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Dossier zur Nutzenbewertung gemäß § 35a SGB V

Semaglutid (Rybelsus®/Ozempic®)

Novo Nordisk Pharma GmbH

Modul 4 E – Anhang 4-G

Zur Behandlung von erwachsenen Patienten mit Typ 2 Diabetes mellitus und hohem kardiovaskulären Risiko

Medizinischer Nutzen und
medizinischer Zusatznutzen,
Patientengruppen mit therapeutisch
bedeutsamem Zusatznutzen

Stand: 26.10.2020

Anhang 4-G: Ergänzende Analysen

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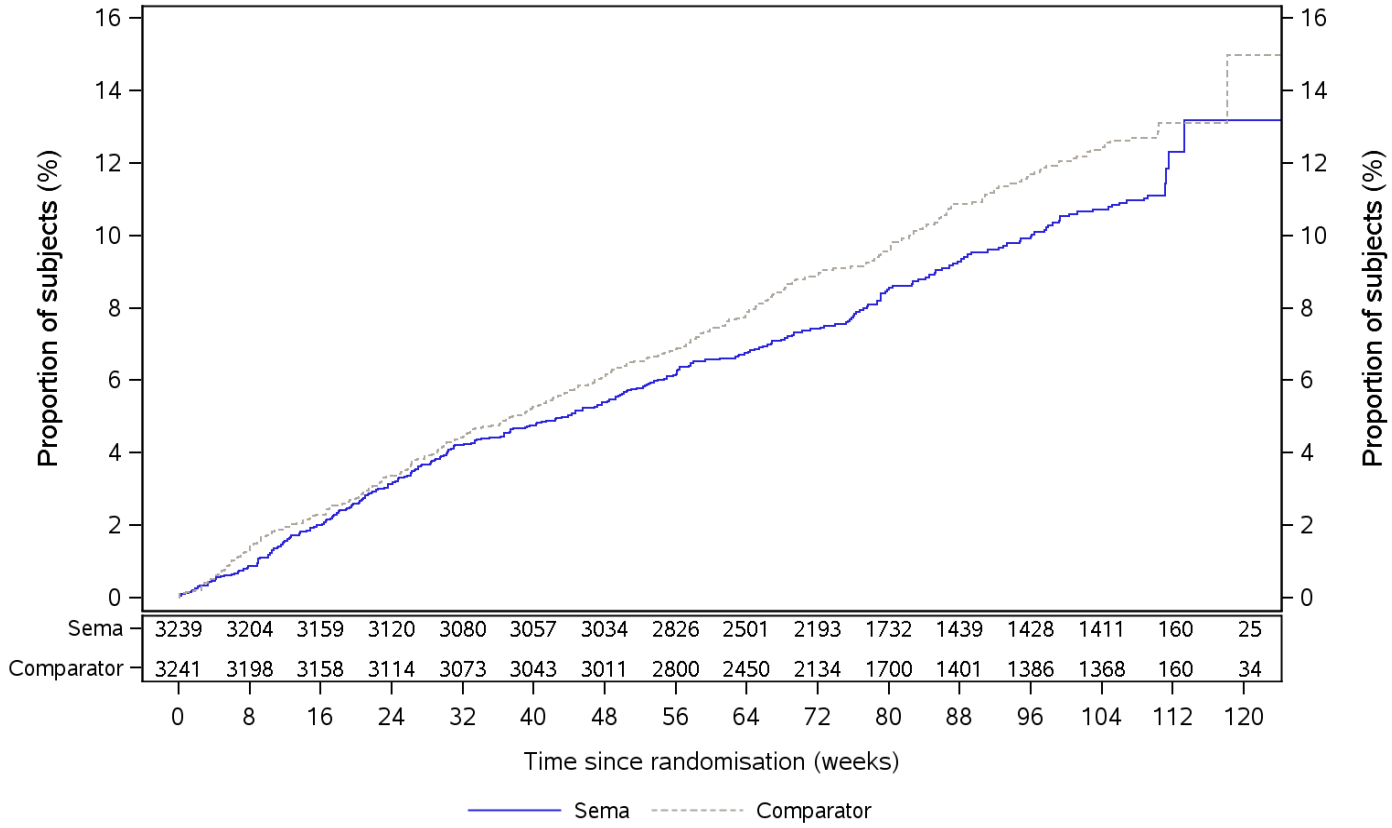
Meta-Analyse PIONEER 6 und SUSTAIN 6 – Kumulative Inzidenz (SUE nach SOC und PT)

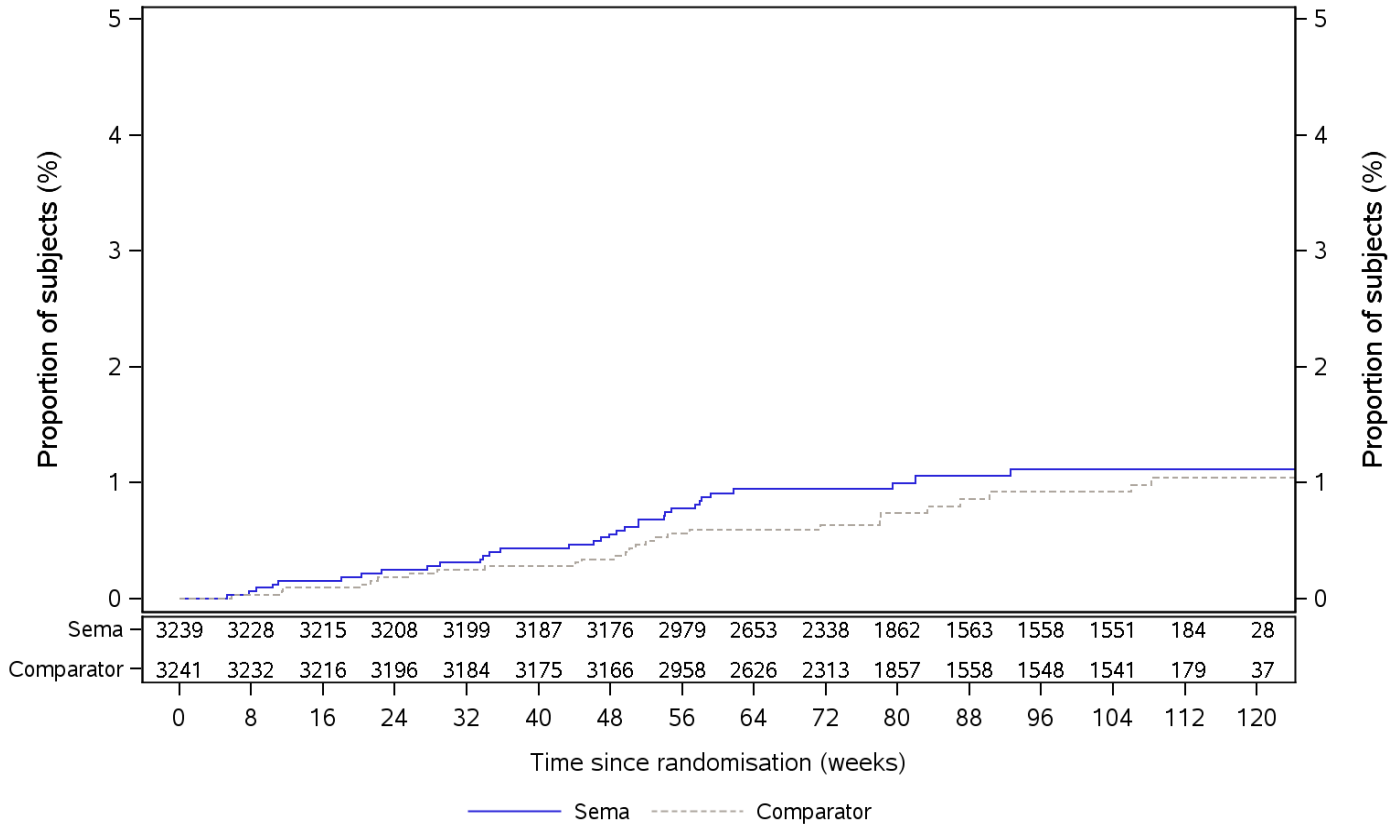
1 Serious adverse events - system organ class "Cardiac disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:29:16 - f_cif_tte_pool.sas/f_cif_soc_cd_sae_pool.png

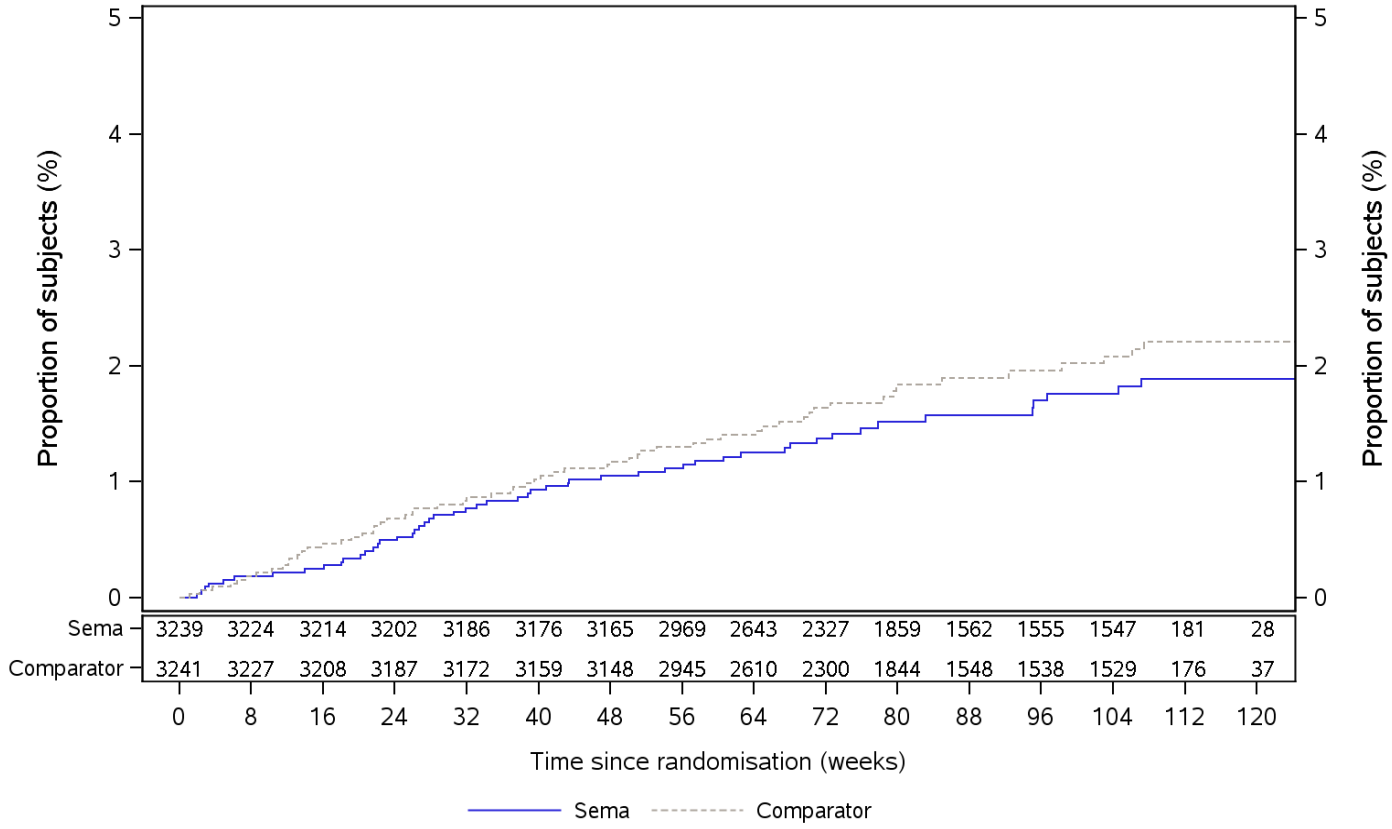
2 Serious adverse events - system organ class "Eye disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:29:59 - f_cif_tte_pool.sas/f_cif_soc_ed_sae_pool.png

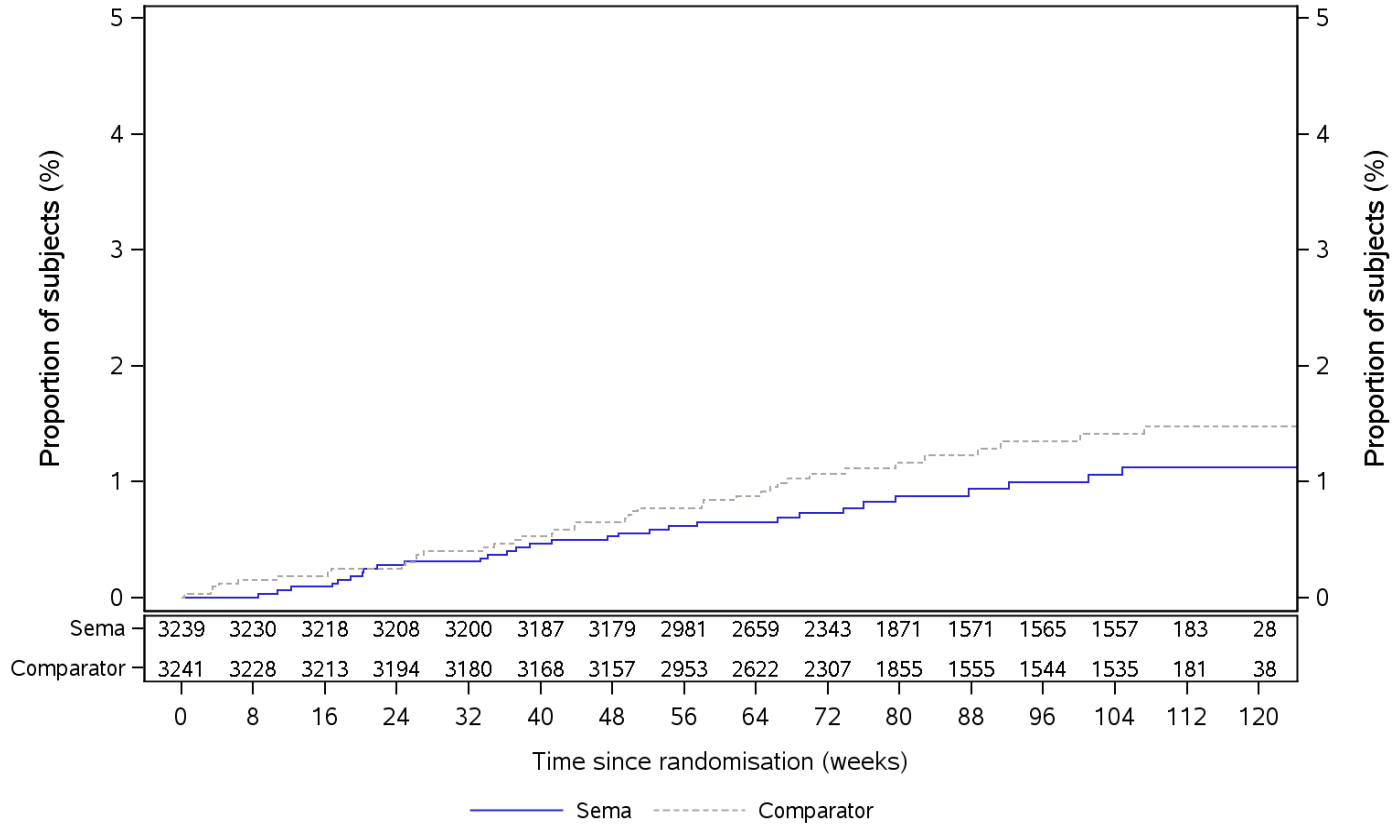
3 Serious adverse events - system organ class "General disorders and administration site conditions" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:31:25 - f_cif_tte_pool.sas/f_cif_soc_gdasc_sae_pool.png

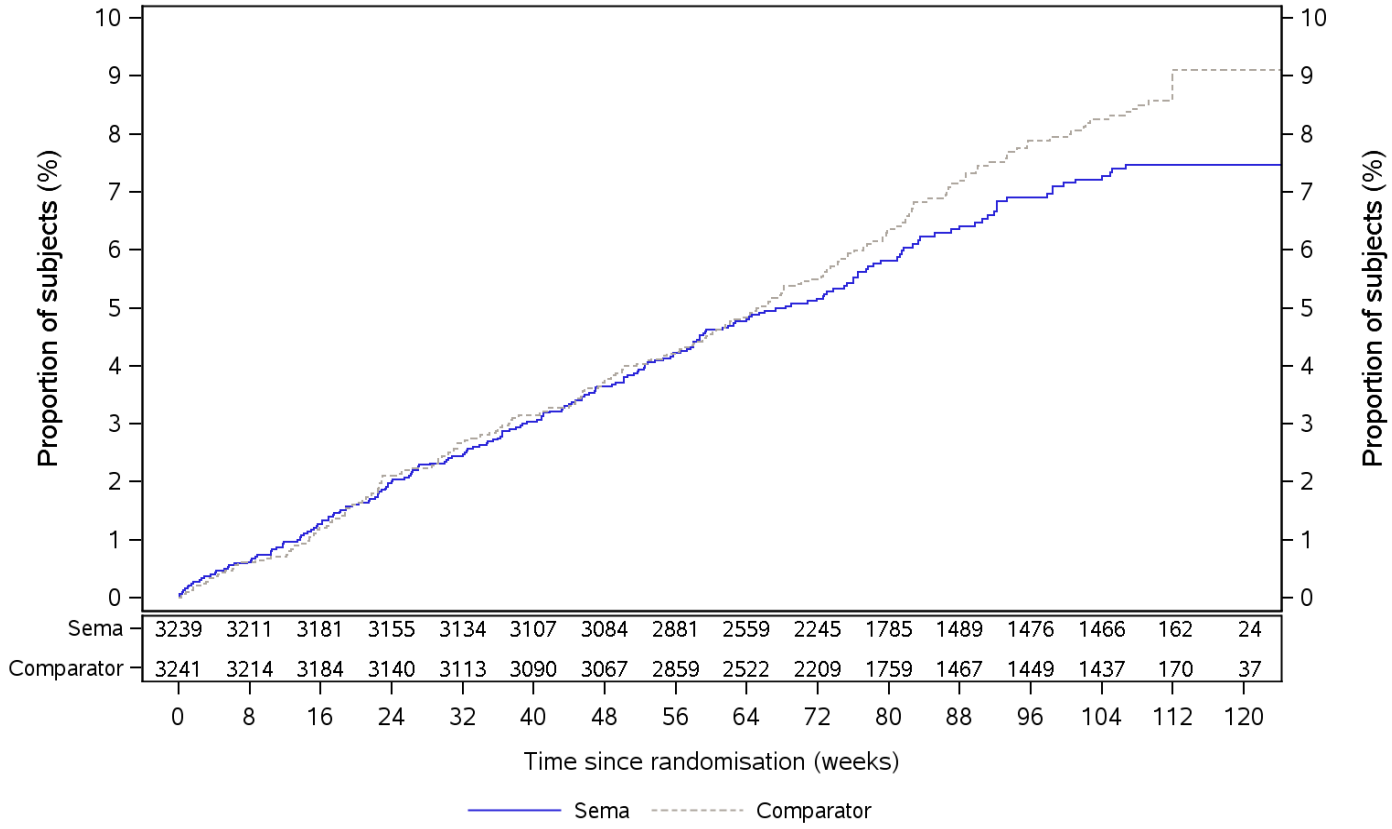
4 Serious adverse events - system organ class "Hepatobiliary disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:31:59 - f_cif_tte_pool.sas/f_cif_soc_hd_sae_pool.png

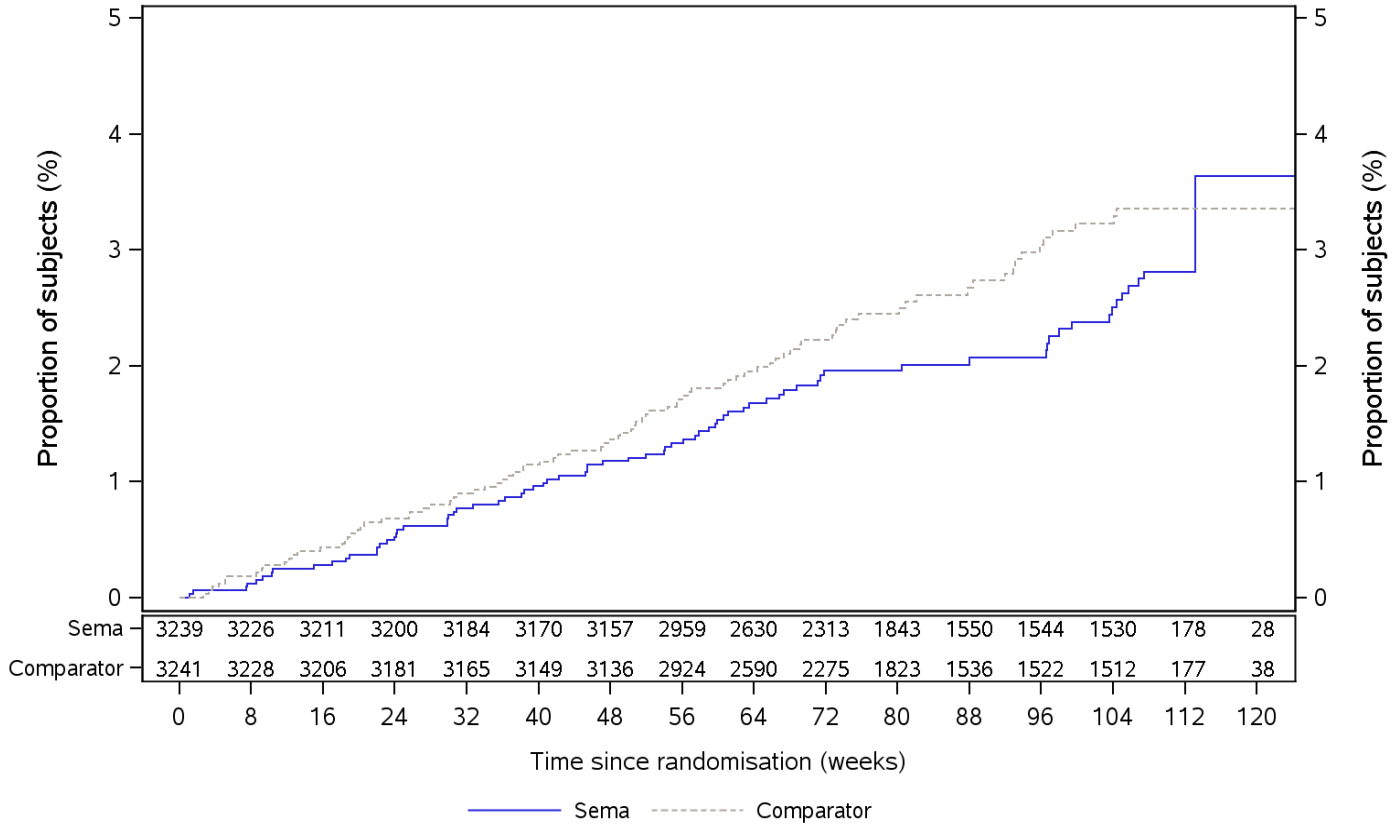
5 Serious adverse events - system organ class "Infections and infestations" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:32:34 - f_cif_tte_pool.sas/f_cif_soc_ii_sae_pool.png

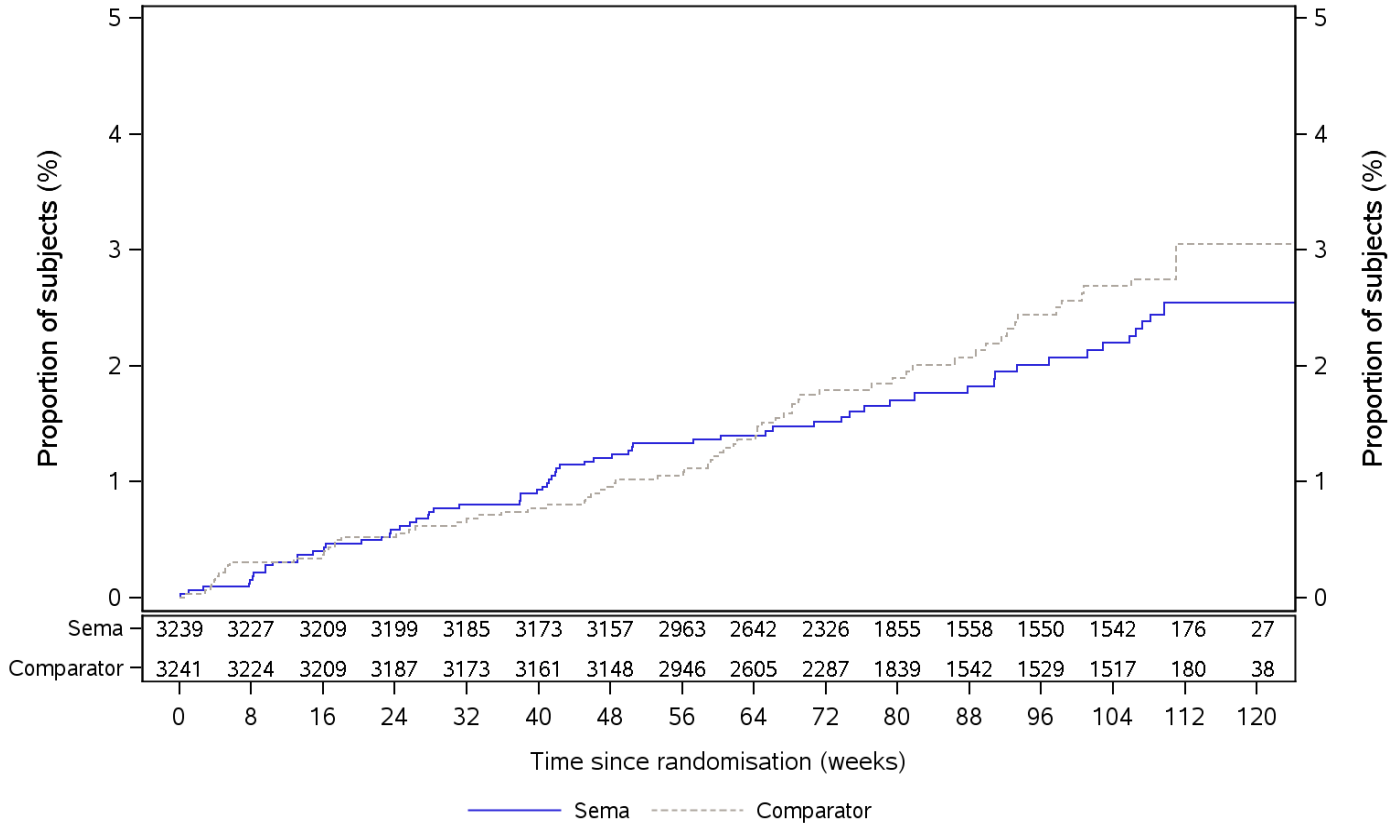
6 Serious adverse events - system organ class "Injury, poisoning and procedural complications" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:33:16 - f_cif_tte_pool.sas/f_cif_soc_ippc_sae_pool.png

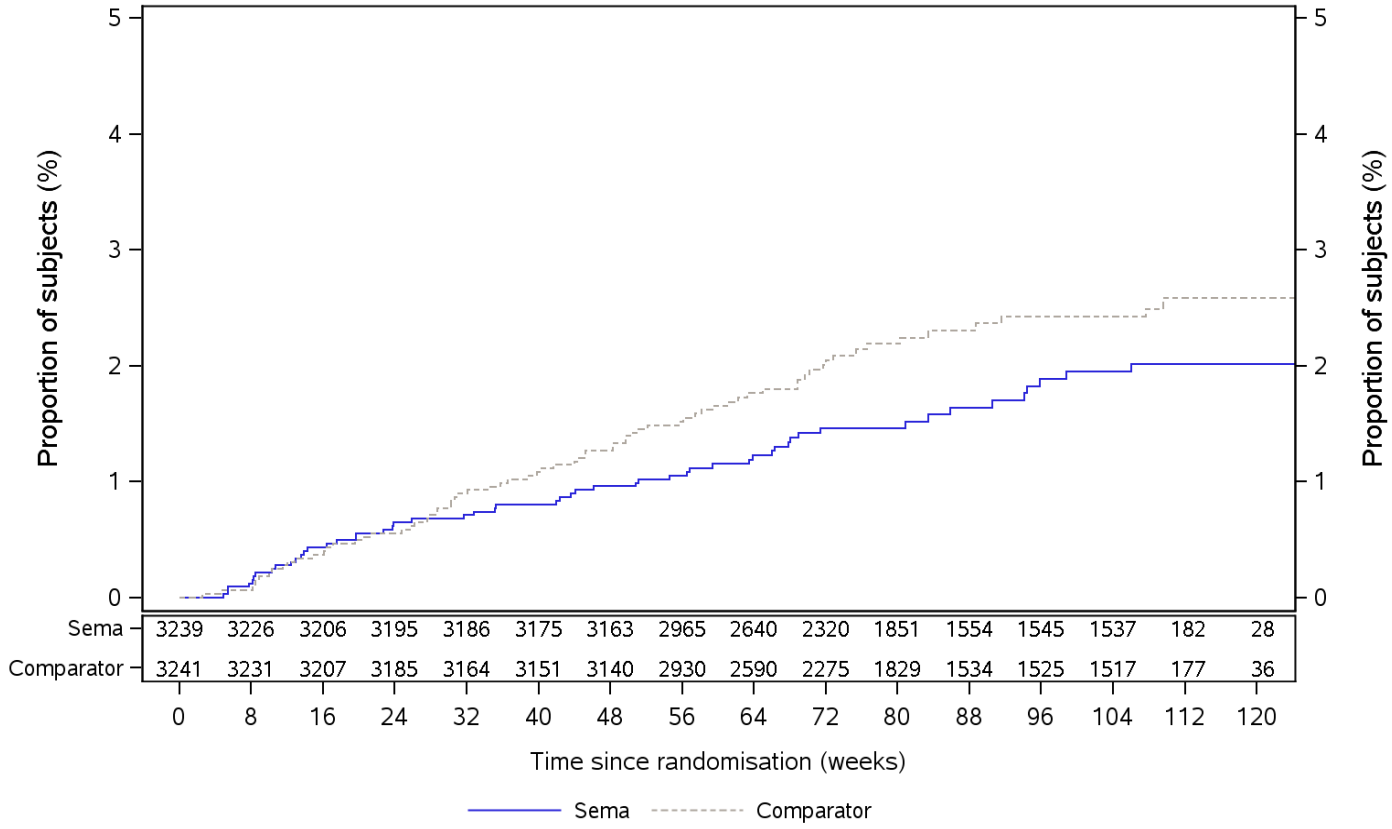
7 Serious adverse events - system organ class "Metabolism and nutrition disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:33:56 - f_cif_tte_pool.sas/f_cif_soc_mnd_sae_pool.png

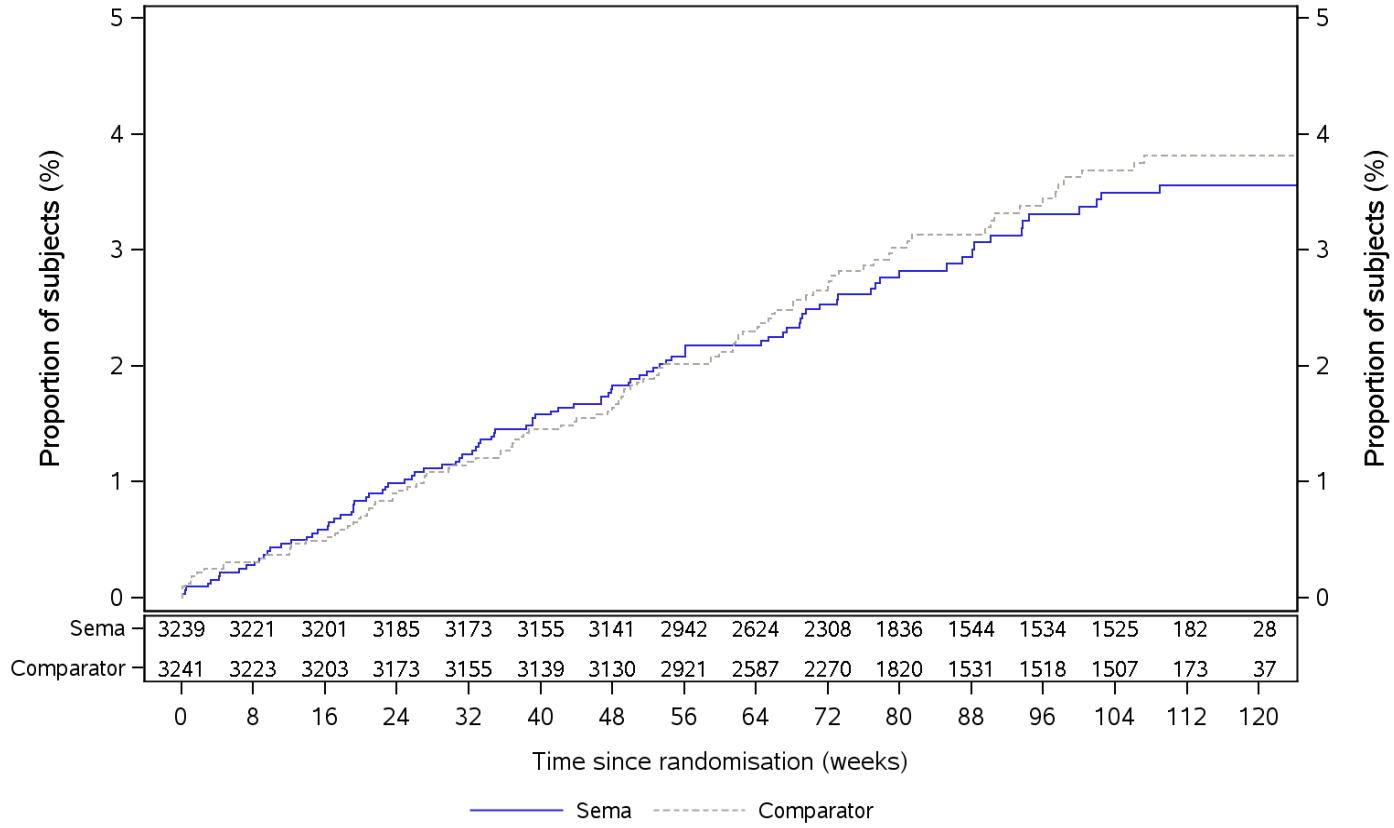
8 Serious adverse events - system organ class "Musculoskeletal and connective tissue disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:34:35 - f_cif_tte_pool.sas/f_cif_soc_mctd_sae_pool.png

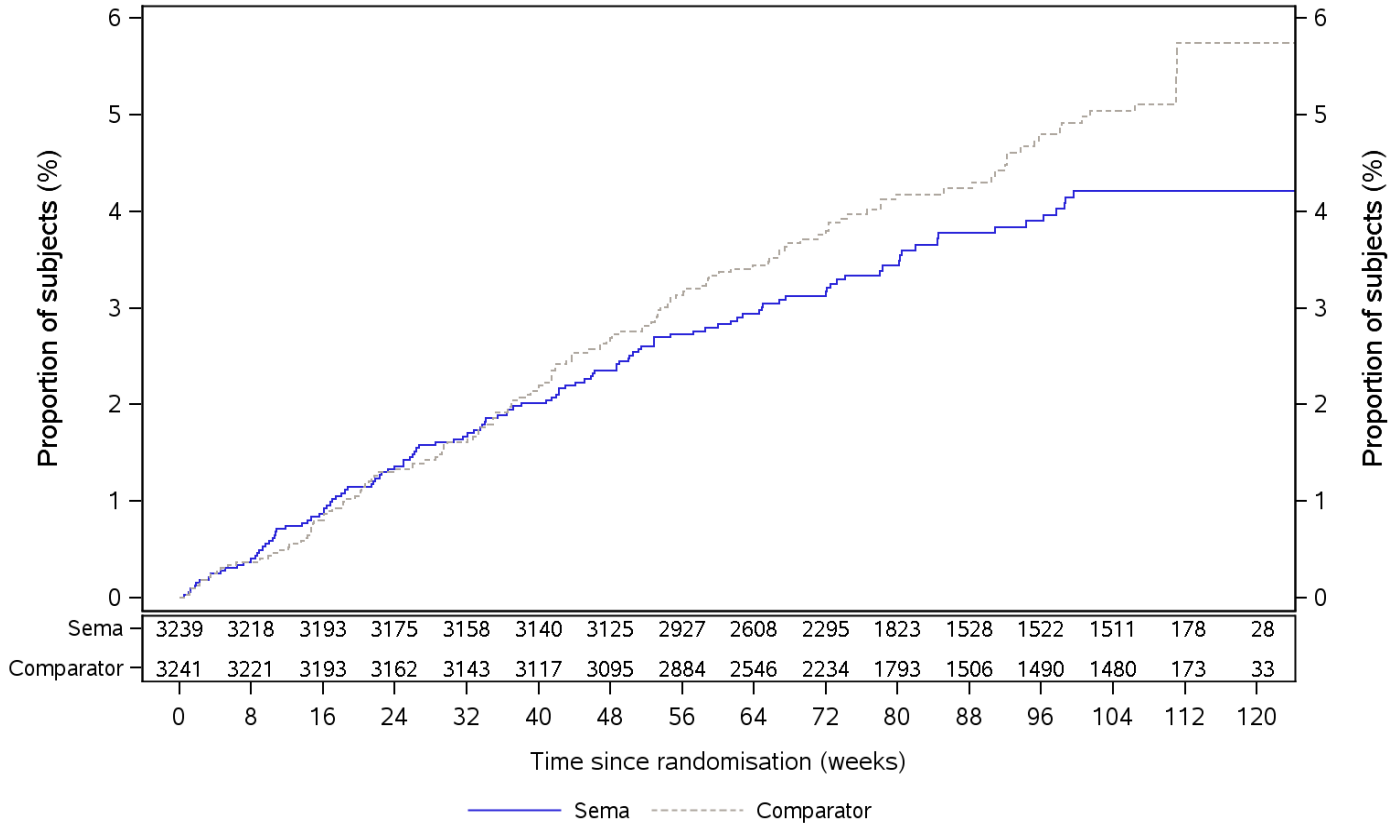
9 Serious adverse events - system organ class "Neoplasms benign, malignant and unspecified (incl cysts and polyps)" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:35:13 - f_cif_tte_pool.sas/f_cif_soc_nbmu_sae_pool.png

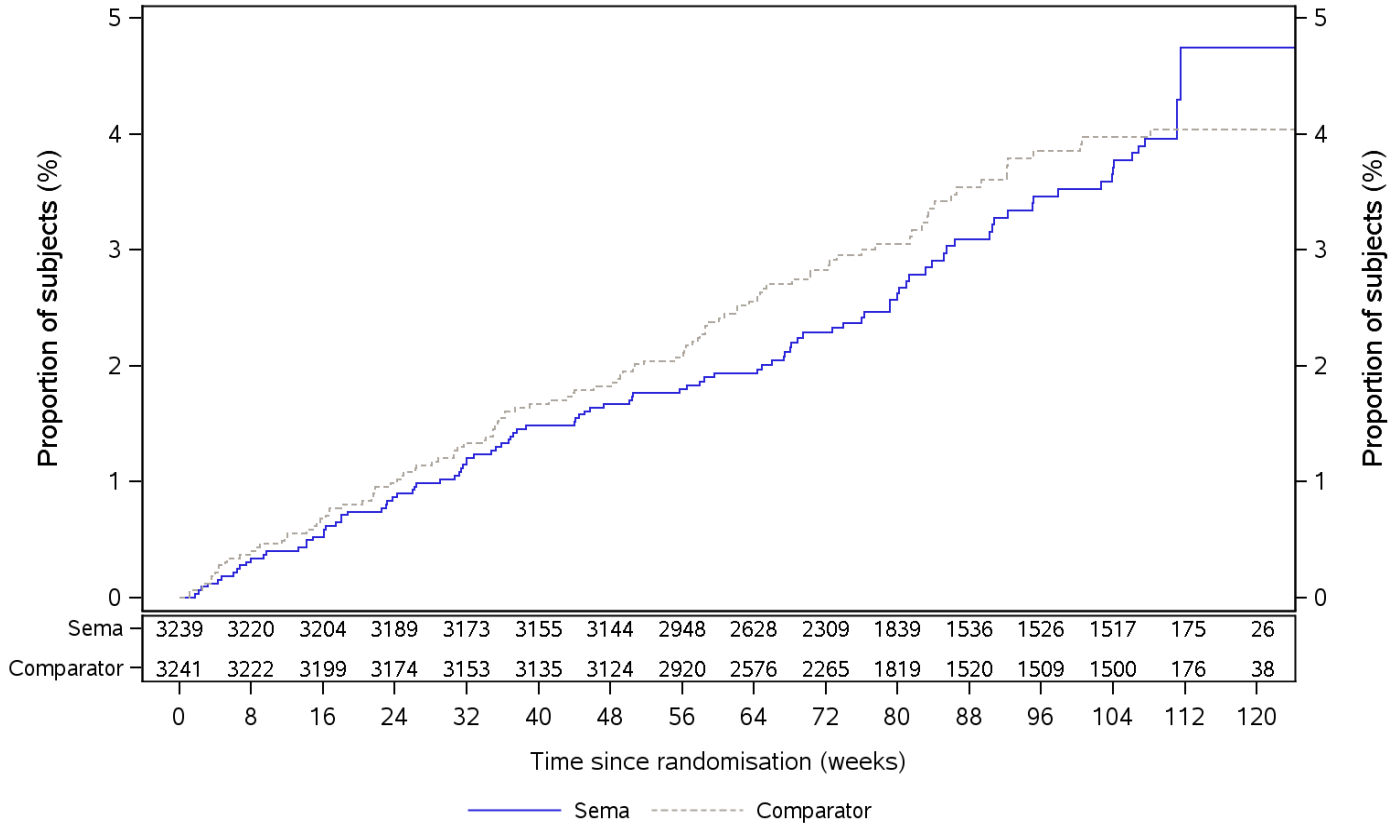
10 Serious adverse events - system organ class "Nervous system disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:35:46 - f_cif_tte_pool.sas/f_cif_soc_nsd_sae_pool.png

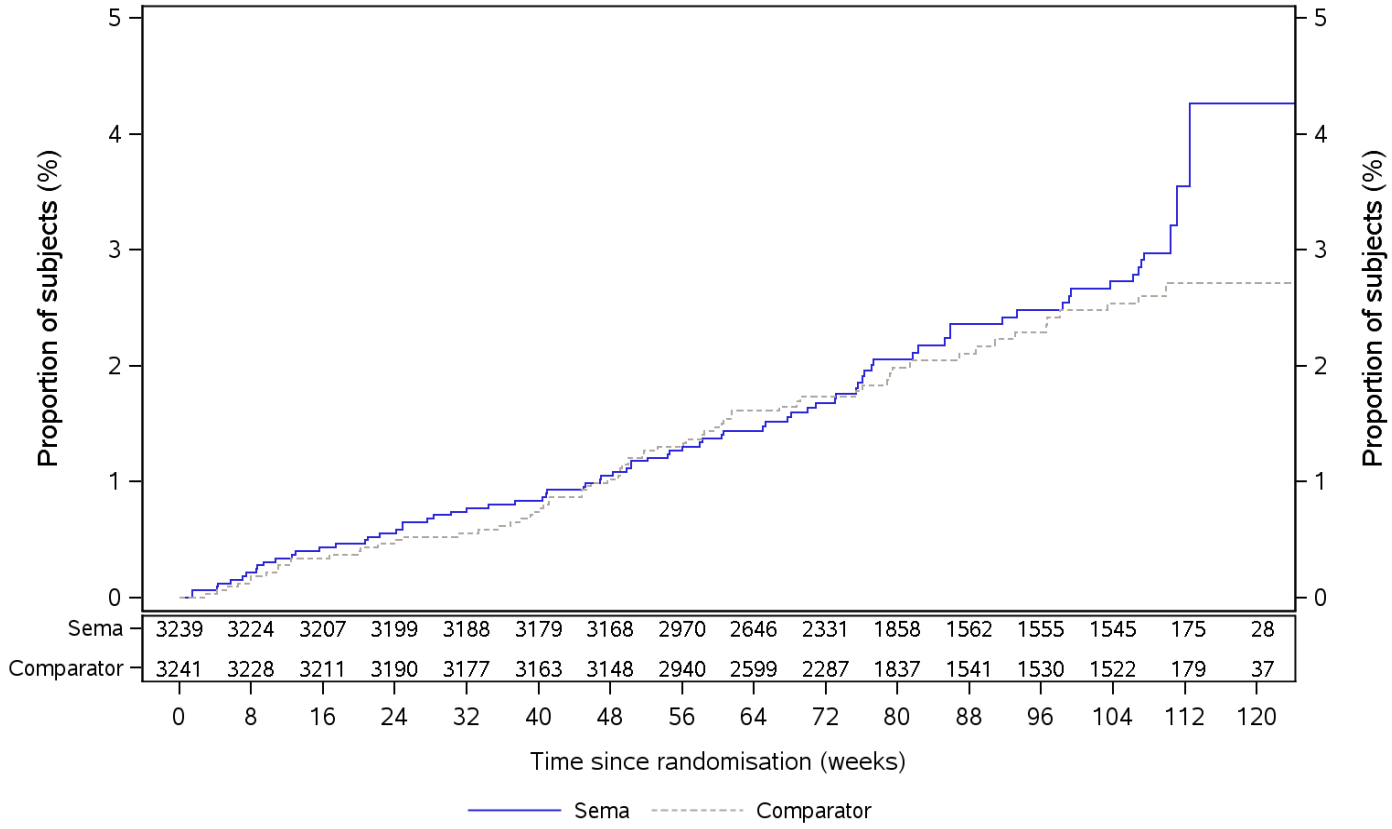
11 Serious adverse events - system organ class "Renal and urinary disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:36:33 - f_cif_tte_pool.sas/f_cif_soc_rud_sae_pool.png

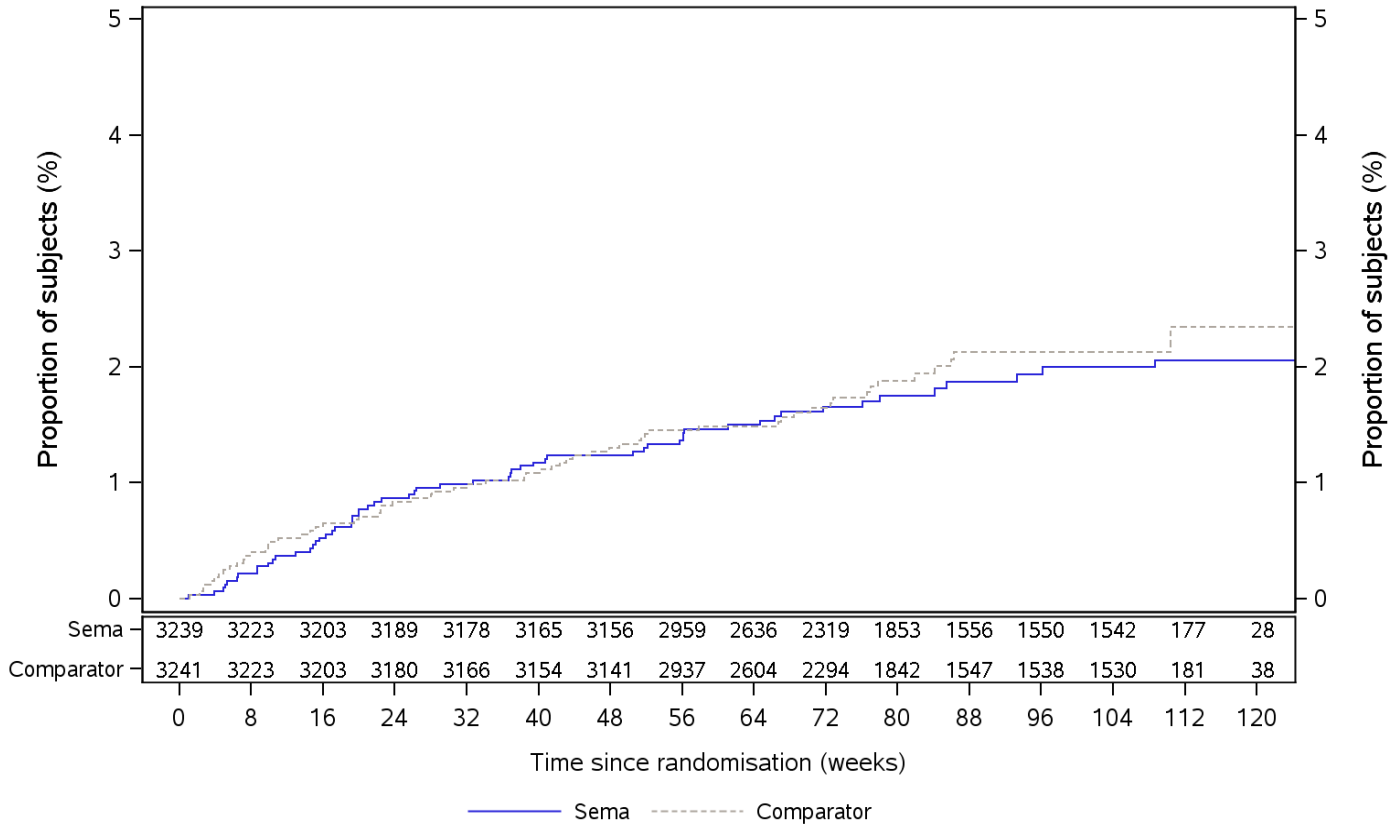
12 Serious adverse events - system organ class "Respiratory, thoracic and mediastinal disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:37:07 - f_cif_tte_pool.sas/f_cif_soc_rtmd_sae_pool.png

13 Serious adverse events - system organ class "Vascular disorders" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

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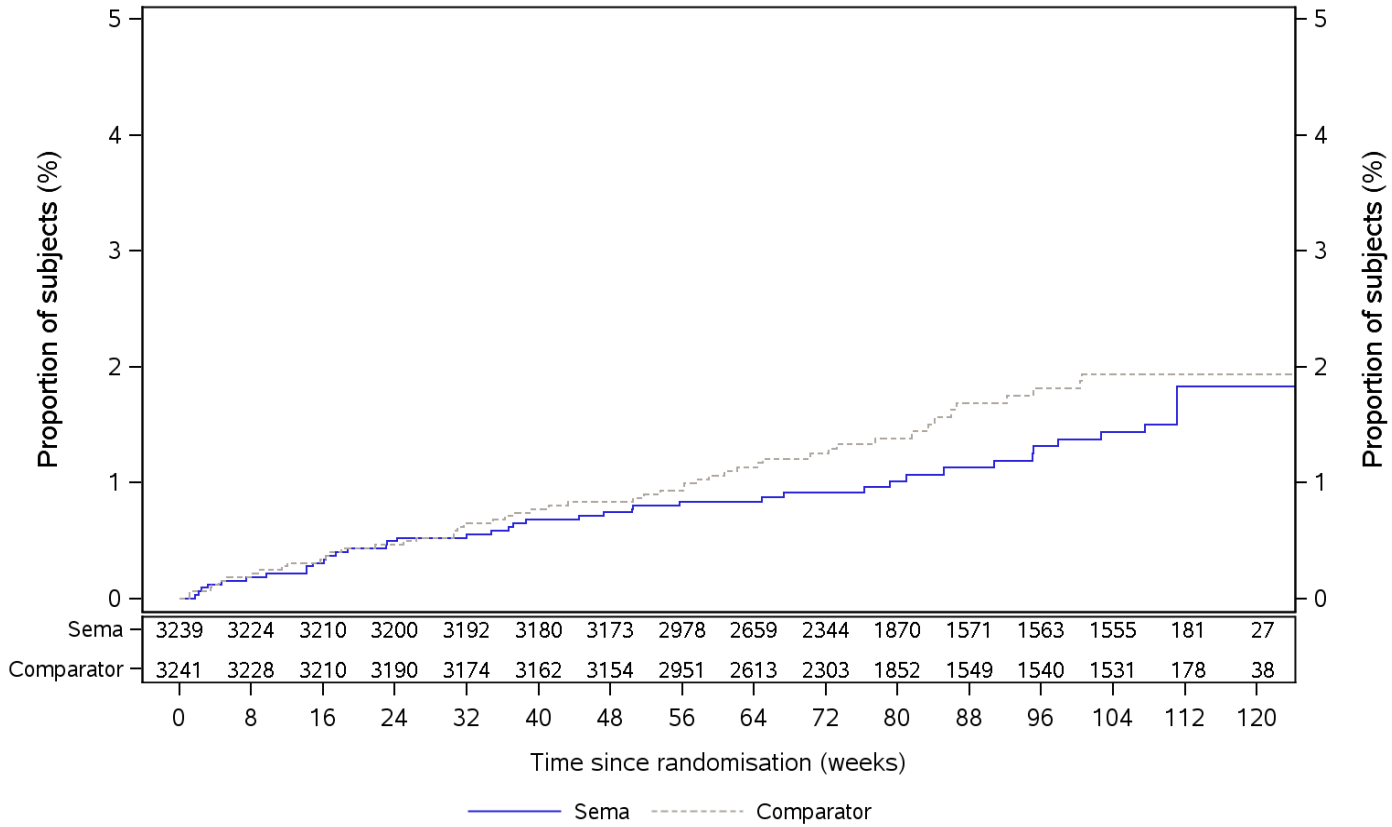
24FEB2020:15:38:32 - f_cif_tte_pool.sas/f_cif_soc_vd_sae_pool.png

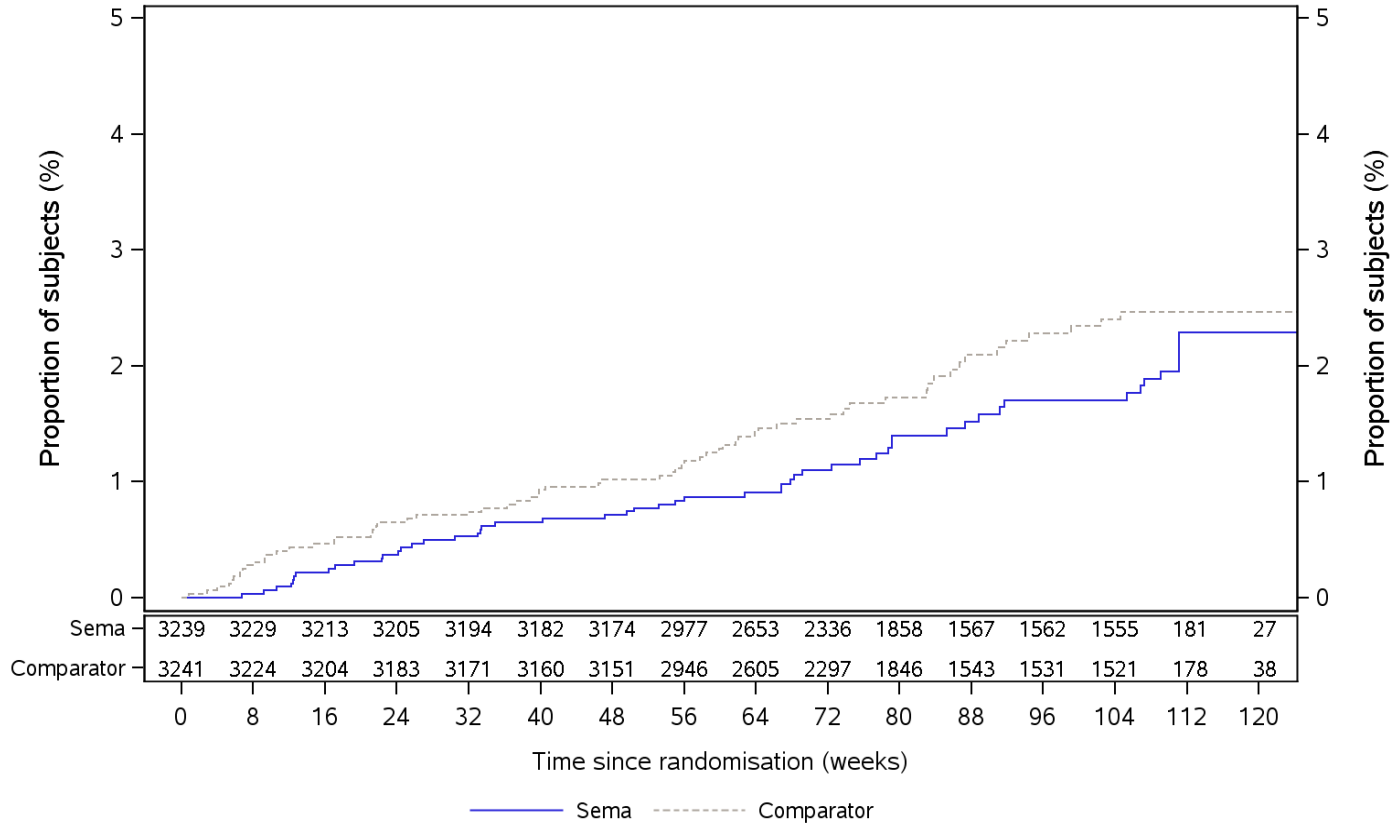
14 Serious adverse events - preferred term "Acute kidney injury" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:39:07 - f_cif_tte_pool.sas/f_cif_pt_aki_sae_pool.png

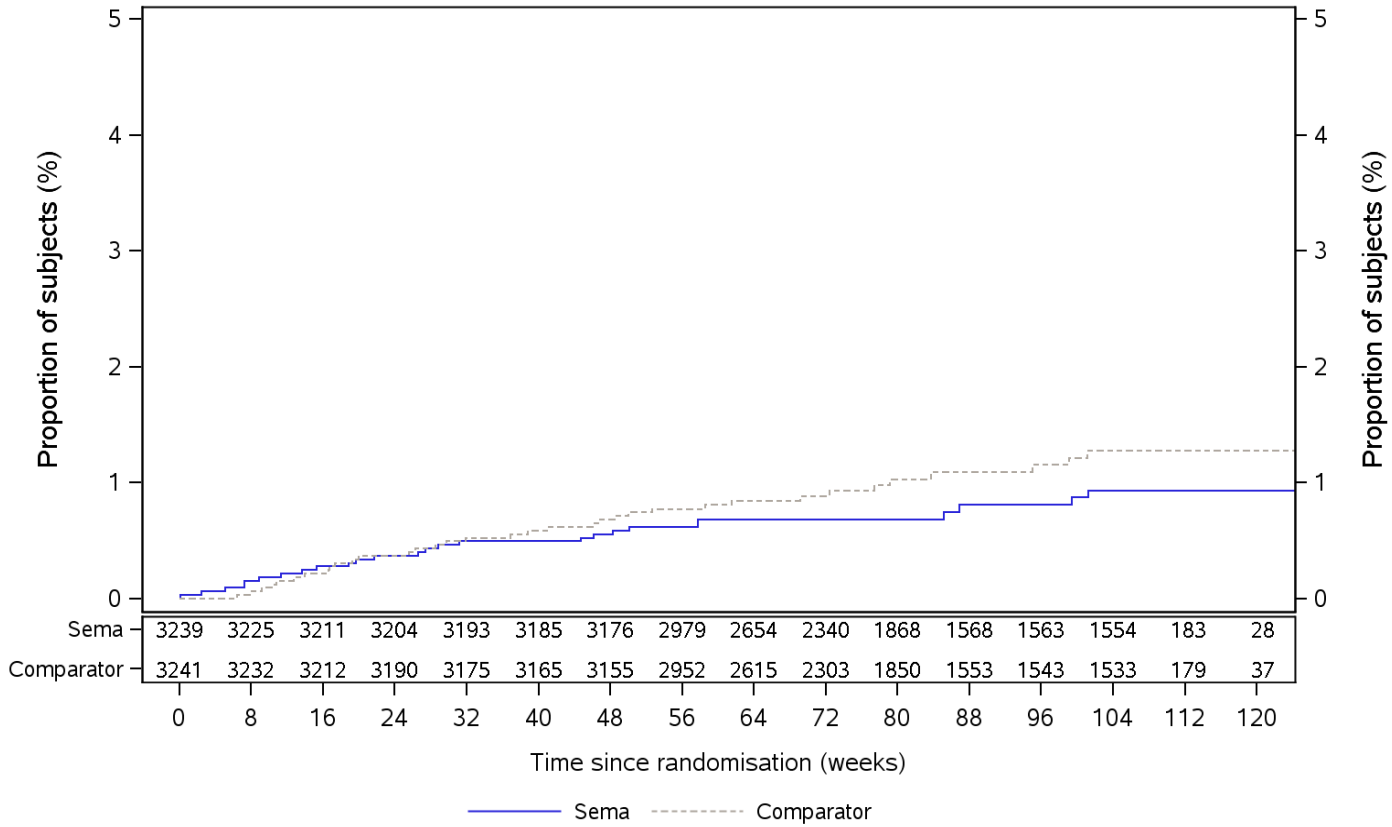
15 Serious adverse events - preferred term "Acute myocardial infarction" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:39:53 - f_cif_tte_pool.sas/f_cif_pt_ami_sae_pool.png

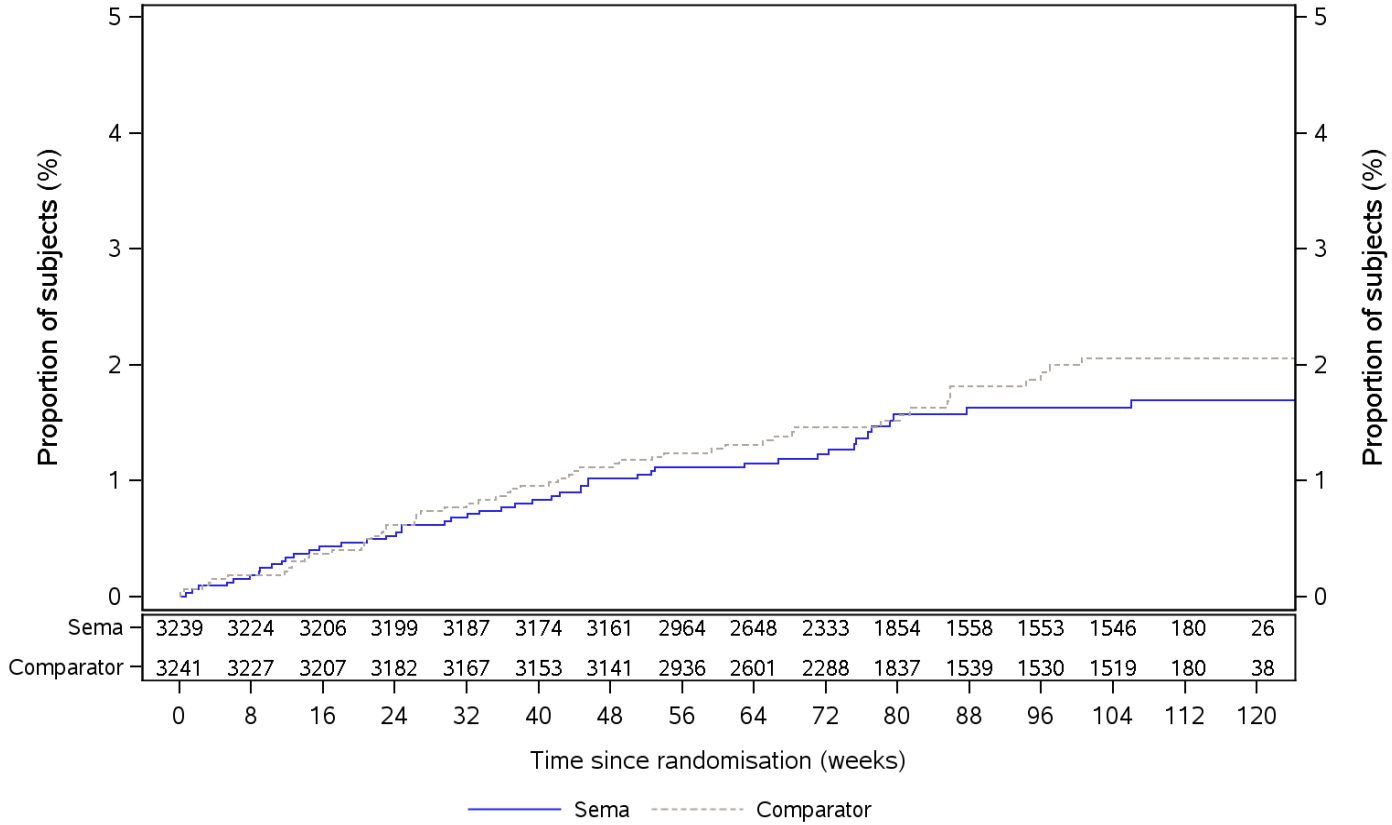
16 Serious adverse events - preferred term "Angina pectoris" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:40:36 - f_cif_tte_pool.sas/f_cif_pt_ap_sae_pool.png

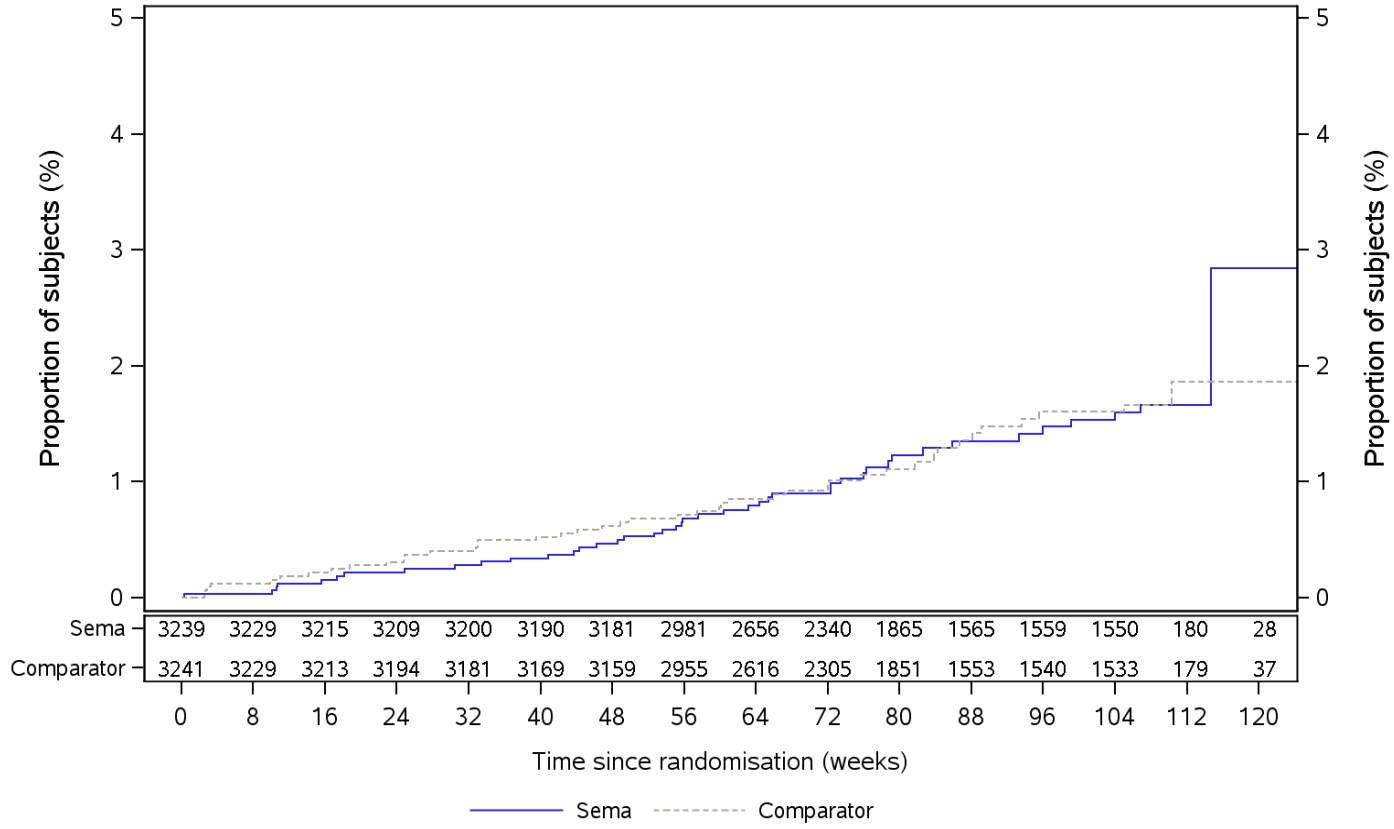
17 Serious adverse events - preferred term "Angina unstable" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:41:14 - f_cif_tte_pool.sas/f_cif_pt_au_sae_pool.png

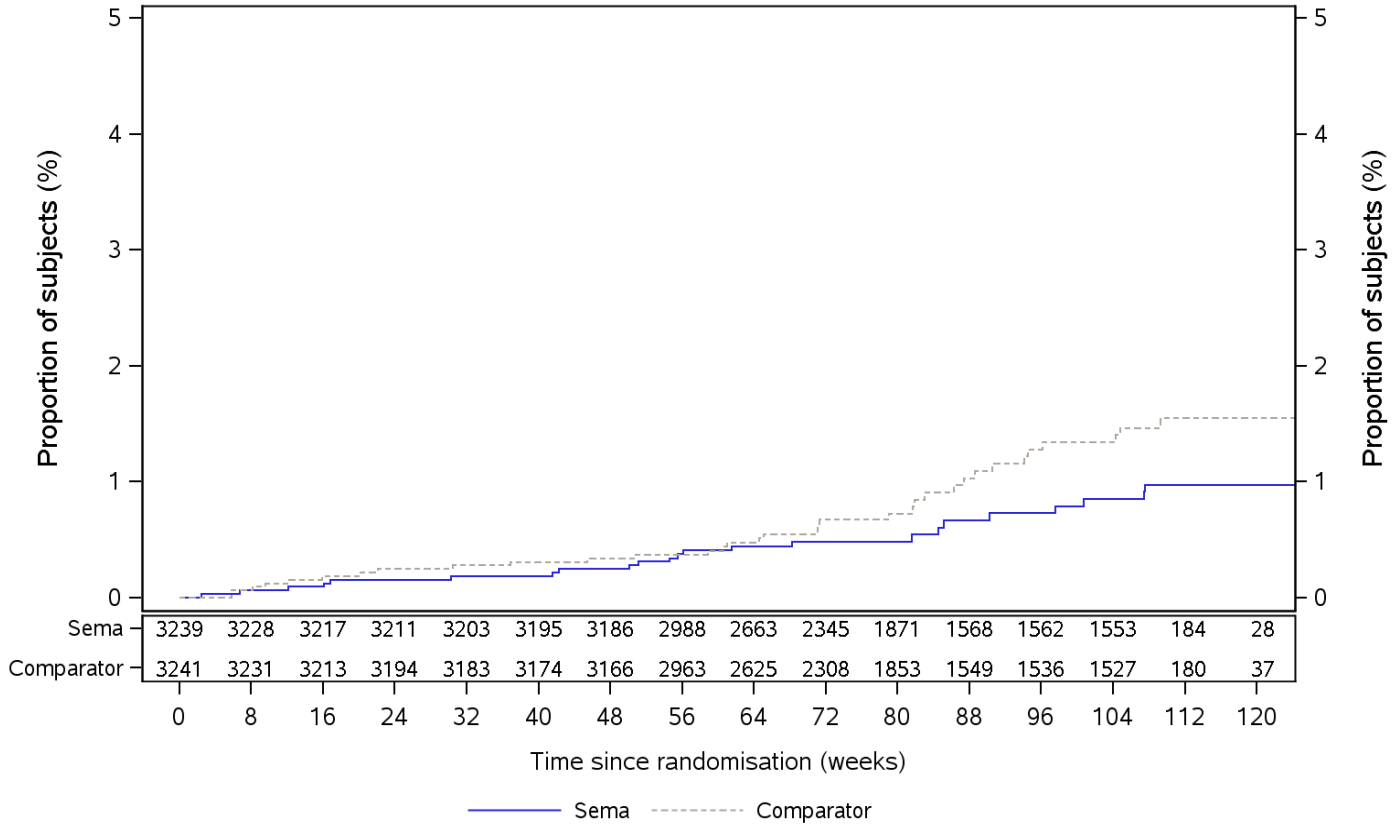
18 Serious adverse events - preferred term "Cardiac failure congestive" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:42:37 - f_cif_tte_pool.sas/f_cif_pt_cfc_sae_pool.png

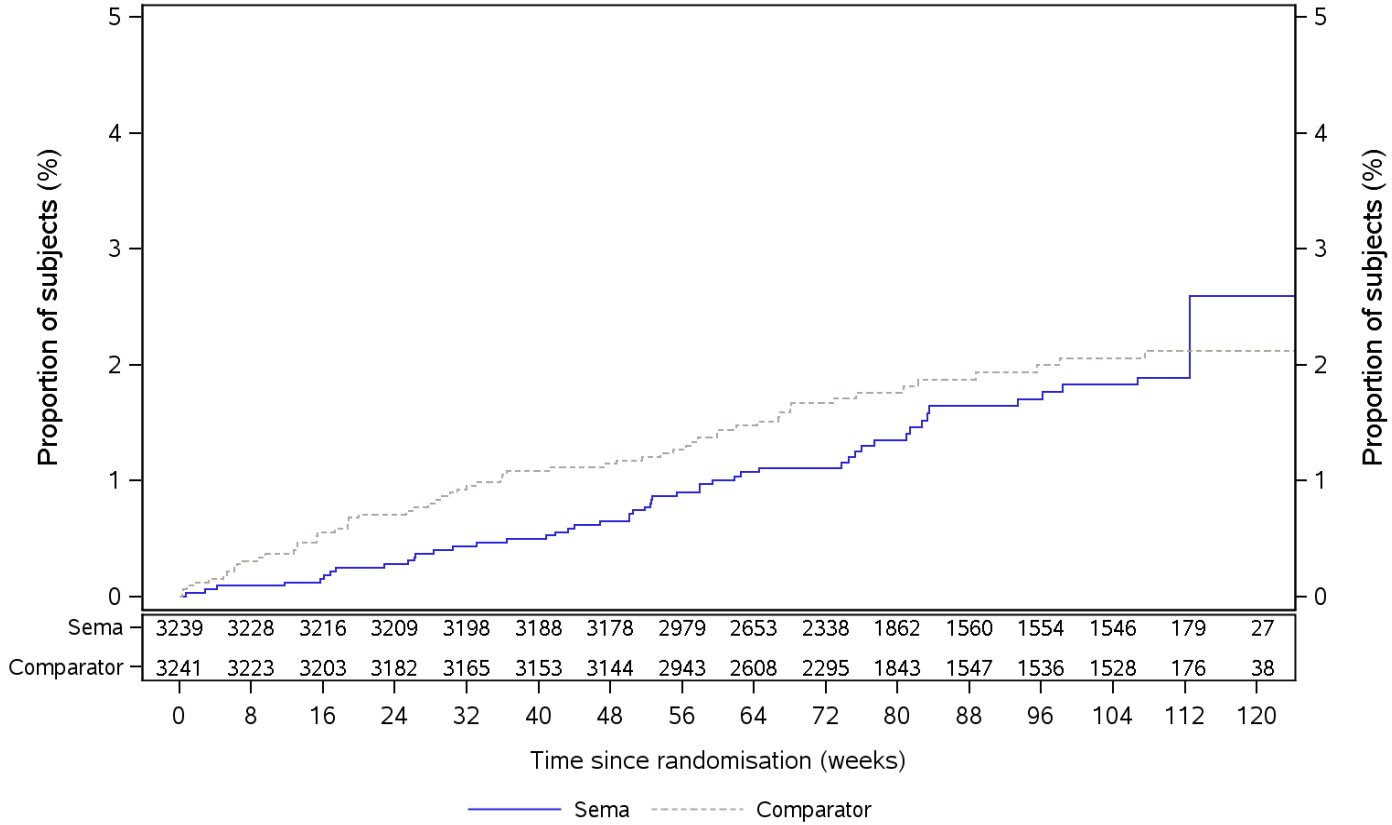
19 Serious adverse events - preferred term "Coronary arterial stent insertion" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:43:14 - f_cif_tte_pool.sas/f_cif_pt_casi_sae_pool.png

20 Serious adverse events - preferred term "Pneumonia" - cumulative incidence plot - Pool - P6 and S6 - in-trial - full analysis set

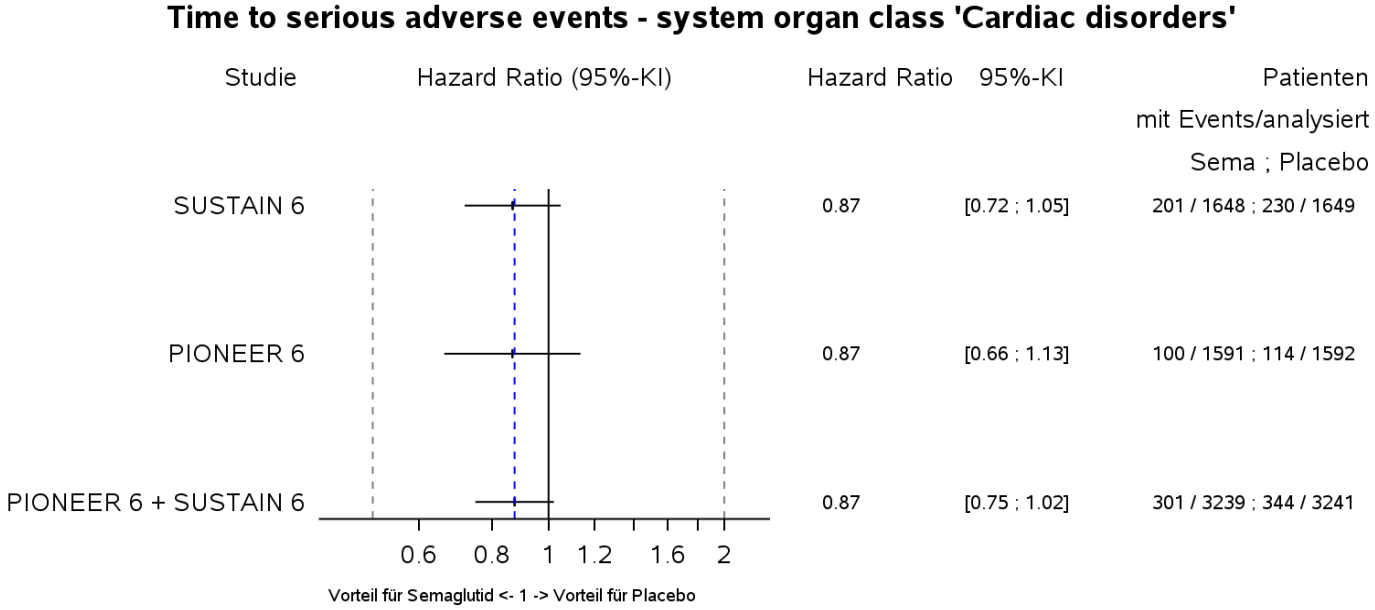


Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
24FEB2020:15:43:58 - f_cif_tte_pool.sas/f_cif_pt_pneu_sae_pool.png

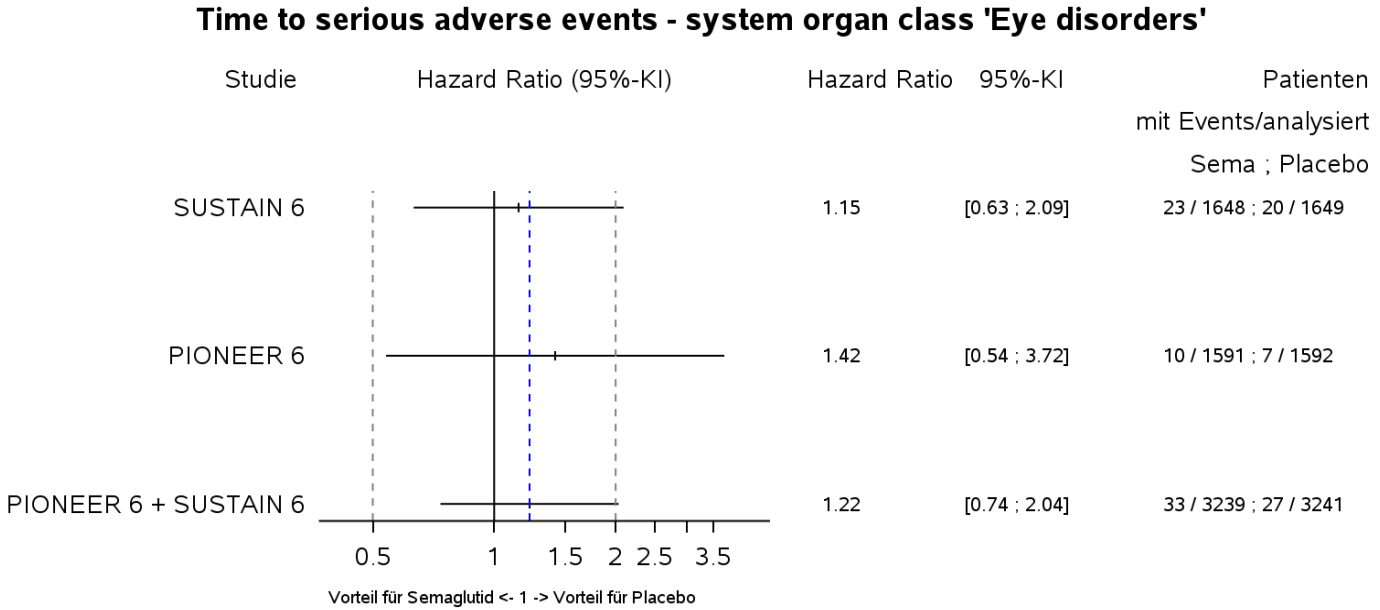
Meta-Analyse PIONEER 6 und SUSTAIN 6 – Forest-Plot (SUE nach SOC und PT)

1 Serious adverse events - system organ class "Cardiac disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



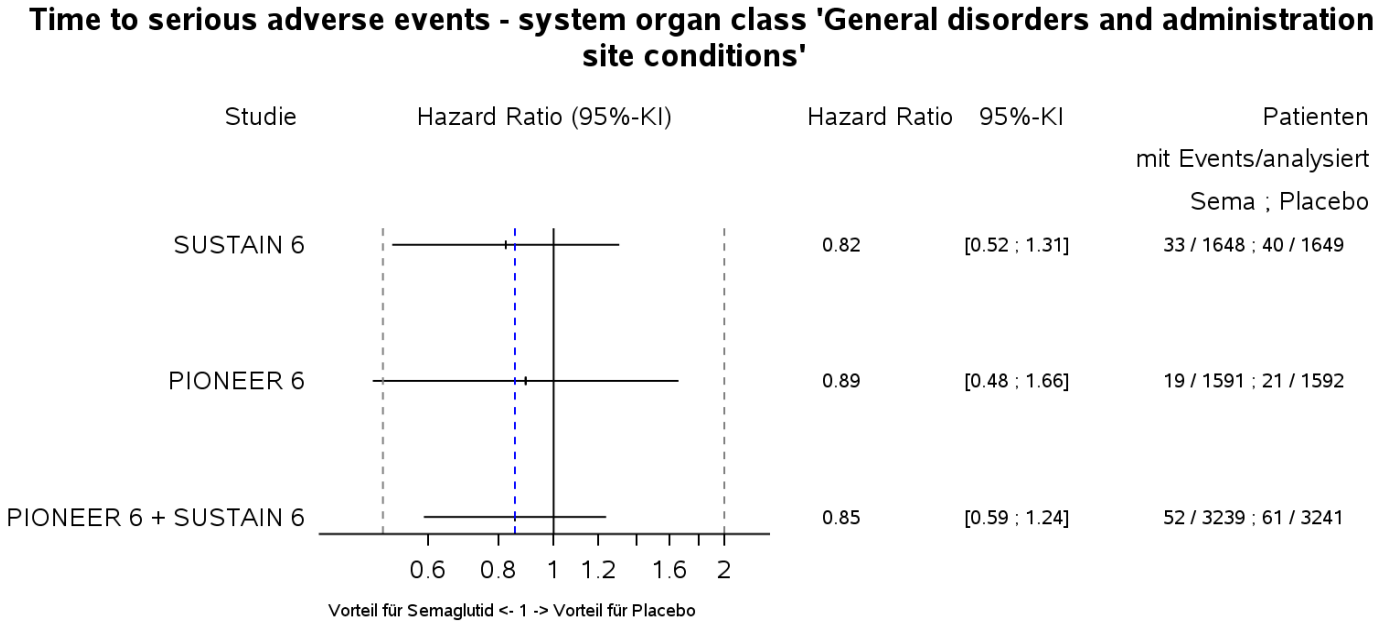
Heterogenität: I-quadrat = 0.0% , p = 0.9381
Test auf Gesamteffekt: p = 0.0895

2 Serious adverse events - system organ class "Eye disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



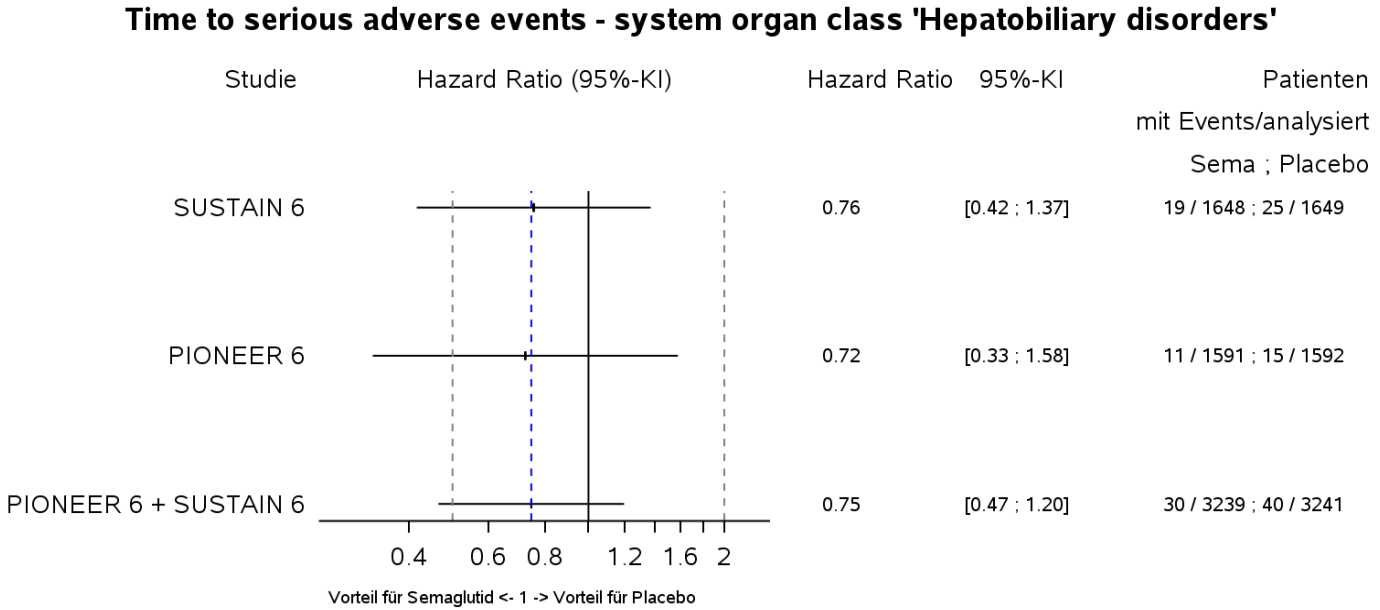
Heterogenität: I-quadrat = 0.0% , p = 0.7254
Test auf Gesamteffekt: p = 0.4365

3 Serious adverse events - system organ class "General disorders and administration site conditions" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



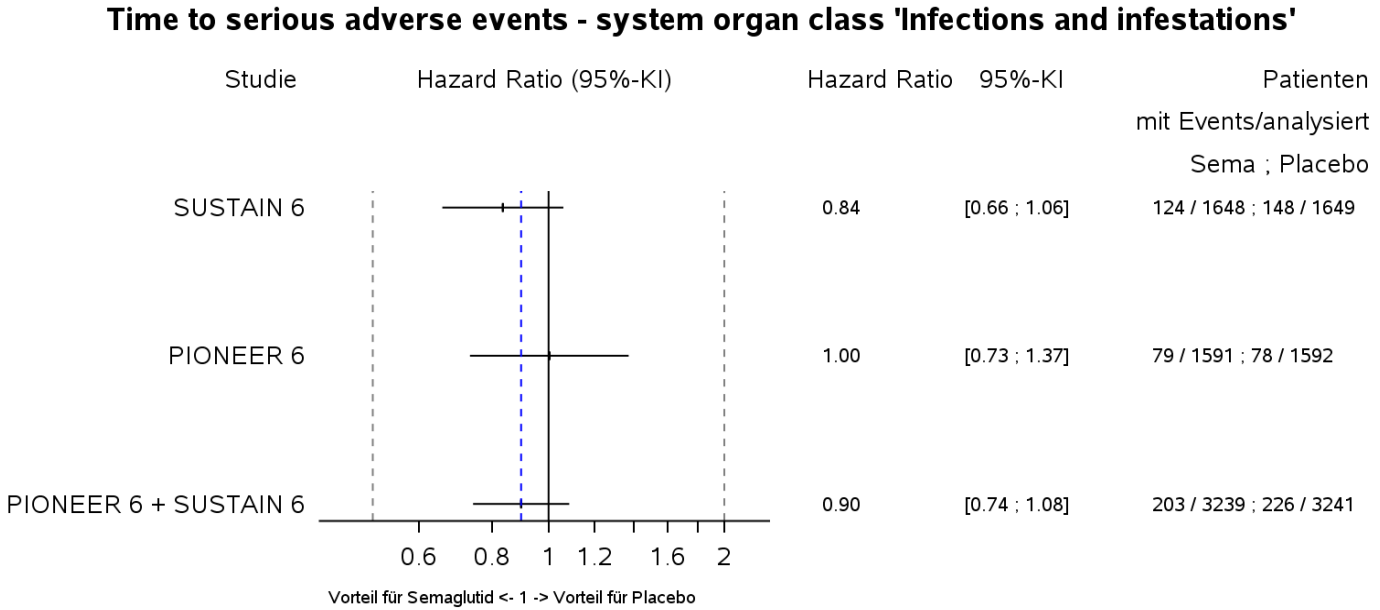
Heterogenität: I-quadrat = 0.0% , p = 0.8652
Test auf Gesamteffekt: p = 0.4060

4 Serious adverse events - system organ class "Hepatobiliary disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



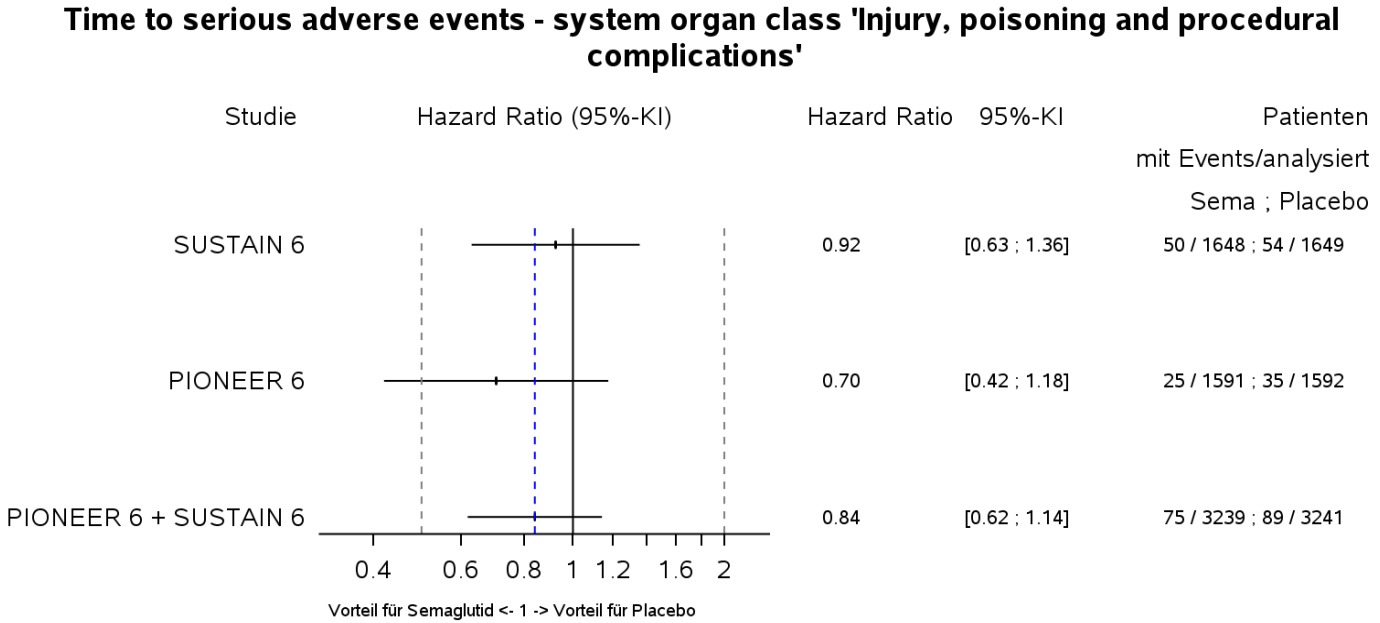
Heterogenität: I-quadrat = 0.0% , p = 0.9230
Test auf Gesamteffekt: p = 0.2270

5 Serious adverse events - system organ class "Infections and infestations" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



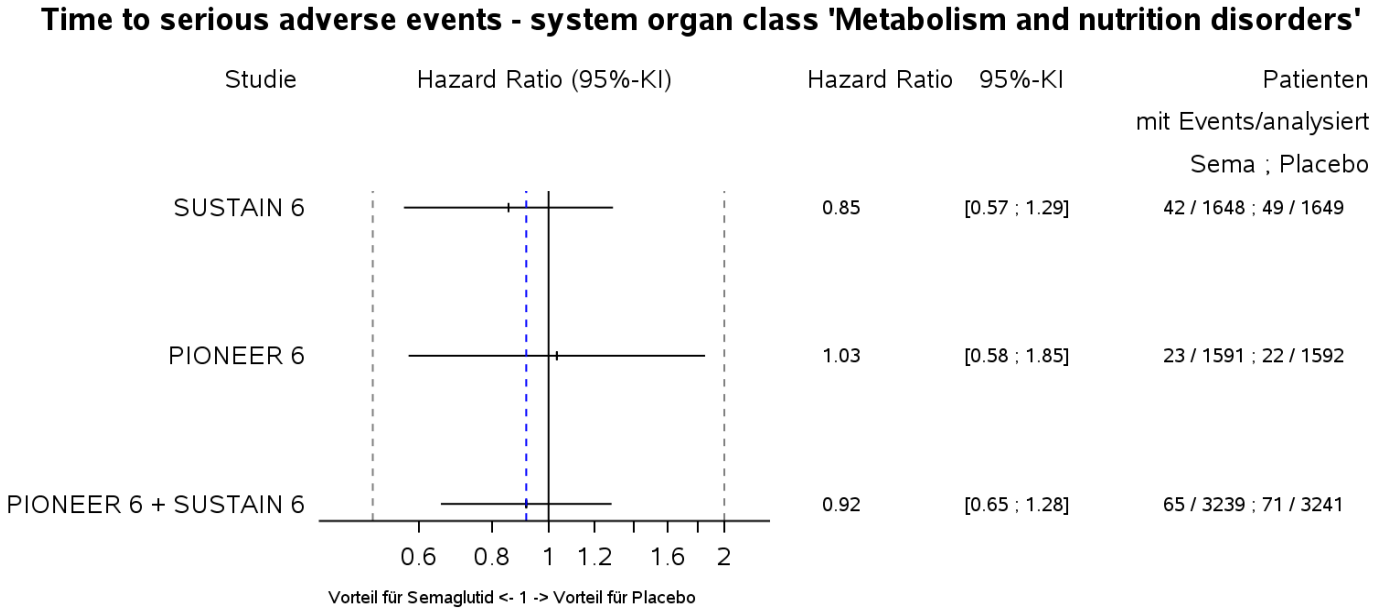
Heterogenität: I-quadrat = 0.0% , p = 0.3830
Test auf Gesamteffekt: p = 0.2636

6 Serious adverse events - system organ class "Injury, poisoning and procedural complications" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



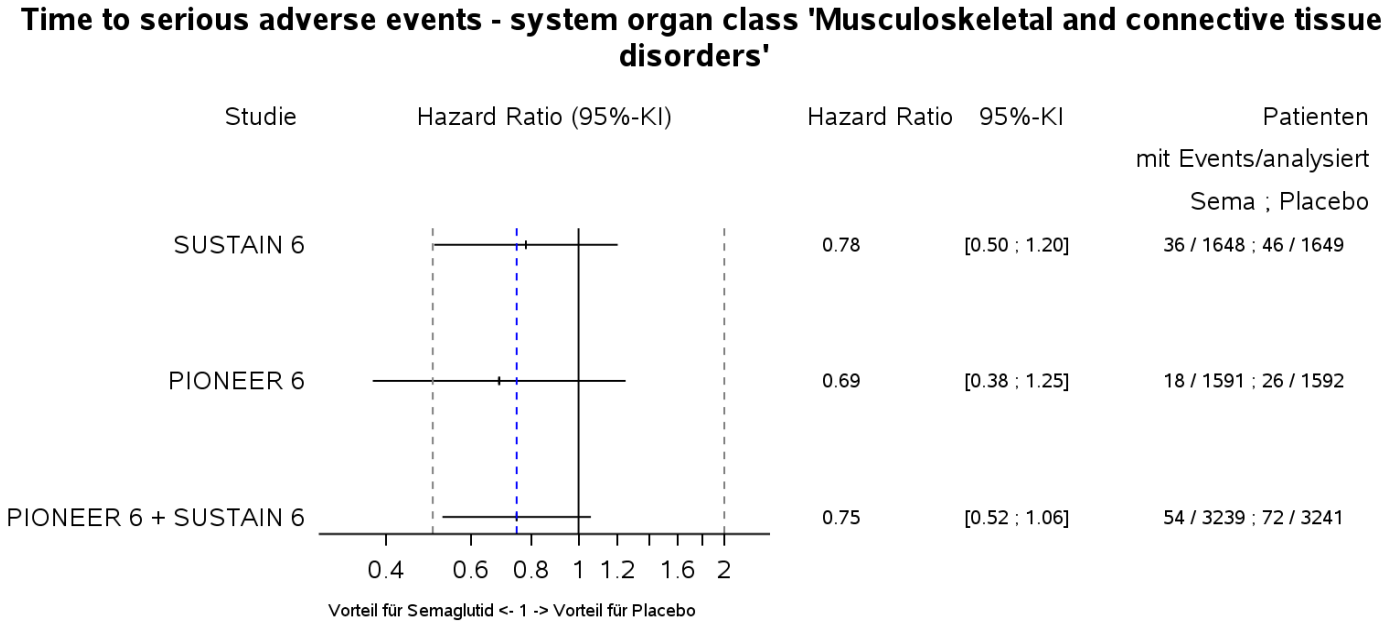
Heterogenität: I-quadrat = 0.0% , p = 0.3965
Test auf Gesamteffekt: p = 0.2659

7 Serious adverse events - system organ class "Metabolism and nutrition disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



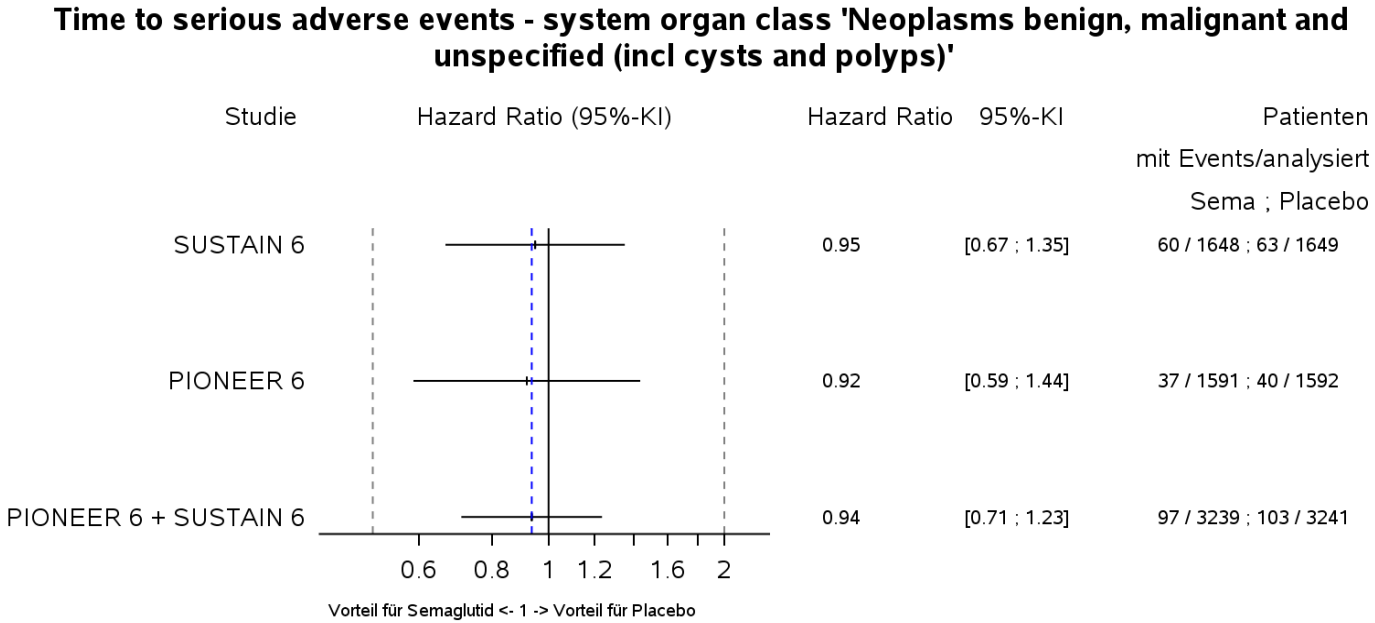
Heterogenität: I-quadrat = 0.0% , p = 0.6212
Test auf Gesamteffekt: p = 0.6081

