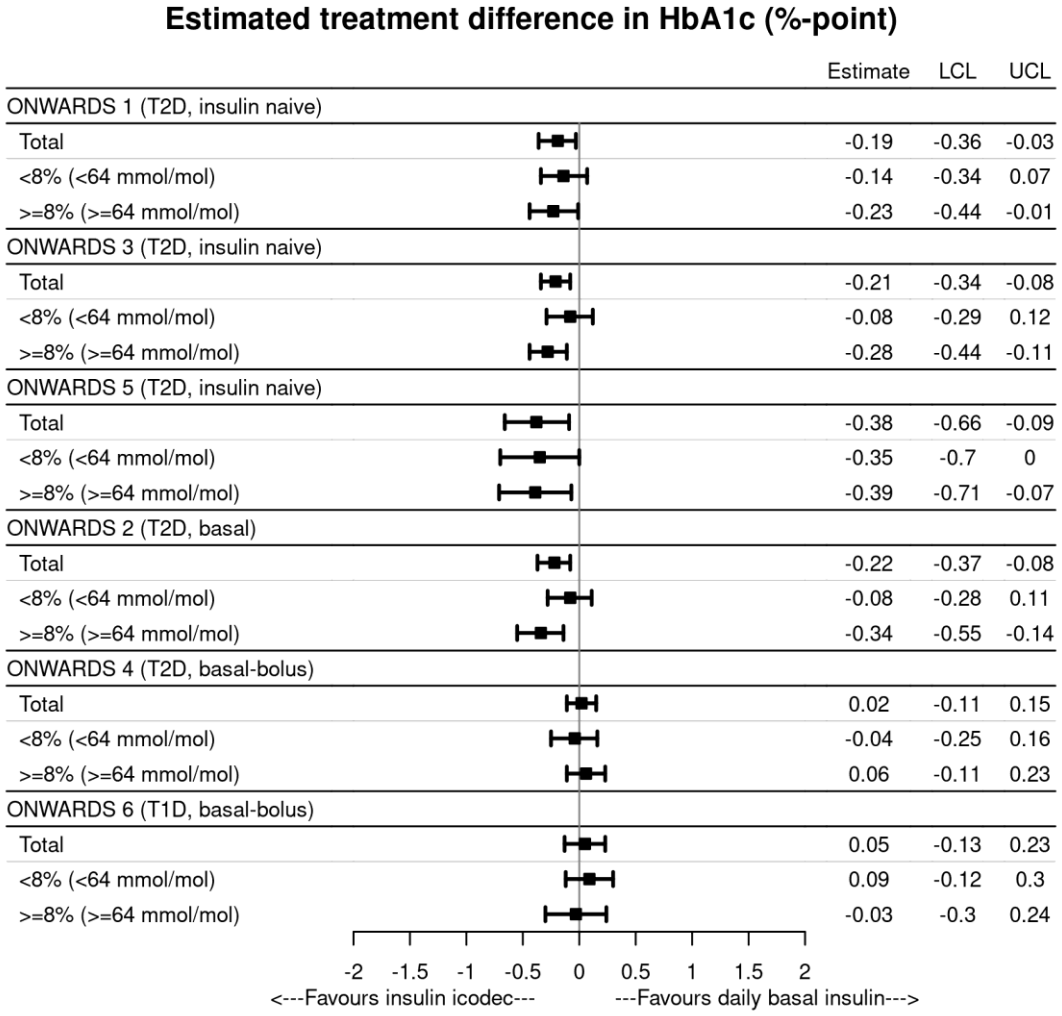
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.48 HbA1c (%) at planned end of treatment by baseline HbA1c group - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<8% (<64 mmol/mol)	189	189	7.30	0.10		
>=8% (>=64 mmol/mol)	101	101	6.87	0.14		
Daily basal insulin						
<8% (<64 mmol/mol)	189	189	7.21	0.09		
>=8% (>=64 mmol/mol)	103	103	6.90	0.14		
LSMeans, change from baseline						
Insulin icodec						
<8% (<64 mmol/mol)	189	189	-0.32	0.10		
>=8% (>=64 mmol/mol)	101	101	-0.74	0.14		
Daily basal insulin						
<8% (<64 mmol/mol)	189	189	-0.40	0.09		
>=8% (>=64 mmol/mol)	103	103	-0.71	0.14		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<8% (<64 mmol/mol)			0.09		[-0.12 ; 0.30]	
>=8% (>=64 mmol/mol)			-0.03		[-0.30 ; 0.24]	
Test for treatment by subgroup interaction						0.4399

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.49 HbA1c (%) at planned end of treatment by baseline HbA1c group - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

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6.3.50 HbA1c (%) at planned end of treatment by duration of diabetes - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<10 years	211	211	6.89	0.08		
>=10 years	281	281	6.96	0.07		
Daily basal insulin						
<10 years	230	230	6.99	0.08		
>=10 years	262	262	7.24	0.06		
LSMeans, change from baseline						
Insulin icodec						
<10 years	211	211	-1.59	0.08		
>=10 years	281	281	-1.52	0.07		
Daily basal insulin						
<10 years	230	230	-1.49	0.08		
>=10 years	262	262	-1.24	0.06		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<10 years			-0.10		[-0.32 ; 0.12]	
>=10 years			-0.28		[-0.48 ; -0.08]	
Test for treatment by subgroup interaction						0.1710

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.51 HbA1c (%) at planned end of treatment by duration of diabetes - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<10 years	137	137	6.97	0.07		
>=10 years	157	157	6.93	0.06		
Daily basal insulin						
<10 years	137	137	7.13	0.07		
>=10 years	157	157	7.17	0.06		
LSMeans, change from baseline						
Insulin icodec						
<10 years	137	137	-1.55	0.07		
>=10 years	157	157	-1.59	0.06		
Daily basal insulin						
<10 years	137	137	-1.38	0.07		
>=10 years	157	157	-1.34	0.06		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<10 years			-0.17		[-0.36 ; 0.02]	
>=10 years			-0.25		[-0.42 ; -0.07]	
Test for treatment by subgroup interaction						0.5357

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.52 HbA1c (%) at planned end of treatment by duration of diabetes - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<10 years	229	229	7.19	0.10		
>=10 years	313	313	7.27	0.11		
Daily basal insulin						
<10 years	242	241	7.53	0.13		
>=10 years	301	301	7.68	0.15		
LSMeans, change from baseline						
Insulin icodec						
<10 years	229	229	-1.73	0.10		
>=10 years	313	313	-1.65	0.11		
Daily basal insulin						
<10 years	242	241	-1.39	0.13		
>=10 years	301	301	-1.24	0.15		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<10 years			-0.34		[-0.65 ; -0.03]	
>=10 years			-0.41		[-0.75 ; -0.07]	
Test for treatment by subgroup interaction						0.6871

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.53 HbA1c (%) at planned end of treatment by duration of diabetes - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<10 years	56	56	7.07	0.11		
>=10 years	207	207	7.24	0.06		
Daily basal insulin						
<10 years	46	46	7.38	0.12		
>=10 years	217	217	7.43	0.06		
LSMeans, change from baseline						
Insulin icodec						
<10 years	56	56	-1.06	0.11		
>=10 years	207	207	-0.90	0.06		
Daily basal insulin						
<10 years	46	46	-0.75	0.12		
>=10 years	217	217	-0.70	0.06		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<10 years			-0.32		[-0.63 ; -0.01]	
>=10 years			-0.20		[-0.36 ; -0.03]	
Test for treatment by subgroup interaction						0.4886

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.54 HbA1c (%) at planned end of treatment by duration of diabetes - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<10 years	56	56	7.12	0.11		
>=10 years	235	235	7.15	0.05		
Daily basal insulin						
<10 years	61	61	7.25	0.11		
>=10 years	230	230	7.09	0.05		
LSMeans, change from baseline						
Insulin icodec						
<10 years	56	56	-1.18	0.11		
>=10 years	235	235	-1.15	0.05		
Daily basal insulin						
<10 years	61	61	-1.06	0.11		
>=10 years	230	230	-1.21	0.05		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<10 years			-0.13		[-0.42 ; 0.17]	
>=10 years			0.06		[-0.09 ; 0.20]	
Test for treatment by subgroup interaction						0.2666

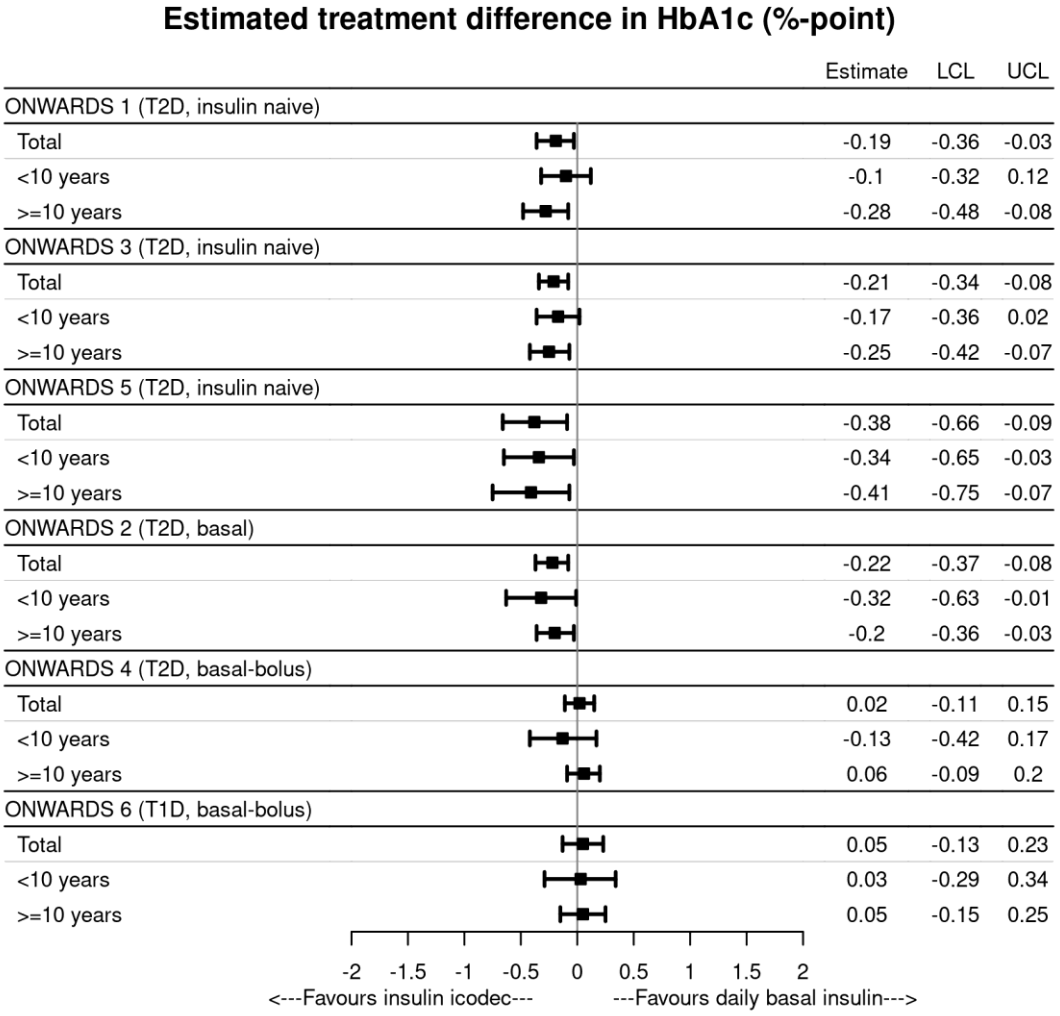
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.55 HbA1c (%) at planned end of treatment by duration of diabetes - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<10 years	75	75	7.02	0.12		
>=10 years	215	215	7.19	0.07		
Daily basal insulin						
<10 years	82	82	7.00	0.10		
>=10 years	210	210	7.14	0.07		
LSMeans, change from baseline						
Insulin icodec						
<10 years	75	75	-0.59	0.12		
>=10 years	215	215	-0.42	0.07		
Daily basal insulin						
<10 years	82	82	-0.61	0.10		
>=10 years	210	210	-0.47	0.07		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<10 years			0.03		[-0.29 ; 0.34]	
>=10 years			0.05		[-0.15 ; 0.25]	
Test for treatment by subgroup interaction						0.8777

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.56 HbA1c (%) at planned end of treatment by duration of diabetes - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

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6.3.57 HbA1c (%) at planned end of treatment by estimated renal function at baseline - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal (>=90)	224	224	6.94	0.08		
Mild impairment (>=60 - <90)	223	223	6.93	0.07		
Moderate or severe impairment (<60)	45	45	6.83	0.21		
Daily basal insulin						
Normal (>=90)	222	222	7.11	0.08		
Mild impairment (>=60 - <90)	213	213	7.12	0.07		
Moderate or severe impairment (<60)	57	57	7.18	0.14		
LSMeans, change from baseline						
Insulin icodec						
Normal (>=90)	224	224	-1.53	0.08		
Mild impairment (>=60 - <90)	223	223	-1.55	0.07		
Moderate or severe impairment (<60)	45	45	-1.64	0.21		
Daily basal insulin						
Normal (>=90)	222	222	-1.37	0.08		
Mild impairment (>=60 - <90)	213	213	-1.35	0.07		
Moderate or severe impairment (<60)	57	57	-1.30	0.14		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal (>=90)			-0.16		[-0.39 ; 0.07]	
Mild impairment (>=60 - <90)			-0.19		[-0.39 ; -0.00]	
Moderate or severe impairment (<60)			-0.34		[-0.82 ; 0.14]	
Test for treatment by subgroup interaction						0.7462

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.58 HbA1c (%) at planned end of treatment by estimated renal function at baseline - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal (>=90)	173	173	6.90	0.06		
Mild impairment (>=60 - <90)	97	97	6.97	0.08		
Moderate impairment (>=30 - <60)	23	23	7.14	0.17		
Daily basal insulin						
Normal (>=90)	185	185	7.18	0.06		
Mild impairment (>=60 - <90)	88	88	7.06	0.08		
Moderate impairment (>=30 - <60)	21	21	7.33	0.18		
LSMeans, change from baseline						
Insulin icodec						
Normal (>=90)	173	173	-1.61	0.06		
Mild impairment (>=60 - <90)	97	97	-1.55	0.08		
Moderate impairment (>=30 - <60)	23	23	-1.38	0.17		
Daily basal insulin						
Normal (>=90)	185	185	-1.34	0.06		
Mild impairment (>=60 - <90)	88	88	-1.46	0.08		
Moderate impairment (>=30 - <60)	21	21	-1.19	0.18		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal (>=90)			-0.28		[-0.44 ; -0.11]	
Mild impairment (>=60 - <90)			-0.09		[-0.31 ; 0.13]	
Moderate impairment (>=30 - <60)			-0.20		[-0.69 ; 0.30]	
Test for treatment by subgroup interaction						0.4317

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.59 HbA1c (%) at planned end of treatment by estimated renal function at baseline - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal (>=90)	311	311	7.23	0.10		
Mild impairment (>=60 - <90)	174	174	7.23	0.13		
Moderate impairment (>=30 - <60)	52	52	7.31	0.23		
Severe impairment (<30)	5	5	7.29	0.58		
Daily basal insulin						
Normal (>=90)	307	307	7.61	0.13		
Mild impairment (>=60 - <90)	171	171	7.65	0.16		
Moderate impairment (>=30 - <60)	61	61	7.49	0.23		
Severe impairment (<30)	3	3	7.87	1.06		
LSMeans, change from baseline						
Insulin icodec						
Normal (>=90)	311	311	-1.69	0.10		
Mild impairment (>=60 - <90)	174	174	-1.70	0.13		
Moderate impairment (>=30 - <60)	52	52	-1.62	0.23		
Severe impairment (<30)	5	5	-1.63	0.58		
Daily basal insulin						
Normal (>=90)	307	307	-1.31	0.13		
Mild impairment (>=60 - <90)	171	171	-1.27	0.16		
Moderate impairment (>=30 - <60)	61	61	-1.44	0.23		
Severe impairment (<30)	3	3	-1.05	1.06		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal (>=90)			-0.38		[-0.69 ; -0.08]	
Mild impairment (>=60 - <90)			-0.43		[-0.81 ; -0.05]	
Moderate impairment (>=30 - <60)			-0.18		[-0.80 ; 0.44]	
Severe impairment (<30)			-0.59		[-2.96 ; 1.79]	
Test for treatment by subgroup interaction						0.8955

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.60 HbA1c (%) at planned end of treatment by estimated renal function at baseline - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal (>=90)	94	94	7.15	0.08		
Mild impairment (>=60 - <90)	135	135	7.27	0.07		
Moderate impairment (>=30 - <60)	34	34	7.02	0.15		
Daily basal insulin						
Normal (>=90)	109	109	7.48	0.08		
Mild impairment (>=60 - <90)	108	108	7.29	0.08		
Moderate impairment (>=30 - <60)	46	46	7.60	0.12		
LSMeans, change from baseline						
Insulin icodec						
Normal (>=90)	94	94	-0.98	0.08		
Mild impairment (>=60 - <90)	135	135	-0.86	0.07		
Moderate impairment (>=30 - <60)	34	34	-1.11	0.15		
Daily basal insulin						
Normal (>=90)	109	109	-0.65	0.08		
Mild impairment (>=60 - <90)	108	108	-0.84	0.08		
Moderate impairment (>=30 - <60)	46	46	-0.53	0.12		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal (>=90)			-0.32		[-0.56 ; -0.09]	
Mild impairment (>=60 - <90)			-0.02		[-0.22 ; 0.19]	
Moderate impairment (>=30 - <60)			-0.58		[-0.94 ; -0.22]	
Test for treatment by subgroup interaction						0.0138

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.61 HbA1c (%) at planned end of treatment by estimated renal function at baseline - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal (>=90)	123	123	7.08	0.07		
Mild impairment (>=60 - <90)	121	121	7.24	0.07		
Moderate impairment (>=30 - <60)	47	47	7.05	0.12		
Daily basal insulin						
Normal (>=90)	127	127	7.19	0.07		
Mild impairment (>=60 - <90)	120	120	7.03	0.07		
Moderate impairment (>=30 - <60)	44	44	7.19	0.12		
LSMeans, change from baseline						
Insulin icodec						
Normal (>=90)	123	123	-1.22	0.07		
Mild impairment (>=60 - <90)	121	121	-1.06	0.07		
Moderate impairment (>=30 - <60)	47	47	-1.25	0.12		
Daily basal insulin						
Normal (>=90)	127	127	-1.11	0.07		
Mild impairment (>=60 - <90)	120	120	-1.27	0.07		
Moderate impairment (>=30 - <60)	44	44	-1.11	0.12		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal (>=90)			-0.11		[-0.31 ; 0.09]	
Mild impairment (>=60 - <90)			0.21		[0.01 ; 0.41]	
Moderate impairment (>=30 - <60)			-0.13		[-0.47 ; 0.20]	
Test for treatment by subgroup interaction						0.0493

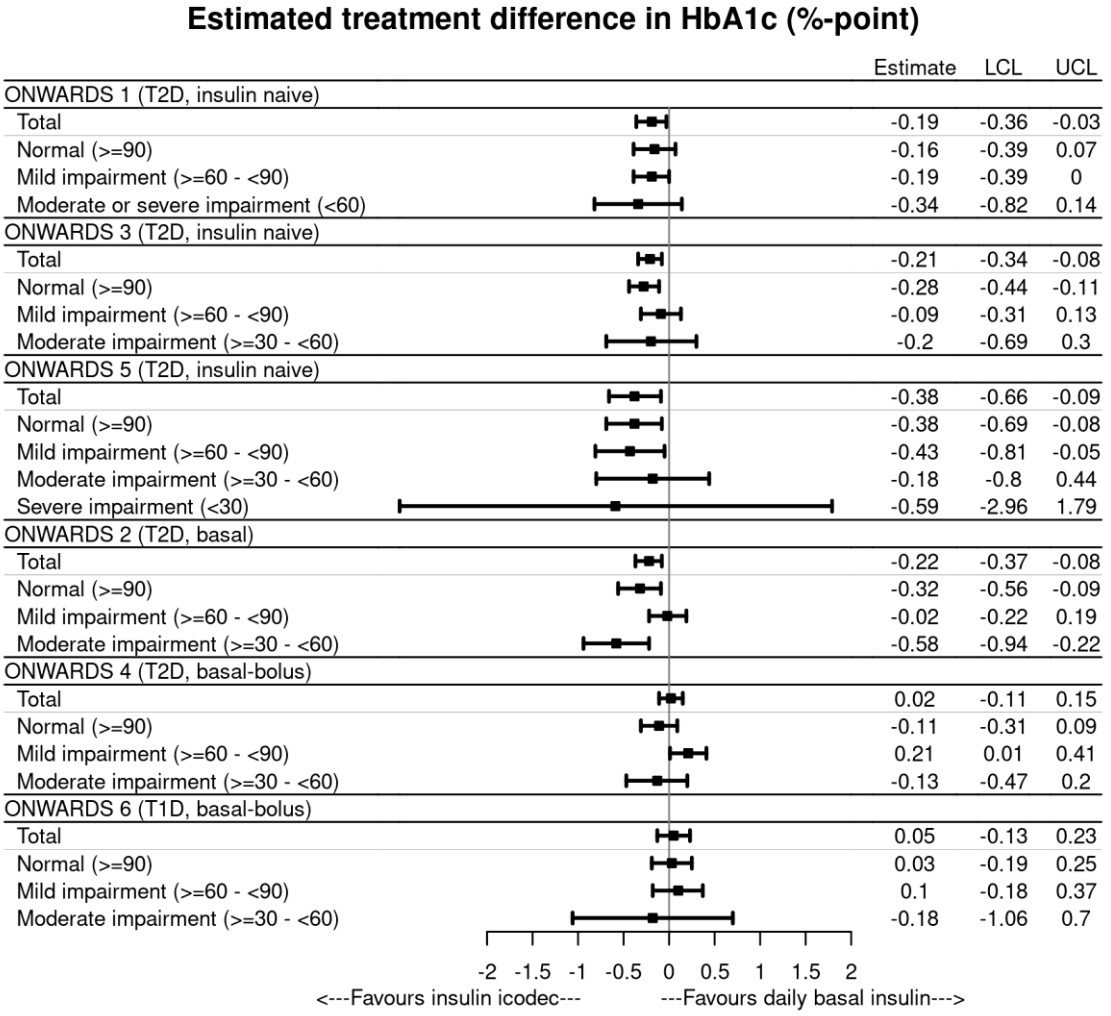
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.62 HbA1c (%) at planned end of treatment by estimated renal function at baseline - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal (>=90)	197	197	7.09	0.08		
Mild impairment (>=60 - <90)	88	88	7.29	0.11		
Moderate impairment (>=30 - <60)	5	5	6.86	0.36		
Daily basal insulin						
Normal (>=90)	190	190	7.06	0.08		
Mild impairment (>=60 - <90)	93	93	7.20	0.09		
Moderate impairment (>=30 - <60)	9	9	7.04	0.27		
LSMeans, change from baseline						
Insulin icodec						
Normal (>=90)	197	197	-0.52	0.08		
Mild impairment (>=60 - <90)	88	88	-0.32	0.11		
Moderate impairment (>=30 - <60)	5	5	-0.75	0.36		
Daily basal insulin						
Normal (>=90)	190	190	-0.56	0.08		
Mild impairment (>=60 - <90)	93	93	-0.42	0.09		
Moderate impairment (>=30 - <60)	9	9	-0.57	0.27		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal (>=90)			0.03		[-0.19 ; 0.25]	
Mild impairment (>=60 - <90)			0.10		[-0.18 ; 0.37]	
Moderate impairment (>=30 - <60)			-0.18		[-1.06 ; 0.70]	
Test for treatment by subgroup interaction						0.8176

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.63 HbA1c (%) at planned end of treatment by estimated renal function at baseline - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

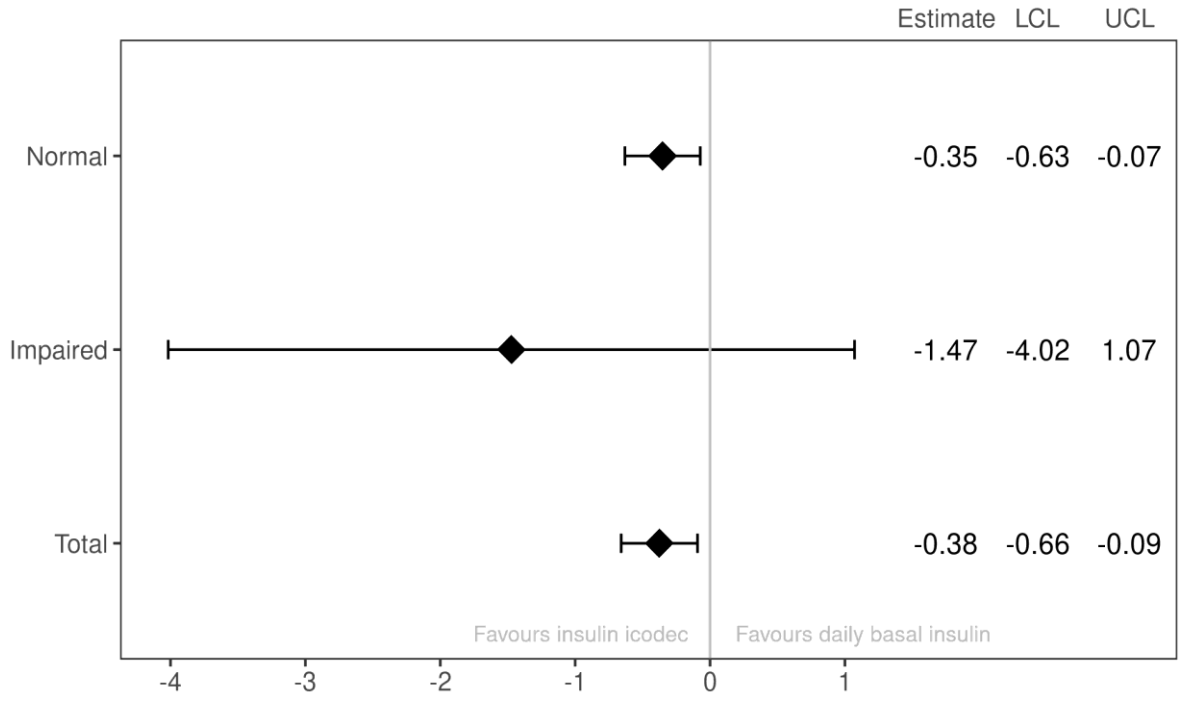
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6.3.64 HbA1c (%) at planned end of treatment by estimated hepatic function at baseline - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal	521	521	7.23	0.09		
Impaired	4	4	7.43	0.63		
Daily basal insulin						
Normal	523	523	7.58	0.12		
Impaired	4	4	8.90	1.13		
LSMeans, change from baseline						
Insulin icodec						
Normal	521	521	-1.69	0.09		
Impaired	4	4	-1.49	0.63		
Daily basal insulin						
Normal	523	523	-1.33	0.12		
Impaired	4	4	-0.01	1.13		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal			-0.35		[-0.63 ; -0.07]	
Impaired			-1.47		[-4.02 ; 1.07]	
Test for treatment by subgroup interaction						0.3738

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.65 HbA1c (%) at planned end of treatment by estimated hepatic function at baseline - change from baseline - ONWARDS 5 - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit. Missing data are imputed using multiple imputation.

