インスリン イコデク（遺伝子組換え）

2.7.3.6 付録
2. 有効性に関するエンドポイント（第 3 相試験）

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6.2 Efficacy endpoints across phase 3a trials

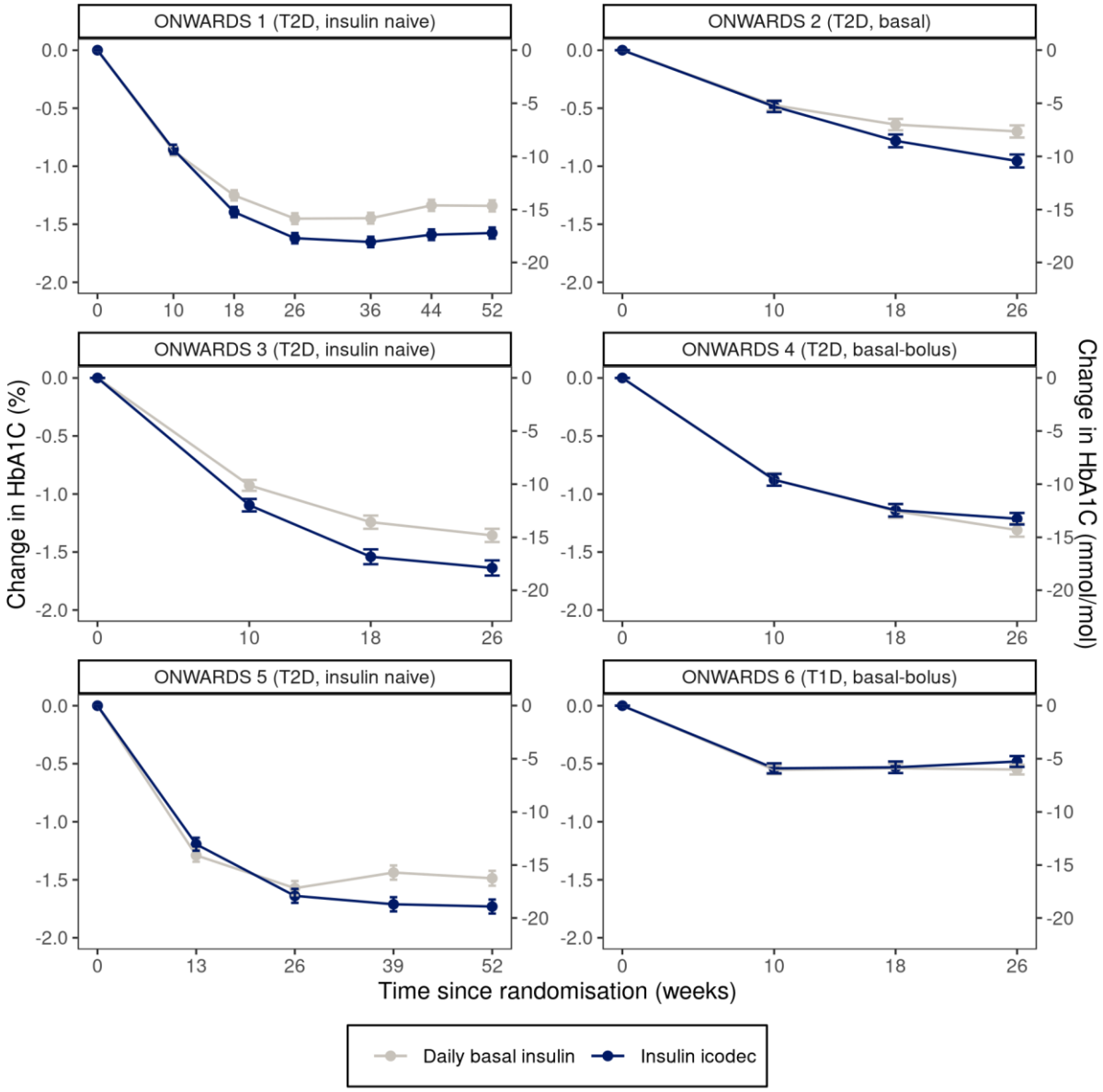
6.2.1 HbA1c at baseline - in-trial - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)
HbA1c (%)				
T2D, insulin naive				
ONWARDS 1	492	8.50 (0.99)	492	8.44 (1.02)
ONWARDS 3	294	8.55 (1.11)	294	8.48 (1.01)
ONWARDS 5	542	8.96 (1.62)	542	8.88 (1.50)
T2D, basal				
ONWARDS 2	263	8.17 (0.77)	263	8.10 (0.77)
T2D, basal-bolus				
ONWARDS 4	291	8.29 (0.86)	291	8.31 (0.90)
T1D, basal-bolus				
ONWARDS 6	290	7.59 (0.96)	292	7.63 (0.93)
HbA1c (mmol/mol)				
T2D, insulin naive				
ONWARDS 1	492	69.44 (10.86)	492	68.79 (11.13)
ONWARDS 3	294	69.96 (12.19)	294	69.23 (11.06)
ONWARDS 5	542	74.43 (17.73)	542	73.60 (16.35)
T2D, basal				
ONWARDS 2	263	65.76 (8.47)	263	65.02 (8.46)
T2D, basal-bolus				
ONWARDS 4	291	67.11 (9.41)	291	67.35 (9.79)
T1D, basal-bolus				
ONWARDS 6	290	59.46 (10.47)	292	59.95 (10.12)

N: Number of subjects, HbA1c: Haemoglobin A1c, SD: Standard deviation, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. 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).

adsl.xpt; variable(s): STDNM DIABTYP HBA1CBL HB1CCBL FASFL TR01PG1 POPGRP; criteria: FASFL == "Y"
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03NOV2022:23:13:28 - tlbblsum/tlbhba1cblsumintfas.txt

6.2.2 HbA1c by treatment week - change from baseline - in-trial - mean plot - full analysis set



Observed data including data obtained after premature treatment discontinuation. Legend: Mean (symbol) and mean ± standard error to the mean (error bars). HbA1c: Haemoglobin A1c, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. 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).

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

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6.2.3 HbA1c at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value for NI	P-value for SUP
HbA1c (%)							
T2D, insulin naive							
ONWARDS 1							
LSMeans							
Insulin icodec	492	492	6.93	0.06			
Daily basal insulin	492	492	7.12	0.05			
LSMeans, change from baseline							
Insulin icodec	492	492	-1.55	0.06			
Daily basal insulin	492	492	-1.35	0.05			
Treatment contrast							
Insulin icodec - Daily basal insulin			-0.19		[-0.36 ; -0.03]	<0.0001	0.0210
ONWARDS 3							
LSMeans							
Insulin icodec	294	294	6.95	0.05			
Daily basal insulin	294	294	7.16	0.05			
LSMeans, change from baseline							
Insulin icodec	294	294	-1.57	0.05			
Daily basal insulin	294	294	-1.36	0.05			
Treatment contrast							
Insulin icodec - Daily basal insulin			-0.21		[-0.34 ; -0.08]	<0.0001	0.0016

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, NA: Not applicable, NI: Non-inferiority, P-value: Two-sided p-value. SE: Standard error of the mean, SUP: Superiority, 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 with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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. A test for superiority was pre-specified as confirmatory secondary hypothesis in ONWARDS 1, 2, 3 and 5.

HbA1c at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value for NI	P-value for SUP
ONWARDS 5							
LSMeans							
Insulin icodec	542	542	7.24	0.09			
Daily basal insulin	543	542	7.61	0.12			
LSMeans, change from baseline							
Insulin icodec	542	542	-1.68	0.09			
Daily basal insulin	543	542	-1.31	0.12			
Treatment contrast							
Insulin icodec - Daily basal insulin			-0.38		[-0.66 ; -0.09]	<0.0001	0.0092
T2D, basal							
ONWARDS 2							
LSMeans							
Insulin icodec	263	263	7.20	0.05			
Daily basal insulin	263	263	7.42	0.06			
LSMeans, change from baseline							
Insulin icodec	263	263	-0.93	0.05			
Daily basal insulin	263	263	-0.71	0.06			
Treatment contrast							
Insulin icodec - Daily basal insulin			-0.22		[-0.37 ; -0.08]	<0.0001	0.0028

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, NA: Not applicable, NI: Non-inferiority, P-value: Two-sided p-value. SE: Standard error of the mean, SUP: Superiority, 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 with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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. A test for superiority was pre-specified as confirmatory secondary hypothesis in ONWARDS 1, 2, 3 and 5.

HbA1c at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value for NI	P-value for SUP
T2D, basal-bolus							
ONWARDS 4							
LSMeans							
Insulin icodec	291	291	7.14	0.05			
Daily basal insulin	291	291	7.12	0.05			
LSMeans, change from baseline							
Insulin icodec	291	291	-1.16	0.05			
Daily basal insulin	291	291	-1.18	0.05			
Treatment contrast							
Insulin icodec - Daily basal insulin			0.02		[-0.11 ; 0.15]	<0.0001	NA
T1D, basal-bolus							
ONWARDS 6							
LSMeans							
Insulin icodec	290	290	7.15	0.07			
Daily basal insulin	292	292	7.10	0.06			
LSMeans, change from baseline							
Insulin icodec	290	290	-0.47	0.07			
Daily basal insulin	292	292	-0.51	0.06			
Treatment contrast							
Insulin icodec - Daily basal insulin			0.05		[-0.13 ; 0.23]	0.0065	NA
HbA1c (mmol/mol)							
T2D, insulin naive							

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, NA: Not applicable, NI: Non-inferiority, P-value: Two-sided p-value. SE: Standard error of the mean, SUP: Superiority, 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 with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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. A test for superiority was pre-specified as confirmatory secondary hypothesis in ONWARDS 1, 2, 3 and 5.

HbA1c at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value for NI	P-value for SUP
ONWARDS 1							
LSMeans							
Insulin icodec	492	492	52.21	0.65			
Daily basal insulin	492	492	54.34	0.59			
LSMeans, change from baseline							
Insulin icodec	492	492	-16.91	0.65			
Daily basal insulin	492	492	-14.78	0.59			
Treatment contrast							
Insulin icodec - Daily basal insulin			-2.13		[-3.93 ; -0.32]	<0.0001	0.0210
ONWARDS 3							
LSMeans							
Insulin icodec	294	294	52.42	0.51			
Daily basal insulin	294	294	54.71	0.52			
LSMeans, change from baseline							
Insulin icodec	294	294	-17.18	0.51			
Daily basal insulin	294	294	-14.88	0.52			
Treatment contrast							
Insulin icodec - Daily basal insulin			-2.30		[-3.73 ; -0.87]	<0.0001	0.0016
ONWARDS 5							

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, NA: Not applicable, NI: Non-inferiority, P-value: Two-sided p-value. SE: Standard error of the mean, SUP: Superiority, 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 with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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. A test for superiority was pre-specified as confirmatory secondary hypothesis in ONWARDS 1, 2, 3 and 5.

HbA1c at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value for NI	P-value for SUP
LSMeans							
Insulin icodec	542	542	55.61	0.94			
Daily basal insulin	543	542	59.71	1.35			
LSMeans, change from baseline							
Insulin icodec	542	542	-18.41	0.94			
Daily basal insulin	543	542	-14.30	1.35			
Treatment contrast							
Insulin icodec - Daily basal insulin			-4.11		[-7.20 ; -1.02]	<0.0001	0.0092
T2D, basal							
ONWARDS 2							
LSMeans							
Insulin icodec	263	263	55.19	0.56			
Daily basal insulin	263	263	57.64	0.62			
LSMeans, change from baseline							
Insulin icodec	263	263	-10.20	0.56			
Daily basal insulin	263	263	-7.75	0.62			
Treatment contrast							
Insulin icodec - Daily basal insulin			-2.45		[-4.05 ; -0.84]	<0.0001	0.0028

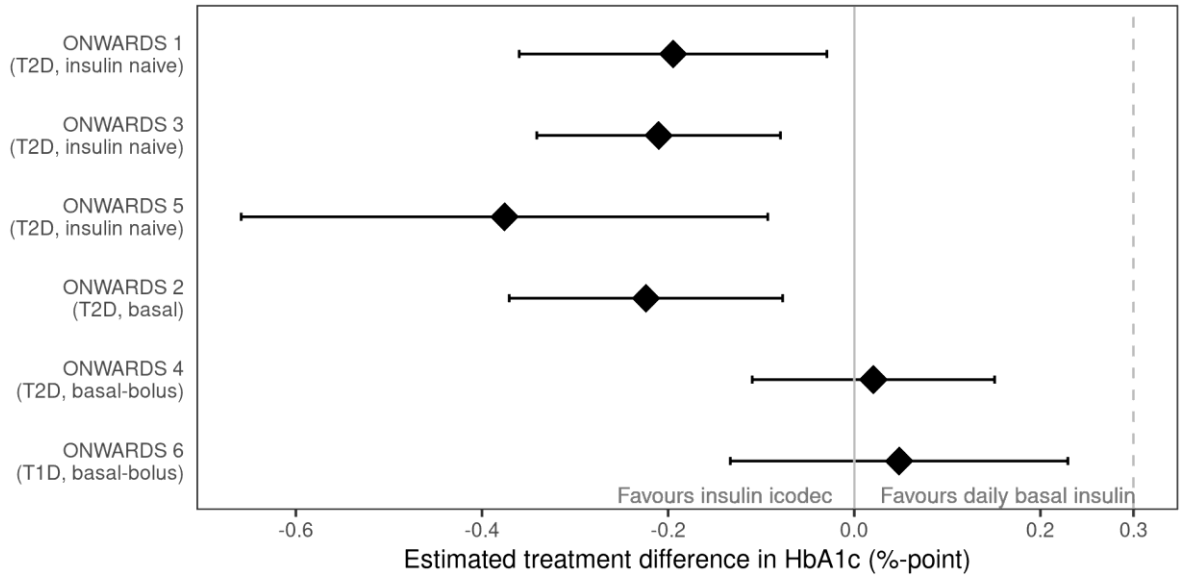
CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, NA: Not applicable, NI: Non-inferiority, P-value: Two-sided p-value. SE: Standard error of the mean, SUP: Superiority, T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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 with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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. A test for superiority was pre-specified as confirmatory secondary hypothesis in ONWARDS 1, 2, 3 and 5.

HbA1c at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value for NI	P-value for SUP
T2D, basal-bolus							
ONWARDS 4							
LSMeans							
Insulin icodec	291	291	54.58	0.51			
Daily basal insulin	291	291	54.35	0.52			
LSMeans, change from baseline							
Insulin icodec	291	291	-12.65	0.51			
Daily basal insulin	291	291	-12.88	0.52			
Treatment contrast							
Insulin icodec - Daily basal insulin			0.22		[-1.20 ; 1.65]	<0.0001	NA
T1D, basal-bolus							
ONWARDS 6							
LSMeans							
Insulin icodec	290	290	54.62	0.76			
Daily basal insulin	292	292	54.09	0.68			
LSMeans, change from baseline							
Insulin icodec	290	290	-5.08	0.76			
Daily basal insulin	292	292	-5.61	0.68			
Treatment contrast							
Insulin icodec - Daily basal insulin			0.53		[-1.46 ; 2.51]	0.0065	NA

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, NA: Not applicable, NI: Non-inferiority, P-value: Two-sided p-value. SE: Standard error of the mean, SUP: Superiority, 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 with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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. A test for superiority was pre-specified as confirmatory secondary hypothesis in ONWARDS 1, 2, 3 and 5.