8 Serious adverse events - system organ class "Musculoskeletal and connective tissue disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



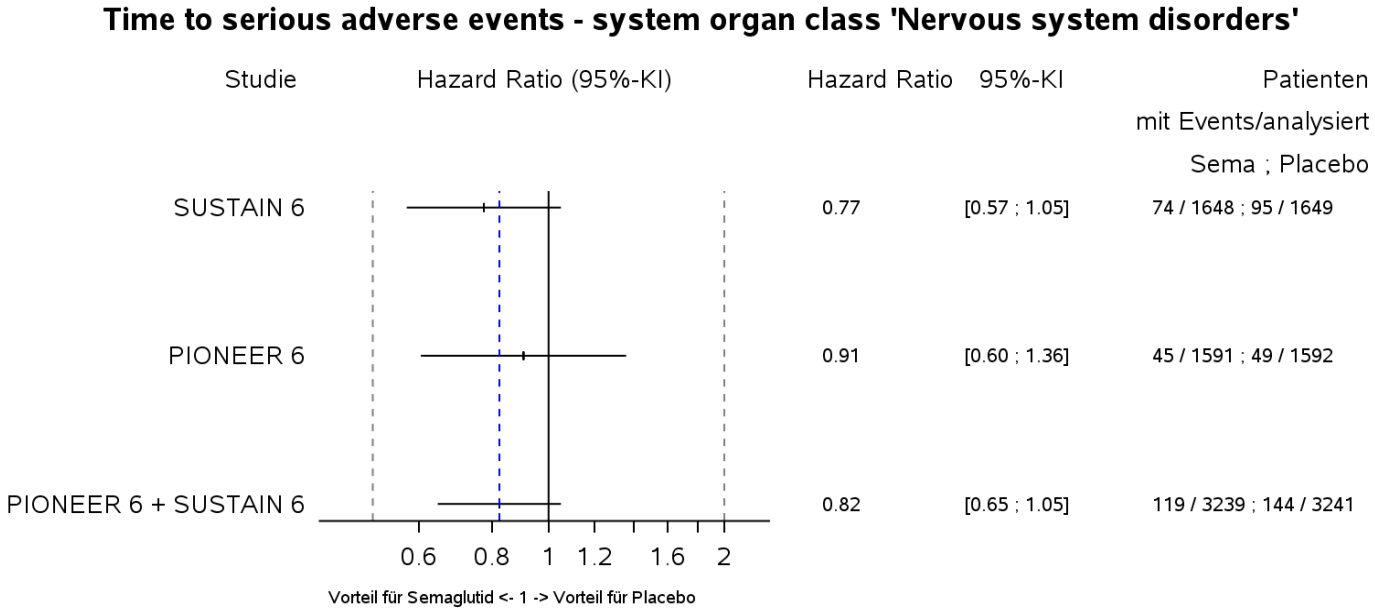
Heterogenität: I-quadrat = 0.0% , p = 0.7370
Test auf Gesamteffekt: p = 0.1023

9 Serious adverse events - system organ class "Neoplasms benign, malignant and unspecified (incl cysts and polyps)" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



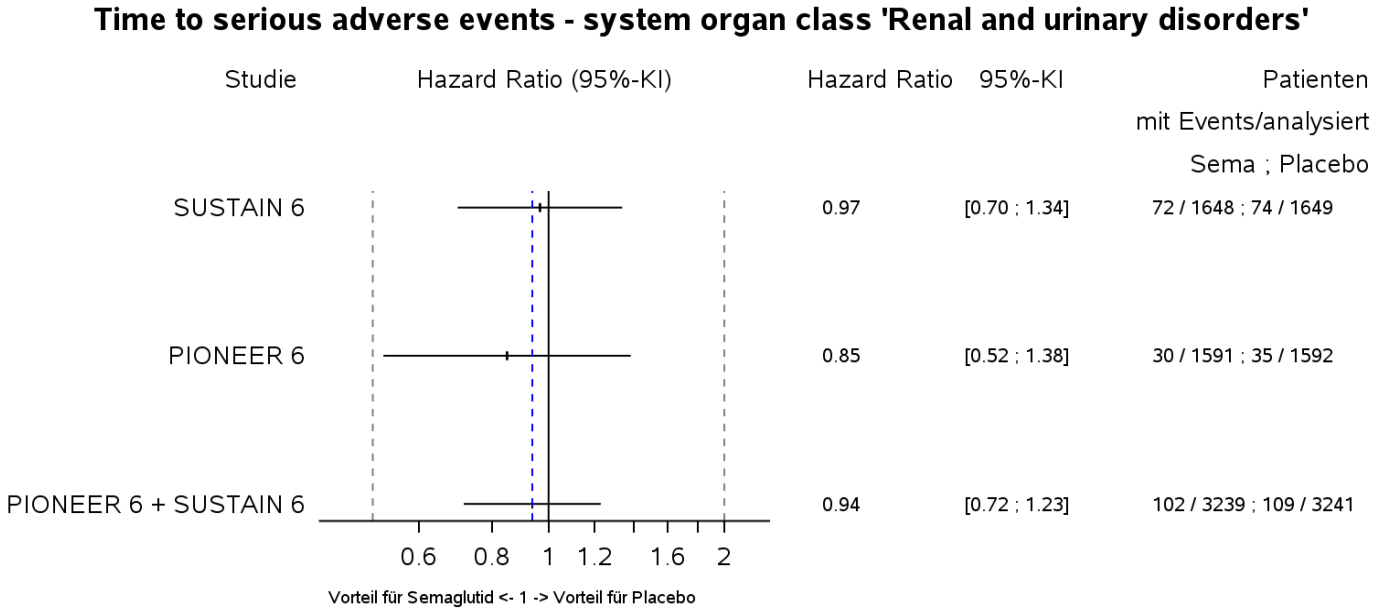
Heterogenität: I-quadrat = 0.0% , p = 0.9147
Test auf Gesamteffekt: p = 0.6379

10 Serious adverse events - system organ class "Nervous system disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



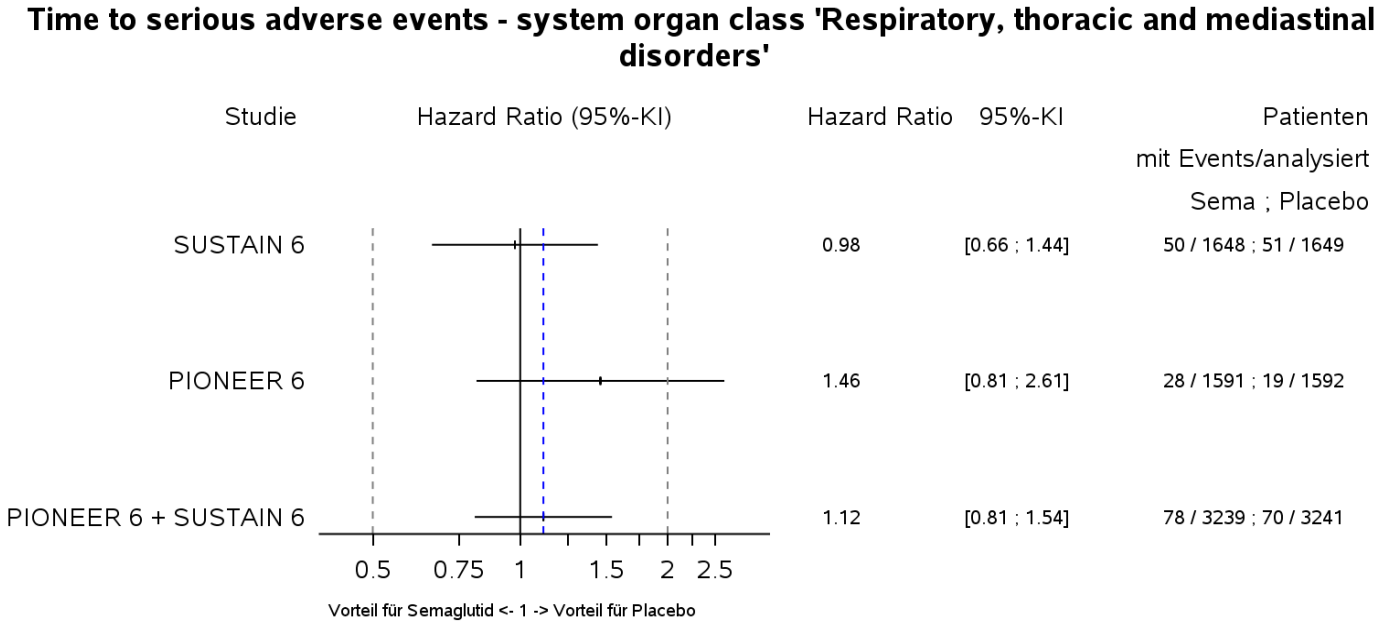
Heterogenität: I-quadrat = 0.0% , p = 0.5650
Test auf Gesamteffekt: p = 0.1172

11 Serious adverse events - system organ class "Renal and urinary disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



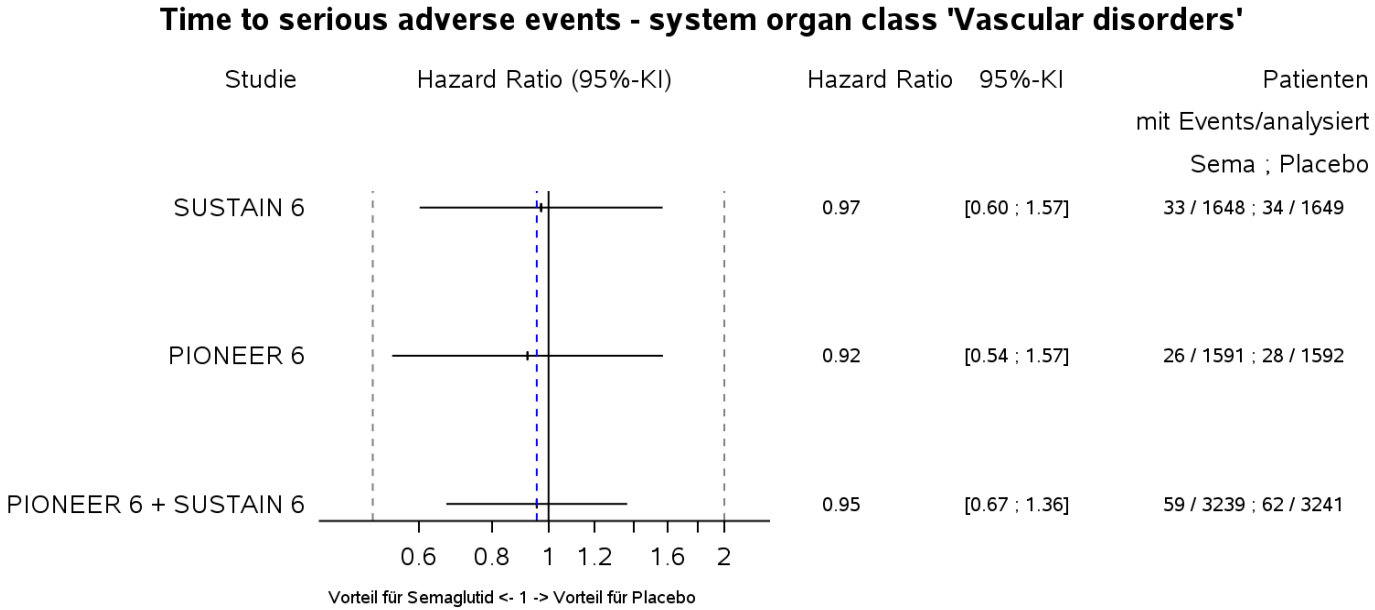
Heterogenität: I-quadrat = 0.0% , p = 0.6303
Test auf Gesamteffekt: p = 0.6408

12 Serious adverse events - system organ class "Respiratory, thoracic and mediastinal disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



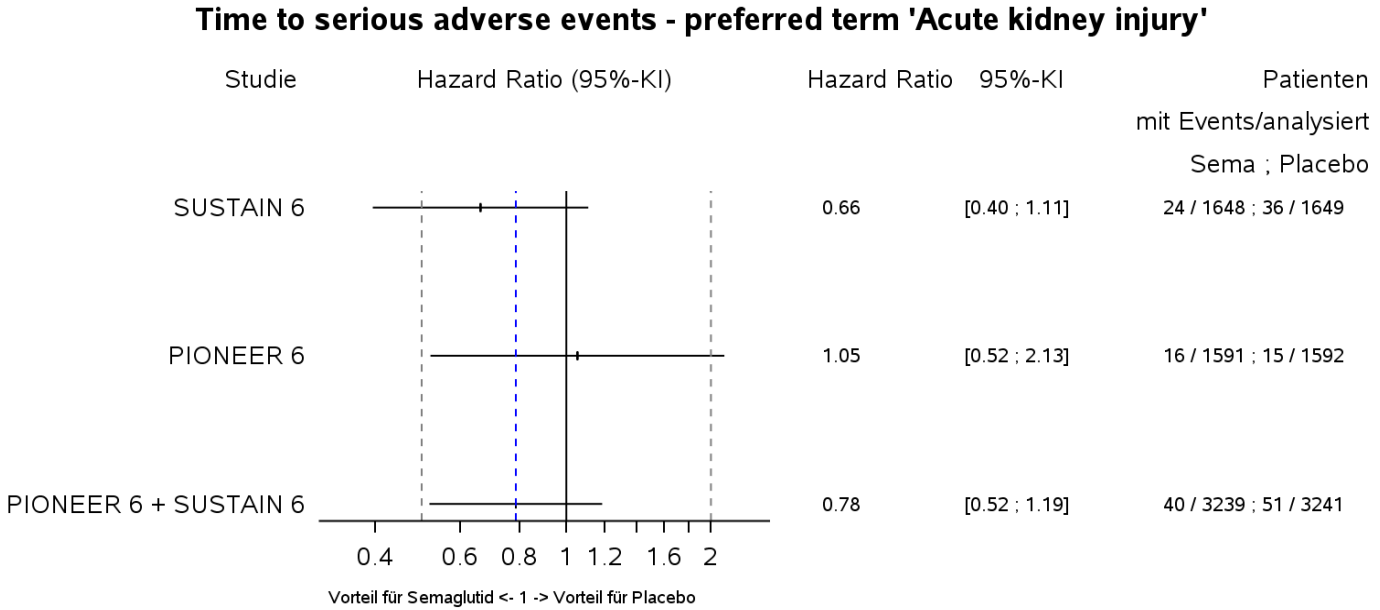
Heterogenität: I-quadrat = 20.8% , p = 0.2746
Test auf Gesamteffekt: p = 0.5082

13 Serious adverse events - system organ class "Vascular disorders" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



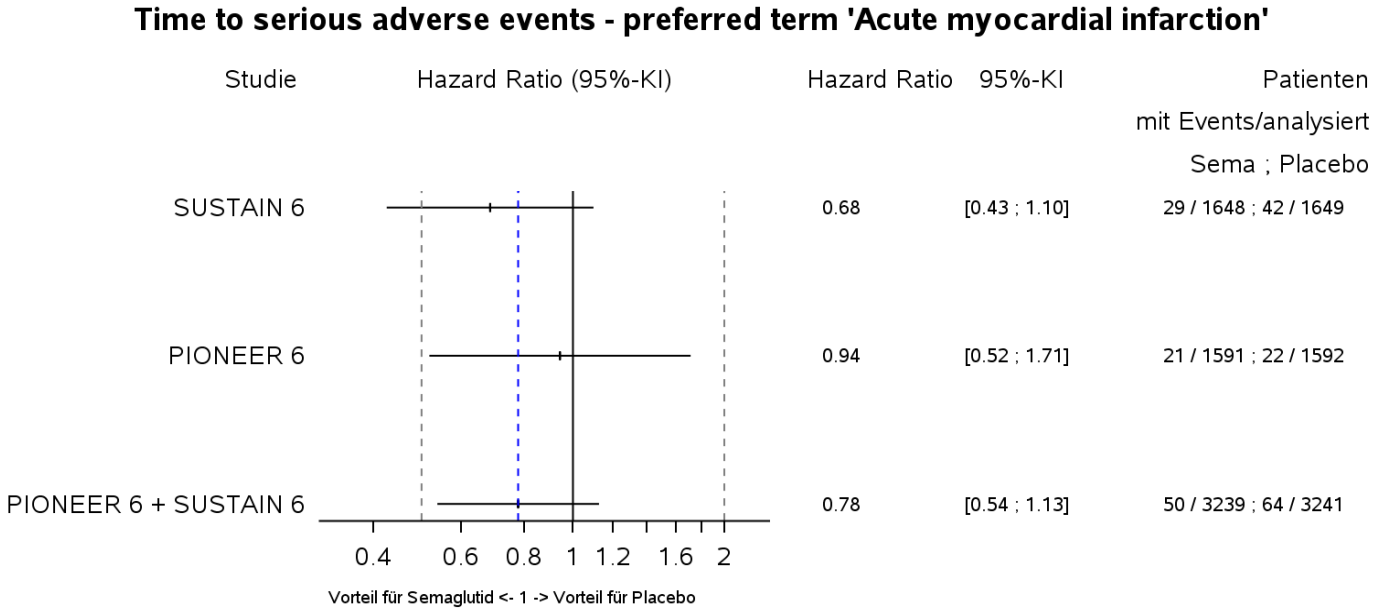
Heterogenität: I-quadrat = 0.0% , p = 0.8575
Test auf Gesamteffekt: p = 0.7982

14 Serious adverse events - preferred term "Acute kidney injury" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



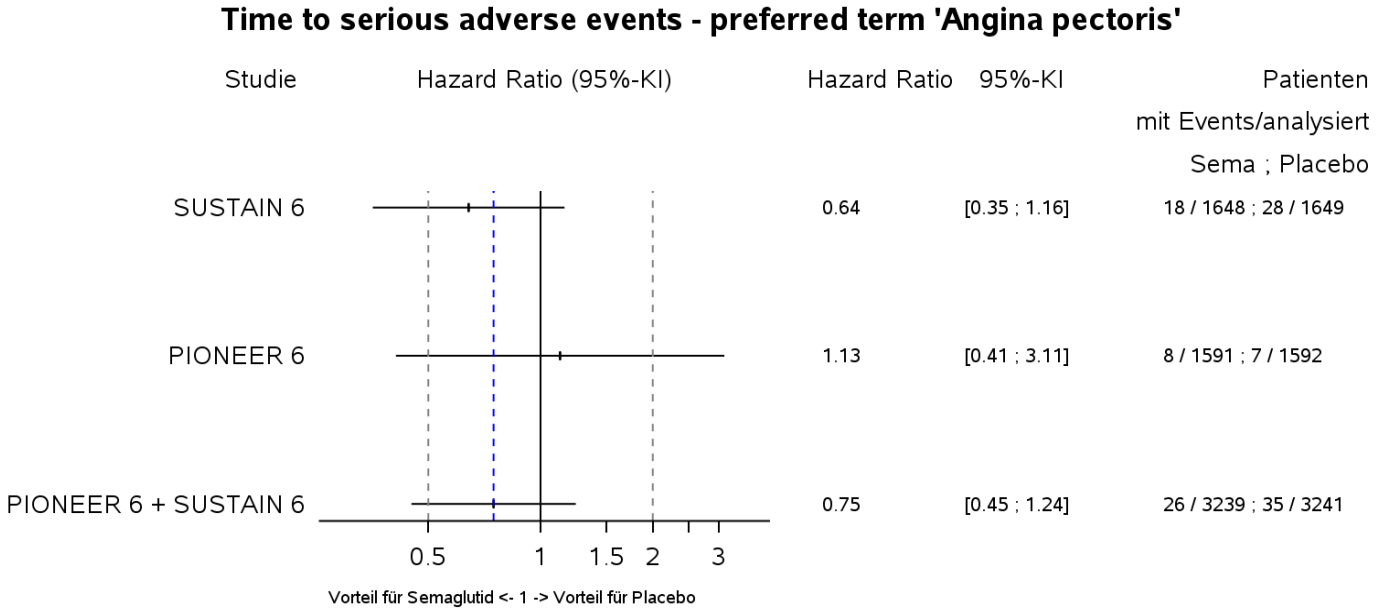
Heterogenität: I-quadrat = 7.9% , p = 0.3109
Test auf Gesamteffekt: p = 0.2516

15 Serious adverse events - preferred term "Acute myocardial infarction" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



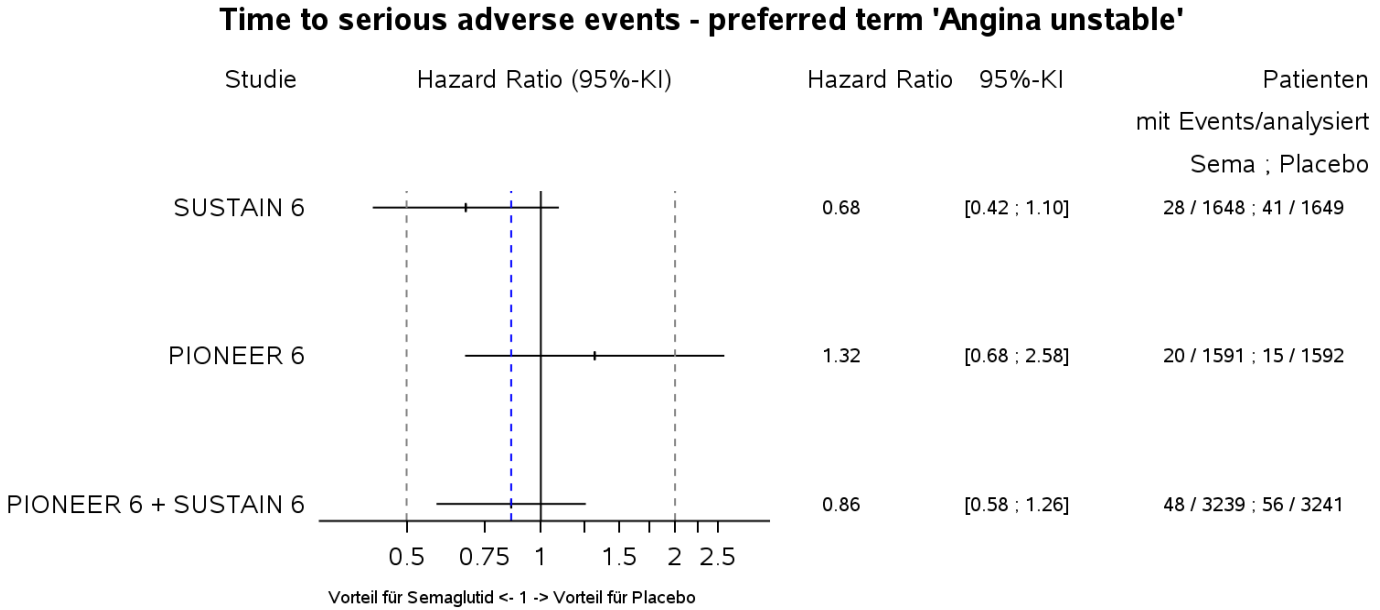
Heterogenität: I-quadrat = 0.0% , p = 0.4263
Test auf Gesamteffekt: p = 0.1841

16 Serious adverse events - preferred term "Angina pectoris" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



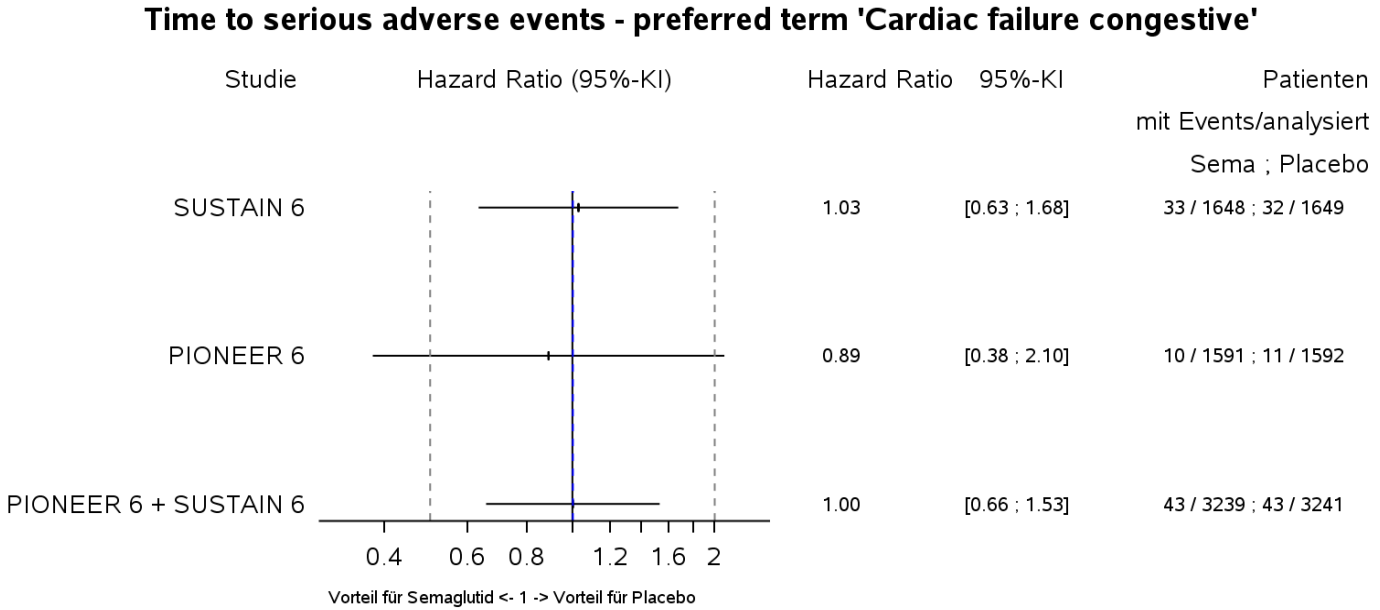
Heterogenität: I-quadrat = 0.0% , p = 0.3594
Test auf Gesamteffekt: p = 0.2631

17 Serious adverse events - preferred term "Angina unstable" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



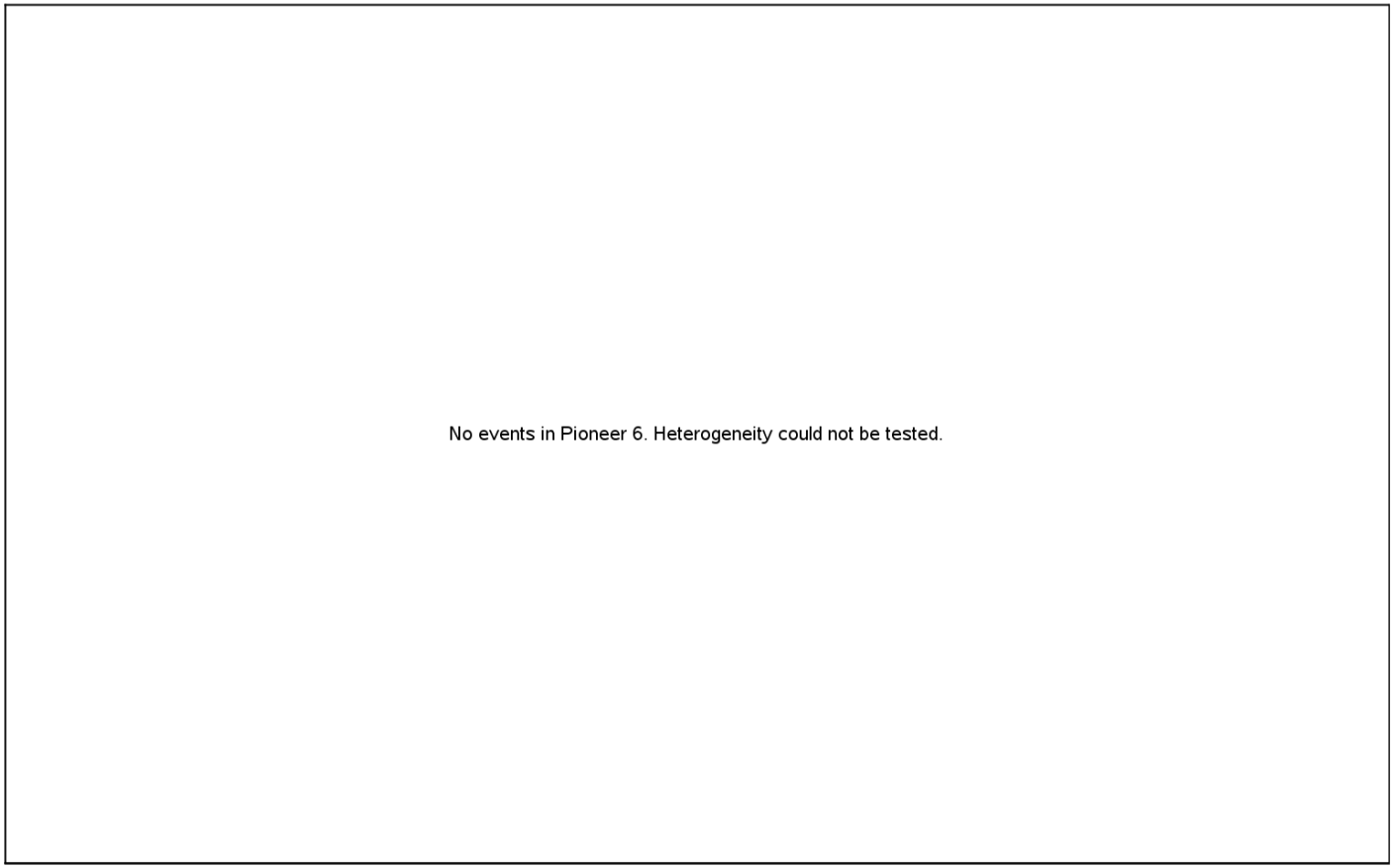
Heterogenität: I-quadrat = 60.1% , p = 0.1199
Test auf Gesamteffekt: p = 0.4360

18 Serious adverse events - preferred term "Cardiac failure congestive" - forest plot - Pool - P6 and S6 - in-trial - full analysis set

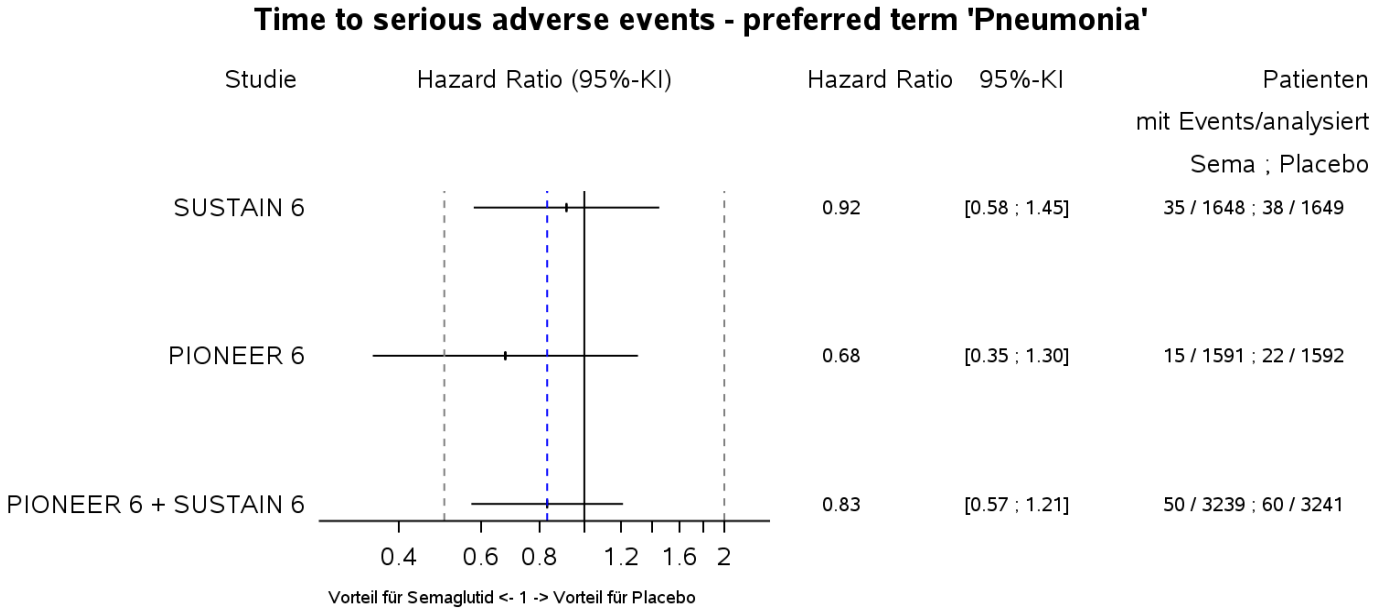


Heterogenität: I-quadrat = 0.0% , p = 0.7551
Test auf Gesamteffekt: p = 0.9911

19 Serious adverse events - preferred term "Coronary arterial stent insertion" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



20 Serious adverse events - preferred term "Pneumonia" - forest plot - Pool - P6 and S6 - in-trial - full analysis set



Heterogenität: I-quadrat = 0.0% , p = 0.4488
Test auf Gesamteffekt: p = 0.3369

Meta-Analyse PIONEER 6 und SUSTAIN 6 – Subgruppenergebnisse

1 EAC-confirmed all-cause death - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	85 (2.6%)	3154 (97.4%)	30 (0.9%)	0 (0.0%)	3241	105 (3.2%)	3136 (96.8%)	46 (1.4%)	0 (0.0%)	0.81 [0.61;1.08]	0.1533	
Gender													0.1524
Female	1142	26 (2.3%)	1116 (97.7%)	12 (1.1%)	0 (0.0%)	1160	23 (2.0%)	1137 (98.0%)	21 (1.8%)	0 (0.0%)	1.15 [0.66;2.02]	0.6201	
Male	2097	59 (2.8%)	2038 (97.2%)	18 (0.9%)	0 (0.0%)	2081	82 (3.9%)	1999 (96.1%)	25 (1.2%)	0 (0.0%)	0.72 [0.51;1.00]	0.0497	
Age													0.9086
< 65	1561	36 (2.3%)	1525 (97.7%)	14 (0.9%)	0 (0.0%)	1479	43 (2.9%)	1436 (97.1%)	28 (1.9%)	0 (0.0%)	0.80 [0.51;1.25]	0.3280	
>= 65	1678	49 (2.9%)	1629 (97.1%)	16 (1.0%)	0 (0.0%)	1762	62 (3.5%)	1700 (96.5%)	18 (1.0%)	0 (0.0%)	0.83 [0.57;1.21]	0.3279	
Region A													0.9110
OECD	2230	58 (2.6%)	2172 (97.4%)	28 (1.3%)	0 (0.0%)	2195	69 (3.1%)	2126 (96.9%)	44 (2.0%)	0 (0.0%)	0.82 [0.58;1.17]	0.2759	
Non-OECD	1009	27 (2.7%)	982 (97.3%)	2 (0.2%)	0 (0.0%)	1046	36 (3.4%)	1010 (96.6%)	2 (0.2%)	0 (0.0%)	0.80 [0.48;1.31]	0.3688	
Region B													0.0781
West Europe	521	12 (2.3%)	509 (97.7%)	4 (0.8%)	0 (0.0%)	475	6 (1.3%)	469 (98.7%)	6 (1.3%)	0 (0.0%)	1.88 [0.71;5.01]	0.2067	
Rest of World	2718	73 (2.7%)	2645 (97.3%)	26 (1.0%)	0 (0.0%)	2766	99 (3.6%)	2667 (96.4%)	40 (1.4%)	0 (0.0%)	0.75 [0.55;1.01]	0.0597	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed all-cause death - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.7737
<= 7.5	983	20 (2.1%)	963 (98.0%)	5 (0.5%)	0 (0.0%)	1052	29 (2.8%)	1023 (97.2%)	13 (1.2%)	0 (0.0%)	0.75 [0.42;1.32]	0.3208	
7.5 <	2246	64 (2.8%)	2182 (97.2%)	25 (1.1%)	0 (0.0%)	2171	75 (3.5%)	2096 (96.5%)	33 (1.5%)	0 (0.0%)	0.83 [0.59;1.15]	0.2598	
Evidence of CV disease at screening													0.8626
CV DISEASE	2703	78 (2.9%)	2625 (97.1%)	26 (1.0%)	0 (0.0%)	2727	96 (3.5%)	2631 (96.5%)	42 (1.5%)	0 (0.0%)	0.82 [0.61;1.10]	0.1880	
CV RISK FACTORS ONLY	536	7 (1.3%)	529 (98.7%)	4 (0.7%)	0 (0.0%)	514	9 (1.7%)	505 (98.2%)	4 (0.8%)	0 (0.0%)	0.75 [0.28;2.01]	0.5627	
Insulin Therapy at baseline													0.7946
No insulin	1315	27 (2.1%)	1288 (97.9%)	18 (1.4%)	0 (0.0%)	1322	37 (2.8%)	1285 (97.2%)	12 (0.9%)	0 (0.0%)	0.73 [0.44;1.20]	0.2094	
Basal only	784	22 (2.8%)	762 (97.2%)	10 (1.3%)	0 (0.0%)	796	24 (3.0%)	772 (97.0%)	19 (2.4%)	0 (0.0%)	0.95 [0.53;1.69]	0.8543	
Insulin (not basal only)	1140	36 (3.1%)	1104 (96.8%)	2 (0.2%)	0 (0.0%)	1123	44 (3.9%)	1079 (96.1%)	15 (1.3%)	0 (0.0%)	0.81 [0.52;1.25]	0.3388	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

2 EAC-confirmed cardiovascular death (including undetermined cause of death) - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	59 (1.8%)	3180 (98.2%)	56 (1.7%)	26 (0.8%)	3241	76 (2.3%)	3165 (97.7%)	75 (2.3%)	29 (0.9%)	0.78 [0.56;1.10]	0.1553	
Gender													0.2734
Female	1142	17 (1.5%)	1125 (98.5%)	21 (1.8%)	9 (0.8%)	1160	16 (1.4%)	1144 (98.6%)	28 (2.4%)	7 (0.6%)	1.09 [0.55;2.15]	0.8130	
Male	2097	42 (2.0%)	2055 (98.0%)	35 (1.7%)	17 (0.8%)	2081	60 (2.9%)	2021 (97.1%)	47 (2.3%)	22 (1.1%)	0.70 [0.47;1.04]	0.0751	
Age													0.6588
< 65	1561	27 (1.8%)	1534 (98.3%)	23 (1.5%)	9 (0.6%)	1479	36 (2.4%)	1443 (97.6%)	35 (2.4%)	7 (0.5%)	0.72 [0.44;1.19]	0.2005	
>= 65	1678	32 (1.9%)	1646 (98.1%)	33 (2.0%)	17 (1.0%)	1762	40 (2.3%)	1722 (97.7%)	40 (2.3%)	22 (1.2%)	0.84 [0.53;1.34]	0.4677	
Region A													0.5292
OECD	2230	40 (1.8%)	2190 (98.2%)	46 (2.1%)	18 (0.8%)	2195	46 (2.1%)	2149 (97.9%)	67 (3.1%)	23 (1.0%)	0.85 [0.56;1.30]	0.4630	
Non-OECD	1009	19 (1.9%)	990 (98.1%)	10 (1.0%)	8 (0.8%)	1046	30 (2.9%)	1016 (97.1%)	8 (0.8%)	6 (0.6%)	0.68 [0.38;1.21]	0.1859	
Region B													0.3237
West Europe	521	5 (1.0%)	516 (99.0%)	11 (2.1%)	7 (1.3%)	475	3 (0.6%)	472 (99.4%)	9 (1.9%)	3 (0.6%)	1.58 [0.38;6.61]	0.5312	
Rest of World	2718	54 (2.0%)	2664 (98.0%)	45 (1.7%)	19 (0.7%)	2766	73 (2.6%)	2693 (97.4%)	66 (2.4%)	26 (0.9%)	0.75 [0.53;1.07]	0.1126	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed cardiovascular death (including undetermined cause of death) - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.4735
<= 7.5	983	14 (1.4%)	969 (98.6%)	11 (1.1%)	6 (0.6%)	1052	16 (1.5%)	1036 (98.5%)	26 (2.5%)	13 (1.2%)	0.96 [0.47;1.96]	0.9076	
7.5 <	2246	44 (2.0%)	2202 (98.0%)	45 (2.0%)	20 (0.9%)	2171	60 (2.8%)	2111 (97.2%)	48 (2.2%)	15 (0.7%)	0.71 [0.48;1.05]	0.0859	
Evidence of CV disease at screening													0.3010
CV DISEASE	2703	54 (2.0%)	2649 (98.0%)	50 (1.8%)	24 (0.9%)	2727	73 (2.7%)	2654 (97.3%)	65 (2.4%)	23 (0.8%)	0.75 [0.52;1.06]	0.1028	
CV RISK FACTORS ONLY	536	5 (0.9%)	531 (99.1%)	6 (1.1%)	2 (0.4%)	514	3 (0.6%)	511 (99.4%)	10 (1.9%)	6 (1.2%)	1.62 [0.39;6.80]	0.5066	
Insulin Therapy at baseline													0.4618
No insulin	1315	16 (1.2%)	1299 (98.8%)	29 (2.2%)	11 (0.8%)	1322	26 (2.0%)	1296 (98.0%)	23 (1.7%)	11 (0.8%)	0.61 [0.33;1.14]	0.1237	
Basal only	784	16 (2.1%)	768 (98.0%)	16 (2.0%)	6 (0.8%)	796	15 (1.9%)	781 (98.1%)	28 (3.5%)	9 (1.1%)	1.11 [0.55;2.25]	0.7704	
Insulin (not basal only)	1140	27 (2.4%)	1113 (97.6%)	11 (1.0%)	9 (0.8%)	1123	35 (3.1%)	1088 (96.9%)	24 (2.1%)	9 (0.8%)	0.77 [0.46;1.27]	0.2978	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

3 EAC-confirmed MACE - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	169 (5.2%)	3070 (94.8%)	51 (1.6%)	22 (0.7%)	3241	222 (6.8%)	3019 (93.2%)	67 (2.1%)	25 (0.8%)	0.76 [0.62;0.92]	0.0062	
Gender													0.2751
Female	1142	49 (4.3%)	1093 (95.7%)	19 (1.7%)	7 (0.6%)	1160	55 (4.7%)	1105 (95.3%)	28 (2.4%)	7 (0.6%)	0.91 [0.62;1.33]	0.6152	
Male	2097	120 (5.7%)	1977 (94.3%)	32 (1.5%)	15 (0.7%)	2081	167 (8.0%)	1914 (92.0%)	39 (1.9%)	18 (0.9%)	0.70 [0.56;0.89]	0.0035	
Age													0.2417
< 65	1561	72 (4.6%)	1489 (95.4%)	22 (1.4%)	8 (0.5%)	1479	103 (6.9%)	1376 (93.0%)	30 (2.0%)	6 (0.4%)	0.66 [0.49;0.90]	0.0078	
>= 65	1678	97 (5.8%)	1581 (94.2%)	29 (1.7%)	14 (0.8%)	1762	119 (6.8%)	1643 (93.2%)	37 (2.1%)	19 (1.1%)	0.85 [0.65;1.11]	0.2201	
Region A													0.5107
OECD	2230	122 (5.5%)	2108 (94.5%)	42 (1.9%)	15 (0.7%)	2195	150 (6.9%)	2045 (93.2%)	59 (2.7%)	19 (0.9%)	0.79 [0.62;1.00]	0.0540	
Non-OECD	1009	47 (4.7%)	962 (95.3%)	9 (0.9%)	7 (0.7%)	1046	72 (6.8%)	974 (93.1%)	8 (0.8%)	6 (0.6%)	0.68 [0.47;0.99]	0.0417	
Region B													0.8790
West Europe	521	23 (4.4%)	498 (95.6%)	10 (1.9%)	6 (1.2%)	475	27 (5.7%)	448 (94.3%)	9 (1.9%)	3 (0.6%)	0.79 [0.45;1.38]	0.4027	
Rest of World	2718	146 (5.4%)	2572 (94.6%)	41 (1.5%)	16 (0.6%)	2766	195 (7.1%)	2571 (93.0%)	58 (2.1%)	22 (0.8%)	0.75 [0.61;0.93]	0.0095	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed MACE - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.6945
<= 7.5	983	41 (4.2%)	942 (95.8%)	9 (0.9%)	4 (0.4%)	1052	55 (5.2%)	997 (94.8%)	21 (2.0%)	11 (1.0%)	0.80 [0.53;1.20]	0.2812	
7.5 <	2246	127 (5.7%)	2119 (94.3%)	42 (1.9%)	18 (0.8%)	2171	167 (7.7%)	2004 (92.3%)	45 (2.1%)	13 (0.6%)	0.73 [0.58;0.92]	0.0073	
Evidence of CV disease at screening													0.9444
CV DISEASE	2703	155 (5.7%)	2548 (94.3%)	45 (1.7%)	20 (0.7%)	2727	205 (7.5%)	2522 (92.5%)	57 (2.1%)	19 (0.7%)	0.75 [0.61;0.93]	0.0082	
CV RISK FACTORS ONLY	536	14 (2.6%)	522 (97.4%)	6 (1.1%)	2 (0.4%)	514	17 (3.3%)	497 (96.7%)	10 (1.9%)	6 (1.2%)	0.77 [0.38;1.57]	0.4795	
Insulin Therapy at baseline													0.4761
No insulin	1315	50 (3.8%)	1265 (96.2%)	28 (2.1%)	10 (0.8%)	1322	77 (5.8%)	1245 (94.2%)	21 (1.6%)	9 (0.7%)	0.64 [0.45;0.92]	0.0147	
Basal only	784	42 (5.4%)	742 (94.6%)	13 (1.7%)	4 (0.5%)	796	48 (6.0%)	748 (94.0%)	26 (3.3%)	8 (1.0%)	0.90 [0.59;1.36]	0.6055	
Insulin (not basal only)	1140	77 (6.7%)	1063 (93.2%)	10 (0.9%)	8 (0.7%)	1123	97 (8.7%)	1026 (91.4%)	20 (1.8%)	8 (0.7%)	0.77 [0.57;1.04]	0.0922	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

4 EAC-confirmed non-fatal myocardial infarction - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	84 (2.6%)	3155 (97.4%)	104 (3.2%)	74 (2.3%)	3241	95 (2.9%)	3146 (97.1%)	141 (4.4%)	98 (3.0%)	0.88 [0.66;1.18]	0.4000	
Gender													0.1419
Female	1142	24 (2.1%)	1118 (97.9%)	32 (2.8%)	20 (1.8%)	1160	19 (1.6%)	1141 (98.4%)	44 (3.8%)	23 (2.0%)	1.30 [0.71;2.37]	0.3949	
Male	2097	60 (2.9%)	2037 (97.1%)	72 (3.4%)	54 (2.6%)	2081	76 (3.7%)	2005 (96.3%)	97 (4.7%)	75 (3.6%)	0.77 [0.55;1.09]	0.1380	
Age													0.2909
< 65	1561	34 (2.2%)	1527 (97.8%)	47 (3.0%)	33 (2.1%)	1479	44 (3.0%)	1435 (97.0%)	65 (4.4%)	40 (2.7%)	0.74 [0.47;1.16]	0.1854	
>= 65	1678	50 (3.0%)	1628 (97.0%)	57 (3.4%)	41 (2.4%)	1762	51 (2.9%)	1711 (97.1%)	76 (4.3%)	58 (3.3%)	1.02 [0.69;1.50]	0.9298	
Region A													0.9563
OECD	2230	61 (2.7%)	2169 (97.3%)	77 (3.5%)	49 (2.2%)	2195	68 (3.1%)	2127 (96.9%)	104 (4.7%)	63 (2.9%)	0.88 [0.62;1.24]	0.4519	
Non-OECD	1009	23 (2.3%)	986 (97.7%)	27 (2.7%)	25 (2.5%)	1046	27 (2.6%)	1019 (97.4%)	37 (3.5%)	35 (3.3%)	0.89 [0.51;1.56]	0.6870	
Region B													0.5800
West Europe	521	10 (1.9%)	511 (98.1%)	14 (2.7%)	10 (1.9%)	475	13 (2.7%)	462 (97.3%)	12 (2.5%)	6 (1.3%)	0.71 [0.31;1.62]	0.4170	
Rest of World	2718	74 (2.7%)	2644 (97.3%)	90 (3.3%)	64 (2.4%)	2766	82 (3.0%)	2684 (97.0%)	129 (4.7%)	92 (3.3%)	0.91 [0.67;1.25]	0.5651	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed non-fatal myocardial infarction - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.4326
<= 7.5	983	23 (2.3%)	960 (97.7%)	21 (2.1%)	16 (1.6%)	1052	23 (2.2%)	1029 (97.8%)	37 (3.5%)	27 (2.6%)	1.07 [0.60;1.91]	0.8203	
7.5 <	2246	61 (2.7%)	2185 (97.3%)	82 (3.7%)	57 (2.5%)	2171	72 (3.3%)	2099 (96.7%)	103 (4.7%)	70 (3.2%)	0.82 [0.58;1.15]	0.2463	
Evidence of CV disease at screening													0.6937
CV DISEASE	2703	78 (2.9%)	2625 (97.1%)	93 (3.4%)	67 (2.5%)	2727	90 (3.3%)	2637 (96.7%)	128 (4.7%)	89 (3.3%)	0.87 [0.64;1.18]	0.3615	
CV RISK FACTORS ONLY	536	6 (1.1%)	530 (98.9%)	11 (2.1%)	7 (1.3%)	514	5 (1.0%)	509 (99.0%)	13 (2.5%)	9 (1.8%)	1.11 [0.34;3.64]	0.8624	
Insulin Therapy at baseline													0.2553
No insulin	1315	23 (1.7%)	1292 (98.3%)	42 (3.2%)	24 (1.8%)	1322	37 (2.8%)	1285 (97.2%)	46 (3.5%)	34 (2.6%)	0.62 [0.37;1.04]	0.0683	
Basal only	784	22 (2.8%)	762 (97.2%)	27 (3.4%)	17 (2.2%)	796	22 (2.8%)	774 (97.2%)	40 (5.0%)	21 (2.6%)	1.02 [0.57;1.85]	0.9358	
Insulin (not basal only)	1140	39 (3.4%)	1101 (96.6%)	35 (3.1%)	33 (2.9%)	1123	36 (3.2%)	1087 (96.8%)	55 (4.9%)	43 (3.8%)	1.06 [0.68;1.67]	0.7869	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

5 EAC-confirmed non-fatal stroke - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	39 (1.2%)	3200 (98.8%)	110 (3.4%)	81 (2.5%)	3241	60 (1.9%)	3181 (98.1%)	145 (4.5%)	100 (3.1%)	0.65 [0.43;0.97]	0.0346	
Gender													0.9905
Female	1142	14 (1.2%)	1128 (98.8%)	36 (3.2%)	24 (2.1%)	1160	22 (1.9%)	1138 (98.1%)	42 (3.6%)	21 (1.8%)	0.65 [0.33;1.26]	0.2001	
Male	2097	25 (1.2%)	2072 (98.8%)	74 (3.5%)	57 (2.7%)	2081	38 (1.8%)	2043 (98.2%)	103 (4.9%)	79 (3.8%)	0.65 [0.39;1.07]	0.0928	
Age													0.3522
< 65	1561	14 (0.9%)	1547 (99.1%)	49 (3.1%)	35 (2.2%)	1479	26 (1.7%)	1453 (98.2%)	69 (4.7%)	42 (2.8%)	0.51 [0.27;0.99]	0.0451	
>= 65	1678	25 (1.5%)	1653 (98.5%)	61 (3.6%)	46 (2.7%)	1762	34 (1.9%)	1728 (98.1%)	76 (4.3%)	58 (3.3%)	0.76 [0.46;1.28]	0.3050	
Region A													0.6710
OECD	2230	30 (1.3%)	2200 (98.7%)	83 (3.7%)	56 (2.5%)	2195	43 (2.0%)	2152 (98.0%)	107 (4.9%)	64 (2.9%)	0.68 [0.43;1.08]	0.1043	
Non-OECD	1009	9 (0.9%)	1000 (99.1%)	27 (2.7%)	25 (2.5%)	1046	17 (1.6%)	1029 (98.4%)	38 (3.6%)	36 (3.4%)	0.56 [0.25;1.25]	0.1534	
Region B													0.4860
West Europe	521	10 (1.9%)	511 (98.1%)	16 (3.1%)	12 (2.3%)	475	11 (2.3%)	464 (97.7%)	12 (2.5%)	6 (1.3%)	0.84 [0.36;1.99]	0.6961	
Rest of World	2718	29 (1.1%)	2689 (98.9%)	94 (3.5%)	69 (2.5%)	2766	49 (1.8%)	2717 (98.2%)	133 (4.8%)	94 (3.4%)	0.60 [0.38;0.94]	0.0276	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed non-fatal stroke - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs. Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.1224
<= 7.5	983	6 (0.6%)	977 (99.4%)	25 (2.5%)	20 (2.0%)	1052	19 (1.8%)	1033 (98.2%)	39 (3.7%)	26 (2.5%)	0.34 [0.14;0.86]	0.0227	
7.5 <	2246	33 (1.5%)	2213 (98.5%)	84 (3.7%)	60 (2.7%)	2171	41 (1.9%)	2130 (98.1%)	105 (4.8%)	73 (3.4%)	0.77 [0.49;1.22]	0.2693	
Evidence of CV disease at screening													0.1740
CV DISEASE	2703	36 (1.3%)	2667 (98.7%)	99 (3.7%)	74 (2.7%)	2727	50 (1.8%)	2677 (98.2%)	133 (4.9%)	92 (3.4%)	0.72 [0.47;1.11]	0.1388	
CV RISK FACTORS ONLY	536	3 (0.6%)	533 (99.4%)	11 (2.1%)	7 (1.3%)	514	10 (2.0%)	504 (98.1%)	12 (2.3%)	8 (1.6%)	0.28 [0.08;1.02]	0.0544	
Insulin Therapy at baseline													0.8149
No insulin	1315	14 (1.1%)	1301 (98.9%)	45 (3.4%)	27 (2.1%)	1322	18 (1.4%)	1304 (98.6%)	46 (3.5%)	34 (2.6%)	0.77 [0.39;1.56]	0.4744	
Basal only	784	9 (1.2%)	775 (98.9%)	30 (3.8%)	21 (2.7%)	796	15 (1.9%)	781 (98.1%)	41 (5.2%)	23 (2.9%)	0.61 [0.27;1.40]	0.2480	
Insulin (not basal only)	1140	16 (1.4%)	1124 (98.6%)	35 (3.1%)	33 (2.9%)	1123	27 (2.4%)	1096 (97.6%)	58 (5.2%)	43 (3.8%)	0.58 [0.31;1.07]	0.0800	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

6 EAC-confirmed unstable angina pectoris requiring hospitalisation - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	33 (1.0%)	3206 (99.0%)	113 (3.5%)	84 (2.6%)	3241	34 (1.0%)	3207 (99.0%)	149 (4.6%)	103 (3.2%)	0.98 [0.60;1.58]	0.9202	
Gender													0.3359
Female	1142	11 (1.0%)	1131 (99.0%)	37 (3.2%)	26 (2.3%)	1160	8 (0.7%)	1152 (99.3%)	44 (3.8%)	23 (2.0%)	1.42 [0.57;3.53]	0.4509	
Male	2097	22 (1.0%)	2075 (99.0%)	76 (3.6%)	58 (2.8%)	2081	26 (1.3%)	2055 (98.8%)	105 (5.0%)	80 (3.8%)	0.84 [0.47;1.48]	0.5422	
Age													0.8201
< 65	1561	17 (1.1%)	1544 (98.9%)	48 (3.1%)	35 (2.2%)	1479	16 (1.1%)	1463 (98.9%)	71 (4.8%)	43 (2.9%)	1.03 [0.52;2.05]	0.9255	
>= 65	1678	16 (1.0%)	1662 (99.0%)	65 (3.9%)	49 (2.9%)	1762	18 (1.0%)	1744 (99.0%)	78 (4.4%)	60 (3.4%)	0.92 [0.47;1.81]	0.8188	
Region A													0.2851
OECD	2230	23 (1.0%)	2207 (99.0%)	84 (3.8%)	57 (2.6%)	2195	27 (1.2%)	2168 (98.8%)	111 (5.1%)	67 (3.1%)	0.83 [0.48;1.45]	0.5215	
Non-OECD	1009	10 (1.0%)	999 (99.0%)	29 (2.9%)	27 (2.7%)	1046	7 (0.7%)	1039 (99.3%)	38 (3.6%)	36 (3.4%)	1.53 [0.58;4.02]	0.3874	
Region B													0.3039
West Europe	521	1 (0.2%)	520 (99.8%)	16 (3.1%)	12 (2.3%)	475	3 (0.6%)	472 (99.4%)	12 (2.5%)	6 (1.3%)	0.31 [0.03;3.00]	0.3126	
Rest of World	2718	32 (1.2%)	2686 (98.8%)	97 (3.6%)	72 (2.6%)	2766	31 (1.1%)	2735 (98.9%)	137 (5.0%)	97 (3.5%)	1.05 [0.64;1.72]	0.8453	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed unstable angina pectoris requiring hospitalisation - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.2417
<= 7.5	983	8 (0.8%)	975 (99.2%)	24 (2.4%)	19 (1.9%)	1052	5 (0.5%)	1047 (99.5%)	41 (3.9%)	28 (2.7%)	1.75 [0.57;5.36]	0.3252	
7.5 <	2246	25 (1.1%)	2221 (98.9%)	88 (3.9%)	64 (2.8%)	2171	29 (1.3%)	2142 (98.7%)	107 (4.9%)	74 (3.4%)	0.84 [0.49;1.43]	0.5118	
Evidence of CV disease at screening													0.9613
CV DISEASE	2703	31 (1.1%)	2672 (98.9%)	103 (3.8%)	78 (2.9%)	2727	32 (1.2%)	2695 (98.8%)	136 (5.0%)	94 (3.4%)	0.98 [0.60;1.60]	0.9320	
CV RISK FACTORS ONLY	536	2 (0.4%)	534 (99.6%)	10 (1.9%)	6 (1.1%)	514	2 (0.4%)	512 (99.6%)	13 (2.5%)	9 (1.8%)	0.93 [0.13;6.61]	0.9429	
Insulin Therapy at baseline													0.4875
No insulin	1315	12 (0.9%)	1303 (99.1%)	44 (3.3%)	27 (2.1%)	1322	13 (1.0%)	1309 (99.0%)	49 (3.7%)	37 (2.8%)	0.92 [0.42;2.03]	0.8448	
Basal only	784	6 (0.8%)	778 (99.2%)	32 (4.1%)	22 (2.8%)	796	10 (1.3%)	786 (98.7%)	42 (5.3%)	23 (2.9%)	0.62 [0.23;1.71]	0.3556	
Insulin (not basal only)	1140	15 (1.3%)	1125 (98.7%)	37 (3.2%)	35 (3.1%)	1123	11 (1.0%)	1112 (99.0%)	58 (5.2%)	43 (3.8%)	1.34 [0.62;2.93]	0.4564	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

7 EAC-confirmed heart failure requiring hospitalisation - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	80 (2.5%)	3159 (97.5%)	97 (3.0%)	67 (2.1%)	3241	78 (2.4%)	3163 (97.6%)	135 (4.2%)	91 (2.8%)	1.03 [0.75;1.40]	0.8677	
Gender													0.7420
Female	1142	24 (2.1%)	1118 (97.9%)	30 (2.6%)	18 (1.6%)	1160	26 (2.2%)	1134 (97.8%)	42 (3.6%)	22 (1.9%)	0.95 [0.54;1.65]	0.8529	
Male	2097	56 (2.7%)	2041 (97.3%)	67 (3.2%)	49 (2.3%)	2081	52 (2.5%)	2029 (97.5%)	93 (4.5%)	69 (3.3%)	1.06 [0.73;1.55]	0.7544	
Age													0.4194
< 65	1561	34 (2.2%)	1527 (97.8%)	41 (2.6%)	27 (1.7%)	1479	27 (1.8%)	1452 (98.2%)	62 (4.2%)	35 (2.4%)	1.22 [0.74;2.02]	0.4431	
>= 65	1678	46 (2.7%)	1632 (97.3%)	56 (3.3%)	40 (2.4%)	1762	51 (2.9%)	1711 (97.1%)	73 (4.1%)	56 (3.2%)	0.93 [0.63;1.39]	0.7402	
Region A													0.2778
OECD	2230	59 (2.6%)	2171 (97.4%)	73 (3.3%)	45 (2.0%)	2195	62 (2.8%)	2133 (97.2%)	103 (4.7%)	61 (2.8%)	0.93 [0.65;1.32]	0.6779	
Non-OECD	1009	21 (2.1%)	988 (97.9%)	24 (2.4%)	22 (2.2%)	1046	16 (1.5%)	1030 (98.5%)	32 (3.1%)	30 (2.9%)	1.40 [0.73;2.68]	0.3125	
Region B													0.1330
West Europe	521	6 (1.1%)	515 (98.8%)	15 (2.9%)	11 (2.1%)	475	11 (2.3%)	464 (97.7%)	11 (2.3%)	5 (1.1%)	0.50 [0.19;1.36]	0.1748	
Rest of World	2718	74 (2.7%)	2644 (97.3%)	82 (3.0%)	56 (2.1%)	2766	67 (2.4%)	2699 (97.6%)	124 (4.5%)	86 (3.1%)	1.12 [0.81;1.56]	0.4964	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed heart failure requiring hospitalisation - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.5481
<= 7.5	983	21 (2.2%)	962 (97.9%)	21 (2.1%)	16 (1.6%)	1052	19 (1.8%)	1033 (98.2%)	39 (3.7%)	27 (2.6%)	1.20 [0.65;2.24]	0.5570	
7.5 <	2246	59 (2.6%)	2187 (97.4%)	75 (3.3%)	50 (2.2%)	2171	59 (2.7%)	2112 (97.3%)	95 (4.4%)	63 (2.9%)	0.97 [0.67;1.39]	0.8535	
Evidence of CV disease at screening													0.8165
CV DISEASE	2703	72 (2.7%)	2631 (97.3%)	87 (3.2%)	61 (2.3%)	2727	70 (2.6%)	2657 (97.4%)	122 (4.5%)	82 (3.0%)	1.04 [0.75;1.44]	0.8168	
CV RISK FACTORS ONLY	536	8 (1.4%)	528 (98.5%)	10 (1.9%)	6 (1.1%)	514	8 (1.6%)	506 (98.4%)	13 (2.5%)	9 (1.8%)	0.92 [0.35;2.45]	0.8673	
Insulin Therapy at baseline													0.6474
No insulin	1315	19 (1.4%)	1296 (98.6%)	41 (3.1%)	23 (1.7%)	1322	19 (1.4%)	1303 (98.6%)	45 (3.4%)	33 (2.5%)	1.01 [0.53;1.90]	0.9831	
Basal only	784	27 (3.5%)	757 (96.6%)	22 (2.8%)	12 (1.5%)	796	22 (2.8%)	774 (97.2%)	39 (4.9%)	21 (2.6%)	1.26 [0.72;2.22]	0.4177	
Insulin (not basal only)	1140	34 (3.0%)	1106 (97.0%)	34 (3.0%)	32 (2.8%)	1123	37 (3.3%)	1086 (96.7%)	51 (4.5%)	37 (3.3%)	0.89 [0.56;1.42]	0.6307	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

8 EAC-confirmed transient ischemic attack - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	15 (0.5%)	3224 (99.5%)	114 (3.5%)	84 (2.6%)	3241	22 (0.7%)	3219 (99.3%)	149 (4.6%)	104 (3.2%)	0.69 [0.36;1.32]	0.2605	
Gender													0.0884
Female	1142	9 (0.8%)	1133 (99.2%)	37 (3.2%)	25 (2.2%)	1160	7 (0.6%)	1153 (99.4%)	44 (3.8%)	23 (2.0%)	1.31 [0.49;3.52]	0.5900	
Male	2097	6 (0.3%)	2091 (99.7%)	77 (3.7%)	59 (2.8%)	2081	15 (0.7%)	2066 (99.3%)	105 (5.0%)	81 (3.9%)	0.40 [0.15;1.03]	0.0574	
Age													0.4929
< 65	1561	6 (0.4%)	1555 (99.6%)	49 (3.1%)	35 (2.2%)	1479	6 (0.4%)	1473 (99.6%)	70 (4.7%)	43 (2.9%)	0.96 [0.31;2.99]	0.9483	
>= 65	1678	9 (0.5%)	1669 (99.5%)	65 (3.9%)	49 (2.9%)	1762	16 (0.9%)	1746 (99.1%)	79 (4.5%)	61 (3.5%)	0.59 [0.26;1.34]	0.2071	
Region A													0.9868
OECD	2230	14 (0.6%)	2216 (99.4%)	85 (3.8%)	57 (2.6%)	2195	22 (1.0%)	2173 (99.0%)	111 (5.1%)	68 (3.1%)	0.63 [0.32;1.22]	0.1708	
Non-OECD	1009	1 (0.1%)	1008 (99.9%)	29 (2.9%)	27 (2.7%)	1046	0 (0.0%)	1046 (100%)	38 (3.6%)	36 (3.4%)	Not est	Not est	
Region B													0.0545
West Europe	521	1 (0.2%)	520 (99.8%)	16 (3.1%)	12 (2.3%)	475	8 (1.7%)	467 (98.3%)	12 (2.5%)	6 (1.3%)	0.12 [0.01;0.94]	0.0430	
Rest of World	2718	14 (0.5%)	2704 (99.5%)	98 (3.6%)	72 (2.6%)	2766	14 (0.5%)	2752 (99.5%)	137 (5.0%)	98 (3.5%)	1.02 [0.49;2.14]	0.9594	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed transient ischemic attack - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.1111
<= 7.5	983	2 (0.2%)	981 (99.8%)	25 (2.5%)	20 (2.0%)	1052	9 (0.8%)	1043 (99.1%)	41 (3.9%)	29 (2.8%)	0.24 [0.05;1.12]	0.0689	
7.5 <	2246	13 (0.6%)	2233 (99.4%)	88 (3.9%)	63 (2.8%)	2171	13 (0.6%)	2158 (99.4%)	107 (4.9%)	74 (3.4%)	0.97 [0.45;2.10]	0.9419	
Evidence of CV disease at screening													0.7763
CV DISEASE	2703	14 (0.5%)	2689 (99.5%)	103 (3.8%)	77 (2.8%)	2727	20 (0.7%)	2707 (99.3%)	136 (5.0%)	95 (3.5%)	0.71 [0.36;1.40]	0.3174	
CV RISK FACTORS ONLY	536	1 (0.2%)	535 (99.8%)	11 (2.1%)	7 (1.3%)	514	2 (0.4%)	512 (99.6%)	13 (2.5%)	9 (1.8%)	0.49 [0.04;5.42]	0.5620	
Insulin Therapy at baseline													0.8059
No insulin	1315	4 (0.3%)	1311 (99.7%)	45 (3.4%)	27 (2.1%)	1322	8 (0.6%)	1314 (99.4%)	49 (3.7%)	37 (2.8%)	0.50 [0.15;1.66]	0.2578	
Basal only	784	5 (0.6%)	779 (99.4%)	32 (4.1%)	22 (2.8%)	796	6 (0.8%)	790 (99.2%)	42 (5.3%)	23 (2.9%)	0.86 [0.26;2.83]	0.8070	
Insulin (not basal only)	1140	6 (0.5%)	1134 (99.5%)	37 (3.2%)	35 (3.1%)	1123	8 (0.7%)	1115 (99.3%)	58 (5.2%)	44 (3.9%)	0.74 [0.26;2.14]	0.5838	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).

9 HbA1c (%) - ANCOVA - Pool - P6 and S6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	3239	3229	2969	8.44 (1.5)	7.28 (1.4)	-1.13 (0.0)	3241	3223	2934	8.44 (1.6)	8.04 (1.5)	-0.37 (0.0)	-0.76 [-0.83;-0.70] <0.0001	-0.52 [-0.57;-0.47]	
Gender															0.0179*
Female	1142	1140	1047	8.57 (1.6)	7.30 (1.4)	-1.15 (0.0)	1160	1153	1040	8.65 (1.7)	8.20 (1.5)	-0.29 (0.0)	-0.87 [-0.97;-0.76] <0.0001	-0.55 [-0.64;-0.46]	
Male	2097	2089	1922	8.36 (1.5)	7.27 (1.3)	-1.12 (0.0)	2081	2070	1894	8.32 (1.5)	7.95 (1.4)	-0.41 (0.0)	-0.71 [-0.79;-0.63] <0.0001	-0.50 [-0.57;-0.44]	
Age															0.0258*
< 65	1561	1558	1435	8.68 (1.7)	7.40 (1.4)	-1.12 (0.0)	1479	1473	1333	8.70 (1.7)	8.25 (1.6)	-0.27 (0.0)	-0.84 [-0.93;-0.75] <0.0001	-0.51 [-0.58;-0.43]	
>= 65	1678	1671	1534	8.21 (1.4)	7.17 (1.3)	-1.14 (0.0)	1762	1750	1601	8.22 (1.5)	7.86 (1.3)	-0.44 (0.0)	-0.70 [-0.79;-0.61] <0.0001	-0.54 [-0.61;-0.47]	
Region A															<0.0001*
OECD	2230	2224	2013	8.35 (1.5)	7.28 (1.4)	-1.09 (0.0)	2195	2184	1949	8.30 (1.5)	7.92 (1.4)	-0.42 (0.0)	-0.67 [-0.74;-0.59] <0.0001	-0.49 [-0.56;-0.43]	
Non-OECD	1009	1005	956	8.63 (1.6)	7.28 (1.3)	-1.21 (0.0)	1046	1039	985	8.72 (1.7)	8.28 (1.6)	-0.25 (0.0)	-0.96 [-1.07;-0.85] <0.0001	-0.58 [-0.67;-0.48]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an
observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, trial (Pioneer 6, Sustain 6), stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

HbA1c (%) - ANCOVA - Pool - P6 and S6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region B															0.0006*
West Europe	521	518	479	8.03 (1.3)	7.22 (1.3)	-1.01 (0.1)	475	471	452	7.91 (1.2)	7.69 (1.2)	-0.49 (0.1)	-0.51 [-0.67;-0.35] <0.0001	-0.49 [-0.62;-0.36]	
Rest of World	2718	2711	2490	8.52 (1.6)	7.29 (1.4)	-1.15 (0.0)	2766	2752	2482	8.53 (1.6)	8.10 (1.5)	-0.34 (0.0)	-0.81 [-0.88;-0.74] <0.0001	-0.53 [-0.59;-0.47]	
HbA1c at baseline (disease severity)**															<0.0001*
<= 7.5	983	983	914	6.92 (0.5)	6.58 (0.8)	-0.32 (0.0)	1052	1052	967	6.93 (0.5)	7.17 (1.0)	0.26 (0.0)	-0.59 [-0.70;-0.48] <0.0001	-0.70 [-0.79;-0.60]	
7.5 <	2246	2246	2047	9.10 (1.4)	7.59 (1.4)	-1.51 (0.0)	2171	2171	1954	9.17 (1.4)	8.47 (1.5)	-0.65 (0.0)	-0.86 [-0.93;-0.78] <0.0001	-0.51 [-0.58;-0.45]	
Evidence of CV disease at screening															0.0757
CV DISEASE	2703	2694	2460	8.43 (1.5)	7.30 (1.4)	-1.10 (0.0)	2727	2714	2450	8.43 (1.6)	8.04 (1.5)	-0.36 (0.0)	-0.74 [-0.81;-0.67] <0.0001	-0.49 [-0.55;-0.44]	
CV RISK FACTORS ONLY	536	535	509	8.49 (1.5)	7.20 (1.2)	-1.26 (0.1)	514	509	484	8.47 (1.5)	8.06 (1.4)	-0.37 (0.1)	-0.89 [-1.04;-0.74] <0.0001	-0.64 [-0.77;-0.51]	
Insulin Therapy at baseline															0.7601

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, trial (Pioneer 6, Sustain 6), stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

HbA1c (%) - ANCOVA - Pool - P6 and S6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
No insulin	1315	1314	1206	8.13 (1.5)	6.93 (1.2)	-1.34 (0.0)	1322	1319	1212	8.08 (1.5)	7.68 (1.4)	-0.57 (0.0)	-0.77 [-0.86;-0.67] <0.0001	-0.55 [-0.63;-0.46]	
Basal only	784	783	713	8.69 (1.5)	7.50 (1.4)	-1.04 (0.0)	796	791	716	8.67 (1.5)	8.29 (1.4)	-0.24 (0.0)	-0.80 [-0.93;-0.68] <0.0001	-0.53 [-0.64;-0.43]	
Insulin (not basal only)	1140	1132	1050	8.62 (1.5)	7.53 (1.4)	-0.94 (0.0)	1123	1113	1006	8.69 (1.6)	8.29 (1.5)	-0.20 (0.0)	-0.74 [-0.84;-0.64] <0.0001	-0.48 [-0.57;-0.39]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, trial (Pioneer 6, Sustain 6), stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

10 Body weight (kg) - ANCOVA - Pool - P6 and S6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	3239	3236	2990	91.68 (21.1)	87.24 (20.7)	-4.22 (0.1)	3241	3237	2943	91.34 (20.8)	90.52 (20.9)	-0.71 (0.1)	-3.52 [-3.80;-3.24] <0.0001	-0.63 [-0.68;-0.58]	
Gender															0.0006*
Female	1142	1142	1057	85.29 (19.9)	80.31 (18.9)	-5.17 (0.2)	1160	1160	1048	85.79 (19.4)	84.75 (19.3)	-1.00 (0.2)	-4.18 [-4.65;-3.71] <0.0001	-0.69 [-0.78;-0.60]	
Male	2097	2094	1933	95.16 (20.8)	91.03 (20.7)	-3.70 (0.1)	2081	2077	1895	94.44 (20.9)	93.71 (21.1)	-0.55 (0.1)	-3.15 [-3.50;-2.81] <0.0001	-0.60 [-0.66;-0.53]	
Age															0.0868
< 65	1561	1559	1442	92.77 (21.7)	88.69 (21.1)	-3.76 (0.1)	1479	1476	1336	92.56 (21.8)	91.91 (21.7)	-0.49 (0.2)	-3.27 [-3.68;-2.86] <0.0001	-0.56 [-0.64;-0.49]	
>= 65	1678	1677	1548	90.66 (20.4)	85.89 (20.3)	-4.65 (0.1)	1762	1761	1607	90.31 (19.9)	89.37 (20.2)	-0.89 (0.1)	-3.76 [-4.15;-3.38] <0.0001	-0.71 [-0.78;-0.63]	
Region A															0.0330*
OECD	2230	2228	2030	95.71 (20.9)	90.92 (20.9)	-4.49 (0.1)	2195	2193	1953	95.31 (20.9)	94.54 (21.0)	-0.76 (0.1)	-3.72 [-4.06;-3.38] <0.0001	-0.63 [-0.69;-0.56]	
Non-OECD	1009	1008	960	82.77 (18.4)	79.48 (18.0)	-3.67 (0.2)	1046	1044	990	83.00 (18.0)	82.58 (18.3)	-0.59 (0.2)	-3.07 [-3.56;-2.58] <0.0001	-0.66 [-0.75;-0.56]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an
observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, trial (Pioneer 6, Sustain 6), stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

Body weight (kg) - ANCOVA - Pool - P6 and S6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region B															0.4321
West Europe	521	521	487	93.32 (17.2)	88.60 (16.9)	-4.54 (0.3)	475	475	451	93.53 (18.4)	92.94 (18.4)	-0.76 (0.3)	-3.77 [-4.48;-3.07] <0.0001	-0.67 [-0.80;-0.54]	
Rest of World	2718	2715	2503	91.36 (21.7)	86.98 (21.4)	-4.16 (0.1)	2766	2762	2492	90.96 (21.2)	90.08 (21.3)	-0.70 (0.1)	-3.46 [-3.77;-3.16] <0.0001	-0.62 [-0.68;-0.57]	
HbA1c at baseline (disease severity)**															0.0700
<= 7.5	983	982	922	91.79 (21.1)	86.56 (20.1)	-4.87 (0.2)	1052	1051	971	92.53 (21.3)	91.51 (21.3)	-0.96 (0.2)	-3.91 [-4.41;-3.41] <0.0001	-0.65 [-0.74;-0.56]	
7.5 <	2246	2244	2059	91.61 (21.1)	87.51 (21.0)	-3.95 (0.1)	2171	2168	1955	90.81 (20.5)	90.07 (20.8)	-0.59 (0.1)	-3.35 [-3.69;-3.01] <0.0001	-0.63 [-0.69;-0.56]	
Evidence of CV disease at screening															0.9050
CV DISEASE	2703	2701	2479	92.10 (20.9)	87.64 (20.7)	-4.21 (0.1)	2727	2723	2455	92.03 (20.9)	91.23 (21.1)	-0.70 (0.1)	-3.51 [-3.82;-3.20] <0.0001	-0.62 [-0.67;-0.56]	
CV RISK FACTORS ONLY	536	535	511	89.54 (21.5)	85.29 (20.7)	-4.29 (0.2)	514	514	488	87.65 (19.7)	86.94 (19.6)	-0.74 (0.2)	-3.55 [-4.24;-2.87] <0.0001	-0.71 [-0.84;-0.58]	
Insulin Therapy at baseline															0.0002*

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, trial (Pioneer 6, Sustain 6), stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

Body weight (kg) - ANCOVA - Pool - P6 and S6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
No insulin	1315	1315	1218	88.88 (19.7)	84.63 (19.4)	-4.14 (0.2)	1322	1319	1214	88.82 (20.1)	87.38 (19.8)	-1.30 (0.2)	-2.84 [-3.28;-2.40] <0.0001	-0.55 [-0.63;-0.47]	
Basal only	784	784	714	93.02 (21.0)	88.86 (20.6)	-4.08 (0.2)	796	796	721	91.42 (20.4)	91.17 (20.8)	-0.38 (0.2)	-3.69 [-4.26;-3.12] <0.0001	-0.65 [-0.76;-0.55]	
Insulin (not basal only)	1140	1137	1058	93.99 (22.2)	89.16 (21.9)	-4.41 (0.2)	1123	1122	1008	94.24 (21.5)	93.84 (21.8)	-0.22 (0.2)	-4.19 [-4.67;-3.72] <0.0001	-0.70 [-0.79;-0.61]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, trial (Pioneer 6, Sustain 6), stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

11 Serious adverse events - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	889 (27.4%)	2350 (72.6%)	25 (0.8%)	1 (0.0%)	3241	998 (30.8%)	2243 (69.2%)	29 (0.9%)	0 (0.0%)	0.88 [0.81;0.97]	0.0074	
Gender													0.4157
Female	1142	278 (24.5%)	864 (75.7%)	9 (0.8%)	0 (0.0%)	1160	335 (28.8%)	825 (71.1%)	16 (1.4%)	0 (0.0%)	0.84 [0.71;0.98]	0.0275	
Male	2097	611 (29.1%)	1486 (70.9%)	16 (0.8%)	1 (0.0%)	2081	663 (31.9%)	1418 (68.1%)	13 (0.6%)	0 (0.0%)	0.91 [0.81;1.01]	0.0790	
Age													0.5199
< 65	1561	386 (24.9%)	1175 (75.3%)	12 (0.8%)	1 (0.1%)	1479	428 (28.8%)	1051 (71.1%)	15 (1.0%)	0 (0.0%)	0.86 [0.75;0.99]	0.0303	
65 <=	1678	503 (29.9%)	1175 (70.0%)	13 (0.8%)	0 (0.0%)	1762	570 (32.4%)	1192 (67.7%)	14 (0.8%)	0 (0.0%)	0.91 [0.81;1.03]	0.1321	
Region A													0.2826
OECD	2230	655 (29.3%)	1575 (70.6%)	23 (1.0%)	1 (0.0%)	2195	740 (33.8%)	1455 (66.3%)	27 (1.2%)	0 (0.0%)	0.85 [0.77;0.95]	0.0032	
Non-OECD	1009	234 (23.3%)	775 (76.8%)	2 (0.2%)	0 (0.0%)	1046	258 (24.5%)	788 (75.3%)	2 (0.2%)	0 (0.0%)	0.96 [0.80;1.14]	0.6169	
Region B													0.8888
West Europe	521	153 (29.3%)	368 (70.6%)	3 (0.6%)	0 (0.0%)	475	161 (33.9%)	314 (66.1%)	2 (0.4%)	0 (0.0%)	0.87 [0.70;1.08]	0.2150	
Rest of World	2718	736 (27.1%)	1982 (72.9%)	22 (0.8%)	1 (0.0%)	2766	837 (30.3%)	1929 (69.7%)	27 (1.0%)	0 (0.0%)	0.88 [0.80;0.98]	0.0151	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Serious adverse events - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.8660
<= 7.5	983	248 (25.4%)	735 (74.8%)	6 (0.6%)	1 (0.1%)	1052	295 (27.9%)	757 (72.0%)	10 (1.0%)	0 (0.0%)	0.90 [0.76;1.06]	0.1987	
7.5 <	2246	638 (28.4%)	1608 (71.6%)	19 (0.8%)	0 (0.0%)	2171	697 (32.1%)	1474 (67.9%)	19 (0.9%)	0 (0.0%)	0.88 [0.79;0.98]	0.0195	
Evidence of CV disease at screening													0.9339
CV DISEASE	2703	780 (28.9%)	1923 (71.1%)	21 (0.8%)	1 (0.0%)	2727	882 (32.3%)	1845 (67.7%)	27 (1.0%)	0 (0.0%)	0.88 [0.80;0.97]	0.0110	
CV RISK FACTORS ONLY	536	109 (20.2%)	427 (79.7%)	4 (0.7%)	0 (0.0%)	514	116 (22.6%)	398 (77.4%)	2 (0.4%)	0 (0.0%)	0.89 [0.69;1.16]	0.3963	
Insulin Therapy at baseline													0.4383
No insulin	1315	319 (24.2%)	996 (75.7%)	14 (1.1%)	0 (0.0%)	1322	365 (27.6%)	957 (72.4%)	10 (0.8%)	0 (0.0%)	0.87 [0.75;1.01]	0.0750	
Basal only	784	208 (26.6%)	576 (73.5%)	8 (1.0%)	0 (0.0%)	796	258 (32.4%)	538 (67.6%)	11 (1.4%)	0 (0.0%)	0.81 [0.67;0.97]	0.0230	
Insulin (not basal only)	1140	362 (31.7%)	778 (68.2%)	3 (0.3%)	1 (0.1%)	1123	375 (33.5%)	748 (66.6%)	8 (0.7%)	0 (0.0%)	0.94 [0.81;1.09]	0.4091	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

12 Serious adverse events excluding morbidity endpoints - comprehensive approach with PTs only - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	747 (23.1%)	2492 (76.9%)	38 (1.2%)	14 (0.4%)	3241	826 (25.5%)	2415 (74.5%)	59 (1.8%)	27 (0.8%)	0.90 [0.82;1.00]	0.0417	
Gender													0.4597
Female	1142	244 (21.5%)	898 (78.6%)	13 (1.1%)	4 (0.4%)	1160	289 (24.8%)	871 (75.1%)	24 (2.1%)	7 (0.6%)	0.86 [0.72;1.01]	0.0733	
Male	2097	503 (23.9%)	1594 (76.0%)	25 (1.2%)	10 (0.5%)	2081	537 (25.9%)	1544 (74.2%)	35 (1.7%)	20 (1.0%)	0.93 [0.82;1.05]	0.2162	
Age													0.3935
< 65	1561	317 (20.4%)	1244 (79.7%)	19 (1.2%)	8 (0.5%)	1479	350 (23.5%)	1129 (76.3%)	36 (2.4%)	19 (1.3%)	0.86 [0.74;1.01]	0.0598	
65 <=	1678	430 (25.5%)	1248 (74.4%)	19 (1.1%)	6 (0.4%)	1762	476 (27.1%)	1286 (73.0%)	23 (1.3%)	8 (0.5%)	0.94 [0.83;1.07]	0.3773	
Region A													0.3120
OECD	2230	556 (24.9%)	1674 (75.1%)	30 (1.3%)	8 (0.4%)	2195	620 (28.3%)	1575 (71.8%)	43 (2.0%)	13 (0.6%)	0.87 [0.78;0.98]	0.0182	
Non-OECD	1009	191 (19.0%)	818 (81.1%)	8 (0.8%)	6 (0.6%)	1046	206 (19.6%)	840 (80.3%)	16 (1.5%)	14 (1.3%)	0.98 [0.80;1.19]	0.8389	
Region B													0.8349
West Europe	521	129 (24.7%)	392 (75.2%)	3 (0.6%)	0 (0.0%)	475	130 (27.4%)	345 (72.6%)	3 (0.6%)	0 (0.0%)	0.92 [0.72;1.18]	0.5152	
Rest of World	2718	618 (22.7%)	2100 (77.3%)	35 (1.3%)	14 (0.5%)	2766	696 (25.2%)	2070 (74.8%)	56 (2.0%)	27 (1.0%)	0.90 [0.80;1.00]	0.0481	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Serious adverse events excluding morbidity endpoints - comprehensive approach with PTs only - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.8544
<= 7.5	983	211 (21.7%)	772 (78.5%)	8 (0.8%)	3 (0.3%)	1052	255 (24.1%)	797 (75.8%)	13 (1.2%)	3 (0.3%)	0.89 [0.74;1.07]	0.2090	
7.5 <	2246	533 (23.7%)	1713 (76.3%)	30 (1.3%)	11 (0.5%)	2171	567 (26.1%)	1604 (73.9%)	46 (2.1%)	24 (1.1%)	0.91 [0.81;1.02]	0.1093	
Evidence of CV disease at screening													0.7169
CV DISEASE	2703	652 (24.2%)	2051 (75.9%)	31 (1.1%)	11 (0.4%)	2727	730 (26.7%)	1997 (73.2%)	56 (2.1%)	26 (1.0%)	0.90 [0.81;1.00]	0.0419	
CV RISK FACTORS ONLY	536	95 (17.7%)	441 (82.3%)	7 (1.3%)	3 (0.6%)	514	96 (18.8%)	418 (81.3%)	3 (0.6%)	1 (0.2%)	0.95 [0.71;1.26]	0.7112	
Insulin Therapy at baseline													0.5402
No insulin	1315	272 (20.7%)	1043 (79.3%)	18 (1.4%)	4 (0.3%)	1322	311 (23.5%)	1011 (76.5%)	19 (1.4%)	9 (0.7%)	0.87 [0.74;1.03]	0.1069	
Basal only	784	179 (22.9%)	605 (77.2%)	11 (1.4%)	3 (0.4%)	796	214 (26.8%)	582 (73.1%)	17 (2.1%)	3 (0.4%)	0.85 [0.69;1.03]	0.1003	
Insulin (not basal only)	1140	296 (25.9%)	844 (74.0%)	9 (0.8%)	7 (0.6%)	1123	301 (26.9%)	822 (73.2%)	23 (2.0%)	15 (1.3%)	0.97 [0.82;1.13]	0.6741	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

13 Adverse events leading to trial product discontinuation - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	399 (12.3%)	2840 (87.7%)	76 (2.3%)	55 (1.7%)	3241	214 (6.6%)	3027 (93.4%)	108 (3.3%)	74 (2.3%)	1.94 [1.64;2.29]	<0.0001	
Gender													0.1779
Female	1142	143 (12.5%)	999 (87.5%)	27 (2.4%)	18 (1.6%)	1160	67 (5.8%)	1093 (94.2%)	34 (2.9%)	17 (1.5%)	2.28 [1.70;3.05]	<0.0001	
Male	2097	256 (12.2%)	1841 (87.8%)	49 (2.3%)	37 (1.8%)	2081	147 (7.1%)	1934 (92.9%)	74 (3.6%)	57 (2.7%)	1.79 [1.46;2.19]	<0.0001	
Age													0.0720
< 65	1561	137 (8.8%)	1424 (91.2%)	36 (2.3%)	26 (1.7%)	1479	83 (5.6%)	1396 (94.4%)	52 (3.5%)	32 (2.2%)	1.61 [1.23;2.12]	0.0006	
65 <=	1678	262 (15.6%)	1416 (84.4%)	40 (2.4%)	29 (1.7%)	1762	131 (7.4%)	1631 (92.6%)	56 (3.2%)	42 (2.4%)	2.21 [1.79;2.73]	<0.0001	
Region A													0.7469
OECD	2230	321 (14.4%)	1909 (85.6%)	56 (2.5%)	37 (1.7%)	2195	169 (7.7%)	2026 (92.3%)	79 (3.6%)	47 (2.1%)	1.96 [1.63;2.36]	<0.0001	
Non-OECD	1009	78 (7.7%)	931 (92.3%)	20 (2.0%)	18 (1.8%)	1046	45 (4.3%)	1001 (95.7%)	29 (2.8%)	27 (2.6%)	1.83 [1.27;2.64]	0.0012	
Region B													0.8386
West Europe	521	86 (16.5%)	435 (83.5%)	7 (1.3%)	5 (1.0%)	475	42 (8.9%)	433 (91.2%)	3 (0.6%)	2 (0.4%)	2.00 [1.38;2.89]	0.0002	
Rest of World	2718	313 (11.5%)	2405 (88.5%)	69 (2.5%)	50 (1.8%)	2766	172 (6.2%)	2594 (93.8%)	105 (3.8%)	72 (2.6%)	1.91 [1.59;2.31]	<0.0001	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Adverse events leading to trial product discontinuation - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.7429
<= 7.5	983	132 (13.4%)	851 (86.6%)	14 (1.4%)	10 (1.0%)	1052	78 (7.4%)	974 (92.6%)	26 (2.5%)	15 (1.4%)	1.88 [1.42;2.49]	<0.0001	
7.5 <	2246	267 (11.9%)	1979 (88.1%)	61 (2.7%)	44 (2.0%)	2171	135 (6.2%)	2036 (93.8%)	82 (3.8%)	59 (2.7%)	1.99 [1.62;2.45]	<0.0001	
Evidence of CV disease at screening													0.2196
CV DISEASE	2703	350 (13.0%)	2353 (87.1%)	68 (2.5%)	50 (1.8%)	2727	196 (7.2%)	2531 (92.8%)	100 (3.7%)	69 (2.5%)	1.87 [1.57;2.23]	<0.0001	
CV RISK FACTORS ONLY	536	49 (9.1%)	487 (90.9%)	8 (1.5%)	5 (0.9%)	514	18 (3.5%)	496 (96.5%)	8 (1.6%)	5 (1.0%)	2.67 [1.56;4.58]	0.0004	
Insulin Therapy at baseline													0.0580
No insulin	1315	156 (11.9%)	1159 (88.1%)	29 (2.2%)	17 (1.3%)	1322	93 (7.0%)	1229 (93.0%)	36 (2.7%)	26 (2.0%)	1.74 [1.35;2.25]	<0.0001	
Basal only	784	115 (14.7%)	669 (85.3%)	19 (2.4%)	12 (1.5%)	796	45 (5.7%)	751 (94.3%)	28 (3.5%)	17 (2.1%)	2.78 [1.97;3.92]	<0.0001	
Insulin (not basal only)	1140	128 (11.2%)	1012 (88.8%)	28 (2.5%)	26 (2.3%)	1123	76 (6.8%)	1047 (93.2%)	44 (3.9%)	31 (2.8%)	1.70 [1.28;2.25]	0.0003	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

14 Serious adverse events - system organ class "Gastrointestinal disorders" – time-to-event analysis - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

Serious adverse events by system organ class - time-to-event analysis - Pool - P6 and S6 - in-trial – full analysis set

		Oral Sema					Comparator					Oral Sema vs.Comparator		
System Organ Class	Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Gastrointestinal disorders	All subjects (total)	3239	104 (3.2%)	3135 (96.8%)	103 (3.2%)	73 (2.3%)	3241	74 (2.3%)	3167 (97.7%)	144 (4.4%)	99 (3.1%)	1.42 [1.06;1.92]	0.0207	
	Gender													0.2489
	Female	1142	43 (3.8%)	1099 (96.2%)	32 (2.8%)	20 (1.8%)	1160	25 (2.1%)	1135 (97.8%)	43 (3.7%)	22 (1.9%)	1.79 [1.09;2.93]	0.0209	
	Male	2097	61 (2.9%)	2036 (97.1%)	71 (3.4%)	53 (2.5%)	2081	49 (2.4%)	2032 (97.6%)	101 (4.9%)	77 (3.7%)	1.24 [0.85;1.81]	0.2603	
	Age													0.1932
	< 65	1561	37 (2.4%)	1524 (97.6%)	44 (2.8%)	30 (1.9%)	1479	32 (2.2%)	1447 (97.8%)	68 (4.6%)	41 (2.8%)	1.12 [0.70;1.80]	0.6322	
	65 <=	1678	67 (4.0%)	1611 (96.0%)	59 (3.5%)	43 (2.6%)	1762	42 (2.4%)	1720 (97.6%)	76 (4.3%)	58 (3.3%)	1.68 [1.14;2.48]	0.0081	
	Region A													0.6523
	OECD	2230	80 (3.6%)	2150 (96.4%)	76 (3.4%)	48 (2.2%)	2195	58 (2.7%)	2137 (97.4%)	107 (4.9%)	64 (2.9%)	1.36 [0.97;1.91]	0.0739	
	Non-OECD	1009	24 (2.4%)	985 (97.6%)	27 (2.7%)	25 (2.5%)	1046	16 (1.5%)	1030 (98.5%)	37 (3.5%)	35 (3.3%)	1.60 [0.85;3.02]	0.1427	
	Region B													0.2509
	West Europe	521	13 (2.5%)	508 (97.5%)	15 (2.9%)	11 (2.1%)	475	13 (2.7%)	462 (97.3%)	10 (2.1%)	4 (0.8%)	0.94 [0.43;2.02]	0.8693	
	Rest of World	2718	91 (3.3%)	2627 (96.7%)	88 (3.2%)	62 (2.3%)	2766	61 (2.2%)	2705 (97.8%)	134 (4.8%)	95 (3.4%)	1.53 [1.11;2.11]	0.0104	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Serious adverse events by system organ class - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

System Organ Class	Subgroup	Oral Sema N	Oral Sema n(adj.%)	Oral Sema nc(%)	Oral Sema nc'(%)	Oral Sema nccr(%)	Comparator N	Comparator n(adj.%)	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Oral Sema vs.Comparator HR [95%-CI]	Oral Sema vs.Comparator p-value	p-value int.
Gastrointestinal disorders	HbA1c at baseline (disease severity)**													0.8834
	<= 7.5	983	30 (3.1%)	953 (96.9%)	22 (2.2%)	17 (1.7%)	1052	24 (2.3%)	1028 (97.7%)	39 (3.7%)	26 (2.5%)	1.38 [0.80;2.36]	0.2431	
	7.5 <	2246	74 (3.3%)	2172 (96.7%)	80 (3.6%)	55 (2.4%)	2171	50 (2.3%)	2121 (97.7%)	104 (4.8%)	72 (3.3%)	1.44 [1.01;2.07]	0.0444	
	Evidence of CV disease at screening													0.2099
	CV DISEASE	2703	92 (3.4%)	2611 (96.6%)	92 (3.4%)	66 (2.4%)	2727	70 (2.6%)	2657 (97.4%)	132 (4.8%)	91 (3.3%)	1.34 [0.98;1.83]	0.0661	
	CV RISK FACTORS ONLY	536	12 (2.2%)	524 (97.8%)	11 (2.1%)	7 (1.3%)	514	4 (0.8%)	510 (99.2%)	12 (2.3%)	8 (1.6%)	2.84 [0.91;8.80]	0.0711	
	Insulin Therapy at baseline													0.4520
	No insulin	1315	41 (3.1%)	1274 (96.9%)	39 (3.0%)	21 (1.6%)	1322	31 (2.3%)	1291 (97.7%)	47 (3.6%)	35 (2.6%)	1.34 [0.84;2.13]	0.2217	
	Basal only	784	20 (2.6%)	764 (97.4%)	29 (3.7%)	19 (2.4%)	796	19 (2.4%)	777 (97.6%)	40 (5.0%)	22 (2.8%)	1.08 [0.58;2.03]	0.8021	
	Insulin (not basal only)	1140	43 (3.8%)	1097 (96.2%)	35 (3.1%)	33 (2.9%)	1123	24 (2.1%)	1099 (97.9%)	57 (5.1%)	42 (3.7%)	1.79 [1.08;2.94]	0.0227	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

15 Serious adverse events - system organ class "Surgical and medical procedures" – time-to-event analysis - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

Serious adverse events by system organ class - time-to-event analysis - Pool - P6 and S6 - in-trial – full analysis set

		Oral Sema					Comparator					Oral Sema vs.Comparator		
System Organ Class	Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	All subjects (total)	3239	95 (2.9%)	3144 (97.1%)	105 (3.2%)	76 (2.3%)	3241	136 (4.2%)	3105 (95.8%)	141 (4.4%)	98 (3.0%)	0.70 [0.54;0.91]	0.0073	
	Gender													0.4213
	Female	1142	34 (3.0%)	1108 (97.0%)	33 (2.9%)	22 (1.9%)	1160	43 (3.7%)	1117 (96.3%)	43 (3.7%)	22 (1.9%)	0.81 [0.52;1.27]	0.3595	
	Male	2097	61 (2.9%)	2036 (97.1%)	72 (3.4%)	54 (2.6%)	2081	93 (4.5%)	1988 (95.5%)	98 (4.7%)	76 (3.7%)	0.65 [0.47;0.89]	0.0079	
	Age													0.4730
	< 65	1561	47 (3.1%)	1514 (97.0%)	44 (2.8%)	31 (2.0%)	1479	72 (4.8%)	1407 (95.1%)	66 (4.5%)	41 (2.8%)	0.64 [0.44;0.92]	0.0159	
	65 <=	1678	48 (2.8%)	1630 (97.1%)	61 (3.6%)	45 (2.7%)	1762	64 (3.7%)	1698 (96.4%)	75 (4.3%)	57 (3.2%)	0.77 [0.53;1.12]	0.1730	
	Region A													0.5410
	OECD	2230	73 (3.2%)	2157 (96.7%)	76 (3.4%)	49 (2.2%)	2195	106 (4.9%)	2089 (95.2%)	106 (4.8%)	65 (3.0%)	0.66 [0.49;0.89]	0.0068	
	Non-OECD	1009	22 (2.2%)	987 (97.8%)	29 (2.9%)	27 (2.7%)	1046	30 (2.8%)	1016 (97.1%)	35 (3.3%)	33 (3.2%)	0.81 [0.46;1.40]	0.4397	
	Region B													0.9505
	West Europe	521	13 (2.5%)	508 (97.5%)	16 (3.1%)	12 (2.3%)	475	17 (3.6%)	458 (96.4%)	12 (2.5%)	6 (1.3%)	0.71 [0.35;1.47]	0.3599	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Serious adverse events by system organ class - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

System Organ Class	Subgroup	Oral Sema N	Oral Sema n(adj.%)	Oral Sema nc(%)	Oral Sema nc'(%)	Oral Sema nccr(%)	Comparator N	Comparator n(adj.%)	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Oral Sema vs.Comparator HR [95%-CI]	Oral Sema vs.Comparator p-value	p-value int.
Surgical and medical procedures	Rest of World	2718	82 (3.0%)	2636 (97.0%)	89 (3.3%)	64 (2.4%)	2766	119 (4.3%)	2647 (95.7%)	129 (4.7%)	92 (3.3%)	0.70 [0.53;0.92]	0.0117	
	HbA1c at baseline (disease severity)**													0.0238*
	<= 7.5	983	28 (2.9%)	955 (97.2%)	22 (2.2%)	17 (1.7%)	1052	27 (2.5%)	1025 (97.4%)	38 (3.6%)	28 (2.7%)	1.19 [0.70;2.01]	0.5241	
	7.5 <	2246	67 (3.0%)	2179 (97.0%)	82 (3.7%)	58 (2.6%)	2171	109 (5.0%)	2062 (95.0%)	102 (4.7%)	69 (3.2%)	0.59 [0.43;0.80]	0.0006	
	Evidence of CV disease at screening													0.0234*
	CV DISEASE	2703	81 (3.0%)	2622 (97.0%)	94 (3.5%)	69 (2.6%)	2727	129 (4.7%)	2598 (95.3%)	128 (4.7%)	89 (3.3%)	0.63 [0.48;0.83]	0.0012	
	CV RISK FACTORS ONLY	536	14 (2.6%)	522 (97.4%)	11 (2.1%)	7 (1.3%)	514	7 (1.4%)	507 (98.6%)	13 (2.5%)	9 (1.8%)	1.89 [0.76;4.69]	0.1684	
	Insulin Therapy at baseline													0.1007
	No insulin	1315	38 (2.9%)	1277 (97.1%)	40 (3.0%)	23 (1.7%)	1322	48 (3.6%)	1274 (96.4%)	46 (3.5%)	34 (2.6%)	0.78 [0.51;1.20]	0.2585	
	Basal only	784	31 (4.0%)	753 (96.0%)	30 (3.8%)	20 (2.6%)	796	34 (4.2%)	762 (95.7%)	41 (5.2%)	22 (2.8%)	0.95 [0.58;1.54]	0.8311	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Serious adverse events by system organ class - time-to-event analysis - Pool - P6 and S6 - in-trial – full analysis set

		Oral Sema					Comparator					Oral Sema vs.Comparator		
System Organ Class	Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	Insulin (not basal only)	1140	26 (2.3%)	1114 (97.7%)	35 (3.1%)	33 (2.9%)	1123	54 (4.8%)	1069 (95.2%)	54 (4.8%)	42 (3.7%)	0.47 [0.29;0.75]	0.0015	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

16 Serious adverse events – preferred term "Atrial fibrillation"– time-to-event analysis - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

Serious adverse events by preferred term - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

