Dossier zur Nutzenbewertung gemäß § 35a SGB V

Insulin icodec (Awiqli®)

Novo Nordisk Pharma GmbH

Modul 4 C – Anhang 4-G

Behandlung von Erwachsenen mit Typ 1 Diabetes mellitus

Stand: 29.08.2024

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1 Auswertung zum Anteil der Patienten mit einer 50 % oder 100 % Aufsättigungsdosis im Studienarm mit Insulin icodec aus ONWARDS 6

1.1 Insulin icodec subjects having additional 50% or 100% loading dose at week 1 - Onwards 6 – Full analysis set

	Ico		IDeg	
	N	n (%)	N	n (%)
Loading dose				
0%	290	0	292	292 (100)
50%	290	215 (74)	292	0
100%	290	75 (26)	292	0

N: number of subjects in population, n: number of subjects in subgroup

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2 Vollständige Auswertung zu Wirksamkeit und Sicherheit inkl. Subgruppenanalysen zur Studienpopulation aus ONWARDS 6

2.1 Change in HbA1c by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico			IDeg			Ico - IDeg		
		N n	Mean (SD)	LS Mean (SE)	N n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI] p-value int.	
HbA1c (%)										
All subjects (total)	Week 10	290 280	-0.54 (0.72)		292 284	-0.55 (0.63)			-0.02 [-0.18; 0.14]	
	Week 18	290 274	-0.53 (0.82)		292 280	-0.54 (0.68)			-0.02 [-0.18; 0.15]	
	Week 26	290 275	-0.48 (0.77)		292 283	-0.55 (0.71)			-0.09 [-0.26; 0.07]	
	Week 36	290 263	-0.42 (0.75)		292 280	-0.49 (0.71)			-0.09 [-0.25; 0.07]	
	Week 44	290 259	-0.39 (0.76)		292 270	-0.48 (0.71)			-0.12 [-0.29; 0.04]	
	Week 52	290 270	-0.39 (0.80)	-0.37 (0.05)	292 278	-0.56 (0.71)	-0.54 (0.05)	0.17 [0.02; 0.31] 0.0213	-0.21 [-0.38;-0.05]	
Gender										
Female	Week 10	125 121	-0.53 (0.60)		120 117	-0.52 (0.62)			0.02 [-0.23; 0.27]	
	Week 18	125 118	-0.49 (0.73)		120 115	-0.53 (0.67)			-0.06 [-0.31; 0.19]	
	Week 26	125 115	-0.40 (0.74)		120 116	-0.55 (0.76)			-0.20 [-0.45; 0.05]	
	Week 36	125 112	-0.34 (0.70)		120 114	-0.48 (0.79)			-0.18 [-0.43; 0.07]	
	Week 44	125 110	-0.27 (0.78)		120 110	-0.50 (0.75)			-0.29 [-0.55;-0.04]	
	Week 52	125 117	-0.26 (0.79)	-0.23 (0.07)	120 114	-0.55 (0.74)	-0.46 (0.08)	0.23 [0.03; 0.44] 0.0268	-0.38 [-0.63;-0.12]	0.3483
Male	Week 10	165 159	-0.55 (0.81)		172 167	-0.58 (0.63)			-0.04 [-0.26; 0.17]	
	Week 18	165 156	-0.56 (0.89)		172 165	-0.55 (0.68)			0.01 [-0.20; 0.22]	
	Week 26	165 160	-0.54 (0.79)		172 167	-0.55 (0.69)			-0.02 [-0.23; 0.20]	
	Week 36	165 151	-0.49 (0.78)		172 166	-0.50 (0.65)			-0.02 [-0.23; 0.20]	
	Week 44	165 149	-0.47 (0.73)		172 160	-0.46 (0.69)			0.01 [-0.20; 0.22]	
	Week 52	165 153	-0.50 (0.80)	-0.48 (0.06)	172 164	-0.56 (0.69)	-0.59 (0.06)	0.11 [-0.06; 0.29] 0.2067	-0.09 [-0.30; 0.13]	

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 52 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment, region (if applicable), HbA1c group at screening and pre-trial basal insulin treatment (and subgroup with interaction between treatment and subgroup, if applicable) as fixed factors, and baseline response as covariate. Missing values at week 52 are imputed using multiple imputation based on the change from LAOT value to week 52 for subjects that have discontinued randomised treatment but have a measurement at week 52. The model includes treatment as a fixed factor and the LAOT value and the time point of this assessment as covariates. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Change in HbA1c by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg			
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]	p-value int.
Age													
<65 years	Week 10	267	258	-0.58 (0.72)		271	263	-0.55 (0.64)				0.04 [-0.13; 0.21]	
	Week 18	267	252	-0.57 (0.81)		271	259	-0.54 (0.69)				0.05 [-0.12; 0.21]	
	Week 26	267	254	-0.51 (0.78)		271	262	-0.55 (0.73)				-0.05 [-0.22; 0.11]	
	Week 36	267	243	-0.46 (0.75)		271	259	-0.50 (0.72)				-0.06 [-0.23; 0.11]	
	Week 44	267	239	-0.42 (0.75)		271	249	-0.49 (0.72)				-0.09 [-0.26; 0.08]	
	Week 52	267	250	-0.43 (0.79)	-0.41 (0.05)	271	257	-0.56 (0.72)	-0.55 (0.06)	0.14 [-0.01; 0.28]	0.0704	-0.17 [-0.34; 0.00]	0.1093
>=65 years	Week 10	23	22	-0.05 (0.63)		21	21	-0.56 (0.46)				-0.89 [-1.51;-0.27]	
	Week 18	23	22	-0.05 (0.82)		21	21	-0.60 (0.56)				-0.77 [-1.39;-0.16]	
	Week 26	23	21	-0.12 (0.62)		21	21	-0.53 (0.54)				-0.68 [-1.29;-0.07]	
	Week 36	23	20	-0.04 (0.64)		21	21	-0.37 (0.59)				-0.52 [-1.12; 0.08]	
	Week 44	23	20	0.05 (0.71)		21	21	-0.36 (0.61)				-0.60 [-1.21; 0.00]	
	Week 52	23	20	0.06 (0.80)	0.05 (0.17)	21	21	-0.51 (0.59)	-0.48 (0.16)	0.53 [0.07; 0.99]	0.0239	-0.79 [-1.41;-0.18]	
HbA1c													
<=8,5%	Week 10	235	227	-0.38 (0.62)		242	234	-0.43 (0.53)				-0.09 [-0.27; 0.09]	
	Week 18	235	222	-0.35 (0.71)		242	231	-0.40 (0.58)				-0.08 [-0.26; 0.10]	
	Week 26	235	222	-0.32 (0.61)		242	234	-0.40 (0.61)				-0.14 [-0.32; 0.04]	
	Week 36	235	214	-0.26 (0.62)		242	233	-0.34 (0.60)				-0.13 [-0.31; 0.05]	
	Week 44	235	210	-0.25 (0.63)		242	224	-0.33 (0.60)				-0.14 [-0.32; 0.04]	
	Week 52	235	216	-0.25 (0.66)	-0.19 (0.06)	242	231	-0.42 (0.61)	-0.36 (0.06)	0.16 [0.01; 0.32]	0.0369	-0.27 [-0.45;-0.09]	0.7183
>8,5%	Week 10	55	53	-1.24 (0.72)		50	50	-1.15 (0.71)				0.13 [-0.26; 0.51]	
	Week 18	55	52	-1.31 (0.85)		50	49	-1.22 (0.70)				0.11 [-0.27; 0.50]	
	Week 26	55	53	-1.17 (0.98)		50	49	-1.24 (0.76)				-0.08 [-0.47; 0.30]	
	Week 36	55	49	-1.13 (0.85)		50	47	-1.23 (0.76)				-0.12 [-0.50; 0.26]	
	Week 44	55	49	-0.99 (0.95)		50	46	-1.20 (0.78)				-0.23 [-0.62; 0.15]	
	Week 52	55	54	-0.96 (1.04)	-1.17 (0.12)	50	47	-1.21 (0.81)	-1.39 (0.13)	0.22 [-0.08; 0.52]	0.1438	-0.27 [-0.65; 0.12]	

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 52 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment, region (if applicable), HbA1c group at screening and pre-trial basal insulin treatment (and subgroup with interaction between treatment and subgroup, if applicable) as fixed factors, and baseline response as covariate. Missing values at week 52 are imputed using multiple imputation based on the change from LAOT value to week 52 for subjects that have discontinued randomised treatment but have a measurement at week 52. The model includes treatment as a fixed factor and the LAOT value and the time point of this assessment as covariates. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Change in HbA1c by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg			
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]	p-value int.
Region													
Europe	Week 10	136	131	-0.62 (0.62)		139	135	-0.61 (0.63)				0.01 [-0.22; 0.25]	
	Week 18	136	128	-0.60 (0.68)		139	135	-0.57 (0.67)				0.04 [-0.19; 0.28]	
	Week 26	136	130	-0.56 (0.65)		139	136	-0.56 (0.73)				0.00 [-0.23; 0.24]	
	Week 36	136	122	-0.52 (0.67)		139	134	-0.55 (0.73)				-0.04 [-0.28; 0.19]	
	Week 44	136	122	-0.46 (0.63)		139	126	-0.58 (0.74)				-0.17 [-0.41; 0.06]	
	Week 52	136	127	-0.46 (0.70)	-0.49 (0.07)	139	130	-0.56 (0.71)	-0.57 (0.08)	0.08 [-0.12; 0.29]	0.4248	-0.14 [-0.37; 0.10]	0.2205
North and South America	Week 10	106	101	-0.48 (0.78)		85	81	-0.50 (0.67)				-0.02 [-0.31; 0.26]	
	Week 18	106	98	-0.52 (0.83)		85	78	-0.53 (0.71)				-0.01 [-0.29; 0.28]	
	Week 26	106	97	-0.45 (0.79)		85	79	-0.52 (0.75)				-0.09 [-0.37; 0.20]	
	Week 36	106	95	-0.39 (0.75)		85	78	-0.46 (0.76)				-0.08 [-0.37; 0.20]	
	Week 44	106	92	-0.37 (0.79)		85	77	-0.37 (0.75)				-0.01 [-0.29; 0.28]	
	Week 52	106	96	-0.38 (0.82)	-0.31 (0.08)	85	80	-0.51 (0.82)	-0.47 (0.09)	0.16 [-0.08; 0.39]	0.1878	-0.15 [-0.44; 0.13]	
Asia	Week 10	48	48	-0.44 (0.85)		68	68	-0.50 (0.55)				-0.09 [-0.46; 0.28]	
	Week 18	48	48	-0.37 (1.12)		68	67	-0.51 (0.65)				-0.17 [-0.54; 0.20]	
	Week 26	48	48	-0.31 (0.98)		68	68	-0.56 (0.65)				-0.31 [-0.68; 0.07]	
	Week 36	48	46	-0.23 (0.89)		68	68	-0.40 (0.60)				-0.23 [-0.60; 0.14]	
	Week 44	48	45	-0.22 (0.97)		68	67	-0.40 (0.60)				-0.23 [-0.60; 0.14]	
	Week 52	48	47	-0.23 (1.01)	-0.19 (0.11)	68	68	-0.61 (0.59)	-0.58 (0.09)	0.39 [0.11; 0.66]	0.0054	-0.48 [-0.85;-0.10]	

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 52 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment, region (if applicable),HbA1c group at screening and pre-trial basal insulin treatment (and subgroup with interaction between treatment and subgroup, if applicable) as fixed factors, and baseline response as covariate. Missing values at week 52 are imputed using multiple imputation based on the change from LAOT value to week 52 for subjects that have discontinued randomised treatment but have a measurement at week 52. The model includes treatment as a fixed factor and the LAOT value and the time point of this assessment as covariates. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Change in HbA1c by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI] p-value int.
Race												
White	Week 10	230	220	-0.55 (0.68)		218	210	-0.57 (0.65)				-0.03 [-0.21; 0.16]
	Week 18	230	214	-0.55 (0.73)		218	207	-0.54 (0.69)				0.01 [-0.17; 0.20]
	Week 26	230	216	-0.50 (0.69)		218	209	-0.54 (0.74)				-0.05 [-0.24; 0.13]
	Week 36	230	206	-0.45 (0.69)		218	206	-0.51 (0.75)				-0.09 [-0.27; 0.10]
	Week 44	230	203	-0.41 (0.68)		218	198	-0.50 (0.76)				-0.12 [-0.31; 0.06]
	Week 52	230	212	-0.41 (0.73)	-0.38 (0.07)	218	204	-0.54 (0.76)	-0.51 (0.08)	0.14 [-0.03; 0.30]	0.1141	-0.18 [-0.37; 0.00] 0.3527
Not white	Week 10	60	60	-0.52 (0.86)		74	74	-0.52 (0.54)				0.00 [-0.34; 0.34]
	Week 18	60	60	-0.47 (1.09)		74	73	-0.56 (0.64)				-0.11 [-0.45; 0.24]
	Week 26	60	59	-0.41 (1.01)		74	74	-0.58 (0.63)				-0.21 [-0.55; 0.13]
	Week 36	60	57	-0.34 (0.93)		74	74	-0.43 (0.60)				-0.11 [-0.45; 0.23]
	Week 44	60	56	-0.29 (0.98)		74	72	-0.41 (0.59)				-0.16 [-0.50; 0.18]
	Week 52	60	58	-0.34 (1.03)	-0.36 (0.15)	74	74	-0.59 (0.58)	-0.64 (0.16)	0.28 [0.02; 0.54]	0.0320	-0.31 [-0.65; 0.03]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 52 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment, region (if applicable), HbA1c group at screening and pre-trial basal insulin treatment (and subgroup with interaction between treatment and subgroup, if applicable) as fixed factors, and baseline response as covariate. Missing values at week 52 are imputed using multiple imputation based on the change from LAOT value to week 52 for subjects that have discontinued randomised treatment but have a measurement at week 52. The model includes treatment as a fixed factor and the LAOT value and the time point of this assessment as covariates. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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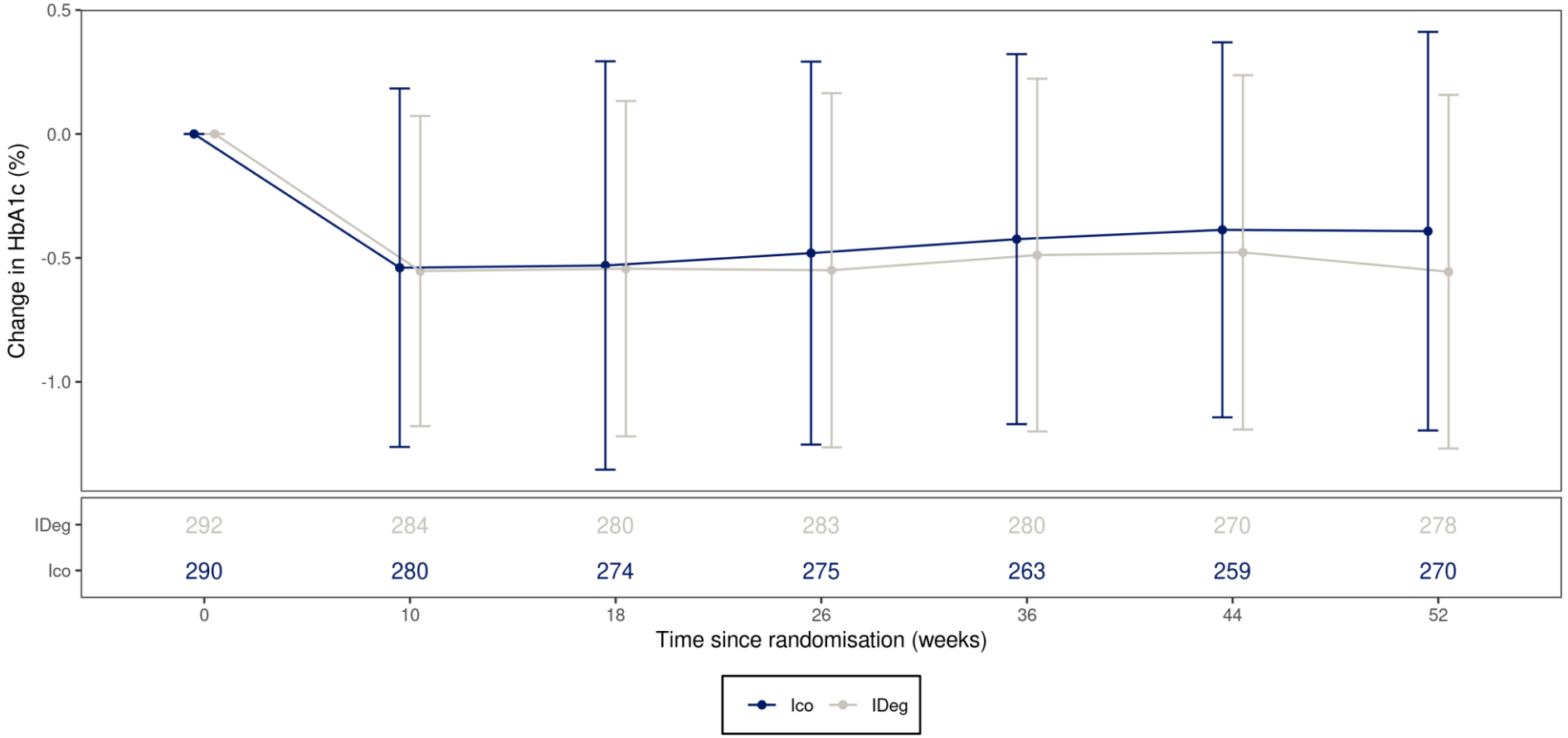
2.2 Change in HbA1c by treatment week - Mean plot - Onwards 6 - in-trial - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).
HbA1c: Haemoglobin A1c.