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



Estimates with 95% confidence interval. 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). 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. HbA1c: Haemoglobin A1c, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. ANCOVA with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. Vertical line at 0.3%-point non-inferiority margin. A test for superiority was pre-specified as confirmatory secondary hypothesis in ONWARDS 1, 2, 3 and 5.

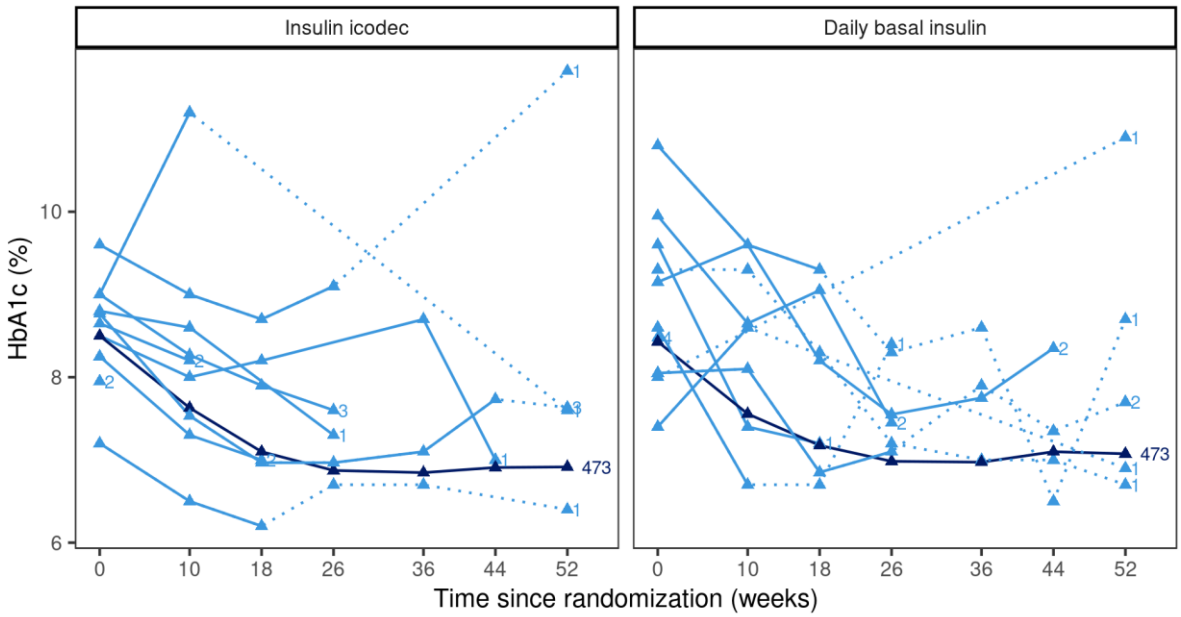
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6.2.5 Subjects status and HbA1c assessments at planned end of treatment - in-trial - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	(%)	N	(%)
T2D, insulin naive				
ONWARDS 1				
Full analysis set	492		492	
Treatment completers with final assessment	473	(96.1)	477	(97.0)
Retrieved data, premature treatment discontinuation	6	(1.2)	2	(0.4)
Missing assessment, premature treatment discontinuation	11	(2.2)	10	(2.0)
Missing assessment, treatment completers (missing-at-random)	2	(0.4)	3	(0.6)
ONWARDS 3				
Full analysis set	294		294	
Treatment completers with final assessment	279	(94.9)	283	(96.3)
Retrieved data, premature treatment discontinuation	4	(1.4)	2	(0.7)
Missing assessment, premature treatment discontinuation	9	(3.1)	9	(3.1)
Missing assessment, treatment completers (missing-at-random)	2	(0.7)	0	
ONWARDS 5				
Full analysis set	542		543	
Treatment completers with final assessment	475	(87.6)	490	(90.2)
Retrieved data, premature treatment discontinuation	14	(2.6)	3	(0.6)
Missing assessment, premature treatment discontinuation	45	(8.3)	47	(8.7)
Missing assessment, treatment completers (missing-at-random)	8	(1.5)	3	(0.6)
T2D, basal				
ONWARDS 2				
Full analysis set	263		263	
Treatment completers with final assessment	254	(96.6)	251	(95.4)
Retrieved data, premature treatment discontinuation	2	(0.8)	2	(0.8)
Missing assessment, premature treatment discontinuation	5	(1.9)	8	(3.0)
Missing assessment, treatment completers (missing-at-random)	2	(0.8)	2	(0.8)
T2D, basal-bolus				
ONWARDS 4				
Full analysis set	291		291	
Treatment completers with final assessment	272	(93.5)	263	(90.4)
Retrieved data, premature treatment discontinuation	3	(1.0)	1	(0.3)
Missing assessment, premature treatment discontinuation	14	(4.8)	21	(7.2)
Missing assessment, treatment completers (missing-at-random)	2	(0.7)	6	(2.1)
T1D, basal-bolus				
ONWARDS 6				
Full analysis set	290		292	
Treatment completers with final assessment	269	(92.8)	281	(96.2)
Retrieved data, premature treatment discontinuation	5	(1.7)	2	(0.7)
Missing assessment, premature treatment discontinuation	13	(4.5)	7	(2.4)
Missing assessment, treatment completers (missing-at-random)	3	(1.0)	2	(0.7)

%: Percentage of subjects, HbA1c: Haemoglobin A1c, N: Number of subjects, Retrieved data: data collected after premature treatment discontinuation, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. 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). 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.

6.2.6 HbA1c (%) by treatment week - ONWARDS 1 - in-trial - missing pattern plot - full analysis set

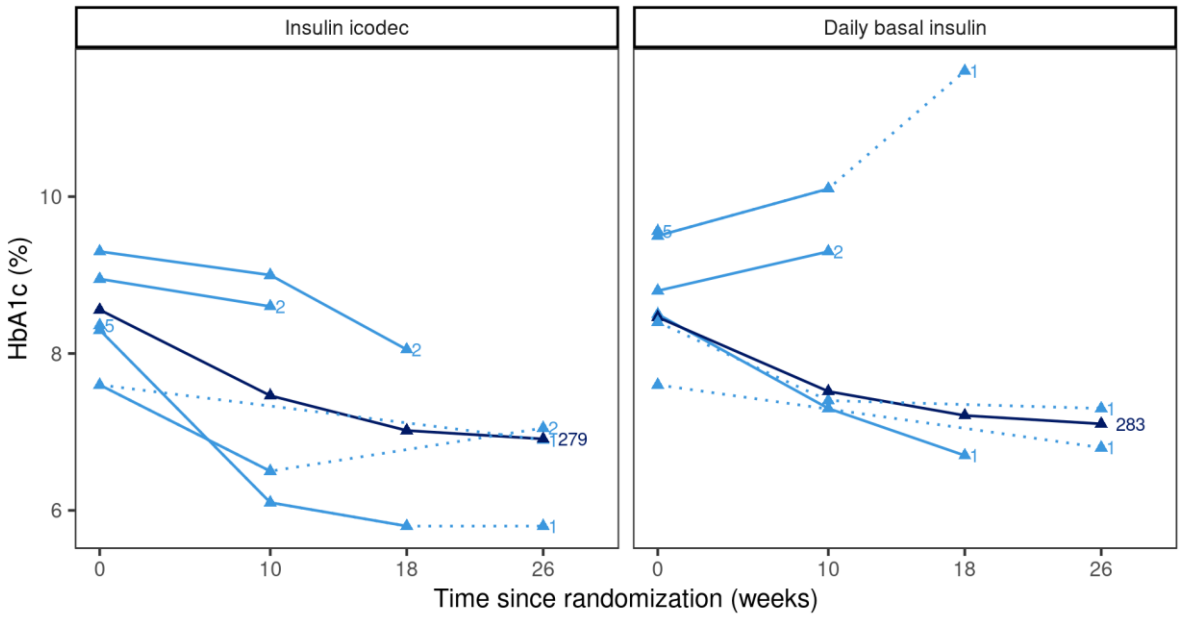


Observed data. HbA1c: Haemoglobin A1c. Daily basal insulin: IGlar U100. Legend: Mean HbA1c and number of subjects contributing to curve are shown for subjects completing week 52 visit (dark blue) and for subjects with intercurrent events (light blue). Lines are solid until intercurrent event.. Intercurrent event: Treatment discontinuation (ONWARDS 1-6) or initiation of bolus insulin (ONWARDS 1-3).

adsl.xpt; variable(s): EOTSTT EOTDT EOSDT BOLPERFL BOLPERDT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4477"
adlb.xpt; variable(s): AVISITN AVAL ADT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4477" & PARAMCD == "HBA1CB" & ANELFL == "Y" & ANL01FL == "Y" & FASFL == "Y" & AVISITN %in% c(200, 1200, 2000, 2800, 3600, 4000, 4600)

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6.2.7 HbA1c (%) by treatment week - ONWARDS 3 - in-trial - missing pattern plot - full analysis set

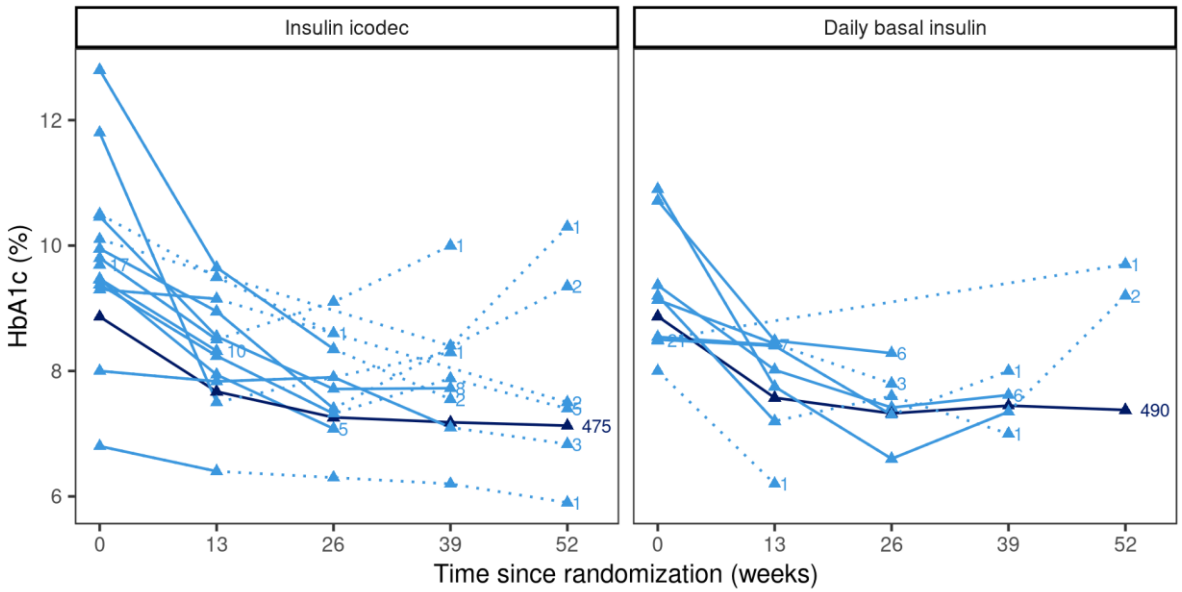


Observed data. HbA1c: Haemoglobin A1c. Daily basal insulin: IDeg. Legend: Mean HbA1c and number of subjects contributing to curve are shown for subjects completing week 26 visit (dark blue) and for subjects with intercurrent events (light blue). Lines are solid until intercurrent event.. Intercurrent event: Treatment discontinuation (ONWARDS 1-6) or initiation of bolus insulin (ONWARDS 1-3).

adsl.xpt; variable(s): EOTSTT EOTDT EOSDT BOLPERFL BOLPERDT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4479"
adlb.xpt; variable(s): AVISITN AVAL ADT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4479" & PARAMCD == "HBA1CB" & ANELFL == "Y" & ANL01FL == "Y" & FASFL == "Y" & AVISITN %in% c(200, 1200, 2000, 2800)

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6.2.8 HbA1c (%) by treatment week - ONWARDS 5 - in-trial - missing pattern plot - full analysis set

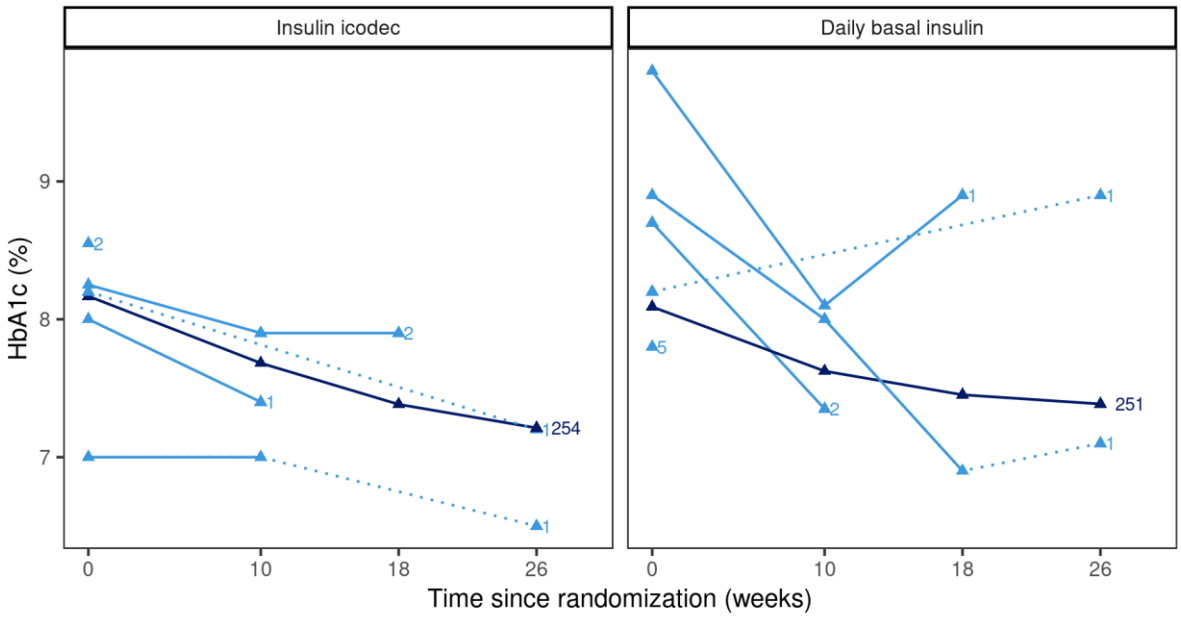


Observed data. HbA1c: Haemoglobin A1c. Daily basal insulin: once-daily analogues (IDeg, IGlar U100, IGlar U300). Legend: Mean HbA1c and number of subjects contributing to curve are shown for subjects completing week 52 visit (dark blue) and for subjects with intercurrent events (light blue). Lines are solid until intercurrent event.. Intercurrent event: Treatment discontinuation (ONWARDS 1-6) or initiation of bolus insulin (ONWARDS 1-3). OD analogues: Once-daily basal insulin analogues (IDeg, IGlar U100, IGlar U300).