		Oral Sema					Comparator					Oral Sema vs.Comparator		
Preferred Term	Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Atrial fibrillation	All subjects (total)	3239	32 (1.0%)	3207 (99.0%)	113 (3.5%)	83 (2.6%)	3241	52 (1.6%)	3189 (98.4%)	144 (4.4%)	98 (3.0%)	0.62 [0.40;0.96]	0.0316	
	Gender													0.9085
	Female	1142	10 (0.9%)	1132 (99.1%)	38 (3.3%)	26 (2.3%)	1160	16 (1.4%)	1144 (98.6%)	44 (3.8%)	23 (2.0%)	0.64 [0.29;1.41]	0.2679	
	Male	2097	22 (1.0%)	2075 (99.0%)	75 (3.6%)	57 (2.7%)	2081	36 (1.7%)	2045 (98.3%)	100 (4.8%)	75 (3.6%)	0.61 [0.36;1.03]	0.0635	
	Age													0.4963
	< 65	1561	12 (0.8%)	1549 (99.2%)	50 (3.2%)	36 (2.3%)	1479	15 (1.0%)	1464 (99.0%)	70 (4.7%)	42 (2.8%)	0.78 [0.36;1.66]	0.5126	
	65 <=	1678	20 (1.2%)	1658 (98.8%)	63 (3.8%)	47 (2.8%)	1762	37 (2.1%)	1725 (97.9%)	74 (4.2%)	56 (3.2%)	0.56 [0.33;0.97]	0.0374	
	Region A													0.5782
	OECD	2230	26 (1.2%)	2204 (98.8%)	84 (3.8%)	56 (2.5%)	2195	44 (2.0%)	2151 (98.0%)	106 (4.8%)	62 (2.8%)	0.58 [0.35;0.94]	0.0257	
	Non-OECD	1009	6 (0.6%)	1003 (99.4%)	29 (2.9%)	27 (2.7%)	1046	8 (0.8%)	1038 (99.2%)	38 (3.6%)	36 (3.4%)	0.80 [0.28;2.31]	0.6815	
	Region B													0.2643
	West Europe	521	7 (1.3%)	514 (98.7%)	15 (2.9%)	11 (2.1%)	475	6 (1.3%)	469 (98.7%)	12 (2.5%)	6 (1.3%)	1.09 [0.37;3.24]	0.8787	
	Rest of World	2718	25 (0.9%)	2693 (99.1%)	98 (3.6%)	72 (2.6%)	2766	46 (1.7%)	2720 (98.3%)	132 (4.8%)	92 (3.3%)	0.55 [0.34;0.90]	0.0166	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).MedDRA version 20.1

Serious adverse events by preferred term - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

		Oral Sema				Comparator					Oral Sema vs.Comparator		
Preferred Term	Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Atrial fibrillation	HbA1c at baseline (disease severity)**													0.4065
	<= 7.5	983	8 (0.8%)	975 (99.2%)	25 (2.5%)	20 (2.0%)	1052	19 (1.8%)	1033 (98.2%)	39 (3.7%)	26 (2.5%)	0.46 [0.20;1.06]	0.0685	
	7.5 <	2246	24 (1.1%)	2222 (98.9%)	87 (3.9%)	62 (2.8%)	2171	33 (1.5%)	2138 (98.5%)	104 (4.8%)	71 (3.3%)	0.70 [0.42;1.19]	0.1880	
	Evidence of CV disease at screening													0.2709
	CV DISEASE	2703	30 (1.1%)	2673 (98.9%)	102 (3.8%)	76 (2.8%)	2727	45 (1.6%)	2682 (98.3%)	132 (4.8%)	90 (3.3%)	0.67 [0.42;1.07]	0.0936	
	CV RISK FACTORS ONLY	536	2 (0.4%)	534 (99.6%)	11 (2.1%)	7 (1.3%)	514	7 (1.4%)	507 (98.6%)	12 (2.3%)	8 (1.6%)	0.27 [0.06;1.29]	0.1009	
	Insulin Therapy at baseline													0.1276
	No insulin	1315	13 (1.0%)	1302 (99.0%)	43 (3.3%)	25 (1.9%)	1322	12 (0.9%)	1310 (99.1%)	47 (3.6%)	35 (2.6%)	1.09 [0.50;2.38]	0.8382	
	Basal only	784	8 (1.0%)	776 (99.0%)	32 (4.1%)	22 (2.8%)	796	24 (3.0%)	772 (97.0%)	40 (5.0%)	21 (2.6%)	0.34 [0.15;0.76]	0.0086	
	Insulin (not basal only)	1140	11 (1.0%)	1129 (99.0%)	38 (3.3%)	36 (3.2%)	1123	16 (1.4%)	1107 (98.6%)	57 (5.1%)	42 (3.7%)	0.68 [0.31;1.45]	0.3159	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

17 Neoplasms – serious adverse events - pre-defined MedDRA search - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	103 (3.2%)	3136 (96.8%)	92 (2.8%)	63 (1.9%)	3241	115 (3.5%)	3126 (96.5%)	130 (4.0%)	86 (2.7%)	0.89 [0.68;1.16]	0.3878	
Gender													0.5203
Female	1142	31 (2.7%)	1111 (97.3%)	31 (2.7%)	20 (1.8%)	1160	31 (2.7%)	1129 (97.3%)	40 (3.4%)	19 (1.6%)	1.02 [0.62;1.67]	0.9452	
Male	2097	72 (3.4%)	2025 (96.6%)	61 (2.9%)	43 (2.1%)	2081	84 (4.0%)	1997 (96.0%)	90 (4.3%)	67 (3.2%)	0.84 [0.61;1.15]	0.2739	
Age													0.0102*
< 65	1561	29 (1.9%)	1532 (98.1%)	43 (2.8%)	30 (1.9%)	1479	49 (3.3%)	1430 (96.7%)	65 (4.4%)	39 (2.6%)	0.56 [0.35;0.88]	0.0126	
65 <=	1678	74 (4.4%)	1604 (95.6%)	49 (2.9%)	33 (2.0%)	1762	66 (3.8%)	1696 (96.3%)	65 (3.7%)	47 (2.7%)	1.17 [0.84;1.63]	0.3505	
Region A													0.4474
OECD	2230	84 (3.8%)	2146 (96.2%)	68 (3.0%)	41 (1.8%)	2195	88 (4.0%)	2107 (96.0%)	96 (4.4%)	54 (2.5%)	0.93 [0.69;1.26]	0.6484	
Non-OECD	1009	19 (1.9%)	990 (98.1%)	24 (2.4%)	22 (2.2%)	1046	27 (2.6%)	1019 (97.4%)	34 (3.3%)	32 (3.1%)	0.72 [0.40;1.30]	0.2780	
Region B													0.0210*
West Europe	521	32 (6.1%)	489 (93.9%)	10 (1.9%)	6 (1.2%)	475	19 (4.0%)	456 (96.0%)	9 (1.9%)	4 (0.8%)	1.59 [0.90;2.80]	0.1116	
Rest of World	2718	71 (2.6%)	2647 (97.4%)	82 (3.0%)	57 (2.1%)	2766	96 (3.5%)	2670 (96.5%)	121 (4.4%)	82 (3.0%)	0.74 [0.55;1.01]	0.0560	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Neoplasms – serious adverse events - pre-defined MedDRA search - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.6374
<= 7.5	983	42 (4.3%)	941 (95.7%)	19 (1.9%)	14 (1.4%)	1052	47 (4.4%)	1005 (95.5%)	30 (2.9%)	18 (1.7%)	0.96 [0.63;1.46]	0.8561	
7.5 <	2246	60 (2.7%)	2186 (97.3%)	72 (3.2%)	48 (2.1%)	2171	68 (3.1%)	2103 (96.9%)	99 (4.6%)	67 (3.1%)	0.84 [0.60;1.20]	0.3404	
Evidence of CV disease at screening													0.4610
CV DISEASE	2703	84 (3.1%)	2619 (96.9%)	83 (3.1%)	58 (2.1%)	2727	99 (3.6%)	2628 (96.4%)	120 (4.4%)	80 (2.9%)	0.85 [0.64;1.14]	0.2779	
CV RISK FACTORS ONLY	536	19 (3.5%)	517 (96.5%)	9 (1.7%)	5 (0.9%)	514	16 (3.1%)	498 (96.9%)	10 (1.9%)	6 (1.2%)	1.12 [0.58;2.18]	0.7412	
Insulin Therapy at baseline													0.9150
No insulin	1315	44 (3.3%)	1271 (96.7%)	35 (2.7%)	18 (1.4%)	1322	47 (3.6%)	1275 (96.4%)	40 (3.0%)	28 (2.1%)	0.93 [0.62;1.40]	0.7279	
Basal only	784	23 (2.9%)	761 (97.1%)	27 (3.4%)	17 (2.2%)	796	29 (3.6%)	767 (96.4%)	40 (5.0%)	21 (2.6%)	0.80 [0.47;1.39]	0.4352	
Insulin (not basal only)	1140	36 (3.2%)	1104 (96.8%)	30 (2.6%)	28 (2.5%)	1123	39 (3.5%)	1084 (96.5%)	50 (4.5%)	37 (3.3%)	0.90 [0.57;1.42]	0.6526	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

18 Hypoglycaemic episodes – serious adverse events - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	34 (1.0%)	3205 (99.0%)	110 (3.4%)	81 (2.5%)	3241	27 (0.8%)	3214 (99.2%)	148 (4.6%)	103 (3.2%)	1.26 [0.76;2.08]	0.3748	
Gender													0.4095
Female	1142	12 (1.1%)	1130 (98.9%)	35 (3.1%)	23 (2.0%)	1160	7 (0.6%)	1153 (99.4%)	44 (3.8%)	23 (2.0%)	1.74 [0.68;4.42]	0.2451	
Male	2097	22 (1.0%)	2075 (99.0%)	75 (3.6%)	58 (2.8%)	2081	20 (1.0%)	2061 (99.0%)	104 (5.0%)	80 (3.8%)	1.09 [0.59;2.00]	0.7832	
Age													0.2105
< 65	1561	19 (1.2%)	1542 (98.8%)	47 (3.0%)	33 (2.1%)	1479	10 (0.7%)	1469 (99.3%)	71 (4.8%)	43 (2.9%)	1.79 [0.83;3.86]	0.1351	
65 <=	1678	15 (0.9%)	1663 (99.1%)	63 (3.8%)	48 (2.9%)	1762	17 (1.0%)	1745 (99.0%)	77 (4.4%)	60 (3.4%)	0.93 [0.46;1.85]	0.8288	
Region A													0.4173
OECD	2230	25 (1.1%)	2205 (98.9%)	82 (3.7%)	55 (2.5%)	2195	22 (1.0%)	2173 (99.0%)	110 (5.0%)	67 (3.1%)	1.12 [0.63;1.98]	0.7061	
Non-OECD	1009	9 (0.9%)	1000 (99.1%)	28 (2.8%)	26 (2.6%)	1046	5 (0.5%)	1041 (99.5%)	38 (3.6%)	36 (3.4%)	1.86 [0.62;5.55]	0.2656	
Region B													0.0625
West Europe	521	1 (0.2%)	520 (99.8%)	16 (3.1%)	12 (2.3%)	475	5 (1.1%)	470 (98.9%)	11 (2.3%)	6 (1.3%)	0.19 [0.02;1.58]	0.1237	
Rest of World	2718	33 (1.2%)	2685 (98.8%)	94 (3.5%)	69 (2.5%)	2766	22 (0.8%)	2744 (99.2%)	137 (5.0%)	97 (3.5%)	1.52 [0.89;2.60]	0.1294	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Hypoglycaemic episodes - serious adverse events - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.3517
<= 7.5	983	6 (0.6%)	977 (99.4%)	25 (2.5%)	20 (2.0%)	1052	8 (0.8%)	1044 (99.2%)	40 (3.8%)	27 (2.6%)	0.80 [0.28;2.31]	0.6793	
7.5 <	2246	28 (1.2%)	2218 (98.8%)	84 (3.7%)	60 (2.7%)	2171	19 (0.9%)	2152 (99.1%)	107 (4.9%)	75 (3.5%)	1.42 [0.79;2.54]	0.2378	
Evidence of CV disease at screening													0.7157
CV DISEASE	2703	29 (1.1%)	2674 (98.9%)	99 (3.7%)	74 (2.7%)	2727	24 (0.9%)	2703 (99.1%)	136 (5.0%)	95 (3.5%)	1.21 [0.71;2.08]	0.4857	
CV RISK FACTORS ONLY	536	5 (0.9%)	531 (99.1%)	11 (2.1%)	7 (1.3%)	514	3 (0.6%)	511 (99.4%)	12 (2.3%)	8 (1.6%)	1.61 [0.38;6.75]	0.5139	
Insulin Therapy at baseline													0.9151
No insulin	1315	5 (0.4%)	1310 (99.6%)	44 (3.3%)	26 (2.0%)	1322	5 (0.4%)	1317 (99.6%)	47 (3.6%)	36 (2.7%)	1.00 [0.29;3.46]	0.9976	
Basal only	784	7 (0.9%)	777 (99.1%)	31 (4.0%)	22 (2.8%)	796	5 (0.6%)	791 (99.4%)	43 (5.4%)	24 (3.0%)	1.43 [0.45;4.51]	0.5403	
Insulin (not basal only)	1140	22 (1.9%)	1118 (98.1%)	35 (3.1%)	33 (2.9%)	1123	17 (1.5%)	1106 (98.5%)	58 (5.2%)	43 (3.8%)	1.27 [0.67;2.39]	0.4647	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

19 Pancreatitis – serious adverse events - pre-defined MedDRA search - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	5 (0.2%)	3234 (99.8%)	115 (3.6%)	85 (2.6%)	3241	11 (0.3%)	3230 (99.7%)	149 (4.6%)	104 (3.2%)	0.46 [0.16;1.31]	0.1453	
Gender													0.9905
Female	1142	1 (0.1%)	1141 (99.9%)	38 (3.3%)	26 (2.3%)	1160	0 (0.0%)	1160 (100%)	44 (3.8%)	23 (2.0%)	Not est	Not est	
Male	2097	4 (0.2%)	2093 (99.8%)	77 (3.7%)	59 (2.8%)	2081	11 (0.5%)	2070 (99.5%)	105 (5.0%)	81 (3.9%)	0.36 [0.11;1.12]	0.0785	
Age													0.2357
< 65	1561	4 (0.3%)	1557 (99.7%)	50 (3.2%)	36 (2.3%)	1479	5 (0.3%)	1474 (99.7%)	70 (4.7%)	43 (2.9%)	0.78 [0.21;2.90]	0.7083	
65 <=	1678	1 (0.1%)	1677 (99.9%)	65 (3.9%)	49 (2.9%)	1762	6 (0.3%)	1756 (99.7%)	79 (4.5%)	61 (3.5%)	0.17 [0.02;1.43]	0.1035	
Region A													0.9997
OECD	2230	5 (0.2%)	2225 (99.8%)	86 (3.9%)	58 (2.6%)	2195	11 (0.5%)	2184 (99.5%)	111 (5.1%)	68 (3.1%)	0.44 [0.15;1.28]	0.1316	
Non-OECD	1009	0 (0.0%)	1009 (100%)	29 (2.9%)	27 (2.7%)	1046	0 (0.0%)	1046 (100%)	38 (3.6%)	36 (3.4%)	Not est	Not est	
Region B													0.9914
West Europe	521	0 (0.0%)	521 (100%)	16 (3.1%)	12 (2.3%)	475	4 (0.8%)	471 (99.2%)	11 (2.3%)	5 (1.1%)	Not est	Not est	
Rest of World	2718	5 (0.2%)	2713 (99.8%)	99 (3.6%)	73 (2.7%)	2766	7 (0.3%)	2759 (99.7%)	138 (5.0%)	99 (3.6%)	0.73 [0.23;2.29]	0.5840	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

Pancreatitis - serious adverse events - pre-defined MedDRA search - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.8219
<= 7.5	983	1 (0.1%)	982 (99.9%)	25 (2.5%)	20 (2.0%)	1052	3 (0.3%)	1049 (99.7%)	41 (3.9%)	28 (2.7%)	0.36 [0.04;3.48]	0.3786	
7.5 <	2246	4 (0.2%)	2242 (99.8%)	89 (4.0%)	64 (2.8%)	2171	8 (0.4%)	2163 (99.6%)	107 (4.9%)	75 (3.5%)	0.49 [0.15;1.61]	0.2381	
Evidence of CV disease at screening													0.9901
CV DISEASE	2703	4 (0.1%)	2699 (99.9%)	104 (3.8%)	78 (2.9%)	2727	11 (0.4%)	2716 (99.6%)	136 (5.0%)	95 (3.5%)	0.37 [0.12;1.15]	0.0861	
CV RISK FACTORS ONLY	536	1 (0.2%)	535 (99.8%)	11 (2.1%)	7 (1.3%)	514	0 (0.0%)	514 (100%)	13 (2.5%)	9 (1.8%)	Not est	Not est	
Insulin Therapy at baseline													0.8208
No insulin	1315	1 (0.1%)	1314 (99.9%)	45 (3.4%)	27 (2.1%)	1322	2 (0.2%)	1320 (99.8%)	49 (3.7%)	37 (2.8%)	0.50 [0.05;5.51]	0.5713	
Basal only	784	1 (0.1%)	783 (99.9%)	32 (4.1%)	22 (2.8%)	796	4 (0.5%)	792 (99.5%)	42 (5.3%)	24 (3.0%)	0.26 [0.03;2.30]	0.2238	
Insulin (not basal only)	1140	3 (0.3%)	1137 (99.7%)	38 (3.3%)	36 (3.2%)	1123	5 (0.4%)	1118 (99.6%)	58 (5.2%)	43 (3.8%)	0.59 [0.14;2.48]	0.4725	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

20 Acute kidney injury (preferred term) - serious adverse events - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
All subjects (total)	3239	40 (1.2%)	3199 (98.8%)	106 (3.3%)	76 (2.3%)	3241	51 (1.6%)	3190 (98.4%)	137 (4.2%)	92 (2.8%)	0.78 [0.52;1.19]	0.2516	
Gender													0.4345
Female	1142	17 (1.5%)	1125 (98.5%)	34 (3.0%)	22 (1.9%)	1160	18 (1.5%)	1142 (98.4%)	40 (3.4%)	20 (1.7%)	0.97 [0.50;1.88]	0.9212	
Male	2097	23 (1.1%)	2074 (98.9%)	72 (3.4%)	54 (2.6%)	2081	33 (1.6%)	2048 (98.4%)	97 (4.7%)	72 (3.5%)	0.69 [0.40;1.17]	0.1703	
Age													0.8543
< 65	1561	18 (1.2%)	1543 (98.8%)	45 (2.9%)	31 (2.0%)	1479	21 (1.4%)	1458 (98.6%)	64 (4.3%)	37 (2.5%)	0.83 [0.44;1.55]	0.5494	
65 <=	1678	22 (1.3%)	1656 (98.7%)	61 (3.6%)	45 (2.7%)	1762	30 (1.7%)	1732 (98.3%)	73 (4.1%)	55 (3.1%)	0.76 [0.44;1.32]	0.3349	
Region A													0.9656
OECD	2230	35 (1.6%)	2195 (98.4%)	79 (3.5%)	51 (2.3%)	2195	44 (2.0%)	2151 (98.0%)	101 (4.6%)	58 (2.6%)	0.78 [0.50;1.21]	0.2648	
Non-OECD	1009	5 (0.5%)	1004 (99.5%)	27 (2.7%)	25 (2.5%)	1046	7 (0.7%)	1039 (99.3%)	36 (3.4%)	34 (3.3%)	0.76 [0.24;2.38]	0.6329	
Region B													0.8050
West Europe	521	4 (0.8%)	517 (99.2%)	16 (3.1%)	12 (2.3%)	475	4 (0.8%)	471 (99.2%)	12 (2.5%)	6 (1.3%)	0.93 [0.23;3.73]	0.9203	
Rest of World	2718	36 (1.3%)	2682 (98.7%)	90 (3.3%)	64 (2.4%)	2766	47 (1.7%)	2719 (98.3%)	125 (4.5%)	86 (3.1%)	0.78 [0.50;1.20]	0.2522	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

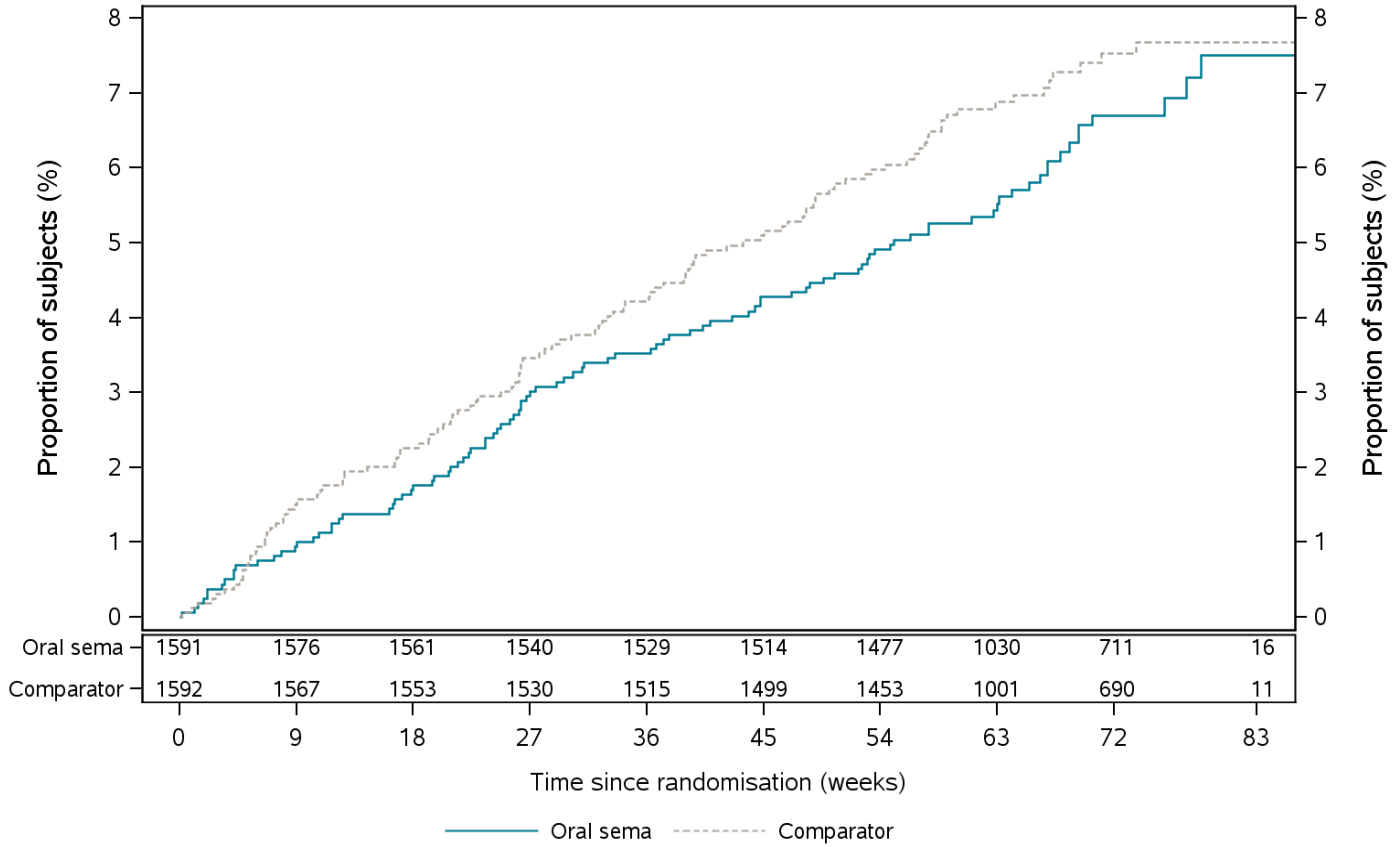
Acute kidney injury (preferred term) - serious adverse events - time-to-event analysis - Pool - P6 and S6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	N	n(adj.%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
HbA1c at baseline (disease severity)**													0.4405
<= 7.5	983	13 (1.3%)	970 (98.7%)	22 (2.2%)	17 (1.7%)	1052	14 (1.3%)	1038 (98.7%)	35 (3.3%)	22 (2.1%)	1.01 [0.47;2.14]	0.9870	
7.5 <	2246	27 (1.2%)	2219 (98.8%)	83 (3.7%)	58 (2.6%)	2171	37 (1.7%)	2134 (98.3%)	101 (4.7%)	69 (3.2%)	0.71 [0.43;1.16]	0.1676	
Evidence of CV disease at screening													0.1752
CV DISEASE	2703	39 (1.4%)	2664 (98.6%)	95 (3.5%)	69 (2.6%)	2727	46 (1.7%)	2681 (98.3%)	125 (4.6%)	84 (3.1%)	0.85 [0.56;1.31]	0.4630	
CV RISK FACTORS ONLY	536	1 (0.2%)	535 (99.8%)	11 (2.1%)	7 (1.3%)	514	5 (1.0%)	509 (99.0%)	12 (2.3%)	8 (1.6%)	0.19 [0.02;1.61]	0.1265	
Insulin Therapy at baseline													0.1884
No insulin	1315	10 (0.8%)	1305 (99.2%)	42 (3.2%)	24 (1.8%)	1322	19 (1.4%)	1303 (98.6%)	46 (3.5%)	34 (2.6%)	0.52 [0.24;1.13]	0.0983	
Basal only	784	8 (1.0%)	776 (99.0%)	30 (3.8%)	20 (2.6%)	796	14 (1.7%)	782 (98.2%)	37 (4.6%)	19 (2.4%)	0.59 [0.25;1.40]	0.2277	
Insulin (not basal only)	1140	22 (1.9%)	1118 (98.1%)	34 (3.0%)	32 (2.8%)	1123	18 (1.6%)	1105 (98.4%)	54 (4.8%)	39 (3.5%)	1.21 [0.65;2.25]	0.5533	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, adj.%: Cochran-Mantel-Haenszel
adjusted proportion of subjects with at least one event, %: proportion of subjects, HR: Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value int. < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by trial (Pioneer 6, Sustain 6) and CV disease status at screening (CV disease at screening, CV risk factors only at screening).
MedDRA version 20.1

PIONEER 6 – Kumulative Inzidenz (SUE nach SOC und PT)

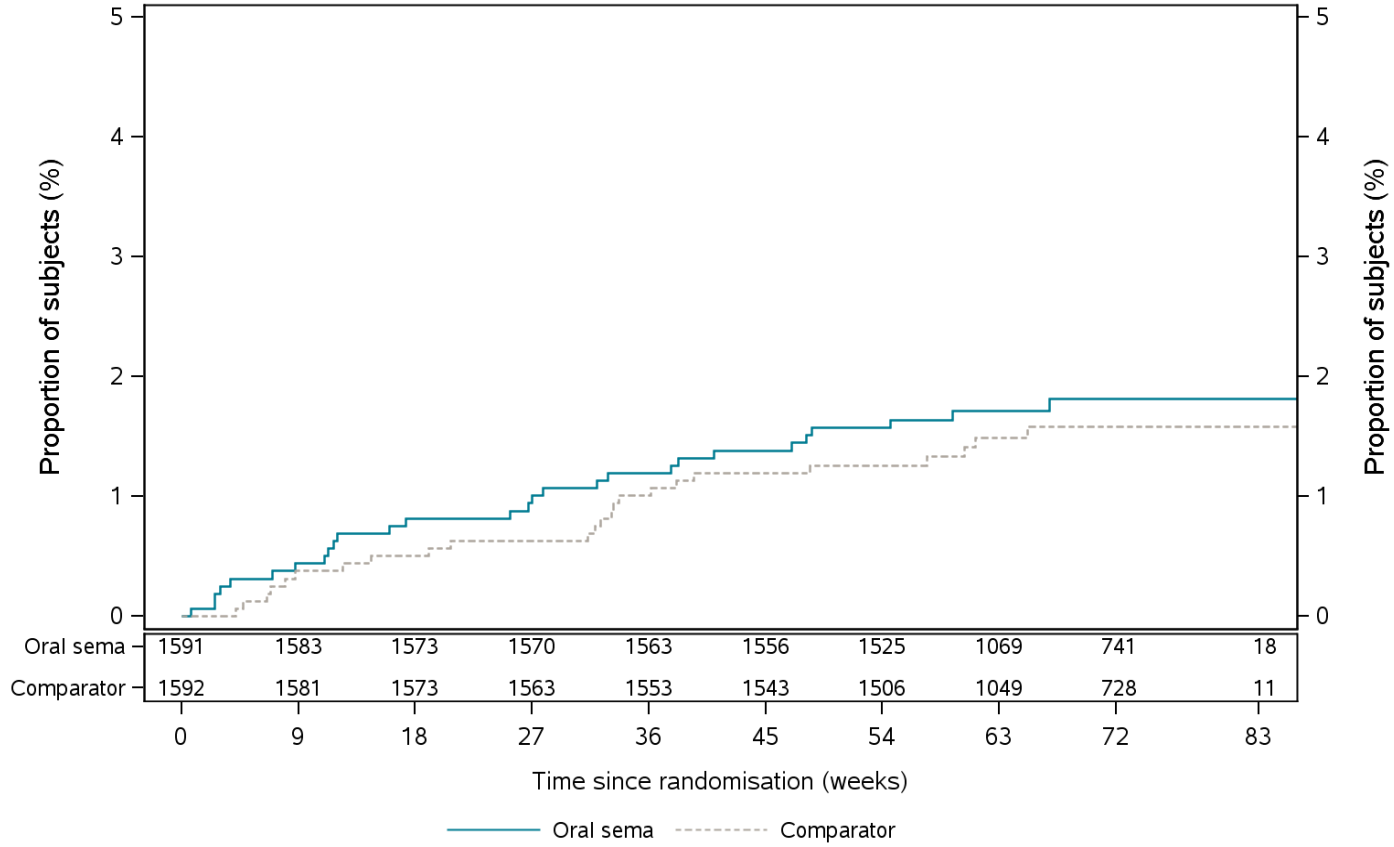
1 Serious adverse events - system organ class "Cardiac disorders" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:33:06 - f_cif_tte_p6.sas/f_cif_soc_cd_sae_p6.png

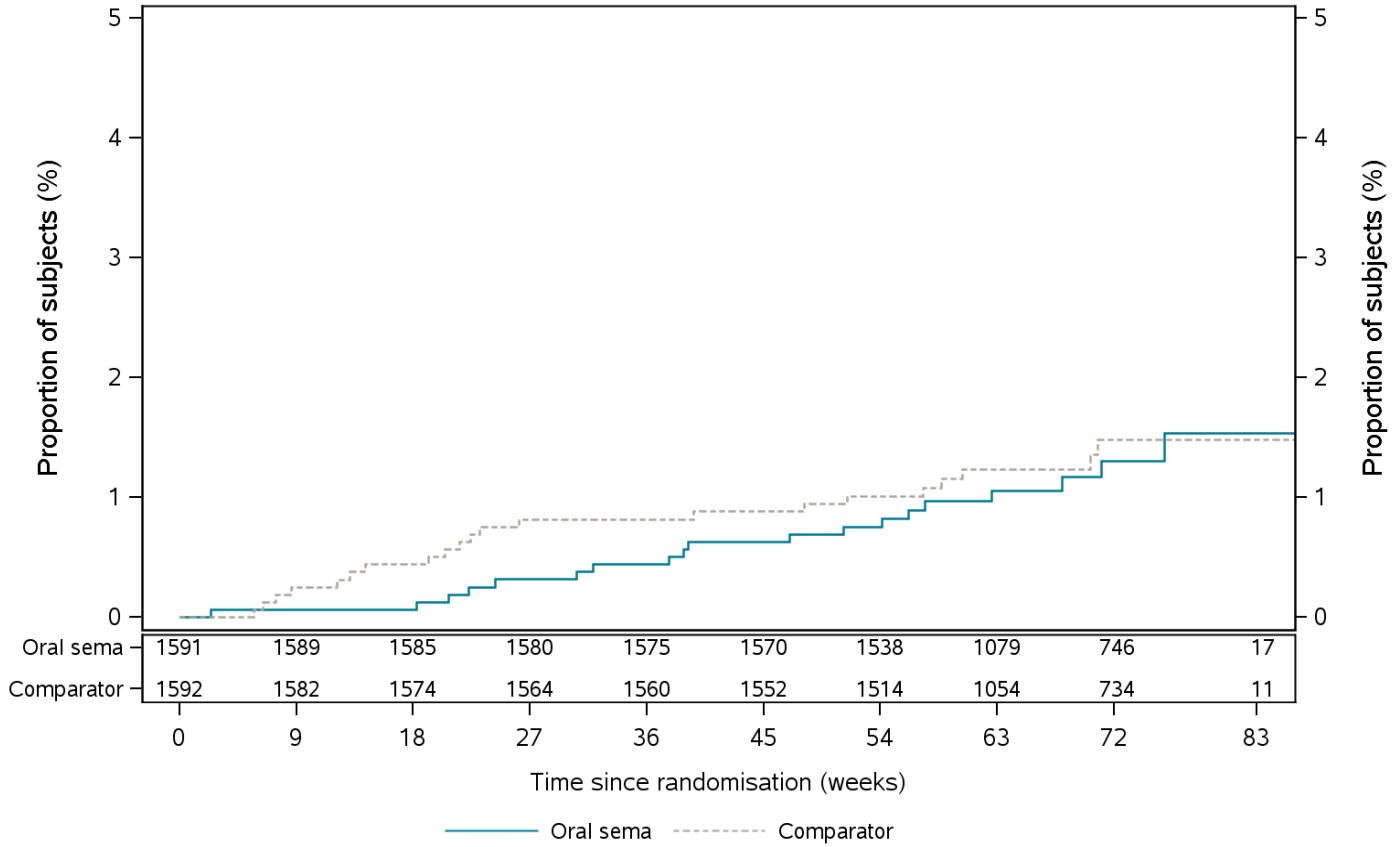
2 Serious adverse events - system organ class "Gastrointestinal disorders" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:33:18 - f_cif_tte_p6.sas/f_cif_soc_gd_sae_p6.png

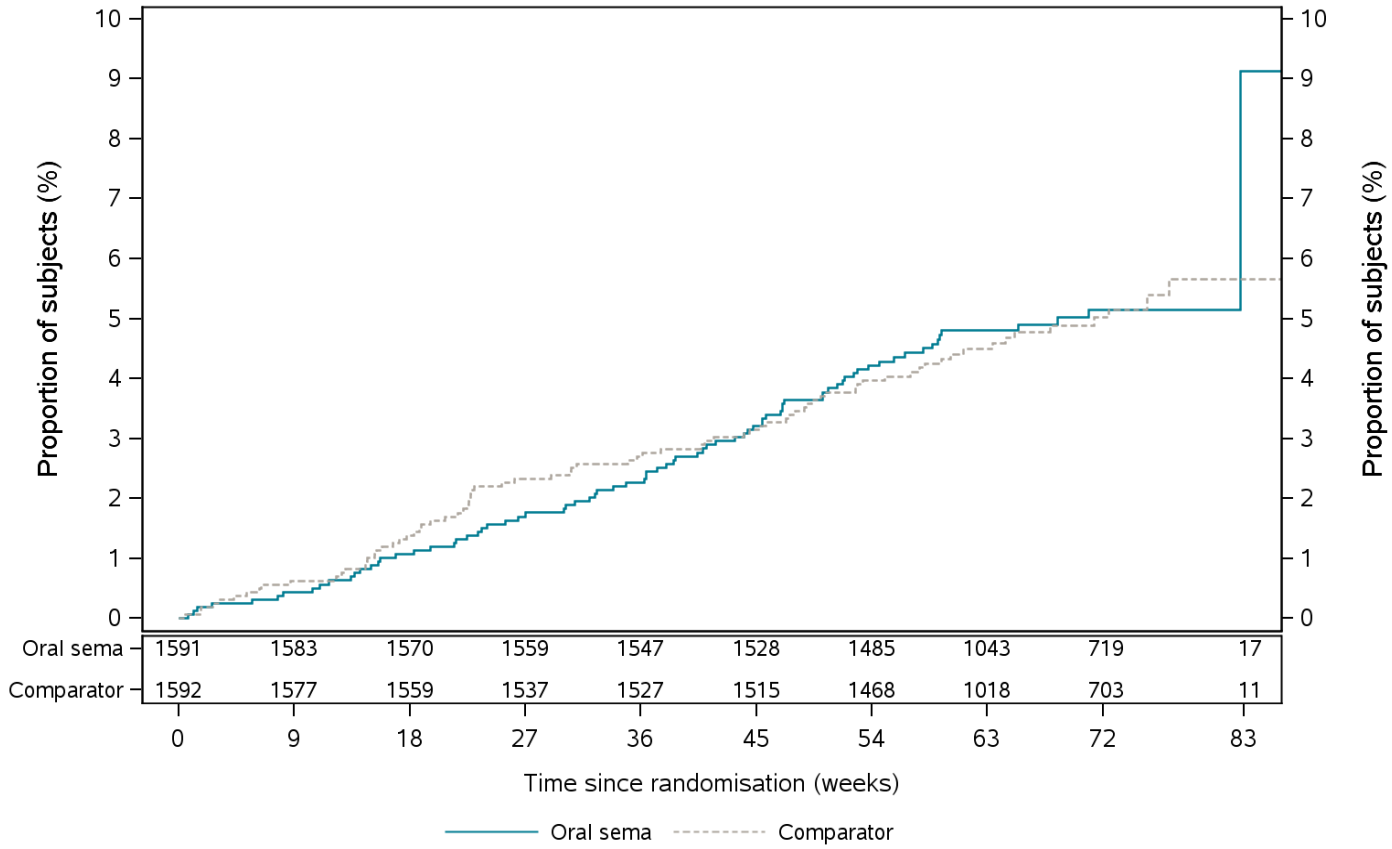
3 Serious adverse events - system organ class "General disorders and administration site conditions" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:33:31 - f_cif_tte_p6.sas/f_cif_soc_gdasc_sae_p6.png

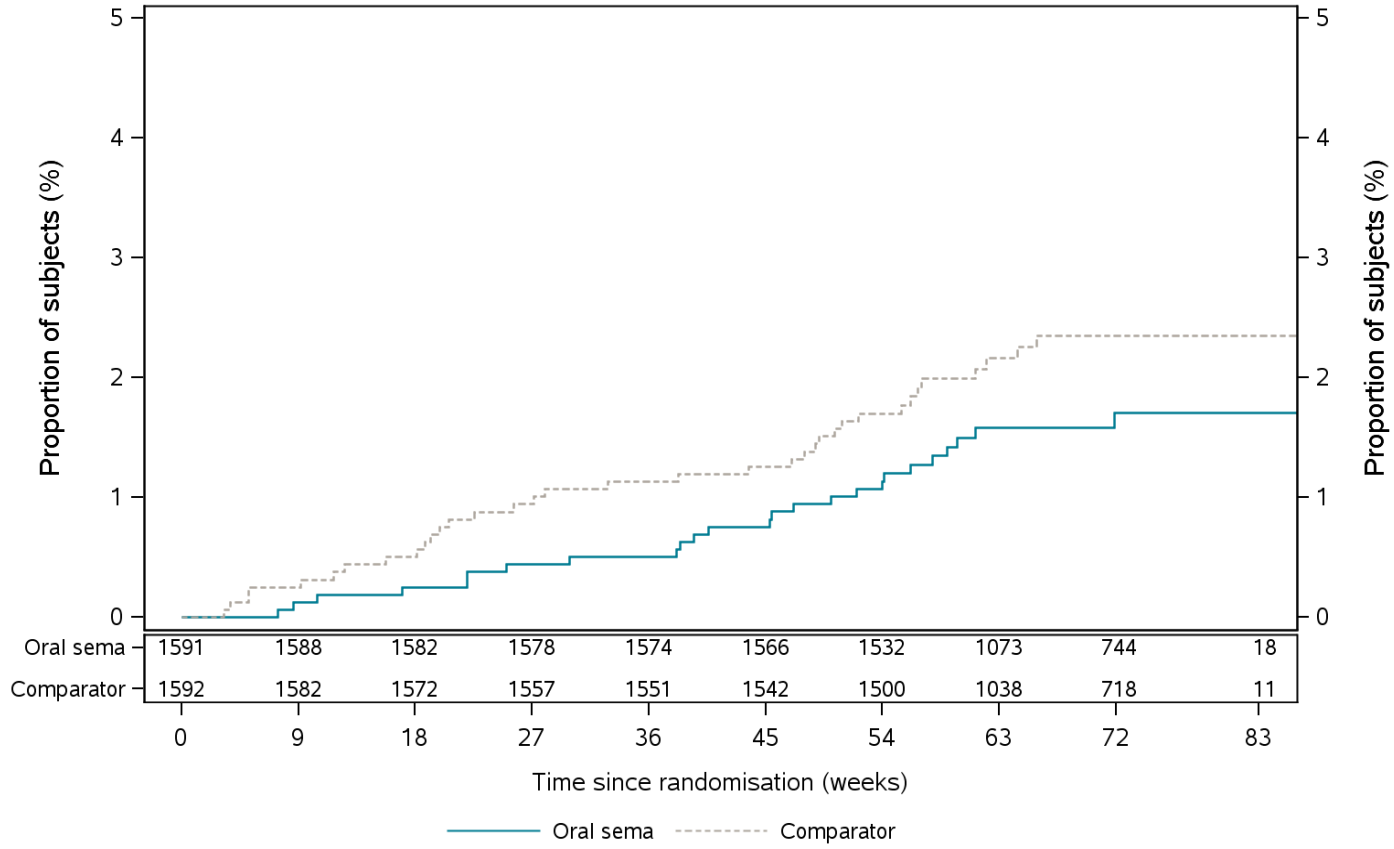
4 Serious adverse events - system organ class "Infections and infestations" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:33:43 - f_cif_tte_p6.sas/f_cif_soc_ii_sae_p6.png

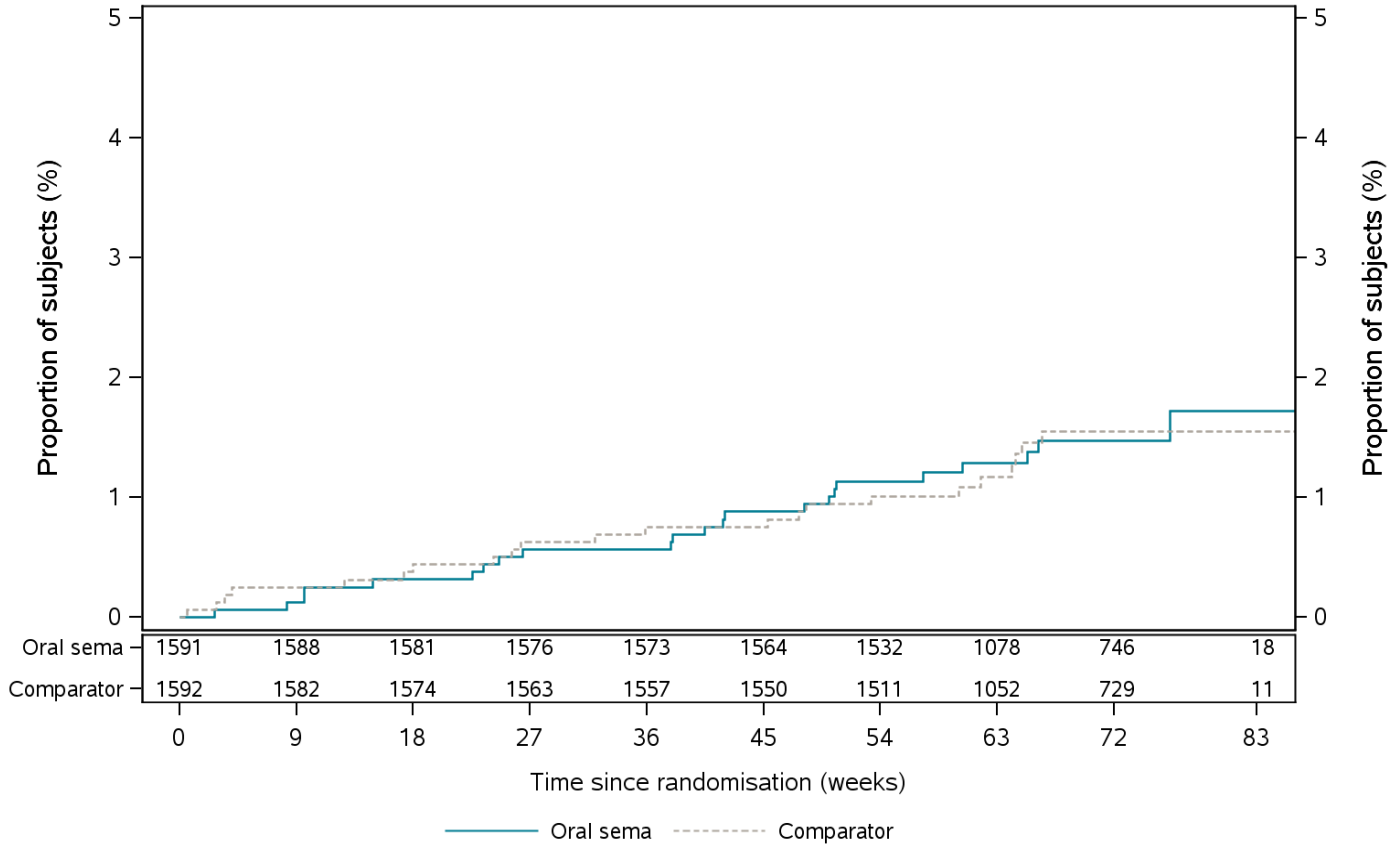
5 Serious adverse events - system organ class "Injury, poisoning and procedural complications" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:33:56 - f_cif_tte_p6.sas/f_cif_soc_ippc_sae_p6.png

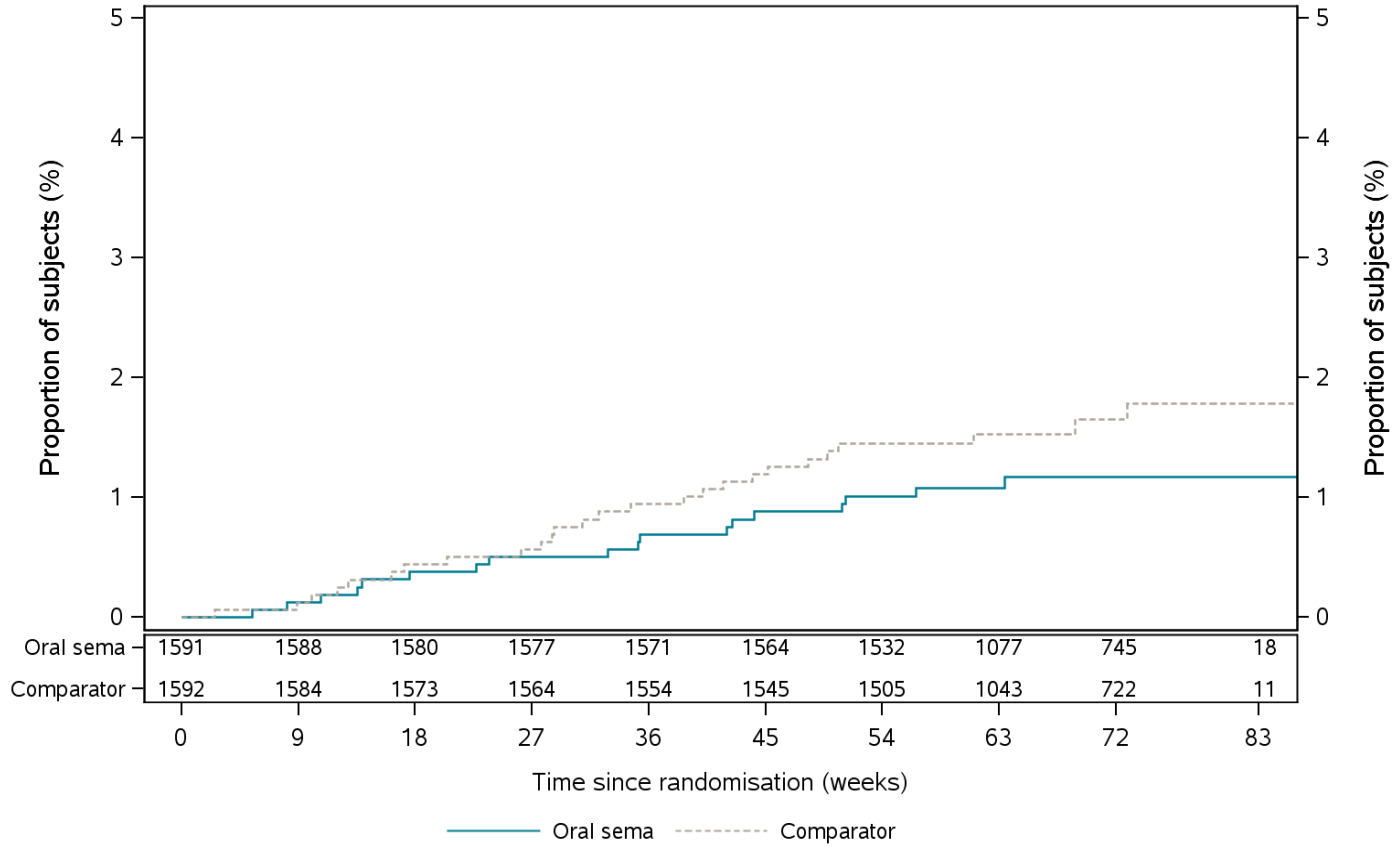
6 Serious adverse events - system organ class "Metabolism and nutrition disorders" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:34:08 - f_cif_tte_p6.sas/f_cif_soc_mnd_sae_p6.png

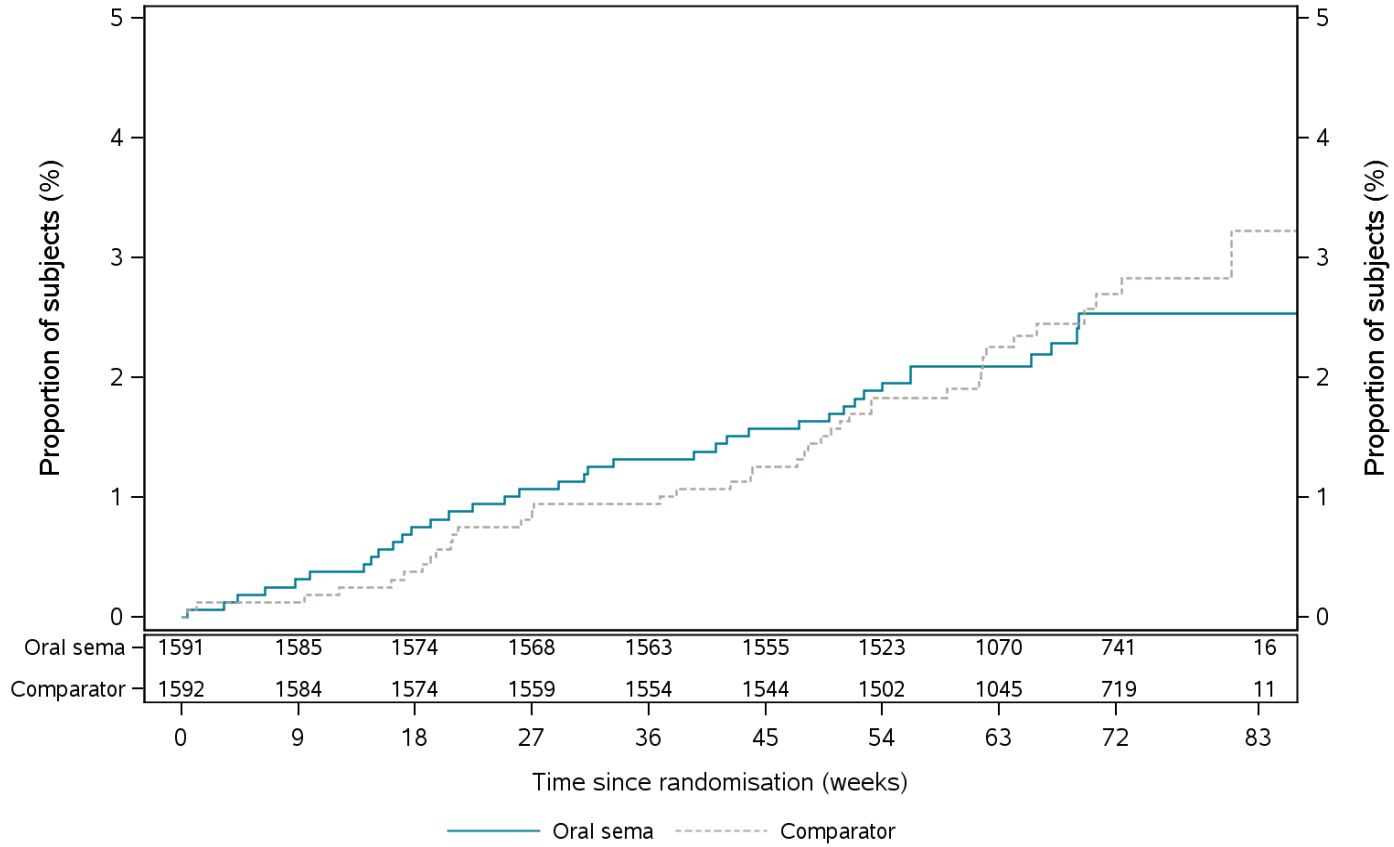
7 Serious adverse events - system organ class "Musculoskeletal and connective tissue disorders" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:34:20 - f_cif_tte_p6.sas/f_cif_soc_mctd_sae_p6.png

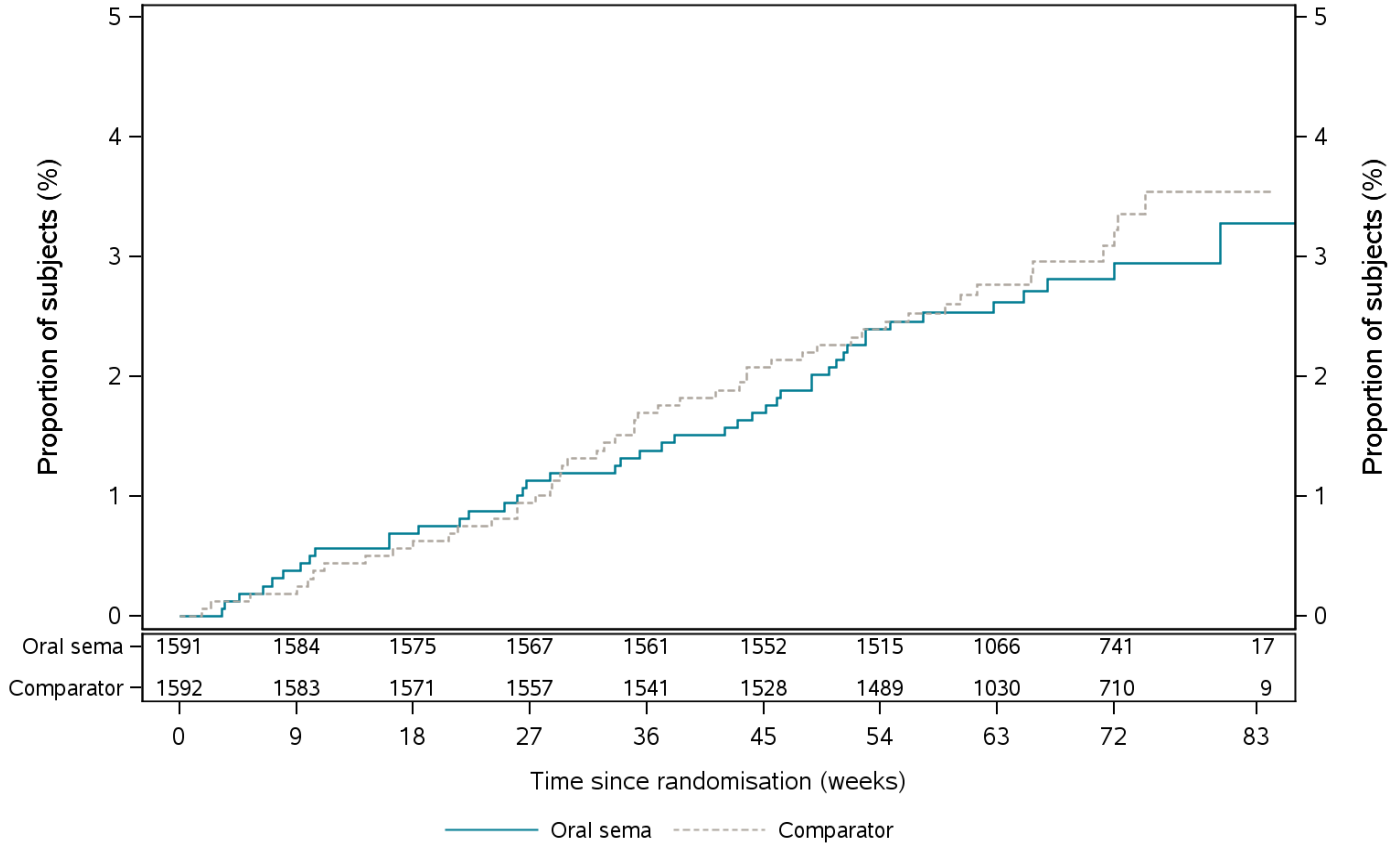
8 Serious adverse events - system organ class "Neoplasms benign, malignant and unspecified (incl cysts and polyps)" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:34:32 - f_cif_tte_p6.sas/f_cif_soc_nbmu_sae_p6.png

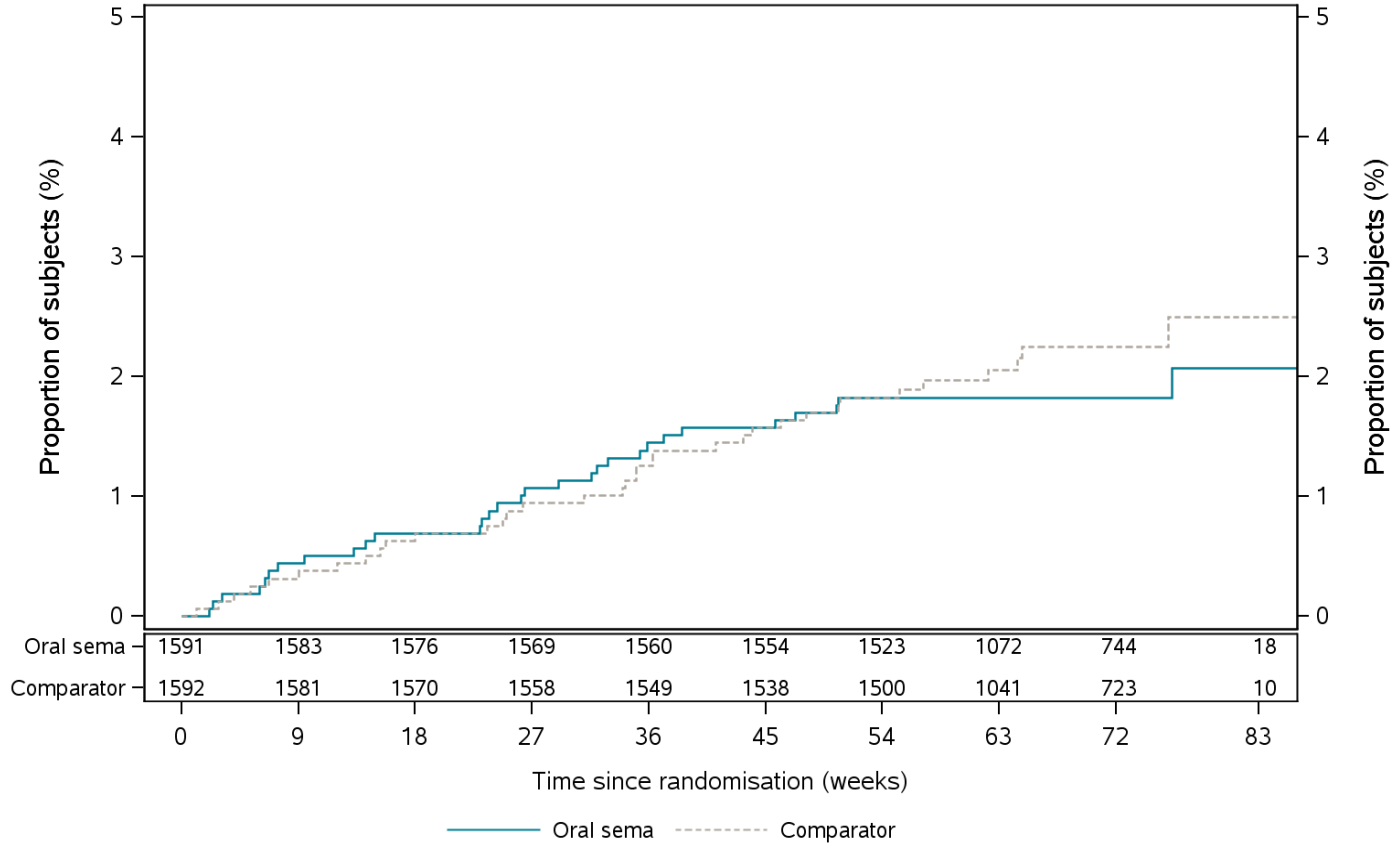
9 Serious adverse events - system organ class "Nervous system disorders" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:34:44 - f_cif_tte_p6.sas/f_cif_soc_nsd_sae_p6.png

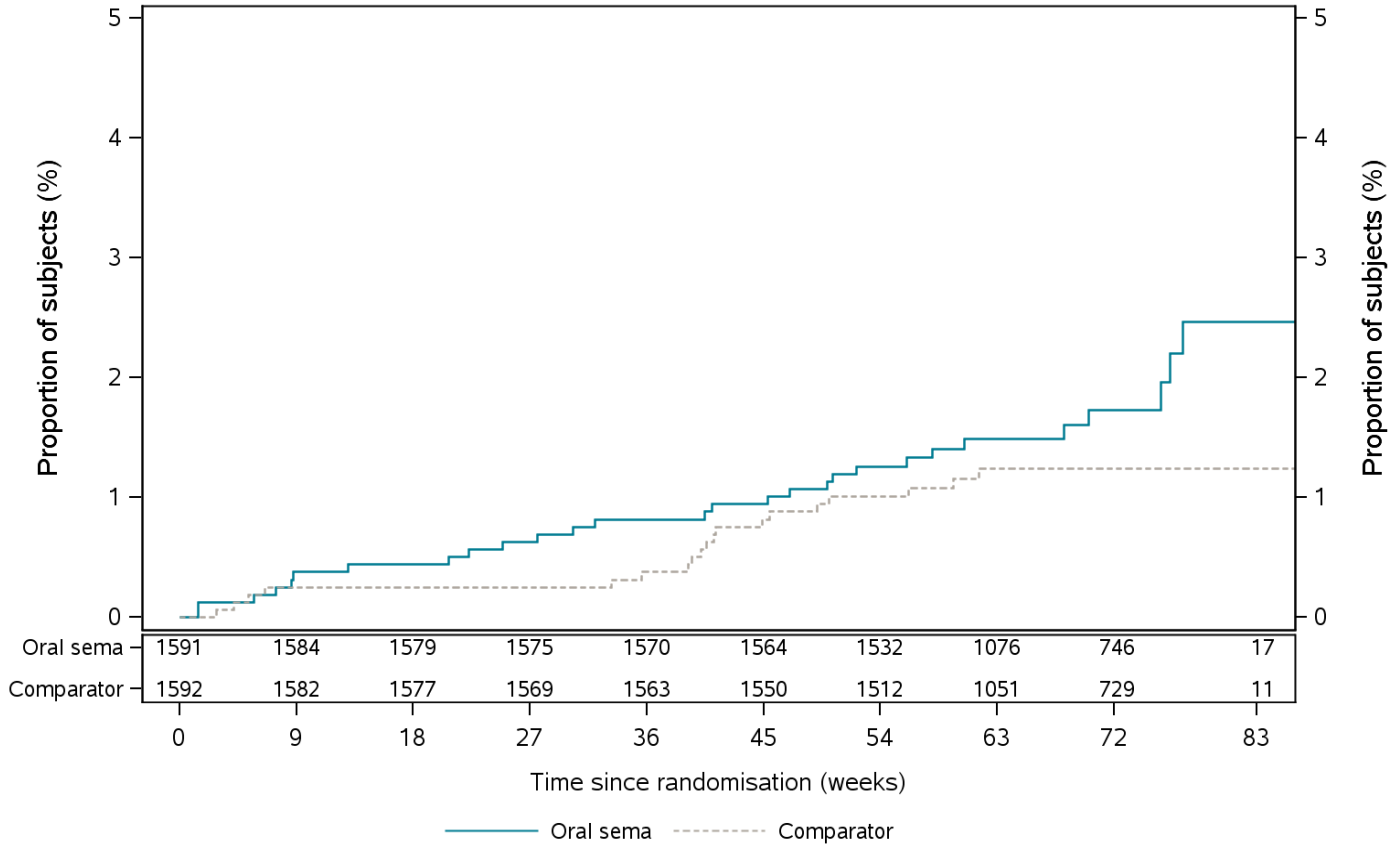
10 Serious adverse events - system organ class "Renal and urinary disorders" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:34:57 - f_cif_tte_p6.sas/f_cif_soc_rud_sae_p6.png

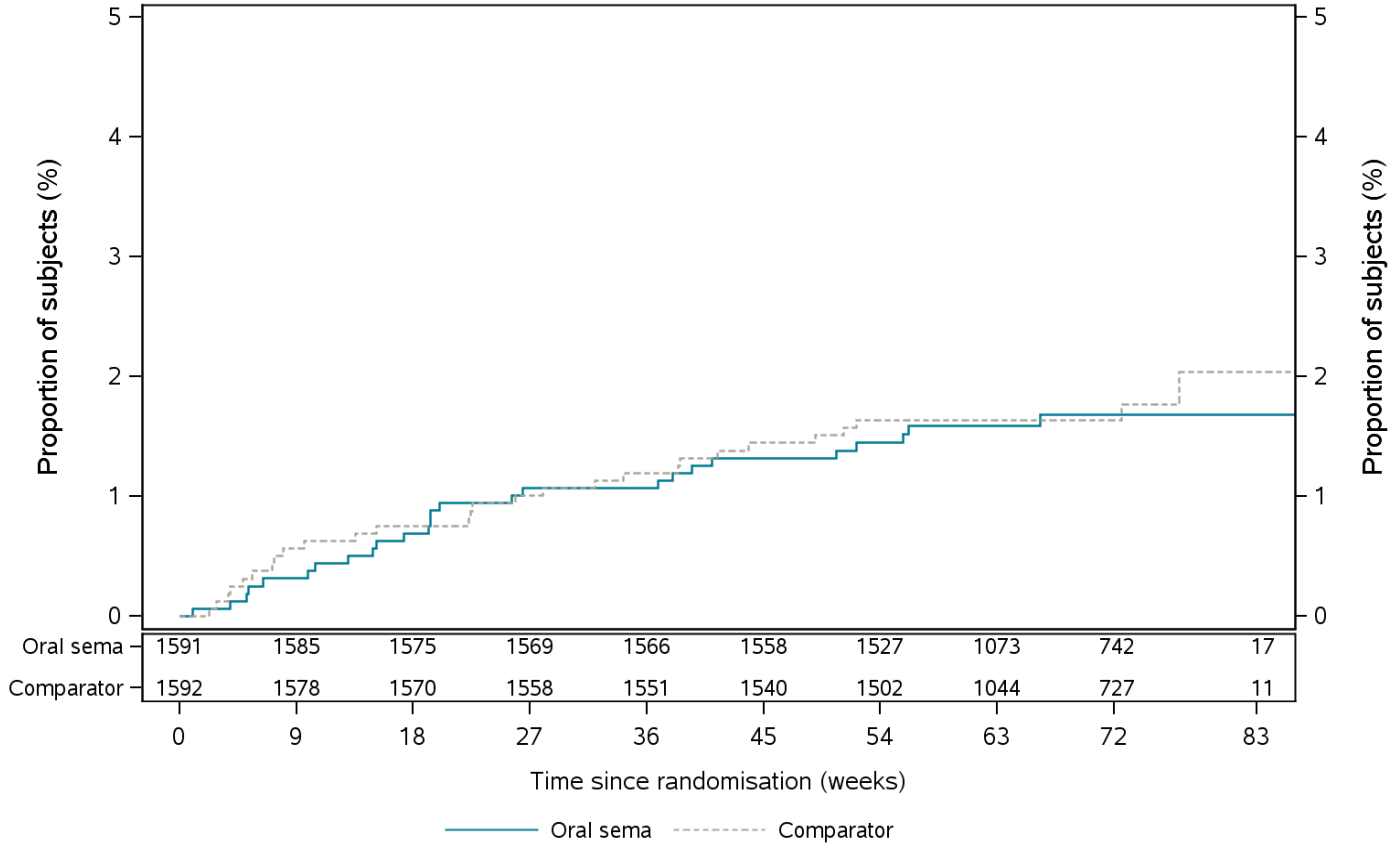
11 Serious adverse events - system organ class "Respiratory, thoracic and mediastinal disorders" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:35:09 - f_cif_tte_p6.sas/f_cif_soc_rtmd_sae_p6.png

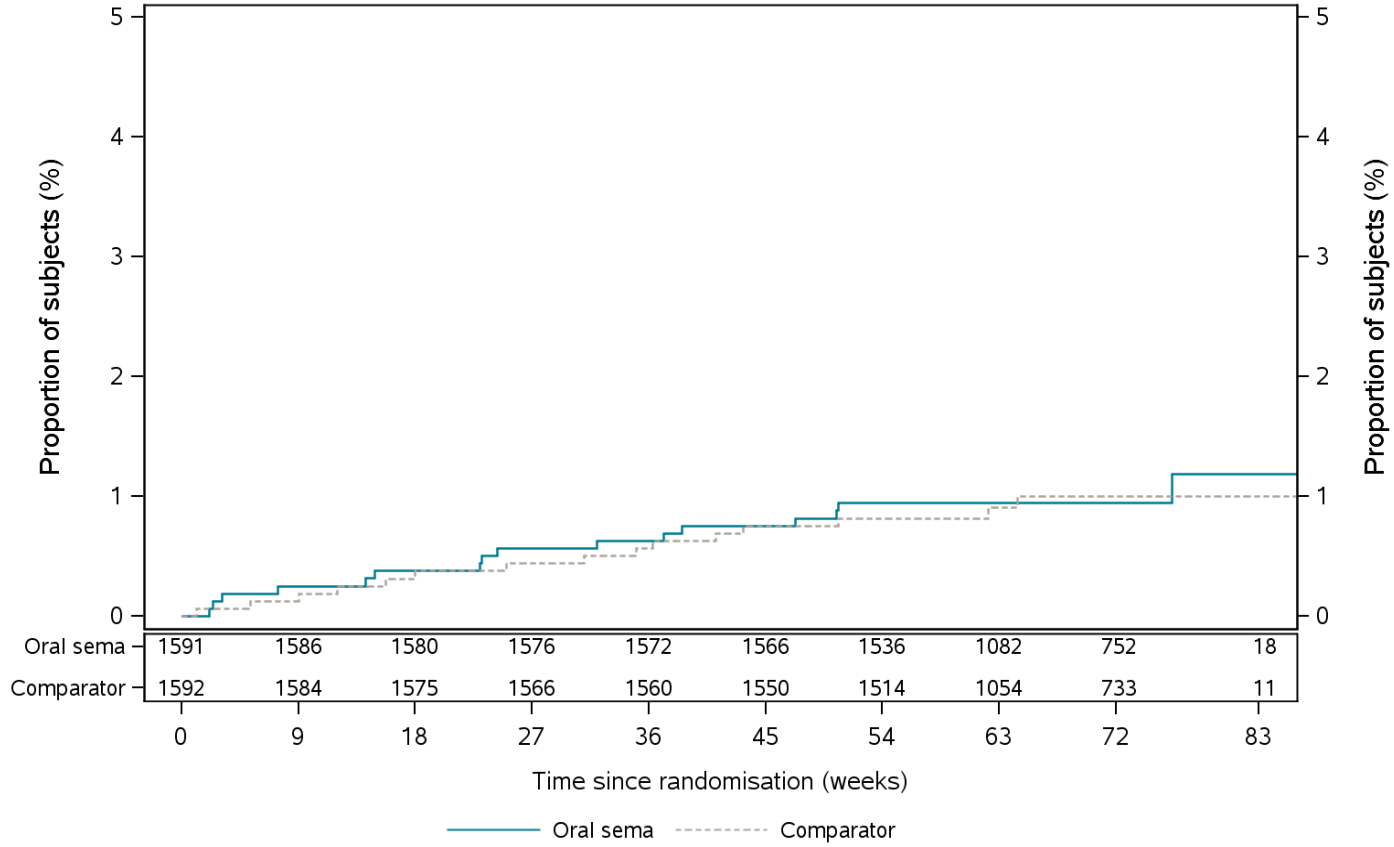
12 Serious adverse events - system organ class "Vascular disorders" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:35:21 - f_cif_tte_p6.sas/f_cif_soc_vd_sae_p6.png

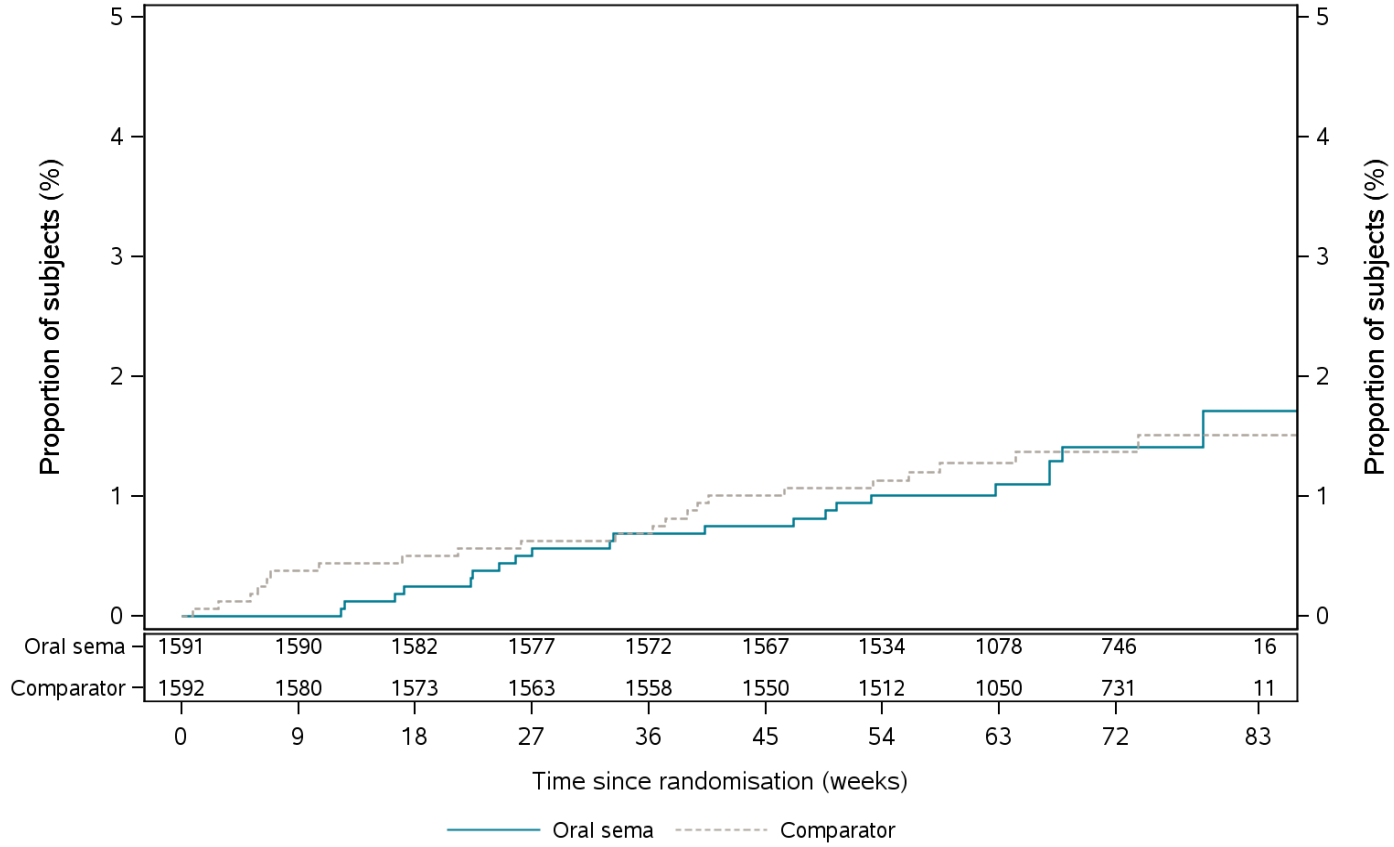
13 Serious adverse events - preferred term "Acute kidney injury" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:35:33 - f_cif_tte_p6.sas/f_cif_pt_aki_sae_p6.png

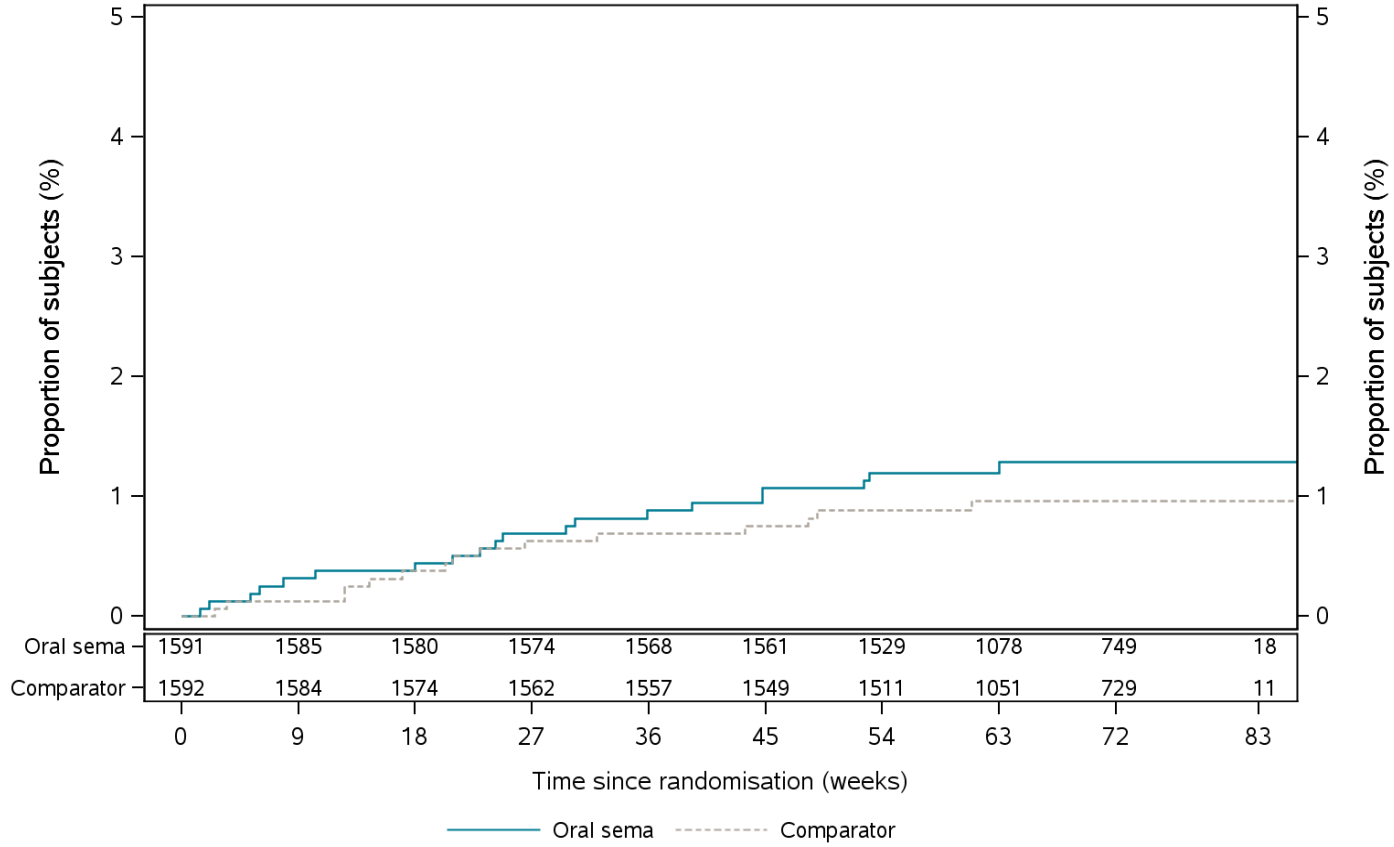
14 Serious adverse events - preferred term "Acute myocardial infarction" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:35:45 - f_cif_tte_p6.sas/f_cif_pt_ami_sae_p6.png

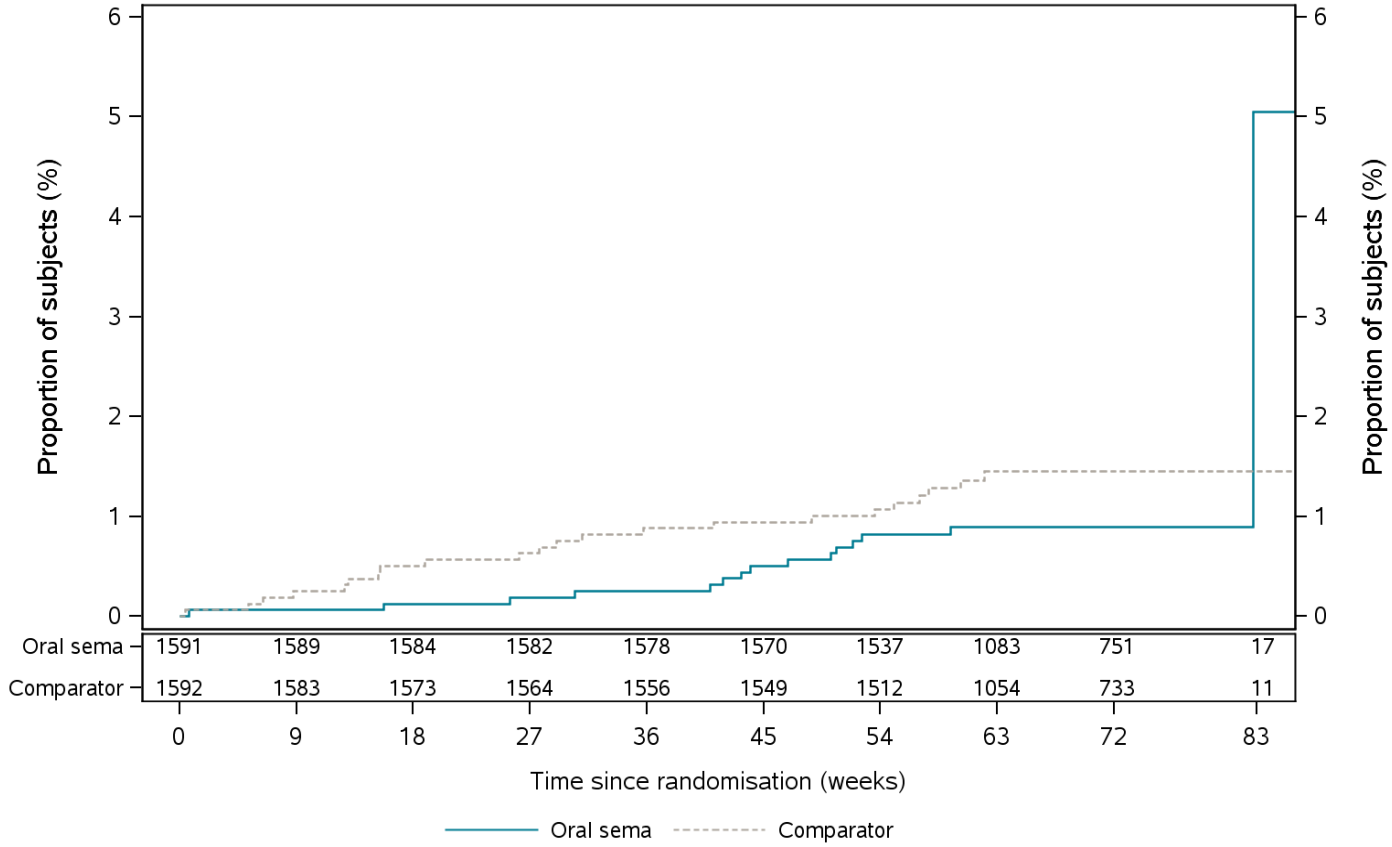
15 Serious adverse events - preferred term "Angina unstable" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:35:58 - f_cif_tte_p6.sas/f_cif_pt_au_sae_p6.png

16 Serious adverse events - preferred term "Pneumonia" - cumulative incidence plot - Pioneer 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).

nn9924/nn9924-submission-package/germany
28APR2020:10:36:10 - f_cif_tte_p6.sas/f_cif_pt_pneu_sae_p6.png

PIONEER 6 – Subgruppenergebnisse – Mortalität / Morbidität / Sicherheit

1 EAC-confirmed all-cause death - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	23 (1.4%)	1568 (98.6%)	5 (0.3%)	0 (0.0%)	1592	45 (2.8%)	1547 (97.2%)	6 (0.4%)	0 (0.0%)	0.51 [0.31;0.84]	0.0078	
Gender													0.9624
Female	507	3 (0.6%)	504 (99.4%)	2 (0.4%)	0 (0.0%)	500	6 (1.2%)	494 (98.8%)	1 (0.2%)	0 (0.0%)	0.49 [0.12;1.96]	0.3148	
Male	1084	20 (1.8%)	1064 (98.2%)	3 (0.3%)	0 (0.0%)	1092	39 (3.6%)	1053 (96.4%)	5 (0.5%)	0 (0.0%)	0.51 [0.30;0.87]	0.0141	
Age													0.0097*
< 65	700	4 (0.6%)	696 (99.4%)	1 (0.1%)	0 (0.0%)	634	21 (3.3%)	613 (96.7%)	2 (0.3%)	0 (0.0%)	0.17 [0.06;0.49]	0.0011	
65 <=	891	19 (2.1%)	872 (97.9%)	4 (0.4%)	0 (0.0%)	958	24 (2.5%)	934 (97.5%)	4 (0.4%)	0 (0.0%)	0.85 [0.47;1.55]	0.5950	
Region B													0.6745
OECD	1056	13 (1.2%)	1043 (98.8%)	4 (0.4%)	0 (0.0%)	1059	28 (2.6%)	1031 (97.4%)	5 (0.5%)	0 (0.0%)	0.46 [0.24;0.89]	0.0212	
Non-OECD	535	10 (1.9%)	525 (98.1%)	1 (0.2%)	0 (0.0%)	533	17 (3.2%)	516 (96.8%)	1 (0.2%)	0 (0.0%)	0.57 [0.26;1.25]	0.1642	
Region C													0.6575
West Europe	293	3 (1.0%)	290 (99.0%)	1 (0.3%)	0 (0.0%)	270	4 (1.5%)	266 (98.5%)	1 (0.4%)	0 (0.0%)	0.70 [0.16;3.13]	0.6407	
Rest of World	1298	20 (1.5%)	1278 (98.5%)	4 (0.3%)	0 (0.0%)	1322	41 (3.1%)	1281 (96.9%)	5 (0.4%)	0 (0.0%)	0.49 [0.29;0.83]	0.0087	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed all-cause death - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.1051
<= 8.5	1068	18 (1.7%)	1050 (98.3%)	3 (0.3%)	0 (0.0%)	1057	27 (2.6%)	1030 (97.4%)	4 (0.4%)	0 (0.0%)	0.65 [0.36;1.18]	0.1608	
8.5 <	513	4 (0.8%)	509 (99.2%)	2 (0.4%)	0 (0.0%)	517	17 (3.3%)	500 (96.7%)	2 (0.4%)	0 (0.0%)	0.23 [0.08;0.69]	0.0089	
HbA1c at baseline (disease severity) B**													0.9497
<= 7.5	627	9 (1.4%)	618 (98.6%)	3 (0.5%)	0 (0.0%)	649	19 (2.9%)	630 (97.1%)	3 (0.5%)	0 (0.0%)	0.48 [0.22;1.07]	0.0720	
7.5 <	954	13 (1.4%)	941 (98.6%)	2 (0.2%)	0 (0.0%)	925	25 (2.7%)	900 (97.3%)	3 (0.3%)	0 (0.0%)	0.50 [0.26;0.98]	0.0422	
Race B													0.8118
White	1148	14 (1.2%)	1134 (98.8%)	3 (0.3%)	0 (0.0%)	1152	29 (2.5%)	1123 (97.5%)	4 (0.3%)	0 (0.0%)	0.48 [0.25;0.91]	0.0244	
Non-White	443	9 (2.0%)	434 (98.0%)	2 (0.5%)	0 (0.0%)	440	16 (3.6%)	424 (96.4%)	2 (0.5%)	0 (0.0%)	0.55 [0.24;1.23]	0.1455	
Evidence of CV disease at screening													0.7763
CV DISEASE	1350	20 (1.5%)	1330 (98.5%)	4 (0.3%)	0 (0.0%)	1345	40 (3.0%)	1305 (97.0%)	5 (0.4%)	0 (0.0%)	0.49 [0.29;0.84]	0.0096	
CV RISK FACTORS ONLY	241	3 (1.2%)	238 (98.8%)	1 (0.4%)	0 (0.0%)	247	5 (2.0%)	242 (98.0%)	1 (0.4%)	0 (0.0%)	0.61 [0.15;2.57]	0.5046	
Insulin Therapy at baseline													0.7413

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed all-cause death - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
No insulin	623	6 (1.0%)	617 (99.0%)	4 (0.6%)	0 (0.0%)	630	11 (1.7%)	619 (98.3%)	1 (0.2%)	0 (0.0%)	0.55 [0.20;1.48]	0.2360	
Basal only	269	2 (0.7%)	267 (99.3%)	1 (0.4%)	0 (0.0%)	265	7 (2.6%)	258 (97.4%)	1 (0.4%)	0 (0.0%)	0.28 [0.06;1.36]	0.1148	
Insulin (not basal only)	699	15 (2.1%)	684 (97.9%)	0 (0.0%)	0 (0.0%)	697	27 (3.9%)	670 (96.1%)	4 (0.6%)	0 (0.0%)	0.54 [0.29;1.02]	0.0572	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

2 EAC-confirmed cardiovascular death (including undetermined cause of death) - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	15 (0.9%)	1576 (99.1%)	13 (0.8%)	8 (0.5%)	1592	30 (1.9%)	1562 (98.1%)	21 (1.3%)	15 (0.9%)	0.49 [0.27;0.92]	0.0261	
Gender													0.5682
Female	507	3 (0.6%)	504 (99.4%)	2 (0.4%)	0 (0.0%)	500	4 (0.8%)	496 (99.2%)	3 (0.6%)	2 (0.4%)	0.74 [0.17;3.30]	0.6925	
Male	1084	12 (1.1%)	1072 (98.9%)	11 (1.0%)	8 (0.7%)	1092	26 (2.4%)	1066 (97.6%)	18 (1.6%)	13 (1.2%)	0.46 [0.23;0.91]	0.0252	
Age													0.0078*
< 65	700	3 (0.4%)	697 (99.6%)	2 (0.3%)	1 (0.1%)	634	18 (2.8%)	616 (97.2%)	5 (0.8%)	3 (0.5%)	0.15 [0.04;0.50]	0.0022	
65 <=	891	12 (1.3%)	879 (98.7%)	11 (1.2%)	7 (0.8%)	958	12 (1.3%)	946 (98.7%)	16 (1.7%)	12 (1.3%)	1.07 [0.48;2.39]	0.8635	
Region B													0.4971
OECD	1056	10 (0.9%)	1046 (99.1%)	7 (0.7%)	3 (0.3%)	1059	17 (1.6%)	1042 (98.4%)	16 (1.5%)	11 (1.0%)	0.59 [0.27;1.28]	0.1802	
Non-OECD	535	5 (0.9%)	530 (99.1%)	6 (1.1%)	5 (0.9%)	533	13 (2.4%)	520 (97.6%)	5 (0.9%)	4 (0.8%)	0.37 [0.13;1.05]	0.0619	
Region C													0.6514
West Europe	293	1 (0.3%)	292 (99.7%)	3 (1.0%)	2 (0.7%)	270	1 (0.4%)	269 (99.6%)	4 (1.5%)	3 (1.1%)	0.93 [0.06;14.91]	0.9606	
Rest of World	1298	14 (1.1%)	1284 (98.9%)	10 (0.8%)	6 (0.5%)	1322	29 (2.2%)	1293 (97.8%)	17 (1.3%)	12 (0.9%)	0.48 [0.26;0.92]	0.0258	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed cardiovascular death (including undetermined cause of death) - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.0855
<= 8.5	1068	11 (1.0%)	1057 (99.0%)	10 (0.9%)	7 (0.7%)	1057	15 (1.4%)	1042 (98.6%)	16 (1.5%)	12 (1.1%)	0.72 [0.33;1.56]	0.4053	
8.5 <	513	3 (0.6%)	510 (99.4%)	3 (0.6%)	1 (0.2%)	517	15 (2.9%)	502 (97.1%)	4 (0.8%)	2 (0.4%)	0.20 [0.06;0.69]	0.0107	
HbA1c at baseline (disease severity) B**													0.1117
<= 7.5	627	7 (1.1%)	620 (98.9%)	5 (0.8%)	2 (0.3%)	649	8 (1.2%)	641 (98.8%)	14 (2.2%)	11 (1.7%)	0.89 [0.32;2.47]	0.8298	
7.5 <	954	7 (0.7%)	947 (99.3%)	8 (0.8%)	6 (0.6%)	925	22 (2.4%)	903 (97.6%)	6 (0.6%)	3 (0.3%)	0.31 [0.13;0.72]	0.0063	
Race B													0.3616
White	1148	11 (1.0%)	1137 (99.0%)	6 (0.5%)	3 (0.3%)	1152	18 (1.6%)	1134 (98.4%)	15 (1.3%)	11 (1.0%)	0.61 [0.29;1.29]	0.1948	
Non-White	443	4 (0.9%)	439 (99.1%)	7 (1.6%)	5 (1.1%)	440	12 (2.7%)	428 (97.3%)	6 (1.4%)	4 (0.9%)	0.32 [0.10;1.00]	0.0507	
Evidence of CV disease at screening													0.1869
CV DISEASE	1350	12 (0.9%)	1338 (99.1%)	12 (0.9%)	8 (0.6%)	1345	28 (2.1%)	1317 (97.9%)	17 (1.3%)	12 (0.9%)	0.42 [0.21;0.83]	0.0125	
CV RISK FACTORS ONLY	241	3 (1.2%)	238 (98.8%)	1 (0.4%)	0 (0.0%)	247	2 (0.8%)	245 (99.2%)	4 (1.6%)	3 (1.2%)	1.53 [0.26;9.17]	0.6403	
Insulin Therapy at baseline													0.8062

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed cardiovascular death (including undetermined cause of death) - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
No insulin	623	3 (0.5%)	620 (99.5%)	7 (1.1%)	3 (0.5%)	630	6 (1.0%)	624 (99.0%)	6 (1.0%)	5 (0.8%)	0.50 [0.13;2.01]	0.3295	
Basal only	269	1 (0.4%)	268 (99.6%)	2 (0.7%)	1 (0.4%)	265	4 (1.5%)	261 (98.5%)	4 (1.5%)	3 (1.1%)	0.25 [0.03;2.22]	0.2121	
Insulin (not basal only)	699	11 (1.6%)	688 (98.4%)	4 (0.6%)	4 (0.6%)	697	20 (2.9%)	677 (97.1%)	11 (1.6%)	7 (1.0%)	0.54 [0.26;1.12]	0.0982	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

3 EAC-confirmed MACE - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	61 (3.8%)	1530 (96.2%)	13 (0.8%)	8 (0.5%)	1592	76 (4.8%)	1516 (95.2%)	19 (1.2%)	13 (0.8%)	0.79 [0.57;1.11]	0.1749	
Gender													0.2805
Female	507	14 (2.8%)	493 (97.2%)	2 (0.4%)	0 (0.0%)	500	12 (2.4%)	488 (97.6%)	3 (0.6%)	2 (0.4%)	1.16 [0.54;2.51]	0.7072	
Male	1084	47 (4.3%)	1037 (95.7%)	11 (1.0%)	8 (0.7%)	1092	64 (5.9%)	1028 (94.1%)	16 (1.5%)	11 (1.0%)	0.72 [0.50;1.05]	0.0910	
Age													0.0515
< 65	700	19 (2.7%)	681 (97.3%)	2 (0.3%)	1 (0.1%)	634	33 (5.2%)	601 (94.8%)	4 (0.6%)	2 (0.3%)	0.51 [0.29;0.90]	0.0208	
65 <=	891	42 (4.7%)	849 (95.3%)	11 (1.2%)	7 (0.8%)	958	43 (4.5%)	915 (95.5%)	15 (1.6%)	11 (1.1%)	1.04 [0.68;1.59]	0.8658	
Region A													0.4434
Non North America	1035	42 (4.1%)	993 (95.9%)	9 (0.9%)	7 (0.7%)	1042	48 (4.6%)	994 (95.4%)	10 (1.0%)	8 (0.8%)	0.87 [0.58;1.32]	0.5153	
North America	556	19 (3.4%)	537 (96.6%)	4 (0.7%)	1 (0.2%)	550	28 (5.1%)	522 (94.9%)	9 (1.6%)	5 (0.9%)	0.66 [0.37;1.18]	0.1606	
Region B													0.3934
OECD	1056	44 (4.2%)	1012 (95.8%)	7 (0.7%)	3 (0.3%)	1059	50 (4.7%)	1009 (95.3%)	14 (1.3%)	9 (0.8%)	0.87 [0.58;1.31]	0.5164	
Non-OECD	535	17 (3.2%)	518 (96.8%)	6 (1.1%)	5 (0.9%)	533	26 (4.9%)	507 (95.1%)	5 (0.9%)	4 (0.8%)	0.64 [0.34;1.17]	0.1460	
Region C													0.6950

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed MACE - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
West Europe	293	11 (3.8%)	282 (96.2%)	3 (1.0%)	2 (0.7%)	270	11 (4.1%)	259 (95.9%)	4 (1.5%)	3 (1.1%)	0.92 [0.40;2.13]	0.8541	
Rest of World	1298	50 (3.9%)	1248 (96.1%)	10 (0.8%)	6 (0.5%)	1322	65 (4.9%)	1257 (95.1%)	15 (1.1%)	10 (0.8%)	0.77 [0.53;1.11]	0.1651	
HbA1c at baseline (disease severity) A**													0.7706
<= 8.5	1068	38 (3.6%)	1030 (96.4%)	10 (0.9%)	7 (0.7%)	1057	46 (4.4%)	1011 (95.6%)	15 (1.4%)	11 (1.0%)	0.81 [0.53;1.24]	0.3294	
8.5 <	513	22 (4.3%)	491 (95.7%)	3 (0.6%)	1 (0.2%)	517	30 (5.8%)	487 (94.2%)	3 (0.6%)	1 (0.2%)	0.73 [0.42;1.26]	0.2578	
HbA1c at baseline (disease severity) B**													0.3498
<= 7.5	627	22 (3.5%)	605 (96.5%)	5 (0.8%)	2 (0.3%)	649	23 (3.5%)	626 (96.5%)	13 (2.0%)	10 (1.5%)	0.97 [0.54;1.74]	0.9195	
7.5 <	954	38 (4.0%)	916 (96.0%)	8 (0.8%)	6 (0.6%)	925	53 (5.7%)	872 (94.3%)	5 (0.5%)	2 (0.2%)	0.69 [0.45;1.05]	0.0796	
Race A													0.1409
White	1148	46 (4.0%)	1102 (96.0%)	6 (0.5%)	3 (0.3%)	1152	55 (4.8%)	1097 (95.2%)	13 (1.1%)	9 (0.8%)	0.83 [0.56;1.23]	0.3500	
Black or African American	89	5 (5.6%)	84 (94.4%)	1 (1.1%)	0 (0.0%)	103	1 (1.0%)	102 (99.0%)	3 (2.9%)	1 (1.0%)	5.67 [0.66;48.51]	0.1133	
Asian	324	9 (2.8%)	315 (97.2%)	6 (1.9%)	5 (1.5%)	306	19 (6.2%)	287 (93.8%)	2 (0.7%)	2 (0.7%)	0.44 [0.20;0.97]	0.0408	
Other	30	1 (3.3%)	29 (96.7%)	0 (0.0%)	0 (0.0%)	31	1 (3.2%)	30 (96.8%)	1 (3.2%)	1 (3.2%)	1.04 [0.06;16.59]	0.9791	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed MACE - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
Race B													0.6521
White	1148	46 (4.0%)	1102 (96.0%)	6 (0.5%)	3 (0.3%)	1152	55 (4.8%)	1097 (95.2%)	13 (1.1%)	9 (0.8%)	0.83 [0.56;1.23]	0.3498	
Non-White	443	15 (3.4%)	428 (96.6%)	7 (1.6%)	5 (1.1%)	440	21 (4.8%)	419 (95.2%)	6 (1.4%)	4 (0.9%)	0.70 [0.36;1.35]	0.2818	
Body mass index (BMI)**													0.2011
<= 30	650	23 (3.5%)	627 (96.5%)	8 (1.2%)	6 (0.9%)	629	35 (5.6%)	594 (94.4%)	9 (1.4%)	8 (1.3%)	0.61 [0.36;1.03]	0.0649	
30 <	940	38 (4.0%)	902 (96.0%)	5 (0.5%)	2 (0.2%)	963	41 (4.3%)	922 (95.7%)	10 (1.0%)	5 (0.5%)	0.95 [0.61;1.48]	0.8332	
Myocardial infarction or stroke prior to randomisation**													0.1625
No	884	20 (2.3%)	864 (97.7%)	8 (0.9%)	4 (0.5%)	845	32 (3.8%)	813 (96.2%)	10 (1.2%)	7 (0.8%)	0.59 [0.34;1.03]	0.0639	
Yes	693	41 (5.9%)	652 (94.1%)	5 (0.7%)	4 (0.6%)	735	44 (6.0%)	691 (94.0%)	9 (1.2%)	6 (0.8%)	0.97 [0.64;1.49]	0.8982	
Renal function (eGFR) as per CKD-EPI**													0.8024
< 60	434	20 (4.6%)	414 (95.4%)	5 (1.2%)	2 (0.5%)	422	25 (5.9%)	397 (94.1%)	10 (2.4%)	8 (1.9%)	0.74 [0.41;1.33]	0.3141	
60 <=	1150	41 (3.6%)	1109 (96.4%)	8 (0.7%)	6 (0.5%)	1158	51 (4.4%)	1107 (95.6%)	9 (0.8%)	5 (0.4%)	0.81 [0.54;1.22]	0.3157	
Evidence of CV disease at screening													0.4425