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6.3.66 HbA1c (%) at planned end of treatment by pre-trial SU use - change from baseline - ONWARDS 1 - in- trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No SU use	273	273	6.81	0.08		
SU use	219	219	7.08	0.07		
Daily basal insulin						
No SU use	265	265	6.97	0.07		
SU use	227	227	7.30	0.07		
LSMeans, change from baseline						
Insulin icodec						
No SU use	273	273	-1.67	0.08		
SU use	219	219	-1.40	0.07		
Daily basal insulin						
No SU use	265	265	-1.50	0.07		
SU use	227	227	-1.18	0.07		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No SU use			-0.16		[-0.37 ; 0.05]	
SU use			-0.22		[-0.42 ; -0.02]	
Test for treatment by subgroup interaction						0.6467

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, SU: Sulfonylureas, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.67 HbA1c (%) at planned end of treatment by pre-trial SU use - change from baseline - ONWARDS 3 - in- trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No SU use	162	162	7.01	0.09		
SU use	132	132	6.87	0.11		
Daily basal insulin						
No SU use	166	166	7.26	0.09		
SU use	128	128	7.02	0.11		
LSMeans, change from baseline						
Insulin icodec						
No SU use	162	162	-1.51	0.09		
SU use	132	132	-1.65	0.11		
Daily basal insulin						
No SU use	166	166	-1.25	0.09		
SU use	128	128	-1.50	0.11		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No SU use			-0.26		[-0.43 ; -0.09]	
SU use			-0.15		[-0.34 ; 0.05]	
Test for treatment by subgroup interaction						0.3908

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, SU: Sulfonylureas, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.68 HbA1c (%) at planned end of treatment by pre-trial SU use - change from baseline - ONWARDS 5 - in- trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No SU use	333	333	7.20	0.09		
SU use	209	209	7.30	0.13		
Daily basal insulin						
No SU use	313	312	7.51	0.13		
SU use	230	230	7.75	0.15		
LSMeans, change from baseline						
Insulin icodec						
No SU use	333	333	-1.72	0.09		
SU use	209	209	-1.63	0.13		
Daily basal insulin						
No SU use	313	312	-1.41	0.13		
SU use	230	230	-1.17	0.15		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No SU use			-0.31		[-0.61 ; -0.01]	
SU use			-0.45		[-0.84 ; -0.07]	
Test for treatment by subgroup interaction						0.4455

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, SU: Sulfonylureas, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.69 HbA1c (%) at planned end of treatment by pre-trial SU use - change from baseline - ONWARDS 2 - in- trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No SU use	204	204	7.15	0.06		
SU use	59	59	7.37	0.11		
Daily basal insulin						
No SU use	208	208	7.35	0.06		
SU use	55	55	7.68	0.12		
LSMeans, change from baseline						
Insulin icodec						
No SU use	204	204	-0.98	0.06		
SU use	59	59	-0.76	0.11		
Daily basal insulin						
No SU use	208	208	-0.78	0.06		
SU use	55	55	-0.45	0.12		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No SU use			-0.20		[-0.36 ; -0.05]	
SU use			-0.31		[-0.63 ; 0.01]	
Test for treatment by subgroup interaction						0.5349

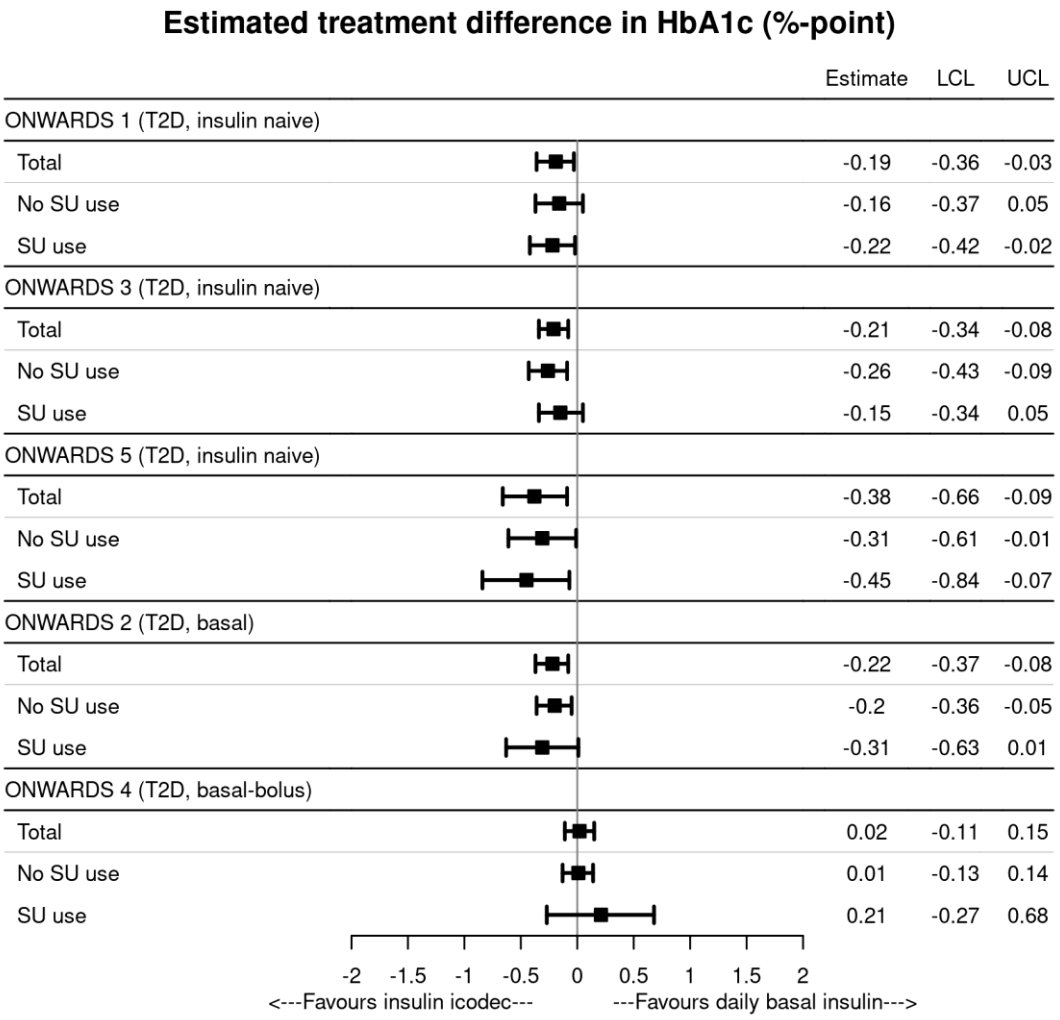
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, SU: Sulfonylureas, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.70 HbA1c (%) at planned end of treatment by pre-trial SU use - change from baseline - ONWARDS 4 - in- trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No SU use	263	263	7.14	0.05		
SU use	28	28	7.17	0.15		
Daily basal insulin						
No SU use	275	275	7.13	0.05		
SU use	16	16	6.97	0.20		
LSMeans, change from baseline						
Insulin icodec						
No SU use	263	263	-1.16	0.05		
SU use	28	28	-1.13	0.15		
Daily basal insulin						
No SU use	275	275	-1.17	0.05		
SU use	16	16	-1.33	0.20		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No SU use			0.01		[-0.13 ; 0.14]	
SU use			0.21		[-0.27 ; 0.68]	
Test for treatment by subgroup interaction						0.4291

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, SU: Sulfonylureas, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.71 HbA1c (%) at planned end of treatment by pre-trial SU use - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, SU: Sulfonylureas, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

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6.3.72 HbA1c (%) at planned end of treatment by GLP-1 RA use at baseline - change from baseline - ONWARDS 1 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No GLP-1 RA use	409	409	6.94	0.07		
GLP-1 RA use	83	83	6.88	0.10		
Daily basal insulin						
No GLP-1 RA use	400	400	7.16	0.06		
GLP-1 RA use	92	92	6.96	0.11		
LSMeans, change from baseline						
Insulin icodec						
No GLP-1 RA use	409	409	-1.54	0.07		
GLP-1 RA use	83	83	-1.60	0.10		
Daily basal insulin						
No GLP-1 RA use	400	400	-1.32	0.06		
GLP-1 RA use	92	92	-1.51	0.11		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No GLP-1 RA use			-0.22		[-0.40 ; -0.04]	
GLP-1 RA use			-0.09		[-0.38 ; 0.21]	
Test for treatment by subgroup interaction						0.4096

CI: Confidence interval, FAS: Number of subjects in full analysis set, GLP-1 RA: Glucagon-like peptide-1 receptor agonist, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.73 HbA1c (%) at planned end of treatment by GLP-1 RA use at baseline - change from baseline - ONWARDS 3 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No GLP-1 RA use	230	230	6.96	0.05		
GLP-1 RA use	64	64	6.89	0.10		
Daily basal insulin						
No GLP-1 RA use	246	246	7.17	0.05		
GLP-1 RA use	48	48	7.10	0.12		
LSMeans, change from baseline						
Insulin icodec						
No GLP-1 RA use	230	230	-1.56	0.05		
GLP-1 RA use	64	64	-1.63	0.10		
Daily basal insulin						
No GLP-1 RA use	246	246	-1.35	0.05		
GLP-1 RA use	48	48	-1.42	0.12		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No GLP-1 RA use			-0.21		[-0.35 ; -0.06]	
GLP-1 RA use			-0.21		[-0.50 ; 0.08]	
Test for treatment by subgroup interaction						0.9750

CI: Confidence interval, FAS: Number of subjects in full analysis set, GLP-1 RA: Glucagon-like peptide-1 receptor agonist, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.74 HbA1c (%) at planned end of treatment by GLP-1 RA use at baseline - change from baseline - ONWARDS 5 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No GLP-1 RA use	394	394	7.23	0.10		
GLP-1 RA use	148	148	7.26	0.11		
Daily basal insulin						
No GLP-1 RA use	385	384	7.62	0.13		
GLP-1 RA use	158	158	7.59	0.15		
LSMeans, change from baseline						
Insulin icodec						
No GLP-1 RA use	394	394	-1.69	0.10		
GLP-1 RA use	148	148	-1.66	0.11		
Daily basal insulin						
No GLP-1 RA use	385	384	-1.30	0.13		
GLP-1 RA use	158	158	-1.33	0.15		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No GLP-1 RA use			-0.39		[-0.71 ; -0.07]	
GLP-1 RA use			-0.33		[-0.69 ; 0.03]	
Test for treatment by subgroup interaction						0.7561

CI: Confidence interval, FAS: Number of subjects in full analysis set, GLP-1 RA: Glucagon-like peptide-1 receptor agonist, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.75 HbA1c (%) at planned end of treatment by GLP-1 RA use at baseline - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No GLP-1 RA use	195	195	7.26	0.06		
GLP-1 RA use	68	68	7.01	0.09		
Daily basal insulin						
No GLP-1 RA use	194	194	7.52	0.07		
GLP-1 RA use	69	69	7.14	0.09		
LSMeans, change from baseline						
Insulin icodec						
No GLP-1 RA use	195	195	-0.87	0.06		
GLP-1 RA use	68	68	-1.12	0.09		
Daily basal insulin						
No GLP-1 RA use	194	194	-0.61	0.07		
GLP-1 RA use	69	69	-0.99	0.09		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No GLP-1 RA use			-0.26		[-0.43 ; -0.09]	
GLP-1 RA use			-0.13		[-0.38 ; 0.13]	
Test for treatment by subgroup interaction						0.3902

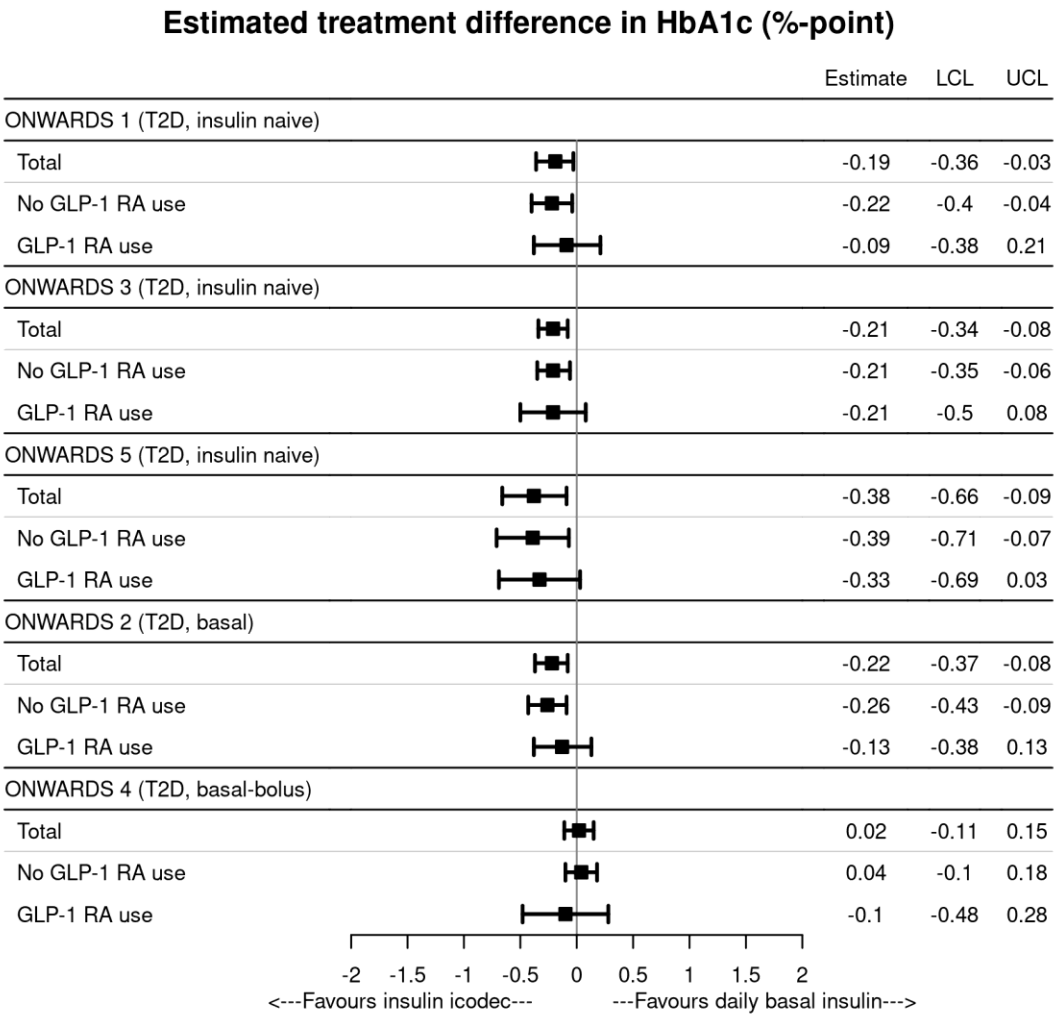
CI: Confidence interval, FAS: Number of subjects in full analysis set, GLP-1 RA: Glucagon-like peptide-1 receptor agonist, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.76 HbA1c (%) at planned end of treatment by GLP-1 RA use at baseline - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No GLP-1 RA use	254	254	7.14	0.05		
GLP-1 RA use	37	37	7.16	0.14		
Daily basal insulin						
No GLP-1 RA use	257	257	7.10	0.05		
GLP-1 RA use	34	34	7.26	0.14		
LSMeans, change from baseline						
Insulin icodec						
No GLP-1 RA use	254	254	-1.16	0.05		
GLP-1 RA use	37	37	-1.14	0.14		
Daily basal insulin						
No GLP-1 RA use	257	257	-1.20	0.05		
GLP-1 RA use	34	34	-1.04	0.14		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No GLP-1 RA use			0.04		[-0.10 ; 0.18]	
GLP-1 RA use			-0.10		[-0.48 ; 0.28]	
Test for treatment by subgroup interaction						0.5008

CI: Confidence interval, FAS: Number of subjects in full analysis set, GLP-1 RA: Glucagon-like peptide-1 receptor agonist, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.77 HbA1c (%) at planned end of treatment by GLP-1 RA use at baseline - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, GLP-1 RA: Glucagon-like peptide-1 receptor agonist, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

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6.3.78 HbA1c (%) at planned end of treatment by pre-trial basal insulin regimen - change from baseline - ONWARDS 2 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Insulin degludec	75	75	7.14	0.09		
Insulin glargine U100	111	111	7.18	0.08		
Insulin glargine U300	38	38	7.03	0.12		
Other	39	39	7.56	0.13		
Daily basal insulin						
Insulin degludec	73	73	7.14	0.09		
Insulin glargine U100	108	108	7.51	0.10		
Insulin glargine U300	44	44	7.39	0.11		
Other	38	38	7.73	0.13		
LSMeans, change from baseline						
Insulin icodec						
Insulin degludec	75	75	-0.99	0.09		
Insulin glargine U100	111	111	-0.96	0.08		
Insulin glargine U300	38	38	-1.10	0.12		
Other	39	39	-0.57	0.13		
Daily basal insulin						
Insulin degludec	73	73	-0.99	0.09		
Insulin glargine U100	108	108	-0.62	0.10		
Insulin glargine U300	44	44	-0.74	0.11		
Other	38	38	-0.41	0.13		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Insulin degludec			0.00		[-0.25 ; 0.25]	
Insulin glargine U100			-0.33		[-0.57 ; -0.10]	
Insulin glargine U300			-0.36		[-0.68 ; -0.03]	
Other			-0.16		[-0.51 ; 0.18]	
Test for treatment by subgroup interaction						0.1808

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.79 HbA1c (%) at planned end of treatment by pre-trial basal insulin regimen - change from baseline - ONWARDS 4 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Insulin degludec	73	73	7.27	0.09		
Insulin glargine U100	146	146	7.11	0.07		
Insulin glargine U300	56	56	7.10	0.11		
Other	16	16	6.99	0.20		
Daily basal insulin						
Insulin degludec	67	67	7.07	0.10		
Insulin glargine U100	132	132	7.19	0.07		
Insulin glargine U300	67	67	7.12	0.10		
Other	25	25	6.93	0.16		
LSMeans, change from baseline						
Insulin icodec						
Insulin degludec	73	73	-1.03	0.09		
Insulin glargine U100	146	146	-1.19	0.07		
Insulin glargine U300	56	56	-1.20	0.11		
Other	16	16	-1.31	0.20		
Daily basal insulin						
Insulin degludec	67	67	-1.24	0.10		
Insulin glargine U100	132	132	-1.11	0.07		
Insulin glargine U300	67	67	-1.18	0.10		
Other	25	25	-1.37	0.16		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Insulin degludec			0.21		[-0.06 ; 0.47]	
Insulin glargine U100			-0.08		[-0.27 ; 0.11]	
Insulin glargine U300			-0.02		[-0.30 ; 0.26]	
Other			0.06		[-0.44 ; 0.56]	
Test for treatment by subgroup interaction						0.3855

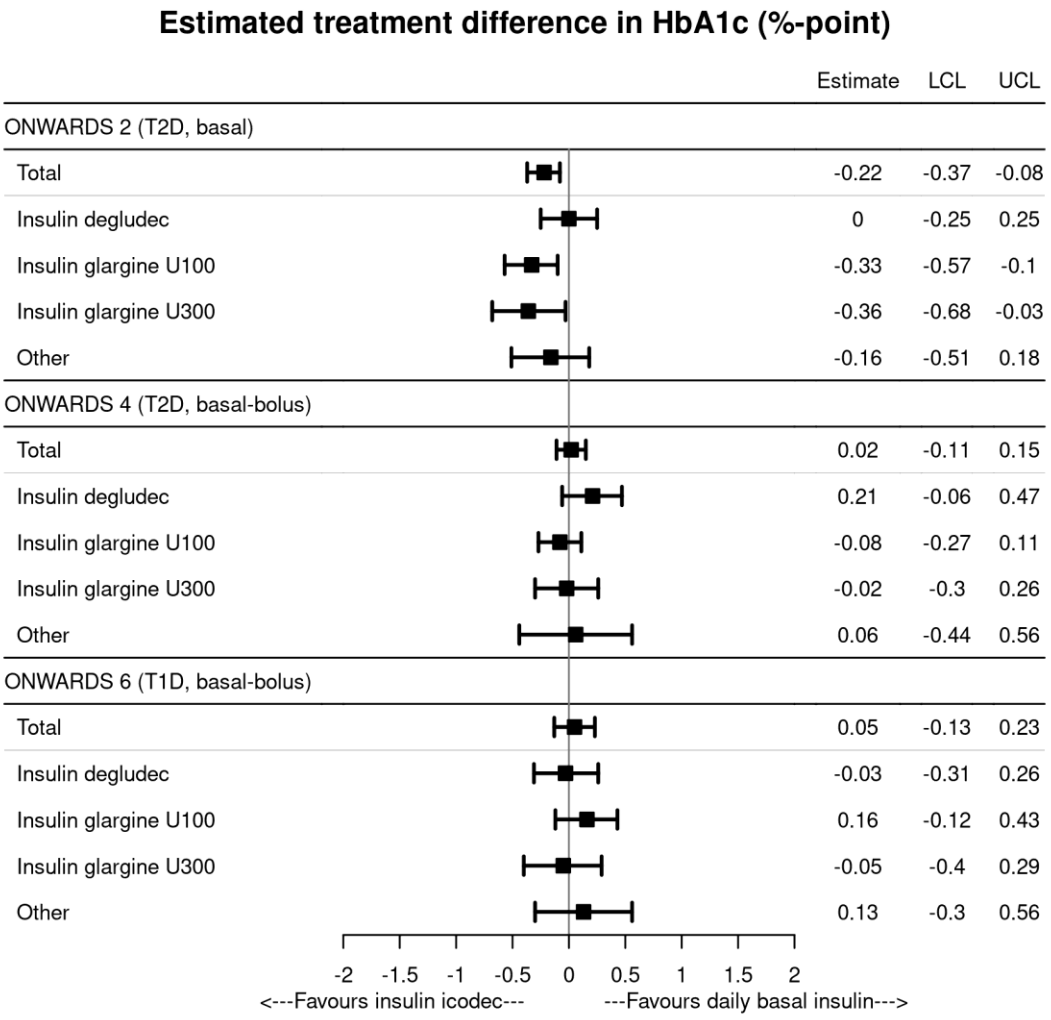
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.80 HbA1c (%) at planned end of treatment by pre-trial basal insulin regimen - change from baseline - ONWARDS 6 - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Insulin degludec	120	120	7.21	0.10		
Insulin glargine U100	98	98	7.13	0.10		
Insulin glargine U300	49	49	7.03	0.15		
Other	23	23	7.11	0.18		
Daily basal insulin						
Insulin degludec	113	113	7.24	0.11		
Insulin glargine U100	88	88	6.97	0.10		
Insulin glargine U300	60	60	7.08	0.11		
Other	31	31	6.98	0.16		
LSMeans, change from baseline						
Insulin icodec						
Insulin degludec	120	120	-0.40	0.10		
Insulin glargine U100	98	98	-0.48	0.10		
Insulin glargine U300	49	49	-0.58	0.15		
Other	23	23	-0.50	0.18		
Daily basal insulin						
Insulin degludec	113	113	-0.37	0.11		
Insulin glargine U100	88	88	-0.64	0.10		
Insulin glargine U300	60	60	-0.53	0.11		
Other	31	31	-0.63	0.16		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Insulin degludec			-0.03		[-0.31 ; 0.26]	
Insulin glargine U100			0.16		[-0.12 ; 0.43]	
Insulin glargine U300			-0.05		[-0.40 ; 0.29]	
Other			0.13		[-0.30 ; 0.56]	
Test for treatment by subgroup interaction						0.6590

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. End of treatment: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 52, ONWARDS 2-4 and 6 (main part): Week 26. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.3.81 HbA1c (%) at planned end of treatment by pre-trial basal insulin regimen - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



HbA1c: Haemoglobin A1c, LCL: lower 95% confidence limit, UCL: upper 95% confidence limit, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Missing data are imputed using multiple imputation.