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2.3 Absolute HbA1c by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico			IDeg			Ico - IDeg
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
HbA1c (%)								
All subjects (total)	Week 0	290	290	7.59 (0.96)	292	292	7.63 (0.93)	0.05 [-0.12; 0.21]
	Week 10	290	280	7.05 (0.83)	292	284	7.08 (0.77)	0.04 [-0.12; 0.20]
	Week 18	290	274	7.06 (0.91)	292	280	7.09 (0.79)	0.04 [-0.12; 0.20]
	Week 26	290	275	7.12 (0.88)	292	283	7.08 (0.79)	-0.04 [-0.20; 0.12]
	Week 36	290	263	7.17 (0.86)	292	280	7.13 (0.80)	-0.04 [-0.20; 0.12]
	Week 44	290	259	7.21 (0.90)	292	270	7.14 (0.81)	-0.08 [-0.24; 0.08]
	Week 52	290	270	7.21 (0.96)	292	278	7.06 (0.80)	-0.17 [-0.33; 0.00]
Gender								
Female	Week 0	125	125	7.62 (0.97)	120	120	7.72 (0.98)	0.10 [-0.15; 0.35]
	Week 10	125	121	7.09 (0.82)	120	117	7.21 (0.81)	0.14 [-0.11; 0.39]
	Week 18	125	118	7.12 (0.92)	120	115	7.19 (0.82)	0.08 [-0.17; 0.33]
	Week 26	125	115	7.22 (0.94)	120	116	7.16 (0.80)	-0.07 [-0.32; 0.19]
	Week 36	125	112	7.26 (0.90)	120	114	7.21 (0.86)	-0.05 [-0.30; 0.20]
	Week 44	125	110	7.32 (0.96)	120	110	7.17 (0.84)	-0.16 [-0.41; 0.09]
	Week 52	125	117	7.37 (1.03)	120	114	7.15 (0.80)	-0.23 [-0.49; 0.02]
Male	Week 0	165	165	7.57 (0.95)	172	172	7.57 (0.88)	0.01 [-0.21; 0.22]
	Week 10	165	159	7.02 (0.83)	172	167	7.00 (0.73)	-0.03 [-0.24; 0.18]
	Week 18	165	156	7.01 (0.90)	172	165	7.02 (0.76)	0.01 [-0.20; 0.23]
	Week 26	165	160	7.04 (0.83)	172	167	7.03 (0.77)	-0.02 [-0.23; 0.19]
	Week 36	165	151	7.10 (0.83)	172	166	7.08 (0.76)	-0.02 [-0.24; 0.19]
	Week 44	165	149	7.12 (0.84)	172	160	7.11 (0.79)	-0.01 [-0.22; 0.20]
	Week 52	165	153	7.08 (0.89)	172	164	6.99 (0.79)	-0.10 [-0.32; 0.11]
Age								
<65 years	Week 0	267	267	7.61 (0.98)	271	271	7.62 (0.94)	0.02 [-0.15; 0.18]
	Week 10	267	258	7.03 (0.84)	271	263	7.07 (0.78)	0.05 [-0.12; 0.22]
	Week 18	267	252	7.04 (0.91)	271	259	7.09 (0.80)	0.06 [-0.11; 0.23]
	Week 26	267	254	7.11 (0.90)	271	262	7.07 (0.79)	-0.04 [-0.21; 0.12]
	Week 36	267	243	7.15 (0.88)	271	259	7.11 (0.80)	-0.05 [-0.22; 0.12]
	Week 44	267	239	7.19 (0.91)	271	249	7.12 (0.82)	-0.08 [-0.25; 0.08]
	Week 52	267	250	7.19 (0.97)	271	257	7.04 (0.82)	-0.17 [-0.33; 0.00]
>=65 years	Week 0	23	23	7.37 (0.58)	21	21	7.77 (0.67)	0.63 [0.02; 1.23]
	Week 10	23	22	7.31 (0.69)	21	21	7.21 (0.59)	-0.15 [-0.74; 0.44]
	Week 18	23	22	7.32 (0.81)	21	21	7.17 (0.68)	-0.20 [-0.79; 0.39]
	Week 26	23	21	7.22 (0.56)	21	21	7.24 (0.66)	0.03 [-0.56; 0.62]
	Week 36	23	20	7.32 (0.66)	21	21	7.40 (0.76)	0.10 [-0.49; 0.70]
	Week 44	23	20	7.42 (0.80)	21	21	7.41 (0.70)	-0.01 [-0.60; 0.58]
	Week 52	23	20	7.39 (0.89)	21	21	7.26 (0.53)	-0.17 [-0.76; 0.42]
HbA1c								
<=8,5%	Week 0	235	235	7.26 (0.73)	242	242	7.34 (0.71)	0.11 [-0.07; 0.29]
	Week 10	235	227	6.89 (0.77)	242	234	6.91 (0.66)	0.03 [-0.15; 0.21]
	Week 18	235	222	6.91 (0.86)	242	231	6.94 (0.70)	0.03 [-0.15; 0.21]
	Week 26	235	222	6.95 (0.76)	242	234	6.93 (0.70)	-0.02 [-0.20; 0.16]
	Week 36	235	214	7.01 (0.79)	242	233	7.00 (0.73)	-0.01 [-0.19; 0.17]
	Week 44	235	210	7.02 (0.78)	242	224	6.99 (0.73)	-0.04 [-0.22; 0.14]
	Week 52	235	216	7.00 (0.83)	242	231	6.90 (0.70)	-0.13 [-0.31; 0.05]
>8,5%	Week 0	55	55	8.99 (0.36)	50	50	9.04 (0.42)	0.14 [-0.25; 0.52]
	Week 10	55	53	7.76 (0.70)	50	50	7.89 (0.74)	0.18 [-0.20; 0.57]
	Week 18	55	52	7.68 (0.84)	50	49	7.84 (0.74)	0.20 [-0.19; 0.58]
	Week 26	55	53	7.82 (0.99)	50	49	7.79 (0.79)	-0.03 [-0.41; 0.36]
	Week 36	55	49	7.86 (0.85)	50	47	7.81 (0.79)	-0.07 [-0.45; 0.32]
	Week 44	55	49	8.01 (0.94)	50	46	7.85 (0.79)	-0.18 [-0.56; 0.21]
	Week 52	55	54	8.02 (1.02)	50	47	7.83 (0.81)	-0.20 [-0.59; 0.18]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval. nn1436/nn1436-amnog/current
23JAN2024:13:34:49 - /HbA1c_4625.txt

Absolute HbA1c by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico			IDeg			Ico - IDeg
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
Region								
Europe	Week 0	136	136	7.50 (0.91)	139	139	7.57 (0.94)	0.08 [-0.16; 0.31]
	Week 10	136	131	6.88 (0.77)	139	135	6.96 (0.77)	0.10 [-0.13; 0.34]
	Week 18	136	128	6.90 (0.78)	139	135	7.00 (0.78)	0.12 [-0.12; 0.36]
	Week 26	136	130	6.95 (0.76)	139	136	6.99 (0.77)	0.05 [-0.18; 0.29]
	Week 36	136	122	6.99 (0.81)	139	134	7.00 (0.80)	0.01 [-0.23; 0.24]
	Week 44	136	122	7.05 (0.88)	139	126	6.95 (0.79)	-0.11 [-0.35; 0.12]
	Week 52	136	127	7.07 (0.97)	139	130	6.96 (0.79)	-0.13 [-0.36; 0.11]
North and South America	Week 0	106	106	7.69 (1.09)	85	85	7.69 (1.01)	0.00 [-0.28; 0.29]
	Week 10	106	101	7.22 (0.83)	85	81	7.21 (0.75)	-0.02 [-0.30; 0.27]
	Week 18	106	98	7.17 (0.89)	85	78	7.19 (0.77)	0.02 [-0.26; 0.31]
	Week 26	106	97	7.24 (0.95)	85	79	7.20 (0.80)	-0.05 [-0.33; 0.24]
	Week 36	106	95	7.29 (0.89)	85	78	7.24 (0.81)	-0.07 [-0.35; 0.22]
	Week 44	106	92	7.32 (0.86)	85	77	7.32 (0.84)	-0.01 [-0.30; 0.28]
	Week 52	106	96	7.30 (0.88)	85	80	7.20 (0.85)	-0.11 [-0.40; 0.17]
Asia	Week 0	48	48	7.62 (0.77)	68	68	7.69 (0.79)	0.09 [-0.28; 0.45]
	Week 10	48	48	7.18 (0.89)	68	68	7.19 (0.77)	0.01 [-0.36; 0.38]
	Week 18	48	48	7.25 (1.16)	68	67	7.18 (0.80)	-0.08 [-0.45; 0.29]
	Week 26	48	48	7.31 (0.96)	68	68	7.13 (0.79)	-0.21 [-0.58; 0.16]
	Week 36	48	46	7.37 (0.87)	68	68	7.29 (0.77)	-0.11 [-0.48; 0.26]
	Week 44	48	45	7.40 (0.98)	68	67	7.28 (0.75)	-0.13 [-0.50; 0.24]
	Week 52	48	47	7.37 (1.06)	68	68	7.08 (0.74)	-0.33 [-0.70; 0.04]
Race								
White	Week 0	230	230	7.56 (0.98)	218	218	7.60 (0.97)	0.05 [-0.14; 0.23]
	Week 10	230	220	7.01 (0.80)	218	210	7.04 (0.77)	0.03 [-0.15; 0.22]
	Week 18	230	214	7.00 (0.84)	218	207	7.06 (0.79)	0.07 [-0.11; 0.26]
	Week 26	230	216	7.07 (0.85)	218	209	7.06 (0.79)	-0.02 [-0.20; 0.17]
	Week 36	230	206	7.12 (0.85)	218	206	7.07 (0.81)	-0.06 [-0.24; 0.13]
	Week 44	230	203	7.15 (0.86)	218	198	7.08 (0.83)	-0.09 [-0.27; 0.10]
	Week 52	230	212	7.17 (0.93)	218	204	7.03 (0.81)	-0.16 [-0.35; 0.03]
Not white	Week 0	60	60	7.72 (0.84)	74	74	7.74 (0.78)	0.02 [-0.32; 0.36]
	Week 10	60	60	7.21 (0.92)	74	74	7.22 (0.76)	0.01 [-0.33; 0.36]
	Week 18	60	60	7.26 (1.11)	74	73	7.18 (0.78)	-0.08 [-0.42; 0.26]
	Week 26	60	59	7.29 (0.97)	74	74	7.16 (0.77)	-0.15 [-0.49; 0.20]
	Week 36	60	57	7.34 (0.89)	74	74	7.31 (0.76)	-0.04 [-0.38; 0.30]
	Week 44	60	56	7.41 (1.01)	74	72	7.31 (0.74)	-0.11 [-0.45; 0.23]
	Week 52	60	58	7.34 (1.06)	74	74	7.15 (0.77)	-0.22 [-0.56; 0.12]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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2.4 Change in fasting plasma glucose (FPG) by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg	
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]
FPG (mg/dL)											
All subjects (total)	Week 10	290	264	-22.28 (86.52)		292	271	-28.67 (85.65)			-0.07 [-0.24; 0.09]
	Week 18	290	252	-18.76 (88.32)		292	269	-28.54 (77.97)			-0.12 [-0.28; 0.05]
	Week 26	290	256	-19.24 (90.08)		292	274	-32.42 (83.31)			-0.15 [-0.31; 0.01]
	Week 52	290	239	-15.31 (86.95)	-10.46 (3.74)	292	257	-34.67 (83.67)	-33.81 (3.62)	23.35 [13.11;33.59] <0.0001	-0.23 [-0.39;-0.06]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The change from baseline in response after 52 weeks are analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and baseline response as covariate. Missing values at week 52 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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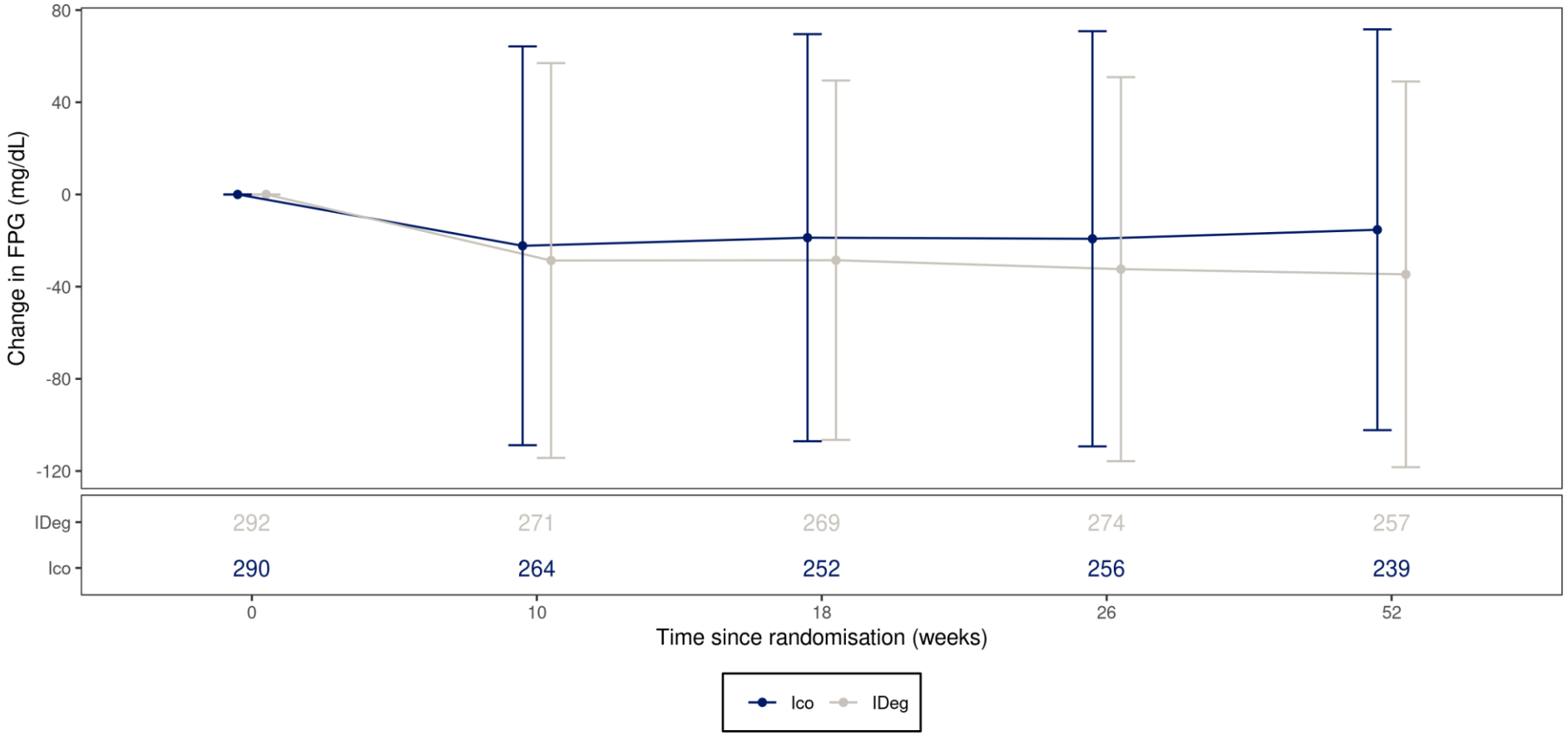
2.5 Change in fasting plasma glucose (FPG) by treatment week - Mean plot - Onwards 6 - in-trial - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).
FPG : Fasting plasma glucose

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23JAN2024:13:35:57 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/FPG2chg4625.png

2.6 Change in fasting plasma glucose (FPG) by treatment week - Onwards 6 - in-trial - Full analysis set

		Ico				IDeg				Ico - IDeg	
	Week	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]
FPG (mmol/L)											
All subjects (total)	Week 10	290	264	-1.24 (4.80)		292	271	-1.59 (4.75)			-0.07 [-0.24; 0.09]
	Week 18	290	252	-1.04 (4.90)		292	269	-1.58 (4.33)			-0.12 [-0.28; 0.05]
	Week 26	290	256	-1.07 (5.00)		292	274	-1.80 (4.62)			-0.15 [-0.31; 0.01]
	Week 52	290	239	-0.85 (4.83)	-0.58 (0.21)	292	257	-1.92 (4.64)	-1.88 (0.20)	1.30 [0.73; 1.86] <0.0001	-0.23 [-0.39;-0.06]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test).The change from baseline in response after 52 weeks are analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and baseline response as covariate. Missing values at week 52 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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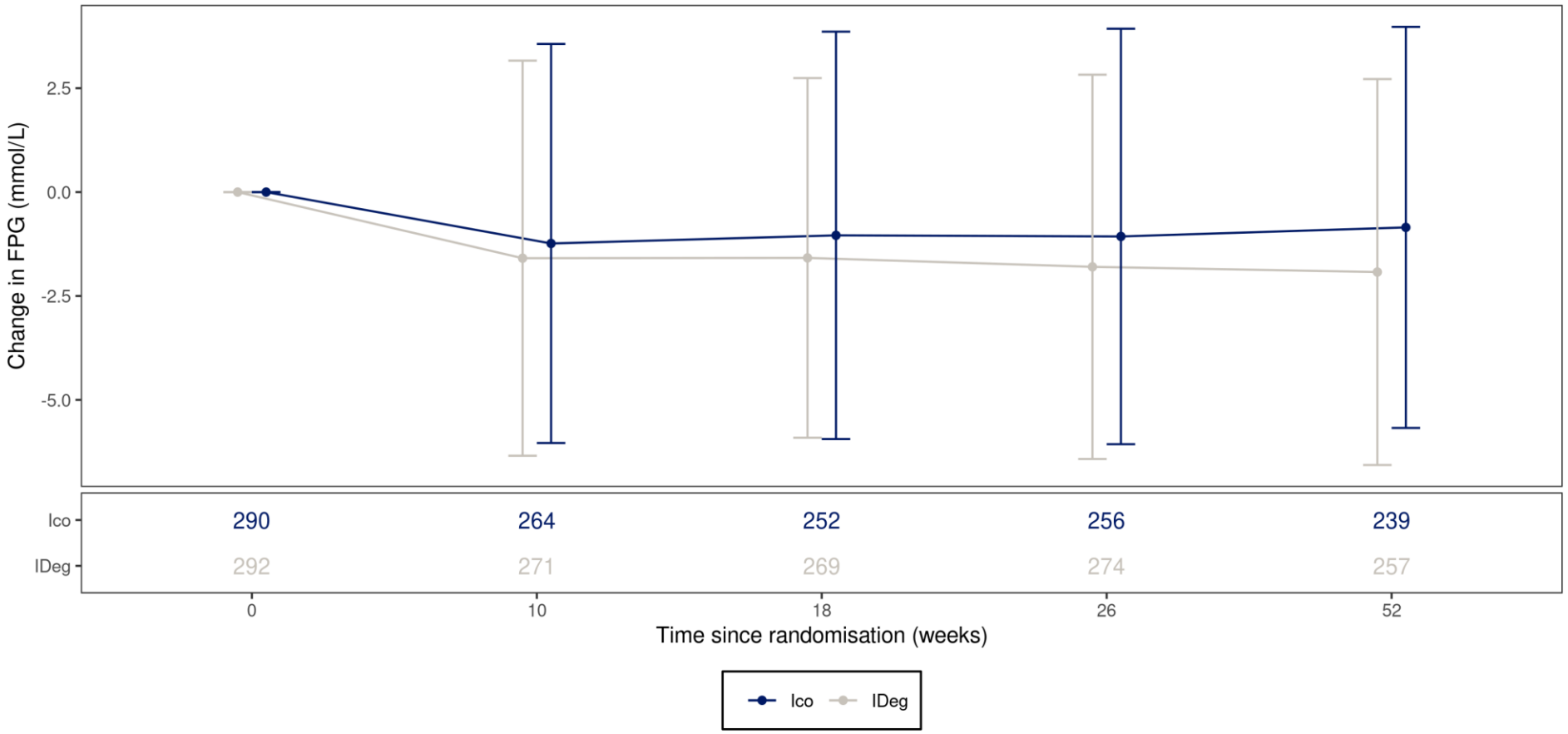
21JUL2023:15:58:55 - /ChangeFPG_4625.txt

2.7 Change in fasting plasma glucose (FPG) by treatment week - Mean plot - Onwards 6 - in-trial - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).
FPG : Fasting plasma glucose

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21JUL2023:13:54:41 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/FPGchg4625.png

2.8 Absolute fasting plasma glucose (FPG) by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico			IDeg			Ico - IDeg
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
FPG (mg/dL)								
All subjects (total)	Week 0	290	276	179.17 (73.86)	292	287	172.31 (72.30)	-0.09 [-0.26; 0.07]
	Week 10	290	273	159.06 (64.18)	292	276	144.62 (58.81)	-0.23 [-0.40;-0.07]
	Week 18	290	261	163.91 (63.02)	292	272	143.44 (55.69)	-0.34 [-0.51;-0.18]
	Week 26	290	265	159.75 (63.81)	292	277	141.38 (51.31)	-0.32 [-0.48;-0.15]
	Week 52	290	247	164.81 (61.50)	292	260	140.71 (51.49)	-0.42 [-0.59;-0.26]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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2.9 Absolute Fasting plasma glucose (FPG) by treatment week - Onwards 6 - in-trial - Full analysis set

		Ico			IDeg			Ico - IDeg
	Week	N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
FPG (mmol/L)								
All subjects (total)	Week 0	290	276	9.94 (4.10)	292	287	9.56 (4.01)	-0.09 [-0.26; 0.07]
	Week 10	290	273	8.83 (3.56)	292	276	8.03 (3.26)	-0.23 [-0.40;-0.07]
	Week 18	290	261	9.10 (3.50)	292	272	7.96 (3.09)	-0.34 [-0.51;-0.18]
	Week 26	290	265	8.87 (3.54)	292	277	7.85 (2.85)	-0.32 [-0.48;-0.15]
	Week 52	290	247	9.15 (3.41)	292	260	7.81 (2.86)	-0.42 [-0.59;-0.26]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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21JUL2023:15:58:56 - /FPG_4625.txt