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed MACE - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
CV DISEASE	1350	57 (4.2%)	1293 (95.8%)	12 (0.9%)	8 (0.6%)	1345	68 (5.1%)	1277 (94.9%)	15 (1.1%)	10 (0.7%)	0.83 [0.58;1.17]	0.2847	
CV RISK FACTORS ONLY	241	4 (1.7%)	237 (98.3%)	1 (0.4%)	0 (0.0%)	247	8 (3.2%)	239 (96.8%)	4 (1.6%)	3 (1.2%)	0.51 [0.15;1.68]	0.2653	
Insulin Therapy at baseline													0.4688
No insulin	623	20 (3.2%)	603 (96.8%)	7 (1.1%)	3 (0.5%)	630	20 (3.2%)	610 (96.8%)	6 (1.0%)	5 (0.8%)	1.01 [0.54;1.87]	0.9852	
Basal only	269	6 (2.2%)	263 (97.8%)	2 (0.7%)	1 (0.4%)	265	12 (4.5%)	253 (95.5%)	3 (1.1%)	2 (0.8%)	0.49 [0.18;1.30]	0.1518	
Insulin (not basal only)	699	35 (5.0%)	664 (95.0%)	4 (0.6%)	4 (0.6%)	697	44 (6.3%)	653 (93.7%)	10 (1.4%)	6 (0.9%)	0.78 [0.50;1.21]	0.2605	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

4 EAC-confirmed non-fatal myocardial infarction - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1591	37 (2.3%)	1554 (97.7%)	26 (1.6%)	21 (1.3%)	1592	31 (1.9%)	1561 (98.1%)	49 (3.1%)	43 (2.7%)	1.18 [0.73;1.90]	0.5044	
Gender													0.1144
Female	507	9 (1.8%)	498 (98.2%)	3 (0.6%)	1 (0.2%)	500	3 (0.6%)	497 (99.4%)	7 (1.4%)	6 (1.2%)	3.03 [0.82;11.21]	0.0959	
Male	1084	28 (2.6%)	1056 (97.4%)	23 (2.1%)	20 (1.8%)	1092	28 (2.6%)	1064 (97.4%)	42 (3.8%)	37 (3.4%)	0.98 [0.58;1.65]	0.9280	
Age													0.9152
< 65	700	14 (2.0%)	686 (98.0%)	4 (0.6%)	3 (0.4%)	634	11 (1.7%)	623 (98.3%)	22 (3.5%)	20 (3.2%)	1.15 [0.52;2.53]	0.7310	
65 <=	891	23 (2.6%)	868 (97.4%)	22 (2.5%)	18 (2.0%)	958	20 (2.1%)	938 (97.9%)	27 (2.8%)	23 (2.4%)	1.21 [0.67;2.21]	0.5293	
Region B													0.9294
OECD	1056	27 (2.6%)	1029 (97.4%)	15 (1.4%)	11 (1.0%)	1059	23 (2.2%)	1036 (97.8%)	31 (2.9%)	26 (2.5%)	1.16 [0.67;2.03]	0.5954	
Non-OECD	535	10 (1.9%)	525 (98.1%)	11 (2.1%)	10 (1.9%)	533	8 (1.5%)	525 (98.5%)	18 (3.4%)	17 (3.2%)	1.22 [0.48;3.09]	0.6738	
Region C													0.6682
West Europe	293	5 (1.7%)	288 (98.3%)	4 (1.4%)	3 (1.0%)	270	5 (1.9%)	265 (98.1%)	5 (1.9%)	4 (1.5%)	0.92 [0.27;3.18]	0.8941	
Rest of World	1298	32 (2.5%)	1266 (97.5%)	22 (1.7%)	18 (1.4%)	1322	26 (2.0%)	1296 (98.0%)	44 (3.3%)	39 (3.0%)	1.23 [0.73;2.07]	0.4274	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed non-fatal myocardial infarction - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.8077
<= 8.5	1068	23 (2.2%)	1045 (97.8%)	20 (1.9%)	17 (1.6%)	1057	20 (1.9%)	1037 (98.1%)	30 (2.8%)	26 (2.5%)	1.12 [0.62;2.04]	0.7066	
8.5 <	513	14 (2.7%)	499 (97.3%)	5 (1.0%)	3 (0.6%)	517	11 (2.1%)	506 (97.9%)	18 (3.5%)	16 (3.1%)	1.27 [0.58;2.80]	0.5543	
HbA1c at baseline (disease severity) B**													0.5814
<= 7.5	627	14 (2.2%)	613 (97.8%)	11 (1.8%)	8 (1.3%)	649	10 (1.5%)	639 (98.5%)	21 (3.2%)	18 (2.8%)	1.41 [0.62;3.16]	0.4112	
7.5 <	954	23 (2.4%)	931 (97.6%)	14 (1.5%)	12 (1.3%)	925	21 (2.3%)	904 (97.7%)	27 (2.9%)	24 (2.6%)	1.06 [0.59;1.91]	0.8483	
Race B													0.9451
White	1148	30 (2.6%)	1118 (97.4%)	15 (1.3%)	12 (1.0%)	1152	25 (2.2%)	1127 (97.8%)	31 (2.7%)	27 (2.3%)	1.19 [0.70;2.02]	0.5245	
Non-White	443	7 (1.6%)	436 (98.4%)	11 (2.5%)	9 (2.0%)	440	6 (1.4%)	434 (98.6%)	18 (4.1%)	16 (3.6%)	1.14 [0.38;3.39]	0.8156	
Evidence of CV disease at screening													0.9794
CV DISEASE	1350	37 (2.7%)	1313 (97.3%)	22 (1.6%)	18 (1.3%)	1345	29 (2.2%)	1316 (97.8%)	43 (3.2%)	38 (2.8%)	1.26 [0.77;2.04]	0.3563	
CV RISK FACTORS ONLY	241	0 (0.0%)	241 (100%)	4 (1.7%)	3 (1.2%)	247	2 (0.8%)	245 (99.2%)	6 (2.4%)	5 (2.0%)	Not est	Not est	
Insulin Therapy at baseline													0.7880

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed non-fatal myocardial infarction - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator	
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value p-value
No insulin	623	12 (1.9%)	611 (98.1%)	10 (1.6%)	6 (1.0%)	630	10 (1.6%)	620 (98.4%)	12 (1.9%)	11 (1.7%)	1.21 [0.52;2.81]	0.6517
Basal only	269	5 (1.9%)	264 (98.1%)	3 (1.1%)	2 (0.7%)	265	6 (2.3%)	259 (97.7%)	7 (2.6%)	6 (2.3%)	0.81 [0.25;2.64]	0.7215
Insulin (not basal only)	699	20 (2.9%)	679 (97.1%)	13 (1.9%)	13 (1.9%)	697	15 (2.2%)	682 (97.8%)	30 (4.3%)	26 (3.7%)	1.30 [0.66;2.53]	0.4469

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

5 EAC-confirmed non-fatal stroke - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	12 (0.8%)	1579 (99.2%)	27 (1.7%)	22 (1.4%)	1592	16 (1.0%)	1576 (99.0%)	50 (3.1%)	44 (2.8%)	0.74 [0.35;1.57]	0.4350	
Gender													0.5927
Female	507	5 (1.0%)	502 (99.0%)	4 (0.8%)	2 (0.4%)	500	5 (1.0%)	495 (99.0%)	7 (1.4%)	6 (1.2%)	0.97 [0.28;3.36]	0.9645	
Male	1084	7 (0.6%)	1077 (99.4%)	23 (2.1%)	20 (1.8%)	1092	11 (1.0%)	1081 (99.0%)	43 (3.9%)	38 (3.5%)	0.63 [0.25;1.64]	0.3476	
Age													0.8089
< 65	700	4 (0.6%)	696 (99.4%)	4 (0.6%)	3 (0.4%)	634	4 (0.6%)	630 (99.4%)	23 (3.6%)	21 (3.3%)	0.88 [0.22;3.52]	0.8555	
65 <=	891	8 (0.9%)	883 (99.1%)	23 (2.6%)	19 (2.1%)	958	12 (1.3%)	946 (98.7%)	27 (2.8%)	23 (2.4%)	0.72 [0.29;1.75]	0.4666	
Region B													0.3646
OECD	1056	10 (0.9%)	1046 (99.1%)	16 (1.5%)	12 (1.1%)	1059	11 (1.0%)	1048 (99.0%)	32 (3.0%)	27 (2.5%)	0.91 [0.39;2.14]	0.8293	
Non-OECD	535	2 (0.4%)	533 (99.6%)	11 (2.1%)	10 (1.9%)	533	5 (0.9%)	528 (99.1%)	18 (3.4%)	17 (3.2%)	0.39 [0.08;1.99]	0.2562	
Region C													0.6281
West Europe	293	5 (1.7%)	288 (98.3%)	4 (1.4%)	3 (1.0%)	270	5 (1.9%)	265 (98.1%)	5 (1.9%)	4 (1.5%)	0.94 [0.27;3.24]	0.9186	
Rest of World	1298	7 (0.5%)	1291 (99.5%)	23 (1.8%)	19 (1.5%)	1322	11 (0.8%)	1311 (99.2%)	45 (3.4%)	40 (3.0%)	0.64 [0.25;1.64]	0.3517	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed non-fatal stroke - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.0807
<= 8.5	1068	5 (0.5%)	1063 (99.5%)	21 (2.0%)	18 (1.7%)	1057	12 (1.1%)	1045 (98.9%)	30 (2.8%)	26 (2.5%)	0.41 [0.14;1.16]	0.0940	
8.5 <	513	7 (1.4%)	506 (98.6%)	5 (1.0%)	3 (0.6%)	517	4 (0.8%)	513 (99.2%)	19 (3.7%)	17 (3.3%)	1.72 [0.50;5.89]	0.3849	
HbA1c at baseline (disease severity) B**													0.2750
<= 7.5	627	2 (0.3%)	625 (99.7%)	12 (1.9%)	9 (1.4%)	649	6 (0.9%)	643 (99.1%)	21 (3.2%)	18 (2.8%)	0.34 [0.07;1.71]	0.1922	
7.5 <	954	10 (1.0%)	944 (99.0%)	14 (1.5%)	12 (1.3%)	925	10 (1.1%)	915 (98.9%)	28 (3.0%)	25 (2.7%)	0.95 [0.40;2.29]	0.9136	
Race B													0.4022
White	1148	8 (0.7%)	1140 (99.3%)	16 (1.4%)	13 (1.1%)	1152	13 (1.1%)	1139 (98.9%)	32 (2.8%)	28 (2.4%)	0.61 [0.25;1.48]	0.2779	
Non-White	443	4 (0.9%)	439 (99.1%)	11 (2.5%)	9 (2.0%)	440	3 (0.7%)	437 (99.3%)	18 (4.1%)	16 (3.6%)	1.29 [0.29;5.76]	0.7387	
Evidence of CV disease at screening													0.2881
CV DISEASE	1350	11 (0.8%)	1339 (99.2%)	23 (1.7%)	19 (1.4%)	1345	12 (0.9%)	1333 (99.1%)	44 (3.3%)	39 (2.9%)	0.90 [0.40;2.04]	0.8049	
CV RISK FACTORS ONLY	241	1 (0.4%)	240 (99.6%)	4 (1.7%)	3 (1.2%)	247	4 (1.6%)	243 (98.4%)	6 (2.4%)	5 (2.0%)	0.25 [0.03;2.27]	0.2201	
Insulin Therapy at baseline													0.8441

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed non-fatal stroke - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
No insulin	623	5 (0.8%)	618 (99.2%)	10 (1.6%)	6 (1.0%)	630	4 (0.6%)	626 (99.4%)	12 (1.9%)	11 (1.7%)	1.25 [0.33;4.64]	0.7438	
Basal only	269	0 (0.0%)	269 (100%)	3 (1.1%)	2 (0.7%)	265	3 (1.1%)	262 (98.9%)	7 (2.6%)	6 (2.3%)	Not est	Not est	
Insulin (not basal only)	699	7 (1.0%)	692 (99.0%)	14 (2.0%)	14 (2.0%)	697	9 (1.3%)	688 (98.7%)	31 (4.4%)	27 (3.9%)	0.76 [0.28;2.05]	0.5934	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

6 EAC-confirmed unstable angina pectoris requiring hospitalisation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	11 (0.7%)	1580 (99.3%)	27 (1.7%)	22 (1.4%)	1592	7 (0.4%)	1585 (99.6%)	51 (3.2%)	45 (2.8%)	1.56 [0.60;4.01]	0.3605	
Gender													0.9901
Female	507	2 (0.4%)	505 (99.6%)	5 (1.0%)	3 (0.6%)	500	0 (0.0%)	500 (100%)	7 (1.4%)	6 (1.2%)	Not est	Not est	
Male	1084	9 (0.8%)	1075 (99.2%)	22 (2.0%)	19 (1.8%)	1092	7 (0.6%)	1085 (99.4%)	44 (4.0%)	39 (3.6%)	1.27 [0.47;3.41]	0.6372	
Age													0.3001
< 65	700	4 (0.6%)	696 (99.4%)	4 (0.6%)	3 (0.4%)	634	4 (0.6%)	630 (99.4%)	23 (3.6%)	21 (3.3%)	0.89 [0.22;3.58]	0.8751	
65 <=	891	7 (0.8%)	884 (99.2%)	23 (2.6%)	19 (2.1%)	958	3 (0.3%)	955 (99.7%)	28 (2.9%)	24 (2.5%)	2.49 [0.64;9.64]	0.1859	
Region B													0.9397
OECD	1056	8 (0.8%)	1048 (99.2%)	16 (1.5%)	12 (1.1%)	1059	5 (0.5%)	1054 (99.5%)	33 (3.1%)	28 (2.6%)	1.59 [0.52;4.87]	0.4142	
Non-OECD	535	3 (0.6%)	532 (99.4%)	11 (2.1%)	10 (1.9%)	533	2 (0.4%)	531 (99.6%)	18 (3.4%)	17 (3.2%)	1.47 [0.25;8.79]	0.6739	
Region C													0.6952
West Europe	293	1 (0.3%)	292 (99.7%)	4 (1.4%)	3 (1.0%)	270	1 (0.4%)	269 (99.6%)	5 (1.9%)	4 (1.5%)	0.93 [0.06;14.84]	0.9580	
Rest of World	1298	10 (0.8%)	1288 (99.2%)	23 (1.8%)	19 (1.5%)	1322	6 (0.5%)	1316 (99.5%)	46 (3.5%)	41 (3.1%)	1.67 [0.61;4.61]	0.3183	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed unstable angina pectoris requiring hospitalisation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.6221
<= 8.5	1068	9 (0.8%)	1059 (99.2%)	20 (1.9%)	17 (1.6%)	1057	5 (0.5%)	1052 (99.5%)	31 (2.9%)	27 (2.6%)	1.76 [0.59;5.26]	0.3100	
8.5 <	513	2 (0.4%)	511 (99.6%)	6 (1.2%)	4 (0.8%)	517	2 (0.4%)	515 (99.6%)	19 (3.7%)	17 (3.3%)	1.00 [0.14;7.11]	0.9985	
HbA1c at baseline (disease severity) B**													0.8789
<= 7.5	627	5 (0.8%)	622 (99.2%)	11 (1.8%)	8 (1.3%)	649	3 (0.5%)	646 (99.5%)	22 (3.4%)	19 (2.9%)	1.69 [0.40;7.06]	0.4742	
7.5 <	954	6 (0.6%)	948 (99.4%)	15 (1.6%)	13 (1.4%)	925	4 (0.4%)	921 (99.6%)	28 (3.0%)	25 (2.7%)	1.45 [0.41;5.15]	0.5621	
Race B													0.4852
White	1148	8 (0.7%)	1140 (99.3%)	16 (1.4%)	13 (1.1%)	1152	4 (0.3%)	1148 (99.7%)	33 (2.9%)	29 (2.5%)	1.99 [0.60;6.61]	0.2609	
Non-White	443	3 (0.7%)	440 (99.3%)	11 (2.5%)	9 (2.0%)	440	3 (0.7%)	437 (99.3%)	18 (4.1%)	16 (3.6%)	0.98 [0.20;4.84]	0.9766	
Evidence of CV disease at screening													0.9909
CV DISEASE	1350	10 (0.7%)	1340 (99.3%)	24 (1.8%)	20 (1.5%)	1345	7 (0.5%)	1338 (99.5%)	45 (3.3%)	40 (3.0%)	1.41 [0.54;3.71]	0.4842	
CV RISK FACTORS ONLY	241	1 (0.4%)	240 (99.6%)	3 (1.2%)	2 (0.8%)	247	0 (0.0%)	247 (100%)	6 (2.4%)	5 (2.0%)	Not est	Not est	
Insulin Therapy at baseline													0.8955

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed unstable angina pectoris requiring hospitalisation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs. Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
No insulin	623	3 (0.5%)	620 (99.5%)	10 (1.6%)	6 (1.0%)	630	2 (0.3%)	628 (99.7%)	12 (1.9%)	11 (1.7%)	1.52 [0.25;9.12]	0.6446	
Basal only	269	0 (0.0%)	269 (100%)	3 (1.1%)	2 (0.7%)	265	2 (0.8%)	263 (99.2%)	8 (3.0%)	7 (2.6%)	Not est	Not est	
Insulin (not basal only)	699	8 (1.1%)	691 (98.9%)	14 (2.0%)	14 (2.0%)	697	3 (0.4%)	694 (99.6%)	31 (4.4%)	27 (3.9%)	2.60 [0.69;9.79]	0.1585	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

7 EAC-confirmed heart failure requiring hospitalisation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	21 (1.3%)	1570 (98.7%)	25 (1.6%)	20 (1.3%)	1592	24 (1.5%)	1568 (98.5%)	48 (3.0%)	42 (2.6%)	0.86 [0.48;1.55]	0.6227	
Gender													0.7612
Female	507	6 (1.2%)	501 (98.8%)	4 (0.8%)	2 (0.4%)	500	6 (1.2%)	494 (98.8%)	7 (1.4%)	6 (1.2%)	1.00 [0.32;3.11]	0.9966	
Male	1084	15 (1.4%)	1069 (98.6%)	21 (1.9%)	18 (1.7%)	1092	18 (1.6%)	1074 (98.4%)	41 (3.8%)	36 (3.3%)	0.82 [0.41;1.62]	0.5622	
Age													0.2430
< 65	700	6 (0.9%)	694 (99.1%)	3 (0.4%)	2 (0.3%)	634	10 (1.6%)	624 (98.4%)	20 (3.2%)	18 (2.8%)	0.54 [0.20;1.48]	0.2316	
65 <=	891	15 (1.7%)	876 (98.3%)	22 (2.5%)	18 (2.0%)	958	14 (1.5%)	944 (98.5%)	28 (2.9%)	24 (2.5%)	1.13 [0.55;2.35]	0.7363	
Region B													0.3698
OECD	1056	18 (1.7%)	1038 (98.3%)	15 (1.4%)	11 (1.0%)	1059	18 (1.7%)	1041 (98.3%)	32 (3.0%)	27 (2.5%)	0.99 [0.51;1.90]	0.9739	
Non-OECD	535	3 (0.6%)	532 (99.4%)	10 (1.9%)	9 (1.7%)	533	6 (1.1%)	527 (98.9%)	16 (3.0%)	15 (2.8%)	0.49 [0.12;1.96]	0.3140	
Region C													0.2069
West Europe	293	1 (0.3%)	292 (99.7%)	4 (1.4%)	3 (1.0%)	270	4 (1.5%)	266 (98.5%)	5 (1.9%)	4 (1.5%)	0.23 [0.03;2.07]	0.1900	
Rest of World	1298	20 (1.5%)	1278 (98.5%)	21 (1.6%)	17 (1.3%)	1322	20 (1.5%)	1302 (98.5%)	43 (3.3%)	38 (2.9%)	1.00 [0.54;1.86]	0.9972	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed heart failure requiring hospitalisation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.7615
<= 8.5	1068	15 (1.4%)	1053 (98.6%)	19 (1.8%)	16 (1.5%)	1057	16 (1.5%)	1041 (98.5%)	30 (2.8%)	26 (2.5%)	0.91 [0.45;1.85]	0.8010	
8.5 <	513	6 (1.2%)	507 (98.8%)	5 (1.0%)	3 (0.6%)	517	8 (1.5%)	509 (98.5%)	17 (3.3%)	15 (2.9%)	0.75 [0.26;2.16]	0.5945	
HbA1c at baseline (disease severity) B**													0.9554
<= 7.5	627	7 (1.1%)	620 (98.9%)	11 (1.8%)	8 (1.3%)	649	8 (1.2%)	641 (98.8%)	21 (3.2%)	18 (2.8%)	0.88 [0.32;2.42]	0.8015	
7.5 <	954	14 (1.5%)	940 (98.5%)	13 (1.4%)	11 (1.2%)	925	16 (1.7%)	909 (98.3%)	26 (2.8%)	23 (2.5%)	0.85 [0.41;1.74]	0.6510	
Race B													0.5526
White	1148	15 (1.3%)	1133 (98.7%)	16 (1.4%)	13 (1.1%)	1152	19 (1.6%)	1133 (98.4%)	32 (2.8%)	28 (2.4%)	0.78 [0.40;1.53]	0.4714	
Non-White	443	6 (1.4%)	437 (98.6%)	9 (2.0%)	7 (1.6%)	440	5 (1.1%)	435 (98.9%)	16 (3.6%)	14 (3.2%)	1.18 [0.36;3.87]	0.7850	
Evidence of CV disease at screening													0.9869
CV DISEASE	1350	21 (1.6%)	1329 (98.4%)	21 (1.6%)	17 (1.3%)	1345	22 (1.6%)	1323 (98.4%)	42 (3.1%)	37 (2.8%)	0.94 [0.52;1.71]	0.8397	
CV RISK FACTORS ONLY	241	0 (0.0%)	241 (100%)	4 (1.7%)	3 (1.2%)	247	2 (0.8%)	245 (99.2%)	6 (2.4%)	5 (2.0%)	Not est	Not est	
Insulin Therapy at baseline													0.9343

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed heart failure requiring hospitalisation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator	
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
No insulin	623	3 (0.5%)	620 (99.5%)	9 (1.4%)	5 (0.8%)	630	3 (0.5%)	627 (99.5%)	12 (1.9%)	11 (1.7%)	1.01 [0.20;5.03]	0.9858
Basal only	269	5 (1.9%)	264 (98.1%)	2 (0.7%)	1 (0.4%)	265	5 (1.9%)	260 (98.1%)	8 (3.0%)	7 (2.6%)	0.97 [0.28;3.36]	0.9653
Insulin (not basal only)	699	13 (1.9%)	686 (98.1%)	14 (2.0%)	14 (2.0%)	697	16 (2.3%)	681 (97.7%)	28 (4.0%)	24 (3.4%)	0.79 [0.38;1.63]	0.5197
p-value interaction												

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

8 EAC-confirmed transient ischemic attack - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	5 (0.3%)	1586 (99.7%)	27 (1.7%)	22 (1.4%)	1592	9 (0.6%)	1583 (99.4%)	51 (3.2%)	45 (2.8%)	0.55 [0.18;1.64]	0.2843	
Gender													0.8653
Female	507	2 (0.4%)	505 (99.6%)	4 (0.8%)	2 (0.4%)	500	4 (0.8%)	496 (99.2%)	7 (1.4%)	6 (1.2%)	0.49 [0.09;2.69]	0.4124	
Male	1084	3 (0.3%)	1081 (99.7%)	23 (2.1%)	20 (1.8%)	1092	5 (0.5%)	1087 (99.5%)	44 (4.0%)	39 (3.6%)	0.60 [0.14;2.49]	0.4784	
Age													0.2872
< 65	700	2 (0.3%)	698 (99.7%)	4 (0.6%)	3 (0.4%)	634	1 (0.2%)	633 (99.8%)	23 (3.6%)	21 (3.3%)	1.78 [0.16;19.63]	0.6379	
65 <=	891	3 (0.3%)	888 (99.7%)	23 (2.6%)	19 (2.1%)	958	8 (0.8%)	950 (99.2%)	28 (2.9%)	24 (2.5%)	0.40 [0.11;1.51]	0.1774	
Region B													0.9998
OECD	1056	5 (0.5%)	1051 (99.5%)	16 (1.5%)	12 (1.1%)	1059	9 (0.8%)	1050 (99.2%)	33 (3.1%)	28 (2.6%)	0.55 [0.18;1.65]	0.2859	
Non-OECD	535	0 (0.0%)	535 (100%)	11 (2.1%)	10 (1.9%)	533	0 (0.0%)	533 (100%)	18 (3.4%)	17 (3.2%)	Not est	Not est	
Region C													0.3425
West Europe	293	1 (0.3%)	292 (99.7%)	4 (1.4%)	3 (1.0%)	270	4 (1.5%)	266 (98.5%)	5 (1.9%)	4 (1.5%)	0.23 [0.03;2.09]	0.1927	
Rest of World	1298	4 (0.3%)	1294 (99.7%)	23 (1.8%)	19 (1.5%)	1322	5 (0.4%)	1317 (99.6%)	46 (3.5%)	41 (3.1%)	0.80 [0.22;2.99]	0.7441	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed transient ischemic attack - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.8820
<= 8.5	1068	3 (0.3%)	1065 (99.7%)	21 (2.0%)	18 (1.7%)	1057	5 (0.5%)	1052 (99.5%)	31 (2.9%)	27 (2.6%)	0.59 [0.14;2.46]	0.4681	
8.5 <	513	2 (0.4%)	511 (99.6%)	5 (1.0%)	3 (0.6%)	517	4 (0.8%)	513 (99.2%)	19 (3.7%)	17 (3.3%)	0.50 [0.09;2.72]	0.4203	
HbA1c at baseline (disease severity) B**													0.9894
<= 7.5	627	0 (0.0%)	627 (100%)	12 (1.9%)	9 (1.4%)	649	4 (0.6%)	645 (99.4%)	22 (3.4%)	19 (2.9%)	Not est	Not est	
7.5 <	954	5 (0.5%)	949 (99.5%)	14 (1.5%)	12 (1.3%)	925	5 (0.5%)	920 (99.5%)	28 (3.0%)	25 (2.7%)	0.96 [0.28;3.32]	0.9516	
Race B													0.9998
White	1148	5 (0.4%)	1143 (99.6%)	16 (1.4%)	13 (1.1%)	1152	9 (0.8%)	1143 (99.2%)	33 (2.9%)	29 (2.5%)	0.55 [0.19;1.65]	0.2889	
Non-White	443	0 (0.0%)	443 (100%)	11 (2.5%)	9 (2.0%)	440	0 (0.0%)	440 (100%)	18 (4.1%)	16 (3.6%)	Not est	Not est	
Evidence of CV disease at screening													0.6353
CV DISEASE	1350	4 (0.3%)	1346 (99.7%)	23 (1.7%)	19 (1.4%)	1345	8 (0.6%)	1337 (99.4%)	45 (3.3%)	40 (3.0%)	0.49 [0.15;1.64]	0.2477	
CV RISK FACTORS ONLY	241	1 (0.4%)	240 (99.6%)	4 (1.7%)	3 (1.2%)	247	1 (0.4%)	246 (99.6%)	6 (2.4%)	5 (2.0%)	1.02 [0.06;16.36]	0.9871	
Insulin Therapy at baseline													0.8872

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed transient ischemic attack - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
No insulin	623	0 (0.0%)	623 (100%)	10 (1.6%)	6 (1.0%)	630	3 (0.5%)	627 (99.5%)	12 (1.9%)	11 (1.7%)	Not est	Not est	
Basal only	269	1 (0.4%)	268 (99.6%)	3 (1.1%)	2 (0.7%)	265	2 (0.8%)	263 (99.2%)	8 (3.0%)	7 (2.6%)	0.49 [0.04;5.41]	0.5607	
Insulin (not basal only)	699	4 (0.6%)	695 (99.4%)	14 (2.0%)	14 (2.0%)	697	4 (0.6%)	693 (99.4%)	31 (4.4%)	27 (3.9%)	0.98 [0.24;3.92]	0.9766	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

9 EAC-confirmed acute kidney injury - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	38 (2.4%)	1553 (97.6%)	24 (1.5%)	19 (1.2%)	1592	38 (2.4%)	1554 (97.6%)	47 (3.0%)	41 (2.6%)	0.99 [0.63;1.55]	0.9645	
Gender													0.4407
Female	507	14 (2.8%)	493 (97.2%)	3 (0.6%)	1 (0.2%)	500	11 (2.2%)	489 (97.8%)	7 (1.4%)	6 (1.2%)	1.28 [0.58;2.81]	0.5435	
Male	1084	24 (2.2%)	1060 (97.8%)	21 (1.9%)	18 (1.7%)	1092	27 (2.5%)	1065 (97.5%)	40 (3.7%)	35 (3.2%)	0.87 [0.50;1.52]	0.6334	
Age													0.9253
< 65	700	13 (1.9%)	687 (98.1%)	3 (0.4%)	2 (0.3%)	634	12 (1.9%)	622 (98.1%)	22 (3.5%)	20 (3.2%)	0.98 [0.45;2.14]	0.9508	
65 <=	891	25 (2.8%)	866 (97.2%)	21 (2.4%)	17 (1.9%)	958	26 (2.7%)	932 (97.3%)	25 (2.6%)	21 (2.2%)	1.02 [0.59;1.77]	0.9398	
Region B													0.9701
OECD	1056	30 (2.8%)	1026 (97.2%)	15 (1.4%)	11 (1.0%)	1059	30 (2.8%)	1029 (97.2%)	29 (2.7%)	24 (2.3%)	1.00 [0.60;1.65]	0.9896	
Non-OECD	535	8 (1.5%)	527 (98.5%)	9 (1.7%)	8 (1.5%)	533	8 (1.5%)	525 (98.5%)	18 (3.4%)	17 (3.2%)	0.98 [0.37;2.60]	0.9610	
Region C													0.3443
West Europe	293	6 (2.0%)	287 (98.0%)	4 (1.4%)	3 (1.0%)	270	3 (1.1%)	267 (98.9%)	5 (1.9%)	4 (1.5%)	1.86 [0.47;7.44]	0.3794	
Rest of World	1298	32 (2.5%)	1266 (97.5%)	20 (1.5%)	16 (1.2%)	1322	35 (2.6%)	1287 (97.4%)	42 (3.2%)	37 (2.8%)	0.92 [0.57;1.48]	0.7251	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed acute kidney injury - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.3552
<= 8.5	1068	27 (2.5%)	1041 (97.5%)	19 (1.8%)	16 (1.5%)	1057	23 (2.2%)	1034 (97.8%)	28 (2.6%)	24 (2.3%)	1.15 [0.66;2.01]	0.6224	
8.5 <	513	11 (2.1%)	502 (97.9%)	4 (0.8%)	2 (0.4%)	517	15 (2.9%)	502 (97.1%)	18 (3.5%)	16 (3.1%)	0.73 [0.34;1.59]	0.4328	
HbA1c at baseline (disease severity) B**													0.4260
<= 7.5	627	19 (3.0%)	608 (97.0%)	11 (1.8%)	8 (1.3%)	649	16 (2.5%)	633 (97.5%)	19 (2.9%)	16 (2.5%)	1.21 [0.62;2.34]	0.5823	
7.5 <	954	19 (2.0%)	935 (98.0%)	12 (1.3%)	10 (1.0%)	925	22 (2.4%)	903 (97.6%)	27 (2.9%)	24 (2.6%)	0.83 [0.45;1.54]	0.5633	
Race B													0.8289
White	1148	25 (2.2%)	1123 (97.8%)	15 (1.3%)	12 (1.0%)	1152	26 (2.3%)	1126 (97.7%)	30 (2.6%)	26 (2.3%)	0.96 [0.55;1.65]	0.8702	
Non-White	443	13 (2.9%)	430 (97.1%)	9 (2.0%)	7 (1.6%)	440	12 (2.7%)	428 (97.3%)	17 (3.9%)	15 (3.4%)	1.06 [0.48;2.33]	0.8812	
Evidence of CV disease at screening													0.9812
CV DISEASE	1350	38 (2.8%)	1312 (97.2%)	20 (1.5%)	16 (1.2%)	1345	34 (2.5%)	1311 (97.5%)	42 (3.1%)	37 (2.8%)	1.10 [0.70;1.75]	0.6744	
CV RISK FACTORS ONLY	241	0 (0.0%)	241 (100%)	4 (1.7%)	3 (1.2%)	247	4 (1.6%)	243 (98.4%)	5 (2.0%)	4 (1.6%)	Not est	Not est	
Insulin Therapy at baseline													0.5674

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

EAC-confirmed acute kidney injury - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator	
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value p-value
No insulin	623	9 (1.4%)	614 (98.6%)	8 (1.3%)	4 (0.6%)	630	11 (1.7%)	619 (98.3%)	11 (1.7%)	10 (1.6%)	0.83 [0.34;2.00]	0.6772
Basal only	269	6 (2.2%)	263 (97.8%)	3 (1.1%)	2 (0.7%)	265	3 (1.1%)	262 (98.9%)	6 (2.3%)	5 (1.9%)	1.96 [0.49;7.85]	0.3400
Insulin (not basal only)	699	23 (3.3%)	676 (96.7%)	13 (1.9%)	13 (1.9%)	697	24 (3.4%)	673 (96.6%)	30 (4.3%)	26 (3.7%)	0.93 [0.53;1.65]	0.8092

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

10 HbA1c (%) - ANCOVA - Pioneer 6 - in-trial - full analysis set

	Oral Sema						Comparator						Oral Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1591	1581	1497	8.16 (1.6)	7.16 (1.2)	-1.00 (0.0)	1592	1574	1486	8.16 (1.6)	7.81 (1.3)	-0.34 (0.0)	-0.66 [-0.74;-0.59] <0.0001	-0.50 [-0.57;-0.43]	
Gender															0.0218*
Female	507	505	484	8.28 (1.6)	7.17 (1.3)	-1.04 (0.0)	500	493	471	8.38 (1.8)	7.98 (1.4)	-0.25 (0.0)	-0.79 [-0.93;-0.66] <0.0001	-0.56 [-0.69;-0.43]	
Male	1084	1076	1013	8.10 (1.6)	7.16 (1.2)	-0.99 (0.0)	1092	1081	1015	8.06 (1.5)	7.73 (1.3)	-0.38 (0.0)	-0.60 [-0.70;-0.51] <0.0001	-0.47 [-0.56;-0.38]	
Age															0.2357
< 65	700	697	665	8.36 (1.7)	7.27 (1.3)	-0.98 (0.0)	634	628	588	8.40 (1.8)	8.00 (1.5)	-0.26 (0.0)	-0.72 [-0.84;-0.61] <0.0001	-0.47 [-0.58;-0.36]	
65 <=	891	884	832	8.00 (1.4)	7.08 (1.2)	-1.02 (0.0)	958	946	898	8.00 (1.5)	7.69 (1.2)	-0.39 (0.0)	-0.63 [-0.73;-0.53] <0.0001	-0.53 [-0.62;-0.43]	
Region B															0.0008*
OECD	1056	1050	989	8.04 (1.5)	7.15 (1.2)	-0.97 (0.0)	1059	1048	985	8.03 (1.6)	7.70 (1.2)	-0.39 (0.0)	-0.57 [-0.66;-0.48] <0.0001	-0.48 [-0.57;-0.39]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an
observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

HbA1c (%) - ANCOVA - Pioneer 6 - in-trial - full analysis set

	Oral Sema						Comparator						Oral Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Non-OECD	535	531	508	8.39 (1.7)	7.18 (1.3)	-1.08 (0.0)	533	526	501	8.43 (1.7)	8.04 (1.5)	-0.23 (0.0)	-0.84 [-0.97;-0.72] <0.0001	-0.54 [-0.66;-0.41]	
Region C															0.0112*
West Europe	293	290	275	7.82 (1.3)	7.15 (1.1)	-0.86 (0.1)	270	266	259	7.66 (1.2)	7.54 (1.0)	-0.41 (0.1)	-0.45 [-0.63;-0.28] <0.0001	-0.57 [-0.75;-0.40]	
Rest of World	1298	1291	1222	8.24 (1.6)	7.16 (1.3)	-1.04 (0.0)	1322	1308	1227	8.26 (1.7)	7.87 (1.4)	-0.33 (0.0)	-0.71 [-0.79;-0.63] <0.0001	-0.50 [-0.58;-0.42]	
HbA1c at baseline (disease severity) A**															0.0004*
<= 8.5	1068	1068	1005	7.29 (0.8)	6.78 (0.9)	-0.50 (0.0)	1057	1057	994	7.26 (0.8)	7.34 (1.0)	0.07 (0.0)	-0.57 [-0.66;-0.48] <0.0001	-0.68 [-0.77;-0.59]	
8.5 <	513	513	484	9.97 (1.2)	7.93 (1.4)	-2.04 (0.0)	517	517	479	10.00 (1.4)	8.79 (1.5)	-1.18 (0.0)	-0.86 [-0.99;-0.73] <0.0001	-0.52 [-0.65;-0.39]	
HbA1c at baseline (disease severity) B**															<0.0001*

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

HbA1c (%) - ANCOVA - Pioneer 6 - in-trial - full analysis set

	Oral Sema						Comparator						Oral Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
<= 7.5	627	627	589	6.76 (0.5)	6.51 (0.8)	-0.26 (0.0)	649	649	608	6.76 (0.6)	6.99 (0.9)	0.23 (0.0)	-0.48 [-0.60;-0.36] <0.0001	-0.65 [-0.77;-0.54]	
7.5 <	954	954	900	9.08 (1.3)	7.58 (1.3)	-1.51 (0.0)	925	925	865	9.14 (1.4)	8.39 (1.3)	-0.72 (0.0)	-0.79 [-0.89;-0.70] <0.0001	-0.52 [-0.62;-0.43]	
Race B															0.0004*
White	1148	1142	1086	8.04 (1.5)	7.16 (1.2)	-0.95 (0.0)	1152	1140	1082	8.05 (1.6)	7.73 (1.3)	-0.37 (0.0)	-0.58 [-0.67;-0.49] <0.0001	-0.46 [-0.55;-0.38]	
Non-White	443	439	411	8.48 (1.7)	7.17 (1.3)	-1.14 (0.1)	440	434	404	8.46 (1.8)	8.03 (1.5)	-0.26 (0.1)	-0.89 [-1.03;-0.74] <0.0001	-0.59 [-0.73;-0.45]	
Evidence of CV disease at screening															0.0534
CV DISEASE	1350	1341	1264	8.14 (1.6)	7.18 (1.2)	-0.97 (0.0)	1345	1332	1250	8.16 (1.6)	7.82 (1.3)	-0.34 (0.0)	-0.63 [-0.71;-0.55] <0.0001	-0.46 [-0.54;-0.38]	
CV RISK FACTORS ONLY	241	240	233	8.30 (1.6)	7.04 (1.1)	-1.19 (0.1)	247	242	236	8.15 (1.6)	7.79 (1.4)	-0.36 (0.1)	-0.84 [-1.03;-0.65] <0.0001	-0.71 [-0.90;-0.52]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

HbA1c (%) - ANCOVA - Pioneer 6 - in-trial - full analysis set

	Oral Sema						Comparator						Oral Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Insulin Therapy at baseline															0.3111
No insulin	623	622	588	7.74 (1.6)	6.79 (1.0)	-1.19 (0.0)	630	627	597	7.70 (1.5)	7.36 (1.1)	-0.59 (0.0)	-0.61 [-0.72;-0.49] <0.0001	-0.50 [-0.62;-0.39]	
Basal only	269	268	253	8.29 (1.5)	7.28 (1.3)	-0.93 (0.1)	265	260	252	8.24 (1.5)	7.92 (1.2)	-0.28 (0.1)	-0.65 [-0.83;-0.47] <0.0001	-0.50 [-0.68;-0.32]	
Insulin (not basal only)	699	691	656	8.48 (1.5)	7.45 (1.3)	-0.86 (0.0)	697	687	637	8.55 (1.7)	8.20 (1.5)	-0.13 (0.0)	-0.73 [-0.84;-0.62] <0.0001	-0.50 [-0.61;-0.39]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

11 Body weight (kg) - ANCOVA - Pioneer 6 - in-trial - full analysis set

	Oral Sema						Comparator						Oral Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1591	1590	1511	91.00 (21.4)	86.60 (20.7)	-4.22 (0.1)	1592	1592	1493	90.80 (21.0)	89.93 (21.2)	-0.83 (0.1)	-3.38 [-3.75;-3.02] <0.0001	-0.66 [-0.73;-0.58]	
Gender															0.0005*
Female	507	507	489	85.10 (21.0)	80.10 (19.9)	-5.23 (0.2)	500	500	475	85.55 (20.8)	84.62 (20.9)	-0.92 (0.2)	-4.31 [-4.95;-3.67] <0.0001	-0.75 [-0.88;-0.62]	
Male	1084	1083	1022	93.77 (21.1)	89.71 (20.4)	-3.73 (0.2)	1092	1092	1018	93.20 (20.7)	92.40 (20.9)	-0.79 (0.2)	-2.94 [-3.38;-2.50] <0.0001	-0.61 [-0.70;-0.52]	
Age															0.0958
< 65	700	699	668	91.29 (22.1)	87.19 (21.1)	-3.77 (0.2)	634	634	593	91.54 (21.9)	90.61 (21.6)	-0.73 (0.2)	-3.04 [-3.60;-2.48] <0.0001	-0.54 [-0.65;-0.42]	
65 <=	891	891	843	90.78 (20.9)	86.13 (20.4)	-4.57 (0.2)	958	958	900	90.31 (20.5)	89.48 (21.0)	-0.90 (0.2)	-3.67 [-4.14;-3.19] <0.0001	-0.77 [-0.87;-0.67]	
Region B															0.0089*
OECD	1056	1056	1000	97.03 (21.0)	92.04 (20.6)	-4.46 (0.2)	1059	1059	987	95.95 (20.6)	95.18 (20.8)	-0.73 (0.2)	-3.73 [-4.18;-3.28] <0.0001	-0.68 [-0.77;-0.59]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an
observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

Body weight (kg) - ANCOVA - Pioneer 6 - in-trial - full analysis set

	Oral Sema						Comparator						Oral Sema vs Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Non-OECD	535	534	511	79.08 (16.9)	75.95 (16.3)	-3.74 (0.2)	533	533	506	80.56 (18.0)	79.68 (18.0)	-1.03 (0.2)	-2.70 [-3.33;-2.08] <0.0001	-0.63 [-0.75;-0.50]	
Region C															0.3698
West Europe	293	293	281	94.61 (17.4)	89.45 (16.9)	-4.78 (0.3)	270	270	259	94.15 (18.2)	93.26 (18.4)	-1.05 (0.3)	-3.73 [-4.59;-2.87] <0.0001	-0.65 [-0.82;-0.48]	
Rest of World	1298	1297	1230	90.19 (22.2)	85.95 (21.5)	-4.09 (0.1)	1322	1322	1234	90.11 (21.5)	89.23 (21.7)	-0.79 (0.1)	-3.30 [-3.70;-2.90] <0.0001	-0.66 [-0.74;-0.58]	
HbA1c at baseline (disease severity) A**															0.3331
<= 8.5	1068	1067	1014	91.29 (21.4)	86.46 (20.4)	-4.59 (0.2)	1057	1057	996	91.14 (21.1)	89.93 (21.1)	-1.08 (0.2)	-3.51 [-3.95;-3.06] <0.0001	-0.67 [-0.76;-0.58]	
8.5 <	513	513	488	90.34 (21.7)	86.72 (21.5)	-3.51 (0.2)	517	517	480	90.28 (21.1)	90.04 (21.5)	-0.38 (0.2)	-3.12 [-3.76;-2.48] <0.0001	-0.62 [-0.75;-0.49]	
HbA1c at baseline (disease severity) B**															0.3808

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

Body weight (kg) - ANCOVA - Pioneer 6 - in-trial - full analysis set

	Oral Sema						Comparator						Oral Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
<= 7.5	627	626	594	91.27 (22.0)	86.40 (20.9)	-4.57 (0.2)	649	649	610	92.14 (21.8)	90.94 (21.9)	-0.98 (0.2)	-3.59 [-4.16;-3.01] <0.0001	-0.63 [-0.75;-0.51]	
7.5 <	954	954	908	90.79 (21.1)	86.64 (20.7)	-4.02 (0.2)	925	925	866	89.96 (20.5)	89.28 (20.7)	-0.76 (0.2)	-3.26 [-3.73;-2.78] <0.0001	-0.68 [-0.78;-0.59]	
Race B															0.9486
White	1148	1148	1097	95.82 (20.3)	91.12 (19.9)	-4.15 (0.2)	1152	1152	1084	95.29 (20.1)	94.41 (20.2)	-0.78 (0.2)	-3.38 [-3.80;-2.95] <0.0001	-0.63 [-0.71;-0.54]	
Non-White	443	442	414	78.49 (19.2)	74.61 (17.8)	-4.39 (0.3)	440	440	409	79.03 (18.8)	78.04 (19.1)	-0.98 (0.3)	-3.40 [-4.10;-2.71] <0.0001	-0.75 [-0.89;-0.61]	
Evidence of CV disease at screening															0.7470
CV DISEASE	1350	1349	1278	91.10 (21.3)	86.73 (20.7)	-4.20 (0.1)	1345	1345	1256	91.27 (21.3)	90.35 (21.5)	-0.84 (0.1)	-3.36 [-3.75;-2.96] <0.0001	-0.64 [-0.72;-0.56]	
CV RISK FACTORS ONLY	241	241	233	90.49 (22.2)	85.91 (21.0)	-4.32 (0.3)	247	247	237	88.22 (19.5)	87.67 (19.7)	-0.80 (0.3)	-3.52 [-4.44;-2.60] <0.0001	-0.74 [-0.92;-0.55]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

Body weight (kg) - ANCOVA - Pioneer 6 - in-trial - full analysis set

	Oral Sema						Comparator						Oral Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Insulin Therapy at baseline															0.0006*
No insulin	623	623	593	86.54 (20.0)	82.60 (19.5)	-3.96 (0.2)	630	630	600	85.65 (19.2)	84.19 (18.9)	-1.41 (0.2)	-2.54 [-3.12;-1.97] <0.0001	-0.57 [-0.69;-0.46]	
Basal only	269	269	253	92.15 (20.7)	87.48 (19.3)	-4.04 (0.3)	265	265	252	92.06 (20.2)	91.46 (20.3)	-0.55 (0.3)	-3.49 [-4.37;-2.60] <0.0001	-0.67 [-0.85;-0.49]	
Insulin (not basal only)	699	698	665	94.54 (22.3)	89.84 (21.7)	-4.52 (0.2)	697	697	641	94.97 (21.9)	94.69 (22.3)	-0.40 (0.2)	-4.11 [-4.67;-3.56] <0.0001	-0.72 [-0.83;-0.61]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Change from baseline was analysed using an ANCOVA model with treatment, stratification factor (CV disease status at screening), (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

12 Serious adverse events - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1591	324 (20.4%)	1267 (79.6%)	4 (0.3%)	0 (0.0%)	1592	371 (23.3%)	1221 (76.7%)	4 (0.3%)	0 (0.0%)	0.85 [0.73;0.99]	0.0349	
Gender													0.2034
Female	507	75 (14.8%)	432 (85.2%)	2 (0.4%)	0 (0.0%)	500	99 (19.8%)	401 (80.2%)	1 (0.2%)	0 (0.0%)	0.72 [0.53;0.97]	0.0330	
Male	1084	249 (23.0%)	835 (77.0%)	2 (0.2%)	0 (0.0%)	1092	272 (24.9%)	820 (75.1%)	3 (0.3%)	0 (0.0%)	0.90 [0.76;1.07]	0.2449	
Age													0.9181
< 65	700	123 (17.6%)	577 (82.4%)	1 (0.1%)	0 (0.0%)	634	127 (20.0%)	507 (80.0%)	2 (0.3%)	0 (0.0%)	0.87 [0.68;1.11]	0.2670	
65 <=	891	201 (22.6%)	690 (77.4%)	3 (0.3%)	0 (0.0%)	958	244 (25.5%)	714 (74.5%)	2 (0.2%)	0 (0.0%)	0.85 [0.71;1.03]	0.1000	
Region B													0.2912
OECD	1056	232 (22.0%)	824 (78.0%)	3 (0.3%)	0 (0.0%)	1059	278 (26.3%)	781 (73.7%)	3 (0.3%)	0 (0.0%)	0.81 [0.68;0.97]	0.0185	
Non-OECD	535	92 (17.2%)	443 (82.8%)	1 (0.2%)	0 (0.0%)	533	93 (17.4%)	440 (82.6%)	1 (0.2%)	0 (0.0%)	0.97 [0.73;1.30]	0.8482	
Region C													0.2415
West Europe	293	67 (22.9%)	226 (77.1%)	0 (0.0%)	0 (0.0%)	270	81 (30.0%)	189 (70.0%)	0 (0.0%)	0 (0.0%)	0.71 [0.52;0.99]	0.0410	
Rest of World	1298	257 (19.8%)	1041 (80.2%)	4 (0.3%)	0 (0.0%)	1322	290 (21.9%)	1032 (78.1%)	4 (0.3%)	0 (0.0%)	0.89 [0.75;1.05]	0.1629	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Serious adverse events - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.8465
<= 8.5	1068	214 (20.0%)	854 (80.0%)	3 (0.3%)	0 (0.0%)	1057	241 (22.8%)	816 (77.2%)	3 (0.3%)	0 (0.0%)	0.85 [0.70;1.02]	0.0747	
8.5 <	513	107 (20.9%)	406 (79.1%)	1 (0.2%)	0 (0.0%)	517	124 (24.0%)	393 (76.0%)	1 (0.2%)	0 (0.0%)	0.87 [0.67;1.13]	0.3027	
HbA1c at baseline (disease severity) B**													0.3714
<= 7.5	627	113 (18.0%)	514 (82.0%)	3 (0.5%)	0 (0.0%)	649	143 (22.0%)	506 (78.0%)	3 (0.5%)	0 (0.0%)	0.78 [0.61;1.00]	0.0492	
7.5 <	954	208 (21.8%)	746 (78.2%)	1 (0.1%)	0 (0.0%)	925	222 (24.0%)	703 (76.0%)	1 (0.1%)	0 (0.0%)	0.90 [0.74;1.09]	0.2734	
Race B													0.2983
White	1148	234 (20.4%)	914 (79.6%)	2 (0.2%)	0 (0.0%)	1152	281 (24.4%)	871 (75.6%)	3 (0.3%)	0 (0.0%)	0.81 [0.68;0.97]	0.0191	
Non-White	443	90 (20.3%)	353 (79.7%)	2 (0.5%)	0 (0.0%)	440	90 (20.5%)	350 (79.5%)	1 (0.2%)	0 (0.0%)	0.97 [0.73;1.30]	0.8558	
Evidence of CV disease at screening													0.7353
CV DISEASE	1350	284 (21.0%)	1066 (79.0%)	3 (0.2%)	0 (0.0%)	1345	321 (23.9%)	1024 (76.1%)	4 (0.3%)	0 (0.0%)	0.86 [0.73;1.01]	0.0648	
CV RISK FACTORS ONLY	241	40 (16.6%)	201 (83.4%)	1 (0.4%)	0 (0.0%)	247	50 (20.2%)	197 (79.8%)	0 (0.0%)	0 (0.0%)	0.80 [0.53;1.21]	0.2840	
Insulin Therapy at baseline													0.2298

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Serious adverse events - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator	
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value p-value
No insulin	623	101 (16.2%)	522 (83.8%)	3 (0.5%)	0 (0.0%)	630	123 (19.5%)	507 (80.5%)	0 (0.0%)	0 (0.0%)	0.80 [0.62;1.05]	0.1050
Basal only	269	47 (17.5%)	222 (82.5%)	1 (0.4%)	0 (0.0%)	265	65 (24.5%)	200 (75.5%)	1 (0.4%)	0 (0.0%)	0.67 [0.46;0.97]	0.0355
Insulin (not basal only)	699	176 (25.2%)	523 (74.8%)	0 (0.0%)	0 (0.0%)	697	183 (26.3%)	514 (73.7%)	3 (0.4%)	0 (0.0%)	0.95 [0.78;1.17]	0.6592

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

13 Serious adverse events excluding morbidity endpoints - comprehensive approach with PTs only - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1591	255 (16.0%)	1336 (84.0%)	8 (0.5%)	4 (0.3%)	1592	282 (17.7%)	1310 (82.3%)	20 (1.3%)	16 (1.0%)	0.89 [0.75;1.05]	0.1691	
Gender													0.1293
Female	507	60 (11.8%)	447 (88.2%)	2 (0.4%)	0 (0.0%)	500	80 (16.0%)	420 (84.0%)	4 (0.8%)	3 (0.6%)	0.71 [0.51;1.00]	0.0475	
Male	1084	195 (18.0%)	889 (82.0%)	6 (0.6%)	4 (0.4%)	1092	202 (18.5%)	890 (81.5%)	16 (1.5%)	13 (1.2%)	0.96 [0.79;1.17]	0.7048	
Age													0.7975
< 65	700	98 (14.0%)	602 (86.0%)	2 (0.3%)	1 (0.1%)	634	95 (15.0%)	539 (85.0%)	12 (1.9%)	10 (1.6%)	0.92 [0.70;1.23]	0.5822	
65 <=	891	157 (17.6%)	734 (82.4%)	6 (0.7%)	3 (0.3%)	958	187 (19.5%)	771 (80.5%)	8 (0.8%)	6 (0.6%)	0.88 [0.71;1.09]	0.2467	
Region B													0.2571
OECD	1056	178 (16.9%)	878 (83.1%)	6 (0.6%)	3 (0.3%)	1059	209 (19.7%)	850 (80.3%)	11 (1.0%)	8 (0.8%)	0.84 [0.68;1.02]	0.0773	
Non-OECD	535	77 (14.4%)	458 (85.6%)	2 (0.4%)	1 (0.2%)	533	73 (13.7%)	460 (86.3%)	9 (1.7%)	8 (1.5%)	1.04 [0.75;1.43]	0.8157	
Region C													0.4279
West Europe	293	52 (17.7%)	241 (82.3%)	0 (0.0%)	0 (0.0%)	270	60 (22.2%)	210 (77.8%)	0 (0.0%)	0 (0.0%)	0.77 [0.53;1.12]	0.1764	
Rest of World	1298	203 (15.6%)	1095 (84.4%)	8 (0.6%)	4 (0.3%)	1322	222 (16.8%)	1100 (83.2%)	20 (1.5%)	16 (1.2%)	0.92 [0.76;1.11]	0.3684	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Serious adverse events excluding morbidity endpoints - comprehensive approach with PTs only - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.4454
<= 8.5	1068	166 (15.5%)	902 (84.5%)	6 (0.6%)	3 (0.3%)	1057	188 (17.8%)	869 (82.2%)	10 (0.9%)	7 (0.7%)	0.85 [0.69;1.04]	0.1153	
8.5 <	513	86 (16.8%)	427 (83.2%)	2 (0.4%)	1 (0.2%)	517	90 (17.4%)	427 (82.6%)	10 (1.9%)	9 (1.7%)	0.97 [0.72;1.31]	0.8588	
HbA1c at baseline (disease severity) B**													0.1015
<= 7.5	627	86 (13.7%)	541 (86.3%)	5 (0.8%)	2 (0.3%)	649	116 (17.9%)	533 (82.1%)	5 (0.8%)	2 (0.3%)	0.74 [0.56;0.97]	0.0319	
7.5 <	954	166 (17.4%)	788 (82.6%)	3 (0.3%)	2 (0.2%)	925	162 (17.5%)	763 (82.5%)	15 (1.6%)	14 (1.5%)	0.99 [0.80;1.23]	0.9257	
Race B													0.5652
White	1148	184 (16.0%)	964 (84.0%)	6 (0.5%)	4 (0.3%)	1152	211 (18.3%)	941 (81.7%)	10 (0.9%)	7 (0.6%)	0.86 [0.71;1.05]	0.1409	
Non-White	443	71 (16.0%)	372 (84.0%)	2 (0.5%)	0 (0.0%)	440	71 (16.1%)	369 (83.9%)	10 (2.3%)	9 (2.0%)	0.96 [0.69;1.34]	0.8304	
Evidence of CV disease at screening													0.6116
CV DISEASE	1350	218 (16.1%)	1132 (83.9%)	5 (0.4%)	2 (0.1%)	1345	244 (18.1%)	1101 (81.9%)	19 (1.4%)	15 (1.1%)	0.87 [0.73;1.05]	0.1430	
CV RISK FACTORS ONLY	241	37 (15.4%)	204 (84.6%)	3 (1.2%)	2 (0.8%)	247	38 (15.4%)	209 (84.6%)	1 (0.4%)	1 (0.4%)	0.99 [0.63;1.56]	0.9657	
Insulin Therapy at baseline													0.1380

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Serious adverse events excluding morbidity endpoints - comprehensive approach with PTs only - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
No insulin	623	76 (12.2%)	547 (87.8%)	4 (0.6%)	1 (0.2%)	630	98 (15.6%)	532 (84.4%)	3 (0.5%)	3 (0.5%)	0.76 [0.56;1.02]	0.0704	
Basal only	269	38 (14.1%)	231 (85.9%)	1 (0.4%)	0 (0.0%)	265	50 (18.9%)	215 (81.1%)	1 (0.4%)	0 (0.0%)	0.72 [0.47;1.10]	0.1298	
Insulin (not basal only)	699	141 (20.2%)	558 (79.8%)	3 (0.4%)	3 (0.4%)	697	134 (19.2%)	563 (80.8%)	16 (2.3%)	13 (1.9%)	1.05 [0.83;1.33]	0.6751	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

14 Adverse events leading to permanent trial product discontinuation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1591	184 (11.6%)	1407 (88.4%)	11 (0.7%)	9 (0.6%)	1592	104 (6.5%)	1488 (93.5%)	29 (1.8%)	24 (1.5%)	1.81 [1.43;2.31]	<0.0001	
Gender													0.5176
Female	507	54 (10.7%)	453 (89.3%)	3 (0.6%)	1 (0.2%)	500	27 (5.4%)	473 (94.6%)	4 (0.8%)	3 (0.6%)	2.06 [1.30;3.27]	0.0021	
Male	1084	130 (12.0%)	954 (88.0%)	8 (0.7%)	8 (0.7%)	1092	77 (7.1%)	1015 (92.9%)	25 (2.3%)	21 (1.9%)	1.72 [1.30;2.29]	0.0002	
Age													0.3087
< 65	700	55 (7.9%)	645 (92.1%)	3 (0.4%)	2 (0.3%)	634	33 (5.2%)	601 (94.8%)	14 (2.2%)	12 (1.9%)	1.54 [1.00;2.37]	0.0506	
65 <=	891	129 (14.5%)	762 (85.5%)	8 (0.9%)	7 (0.8%)	958	71 (7.4%)	887 (92.6%)	15 (1.6%)	12 (1.3%)	2.01 [1.51;2.69]	<0.0001	
Region B													0.9731
OECD	1056	132 (12.5%)	924 (87.5%)	7 (0.7%)	6 (0.6%)	1059	75 (7.1%)	984 (92.9%)	18 (1.7%)	14 (1.3%)	1.82 [1.37;2.42]	<0.0001	
Non-OECD	535	52 (9.7%)	483 (90.3%)	4 (0.7%)	3 (0.6%)	533	29 (5.4%)	504 (94.6%)	11 (2.1%)	10 (1.9%)	1.80 [1.14;2.84]	0.0110	
Region C													0.7913
West Europe	293	34 (11.6%)	259 (88.4%)	0 (0.0%)	0 (0.0%)	270	19 (7.0%)	251 (93.0%)	2 (0.7%)	2 (0.7%)	1.69 [0.97;2.97]	0.0664	
Rest of World	1298	150 (11.6%)	1148 (88.4%)	11 (0.8%)	9 (0.7%)	1322	85 (6.4%)	1237 (93.6%)	27 (2.0%)	22 (1.7%)	1.84 [1.41;2.40]	<0.0001	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Adverse events leading to permanent trial product discontinuation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.7058
<= 8.5	1068	131 (12.3%)	937 (87.7%)	8 (0.7%)	6 (0.6%)	1057	75 (7.1%)	982 (92.9%)	14 (1.3%)	11 (1.0%)	1.77 [1.33;2.35]	<0.0001	
8.5 <	513	53 (10.3%)	460 (89.7%)	2 (0.4%)	2 (0.4%)	517	28 (5.4%)	489 (94.6%)	15 (2.9%)	13 (2.5%)	1.96 [1.24;3.10]	0.0039	
HbA1c at baseline (disease severity) B**													0.5995
<= 7.5	627	81 (12.9%)	546 (87.1%)	5 (0.8%)	3 (0.5%)	649	50 (7.7%)	599 (92.3%)	10 (1.5%)	7 (1.1%)	1.70 [1.20;2.43]	0.0030	
7.5 <	954	103 (10.8%)	851 (89.2%)	5 (0.5%)	5 (0.5%)	925	53 (5.7%)	872 (94.3%)	19 (2.1%)	17 (1.8%)	1.94 [1.39;2.70]	<0.0001	
Race B													0.5224
White	1148	138 (12.0%)	1010 (88.0%)	7 (0.6%)	7 (0.6%)	1152	75 (6.5%)	1077 (93.5%)	18 (1.6%)	15 (1.3%)	1.90 [1.43;2.52]	<0.0001	
Non-White	443	46 (10.4%)	397 (89.6%)	4 (0.9%)	2 (0.5%)	440	29 (6.6%)	411 (93.4%)	11 (2.5%)	9 (2.0%)	1.59 [1.00;2.53]	0.0500	
Evidence of CV disease at screening													0.2849
CV DISEASE	1350	165 (12.2%)	1185 (87.8%)	8 (0.6%)	7 (0.5%)	1345	97 (7.2%)	1248 (92.8%)	25 (1.9%)	21 (1.6%)	1.74 [1.35;2.23]	<0.0001	
CV RISK FACTORS ONLY	241	19 (7.9%)	222 (92.1%)	3 (1.2%)	2 (0.8%)	247	7 (2.8%)	240 (97.2%)	4 (1.6%)	3 (1.2%)	2.84 [1.20;6.76]	0.0181	
Insulin Therapy at baseline													0.3081

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Adverse events leading to permanent trial product discontinuation - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator	
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
No insulin	623	66 (10.6%)	557 (89.4%)	3 (0.5%)	1 (0.2%)	630	45 (7.1%)	585 (92.9%)	6 (1.0%)	6 (1.0%)	1.52 [1.04;2.21]	0.0315
Basal only	269	36 (13.4%)	233 (86.6%)	0 (0.0%)	0 (0.0%)	265	14 (5.3%)	251 (94.7%)	4 (1.5%)	3 (1.1%)	2.66 [1.44;4.94]	0.0019
Insulin (not basal only)	699	82 (11.7%)	617 (88.3%)	8 (1.1%)	8 (1.1%)	697	45 (6.5%)	652 (93.5%)	19 (2.7%)	15 (2.2%)	1.85 [1.28;2.65]	0.0010
p-value interaction												

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

15 Neoplasms – serious adverse events – pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	39 (2.5%)	1552 (97.5%)	19 (1.2%)	14 (0.9%)	1592	42 (2.6%)	1550 (97.4%)	40 (2.5%)	34 (2.1%)	0.92 [0.60;1.43]	0.7141	
Gender													0.8654
Female	507	7 (1.4%)	500 (98.6%)	4 (0.8%)	2 (0.4%)	500	8 (1.6%)	492 (98.4%)	6 (1.2%)	5 (1.0%)	0.85 [0.31;2.36]	0.7617	
Male	1084	32 (3.0%)	1052 (97.0%)	15 (1.4%)	12 (1.1%)	1092	34 (3.1%)	1058 (96.9%)	34 (3.1%)	29 (2.7%)	0.94 [0.58;1.53]	0.8083	
Age													0.0939
< 65	700	8 (1.1%)	692 (98.9%)	4 (0.6%)	3 (0.4%)	634	14 (2.2%)	620 (97.8%)	20 (3.2%)	18 (2.8%)	0.51 [0.21;1.20]	0.1233	
65 <=	891	31 (3.5%)	860 (96.5%)	15 (1.7%)	11 (1.2%)	958	28 (2.9%)	930 (97.1%)	20 (2.1%)	16 (1.7%)	1.20 [0.72;1.99]	0.4941	
Region B													0.8889
OECD	1056	30 (2.8%)	1026 (97.2%)	11 (1.0%)	7 (0.7%)	1059	33 (3.1%)	1026 (96.9%)	25 (2.4%)	20 (1.9%)	0.91 [0.55;1.49]	0.7047	
Non-OECD	535	9 (1.7%)	526 (98.3%)	8 (1.5%)	7 (1.3%)	533	9 (1.7%)	524 (98.3%)	15 (2.8%)	14 (2.6%)	0.98 [0.39;2.47]	0.9646	
Region C													0.7376
West Europe	293	11 (3.8%)	282 (96.2%)	2 (0.7%)	1 (0.3%)	270	10 (3.7%)	260 (96.3%)	3 (1.1%)	2 (0.7%)	1.04 [0.44;2.45]	0.9272	
Rest of World	1298	28 (2.2%)	1270 (97.8%)	17 (1.3%)	13 (1.0%)	1322	32 (2.4%)	1290 (97.6%)	37 (2.8%)	32 (2.4%)	0.88 [0.53;1.46]	0.6148	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Neoplasms – serious adverse events – pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.7732
<= 8.5	1068	30 (2.8%)	1038 (97.2%)	13 (1.2%)	10 (0.9%)	1057	32 (3.0%)	1025 (97.0%)	20 (1.9%)	16 (1.5%)	0.92 [0.56;1.52]	0.7568	
8.5 <	513	8 (1.6%)	505 (98.4%)	5 (1.0%)	3 (0.6%)	517	10 (1.9%)	507 (98.1%)	19 (3.7%)	17 (3.3%)	0.79 [0.31;2.01]	0.6222	
HbA1c at baseline (disease severity) B**													0.9259
<= 7.5	627	18 (2.9%)	609 (97.1%)	8 (1.3%)	5 (0.8%)	649	21 (3.2%)	628 (96.8%)	14 (2.2%)	11 (1.7%)	0.88 [0.47;1.65]	0.6873	
7.5 <	954	20 (2.1%)	934 (97.9%)	10 (1.0%)	8 (0.8%)	925	21 (2.3%)	904 (97.7%)	25 (2.7%)	22 (2.4%)	0.92 [0.50;1.69]	0.7791	
Race B													0.8661
White	1148	31 (2.7%)	1117 (97.3%)	11 (1.0%)	8 (0.7%)	1152	33 (2.9%)	1119 (97.1%)	26 (2.3%)	22 (1.9%)	0.94 [0.58;1.54]	0.8114	
Non-White	443	8 (1.8%)	435 (98.2%)	8 (1.8%)	6 (1.4%)	440	9 (2.0%)	431 (98.0%)	14 (3.2%)	12 (2.7%)	0.86 [0.33;2.23]	0.7547	
Evidence of CV disease at screening													0.6070
CV DISEASE	1350	33 (2.4%)	1317 (97.6%)	15 (1.1%)	11 (0.8%)	1345	37 (2.8%)	1308 (97.2%)	34 (2.5%)	29 (2.2%)	0.88 [0.55;1.41]	0.5960	
CV RISK FACTORS ONLY	241	6 (2.5%)	235 (97.5%)	4 (1.7%)	3 (1.2%)	247	5 (2.0%)	242 (98.0%)	6 (2.4%)	5 (2.0%)	1.23 [0.38;4.03]	0.7312	
Insulin Therapy at baseline													0.2677

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Neoplasms – serious adverse events – pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator	
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value p-value
No insulin	623	13 (2.1%)	610 (97.9%)	8 (1.3%)	4 (0.6%)	630	9 (1.4%)	621 (98.6%)	10 (1.6%)	9 (1.4%)	1.44 [0.62;3.38]	0.3965
Basal only	269	6 (2.2%)	263 (97.8%)	2 (0.7%)	1 (0.4%)	265	12 (4.5%)	253 (95.5%)	5 (1.9%)	4 (1.5%)	0.49 [0.19;1.32]	0.1580
Insulin (not basal only)	699	20 (2.9%)	679 (97.1%)	9 (1.3%)	9 (1.3%)	697	21 (3.0%)	676 (97.0%)	25 (3.6%)	21 (3.0%)	0.94 [0.51;1.74]	0.8463

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

16 Hypoglycaemic episodes – serious adverse events - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	17 (1.1%)	1574 (98.9%)	26 (1.6%)	21 (1.3%)	1592	12 (0.8%)	1580 (99.2%)	48 (3.0%)	43 (2.7%)	1.40 [0.67;2.94]	0.3687	
Gender													0.4460
Female	507	5 (1.0%)	502 (99.0%)	4 (0.8%)	2 (0.4%)	500	2 (0.4%)	498 (99.6%)	7 (1.4%)	6 (1.2%)	2.45 [0.47;12.62]	0.2846	
Male	1084	12 (1.1%)	1072 (98.9%)	22 (2.0%)	19 (1.8%)	1092	10 (0.9%)	1082 (99.1%)	41 (3.8%)	37 (3.4%)	1.20 [0.52;2.77]	0.6764	
Age													0.9130
< 65	700	9 (1.3%)	691 (98.7%)	4 (0.6%)	3 (0.4%)	634	6 (0.9%)	628 (99.1%)	23 (3.6%)	21 (3.3%)	1.32 [0.47;3.72]	0.5957	
65 <=	891	8 (0.9%)	883 (99.1%)	22 (2.5%)	18 (2.0%)	958	6 (0.6%)	952 (99.4%)	25 (2.6%)	22 (2.3%)	1.44 [0.50;4.14]	0.5025	
Region B													0.4438
OECD	1056	12 (1.1%)	1044 (98.9%)	15 (1.4%)	11 (1.0%)	1059	10 (0.9%)	1049 (99.1%)	30 (2.8%)	26 (2.5%)	1.19 [0.52;2.76]	0.6780	
Non-OECD	535	5 (0.9%)	530 (99.1%)	11 (2.1%)	10 (1.9%)	533	2 (0.4%)	531 (99.6%)	18 (3.4%)	17 (3.2%)	2.45 [0.48;12.64]	0.2834	
Region C													0.7615
West Europe	293	1 (0.3%)	292 (99.7%)	4 (1.4%)	3 (1.0%)	270	1 (0.4%)	269 (99.6%)	4 (1.5%)	4 (1.5%)	0.94 [0.06;14.94]	0.9622	
Rest of World	1298	16 (1.2%)	1282 (98.8%)	22 (1.7%)	18 (1.4%)	1322	11 (0.8%)	1311 (99.2%)	44 (3.3%)	39 (3.0%)	1.46 [0.68;3.15]	0.3343	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Hypoglycaemic episodes - serious adverse events - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.0748
<= 8.5	1068	10 (0.9%)	1058 (99.1%)	20 (1.9%)	17 (1.6%)	1057	11 (1.0%)	1046 (99.0%)	28 (2.6%)	25 (2.4%)	0.89 [0.38;2.10]	0.7916	
8.5 <	513	7 (1.4%)	506 (98.6%)	5 (1.0%)	3 (0.6%)	517	1 (0.2%)	516 (99.8%)	19 (3.7%)	17 (3.3%)	6.97 [0.86;56.67]	0.0693	
HbA1c at baseline (disease severity) B**													0.5538
<= 7.5	627	5 (0.8%)	622 (99.2%)	12 (1.9%)	9 (1.4%)	649	5 (0.8%)	644 (99.2%)	20 (3.1%)	17 (2.6%)	1.03 [0.30;3.55]	0.9659	
7.5 <	954	12 (1.3%)	942 (98.7%)	13 (1.4%)	11 (1.2%)	925	7 (0.8%)	918 (99.2%)	27 (2.9%)	25 (2.7%)	1.64 [0.65;4.17]	0.2973	
Race B													0.5368
White	1148	13 (1.1%)	1135 (98.9%)	15 (1.3%)	12 (1.0%)	1152	8 (0.7%)	1144 (99.3%)	31 (2.7%)	28 (2.4%)	1.62 [0.67;3.92]	0.2808	
Non-White	443	4 (0.9%)	439 (99.1%)	11 (2.5%)	9 (2.0%)	440	4 (0.9%)	436 (99.1%)	17 (3.9%)	15 (3.4%)	0.97 [0.24;3.87]	0.9631	
Evidence of CV disease at screening													0.7382
CV DISEASE	1350	15 (1.1%)	1335 (98.9%)	22 (1.6%)	18 (1.3%)	1345	10 (0.7%)	1335 (99.3%)	43 (3.2%)	39 (2.9%)	1.48 [0.66;3.29]	0.3395	
CV RISK FACTORS ONLY	241	2 (0.8%)	239 (99.2%)	4 (1.7%)	3 (1.2%)	247	2 (0.8%)	245 (99.2%)	5 (2.0%)	4 (1.6%)	1.03 [0.15;7.31]	0.9769	
Insulin Therapy at baseline													0.7751

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Hypoglycaemic episodes - serious adverse events - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator	
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
No insulin	623	1 (0.2%)	622 (99.8%)	10 (1.6%)	6 (1.0%)	630	2 (0.3%)	628 (99.7%)	10 (1.6%)	10 (1.6%)	0.50 [0.05;5.55]	0.5752
Basal only	269	3 (1.1%)	266 (98.9%)	3 (1.1%)	2 (0.7%)	265	0 (0.0%)	265 (100%)	8 (3.0%)	7 (2.6%)	Not est	Not est
Insulin (not basal only)	699	13 (1.9%)	686 (98.1%)	13 (1.9%)	13 (1.9%)	697	10 (1.4%)	687 (98.6%)	30 (4.3%)	26 (3.7%)	1.27 [0.56;2.89]	0.5719
p-value interaction												

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

17 Diabetic retinopathy and related complications – pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

Comparator	Oral Sema					Comparator					Oral Sema vs.		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	113 (7.1%)	1478 (92.9%)	26 (1.6%)	21 (1.3%)	1592	101 (6.3%)	1491 (93.7%)	50 (3.1%)	44 (2.8%)	1.11 [0.85;1.45]	0.4568	
Gender													0.8048
Female	507	32 (6.3%)	475 (93.7%)	5 (1.0%)	3 (0.6%)	500	30 (6.0%)	470 (94.0%)	7 (1.4%)	6 (1.2%)	1.05 [0.64;1.73]	0.8461	
Male	1084	81 (7.5%)	1003 (92.5%)	21 (1.9%)	18 (1.7%)	1092	71 (6.5%)	1021 (93.5%)	43 (3.9%)	38 (3.5%)	1.13 [0.82;1.56]	0.4459	
Age													0.9827
< 65	700	48 (6.9%)	652 (93.1%)	5 (0.7%)	4 (0.6%)	634	38 (6.0%)	596 (94.0%)	22 (3.5%)	20 (3.2%)	1.11 [0.72;1.69]	0.6404	
65 <=	891	65 (7.3%)	826 (92.7%)	21 (2.4%)	17 (1.9%)	958	63 (6.6%)	895 (93.4%)	28 (2.9%)	24 (2.5%)	1.11 [0.79;1.57]	0.5430	
Region B													0.7512
OECD	1056	83 (7.9%)	973 (92.1%)	16 (1.5%)	12 (1.1%)	1059	73 (6.9%)	986 (93.1%)	32 (3.0%)	27 (2.5%)	1.14 [0.83;1.56]	0.4167	
Non-OECD	535	30 (5.6%)	505 (94.4%)	10 (1.9%)	9 (1.7%)	533	28 (5.3%)	505 (94.7%)	18 (3.4%)	17 (3.2%)	1.03 [0.62;1.73]	0.9009	
Region C													0.9118
West Europe	293	25 (8.5%)	268 (91.5%)	4 (1.4%)	3 (1.0%)	270	22 (8.1%)	248 (91.9%)	4 (1.5%)	3 (1.1%)	1.07 [0.61;1.91]	0.8067	
Rest of World	1298	88 (6.8%)	1210 (93.2%)	22 (1.7%)	18 (1.4%)	1322	79 (6.0%)	1243 (94.0%)	46 (3.5%)	41 (3.1%)	1.11 [0.82;1.51]	0.4852	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Diabetic retinopathy and related complications – pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.0946
<= 8.5	1068	73 (6.8%)	995 (93.2%)	19 (1.8%)	16 (1.5%)	1057	53 (5.0%)	1004 (95.0%)	30 (2.8%)	26 (2.5%)	1.36 [0.96;1.94]	0.0863	
8.5 <	513	39 (7.6%)	474 (92.4%)	6 (1.2%)	4 (0.8%)	517	45 (8.7%)	472 (91.3%)	19 (3.7%)	17 (3.3%)	0.85 [0.55;1.30]	0.4523	
HbA1c at baseline (disease severity) B**													0.6750
<= 7.5	627	33 (5.3%)	594 (94.7%)	12 (1.9%)	9 (1.4%)	649	33 (5.1%)	616 (94.9%)	21 (3.2%)	18 (2.8%)	1.03 [0.63;1.67]	0.9110	
7.5 <	954	79 (8.3%)	875 (91.7%)	13 (1.4%)	11 (1.2%)	925	65 (7.0%)	860 (93.0%)	28 (3.0%)	25 (2.7%)	1.16 [0.84;1.62]	0.3629	
Race B													0.8748
White	1148	83 (7.2%)	1065 (92.8%)	16 (1.4%)	13 (1.1%)	1152	76 (6.6%)	1076 (93.4%)	32 (2.8%)	28 (2.4%)	1.09 [0.80;1.49]	0.5718	
Non-White	443	30 (6.8%)	413 (93.2%)	10 (2.3%)	8 (1.8%)	440	25 (5.7%)	415 (94.3%)	18 (4.1%)	16 (3.6%)	1.15 [0.68;1.95]	0.6072	
Evidence of CV disease at screening													0.2909
CV DISEASE	1350	93 (6.9%)	1257 (93.1%)	22 (1.6%)	18 (1.3%)	1345	88 (6.5%)	1257 (93.5%)	44 (3.3%)	39 (2.9%)	1.04 [0.78;1.39]	0.7877	
CV RISK FACTORS ONLY	241	20 (8.3%)	221 (91.7%)	4 (1.7%)	3 (1.2%)	247	13 (5.3%)	234 (94.7%)	6 (2.4%)	5 (2.0%)	1.56 [0.78;3.15]	0.2088	
Insulin Therapy at baseline													0.3414

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Diabetic retinopathy and related complications – pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
No insulin	623	30 (4.8%)	593 (95.2%)	10 (1.6%)	6 (1.0%)	630	27 (4.3%)	603 (95.7%)	12 (1.9%)	11 (1.7%)	1.10 [0.66;1.86]	0.7109	
Basal only	269	18 (6.7%)	251 (93.3%)	2 (0.7%)	1 (0.4%)	265	24 (9.1%)	241 (90.9%)	8 (3.0%)	7 (2.6%)	0.75 [0.41;1.38]	0.3554	
Insulin (not basal only)	699	65 (9.3%)	634 (90.7%)	14 (2.0%)	14 (2.0%)	697	50 (7.2%)	647 (92.8%)	30 (4.3%)	26 (3.7%)	1.28 [0.88;1.85]	0.1917	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

18 Pancreatitis – serious adverse events – pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1591	1 (0.1%)	1590 (99.9%)	28 (1.8%)	23 (1.4%)	1592	3 (0.2%)	1589 (99.8%)	50 (3.1%)	44 (2.8%)	0.33 [0.03;3.17]	0.3364	
Gender													0.9998
Female	507	0 (0.0%)	507 (100%)	5 (1.0%)	3 (0.6%)	500	0 (0.0%)	500 (100%)	7 (1.4%)	6 (1.2%)	Not est	Not est	
Male	1084	1 (0.1%)	1083 (99.9%)	23 (2.1%)	20 (1.8%)	1092	3 (0.3%)	1089 (99.7%)	43 (3.9%)	38 (3.5%)	0.33 [0.03;3.13]	0.3311	
Age													0.9947
< 65	700	1 (0.1%)	699 (99.9%)	5 (0.7%)	4 (0.6%)	634	2 (0.3%)	632 (99.7%)	23 (3.6%)	21 (3.3%)	0.46 [0.04;5.03]	0.5217	
65 <=	891	0 (0.0%)	891 (100%)	23 (2.6%)	19 (2.1%)	958	1 (0.1%)	957 (99.9%)	27 (2.8%)	23 (2.4%)	Not est	Not est	
Region B													0.9998
OECD	1056	1 (0.1%)	1055 (99.9%)	17 (1.6%)	13 (1.2%)	1059	3 (0.3%)	1056 (99.7%)	32 (3.0%)	27 (2.5%)	0.33 [0.03;3.17]	0.3371	
Non-OECD	535	0 (0.0%)	535 (100%)	11 (2.1%)	10 (1.9%)	533	0 (0.0%)	533 (100%)	18 (3.4%)	17 (3.2%)	Not est	Not est	
Region C													0.9943
West Europe	293	0 (0.0%)	293 (100%)	4 (1.4%)	3 (1.0%)	270	2 (0.7%)	268 (99.3%)	4 (1.5%)	3 (1.1%)	Not est	Not est	
Rest of World	1298	1 (0.1%)	1297 (99.9%)	24 (1.8%)	20 (1.5%)	1322	1 (0.1%)	1321 (99.9%)	46 (3.5%)	41 (3.1%)	1.01 [0.06;16.07]	0.9972	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Pancreatitis - serious adverse events - pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
HbA1c at baseline (disease severity) A**													0.9998
<= 8.5	1068	1 (0.1%)	1067 (99.9%)	21 (2.0%)	18 (1.7%)	1057	3 (0.3%)	1054 (99.7%)	30 (2.8%)	26 (2.5%)	0.32 [0.03;3.12]	0.3301	
8.5 <	513	0 (0.0%)	513 (100%)	6 (1.2%)	4 (0.8%)	517	0 (0.0%)	517 (100%)	19 (3.7%)	17 (3.3%)	Not est	Not est	
HbA1c at baseline (disease severity) B**													0.9945
<= 7.5	627	1 (0.2%)	626 (99.8%)	12 (1.9%)	9 (1.4%)	649	2 (0.3%)	647 (99.7%)	21 (3.2%)	18 (2.8%)	0.50 [0.04;5.47]	0.5672	
7.5 <	954	0 (0.0%)	954 (100%)	15 (1.6%)	13 (1.4%)	925	1 (0.1%)	924 (99.9%)	28 (3.0%)	25 (2.7%)	Not est	Not est	
Race B													0.9998
White	1148	1 (0.1%)	1147 (99.9%)	17 (1.5%)	14 (1.2%)	1152	3 (0.3%)	1149 (99.7%)	32 (2.8%)	28 (2.4%)	0.33 [0.03;3.17]	0.3366	
Non-White	443	0 (0.0%)	443 (100%)	11 (2.5%)	9 (2.0%)	440	0 (0.0%)	440 (100%)	18 (4.1%)	16 (3.6%)	Not est	Not est	
Evidence of CV disease at screening													
CV DISEASE	1350	1 (0.1%)	1349 (99.9%)	24 (1.8%)	20 (1.5%)	1345	3 (0.2%)	1342 (99.8%)	44 (3.3%)	39 (2.9%)	0.33 [0.03;3.17]	0.3364	
CV RISK FACTORS ONLY	241	0 (0.0%)	241 (100%)	4 (1.7%)	3 (1.2%)	247	0 (0.0%)	247 (100%)	6 (2.4%)	5 (2.0%)	Not est	Not est	
Insulin Therapy at baseline													1.0000

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

Pancreatitis - serious adverse events - pre-defined MedDRA search - time-to-event analysis - Pioneer 6 - in-trial - full analysis set

	Oral Sema					Comparator					Oral Sema vs.Comparator	
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
No insulin	623	0 (0.0%)	623 (100%)	10 (1.6%)	6 (1.0%)	630	1 (0.2%)	629 (99.8%)	12 (1.9%)	11 (1.7%)	Not est	Not est
Basal only	269	0 (0.0%)	269 (100%)	3 (1.1%)	2 (0.7%)	265	0 (0.0%)	265 (100%)	8 (3.0%)	7 (2.6%)	Not est	Not est
Insulin (not basal only)	699	1 (0.1%)	698 (99.9%)	15 (2.1%)	15 (2.1%)	697	2 (0.3%)	695 (99.7%)	30 (4.3%)	26 (3.7%)	0.49 [0.04;5.35]	0.5550

p-value interaction

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated, **: due to missing baseline data it was not possible to classify all subjects in the analysis set into a level of the subgroup
Time-to-event endpoints (time from randomisation to first event) were analysed using a stratified Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factors. The model was stratified by CV disease status at screening (CV disease at screening, CV risk factors only at screening).

SUSTAIN 6 – UE nach Schweregrad (mild)

1 Mild adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema					Comparator					Sema vs.Comparator	
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Blood and lymphatic system disorders	All subjects (total)	1648	90 (5.5%)	1558 (94.5%)	80 (4.9%)	55 (3.3%)	1649	107 (6.5%)	1542 (93.5%)	91 (5.5%)	52 (3.2%)	0.84 [0.63;1.11]	0.2140
Cardiac disorders		1648	148 (9.0%)	1500 (91.0%)	76 (4.6%)	52 (3.2%)	1649	151 (9.2%)	1498 (90.8%)	87 (5.3%)	48 (2.9%)	0.98 [0.78;1.22]	0.8315
Ear and labyrinth disorders		1648	49 (3.0%)	1599 (97.0%)	86 (5.2%)	61 (3.7%)	1649	39 (2.4%)	1610 (97.6%)	97 (5.9%)	58 (3.5%)	1.26 [0.83;1.92]	0.2819
Endocrine disorders		1648	42 (2.5%)	1606 (97.5%)	81 (4.9%)	57 (3.5%)	1649	33 (2.0%)	1616 (98.0%)	99 (6.0%)	59 (3.6%)	1.28 [0.81;2.01]	0.2941
Eye disorders		1648	249 (15.1%)	1399 (84.9%)	78 (4.7%)	54 (3.3%)	1649	215 (13.0%)	1434 (87.0%)	95 (5.8%)	56 (3.4%)	1.16 [0.97;1.40]	0.1014
Gastrointestinal disorders		1648	674 (40.9%)	974 (59.1%)	56 (3.4%)	41 (2.5%)	1649	467 (28.3%)	1182 (71.7%)	70 (4.2%)	42 (2.5%)	1.62 [1.44;1.82]	<0.0001
General disorders and administration site conditions													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated. Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed factor.
MedDRA version 20.1

Mild adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value
General disorders and administration site conditions		1648	196 (11.9%)	1452 (88.1%)	76 (4.6%)	57 (3.5%)	1649	203 (12.3%)	1446 (87.7%)	86 (5.2%)	50 (3.0%)	0.97 [0.80;1.18]	0.7438
Hepatobiliary disorders		1648	62 (3.8%)	1586 (96.2%)	82 (5.0%)	57 (3.5%)	1649	68 (4.1%)	1581 (95.9%)	98 (5.9%)	58 (3.5%)	0.91 [0.65;1.29]	0.5970
Immune system disorders		1648	18 (1.1%)	1630 (98.9%)	86 (5.2%)	61 (3.7%)	1649	9 (0.5%)	1640 (99.5%)	99 (6.0%)	59 (3.6%)	2.00 [0.90;4.46]	0.0890
Infections and infestations		1648	557 (33.8%)	1091 (66.2%)	67 (4.1%)	48 (2.9%)	1649	573 (34.7%)	1076 (65.3%)	71 (4.3%)	42 (2.5%)	0.96 [0.86;1.08]	0.5065
Injury, poisoning and procedural complications		1648	158 (9.6%)	1490 (90.4%)	79 (4.8%)	57 (3.5%)	1649	200 (12.1%)	1449 (87.9%)	88 (5.3%)	51 (3.1%)	0.78 [0.63;0.96]	0.0174
Investigations		1648	332 (20.1%)	1316 (79.9%)	71 (4.3%)	51 (3.1%)	1649	309 (18.7%)	1340 (81.3%)	83 (5.0%)	47 (2.9%)	1.09 [0.93;1.27]	0.3004
Metabolism and nutrition disorders													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Metabolism and nutrition disorders		1648	317 (19.2%)	1331 (80.8%)	70 (4.2%)	51 (3.1%)	1649	267 (16.2%)	1382 (83.8%)	83 (5.0%)	48 (2.9%)	1.23 [1.05;1.45]	0.0116
Musculoskeletal and connective tissue disorders		1648	309 (18.8%)	1339 (81.3%)	75 (4.6%)	54 (3.3%)	1649	333 (20.2%)	1316 (79.8%)	87 (5.3%)	53 (3.2%)	0.92 [0.79;1.07]	0.2788
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		1648	85 (5.2%)	1563 (94.8%)	87 (5.3%)	62 (3.8%)	1649	56 (3.4%)	1593 (96.6%)	99 (6.0%)	60 (3.6%)	1.53 [1.09;2.15]	0.0130
Nervous system disorders		1648	273 (16.6%)	1375 (83.4%)	72 (4.4%)	52 (3.2%)	1649	283 (17.2%)	1366 (82.8%)	90 (5.5%)	54 (3.3%)	0.96 [0.81;1.14]	0.6423
Psychiatric disorders		1648	89 (5.4%)	1559 (94.6%)	85 (5.2%)	60 (3.6%)	1649	59 (3.6%)	1590 (96.4%)	98 (5.9%)	58 (3.5%)	1.53 [1.10;2.12]	0.0117
Renal and urinary disorders		1648	201 (12.2%)	1447 (87.8%)	72 (4.4%)	49 (3.0%)	1649	260 (15.8%)	1389 (84.2%)	82 (5.0%)	44 (2.7%)	0.76 [0.63;0.91]	0.0030

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.