adsl.xpt; variable(s): EOTSTT EOTDT EOSDT BOLPERFL BOLPERDT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4481"
adlb.xpt; variable(s): AVISITN AVAL ADT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4481" & PARAMCD == "HBA1CB" & ANELFL == "Y" & ANL01FL == "Y" & FASFL == "Y" & AVISITN %in% c(200, 300, 400, 500, 600)

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6.2.9 HbA1c (%) by treatment week - ONWARDS 2 - in-trial - missing pattern plot - full analysis set

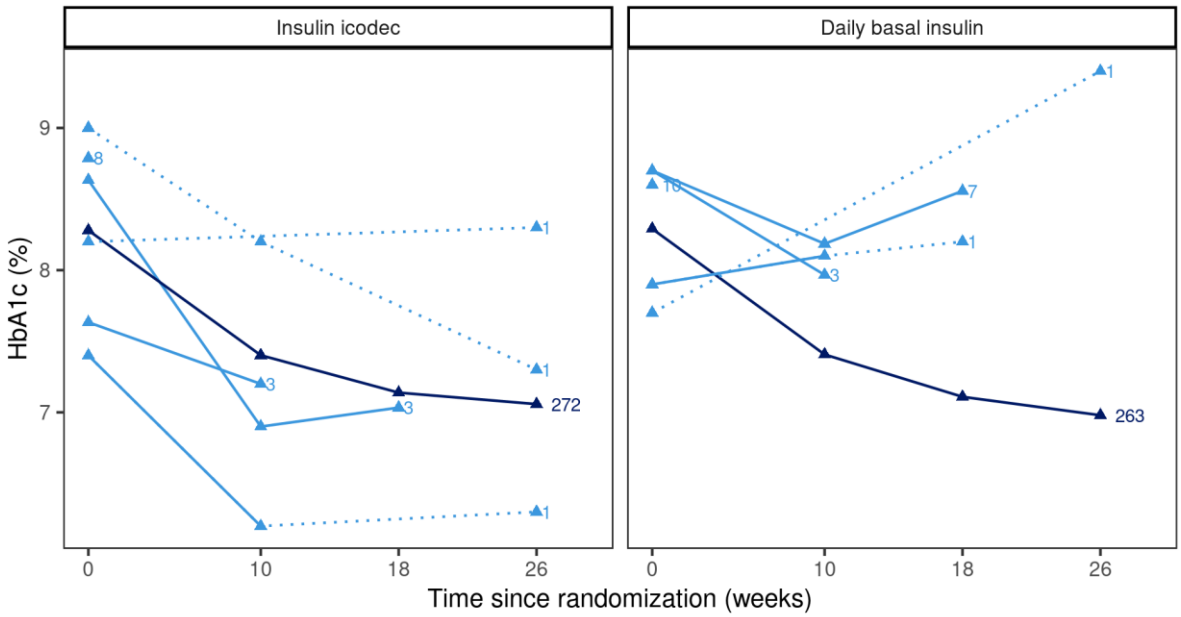


Observed data. HbA1c: Haemoglobin A1c. Daily basal insulin: IDeg. Legend: Mean HbA1c and number of subjects contributing to curve are shown for subjects completing week 26 visit (dark blue) and for subjects with intercurrent events (light blue). Lines are solid until intercurrent event.. Intercurrent event: Treatment discontinuation (ONWARDS 1-6) or initiation of bolus insulin (ONWARDS 1-3).

adsl.xpt; variable(s): EOTSTT EOTDT EOSDT BOLPERFL BOLPERDT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4478"
adlb.xpt; variable(s): AVISITN AVAL ADT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4478" & PARAMCD == "HBA1CB" & ANELFL == "Y" & ANL01FL == "Y" & FASFL == "Y" & AVISITN %in% c(200, 1200, 2000, 2800)

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6.2.10 HbA1c (%) by treatment week - ONWARDS 4 - in-trial - missing pattern plot - full analysis set

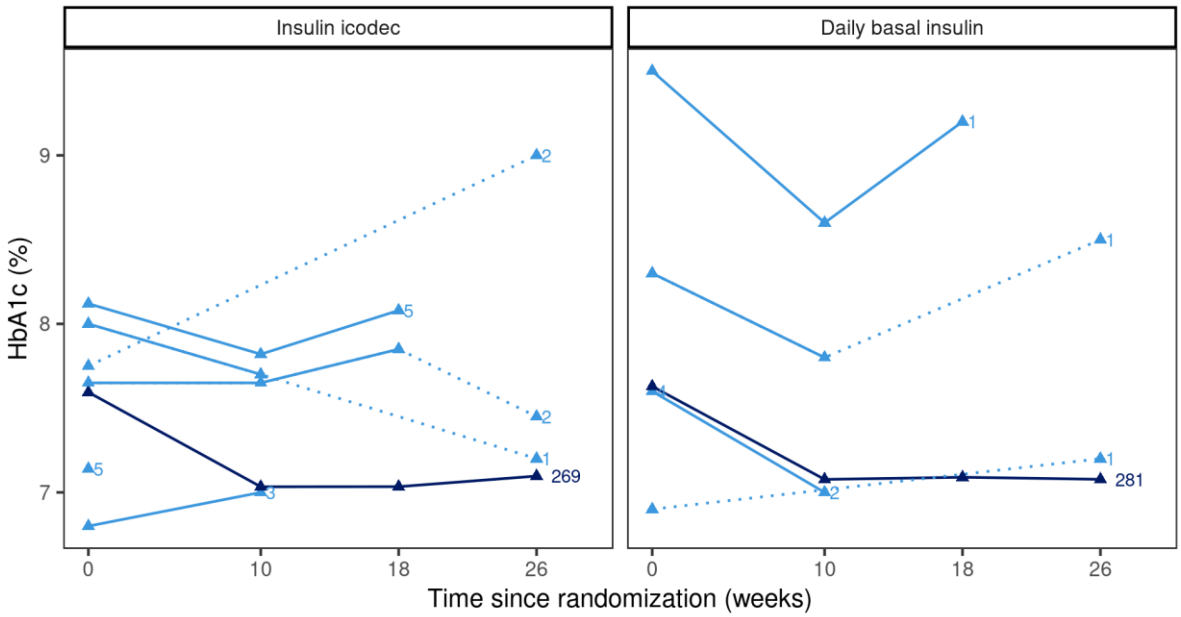


Observed data. HbA1c: Haemoglobin A1c. Daily basal insulin: IGlar U100. Legend: Mean HbA1c and number of subjects contributing to curve are shown for subjects completing week 26 visit (dark blue) and for subjects with intercurrent events (light blue). Lines are solid until intercurrent event.. Intercurrent event: Treatment discontinuation (ONWARDS 1-6) or initiation of bolus insulin (ONWARDS 1-3).

adsl.xpt; variable(s): EOTSTT EOTDT EOSDT BOLPERFL BOLPERDT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4480"
adlb.xpt; variable(s): AVISITN AVAL ADT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4480" & PARAMCD == "HBA1CB" & ANELFL == "Y" & ANL01FL == "Y" & FASFL == "Y" & AVISITN %in% c(200, 1200, 2000, 2800)

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6.2.11 HbA1c (%) by treatment week - ONWARDS 6 - in-trial - missing pattern plot - full analysis set

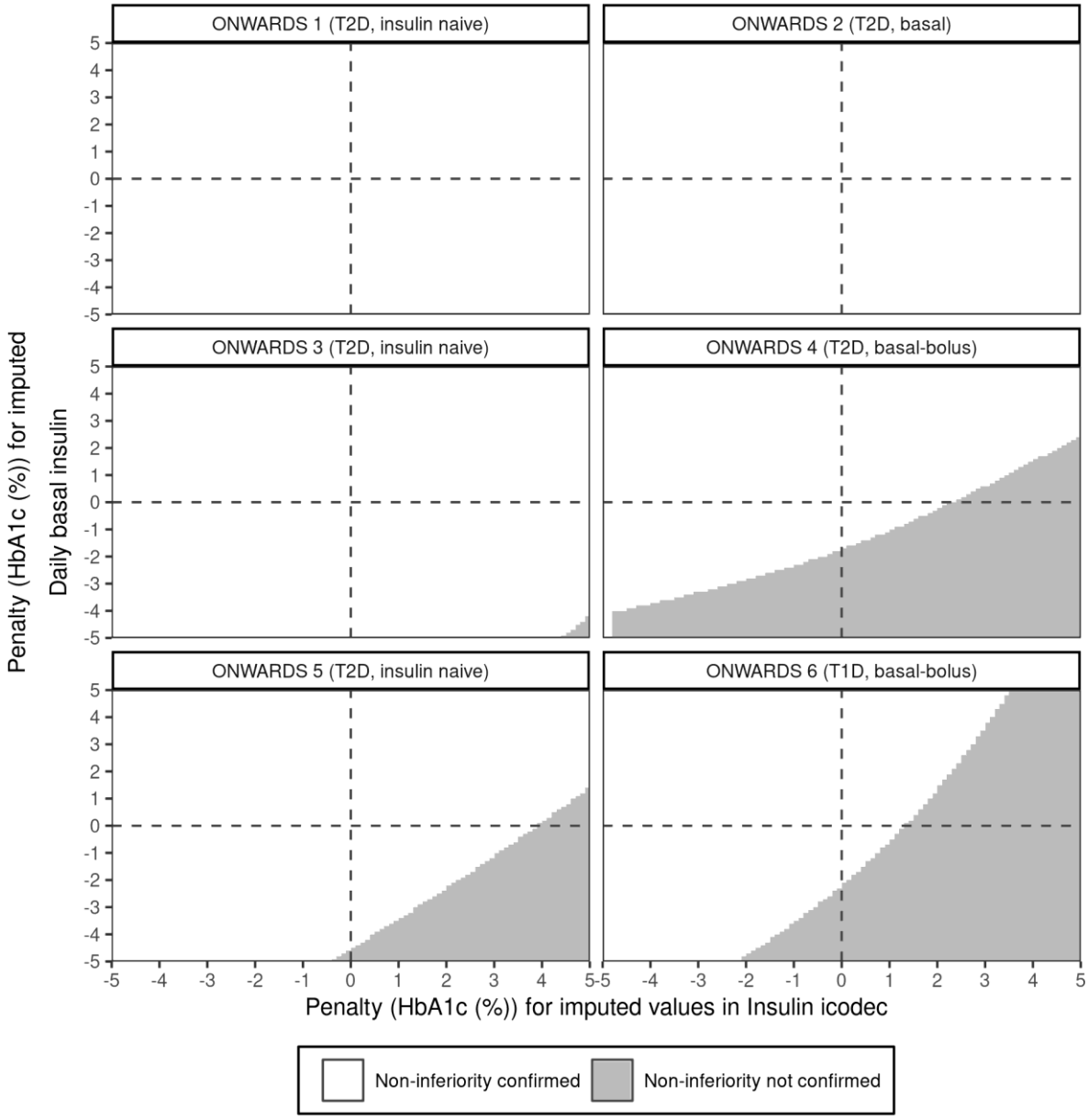


Observed data. HbA1c: Haemoglobin A1c. Daily basal insulin: IDeg. Legend: Mean HbA1c and number of subjects contributing to curve are shown for subjects completing week 26 visit (dark blue) and for subjects with intercurrent events (light blue). Lines are solid until intercurrent event.. Intercurrent event: Treatment discontinuation (ONWARDS 1-6) or initiation of bolus insulin (ONWARDS 1-3).

adsl.xpt; variable(s): EOTSTT EOTDT EOSDT BOLPERFL BOLPERDT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4625"
adlb.xpt; variable(s): AVISITN AVAL ADT; criteria: (FASFL == "Y") & STUDYID == "NN1436-4625" & PARAMCD == "HBA1CB" & ANELFL == "Y" & ANL01FL == "Y" & FASFL == "Y" & AVISITN %in% c(200, 1200, 2000, 2800)

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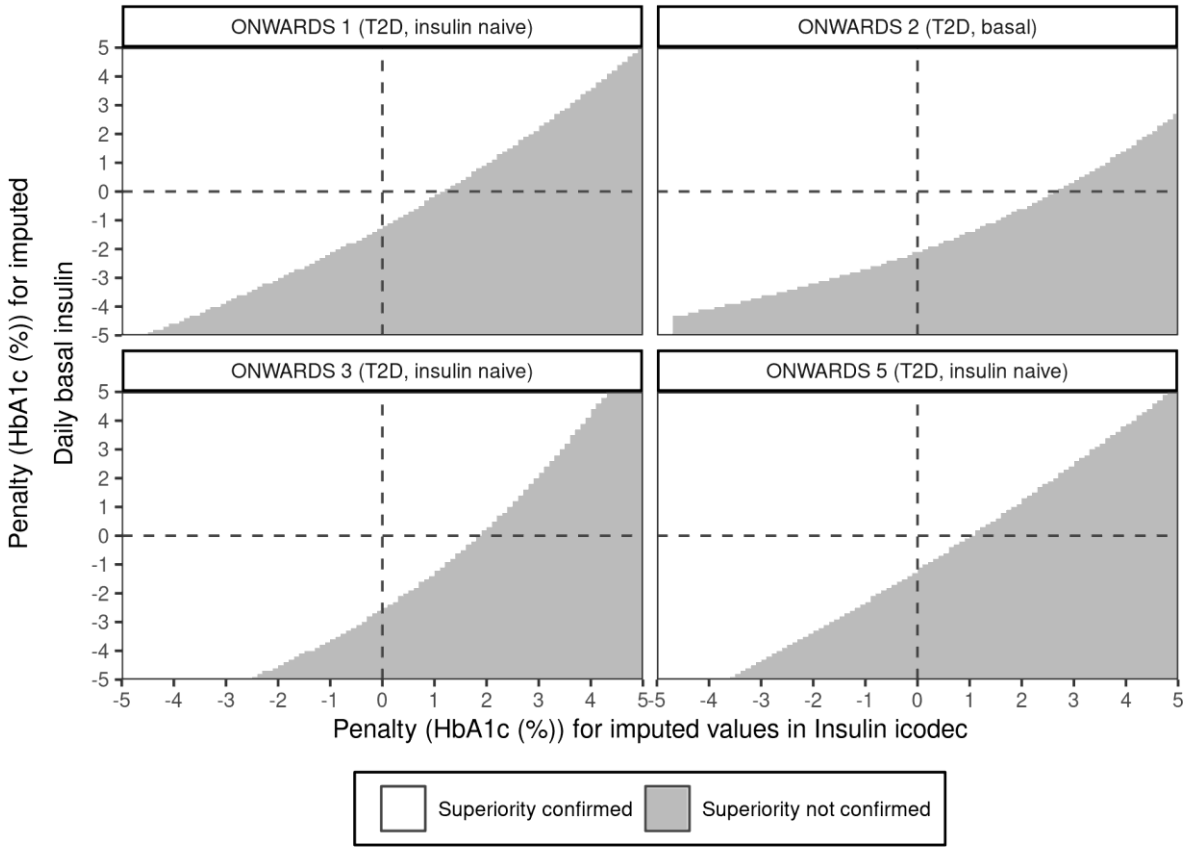
6.2.12 HbA1c (%) at planned end of treatment - change from baseline - in-trial - statistical sensitivity analysis - tipping point plot for non-inferiority - full analysis set



HbA1c: Haemoglobin A1c, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Observed data with missing values imputed using multiple imputation. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3), IGlar U100 (ONWARDS 1), 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.