インスリン イコデク（遺伝子組換え）

2.7.3.6 付録
4. 推奨用法・用量に関するデータ（第 3 相試験）

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6.4 Analyses across phase 3a trials related to dosing recommendation

6.4.1 Actual weekly total basal insulin dose at screening - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	Geometric mean (CV%)	N	Geometric mean (CV%)
Total weekly basal insulin dose (U)				
T2D, basal				
ONWARDS 2	263	177.05 (82.1)	263	193.66 (76.6)
T2D, basal-bolus				
ONWARDS 4	291	203.75 (75.7)	290	198.76 (81.1)
T1D, basal-bolus				
ONWARDS 6	290	154.40 (54.8)	292	146.79 (63.0)
Total weekly basal insulin dose (U/kg)				
T2D, basal				
ONWARDS 2	263	2.16 (71.2)	263	2.43 (67.5)
T2D, basal-bolus				
ONWARDS 4	291	2.43 (64.4)	290	2.44 (72.4)
T1D, basal-bolus				
ONWARDS 6	290	2.01 (45.1)	292	1.95 (52.0)

N: Number of subjects, CV: Coefficient of variation, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 6), IGlar U100 (ONWARDS 4). Data from ONWARDS 2, 4 and 6, only main part of ONWARDS 6.

6.4.2 Actual weekly total basal insulin dose during last two weeks of planned treatment - on-treatment - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
Average weekly basal insulin dose last 2 weeks of treatment (U)					
T2D, insulin naive					
ONWARDS 1					
LSMeans					
Insulin icodec	492	492	214.23		
Daily basal insulin	492	492	222.39		
Treatment ratio					
Insulin icodec / Daily basal insulin			0.96	[0.89 ; 1.05]	0.3701
ONWARDS 3					
LSMeans					
Insulin icodec	294	294	204.28		
Daily basal insulin	294	294	186.52		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.10	[0.98 ; 1.22]	0.0932
ONWARDS 5					
LSMeans					
Insulin icodec	542	542	226.51		
Daily basal insulin	543	543	185.23		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.22	[1.12 ; 1.33]	<0.0001
T2D, basal					
ONWARDS 2					
LSMeans					
Insulin icodec	263	263	267.96		
Daily basal insulin	263	263	244.22		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.10	[1.01 ; 1.20]	0.0348
T2D, basal-bolus					
ONWARDS 4					
LSMeans					
Insulin icodec	291	291	305.06		
Daily basal insulin	291	290	279.42		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.09	[1.01 ; 1.18]	0.0286

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, P-value: Two-sided p-value for test of no treatment difference. T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. ANCOVA based on log-transformed values with treatment, region and, if applicable, additional relevant factors as fixed factors, and (ONWARDS 2, 4 and 6) log-transformed baseline response as covariate. Missing data are imputed using multiple imputation. Last two weeks of treatment: Last two weeks of planned treatment or last two weeks of the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 50-52, ONWARDS 2-4 and 6 (main part): Week 24-26.

Actual weekly total basal insulin dose during last two weeks of planned treatment - on-treatment - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
T1D, basal-bolus					
ONWARDS 6					
LSMeans					
Insulin icodec	290	290	169.96		
Daily basal insulin	292	292	151.24		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.12	[1.07 ; 1.18]	<0.0001
Average weekly basal insulin dose last 2 weeks of treatment (U/kg)					
T2D, insulin naive					
ONWARDS 1					
LSMeans					
Insulin icodec	492	492	2.52		
Daily basal insulin	492	492	2.64		
Treatment ratio					
Insulin icodec / Daily basal insulin			0.95	[0.88 ; 1.03]	0.1945
ONWARDS 3					
LSMeans					
Insulin icodec	294	294	2.38		
Daily basal insulin	294	294	2.24		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.06	[0.97 ; 1.17]	0.2095
ONWARDS 5					
LSMeans					
Insulin icodec	542	542	2.50		
Daily basal insulin	543	543	2.02		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.24	[1.14 ; 1.34]	<0.0001
T2D, basal					
ONWARDS 2					
LSMeans					
Insulin icodec	263	263	3.26		
Daily basal insulin	263	263	3.05		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.07	[0.99 ; 1.16]	0.0977

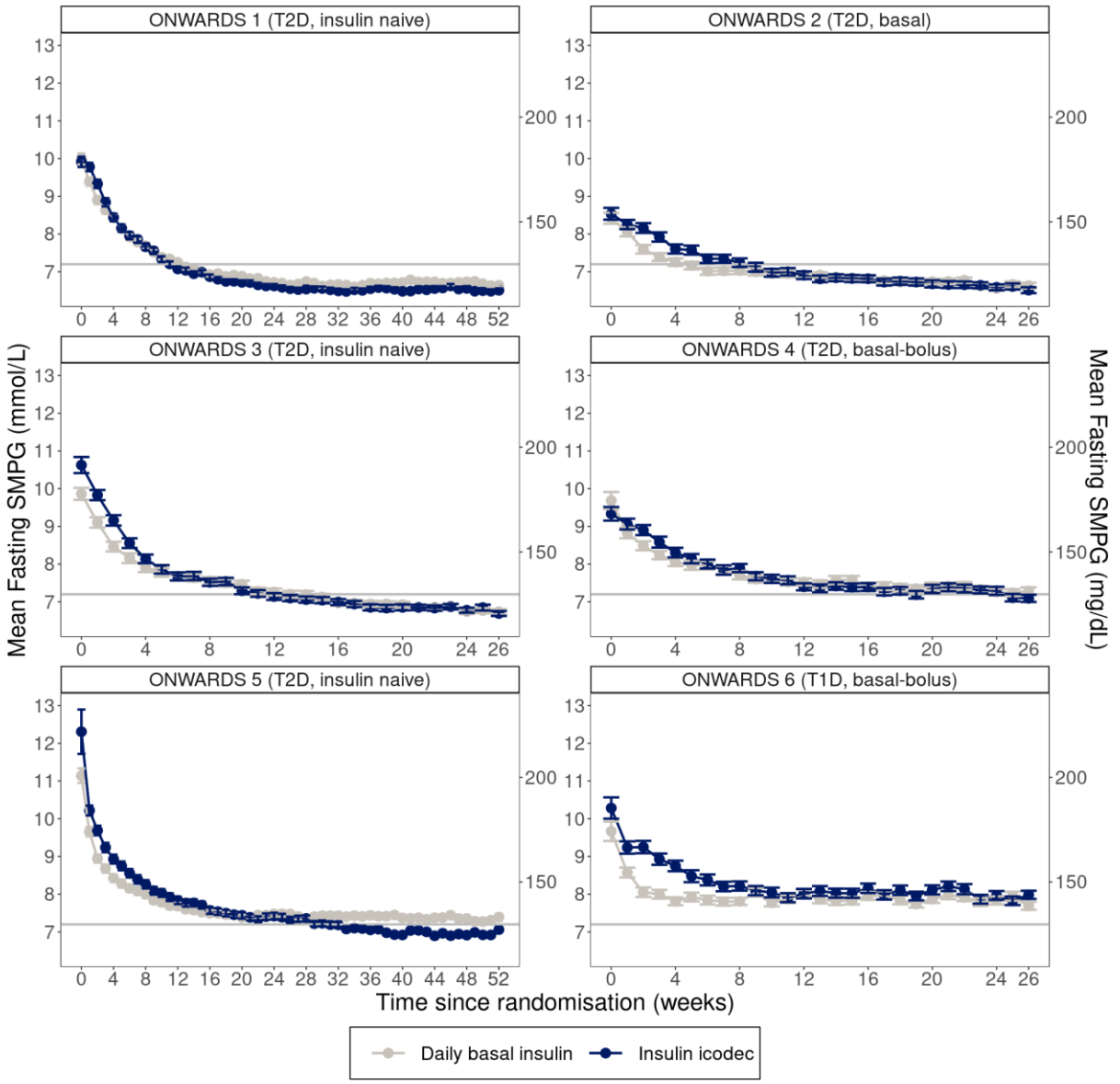
CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, P-value: Two-sided p-value for test of no treatment difference. T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. ANCOVA based on log-transformed values with treatment, region and, if applicable, additional relevant factors as fixed factors, and (ONWARDS 2, 4 and 6) log-transformed baseline response as covariate. Missing data are imputed using multiple imputation. Last two weeks of treatment: Last two weeks of planned treatment or last two weeks of the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 50-52, ONWARDS 2-4 and 6 (main part): Week 24-26.

Actual weekly total basal insulin dose during last two weeks of planned treatment - on-treatment - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
T2D, basal-bolus					
ONWARDS 4					
LSMeans					
Insulin icodec	291	291	3.59		
Daily basal insulin	291	290	3.34		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.08	[1.00 ; 1.16]	0.0520
T1D, basal-bolus					
ONWARDS 6					
LSMeans					
Insulin icodec	290	290	2.21		
Daily basal insulin	292	292	1.97		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.12	[1.07 ; 1.18]	<0.0001

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, P-value: Two-sided p-value for test of no treatment difference. T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. ANCOVA based on log-transformed values with treatment, region and, if applicable, additional relevant factors as fixed factors, and (ONWARDS 2, 4 and 6) log-transformed baseline response as covariate. Missing data are imputed using multiple imputation. Last two weeks of treatment: Last two weeks of planned treatment or last two weeks of the main part of the trials, as applicable; ONWARDS 1 (main part) and 5: Week 50-52, ONWARDS 2-4 and 6 (main part): Week 24-26.

6.4.3 Mean fasting self-measured plasma glucose during the entire week by treatment week - in trial - mean plot - full analysis set

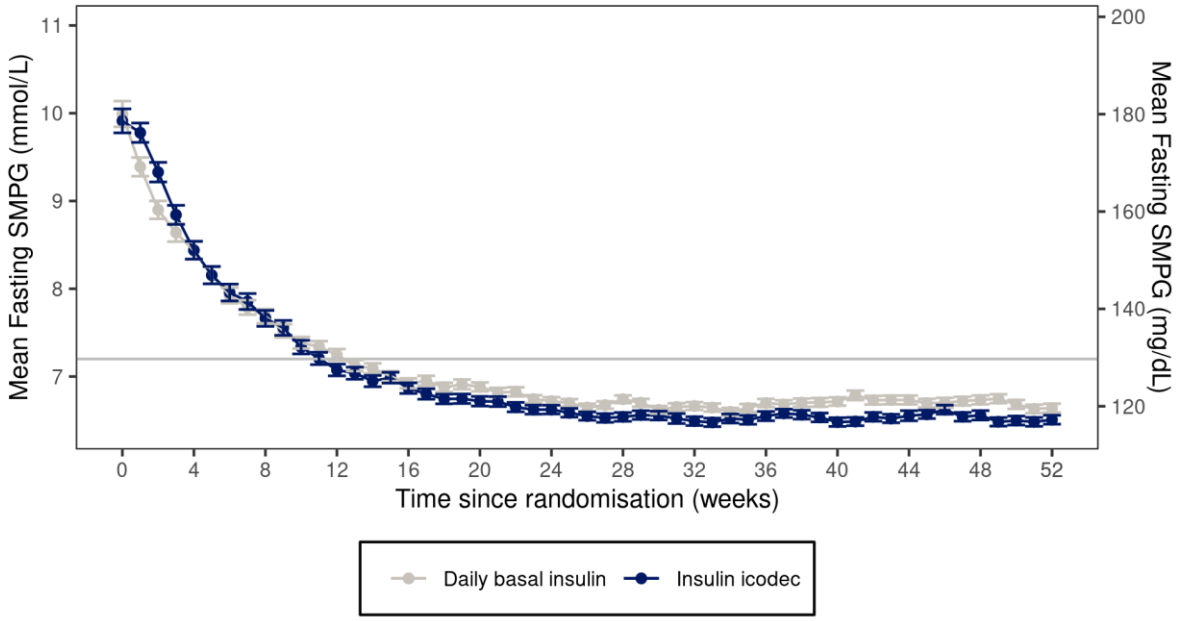


Observed data. SMPG: Self-measured plasma glucose assessed with glucose meter as plasma equivalent values of capillary whole blood glucose, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Legend: Mean (symbol) and mean ± standard error to the mean (error bars). Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6.

adsl.xpt; variable(s):STDNM POPGRP TR01PG1; criteria: FASFL == "Y"
adsmpgen.xpt; variable(s):STDNM POPGRP PARAMCD AWEEKN TRPG1 AVAL; criteria: FASFL == "Y" & PARAMCD %in% c("SMPGXMP3", "SMPGXMP4") & ANELFL == "Y" & ANL01FL == "Y" & !is.na(AWEEKN)

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6.4.4 Mean fasting self-measured plasma glucose during the entire week by treatment week - ONWARDS 1 - in trial - mean plot - full analysis set

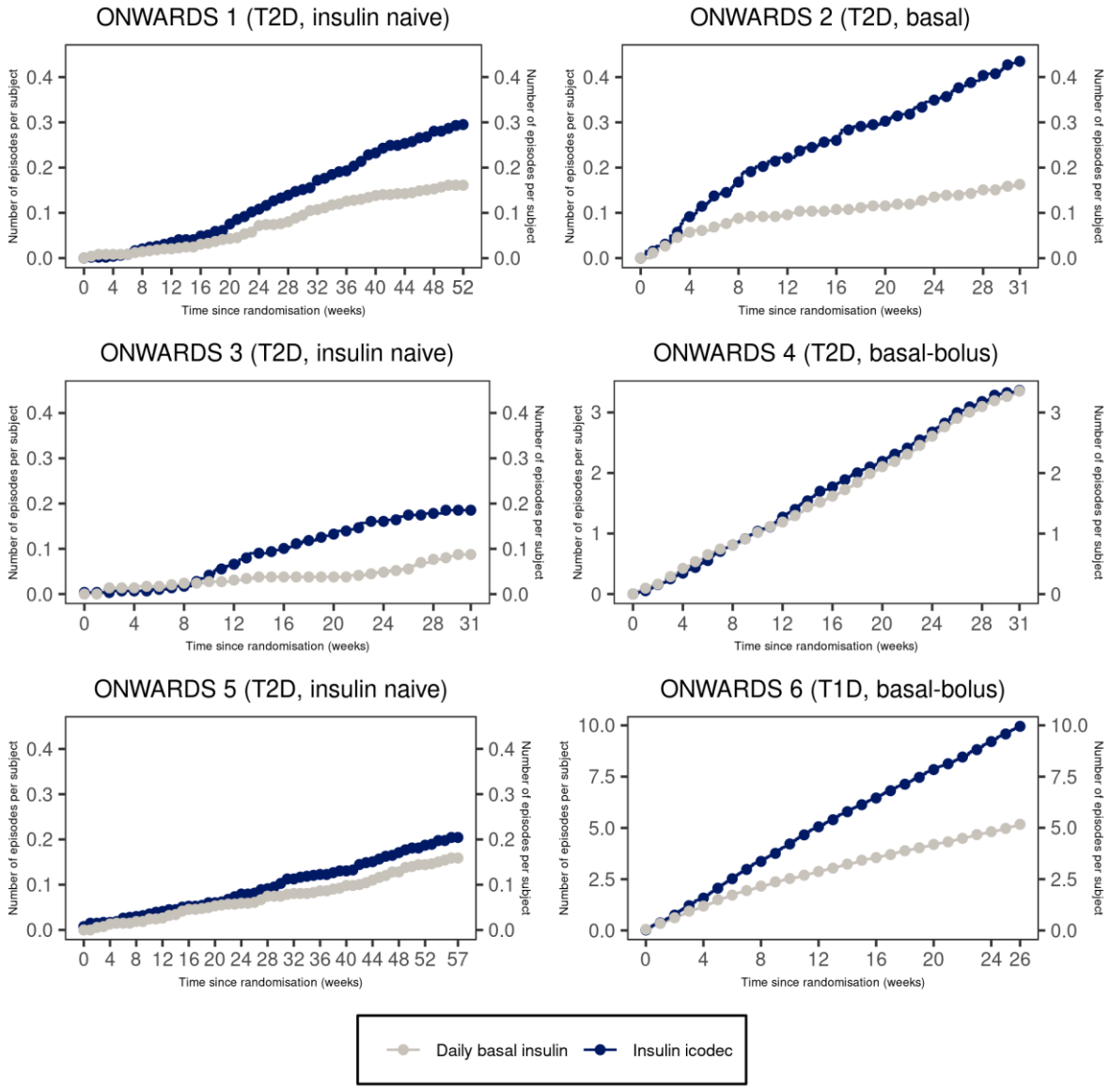


Observed data. SMPG: Self-measured plasma glucose assessed with glucose meter as plasma equivalent values of capillary whole blood glucose. Legend: Mean (symbol) and mean ± standard error to the mean (error bars). Daily basal insulin: IGlar U100. Data from main part of ONWARDS 1.

adsl.xpt; variable(s):POPGRP TR01PG1; criteria: FASFL == "Y"
adsmpgen.xpt; variable(s):POPGRP PARAMCD AWEEKN TRPG1 AVAL; criteria: FASFL == "Y" & PARAMCD %in% c("SMPGXMP3", "SMPGXMP4") & ANELFL == "Y" & ANL01FL == "Y" & !is.na(AWEEKN) & STDNM == "ONWARDS 1"

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03NOV2022:23:38:54 - fsmpgmean/fsmpgallmeanintow1fas.png

6.4.5 Severe (level 3) or clinically significant (level 2) hypoglycaemia - on-treatment - mean cumulative function - safety analysis set



Observed data. BG: Blood glucose, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6.

adsl.xpt; variable(s): STDNM ONTRDURD; criteria: SAFFL == "Y"
adhypo.xpt; variable(s): STDNM POPGRP TRAG1 ASTDY; criteria: SAFFL == "Y" & ACAT4N %in% (2:3) & ANELFL == "Y" & ((STUDYID %in% c("NN1436-4477", "NN1436-4625") & ANL05FL == "Y") | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ANL02FL == "Y"))

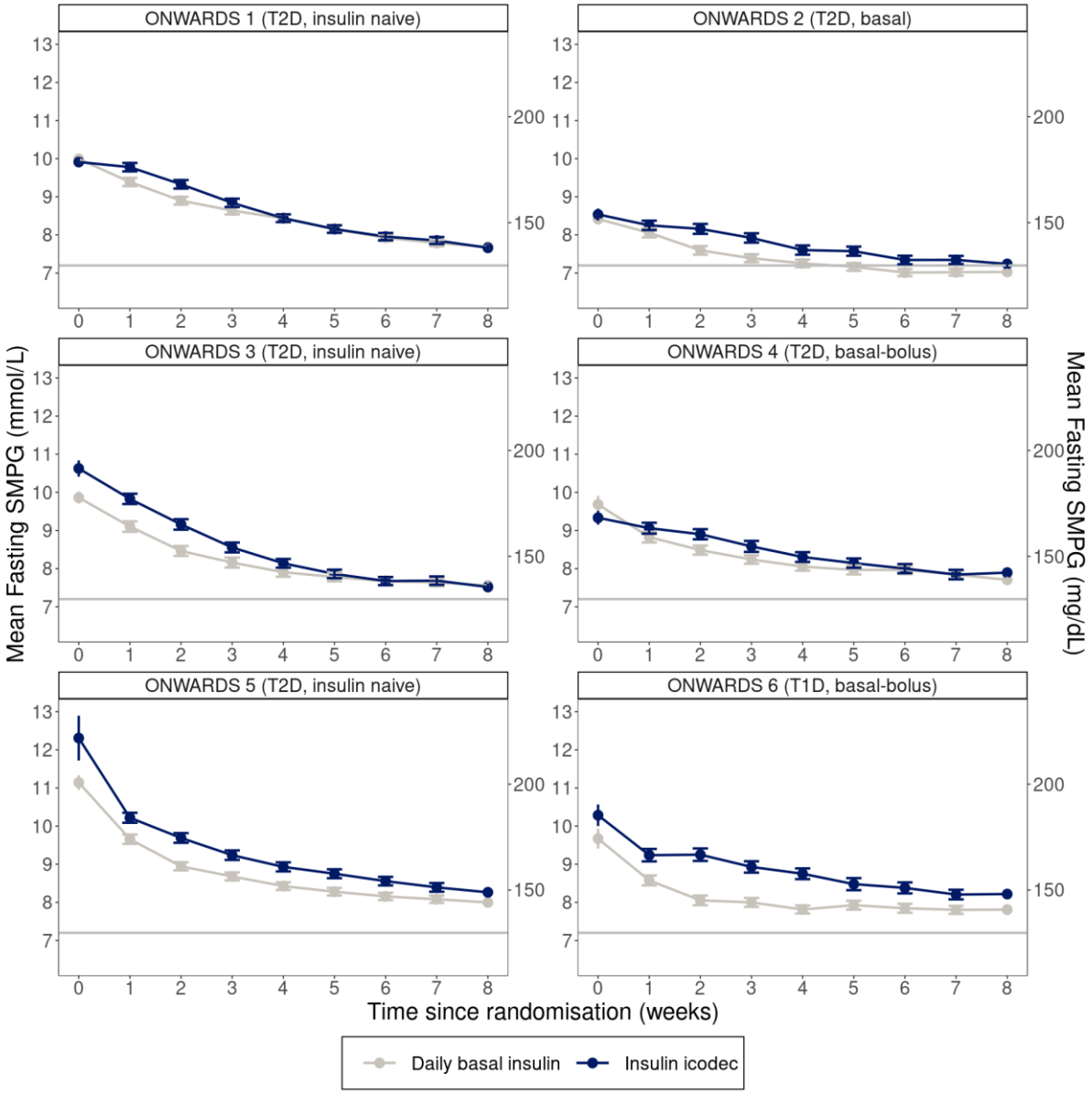
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03NOV2022:23:16:36 - fhypomcf/fhypolev23mcfontsas.png

6.4.6 Time to achievement of before breakfast plasma glucose target 4.4-7.2 mmol/l (80-130 mg/dL) is met for the first time (week) - in trial - summary - full analysis set

	Insulin icodec	Daily basal insulin
T2D, insulin naive		
ONWARDS 1		
25% percentile	3	2
Median	7	6
75% percentile	13	12
ONWARDS 3		
25% percentile	3	2
Median	5	4
75% percentile	11	10
ONWARDS 5		
25% percentile	4	
Median	9	
75% percentile	18	
T2D, basal		
ONWARDS 2		
25% percentile	2	2
Median	5	3
75% percentile	10	6
T2D, basal-bolus		
ONWARDS 4		
25% percentile	3	2
Median	8	4
75% percentile	17	8
T1D, basal-bolus		
ONWARDS 6		
25% percentile	3	2
Median	6	3
75% percentile	12	7

T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. In ONWARDS 5 titration of daily basal insulin was done according to local clinical practice, hence the achievement of target was not assessed.