Mild adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Reproductive system and breast disorders		1648	50 (3.0%)	1598 (97.0%)	86 (5.2%)	61 (3.7%)	1649	48 (2.9%)	1601 (97.1%)	99 (6.0%)	59 (3.6%)	1.04 [0.70;1.55]	0.8345
Respiratory, thoracic and mediastinal disorders		1648	184 (11.2%)	1464 (88.8%)	74 (4.5%)	50 (3.0%)	1649	219 (13.3%)	1430 (86.7%)	84 (5.1%)	48 (2.9%)	0.83 [0.68;1.01]	0.0613
Skin and subcutaneous tissue disorders		1648	146 (8.9%)	1502 (91.1%)	78 (4.7%)	55 (3.3%)	1649	166 (10.1%)	1483 (89.9%)	91 (5.5%)	54 (3.3%)	0.88 [0.70;1.09]	0.2450
Surgical and medical procedures		1648	30 (1.8%)	1618 (98.2%)	86 (5.2%)	61 (3.7%)	1649	37 (2.2%)	1612 (97.8%)	99 (6.0%)	59 (3.6%)	0.81 [0.50;1.31]	0.3843
Vascular disorders		1648	115 (7.0%)	1533 (93.0%)	79 (4.8%)	55 (3.3%)	1649	115 (7.0%)	1534 (93.0%)	94 (5.7%)	55 (3.3%)	1.00 [0.77;1.30]	0.9957

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

2 Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Comparator__ Preferred Term	Subgroup	Sema					Comparator					Sema vs.	
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Abdominal discomfort	All subjects (total)	1648	61 (3.7%)	1587 (96.3%)	87 (5.3%)	62 (3.8%)	1649	30 (1.8%)	1619 (98.2%)	99 (6.0%)	60 (3.6%)	2.06 [1.33;3.18]	0.0012
Abdominal distension		1648	26 (1.6%)	1622 (98.4%)	84 (5.1%)	62 (3.8%)	1649	15 (0.9%)	1634 (99.1%)	98 (5.9%)	58 (3.5%)	1.74 [0.92;3.29]	0.0861
Abdominal pain		1648	48 (2.9%)	1600 (97.1%)	83 (5.0%)	59 (3.6%)	1649	41 (2.5%)	1608 (97.5%)	97 (5.9%)	59 (3.6%)	1.17 [0.77;1.78]	0.4550
Abdominal pain upper		1648	45 (2.7%)	1603 (97.3%)	86 (5.2%)	61 (3.7%)	1649	31 (1.9%)	1618 (98.1%)	99 (6.0%)	60 (3.6%)	1.46 [0.93;2.31]	0.1037
Amylase increased		1648	64 (3.9%)	1584 (96.1%)	85 (5.2%)	60 (3.6%)	1649	46 (2.8%)	1603 (97.2%)	99 (6.0%)	59 (3.6%)	1.40 [0.96;2.04]	0.0822
Anaemia		1648	54 (3.3%)	1594 (96.7%)	83 (5.0%)	58 (3.5%)	1649	73 (4.4%)	1576 (95.6%)	92 (5.6%)	53 (3.2%)	0.73 [0.52;1.04]	0.0859
Angina pectoris		1648	14 (0.8%)	1634 (99.2%)	86 (5.2%)	61 (3.7%)	1649	21 (1.3%)	1628 (98.7%)	98 (5.9%)	59 (3.6%)	0.66 [0.34;1.31]	0.2349
Anxiety		1648	19 (1.2%)	1629 (98.8%)	87 (5.3%)	62 (3.8%)	1649	17 (1.0%)	1632 (99.0%)	100 (6.1%)	60 (3.6%)	1.12 [0.58;2.15]	0.7394

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixedfactor. MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Arthralgia		1648	48 (2.9%)	1600 (97.1%)	86 (5.2%)	61 (3.7%)	1649	66 (4.0%)	1583 (96.0%)	97 (5.9%)	57 (3.5%)	0.72 [0.50;1.05]	0.0846
Asthenia		1648	32 (1.9%)	1616 (98.1%)	82 (5.0%)	59 (3.6%)	1649	17 (1.0%)	1632 (99.0%)	99 (6.0%)	59 (3.6%)	1.89 [1.05;3.41]	0.0334
Atrial fibrillation		1648	23 (1.4%)	1625 (98.6%)	87 (5.3%)	62 (3.8%)	1649	21 (1.3%)	1628 (98.7%)	97 (5.9%)	57 (3.5%)	1.09 [0.61;1.98]	0.7654
Back pain		1648	69 (4.2%)	1579 (95.8%)	85 (5.2%)	60 (3.6%)	1649	56 (3.4%)	1593 (96.6%)	97 (5.9%)	58 (3.5%)	1.24 [0.87;1.76]	0.2355
Benign prostatic hyperplasia		1648	18 (1.1%)	1630 (98.9%)	87 (5.3%)	62 (3.8%)	1649	10 (0.6%)	1639 (99.4%)	99 (6.0%)	59 (3.6%)	1.80 [0.83;3.91]	0.1349
Blood creatinine increased		1648	27 (1.6%)	1621 (98.4%)	85 (5.2%)	60 (3.6%)	1649	30 (1.8%)	1619 (98.2%)	100 (6.1%)	60 (3.6%)	0.90 [0.53;1.51]	0.6866
Bronchitis		1648	39 (2.4%)	1609 (97.6%)	84 (5.1%)	60 (3.6%)	1649	54 (3.3%)	1595 (96.7%)	100 (6.1%)	60 (3.6%)	0.72 [0.48;1.08]	0.1139
Cataract													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

Preferred Term	Subgroup	Sema					Comparator					Sema vs.Comparator	
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Cataract		1648	74 (4.5%)	1574 (95.5%)	86 (5.2%)	61 (3.7%)	1649	61 (3.7%)	1588 (96.3%)	99 (6.0%)	60 (3.6%)	1.21 [0.86;1.70]	0.2675
Cellulitis		1648	17 (1.0%)	1631 (99.0%)	85 (5.2%)	60 (3.6%)	1649	17 (1.0%)	1632 (99.0%)	100 (6.1%)	60 (3.6%)	1.00 [0.51;1.95]	0.9954
Chest pain		1648	9 (0.5%)	1639 (99.5%)	87 (5.3%)	62 (3.8%)	1649	17 (1.0%)	1632 (99.0%)	99 (6.0%)	59 (3.6%)	0.53 [0.24;1.18]	0.1212
Cholelithiasis		1648	24 (1.5%)	1624 (98.5%)	84 (5.1%)	59 (3.6%)	1649	23 (1.4%)	1626 (98.6%)	99 (6.0%)	59 (3.6%)	1.04 [0.59;1.84]	0.8899
Chronic kidney disease		1648	10 (0.6%)	1638 (99.4%)	85 (5.2%)	60 (3.6%)	1649	17 (1.0%)	1632 (99.0%)	99 (6.0%)	59 (3.6%)	0.59 [0.27;1.28]	0.1800
Conjunctivitis		1648	18 (1.1%)	1630 (98.9%)	87 (5.3%)	62 (3.8%)	1649	11 (0.7%)	1638 (99.3%)	99 (6.0%)	59 (3.6%)	1.63 [0.77;3.46]	0.1997
Constipation		1648	96 (5.8%)	1552 (94.2%)	81 (4.9%)	58 (3.5%)	1649	51 (3.1%)	1598 (96.9%)	93 (5.6%)	55 (3.3%)	1.92 [1.37;2.70]	0.0002
Contusion		1648	12 (0.7%)	1636 (99.3%)	87 (5.3%)	62 (3.8%)	1649	25 (1.5%)	1624 (98.5%)	97 (5.9%)	58 (3.5%)	0.48 [0.24;0.95]	0.0359

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Cough		1648	46 (2.8%)	1602 (97.2%)	84 (5.1%)	59 (3.6%)	1649	65 (3.9%)	1584 (96.1%)	98 (5.9%)	58 (3.5%)	0.70 [0.48;1.03]	0.0687
Cystitis		1648	17 (1.0%)	1631 (99.0%)	87 (5.3%)	62 (3.8%)	1649	13 (0.8%)	1636 (99.2%)	100 (6.1%)	60 (3.6%)	1.31 [0.63;2.69]	0.4673
Decreased appetite		1648	121 (7.3%)	1527 (92.7%)	80 (4.9%)	58 (3.5%)	1649	20 (1.2%)	1629 (98.8%)	99 (6.0%)	59 (3.6%)	6.27 [3.90;10.06]	<0.0001
Depression		1648	28 (1.7%)	1620 (98.3%)	87 (5.3%)	62 (3.8%)	1649	16 (1.0%)	1633 (99.0%)	100 (6.1%)	60 (3.6%)	1.75 [0.95;3.24]	0.0728
Diabetes mellitus		1648	8 (0.5%)	1640 (99.5%)	87 (5.3%)	62 (3.8%)	1649	19 (1.2%)	1630 (98.8%)	99 (6.0%)	59 (3.6%)	0.42 [0.18;0.96]	0.0386
Diabetes mellitus inadequate control		1648	14 (0.8%)	1634 (99.2%)	87 (5.3%)	62 (3.8%)	1649	23 (1.4%)	1626 (98.6%)	99 (6.0%)	59 (3.6%)	0.60 [0.31;1.17]	0.1367
Diabetic neuropathy		1648	18 (1.1%)	1630 (98.9%)	86 (5.2%)	61 (3.7%)	1649	18 (1.1%)	1631 (98.9%)	100 (6.1%)	60 (3.6%)	1.00 [0.52;1.92]	0.9940
Diabetic retinopathy													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

Preferred Term	Subgroup	Sema					Comparator					Sema vs.Comparator	
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Diabetic retinopathy		1648	66 (4.0%)	1582 (96.0%)	85 (5.2%)	60 (3.6%)	1649	59 (3.6%)	1590 (96.4%)	99 (6.0%)	59 (3.6%)	1.12 [0.79;1.59]	0.5372
Diarrhoea		1648	227 (13.8%)	1421 (86.2%)	76 (4.6%)	53 (3.2%)	1649	132 (8.0%)	1517 (92.0%)	89 (5.4%)	56 (3.4%)	1.78 [1.43;2.20]	<0.0001
Dizziness		1648	80 (4.9%)	1568 (95.1%)	81 (4.9%)	60 (3.6%)	1649	64 (3.9%)	1585 (96.1%)	96 (5.8%)	57 (3.5%)	1.26 [0.91;1.75]	0.1718
Dyslipidaemia		1648	40 (2.4%)	1608 (97.6%)	86 (5.2%)	61 (3.7%)	1649	41 (2.5%)	1608 (97.5%)	99 (6.0%)	59 (3.6%)	0.97 [0.63;1.51]	0.9085
Dyspepsia		1648	73 (4.4%)	1575 (95.6%)	86 (5.2%)	61 (3.7%)	1649	32 (1.9%)	1617 (98.1%)	99 (6.0%)	59 (3.6%)	2.32 [1.53;3.52]	<0.0001
Dyspnoea		1648	26 (1.6%)	1622 (98.4%)	85 (5.2%)	61 (3.7%)	1649	29 (1.8%)	1620 (98.2%)	98 (5.9%)	58 (3.5%)	0.89 [0.53;1.51]	0.6727
Eructation		1648	20 (1.2%)	1628 (98.8%)	86 (5.2%)	62 (3.8%)	1649	0 (0.0%)	1649 (100%)	100 (6.1%)	60 (3.6%)	Not est	Not est
Fall		1648	24 (1.5%)	1624 (98.5%)	86 (5.2%)	61 (3.7%)	1649	30 (1.8%)	1619 (98.2%)	99 (6.0%)	59 (3.6%)	0.80 [0.47;1.36]	0.4078

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Fatigue		1648	49 (3.0%)	1599 (97.0%)	85 (5.2%)	62 (3.8%)	1649	27 (1.6%)	1622 (98.4%)	100 (6.1%)	60 (3.6%)	1.83 [1.14;2.92]	0.0120
Flatulence		1648	39 (2.4%)	1609 (97.6%)	84 (5.1%)	60 (3.6%)	1649	14 (0.8%)	1635 (99.2%)	98 (5.9%)	59 (3.6%)	2.81 [1.52;5.17]	0.0009
Gastritis		1648	20 (1.2%)	1628 (98.8%)	87 (5.3%)	62 (3.8%)	1649	12 (0.7%)	1637 (99.3%)	99 (6.0%)	60 (3.6%)	1.67 [0.82;3.42]	0.1590
Gastroenteritis		1648	28 (1.7%)	1620 (98.3%)	87 (5.3%)	62 (3.8%)	1649	23 (1.4%)	1626 (98.6%)	100 (6.1%)	60 (3.6%)	1.22 [0.70;2.12]	0.4750
Gastrooesophageal reflux disease		1648	40 (2.4%)	1608 (97.6%)	84 (5.1%)	60 (3.6%)	1649	10 (0.6%)	1639 (99.4%)	99 (6.0%)	59 (3.6%)	4.05 [2.02;8.09]	<0.0001
Haemorrhoids		1648	19 (1.2%)	1629 (98.8%)	87 (5.3%)	62 (3.8%)	1649	12 (0.7%)	1637 (99.3%)	100 (6.1%)	60 (3.6%)	1.59 [0.77;3.27]	0.2116
Headache		1648	81 (4.9%)	1567 (95.1%)	81 (4.9%)	58 (3.5%)	1649	109 (6.6%)	1540 (93.4%)	98 (5.9%)	59 (3.6%)	0.74 [0.55;0.98]	0.0389
Hepatic steatosis													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

Preferred Term	Subgroup	Sema					Comparator					Sema vs.Comparator	
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Hepatic steatosis		1648	30 (1.8%)	1618 (98.2%)	86 (5.2%)	61 (3.7%)	1649	33 (2.0%)	1616 (98.0%)	100 (6.1%)	60 (3.6%)	0.91 [0.55;1.49]	0.7029
Herpes zoster		1648	17 (1.0%)	1631 (99.0%)	85 (5.2%)	60 (3.6%)	1649	10 (0.6%)	1639 (99.4%)	100 (6.1%)	60 (3.6%)	1.70 [0.78;3.71]	0.1833
Hypercalcaemia		1648	24 (1.5%)	1624 (98.5%)	87 (5.3%)	62 (3.8%)	1649	19 (1.2%)	1630 (98.8%)	98 (5.9%)	59 (3.6%)	1.26 [0.69;2.31]	0.4449
Hyperglycaemia		1648	11 (0.7%)	1637 (99.3%)	86 (5.2%)	61 (3.7%)	1649	34 (2.1%)	1615 (97.9%)	99 (6.0%)	59 (3.6%)	0.32 [0.16;0.63]	0.0010
Hyperkalaemia		1648	34 (2.1%)	1614 (97.9%)	84 (5.1%)	60 (3.6%)	1649	35 (2.1%)	1614 (97.9%)	97 (5.9%)	59 (3.6%)	0.97 [0.60;1.55]	0.8927
Hypertension		1648	42 (2.5%)	1606 (97.5%)	86 (5.2%)	61 (3.7%)	1649	48 (2.9%)	1601 (97.1%)	97 (5.9%)	58 (3.5%)	0.87 [0.58;1.32]	0.5219
Hypertriglyceridaemia		1648	20 (1.2%)	1628 (98.8%)	87 (5.3%)	62 (3.8%)	1649	25 (1.5%)	1624 (98.5%)	100 (6.1%)	60 (3.6%)	0.80 [0.44;1.44]	0.4523
Hypokalaemia		1648	17 (1.0%)	1631 (99.0%)	87 (5.3%)	62 (3.8%)	1649	22 (1.3%)	1627 (98.7%)	97 (5.9%)	57 (3.5%)	0.77 [0.41;1.46]	0.4246

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Hypotension		1648	16 (1.0%)	1632 (99.0%)	85 (5.2%)	60 (3.6%)	1649	20 (1.2%)	1629 (98.8%)	100 (6.1%)	60 (3.6%)	0.80 [0.41;1.54]	0.5065
Influenza		1648	65 (3.9%)	1583 (96.1%)	86 (5.2%)	61 (3.7%)	1649	62 (3.8%)	1587 (96.2%)	99 (6.0%)	59 (3.6%)	1.05 [0.74;1.48]	0.7971
Insomnia		1648	26 (1.6%)	1622 (98.4%)	86 (5.2%)	61 (3.7%)	1649	16 (1.0%)	1633 (99.0%)	99 (6.0%)	59 (3.6%)	1.63 [0.87;3.04]	0.1244
Large intestine polyp		1648	18 (1.1%)	1630 (98.9%)	87 (5.3%)	62 (3.8%)	1649	14 (0.8%)	1635 (99.2%)	98 (5.9%)	59 (3.6%)	1.28 [0.64;2.58]	0.4856
Lipase increased		1648	142 (8.6%)	1506 (91.4%)	84 (5.1%)	59 (3.6%)	1649	104 (6.3%)	1545 (93.7%)	96 (5.8%)	57 (3.5%)	1.38 [1.07;1.78]	0.0129
Microalbuminuria		1648	50 (3.0%)	1598 (97.0%)	84 (5.1%)	60 (3.6%)	1649	73 (4.4%)	1576 (95.6%)	98 (5.9%)	58 (3.5%)	0.68 [0.47;0.97]	0.0351
Muscle spasms		1648	21 (1.3%)	1627 (98.7%)	86 (5.2%)	61 (3.7%)	1649	20 (1.2%)	1629 (98.8%)	100 (6.1%)	60 (3.6%)	1.05 [0.57;1.93]	0.8794
Musculoskeletal chest pain													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value
Musculoskeletal chest pain		1648	9 (0.5%)	1639 (99.5%)	87 (5.3%)	62 (3.8%)	1649	17 (1.0%)	1632 (99.0%)	99 (6.0%)	60 (3.6%)	0.53 [0.24;1.18]	0.1213
Musculoskeletal pain		1648	32 (1.9%)	1616 (98.1%)	87 (5.3%)	62 (3.8%)	1649	27 (1.6%)	1622 (98.4%)	98 (5.9%)	59 (3.6%)	1.18 [0.71;1.98]	0.5176
Myalgia		1648	11 (0.7%)	1637 (99.3%)	85 (5.2%)	60 (3.6%)	1649	27 (1.6%)	1622 (98.4%)	100 (6.1%)	60 (3.6%)	0.41 [0.20;0.82]	0.0116
Nasopharyngitis		1648	111 (6.7%)	1537 (93.3%)	83 (5.0%)	59 (3.6%)	1649	120 (7.3%)	1529 (92.7%)	94 (5.7%)	57 (3.5%)	0.92 [0.71;1.19]	0.5365
Nausea		1648	232 (14.1%)	1416 (85.9%)	73 (4.4%)	54 (3.3%)	1649	104 (6.3%)	1545 (93.7%)	91 (5.5%)	57 (3.5%)	2.33 [1.85;2.94]	<0.0001
Nephrolithiasis		1648	10 (0.6%)	1638 (99.4%)	86 (5.2%)	61 (3.7%)	1649	22 (1.3%)	1627 (98.7%)	98 (5.9%)	58 (3.5%)	0.45 [0.21;0.96]	0.0379
Nephropathy		1648	8 (0.5%)	1640 (99.5%)	86 (5.2%)	61 (3.7%)	1649	18 (1.1%)	1631 (98.9%)	99 (6.0%)	59 (3.6%)	0.44 [0.19;1.02]	0.0553
Non-cardiac chest pain		1648	19 (1.2%)	1629 (98.8%)	86 (5.2%)	62 (3.8%)	1649	13 (0.8%)	1636 (99.2%)	99 (6.0%)	59 (3.6%)	1.46 [0.72;2.97]	0.2890

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Oedema peripheral		1648	24 (1.5%)	1624 (98.5%)	85 (5.2%)	61 (3.7%)	1649	42 (2.5%)	1607 (97.5%)	95 (5.8%)	56 (3.4%)	0.57 [0.34;0.93]	0.0261
Oropharyngeal pain		1648	12 (0.7%)	1636 (99.3%)	87 (5.3%)	62 (3.8%)	1649	21 (1.3%)	1628 (98.7%)	99 (6.0%)	60 (3.6%)	0.57 [0.28;1.15]	0.1176
Osteoarthritis		1648	32 (1.9%)	1616 (98.1%)	86 (5.2%)	61 (3.7%)	1649	28 (1.7%)	1621 (98.3%)	100 (6.1%)	60 (3.6%)	1.14 [0.69;1.90]	0.6054
Pain in extremity		1648	40 (2.4%)	1608 (97.6%)	86 (5.2%)	61 (3.7%)	1649	54 (3.3%)	1595 (96.7%)	96 (5.8%)	57 (3.5%)	0.74 [0.49;1.11]	0.1402
Pancreatic enzymes increased		1648	17 (1.0%)	1631 (99.0%)	86 (5.2%)	62 (3.8%)	1649	12 (0.7%)	1637 (99.3%)	100 (6.1%)	60 (3.6%)	1.42 [0.68;2.97]	0.3534
Pharyngitis		1648	22 (1.3%)	1626 (98.7%)	86 (5.2%)	62 (3.8%)	1649	17 (1.0%)	1632 (99.0%)	100 (6.1%)	60 (3.6%)	1.29 [0.69;2.44]	0.4246
Pneumonia		1648	27 (1.6%)	1621 (98.4%)	87 (5.3%)	62 (3.8%)	1649	20 (1.2%)	1629 (98.8%)	98 (5.9%)	58 (3.5%)	1.35 [0.76;2.41]	0.3080
Proteinuria													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value
Proteinuria		1648	22 (1.3%)	1626 (98.7%)	86 (5.2%)	62 (3.8%)	1649	28 (1.7%)	1621 (98.3%)	99 (6.0%)	59 (3.6%)	0.78 [0.45;1.37]	0.3902
Pruritus		1648	23 (1.4%)	1625 (98.6%)	86 (5.2%)	61 (3.7%)	1649	15 (0.9%)	1634 (99.1%)	99 (6.0%)	59 (3.6%)	1.54 [0.80;2.94]	0.1963
Pyrexia		1648	10 (0.6%)	1638 (99.4%)	87 (5.3%)	62 (3.8%)	1649	20 (1.2%)	1629 (98.8%)	97 (5.9%)	58 (3.5%)	0.50 [0.23;1.07]	0.0728
Rash		1648	18 (1.1%)	1630 (98.9%)	86 (5.2%)	61 (3.7%)	1649	21 (1.3%)	1628 (98.7%)	99 (6.0%)	60 (3.6%)	0.85 [0.45;1.60]	0.6217
Renal cyst		1648	28 (1.7%)	1620 (98.3%)	84 (5.1%)	59 (3.6%)	1649	40 (2.4%)	1609 (97.6%)	97 (5.9%)	57 (3.5%)	0.70 [0.43;1.13]	0.1439
Sinusitis		1648	33 (2.0%)	1615 (98.0%)	86 (5.2%)	62 (3.8%)	1649	36 (2.2%)	1613 (97.8%)	96 (5.8%)	59 (3.6%)	0.92 [0.57;1.47]	0.7172
Tooth infection		1648	19 (1.2%)	1629 (98.8%)	86 (5.2%)	61 (3.7%)	1649	7 (0.4%)	1642 (99.6%)	100 (6.1%)	60 (3.6%)	2.72 [1.14;6.46]	0.0238
Toothache		1648	16 (1.0%)	1632 (99.0%)	86 (5.2%)	61 (3.7%)	1649	17 (1.0%)	1632 (99.0%)	98 (5.9%)	58 (3.5%)	0.94 [0.47;1.86]	0.8579

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Mild adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Upper respiratory tract infection		1648	69 (4.2%)	1579 (95.8%)	83 (5.0%)	61 (3.7%)	1649	89 (5.4%)	1560 (94.6%)	96 (5.8%)	56 (3.4%)	0.77 [0.56;1.05]	0.1020
Urinary tract infection		1648	105 (6.4%)	1543 (93.6%)	82 (5.0%)	57 (3.5%)	1649	101 (6.1%)	1548 (93.9%)	95 (5.8%)	57 (3.5%)	1.04 [0.79;1.37]	0.7748
Vertigo		1648	20 (1.2%)	1628 (98.8%)	87 (5.3%)	62 (3.8%)	1649	13 (0.8%)	1636 (99.2%)	100 (6.1%)	60 (3.6%)	1.54 [0.77;3.10]	0.2256
Vitamin D deficiency		1648	18 (1.1%)	1630 (98.9%)	87 (5.3%)	62 (3.8%)	1649	17 (1.0%)	1632 (99.0%)	99 (6.0%)	60 (3.6%)	1.06 [0.55;2.05]	0.8686
Vomiting		1648	128 (7.8%)	1520 (92.2%)	79 (4.8%)	56 (3.4%)	1649	53 (3.2%)	1596 (96.8%)	96 (5.8%)	58 (3.5%)	2.47 [1.80;3.41]	<0.0001

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

SUSTAIN 6 – UE nach Schweregrad (moderat)

1 Moderate adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value
Blood and lymphatic system disorders	All subjects (total)	1648	44 (2.7%)	1604 (97.3%)	79 (4.8%)	55 (3.3%)	1649	30 (1.8%)	1619 (98.2%)	94 (5.7%)	55 (3.3%)	1.48 [0.93;2.35]	0.1001
Cardiac disorders		1648	153 (9.3%)	1495 (90.7%)	73 (4.4%)	49 (3.0%)	1649	180 (10.9%)	1469 (89.1%)	82 (5.0%)	47 (2.9%)	0.85 [0.69;1.05]	0.1394
Ear and labyrinth disorders		1648	21 (1.3%)	1627 (98.7%)	87 (5.3%)	62 (3.8%)	1649	17 (1.0%)	1632 (99.0%)	100 (6.1%)	60 (3.6%)	1.24 [0.65;2.34]	0.5168
Eye disorders		1648	102 (6.2%)	1546 (93.8%)	83 (5.0%)	59 (3.6%)	1649	83 (5.0%)	1566 (95.0%)	97 (5.9%)	57 (3.5%)	1.23 [0.92;1.65]	0.1535
Gastrointestinal disorders		1648	368 (22.3%)	1280 (77.7%)	66 (4.0%)	44 (2.7%)	1649	231 (14.0%)	1418 (86.0%)	84 (5.1%)	48 (2.9%)	1.71 [1.45;2.02]	<0.0001
General disorders and administration site conditions		1648	95 (5.8%)	1553 (94.2%)	80 (4.9%)	56 (3.4%)	1649	101 (6.1%)	1548 (93.9%)	90 (5.5%)	54 (3.3%)	0.94 [0.71;1.24]	0.6684
Hepatobiliary disorders													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed factor.
MedDRA version 20.1

Moderate adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Hepatobiliary disorders		1648	27 (1.6%)	1621 (98.4%)	85 (5.2%)	60 (3.6%)	1649	35 (2.1%)	1614 (97.9%)	97 (5.9%)	57 (3.5%)	0.77 [0.47;1.27]	0.3050
Infections and infestations		1648	359 (21.8%)	1289 (78.2%)	70 (4.2%)	49 (3.0%)	1649	366 (22.2%)	1283 (77.8%)	83 (5.0%)	51 (3.1%)	0.98 [0.85;1.14]	0.8126
Injury, poisoning and procedural complications		1648	120 (7.3%)	1528 (92.7%)	84 (5.1%)	60 (3.6%)	1649	139 (8.4%)	1510 (91.6%)	88 (5.3%)	53 (3.2%)	0.86 [0.67;1.09]	0.2164
Investigations		1648	123 (7.5%)	1525 (92.5%)	79 (4.8%)	55 (3.3%)	1649	112 (6.8%)	1537 (93.2%)	89 (5.4%)	53 (3.2%)	1.10 [0.85;1.42]	0.4588
Metabolism and nutrition disorders		1648	137 (8.3%)	1511 (91.7%)	72 (4.4%)	53 (3.2%)	1649	137 (8.3%)	1512 (91.7%)	86 (5.2%)	51 (3.1%)	1.00 [0.79;1.27]	0.9720
Musculoskeletal and connective tissue disorders		1648	203 (12.3%)	1445 (87.7%)	81 (4.9%)	57 (3.5%)	1649	237 (14.4%)	1412 (85.6%)	88 (5.3%)	55 (3.3%)	0.85 [0.70;1.02]	0.0850

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Moderate adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		1648	37 (2.2%)	1611 (97.8%)	85 (5.2%)	61 (3.7%)	1649	45 (2.7%)	1604 (97.3%)	94 (5.7%)	56 (3.4%)	0.82 [0.53;1.27]	0.3699
Nervous system disorders		1648	171 (10.4%)	1477 (89.6%)	76 (4.6%)	56 (3.4%)	1649	164 (9.9%)	1485 (90.1%)	87 (5.3%)	51 (3.1%)	1.05 [0.85;1.30]	0.6554
Psychiatric disorders		1648	47 (2.9%)	1601 (97.1%)	79 (4.8%)	56 (3.4%)	1649	38 (2.3%)	1611 (97.7%)	94 (5.7%)	57 (3.5%)	1.24 [0.81;1.90]	0.3252
Renal and urinary disorders		1648	110 (6.7%)	1538 (93.3%)	79 (4.8%)	54 (3.3%)	1649	130 (7.9%)	1519 (92.1%)	82 (5.0%)	46 (2.8%)	0.84 [0.65;1.09]	0.1865
Reproductive system and breast disorders		1648	23 (1.4%)	1625 (98.6%)	86 (5.2%)	61 (3.7%)	1649	21 (1.3%)	1628 (98.7%)	98 (5.9%)	59 (3.6%)	1.09 [0.61;1.98]	0.7657
Respiratory, thoracic and mediastinal disorders		1648	99 (6.0%)	1549 (94.0%)	75 (4.6%)	51 (3.1%)	1649	100 (6.1%)	1549 (93.9%)	85 (5.2%)	50 (3.0%)	0.99 [0.75;1.30]	0.9166

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Moderate adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Skin and subcutaneous tissue disorders		1648	59 (3.6%)	1589 (96.4%)	83 (5.0%)	58 (3.5%)	1649	70 (4.2%)	1579 (95.8%)	98 (5.9%)	58 (3.5%)	0.84 [0.59;1.19]	0.3274
Surgical and medical procedures		1648	56 (3.4%)	1592 (96.6%)	81 (4.9%)	57 (3.5%)	1649	77 (4.7%)	1572 (95.3%)	94 (5.7%)	56 (3.4%)	0.72 [0.51;1.02]	0.0639
Vascular disorders		1648	93 (5.6%)	1555 (94.4%)	77 (4.7%)	52 (3.2%)	1649	103 (6.2%)	1546 (93.8%)	94 (5.7%)	55 (3.3%)	0.90 [0.68;1.19]	0.4619

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N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

2 Moderate adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema					Comparator					Sema vs.Comparator	
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Abdominal discomfort	All subjects (total)	1648	18 (1.1%)	1630 (98.9%)	86 (5.2%)	61 (3.7%)	1649	9 (0.5%)	1640 (99.5%)	100 (6.1%)	60 (3.6%)	2.01 [0.90;4.47]	0.0881
Abdominal pain		1648	35 (2.1%)	1613 (97.9%)	85 (5.2%)	60 (3.6%)	1649	24 (1.5%)	1625 (98.5%)	98 (5.9%)	58 (3.5%)	1.46 [0.87;2.46]	0.1507
Abdominal pain upper		1648	32 (1.9%)	1616 (98.1%)	84 (5.1%)	59 (3.6%)	1649	11 (0.7%)	1638 (99.3%)	100 (6.1%)	60 (3.6%)	2.92 [1.47;5.80]	0.0021
Acute kidney injury		1648	14 (0.8%)	1634 (99.2%)	86 (5.2%)	61 (3.7%)	1649	22 (1.3%)	1627 (98.7%)	96 (5.8%)	57 (3.5%)	0.63 [0.32;1.24]	0.1834
Amylase increased		1648	21 (1.3%)	1627 (98.7%)	87 (5.3%)	62 (3.8%)	1649	10 (0.6%)	1639 (99.4%)	100 (6.1%)	60 (3.6%)	2.10 [0.99;4.47]	0.0530
Anaemia		1648	25 (1.5%)	1623 (98.5%)	82 (5.0%)	58 (3.5%)	1649	20 (1.2%)	1629 (98.8%)	95 (5.8%)	56 (3.4%)	1.26 [0.70;2.26]	0.4488
Angina pectoris		1648	19 (1.2%)	1629 (98.8%)	84 (5.1%)	60 (3.6%)	1649	30 (1.8%)	1619 (98.2%)	97 (5.9%)	58 (3.5%)	0.63 [0.36;1.12]	0.1166
Angina unstable		1648	22 (1.3%)	1626 (98.7%)	86 (5.2%)	61 (3.7%)	1649	27 (1.6%)	1622 (98.4%)	98 (5.9%)	58 (3.5%)	0.81 [0.46;1.43]	0.4687

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Moderate adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value
Arthralgia		1648	28 (1.7%)	1620 (98.3%)	87 (5.3%)	62 (3.8%)	1649	54 (3.3%)	1595 (96.7%)	97 (5.9%)	59 (3.6%)	0.51 [0.33;0.81]	0.0043
Atrial fibrillation		1648	26 (1.6%)	1622 (98.4%)	85 (5.2%)	60 (3.6%)	1649	30 (1.8%)	1619 (98.2%)	96 (5.8%)	56 (3.4%)	0.86 [0.51;1.46]	0.5871
Back pain		1648	35 (2.1%)	1613 (97.9%)	86 (5.2%)	61 (3.7%)	1649	41 (2.5%)	1608 (97.5%)	96 (5.8%)	58 (3.5%)	0.85 [0.54;1.33]	0.4772
Bronchitis		1648	51 (3.1%)	1597 (96.9%)	84 (5.1%)	59 (3.6%)	1649	49 (3.0%)	1600 (97.0%)	99 (6.0%)	60 (3.6%)	1.04 [0.70;1.54]	0.8496
Cardiac failure congestive		1648	19 (1.2%)	1629 (98.8%)	80 (4.9%)	55 (3.3%)	1649	22 (1.3%)	1627 (98.7%)	95 (5.8%)	58 (3.5%)	0.86 [0.47;1.59]	0.6375
Cataract		1648	26 (1.6%)	1622 (98.4%)	86 (5.2%)	62 (3.8%)	1649	24 (1.5%)	1625 (98.5%)	99 (6.0%)	59 (3.6%)	1.08 [0.62;1.88]	0.7856
Cellulitis		1648	13 (0.8%)	1635 (99.2%)	87 (5.3%)	62 (3.8%)	1649	28 (1.7%)	1621 (98.3%)	98 (5.9%)	60 (3.6%)	0.46 [0.24;0.89]	0.0214
Chronic kidney disease													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Moderate adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Chronic kidney disease		1648	9 (0.5%)	1639 (99.5%)	87 (5.3%)	62 (3.8%)	1649	22 (1.3%)	1627 (98.7%)	98 (5.9%)	59 (3.6%)	0.41 [0.19;0.88]	0.0229
Chronic obstructive pulmonary disease		1648	6 (0.4%)	1642 (99.6%)	86 (5.2%)	61 (3.7%)	1649	20 (1.2%)	1629 (98.8%)	98 (5.9%)	58 (3.5%)	0.30 [0.12;0.74]	0.0095
Constipation		1648	37 (2.2%)	1611 (97.8%)	81 (4.9%)	56 (3.4%)	1649	22 (1.3%)	1627 (98.7%)	98 (5.9%)	59 (3.6%)	1.70 [1.00;2.87]	0.0500
Coronary arterial stent insertion		1648	13 (0.8%)	1635 (99.2%)	85 (5.2%)	60 (3.6%)	1649	22 (1.3%)	1627 (98.7%)	98 (5.9%)	59 (3.6%)	0.59 [0.30;1.17]	0.1285
Cough		1648	22 (1.3%)	1626 (98.7%)	85 (5.2%)	60 (3.6%)	1649	22 (1.3%)	1627 (98.7%)	98 (5.9%)	59 (3.6%)	1.00 [0.55;1.80]	0.9894
Decreased appetite		1648	40 (2.4%)	1608 (97.6%)	81 (4.9%)	59 (3.6%)	1649	7 (0.4%)	1642 (99.6%)	99 (6.0%)	59 (3.6%)	5.77 [2.59;12.88]	<0.0001
Depression		1648	18 (1.1%)	1630 (98.9%)	86 (5.2%)	61 (3.7%)	1649	14 (0.8%)	1635 (99.2%)	98 (5.9%)	60 (3.6%)	1.28 [0.64;2.58]	0.4826
Diabetes mellitus													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Moderate adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value
Diabetes mellitus		1648	14 (0.8%)	1634 (99.2%)	86 (5.2%)	62 (3.8%)	1649	17 (1.0%)	1632 (99.0%)	99 (6.0%)	60 (3.6%)	0.82 [0.40;1.66]	0.5804
Diabetic retinopathy		1648	38 (2.3%)	1610 (97.7%)	87 (5.3%)	62 (3.8%)	1649	19 (1.2%)	1630 (98.8%)	99 (6.0%)	59 (3.6%)	2.01 [1.16;3.48]	0.0132
Diarrhoea		1648	109 (6.6%)	1539 (93.4%)	82 (5.0%)	59 (3.6%)	1649	71 (4.3%)	1578 (95.7%)	97 (5.9%)	57 (3.5%)	1.56 [1.16;2.10]	0.0035
Dizziness		1648	21 (1.3%)	1627 (98.7%)	84 (5.1%)	60 (3.6%)	1649	19 (1.2%)	1630 (98.8%)	98 (5.9%)	58 (3.5%)	1.11 [0.60;2.06]	0.7464
Dyspepsia		1648	40 (2.4%)	1608 (97.6%)	84 (5.1%)	60 (3.6%)	1649	9 (0.5%)	1640 (99.5%)	99 (6.0%)	59 (3.6%)	4.50 [2.18;9.28]	<0.0001
Dyspnoea		1648	17 (1.0%)	1631 (99.0%)	84 (5.1%)	60 (3.6%)	1649	16 (1.0%)	1633 (99.0%)	99 (6.0%)	59 (3.6%)	1.06 [0.54;2.10]	0.8642
Fall		1648	25 (1.5%)	1623 (98.5%)	86 (5.2%)	61 (3.7%)	1649	33 (2.0%)	1616 (98.0%)	95 (5.8%)	57 (3.5%)	0.75 [0.45;1.27]	0.2889
Fatigue		1648	18 (1.1%)	1630 (98.9%)	85 (5.2%)	60 (3.6%)	1649	16 (1.0%)	1633 (99.0%)	98 (5.9%)	58 (3.5%)	1.13 [0.57;2.21]	0.7311

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Moderate adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value
Gastritis		1648	20 (1.2%)	1628 (98.8%)	87 (5.3%)	62 (3.8%)	1649	10 (0.6%)	1639 (99.4%)	100 (6.1%)	60 (3.6%)	2.01 [0.94;4.29]	0.0719
Gastroenteritis		1648	23 (1.4%)	1625 (98.6%)	86 (5.2%)	62 (3.8%)	1649	18 (1.1%)	1631 (98.9%)	100 (6.1%)	60 (3.6%)	1.28 [0.69;2.37]	0.4355
Gastrooesophageal reflux disease		1648	26 (1.6%)	1622 (98.4%)	87 (5.3%)	62 (3.8%)	1649	12 (0.7%)	1637 (99.3%)	99 (6.0%)	59 (3.6%)	2.18 [1.10;4.31]	0.0259
Headache		1648	38 (2.3%)	1610 (97.7%)	87 (5.3%)	62 (3.8%)	1649	39 (2.4%)	1610 (97.6%)	98 (5.9%)	60 (3.6%)	0.97 [0.62;1.52]	0.9052
Hyperglycaemia		1648	16 (1.0%)	1632 (99.0%)	85 (5.2%)	61 (3.7%)	1649	22 (1.3%)	1627 (98.7%)	99 (6.0%)	60 (3.6%)	0.72 [0.38;1.37]	0.3216
Hypertension		1648	27 (1.6%)	1621 (98.4%)	86 (5.2%)	61 (3.7%)	1649	33 (2.0%)	1616 (98.0%)	97 (5.9%)	57 (3.5%)	0.81 [0.49;1.35]	0.4296
Influenza		1648	33 (2.0%)	1615 (98.0%)	86 (5.2%)	61 (3.7%)	1649	39 (2.4%)	1610 (97.6%)	100 (6.1%)	60 (3.6%)	0.84 [0.53;1.34]	0.4686
Lipase increased													

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Moderate adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Lipase increased		1648	53 (3.2%)	1595 (96.8%)	86 (5.2%)	61 (3.7%)	1649	32 (1.9%)	1617 (98.1%)	98 (5.9%)	59 (3.6%)	1.66 [1.07;2.58]	0.0229
Musculoskeletal pain		1648	18 (1.1%)	1630 (98.9%)	86 (5.2%)	61 (3.7%)	1649	19 (1.2%)	1630 (98.8%)	97 (5.9%)	57 (3.5%)	0.95 [0.50;1.80]	0.8662
Nasopharyngitis		1648	24 (1.5%)	1624 (98.5%)	87 (5.3%)	62 (3.8%)	1649	27 (1.6%)	1622 (98.4%)	100 (6.1%)	60 (3.6%)	0.89 [0.51;1.54]	0.6733
Nausea		1648	103 (6.3%)	1545 (93.8%)	80 (4.9%)	55 (3.3%)	1649	35 (2.1%)	1614 (97.9%)	98 (5.9%)	58 (3.5%)	3.02 [2.06;4.43]	<0.0001
Non-cardiac chest pain		1648	14 (0.8%)	1634 (99.2%)	87 (5.3%)	62 (3.8%)	1649	20 (1.2%)	1629 (98.8%)	99 (6.0%)	60 (3.6%)	0.70 [0.35;1.38]	0.3016
Oedema peripheral		1648	9 (0.5%)	1639 (99.5%)	84 (5.1%)	59 (3.6%)	1649	17 (1.0%)	1632 (99.0%)	98 (5.9%)	59 (3.6%)	0.53 [0.23;1.18]	0.1194
Osteoarthritis		1648	42 (2.5%)	1606 (97.5%)	86 (5.2%)	61 (3.7%)	1649	26 (1.6%)	1623 (98.4%)	100 (6.1%)	60 (3.6%)	1.62 [0.99;2.64]	0.0537
Pain in extremity		1648	26 (1.6%)	1622 (98.4%)	87 (5.3%)	62 (3.8%)	1649	33 (2.0%)	1616 (98.0%)	96 (5.8%)	59 (3.6%)	0.78 [0.47;1.31]	0.3536

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Moderate adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value
Pneumonia		1648	30 (1.8%)	1618 (98.2%)	82 (5.0%)	57 (3.5%)	1649	40 (2.4%)	1609 (97.6%)	97 (5.9%)	58 (3.5%)	0.74 [0.46;1.19]	0.2206
Sinusitis		1648	23 (1.4%)	1625 (98.6%)	86 (5.2%)	61 (3.7%)	1649	26 (1.6%)	1623 (98.4%)	99 (6.0%)	60 (3.6%)	0.88 [0.50;1.55]	0.6625
Upper respiratory tract infection		1648	41 (2.5%)	1607 (97.5%)	85 (5.2%)	61 (3.7%)	1649	48 (2.9%)	1601 (97.1%)	97 (5.9%)	58 (3.5%)	0.85 [0.56;1.29]	0.4525
Urinary tract infection		1648	59 (3.6%)	1589 (96.4%)	86 (5.2%)	61 (3.7%)	1649	50 (3.0%)	1599 (97.0%)	97 (5.9%)	58 (3.5%)	1.18 [0.81;1.72]	0.3862
Vomiting		1648	87 (5.3%)	1561 (94.7%)	81 (4.9%)	56 (3.4%)	1649	26 (1.6%)	1623 (98.4%)	97 (5.9%)	58 (3.5%)	3.42 [2.21;5.31]	<0.0001

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

SUSTAIN 6 – UE nach Schweregrad (schwer)

1 Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Cardiac disorders	All subjects (total)	1648	104 (6.3%)	1544 (93.7%)	54 (3.3%)	30 (1.8%)	1649	124 (7.5%)	1525 (92.5%)	64 (3.9%)	28 (1.7%)	0.83 [0.64;1.08]	0.1711
Gastrointestinal disorders		1648	96 (5.8%)	1552 (94.2%)	74 (4.5%)	52 (3.2%)	1649	33 (2.0%)	1616 (98.0%)	97 (5.9%)	57 (3.5%)	2.99 [2.02;4.44]	<0.0001
General disorders and administration site conditions		1648	18 (1.1%)	1630 (98.9%)	79 (4.8%)	54 (3.3%)	1649	17 (1.0%)	1632 (99.0%)	91 (5.5%)	51 (3.1%)	1.06 [0.55;2.05]	0.8655
Hepatobiliary disorders		1648	17 (1.0%)	1631 (99.0%)	84 (5.1%)	59 (3.6%)	1649	10 (0.6%)	1639 (99.4%)	100 (6.1%)	60 (3.6%)	1.70 [0.78;3.71]	0.1835
Infections and infestations		1648	69 (4.2%)	1579 (95.8%)	74 (4.5%)	49 (3.0%)	1649	88 (5.3%)	1561 (94.7%)	83 (5.0%)	47 (2.9%)	0.78 [0.57;1.07]	0.1277
Injury, poisoning and procedural complications		1648	31 (1.9%)	1617 (98.1%)	85 (5.2%)	60 (3.6%)	1649	36 (2.2%)	1613 (97.8%)	94 (5.7%)	54 (3.3%)	0.86 [0.53;1.39]	0.5314

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Investigations		1648	20 (1.2%)	1628 (98.8%)	83 (5.0%)	58 (3.5%)	1649	13 (0.8%)	1636 (99.2%)	99 (6.0%)	59 (3.6%)	1.54 [0.77;3.10]	0.2245
Metabolism and nutrition disorders		1648	33 (2.0%)	1615 (98.0%)	82 (5.0%)	57 (3.5%)	1649	38 (2.3%)	1611 (97.7%)	92 (5.6%)	54 (3.3%)	0.87 [0.54;1.38]	0.5501
Musculoskeletal and connective tissue disorders		1648	26 (1.6%)	1622 (98.4%)	87 (5.3%)	62 (3.8%)	1649	43 (2.6%)	1606 (97.4%)	97 (5.9%)	59 (3.6%)	0.60 [0.37;0.98]	0.0404
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		1648	28 (1.7%)	1620 (98.3%)	74 (4.5%)	50 (3.0%)	1649	30 (1.8%)	1619 (98.2%)	95 (5.8%)	55 (3.3%)	0.93 [0.56;1.56]	0.7818
Nervous system disorders		1648	50 (3.0%)	1598 (97.0%)	75 (4.6%)	51 (3.1%)	1649	59 (3.6%)	1590 (96.4%)	87 (5.3%)	50 (3.0%)	0.85 [0.58;1.23]	0.3873
Renal and urinary disorders		1648	37 (2.2%)	1611 (97.8%)	77 (4.7%)	52 (3.2%)	1649	38 (2.3%)	1611 (97.7%)	87 (5.3%)	49 (3.0%)	0.97 [0.62;1.53]	0.8990

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Respiratory, thoracic and mediastinal disorders		1648	41 (2.5%)	1607 (97.5%)	69 (4.2%)	45 (2.7%)	1649	27 (1.6%)	1622 (98.4%)	88 (5.3%)	49 (3.0%)	1.52 [0.94;2.47]	0.0904
Surgical and medical procedures		1648	42 (2.5%)	1606 (97.5%)	82 (5.0%)	57 (3.5%)	1649	69 (4.2%)	1580 (95.8%)	95 (5.8%)	56 (3.4%)	0.60 [0.41;0.88]	0.0095
Vascular disorders		1648	20 (1.2%)	1628 (98.8%)	86 (5.2%)	61 (3.7%)	1649	25 (1.5%)	1624 (98.5%)	94 (5.7%)	55 (3.3%)	0.80 [0.44;1.44]	0.4575

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

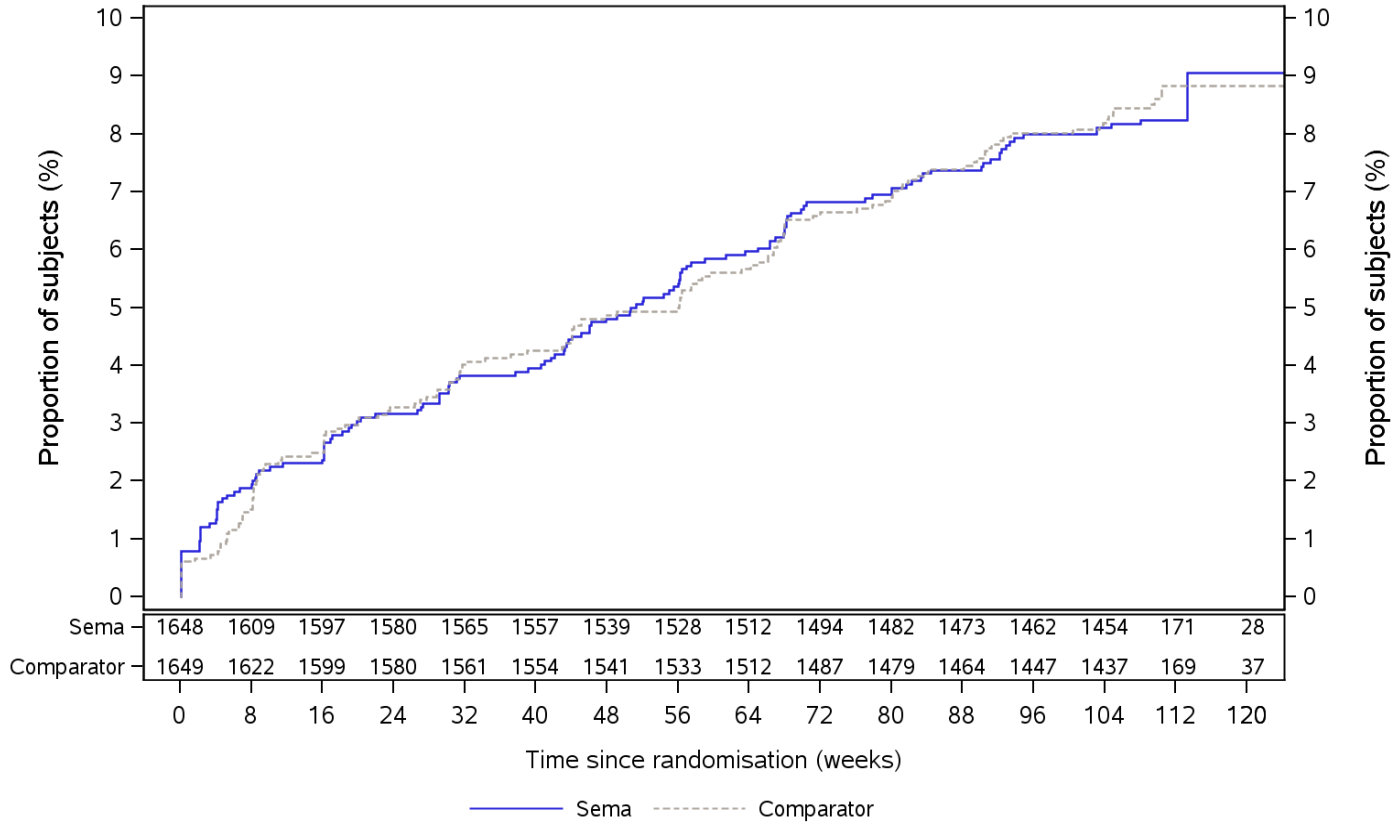
2 Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator	
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
Acute myocardial infarction	All subjects (total)	1648	19 (1.2%)	1629 (98.8%)	79 (4.8%)	54 (3.3%)	1649	30 (1.8%)	1619 (98.2%)	94 (5.7%)	55 (3.3%)	0.63 [0.35;1.12]	0.1131
Cardiac failure congestive		1648	17 (1.0%)	1631 (99.0%)	80 (4.9%)	55 (3.3%)	1649	16 (1.0%)	1633 (99.0%)	93 (5.6%)	54 (3.3%)	1.06 [0.54;2.10]	0.8673
Coronary artery bypass		1648	9 (0.5%)	1639 (99.5%)	87 (5.3%)	62 (3.8%)	1649	19 (1.2%)	1630 (98.8%)	98 (5.9%)	58 (3.5%)	0.47 [0.21;1.04]	0.0626
Nausea		1648	25 (1.5%)	1623 (98.5%)	83 (5.0%)	60 (3.6%)	1649	1 (0.1%)	1648 (99.9%)	100 (6.1%)	60 (3.6%)	25.22 [3.42;186.10]	0.0016
Pneumonia		1648	14 (0.8%)	1634 (99.2%)	81 (4.9%)	56 (3.4%)	1649	19 (1.2%)	1630 (98.8%)	95 (5.8%)	57 (3.5%)	0.73 [0.37;1.46]	0.3793

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment as fixed
factor.
MedDRA version 20.1

SUSTAIN 6 – Kumulative Inzidenz (UE nach SOC und PT)

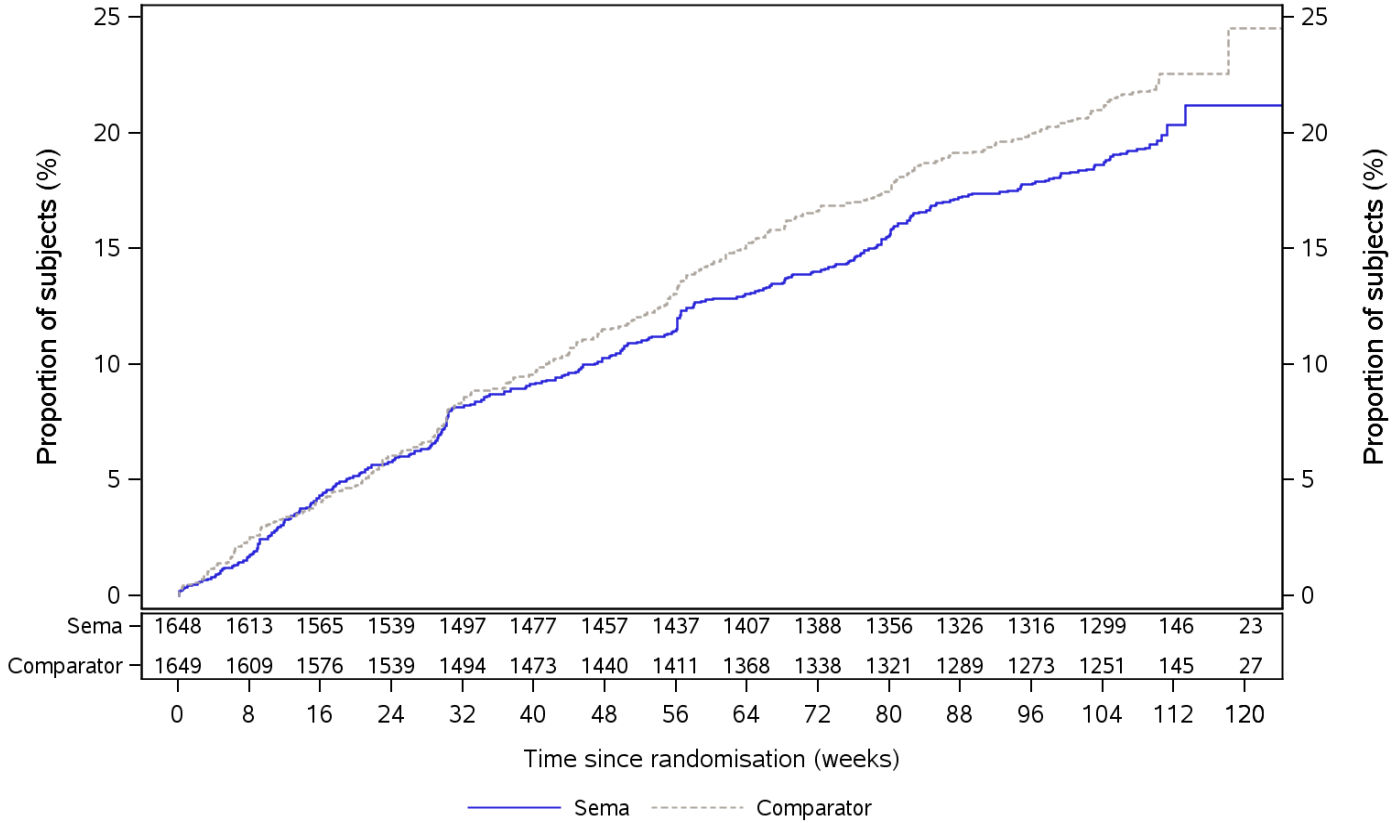
1 Adverse events - system organ class "Blood and lymphatic system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:42:26 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_blsd_ae_all_s6.png

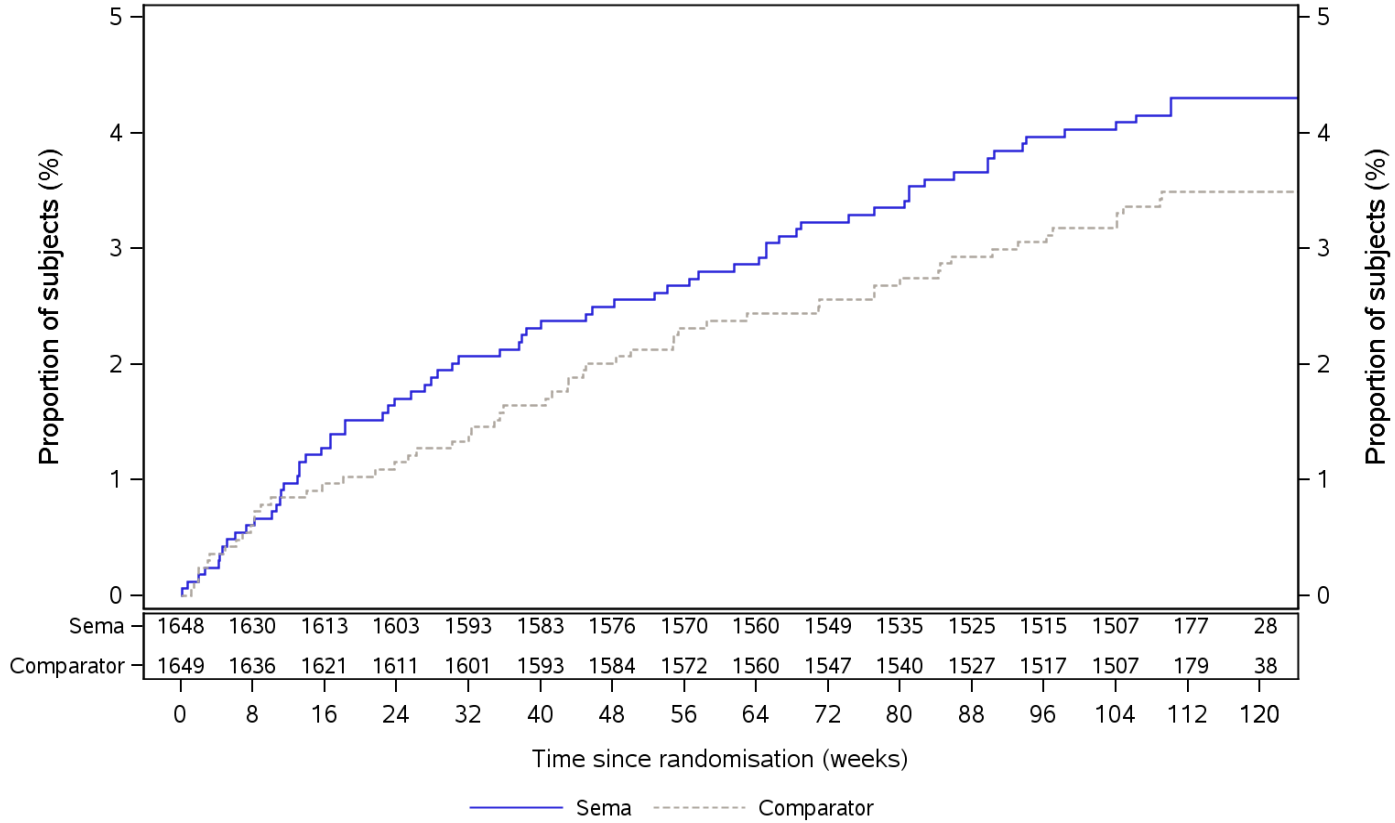
2 Adverse events - system organ class "Cardiac disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:42:48 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_cd_ae_all_s6.png

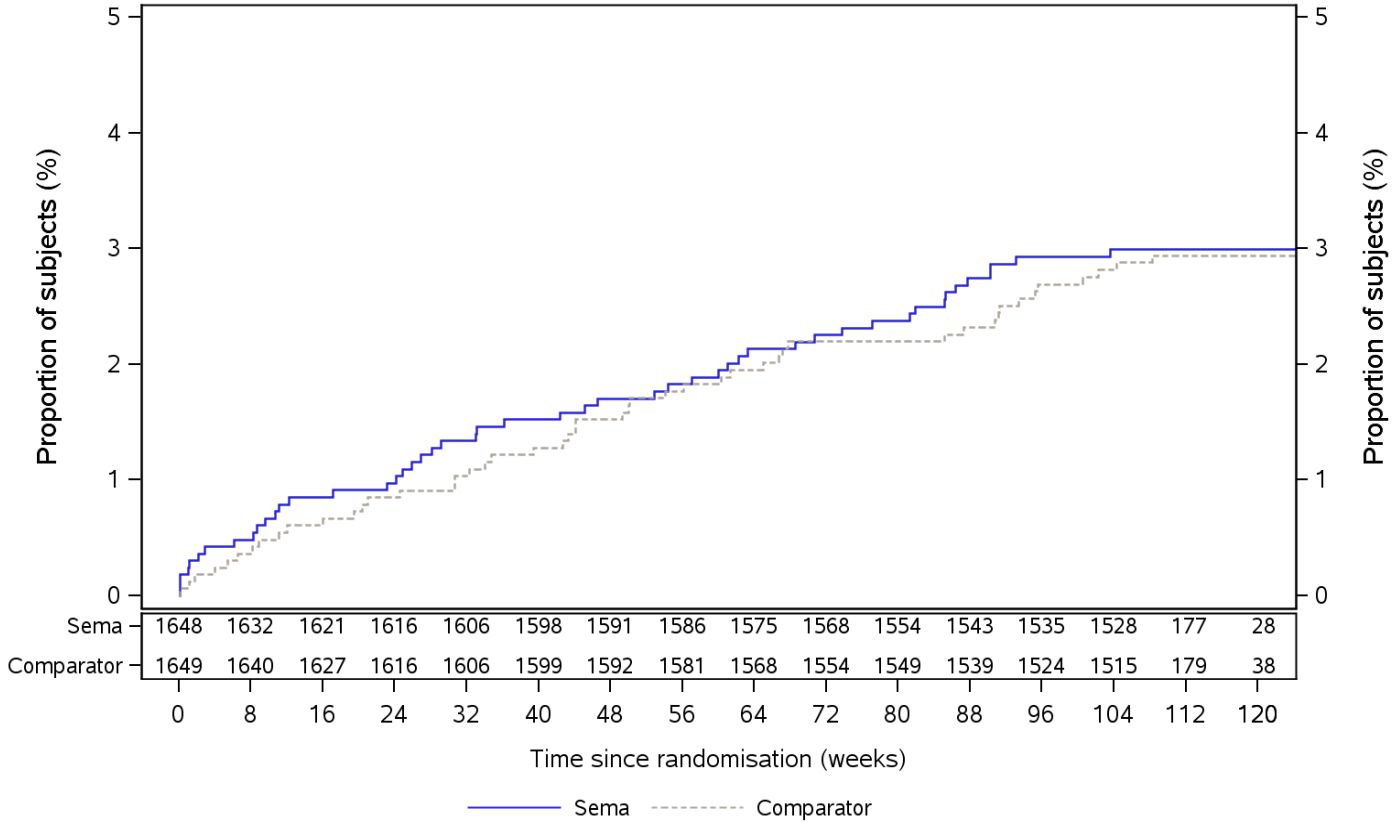
3 Adverse events - system organ class "Ear and labyrinth disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:43:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_earandlab_ae_all_s6.png

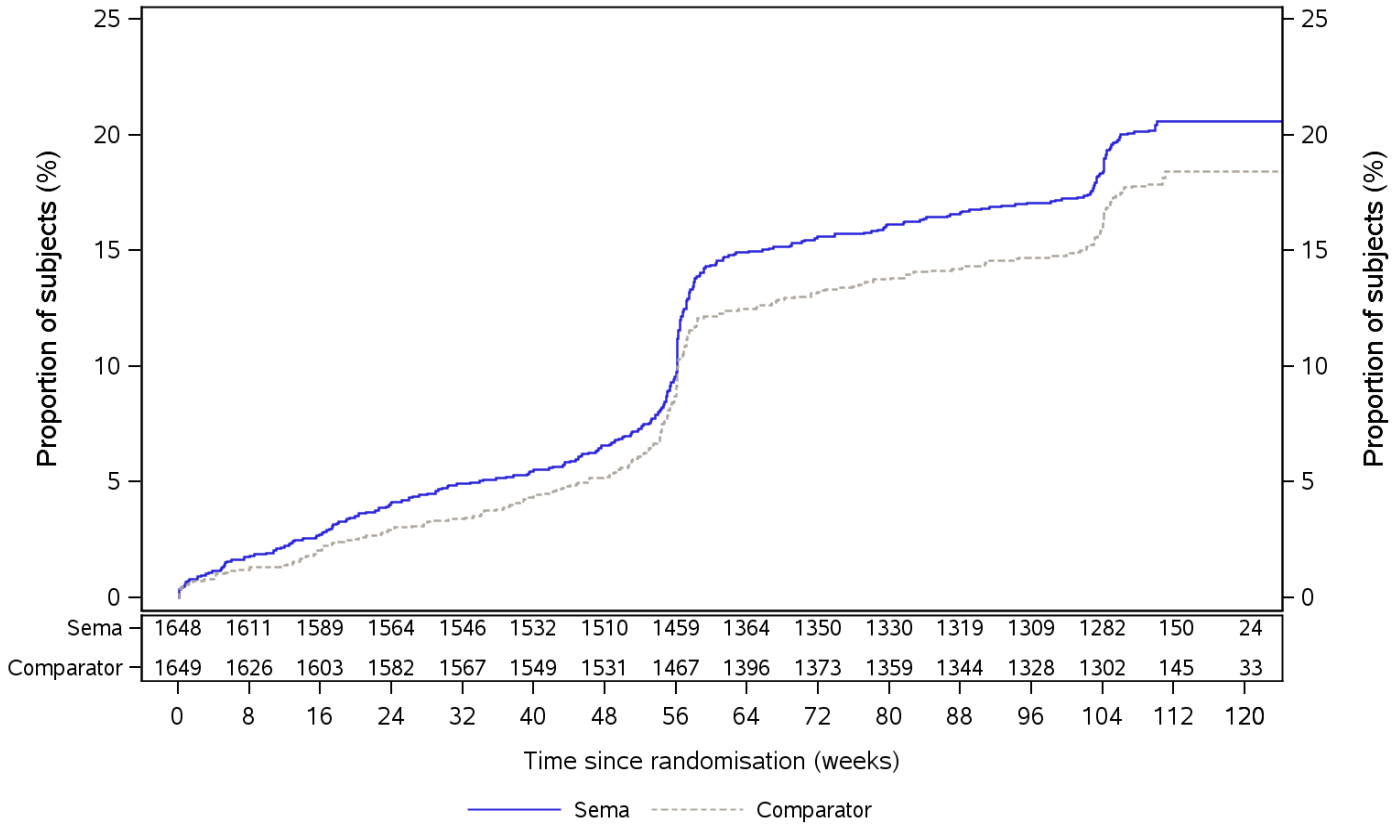
4 Adverse events - system organ class "Endocrine disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:43:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_endodiso_ae_all_s6.png

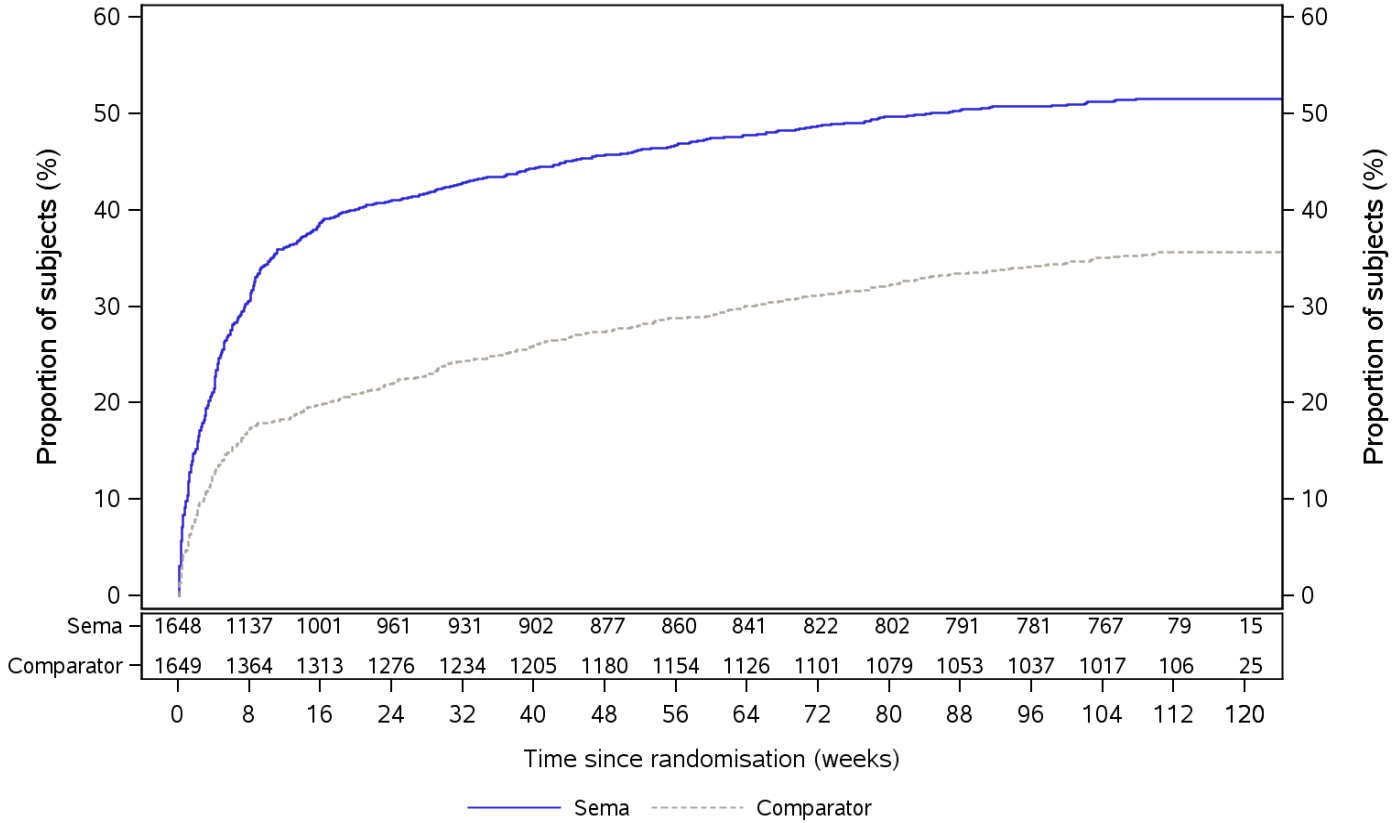
5 Adverse events - system organ class "Eye disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:43:43 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ed_ae_all_s6.png

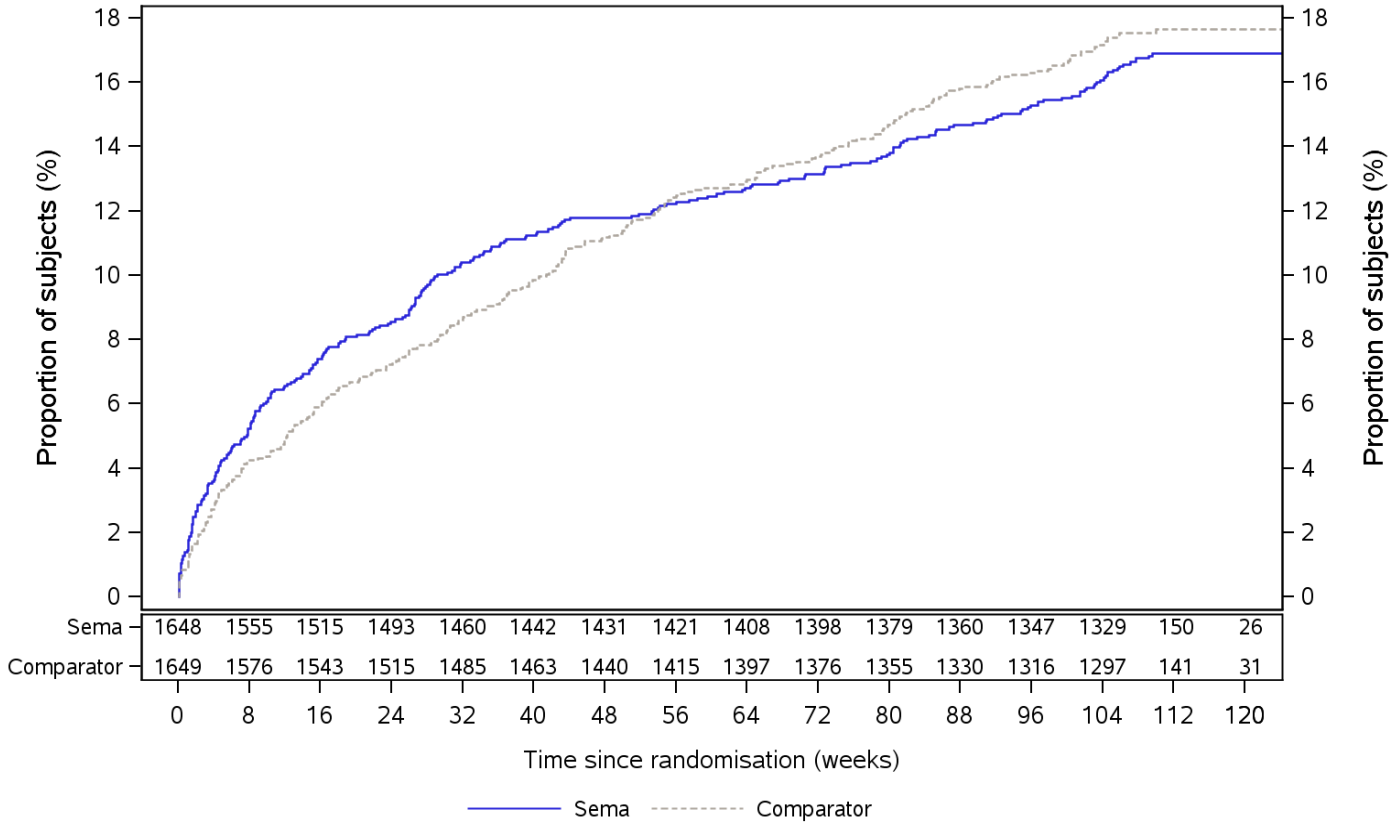
6 Adverse events - system organ class "Gastrointestinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:43:57 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_gd_ae_all_s6.png

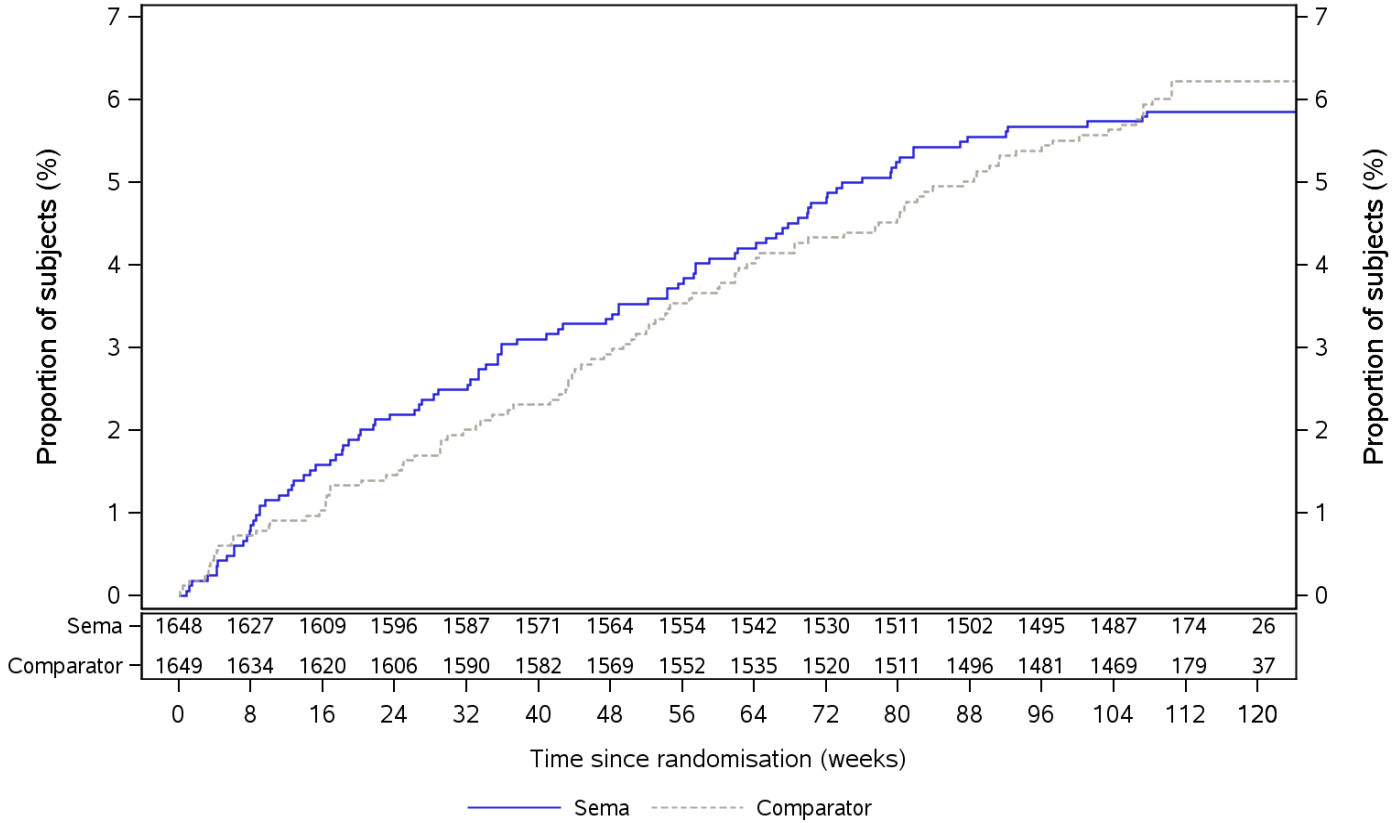
7 Adverse events - system organ class "General disorders and administration site conditions" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:44:14 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_gdasc_ae_all_s6.png

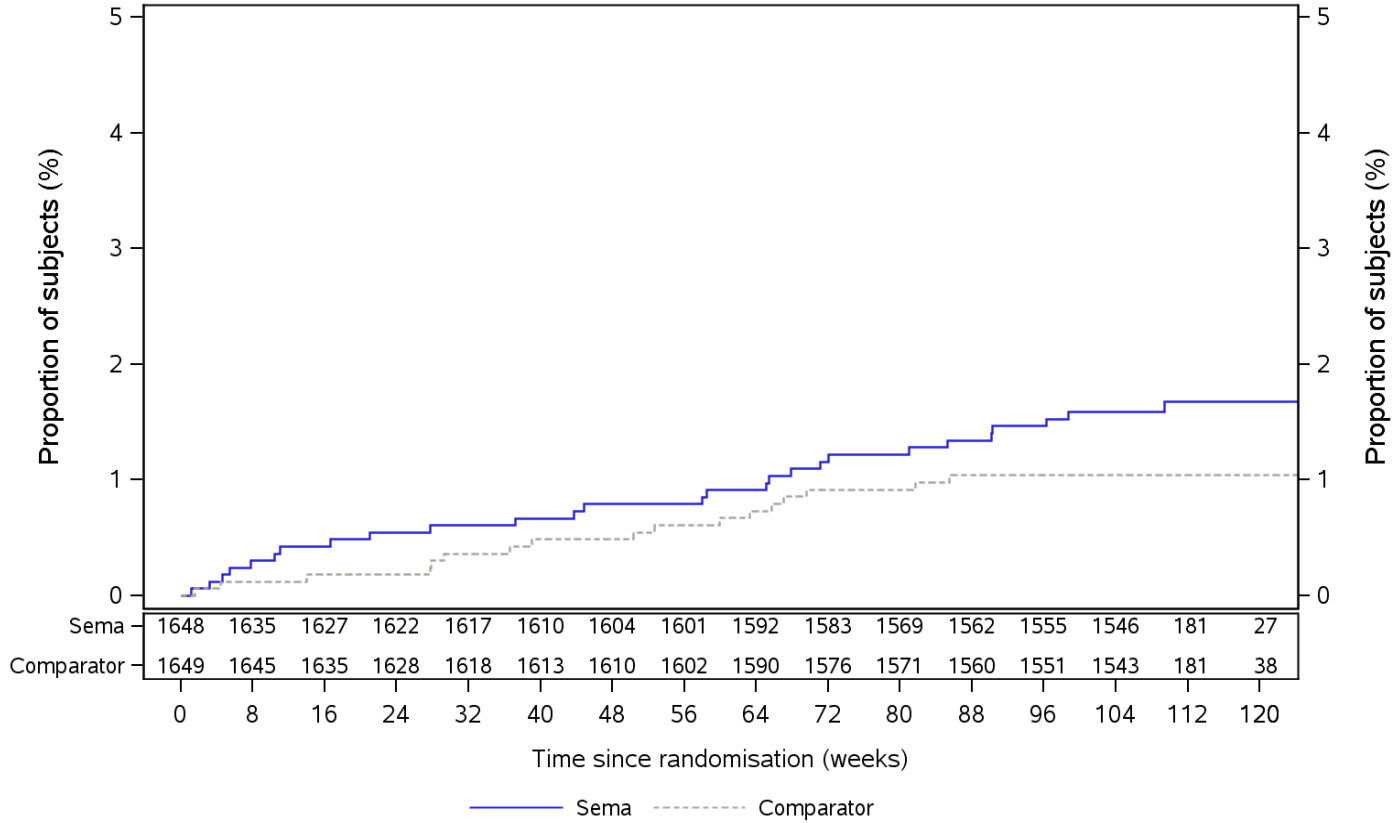
8 Adverse events - system organ class "Hepatobiliary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:44:32 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_hd_ae_all_s6.png

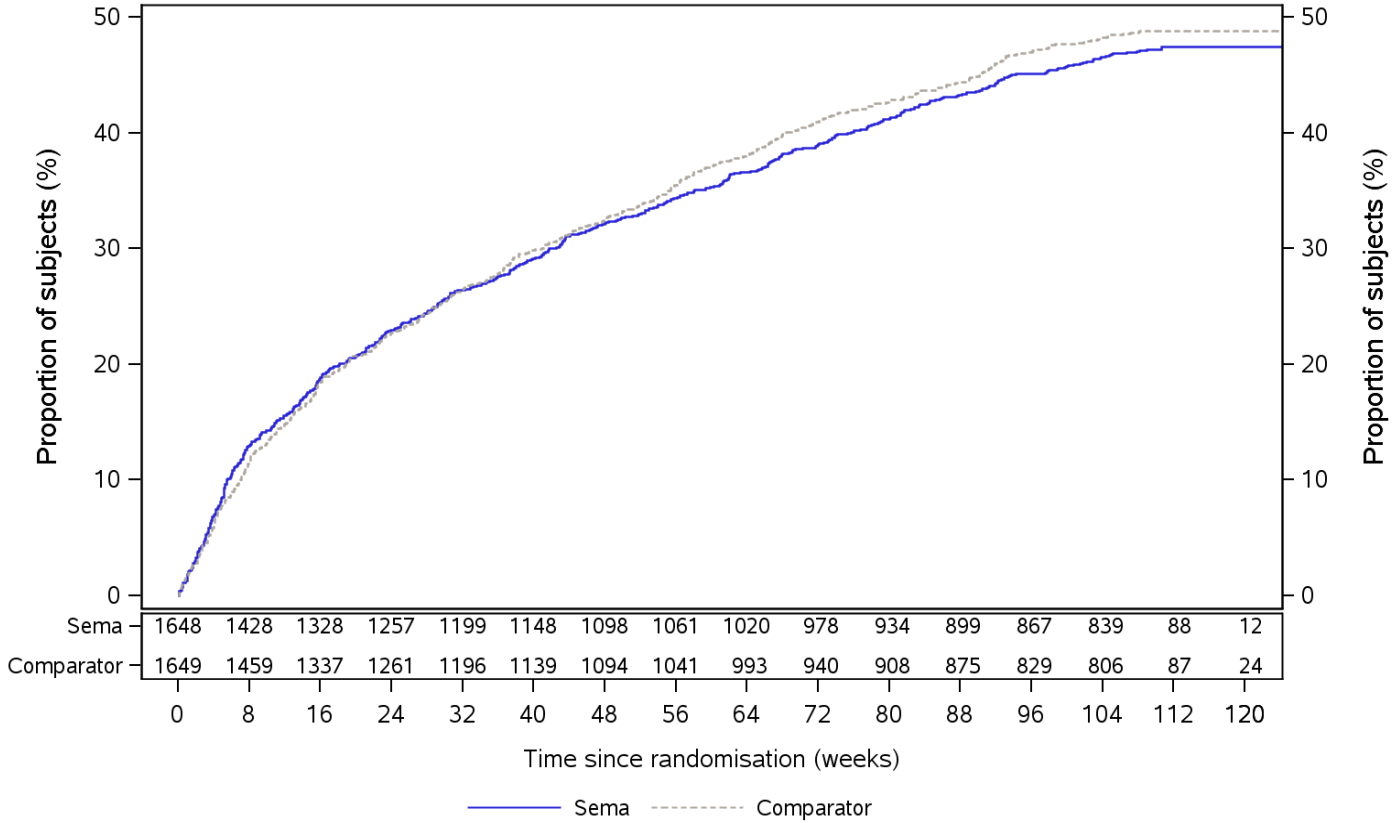
9 Adverse events - system organ class "Immune system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:44:51 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_immsysdis_ae_all_s6.png

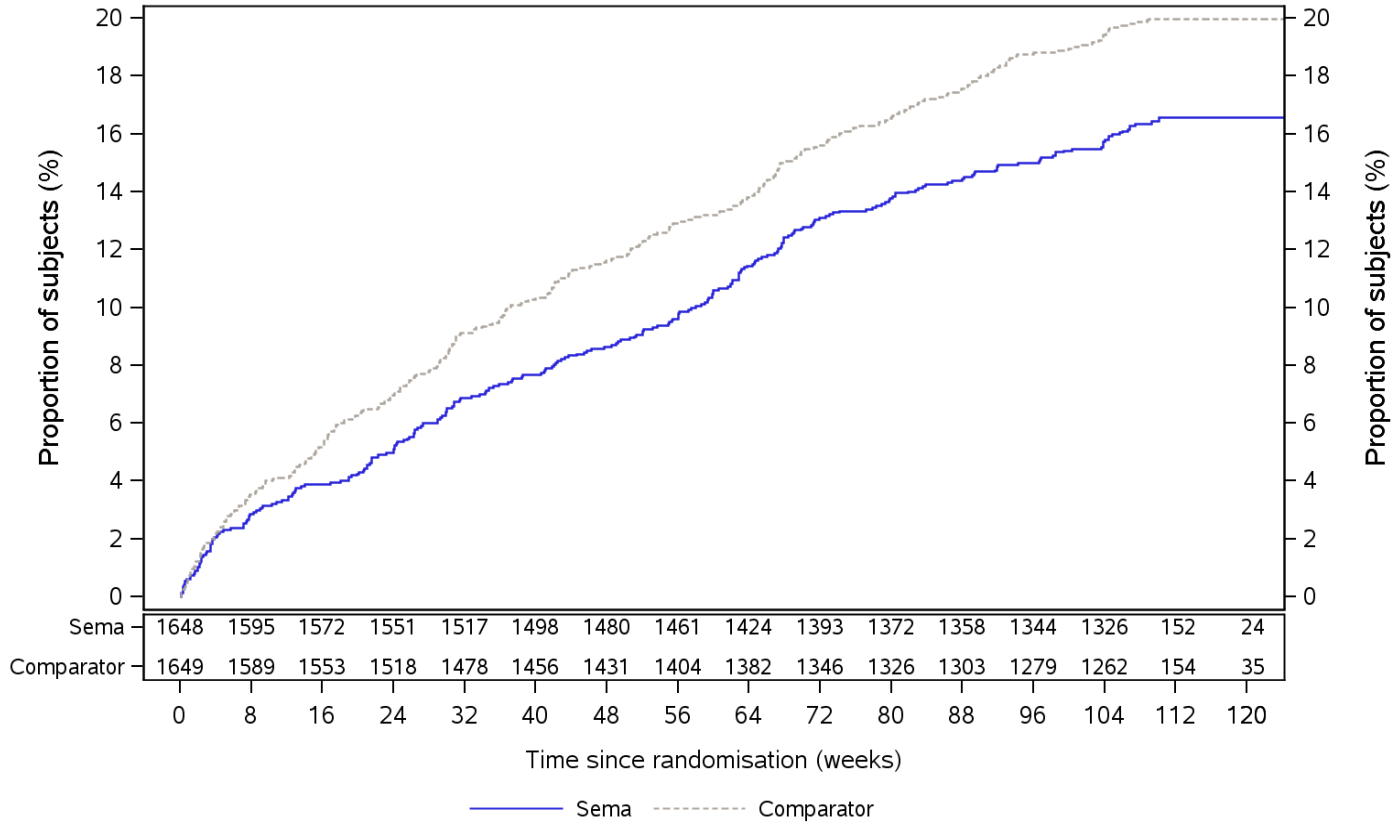
10 Adverse events - system organ class "Infections and infestations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:45:05 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ii_ae_all_s6.png

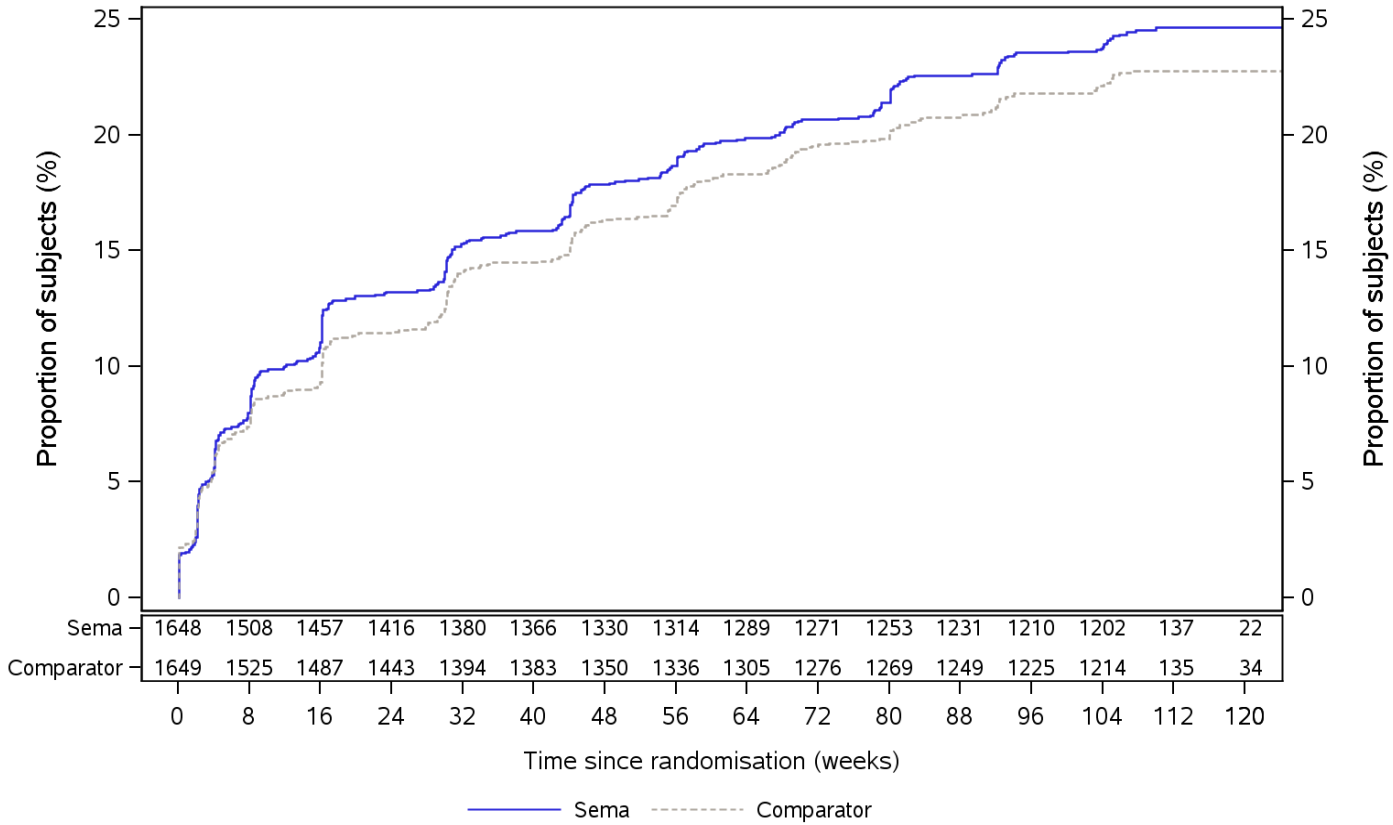
11 Adverse events - system organ class "Injury, poisoning and procedural complications" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:45:22 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ippc_ae_all_s6.png

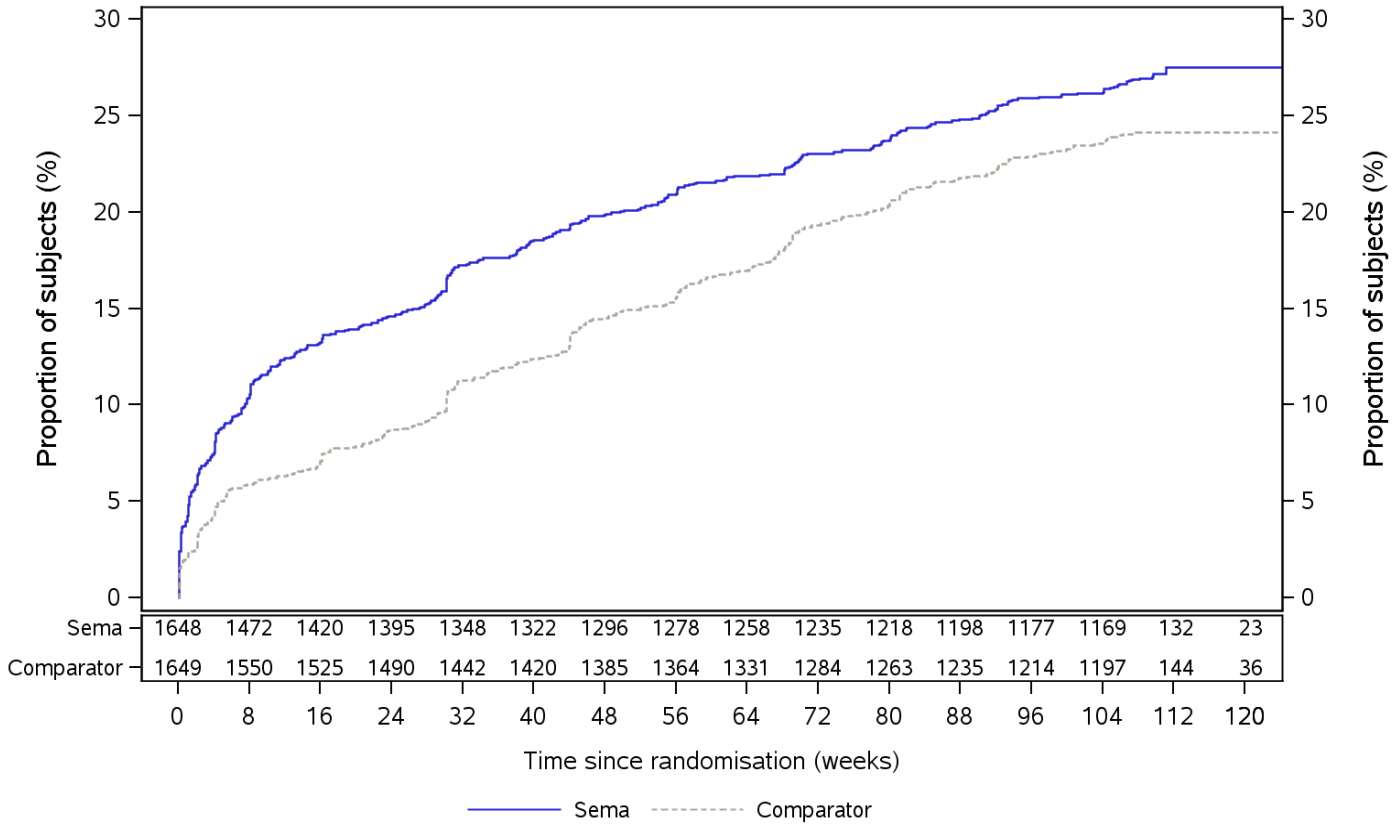
12 Adverse events - system organ class "Investigations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:45:39 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_investig_ae_all_s6.png

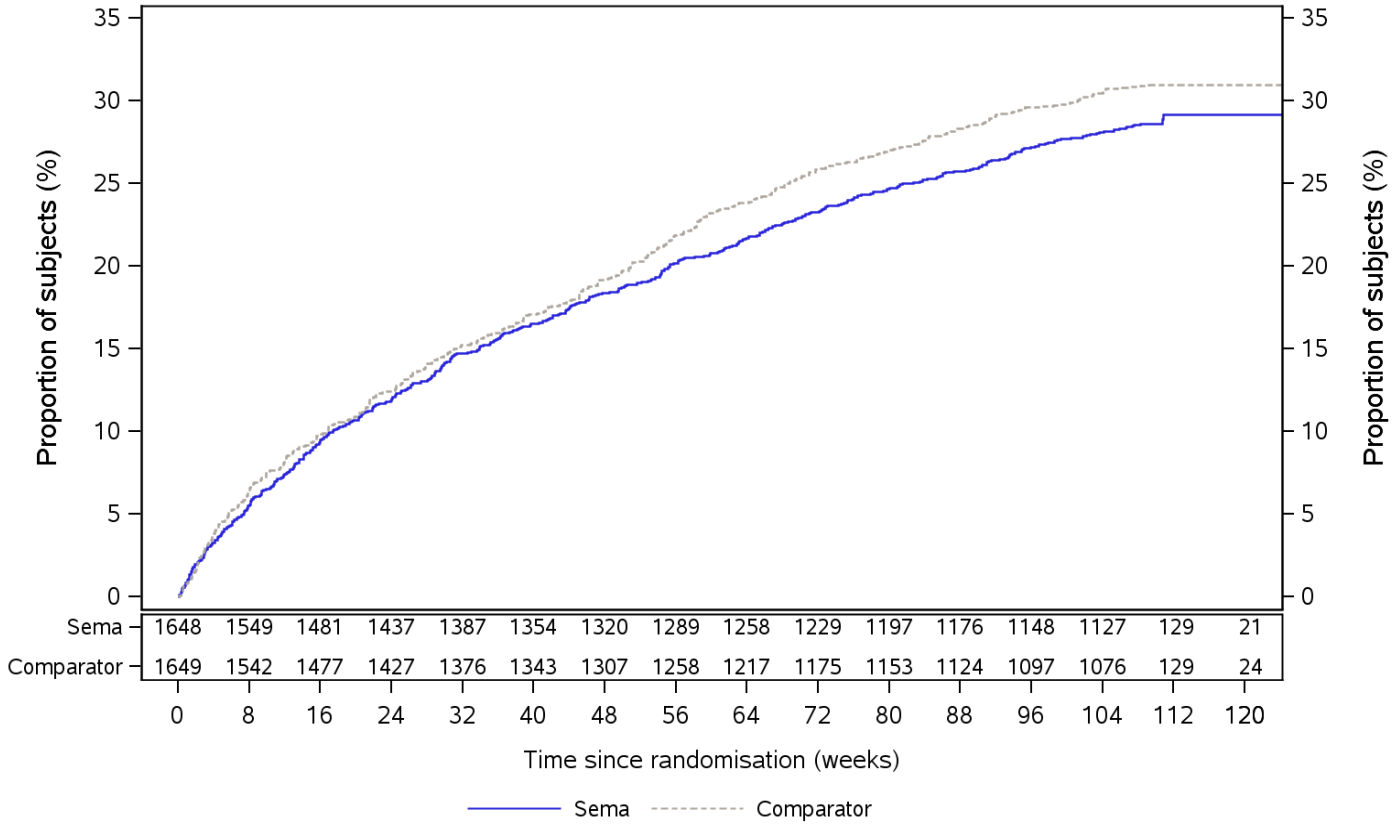
13 Adverse events - system organ class "Metabolism and nutrition disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:45:56 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_mnd_ae_all_s6.png

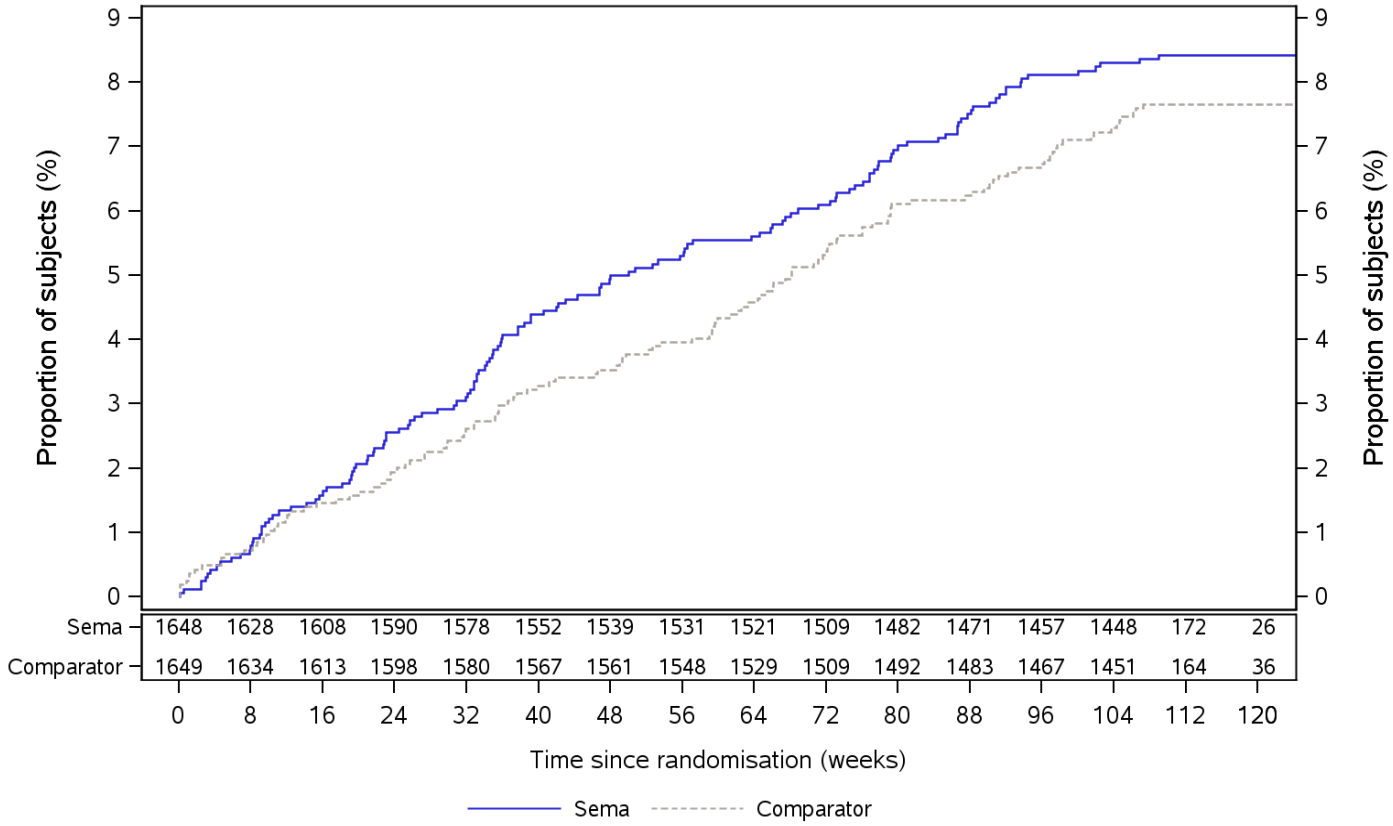
14 Adverse events - system organ class "Musculoskeletal and connective tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:46:12 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_mctd_ae_all_s6.png

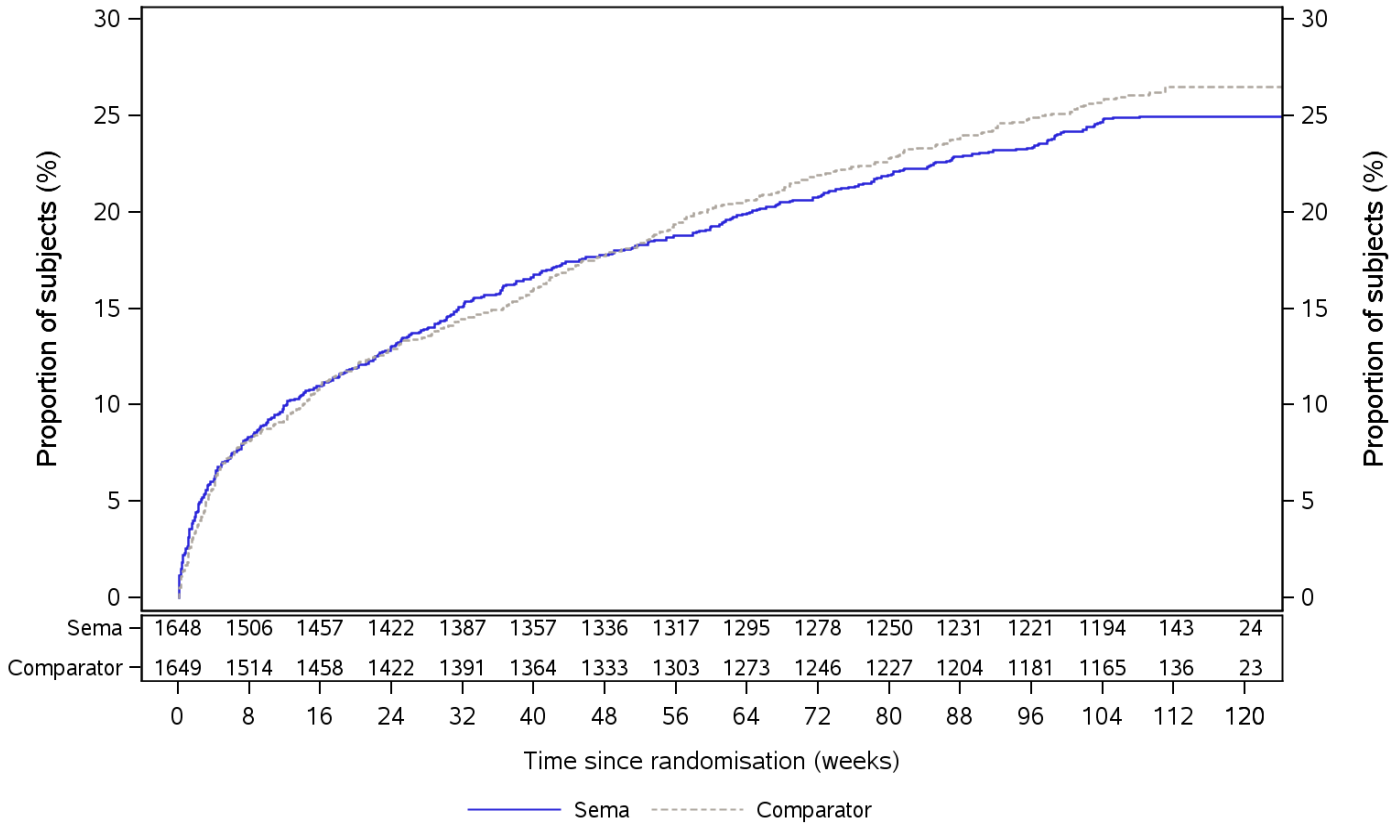
15 Adverse events - system organ class "Neoplasms benign, malignant and unspecified (incl cysts and polyps)" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:46:30 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_nbmu_ae_all_s6.png

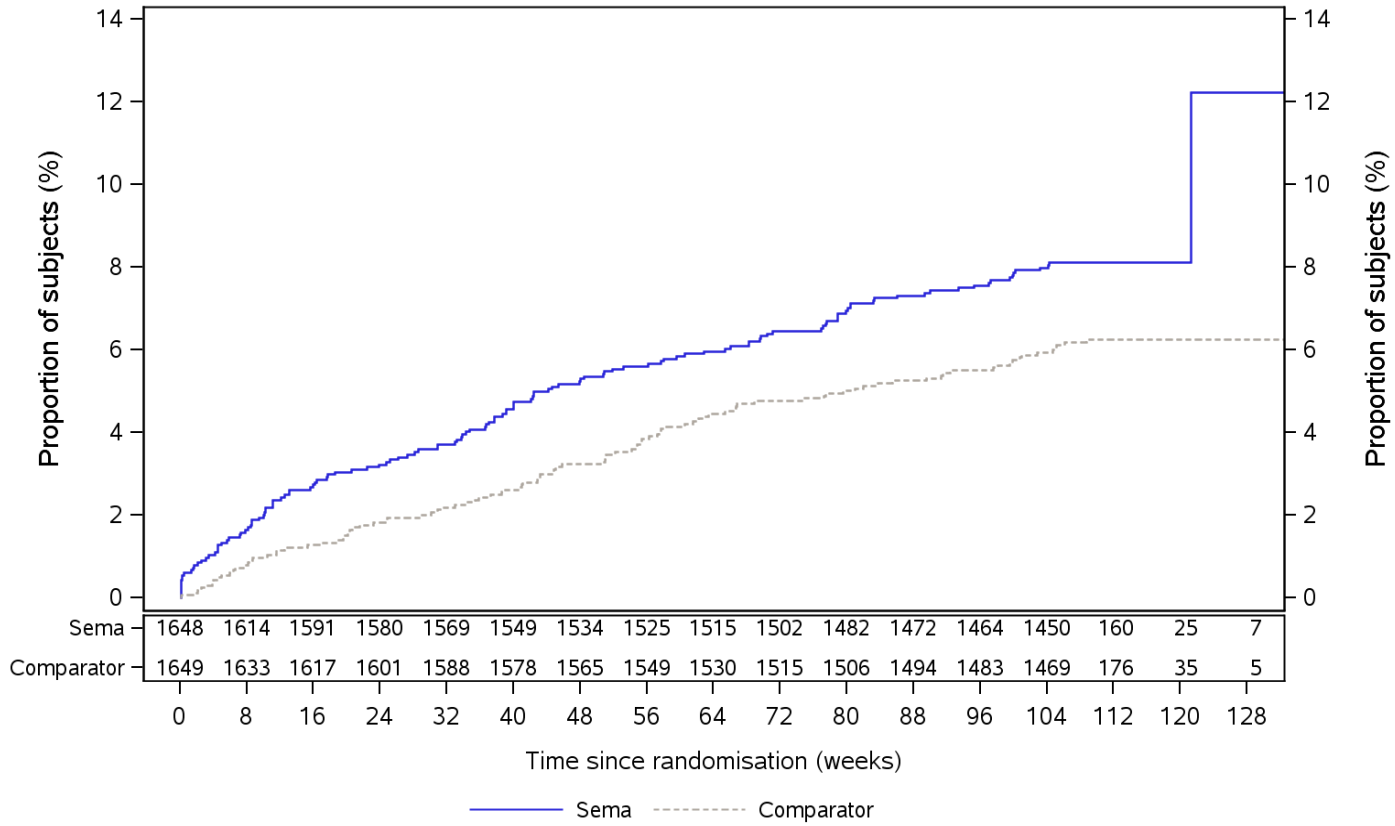
16 Adverse events - system organ class "Nervous system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:46:47 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_nsd_ae_all_s6.png

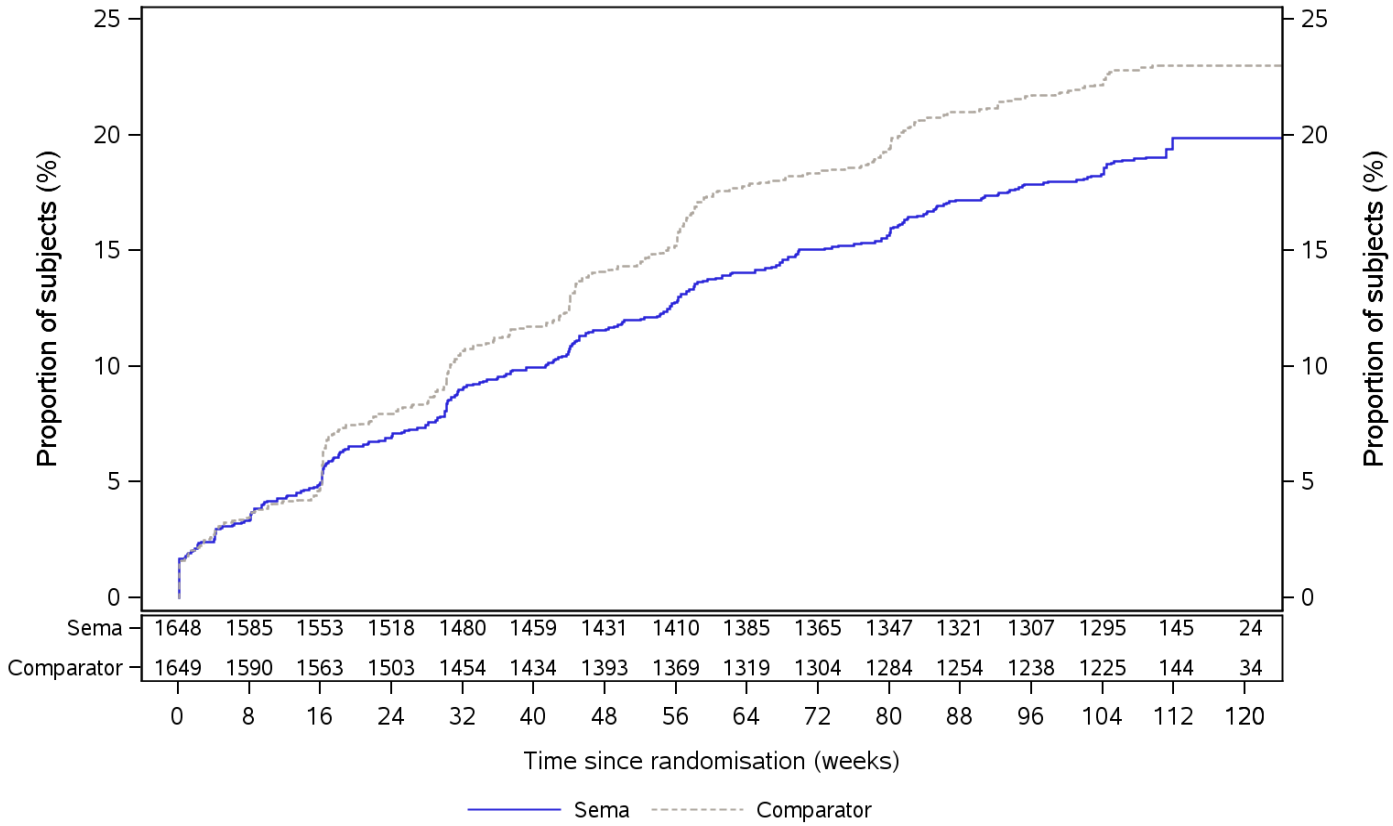
17 Adverse events - system organ class "Psychiatric disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:47:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_psycdiso_ae_all_s6.png