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6.2.13 HbA1c (%) at planned end of treatment - change from baseline - in-trial - statistical sensitivity analysis - tipping point plot for superiority - full analysis set



HbA1c: Haemoglobin A1c, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Observed data with missing values imputed using multiple imputation. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3), IGlar U100 (ONWARDS 1), and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). Data from ONWARDS 1, 2, 3 and 5, only main part of ONWARDS 1. 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 and 3 (main part): Week 26.

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6.2.14 Fasting plasma glucose at baseline - in-trial - summary - full analysis set

	Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)
Fasting Plasma Glucose (mmol/L)				
T2D, insulin naive				
ONWARDS 1	480	10.28 (2.72)	474	10.31 (2.87)
ONWARDS 3	284	10.37 (3.01)	290	9.78 (2.55)
T2D, basal				
ONWARDS 2	260	8.45 (2.63)	257	8.36 (2.27)
T2D, basal-bolus				
ONWARDS 4	283	9.24 (3.00)	284	9.60 (3.52)
T1D, basal-bolus				
ONWARDS 6	276	9.94 (4.10)	287	9.56 (4.01)
Fasting plasma glucose (mg/dL)				
T2D, insulin naive				
ONWARDS 1	480	185.31 (48.96)	474	185.71 (51.66)
ONWARDS 3	284	186.78 (54.20)	290	176.20 (45.90)
T2D, basal				
ONWARDS 2	260	152.24 (47.47)	257	150.70 (40.92)
T2D, basal-bolus				
ONWARDS 4	283	166.59 (54.10)	284	173.05 (63.46)
T1D, basal-bolus				
ONWARDS 6	276	179.17 (73.86)	287	172.31 (72.30)

N: Number of subjects, SD: Standard deviation, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4). Data from ONWARDS 1-4 and 6, only main part of ONWARDS 1 and 6.

6.2.15 Fasting plasma glucose at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
FPG (mmol/L)						
T2D, insulin naive						
ONWARDS 1						
LSMeans						
Insulin icodec	492	480	6.95	0.09		
Daily basal insulin	492	474	6.96	0.09		
LSMeans, change from baseline						
Insulin icodec	492	480	-3.35	0.09		
Daily basal insulin	492	474	-3.33	0.09		
Treatment contrast						
Insulin icodec - Daily basal insulin			-0.01		[-0.27 ; 0.24]	0.9200
ONWARDS 3						
LSMeans						
Insulin icodec	294	284	7.06	0.11		
Daily basal insulin	294	290	7.08	0.11		
LSMeans, change from baseline						
Insulin icodec	294	284	-3.01	0.11		
Daily basal insulin	294	290	-2.99	0.11		
Treatment contrast						
Insulin icodec - Daily basal insulin			-0.02		[-0.34 ; 0.29]	0.8965
T2D, basal						
ONWARDS 2						
LSMeans						
Insulin icodec	263	260	6.83	0.12		
Daily basal insulin	263	257	6.79	0.12		
LSMeans, change from baseline						
Insulin icodec	263	260	-1.58	0.12		
Daily basal insulin	263	257	-1.62	0.12		
Treatment contrast						
Insulin icodec - Daily basal insulin			0.04		[-0.28 ; 0.36]	0.8121
T2D, basal-bolus						
ONWARDS 4						
LSMeans						
Insulin icodec	291	283	7.67	0.16		
Daily basal insulin	291	284	7.81	0.16		
LSMeans, change from baseline						
Insulin icodec	291	283	-1.75	0.16		
Daily basal insulin	291	284	-1.61	0.16		
Treatment contrast						
Insulin icodec - Daily basal insulin			-0.14		[-0.59 ; 0.31]	0.5489

CI: Confidence interval, FAS: Number of subjects in full analysis set, FPG: Fasting plasma glucose, N: Number of subjects contributing to the analysis, T1D: Type 1 diabetes, T2D: Type 2 diabetes, P-value: Two-sided p-value for test of no treatment difference. SE: Standard error of the mean. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4). Data from ONWARDS 1-4 and 6, only main part of ONWARDS 1 and 6. ANCOVA with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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): Week 52, ONWARDS 2-4 and 6 (main part): Week 26.

Fasting plasma glucose at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
T1D, basal-bolus						
ONWARDS 6						
LSMeans						
Insulin icodec	290	276	8.91	0.20		
Daily basal insulin	292	287	7.88	0.20		
LSMeans, change from baseline						
Insulin icodec	290	276	-0.84	0.20		
Daily basal insulin	292	287	-1.87	0.20		
Treatment contrast						
Insulin icodec - Daily basal insulin			1.03		[0.48 ; 1.59]	0.0003
FPG (mg/dL)						
T2D, insulin naive						
ONWARDS 1						
LSMeans						
Insulin icodec	492	480	125.19	1.67		
Daily basal insulin	492	474	125.43	1.68		
LSMeans, change from baseline						
Insulin icodec	492	480	-60.32	1.67		
Daily basal insulin	492	474	-60.08	1.68		
Treatment contrast						
Insulin icodec - Daily basal insulin			-0.24		[-4.89 ; 4.41]	0.9200
ONWARDS 3						
LSMeans						
Insulin icodec	294	284	127.16	2.06		
Daily basal insulin	294	290	127.53	2.02		
LSMeans, change from baseline						
Insulin icodec	294	284	-54.28	2.06		
Daily basal insulin	294	290	-53.90	2.02		
Treatment contrast						
Insulin icodec - Daily basal insulin			-0.38		[-6.05 ; 5.30]	0.8965
T2D, basal						
ONWARDS 2						
LSMeans						
Insulin icodec	263	260	123.01	2.08		
Daily basal insulin	263	257	122.30	2.10		
LSMeans, change from baseline						
Insulin icodec	263	260	-28.47	2.08		
Daily basal insulin	263	257	-29.18	2.10		
Treatment contrast						
Insulin icodec - Daily basal insulin			0.71		[-5.12 ; 6.54]	0.8121

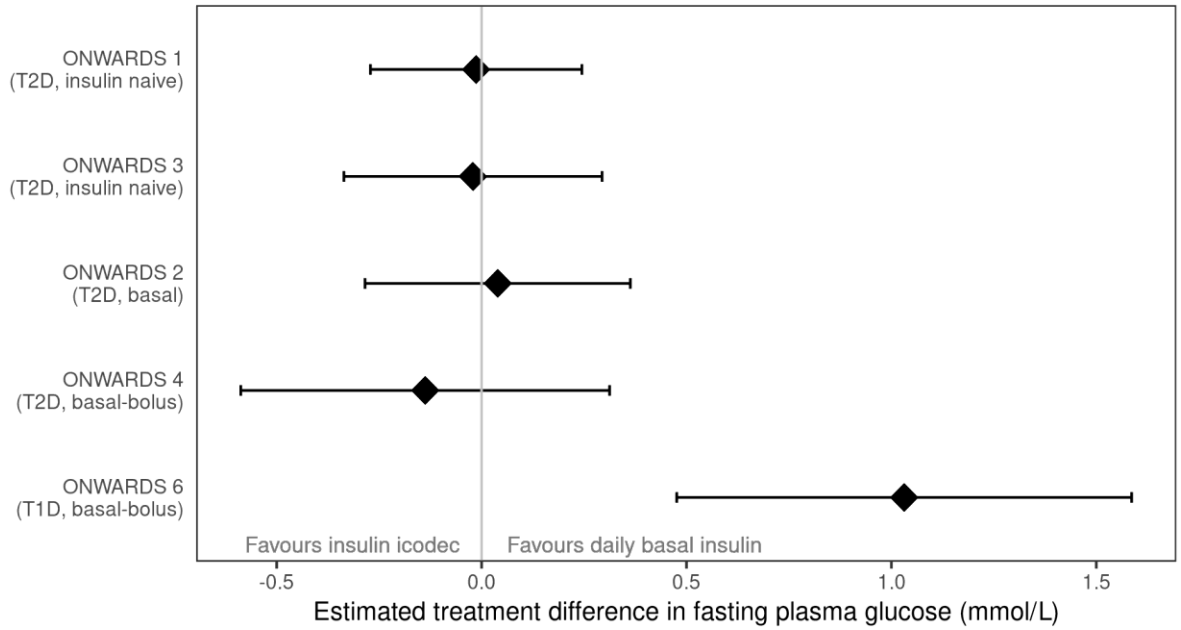
CI: Confidence interval, FAS: Number of subjects in full analysis set, FPG: Fasting plasma glucose, N: Number of subjects contributing to the analysis, T1D: Type 1 diabetes, T2D: Type 2 diabetes, P-value: Two-sided p-value for test of no treatment difference. SE: Standard error of the mean. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4). Data from ONWARDS 1-4 and 6, only main part of ONWARDS 1 and 6. ANCOVA with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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): Week 52, ONWARDS 2-4 and 6 (main part): Week 26.

Fasting plasma glucose at planned end of treatment - change from baseline - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
T2D, basal-bolus						
ONWARDS 4						
LSMeans						
Insulin icodec	291	283	138.28	2.90		
Daily basal insulin	291	284	140.76	2.93		
LSMeans, change from baseline						
Insulin icodec	291	283	-31.54	2.90		
Daily basal insulin	291	284	-29.06	2.93		
Treatment contrast						
Insulin icodec - Daily basal insulin			-2.48		[-10.59 ; 5.63]	0.5489
T1D, basal-bolus						
ONWARDS 6						
LSMeans						
Insulin icodec	290	276	160.60	3.65		
Daily basal insulin	292	287	142.02	3.55		
LSMeans, change from baseline						
Insulin icodec	290	276	-15.08	3.65		
Daily basal insulin	292	287	-33.66	3.55		
Treatment contrast						
Insulin icodec - Daily basal insulin			18.58		[8.58 ; 28.58]	0.0003

CI: Confidence interval, FAS: Number of subjects in full analysis set, FPG: Fasting plasma glucose, N: Number of subjects contributing to the analysis, T1D: Type 1 diabetes, T2D: Type 2 diabetes, P-value: Two-sided p-value for test of no treatment difference. SE: Standard error of the mean. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4). Data from ONWARDS 1-4 and 6, only main part of ONWARDS 1 and 6. ANCOVA with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation. 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): Week 52, ONWARDS 2-4 and 6 (main part): Week 26.

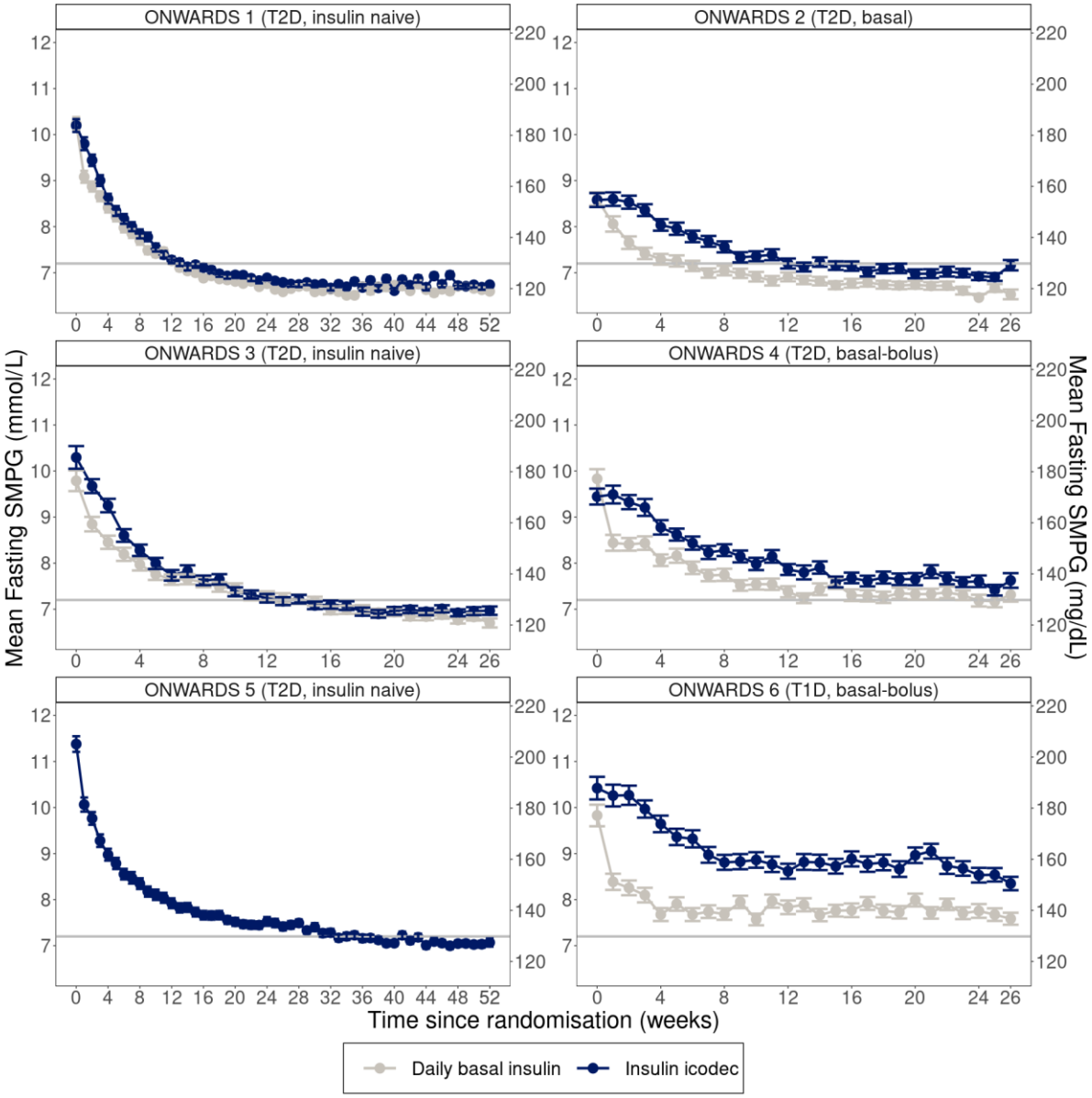
6.2.16 Fasting plasma glucose (mmol/L) at planned end of treatment - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



Estimates with 95% confidence interval. T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 3, ONWARDS 6), IGlar U100 (ONWARDS 1, ONWARDS 4). 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): Week 52, ONWARDS 2-4 and 6 (main part): Week 26. Data from ONWARDS 1-4 and 6, only main part of ONWARDS 1 and 6. ANCOVA with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation.