6.4.7 Mean fasting self-measured plasma glucose during the entire week from week 0 to week 8 - in trial - mean plot - full analysis set



Observed data. SMPG: Self-measured plasma glucose assessed with glucose meter as plasma equivalent values of capillary whole blood glucose, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Legend: Mean (symbol) and mean ± standard error to the mean (error bars). Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6.

adsl.xpt; variable(s):STDNM POPGRP TR01PG1; criteria: FASFL == "Y"
adsmpgen.xpt; variable(s):STDNM POPGRP PARAMCD AWEEKN TRPG1 AVAL; criteria: FASFL == "Y" & PARAMCD %in% c("SMPGXMP3", "SMPGXMP4") & ANELFL == "Y" & ANL01FL == "Y" & !is.na(AWEEKN) & AWEEKN <= 8

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6.4.8 Time in range 3.9-10.0 mmol/L (70-180 mg/dL) (%) from week 0 to week 4 - in-trial - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)
Time in range 3.9-10.0 mmol/L (70-180 mg/dL) (%)				
T2D, insulin naïve				
ONWARDS 1	470	50.12 (26.83)	463	52.51 (26.13)
T2D, basal				
ONWARDS 2	252	51.17 (21.42)	244	53.42 (20.16)
T2D, basal-bolus				
ONWARDS 4	268	56.58 (20.96)	262	56.14 (20.11)
T1D				
ONWARDS 6	284	60.73 (14.78)	284	63.20 (14.66)

N: Number of subjects, SD: Standard deviation, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 6), and IGlar U100 (ONWARDS 1, ONWARDS 4). Data from ONWARDS 1, 2, 4 and 6, only main part of ONWARDS 1 and 6.

adcgmen.xpt; variable(s): STDNM POPGRP PARAM AVISIT AVAL; criteria: FASFL == "Y" & PARAMCD %in% c("TXIG3910") & AVISITN == 600 & ANELFL == "Y" & DTYPE %in% c("") & STDNM %in% c("ONWARDS 1", "ONWARDS 2", "ONWARDS 4", "ONWARDS 6")
nn1436/nn1436-ise/submission_20221031_er
03NOV2022:23:19:04 - tcgmsum/tcgmtirweek04sumintfas.txt

6.4.9 Time spent below range from week 0 to week 4 - in-trial - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)
Time spent < 3.0 mmol/L (54 mg/dL) (%)				
T2D, insulin naïve				
ONWARDS 1	470	0.10 (0.36)	463	0.08 (0.24)
T2D, basal				
ONWARDS 2	252	0.21 (0.67)	244	0.14 (0.45)
T2D, basal-bolus				
ONWARDS 4	268	0.54 (1.22)	262	0.45 (0.97)
T1D				
ONWARDS 6	284	0.87 (1.15)	284	0.70 (1.15)
Time spent < 3.9 mmol/L (70 mg/dL) (%)				
T2D, insulin naïve				
ONWARDS 1	470	0.33 (0.89)	463	0.28 (0.66)
T2D, basal				
ONWARDS 2	252	0.76 (1.77)	244	0.69 (1.91)
T2D, basal-bolus				
ONWARDS 4	268	1.87 (3.18)	262	1.68 (2.62)
T1D				
ONWARDS 6	284	3.56 (3.15)	284	3.19 (3.16)

N: Number of subjects, SD: Standard deviation, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 6), and IGlar U100 (ONWARDS 1, ONWARDS 4). Data from ONWARDS 1, 2, 4 and 6, only main part of ONWARDS 1 and 6.

adcgmen.xpt; variable(s): STDNM POPGRP PARAM AVISIT AVAL; criteria: FASFL == "Y" & PARAMCD %in% c("TLXIG39", "TXIG30") & AVISITN == 600 & ANELFL == "Y" & DTYPE %in% c("") & STDNM %in% c("ONWARDS 1", "ONWARDS 2", "ONWARDS 4", "ONWARDS 6")
nn1436/nn1436-ise/submission_20221031_er
03NOV2022:23:19:06 - tcgmsum/tcgmtbrweek04sumintfas.txt

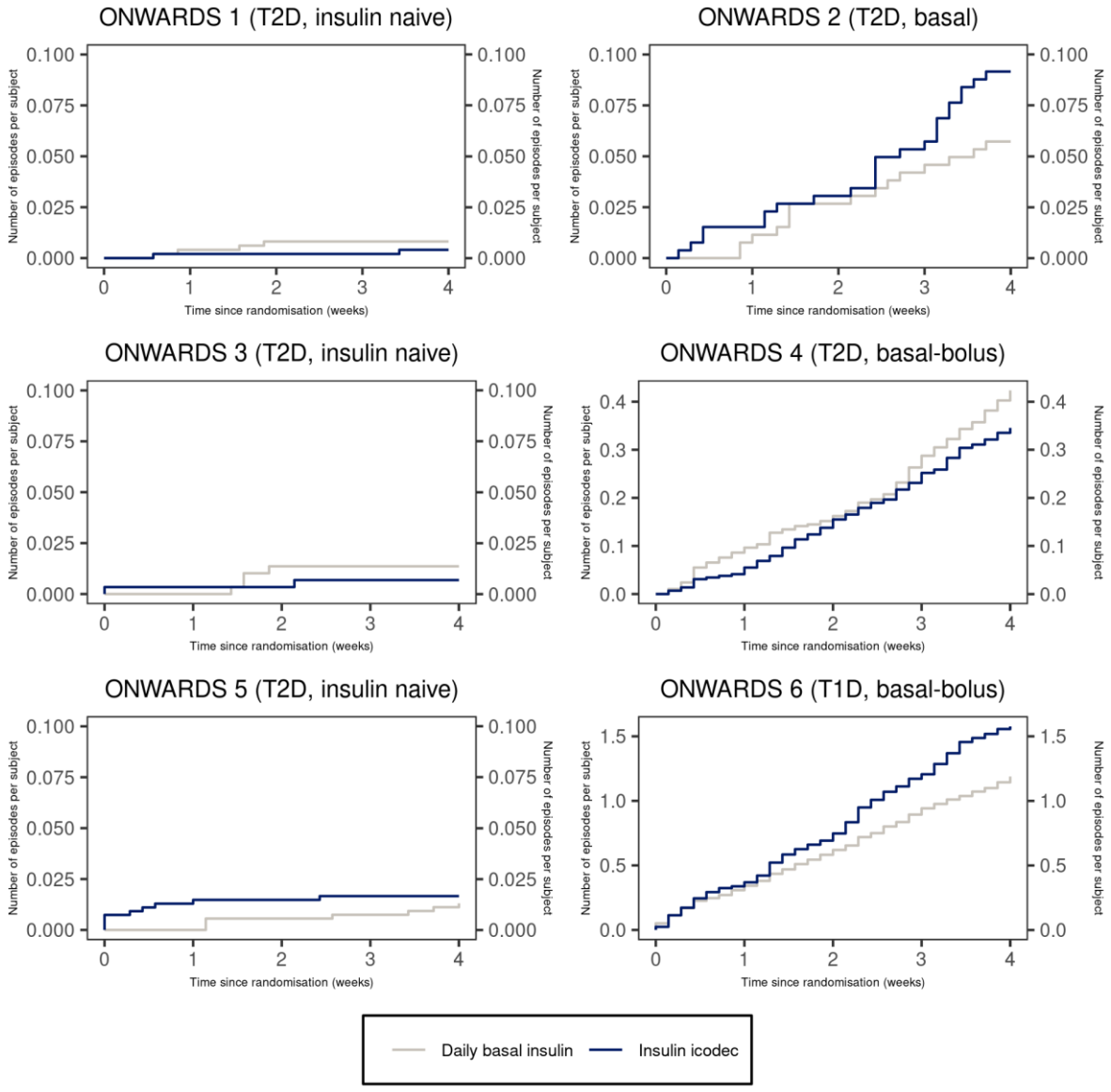
6.4.10 Time spent above range from week 0 to week 4 - in-trial - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)
Time spent > 10.0 mmol/L (180 mg/dL) (%)				
T2D, insulin naïve				
ONWARDS 1	470	49.55 (27.04)	463	47.21 (26.33)
T2D, basal				
ONWARDS 2	252	48.08 (21.89)	244	45.89 (20.76)
T2D, basal-bolus				
ONWARDS 4	268	41.55 (21.90)	262	42.18 (20.82)
T1D				
ONWARDS 6	284	35.70 (15.31)	284	33.62 (15.34)
Time spent > 13.9 mmol/L (250 mg/dL) (%)				
T2D, insulin naïve				
ONWARDS 1	470	18.09 (21.03)	463	16.98 (20.82)
T2D, basal				
ONWARDS 2	252	16.90 (16.26)	244	16.05 (15.60)
T2D, basal-bolus				
ONWARDS 4	268	13.71 (14.64)	262	14.43 (14.72)
T1D				
ONWARDS 6	284	12.22 (9.87)	284	10.62 (9.66)

N: Number of subjects, SD: Standard deviation, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 6), and IGlar U100 (ONWARDS 1, ONWARDS 4). Data from ONWARDS 1, 2, 4 and 6, only main part of ONWARDS 1 and 6.

adcgmen.xpt; variable(s): STDNM POPGRP PARAM AVISIT AVAL; criteria: FASFL == "Y" & PARAMCD %in% c("HXIGX100", "HXIGG139") & AVISITN == 600 & ANELFL == "Y" & DTYPE %in% c("") & STDNM %in% c("ONWARDS 1", "ONWARDS 2", "ONWARDS 4", "ONWARDS 6")
nn1436/nn1436-ise/submission_20221031_er
03NOV2022:23:19:09 - tcgmsum/tcgmtarweek04sumintfas.txt

6.4.11 Severe (level 3) or clinically significant (level 2) hypoglycaemia from week 0 to week 4 - on-treatment - mean cumulative function - safety analysis set



Observed data. BG: Blood glucose, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6.

adsl.xpt; variable(s): STDNM POPGRP ONTRDURD; criteria: SAFFL == "Y"
adhypo.xpt; variable(s): STDNM POPGRP TRAG1 ASTDY; criteria: SAFFL == "Y" & ACAT4N %in% (2:3) & ASTDY <= 29 & ANELFL == "Y" & ((STUDYID %in% c("NN1436-4477", "NN1436-4625") & ANL05FL == "Y") | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ANL05FL == "Y"))

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6.4.12 Change of weekly insulin dosing day - insulin icodec - on-treatment - summary - safety analysis set

	ONWARDS 1	ONWARDS 3	ONWARDS 5	ONWARDS 2	ONWARDS 4	ONWARDS 6
Number of subjects	492	293	542	262	291	290
Subjects changing dosing day at any time						
Yes	332	147	469	159	142	172
No	160	146	73	103	149	118
Number of times dosing day changed during trial						
N	332	147	469	159	142	172
Mean (SD)	6.98 (6.48)	3.54 (2.76)	8.07 (5.62)	4.57 (3.66)	4.12 (3.25)	4.25 (3.34)
Median	4.00	2.00	7.00	3.00	3.00	3.00
Min ; Max	1 ; 33	1 ; 15	1 ; 27	1 ; 16	1 ; 17	1 ; 16
Average number of days by which the dosing day changed						
N	332	147	469	159	142	172
Mean (SD)	1.35 (0.48)	1.37 (0.51)	1.30 (0.39)	1.31 (0.47)	1.45 (0.53)	1.23 (0.39)
Median	1.15	1.00	1.20	1.00	1.25	1.00
Min ; Max	1.00 ; 3.00	1.00 ; 3.00	1.00 ; 3.00	1.00 ; 3.00	1.00 ; 3.00	1.00 ; 3.00

N: Number of subjects changing the dosing day at any time, SD: Standard deviation. The average number of days is calculated based on the absolute number of days by which the dosing day changed. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. Change of the dosing day of weekly insulin icodec up to +/-3 days is allowed in ONWARDS 1-5.

adsl.xpt; variable(s): STDNM; criteria: SAFFL == "Y" & TRT01AN == 1
adec.xpt; variable(s): DAYSDEV FLEXFL; criteria: SAFFL == "Y" & TRTAN == 1 & ANL02FL == "Y" & PARAMCD == "I287COMP" & COMPDOS == "ACTUAL" & (STUDYID != "NN1436-4479" | (STUDYID == "NN1436-4479" & ECDOSFRQ == "EVERY WEEK")) & (STUDYID %in% c("NN1436-4477", "NN1436-4625") & ADT <= MONTEDT) | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ADT <= TRTEDT) & FLEXFL == "Y" & DAYSDEV <= 3 & DAYSDEV >= -3
nn1436/nn1436-ise/submission_20221031_er
04NOV2022:00:28:18 - tecflex/tecflexicomeanontsas.txt

6.4.13 Missed dose of weekly insulin dosing - insulin icodec - on-treatment - summary - safety analysis set

	ONWARDS 1	ONWARDS 3	ONWARDS 5	ONWARDS 2	ONWARDS 4	ONWARDS 6
Number of subjects	492	293	542	262	291	290
Subjects delaying dose at any time						
Yes	305	125	463	140	115	164
No	187	168	79	122	176	126
Number of delayed doses during trial						
N	305	125	463	140	115	164
Mean (SD)	3.74 (3.29)	1.97 (1.29)	4.27 (3.00)	2.49 (1.95)	2.21 (1.61)	2.43 (1.72)
Median	2.00	1.00	4.00	2.00	2.00	2.00
Min ; Max	1 ; 16	1 ; 6	1 ; 15	1 ; 9	1 ; 7	1 ; 9
Average number of days delay from OW schedule						
N	305	125	463	140	115	164
Mean (SD)	1.34 (0.49)	1.31 (0.51)	1.31 (0.40)	1.29 (0.48)	1.34 (0.48)	1.24 (0.40)
Median	1.00	1.00	1.20	1.00	1.00	1.00
Min ; Max	1.00 ; 3.00	1.00 ; 3.00	1.00 ; 3.00	1.00 ; 3.00	1.00 ; 3.00	1.00 ; 3.00

N: Number of subjects delaying the dose at any time, SD: Standard deviation, Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. OW: Once weekly. A missed dose is defined as a dose that was taken with up to +3 days delay according to the weekly schedule.

adsl.xpt; variable(s): STDNM; criteria: SAFFL == "Y" & TRT01AN == 1
adec.xpt; variable(s): DAYSDEV FLEXFL; criteria: SAFFL == "Y" & TRTAN == 1 & ANL02FL == "Y" & PARAMCD == "I287COMP" & COMPDOS == "ACTUAL" & (STUDYID != "NN1436-4479" | (STUDYID == "NN1436-4479" & ECDOSFRQ == "EVERY WEEK")) & (STUDYID %in% c("NN1436-4477", "NN1436-4625") & ADT <= MONTEDT) | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ADT <= TRTEDT) & FLEXFL == "Y" & DAYSDEV <= 3 & DAYSDEV > 0
nn1436/nn1436-ise/submission_20221031_er
04NOV2022:00:28:20 - tecflex/tecmissicomeanontsas.txt

6.4.14 Frequency deviation days from weekly schedule - insulin icodec - on treatment - summary - safety analysis set

	ONWARDS 1 N	(%)	ONWARDS 3 N	(%)	ONWARDS 5 N	(%)	ONWARDS 2 N	(%)	ONWARDS 4 N	(%)	ONWARDS 6 N	(%)
Total number of doses taken	25733		7562		24068		7099		7388		7373	
Deviation type												
-3	78	(0.30)	21	(0.28)	122	(0.51)	29	(0.41)	46	(0.62)	18	(0.24)
-2	234	(0.91)	63	(0.83)	283	(1.18)	77	(1.08)	85	(1.15)	48	(0.65)
-1	862	(3.35)	190	(2.51)	1404	(5.83)	272	(3.83)	200	(2.71)	267	(3.62)
1	853	(3.31)	182	(2.41)	1500	(6.23)	260	(3.66)	176	(2.38)	309	(4.19)
2	196	(0.76)	45	(0.60)	295	(1.23)	68	(0.96)	55	(0.74)	70	(0.95)
3	93	(0.36)	19	(0.25)	181	(0.75)	21	(0.30)	23	(0.31)	19	(0.26)

Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. N: Number of doses taken where the deviation type was used. %: Percentage of doses. Change of the dosing day of weekly insulin icodec up to +/-3 days is allowed in ONWARDS 1-5.

adec.xpt; variable(s): DAYSDEV FLEXFL; criteria: SAFFL == "Y" & TRTAN == 1 & ANL02FL == "Y" & PARAMCD == "I287COMP" & COMPDOS == "ACTUAL" & (STUDYID != "NN1436-4479" | (STUDYID == "NN1436-4479" & ECDOSFRQ == "EVERY WEEK")) & (STUDYID %in% c("NN1436-4477", "NN1436-4625") & ADT <= MONTEDT) | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ADT <= TRTEDT) & FLEXFL == "Y" & DAYSDEV <= 3 & DAYSDEV >= -3

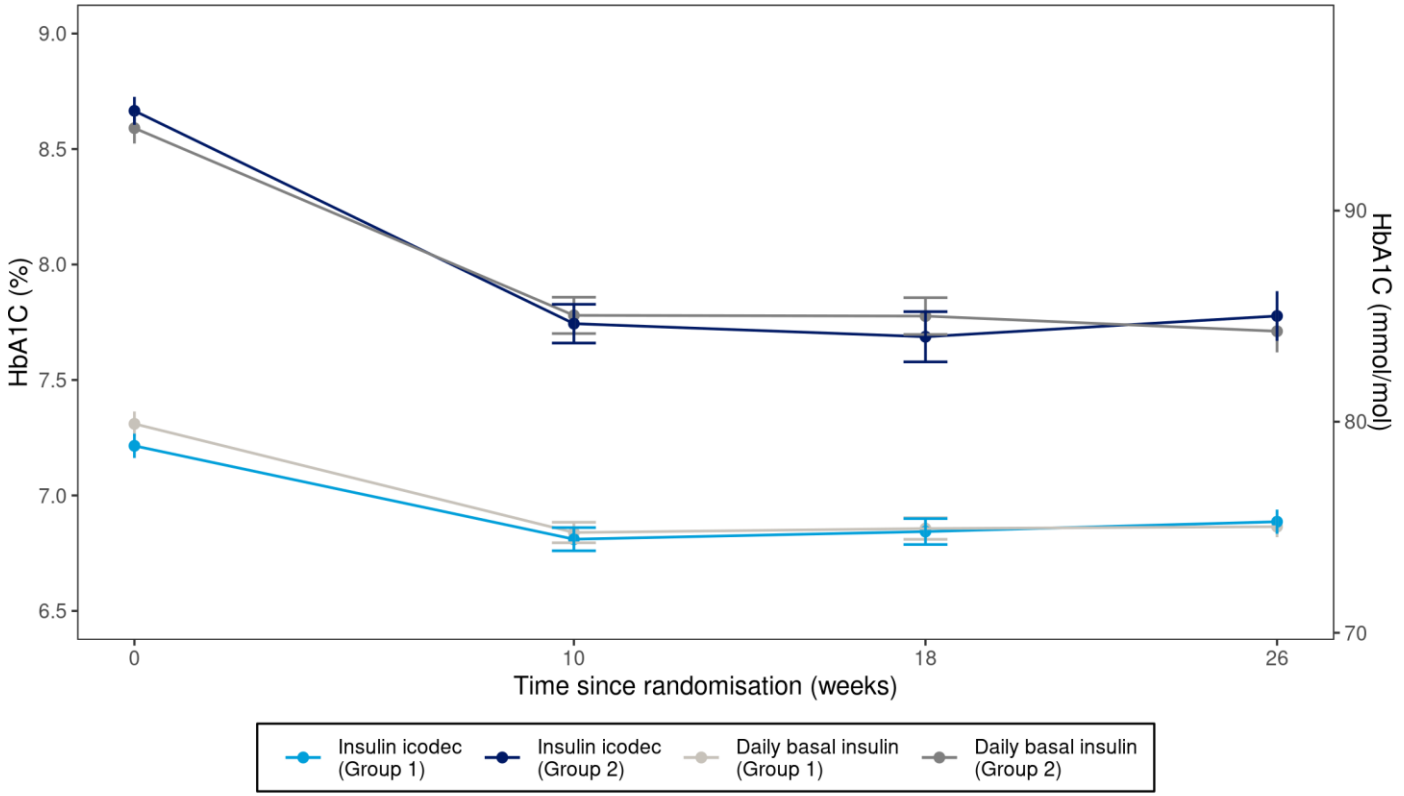
6.4.15 Subjects by grouping based on stratification - summary - ONWARDS 6 - full analysis set

	Insulin icodec		Daily basal insulin		Total	
	N	(%)	N	(%)	N	(%)
Number of subjects	290		292		582	
Group 1 (Insulin icodec: planned one-time additional 50% dose)	215	(74.1)	218	(74.7)	433	(74.4)
Group 2 (Insulin icodec: planned one-time additional 100% dose)	75	(25.9)	74	(25.3)	149	(25.6)

N: Number of subjects, %: Percentage of subjects, Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm). Daily basal insulin: IDeg. Data from main part of ONWARDS 6.

adsl.xpt; variable(s): TR01PG1 STRATA1 STRATA2; criteria: STUDYID == "NN1436-4625" & FASFL == "Y"
nn1436/nn1436-ise/submission_20221031_er
03NOV2022:23:13:43 - tslstratasum/tslstratasumfas.txt

6.4.16 HbA1c by treatment week and grouping based on stratification - ONWARDS 6 - in-trial - mean plot - full analysis set

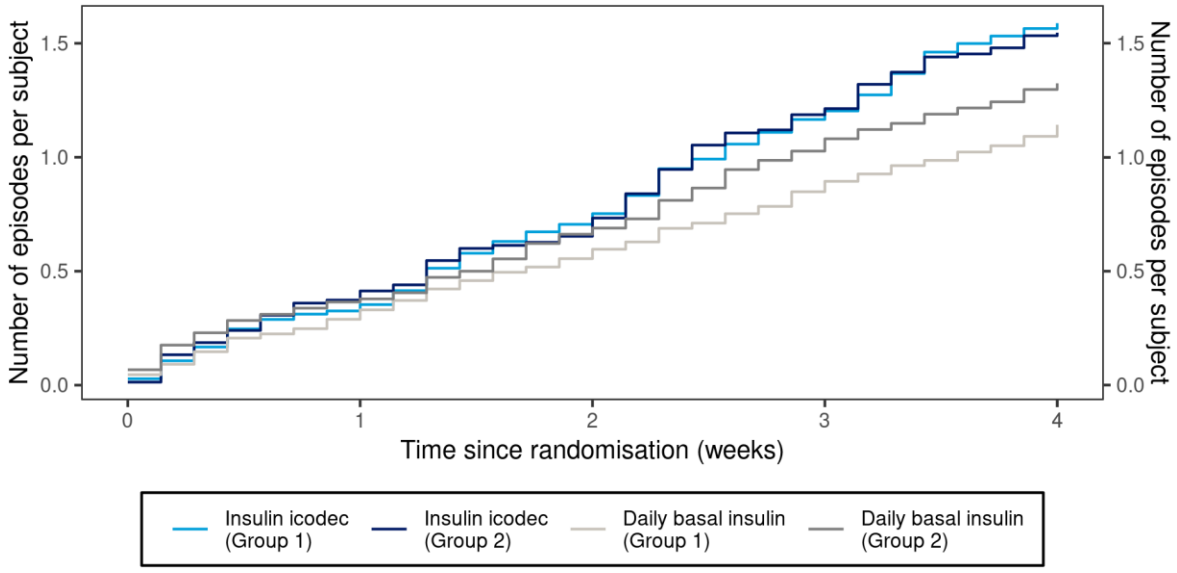


Observed data including data obtained after premature treatment discontinuation. Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm), Legend: Mean (symbol) and mean ± standard error to the mean (error bars). HbA1c: Haemoglobin A1c. Daily basal insulin: IDeg. Data from main part of ONWARDS 6.

adlb.xpt; variable(s): PARAMCD STRATA1 STRATA2 TRPG1 AVISIT2N AVAL; criteria: FASFL == "Y" & STUDYID == "NN1436-4625" & PARAMCD %in% c("HBA1CB", "HBA1CB2") & AVISITN != 100 & ANELFL == "Y" & ANL01FL == "Y" & DTYPE %in% c("", "LVPD")

nn1436/nn1436-ise/submission_20221031_er
04NOV2022:00:55:21 - flbmeanstrata/flbhba1cmeanstratafas.png

6.4.17 Severe (level 3) or clinically significant (level 2) hypoglycaemia by grouping based on stratification - ONWARDS 6 - on-treatment - mean cumulative function - safety analysis set



Observed data. BG: Blood glucose, Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Daily basal insulin: IDeg. Data from main part of ONWARDS 6. Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm).

adsl.xpt; variable(s): TR01AG1 STRATA1 STRATA2 ONTRDURD; criteria: SAFFL == "Y"
adhypo.xpt; variable(s): STDNM POPGRP ASTDY; criteria: SAFFL == "Y" & ACAT4N %in% (2:3) & ASTDY <= 29 & ANELFL == "Y" & STUDYID == "NN1436-4625" & ANL05FL == "Y"

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03NOV2022:23:16:35 - fhypomcfstrata/fhypolev23mcf04ontow6sas.png

6.4.18 Time in range 3.9-10.0 mmol/L (70-180 mg/dL) (%) from week 0 to week 4 by grouping based on stratification - ONWARDS 6 - in-trial - summary - full analysis set

	Insulin icodec N	Insulin icodec Mean (SD)	Daily basal insulin N	Daily basal insulin Mean (SD)
Time in range 3.9-10.0 mmol/L (70-180 mg/dL) (%)				
Group 1 (Insulin icodec: planned one-time additional 50% dose)				
Visit 2 to 4 (Week 0-2)	208	62.96 (15.52)	213	65.97 (14.53)
Visit 4 to 6 (Week 2-4)	211	64.39 (14.79)	209	67.23 (14.21)
Group 2 (Insulin icodec: planned one-time additional 100% dose)				
Visit 2 to 4 (Week 0-2)	70	51.91 (12.08)	67	52.83 (14.57)
Visit 4 to 6 (Week 2-4)	73	52.31 (14.25)	70	53.54 (14.09)

N: Number of subjects, SD: Standard deviation, Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm). Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg. Data from main part of ONWARDS 6.

adcgmen2.xpt; variable(s): PARAMCD STRATA1 STRATA2 TRTP AVISIT2 AVAL; criteria: PARAMCD %in% c("TXIG3910") & AVISIT2N %in% c(400, 600) & ANELFL == "Y" & DTYPE %in% c("") & STUDYID == "NN1436-4625"

nn1436/nn1436-ise/submission_20221031_er
03NOV2022:23:17:49 - tcgmsumstrata/tcgmtirweek04sumintow6fas.txt

6.4.19 Time spent below range from week 0 to week 4 by grouping based on stratification - ONWARDS 6 - in- trial - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)
Time spent < 3.0 mmol/L (54 mg/dL) (%)				
Group 1 (Insulin icodec: planned one-time additional 50% dose)				
Visit 2 to 4 (Week 0-2)	208	0.80 (1.12)	213	0.59 (0.85)
Visit 4 to 6 (Week 2-4)	211	0.88 (1.29)	209	0.59 (1.11)
Group 2 (Insulin icodec: planned one-time additional 100% dose)				
Visit 2 to 4 (Week 0-2)	70	1.02 (1.55)	67	0.80 (1.53)
Visit 4 to 6 (Week 2-4)	73	0.99 (1.54)	70	1.12 (2.30)
Time spent < 3.9 mmol/L (70 mg/dL) (%)				
Group 1 (Insulin icodec: planned one-time additional 50% dose)				
Visit 2 to 4 (Week 0-2)	208	3.48 (3.18)	213	3.06 (3.08)
Visit 4 to 6 (Week 2-4)	211	3.68 (3.40)	209	3.14 (3.12)
Group 2 (Insulin icodec: planned one-time additional 100% dose)				
Visit 2 to 4 (Week 0-2)	70	3.60 (3.86)	67	3.21 (3.95)
Visit 4 to 6 (Week 2-4)	73	3.79 (3.74)	70	3.57 (4.41)