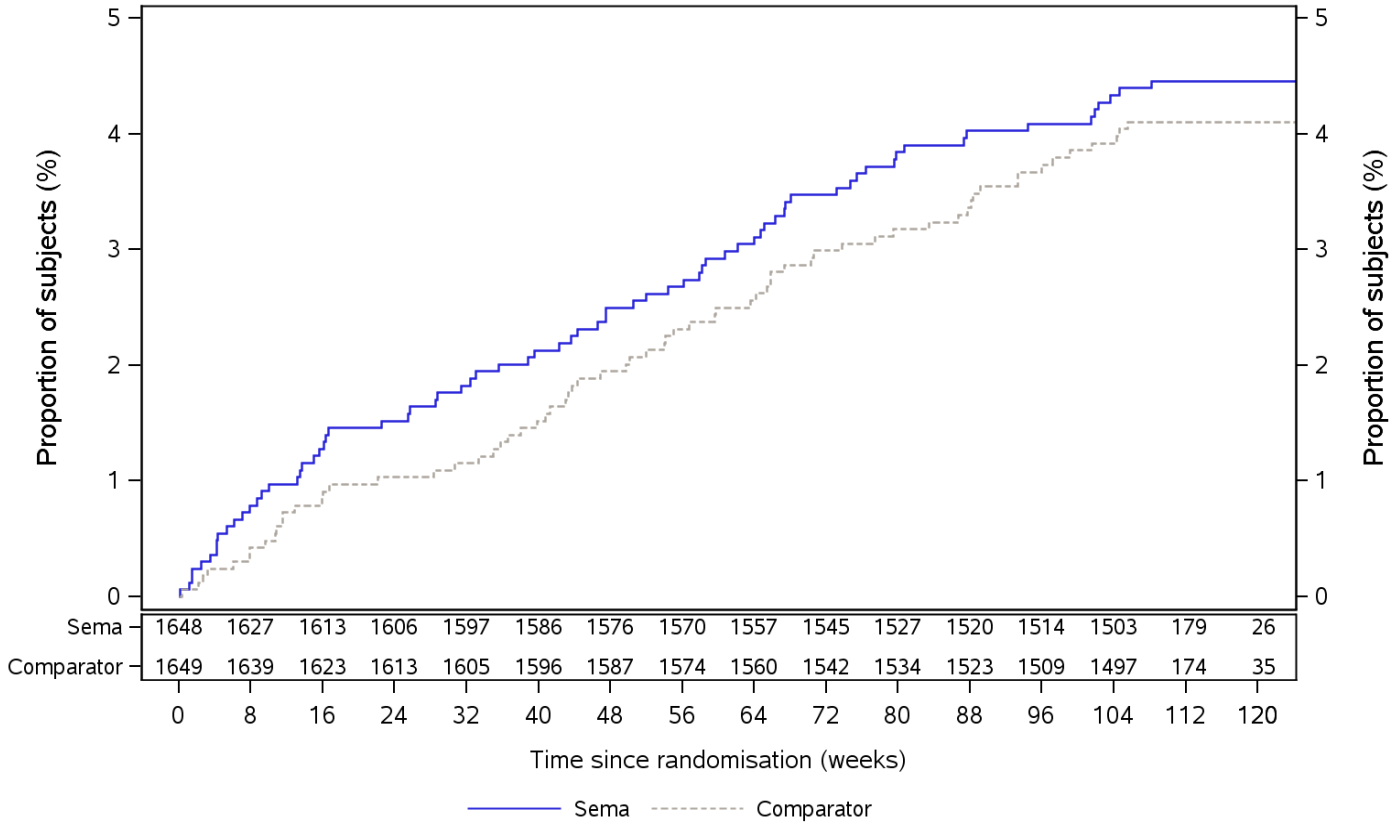
18 Adverse events - system organ class "Renal and urinary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:47:22 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_rud_ae_all_s6.png

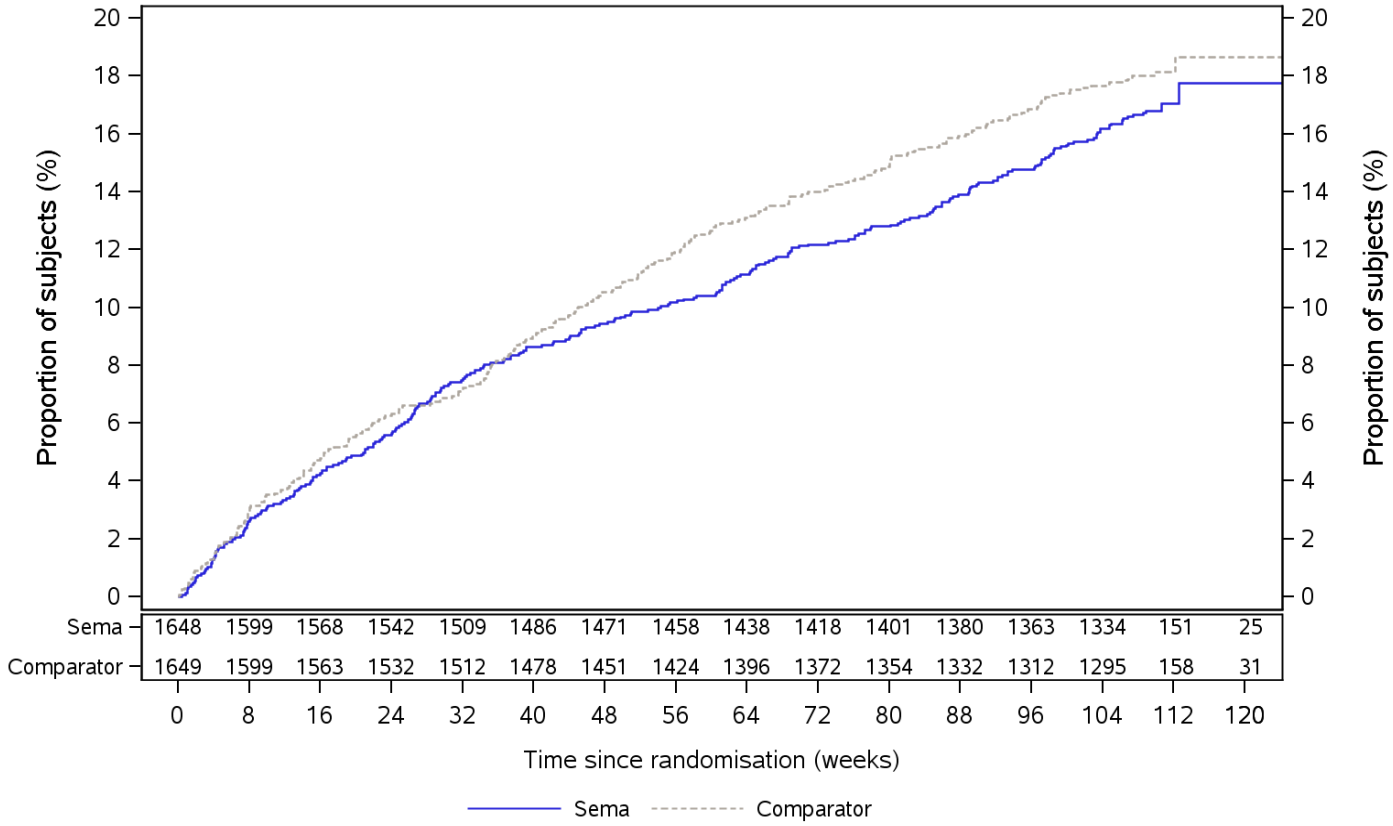
19 Adverse events - system organ class "Reproductive system and breast disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:47:41 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_repsysand_ae_all_s6.png

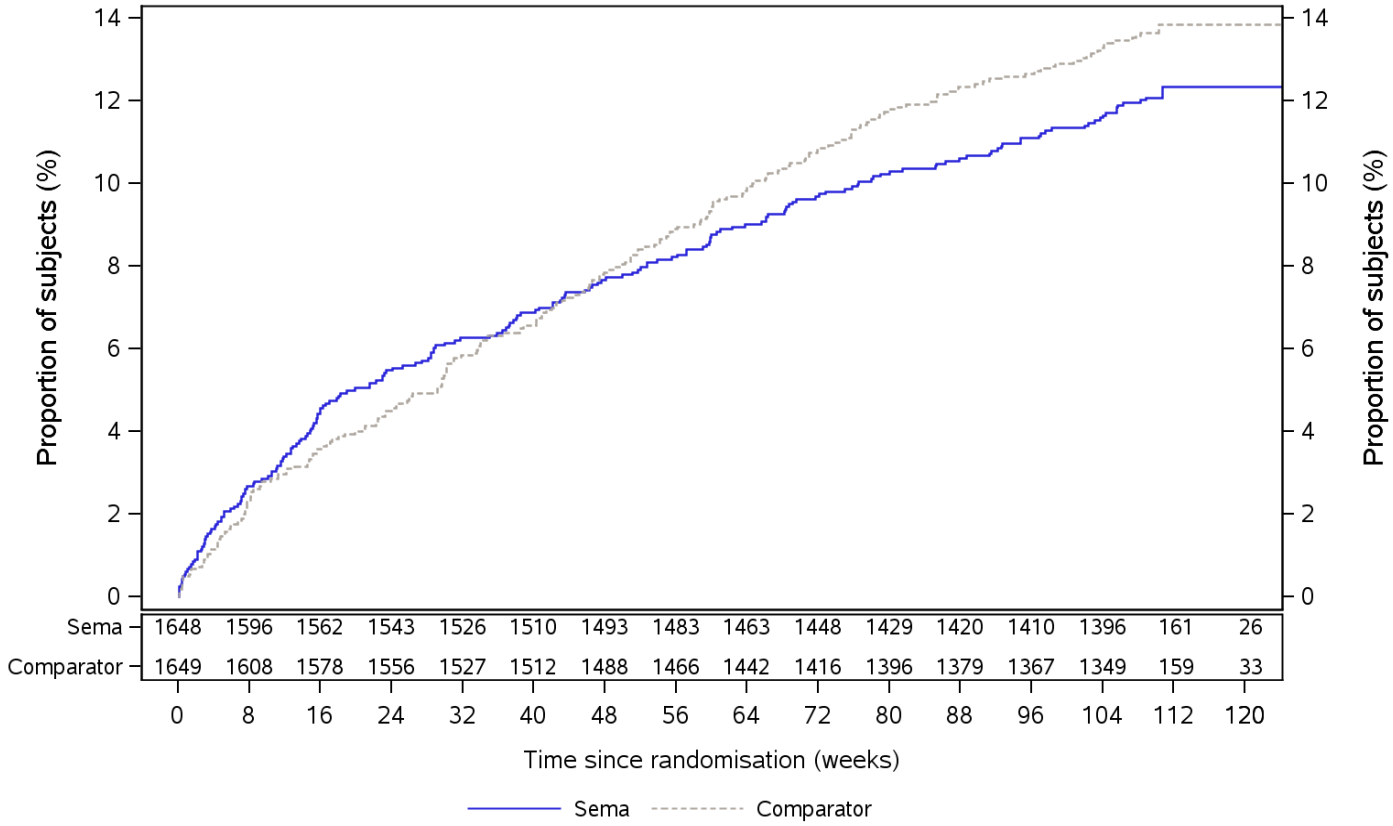
20 Adverse events - system organ class "Respiratory, thoracic and mediastinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:47:59 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_rtmd_ae_all_s6.png

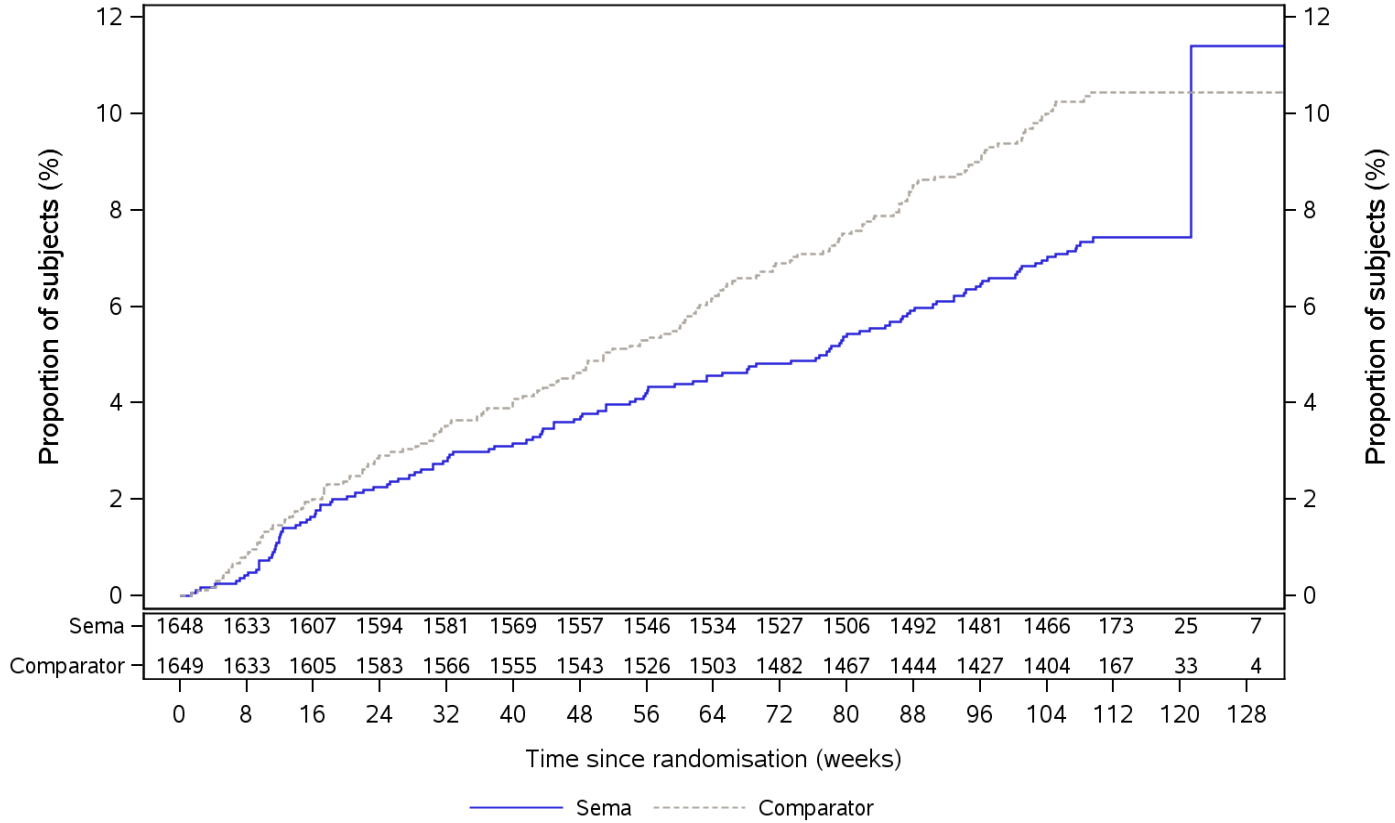
21 Adverse events - system organ class "Skin and subcutaneous tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:48:18 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_sstd_ae_all_s6.png

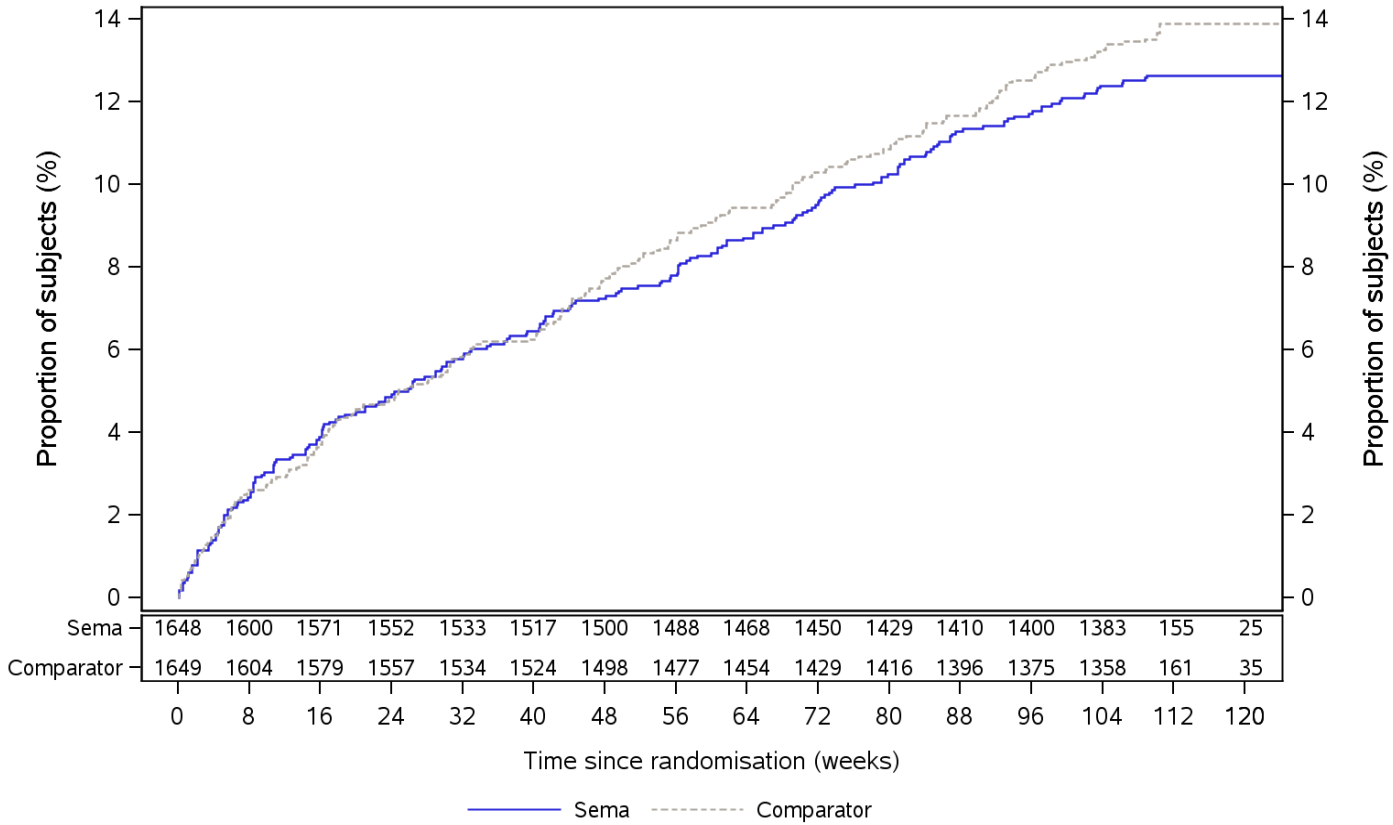
22 Adverse events - system organ class "Surgical and medical procedures" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:48:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_smp_ae_all_s6.png

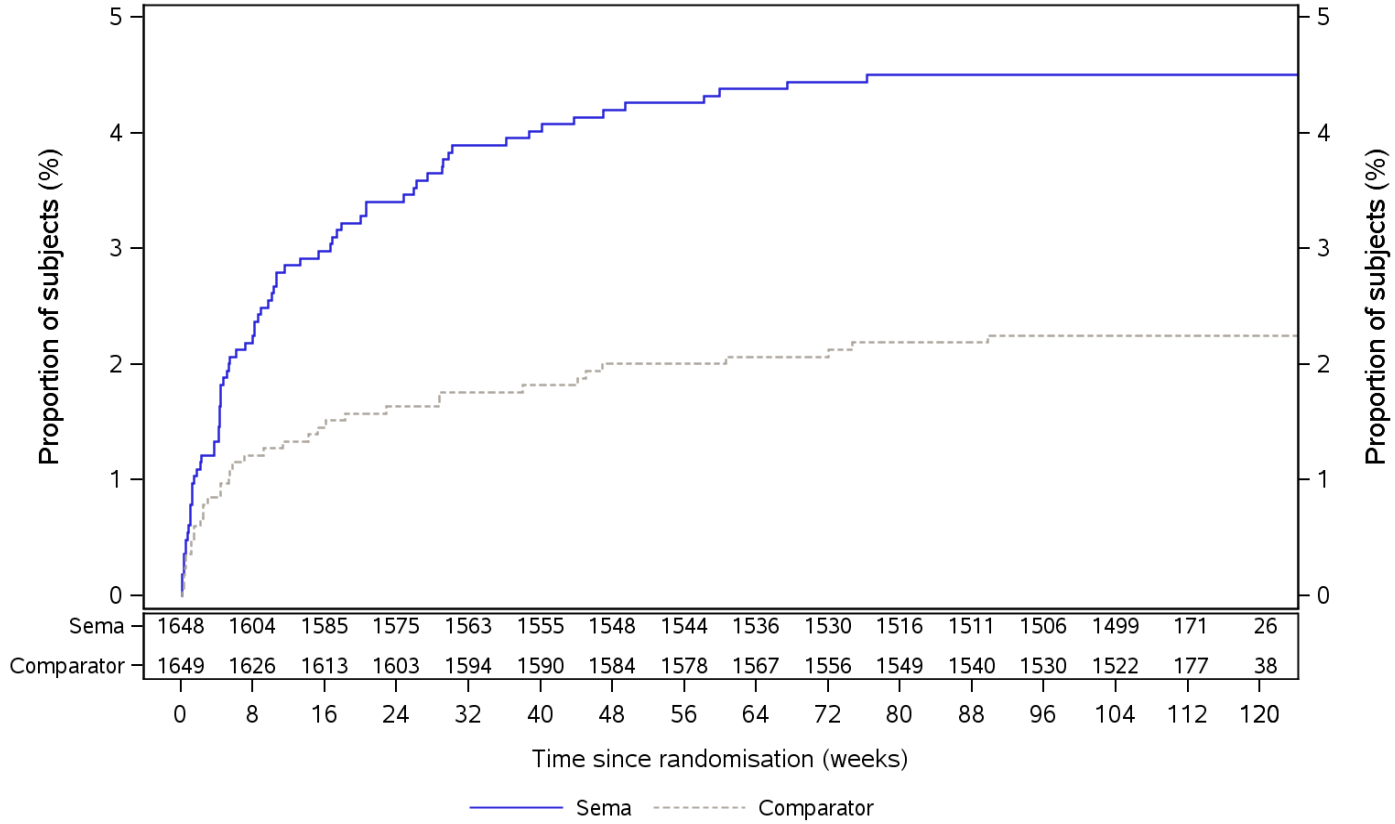
23 Adverse events - system organ class "Vascular disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:48:54 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_vd_ae_all_s6.png

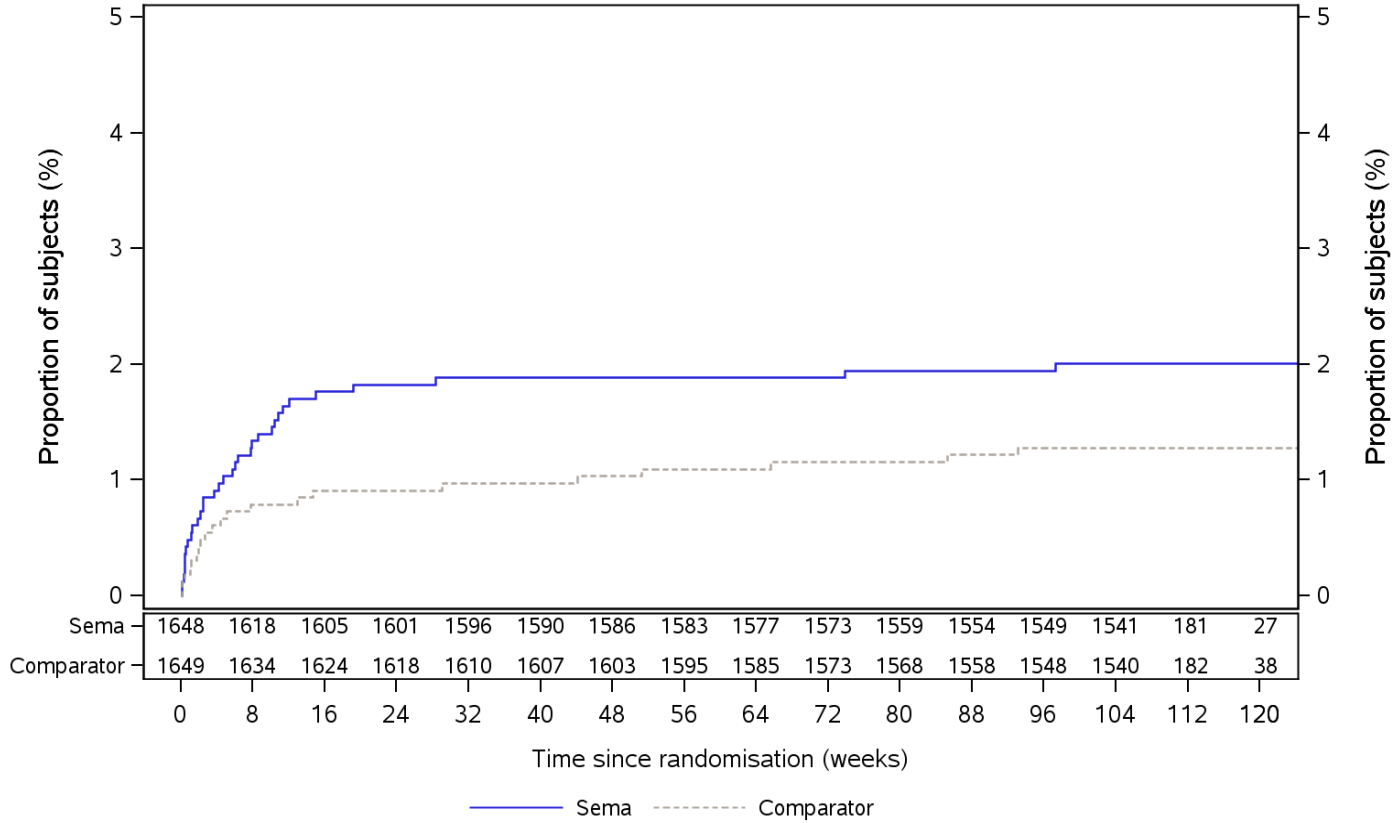
24 Adverse events - preferred term "Abdominal discomfort" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:49:15 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdodisc_ae_all_s6.png

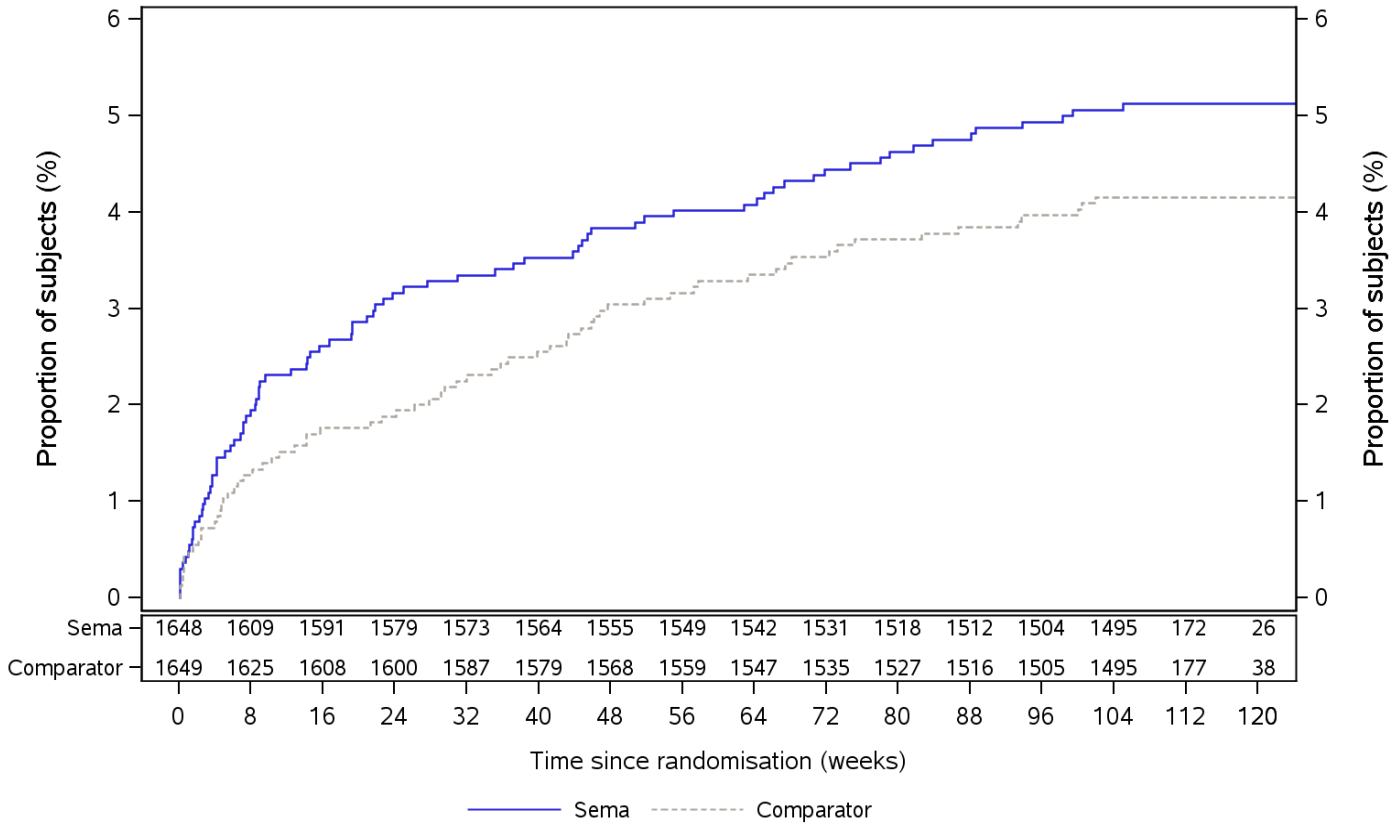
25 Adverse events - preferred term "Abdominal distension" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:49:33 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdodist_ae_all_s6.png

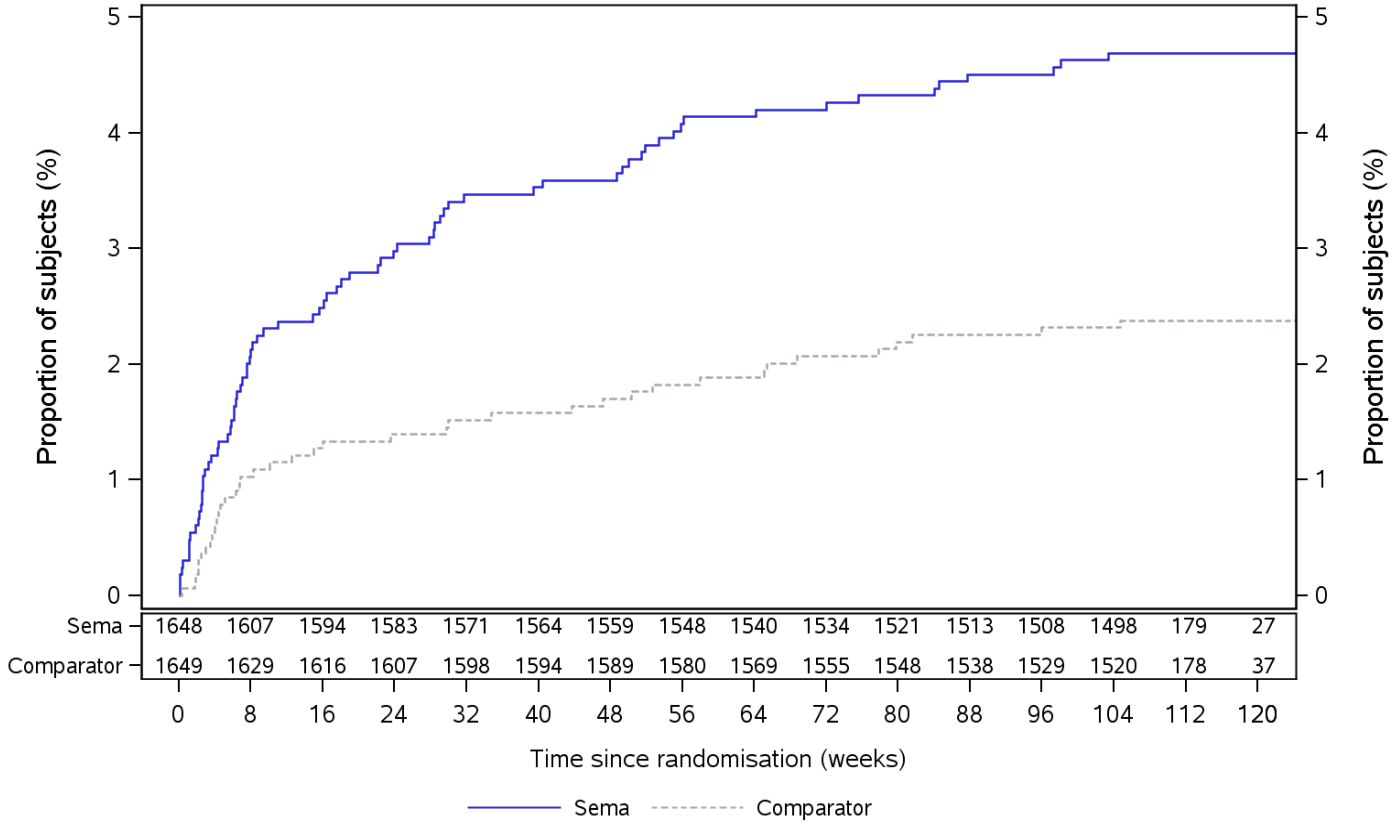
26 Adverse events - preferred term "Abdominal pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:49:52 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdopain_ae_all_s6.png

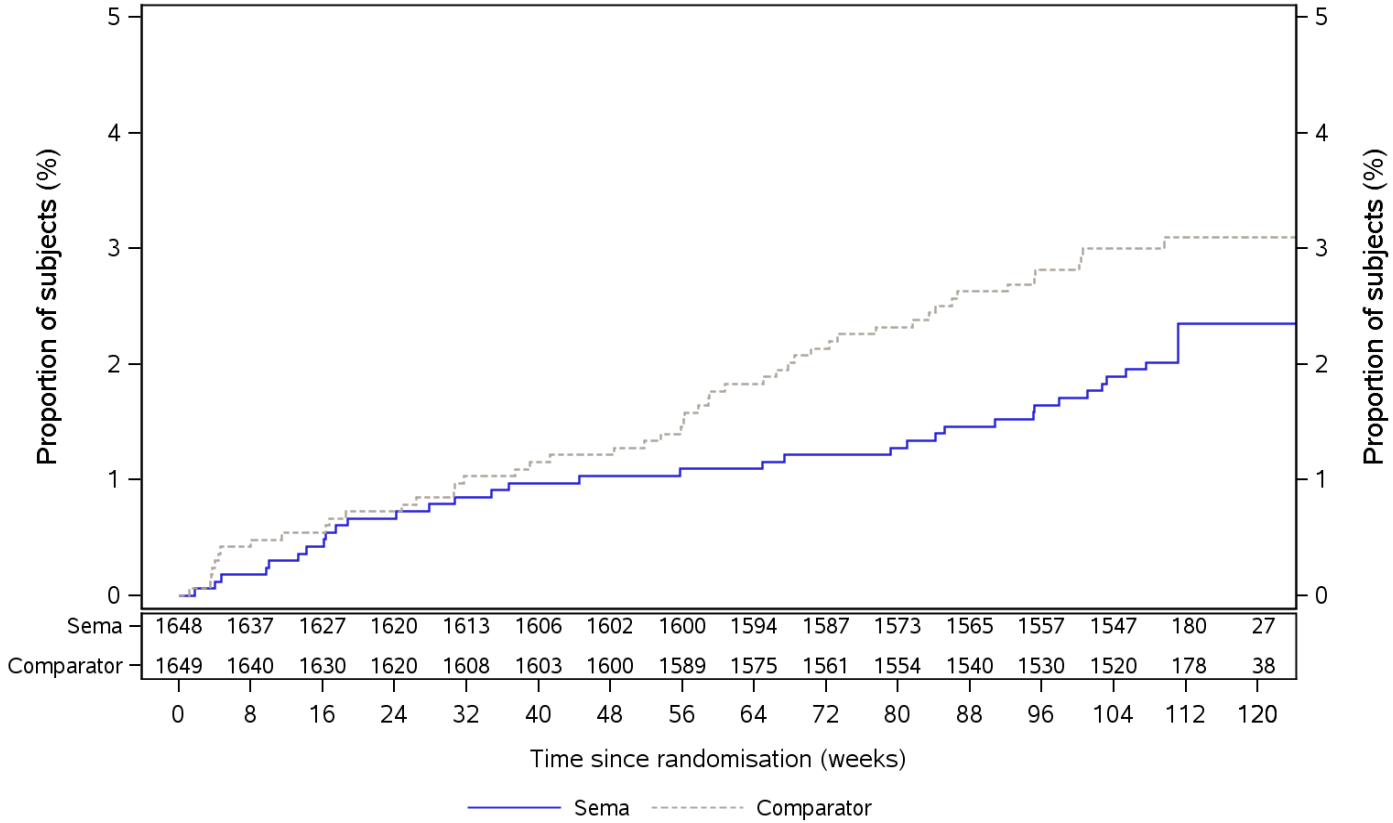
27 Adverse events - preferred term "Abdominal pain upper" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:50:11 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdpaiupp_ae_all_s6.png

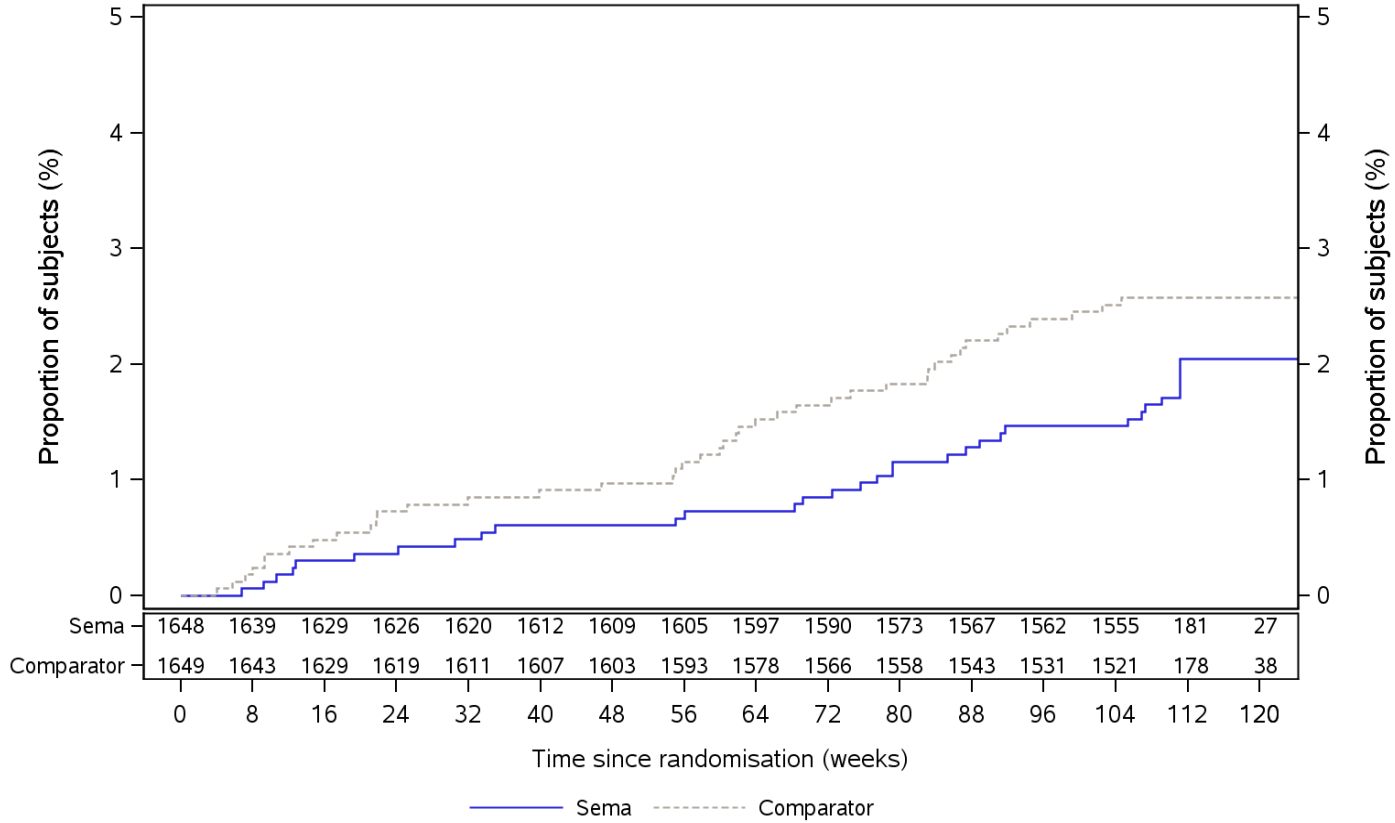
28 Adverse events - preferred term "Acute kidney injury" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:50:30 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_aki_ae_all_s6.png

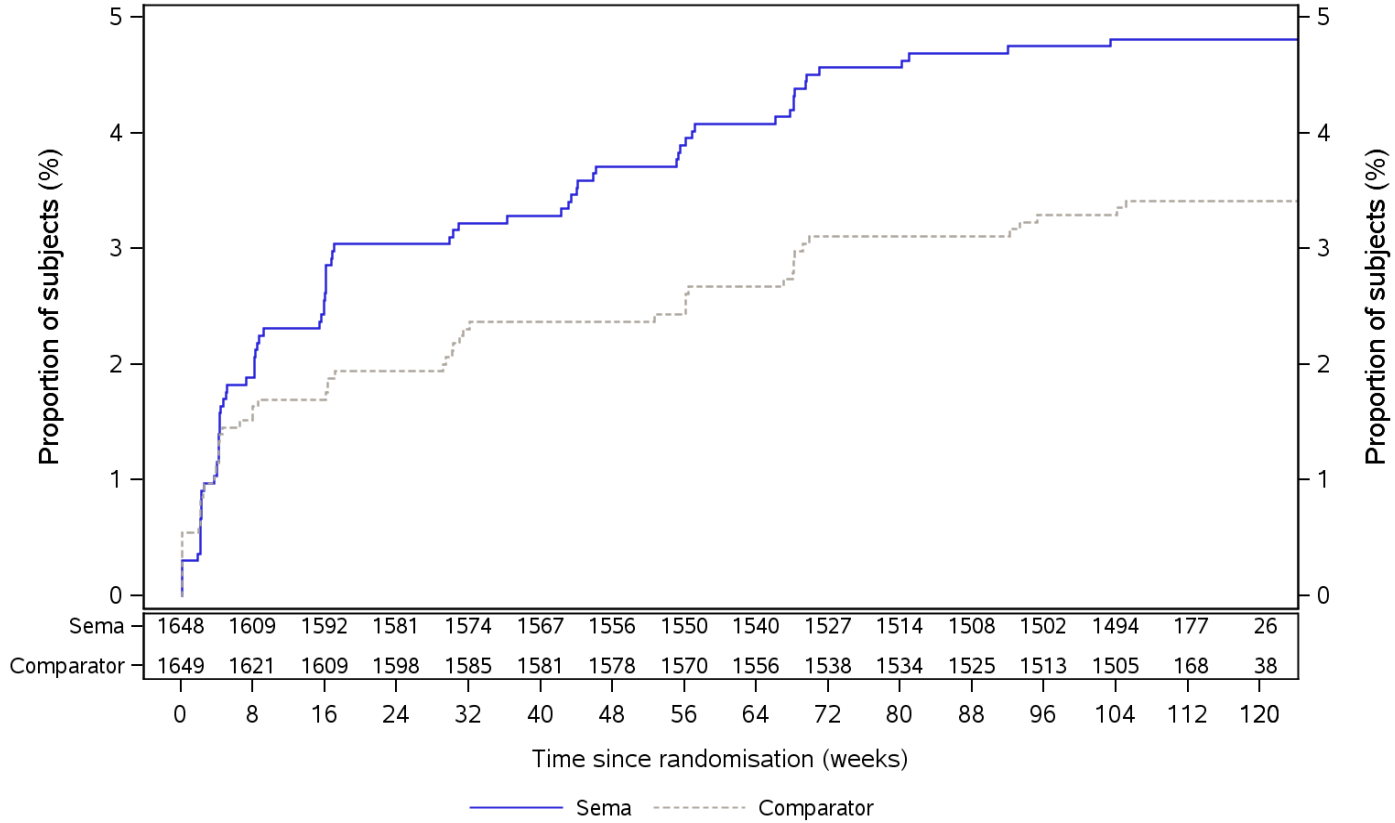
29 Adverse events - preferred term "Acute myocardial infarction" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:50:49 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_ami_ae_all_s6.png

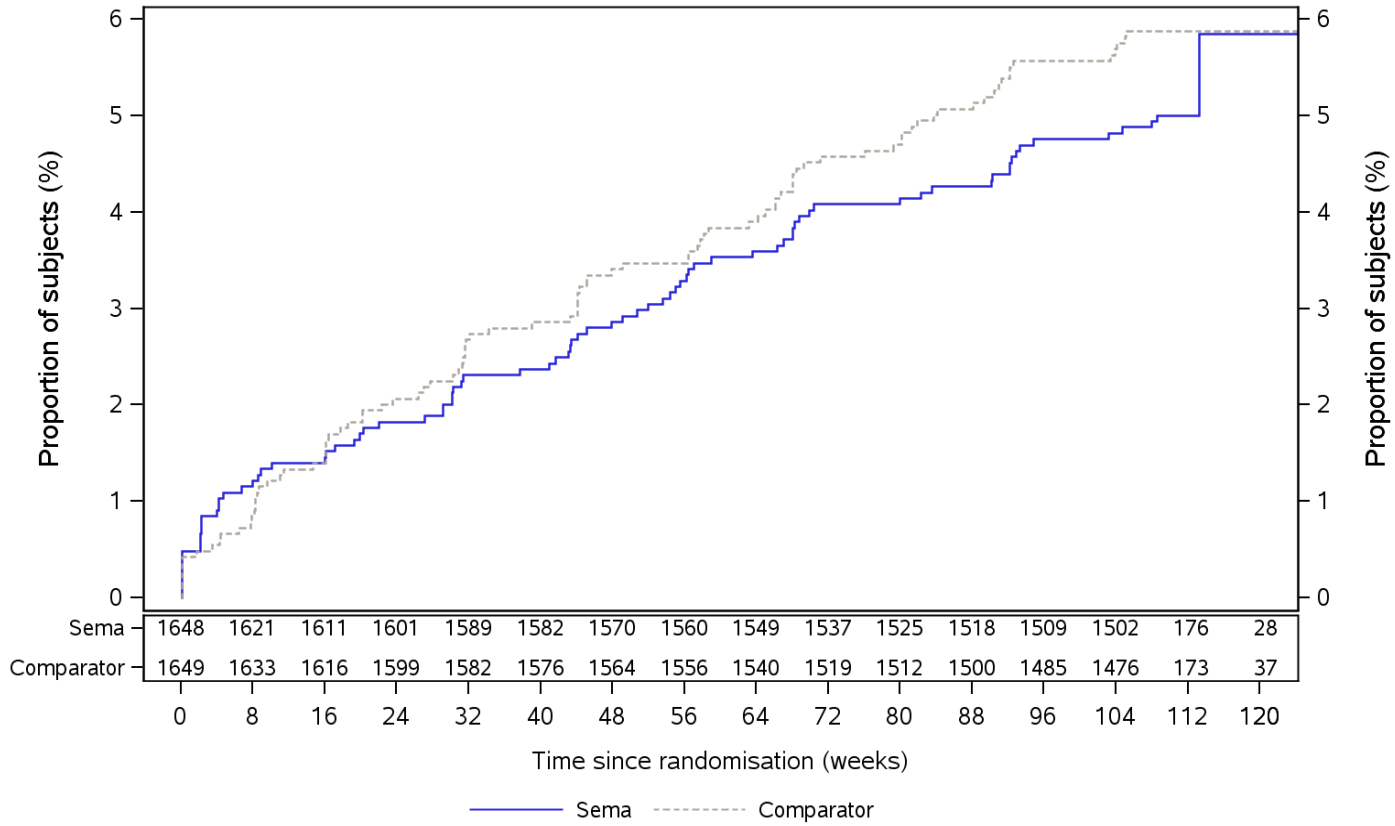
30 Adverse events - preferred term "Amylase increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:51:08 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_amylincr_ae_all_s6.png

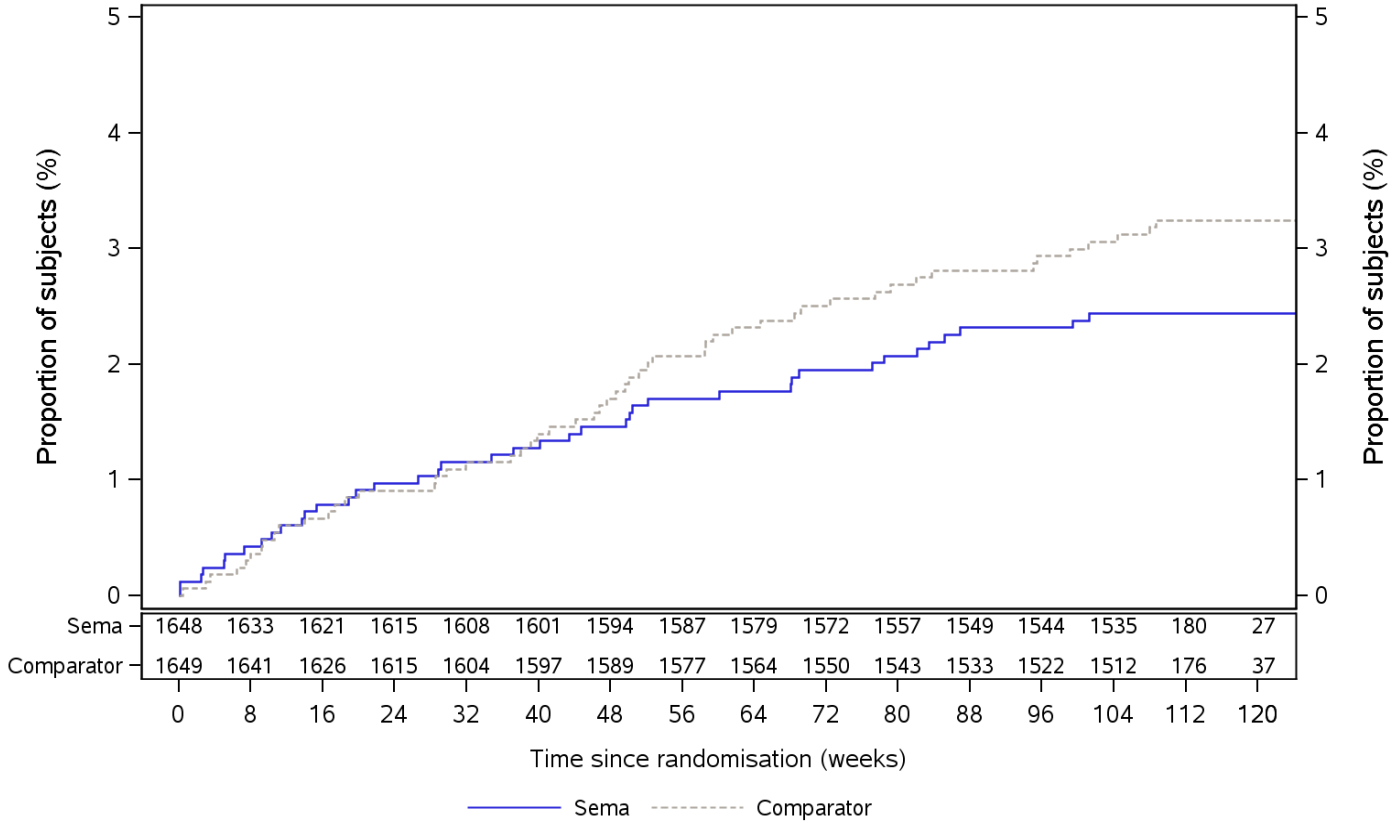
31 Adverse events - preferred term "Anaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:51:26 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_anaemia_ae_all_s6.png

32 Adverse events - preferred term "Angina pectoris" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

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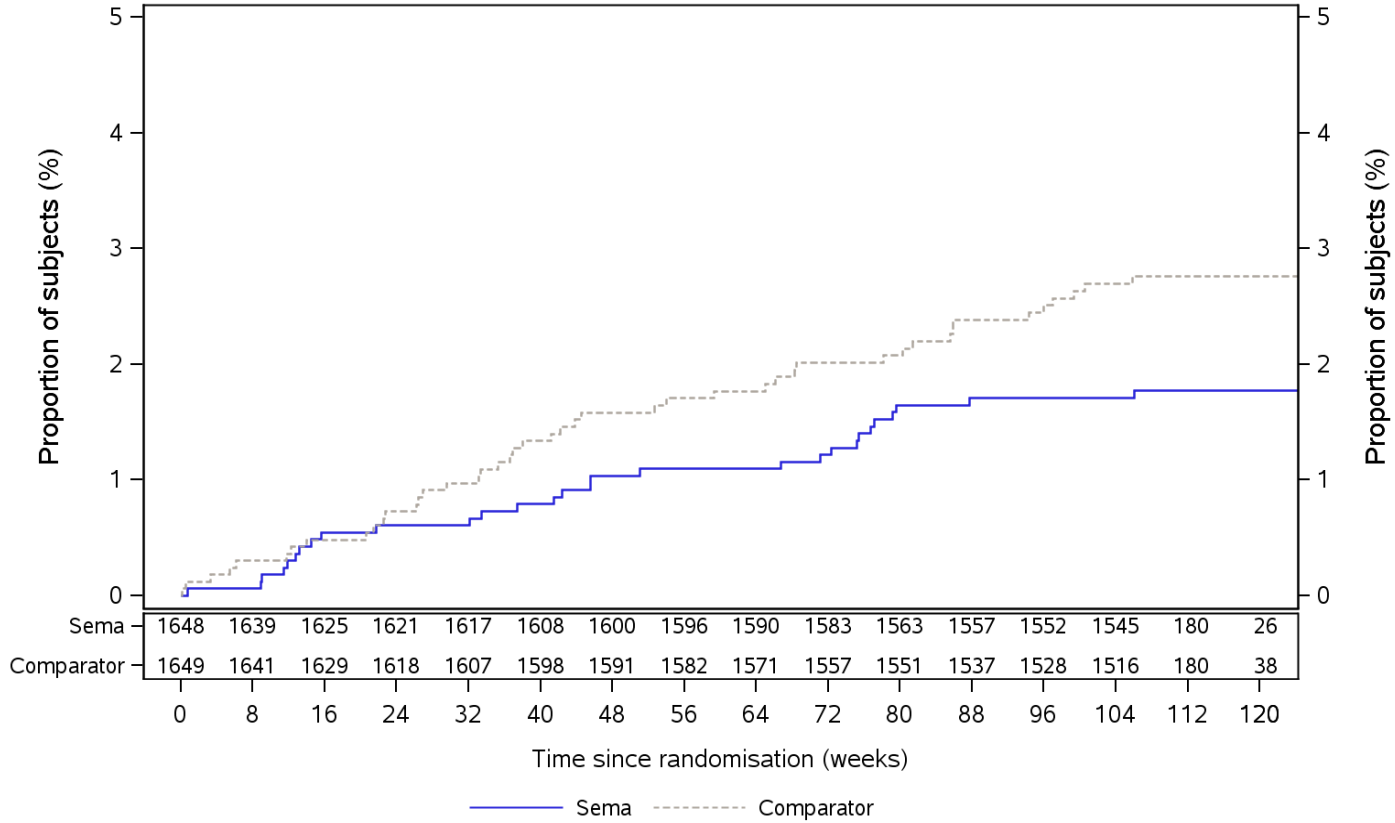
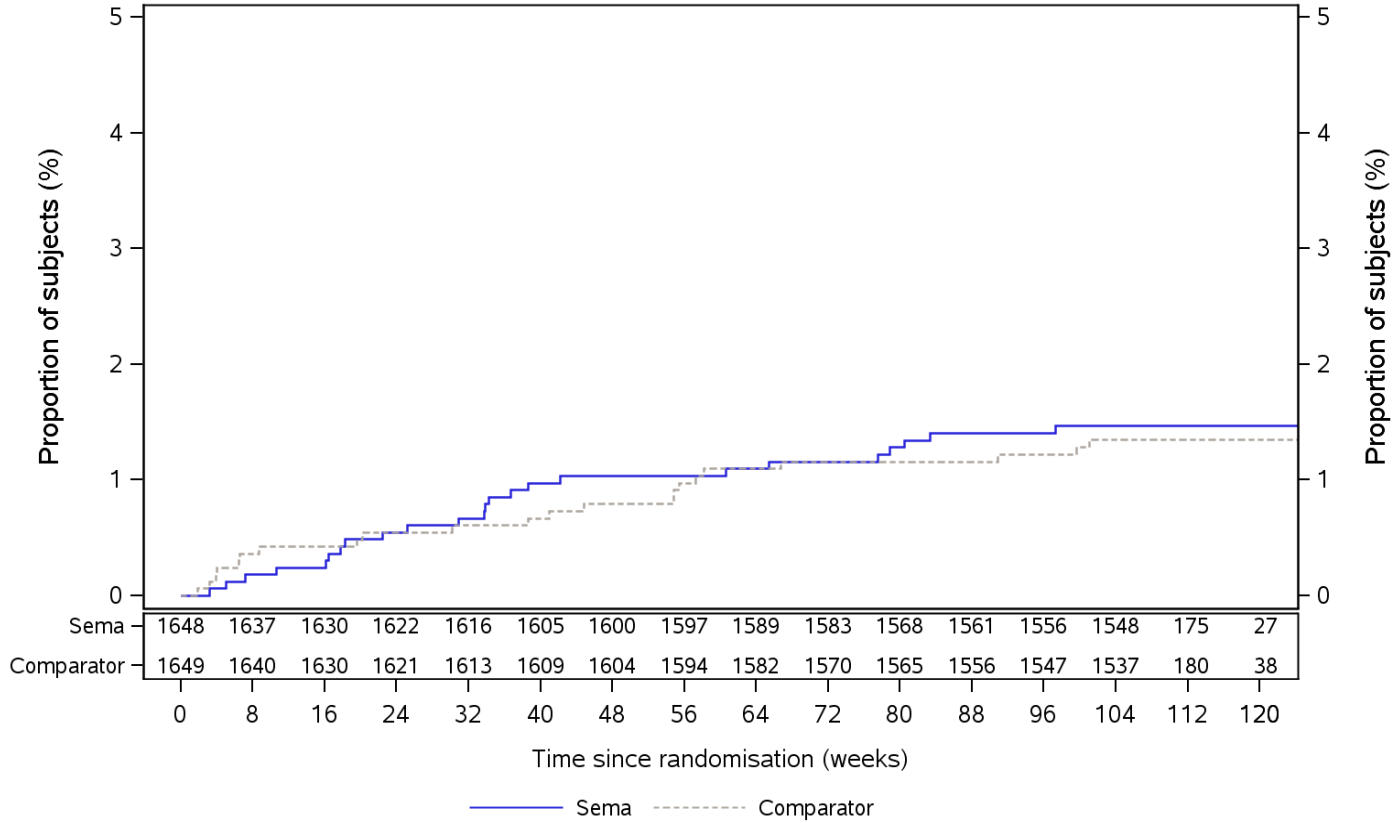
33 Adverse events - preferred term "Angina unstable" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:52:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_au_ae_all_s6.png

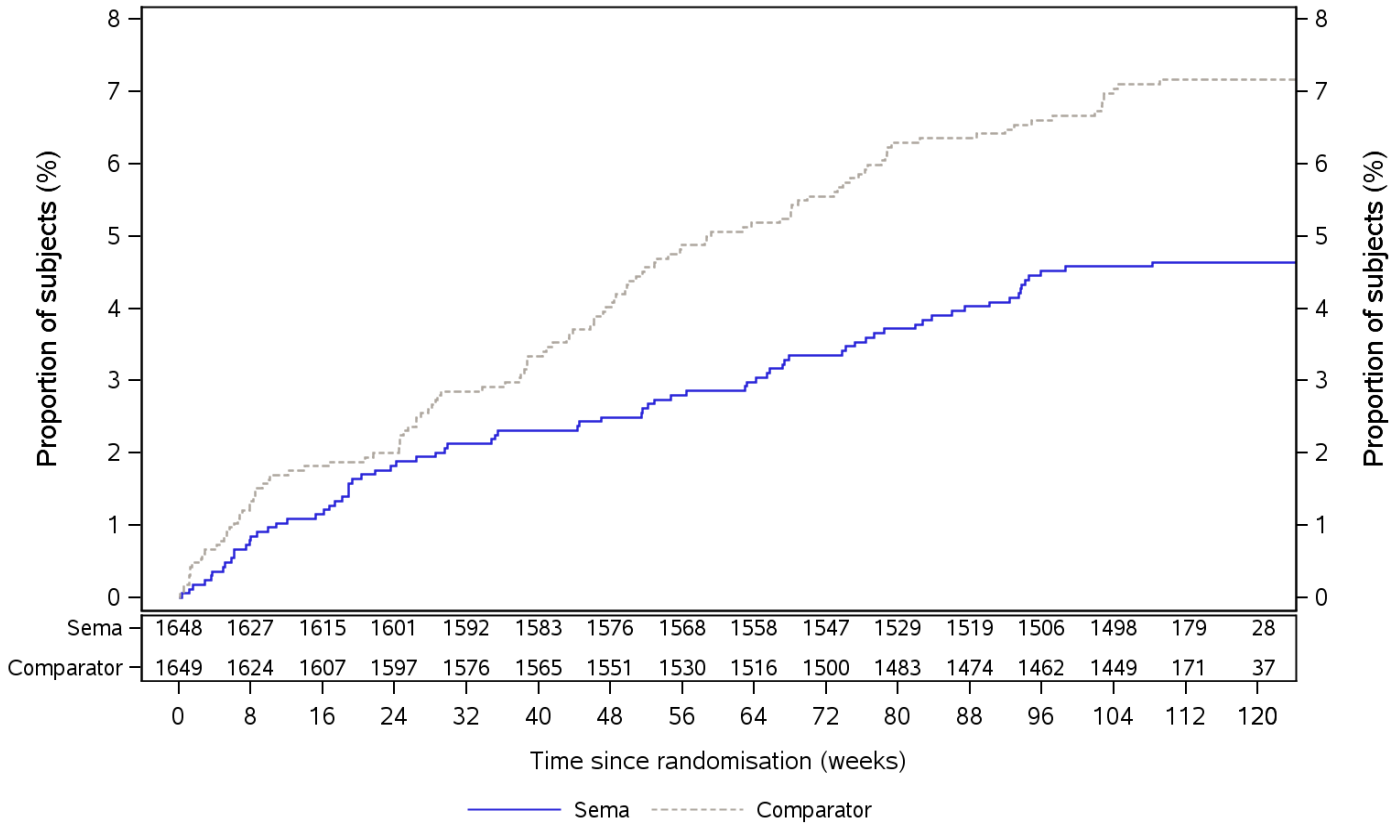
34 Adverse events - preferred term "Anxiety" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:52:26 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_anxiety_ae_all_s6.png

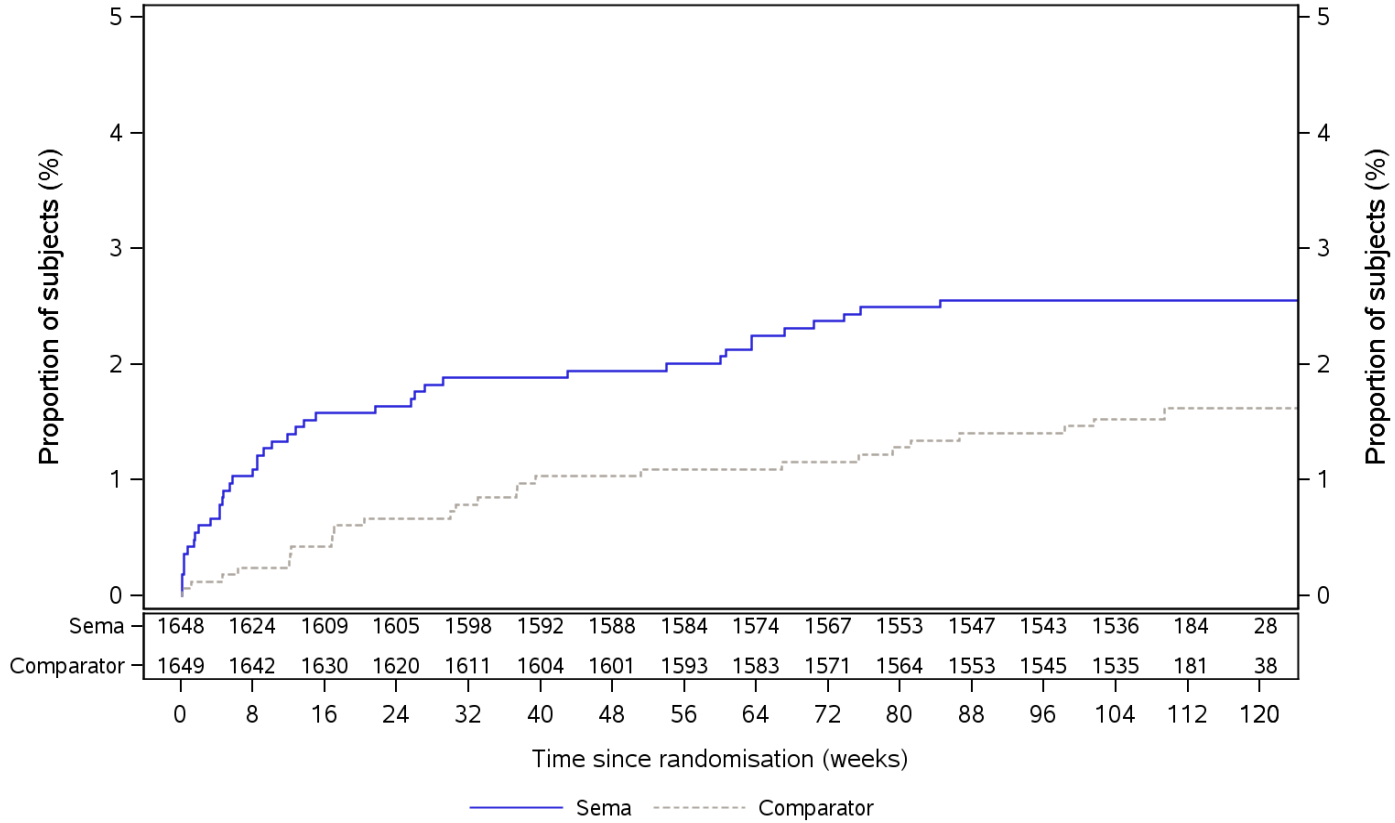
35 Adverse events - preferred term "Arthralgia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:52:45 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_arthralg_ae_all_s6.png

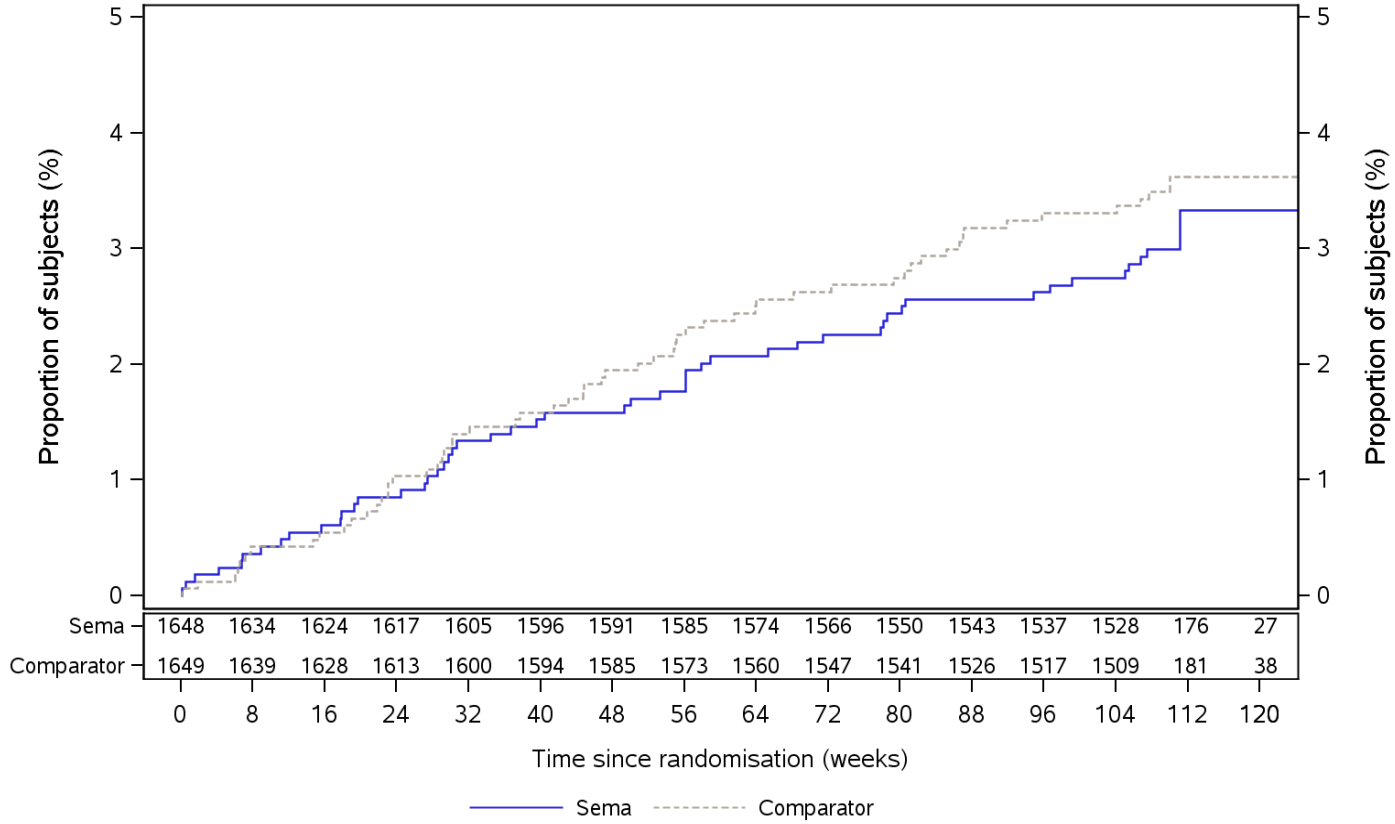
36 Adverse events - preferred term "Asthenia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:53:04 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_asthenia_ae_all_s6.png

37 Adverse events - preferred term "Atrial fibrillation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

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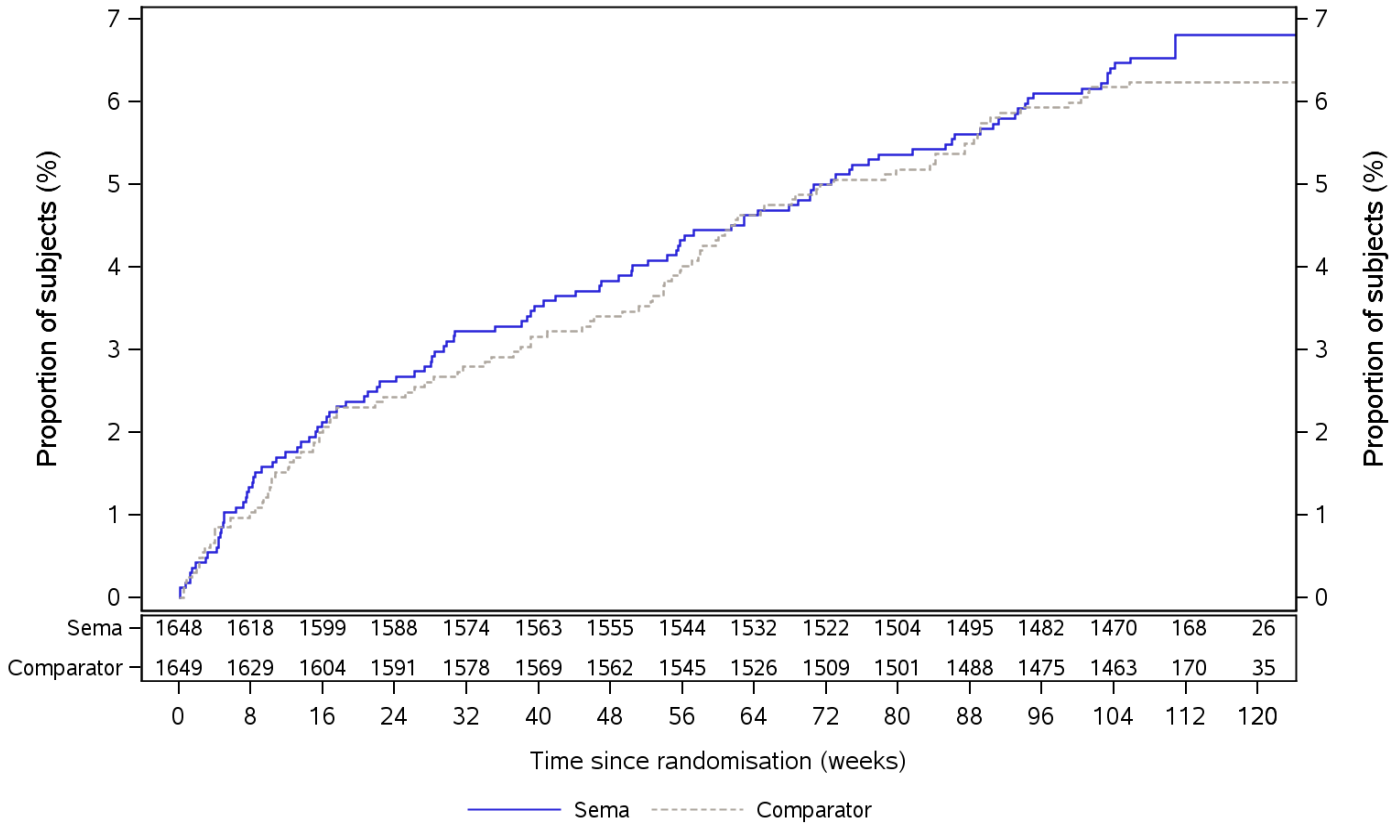
26MAY2020:10:53:24 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_af_ae_all_s6.png

38 Adverse events - preferred term "Back pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
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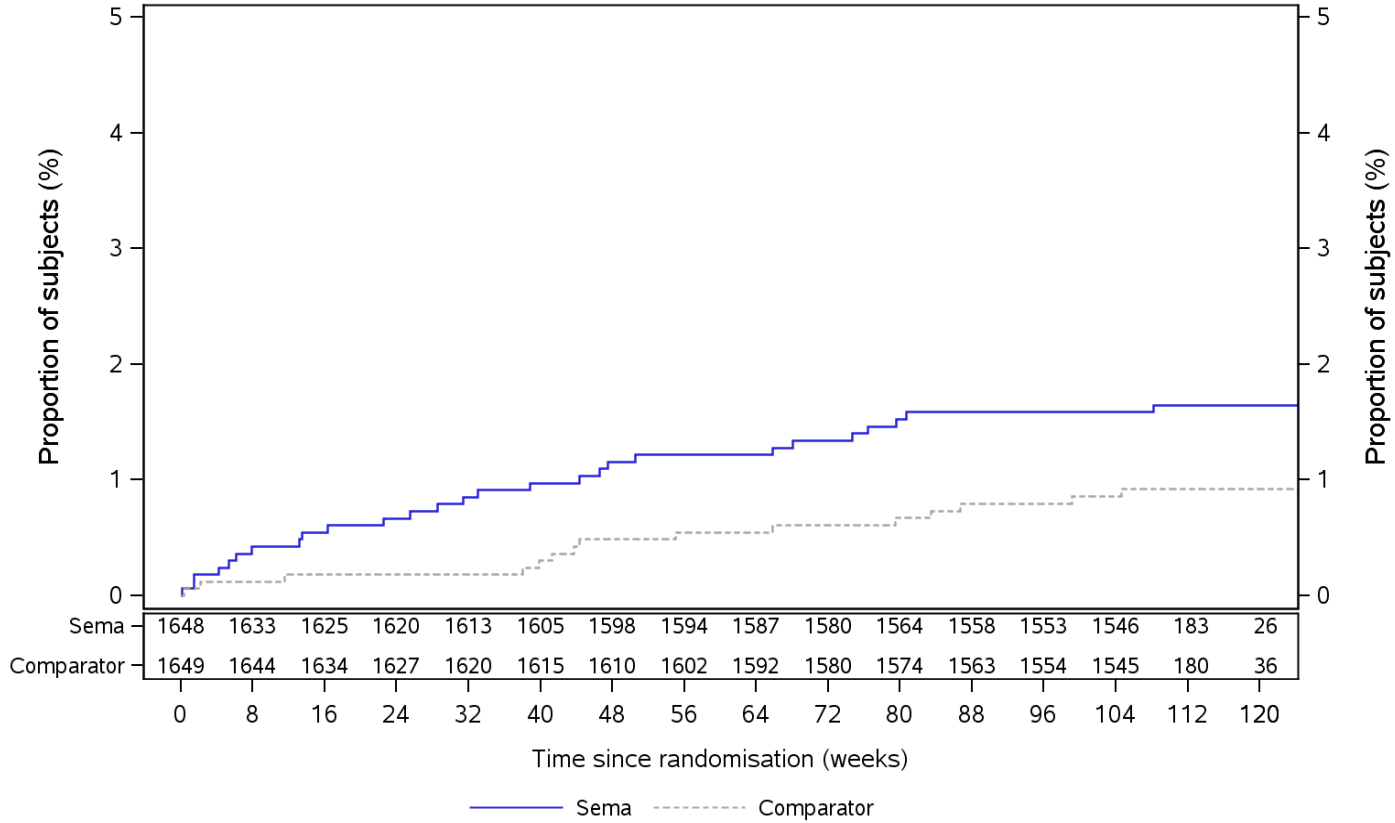
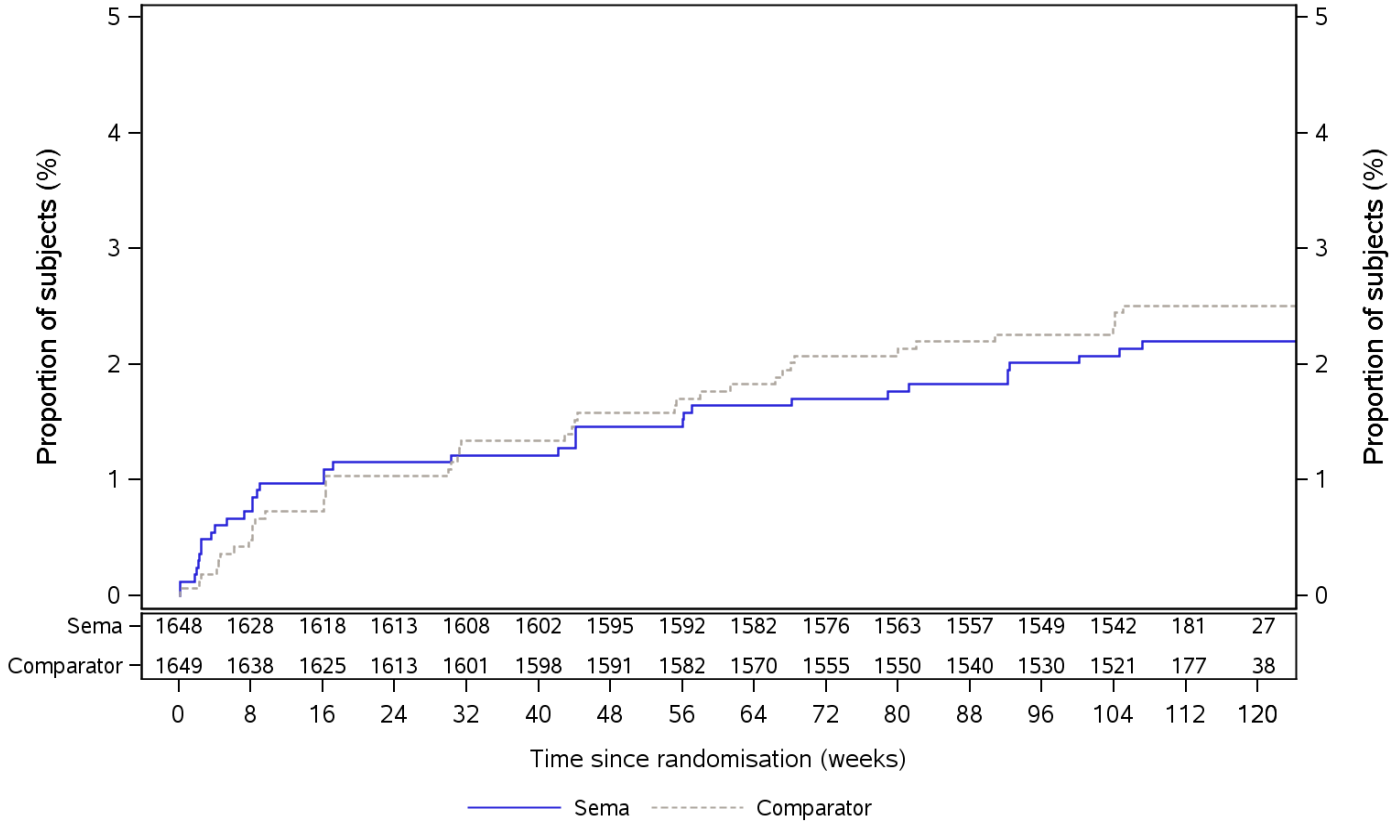
39 Adverse events - preferred term "Benign prostatic hyperplasia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:54:02 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_benprohyp_ae_all_s6.png

40 Adverse events - preferred term "Blood creatinine increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

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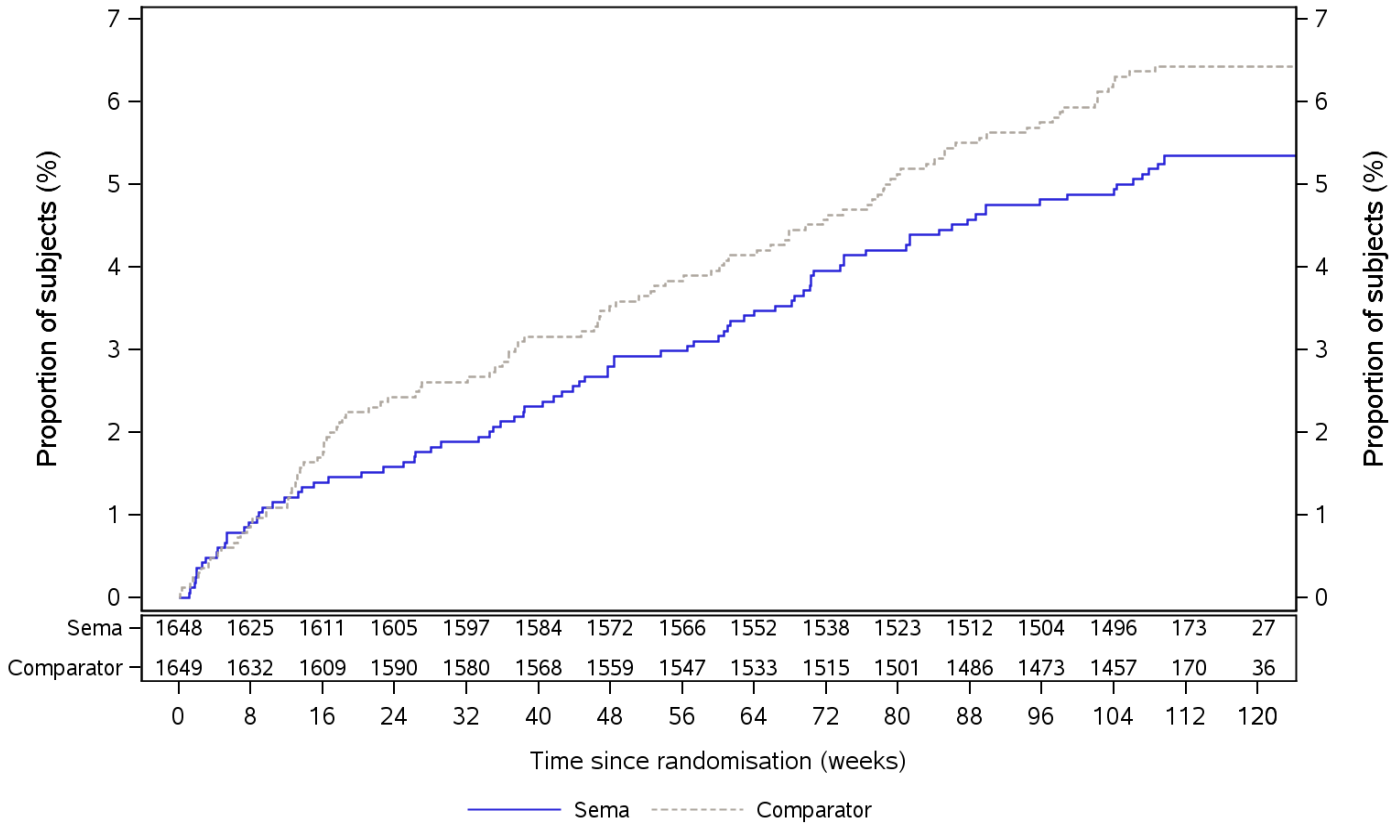
26MAY2020:10:54:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_blocreinc_ae_all_s6.png

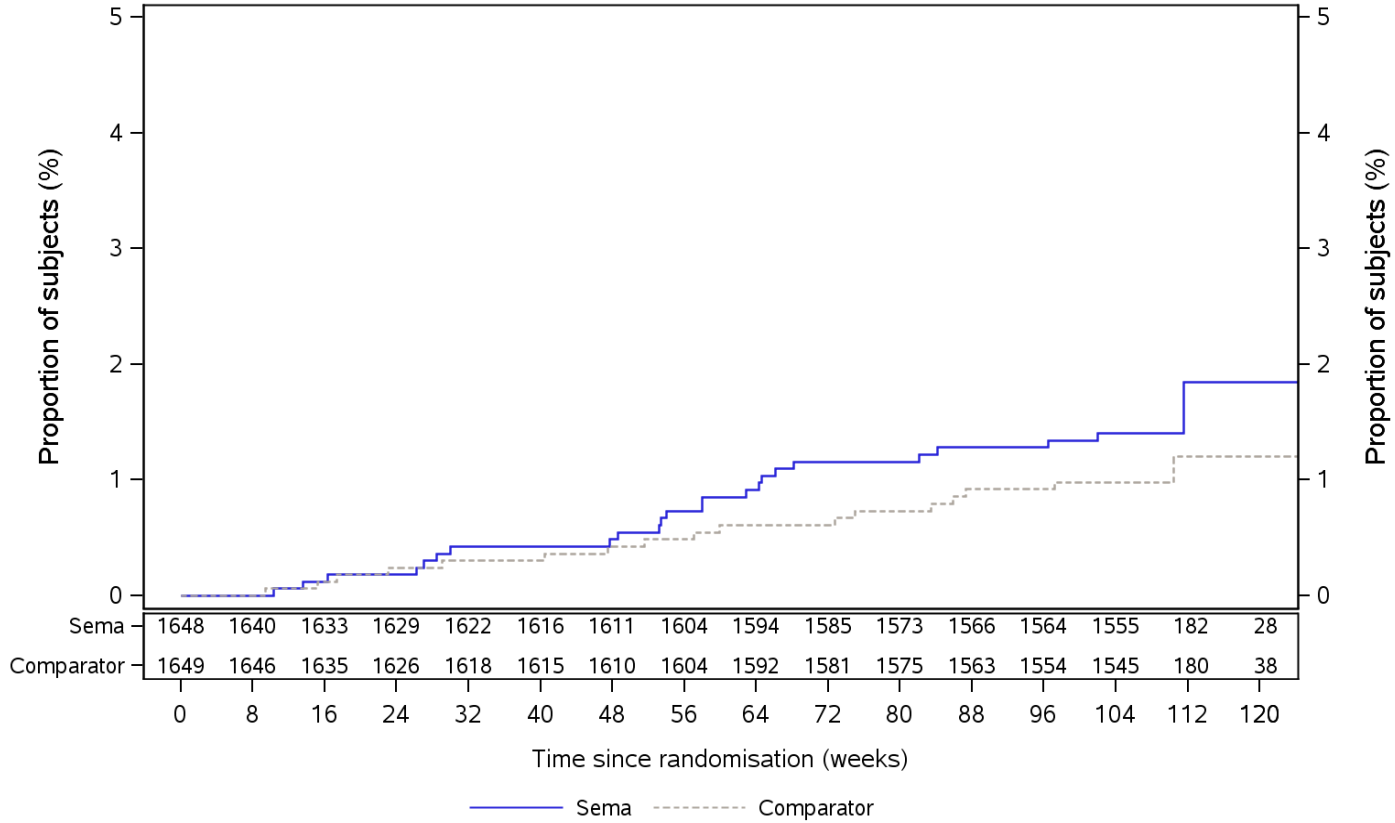
41 Adverse events - preferred term "Bronchitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:54:41 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_bronchit_ae_all_s6.png

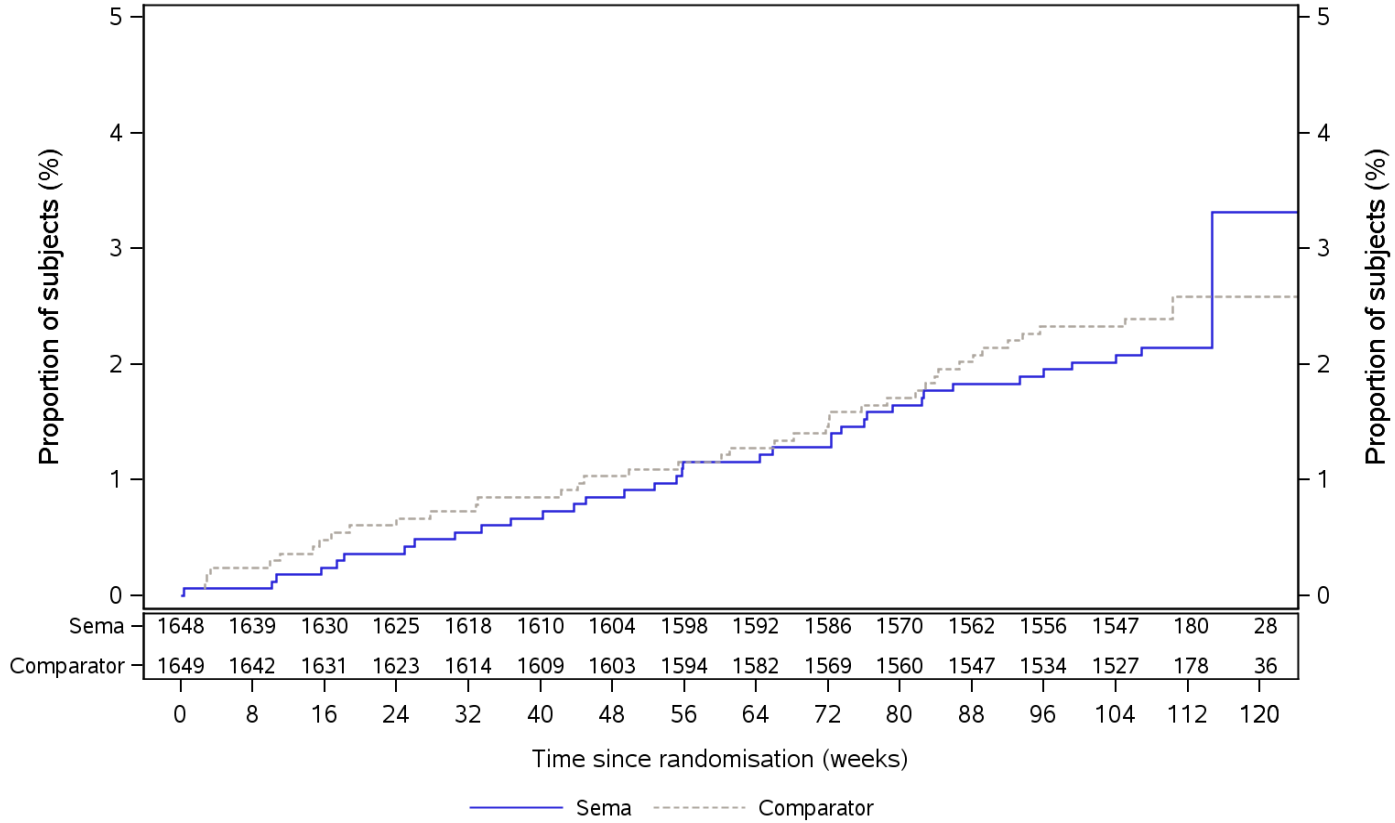
42 Adverse events - preferred term "Cardiac failure" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:55:01 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cf_ae_all_s6.png

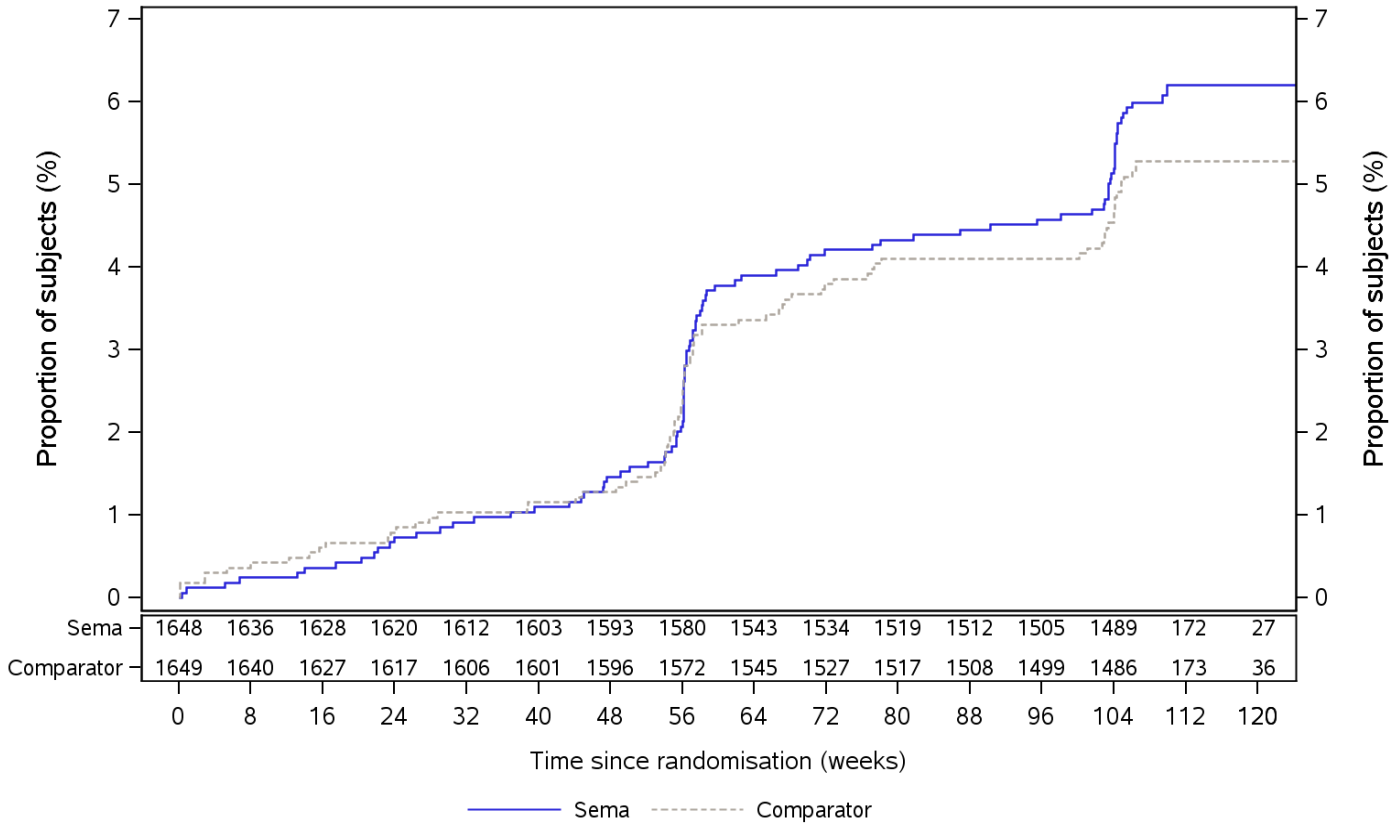
43 Adverse events - preferred term "Cardiac failure congestive" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:55:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cfc_ae_all_s6.png

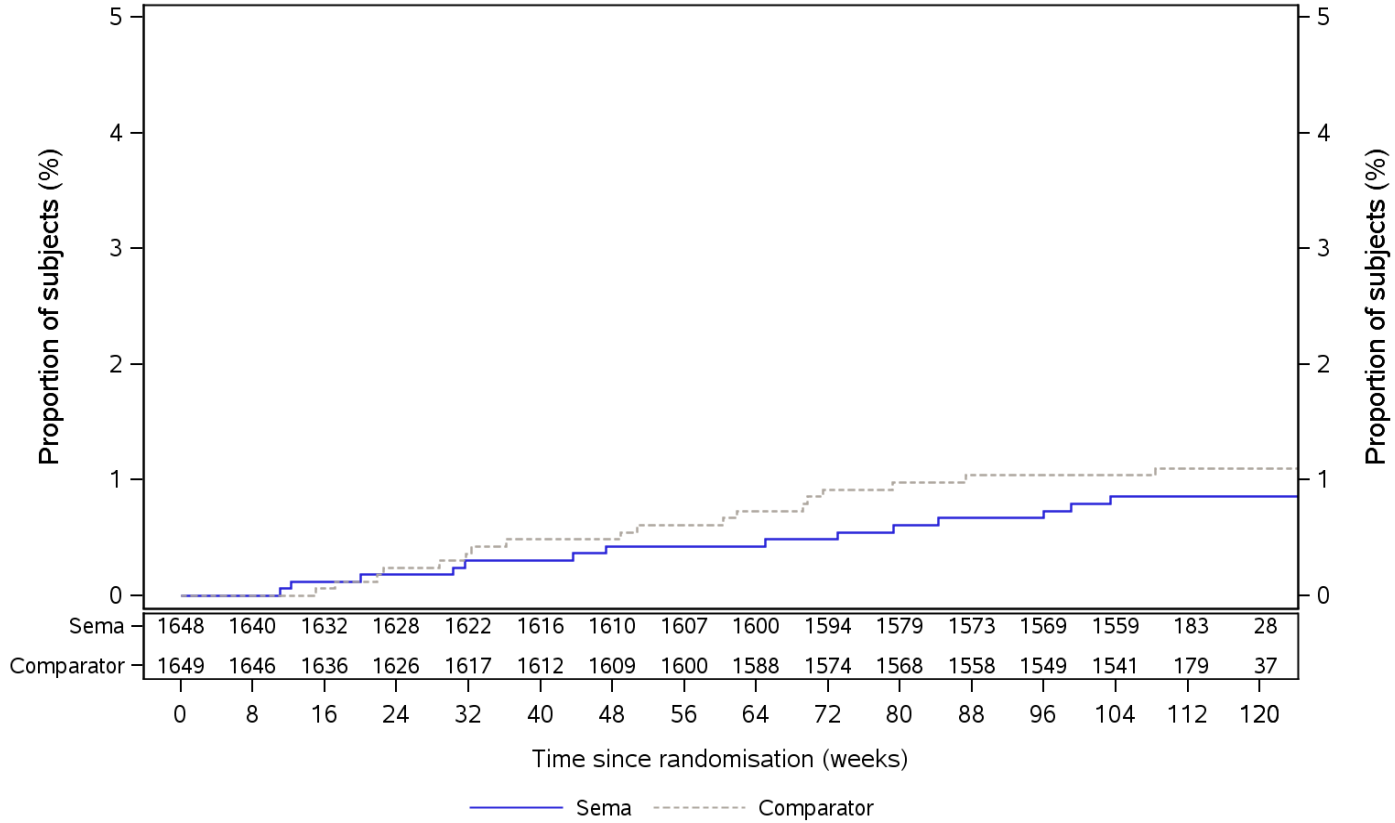
44 Adverse events - preferred term "Cataract" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:55:40 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cataract_ae_all_s6.png