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6.2.17 Mean fasting self-measured plasma glucose for dose adjustment 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("SMPGXMP", "SMPGXMP2") & ANELFL == "Y" & ANL01FL == "Y" & !is.na(AWEEKN) & !(STUDYID == "NN1436-4481" & TRTPN != 1)

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6.2.18 Time in range 3.9-10.0 mmol/L (70-180 mg/dL) at planned end of treatment - 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	439	71.94 (18.23)	440	66.90 (18.19)
T2D, basal				
ONWARDS 2	238	63.13 (17.40)	239	59.50 (18.92)
T2D, basal-bolus				
ONWARDS 4	244	66.88 (15.62)	237	66.44 (16.17)
T1D				
ONWARDS 6	261	59.10 (15.66)	272	60.85 (15.03)

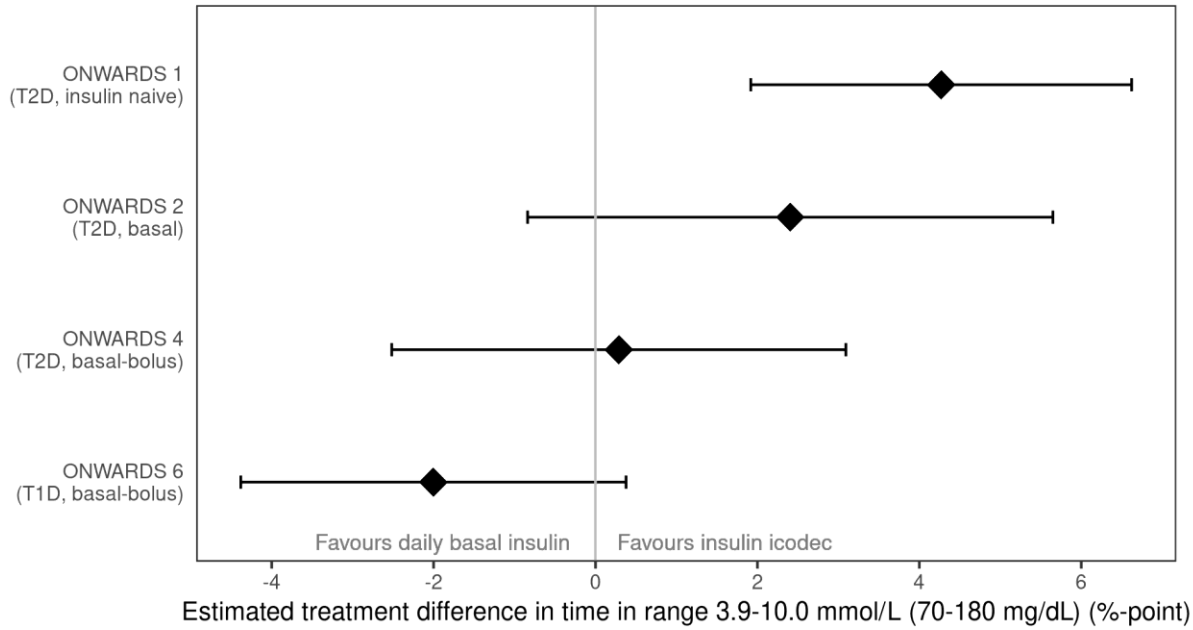
N: Number of subjects, SD: Standard deviation, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 6), and IGlar U100 (ONWARDS 1, ONWARDS 4). Data from ONWARDS 1, 2, 4 and 6, only main part of ONWARDS 1 and 6. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26.

6.2.19 Time in range 3.9-10.0 mmol/L (70-180 mg/dL) at planned end of treatment - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
Time in range 3.9-10.0 mmol/L (70-180 mg/dL) (%)						
T2D, insulin naive						
ONWARDS 1						
LSMeans						
Insulin icodec	492	492	71.27	0.85		
Daily basal insulin	492	492	67.00	0.85		
Treatment contrast						
Insulin icodec - Daily basal insulin			4.27		[1.92 ; 6.62]	0.0004
T2D, basal						
ONWARDS 2						
LSMeans						
Insulin icodec	263	263	62.34	1.16		
Daily basal insulin	263	263	59.93	1.16		
Treatment contrast						
Insulin icodec - Daily basal insulin			2.41		[-0.84 ; 5.65]	0.1461
T2D, basal-bolus						
ONWARDS 4						
LSMeans						
Insulin icodec	291	291	66.75	1.00		
Daily basal insulin	291	291	66.46	1.02		
Treatment contrast						
Insulin icodec - Daily basal insulin			0.29		[-2.52 ; 3.09]	0.8406
T1D, basal-bolus						
ONWARDS 6						
LSMeans						
Insulin icodec	290	290	59.06	0.86		
Daily basal insulin	292	292	61.06	0.85		
Treatment contrast						
Insulin icodec - Daily basal insulin			-2.00		[-4.38 ; 0.38]	0.0991

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, T1D: Type 1 diabetes, T2D: Type 2 diabetes, P-value: Two-sided p-value for test of no treatment difference. P-value (ONWARDS 1): Two-sided p-value for test of superiority. Time in range was a confirmatory secondary endpoint in ONWARDS 1, SE: Standard error of the mean. 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26. ANOVA with treatment, region and, if applicable, additional relevant factors as fixed factors. Missing data are imputed using multiple imputation.

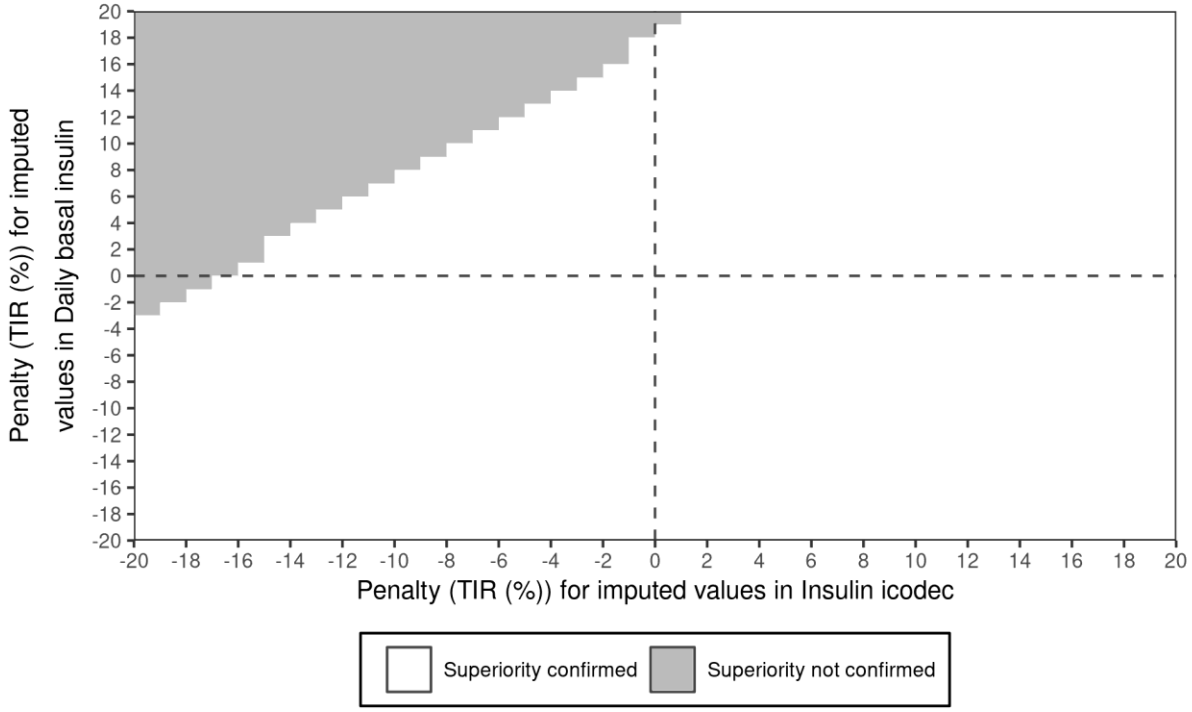
6.2.20 Time in range 3.9-10.0 mmol/L (70-180 mg/dL) (%) at planned end of treatment - in-trial - plot of estimated treatment differences - full analysis set



Estimates with 95% confidence interval. T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. ANOVA with treatment, region and, if applicable, additional relevant factors as fixed factors. Missing data are imputed using multiple imputation.

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6.2.21 Time in range 3.9-10.0 mmol/L (70-180 mg/dL) at planned end of treatment - ONWARDS 1 - in-trial - statistical sensitivity analysis - tipping point plot - full analysis set



TIR: Time in range 3.9-10.0 mmol/L (70-180 mg/dL). Daily basal insulin: IGlar U100 (ONWARDS 1). Data from main part of ONWARDS 1. End of treatment: ONWARDS 1 (main part): Week 48-52.

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6.2.22 Time spent below range at planned end of treatment - in-trial - summary - full analysis set

	TBR < 3.0 mmol/L (54 mg/dL) (%)				TBR < 3.9 mmol/L (70 mg/dL) (%)			
	Insulin icodec		Daily basal insulin		Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
T2D, insulin naïve								
ONWARDS 1	439	0.27 (0.57)	440	0.21 (0.63)	439	1.20 (1.98)	440	0.83 (2.12)
T2D, basal								
ONWARDS 2	238	0.34 (0.88)	239	0.22 (0.45)	238	1.35 (2.23)	239	0.79 (1.12)
T2D, basal-bolus								
ONWARDS 4	244	0.73 (1.14)	237	0.61 (1.07)	244	2.65 (2.92)	237	2.26 (2.62)
T1D								
ONWARDS 6	261	1.02 (1.64)	272	0.68 (1.27)	261	3.86 (3.56)	272	2.90 (2.91)

N: Number of subjects, SD: Standard deviation, TBR: Time below range, 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26.

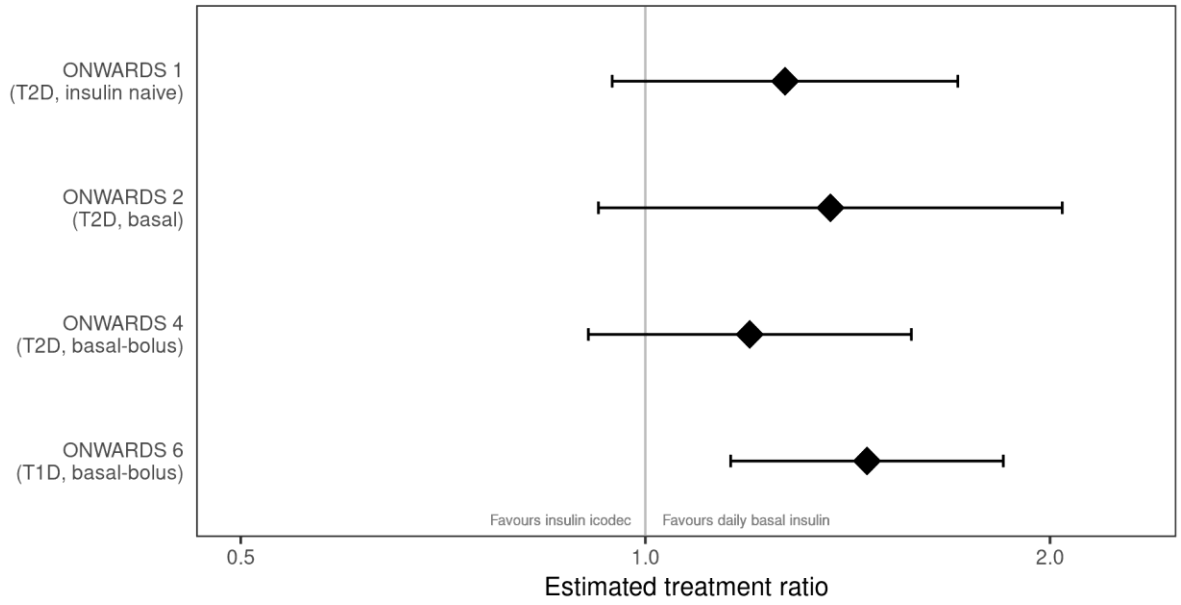
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6.2.23 Time spent < 3.0 mmol/L (54 mg/dL) at planned end of treatment - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
Time spent < 3.0 mmol/L (54 mg/dL) (%)					
T2D, insulin naive					
ONWARDS 1					
LSMeans					
Insulin icodec	492	439	0.21		
Daily basal insulin	492	440	0.16		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.27	[0.94 ; 1.71]	0.1134
T2D, basal					
ONWARDS 2					
LSMeans					
Insulin icodec	263	238	0.33		
Daily basal insulin	263	239	0.24		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.37	[0.92 ; 2.04]	0.1180
T2D, basal-bolus					
ONWARDS 4					
LSMeans					
Insulin icodec	291	244	0.69		
Daily basal insulin	291	237	0.58		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.20	[0.91 ; 1.58]	0.2050
T1D, basal-bolus					
ONWARDS 6					
LSMeans					
Insulin icodec	290	261	0.94		
Daily basal insulin	292	272	0.65		
Treatment ratio					
Insulin icodec / Daily basal insulin			1.46	[1.16 ; 1.85]	0.0014

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, T1D: Type 1 diabetes, T2D: Type 2 diabetes. P-value: Two-sided p-value for test of no treatment difference. 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26. Negative binomial model (log link) on the number of recorded measurements in a given range. The model includes treatment, region and, if applicable, additional relevant factors as fixed factors, and the logarithm of the total number of recorded measurements as an offset.

6.2.24 Time spent < 3.0 mmol/L (54 mg/dL) (%) at planned end of treatment - in-trial - plot of estimated treatment ratios - full analysis set



Estimates with 95% confidence interval. T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Negative binomial model (log link) on the number of recorded measurements in a given range. The model includes treatment, region and, if applicable, additional relevant factors as fixed factors, and the logarithm of the total number of recorded measurements as an offset.

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6.2.25 Time spent above range at planned end of treatment - in-trial - summary - full analysis set

	TAR > 10.0 mmol/L (180 mg/dL) (%)				TAR > 13.9 mmol/L (250 mg/dL) (%)			
	Insulin icodec		Daily basal insulin		Insulin icodec		Daily basal insulin	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
T2D, insulin naïve								
ONWARDS 1	439	26.86 (18.74)	440	32.27 (18.66)	439	6.66 (9.96)	440	8.86 (12.09)
T2D, basal								
ONWARDS 2	238	35.52 (17.95)	239	39.71 (19.34)	238	10.83 (11.07)	239	13.29 (14.14)
T2D, basal-bolus								
ONWARDS 4	244	30.47 (15.90)	237	31.30 (16.67)	244	8.53 (9.45)	237	8.59 (9.94)
T1D								
ONWARDS 6	261	37.03 (16.21)	272	36.25 (15.61)	261	13.24 (11.09)	272	12.18 (10.54)

N: Number of subjects, SD: Standard deviation, TAR: Time above range, 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26.