2.10 Change in body weight by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico			IDeg			Ico - IDeg		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI] p-value int.
Body weight (kg)											
All subjects (total)	Week 14	290	280	1.06 (2.34)		292	284	0.78 (2.16)			-0.13 [-0.29; 0.03]
	Week 26	290	277	1.25 (3.11)		292	284	1.06 (2.88)			-0.06 [-0.23; 0.10]
	Week 52	290	273	1.41 (4.10)	1.25 (0.27)	292	279	1.25 (3.61)	1.67 (0.29)	-0.42 [-1.20; 0.37] 0.2958	-0.04 [-0.20; 0.12]
Gender											
Female	Week 14	125	121	0.94 (2.38)		120	115	0.81 (2.00)			-0.06 [-0.31; 0.19]
	Week 26	125	117	1.16 (3.37)		120	116	1.37 (2.79)			0.07 [-0.18; 0.32]
	Week 52	125	116	1.22 (4.35)	1.03 (0.43)	120	114	1.44 (3.73)	2.05 (0.44)	-1.02 [-2.21; 0.16] 0.0910	0.05 [-0.20; 0.30] 0.1662
Male	Week 14	165	159	1.16 (2.31)		172	169	0.75 (2.27)			-0.18 [-0.39; 0.04]
	Week 26	165	160	1.32 (2.92)		172	168	0.85 (2.93)			-0.16 [-0.38; 0.05]
	Week 52	165	157	1.55 (3.91)	1.41 (0.35)	172	165	1.12 (3.54)	1.40 (0.36)	0.01 [-0.96; 0.98] 0.9858	-0.11 [-0.33; 0.10]
Age											
<65 years	Week 14	267	258	1.05 (2.36)		271	264	0.78 (2.21)			-0.12 [-0.29; 0.05]
	Week 26	267	256	1.27 (3.09)		271	263	1.05 (2.92)			-0.07 [-0.24; 0.10]
	Week 52	267	252	1.53 (4.18)	1.35 (0.28)	271	258	1.25 (3.62)	1.71 (0.30)	-0.36 [-1.17; 0.46] 0.3932	-0.07 [-0.24; 0.10] 0.5788
>=65 years	Week 14	23	22	1.19 (2.11)		21	20	0.70 (1.47)			-0.26 [-0.86; 0.33]
	Week 26	23	21	1.01 (3.47)		21	21	1.16 (2.29)			0.05 [-0.54; 0.64]
	Week 52	23	21	-0.03 (2.71)	0.06 (0.94)	21	21	1.25 (3.65)	1.17 (0.93)	-1.12 [-3.70; 1.47] 0.3970	0.39 [-0.20; 0.99]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 52 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment, region (if applicable),HbA1c group at screening and pre-trial basal insulin treatment (and subgroup with interaction between treatment and subgroup, if applicable) as fixed factors, and baseline response as covariate. Missing values at week 52 are imputed using multiple imputation based on the change from LAOT value to week 52 for subjects that have discontinued randomised treatment but have a measurement at week 52. The model includes treatment as a fixed factor and the LAOT value and the time point of this assessment as covariates. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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23JAN2024:13:34:53 - /ChangeWeight_4625.txt

Change in body weight by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg			
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]	p-value int.
HbA1c													
<=8,5%	Week 14	235	226	0.85 (2.24)		242	236	0.70 (2.22)				-0.07 [-0.25; 0.11]	
	Week 26	235	224	1.05 (2.94)		242	235	0.99 (2.96)				-0.02 [-0.20; 0.16]	
	Week 52	235	219	1.34 (3.65)	1.38 (0.31)	242	231	1.20 (3.68)	1.80 (0.33)	-0.42 [-1.28; 0.44]	0.3408	-0.04 [-0.22; 0.14]	0.9657
>8,5%	Week 14	55	54	1.94 (2.55)		50	48	1.14 (1.81)				-0.36 [-0.74; 0.03]	
	Week 26	55	53	2.11 (3.65)		50	49	1.39 (2.46)				-0.23 [-0.61; 0.16]	
	Week 52	55	54	1.70 (5.61)	0.67 (0.67)	50	48	1.47 (3.32)	1.05 (0.69)	-0.38 [-2.06; 1.30]	0.6599	-0.05 [-0.43; 0.34]	
Region													
Europe	Week 14	136	132	0.93 (2.38)		139	136	0.73 (2.19)				-0.09 [-0.32; 0.15]	
	Week 26	136	131	1.20 (3.20)		139	136	0.95 (2.92)				-0.08 [-0.32; 0.15]	
	Week 52	136	128	1.20 (3.69)	1.08 (0.39)	139	131	0.99 (3.57)	1.57 (0.42)	-0.49 [-1.60; 0.62]	0.3855	-0.06 [-0.29; 0.18]	0.8996
North and South America	Week 14	106	100	1.18 (2.41)		85	80	0.98 (2.33)				-0.08 [-0.37; 0.21]	
	Week 26	106	98	1.38 (3.33)		85	80	1.30 (3.39)				-0.02 [-0.31; 0.26]	
	Week 52	106	98	1.83 (4.73)	1.62 (0.46)	85	80	1.73 (4.21)	2.14 (0.51)	-0.52 [-1.85; 0.81]	0.4456	-0.02 [-0.31; 0.26]	
Asia	Week 14	48	48	1.21 (2.10)		68	68	0.63 (1.89)				-0.29 [-0.66; 0.08]	
	Week 26	48	48	1.13 (2.36)		68	68	1.00 (2.04)				-0.06 [-0.43; 0.31]	
	Week 52	48	47	1.09 (3.77)	1.08 (0.64)	68	68	1.18 (2.86)	1.15 (0.55)	-0.08 [-1.66; 1.51]	0.9248	0.03 [-0.34; 0.39]	
Race													
White	Week 14	230	220	1.03 (2.39)		218	210	0.81 (2.26)				-0.09 [-0.28; 0.09]	
	Week 26	230	218	1.26 (3.20)		218	210	1.05 (3.12)				-0.07 [-0.25; 0.12]	
	Week 52	230	215	1.49 (4.13)	1.46 (0.38)	218	205	1.28 (3.81)	1.96 (0.42)	-0.50 [-1.42; 0.41]	0.2805	-0.05 [-0.24; 0.13]	0.6063
Not white	Week 14	60	60	1.20 (2.16)		74	74	0.67 (1.84)				-0.26 [-0.60; 0.08]	
	Week 26	60	59	1.23 (2.78)		74	74	1.09 (2.09)				-0.06 [-0.40; 0.29]	
	Week 52	60	58	1.09 (4.03)	0.62 (0.89)	74	74	1.16 (3.04)	0.67 (0.95)	-0.05 [-1.53; 1.44]	0.9525	0.02 [-0.32; 0.36]	

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 52 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment, region (if applicable), HbA1c group at screening and pre-trial basal insulin treatment (and subgroup with interaction between treatment and subgroup, if applicable) as fixed factors, and baseline response as covariate. Missing values at week 52 are imputed using multiple imputation based on the change from LAOT value to week 52 for subjects that have discontinued randomised treatment but have a measurement at week 52. The model includes treatment as a fixed factor and the LAOT value and the time point of this assessment as covariates. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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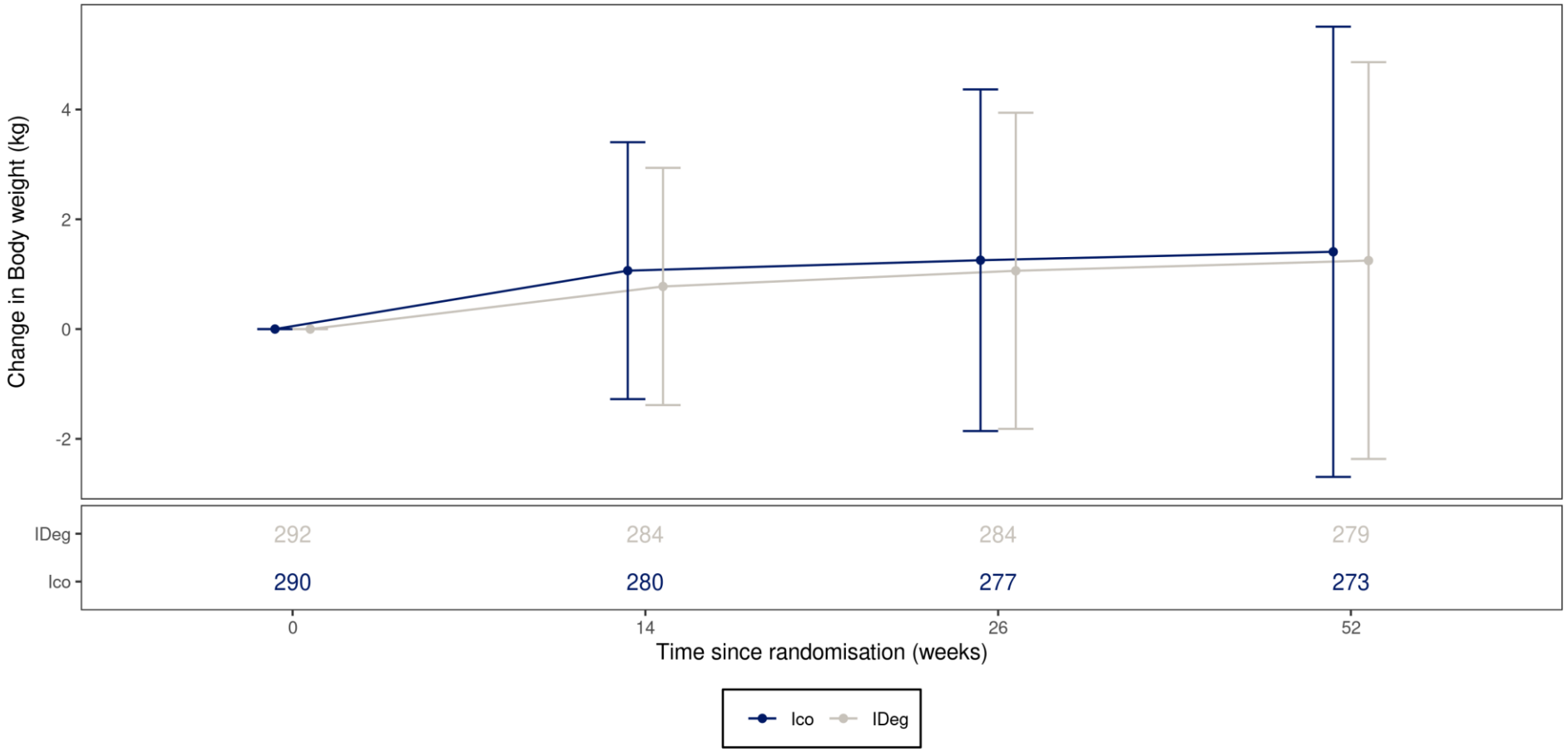
2.11 Change in body weight by treatment week - Mean plot - Onwards 6 - in-trial - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).

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23JAN2024:13:35:58 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/WEIGHTchg4625.png

2.12 Absolute body weight by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico			IDeg			Ico - IDeg
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
Body weight (kg)								
All subjects (total)	Week 0	290	290	78.65 (17.62)	292	292	77.10 (16.78)	-0.09 [-0.25; 0.07]
	Week 14	290	280	79.76 (18.02)	292	284	77.63 (17.09)	-0.12 [-0.28; 0.04]
	Week 26	290	277	79.97 (18.11)	292	284	78.13 (17.12)	-0.10 [-0.27; 0.06]
	Week 52	290	273	80.15 (18.28)	292	279	78.21 (17.35)	-0.11 [-0.27; 0.05]
Gender								
Female	Week 0	125	125	70.99 (15.51)	120	120	68.87 (15.34)	-0.14 [-0.39; 0.11]
	Week 14	125	121	71.72 (15.57)	120	115	69.12 (15.17)	-0.17 [-0.42; 0.08]
	Week 26	125	117	71.76 (15.69)	120	116	70.26 (15.74)	-0.09 [-0.35; 0.16]
	Week 52	125	116	71.81 (16.06)	120	114	70.37 (16.06)	-0.09 [-0.34; 0.16]
Male	Week 0	165	165	84.45 (16.94)	172	172	82.84 (15.33)	-0.10 [-0.31; 0.11]
	Week 14	165	159	85.88 (17.37)	172	169	83.42 (15.88)	-0.15 [-0.36; 0.07]
	Week 26	165	160	85.97 (17.44)	172	168	83.56 (15.93)	-0.14 [-0.36; 0.07]
	Week 52	165	157	86.32 (17.38)	172	165	83.63 (16.14)	-0.16 [-0.37; 0.05]
Age								
<65 years	Week 0	267	267	78.36 (17.68)	271	271	77.30 (16.72)	-0.06 [-0.23; 0.11]
	Week 14	267	258	79.50 (18.08)	271	264	77.86 (17.04)	-0.09 [-0.26; 0.08]
	Week 26	267	256	79.71 (18.17)	271	263	78.34 (17.12)	-0.08 [-0.25; 0.09]
	Week 52	267	252	79.99 (18.40)	271	258	78.42 (17.34)	-0.09 [-0.26; 0.08]
>=65 years	Week 0	23	23	82.02 (16.91)	21	21	74.43 (17.84)	-0.43 [-1.03; 0.17]
	Week 14	23	22	82.73 (17.42)	21	20	74.58 (17.88)	-0.45 [-1.05; 0.15]
	Week 26	23	21	83.12 (17.53)	21	21	75.58 (17.38)	-0.42 [-1.02; 0.17]
	Week 52	23	21	82.08 (16.97)	21	21	75.67 (17.69)	-0.36 [-0.96; 0.23]
HbA1c								
<=8,5%	Week 0	235	235	78.74 (18.03)	242	242	77.19 (16.33)	-0.09 [-0.27; 0.09]
	Week 14	235	226	79.61 (18.46)	242	236	77.71 (16.61)	-0.11 [-0.29; 0.07]
	Week 26	235	224	79.83 (18.63)	242	235	78.07 (16.70)	-0.10 [-0.28; 0.08]
	Week 52	235	219	80.18 (18.72)	242	231	78.07 (16.94)	-0.12 [-0.30; 0.06]
>8,5%	Week 0	55	55	78.28 (15.91)	50	50	76.63 (18.99)	-0.09 [-0.48; 0.29]
	Week 14	55	54	80.38 (16.16)	50	48	77.26 (19.45)	-0.17 [-0.56; 0.21]
	Week 26	55	53	80.52 (15.92)	50	49	78.44 (19.21)	-0.12 [-0.50; 0.27]
	Week 52	55	54	80.05 (16.52)	50	48	78.87 (19.40)	-0.06 [-0.45; 0.32]
Region								
Europe	Week 0	136	136	77.92 (14.72)	139	139	79.13 (15.05)	0.08 [-0.16; 0.32]
	Week 14	136	132	79.07 (14.84)	139	136	79.63 (15.37)	0.04 [-0.20; 0.27]
	Week 26	136	131	79.40 (15.03)	139	136	80.14 (15.14)	0.05 [-0.19; 0.29]
	Week 52	136	128	79.31 (15.31)	139	131	80.32 (15.96)	0.06 [-0.17; 0.30]
North and South America	Week 0	106	106	86.25 (18.54)	85	85	84.65 (16.46)	-0.09 [-0.38; 0.20]
	Week 14	106	100	87.68 (19.10)	85	80	85.72 (16.83)	-0.11 [-0.39; 0.18]
	Week 26	106	98	88.03 (19.05)	85	80	86.31 (17.33)	-0.09 [-0.38; 0.19]
	Week 52	106	98	88.31 (19.16)	85	80	86.28 (17.12)	-0.11 [-0.40; 0.18]
Asia	Week 0	48	48	63.92 (12.88)	68	68	63.50 (12.20)	-0.03 [-0.40; 0.34]
	Week 14	48	48	65.13 (13.82)	68	68	64.13 (12.33)	-0.08 [-0.45; 0.29]
	Week 26	48	48	65.05 (13.75)	68	68	64.49 (12.08)	-0.04 [-0.41; 0.33]
	Week 52	48	47	65.46 (13.77)	68	68	64.67 (11.72)	-0.06 [-0.43; 0.31]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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Absolute body weight by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico			IDeg			Ico - IDeg
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
Race								
White	Week 0	230	230	81.47 (17.07)	218	218	81.37 (15.83)	-0.01 [-0.19; 0.18]
	Week 14	230	220	82.69 (17.39)	218	210	82.02 (16.22)	-0.04 [-0.23; 0.15]
	Week 26	230	218	82.95 (17.46)	218	210	82.54 (16.28)	-0.02 [-0.21; 0.16]
	Week 52	230	215	83.10 (17.70)	218	205	82.74 (16.69)	-0.02 [-0.21; 0.16]
Not white	Week 0	60	60	67.82 (15.50)	74	74	64.52 (12.79)	-0.23 [-0.57; 0.11]
	Week 14	60	60	69.02 (16.22)	74	74	65.20 (12.90)	-0.26 [-0.60; 0.08]
	Week 26	60	59	68.93 (16.22)	74	74	65.61 (12.78)	-0.23 [-0.57; 0.11]
	Week 52	60	58	69.22 (16.23)	74	74	65.68 (12.30)	-0.25 [-0.59; 0.09]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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2.13 Total weekly insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

	Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Total Weekly Actual Insulin Dose (U)											
All subjects (total)	Week 1	290	289	460.24 (229.38)		292	291	347.76 (161.85)			-0.57 [-0.73;-0.40]
	Week 2	290	289	357.45 (172.88)		292	291	349.57 (165.49)			-0.05 [-0.21; 0.12]
	Week 3	290	288	352.34 (166.83)		292	289	341.93 (158.36)			-0.06 [-0.23; 0.10]
	Week 4	290	288	353.33 (170.20)		292	289	338.81 (156.99)			-0.09 [-0.25; 0.07]
	Week 5	290	288	351.61 (172.01)		292	288	339.39 (156.84)			-0.07 [-0.24; 0.09]
	Week 6	290	286	353.48 (177.66)		292	288	341.97 (160.97)			-0.07 [-0.23; 0.09]
	Week 7	290	286	351.79 (183.37)		292	287	341.06 (161.94)			-0.06 [-0.22; 0.10]
	Week 8	290	286	355.87 (183.12)		292	287	340.17 (159.50)			-0.09 [-0.25; 0.07]
	Week 9	290	284	354.14 (181.80)		292	286	340.46 (160.03)			-0.08 [-0.24; 0.08]
	Week 10	290	284	351.09 (190.44)		292	287	341.09 (162.48)			-0.06 [-0.22; 0.11]
	Week 11	290	282	349.26 (184.01)		292	286	343.99 (169.31)			-0.03 [-0.19; 0.13]
	Week 12	290	280	350.75 (186.74)		292	286	344.52 (167.58)			-0.04 [-0.20; 0.13]
	Week 13	290	279	354.18 (187.16)		292	284	346.02 (164.20)			-0.05 [-0.21; 0.12]
	Week 14	290	280	354.34 (193.73)		292	284	347.96 (167.48)			-0.04 [-0.20; 0.13]
	Week 15	290	280	351.61 (182.97)		292	284	346.72 (169.47)			-0.03 [-0.19; 0.13]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Total weekly insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Week 16	290	279	354.66 (190.61)		292	282	345.96 (168.75)			-0.05 [-0.21; 0.11]
Week 17	290	279	355.43 (196.20)		292	282	345.91 (166.82)			-0.05 [-0.21; 0.11]
Week 18	290	279	352.07 (194.36)		292	282	344.76 (174.46)			-0.04 [-0.20; 0.12]
Week 19	290	276	348.90 (194.66)		292	282	348.33 (175.95)			0.00 [-0.17; 0.16]
Week 20	290	276	351.75 (195.39)		292	282	347.47 (173.16)			-0.02 [-0.19; 0.14]
Week 21	290	274	355.14 (197.67)		292	282	345.82 (165.95)			-0.05 [-0.21; 0.11]
Week 22	290	274	355.14 (193.64)		292	282	345.21 (166.37)			-0.05 [-0.22; 0.11]
Week 23	290	273	357.35 (195.37)		292	282	347.98 (171.56)			-0.05 [-0.21; 0.11]
Week 24	290	270	352.41 (200.66)		292	282	347.57 (173.94)			-0.03 [-0.19; 0.14]
Week 25	290	271	351.57 (197.46)		292	282	348.89 (172.66)			-0.01 [-0.18; 0.15]
Week 26	290	271	356.00 (203.12)		292	282	347.00 (169.20)			-0.05 [-0.21; 0.11]
Week 27	290	270	353.53 (201.37)		292	282	346.44 (172.24)			-0.04 [-0.20; 0.12]
Week 28	290	270	354.69 (207.82)		292	282	348.62 (170.41)			-0.03 [-0.19; 0.13]
Week 29	290	267	353.24 (205.59)		292	281	351.05 (172.81)			-0.01 [-0.17; 0.15]
Week 30	290	265	353.34 (209.44)		292	279	351.74 (173.99)			-0.01 [-0.17; 0.15]
Week 31	290	265	357.35 (208.36)		292	280	350.98 (179.89)			-0.03 [-0.20; 0.13]
Week 32	290	265	355.72 (207.77)		292	280	349.45 (172.96)			-0.03 [-0.20; 0.13]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Total weekly insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Week 33	290	264	352.97 (208.55)		292	277	351.49 (171.36)			-0.01 [-0.17; 0.15]
Week 34	290	263	356.75 (207.02)		292	279	349.40 (173.08)			-0.04 [-0.20; 0.12]
Week 35	290	262	356.75 (208.68)		292	279	350.96 (177.02)			-0.03 [-0.19; 0.13]
Week 36	290	262	351.34 (211.81)		292	279	349.42 (175.92)			-0.01 [-0.17; 0.15]
Week 37	290	262	353.32 (212.80)		292	278	347.23 (179.10)			-0.03 [-0.19; 0.13]
Week 38	290	262	355.53 (207.33)		292	274	349.33 (177.29)			-0.03 [-0.19; 0.13]
Week 39	290	262	354.35 (210.46)		292	276	346.79 (176.26)			-0.04 [-0.20; 0.12]
Week 40	290	260	353.87 (214.39)		292	276	349.42 (175.27)			-0.02 [-0.19; 0.14]
Week 41	290	259	353.24 (209.11)		292	276	349.42 (176.93)			-0.02 [-0.18; 0.14]
Week 42	290	258	353.94 (216.56)		292	277	345.07 (174.56)			-0.05 [-0.21; 0.12]
Week 43	290	259	357.49 (219.22)		292	278	350.61 (179.70)			-0.03 [-0.20; 0.13]
Week 44	290	257	360.93 (219.45)		292	277	352.93 (184.64)			-0.04 [-0.20; 0.12]
Week 45	290	258	356.56 (216.56)		292	277	352.08 (179.96)			-0.02 [-0.18; 0.14]
Week 46	290	259	353.44 (212.44)		292	277	347.75 (180.26)			-0.03 [-0.19; 0.13]
Week 47	290	257	362.67 (212.47)		292	276	346.42 (178.38)			-0.08 [-0.25; 0.08]
Week 48	290	259	356.90 (215.96)		292	276	348.87 (180.78)			-0.04 [-0.20; 0.12]
Week 49	290	259	355.91 (210.85)		292	276	346.08 (180.03)			-0.05 [-0.21; 0.11]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Total weekly insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg		Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI]	p-value	Hedges' g [95%-CI]
Week 50	290	256	360.40 (217.87)		292	276	349.00 (183.03)				-0.06 [-0.22; 0.11]
Week 51	290	257	356.21 (208.89)		292	274	348.25 (182.26)				-0.04 [-0.20; 0.12]
Week 52	290	257	351.65 (208.72)	308.44 (0.03)	292	273	348.86 (176.89)	329.14 (0.03)	0.94 [0.87;1.01]	0.0770	-0.01 [-0.18; 0.15]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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2.14 Total weekly basal insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

	Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Weekly insulin dose (U)											
All subjects (total)	Week 1	290	283	284.16 (157.64)		292	291	160.59 (92.12)			-0.96 [-1.13;-0.79]
	Week 2	290	286	178.62 (89.27)		292	291	164.23 (93.49)			-0.16 [-0.32; 0.01]
	Week 3	290	283	181.61 (88.29)		292	289	164.89 (92.17)			-0.19 [-0.35;-0.02]
	Week 4	290	282	186.47 (89.56)		292	289	163.56 (91.06)			-0.25 [-0.42;-0.09]
	Week 5	290	281	189.98 (93.59)		292	288	165.14 (91.50)			-0.27 [-0.43;-0.10]
	Week 6	290	279	193.78 (96.99)		292	288	165.73 (90.93)			-0.30 [-0.46;-0.13]
	Week 7	290	277	194.66 (99.41)		292	286	166.75 (92.74)			-0.29 [-0.45;-0.13]
	Week 8	290	281	197.62 (100.56)		292	286	166.18 (93.01)			-0.32 [-0.49;-0.16]
	Week 9	290	280	199.91 (101.84)		292	285	166.12 (93.06)			-0.35 [-0.51;-0.18]
	Week 10	290	275	199.89 (104.03)		292	286	167.03 (93.96)			-0.33 [-0.49;-0.17]
	Week 11	290	274	201.28 (104.46)		292	285	167.05 (95.50)			-0.34 [-0.51;-0.18]
	Week 12	290	271	200.35 (105.49)		292	286	167.24 (95.61)			-0.33 [-0.49;-0.16]
	Week 13	290	274	199.96 (107.00)		292	284	167.81 (95.34)			-0.32 [-0.48;-0.15]
	Week 14	290	273	201.03 (109.66)		292	284	169.08 (95.85)			-0.31 [-0.47;-0.15]
	Week 15	290	274	200.57 (106.62)		292	283	169.72 (97.38)			-0.30 [-0.47;-0.14]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Total weekly basal insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Week 16	290	274	199.20 (108.88)		292	281	169.69 (98.67)			-0.28 [-0.45;-0.12]
Week 17	290	274	200.55 (108.93)		292	281	169.78 (98.85)			-0.30 [-0.46;-0.13]
Week 18	290	271	201.00 (108.94)		292	280	170.55 (99.25)			-0.29 [-0.46;-0.13]
Week 19	290	266	202.26 (111.71)		292	280	170.74 (98.73)			-0.30 [-0.46;-0.14]
Week 20	290	267	201.65 (111.04)		292	281	170.50 (99.31)			-0.30 [-0.46;-0.13]
Week 21	290	265	204.98 (114.70)		292	282	170.58 (100.06)			-0.32 [-0.48;-0.16]
Week 22	290	267	203.37 (115.80)		292	282	170.82 (98.37)			-0.30 [-0.47;-0.14]
Week 23	290	267	204.78 (114.59)		292	281	171.33 (98.73)			-0.31 [-0.48;-0.15]
Week 24	290	261	204.18 (114.88)		292	281	172.19 (98.94)			-0.30 [-0.46;-0.13]
Week 25	290	262	204.31 (113.90)		292	281	172.20 (98.45)			-0.30 [-0.46;-0.14]
Week 26	290	265	204.98 (114.77)		292	282	172.05 (98.53)			-0.31 [-0.47;-0.14]
Week 27	290	262	204.47 (115.35)		292	282	171.73 (98.41)			-0.30 [-0.47;-0.14]
Week 28	290	259	204.63 (117.59)		292	281	171.97 (99.04)			-0.30 [-0.46;-0.14]
Week 29	290	259	205.02 (118.19)		292	281	172.06 (99.05)			-0.30 [-0.47;-0.14]
Week 30	290	252	206.87 (120.50)		292	278	172.23 (99.82)			-0.31 [-0.48;-0.15]
Week 31	290	257	206.34 (120.17)		292	279	172.46 (100.52)			-0.31 [-0.47;-0.14]
Week 32	290	258	206.98 (120.91)		292	279	173.11 (100.83)			-0.30 [-0.47;-0.14]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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23JAN2024:13:34:57 - /TotBasDose_4625.txt

Total weekly basal insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Week 33	290	256	206.50 (121.72)		292	277	174.11 (100.96)			-0.29 [-0.45;-0.13]
Week 34	290	257	207.54 (122.90)		292	278	173.92 (100.65)			-0.30 [-0.46;-0.14]
Week 35	290	256	206.80 (123.39)		292	279	173.42 (101.14)			-0.30 [-0.46;-0.13]
Week 36	290	253	207.37 (123.35)		292	279	173.29 (101.15)			-0.30 [-0.47;-0.14]
Week 37	290	254	205.77 (124.26)		292	277	172.98 (101.15)			-0.29 [-0.45;-0.13]
Week 38	290	256	206.48 (124.79)		292	274	172.56 (100.87)			-0.30 [-0.46;-0.14]
Week 39	290	258	205.27 (125.45)		292	275	172.17 (100.24)			-0.29 [-0.45;-0.13]
Week 40	290	250	208.32 (126.78)		292	276	172.51 (100.61)			-0.31 [-0.48;-0.15]
Week 41	290	251	207.19 (127.70)		292	276	172.57 (101.28)			-0.30 [-0.46;-0.14]
Week 42	290	248	209.64 (129.19)		292	276	172.20 (102.17)			-0.32 [-0.48;-0.16]
Week 43	290	253	208.34 (129.50)		292	277	173.11 (102.80)			-0.30 [-0.46;-0.14]
Week 44	290	250	211.08 (129.35)		292	277	173.17 (103.07)			-0.32 [-0.49;-0.16]
Week 45	290	246	210.28 (129.40)		292	277	173.84 (104.43)			-0.31 [-0.47;-0.15]
Week 46	290	248	207.78 (129.35)		292	276	172.85 (103.87)			-0.30 [-0.46;-0.13]
Week 47	290	253	210.20 (129.83)		292	276	173.03 (104.05)			-0.32 [-0.48;-0.15]
Week 48	290	251	210.00 (131.70)		292	276	173.93 (104.92)			-0.30 [-0.47;-0.14]
Week 49	290	250	209.98 (131.30)		292	275	172.61 (104.33)			-0.31 [-0.48;-0.15]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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23JAN2024:13:34:57 - /TotBasDose_4625.txt

Total weekly basal insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg		Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI]	p-value	Hedges' g [95%-CI]
Week 50	290	249	211.24 (131.74)		292	275	173.50 (104.96)				-0.32 [-0.48;-0.15]
Week 51	290	251	209.04 (126.81)		292	274	173.02 (105.13)				-0.31 [-0.47;-0.15]
Week 52	290	245	209.59 (129.58)	167.68 (0.02)	292	273	173.25 (104.39)	152.83 (0.02)	1.10 [1.03;1.17]	0.0033	-0.31 [-0.47;-0.15]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
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2.15 Total weekly bolus insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

	Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Weekly Actual Bolus Dose (U)											
All subjects (total)	Week 1	290	288	182.62 (114.34)		292	289	188.47 (98.55)			0.05 [-0.11; 0.22]
	Week 2	290	286	182.58 (114.78)		292	288	187.27 (97.68)			0.04 [-0.12; 0.21]
	Week 3	290	285	175.72 (111.64)		292	287	178.28 (92.77)			0.02 [-0.14; 0.19]
	Week 4	290	286	171.94 (112.27)		292	287	176.48 (91.68)			0.04 [-0.12; 0.21]
	Week 5	290	286	167.41 (106.30)		292	286	175.47 (91.46)			0.08 [-0.08; 0.24]
	Week 6	290	284	165.60 (107.06)		292	283	179.35 (92.36)			0.14 [-0.03; 0.30]
	Week 7	290	284	164.41 (108.91)		292	285	176.12 (93.47)			0.12 [-0.05; 0.28]
	Week 8	290	283	163.43 (106.79)		292	286	175.18 (90.64)			0.12 [-0.04; 0.28]
	Week 9	290	282	158.16 (105.85)		292	284	176.15 (91.51)			0.18 [0.02; 0.34]
	Week 10	290	283	158.09 (114.15)		292	285	175.87 (91.92)			0.17 [0.01; 0.33]
	Week 11	290	281	154.24 (105.66)		292	284	178.77 (103.98)			0.23 [0.07; 0.40]
	Week 12	290	279	157.40 (110.46)		292	284	178.52 (96.51)			0.20 [0.04; 0.37]
	Week 13	290	278	158.37 (107.56)		292	282	179.47 (93.64)			0.21 [0.05; 0.37]
	Week 14	290	278	159.48 (108.74)		292	283	179.51 (96.74)			0.19 [0.03; 0.36]
	Week 15	290	276	157.59 (103.77)		292	283	178.22 (96.60)			0.21 [0.04; 0.37]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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23JAN2024:13:34:58 - /TotBolDose_4625.txt

Total weekly bolus insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Week 16	290	276	160.77 (108.65)		292	281	177.50 (94.41)			0.16 [0.00; 0.33]
Week 17	290	276	160.19 (114.01)		292	281	177.36 (92.29)			0.17 [0.00; 0.33]
Week 18	290	277	157.97 (110.62)		292	279	177.32 (99.45)			0.18 [0.02; 0.35]
Week 19	290	274	155.10 (108.13)		292	282	178.80 (100.14)			0.23 [0.06; 0.39]
Week 20	290	274	157.82 (111.49)		292	281	178.21 (99.28)			0.19 [0.03; 0.36]
Week 21	290	272	158.05 (107.16)		292	281	175.87 (92.61)			0.18 [0.01; 0.34]
Week 22	290	270	159.29 (104.09)		292	280	175.63 (92.80)			0.17 [0.00; 0.33]
Week 23	290	271	158.22 (105.62)		292	278	179.80 (95.43)			0.21 [0.05; 0.38]
Week 24	290	268	156.19 (112.10)		292	278	178.52 (98.31)			0.21 [0.05; 0.37]
Week 25	290	269	155.19 (107.91)		292	278	179.85 (97.19)			0.24 [0.08; 0.40]
Week 26	290	270	156.13 (114.88)		292	278	177.46 (94.94)			0.20 [0.04; 0.37]
Week 27	290	267	156.86 (110.33)		292	278	177.23 (97.64)			0.20 [0.03; 0.36]
Week 28	290	268	159.58 (117.35)		292	281	177.89 (95.31)			0.17 [0.01; 0.33]
Week 29	290	265	155.53 (112.70)		292	278	180.92 (98.18)			0.24 [0.08; 0.40]
Week 30	290	263	157.81 (113.64)		292	278	180.78 (99.85)			0.21 [0.05; 0.38]
Week 31	290	264	157.84 (112.86)		292	276	181.73 (102.68)			0.22 [0.06; 0.38]
Week 32	290	260	157.17 (113.53)		292	276	179.52 (96.34)			0.21 [0.05; 0.37]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Total weekly bolus insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg	Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Week 33	290	261	154.48 (111.42)		292	275	178.67 (95.75)			0.23 [0.07; 0.40]
Week 34	290	259	156.33 (108.48)		292	275	178.66 (96.36)			0.22 [0.05; 0.38]
Week 35	290	259	156.48 (110.50)		292	276	179.47 (100.17)			0.22 [0.05; 0.38]
Week 36	290	259	152.84 (111.98)		292	276	178.05 (100.56)			0.24 [0.07; 0.40]
Week 37	290	258	156.22 (114.85)		292	274	177.42 (102.38)			0.19 [0.03; 0.36]
Week 38	290	257	156.77 (106.95)		292	272	178.06 (104.19)			0.20 [0.04; 0.36]
Week 39	290	256	155.78 (108.79)		292	274	176.52 (102.02)			0.20 [0.03; 0.36]
Week 40	290	256	155.97 (110.13)		292	273	178.86 (101.25)			0.22 [0.05; 0.38]
Week 41	290	255	154.84 (107.54)		292	274	178.15 (103.62)			0.22 [0.06; 0.38]
Week 42	290	254	154.83 (111.07)		292	275	174.75 (101.45)			0.19 [0.02; 0.35]
Week 43	290	255	156.39 (117.42)		292	277	178.76 (104.41)			0.20 [0.04; 0.36]
Week 44	290	254	157.44 (117.03)		292	274	181.74 (108.71)			0.21 [0.05; 0.38]
Week 45	290	253	159.14 (113.98)		292	275	179.54 (103.91)			0.19 [0.02; 0.35]
Week 46	290	253	158.15 (112.07)		292	274	177.45 (104.10)			0.18 [0.02; 0.34]
Week 47	290	251	159.47 (112.70)		292	269	177.90 (102.13)			0.17 [0.01; 0.33]
Week 48	290	252	157.65 (113.87)		292	272	177.52 (102.80)			0.18 [0.02; 0.35]
Week 49	290	252	157.48 (111.01)		292	271	177.31 (100.89)			0.19 [0.02; 0.35]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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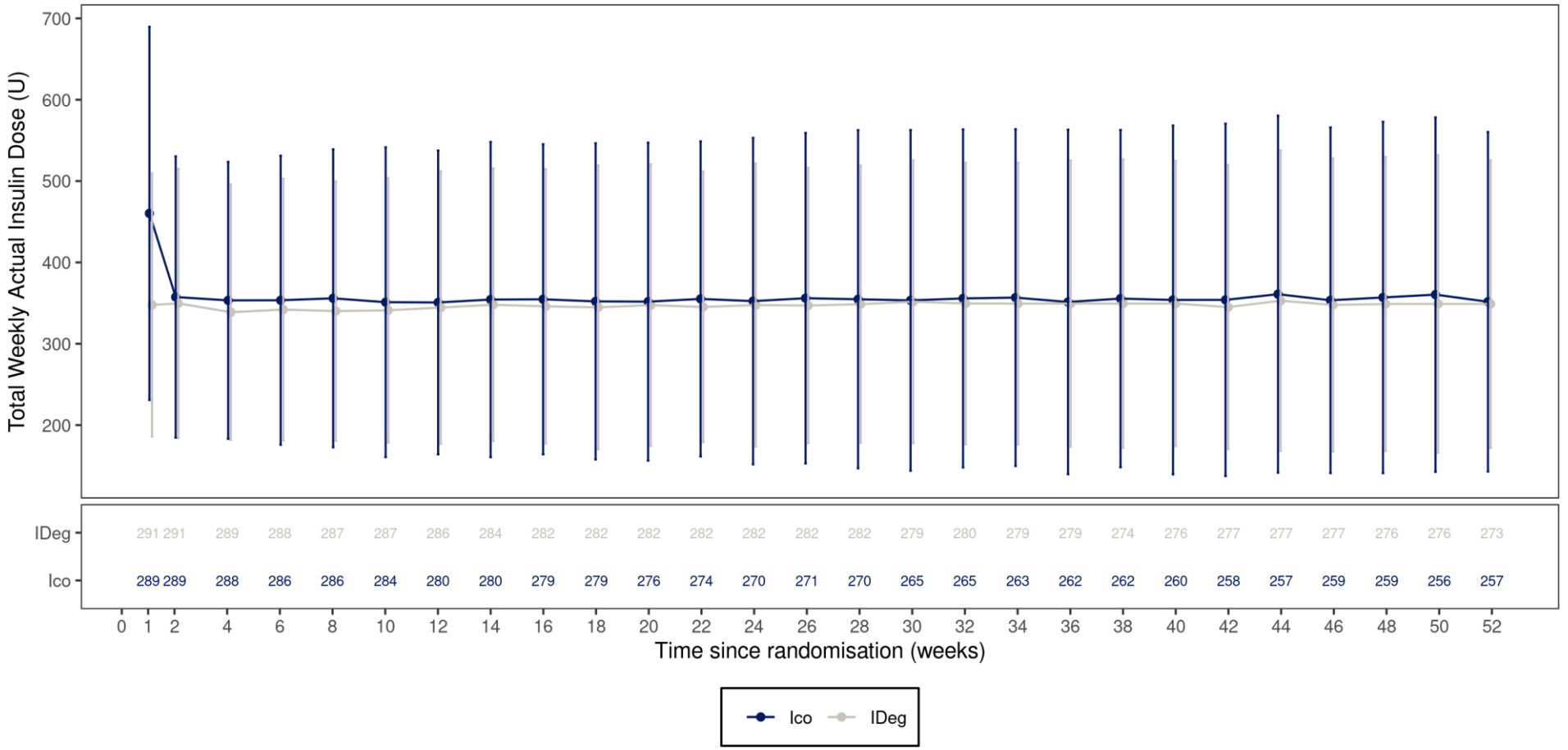
Total weekly bolus insulin dose by treatment week (U) - Onwards 6 - on-treatment - Full analysis set

Week	Ico				IDeg				Ico / IDeg		Ico - IDeg
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI]	p-value	Hedges' g [95%-CI]
Week 50	290	249	159.28 (116.53)		292	270	180.05 (103.38)				0.19 [0.03; 0.35]
Week 51	290	249	156.93 (114.47)		292	271	177.17 (103.35)				0.19 [0.02; 0.35]
Week 52	290	248	157.35 (112.35)	136.32 (0.04)	292	272	176.26 (98.72)	161.22 (0.04)	0.85 [0.76;0.94]	0.0014	0.18 [0.02; 0.34]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The log-transformed response at week 52 is s analysed using an analysis of covariance (ANCOVA) model with treatment, region, HbA1c group at screening and pre-trial basal insulin treatment as fixed factors, and log-transformed screening response as covariate. Missing values at week 52 areare imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:34:58 - /TotBolDose_4625.txt

2.16 Total weekly insulin dose by treatment week (U) - Mean plot - Onwards 6 - on-treatment - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).

nn1436/nn1436-amnog/current
23JAN2024:13:35:54 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/TOTDWACtotal4625.png