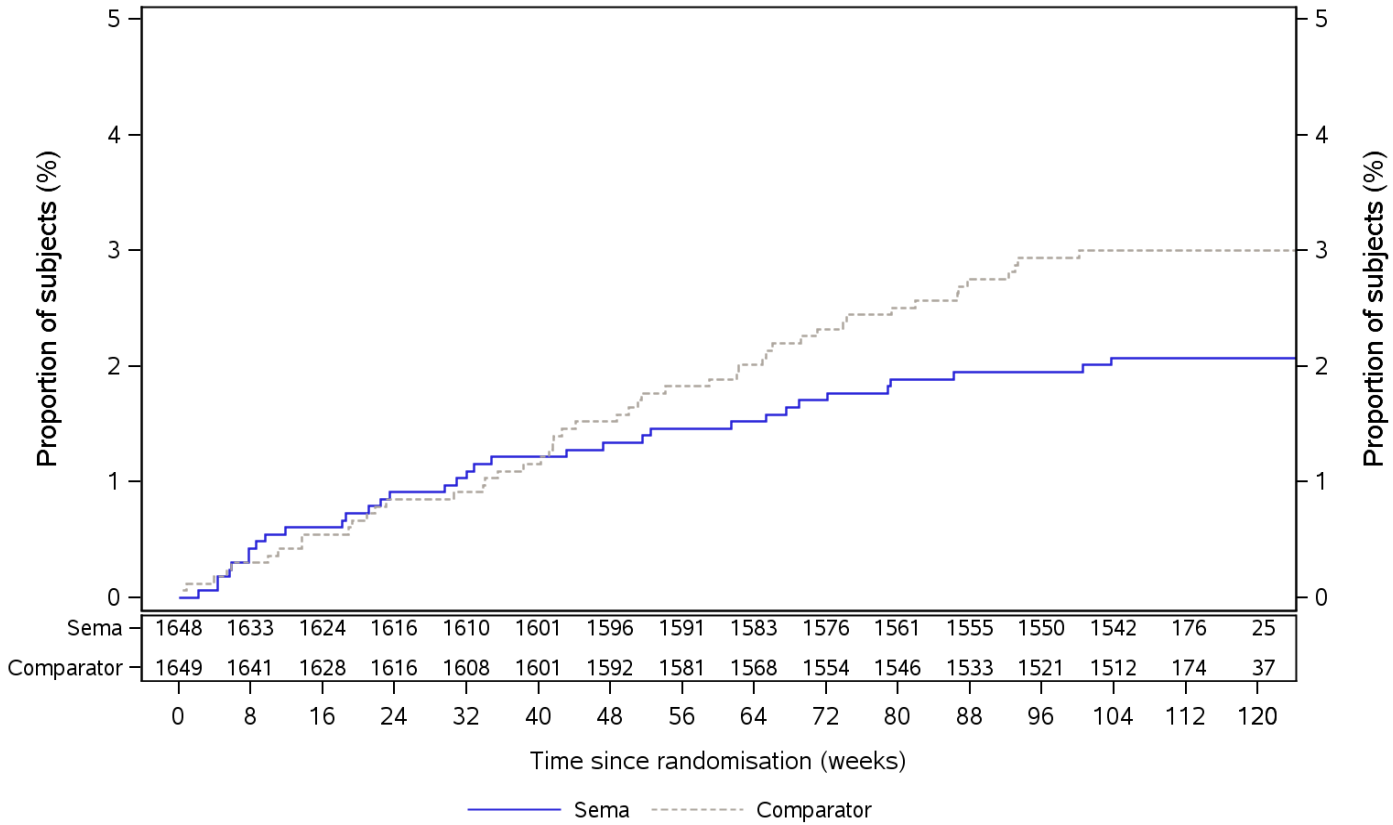
45 Adverse events - preferred term "Cataract operation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:56:00 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cataoper_ae_all_s6.png

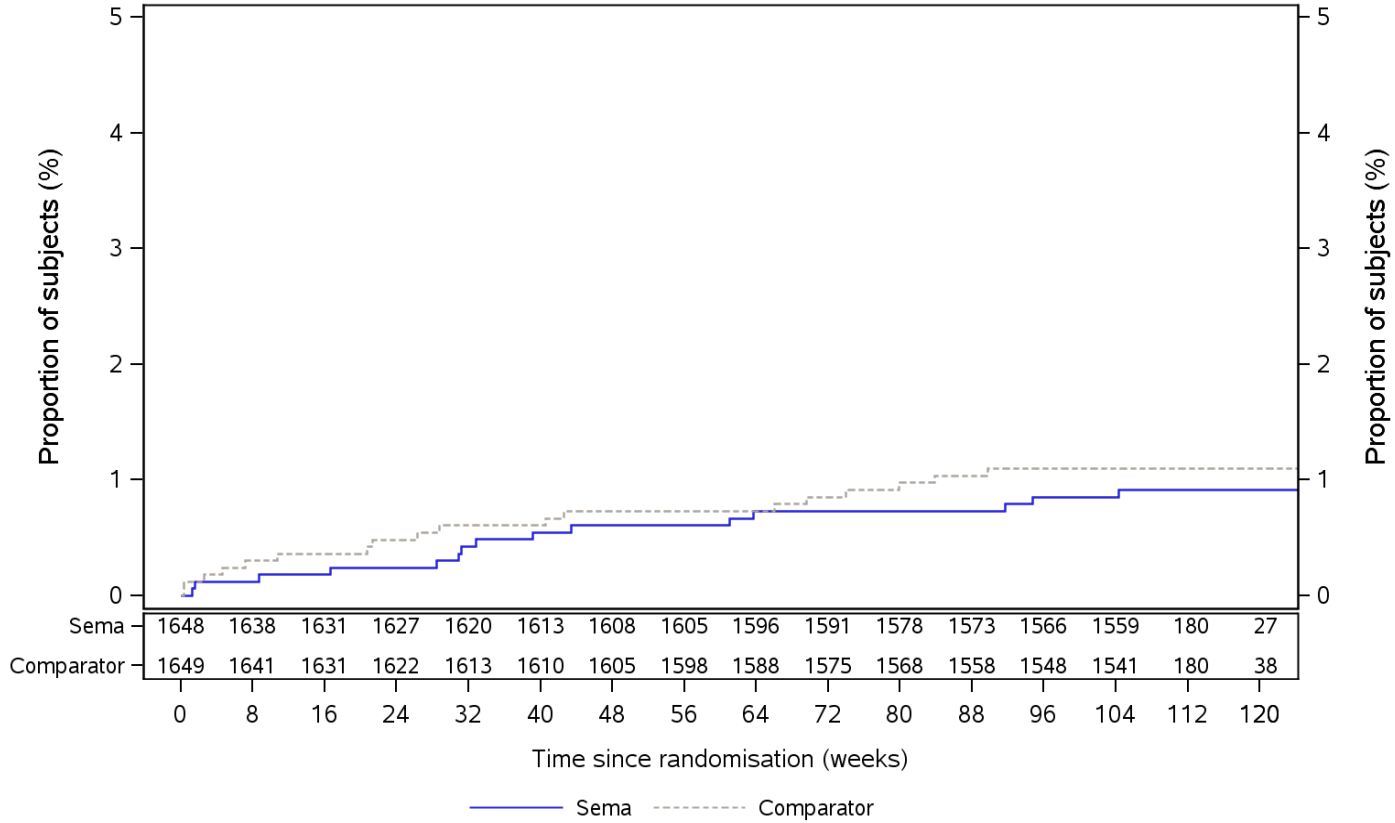
46 Adverse events - preferred term "Cellulitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:56:19 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cellulit_ae_all_s6.png

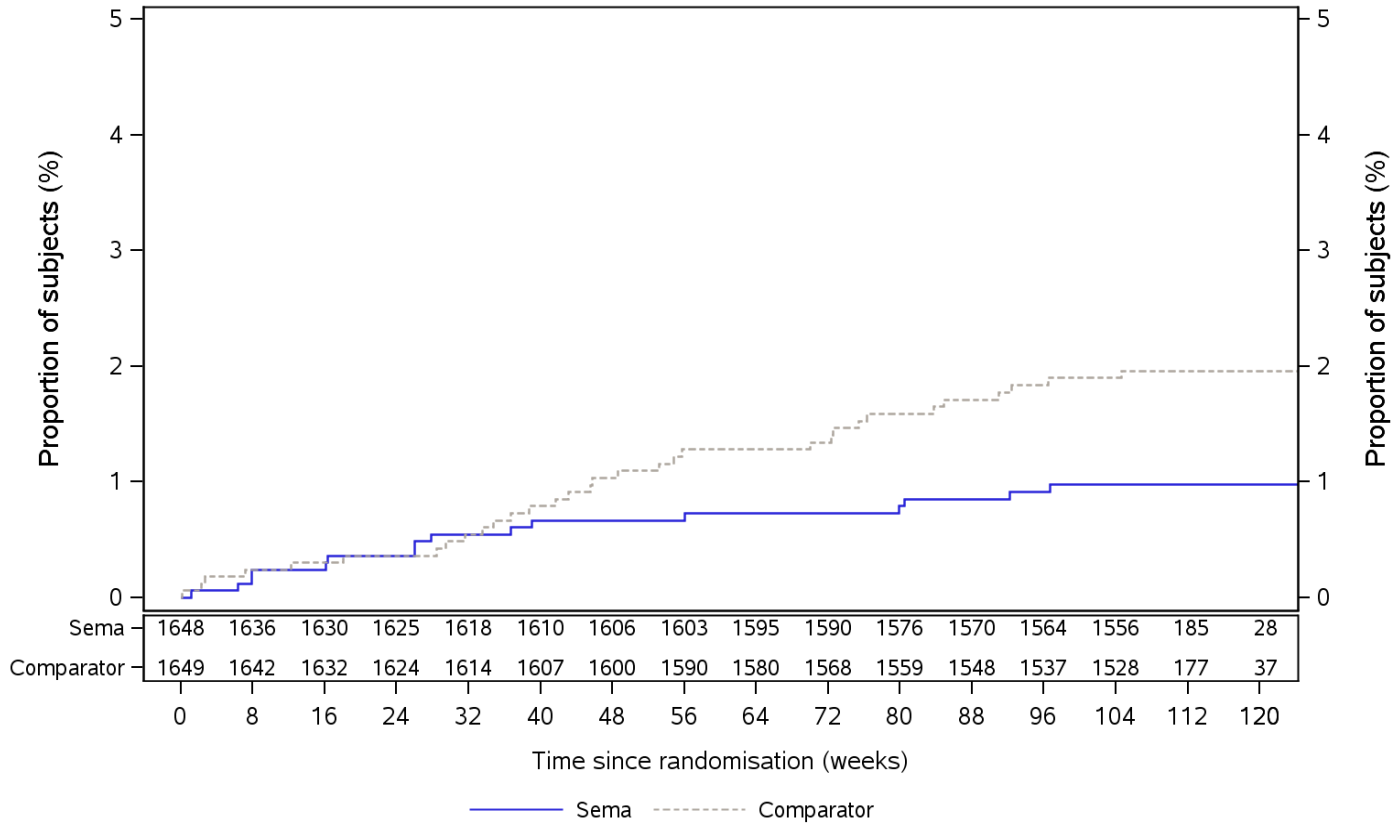
47 Adverse events - preferred term "Chest discomfort" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:56:38 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_chesdisc_ae_all_s6.png

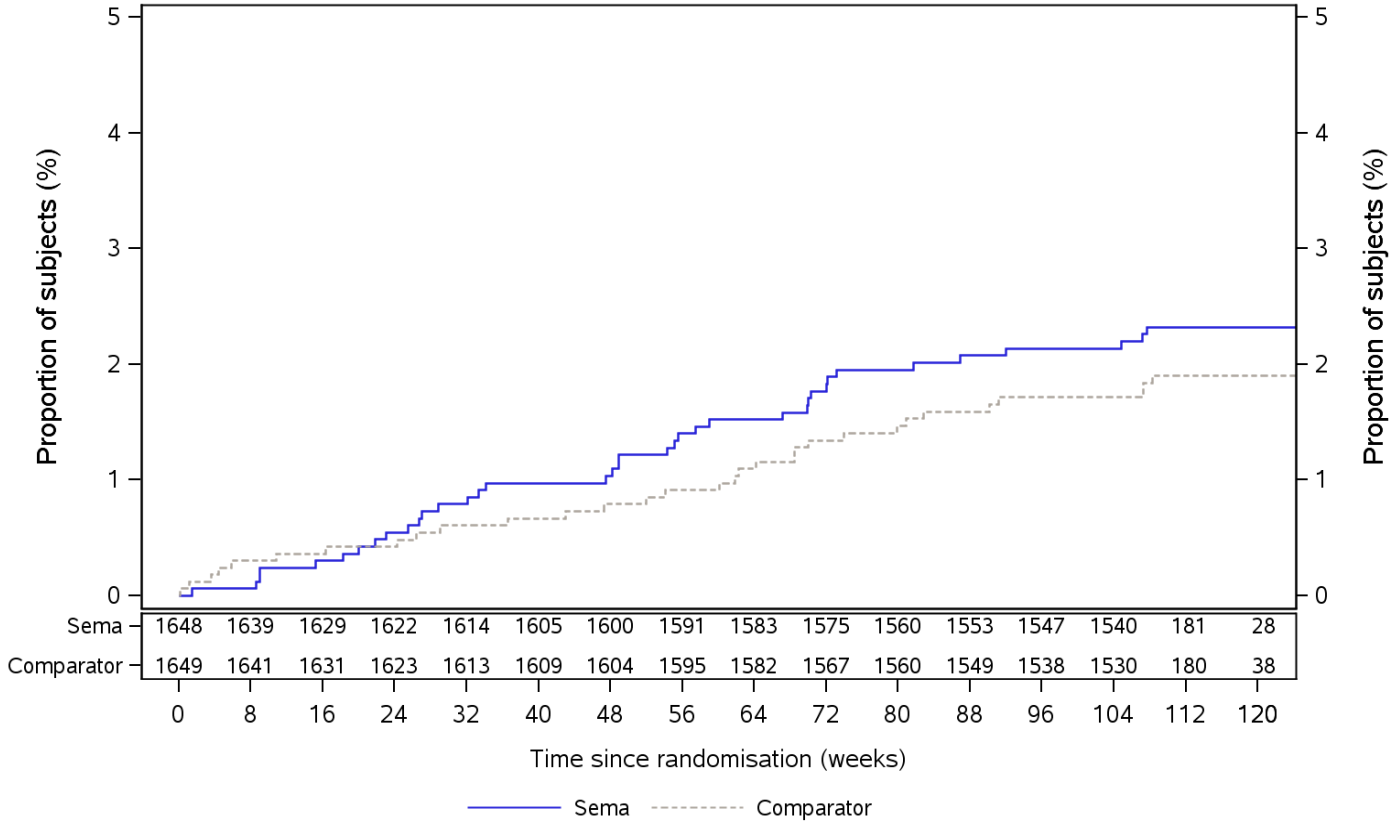
48 Adverse events - preferred term "Chest pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:56:58 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_chespain_ae_all_s6.png

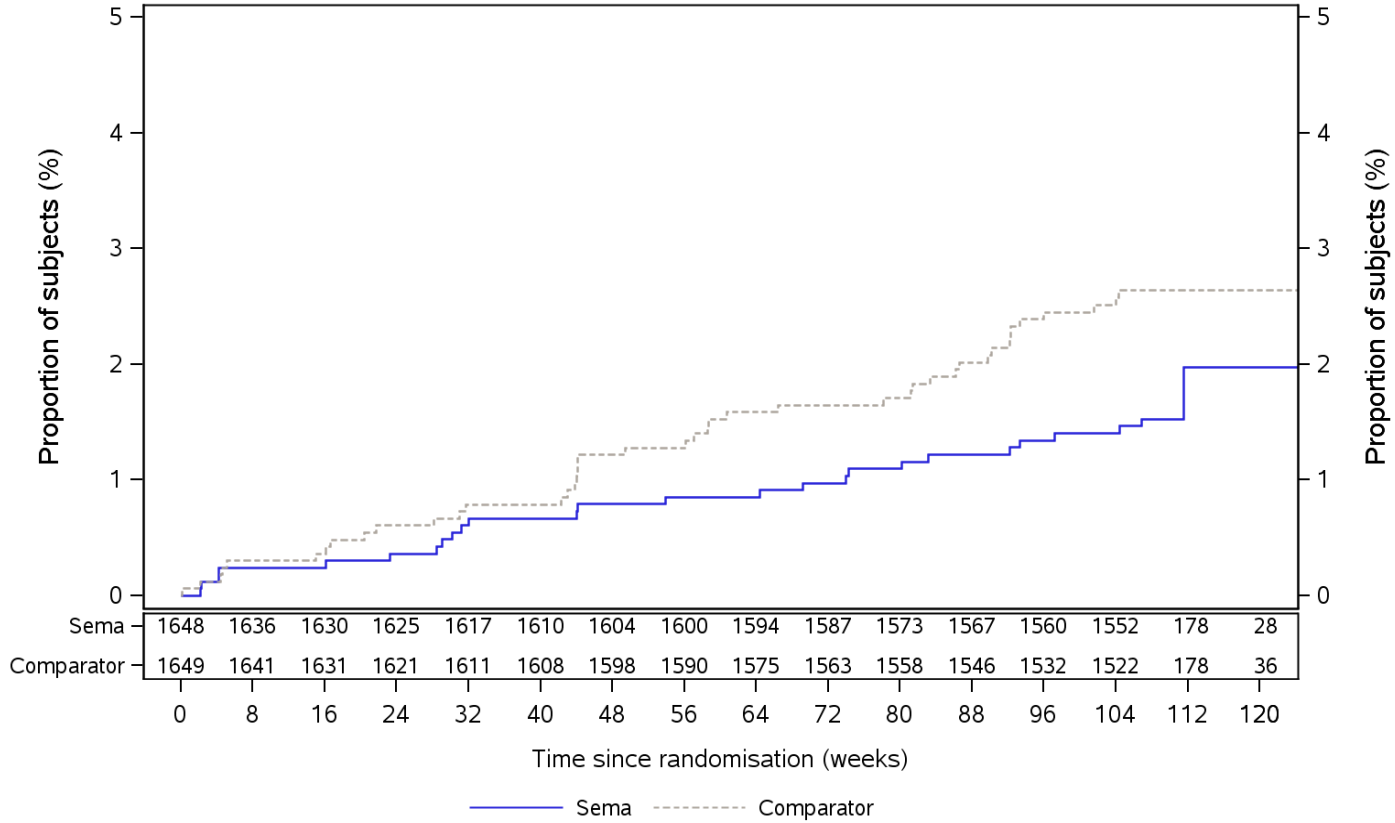
49 Adverse events - preferred term "Cholelithiasis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:57:17 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cholelit_ae_all_s6.png

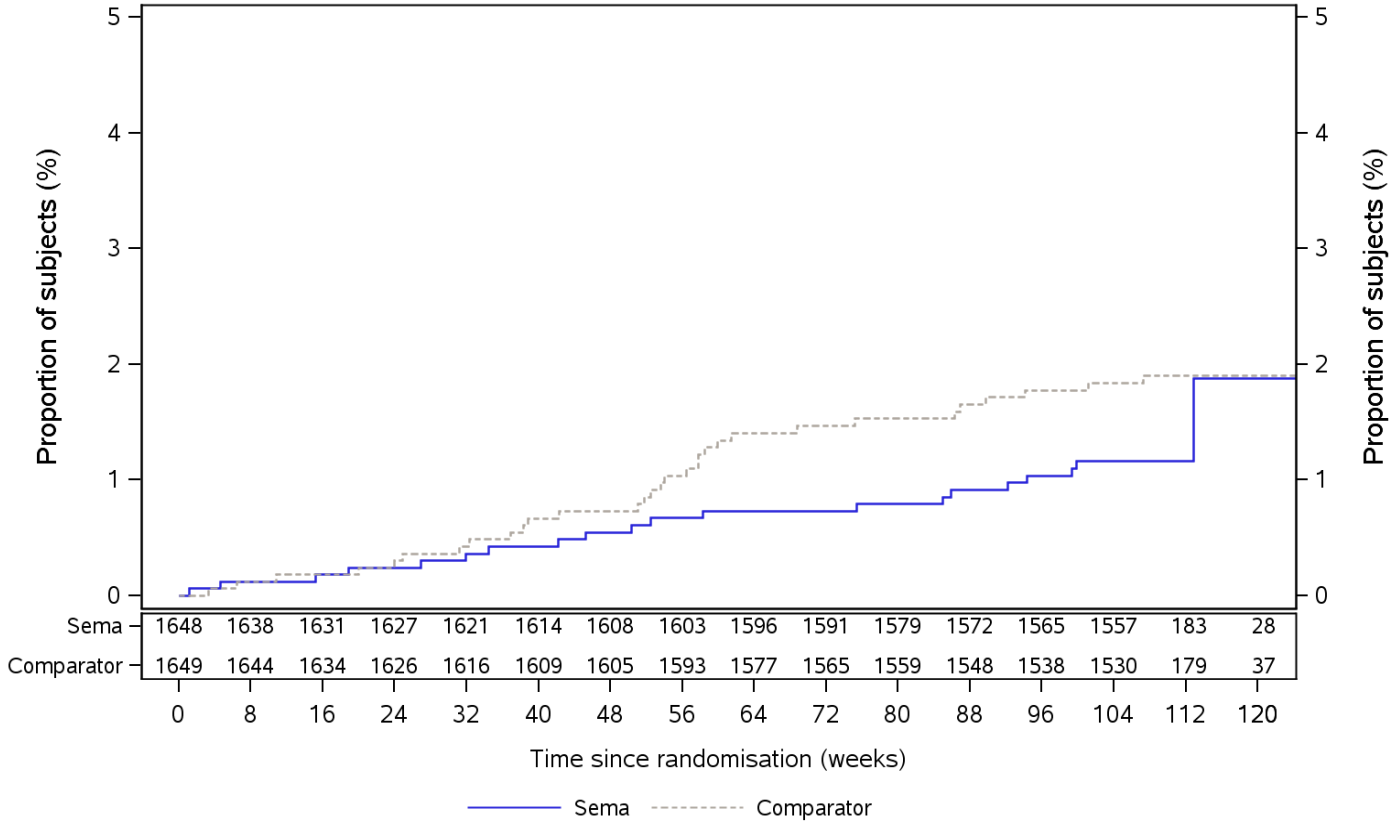
50 Adverse events - preferred term "Chronic kidney disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:57:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_chrkiddis_ae_all_s6.png

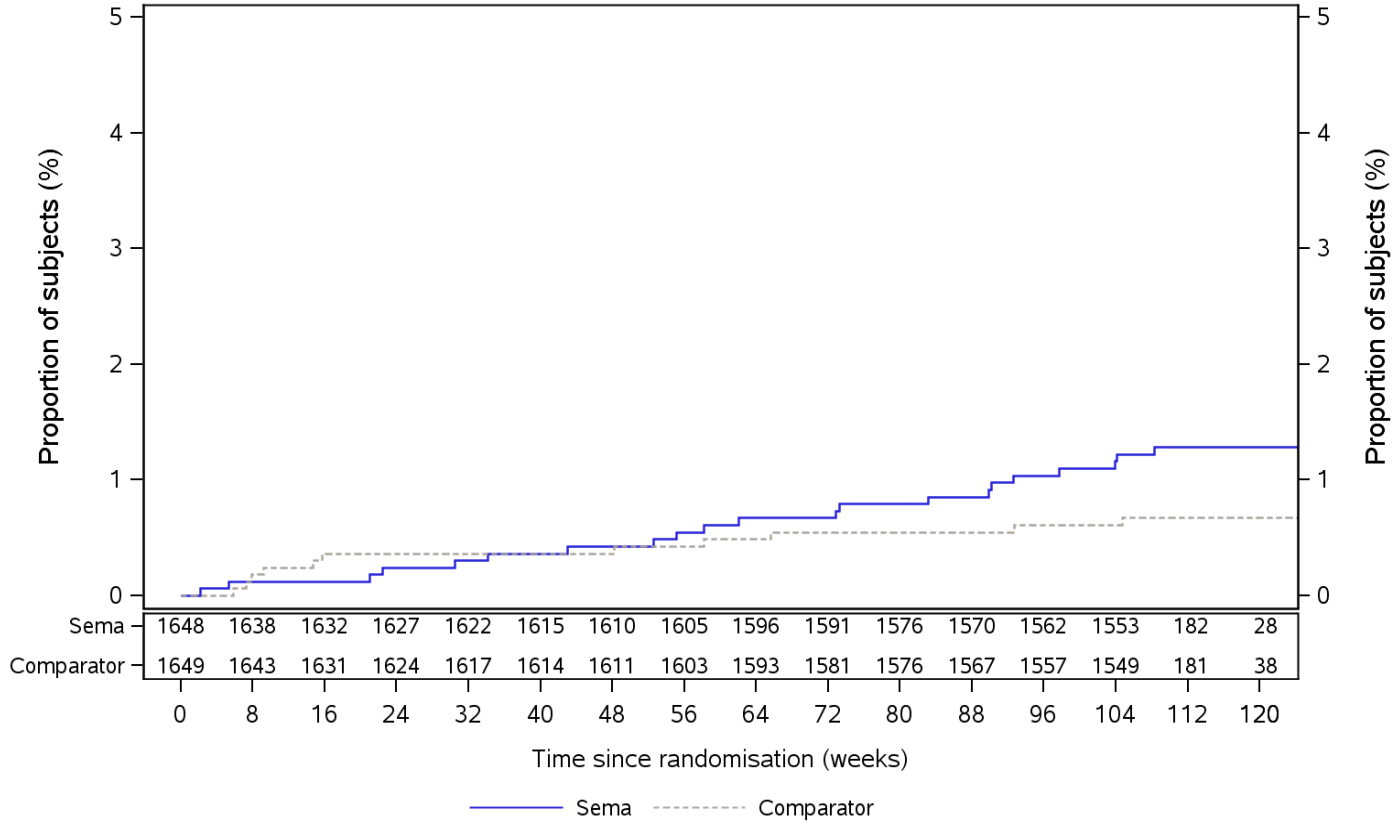
51 Adverse events - preferred term "Chronic obstructive pulmonary disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:57:54 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_chrobspul_ae_all_s6.png

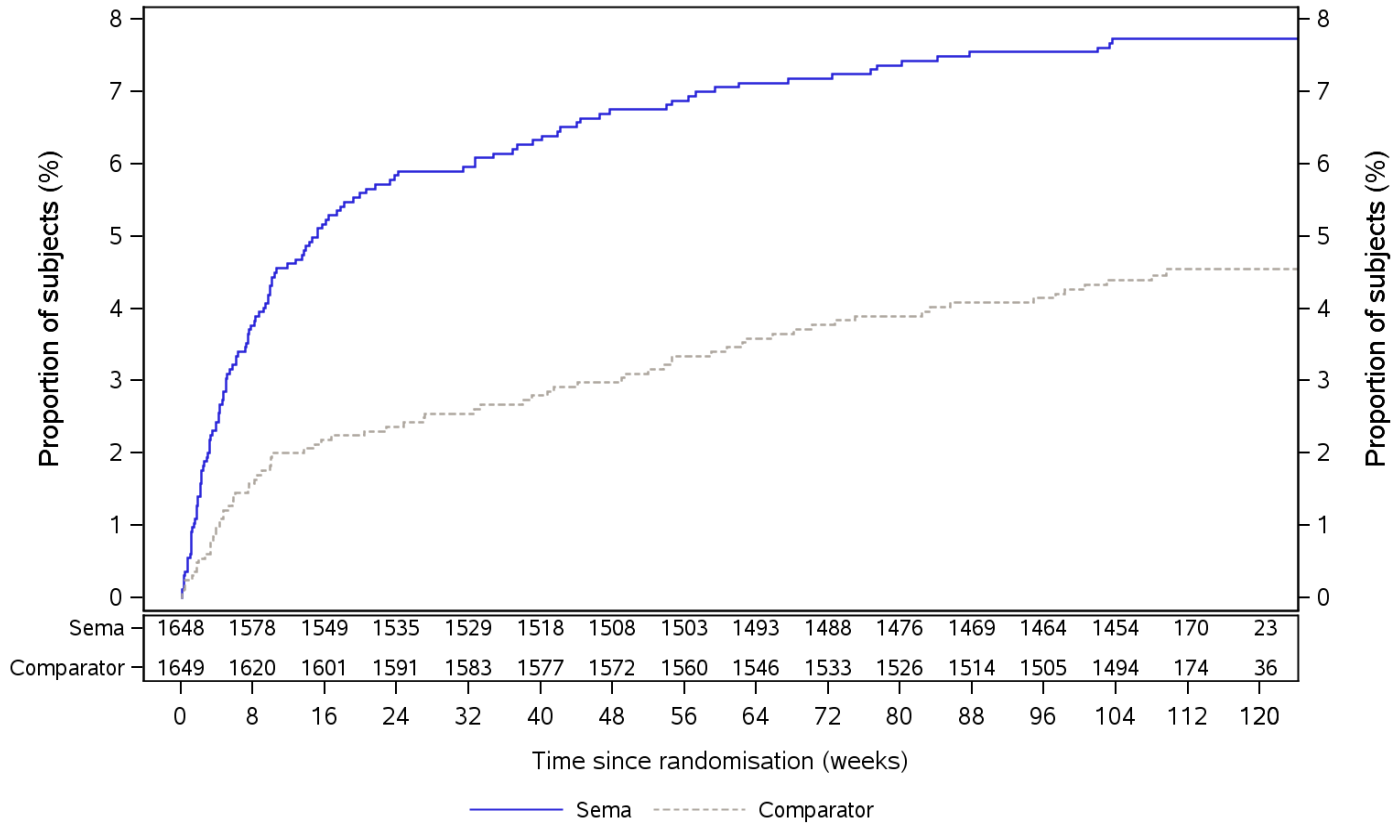
52 Adverse events - preferred term "Conjunctivitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:58:14 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_conjunct_ae_all_s6.png

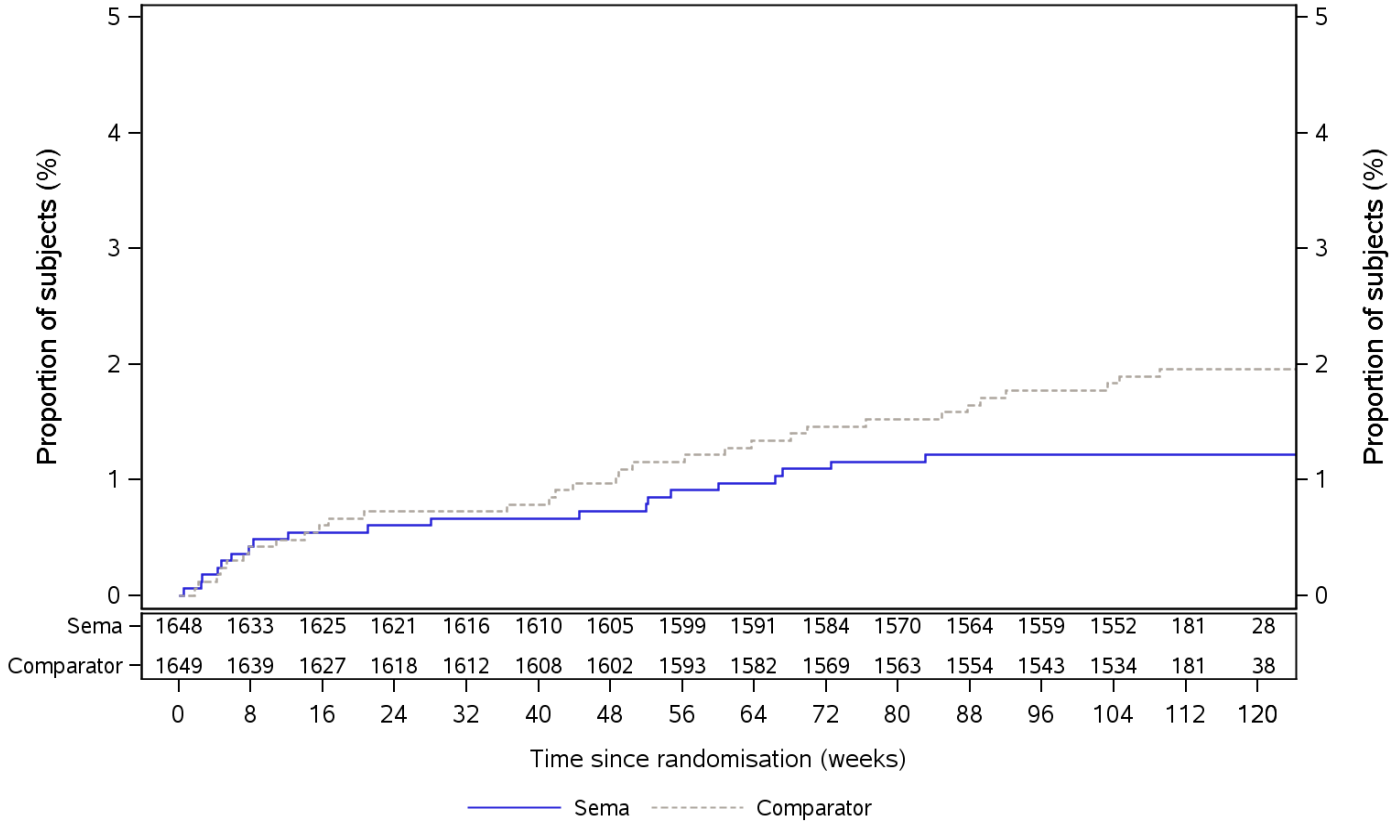
53 Adverse events - preferred term "Constipation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:58:33 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_constipa_ae_all_s6.png

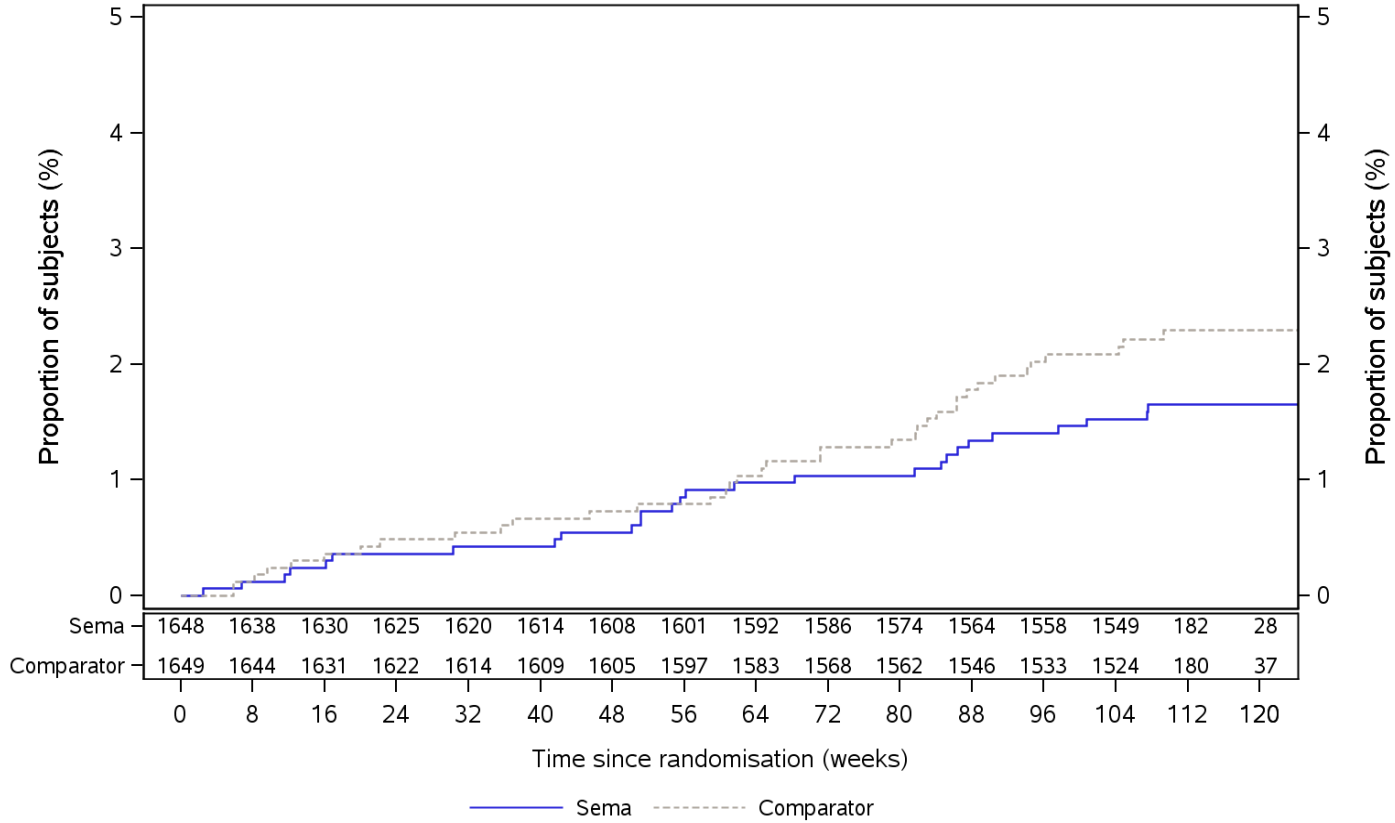
54 Adverse events - preferred term "Contusion" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:58:52 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_contusio_ae_all_s6.png

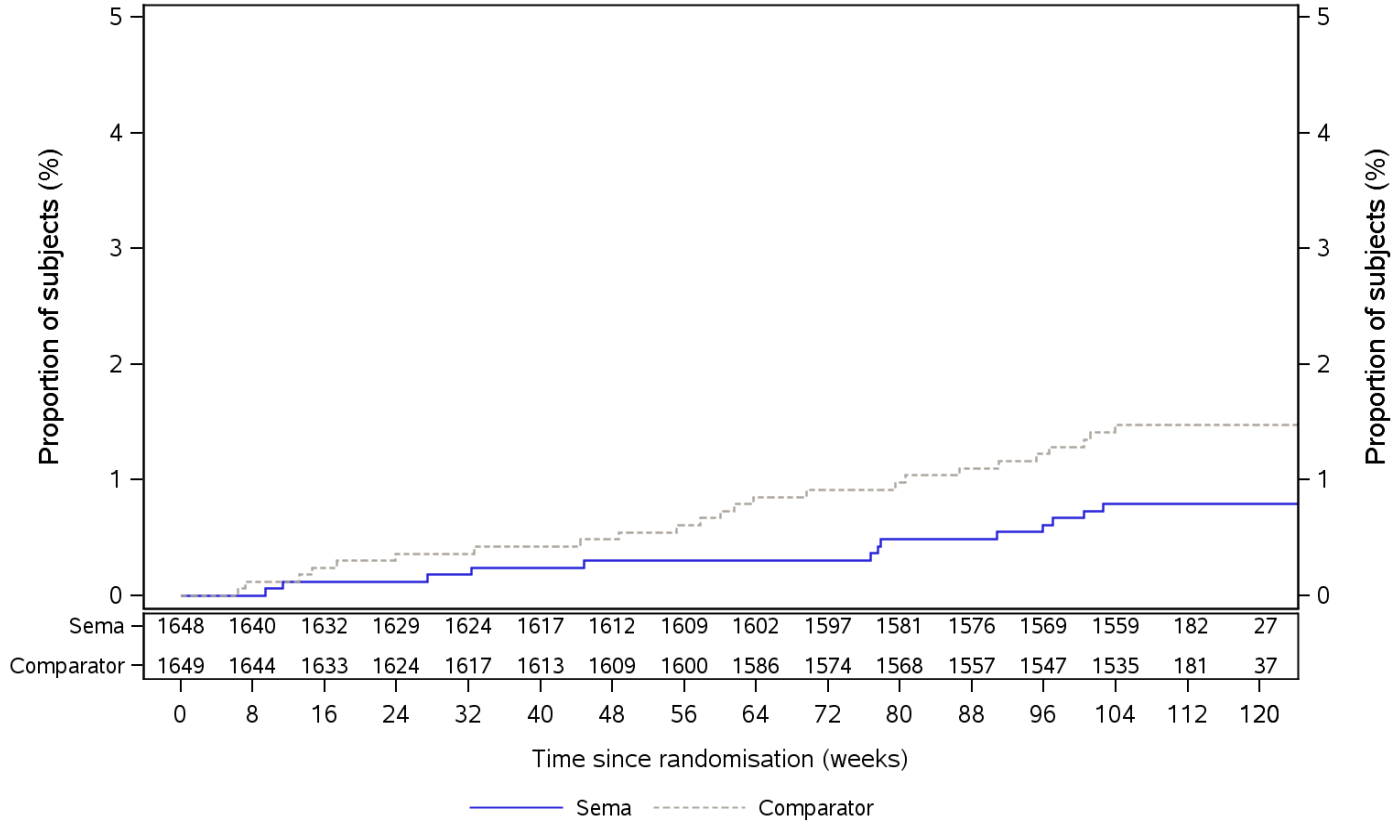
55 Adverse events - preferred term "Coronary arterial stent insertion" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:59:13 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_casi_ae_all_s6.png

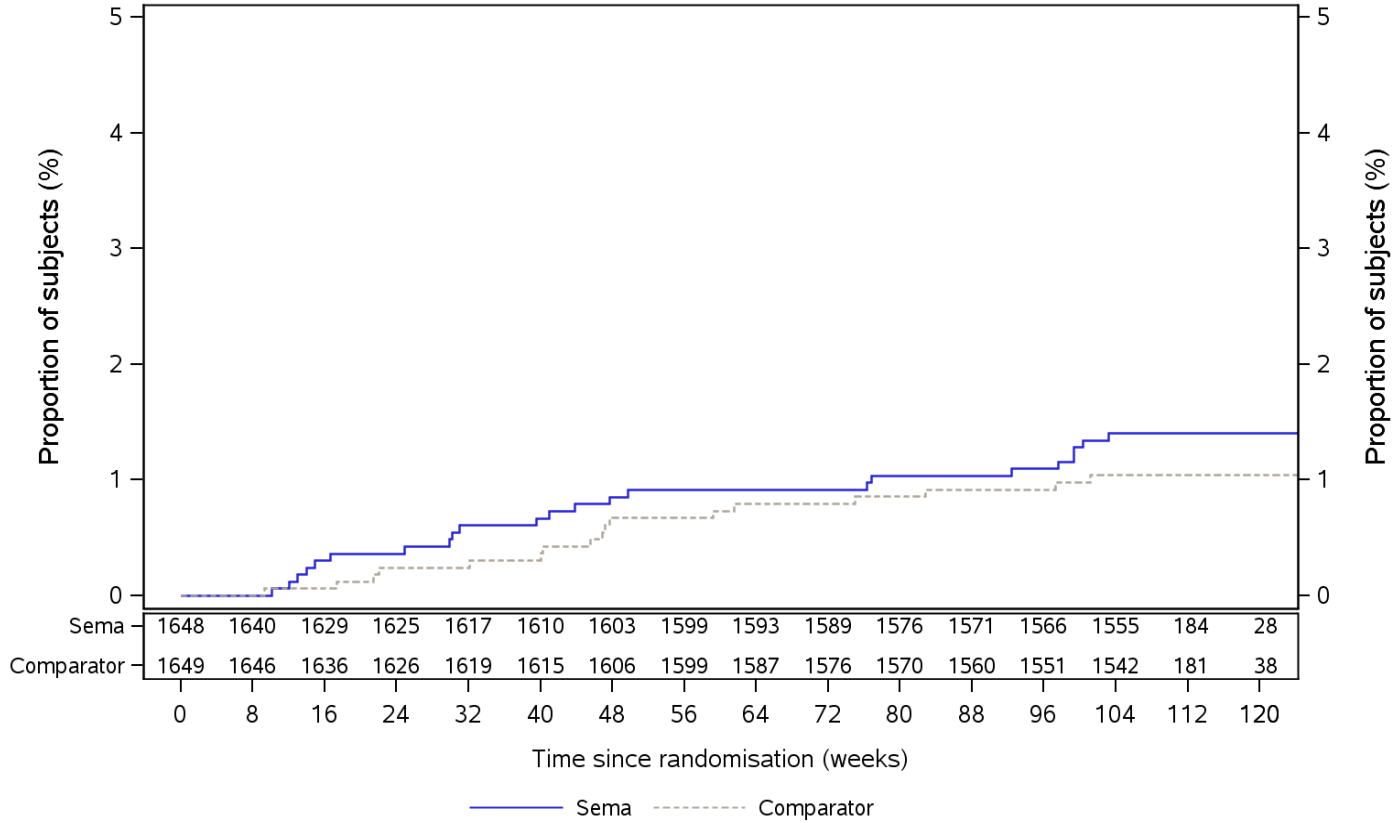
56 Adverse events - preferred term "Coronary artery bypass" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:59:32 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cab_ae_all_s6.png

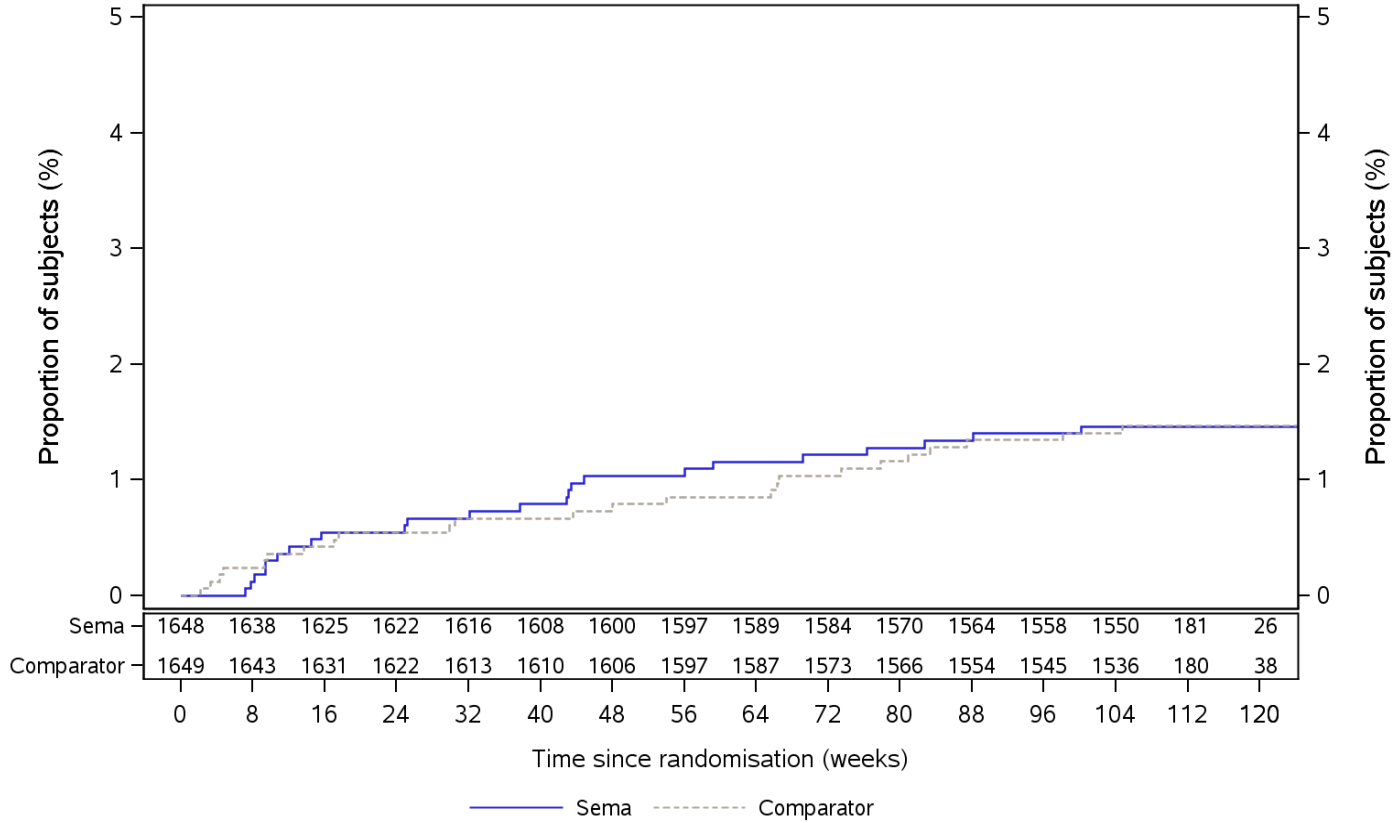
57 Adverse events - preferred term "Coronary artery disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:59:51 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cad_ae_all_s6.png

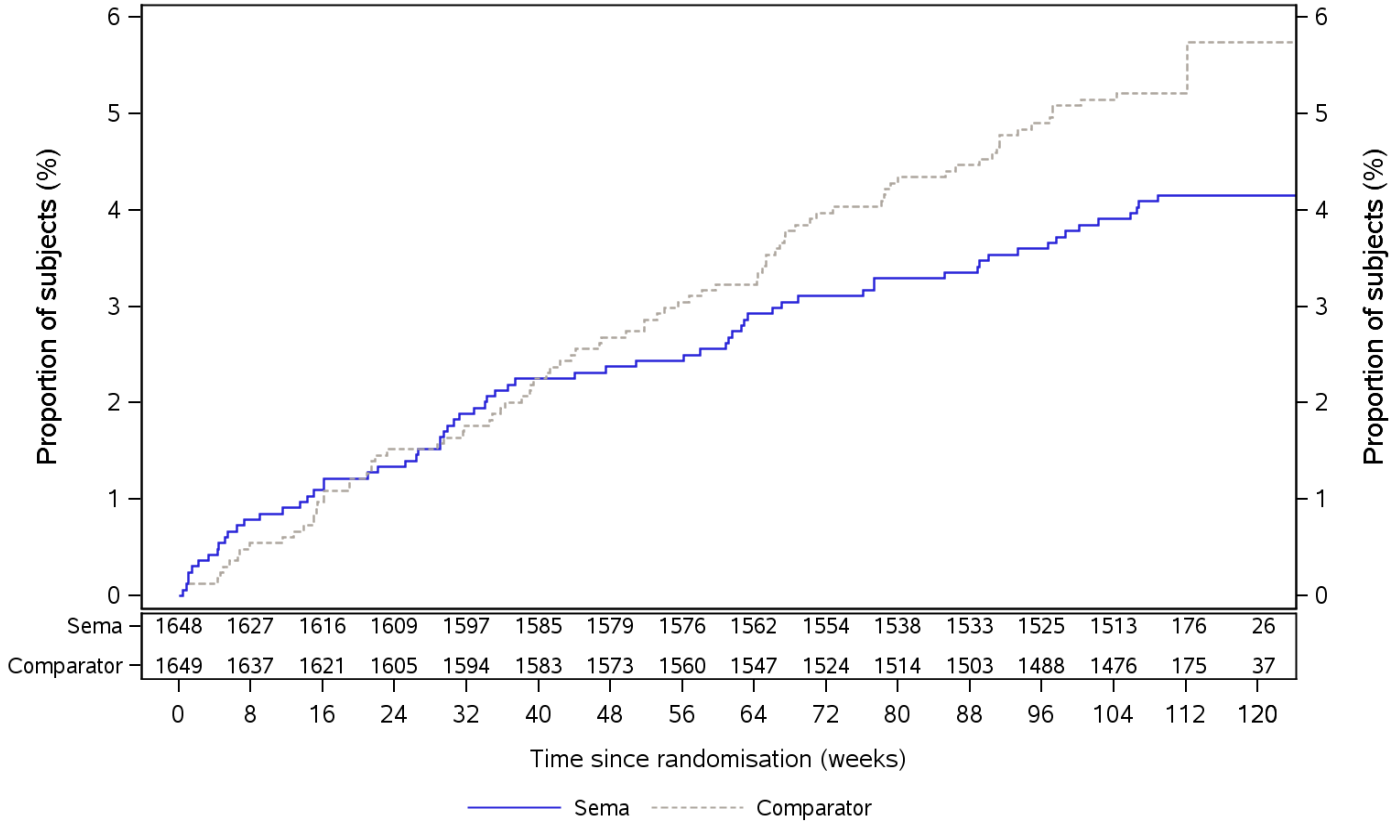
58 Adverse events - preferred term "Coronary revascularisation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:00:11 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cr_ae_all_s6.png

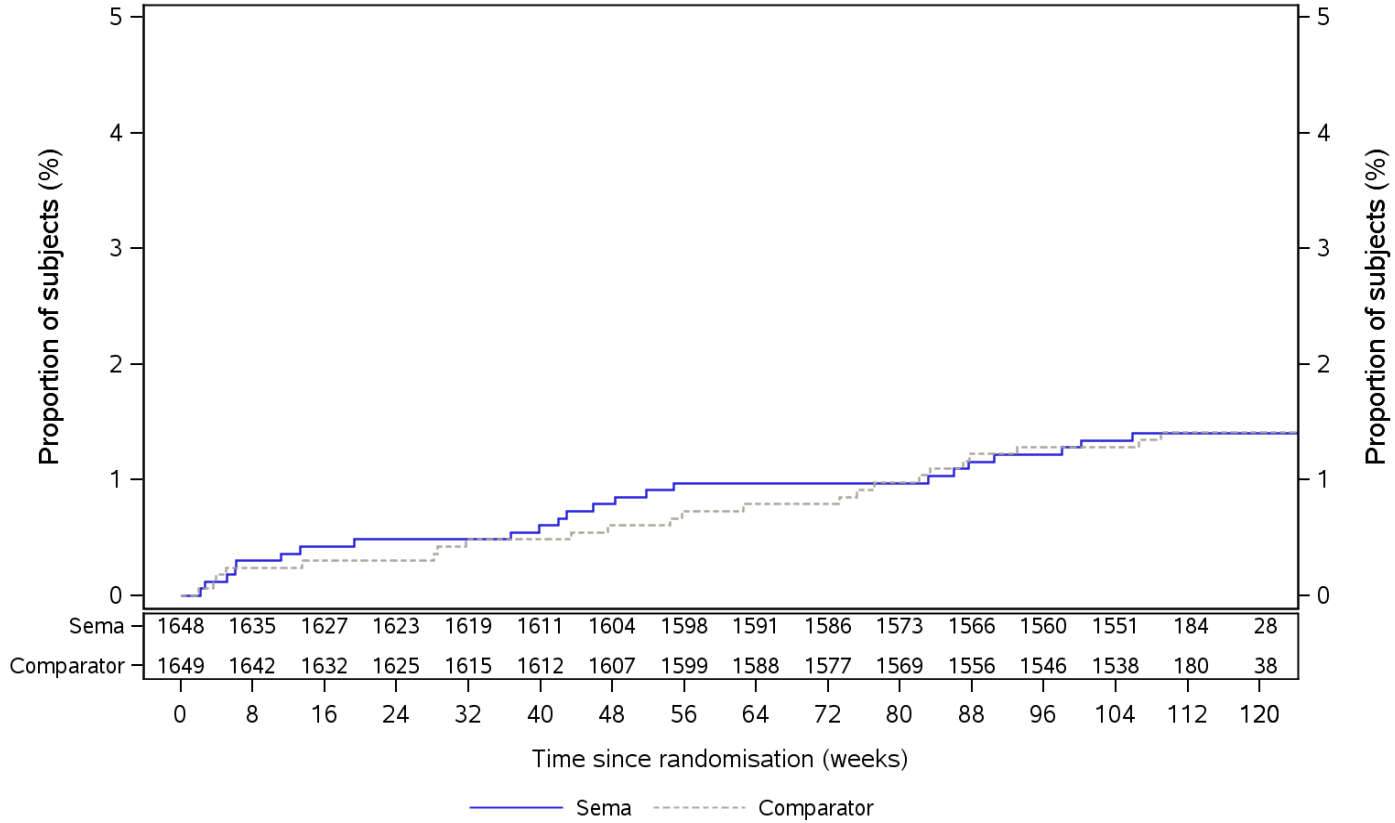
59 Adverse events - preferred term "Cough" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:00:30 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cough_ae_all_s6.png

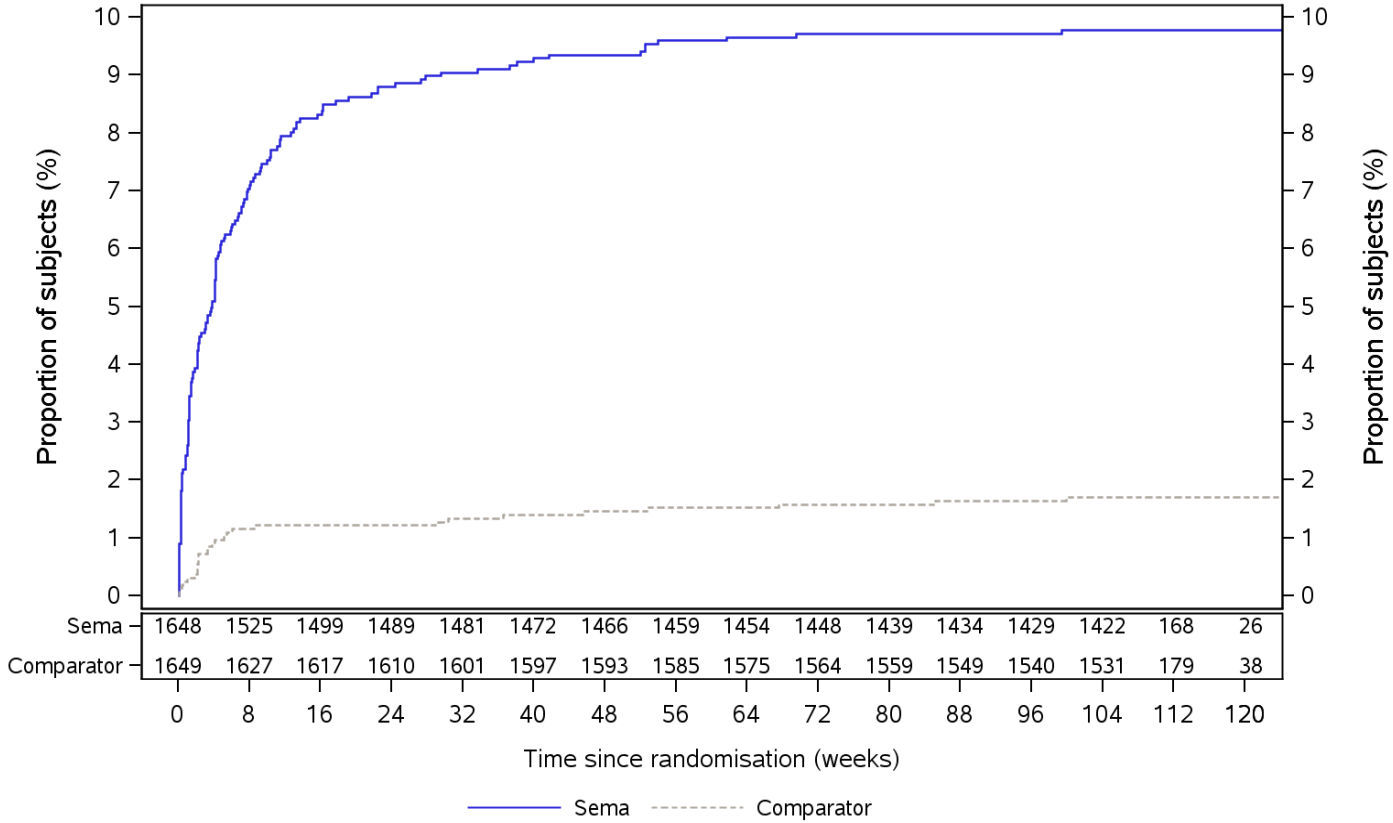
60 Adverse events - preferred term "Cystitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:00:49 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cystitis_ae_all_s6.png

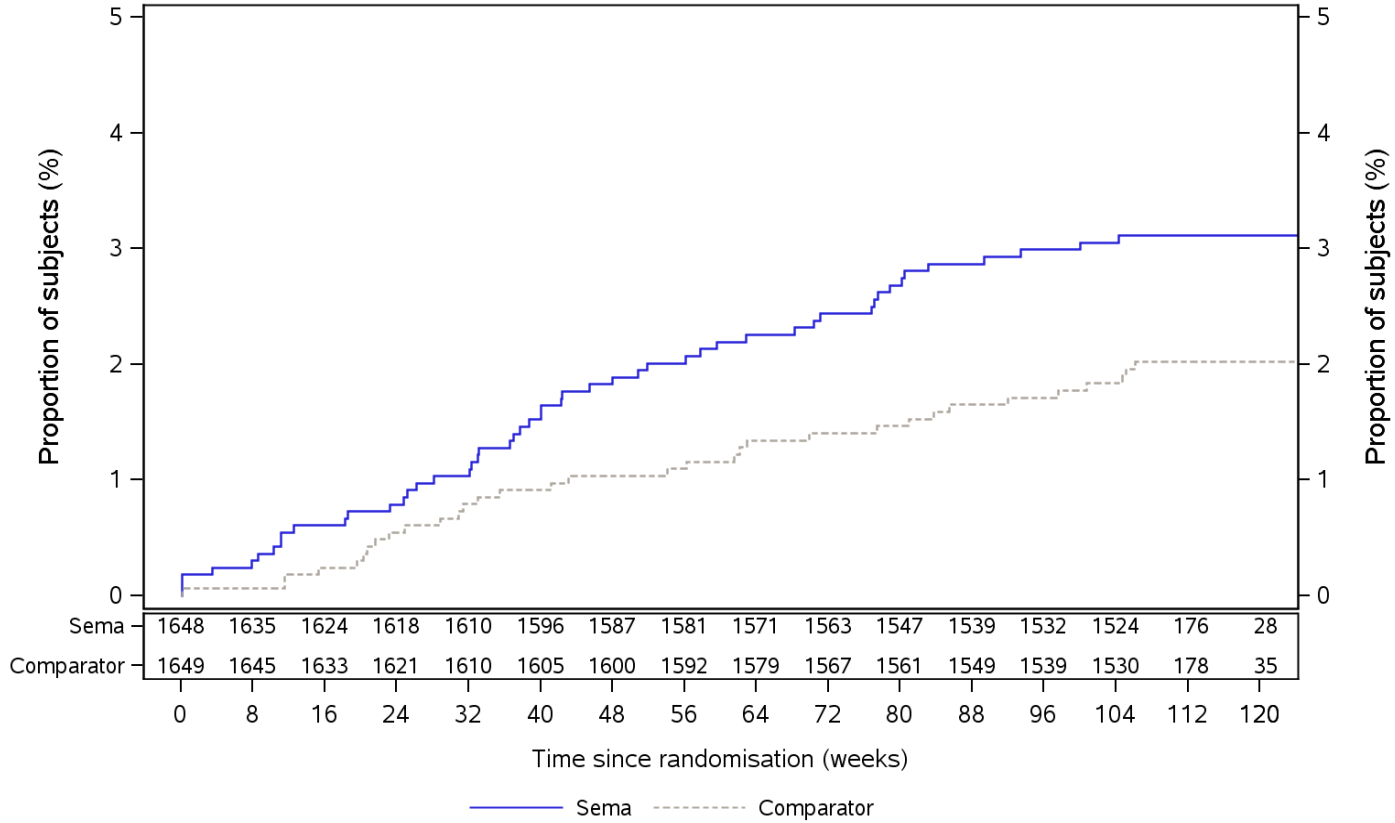
61 Adverse events - preferred term "Decreased appetite" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:01:07 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_decrappe_ae_all_s6.png

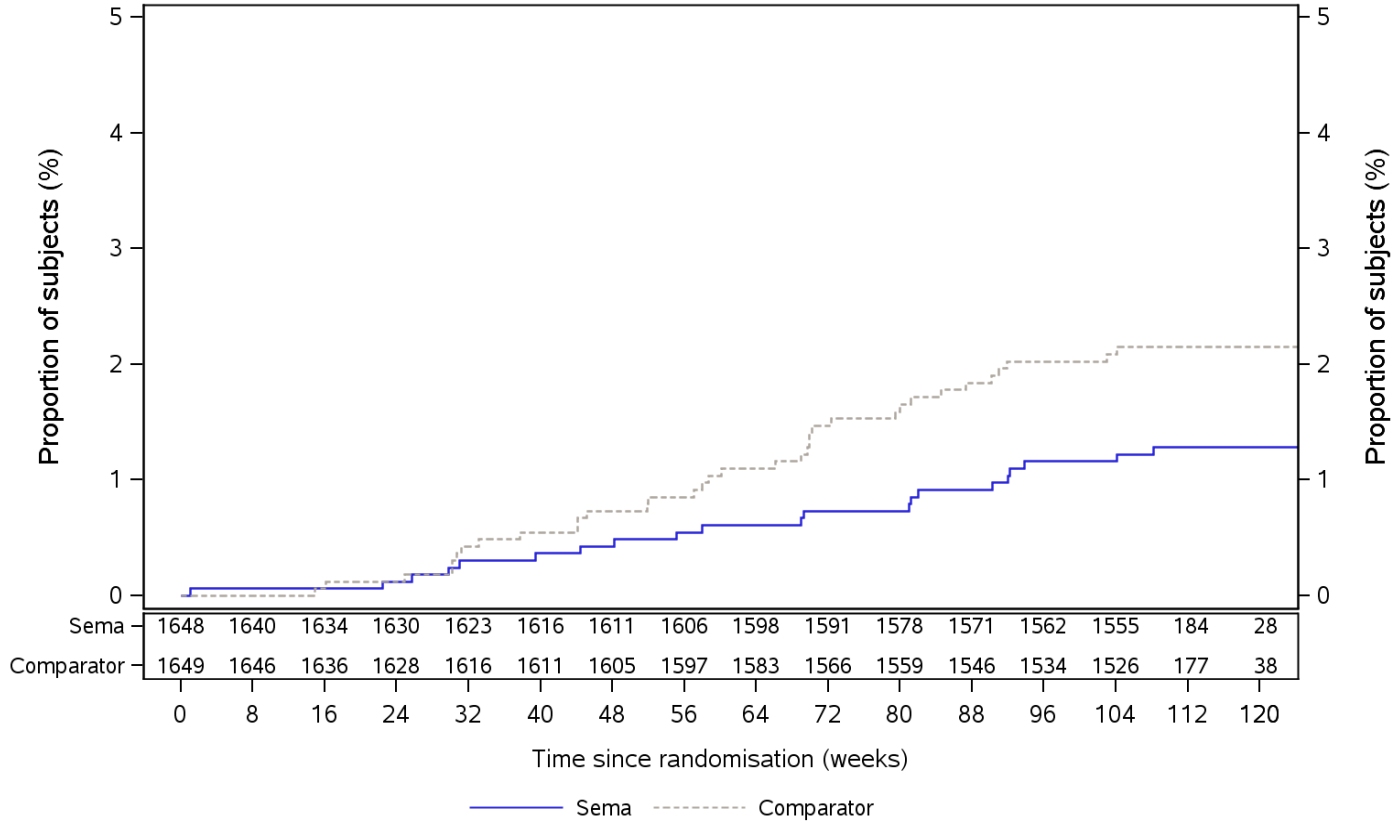
62 Adverse events - preferred term "Depression" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:01:26 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_depressi_ae_all_s6.png

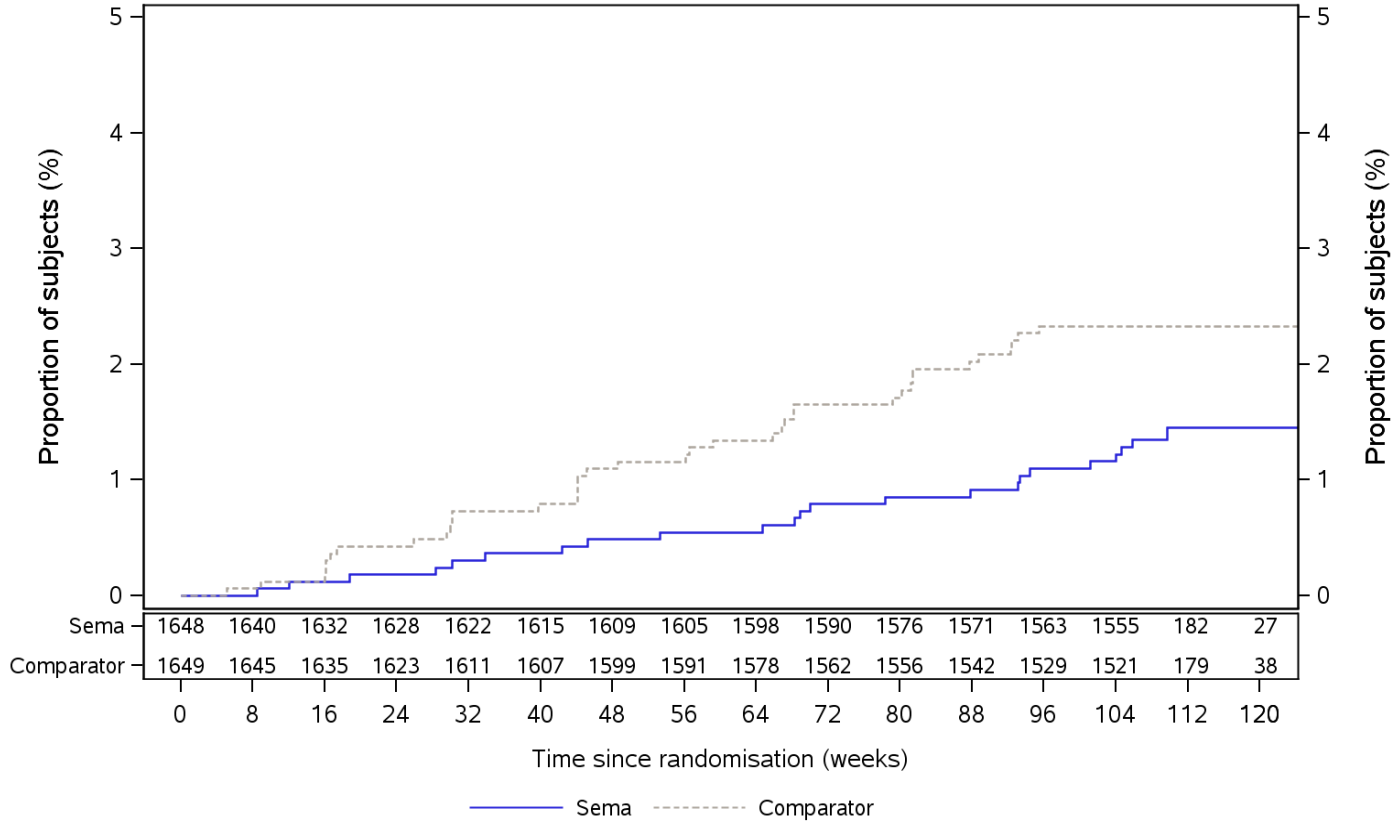
63 Adverse events - preferred term "Diabetes mellitus" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:01:45 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabmell_ae_all_s6.png

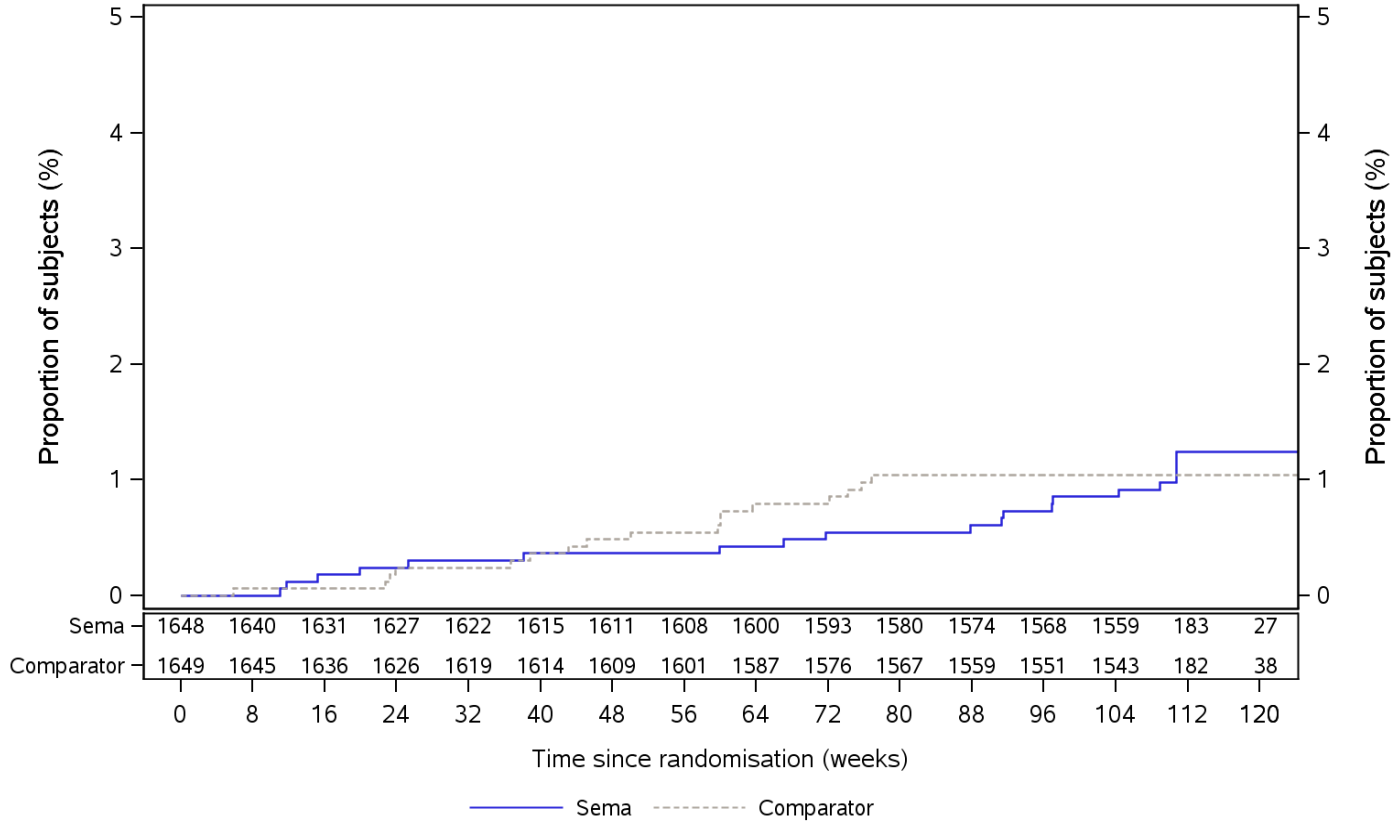
64 Adverse events - preferred term "Diabetes mellitus inadequate control" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:02:04 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diamelina_ae_all_s6.png

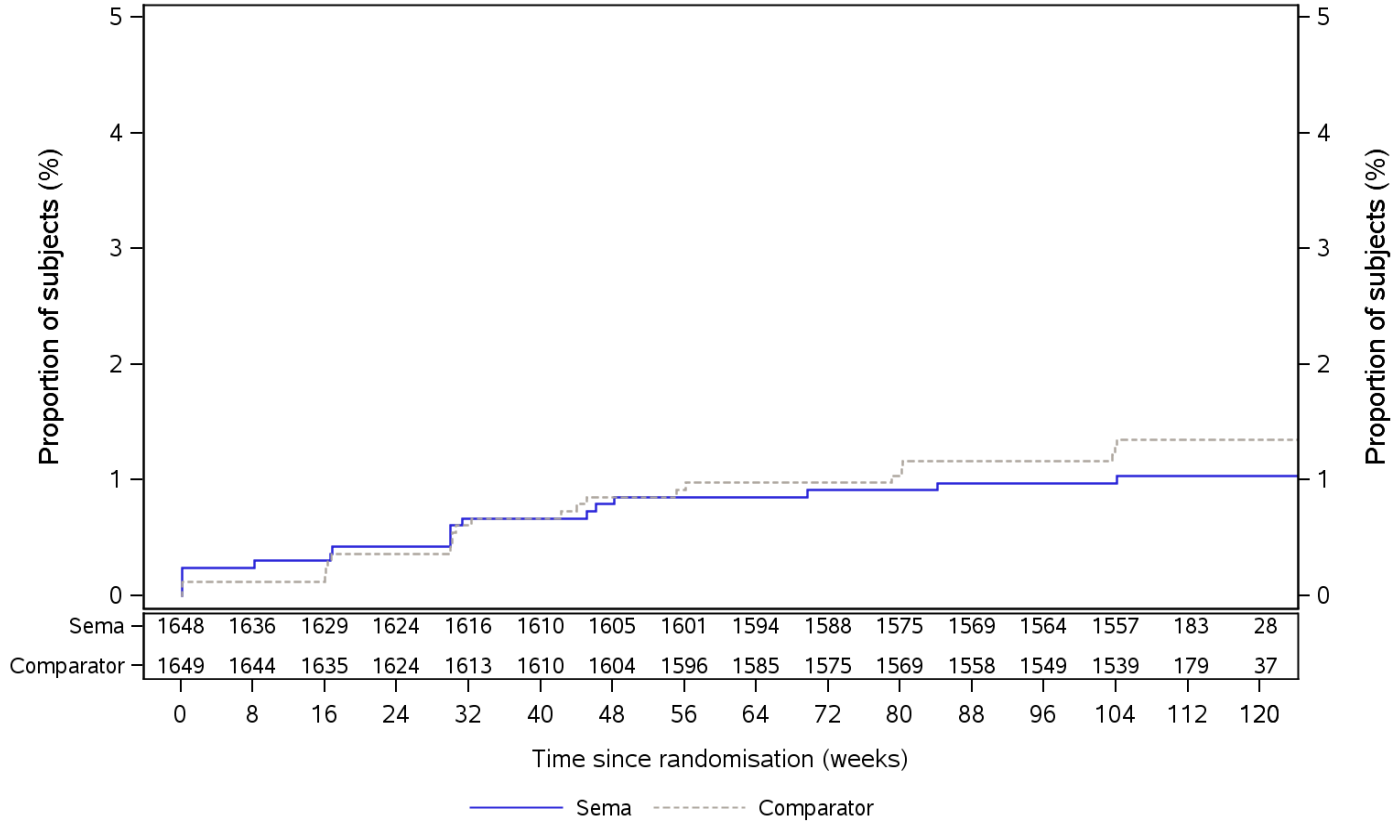
65 Adverse events - preferred term "Diabetic foot" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:02:24 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabfoot_ae_all_s6.png

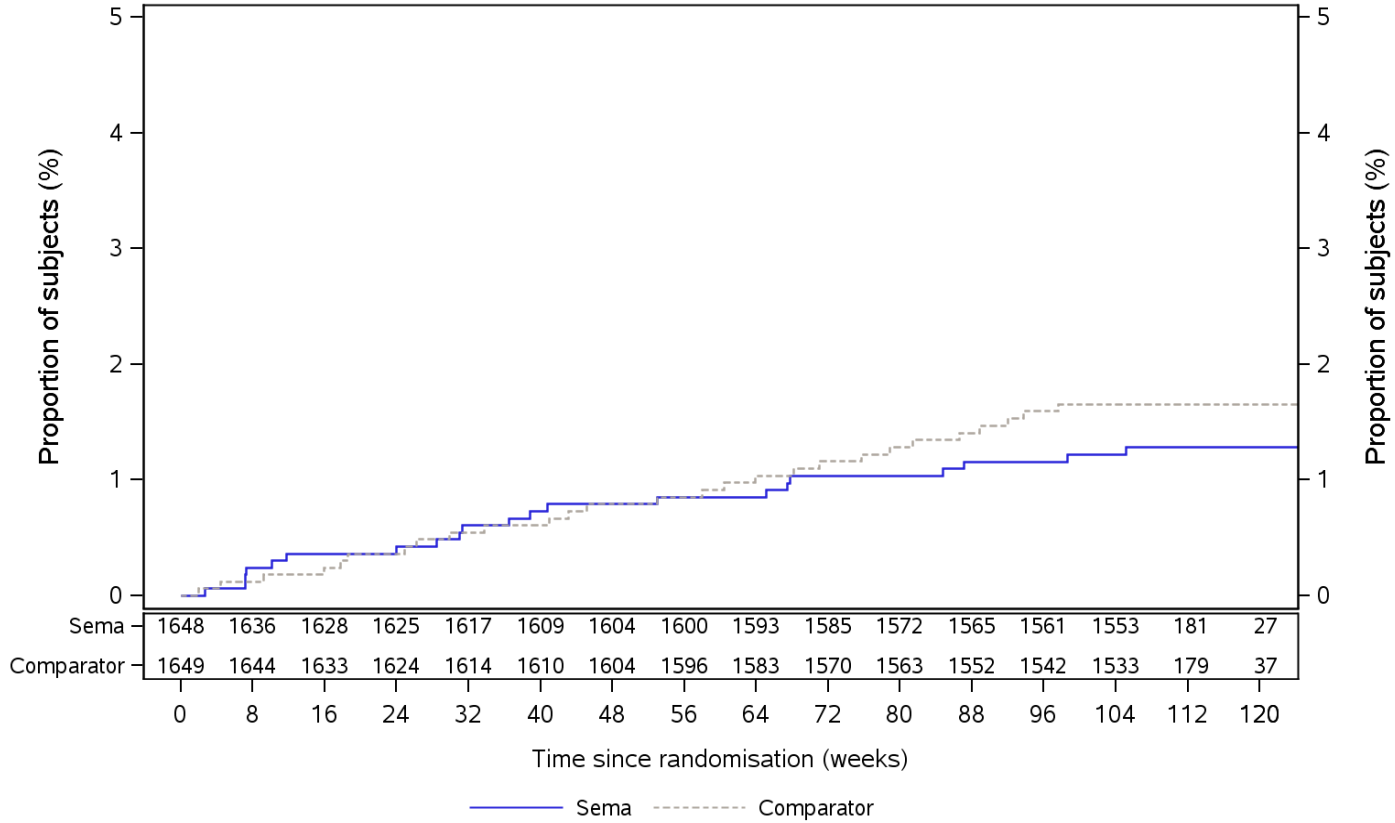
66 Adverse events - preferred term "Diabetic nephropathy" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:02:44 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabneph_ae_all_s6.png

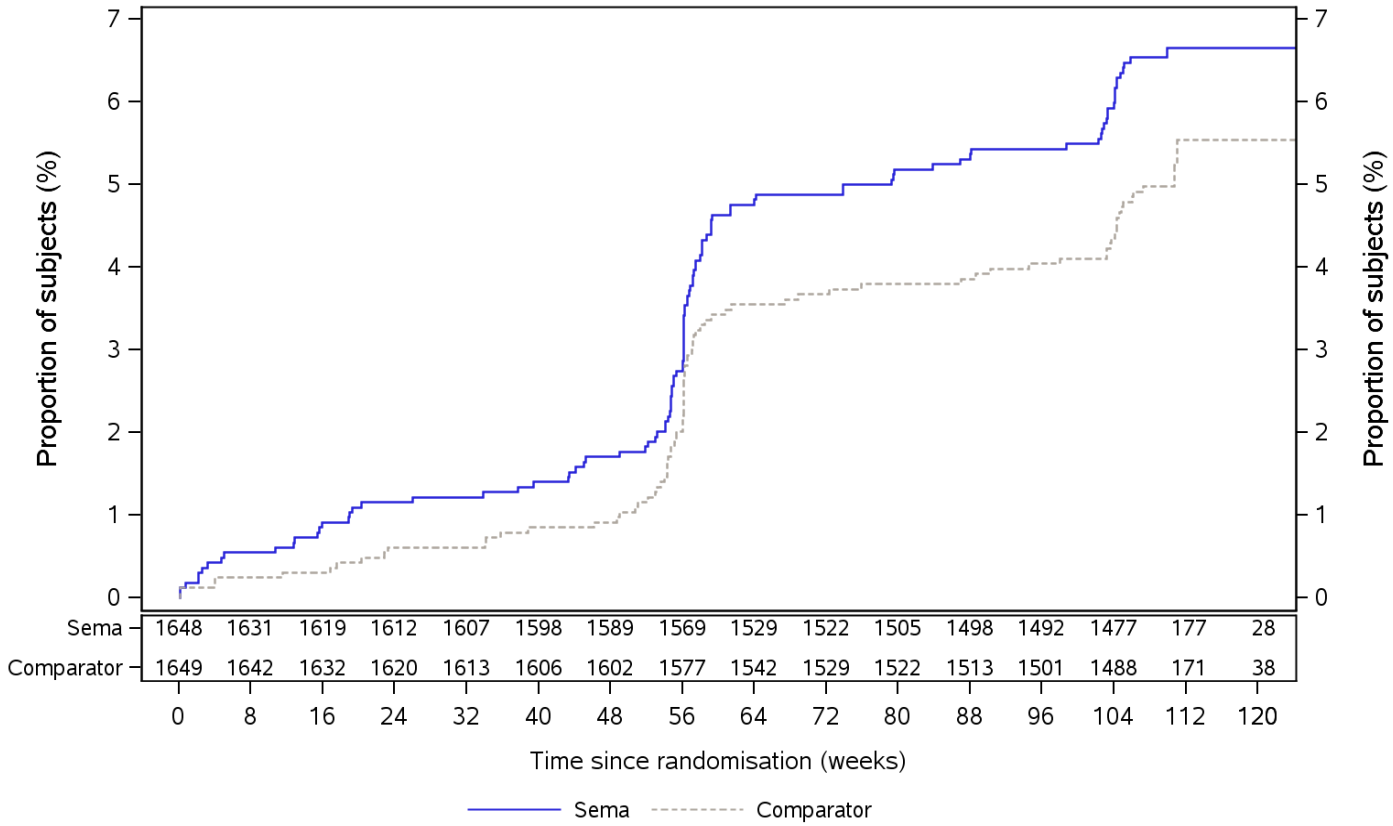
67 Adverse events - preferred term "Diabetic neuropathy" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:03:02 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabneur_ae_all_s6.png

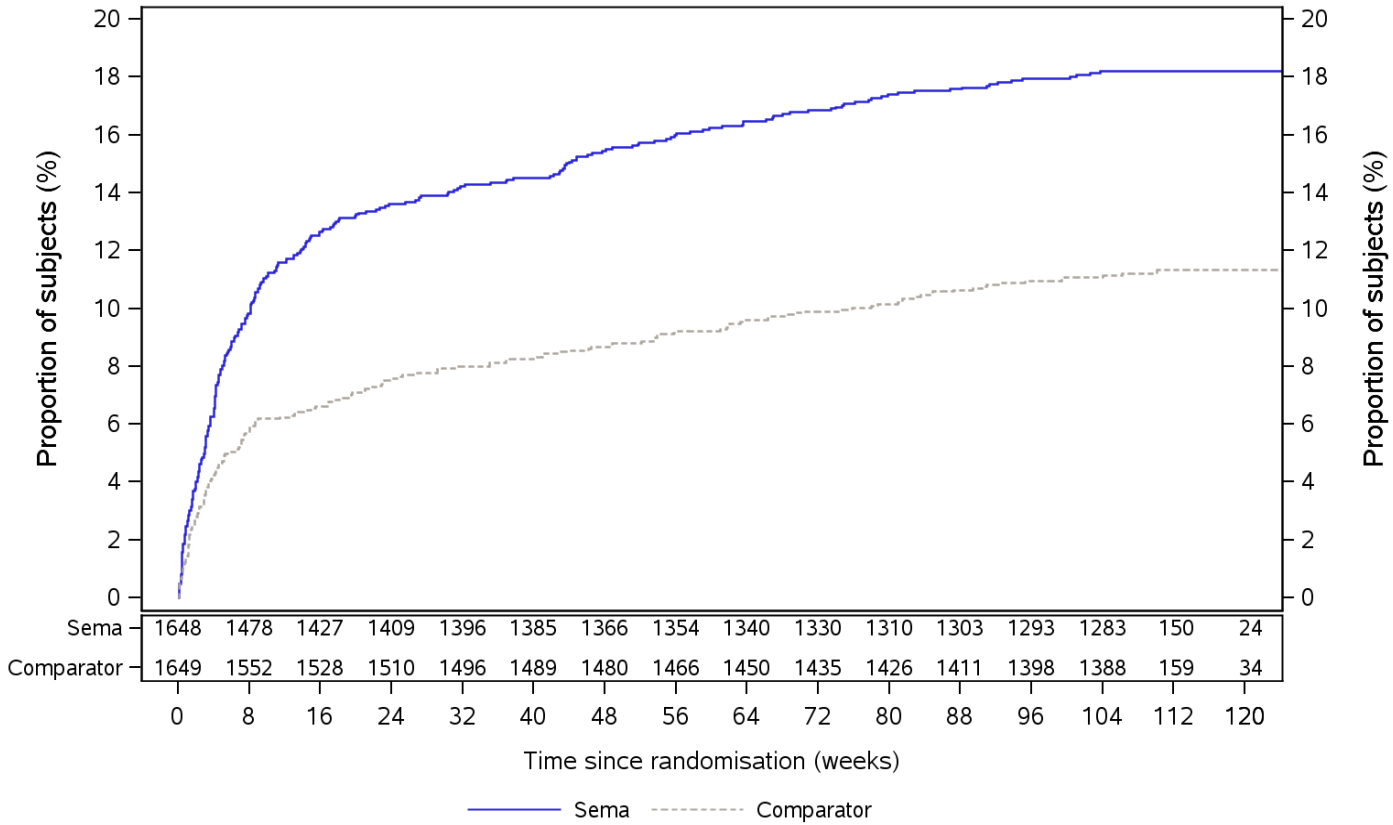
68 Adverse events - preferred term "Diabetic retinopathy" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:03:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabreti_ae_all_s6.png

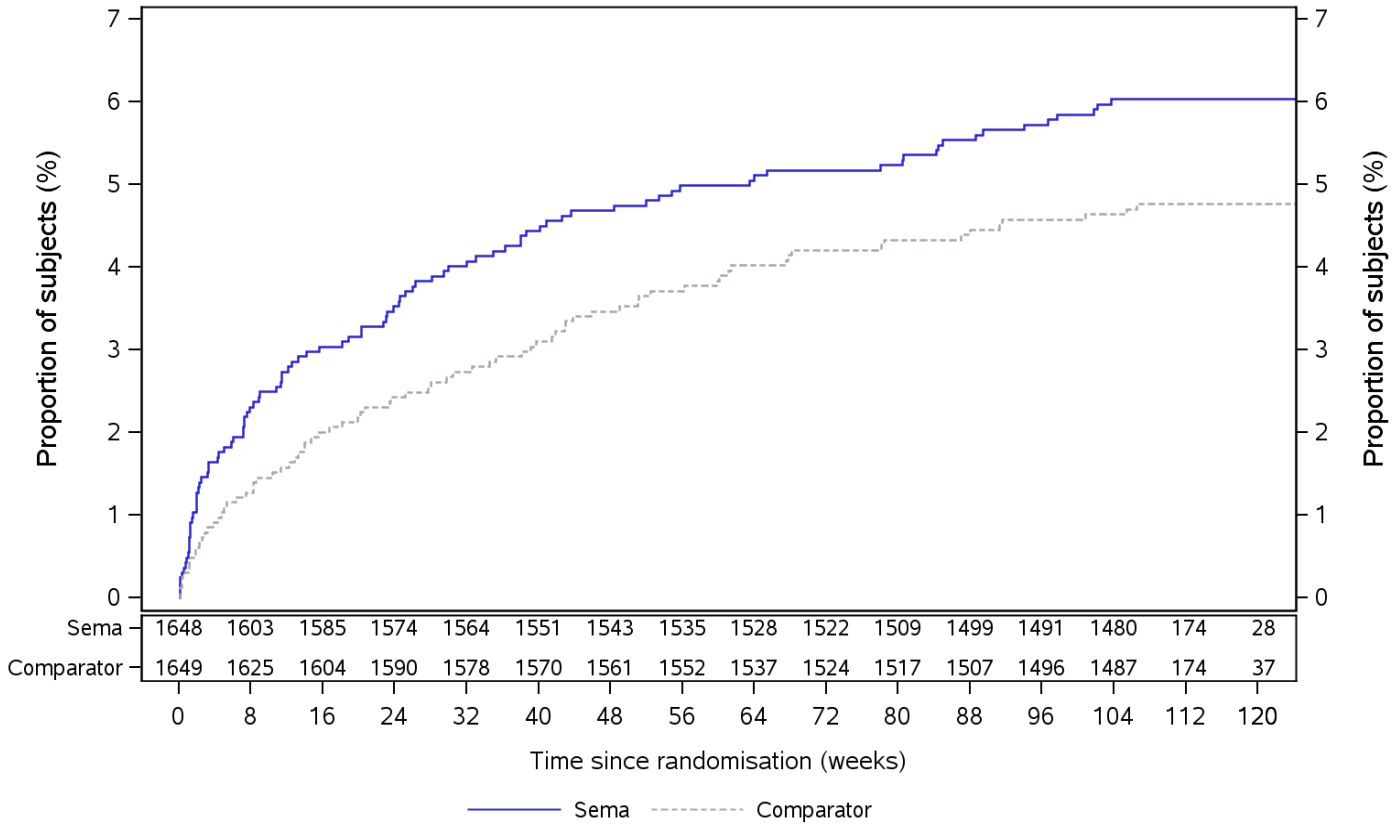
69 Adverse events - preferred term "Diarrhoea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:03:39 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diarrhoe_ae_all_s6.png

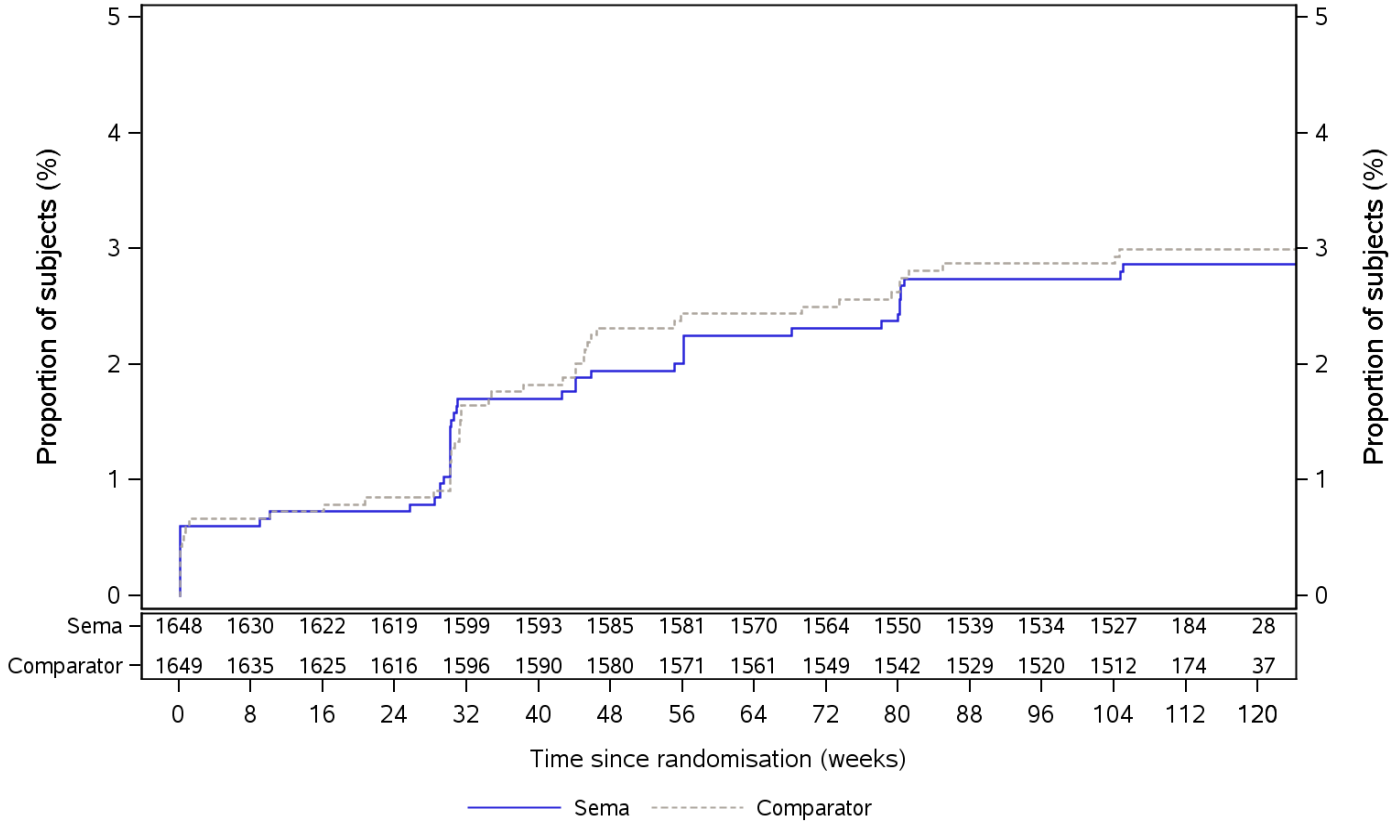
70 Adverse events - preferred term "Dizziness" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:03:57 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dizzines_ae_all_s6.png

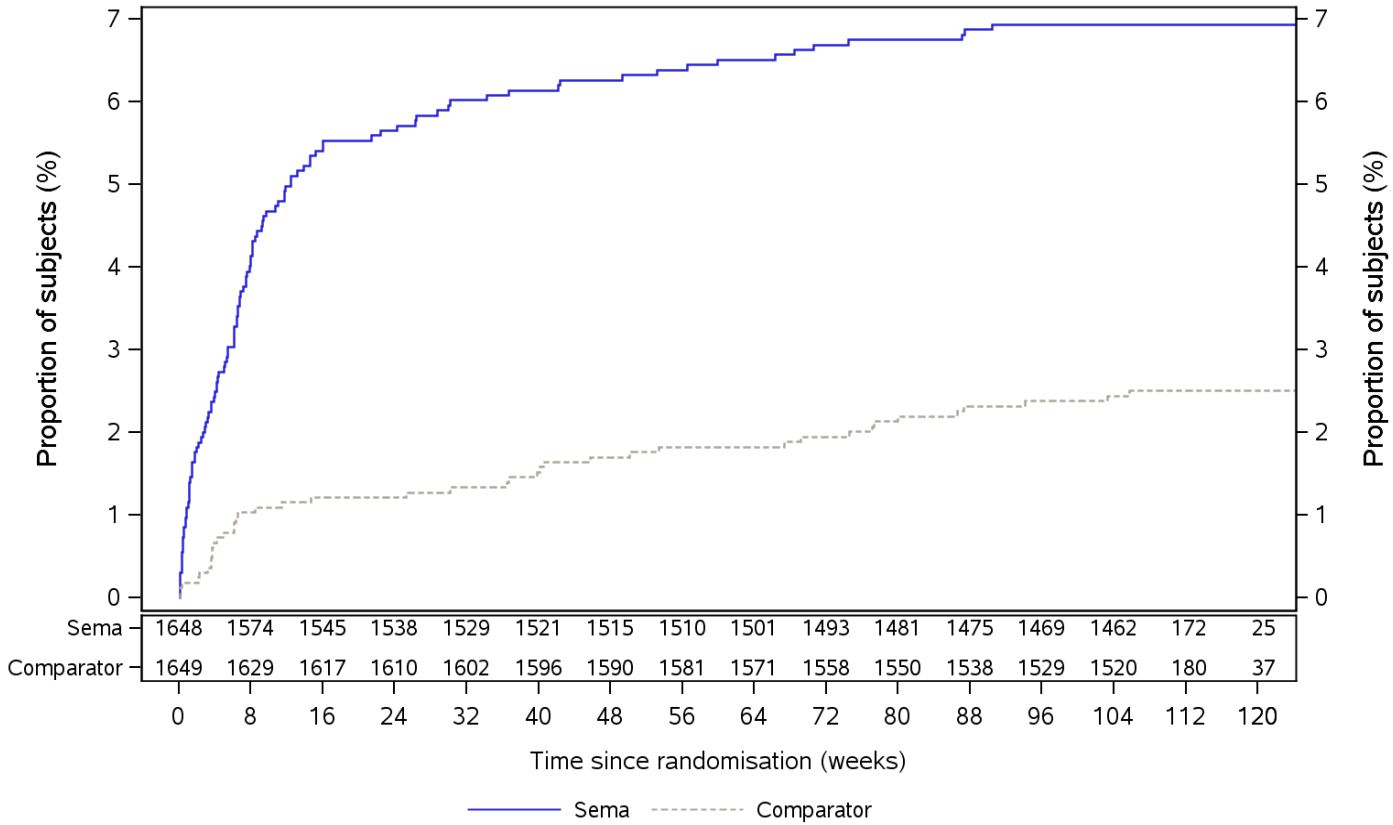
71 Adverse events - preferred term "Dyslipidaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:04:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dyslipid_ae_all_s6.png

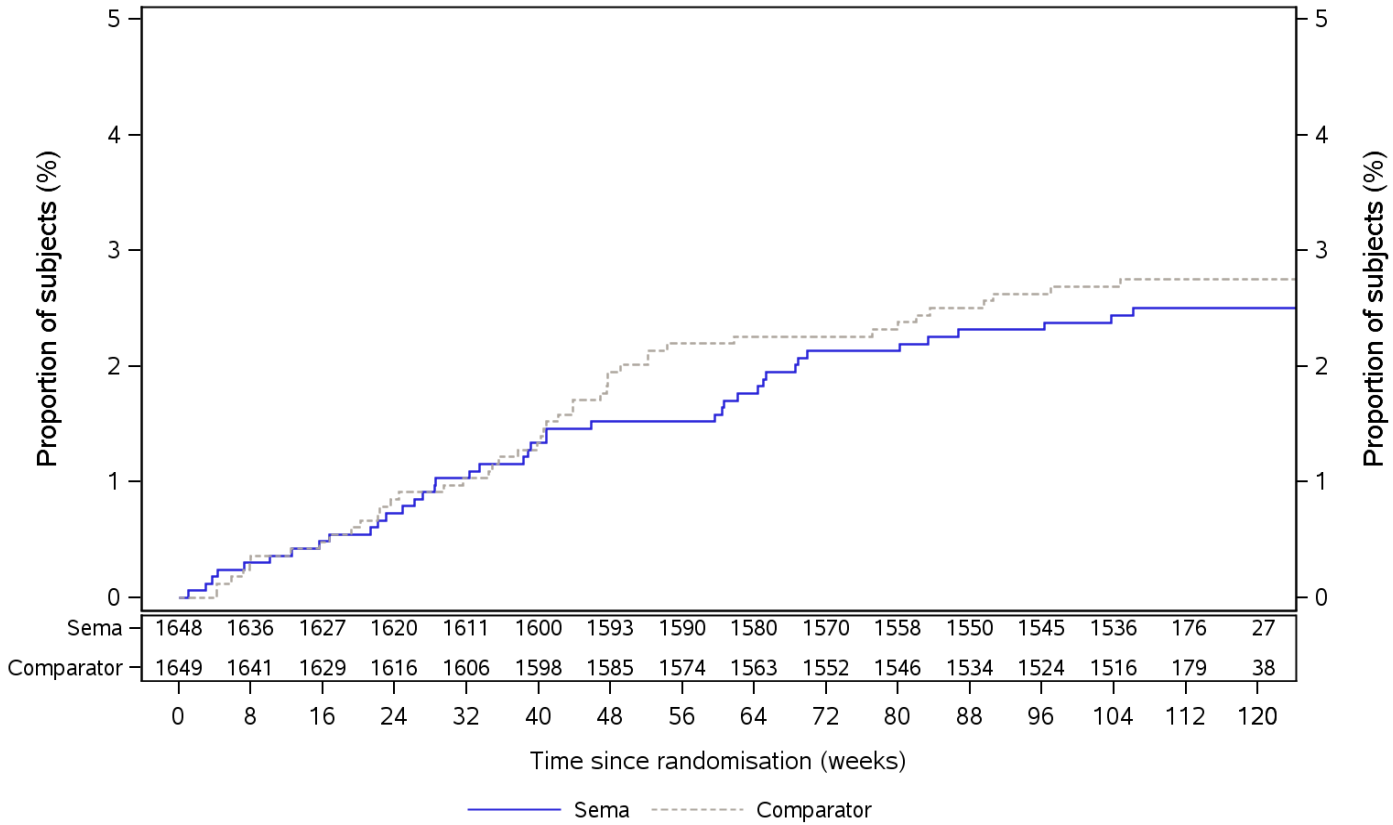
72 Adverse events - preferred term "Dyspepsia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:04:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dyspepsi_ae_all_s6.png