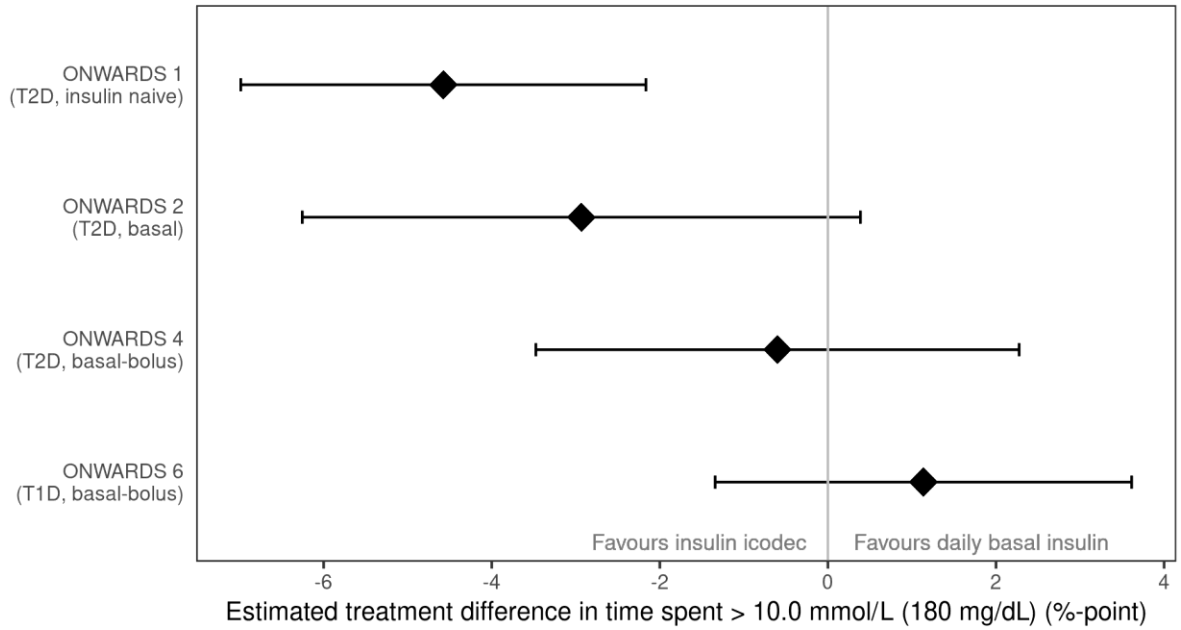
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6.2.26 Time spent > 10.0 mmol/L (180 mg/dL) at planned end of treatment - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	SE	95% CI	P-value
Time spent > 10.0 mmol/L (180 mg/dL) (%)						
T2D, insulin naive						
ONWARDS 1						
LSMeans						
Insulin icodec	492	492	27.56	0.87		
Daily basal insulin	492	492	32.13	0.87		
Treatment contrast						
Insulin icodec - Daily basal insulin			-4.58		[-6.99 ; -2.17]	0.0002
T2D, basal						
ONWARDS 2						
LSMeans						
Insulin icodec	263	263	36.34	1.19		
Daily basal insulin	263	263	39.28	1.19		
Treatment contrast						
Insulin icodec - Daily basal insulin			-2.93		[-6.25 ; 0.39]	0.0833
T2D, basal-bolus						
ONWARDS 4						
LSMeans						
Insulin icodec	291	291	30.64	1.03		
Daily basal insulin	291	291	31.24	1.04		
Treatment contrast						
Insulin icodec - Daily basal insulin			-0.60		[-3.47 ; 2.28]	0.6826
T1D, basal-bolus						
ONWARDS 6						
LSMeans						
Insulin icodec	290	290	37.16	0.90		
Daily basal insulin	292	292	36.03	0.88		
Treatment contrast						
Insulin icodec - Daily basal insulin			1.14		[-1.34 ; 3.61]	0.3689

CI: Confidence interval, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, T1D: Type 1 diabetes, T2D: Type 2 diabetes, P-value: Two-sided p-value for test of no treatment difference. SE: Standard error of the mean. 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26. ANOVA with treatment, region and, if applicable, additional relevant factors as fixed factors. Missing data are imputed using multiple imputation.

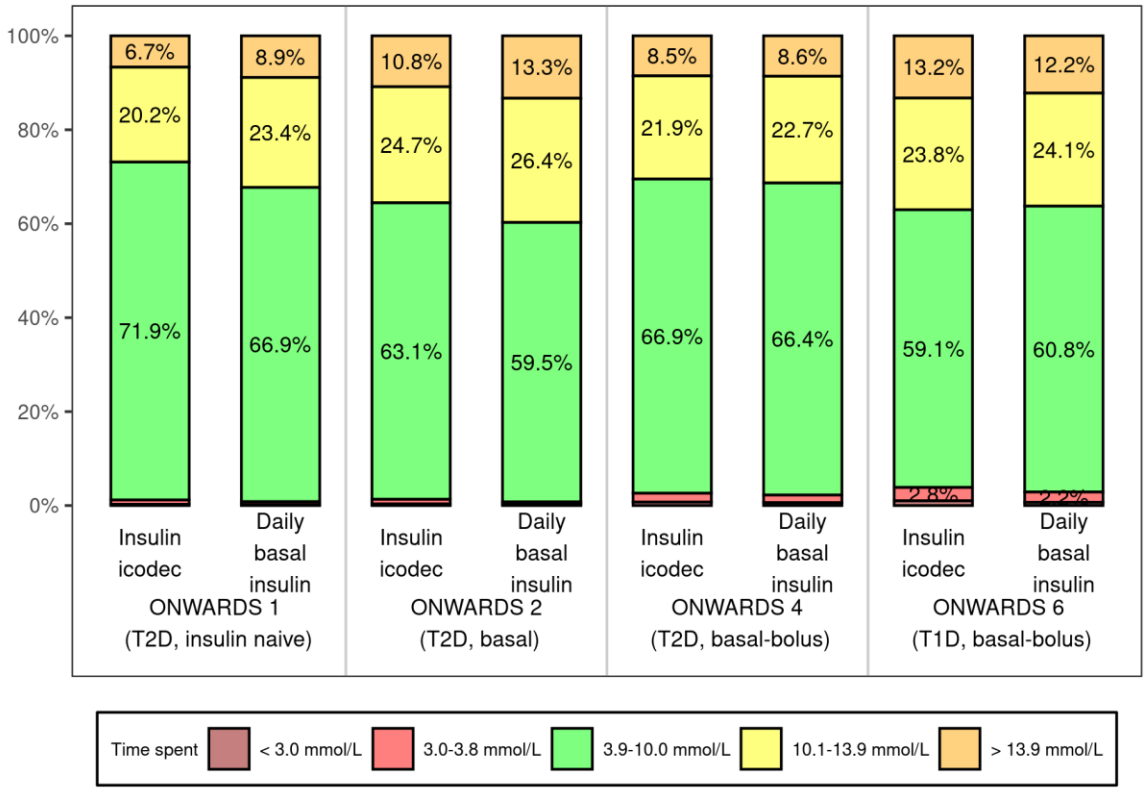
6.2.27 Time spent > 10.0 mmol/L (180 mg/dL) (%) at planned end of treatment - in-trial - plot of estimated treatment differences - full analysis set



Estimates with 95% confidence interval. T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. ANOVA with treatment, region and, if applicable, additional relevant factors as fixed factors. Missing data are imputed using multiple imputation.

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6.2.28 CGM ranges (%) at planned end of treatment - in-trial - bar chart - full analysis set



Observed data. Values <2% are shown on the plot but the numbers are not displayed. CGM: Continuous glucose monitoring, T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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. End of treatment: ONWARDS 1 (main part): Week 48-52, ONWARDS 2, 4 and 6 (main part): Week 22-26. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements.

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6.2.29 Achievement of HbA1c<7.0% at planned end of treatment - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
HbA1c <7.0%					
T2D, insulin naive					
ONWARDS 1					
LSMeans, frequency					
Insulin icodec	492	492	57.57		
Daily basal insulin	492	492	45.44		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.63	[1.24 ; 2.14]	0.0005
ONWARDS 3					
LSMeans, frequency					
Insulin icodec	294	294	56.83		
Daily basal insulin	294	294	41.64		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.85	[1.29 ; 2.64]	0.0008
ONWARDS 5					
LSMeans, frequency					
Insulin icodec	542	542	46.76		
Daily basal insulin	543	542	34.65		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.66	[1.24 ; 2.21]	0.0006
T2D, basal					
ONWARDS 2					
LSMeans, frequency					
Insulin icodec	263	263	40.32		
Daily basal insulin	263	263	26.49		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.88	[1.26 ; 2.79]	0.0019
T2D, basal-bolus					
ONWARDS 4					
LSMeans, frequency					
Insulin icodec	291	291	40.69		
Daily basal insulin	291	291	45.48		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.82	[0.58 ; 1.17]	0.2746

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, T1D: Type 1 diabetes, T2D: Type 2 diabetes. P-value: Two-sided p-value for test of no treatment difference. 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. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

Achievement of HbA1c<7.0% at planned end of treatment - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
T1D, basal-bolus					
ONWARDS 6					
LSMeans, frequency					
Insulin icodec	290	290	40.20		
Daily basal insulin	292	292	45.72		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.80	[0.53 ; 1.19]	0.2694

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, T1D: Type 1 diabetes, T2D: Type 2 diabetes. P-value: Two-sided p-value for test of no treatment difference. 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. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

6.2.30 Achievement of HbA1c<=6.5% at planned end of treatment - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
HbA1c <=6.5%					
T2D, insulin naive					
ONWARDS 1					
LSMeans, frequency					
Insulin icodec	492	492	33.24		
Daily basal insulin	492	492	24.96		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.50	[1.12 ; 2.01]	0.0072
ONWARDS 3					
LSMeans, frequency					
Insulin icodec	294	294	31.00		
Daily basal insulin	294	294	19.60		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.84	[1.25 ; 2.71]	0.0019
ONWARDS 5					
LSMeans, frequency					
Insulin icodec	542	542	24.91		
Daily basal insulin	543	542	17.21		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.60	[1.15 ; 2.21]	0.0050
T2D, basal					
ONWARDS 2					
LSMeans, frequency					
Insulin icodec	263	263	13.51		
Daily basal insulin	263	263	7.49		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.93	[1.13 ; 3.28]	0.0156
T2D, basal-bolus					
ONWARDS 4					
LSMeans, frequency					
Insulin icodec	291	291	19.81		
Daily basal insulin	291	291	21.64		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.89	[0.60 ; 1.33]	0.5811

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

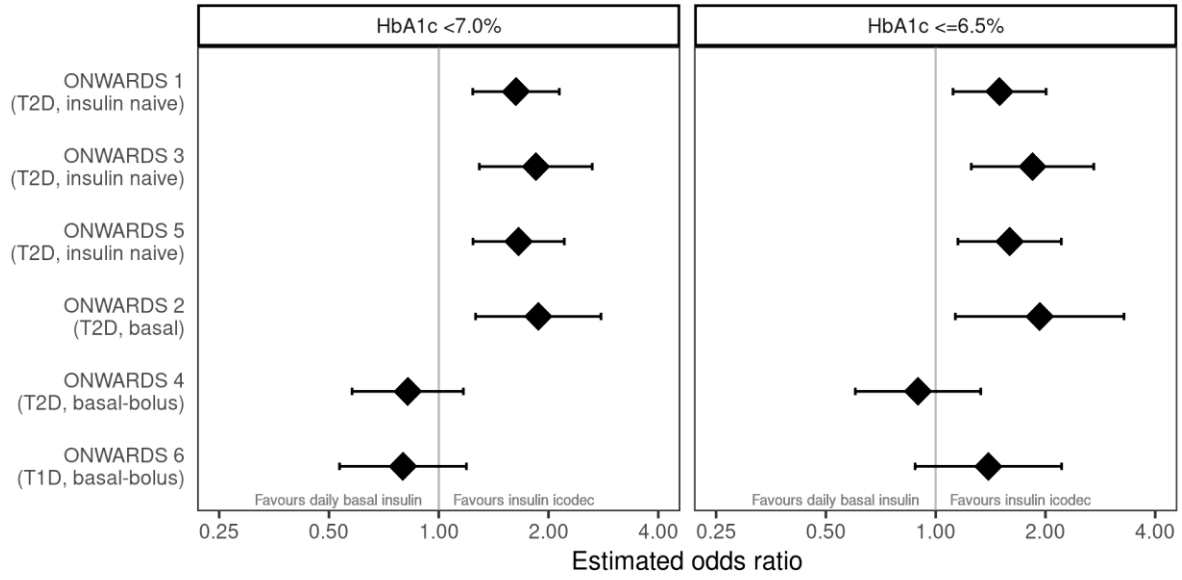
Achievement of HbA1c<=6.5% at planned end of treatment - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
T1D, basal-bolus					
ONWARDS 6					
LSMeans, frequency					
Insulin icodec	290	290	23.95		
Daily basal insulin	292	292	18.42		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.39	[0.88 ; 2.22]	0.1584

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

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6.2.31 Achievement of HbA1c targets at planned end of treatment - in-trial - plot of estimated odds ratios - full analysis set



Estimates with 95% confidence interval. HbA1c: Haemoglobin A1c, 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). 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. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis.