2.17 Time spent below range < 3.0 mmol/L (54 mg/dL) by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]
Time spent < 3.0 mmol/L (54 mg/dL) (%)												
All subjects (total)	Week 0-4	290	284	0.87 (1.15)		292	284	0.70 (1.15)				-0.15 [-0.31; 0.01]
	Week 22-26	290	261	1.02 (1.64)		292	272	0.68 (1.27)				-0.23 [-0.39;-0.06]
	Week 48-52	290	241	0.84 (1.29)	0.82 (0.09)	292	264	0.80 (1.60)	0.81 (0.09)	0.01 [-0.25; 0.27]	0.9130	-0.03 [-0.19; 0.14]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The response from week 48 to week 52 is analysed using an analysis of variance (ANOVA) model with treatment, region, HbA1c group at screening and pre trial basal insulin treatment as fixed factors. Missing values are imputed using multiple imputation based on values for subjects from the comparator group who completed randomised treatment. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:35:03 - /TBR_4625.txt

2.18 Time in range 3.0-3.9 mmol/L (54-70 mg/dL) by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]
Time Spent in Range 3.0-3.9 mmol/L (54-70 mg/dL) (%)												
All subjects (total)	Week 0-4	290	284	2.69 (2.15)		292	284	2.49 (2.21)				-0.09 [-0.26; 0.07]
	Week 22-26	290	261	2.85 (2.17)		292	272	2.22 (1.89)				-0.31 [-0.47;-0.14]
	Week 48-52	290	241	2.59 (2.09)	2.52 (0.14)	292	264	2.35 (2.33)	2.38 (0.14)	0.14 [-0.25; 0.53]	0.4753	-0.11 [-0.27; 0.06]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The response from week 48 to week 52 is analysed using an analysis of variance (ANOVA) model with treatment, region, HbA1c group at screening and pre trial basal insulin treatment as fixed factors. Missing values are imputed using multiple imputation based on values for subjects from the comparator group who completed randomised treatment. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:35:04 - /TIRL_4625.txt

2.19 Time in range 3.9-10.0 mmol/L (70-180mg/dL) by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]
Time in range 3.9-10.0 mmol/L (70-180 mg/dL) (%)												
All subjects (total)	Week 0-4	290	284	60.73 (14.78)		292	284	63.20 (14.66)				0.17 [0.00; 0.33]
	Week 22-26	290	261	59.10 (15.66)		292	272	60.85 (15.03)				0.11 [-0.05; 0.28]
	Week 48-52	290	241	57.26 (15.97)	57.40 (0.91)	292	264	59.60 (15.08)	59.82 (0.88)	-2.42 [-4.90; 0.07]	0.0563	0.15 [-0.01; 0.31]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The response from week 48 to week 52 is analysed using an analysis of variance (ANOVA) model with treatment, region, HbA1c group at screening and pre trial basal insulin treatment as fixed factors. Missing values are imputed using multiple imputation based on values for subjects from the comparator group who completed randomised treatment. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:35:05 - /TIR_4625.txt

2.20 Time in range 10.0-13.9 mmol/L (180-250.2 mg/dL) by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]
Time Spent in Range 10.0-13.9 mmol/L (180-250.2 mg/dL) (%)												
All subjects (total)	Week 0-4	290	284	23.48 (7.78)		292	284	23.00 (7.95)				-0.06 [-0.22; 0.10]
	Week 22-26	290	261	23.79 (7.48)		292	272	24.06 (7.28)				0.04 [-0.13; 0.20]
	Week 48-52	290	241	24.35 (7.41)	24.39 (0.47)	292	264	24.37 (7.78)	24.32 (0.46)	0.08 [-1.22; 1.37]	0.9097	0.00 [-0.16; 0.17]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The response from week 48 to week 52 is analysed using an analysis of variance (ANOVA) model with treatment, region, HbA1c group at screening and pre trial basal insulin treatment as fixed factors. Missing values are imputed using multiple imputation based on values for subjects from the comparator group who completed randomised treatment. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:35:06 - /TIRH_4625.txt

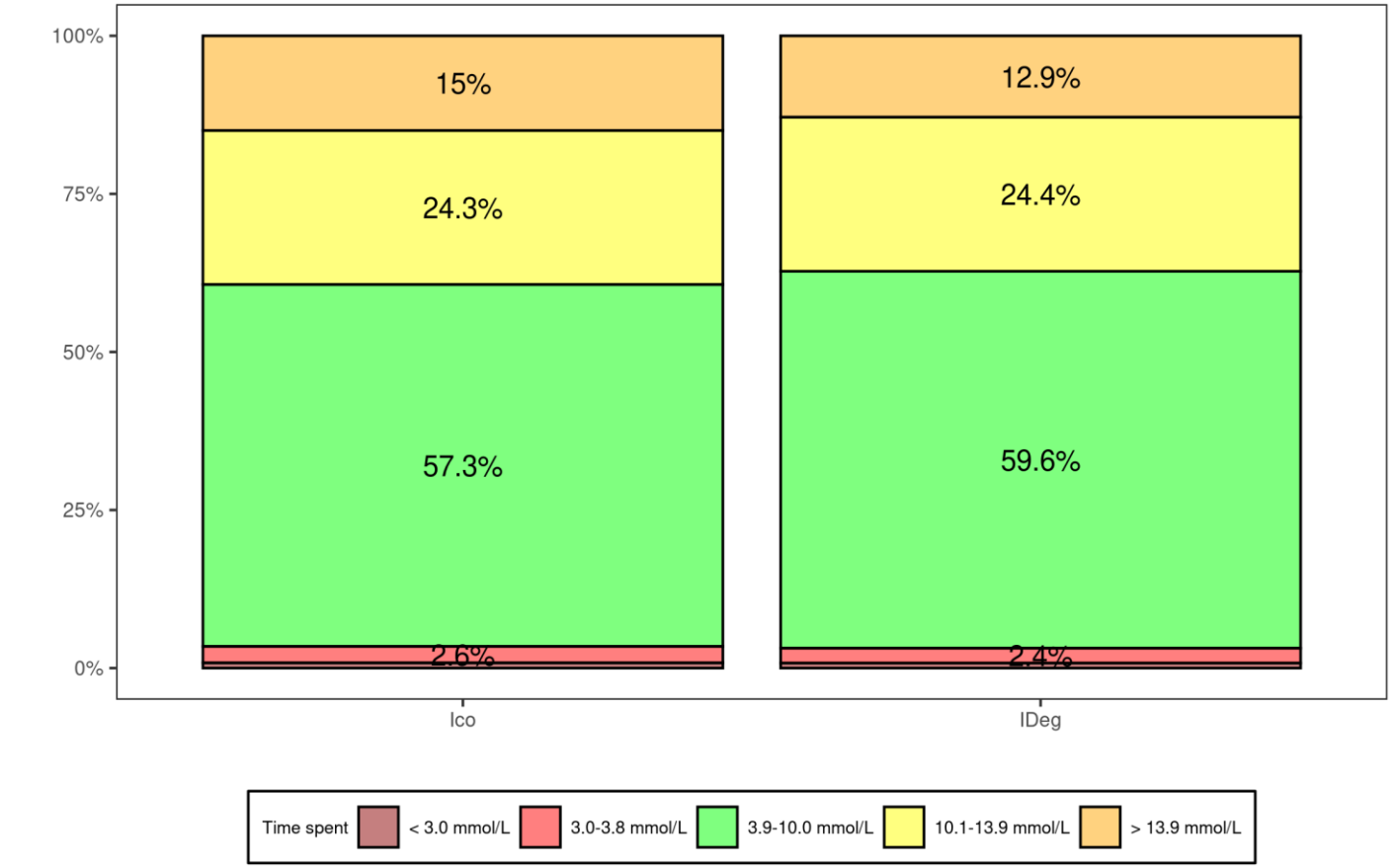
2.21 Time spent above range > 13.9 mmol/L (250 mg/dL) by treatment week - Onwards 6 - in-trial - Full analysis set

	Week	Ico				IDeg				Ico - IDeg		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]
Time spent > 13.9 mmol/L (250 mg/dL) (%)												
All subjects (total)	Week 0-4	290	284	12.22 (9.87)		292	284	10.62 (9.66)				-0.16 [-0.33; 0.00]
	Week 22-26	290	261	13.24 (11.09)		292	272	12.18 (10.54)				-0.10 [-0.26; 0.07]
	Week 48-52	290	241	14.97 (12.11)	14.84 (0.67)	292	264	12.88 (10.93)	12.64 (0.65)	2.20 [0.37; 4.03]	0.0187	-0.18 [-0.34;-0.02]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The response from week 48 to week 52 is analysed using an analysis of variance (ANOVA) model with treatment, region, HbA1c group at screening and pre trial basal insulin treatment as fixed factors. Missing values are imputed using multiple imputation based on values for subjects from the comparator group who completed randomised treatment. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:35:07 - /TAR_4625.txt

2.22 CGM ranges from week 48-52 - Onwards 6 - in-trial - Full analysis set



Observed data including data obtained after premature treatment discontinuation. Time spent is defined as 100 times the number of recorded measurements in a given range, divided by the total number of recorded measurements. Values <2% are shown on the plot but the numbers are not displayed.

nn1436/nn1436-amnog/current
23JAN2024:13:36:09 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/fcgmrangebar.R/fcgmrangesintfasow6.png

2.23 All-cause mortality - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	1 (0.3)	292	0 (0.0)	3.03 (0.12, 74.71)	3.02 (0.12, 73.84)	0.34 (-0.33, 1.02)	0.3699	
Gender									NA
Female	125	0 (0.0)	120	0 (0.0)	0.96 (0.02, 48.78)	0.96 (0.02, 48.01)	0.00 (0.00, 0.00)	NA	
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)	0.3667	
Age									NA
<65 years	267	0 (0.0)	271	0 (0.0)	1.01 (0.02, 51.34)	1.01 (0.02, 50.96)	0.00 (0.00, 0.00)	NA	
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)	0.5138	
HbA1c									NA
<=8,5%	235	1 (0.4)	242	0 (0.0)	3.10 (0.13, 76.54)	3.09 (0.13, 75.45)	0.43 (-0.41, 1.26)	0.3681	
>8,5%	55	0 (0.0)	50	0 (0.0)	0.91 (0.02, 46.71)	0.91 (0.02, 45.06)	0.00 (0.00, 0.00)	NA	
Region									NA
Europe	136	0 (0.0)	139	0 (0.0)	1.02 (0.02, 51.87)	1.02 (0.02, 51.14)	0.00 (0.00, 0.00)	NA	
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)	0.5166	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	1 (0.4)	218	0 (0.0)	2.86 (0.12, 70.49)	2.84 (0.12, 69.44)	0.43 (-0.42, 1.29)	0.5118	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:41 - /ACM_4625.txt

2.24 Adverse events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	240 (82.8)	292	236 (80.8)	1.14 (0.75, 1.74)	1.02 (0.95, 1.11)	1.94 (-4.33, 8.21)	0.5917	
Gender									0.0358
Female	125	109 (87.2)	120	93 (77.5)	1.98 (1.00, 3.89)	1.13 (1.00, 1.27)	9.70 (0.21, 19.19)	0.0638	
Male	165	131 (79.4)	172	143 (83.1)	0.78 (0.45, 1.35)	0.95 (0.86, 1.06)	-3.75 (-12.08, 4.58)	0.4040	
Age									0.6073
<65 years	267	220 (82.4)	271	217 (80.1)	1.16 (0.75, 1.80)	1.03 (0.95, 1.12)	2.32 (-4.27, 8.92)	0.5093	
>=65 years	23	20 (87.0)	21	19 (90.5)	0.70 (0.11, 4.67)	0.96 (0.78, 1.19)	-3.52 (-22.15, 15.11)	0.7673	
HbA1c									0.1960
<=8,5%	235	194 (82.6)	242	200 (82.6)	0.99 (0.62, 1.60)	1.00 (0.92, 1.08)	-0.09 (-6.90, 6.71)	1.0000	
>8,5%	55	46 (83.6)	50	36 (72.0)	1.99 (0.77, 5.11)	1.16 (0.94, 1.43)	11.64 (-4.19, 27.46)	0.1717	
Region									0.3722
Europe	136	117 (86.0)	139	112 (80.6)	1.48 (0.78, 2.82)	1.07 (0.96, 1.19)	5.45 (-3.33, 14.24)	0.2595	
North and South America	106	85 (80.2)	85	72 (84.7)	0.73 (0.34, 1.56)	0.95 (0.83, 1.08)	-4.52 (-15.29, 6.26)	0.5168	
Asia	48	38 (79.2)	68	52 (76.5)	1.17 (0.48, 2.86)	1.04 (0.85, 1.26)	2.70 (-12.59, 17.98)	0.7722	
Race									0.8706
White	230	192 (83.5)	218	179 (82.1)	1.10 (0.67, 1.80)	1.02 (0.93, 1.11)	1.37 (-5.63, 8.36)	0.7091	
Not white	60	48 (80.0)	74	57 (77.0)	1.19 (0.52, 2.74)	1.04 (0.87, 1.24)	2.97 (-10.97, 16.91)	0.6892	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:42 - /AE_4625.txt

2.25 Severe adverse events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	20 (6.9)	292	10 (3.4)	2.09 (0.96, 4.54)	2.01 (0.96, 4.23)	3.47 (-0.11, 7.06)	0.0628	
Gender									0.0930
Female	125	8 (6.4)	120	7 (5.8)	1.10 (0.39, 3.14)	1.10 (0.41, 2.93)	0.57 (-5.43, 6.57)	0.8781	
Male	165	12 (7.3)	172	3 (1.7)	4.42 (1.22, 15.95)	4.17 (1.20, 14.51)	5.53 (1.11, 9.95)	0.0141	
Age									0.2030
<65 years	267	17 (6.4)	271	10 (3.7)	1.77 (0.80, 3.95)	1.73 (0.80, 3.70)	2.68 (-1.01, 6.37)	0.1603	
>=65 years	23	3 (13.0)	21	0 (0.0)	7.34 (0.36, 151.09)	6.42 (0.35, 117.34)	13.04 (-0.72, 26.81)	0.0971	
HbA1c									0.3185
<=8,5%	235	15 (6.4)	242	6 (2.5)	2.68 (1.02, 7.04)	2.57 (1.02, 6.52)	3.90 (0.21, 7.59)	0.0391	
>8,5%	55	5 (9.1)	50	4 (8.0)	1.15 (0.29, 4.55)	1.14 (0.32, 4.00)	1.09 (-9.60, 11.78)	0.8699	
Region									0.9156
Europe	136	10 (7.4)	139	6 (4.3)	1.76 (0.62, 4.98)	1.70 (0.64, 4.56)	3.04 (-2.50, 8.57)	0.2918	
North and South America	106	8 (7.5)	85	3 (3.5)	2.23 (0.57, 8.68)	2.14 (0.59, 7.81)	4.02 (-2.36, 10.40)	0.2653	
Asia	48	2 (4.2)	68	1 (1.5)	2.91 (0.26, 33.08)	2.83 (0.26, 30.37)	2.70 (-3.64, 9.03)	0.4268	
Race									0.5933
White	230	18 (7.8)	218	8 (3.7)	2.23 (0.95, 5.24)	2.13 (0.95, 4.80)	4.16 (-0.12, 8.43)	0.0621	
Not white	60	2 (3.3)	74	2 (2.7)	1.24 (0.17, 9.08)	1.23 (0.18, 8.50)	0.63 (-5.22, 6.49)	0.9112	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:44 - /SevAE_4625.txt

2.26 Serious adverse events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	24 (8.3)	292	21 (7.2)	1.16 (0.63, 2.14)	1.15 (0.66, 2.02)	1.08 (-3.26, 5.42)	0.6814	
Gender									0.1215
Female	125	10 (8.0)	120	13 (10.8)	0.72 (0.30, 1.70)	0.74 (0.34, 1.62)	-2.83 (-10.15, 4.48)	0.5323	
Male	165	14 (8.5)	172	8 (4.7)	1.90 (0.78, 4.66)	1.82 (0.79, 4.23)	3.83 (-1.46, 9.12)	0.1600	
Age									0.3934
<65 years	267	21 (7.9)	271	20 (7.4)	1.07 (0.57, 2.03)	1.07 (0.59, 1.92)	0.49 (-4.00, 4.97)	0.8796	
>=65 years	23	3 (13.0)	21	1 (4.8)	3.00 (0.29, 31.35)	2.74 (0.31, 24.34)	8.28 (-8.22, 24.79)	0.5278	
HbA1c									0.5766
<=8,5%	235	16 (6.8)	242	16 (6.6)	1.03 (0.50, 2.11)	1.03 (0.53, 2.01)	0.20 (-4.29, 4.69)	0.9489	
>8,5%	55	8 (14.5)	50	5 (10.0)	1.53 (0.47, 5.03)	1.45 (0.51, 4.16)	4.55 (-7.94, 17.03)	0.5318	
Region									0.5970
Europe	136	16 (11.8)	139	12 (8.6)	1.41 (0.64, 3.11)	1.36 (0.67, 2.77)	3.13 (-4.02, 10.28)	0.5293	
North and South America	106	6 (5.7)	85	4 (4.7)	1.22 (0.33, 4.45)	1.20 (0.35, 4.13)	0.95 (-5.34, 7.25)	0.8038	
Asia	48	2 (4.2)	68	5 (7.4)	0.55 (0.10, 2.95)	0.57 (0.11, 2.80)	-3.19 (-11.58, 5.21)	0.5714	
Race									0.2515
White	230	22 (9.6)	218	16 (7.3)	1.34 (0.68, 2.62)	1.30 (0.70, 2.41)	2.23 (-2.92, 7.37)	0.5309	
Not white	60	2 (3.3)	74	5 (6.8)	0.48 (0.09, 2.54)	0.49 (0.10, 2.45)	-3.42 (-10.73, 3.88)	0.5161	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:44 - /SerAE_4625.txt

2.27 Adverse events leading to permanent trial product discontinuation - Onwards 6 - in- trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	2 (0.7)	292	1 (0.3)	2.02 (0.18, 22.41)	2.01 (0.18, 22.09)	0.35 (-0.82, 1.51)	0.6018	
Gender									0.4005
Female	125	1 (0.8)	120	0 (0.0)	2.90 (0.12, 71.98)	2.88 (0.12, 70.03)	0.80 (-0.76, 2.36)	0.5148	
Male	165	1 (0.6)	172	1 (0.6)	1.04 (0.06, 16.81)	1.04 (0.07, 16.53)	0.02 (-1.62, 1.67)	1.0000	
Age									0.4000
<65 years	267	1 (0.4)	271	1 (0.4)	1.02 (0.06, 16.31)	1.01 (0.06, 16.14)	0.01 (-1.02, 1.03)	1.0000	
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)	0.5138	
HbA1c									0.4066
<=8,5%	235	1 (0.4)	242	1 (0.4)	1.03 (0.06, 16.56)	1.03 (0.06, 16.37)	0.01 (-1.15, 1.17)	1.0000	
>8,5%	55	1 (1.8)	50	0 (0.0)	2.78 (0.11, 69.81)	2.73 (0.11, 65.57)	1.82 (-1.71, 5.35)	0.5150	
Region									NA
Europe	136	1 (0.7)	139	1 (0.7)	1.02 (0.06, 16.51)	1.02 (0.06, 16.18)	0.02 (-1.99, 2.02)	1.0000	
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)	0.5166	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	2 (0.9)	218	1 (0.5)	1.90 (0.17, 21.14)	1.90 (0.17, 20.76)	0.41 (-1.09, 1.91)	0.6831	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:47 - /AEdisc_4625.txt

2.28 Adverse events leading to study withdrawal - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
09MAY2024:13:26:47 - /AEwith_4625.txt