N: Number of subjects, SD: Standard deviation, Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm). Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg. Data from main part of ONWARDS 6.

adcgmen2.xpt; variable(s): PARAMCD STRATA1 STRATA2 TRTP AVISIT2 AVAL; criteria: PARAMCD %in% c("TLXIG39", "TXIG30") & AVISIT2N %in% c(400, 600) & ANELFL == "Y" & DTYPE %in% c("") & STUDYID == "NN1436-4625"

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03NOV2022:23:17:57 - tcgmsumstrata/tcgmtbrweek04sumintow6fas.txt

6.4.20 Time spent above range from week 0 to week 4 by grouping based on stratification - ONWARDS 6 - in- trial - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)
Time spent > 10.0 mmol/L (180 mg/dL) (%)				
Group 1 (Insulin icodec: planned one-time additional 50% dose)				
Visit 2 to 4 (Week 0-2)	208	33.56 (16.02)	213	30.97 (15.40)
Visit 4 to 6 (Week 2-4)	211	31.93 (15.23)	209	29.64 (14.69)
Group 2 (Insulin icodec: planned one-time additional 100% dose)				
Visit 2 to 4 (Week 0-2)	70	44.49 (13.22)	67	43.95 (16.04)
Visit 4 to 6 (Week 2-4)	73	43.90 (15.54)	70	42.89 (15.46)
Time spent > 13.9 mmol/L (250 mg/dL) (%)				
Group 1 (Insulin icodec: planned one-time additional 50% dose)				
Visit 2 to 4 (Week 0-2)	208	10.77 (10.00)	213	8.72 (8.64)
Visit 4 to 6 (Week 2-4)	211	9.94 (8.67)	209	8.16 (7.84)
Group 2 (Insulin icodec: planned one-time additional 100% dose)				
Visit 2 to 4 (Week 0-2)	70	17.33 (11.15)	67	17.69 (12.94)
Visit 4 to 6 (Week 2-4)	73	17.62 (12.18)	70	16.57 (12.05)

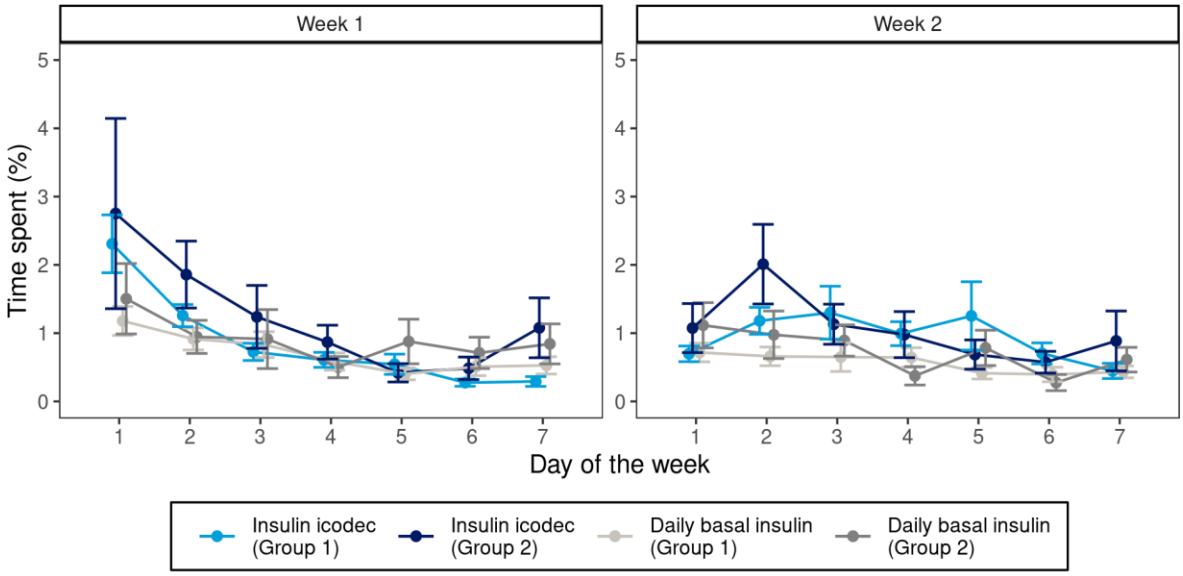
N: Number of subjects, SD: Standard deviation, Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm). Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg. Data from main part of ONWARDS 6.

adcgmen2.xpt; variable(s): PARAMCD STRATA1 STRATA2 TRTP AVISIT2 AVAL; criteria: PARAMCD %in% c("HXIGX100", "HXIGG139") & AVISIT2N %in% c(400, 600) & ANELFL == "Y" & DTYPE %in% c("") & STUDYID == "NN1436-4625"

nn1436/nn1436-ise/submission_20221031_er

03NOV2022:23:18:02 - tcgmsumstrata/tcgmtarweek04sumintow6fas.txt

6.4.21 Time spent < 3.0 mmol/L (54 mg/dL) by day by grouping based on stratification - week 1 and 2 - ONWARDS 6 - in-trial - summary - full analysis set

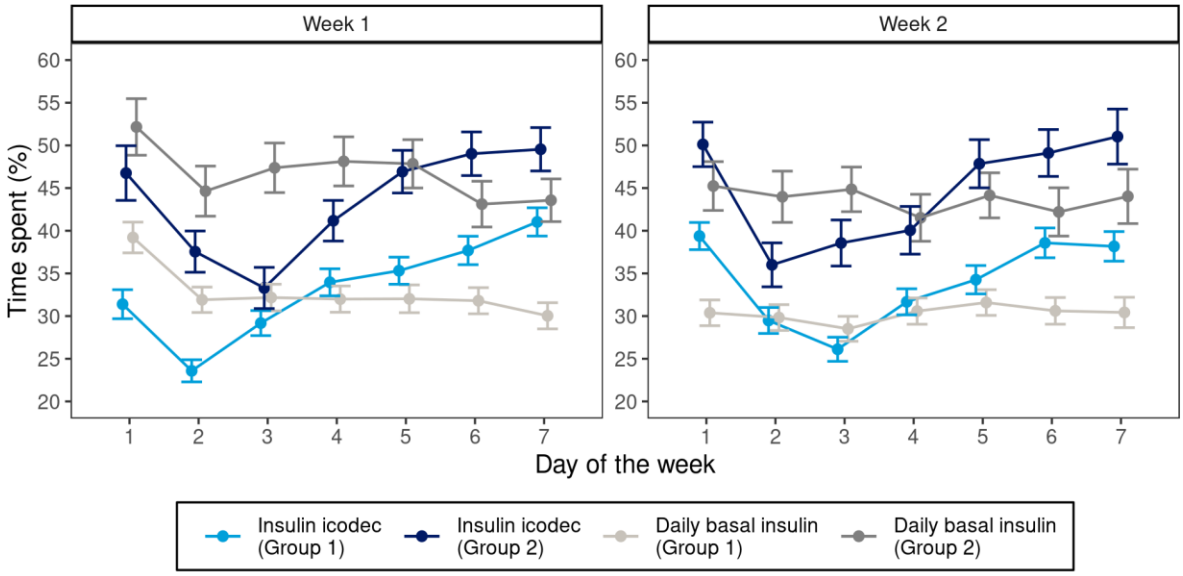


Legend: Mean (symbol) and mean ± standard error to the mean (error bars). Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm). Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg. Data from main part of ONWARDS 6.

adsl.xpt; variable(s): TRTP STRATA1 STRATA2 TRTSDT; criteria: STUDYID == "NN1436-4625" & FASFL == "Y"
adcgm.xpt; variable(s): ADT AVAL; criteria: STUDYID == "NN1436-4625" & FASFL == "Y" & AVISIT2N == 400 & TRTSDT <= ADT & ADT <= TRTSDT + 14 & AVAL < 54 & !is.na(AVISIT) & LBSTAT != "NOT DONE"

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04NOV2022:04:32:41 - fcgmdaystrata/fcgmtbr30meandayfas.png

6.4.22 Time spent > 10.0 mmol/L (180 mg/dL) by day by grouping based on stratification - week 1 and 2 - ONWARDS 6 - in-trial - summary - full analysis set

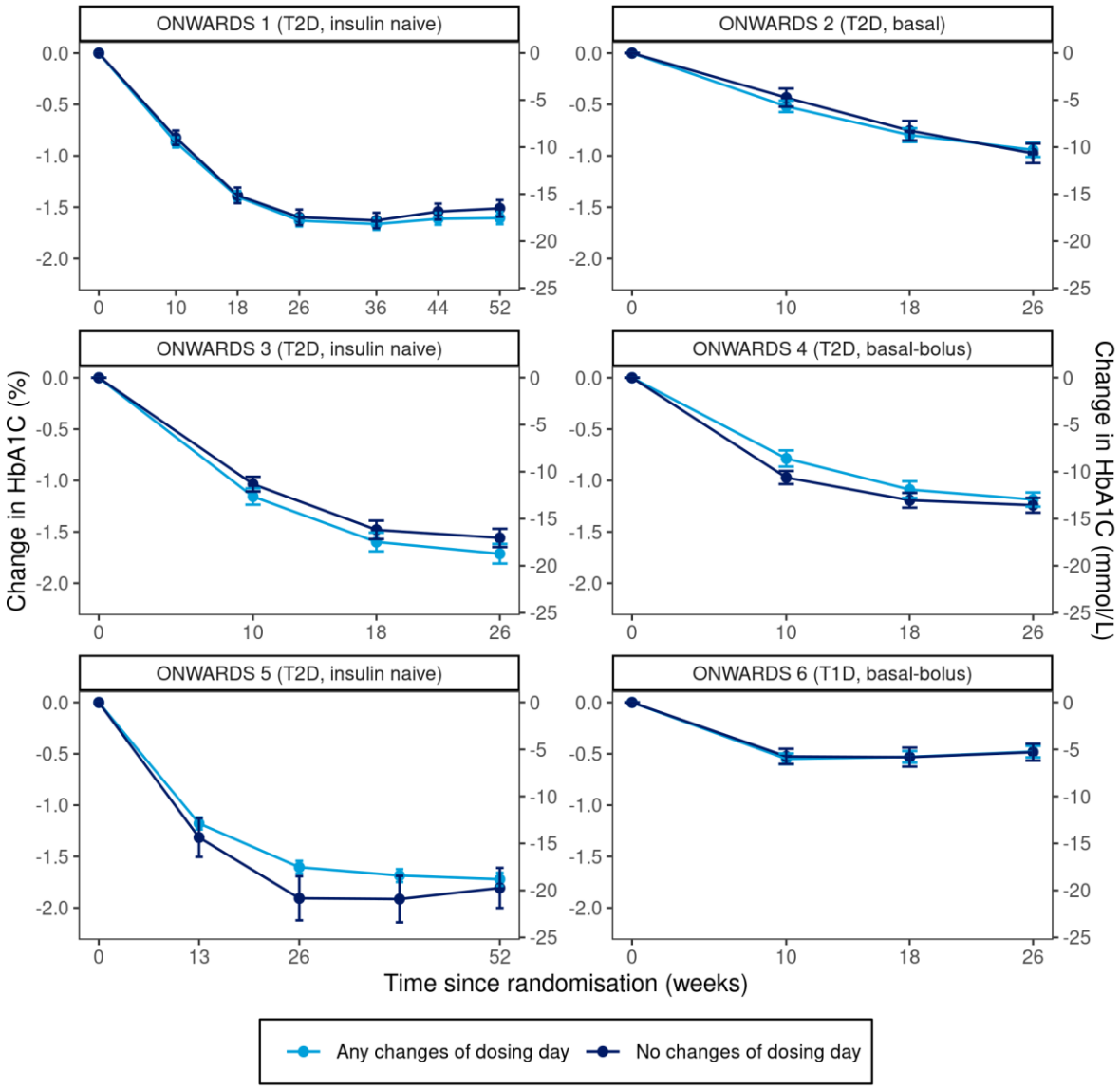


Legend: Mean (symbol) and mean ± standard error to the mean (error bars). Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm). Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg. Data from main part of ONWARDS 6.

adsl.xpt; variable(s): TRTP STRATA1 STRATA2 TRTSDT; criteria: STUDYID == "NN1436-4625" & FASFL == "Y"
adcgm.xpt; variable(s): ADT AVAL; criteria: STUDYID == "NN1436-4625" & FASFL == "Y" & AVISIT2N == 400 & TRTSDT <= ADT & ADT <= TRTSDT + 14 & AVAL > 180 & !is.na(AVISIT) & LBSTAT != "NOT DONE"

nn1436/nn1436-ise/submission_20221031_er
04NOV2022:04:32:51 - fcgmdaystrata/fcgmtar100meandayfas.png

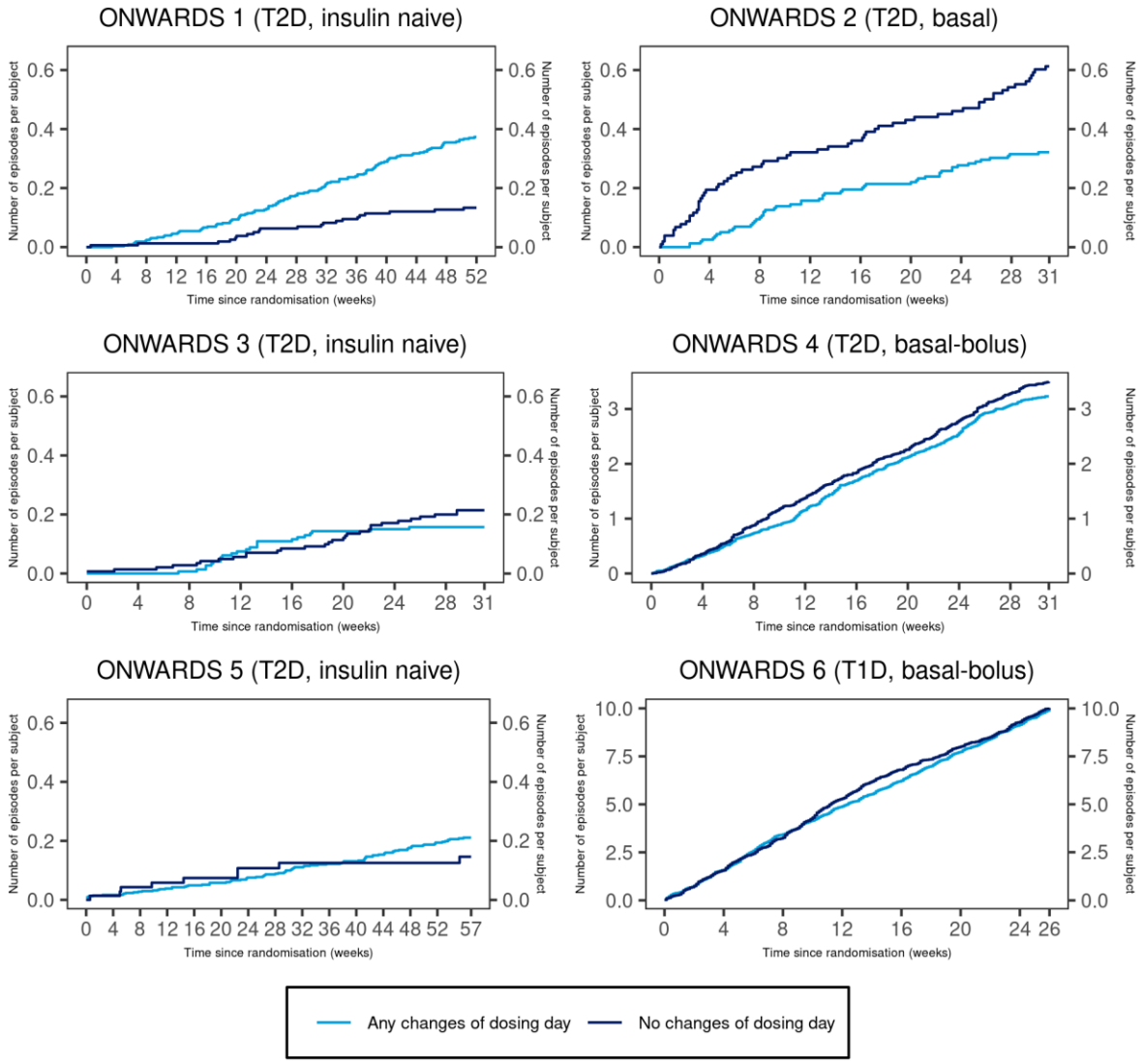
6.4.23 HbA1c by treatment week and change of dosing day status - insulin icodec - change from baseline - in-trial - mean plot - full analysis set



Observed data including data obtained after premature treatment discontinuation. T1D: Type 1 diabetes, T2D: Type 2 diabetes, Legend: Mean (symbol) and mean ± standard error to the mean (error bars). HbA1c: Haemoglobin A1c. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. Change of the dosing day of weekly insulin icodec up to +/-3 days is allowed in ONWARDS 1-5.

adsl.xpt; variable(s): NA; criteria: FASFL == "Y" & TRT01AN == 1
adec.xpt; variable(s): DAYSDEV FLEXFL; criteria: SAFFL == "Y" & TRTAN == 1 & ANL02FL == "Y" & PARAMCD == "I287COMP" & COMPDOS == "ACTUAL" & (STUDYID != "NN1436-4479" | (STUDYID == "NN1436-4479" & ECDOSFRQ == "EVERY WEEK")) & ((STUDYID %in% c("NN1436-4477", "NN1436-4625") & ADT <= MONTEDT) | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ADT <= TRTEDT)) & FLEXFL == "Y" & DAYSDEV <= 3 & DAYSDEV >= -3
adlb.xpt; variable(s): PARAMCD STDNM POPGRP TRPG1 AVISIT2N CHG; criteria: FASFL == "Y" & TRTPN == 1 & PARAMCD %in% c("HBA1CB", "HBA1CB2") & AVISITN != 100 & ANELFL == "Y" & ANL01FL == "Y" & DTYPE %in% c("", "LVPD")
nn1436/nn1436-ise/submission_20221031_er
04NOV2022:00:55:30 - flbmeanmissdose/flbhba1cmeanchgdosefas.png

6.4.24 Severe (level 3) or clinically significant (level 2) hypoglycaemia by change of dosing day status - insulin icodec - on-treatment - mean cumulative function - safety analysis set

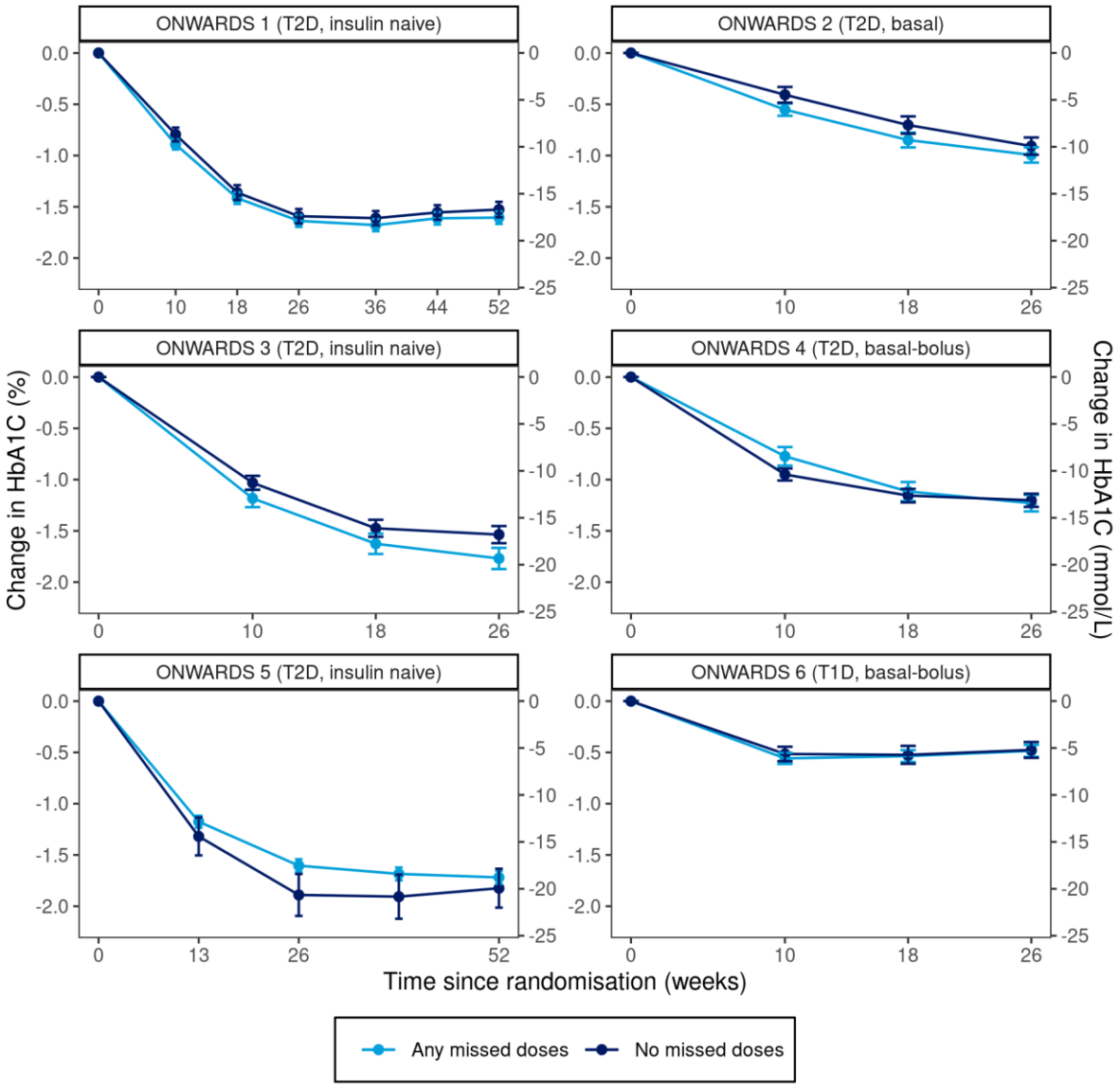


Observed data. BG: Blood glucose, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. Change of the dosing day of weekly insulin icodec up to +/-3 days is allowed in ONWARDS 1-5.

adsl.xpt; variable(s): STDNM POPGRP ONTRDURD; criteria: SAFFL == "Y" & TRT01AN == 1
adec.xpt; variable(s): DAYSDEV FLEXFL; criteria: SAFFL == "Y" & TRTAN == 1 & ANL02FL == "Y" & PARAMCD == "I287COMP" & COMPDOS == "ACTUAL" & (STUDYID != "NN1436-4479" | (STUDYID == "NN1436-4479" & ECDOSFRQ == "EVERY WEEK")) & ((STUDYID %in% c("NN1436-4477", "NN1436-4625") & ADT <= MONTEDT) | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ADT <= TRTEDT)) & FLEXFL == "Y" & DAYSDEV <= 3 & DAYSDEV >= -3
adhypo.xpt; variable(s): STDNM POPGRP ASTDY; criteria: SAFFL == "Y" & TRTAN == 1 & ACAT4N %in% (2:3) & ANELFL == "Y" & ((STUDYID %in% c("NN1436-4477", "NN1436-4625") & ANL05FL == "Y") | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ANL02FL == "Y"))

nn1436/nn1436-ise/submission_20221031_er
04NOV2022:00:28:26 - fhypomcfmissdose/fhypolev23mcfchgdoseontsas.png

6.4.25 HbA1c by treatment week and missed dose status - insulin icodec - change from baseline - in-trial - mean plot - full analysis set



Observed data including data obtained after premature treatment discontinuation. T1D: Type 1 diabetes, T2D: Type 2 diabetes, Legend: Mean (symbol) and mean ± standard error to the mean (error bars). HbA1c: Haemoglobin A1c. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. A missed dose is defined as a dose that was taken with up to +3 days delay according to the weekly schedule.