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6.2.32 Achievement of HbA1c<7.0% at planned end of treatment without severe hypoglycaemic episodes (level 3) during the prior 12 weeks - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
HbA1c <7.0% w/o level 3 hypoglycaemic episodes					
T2D, insulin naive					
ONWARDS 1					
LSMeans, frequency					
Insulin icodec	492	492	55.69		
Daily basal insulin	492	492	44.42		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.57	[1.21 ; 2.05]	0.0008
ONWARDS 3					
LSMeans, frequency					
Insulin icodec	294	294	55.21		
Daily basal insulin	294	294	40.57		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.81	[1.27 ; 2.56]	0.0010
ONWARDS 5					
LSMeans, frequency					
Insulin icodec	542	542	42.43		
Daily basal insulin	543	542	33.05		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.49	[1.15 ; 1.94]	0.0027
T2D, basal					
ONWARDS 2					
LSMeans, frequency					
Insulin icodec	263	263	39.09		
Daily basal insulin	263	263	26.27		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.80	[1.22 ; 2.67]	0.0033
T2D, basal-bolus					
ONWARDS 4					
LSMeans, frequency					
Insulin icodec	291	291	39.63		
Daily basal insulin	291	291	44.20		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.83	[0.59 ; 1.17]	0.2896

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, w/o: without, T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

Achievement of HbA1c<7.0% at planned end of treatment without severe hypoglycaemic episodes (level 3) during the prior 12 weeks - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
T1D, basal-bolus					
ONWARDS 6					
LSMeans, frequency					
Insulin icodec	290	290	37.55		
Daily basal insulin	292	292	44.20		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.76	[0.52 ; 1.12]	0.1612

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, w/o: without, T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

6.2.33 Achievement of HbA1c<=6.5% at planned end of treatment without severe hypoglycaemic episodes (level 3) during the prior 12 weeks - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
HbA1c <=6.5% w/o level 3 hypoglycaemic episodes					
T2D, insulin naive					
ONWARDS 1					
LSMeans, frequency					
Insulin icodec	492	492	31.52		
Daily basal insulin	492	492	24.25		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.44	[1.08 ; 1.92]	0.0133
ONWARDS 3					
LSMeans, frequency					
Insulin icodec	294	294	30.50		
Daily basal insulin	294	294	19.04		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.87	[1.27 ; 2.75]	0.0016
ONWARDS 5					
LSMeans, frequency					
Insulin icodec	542	542	21.84		
Daily basal insulin	543	542	15.85		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.48	[1.09 ; 2.01]	0.0110
T2D, basal					
ONWARDS 2					
LSMeans, frequency					
Insulin icodec	263	263	12.92		
Daily basal insulin	263	263	7.45		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.84	[1.08 ; 3.13]	0.0237
T2D, basal-bolus					
ONWARDS 4					
LSMeans, frequency					
Insulin icodec	291	291	19.51		
Daily basal insulin	291	291	21.65		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.88	[0.59 ; 1.30]	0.5159

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, w/o: without, T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

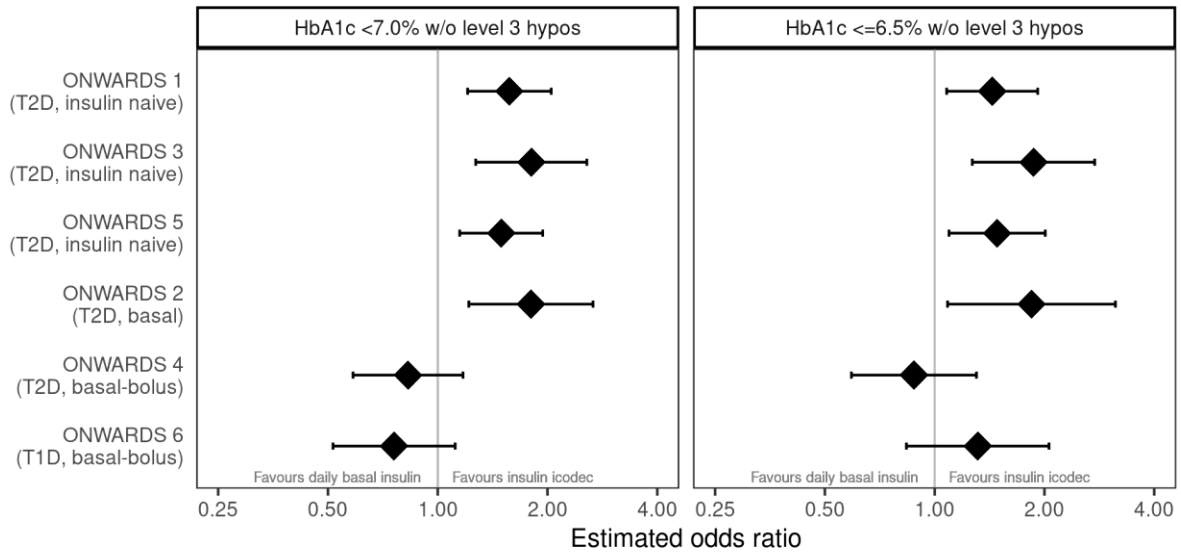
Achievement of HbA1c<=6.5% at planned end of treatment without severe hypoglycaemic episodes (level 3) during the prior 12 weeks - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
T1D, basal-bolus					
ONWARDS 6					
LSMeans, frequency					
Insulin icodec	290	290	21.87		
Daily basal insulin	292	292	17.58		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.31	[0.84 ; 2.06]	0.2367

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, w/o: without, T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

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6.2.34 Achievement of HbA1c targets at planned end of treatment without severe hypoglycaemic episodes (level 3) during the prior 12 weeks - in-trial - plot of estimated odds ratios - full analysis set



Estimates with 95% confidence interval. HbA1c: Haemoglobin A1c, w/o: without, T1D: Type 1 diabetes, T2D: Type 2 diabetes. 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). 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. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis.

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6.2.35 Achievement of HbA1c<7.0% at planned end of treatment without severe (level 3) or clinically significant (level 2) hypoglycaemic episodes during the prior 12 weeks - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
HbA1c <7.0% w/o level 2 or 3 hypoglycaemic episodes					
T2D, insulin naive					
ONWARDS 1					
LSMeans, frequency					
Insulin icodec	492	492	52.56		
Daily basal insulin	492	492	42.58		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.49	[1.15 ; 1.94]	0.0028
ONWARDS 3					
LSMeans, frequency					
Insulin icodec	294	294	52.13		
Daily basal insulin	294	294	39.86		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.64	[1.16 ; 2.33]	0.0054
ONWARDS 5					
LSMeans, frequency					
Insulin icodec	542	542	40.53		
Daily basal insulin	543	542	31.61		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.47	[1.13 ; 1.92]	0.0040
T2D, basal					
ONWARDS 2					
LSMeans, frequency					
Insulin icodec	263	263	36.73		
Daily basal insulin	263	263	26.79		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.59	[1.07 ; 2.36]	0.0223
T2D, basal-bolus					
ONWARDS 4					
LSMeans, frequency					
Insulin icodec	291	291	26.48		
Daily basal insulin	291	291	25.24		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.07	[0.73 ; 1.55]	0.7352

CI: Confidence interval, HbA1c: Haemoglobin A1c, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, w/o: without, 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

Achievement of HbA1c<7.0% at planned end of treatment without severe (level 3) or clinically significant (level 2) hypoglycaemic episodes during the prior 12 weeks - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
T1D, basal-bolus					
ONWARDS 6					
LSMeans, frequency					
Insulin icodec	290	290	9.55		
Daily basal insulin	292	292	16.74		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.52	[0.33 ; 0.85]	0.0080

CI: Confidence interval, HbA1c: Haemoglobin A1c, FAS: Number of subjects in full analysis set, N: Number of subjects contributing to the analysis, w/o: without, 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

6.2.36 Achievement of HbA1c<=6.5% at planned end of treatment without severe (level 3) or clinically significant (level 2) hypoglycaemic episodes during the prior 12 weeks - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
HbA1c <=6.5% w/o level 2 or 3 hypoglycaemic episodes					
T2D, insulin naive					
ONWARDS 1					
LSMeans, frequency					
Insulin icodec	492	492	29.68		
Daily basal insulin	492	492	22.74		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.43	[1.07 ; 1.92]	0.0149
ONWARDS 3					
LSMeans, frequency					
Insulin icodec	294	294	28.33		
Daily basal insulin	294	294	18.69		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.72	[1.16 ; 2.54]	0.0065
ONWARDS 5					
LSMeans, frequency					
Insulin icodec	542	542	20.43		
Daily basal insulin	543	542	14.73		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.49	[1.09 ; 2.03]	0.0123
T2D, basal					
ONWARDS 2					
LSMeans, frequency					
Insulin icodec	263	263	12.54		
Daily basal insulin	263	263	7.77		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			1.70	[1.00 ; 2.91]	0.0517
T2D, basal-bolus					
ONWARDS 4					
LSMeans, frequency					
Insulin icodec	291	291	11.24		
Daily basal insulin	291	291	12.64		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.88	[0.54 ; 1.41]	0.5837

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, w/o: without, 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

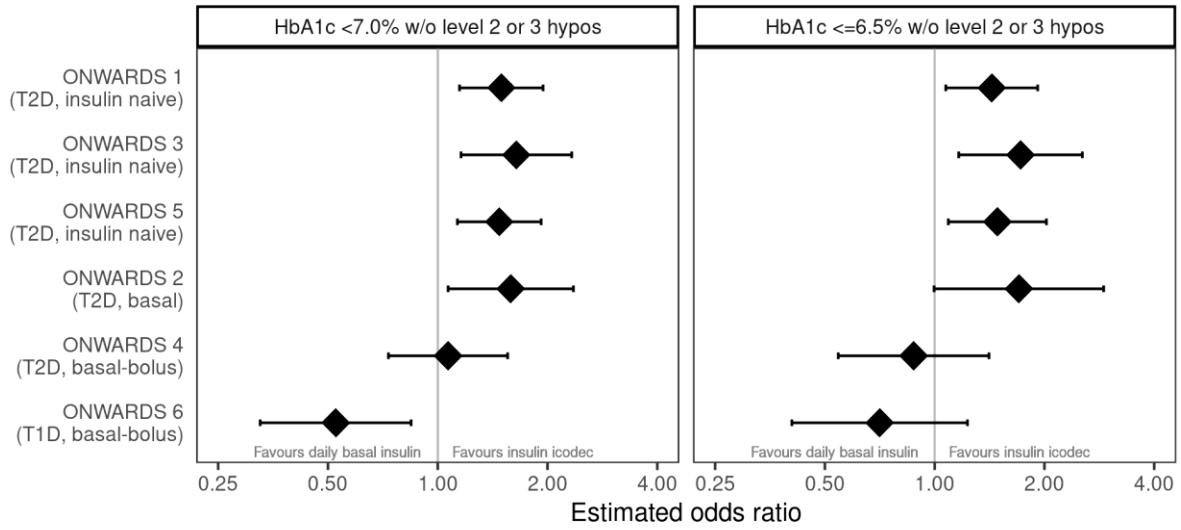
Achievement of HbA1c<=6.5% at planned end of treatment without severe (level 3) or clinically significant (level 2) hypoglycaemic episodes during the prior 12 weeks - in-trial - statistical analysis - full analysis set

	FAS	N	Estimate	95% CI	P-value
T1D, basal-bolus					
ONWARDS 6					
LSMeans, frequency					
Insulin icodec	290	290	5.48		
Daily basal insulin	292	292	7.59		
Treatment odds ratio					
Insulin icodec / Daily basal insulin			0.71	[0.41 ; 1.23]	0.2197

CI: Confidence interval, FAS: Number of subjects in full analysis set, HbA1c: Haemoglobin A1c, N: Number of subjects contributing to the analysis, w/o: without, 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. P-value: Two-sided p-value for test of no treatment difference. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis. 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.

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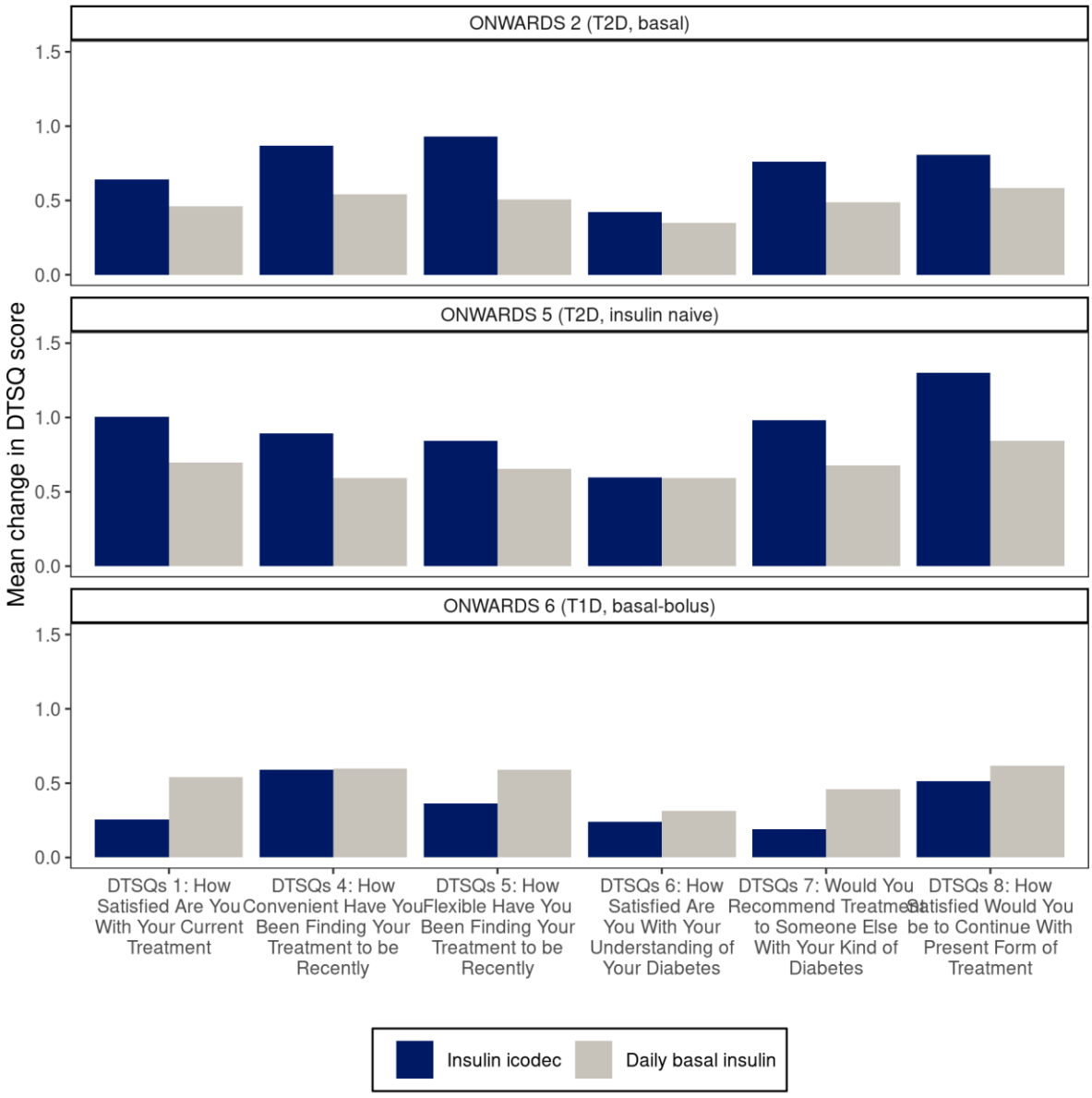
6.2.37 Achievement of HbA1c targets at planned end of treatment without severe (level 3) or clinically significant (level 2) hypoglycaemic episodes during the prior 12 weeks - in-trial - plot of estimated odds ratios - full analysis set



Estimates with 95% confidence interval. HbA1c: Haemoglobin A1c, w/o: without, 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). 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. Data from ONWARDS 1-6, only main part of ONWARDS 1 and 6. Logistic regression model (logit link) with treatment, region, and, if applicable, additional relevant factors as fixed factors, and the baseline HbA1c value as covariate. Missing HbA1c measurements are imputed using the same method as specified for the primary analysis.