2.29 Adverse events excluding disease-associated events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	240 (82.8)	292	236 (80.8)	1.14 (0.75, 1.74)	1.02 (0.95, 1.11)	1.94 (-4.33, 8.21)	0.5917	
Gender									0.0358
Female	125	109 (87.2)	120	93 (77.5)	1.98 (1.00, 3.89)	1.13 (1.00, 1.27)	9.70 (0.21, 19.19)	0.0638	
Male	165	131 (79.4)	172	143 (83.1)	0.78 (0.45, 1.35)	0.95 (0.86, 1.06)	-3.75 (-12.08, 4.58)	0.4040	
Age									0.6073
<65 years	267	220 (82.4)	271	217 (80.1)	1.16 (0.75, 1.80)	1.03 (0.95, 1.12)	2.32 (-4.27, 8.92)	0.5093	
>=65 years	23	20 (87.0)	21	19 (90.5)	0.70 (0.11, 4.67)	0.96 (0.78, 1.19)	-3.52 (-22.15, 15.11)	0.7673	
HbA1c									0.1960
<=8,5%	235	194 (82.6)	242	200 (82.6)	0.99 (0.62, 1.60)	1.00 (0.92, 1.08)	-0.09 (-6.90, 6.71)	1.0000	
>8,5%	55	46 (83.6)	50	36 (72.0)	1.99 (0.77, 5.11)	1.16 (0.94, 1.43)	11.64 (-4.19, 27.46)	0.1717	
Region									0.3722
Europe	136	117 (86.0)	139	112 (80.6)	1.48 (0.78, 2.82)	1.07 (0.96, 1.19)	5.45 (-3.33, 14.24)	0.2595	
North and South America	106	85 (80.2)	85	72 (84.7)	0.73 (0.34, 1.56)	0.95 (0.83, 1.08)	-4.52 (-15.29, 6.26)	0.5168	
Asia	48	38 (79.2)	68	52 (76.5)	1.17 (0.48, 2.86)	1.04 (0.85, 1.26)	2.70 (-12.59, 17.98)	0.7722	
Race									0.8706
White	230	192 (83.5)	218	179 (82.1)	1.10 (0.67, 1.80)	1.02 (0.93, 1.11)	1.37 (-5.63, 8.36)	0.7091	
Not white	60	48 (80.0)	74	57 (77.0)	1.19 (0.52, 2.74)	1.04 (0.87, 1.24)	2.97 (-10.97, 16.91)	0.6892	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

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2.30 Severe adverse events excluding disease-associated events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	14 (4.8)	292	9 (3.1)	1.60 (0.68, 3.75)	1.57 (0.69, 3.56)	1.75 (-1.42, 4.91)	0.2904	
Gender									0.3752
Female	125	7 (5.6)	120	6 (5.0)	1.13 (0.37, 3.46)	1.12 (0.39, 3.24)	0.60 (-5.01, 6.21)	0.8600	
Male	165	7 (4.2)	172	3 (1.7)	2.50 (0.63, 9.82)	2.43 (0.64, 9.25)	2.50 (-1.15, 6.14)	0.2258	
Age									0.1405
<65 years	267	11 (4.1)	271	9 (3.3)	1.25 (0.51, 3.07)	1.24 (0.52, 2.95)	0.80 (-2.40, 4.00)	0.6829	
>=65 years	23	3 (13.0)	21	0 (0.0)	7.34 (0.36, 151.09)	6.42 (0.35, 117.34)	13.04 (-0.72, 26.81)	0.0971	
HbA1c									0.1831
<=8,5%	235	11 (4.7)	242	5 (2.1)	2.33 (0.80, 6.81)	2.27 (0.80, 6.42)	2.61 (-0.63, 5.86)	0.1276	
>8,5%	55	3 (5.5)	50	4 (8.0)	0.66 (0.14, 3.12)	0.68 (0.16, 2.90)	-2.55 (-12.17, 7.08)	0.6427	
Region									0.4813
Europe	136	4 (2.9)	139	5 (3.6)	0.81 (0.21, 3.09)	0.82 (0.22, 2.98)	-0.66 (-4.86, 3.54)	0.8307	
North and South America	106	8 (7.5)	85	3 (3.5)	2.23 (0.57, 8.68)	2.14 (0.59, 7.81)	4.02 (-2.36, 10.40)	0.2653	
Asia	48	2 (4.2)	68	1 (1.5)	2.91 (0.26, 33.08)	2.83 (0.26, 30.37)	2.70 (-3.64, 9.03)	0.4268	
Race									0.7962
White	230	12 (5.2)	218	7 (3.2)	1.66 (0.64, 4.30)	1.62 (0.65, 4.05)	2.01 (-1.70, 5.71)	0.3275	
Not white	60	2 (3.3)	74	2 (2.7)	1.24 (0.17, 9.08)	1.23 (0.18, 8.50)	0.63 (-5.22, 6.49)	0.9112	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

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2.31 Serious adverse events excluding disease-associated events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	17 (5.9)	292	20 (6.8)	0.85 (0.43, 1.65)	0.86 (0.46, 1.60)	-0.99 (-4.95, 2.98)	0.6814	
Gender									0.5583
Female	125	9 (7.2)	120	12 (10.0)	0.70 (0.28, 1.72)	0.72 (0.31, 1.65)	-2.80 (-9.82, 4.22)	0.5307	
Male	165	8 (4.8)	172	8 (4.7)	1.04 (0.38, 2.85)	1.04 (0.40, 2.71)	0.20 (-4.35, 4.74)	0.9870	
Age									0.2379
<65 years	267	14 (5.2)	271	19 (7.0)	0.73 (0.36, 1.50)	0.75 (0.38, 1.46)	-1.77 (-5.82, 2.28)	0.5293	
>=65 years	23	3 (13.0)	21	1 (4.8)	3.00 (0.29, 31.35)	2.74 (0.31, 24.34)	8.28 (-8.22, 24.79)	0.5278	
HbA1c									0.6029
<=8,5%	235	11 (4.7)	242	15 (6.2)	0.74 (0.33, 1.65)	0.76 (0.35, 1.61)	-1.52 (-5.58, 2.55)	0.5320	
>8,5%	55	6 (10.9)	50	5 (10.0)	1.10 (0.31, 3.86)	1.09 (0.35, 3.35)	0.91 (-10.80, 12.62)	0.9207	
Region									0.8377
Europe	136	10 (7.4)	139	11 (7.9)	0.92 (0.38, 2.25)	0.93 (0.41, 2.12)	-0.56 (-6.84, 5.71)	0.8913	
North and South America	106	5 (4.7)	85	4 (4.7)	1.00 (0.26, 3.85)	1.00 (0.28, 3.62)	0.01 (-6.03, 6.06)	1.0000	
Asia	48	2 (4.2)	68	5 (7.4)	0.55 (0.10, 2.95)	0.57 (0.11, 2.80)	-3.19 (-11.58, 5.21)	0.5714	
Race									0.4592
White	230	15 (6.5)	218	15 (6.9)	0.94 (0.45, 1.98)	0.95 (0.47, 1.89)	-0.36 (-4.99, 4.27)	0.9102	
Not white	60	2 (3.3)	74	5 (6.8)	0.48 (0.09, 2.54)	0.49 (0.10, 2.45)	-3.42 (-10.73, 3.88)	0.5161	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

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09MAY2024:13:26:50 - /SerAEexcl_4625.txt

2.32 Non-severe hypoglycaemic episodes (G-BA definition) - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	3 (1.0)	292	5 (1.7)	0.60 (0.14, 2.53)	0.60 (0.15, 2.50)	-0.68 (-2.57, 1.21)	0.5328	
Gender									0.8955
Female	125	2 (1.6)	120	3 (2.5)	0.63 (0.10, 3.86)	0.64 (0.11, 3.76)	-0.90 (-4.46, 2.66)	0.7112	
Male	165	1 (0.6)	172	2 (1.2)	0.52 (0.05, 5.77)	0.52 (0.05, 5.69)	-0.56 (-2.55, 1.44)	0.6828	
Age									NA
<65 years	267	3 (1.1)	271	5 (1.8)	0.60 (0.14, 2.56)	0.61 (0.15, 2.52)	-0.72 (-2.76, 1.32)	0.5317	
>=65 years	23	0 (0.0)	21	0 (0.0)	0.91 (0.02, 48.15)	0.92 (0.02, 44.26)	0.00 (0.00, 0.00)	NA	
HbA1c									NA
<=8,5%	235	3 (1.3)	242	5 (2.1)	0.61 (0.14, 2.59)	0.62 (0.15, 2.56)	-0.79 (-3.09, 1.51)	0.5405	
>8,5%	55	0 (0.0)	50	0 (0.0)	0.91 (0.02, 46.71)	0.91 (0.02, 45.06)	0.00 (0.00, 0.00)	NA	
Region									0.5527
Europe	136	2 (1.5)	139	2 (1.4)	1.02 (0.14, 7.36)	1.02 (0.15, 7.15)	0.03 (-2.80, 2.86)	1.0000	
North and South America	106	1 (0.9)	85	1 (1.2)	0.80 (0.05, 12.98)	0.80 (0.05, 12.63)	-0.23 (-3.17, 2.71)	0.9609	
Asia	48	0 (0.0)	68	2 (2.9)	0.27 (0.01, 5.84)	0.28 (0.01, 5.74)	-2.94 (-6.96, 1.07)	0.2826	
Race									0.2524
White	230	3 (1.3)	218	3 (1.4)	0.95 (0.19, 4.74)	0.95 (0.19, 4.65)	-0.07 (-2.20, 2.06)	0.9995	
Not white	60	0 (0.0)	74	2 (2.7)	0.24 (0.01, 5.09)	0.25 (0.01, 5.03)	-2.70 (-6.40, 0.99)	0.2275	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. Non-severe hypoglycaemic episodes are defined as being blood-glucose confirmed (< 3.0 mmol/L) with symptoms and not requiring medical assistance. Medical assistance is defined as an event either requiring administration of i.v. glucose or glucagon, is life threatening, leads to hospitalisation, calling of an emergency doctor, or is associated with the subject entering a coma or unconscious.

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09MAY2024:13:26:51 - /nonsevhypo_4625.txt

2.33 Severe hypoglycaemic episodes (G-BA definition) - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	11 (3.8)	292	6 (2.1)	1.88 (0.69, 5.15)	1.85 (0.69, 4.93)	1.74 (-1.00, 4.47)	0.2472	
Gender									0.1383
Female	125	2 (1.6)	120	3 (2.5)	0.63 (0.10, 3.86)	0.64 (0.11, 3.76)	-0.90 (-4.46, 2.66)	0.7112	
Male	165	9 (5.5)	172	3 (1.7)	3.25 (0.86, 12.22)	3.13 (0.86, 11.35)	3.71 (-0.27, 7.69)	0.0722	
Age									0.0306
<65 years	267	11 (4.1)	271	4 (1.5)	2.87 (0.90, 9.12)	2.79 (0.90, 8.66)	2.64 (-0.14, 5.43)	0.0695	
>=65 years	23	0 (0.0)	21	2 (9.5)	0.17 (0.01, 3.67)	0.18 (0.01, 3.61)	-9.52 (-22.08, 3.03)	0.1612	
HbA1c									0.1764
<=8,5%	235	8 (3.4)	242	6 (2.5)	1.39 (0.47, 4.06)	1.37 (0.48, 3.90)	0.92 (-2.11, 3.96)	0.6008	
>8,5%	55	3 (5.5)	50	0 (0.0)	6.73 (0.34, 133.66)	6.38 (0.34, 120.44)	5.45 (-0.55, 11.46)	0.1033	
Region									0.5053
Europe	136	6 (4.4)	139	3 (2.2)	2.09 (0.51, 8.54)	2.04 (0.52, 8.01)	2.25 (-1.96, 6.47)	0.3138	
North and South America	106	2 (1.9)	85	2 (2.4)	0.80 (0.11, 5.79)	0.80 (0.12, 5.57)	-0.47 (-4.60, 3.67)	0.8514	
Asia	48	3 (6.2)	68	1 (1.5)	4.47 (0.45, 44.31)	4.25 (0.46, 39.64)	4.78 (-2.64, 12.20)	0.1930	
Race									0.4741
White	230	8 (3.5)	218	5 (2.3)	1.54 (0.49, 4.77)	1.52 (0.50, 4.56)	1.18 (-1.91, 4.28)	0.5329	
Not white	60	3 (5.0)	74	1 (1.4)	3.84 (0.39, 37.92)	3.70 (0.39, 34.67)	3.65 (-2.46, 9.76)	0.2640	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. Severe hypoglycaemic episodes are defined as events requiring medical assistance. Medical assistance is defined as an event either requiring administration of i.v. glucose or glucagon, is life threatening, leads to hospitalisation, calling of an emergency doctor, or is associated with the subject entering a coma or unconscious.

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09MAY2024:13:26:53 - /sevhypo_4625.txt

2.34 Serious adverse events - hypoglycaemia - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	8 (2.8)	292	1 (0.3)	8.26 (1.03, 66.43)	8.06 (1.01, 64.00)	2.42 (0.42, 4.42)	0.0183	
Gender									0.0418
Female	125	1 (0.8)	120	1 (0.8)	0.96 (0.06, 15.52)	0.96 (0.06, 15.17)	-0.03 (-2.29, 2.22)	1.0000	
Male	165	7 (4.2)	172	0 (0.0)	16.32 (0.92, 288.16)	15.63 (0.90, 271.55)	4.24 (1.17, 7.32)	0.0066	
Age									NA
<65 years	267	8 (3.0)	271	1 (0.4)	8.34 (1.04, 67.15)	8.12 (1.02, 64.48)	2.63 (0.46, 4.80)	0.0177	
>=65 years	23	0 (0.0)	21	0 (0.0)	0.91 (0.02, 48.15)	0.92 (0.02, 44.26)	0.00 (0.00, 0.00)	NA	
HbA1c									0.5895
<=8,5%	235	6 (2.6)	242	1 (0.4)	6.31 (0.75, 52.85)	6.18 (0.75, 50.93)	2.14 (-0.03, 4.31)	0.0554	
>8,5%	55	2 (3.6)	50	0 (0.0)	4.72 (0.22, 100.72)	4.55 (0.22, 92.62)	3.64 (-1.31, 8.58)	0.2212	
Region									NA
Europe	136	6 (4.4)	139	1 (0.7)	6.37 (0.76, 53.62)	6.13 (0.75, 50.27)	3.69 (-0.03, 7.42)	0.0550	
North and South America	106	2 (1.9)	85	0 (0.0)	4.09 (0.19, 86.36)	4.02 (0.20, 82.60)	1.89 (-0.70, 4.48)	0.2291	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	8 (3.5)	218	1 (0.5)	7.82 (0.97, 63.05)	7.58 (0.96, 60.13)	3.02 (0.49, 5.55)	0.0237	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

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2.35 Serious adverse events associated with hypoglycaemia (selected preferred terms) - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	9 (3.1)	292	3 (1.0)	3.09 (0.83, 11.51)	3.02 (0.83, 11.05)	2.08 (-0.23, 4.38)	0.0791	
Gender									0.0440
Female	125	1 (0.8)	120	2 (1.7)	0.48 (0.04, 5.32)	0.48 (0.04, 5.22)	-0.87 (-3.64, 1.91)	0.5996	
Male	165	8 (4.8)	172	1 (0.6)	8.71 (1.08, 70.45)	8.34 (1.05, 65.95)	4.27 (0.80, 7.74)	0.0162	
Age									0.0572
<65 years	267	9 (3.4)	271	2 (0.7)	4.69 (1.00, 21.92)	4.57 (1.00, 20.94)	2.63 (0.24, 5.03)	0.0319	
>=65 years	23	0 (0.0)	21	1 (4.8)	0.29 (0.01, 7.54)	0.31 (0.01, 7.12)	-4.76 (-13.87, 4.35)	0.3549	
HbA1c									0.3949
<=8,5%	235	7 (3.0)	242	3 (1.2)	2.45 (0.62, 9.57)	2.40 (0.63, 9.18)	1.74 (-0.84, 4.32)	0.2261	
>8,5%	55	2 (3.6)	50	0 (0.0)	4.72 (0.22, 100.72)	4.55 (0.22, 92.62)	3.64 (-1.31, 8.58)	0.2212	
Region									0.6895
Europe	136	6 (4.4)	139	2 (1.4)	3.16 (0.63, 15.95)	3.07 (0.63, 14.93)	2.97 (-1.01, 6.95)	0.1492	
North and South America	106	2 (1.9)	85	1 (1.2)	1.62 (0.14, 18.12)	1.60 (0.15, 17.39)	0.71 (-2.75, 4.17)	0.7207	
Asia	48	1 (2.1)	68	0 (0.0)	4.33 (0.17, 108.49)	4.22 (0.18, 101.54)	2.08 (-1.96, 6.12)	0.3406	
Race									0.4966
White	230	8 (3.5)	218	3 (1.4)	2.58 (0.68, 9.86)	2.53 (0.68, 9.40)	2.10 (-0.73, 4.93)	0.1567	
Not white	60	1 (1.7)	74	0 (0.0)	3.76 (0.15, 93.89)	3.69 (0.15, 88.94)	1.67 (-1.57, 4.91)	0.3541	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. The selected preferred terms are: Glycopenia, Hypoglycaemia, Hypoglycaemia unawareness, Hypoglycaemic coma, Hypoglycaemic encephalopathy, Hypoglycaemic seizure, Hypoglycaemic unconsciousness, Neuroglycopenia, Postprandial hypoglycaemia, Shock hypoglycaemic.

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09MAY2024:13:26:45 - /SerAEasc_4625.txt

2.36 Any clinically significant hypoglycaemic episodes - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	263 (90.7)	292	250 (85.6)	1.64 (0.98, 2.73)	1.06 (1.00, 1.12)	5.07 (-0.16, 10.31)	0.0722	
Gender									0.2190
Female	125	118 (94.4)	120	104 (86.7)	2.59 (1.03, 6.55)	1.09 (1.00, 1.18)	7.73 (0.44, 15.03)	0.0482	
Male	165	145 (87.9)	172	146 (84.9)	1.29 (0.69, 2.42)	1.04 (0.95, 1.13)	3.00 (-4.32, 10.31)	0.4331	
Age									0.4122
<65 years	267	242 (90.6)	271	234 (86.3)	1.53 (0.89, 2.62)	1.05 (0.99, 1.12)	4.29 (-1.09, 9.67)	0.1378	
>=65 years	23	21 (91.3)	21	16 (76.2)	3.28 (0.56, 19.15)	1.20 (0.91, 1.57)	15.11 (-6.44, 36.66)	0.2178	
HbA1c									0.5831
<=8,5%	235	211 (89.8)	242	206 (85.1)	1.54 (0.89, 2.67)	1.05 (0.99, 1.13)	4.66 (-1.26, 10.59)	0.1311	
>8,5%	55	52 (94.5)	50	44 (88.0)	2.36 (0.56, 10.00)	1.07 (0.95, 1.21)	6.55 (-4.28, 17.37)	0.2538	
Region									0.0460
Europe	136	122 (89.7)	139	117 (84.2)	1.64 (0.80, 3.35)	1.07 (0.97, 1.17)	5.53 (-2.40, 13.46)	0.2115	
North and South America	106	95 (89.6)	85	79 (92.9)	0.66 (0.23, 1.85)	0.96 (0.88, 1.05)	-3.32 (-11.28, 4.64)	0.5168	
Asia	48	46 (95.8)	68	54 (79.4)	5.96 (1.29, 27.62)	1.21 (1.05, 1.38)	16.42 (5.27, 27.57)	0.0116	
Race									0.0179
White	230	206 (89.6)	218	193 (88.5)	1.11 (0.61, 2.01)	1.01 (0.95, 1.08)	1.03 (-4.75, 6.82)	0.7635	
Not white	60	57 (95.0)	74	57 (77.0)	5.67 (1.57, 20.40)	1.23 (1.08, 1.41)	17.97 (6.92, 29.03)	0.0037	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. Clinically significant hypoglycaemia: Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter.

nn1436/nn1436-amnog/current
09MAY2024:13:26:50 - /anycshypo_4625.txt

2.37 EAC evaluated cardiovascular events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	3 (1.0)	292	3 (1.0)	1.01 (0.20, 5.03)	1.01 (0.20, 4.95)	0.01 (-1.63, 1.65)	1.0000	
Gender									0.3834
Female	125	1 (0.8)	120	2 (1.7)	0.48 (0.04, 5.32)	0.48 (0.04, 5.22)	-0.87 (-3.64, 1.91)	0.5996	
Male	165	2 (1.2)	172	1 (0.6)	2.10 (0.19, 23.36)	2.08 (0.19, 22.77)	0.63 (-1.39, 2.65)	0.6002	
Age									0.2896
<65 years	267	2 (0.7)	271	3 (1.1)	0.67 (0.11, 4.07)	0.68 (0.11, 4.02)	-0.36 (-1.98, 1.26)	0.7532	
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)	0.5138	
HbA1c									0.9421
<=8,5%	235	2 (0.9)	242	2 (0.8)	1.03 (0.14, 7.37)	1.03 (0.15, 7.25)	0.02 (-1.61, 1.66)	1.0000	
>8,5%	55	1 (1.8)	50	1 (2.0)	0.91 (0.06, 14.90)	0.91 (0.06, 14.15)	-0.18 (-5.43, 5.06)	0.9994	
Region									NA
Europe	136	2 (1.5)	139	2 (1.4)	1.02 (0.14, 7.36)	1.02 (0.15, 7.15)	0.03 (-2.80, 2.86)	1.0000	
North and South America	106	1 (0.9)	85	1 (1.2)	0.80 (0.05, 12.98)	0.80 (0.05, 12.63)	-0.23 (-3.17, 2.71)	0.9609	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	3 (1.3)	218	3 (1.4)	0.95 (0.19, 4.74)	0.95 (0.19, 4.65)	-0.07 (-2.20, 2.06)	0.9995	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:54 - /allEAC_4625.txt