adsl.xpt; variable(s): NA; criteria: FASFL == "Y" & TRT01AN == 1

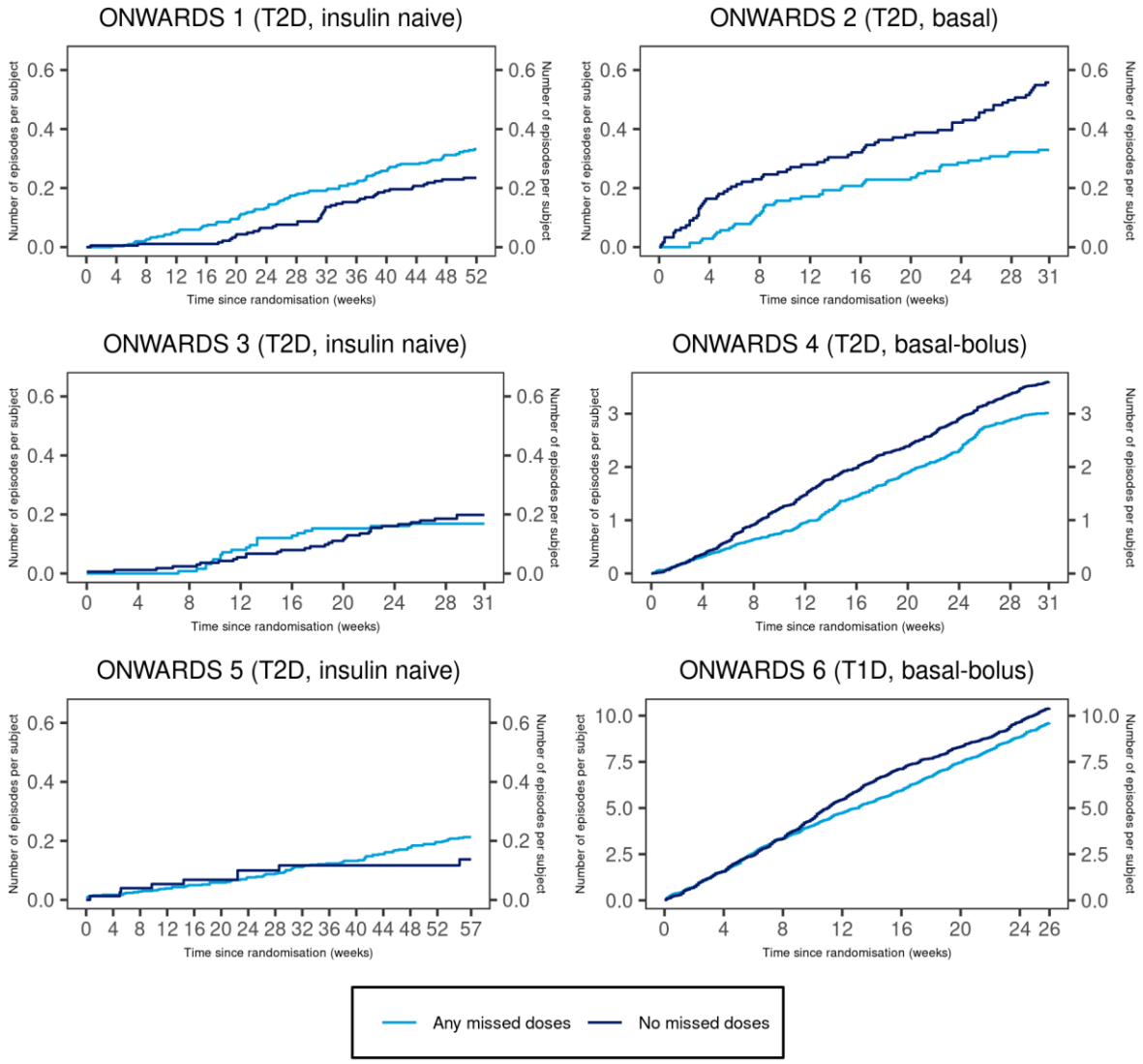
adec.xpt; variable(s): DAYSDEV FLEXFL; criteria: SAFFL == "Y" & TRTAN == 1 & ANL02FL == "Y" & PARAMCD == "I287COMP" & COMPDOS == "ACTUAL" & (STUDYID != "NN1436-4479" | (STUDYID == "NN1436-4479" & ECDOSFRQ == "EVERY WEEK")) & ((STUDYID %in% c("NN1436-4477", "NN1436-4625") & ADT <= MONTEDT) | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ADT <= TRTEDT)) & FLEXFL == "Y" & DAYSDEV <= 3 & DAYSDEV > 0

adlb.xpt; variable(s): PARAMCD STDNM POPGRP TRPG1 AVISIT2N CHG; criteria: FASFL == "Y" & TRTPN == 1 & PARAMCD %in% c("HBA1CB", "HBA1CB2") & AVISITN != 100 & ANELFL == "Y" & ANL01FL == "Y" & DTYPE %in% c("", "LVPD")

nn1436/nn1436-ise/submission_20221031_er

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6.4.26 Severe (level 3) or clinically significant (level 2) hypoglycaemia by missed dose status - insulin icodec - on-treatment - mean cumulative function - safety analysis set



Observed data. BG: Blood glucose, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. A missed dose is defined as a dose that was taken with up to +3 days delay according to the weekly schedule.

adsl.xpt; variable(s): STDNM POPGRP ONTRDURD; criteria: SAFFL == "Y" & TRT01AN == 1
adec.xpt; variable(s): DAYSDEV FLEXFL; criteria: SAFFL == "Y" & TRTAN == 1 & ANL02FL == "Y" & PARAMCD == "I287COMP" & COMPDOS == "ACTUAL" & (STUDYID != "NN1436-4479" | (STUDYID == "NN1436-4479" & ECDOSFRQ == "EVERY WEEK")) & ((STUDYID %in% c("NN1436-4477", "NN1436-4625") & ADT <= MONTEDT) | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ADT <= TRTEDT)) & FLEXFL == "Y" & DAYSDEV <= 3 & DAYSDEV > 0
adhypo.xpt; variable(s): STDNM POPGRP ASTDY; criteria: SAFFL == "Y" & TRTAN == 1 & ACAT4N %in% (2:3) & ANELFL == "Y" & ((STUDYID %in% c("NN1436-4477", "NN1436-4625") & ANL05FL == "Y") | (!(STUDYID %in% c("NN1436-4477", "NN1436-4625")) & ANL02FL == "Y"))

nn1436/nn1436-ise/submission_20221031_er
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インスリン イコデク（遺伝子組換え）

2.7.3.6 付録
5. 日本の推奨用法・用量に関するデータ
（日本人被験者を含む第３相試験）

ノボ ノルディスク ファーマ株式会社

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6.5 Analyses across phase 3 trials including Japanese subjects related to doing recommendation for Japan

6.5.1 First dose of insulin icodec (U) - ONWARDS 1 - summary - safety analysis set

	Insulin icodec	
	N	(%)
Number of subjects	492	
First dose (unit)		
N	492	(100.0)
40	1	(0.2)
50	5	(1.0)
60	2	(0.4)
70	484	(98.4)

N: Number of subjects, %: Percentage of subjects.

adsl.xpt; variable(s): FICODS; criteria: (SAFFL == "Y" & TR01AG1 == "Insulin icodec") & (STDNM == "ONWARDS 1")
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:48 - tsumfdose/tsumfdoseow1.txt

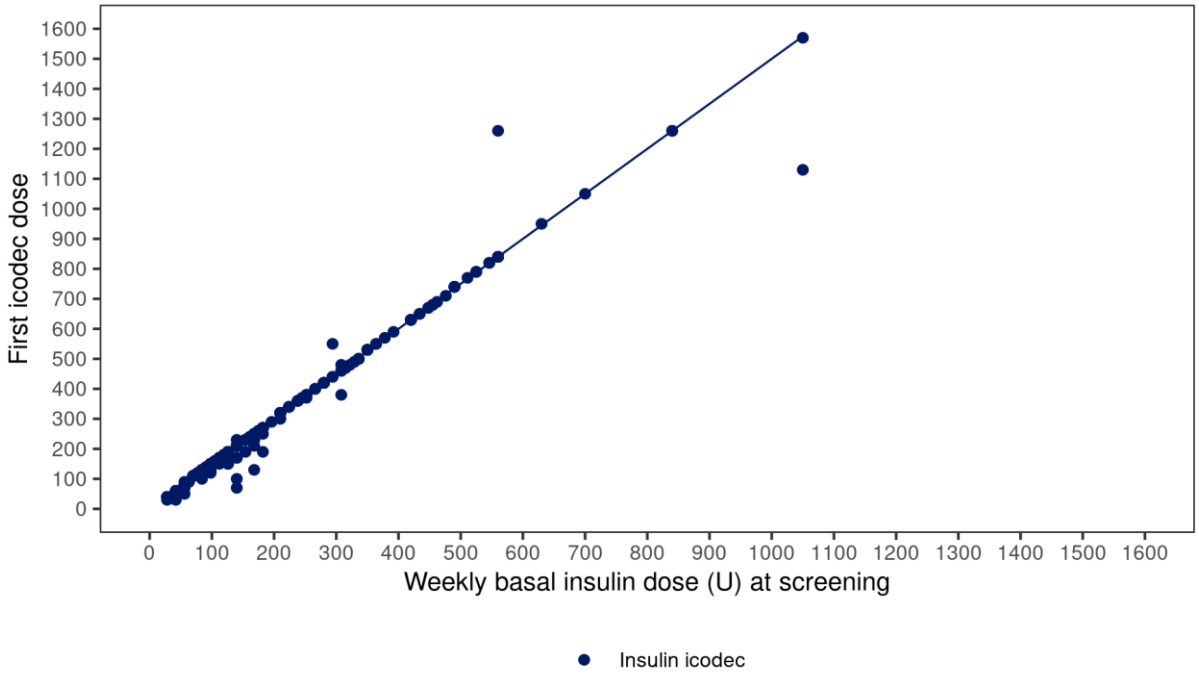
6.5.2 First dose of insulin icodec (U) - ONWARDS 1, Japanese subjects - summary - safety analysis set

	Insulin icodec	
	N	(%)
Number of subjects	78	
First dose (unit)		
N	78	(100.0)
40	1	(1.3)
50	5	(6.4)
60	2	(2.6)
70	70	(89.7)

N: Number of subjects, %: Percentage of subjects.

adsl.xpt; variable(s): FICODS; criteria: (SAFFL == "Y" & TR01AG1 == "Insulin icodec") & (STDNM == "ONWARDS 1" & COUNTRY == "JPN")
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:50 - tsumfdose/tsumfdoseow1jp.txt

6.5.3 First dose of insulin icodec (U) against weekly basal insulin dose at screening (U) - ONWARDS 2 - scatter plot - safety analysis set

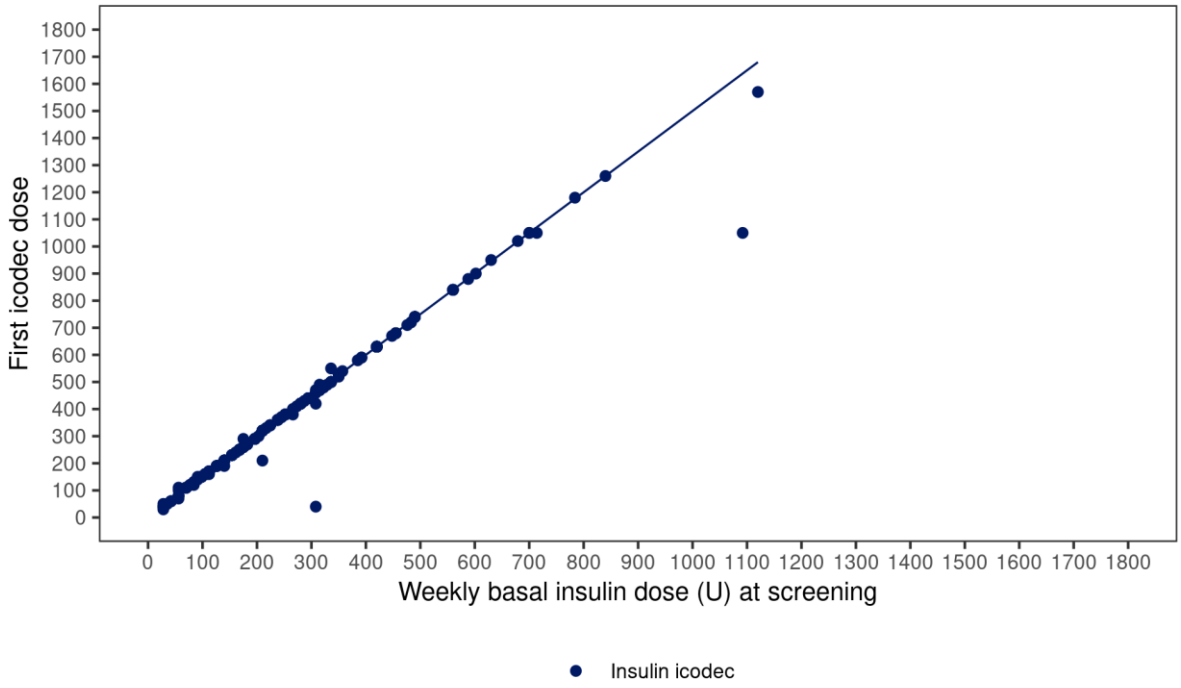


Safety analysis set. Observed data. Reference line: Theoretical dose for one-time additional 50% dose.

adsl.xpt; variable(s): STDNM TR01AG1 TOTBASDS FICODS; criteria: SAFFL == "Y" & STDNM == "ONWARDS 2" & TR01AG1 == "Insulin icodec"

nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:40 - fscafdose/fscadoseow2.png

6.5.4 First dose of insulin icodec (U) against weekly basal insulin dose at screening (U) - ONWARDS 4 - scatter plot - safety analysis set

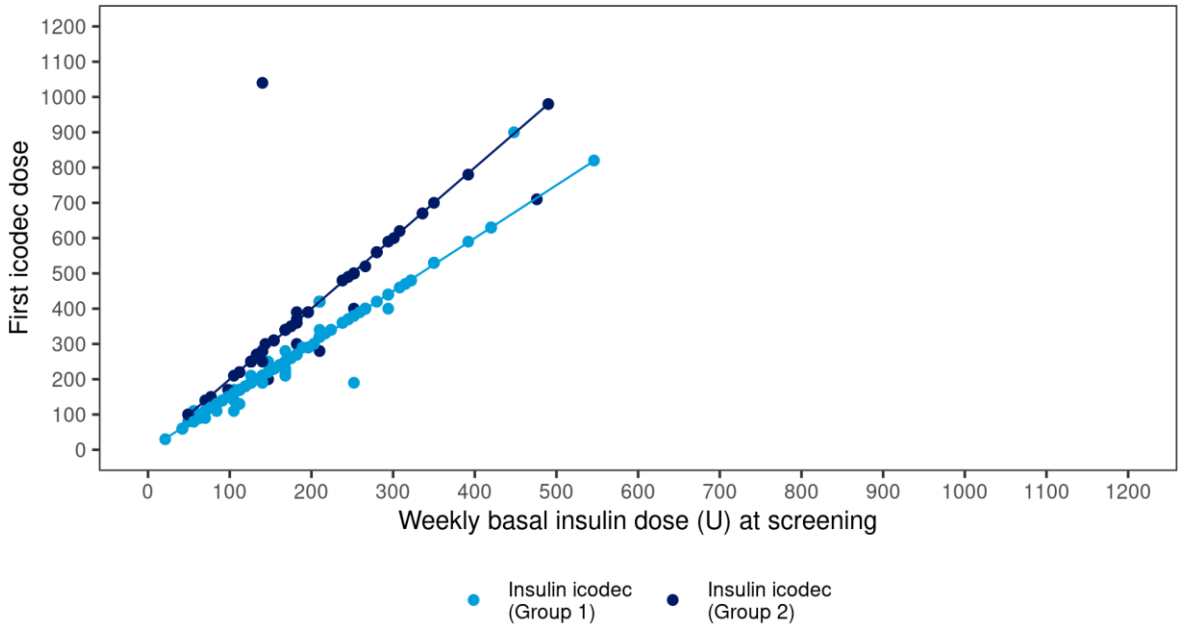


Safety analysis set. Observed data. Reference line: Theoretical dose for one-time additional 50% dose.

adsl.xpt; variable(s): STDNM TR01AG1 TOTBASDS FICODS; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4" & TR01AG1 == "Insulin icodec"

nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:42 - fscafdose/fscadoseow4.png

6.5.5 First dose of insulin icodec (U) against weekly basal insulin dose at screening (U) - ONWARDS 6 - scatter plot - safety analysis set



Safety analysis set. Observed data. Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm), Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm). Reference lines: Theoretical dose for one-time additional 50% and 100% dose.

adsl.xpt; variable(s): STDNM STRATA1 STRATA2 TR01AG1 TOTBASDS FICODS; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & TR01AG1 == "Insulin icodec"

nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:44 - fscafdose/fscadoseow6.png

6.5.6 Actual weekly total basal insulin dose from week 50 to week 52 - ONWARDS 1 (main part) - main-on- treatment - summary - safety analysis set

	Insulin icodec		IGlar	
	N	(%)	N	(%)
Number of subjects	492		492	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	472	(100.0)	477	(100.0)
>=0 - <=560	436	(92.4)	444	(93.1)
>=0 - <=70	39	(8.3)	29	(6.1)
>70 - <=140	90	(19.1)	83	(17.4)
>140 - <=210	101	(21.4)	106	(22.2)
>210 - <=280	73	(15.5)	86	(18.0)
>280 - <=350	52	(11.0)	49	(10.3)
>350 - <=420	38	(8.1)	34	(7.1)
>420 - <=490	29	(6.1)	38	(8.0)
>490 - <=560	14	(3.0)	19	(4.0)
>560 - <=630	11	(2.3)	9	(1.9)
>630 - <=700	8	(1.7)	9	(1.9)
>700 - <=770	8	(1.7)	6	(1.3)
>770 - <=840	4	(0.8)	4	(0.8)
>840 - <=910	3	(0.6)	3	(0.6)
>910 - <=980	2	(0.4)	1	(0.2)
>980 - <=1050	0		1	(0.2)
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 1"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 1" & ANELFL == "Y" & PARAMCD == "IDBAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:54 - tsumldose/tsumlbasdoseow1.txt

6.5.7 Actual weekly total basal insulin dose from week 50 to week 52 - ONWARDS 1 (main part), Japanese subjects - main-on-treatment - summary - safety analysis set

	Insulin icodec		IGlar	
	N	(%)	N	(%)
Number of subjects	78		86	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	77	(100.0)	84	(100.0)
>=0 - <=560	76	(98.7)	84	(100.0)
>=0 - <=70	18	(23.4)	11	(13.1)
>70 - <=140	23	(29.9)	28	(33.3)
>140 - <=210	17	(22.1)	23	(27.4)
>210 - <=280	8	(10.4)	13	(15.5)
>280 - <=350	6	(7.8)	4	(4.8)
>350 - <=420	2	(2.6)	4	(4.8)
>420 - <=490	2	(2.6)	1	(1.2)
>490 - <=560	0		0	
>560 - <=630	0		0	
>630 - <=700	0		0	
>700 - <=770	0		0	
>770 - <=840	1	(1.3)	0	
>840 - <=910	0		0	
>910 - <=980	0		0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 1" & COUNTRY == "JPN"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 1" & COUNTRY == "JPN" & ANELFL == "Y" & PARAMCD == "IDBAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:57 - tsumldose/tsumlbasdoseow1jp.txt

6.5.8 Actual weekly total basal insulin dose from week 24 to week 26 - ONWARDS 2 - on-treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	262		263	
Average weekly insulin dose last 2 weeks of treatment (U)				
N	255	(100.0)	252	(100.0)
>=0 - <=560	221	(86.7)	221	(87.7)
>=0 - <=70	20	(7.8)	12	(4.8)
>70 - <=140	44	(17.3)	39	(15.5)
>140 - <=210	36	(14.1)	46	(18.3)
>210 - <=280	31	(12.2)	43	(17.1)
>280 - <=350	38	(14.9)	28	(11.1)
>350 - <=420	15	(5.9)	18	(7.1)
>420 - <=490	20	(7.8)	14	(5.6)
>490 - <=560	17	(6.7)	21	(8.3)
>560 - <=630	6	(2.4)	10	(4.0)
>630 - <=700	11	(4.3)	5	(2.0)
>700 - <=770	6	(2.4)	10	(4.0)
>770 - <=840	5	(2.0)	1	(0.4)
>840 - <=910	4	(1.6)	1	(0.4)
>910 - <=980	2	(0.8)	0	
>980 - <=1050	0		2	(0.8)
>1050	0		2	(0.8)

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 2"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 2" & ANELFL == "Y" & PARAMCD == "IDAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:00 - tsumldose/tsumlbasdoseow2.txt

6.5.9 Actual weekly total basal insulin dose from week 24 to week 26 - ONWARDS 2, Japanese subjects - on- treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	51		49	
Average weekly insulin dose last 2 weeks of treatment (U)				
N	50	(100.0)	48	(100.0)
>=0 - <=560	48	(96.0)	45	(93.8)
>=0 - <=70	6	(12.0)	6	(12.5)
>70 - <=140	22	(44.0)	10	(20.8)
>140 - <=210	8	(16.0)	12	(25.0)
>210 - <=280	4	(8.0)	7	(14.6)
>280 - <=350	3	(6.0)	4	(8.3)
>350 - <=420	2	(4.0)	3	(6.2)
>420 - <=490	2	(4.0)	2	(4.2)
>490 - <=560	1	(2.0)	1	(2.1)
>560 - <=630	0		1	(2.1)
>630 - <=700	1	(2.0)	0	
>700 - <=770	1	(2.0)	2	(4.2)
>770 - <=840	0		0	
>840 - <=910	0		0	
>910 - <=980	0		0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 2" & COUNTRY == "JPN"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 2" & COUNTRY == "JPN" & ANELFL == "Y" & PARAMCD == "IDAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:02 - tsumldose/tsumlbasdoseow2jp.txt

6.5.10 Actual weekly total basal insulin dose from week 24 to week 26 - ONWARDS 4 - on-treatment - summary - safety analysis set

	Insulin icodec		IGlar	
	N	(%)	N	(%)
Number of subjects	291		291	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	261	(100.0)	264	(100.0)
>=0 - <=560	208	(79.7)	228	(86.4)
>=0 - <=70	6	(2.3)	6	(2.3)
>70 - <=140	22	(8.4)	35	(13.3)
>140 - <=210	34	(13.0)	34	(12.9)
>210 - <=280	31	(11.9)	51	(19.3)
>280 - <=350	34	(13.0)	31	(11.7)
>350 - <=420	31	(11.9)	34	(12.9)
>420 - <=490	31	(11.9)	21	(8.0)
>490 - <=560	19	(7.3)	16	(6.1)
>560 - <=630	19	(7.3)	6	(2.3)
>630 - <=700	12	(4.6)	12	(4.5)
>700 - <=770	8	(3.1)	8	(3.0)
>770 - <=840	4	(1.5)	5	(1.9)
>840 - <=910	3	(1.1)	1	(0.4)
>910 - <=980	2	(0.8)	1	(0.4)
>980 - <=1050	2	(0.8)	1	(0.4)
>1050	3	(1.1)	2	(0.8)

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4" & ANELFL == "Y" & PARAMCD == "IDBAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:05 - tsumldose/tsumlbasdoseow4.txt

6.5.11 Actual weekly total basal insulin dose from week 24 to week 26 - ONWARDS 4, Japanese subjects - on- treatment - summary - safety analysis set

	Insulin icodec		IGlar	
	N	(%)	N	(%)
Number of subjects	44		41	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	42	(100.0)	41	(100.0)
>=0 - <=560	39	(92.9)	40	(97.6)
>=0 - <=70	6	(14.3)	4	(9.8)
>70 - <=140	8	(19.0)	12	(29.3)
>140 - <=210	11	(26.2)	9	(22.0)
>210 - <=280	6	(14.3)	6	(14.6)
>280 - <=350	3	(7.1)	3	(7.3)
>350 - <=420	2	(4.8)	4	(9.8)
>420 - <=490	3	(7.1)	0	
>490 - <=560	0		2	(4.9)
>560 - <=630	2	(4.8)	0	
>630 - <=700	0		0	
>700 - <=770	0		0	
>770 - <=840	1	(2.4)	1	(2.4)
>840 - <=910	0		0	
>910 - <=980	0		0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4" & COUNTRY == "JPN"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4" & COUNTRY == "JPN" & ANELFL == "Y" & PARAMCD == "IDBAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:08 - tsumldose/tsumlbasdoseow4jp.txt

6.5.12 Actual weekly total insulin dose from week 24 to week 26 - ONWARDS 4 - on-treatment - summary - safety analysis set

	Insulin icodec		IGlar	
	N	(%)	N	(%)
Number of subjects	291		291	
Average weekly insulin dose last 2 weeks of treatment (U)				
N	273	(100.0)	266	(100.0)
>=0 - <=560	141	(51.6)	128	(48.1)
>=0 - <=70	1	(0.4)	0	
>70 - <=140	5	(1.8)	0	
>140 - <=210	15	(5.5)	14	(5.3)
>210 - <=280	22	(8.1)	15	(5.6)
>280 - <=350	33	(12.1)	17	(6.4)
>350 - <=420	23	(8.4)	31	(11.7)
>420 - <=490	28	(10.3)	26	(9.8)
>490 - <=560	14	(5.1)	25	(9.4)
>560 - <=630	23	(8.4)	26	(9.8)
>630 - <=700	18	(6.6)	22	(8.3)
>700 - <=770	11	(4.0)	14	(5.3)
>770 - <=840	19	(7.0)	10	(3.8)
>840 - <=910	11	(4.0)	11	(4.1)
>910 - <=980	10	(3.7)	12	(4.5)
>980 - <=1050	11	(4.0)	10	(3.8)
>1050	29	(10.6)	33	(12.4)

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4" & ANELFL == "Y" & PARAMCD == "IDAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:10 - tsumldose/tsumltotdoseow4.txt

6.5.13 Actual weekly total insulin dose from week 24 to week 26 - ONWARDS 4, Japanese subjects - on- treatment - summary - safety analysis set

	Insulin icodec		IGlar	
	N	(%)	N	(%)
Number of subjects	44		41	
Average weekly insulin dose last 2 weeks of treatment (U)				
N	42	(100.0)	41	(100.0)
>=0 - <=560	30	(71.4)	31	(75.6)
>=0 - <=70	0		0	
>70 - <=140	1	(2.4)	0	
>140 - <=210	7	(16.7)	7	(17.1)
>210 - <=280	6	(14.3)	5	(12.2)
>280 - <=350	8	(19.0)	6	(14.6)
>350 - <=420	6	(14.3)	5	(12.2)
>420 - <=490	2	(4.8)	5	(12.2)
>490 - <=560	0		3	(7.3)
>560 - <=630	3	(7.1)	2	(4.9)
>630 - <=700	4	(9.5)	4	(9.8)
>700 - <=770	1	(2.4)	0	
>770 - <=840	0		1	(2.4)
>840 - <=910	0		1	(2.4)
>910 - <=980	1	(2.4)	1	(2.4)
>980 - <=1050	1	(2.4)	0	
>1050	2	(4.8)	1	(2.4)