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6.2.38 DTSQ total treatment satisfaction score by question at planned end of treatment - change from baseline - in-trial - mean plot - full analysis set

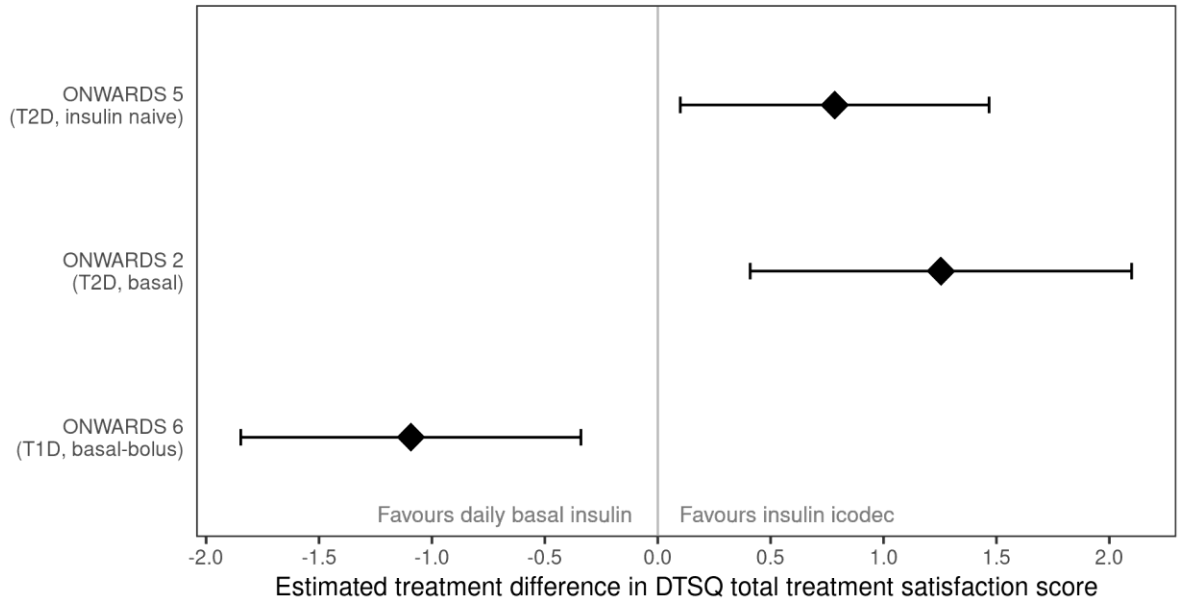


DTSQ: Diabetes treatment satisfaction questionnaire, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Observed data. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 6) and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5).
End-of-treatment visit: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 5: Week 52, ONWARDS 2 and 6 (main part): Week 26. Data from ONWARDS 2, 5 and 6, only main part of ONWARDS 6.

adqsdtsq.xpt; variable(s): PARAM STDNM POPGRP TRPG1 AVAL; criteria: FASFL == "Y" & ANELFL == "Y" & ANL01FL == "Y" & ((STUDYID %in% c("NN1436-4478", "NN1436-4625") & AVISITN == 2800) | (STUDYID %in% c("NN1436-4481") & AVISITN == 600)) & PARAMCD %in% c("DTSQ0101", "DTSQ0104", "DTSQ0105", "DTSQ0106", "DTSQ0107", "DTSQ0108")

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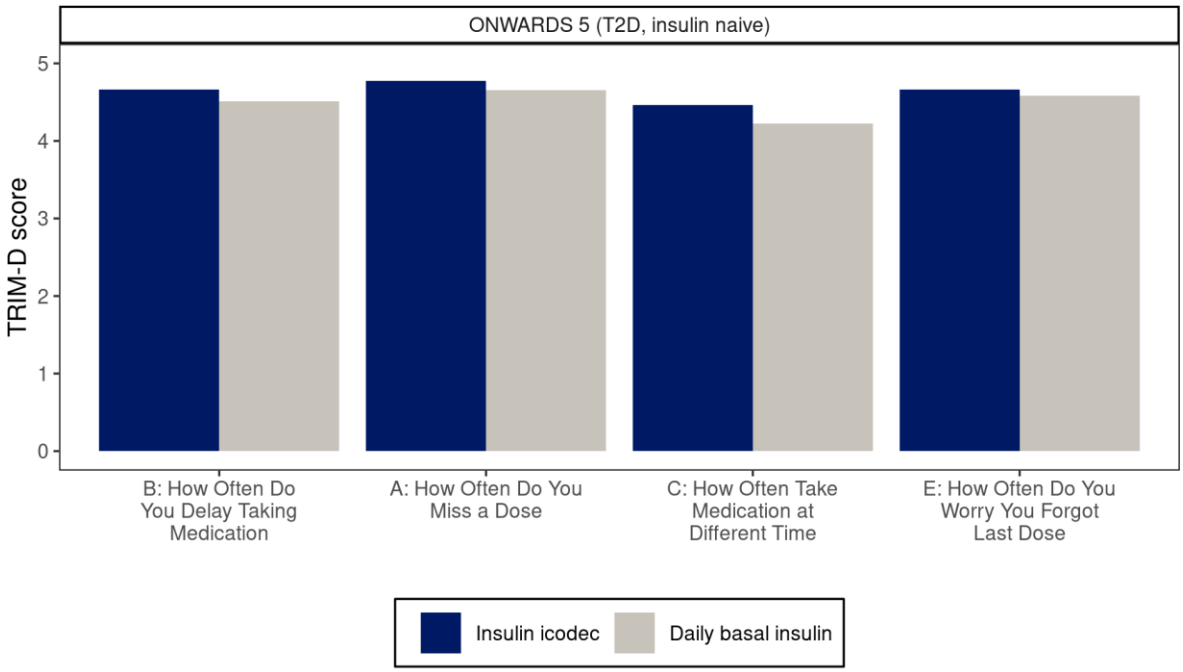
6.2.39 DTSQ total treatment satisfaction score at planned end of treatment - change from baseline - in-trial - plot of estimated treatment differences - full analysis set



Estimates with 95% confidence interval. DTSQ: Diabetes treatment satisfaction questionnaire, T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 2, ONWARDS 6) and once-daily analogues (IDeg, IGlar U100, IGlar U300) (ONWARDS 5). End-of-treatment visit: Planned end-of-treatment visit for the trials or last planned visit in the main part of the trials, as applicable; ONWARDS 5: Week 52, ONWARDS 2 and 6 (main part): Week 26. Data from ONWARDS 2, 5 and 6, only main part of ONWARDS 6. ANCOVA with treatment, region and, if applicable, additional relevant factors as fixed factors, and baseline response as covariate. Missing data are imputed using multiple imputation.

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6.2.40 TRIM-D compliance score by question - ONWARDS 5 - in-trial - mean plot - full analysis set

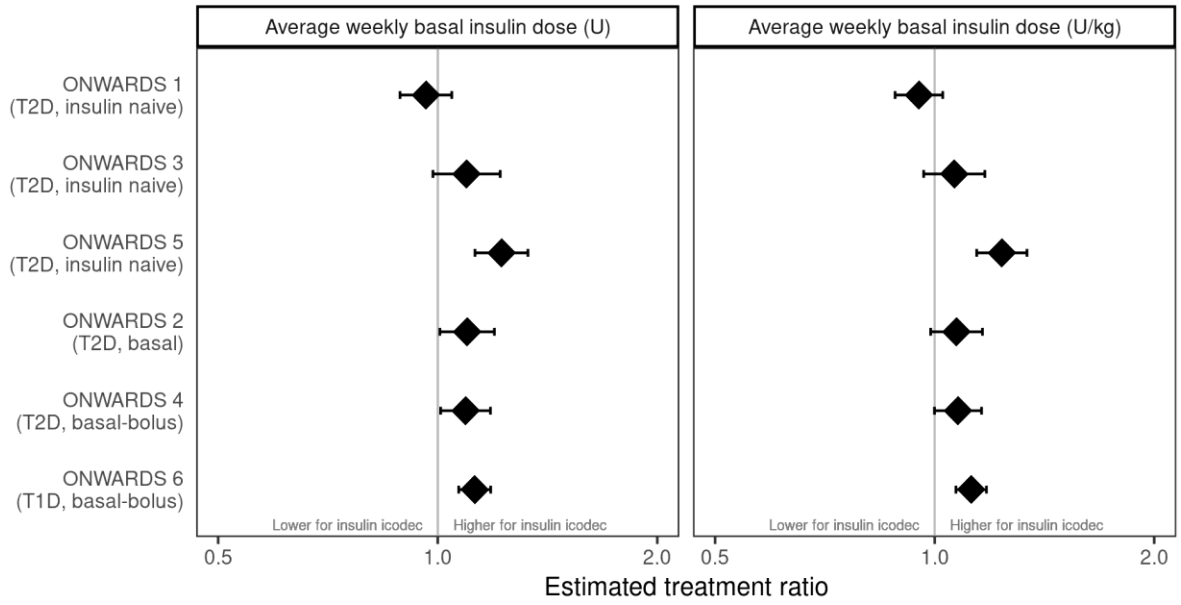


TRIM-D: Treatment Related Impact Measure for Diabetes, T2D: Type 2 diabetes. Observed data. Daily basal insulin: once-daily analogues (IDeg, IGlar U100, IGlar U300). End of treatment: ONWARDS 5: Week 52.

adqstrim.xpt; variable(s): PARAM STDNM POPGRP TRPG1 AVAL; criteria: FASFL == "Y" & ANELFL == "Y" & ANL01FL == "Y" & PARAMCD %in% c("TRIM026A", "TRIM026B", "TRIM026C", "TRIM026E")

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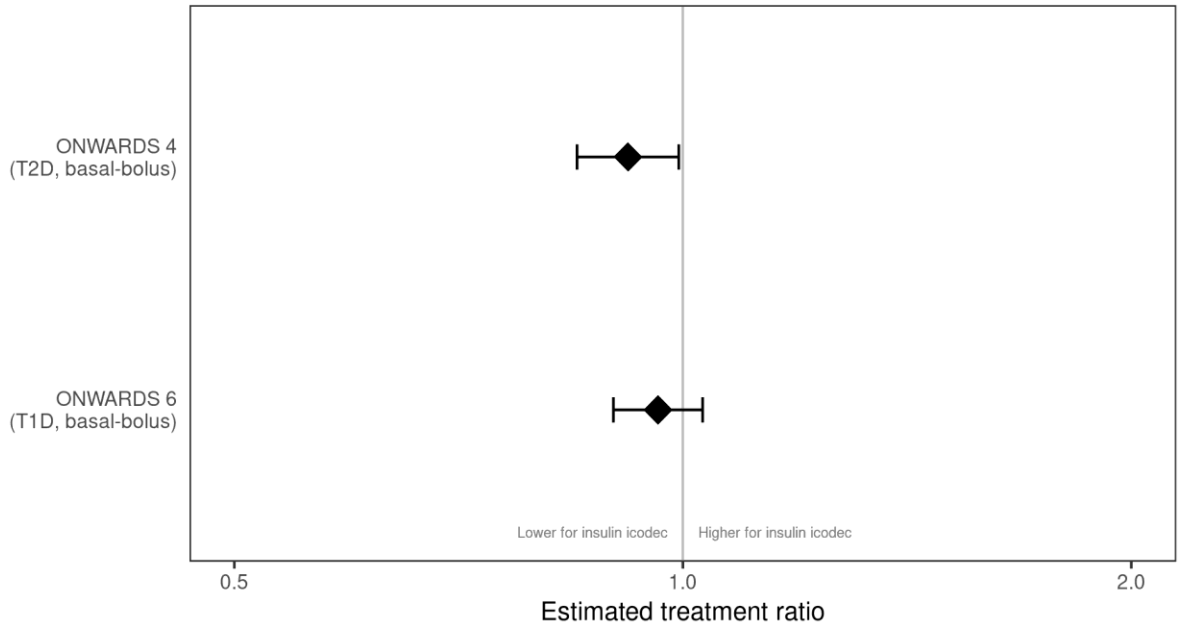
6.2.41 Actual weekly total basal insulin dose during last two weeks of planned treatment - on-treatment - plot of estimated treatment ratios - full analysis set



Estimates with 95% confidence interval. 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). 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. 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.

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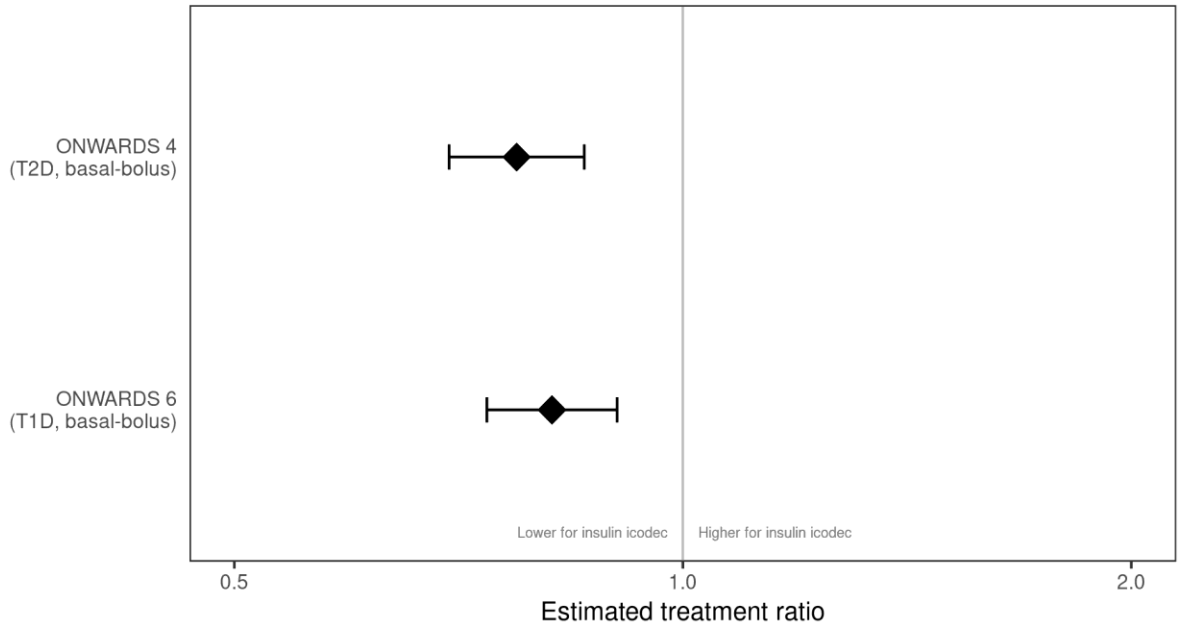
6.2.42 Actual weekly total insulin dose during last two weeks of planned treatment - on-treatment - plot of estimated treatment ratios - full analysis set



Estimates with 95% confidence interval. T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 6), IGlar U100 (ONWARDS 4). 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 4 and 6 (main part): Week 24-26. Data from ONWARDS 4, only main part of ONWARDS 6. ANCOVA based on log-transformed values with treatment, region and, if applicable, additional relevant factors as fixed factors, and (ONWARDS 4 and 6) log-transformed baseline response as covariate. Missing data are imputed using multiple imputation.

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6.2.43 Actual weekly total bolus insulin dose during last two weeks of planned treatment - on-treatment - plot of estimated treatment ratios - full analysis set



Estimates with 95% confidence interval. T1D: Type 1 diabetes, T2D: Type 2 diabetes. Daily basal insulin: IDeg (ONWARDS 6), IGlar U100 (ONWARDS 4). 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 4 and 6 (main part): Week 24-26. Data from ONWARDS 4, only main part of ONWARDS 6. ANCOVA based on log-transformed values with treatment, region and, if applicable, additional relevant factors as fixed factors, and (ONWARDS 4 and 6) log-transformed baseline response as covariate. Missing data are imputed using multiple imputation.

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