2.38 EAC evaluated cardiovascular events - Acute coronary syndrome - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	1 (0.3)	292	2 (0.7)	0.50 (0.05, 5.56)	0.50 (0.05, 5.52)	-0.34 (-1.50, 0.82)
Gender							
Female	125	0 (0.0)	120	2 (1.7)	0.19 (0.01, 3.97)	0.19 (0.01, 3.96)	-1.67 (-3.96, 0.62)
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)
Age							
<65 years	267	0 (0.0)	271	2 (0.7)	0.20 (0.01, 4.22)	0.20 (0.01, 4.21)	-0.74 (-1.76, 0.28)
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)
HbA1c							
<=8,5%	235	1 (0.4)	242	1 (0.4)	1.03 (0.06, 16.56)	1.03 (0.06, 16.37)	0.01 (-1.15, 1.17)
>8,5%	55	0 (0.0)	50	1 (2.0)	0.30 (0.01, 7.47)	0.30 (0.01, 7.29)	-2.00 (-5.88, 1.88)
Region							
Europe	136	0 (0.0)	139	2 (1.4)	0.20 (0.01, 4.24)	0.20 (0.01, 4.22)	-1.44 (-3.42, 0.54)
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	1 (0.4)	218	2 (0.9)	0.47 (0.04, 5.24)	0.47 (0.04, 5.19)	-0.48 (-2.01, 1.04)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:55 - /allEACacs_4625.txt

2.39 EAC evaluated cardiovascular events - Cerebrovascular event - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	2 (0.7)	292	1 (0.3)	2.02 (0.18, 22.41)	2.01 (0.18, 22.09)	0.35 (-0.82, 1.51)
Gender							
Female	125	1 (0.8)	120	0 (0.0)	2.90 (0.12, 71.98)	2.88 (0.12, 70.03)	0.80 (-0.76, 2.36)
Male	165	1 (0.6)	172	1 (0.6)	1.04 (0.06, 16.81)	1.04 (0.07, 16.53)	0.02 (-1.62, 1.67)
Age							
<65 years	267	2 (0.7)	271	1 (0.4)	2.04 (0.18, 22.61)	2.03 (0.19, 22.25)	0.38 (-0.88, 1.64)
>=65 years	23	0 (0.0)	21	0 (0.0)	0.91 (0.02, 48.15)	0.92 (0.02, 44.26)	0.00 (0.00, 0.00)
HbA1c							
<=8,5%	235	1 (0.4)	242	1 (0.4)	1.03 (0.06, 16.56)	1.03 (0.06, 16.37)	0.01 (-1.15, 1.17)
>8,5%	55	1 (1.8)	50	0 (0.0)	2.78 (0.11, 69.81)	2.73 (0.11, 65.57)	1.82 (-1.71, 5.35)
Region							
Europe	136	2 (1.5)	139	0 (0.0)	5.19 (0.25, 109.02)	5.11 (0.25, 105.46)	1.47 (-0.55, 3.49)
North and South America	106	0 (0.0)	85	1 (1.2)	0.26 (0.01, 6.58)	0.27 (0.01, 6.49)	-1.18 (-3.47, 1.12)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	2 (0.9)	218	1 (0.5)	1.90 (0.17, 21.14)	1.90 (0.17, 20.76)	0.41 (-1.09, 1.91)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:56 - /allEACce_4625.txt

2.40 EAC evaluated cardiovascular events - Heart failure - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	1 (0.3)	292	0 (0.0)	3.03 (0.12, 74.71)	3.02 (0.12, 73.84)	0.34 (-0.33, 1.02)
Gender							
Female	125	0 (0.0)	120	0 (0.0)	0.96 (0.02, 48.78)	0.96 (0.02, 48.01)	0.00 (0.00, 0.00)
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)
Age							
<65 years	267	0 (0.0)	271	0 (0.0)	1.01 (0.02, 51.34)	1.01 (0.02, 50.96)	0.00 (0.00, 0.00)
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)
HbA1c							
<=8,5%	235	1 (0.4)	242	0 (0.0)	3.10 (0.13, 76.54)	3.09 (0.13, 75.45)	0.43 (-0.41, 1.26)
>8,5%	55	0 (0.0)	50	0 (0.0)	0.91 (0.02, 46.71)	0.91 (0.02, 45.06)	0.00 (0.00, 0.00)
Region							
Europe	136	0 (0.0)	139	0 (0.0)	1.02 (0.02, 51.87)	1.02 (0.02, 51.14)	0.00 (0.00, 0.00)
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	1 (0.4)	218	0 (0.0)	2.86 (0.12, 70.49)	2.84 (0.12, 69.44)	0.43 (-0.42, 1.29)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:57 - /allEAChf_4625.txt

2.41 EAC evaluated cardiovascular events - Death - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
09MAY2024:13:26:57 - /allEACd_4625.txt

2.42 Severe EAC evaluated cardiovascular events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	2 (0.7)	292	1 (0.3)	2.02 (0.18, 22.41)	2.01 (0.18, 22.09)	0.35 (-0.82, 1.51)	0.6018	
Gender									0.3714
Female	125	1 (0.8)	120	1 (0.8)	0.96 (0.06, 15.52)	0.96 (0.06, 15.17)	-0.03 (-2.29, 2.22)	1.0000	
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)	0.3667	
Age									0.4000
<65 years	267	1 (0.4)	271	1 (0.4)	1.02 (0.06, 16.31)	1.01 (0.06, 16.14)	0.01 (-1.02, 1.03)	1.0000	
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)	0.5138	
HbA1c									0.3644
<=8,5%	235	1 (0.4)	242	0 (0.0)	3.10 (0.13, 76.54)	3.09 (0.13, 75.45)	0.43 (-0.41, 1.26)	0.3681	
>8,5%	55	1 (1.8)	50	1 (2.0)	0.91 (0.06, 14.90)	0.91 (0.06, 14.15)	-0.18 (-5.43, 5.06)	0.9994	
Region									NA
Europe	136	1 (0.7)	139	1 (0.7)	1.02 (0.06, 16.51)	1.02 (0.06, 16.18)	0.02 (-1.99, 2.02)	1.0000	
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)	0.5166	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	2 (0.9)	218	1 (0.5)	1.90 (0.17, 21.14)	1.90 (0.17, 20.76)	0.41 (-1.09, 1.91)	0.6831	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:58 - /SevEAC_4625.txt

2.43 Severe EAC evaluated cardiovascular events - Acute coronary syndrome - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	1 (0.3)	292	1 (0.3)	1.01 (0.06, 16.18)	1.01 (0.06, 16.02)	0.00 (-0.95, 0.95)
Gender							
Female	125	0 (0.0)	120	1 (0.8)	0.32 (0.01, 7.87)	0.32 (0.01, 7.78)	-0.83 (-2.46, 0.79)
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)
Age							
<65 years	267	0 (0.0)	271	1 (0.4)	0.34 (0.01, 8.31)	0.34 (0.01, 8.27)	-0.37 (-1.09, 0.35)
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)
HbA1c							
<=8,5%	235	1 (0.4)	242	0 (0.0)	3.10 (0.13, 76.54)	3.09 (0.13, 75.45)	0.43 (-0.41, 1.26)
>8,5%	55	0 (0.0)	50	1 (2.0)	0.30 (0.01, 7.47)	0.30 (0.01, 7.29)	-2.00 (-5.88, 1.88)
Region							
Europe	136	0 (0.0)	139	1 (0.7)	0.34 (0.01, 8.38)	0.34 (0.01, 8.29)	-0.72 (-2.12, 0.69)
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	1 (0.4)	218	1 (0.5)	0.95 (0.06, 15.24)	0.95 (0.06, 15.06)	-0.02 (-1.26, 1.21)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:26:59 - /SevEACacs_4625.txt

2.44 Severe EAC evaluated cardiovascular events - Cerebrovascular event - Onwards 6 - in- trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	1 (0.3)	292	0 (0.0)	3.03 (0.12, 74.71)	3.02 (0.12, 73.84)	0.34 (-0.33, 1.02)
Gender							
Female	125	1 (0.8)	120	0 (0.0)	2.90 (0.12, 71.98)	2.88 (0.12, 70.03)	0.80 (-0.76, 2.36)
Male	165	0 (0.0)	172	0 (0.0)	1.04 (0.02, 52.83)	1.04 (0.02, 52.22)	0.00 (0.00, 0.00)
Age							
<65 years	267	1 (0.4)	271	0 (0.0)	3.06 (0.12, 75.36)	3.04 (0.12, 74.41)	0.37 (-0.36, 1.11)
>=65 years	23	0 (0.0)	21	0 (0.0)	0.91 (0.02, 48.15)	0.92 (0.02, 44.26)	0.00 (0.00, 0.00)
HbA1c							
<=8,5%	235	0 (0.0)	242	0 (0.0)	1.03 (0.02, 52.11)	1.03 (0.02, 51.68)	0.00 (0.00, 0.00)
>8,5%	55	1 (1.8)	50	0 (0.0)	2.78 (0.11, 69.81)	2.73 (0.11, 65.57)	1.82 (-1.71, 5.35)
Region							
Europe	136	1 (0.7)	139	0 (0.0)	3.09 (0.12, 76.48)	3.07 (0.13, 74.60)	0.74 (-0.70, 2.17)
North and South America	106	0 (0.0)	85	0 (0.0)	0.80 (0.02, 40.88)	0.80 (0.02, 40.09)	0.00 (0.00, 0.00)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	1 (0.4)	218	0 (0.0)	2.86 (0.12, 70.49)	2.84 (0.12, 69.44)	0.43 (-0.42, 1.29)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:00 - /SevEACce_4625.txt

2.45 Severe EAC evaluated cardiovascular events - Heart failure - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	1 (0.3)	292	0 (0.0)	3.03 (0.12, 74.71)	3.02 (0.12, 73.84)	0.34 (-0.33, 1.02)
Gender							
Female	125	0 (0.0)	120	0 (0.0)	0.96 (0.02, 48.78)	0.96 (0.02, 48.01)	0.00 (0.00, 0.00)
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)
Age							
<65 years	267	0 (0.0)	271	0 (0.0)	1.01 (0.02, 51.34)	1.01 (0.02, 50.96)	0.00 (0.00, 0.00)
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)
HbA1c							
<=8,5%	235	1 (0.4)	242	0 (0.0)	3.10 (0.13, 76.54)	3.09 (0.13, 75.45)	0.43 (-0.41, 1.26)
>8,5%	55	0 (0.0)	50	0 (0.0)	0.91 (0.02, 46.71)	0.91 (0.02, 45.06)	0.00 (0.00, 0.00)
Region							
Europe	136	0 (0.0)	139	0 (0.0)	1.02 (0.02, 51.87)	1.02 (0.02, 51.14)	0.00 (0.00, 0.00)
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	1 (0.4)	218	0 (0.0)	2.86 (0.12, 70.49)	2.84 (0.12, 69.44)	0.43 (-0.42, 1.29)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:00 - /SevEAChf_4625.txt

2.46 Severe EAC evaluated cardiovascular events - Death - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
09MAY2024:13:27:01 - /SevEACd_4625.txt

2.47 Serious EAC evaluated cardiovascular events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	2 (0.7)	292	3 (1.0)	0.67 (0.11, 4.03)	0.67 (0.11, 3.99)	-0.34 (-1.84, 1.16)	0.7521	
Gender									0.6740
Female	125	1 (0.8)	120	2 (1.7)	0.48 (0.04, 5.32)	0.48 (0.04, 5.22)	-0.87 (-3.64, 1.91)	0.5996	
Male	165	1 (0.6)	172	1 (0.6)	1.04 (0.06, 16.81)	1.04 (0.07, 16.53)	0.02 (-1.62, 1.67)	1.0000	
Age									0.1851
<65 years	267	1 (0.4)	271	3 (1.1)	0.34 (0.03, 3.25)	0.34 (0.04, 3.23)	-0.73 (-2.18, 0.71)	0.5293	
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)	0.5138	
HbA1c									0.7610
<=8,5%	235	1 (0.4)	242	2 (0.8)	0.51 (0.05, 5.69)	0.51 (0.05, 5.64)	-0.40 (-1.81, 1.01)	0.6819	
>8,5%	55	1 (1.8)	50	1 (2.0)	0.91 (0.06, 14.90)	0.91 (0.06, 14.15)	-0.18 (-5.43, 5.06)	0.9994	
Region									NA
Europe	136	1 (0.7)	139	2 (1.4)	0.51 (0.05, 5.66)	0.51 (0.05, 5.57)	-0.70 (-3.15, 1.74)	0.6823	
North and South America	106	1 (0.9)	85	1 (1.2)	0.80 (0.05, 12.98)	0.80 (0.05, 12.63)	-0.23 (-3.17, 2.71)	0.9609	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	2 (0.9)	218	3 (1.4)	0.63 (0.10, 3.80)	0.63 (0.11, 3.75)	-0.51 (-2.46, 1.45)	0.7116	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:05 - /SerEAC_4625.txt

2.48 Serious EAC evaluated cardiovascular events - Acute coronary syndrome - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	1 (0.3)	292	2 (0.7)	0.50 (0.05, 5.56)	0.50 (0.05, 5.52)	-0.34 (-1.50, 0.82)
Gender							
Female	125	0 (0.0)	120	2 (1.7)	0.19 (0.01, 3.97)	0.19 (0.01, 3.96)	-1.67 (-3.96, 0.62)
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)
Age							
<65 years	267	0 (0.0)	271	2 (0.7)	0.20 (0.01, 4.22)	0.20 (0.01, 4.21)	-0.74 (-1.76, 0.28)
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)
HbA1c							
<=8,5%	235	1 (0.4)	242	1 (0.4)	1.03 (0.06, 16.56)	1.03 (0.06, 16.37)	0.01 (-1.15, 1.17)
>8,5%	55	0 (0.0)	50	1 (2.0)	0.30 (0.01, 7.47)	0.30 (0.01, 7.29)	-2.00 (-5.88, 1.88)
Region							
Europe	136	0 (0.0)	139	2 (1.4)	0.20 (0.01, 4.24)	0.20 (0.01, 4.22)	-1.44 (-3.42, 0.54)
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	1 (0.4)	218	2 (0.9)	0.47 (0.04, 5.24)	0.47 (0.04, 5.19)	-0.48 (-2.01, 1.04)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:06 - /SerEACacs_4625.txt

2.49 Serious EAC evaluated cardiovascular events - Cerebrovascular event - Onwards 6 - in- trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	1 (0.3)	292	1 (0.3)	1.01 (0.06, 16.18)	1.01 (0.06, 16.02)	0.00 (-0.95, 0.95)
Gender							
Female	125	1 (0.8)	120	0 (0.0)	2.90 (0.12, 71.98)	2.88 (0.12, 70.03)	0.80 (-0.76, 2.36)
Male	165	0 (0.0)	172	1 (0.6)	0.35 (0.01, 8.54)	0.35 (0.01, 8.47)	-0.58 (-1.72, 0.55)
Age							
<65 years	267	1 (0.4)	271	1 (0.4)	1.02 (0.06, 16.31)	1.01 (0.06, 16.14)	0.01 (-1.02, 1.03)
>=65 years	23	0 (0.0)	21	0 (0.0)	0.91 (0.02, 48.15)	0.92 (0.02, 44.26)	0.00 (0.00, 0.00)
HbA1c							
<=8,5%	235	0 (0.0)	242	1 (0.4)	0.34 (0.01, 8.43)	0.34 (0.01, 8.38)	-0.41 (-1.22, 0.40)
>8,5%	55	1 (1.8)	50	0 (0.0)	2.78 (0.11, 69.81)	2.73 (0.11, 65.57)	1.82 (-1.71, 5.35)
Region							
Europe	136	1 (0.7)	139	0 (0.0)	3.09 (0.12, 76.48)	3.07 (0.13, 74.60)	0.74 (-0.70, 2.17)
North and South America	106	0 (0.0)	85	1 (1.2)	0.26 (0.01, 6.58)	0.27 (0.01, 6.49)	-1.18 (-3.47, 1.12)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	1 (0.4)	218	1 (0.5)	0.95 (0.06, 15.24)	0.95 (0.06, 15.06)	-0.02 (-1.26, 1.21)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:07 - /SerEACce_4625.txt

2.50 Serious EAC evaluated cardiovascular events - Heart failure - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg		
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)
All subjects (total)	290	1 (0.3)	292	0 (0.0)	3.03 (0.12, 74.71)	3.02 (0.12, 73.84)	0.34 (-0.33, 1.02)
Gender							
Female	125	0 (0.0)	120	0 (0.0)	0.96 (0.02, 48.78)	0.96 (0.02, 48.01)	0.00 (0.00, 0.00)
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)
Age							
<65 years	267	0 (0.0)	271	0 (0.0)	1.01 (0.02, 51.34)	1.01 (0.02, 50.96)	0.00 (0.00, 0.00)
>=65 years	23	1 (4.3)	21	0 (0.0)	2.87 (0.11, 74.28)	2.75 (0.12, 64.04)	4.35 (-3.99, 12.68)
HbA1c							
<=8,5%	235	1 (0.4)	242	0 (0.0)	3.10 (0.13, 76.54)	3.09 (0.13, 75.45)	0.43 (-0.41, 1.26)
>8,5%	55	0 (0.0)	50	0 (0.0)	0.91 (0.02, 46.71)	0.91 (0.02, 45.06)	0.00 (0.00, 0.00)
Region							
Europe	136	0 (0.0)	139	0 (0.0)	1.02 (0.02, 51.87)	1.02 (0.02, 51.14)	0.00 (0.00, 0.00)
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)
Race							
White	230	1 (0.4)	218	0 (0.0)	2.86 (0.12, 70.49)	2.84 (0.12, 69.44)	0.43 (-0.42, 1.29)
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval, EAC: Event adjudication committee. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:07 - /SerEAChf_4625.txt

2.51 Serious EAC evaluated cardiovascular events - Death - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
09MAY2024:13:27:08 - /SerEACd_4625.txt

2.52 Hypersensitivity adverse events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	36 (12.4)	292	42 (14.4)	0.84 (0.52, 1.36)	0.86 (0.57, 1.31)	-1.97 (-7.50, 3.56)	0.5328	
Gender									0.1636
Female	125	17 (13.6)	120	25 (20.8)	0.60 (0.30, 1.17)	0.65 (0.37, 1.15)	-7.23 (-16.66, 2.20)	0.1371	
Male	165	19 (11.5)	172	17 (9.9)	1.19 (0.59, 2.37)	1.17 (0.63, 2.16)	1.63 (-4.97, 8.24)	0.7112	
Age									0.2246
<65 years	267	34 (12.7)	271	37 (13.7)	0.92 (0.56, 1.52)	0.93 (0.60, 1.44)	-0.92 (-6.64, 4.80)	0.8079	
>=65 years	23	2 (8.7)	21	5 (23.8)	0.30 (0.05, 1.78)	0.37 (0.08, 1.69)	-15.11 (-36.66, 6.44)	0.2178	
HbA1c									0.9257
<=8,5%	235	31 (13.2)	242	37 (15.3)	0.84 (0.50, 1.41)	0.86 (0.55, 1.34)	-2.10 (-8.37, 4.17)	0.5405	
>8,5%	55	5 (9.1)	50	5 (10.0)	0.90 (0.24, 3.31)	0.91 (0.28, 2.96)	-0.91 (-12.17, 10.35)	0.8974	
Region									0.4285
Europe	136	15 (11.0)	139	12 (8.6)	1.31 (0.59, 2.92)	1.28 (0.62, 2.63)	2.40 (-4.64, 9.43)	0.5382	
North and South America	106	12 (11.3)	85	11 (12.9)	0.86 (0.36, 2.06)	0.87 (0.41, 1.88)	-1.62 (-10.96, 7.72)	0.7540	
Asia	48	9 (18.8)	68	19 (27.9)	0.60 (0.24, 1.46)	0.67 (0.33, 1.35)	-9.19 (-24.54, 6.16)	0.3406	
Race									0.3756
White	230	25 (10.9)	218	23 (10.6)	1.03 (0.57, 1.88)	1.03 (0.60, 1.76)	0.32 (-5.41, 6.05)	0.9479	
Not white	60	11 (18.3)	74	19 (25.7)	0.65 (0.28, 1.50)	0.71 (0.37, 1.38)	-7.34 (-21.30, 6.62)	0.3599	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:09 - /allCQ01_4625.txt