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4" & COUNTRY == "JPN"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 4" & COUNTRY == "JPN" & ANELFL == "Y" & PARAMCD == "IDAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:12 - tsumldose/tsumltotdoseow4jp.txt

6.5.14 Actual weekly total basal insulin dose from week 24 to week 26 - ONWARDS 6 (main part) - main-on- treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	290		292	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	263	(100.0)	282	(100.0)
>=0 - <=560	258	(98.1)	281	(99.6)
>=0 - <=70	11	(4.2)	25	(8.9)
>70 - <=140	83	(31.6)	107	(37.9)
>140 - <=210	75	(28.5)	79	(28.0)
>210 - <=280	47	(17.9)	37	(13.1)
>280 - <=350	23	(8.7)	17	(6.0)
>350 - <=420	7	(2.7)	9	(3.2)
>420 - <=490	10	(3.8)	6	(2.1)
>490 - <=560	2	(0.8)	1	(0.4)
>560 - <=630	3	(1.1)	0	
>630 - <=700	1	(0.4)	1	(0.4)
>700 - <=770	1	(0.4)	0	
>770 - <=840	0		0	
>840 - <=910	0		0	
>910 - <=980	0		0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & ANELFL == "Y" & PARAMCD == "IDBAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:13 - tsumldose/tsumlbasdoseow6.txt

6.5.15 Actual weekly total basal insulin dose from week 24 to week 26 - ONWARDS 6 (main part), Japanese subjects - main-on-treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	32		48	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	32	(100.0)	48	(100.0)
>=0 - <=560	32	(100.0)	48	(100.0)
>=0 - <=70	6	(18.8)	12	(25.0)
>70 - <=140	12	(37.5)	25	(52.1)
>140 - <=210	6	(18.8)	6	(12.5)
>210 - <=280	5	(15.6)	4	(8.3)
>280 - <=350	2	(6.2)	1	(2.1)
>350 - <=420	0		0	
>420 - <=490	1	(3.1)	0	
>490 - <=560	0		0	
>560 - <=630	0		0	
>630 - <=700	0		0	
>700 - <=770	0		0	
>770 - <=840	0		0	
>840 - <=910	0		0	
>910 - <=980	0		0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & COUNTRY == "JPN"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & COUNTRY == "JPN" & ANELFL == "Y" & PARAMCD == "IDBAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:15 - tsumldose/tsumlbasdoseow6jp.txt

6.5.16 Actual weekly total insulin dose from week 24 to week 26 - ONWARDS 6 (main part) - main-on-treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	290		292	
Average weekly insulin dose last 2 weeks of treatment (U)				
N	269	(100.0)	282	(100.0)
>=0 - <=560	241	(89.6)	248	(87.9)
>=0 - <=70	1	(0.4)	0	
>70 - <=140	12	(4.5)	13	(4.6)
>140 - <=210	38	(14.1)	37	(13.1)
>210 - <=280	64	(23.8)	64	(22.7)
>280 - <=350	50	(18.6)	59	(20.9)
>350 - <=420	37	(13.8)	46	(16.3)
>420 - <=490	27	(10.0)	18	(6.4)
>490 - <=560	12	(4.5)	11	(3.9)
>560 - <=630	7	(2.6)	13	(4.6)
>630 - <=700	2	(0.7)	7	(2.5)
>700 - <=770	7	(2.6)	6	(2.1)
>770 - <=840	0		1	(0.4)
>840 - <=910	1	(0.4)	2	(0.7)
>910 - <=980	6	(2.2)	4	(1.4)
>980 - <=1050	3	(1.1)	1	(0.4)
>1050	2	(0.7)	0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & ANELFL == "Y" & PARAMCD == "IDAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:18 - tsumldose/tsumltotdoseow6.txt

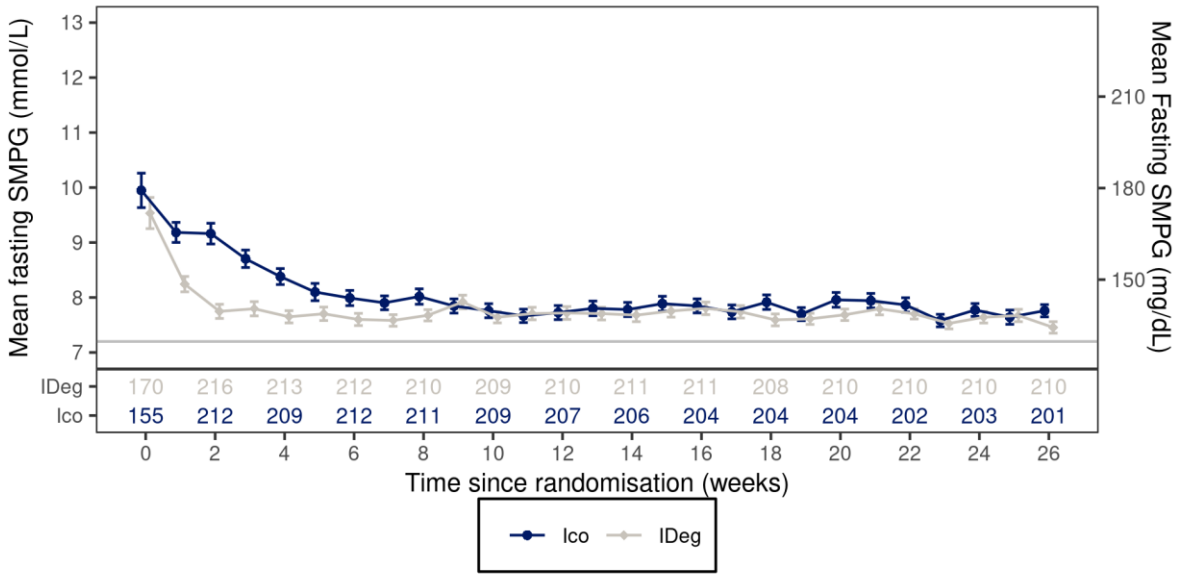
6.5.17 Actual weekly total insulin dose from week 24 to week 26 - ONWARDS 6 (main part), Japanese subjects - main-on-treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	32		48	
Average weekly insulin dose last 2 weeks of treatment (U)				
N	32	(100.0)	48	(100.0)
>=0 - <=560	31	(96.9)	45	(93.8)
>=0 - <=70	0		0	
>70 - <=140	2	(6.2)	3	(6.2)
>140 - <=210	8	(25.0)	14	(29.2)
>210 - <=280	9	(28.1)	10	(20.8)
>280 - <=350	2	(6.2)	11	(22.9)
>350 - <=420	6	(18.8)	4	(8.3)
>420 - <=490	4	(12.5)	2	(4.2)
>490 - <=560	0		1	(2.1)
>560 - <=630	0		2	(4.2)
>630 - <=700	0		1	(2.1)
>700 - <=770	0		0	
>770 - <=840	0		0	
>840 - <=910	0		0	
>910 - <=980	1	(3.1)	0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & COUNTRY == "JPN"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & COUNTRY == "JPN" & ANELFL == "Y" & PARAMCD == "IDAL2W"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:11:20 - tsumldose/tsumltotdoseow6jp.txt

6.5.18 Mean fasting self-measured plasma glucose during the entire week by treatment week - ONWARDS 6 (main part), Group 1 - in-trial - mean plot - full analysis set

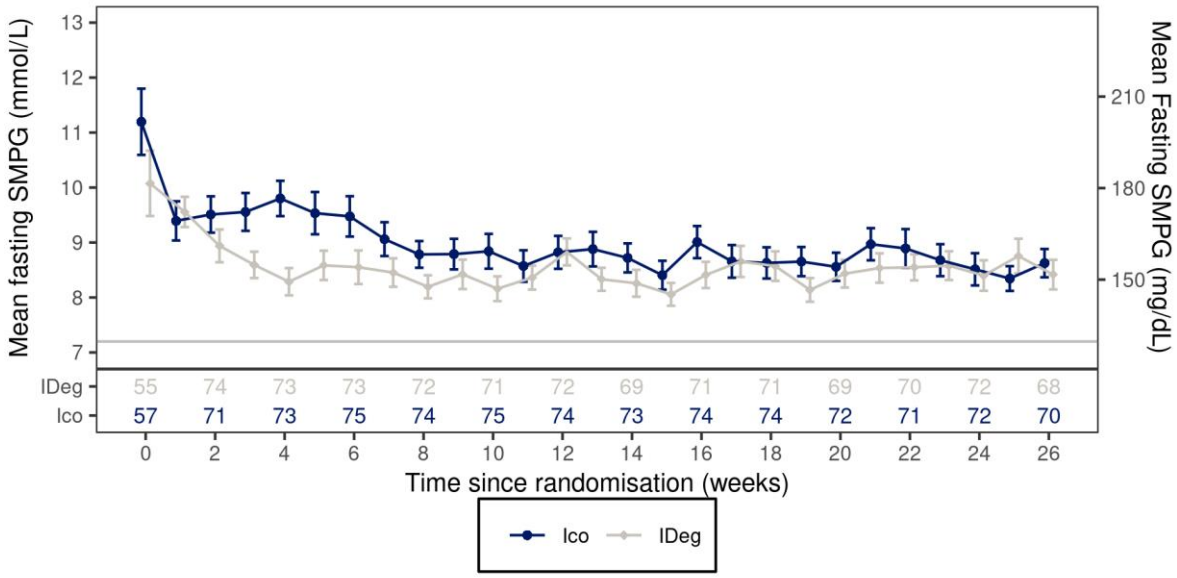


Full analysis set. Observed data including data obtained after premature treatment discontinuation. Number of subjects contributing to the data points appears in the bottom panel. Legend: Mean (symbol) and mean ± standard error to the mean (error bars). SMPG: Self-measured plasma glucose assessed with glucose meter as plasma equivalent values of capillary whole blood glucose. Horizontal line at 7.2 mmol/L. Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm).

adsl.xpt; variable(s): STDNM STRATA1 STRATA2; criteria: FASFL == "Y" & STDNM == "ONWARDS 6" & STRATA1 == "BASAL INSULIN TWICE DAILY /IGLAR U300" | (STRATA1 == "BASAL INSULIN ONCE DAILY" & STRATA2 == "HBA1C <8%")
adsmpgen.xpt; variable(s):AWEEKN PARAMCD PARAM TRTP SUBJID AVAL; criteria: FASFL == "Y" & STDNM == "ONWARDS 6" & PARAMCD %in% c("SMPGXMP3", "SMPGXMP4") & ANELFL == "Y" & ANL01FL == "Y" & !is.na(AWEEKN)

nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:56 - tsumsmpg/fsmpgmeanintow6g50fas.png

6.5.19 Mean fasting self-measured plasma glucose during the entire week by treatment week - ONWARDS 6 (main part), Group 2 - in-trial - mean plot - full analysis set



Full analysis set. Observed data including data obtained after premature treatment discontinuation. Number of subjects contributing to the data points appears in the bottom panel. Legend: Mean (symbol) and mean ± standard error to the mean (error bars). SMPG: Self-measured plasma glucose assessed with glucose meter as plasma equivalent values of capillary whole blood glucose. Horizontal line at 7.2 mmol/L. Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm).

adsl.xpt; variable(s): STDNM STRATA1 STRATA2; criteria: FASFL == "Y" & STDNM == "ONWARDS 6" & STRATA1 == "BASAL INSULIN ONCE DAILY" & STRATA2 == "HBA1C >=8%"
adsmpgen.xpt; variable(s):AWEEKN PARAMCD PARAM TRTP SUBJID AVAL; criteria: FASFL == "Y" & STDNM == "ONWARDS 6" & PARAMCD %in% c("SMPGXMP3", "SMPGXMP4") & ANELFL == "Y" & ANL01FL == "Y" & !is.na(AWEEKN)

nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:59 - tsumsmpg/fsmpgmeanintow6g100fas.png

6.5.20 Hypoglycaemic episodes by classification and month since randomisation - ONWARDS 6 (main part), Group 1 - main-on-treatment - summary - safety analysis set

	Insulin icodec				IDeg			
	N	(%)	E	R	N	(%)	E	R
ONWARDS 6								
Number of subjects	215				218			
PYE (years)	105.17				107.15			
Hypoglycaemia alert value (level 1)	213	(99.1)	8137	7737.07	214	(98.2)	5748	5364.38
0 < to <= 1 month	197	(91.6)	1503	8429.49	194	(89.0)	1267	6962.64
1 < to <= 2 months	195	(91.5)	1567	8818.22	191	(88.0)	1038	5797.53
2 < to <= 3 months	196	(92.5)	1335	7592.79	190	(89.2)	887	4986.94
3 < to <= 4 months	193	(91.9)	1304	7484.07	185	(86.9)	955	5401.68
4 < to <= 5 months	191	(92.3)	1223	7097.25	182	(86.3)	794	4506.39
5 < to <= 6 months	184	(90.2)	1186	7039.10	180	(85.3)	799	4581.03
> 6 months	10	(16.4)	19	3943.04	7	(10.8)	8	1529.84
Clinically significant hypoglycaemia (level 2)	185	(86.0)	2001	1902.65	169	(77.5)	1069	997.66
0 < to <= 1 month	118	(54.9)	358	2007.82	106	(48.6)	262	1439.79
1 < to <= 2 months	125	(58.7)	416	2341.02	90	(41.5)	216	1206.42
2 < to <= 3 months	117	(55.2)	338	1922.37	71	(33.3)	150	843.34
3 < to <= 4 months	109	(51.9)	304	1744.75	86	(40.4)	168	950.24
4 < to <= 5 months	99	(47.8)	265	1537.83	68	(32.2)	124	703.77
5 < to <= 6 months	104	(51.0)	307	1822.10	70	(33.2)	144	825.62
> 6 months	8	(13.1)	13	2697.87	5	(7.7)	5	956.15
Severe hypoglycaemia (level 3)	5	(2.3)	39	37.08	4	(1.8)	12	11.20
0 < to <= 1 month	2	(0.9)	14	78.52	2	(0.9)	4	21.98
1 < to <= 2 months	2	(0.9)	17	95.67	1	(0.5)	2	11.17
2 < to <= 3 months	1	(0.5)	3	17.06	1	(0.5)	1	5.62
3 < to <= 4 months	2	(1.0)	3	17.22	1	(0.5)	1	5.66
4 < to <= 5 months	1	(0.5)	1	5.80	0			
5 < to <= 6 months	1	(0.5)	1	5.94	3	(1.4)	4	22.93
> 6 months	0				0			
Severe (level 3) or clinically significant (level 2) hypoglycaemia	185	(86.0)	2040	1939.73	169	(77.5)	1081	1008.85
0 < to <= 1 month	119	(55.3)	372	2086.34	106	(48.6)	266	1461.77
1 < to <= 2 months	126	(59.2)	433	2436.69	90	(41.5)	218	1217.59
2 < to <= 3 months	117	(55.2)	341	1939.43	71	(33.3)	151	848.96
3 < to <= 4 months	109	(51.9)	307	1761.97	86	(40.4)	169	955.90
4 < to <= 5 months	99	(47.8)	266	1543.64	68	(32.2)	124	703.77
5 < to <= 6 months	104	(51.0)	308	1828.03	71	(33.6)	148	848.55
> 6 months	8	(13.1)	13	2697.87	5	(7.7)	5	956.15

%: Percentage of subjects with one or more events, BG: Blood glucose, E: Number of events, N: Number of subjects with one or more events, PYE: Patient years of exposure (1 PYE = 365.25 days), R: Rate (number of adverse events per 100 PYE). Hypoglycaemia alert value (level 1): Plasma glucose value of < 3.9 mmol/L (70 mg/dL) and >= 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. 1 month = 30.5 days. Daily basal insulin: IDeg. Group 1: Basal insulin twice daily or IGlar U300, or HbA1c <8% (corresponding to planned one-time additional 50% dose in the insulin icodec arm).

adsl.xpt; variable(s): RANDDT OTMTDURY OMTMXXDM(XX=01 to 13); criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & ((STRATA1 == "BASAL INSULIN TWICE DAILY /IGLAR U300") | (STRATA1 == "BASAL INSULIN ONCE DAILY" & STRATA2 == "HBA1C <8%"))
adhypo.xpt; variable(s): ACAT4 ASTDT; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & ((STRATA1 == "BASAL INSULIN TWICE DAILY /IGLAR U300") | (STRATA1 == "BASAL INSULIN ONCE DAILY" & STRATA2 == "HBA1C <8%")) & ANL06FL == "Y" & ANELFL == "Y"
nn1436/nn1436-japan/submission_20221031_er
09NOV2022:10:10:48 - thypomth/thypomonthsumontow6g50sas.txt

6.5.21 Hypoglycaemic episodes by classification and month since randomisation - ONWARDS 6 (main part), Group 2 - main-on-treatment - summary - safety analysis set

	Insulin icodec				IDeg			
	N	(%)	E	R	N	(%)	E	R
ONWARDS 6								
Number of subjects	75				74			
PYE (years)	37.14				36.97			
Hypoglycaemia alert value (level 1)	75	(100.0)	2662	7167.68	73	(98.6)	1653	4471.29
0 < to <= 1 month	66	(88.0)	481	7680.23	61	(82.4)	333	5388.93
1 < to <= 2 months	68	(90.7)	486	7760.07	63	(85.1)	286	4628.33
2 < to <= 3 months	69	(92.0)	441	7105.22	55	(74.3)	264	4272.31
3 < to <= 4 months	69	(93.2)	441	7136.70	60	(81.1)	252	4078.11
4 < to <= 5 months	68	(91.9)	394	6446.07	62	(83.8)	264	4298.02
5 < to <= 6 months	65	(89.0)	418	6963.49	61	(83.6)	251	4181.43
> 6 months	1	(5.9)	1	890.85	3	(14.3)	3	2809.62
Clinically significant hypoglycaemia (level 2)	61	(81.3)	788	2121.76	54	(73.0)	409	1106.33
0 < to <= 1 month	44	(58.7)	130	2075.74	32	(43.2)	102	1650.66
1 < to <= 2 months	44	(58.7)	122	1948.00	36	(48.6)	77	1246.09
2 < to <= 3 months	39	(52.0)	150	2416.74	26	(35.1)	62	1003.35
3 < to <= 4 months	39	(52.7)	147	2378.90	28	(37.8)	49	792.97
4 < to <= 5 months	35	(47.3)	112	1832.39	28	(37.8)	58	944.26
5 < to <= 6 months	40	(54.8)	127	2115.70	24	(32.9)	61	1016.20
> 6 months	0				0			
Severe hypoglycaemia (level 3)	4	(5.3)	8	21.54	5	(6.8)	5	13.52
0 < to <= 1 month	1	(1.3)	1	15.97	3	(4.1)	3	48.55
1 < to <= 2 months	0				1	(1.4)	1	16.18
2 < to <= 3 months	1	(1.3)	1	16.11	0			
3 < to <= 4 months	1	(1.4)	2	32.37	0			
4 < to <= 5 months	0				1	(1.4)	1	16.28
5 < to <= 6 months	3	(4.1)	4	66.64	0			
> 6 months	0				0			
Severe (level 3) or clinically significant (level 2) hypoglycaemia	62	(82.7)	796	2143.30	54	(73.0)	414	1119.85
0 < to <= 1 month	44	(58.7)	131	2091.70	32	(43.2)	105	1699.21
1 < to <= 2 months	44	(58.7)	122	1948.00	36	(48.6)	78	1262.27
2 < to <= 3 months	40	(53.3)	151	2432.85	26	(35.1)	62	1003.35
3 < to <= 4 months	39	(52.7)	149	2411.26	28	(37.8)	49	792.97
4 < to <= 5 months	35	(47.3)	112	1832.39	29	(39.2)	59	960.54
5 < to <= 6 months	41	(56.2)	131	2182.34	24	(32.9)	61	1016.20
> 6 months	0				0			

%: Percentage of subjects with one or more events, BG: Blood glucose, E: Number of events, N: Number of subjects with one or more events, PYE: Patient years of exposure (1 PYE = 365.25 days), R: Rate (number of adverse events per 100 PYE). Hypoglycaemia alert value (level 1): Plasma glucose value of < 3.9 mmol/L (70 mg/dL) and >= 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. 1 month = 30.5 days. Daily basal insulin: IDeg. Group 2: Basal insulin once daily and HbA1c >=8% (corresponding to planned one-time additional 100% dose in the insulin icodec arm).

adsl.xpt; variable(s): RANDDT OTMTDURY OMTMXXDM(XX=01 to 13); criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & STRATA1 == "BASAL INSULIN ONCE DAILY" & STRATA2 == "HBA1C >=8%"
adhypo.xpt; variable(s): ACAT4 ASTDT; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & STRATA1 == "BASAL INSULIN ONCE DAILY" & STRATA2 == "HBA1C >=8%" & ANL06FL == "Y" & ANELFL == "Y"

インスリン イコデク（遺伝子組換え）

2.7.3.6 付録
6. サブグループ別のデータ
〔ONWARDS 1 試験（4477 試験）及び ONWARDS 6 試験（4625 試験）、延長パートを含む〕

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6.6 Subgroup analyses across phase 3a trials (extension part)

6.6.1 HbA1c (%) after 78 weeks by age group - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
18<= to <65 years	333	333	6.91	0.05		
65<= to <75 years	134	134	6.95	0.07		
75<= years	25	25	6.97	0.17		
Daily basal insulin						
18<= to <65 years	332	332	7.06	0.04		
65<= to <75 years	144	144	6.96	0.07		
75<= years	16	16	7.11	0.21		
LSMeans, change from baseline						
Insulin icodec						
18<= to <65 years	333	333	-1.57	0.05		
65<= to <75 years	134	134	-1.52	0.07		
75<= years	25	25	-1.50	0.17		
Daily basal insulin						
18<= to <65 years	332	332	-1.41	0.04		
65<= to <75 years	144	144	-1.52	0.07		
75<= years	16	16	-1.36	0.21		
Treatment contrast						
Insulin icodec - Daily basal insulin						
18<= to <65 years			-0.16		[-0.28 ; -0.03]	
65<= to <75 years			-0.00		[-0.21 ; 0.20]	
75<= years			-0.14		[-0.67 ; 0.39]	
Test for treatment by subgroup interaction						0.4392

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.2 HbA1c (%) after 52 weeks by age group - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
18<= to <65 years	267	267	7.20	0.05		
65<= years	23	23	7.66	0.17		
Daily basal insulin						
18<= to <65 years	271	271	7.07	0.06		
65<= years	21	21	7.13	0.16		
LSMeans, change from baseline						
Insulin icodec						
18<= to <65 years	267	267	-0.41	0.05		
65<= years	23	23	0.05	0.17		
Daily basal insulin						
18<= to <65 years	271	271	-0.55	0.06		
65<= years	21	21	-0.48	0.16		
Treatment contrast						
Insulin icodec - Daily basal insulin						
18<= to <65 years			0.14		[-0.01 ; 0.28]	
65<= years			0.53		[0.07 ; 0.99]	
Test for treatment by subgroup interaction						0.1093

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.3 HbA1c (%) after 78 weeks by sex - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Female	197	197	7.01	0.06		
Male	295	295	6.86	0.05		
Daily basal insulin						
Female	229	229	7.12	0.06		
Male	263	263	6.96	0.05		
LSMeans, change from baseline						
Insulin icodec						
Female	197	197	-1.46	0.06		
Male	295	295	-1.61	0.05		
Daily basal insulin						
Female	229	229	-1.35	0.06		
Male	263	263	-1.52	0.05		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Female			-0.11		[-0.27 ; 0.06]	
Male			-0.09		[-0.23 ; 0.05]	
Test for treatment by subgroup interaction						0.8971

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.4 HbA1c (%) after 52 weeks by sex - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Female	125	125	7.38	0.07		
Male	165	165	7.13	0.06		
Daily basal insulin						
Female	120	120	7.15	0.08		
Male	172	172	7.02	0.06		
LSMeans, change from baseline						
Insulin icodec						
Female	125	125	-0.23	0.07		
Male	165	165	-0.48	0.06		
Daily basal insulin						
Female	120	120	-0.46	0.08		
Male	172	172	-0.59	0.06		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Female			0.23		[0.03 ; 0.44]	
Male			0.11		[-0.06 ; 0.29]	
Test for treatment by subgroup interaction						0.3483