2.53 Severe hypersensitivity adverse events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	3 (1.0)	292	1 (0.3)	3.04 (0.31, 29.41)	3.02 (0.32, 28.87)	0.69 (-0.65, 2.04)	0.3299	
Gender									0.4910
Female	125	2 (1.6)	120	1 (0.8)	1.93 (0.17, 21.62)	1.92 (0.18, 20.90)	0.77 (-1.97, 3.50)	0.6826	
Male	165	1 (0.6)	172	0 (0.0)	3.15 (0.13, 77.78)	3.13 (0.13, 76.21)	0.61 (-0.58, 1.79)	0.3667	
Age									NA
<65 years	267	3 (1.1)	271	1 (0.4)	3.07 (0.32, 29.68)	3.04 (0.32, 29.09)	0.75 (-0.70, 2.21)	0.3293	
>=65 years	23	0 (0.0)	21	0 (0.0)	0.91 (0.02, 48.15)	0.92 (0.02, 44.26)	0.00 (0.00, 0.00)	NA	
HbA1c									0.2290
<=8,5%	235	2 (0.9)	242	0 (0.0)	5.19 (0.25, 108.74)	5.15 (0.25, 106.67)	0.85 (-0.32, 2.03)	0.1594	
>8,5%	55	1 (1.8)	50	1 (2.0)	0.91 (0.06, 14.90)	0.91 (0.06, 14.15)	-0.18 (-5.43, 5.06)	0.9994	
Region									NA
Europe	136	1 (0.7)	139	1 (0.7)	1.02 (0.06, 16.51)	1.02 (0.06, 16.18)	0.02 (-1.99, 2.02)	1.0000	
North and South America	106	2 (1.9)	85	0 (0.0)	4.09 (0.19, 86.36)	4.02 (0.20, 82.60)	1.89 (-0.70, 4.48)	0.2291	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	3 (1.3)	218	1 (0.5)	2.87 (0.30, 27.78)	2.84 (0.30, 27.13)	0.85 (-0.87, 2.56)	0.5292	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:10 - /SevCQ01_4625.txt

2.54 Serious hypersensitivity adverse events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	0 (0.0)	292	1 (0.3)	0.33 (0.01, 8.24)	0.34 (0.01, 8.20)	-0.34 (-1.01, 0.33)	0.5125	
Gender									NA
Female	125	0 (0.0)	120	1 (0.8)	0.32 (0.01, 7.87)	0.32 (0.01, 7.78)	-0.83 (-2.46, 0.79)	0.3663	
Male	165	0 (0.0)	172	0 (0.0)	1.04 (0.02, 52.83)	1.04 (0.02, 52.22)	0.00 (0.00, 0.00)	NA	
Age									NA
<65 years	267	0 (0.0)	271	1 (0.4)	0.34 (0.01, 8.31)	0.34 (0.01, 8.27)	-0.37 (-1.09, 0.35)	0.5150	
>=65 years	23	0 (0.0)	21	0 (0.0)	0.91 (0.02, 48.15)	0.92 (0.02, 44.26)	0.00 (0.00, 0.00)	NA	
HbA1c									NA
<=8,5%	235	0 (0.0)	242	0 (0.0)	1.03 (0.02, 52.11)	1.03 (0.02, 51.68)	0.00 (0.00, 0.00)	NA	
>8,5%	55	0 (0.0)	50	1 (2.0)	0.30 (0.01, 7.47)	0.30 (0.01, 7.29)	-2.00 (-5.88, 1.88)	0.3589	
Region									NA
Europe	136	0 (0.0)	139	1 (0.7)	0.34 (0.01, 8.38)	0.34 (0.01, 8.29)	-0.72 (-2.12, 0.69)	0.5142	
North and South America	106	0 (0.0)	85	0 (0.0)	0.80 (0.02, 40.88)	0.80 (0.02, 40.09)	0.00 (0.00, 0.00)	NA	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	0 (0.0)	218	1 (0.5)	0.31 (0.01, 7.76)	0.32 (0.01, 7.72)	-0.46 (-1.36, 0.44)	0.3655	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:11 - /SerCQ01_4625.txt

2.55 Injection site reactions adverse events - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	290	1 (0.3)	292	2 (0.7)	0.50 (0.05, 5.56)	0.50 (0.05, 5.52)	-0.34 (-1.50, 0.82)	0.6814	
Gender									0.4008
Female	125	1 (0.8)	120	1 (0.8)	0.96 (0.06, 15.52)	0.96 (0.06, 15.17)	-0.03 (-2.29, 2.22)	1.0000	
Male	165	0 (0.0)	172	1 (0.6)	0.35 (0.01, 8.54)	0.35 (0.01, 8.47)	-0.58 (-1.72, 0.55)	0.5134	
Age									NA
<65 years	267	1 (0.4)	271	2 (0.7)	0.51 (0.05, 5.61)	0.51 (0.05, 5.56)	-0.36 (-1.62, 0.89)	0.6829	
>=65 years	23	0 (0.0)	21	0 (0.0)	0.91 (0.02, 48.15)	0.92 (0.02, 44.26)	0.00 (0.00, 0.00)	NA	
HbA1c									0.3621
<=8,5%	235	1 (0.4)	242	1 (0.4)	1.03 (0.06, 16.56)	1.03 (0.06, 16.37)	0.01 (-1.15, 1.17)	1.0000	
>8,5%	55	0 (0.0)	50	1 (2.0)	0.30 (0.01, 7.47)	0.30 (0.01, 7.29)	-2.00 (-5.88, 1.88)	0.3589	
Region									NA
Europe	136	0 (0.0)	139	2 (1.4)	0.20 (0.01, 4.24)	0.20 (0.01, 4.22)	-1.44 (-3.42, 0.54)	0.2113	
North and South America	106	1 (0.9)	85	0 (0.0)	2.43 (0.10, 60.44)	2.41 (0.10, 58.45)	0.94 (-0.90, 2.78)	0.5166	
Asia	48	0 (0.0)	68	0 (0.0)	1.41 (0.03, 72.42)	1.41 (0.03, 69.76)	0.00 (0.00, 0.00)	NA	
Race									NA
White	230	1 (0.4)	218	2 (0.9)	0.47 (0.04, 5.24)	0.47 (0.04, 5.19)	-0.48 (-2.01, 1.04)	0.5999	
Not white	60	0 (0.0)	74	0 (0.0)	1.23 (0.02, 62.97)	1.23 (0.02, 61.07)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
09MAY2024:13:27:12 - /allCQ02_4625.txt

2.56 Severe injection site reactions adverse events - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
09MAY2024:13:27:13 - /SevCQ02_4625.txt

2.57 Serious injection site reactions adverse events - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:26 - /SAEbyPT_4625.txt

2.58 Adverse events by preferred term - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
COVID-19									
All subjects (total)	290	77 (26.6)	292	84 (28.8)	0.90 (0.62, 1.29)	0.92 (0.71, 1.20)	-2.22 (-9.48, 5.05)	0.5654	
Nasopharyngitis									
All subjects (total)	290	48 (16.6)	292	61 (20.9)	0.75 (0.49, 1.14)	0.79 (0.56, 1.11)	-4.34 (-10.67, 1.99)	0.2263	
Diabetic retinopathy									
All subjects (total)	290	24 (8.3)	292	26 (8.9)	0.92 (0.52, 1.65)	0.93 (0.55, 1.58)	-0.63 (-5.18, 3.92)	0.8475	
Pyrexia									
All subjects (total)	290	16 (5.5)	292	20 (6.8)	0.79 (0.40, 1.57)	0.81 (0.43, 1.52)	-1.33 (-5.24, 2.58)	0.5328	
Headache									
All subjects (total)	290	17 (5.9)	292	16 (5.5)	1.07 (0.53, 2.17)	1.07 (0.55, 2.08)	0.38 (-3.38, 4.14)	0.8927	
Arthralgia									
All subjects (total)	290	12 (4.1)	292	15 (5.1)	0.80 (0.37, 1.73)	0.81 (0.38, 1.69)	-1.00 (-4.41, 2.42)	0.6018	
Upper respiratory tract infection									
All subjects (total)	290	15 (5.2)	292	11 (3.8)	1.39 (0.63, 3.09)	1.37 (0.64, 2.94)	1.41 (-1.95, 4.76)	0.5311	
Sinusitis									
All subjects (total)	290	14 (4.8)	292	9 (3.1)	1.60 (0.68, 3.75)	1.57 (0.69, 3.56)	1.75 (-1.42, 4.91)	0.2904	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. Preferred terms are ordered by total number of events in descending sequence.

nn1436/nn1436-amnog/current
21FEB2024:13:16:24 - /AEbyPT_4625.txt

Adverse events by preferred term - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
Back pain									
All subjects (total)	290	5 (1.7)	292	17 (5.8)	0.28 (0.10, 0.78)	0.30 (0.11, 0.79)	-4.10 (-7.17, -1.02)	0.0097	
Gender									0.1548
Female	125	0 (0.0)	120	5 (4.2)	0.08 (0.00, 1.53)	0.09 (0.00, 1.56)	-4.17 (-7.74, -0.59)	0.0219	
Male	165	5 (3.0)	172	12 (7.0)	0.42 (0.14, 1.21)	0.43 (0.16, 1.21)	-3.95 (-8.57, 0.67)	0.1079	
Age									0.7116
<65 years	267	4 (1.5)	271	15 (5.5)	0.26 (0.09, 0.79)	0.27 (0.09, 0.80)	-4.04 (-7.12, -0.95)	0.0113	
>=65 years	23	1 (4.3)	21	2 (9.5)	0.43 (0.04, 5.14)	0.46 (0.04, 4.68)	-5.18 (-20.25, 9.89)	0.5930	
HbA1c									0.7699
<=8,5%	235	3 (1.3)	242	12 (5.0)	0.25 (0.07, 0.89)	0.26 (0.07, 0.90)	-3.68 (-6.77, -0.59)	0.0223	
>8,5%	55	2 (3.6)	50	5 (10.0)	0.34 (0.06, 1.84)	0.36 (0.07, 1.79)	-6.36 (-16.04, 3.31)	0.2254	
Region									0.5738
Europe	136	2 (1.5)	139	11 (7.9)	0.17 (0.04, 0.80)	0.19 (0.04, 0.82)	-6.44 (-11.37, -1.52)	0.0119	
North and South America	106	2 (1.9)	85	4 (4.7)	0.39 (0.07, 2.18)	0.40 (0.08, 2.14)	-2.82 (-8.01, 2.37)	0.3601	
Asia	48	1 (2.1)	68	2 (2.9)	0.70 (0.06, 7.97)	0.71 (0.07, 7.59)	-0.86 (-6.55, 4.84)	0.8277	
Race									0.4830
White	230	4 (1.7)	218	15 (6.9)	0.24 (0.08, 0.73)	0.25 (0.09, 0.75)	-5.14 (-8.90, -1.38)	0.0071	
Not white	60	1 (1.7)	74	2 (2.7)	0.61 (0.05, 6.90)	0.62 (0.06, 6.64)	-1.04 (-5.95, 3.88)	0.7196	
Vomiting									
All subjects (total)	290	11 (3.8)	292	11 (3.8)	1.01 (0.43, 2.36)	1.01 (0.44, 2.29)	0.03 (-3.07, 3.12)	1.0000	
Pain in extremity									
All subjects (total)	290	8 (2.8)	292	13 (4.5)	0.61 (0.25, 1.49)	0.62 (0.26, 1.47)	-1.69 (-4.72, 1.33)	0.2887	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. Preferred terms are ordered by total number of events in descending sequence.

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Adverse events by preferred term - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
Cough									
All subjects (total)	290	9 (3.1)	292	11 (3.8)	0.82 (0.33, 2.01)	0.82 (0.35, 1.96)	-0.66 (-3.62, 2.29)	0.7521	
Urinary tract infection									
All subjects (total)	290	12 (4.1)	292	8 (2.7)	1.53 (0.62, 3.81)	1.51 (0.63, 3.64)	1.40 (-1.56, 4.36)	0.5295	
Nausea									
All subjects (total)	290	9 (3.1)	292	10 (3.4)	0.90 (0.36, 2.26)	0.91 (0.37, 2.20)	-0.32 (-3.21, 2.57)	0.8865	
Gastroenteritis									
All subjects (total)	290	13 (4.5)	292	5 (1.7)	2.69 (0.95, 7.66)	2.62 (0.95, 7.25)	2.77 (-0.04, 5.58)	0.0548	
Medical device site rash									
All subjects (total)	290	7 (2.4)	292	11 (3.8)	0.63 (0.24, 1.65)	0.64 (0.25, 1.63)	-1.35 (-4.16, 1.46)	0.5295	
Oropharyngeal pain									
All subjects (total)	290	8 (2.8)	292	10 (3.4)	0.80 (0.31, 2.06)	0.81 (0.32, 2.01)	-0.67 (-3.48, 2.15)	0.6814	
Diarrhoea									
All subjects (total)	290	10 (3.4)	292	6 (2.1)	1.70 (0.61, 4.75)	1.68 (0.62, 4.56)	1.39 (-1.26, 4.05)	0.3133	
Hypoglycaemia									
All subjects (total)	290	10 (3.4)	292	4 (1.4)	2.57 (0.80, 8.29)	2.52 (0.80, 7.93)	2.08 (-0.41, 4.57)	0.1127	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. Preferred terms are ordered by total number of events in descending sequence.

nn1436/nn1436-amnog/current
21FEB2024:13:16:24 - /AEbyPT_4625.txt

2.59 Adverse events by system organ class - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg			
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value
Infections and infestations								
All subjects (total)	290	159 (54.8)	292	159 (54.5)	1.02 (0.73, 1.41)	1.01 (0.87, 1.17)	0.38 (-7.71, 8.46)	0.9338
General disorders and administration site conditions								
All subjects (total)	290	55 (19.0)	292	65 (22.3)	0.82 (0.55, 1.22)	0.85 (0.62, 1.17)	-3.29 (-9.86, 3.27)	0.5295
Musculoskeletal and connective tissue disorders								
All subjects (total)	290	45 (15.5)	292	56 (19.2)	0.77 (0.50, 1.19)	0.81 (0.57, 1.16)	-3.66 (-9.81, 2.48)	0.2478
Injury, poisoning and procedural complications								
All subjects (total)	290	43 (14.8)	292	50 (17.1)	0.84 (0.54, 1.31)	0.87 (0.60, 1.26)	-2.30 (-8.25, 3.65)	0.5327
Eye disorders								
All subjects (total)	290	43 (14.8)	292	48 (16.4)	0.88 (0.57, 1.39)	0.90 (0.62, 1.32)	-1.61 (-7.51, 4.29)	0.6814
Gastrointestinal disorders								
All subjects (total)	290	47 (16.2)	292	43 (14.7)	1.12 (0.71, 1.76)	1.10 (0.75, 1.61)	1.48 (-4.39, 7.36)	0.6814
Nervous system disorders								
All subjects (total)	290	40 (13.8)	292	39 (13.4)	1.04 (0.65, 1.67)	1.03 (0.69, 1.56)	0.44 (-5.13, 6.00)	0.9158
Skin and subcutaneous tissue disorders								
All subjects (total)	290	36 (12.4)	292	40 (13.7)	0.89 (0.55, 1.45)	0.91 (0.60, 1.38)	-1.28 (-6.76, 4.19)	0.6814

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. System organ classes are ordered by total number of events in descending sequence.

nn1436/nn1436-amnog/current
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Adverse events by system organ class - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg			
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value
Respiratory, thoracic and mediastinal disorders								
All subjects (total)	290	36 (12.4)	292	37 (12.7)	0.98 (0.60, 1.60)	0.98 (0.64, 1.50)	-0.26 (-5.64, 5.12)	0.9441
Investigations								
All subjects (total)	290	19 (6.6)	292	18 (6.2)	1.07 (0.55, 2.08)	1.06 (0.57, 1.98)	0.39 (-3.58, 4.35)	0.8978
Metabolism and nutrition disorders								
All subjects (total)	290	18 (6.2)	292	17 (5.8)	1.07 (0.54, 2.12)	1.07 (0.56, 2.03)	0.38 (-3.48, 4.25)	0.8978
Cardiac disorders								
All subjects (total)	290	16 (5.5)	292	11 (3.8)	1.49 (0.68, 3.27)	1.46 (0.69, 3.10)	1.75 (-1.67, 5.17)	0.3699
Vascular disorders								
All subjects (total)	290	11 (3.8)	292	10 (3.4)	1.11 (0.46, 2.66)	1.11 (0.48, 2.57)	0.37 (-2.66, 3.40)	0.8712
Psychiatric disorders								
All subjects (total)	290	8 (2.8)	292	11 (3.8)	0.72 (0.29, 1.83)	0.73 (0.30, 1.79)	-1.01 (-3.89, 1.88)	0.5328

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval.
The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. System organ classes are ordered by total number of events in descending sequence.

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2.60 Severe adverse events by preferred term - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
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2.61 Severe adverse events by system organ class - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:29 - /SevAEbySOC_4625.txt

2.62 Serious adverse events by preferred term - Onwards 6 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:26 - /SAEbyPT_4625.txt

2.63 Serious adverse events by system organ class - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg		Ico vs. IDeg			
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value
Metabolism and nutrition disorders								
All subjects (total)	290	10 (3.4)	292	3 (1.0)	3.44 (0.94, 12.63)	3.36 (0.93, 12.07)	2.42 (0.02, 4.82)	0.0513

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. System organ classes are ordered by total number of events in descending sequence.

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2.64 Adverse events leading to permanent trial product discontinuation by preferred term - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg	
	N	n (%)	N	n (%)
Cerebral haemorrhage				
All subjects (total)	290	1 (0.3)	292	0 (0.0)
Haemorrhage intracranial				
All subjects (total)	290	1 (0.3)	292	0 (0.0)
Insulin resistance				
All subjects (total)	290	0 (0.0)	292	1 (0.3)

N: number of subjects, n: number of subjects with at least one event. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

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2.65 Adverse events leading to permanent trial product discontinuation by system organ class - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg	
	N	n (%)	N	n (%)
Nervous system disorders				
All subjects (total)	290	2 (0.7)	292	0 (0.0)
Metabolism and nutrition disorders				
All subjects (total)	290	0 (0.0)	292	1 (0.3)

N: number of subjects, n: number of subjects with at least one event. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

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2.66 Adverse events leading to study withdrawal by preferred term - Onwards 6 - in-trial - Safety analysis set

	Ico		IDeg	
	N	n (%)	N	n (%)
All subjects (total)	290	0 (0.0)	292	0 (0.0)

N: number of subjects, n: number of subjects with at least one event. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

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2.67 Adverse events leading to study withdrawal by system organ class - Onwards 6 - in- trial - Safety analysis set

	Ico		IDeg	
	N	n (%)	N	n (%)
All subjects (total)	290	0 (0.0)	292	0 (0.0)

N: number of subjects, n: number of subjects with at least one event. In-trial onset is captured on or after the day of randomisation and no later than week 57 (or week 52 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

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3 Auswertung zum Anteil von Patienten, die in deutschen Studienzentren rekrutiert wurden

3.1 Summary of subjects from Germany in the insulin icodec RCT pool

Study	N	n DE	% DE
ONWARDS 1	984	0	0
ONWARDS 2	526	45	8,6
ONWARDS 3	588	0	0
ONWARDS 4	582	0	0
ONWARDS 5	1085	101	9,3
ONWARDS 6	582	46	7,9
NN1436-4466	154	32	20,8
NN1436-4465	205	38	18,5
NN1436-4462	43	0	0
NN1436-4422	24	0	0
NN1436-4383	247	0	0
NN1436-4314 (I287)	48	48	100
NN1436-4225	66	66	100
NN1436-4057	49	49	100
NN1436-3955 (part 1 and 2 combined)	69	69	100
Sum	**5252**	**494**	**9,4**

N is given as all subjects in the study, independent of having insulin icodec or comparative investigational medicinal product.
DE: Deutschland (Germany); N: number of subjects; n: number of subjects from Germany;
RCT: randomized controlled trial