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.5 HbA1c (%) after 78 weeks by BMI group - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<25 kg/m^2	87	87	7.00	0.09		
25<= to <30 kg/m^2	164	164	6.90	0.07		
30<= to <35 kg/m^2	162	162	6.88	0.07		
>=35 kg/m^2	79	79	6.96	0.09		
Daily basal insulin						
<25 kg/m^2	80	80	7.15	0.10		
25<= to <30 kg/m^2	171	171	7.08	0.06		
30<= to <35 kg/m^2	146	146	6.95	0.07		
>=35 kg/m^2	95	95	6.98	0.08		
LSMeans, change from baseline						
Insulin icodec						
<25 kg/m^2	87	87	-1.47	0.09		
25<= to <30 kg/m^2	164	164	-1.57	0.07		
30<= to <35 kg/m^2	162	162	-1.59	0.07		
>=35 kg/m^2	79	79	-1.52	0.09		
Daily basal insulin						
<25 kg/m^2	80	80	-1.32	0.10		
25<= to <30 kg/m^2	171	171	-1.40	0.06		
30<= to <35 kg/m^2	146	146	-1.53	0.07		
>=35 kg/m^2	95	95	-1.49	0.08		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<25 kg/m^2			-0.15		[-0.41 ; 0.10]	
25<= to <30 kg/m^2			-0.18		[-0.36 ; 0.00]	
30<= to <35 kg/m^2			-0.07		[-0.26 ; 0.13]	
>=35 kg/m^2			-0.03		[-0.27 ; 0.21]	
Test for treatment by subgroup interaction						0.7206

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, BMI: Body mass index, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.6 HbA1c (%) after 52 weeks by BMI group - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<25 kg/m^2	105	105	7.25	0.08		
25<= to <30 kg/m^2	118	118	7.25	0.07		
30<= to <35 kg/m^2	46	46	7.27	0.11		
>=35 kg/m^2	21	21	7.09	0.18		
Daily basal insulin						
<25 kg/m^2	135	135	7.03	0.07		
25<= to <30 kg/m^2	102	102	7.08	0.08		
30<= to <35 kg/m^2	41	41	7.16	0.13		
>=35 kg/m^2	14	14	7.18	0.21		
LSMeans, change from baseline						
Insulin icodec						
<25 kg/m^2	105	105	-0.37	0.08		
25<= to <30 kg/m^2	118	118	-0.36	0.07		
30<= to <35 kg/m^2	46	46	-0.35	0.11		
>=35 kg/m^2	21	21	-0.52	0.18		
Daily basal insulin						
<25 kg/m^2	135	135	-0.58	0.07		
25<= to <30 kg/m^2	102	102	-0.53	0.08		
30<= to <35 kg/m^2	41	41	-0.45	0.13		
>=35 kg/m^2	14	14	-0.44	0.21		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<25 kg/m^2			0.22		[0.01 ; 0.42]	
25<= to <30 kg/m^2			0.17		[-0.05 ; 0.39]	
30<= to <35 kg/m^2			0.11		[-0.23 ; 0.44]	
>=35 kg/m^2			-0.08		[-0.62 ; 0.46]	
Test for treatment by subgroup interaction						0.7423

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, BMI: Body mass index, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.7 HbA1c (%) after 78 weeks by race - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
White	333	333	6.87	0.07		
Black or African American	10	10	6.93	0.28		
Asian	129	129	7.04	0.15		
Other	20	20	6.97	0.26		
Daily basal insulin						
White	317	317	6.99	0.07		
Black or African American	17	17	6.96	0.20		
Asian	145	145	7.13	0.14		
Other	13	13	7.18	0.27		
LSMeans, change from baseline						
Insulin icodec						
White	333	333	-1.60	0.07		
Black or African American	10	10	-1.54	0.28		
Asian	129	129	-1.44	0.15		
Other	20	20	-1.50	0.26		
Daily basal insulin						
White	317	317	-1.48	0.07		
Black or African American	17	17	-1.51	0.20		
Asian	145	145	-1.35	0.14		
Other	13	13	-1.30	0.27		
Treatment contrast						
Insulin icodec - Daily basal insulin						
White			-0.12		[-0.25 ; 0.01]	
Black or African American			-0.03		[-0.68 ; 0.62]	
Asian			-0.09		[-0.28 ; 0.11]	
Other			-0.21		[-0.81 ; 0.39]	
Test for treatment by subgroup interaction						0.9709

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Other race includes American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander. Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.8 HbA1c (%) after 52 weeks by race - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
White	230	230	7.20	0.08		
Black or African American	9	9	6.92	0.27		
Asian	51	51	7.44	0.23		
Daily basal insulin						
White	218	218	7.07	0.09		
Black or African American	2	2	7.67	0.52		
Asian	72	72	7.09	0.23		
LSMeans, change from baseline						
Insulin icodec						
White	230	230	-0.41	0.08		
Black or African American	9	9	-0.70	0.27		
Asian	51	51	-0.17	0.23		
Daily basal insulin						
White	218	218	-0.55	0.09		
Black or African American	2	2	0.06	0.52		
Asian	72	72	-0.53	0.23		
Treatment contrast						
Insulin icodec - Daily basal insulin						
White			0.14		[-0.03 ; 0.30]	
Black or African American			-0.76		[-1.89 ; 0.38]	
Asian			0.35		[0.09 ; 0.62]	
Test for treatment by subgroup interaction						0.1112

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.9 HbA1c (%) after 78 weeks by ethnicity - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Not Hispanic or Latino	439	439	6.88	0.04		
Hispanic or Latino	53	53	7.24	0.13		
Daily basal insulin						
Not Hispanic or Latino	439	439	7.01	0.04		
Hispanic or Latino	53	53	7.24	0.14		
LSMeans, change from baseline						
Insulin icodec						
Not Hispanic or Latino	439	439	-1.59	0.04		
Hispanic or Latino	53	53	-1.24	0.13		
Daily basal insulin						
Not Hispanic or Latino	439	439	-1.47	0.04		
Hispanic or Latino	53	53	-1.24	0.14		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Not Hispanic or Latino			-0.13		[-0.24 ; -0.01]	
Hispanic or Latino			-0.00		[-0.34 ; 0.33]	
Test for treatment by subgroup interaction						0.4805

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.10 HbA1c (%) after 52 weeks by ethnicity - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Not Hispanic or Latino	280	280	7.25	0.05		
Hispanic or Latino	10	10	6.99	0.23		
Daily basal insulin						
Not Hispanic or Latino	282	282	7.08	0.06		
Hispanic or Latino	10	10	6.78	0.24		
LSMeans, change from baseline						
Insulin icodec						
Not Hispanic or Latino	280	280	-0.37	0.05		
Hispanic or Latino	10	10	-0.62	0.23		
Daily basal insulin						
Not Hispanic or Latino	282	282	-0.53	0.06		
Hispanic or Latino	10	10	-0.83	0.24		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Not Hispanic or Latino			0.16		[0.02 ; 0.31]	
Hispanic or Latino			0.21		[-0.43 ; 0.85]	
Test for treatment by subgroup interaction						0.8902

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.11 HbA1c (%) after 78 weeks by region - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Europe	245	245	6.82	0.05		
North America	108	108	7.09	0.09		
Asia	120	120	6.98	0.07		
South America	19	19	6.81	0.20		
Daily basal insulin						
Europe	226	226	7.08	0.05		
North America	112	112	6.91	0.09		
Asia	132	132	7.04	0.07		
South America	22	22	7.16	0.17		
LSMeans, change from baseline						
Insulin icodec						
Europe	245	245	-1.65	0.05		
North America	108	108	-1.38	0.09		
Asia	120	120	-1.49	0.07		
South America	19	19	-1.66	0.20		
Daily basal insulin						
Europe	226	226	-1.39	0.05		
North America	112	112	-1.57	0.09		
Asia	132	132	-1.44	0.07		
South America	22	22	-1.31	0.17		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Europe			-0.26		[-0.41 ; -0.11]	
North America			0.19		[-0.06 ; 0.43]	
Asia			-0.05		[-0.25 ; 0.15]	
South America			-0.35		[-0.86 ; 0.17]	
Test for treatment by subgroup interaction						0.0075

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.12 HbA1c (%) after 52 weeks by region - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Europe	136	136	7.13	0.07		
North America	106	106	7.30	0.08		
Asia	48	48	7.42	0.11		
Daily basal insulin						
Europe	139	139	7.04	0.08		
North America	85	85	7.14	0.09		
Asia	68	68	7.03	0.09		
LSMeans, change from baseline						
Insulin icodec						
Europe	136	136	-0.49	0.07		
North America	106	106	-0.31	0.08		
Asia	48	48	-0.19	0.11		
Daily basal insulin						
Europe	139	139	-0.57	0.08		
North America	85	85	-0.47	0.09		
Asia	68	68	-0.58	0.09		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Europe			0.08		[-0.12 ; 0.29]	
North America			0.16		[-0.08 ; 0.39]	
Asia			0.39		[0.11 ; 0.66]	
Test for treatment by subgroup interaction						0.2205

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.13 HbA1c (%) after 78 weeks by baseline HbA1c group - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<8% (<64 mmol/mol)	170	170	6.91	0.08		
>=8% (>=64 mmol/mol)	322	322	6.93	0.05		
Daily basal insulin						
<8% (<64 mmol/mol)	188	188	7.05	0.07		
>=8% (>=64 mmol/mol)	304	304	7.02	0.05		
LSMeans, change from baseline						
Insulin icodec						
<8% (<64 mmol/mol)	170	170	-1.56	0.08		
>=8% (>=64 mmol/mol)	322	322	-1.55	0.05		
Daily basal insulin						
<8% (<64 mmol/mol)	188	188	-1.42	0.07		
>=8% (>=64 mmol/mol)	304	304	-1.45	0.05		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<8% (<64 mmol/mol)			-0.14		[-0.31 ; 0.03]	
>=8% (>=64 mmol/mol)			-0.09		[-0.23 ; 0.04]	
Test for treatment by subgroup interaction						0.6660

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.14 HbA1c (%) after 52 weeks by baseline HbA1c group - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<8% (<64 mmol/mol)	189	189	7.32	0.08		
>=8% (>=64 mmol/mol)	101	101	7.09	0.12		
Daily basal insulin						
<8% (<64 mmol/mol)	189	189	7.16	0.08		
>=8% (>=64 mmol/mol)	103	103	6.91	0.12		
LSMeans, change from baseline						
Insulin icodec						
<8% (<64 mmol/mol)	189	189	-0.29	0.08		
>=8% (>=64 mmol/mol)	101	101	-0.52	0.12		
Daily basal insulin						
<8% (<64 mmol/mol)	189	189	-0.45	0.08		
>=8% (>=64 mmol/mol)	103	103	-0.70	0.12		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<8% (<64 mmol/mol)			0.16		[-0.01 ; 0.32]	
>=8% (>=64 mmol/mol)			0.18		[-0.05 ; 0.42]	
Test for treatment by subgroup interaction						0.8558

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.15 HbA1c (%) after 78 weeks by duration of diabetes - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<10 years	211	211	6.86	0.06		
>=10 years	281	281	6.96	0.05		
Daily basal insulin						
<10 years	230	230	6.95	0.06		
>=10 years	262	262	7.10	0.05		
LSMeans, change from baseline						
Insulin icodec						
<10 years	211	211	-1.61	0.06		
>=10 years	281	281	-1.51	0.05		
Daily basal insulin						
<10 years	230	230	-1.52	0.06		
>=10 years	262	262	-1.37	0.05		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<10 years			-0.09		[-0.25 ; 0.07]	
>=10 years			-0.14		[-0.28 ; 0.01]	
Test for treatment by subgroup interaction						0.6450

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.16 HbA1c (%) after 52 weeks by duration of diabetes - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
<10 years	75	75	7.17	0.09		
>=10 years	215	215	7.26	0.05		
Daily basal insulin						
<10 years	82	82	7.01	0.09		
>=10 years	210	210	7.10	0.06		
LSMeans, change from baseline						
Insulin icodec						
<10 years	75	75	-0.44	0.09		
>=10 years	215	215	-0.35	0.05		
Daily basal insulin						
<10 years	82	82	-0.60	0.09		
>=10 years	210	210	-0.52	0.06		
Treatment contrast						
Insulin icodec - Daily basal insulin						
<10 years			0.16		[-0.09 ; 0.42]	
>=10 years			0.17		[0.00 ; 0.33]	
Test for treatment by subgroup interaction						0.9808

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.17 HbA1c (%) after 78 weeks by estimated renal function at baseline - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal (>=90)	224	224	6.95	0.06		
Mild impairment (>=60 - <90)	223	223	6.90	0.06		
Moderate or severe impairment (<60)	45	45	6.90	0.14		
Daily basal insulin						
Normal (>=90)	222	222	7.08	0.05		
Mild impairment (>=60 - <90)	213	213	6.99	0.06		
Moderate or severe impairment (<60)	57	57	7.01	0.11		
LSMeans, change from baseline						
Insulin icodec						
Normal (>=90)	224	224	-1.52	0.06		
Mild impairment (>=60 - <90)	223	223	-1.58	0.06		
Moderate or severe impairment (<60)	45	45	-1.57	0.14		
Daily basal insulin						
Normal (>=90)	222	222	-1.40	0.05		
Mild impairment (>=60 - <90)	213	213	-1.48	0.06		
Moderate or severe impairment (<60)	57	57	-1.46	0.11		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal (>=90)			-0.13		[-0.28 ; 0.03]	
Mild impairment (>=60 - <90)			-0.09		[-0.25 ; 0.06]	
Moderate or severe impairment (<60)			-0.11		[-0.46 ; 0.24]	
Test for treatment by subgroup interaction						0.9593

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.18 HbA1c (%) after 52 weeks by estimated renal function at baseline - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Normal (>=90)	197	197	7.19	0.06		
Mild impairment (>=60 - <90)	88	88	7.37	0.09		
Moderate impairment (>=30 - <60)	5	5	6.88	0.33		
Daily basal insulin						
Normal (>=90)	190	190	7.05	0.07		
Mild impairment (>=60 - <90)	93	93	7.13	0.08		
Moderate impairment (>=30 - <60)	9	9	7.02	0.24		
LSMeans, change from baseline						
Insulin icodec						
Normal (>=90)	197	197	-0.43	0.06		
Mild impairment (>=60 - <90)	88	88	-0.24	0.09		
Moderate impairment (>=30 - <60)	5	5	-0.73	0.33		
Daily basal insulin						
Normal (>=90)	190	190	-0.57	0.07		
Mild impairment (>=60 - <90)	93	93	-0.48	0.08		
Moderate impairment (>=30 - <60)	9	9	-0.60	0.24		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Normal (>=90)			0.14		[-0.04 ; 0.32]	
Mild impairment (>=60 - <90)			0.24		[0.02 ; 0.47]	
Moderate impairment (>=30 - <60)			-0.13		[-0.93 ; 0.67]	
Test for treatment by subgroup interaction						0.5840

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.19 HbA1c (%) after 78 weeks by pre-trial SU use - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No SU use	273	273	6.82	0.05		
SU use	219	219	7.05	0.06		
Daily basal insulin						
No SU use	265	265	6.90	0.05		
SU use	227	227	7.18	0.05		
LSMeans, change from baseline						
Insulin icodec						
No SU use	273	273	-1.65	0.05		
SU use	219	219	-1.43	0.06		
Daily basal insulin						
No SU use	265	265	-1.57	0.05		
SU use	227	227	-1.30	0.05		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No SU use			-0.08		[-0.23 ; 0.06]	
SU use			-0.13		[-0.28 ; 0.02]	
Test for treatment by subgroup interaction						0.6642

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, SU: Sulfonylureas, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.20 HbA1c (%) after 78 weeks by pre-trial GLP-1 RA use - change from baseline - ONWARDS 1 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
No GLP-1 RA use	409	409	6.92	0.05		
GLP-1 RA use	83	83	6.90	0.09		
Daily basal insulin						
No GLP-1 RA use	400	400	7.07	0.04		
GLP-1 RA use	92	92	6.87	0.09		
LSMeans, change from baseline						
Insulin icodec						
No GLP-1 RA use	409	409	-1.55	0.05		
GLP-1 RA use	83	83	-1.57	0.09		
Daily basal insulin						
No GLP-1 RA use	400	400	-1.40	0.04		
GLP-1 RA use	92	92	-1.61	0.09		
Treatment contrast						
Insulin icodec - Daily basal insulin						
No GLP-1 RA use			-0.14		[-0.27 ; -0.02]	
GLP-1 RA use			0.03		[-0.21 ; 0.27]	
Test for treatment by subgroup interaction						0.1898

CI: Confidence interval, FAS: Number of subjects in full analysis set, GLP-1 RA: Glucagon-like peptide-1 receptor agonist, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IGlar U100. Planned end of treatment: ONWARDS 1 (extension part): Week 78. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

6.6.21 HbA1c (%) after 52 weeks by pre-trial basal insulin regimen - change from baseline - ONWARDS 6 (extension part) - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
HbA1c (%)						
LSMeans						
Insulin icodec						
Insulin degludec	120	120	7.28	0.08		
Insulin glargine U100	97	97	7.21	0.08		
Insulin glargine U300	50	50	7.23	0.12		
Other	23	23	7.14	0.16		
Daily basal insulin						
Insulin degludec	113	113	7.20	0.09		
Insulin glargine U100	91	91	6.95	0.09		
Insulin glargine U300	57	57	7.05	0.10		
Other	31	31	7.02	0.15		
LSMeans, change from baseline						
Insulin icodec						
Insulin degludec	120	120	-0.33	0.08		
Insulin glargine U100	97	97	-0.40	0.08		
Insulin glargine U300	50	50	-0.38	0.12		
Other	23	23	-0.47	0.16		
Daily basal insulin						
Insulin degludec	113	113	-0.42	0.09		
Insulin glargine U100	91	91	-0.67	0.09		
Insulin glargine U300	57	57	-0.56	0.10		
Other	31	31	-0.59	0.15		
Treatment contrast						
Insulin icodec - Daily basal insulin						
Insulin degludec			0.08		[-0.13 ; 0.30]	
Insulin glargine U100			0.27		[0.03 ; 0.50]	
Insulin glargine U300			0.18		[-0.11 ; 0.47]	
Other			0.12		[-0.30 ; 0.54]	
Test for treatment by subgroup interaction						0.6733

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, SE: Standard error of the mean, Daily basal insulin: IDeg. Planned end of treatment: ONWARDS 6 (extension part): Week 52. ANCOVA with treatment, region, subgroup and treatment by subgroup interaction, and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. P-value: Two-sided p-value for test of no treatment by subgroup interaction.

インスリン イコデク（遺伝子組換え）

2.7.3.6 付録
7. 日本の推奨用法・用量に関するデータ
〔ONWARDS 1 試験（4477 試験）及び ONWARDS 6 試験（4625 試験）、延長パートを含む〕

ノボ ノルディスク ファーマ株式会社

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6.7 Analyses across phase 3 trials (extension part) including Japanese subjects related to doing recommendation for Japan

6.7.1 Actual weekly total basal insulin dose from week 76 to week 78 - ONWARDS 1 (extension part) - on- treatment - summary - safety analysis set

	Insulin icodec		IGlar	
	N	(%)	N	(%)
Number of subjects	492		492	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	459	(100.0)	466	(100.0)
>=0 - <=560	412	(89.8)	421	(90.3)
>=0 - <=70	39	(8.5)	30	(6.4)
>70 - <=140	83	(18.1)	80	(17.2)
>140 - <=210	90	(19.6)	90	(19.3)
>210 - <=280	58	(12.6)	88	(18.9)
>280 - <=350	59	(12.9)	48	(10.3)
>350 - <=420	33	(7.2)	35	(7.5)
>420 - <=490	32	(7.0)	28	(6.0)
>490 - <=560	18	(3.9)	22	(4.7)
>560 - <=630	11	(2.4)	13	(2.8)
>630 - <=700	9	(2.0)	11	(2.4)
>700 - <=770	10	(2.2)	1	(0.2)
>770 - <=840	2	(0.4)	5	(1.1)
>840 - <=910	5	(1.1)	5	(1.1)
>910 - <=980	4	(0.9)	3	(0.6)
>980 - <=1050	3	(0.7)	2	(0.4)
>1050	3	(0.7)	5	(1.1)

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

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6.7.2 Actual weekly total basal insulin dose from week 76 to week 78 - ONWARDS 1 (extension part), Japanese subjects - on-treatment - summary - safety analysis set

	Insulin icodec		IGlar	
	N	(%)	N	(%)
Number of subjects	78		86	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	75	(100.0)	83	(100.0)
>=0 - <=560	74	(98.7)	83	(100.0)
>=0 - <=70	17	(22.7)	12	(14.5)
>70 - <=140	22	(29.3)	23	(27.7)
>140 - <=210	14	(18.7)	25	(30.1)
>210 - <=280	7	(9.3)	13	(15.7)
>280 - <=350	5	(6.7)	4	(4.8)
>350 - <=420	4	(5.3)	3	(3.6)
>420 - <=490	4	(5.3)	2	(2.4)
>490 - <=560	1	(1.3)	1	(1.2)
>560 - <=630	0		0	
>630 - <=700	0		0	
>700 - <=770	0		0	
>770 - <=840	0		0	
>840 - <=910	0		0	
>910 - <=980	0		0	
>980 - <=1050	1	(1.3)	0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 1" & COUNTRY == "JPN"
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6.7.3 Actual weekly total basal insulin dose from week 50 to week 52 - ONWARDS 6 (extension part) - on- treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	290		292	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	250	(100.0)	273	(100.0)
>=0 - <=560	245	(98.0)	271	(99.3)
>=0 - <=70	13	(5.2)	27	(9.9)
>70 - <=140	79	(31.6)	103	(37.7)
>140 - <=210	66	(26.4)	74	(27.1)
>210 - <=280	42	(16.8)	35	(12.8)
>280 - <=350	19	(7.6)	16	(5.9)
>350 - <=420	10	(4.0)	4	(1.5)
>420 - <=490	9	(3.6)	10	(3.7)
>490 - <=560	7	(2.8)	2	(0.7)
>560 - <=630	3	(1.2)	0	
>630 - <=700	0		0	
>700 - <=770	1	(0.4)	1	(0.4)
>770 - <=840	0		0	
>840 - <=910	1	(0.4)	0	
>910 - <=980	0		0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

adsl.xpt; variable(s): NA; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6"
adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & ANELFL == "Y" & PARAMCD == "IDBAL2W"
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6.7.4 Actual weekly total basal insulin dose from week 50 to week 52 - ONWARDS 6 (extension part), Japanese subjects - on-treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	32		48	
Average Weekly Basal Insulin Dose Last 2 Weeks of Treatment (U)				
N	31	(100.0)	48	(100.0)
>=0 - <=560	31	(100.0)	48	(100.0)
>=0 - <=70	6	(19.4)	12	(25.0)
>70 - <=140	12	(38.7)	26	(54.2)
>140 - <=210	3	(9.7)	6	(12.5)
>210 - <=280	7	(22.6)	2	(4.2)
>280 - <=350	1	(3.2)	1	(2.1)
>350 - <=420	1	(3.2)	0	
>420 - <=490	1	(3.2)	1	(2.1)
>490 - <=560	0		0	
>560 - <=630	0		0	
>630 - <=700	0		0	
>700 - <=770	0		0	
>770 - <=840	0		0	
>840 - <=910	0		0	
>910 - <=980	0		0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

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adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & COUNTRY == "JPN" & ANELFL == "Y" & PARAMCD == "IDBAL2W"
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6.7.5 Actual weekly total insulin dose from week 50 to week 52 - ONWARDS 6 (extension part) - on-treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	290		292	
Average weekly insulin dose last 2 weeks of treatment (U)				
N	258	(100.0)	273	(100.0)
>=0 - <=560	229	(88.8)	245	(89.7)
>=0 - <=70	4	(1.6)	0	
>70 - <=140	8	(3.1)	9	(3.3)
>140 - <=210	44	(17.1)	46	(16.8)
>210 - <=280	59	(22.9)	62	(22.7)
>280 - <=350	48	(18.6)	49	(17.9)
>350 - <=420	31	(12.0)	40	(14.7)
>420 - <=490	18	(7.0)	25	(9.2)
>490 - <=560	17	(6.6)	14	(5.1)
>560 - <=630	5	(1.9)	8	(2.9)
>630 - <=700	4	(1.6)	7	(2.6)
>700 - <=770	4	(1.6)	1	(0.4)
>770 - <=840	1	(0.4)	3	(1.1)
>840 - <=910	9	(3.5)	2	(0.7)
>910 - <=980	2	(0.8)	2	(0.7)
>980 - <=1050	2	(0.8)	1	(0.4)
>1050	2	(0.8)	3	(1.1)

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

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adecen.xpt; variable(s): PARAM AVAL; criteria: SAFFL == "Y" & STDNM == "ONWARDS 6" & ANELFL == "Y" & PARAMCD == "IDAL2W"
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6.7.6 Actual weekly total insulin dose from week 50 to week 52 - ONWARDS 6 (extension part), Japanese subjects - on-treatment - summary - safety analysis set

	Insulin icodec		IDeg	
	N	(%)	N	(%)
Number of subjects	32		48	
Average weekly insulin dose last 2 weeks of treatment (U)				
N	31	(100.0)	48	(100.0)
>=0 - <=560	30	(96.8)	46	(95.8)
>=0 - <=70	0		0	
>70 - <=140	3	(9.7)	3	(6.2)
>140 - <=210	6	(19.4)	13	(27.1)
>210 - <=280	5	(16.1)	13	(27.1)
>280 - <=350	9	(29.0)	7	(14.6)
>350 - <=420	3	(9.7)	5	(10.4)
>420 - <=490	2	(6.5)	4	(8.3)
>490 - <=560	2	(6.5)	1	(2.1)
>560 - <=630	0		1	(2.1)
>630 - <=700	0		0	
>700 - <=770	0		0	
>770 - <=840	0		1	(2.1)
>840 - <=910	1	(3.2)	0	
>910 - <=980	0		0	
>980 - <=1050	0		0	
>1050	0		0	

N: Number of subjects, %: Percentage of subjects. Weekly dose in comparator group is derived as 7 times average daily dose.

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