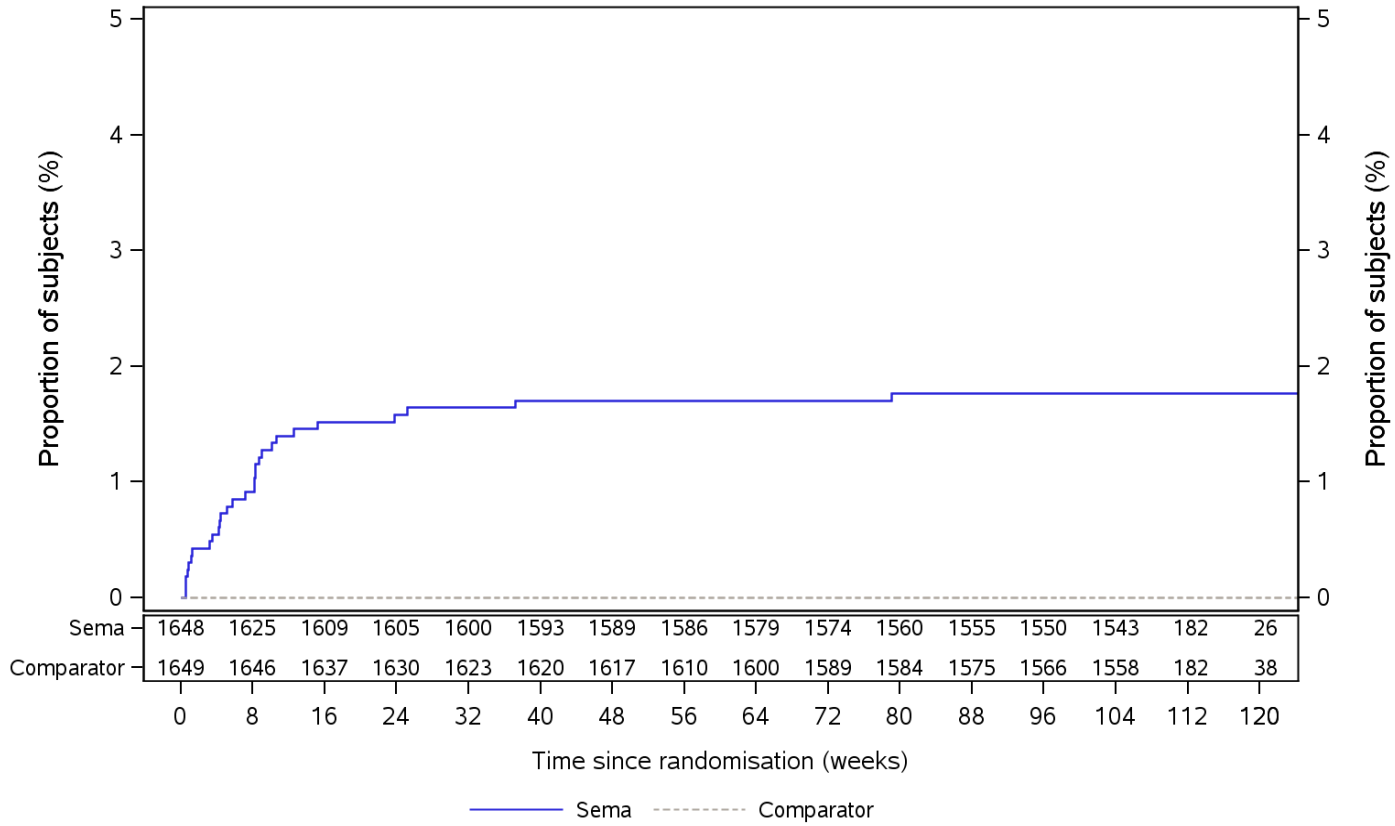
73 Adverse events - preferred term "Dyspnoea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:04:54 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dyspnoea_ae_all_s6.png

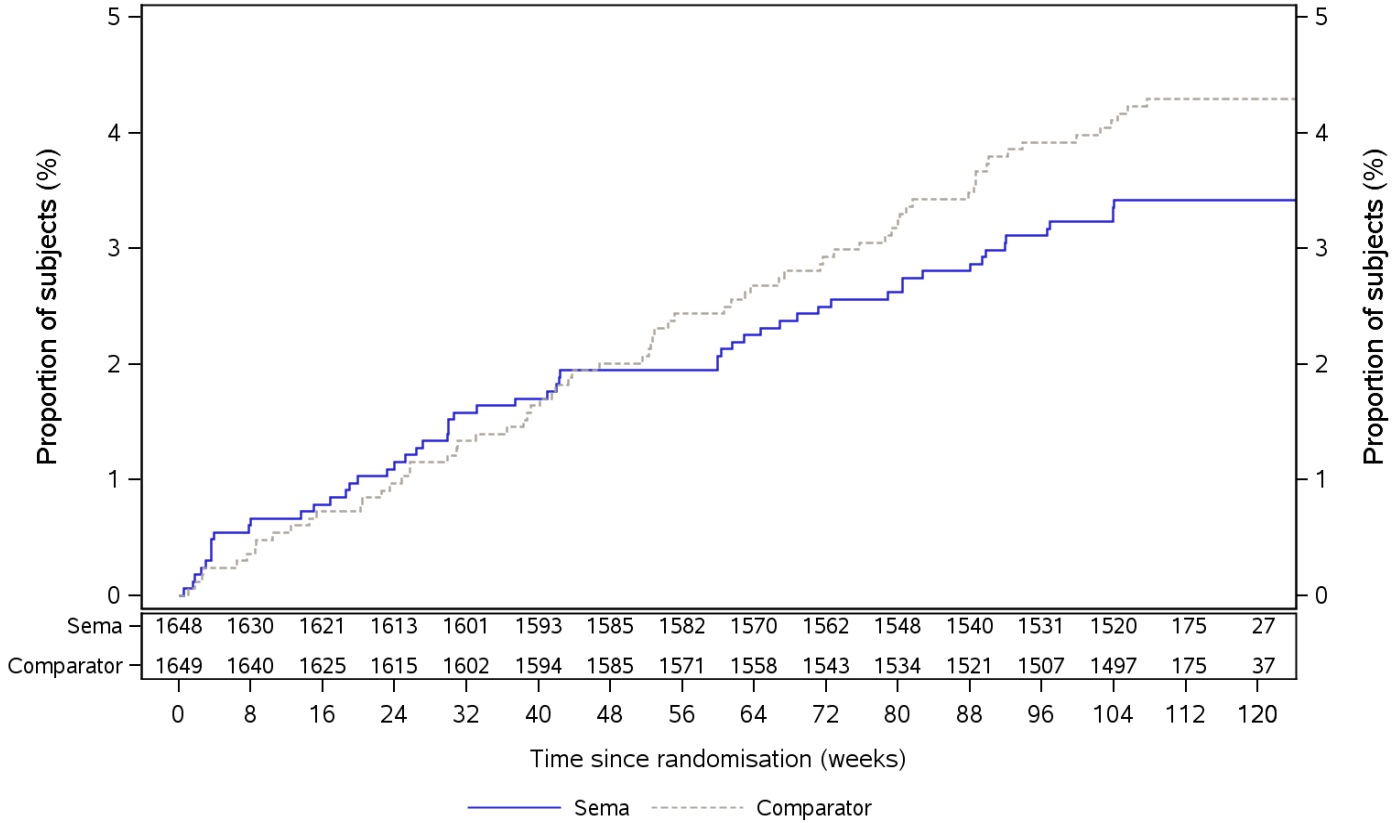
74 Adverse events - preferred term "Eructation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:05:13 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_eructati_ae_all_s6.png

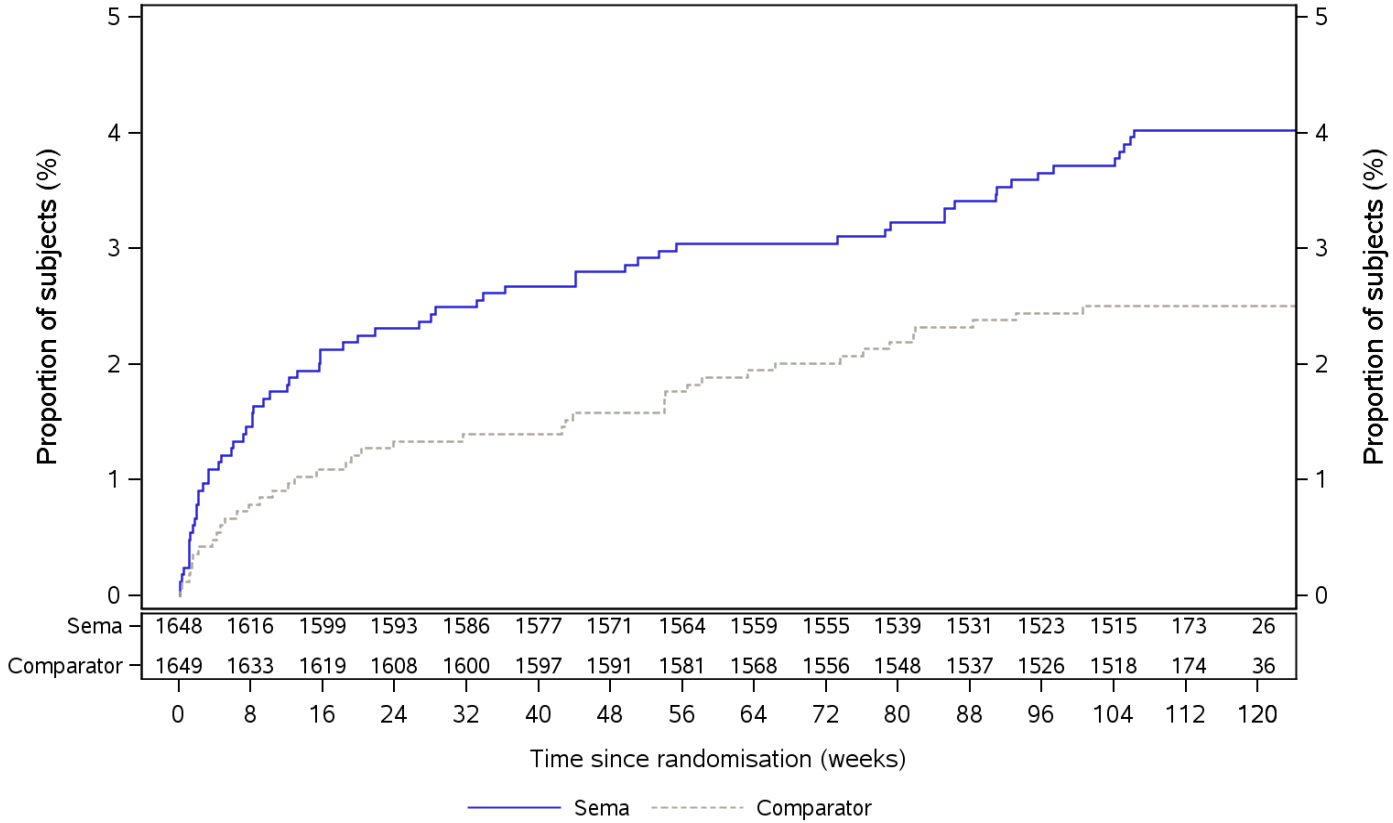
75 Adverse events - preferred term "Fall" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:05:33 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_fall_ae_all_s6.png

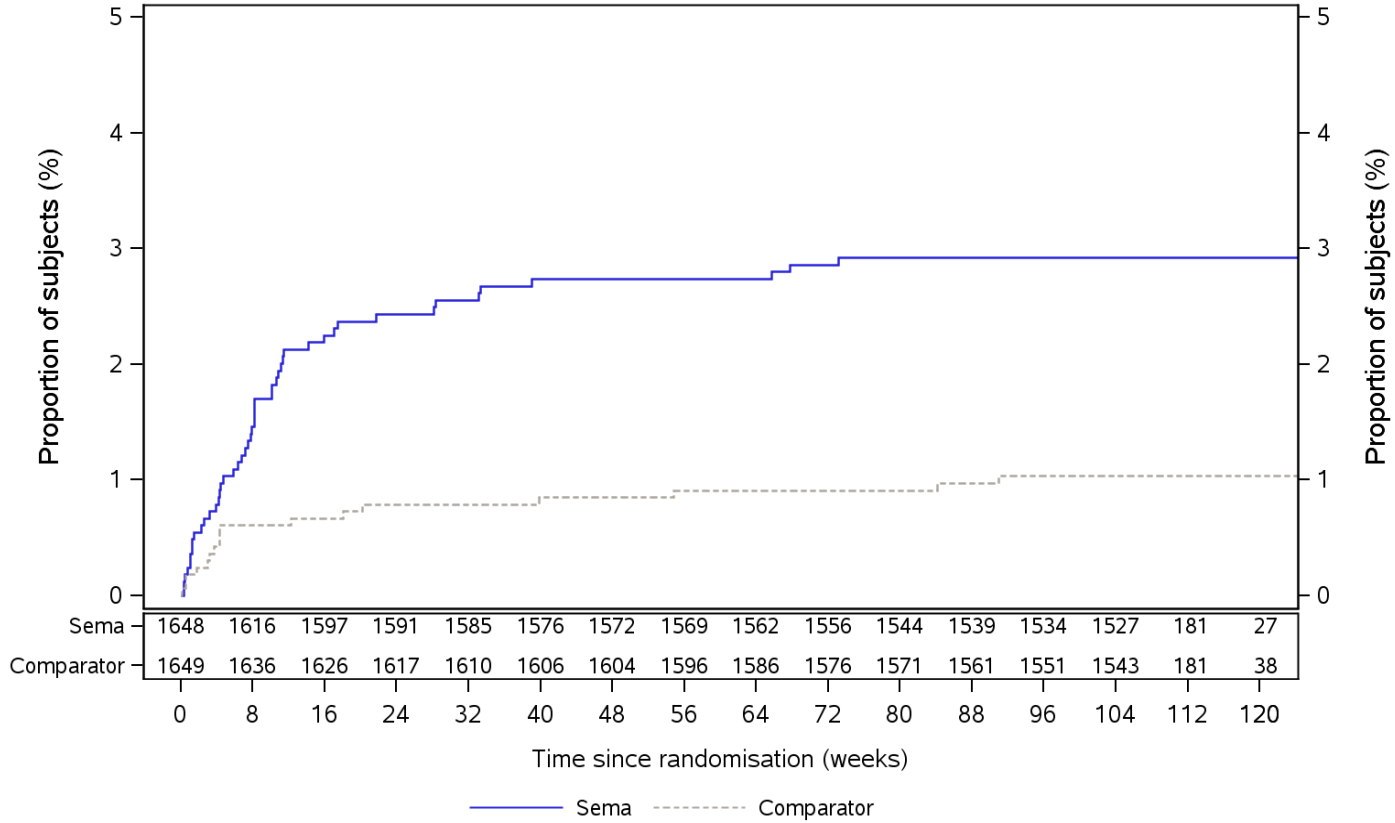
76 Adverse events - preferred term "Fatigue" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:05:51 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_fatigue_ae_all_s6.png

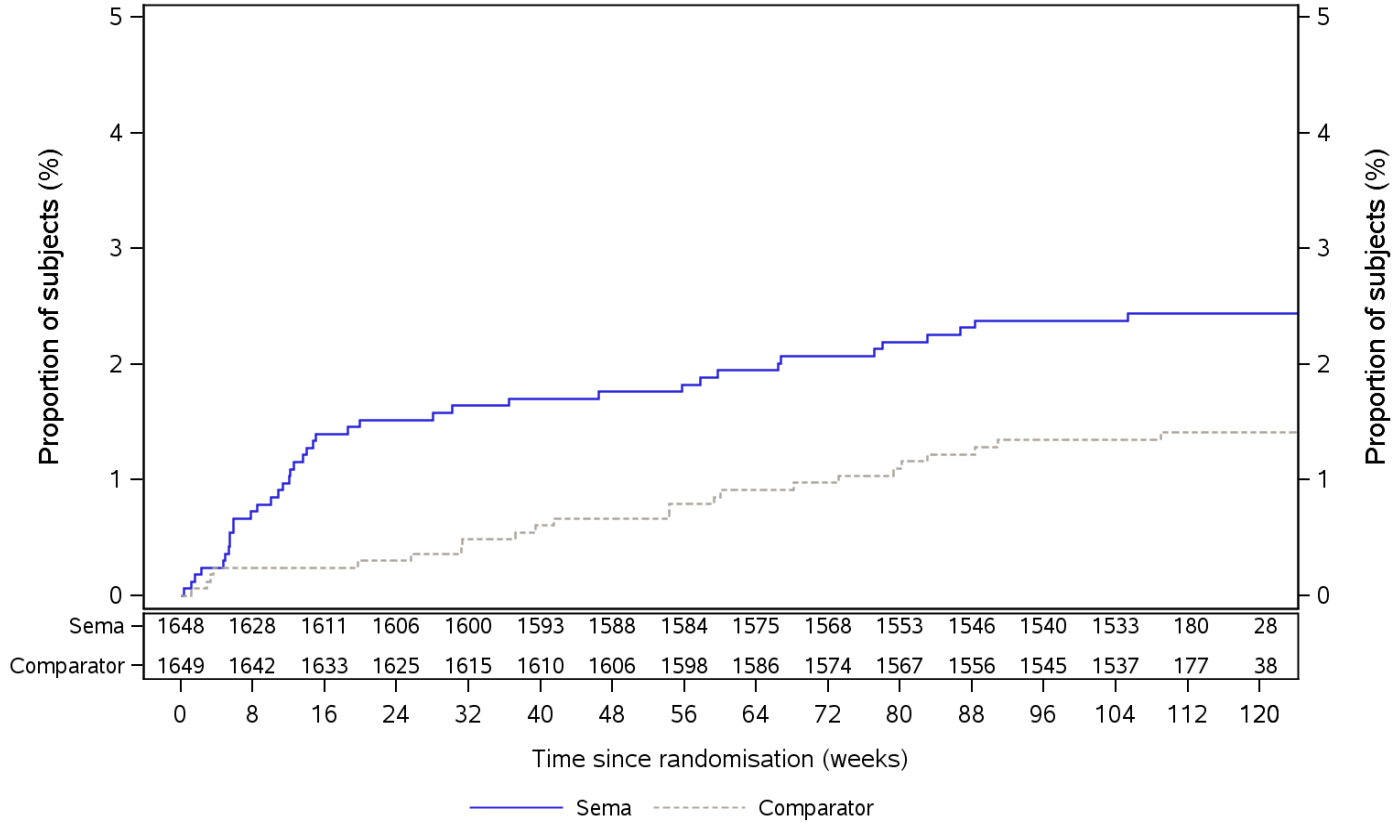
77 Adverse events - preferred term "Flatulence" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:06:11 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_flatulen_ae_all_s6.png

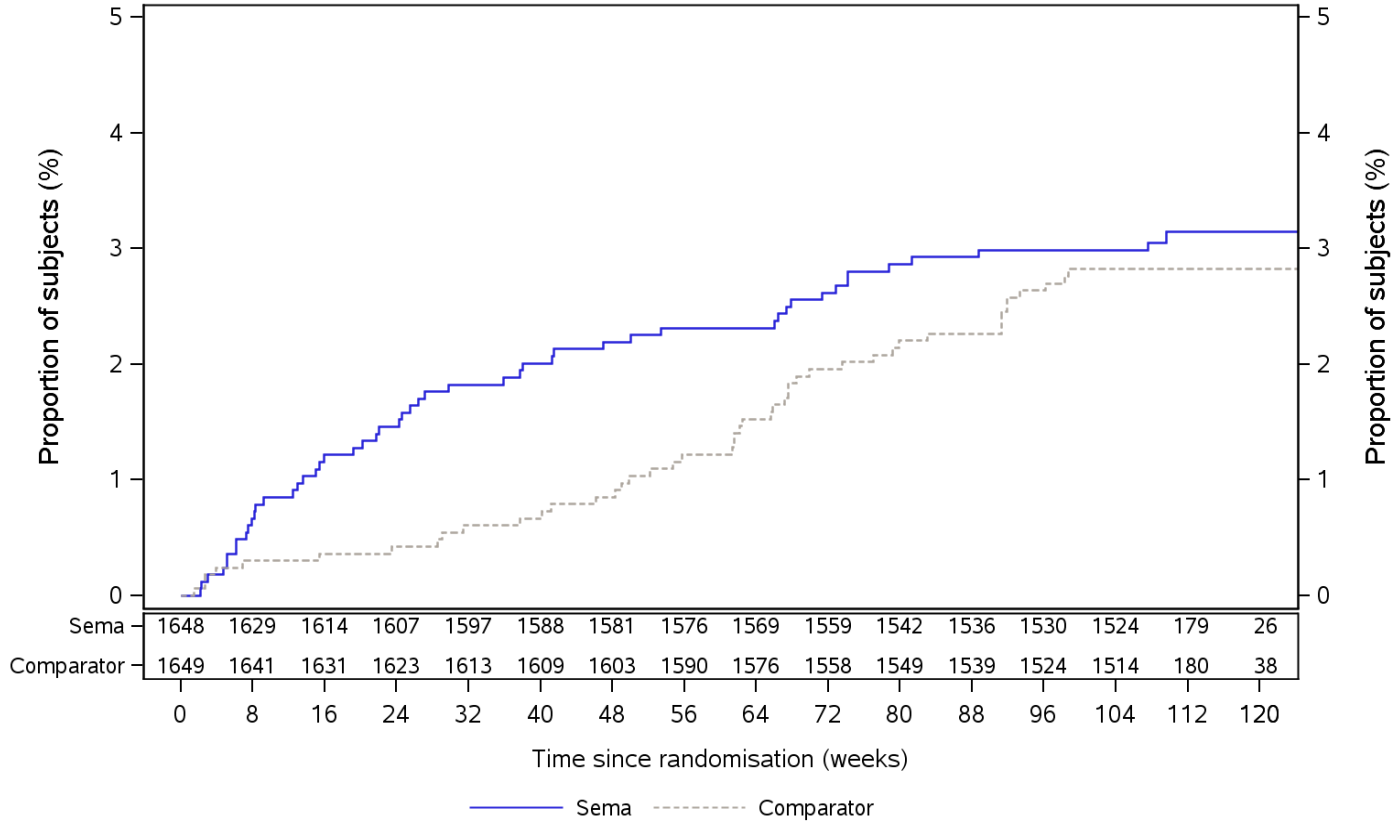
78 Adverse events - preferred term "Gastritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:06:37 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gastriti_ae_all_s6.png

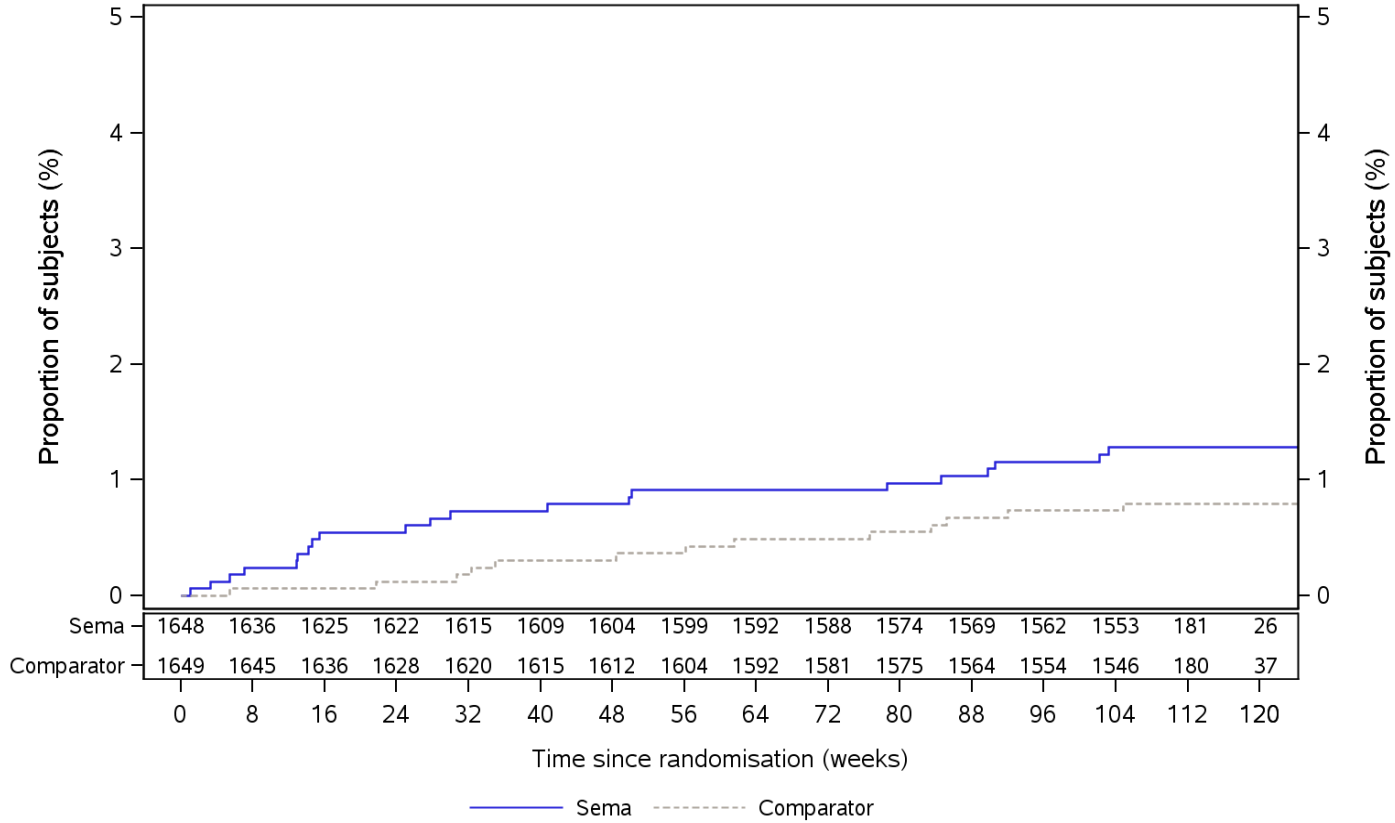
79 Adverse events - preferred term "Gastroenteritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:07:01 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gastroen_ae_all_s6.png

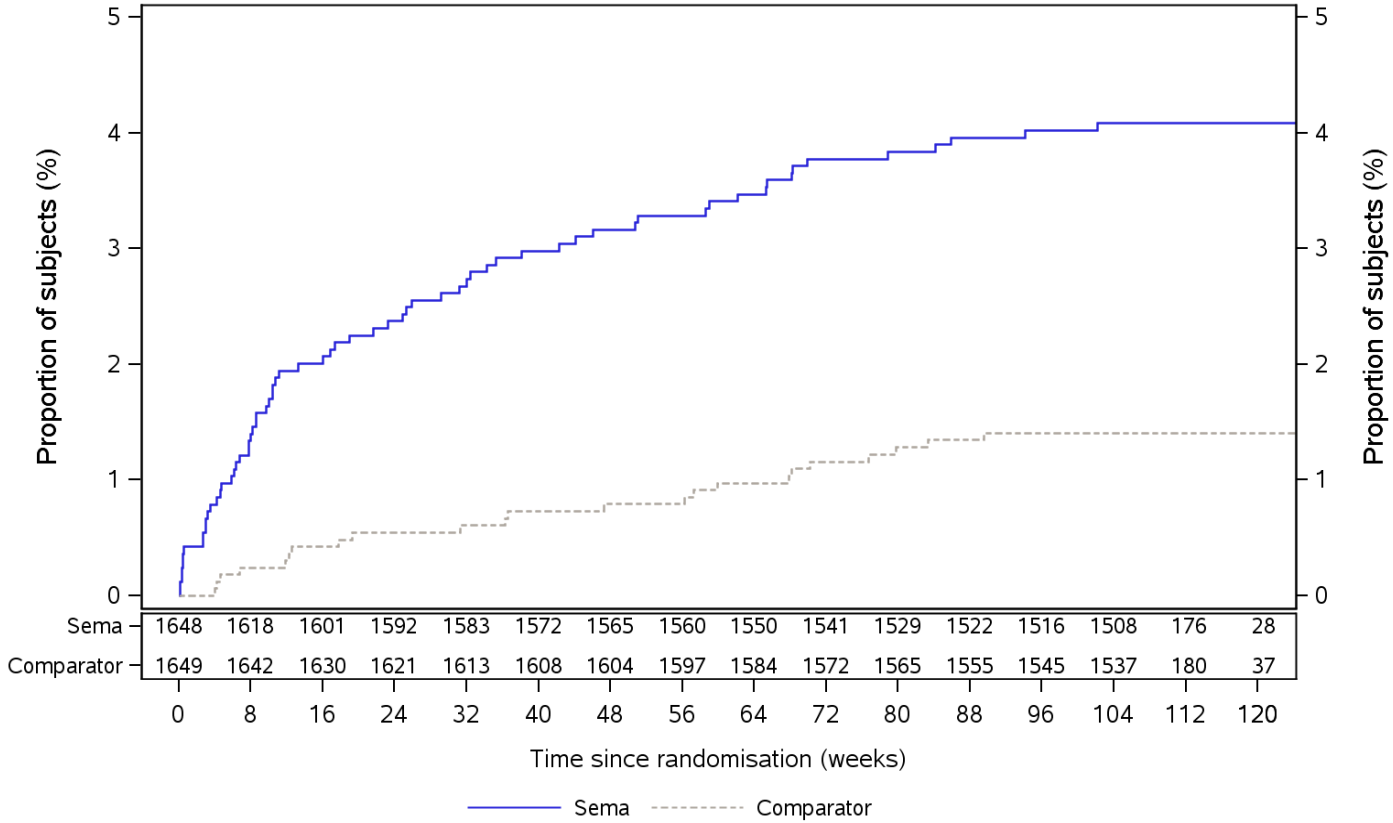
80 Adverse events - preferred term "Gastroenteritis viral" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:07:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gastvira_ae_all_s6.png

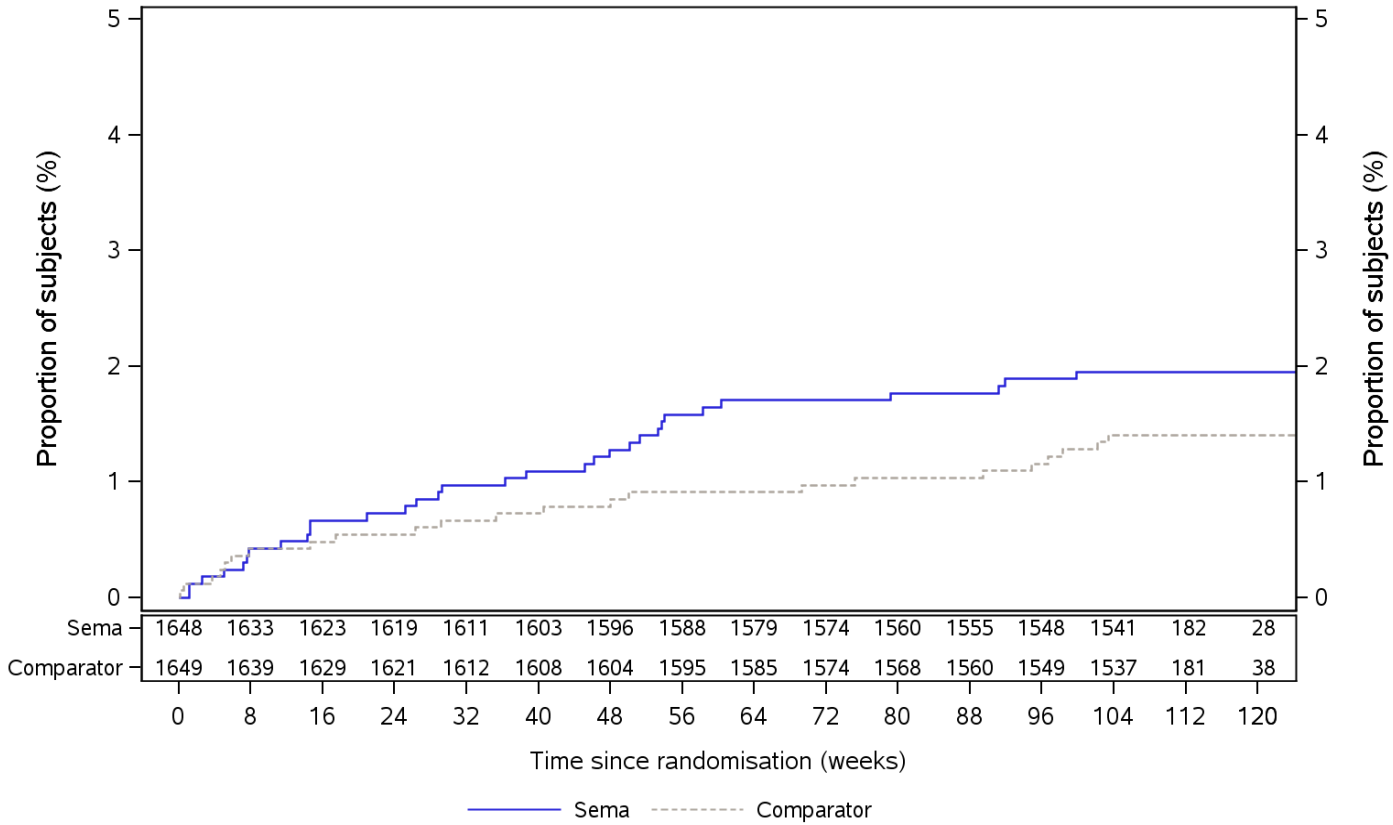
81 Adverse events - preferred term "Gastrooesophageal reflux disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:07:40 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gasrefdis_ae_all_s6.png

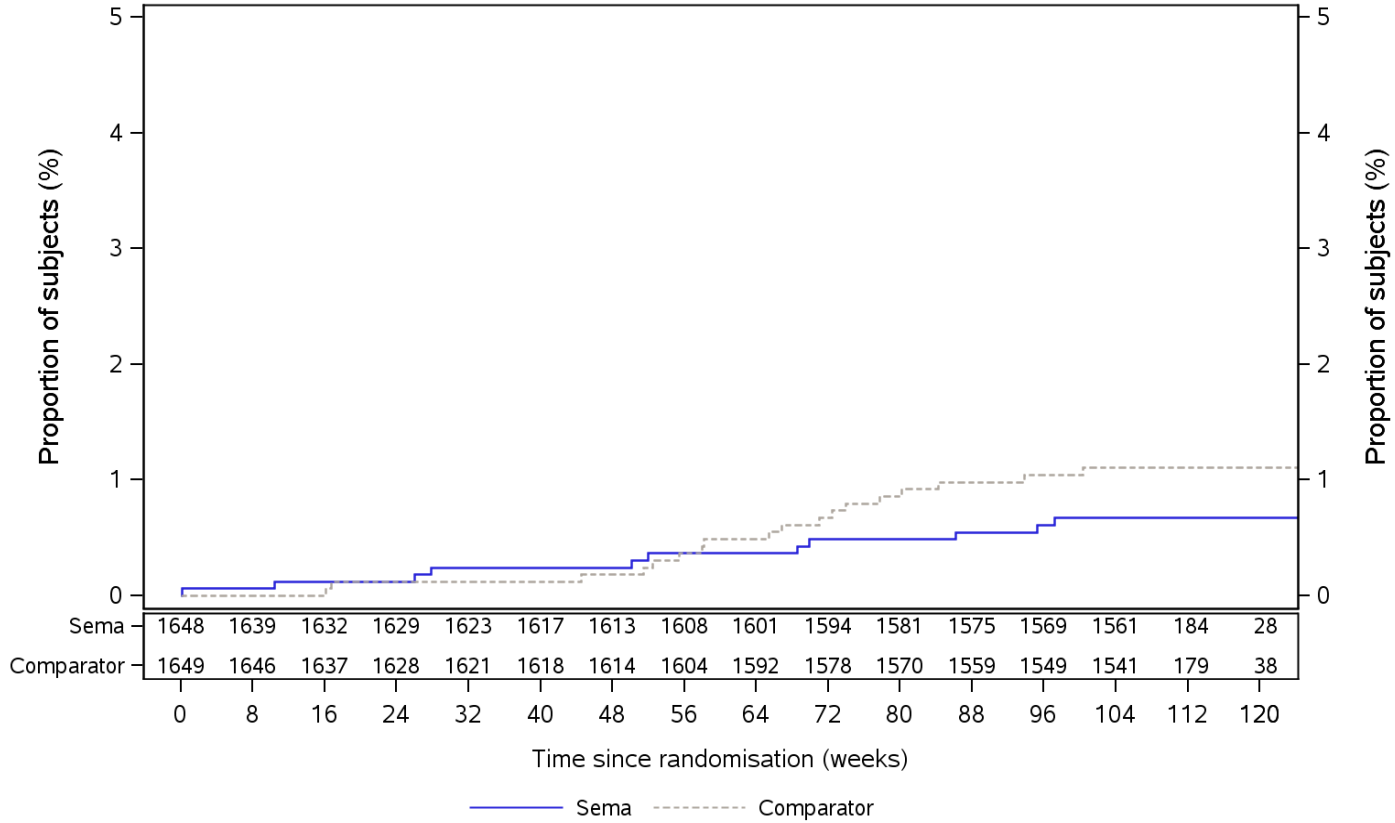
82 Adverse events - preferred term "Gout" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:07:59 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gout_ae_all_s6.png

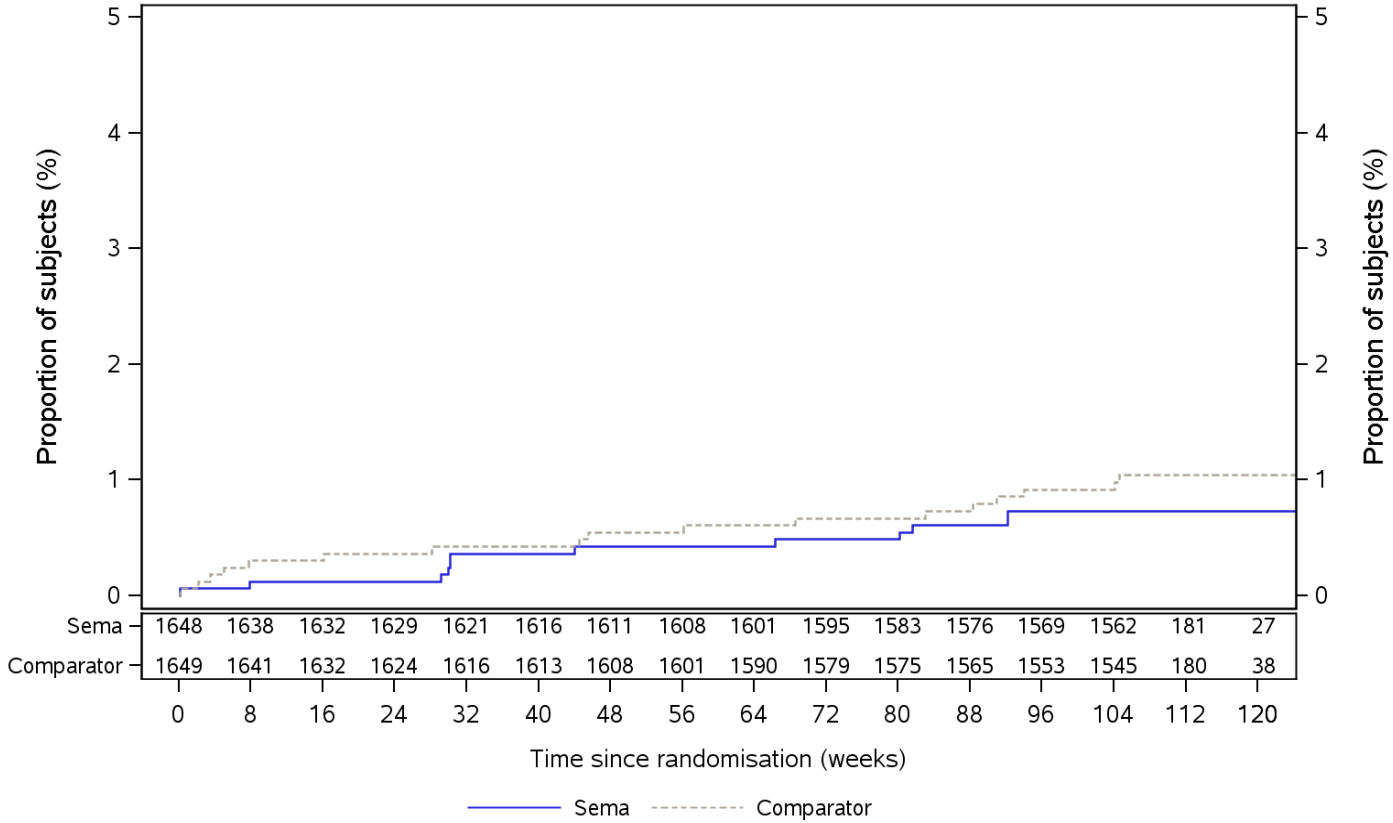
83 Adverse events - preferred term "Haematuria" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:08:18 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_haematur_ae_all_s6.png

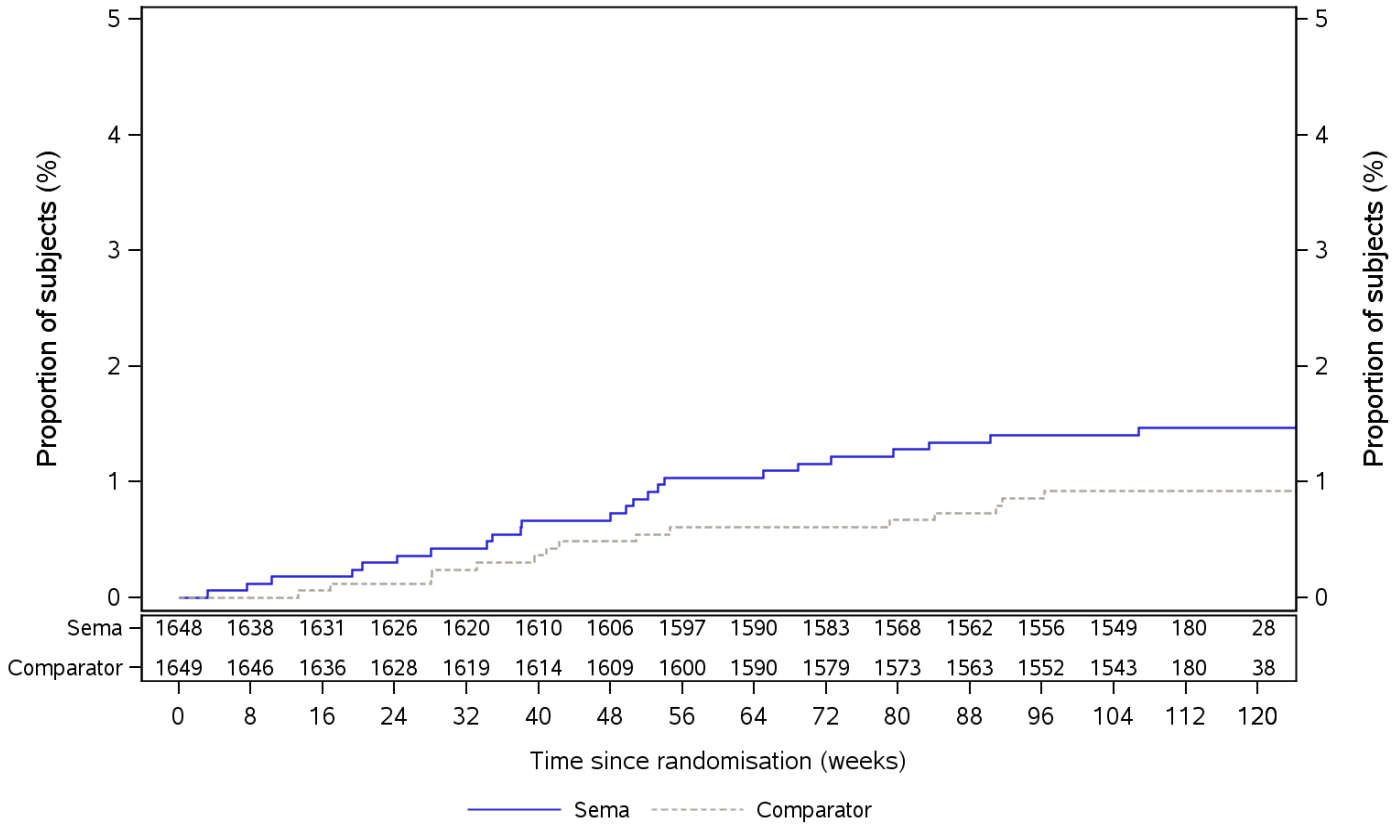
84 Adverse events - preferred term "Haemoglobin decreased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:08:38 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_haemdecr_ae_all_s6.png

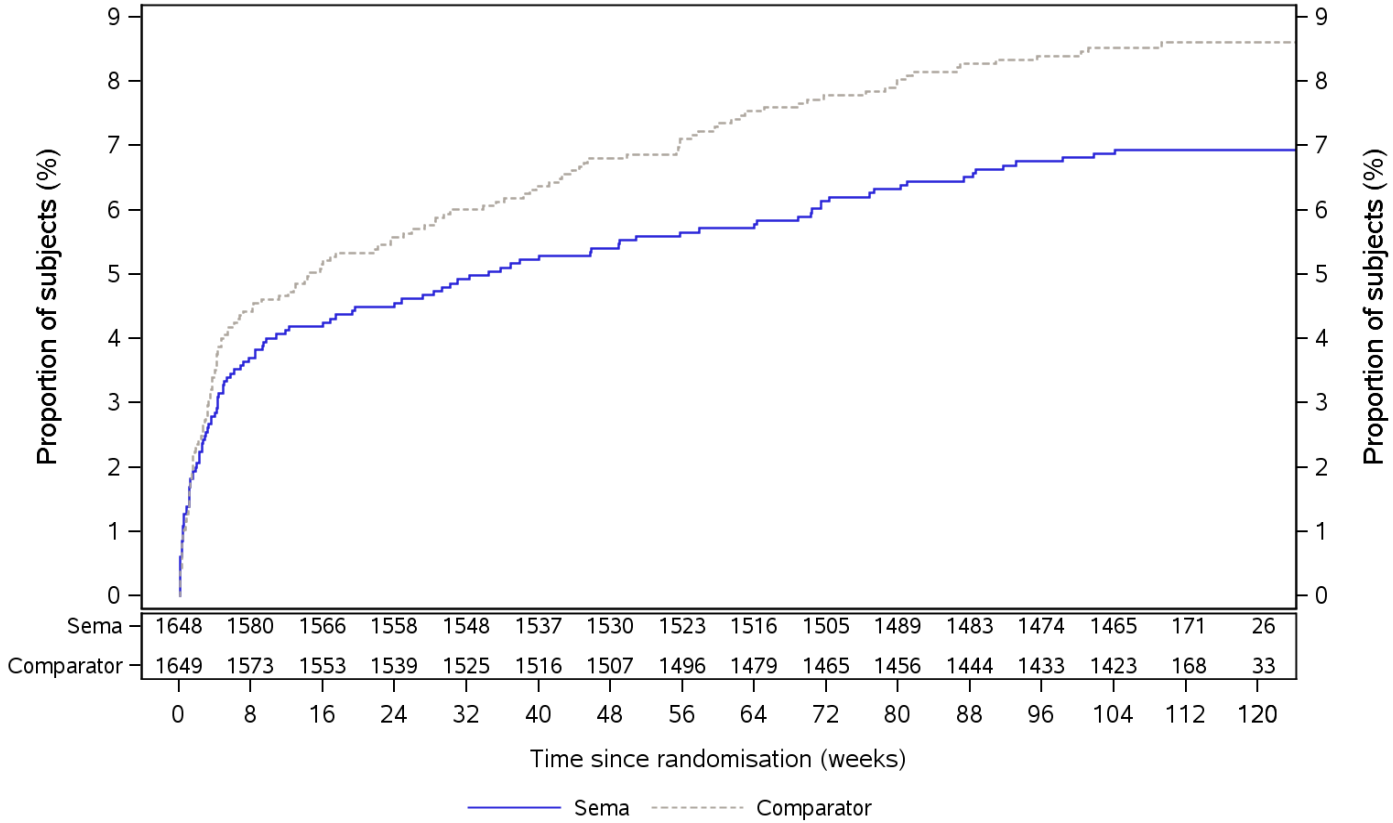
85 Adverse events - preferred term "Haemorrhoids" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:08:58 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_haemorrh_ae_all_s6.png

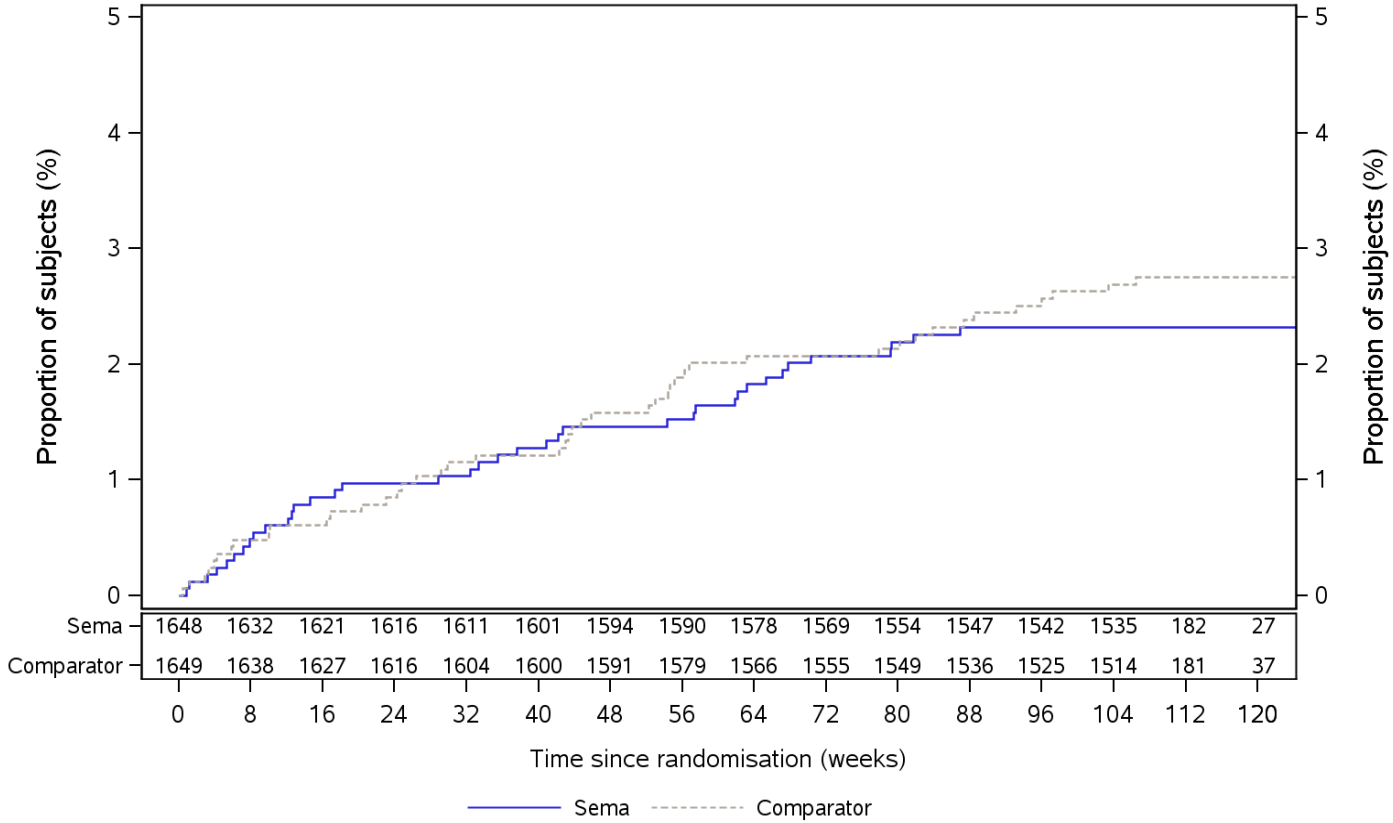
86 Adverse events - preferred term "Headache" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:09:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_headache_ae_all_s6.png

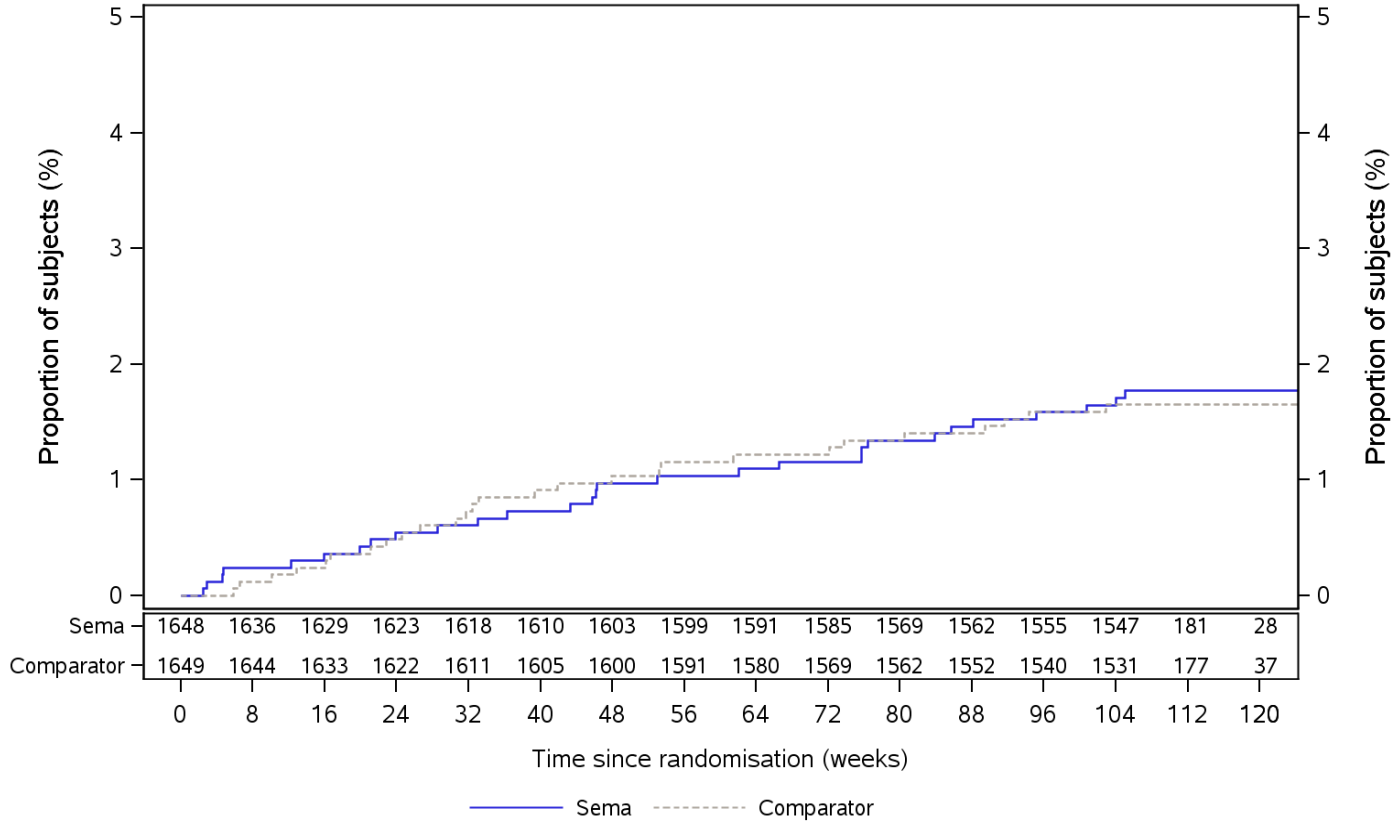
87 Adverse events - preferred term "Hepatic steatosis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:09:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hepastea_ae_all_s6.png

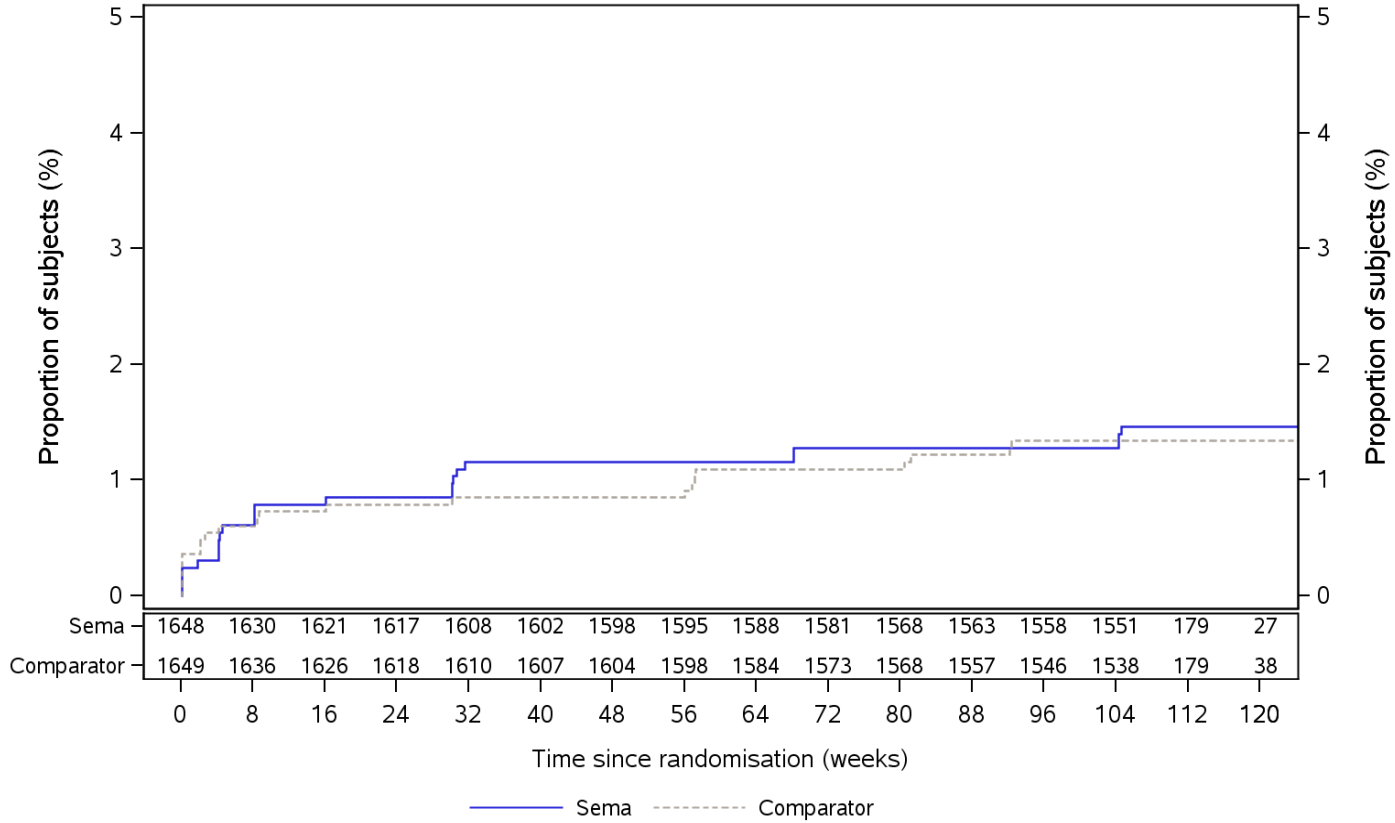
88 Adverse events - preferred term "Herpes zoster" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:09:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_herpzost_ae_all_s6.png

89 Adverse events - preferred term "Hypercalcaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

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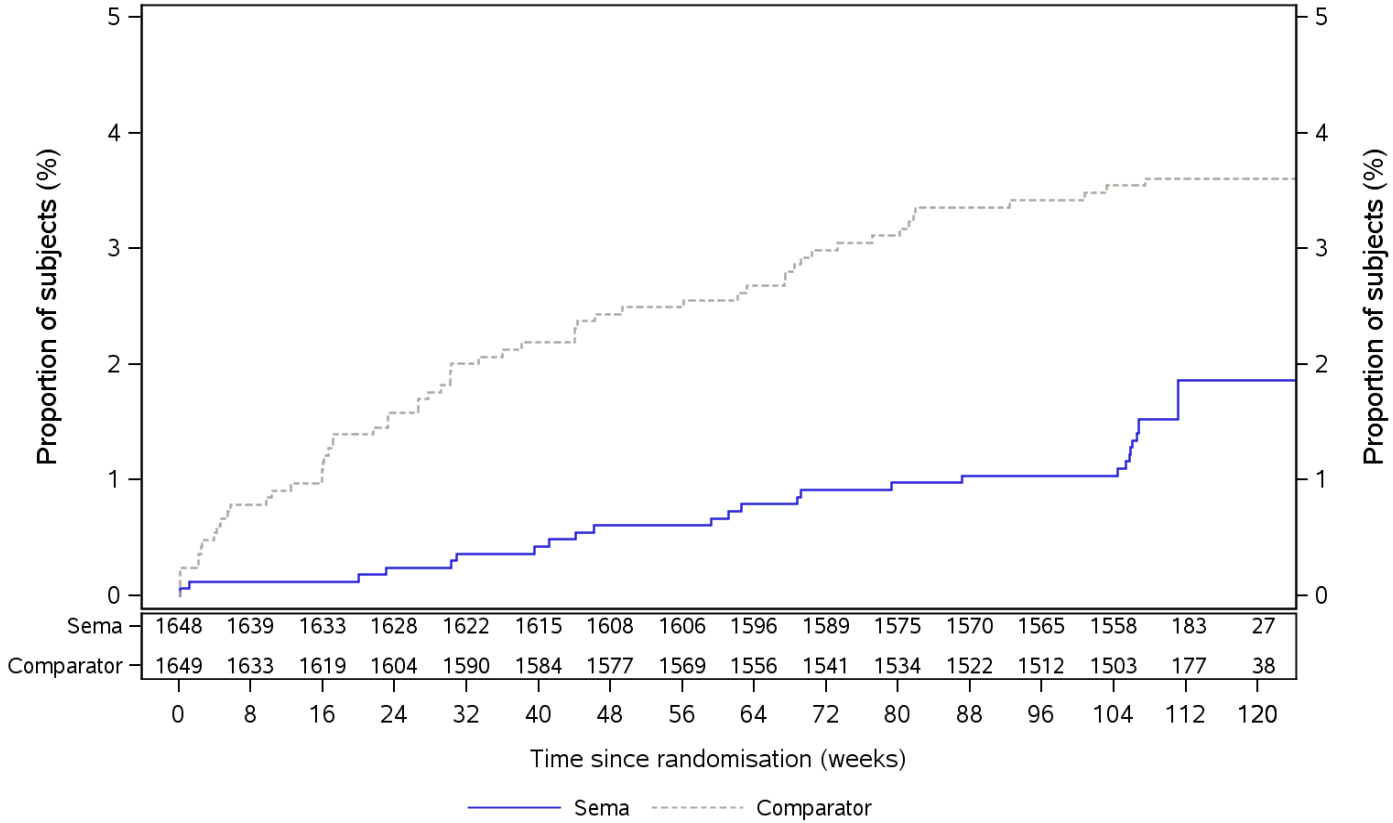
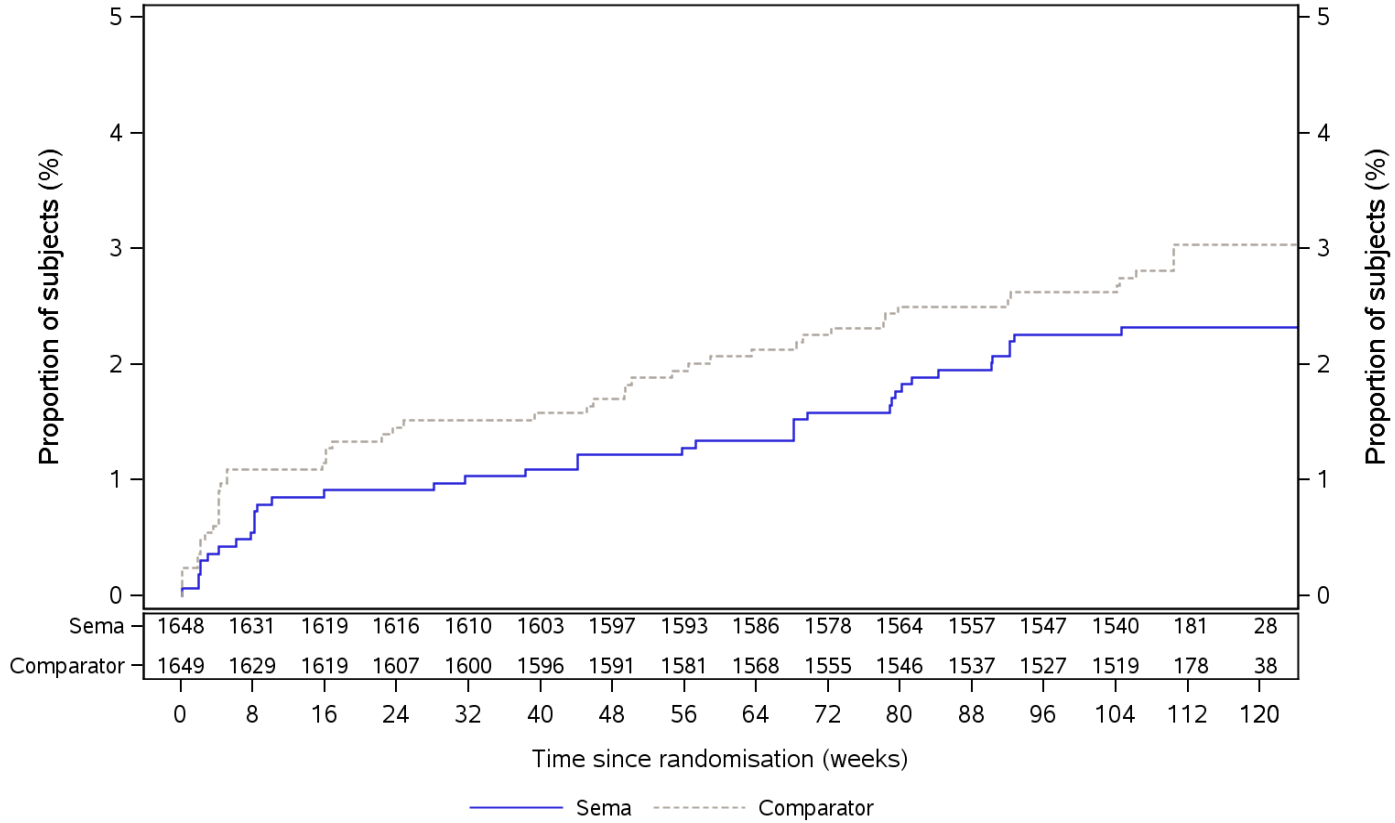
90 Adverse events - preferred term "Hyperglycaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:10:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypergly_ae_all_s6.png

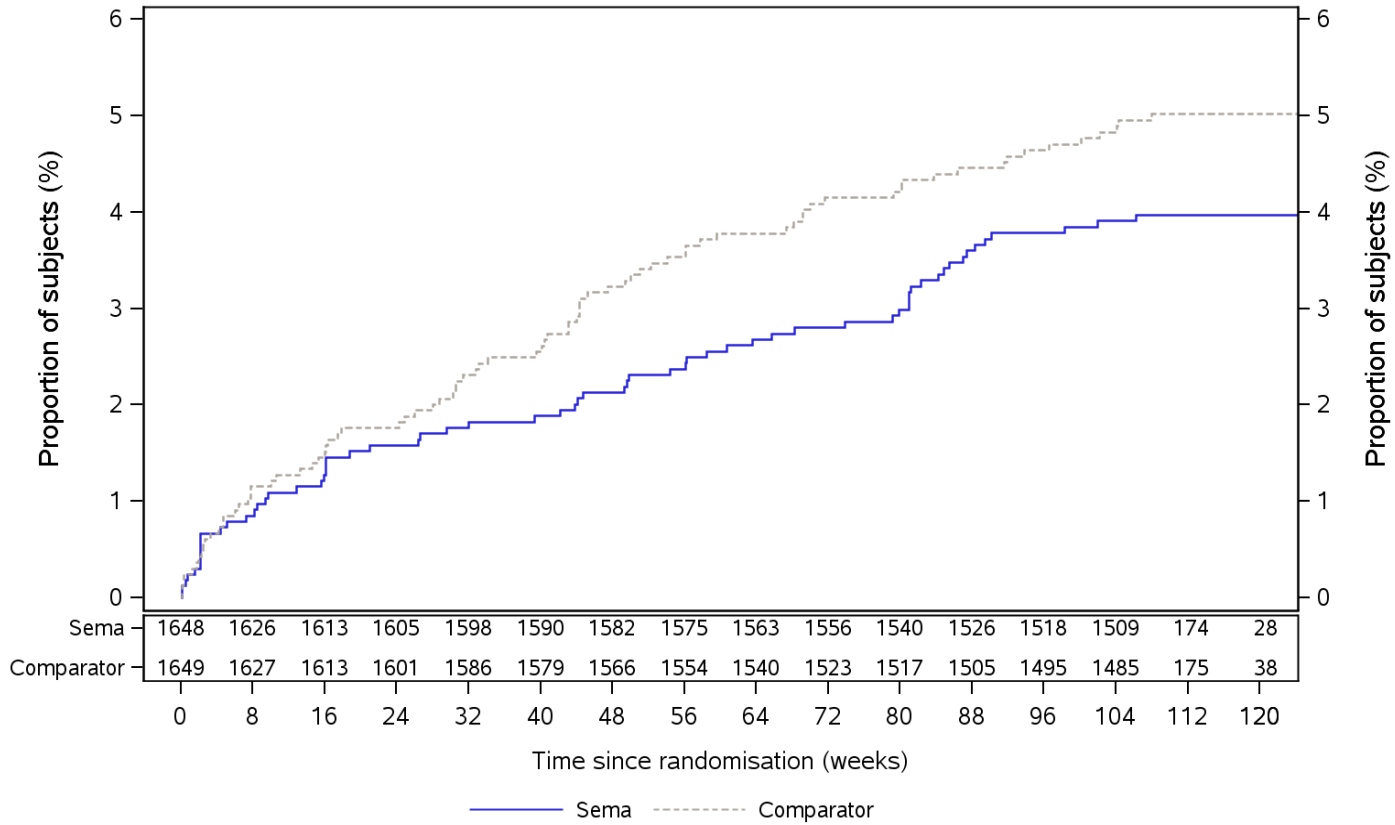
91 Adverse events - preferred term "Hyperkalaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:10:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hyperkal_ae_all_s6.png

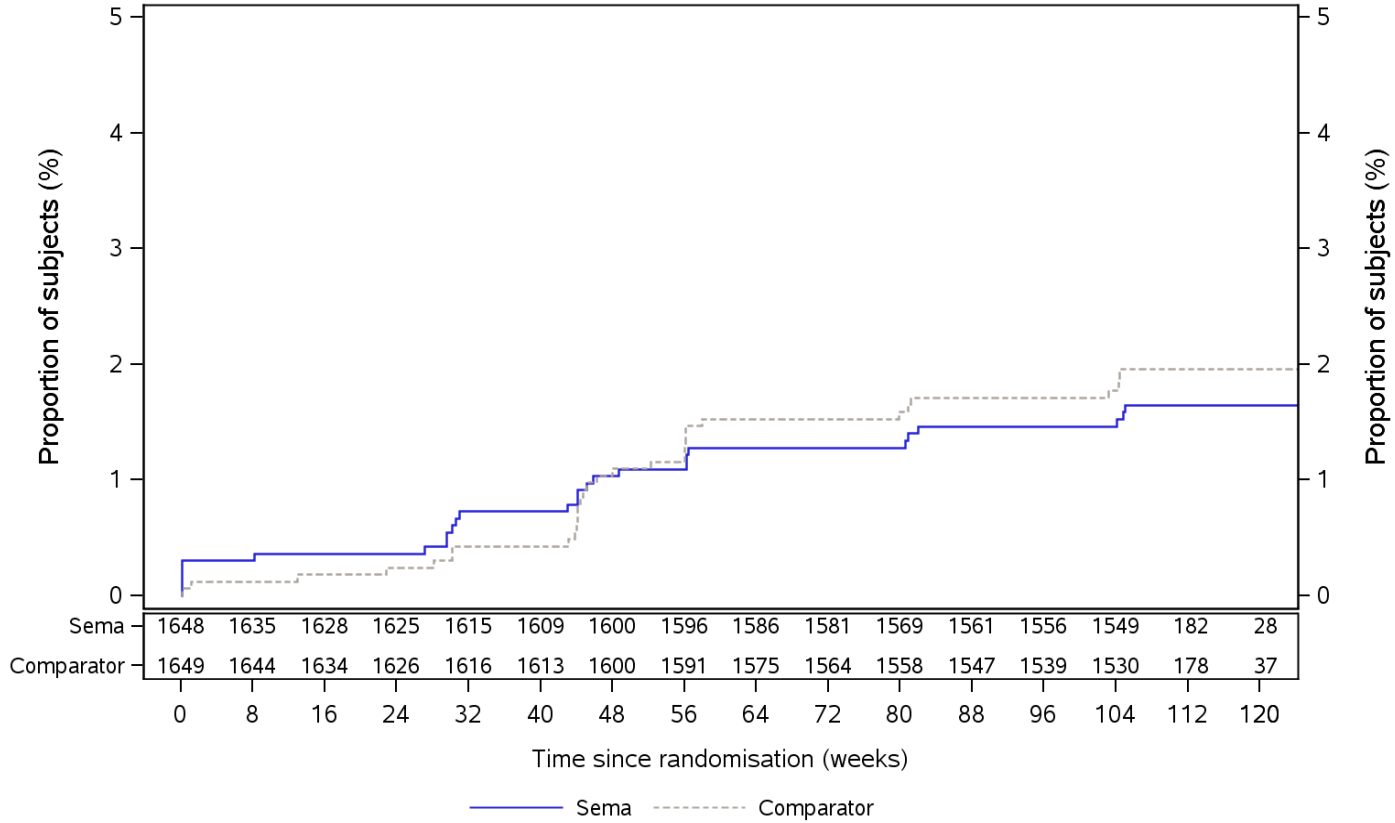
92 Adverse events - preferred term "Hypertension" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:11:14 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hyperten_ae_all_s6.png

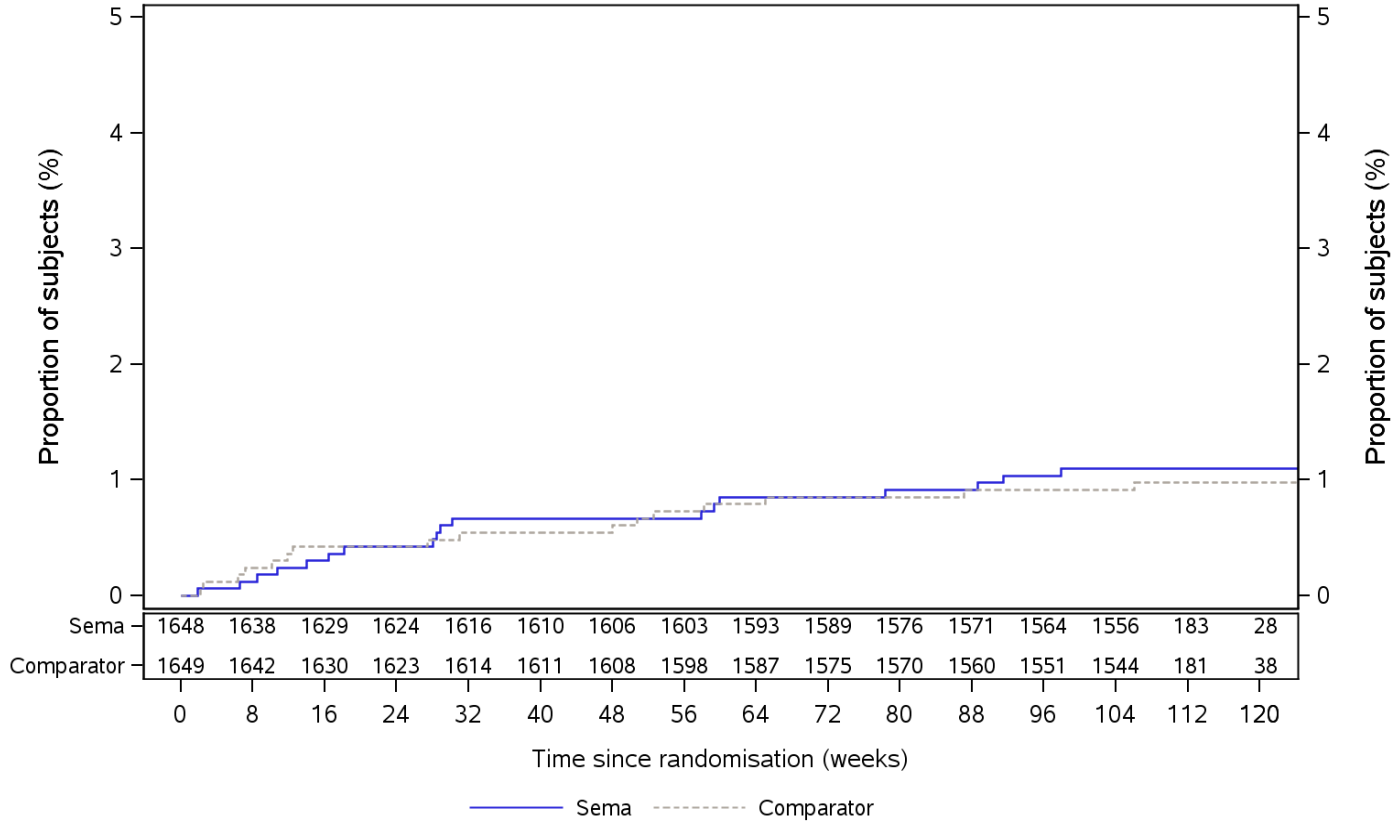
93 Adverse events - preferred term "Hypertriglyceridaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:11:34 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypertri_ae_all_s6.png

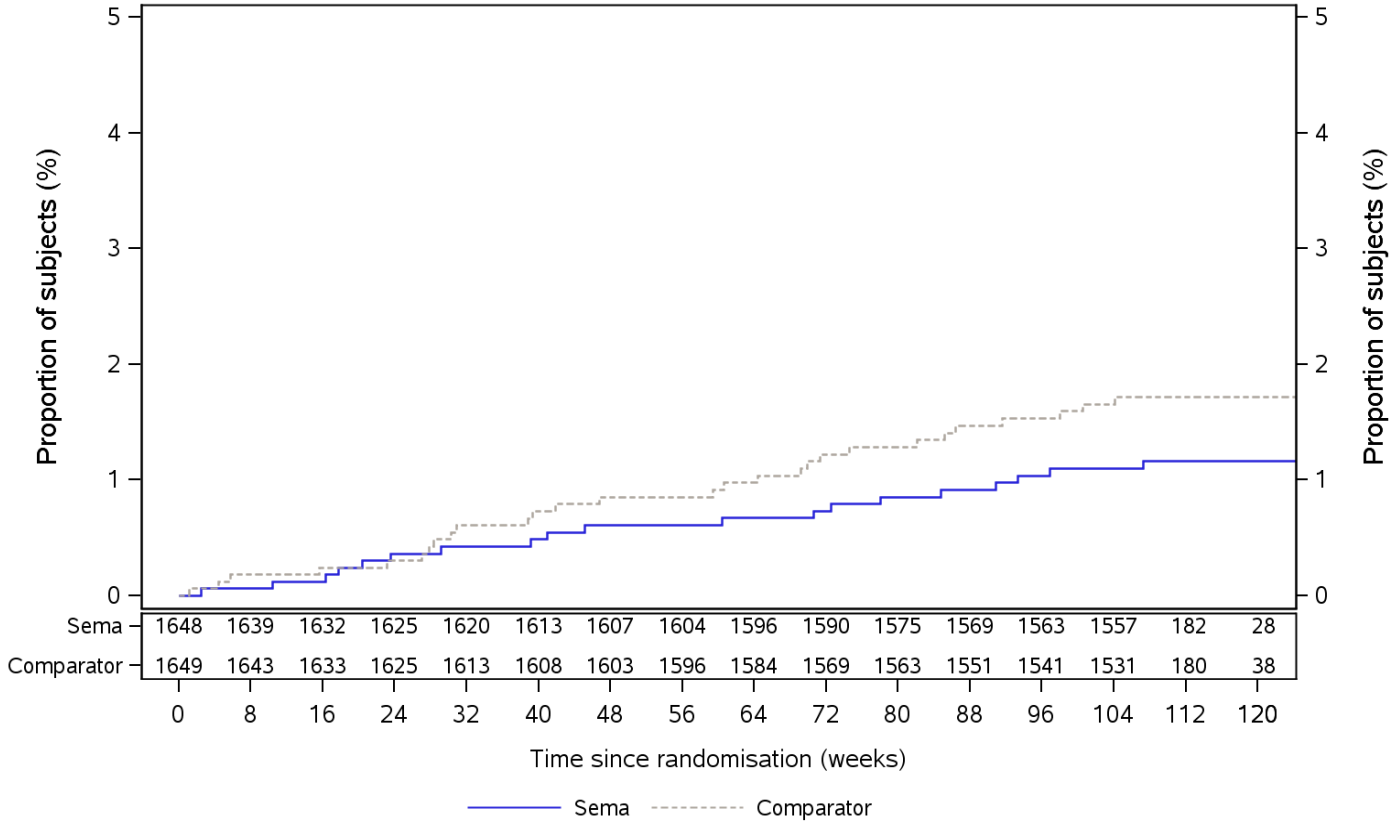
94 Adverse events - preferred term "Hypoaesthesia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:11:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypoaest_ae_all_s6.png

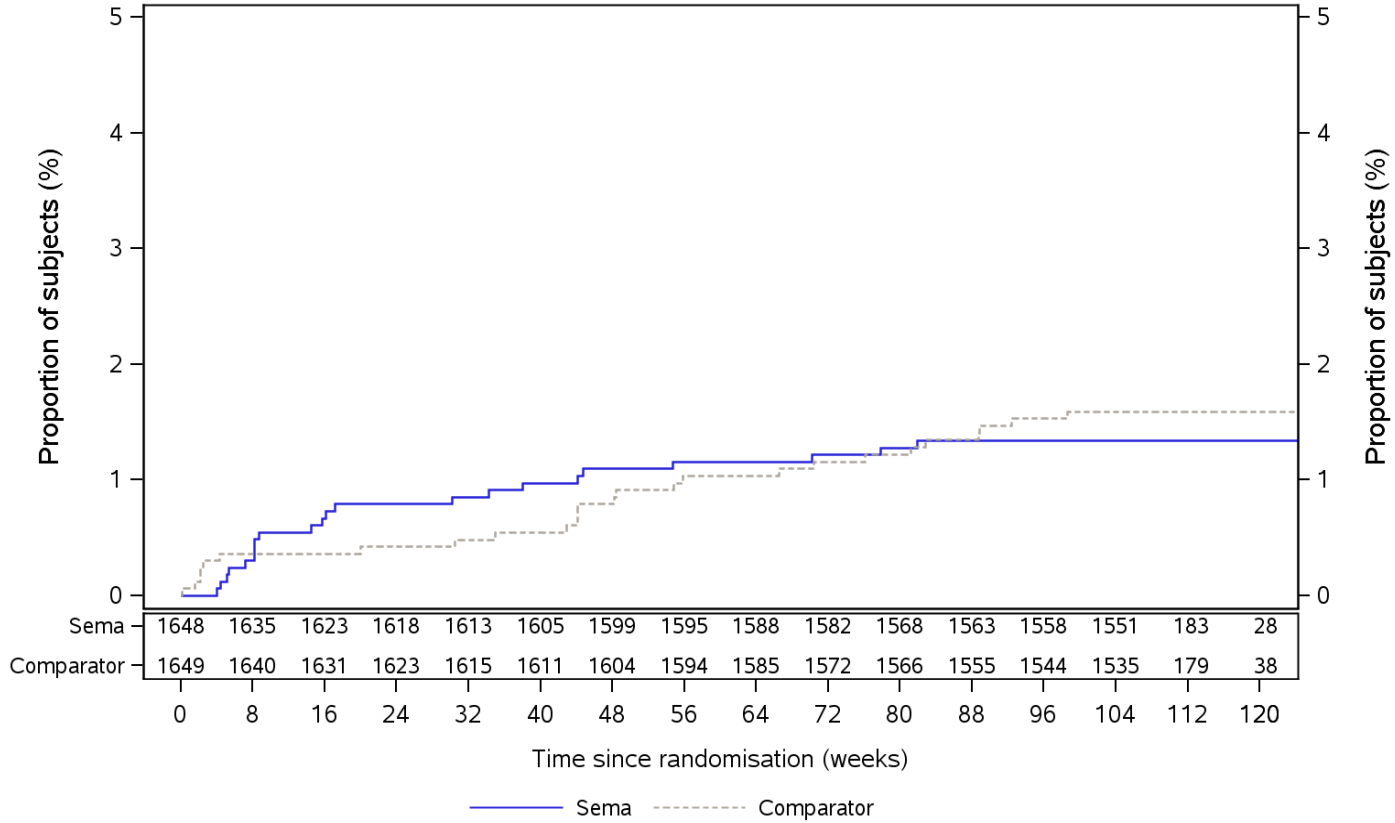
95 Adverse events - preferred term "Hypoglycaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:12:15 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypoglyc_ae_all_s6.png

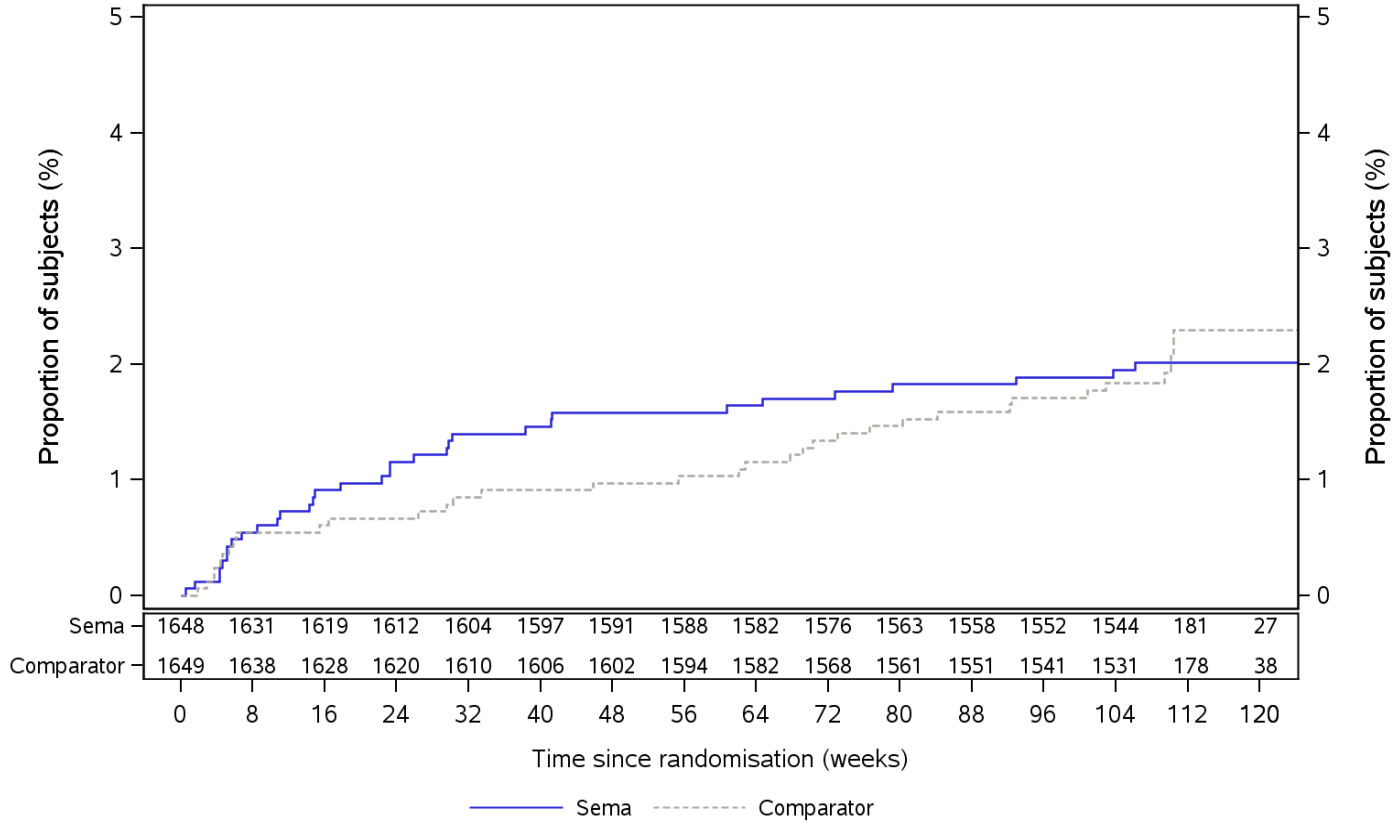
96 Adverse events - preferred term "Hypokalaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:12:36 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypokala_ae_all_s6.png

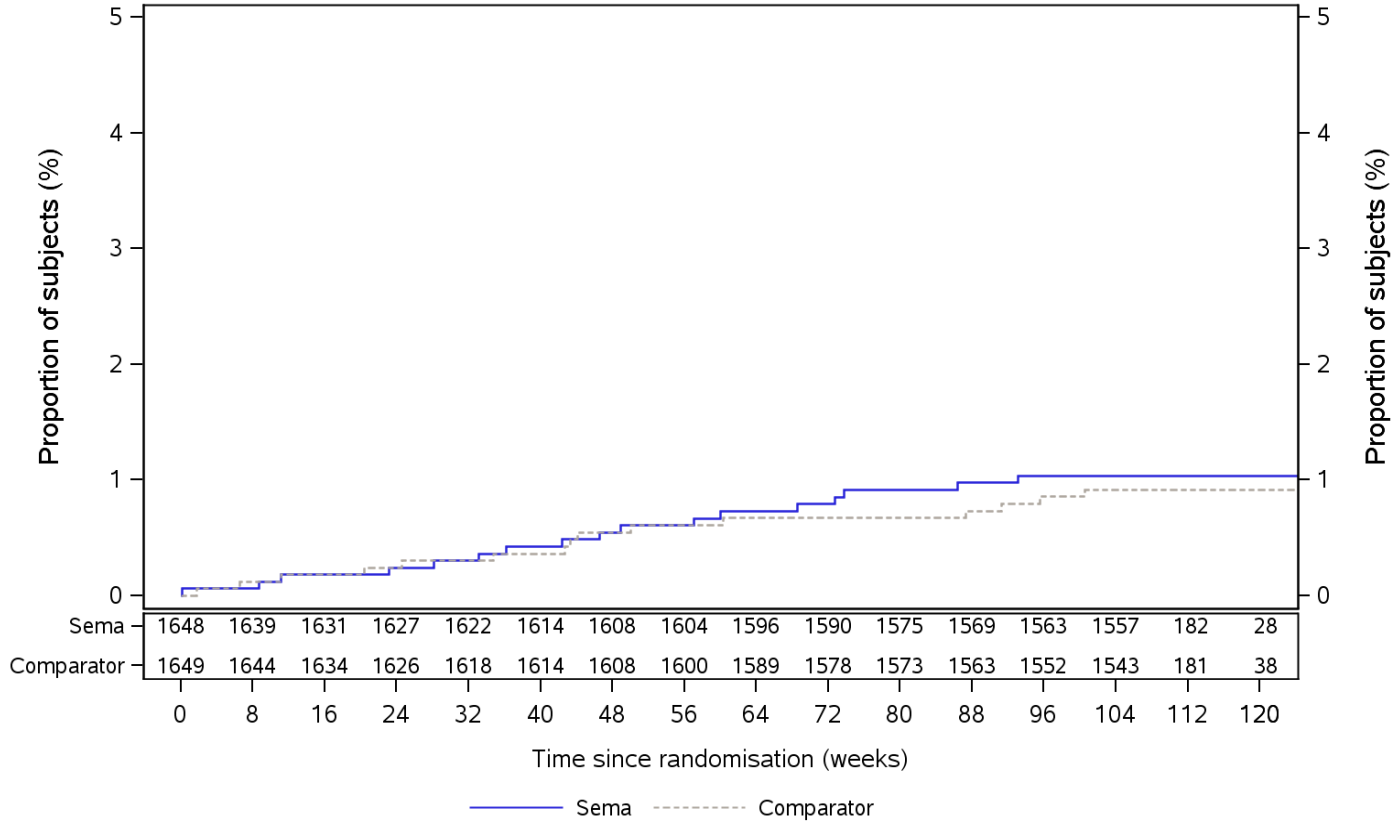
97 Adverse events - preferred term "Hypotension" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:12:56 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypotens_ae_all_s6.png

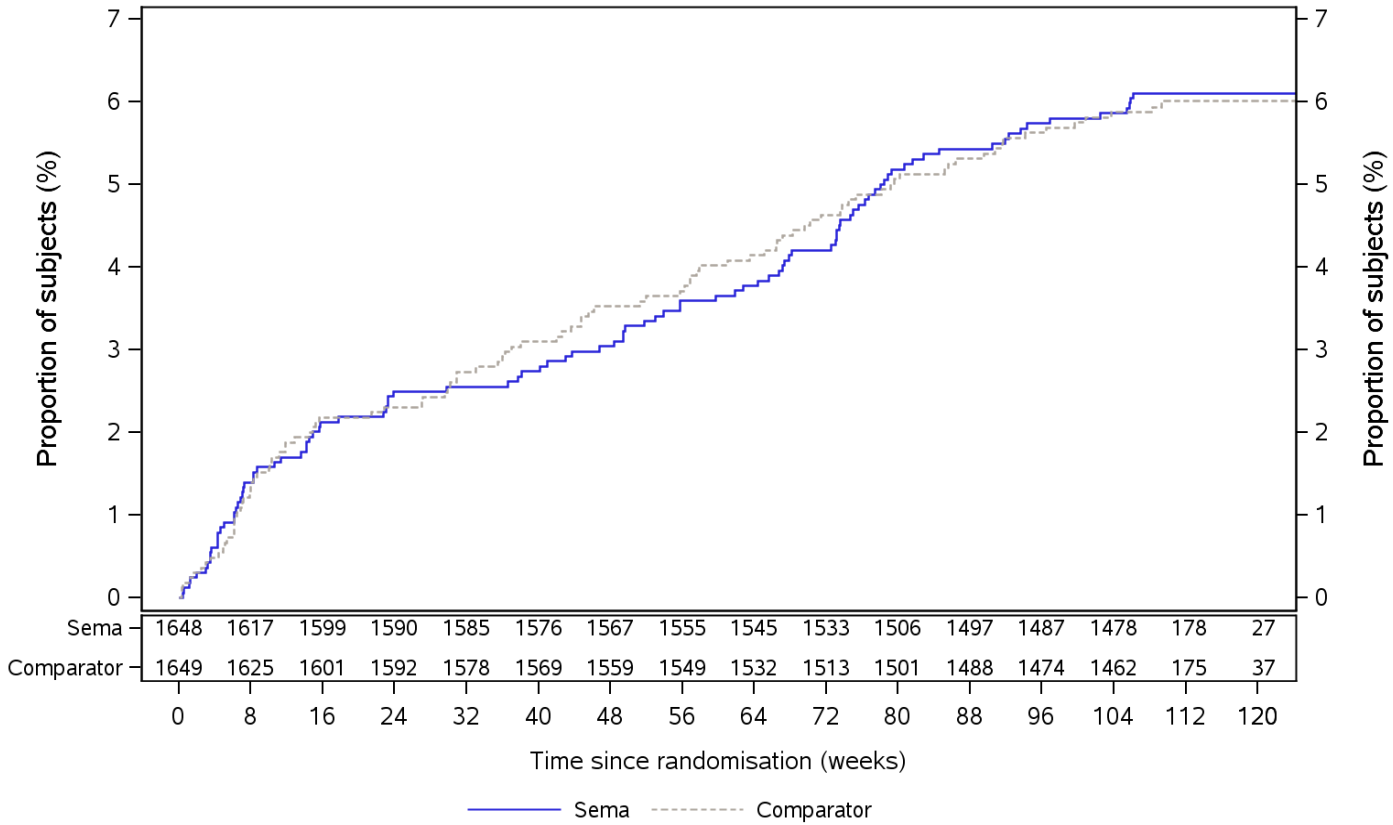
98 Adverse events - preferred term "Hypothyroidism" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:13:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypothyr_ae_all_s6.png

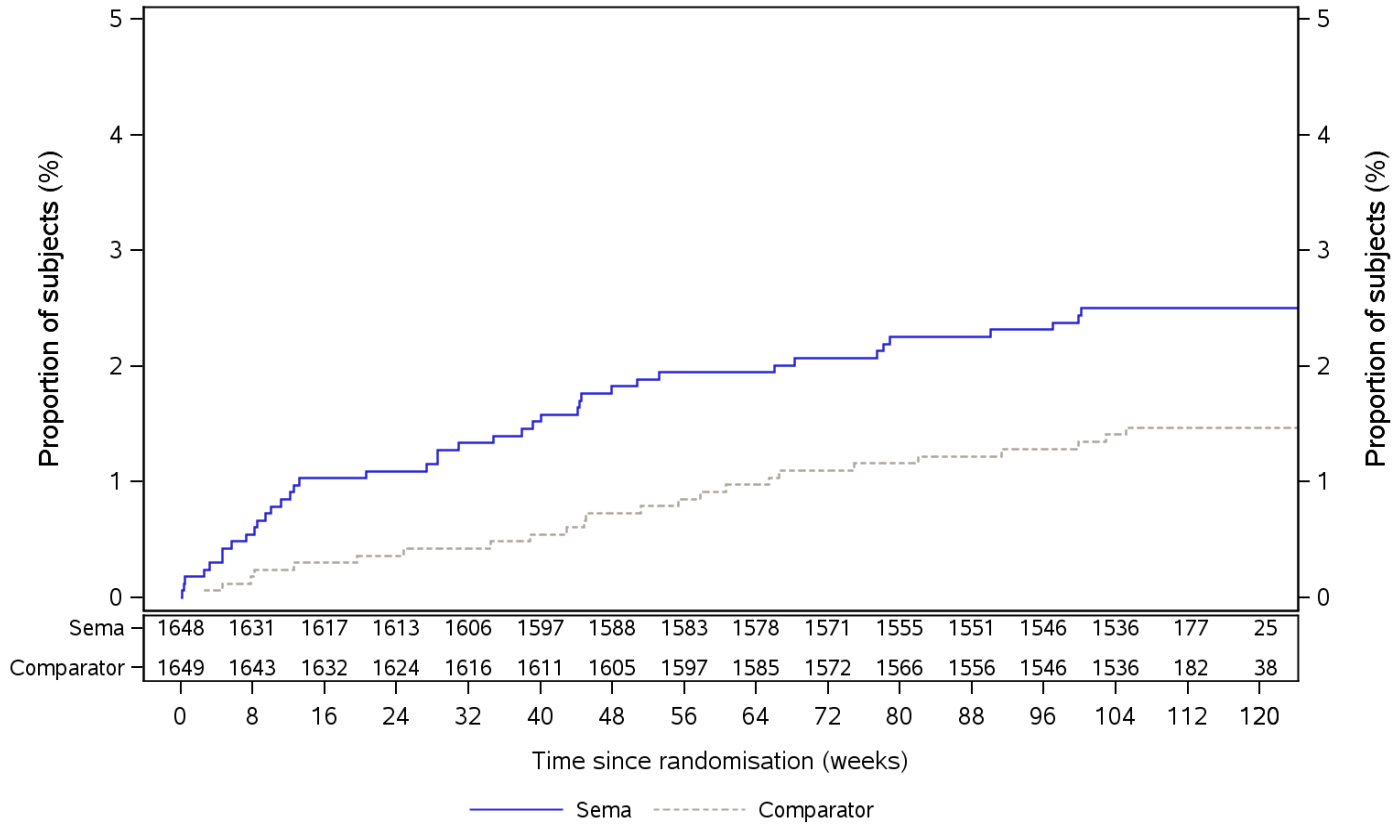
99 Adverse events - preferred term "Influenza" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:13:36 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_influenz_ae_all_s6.png

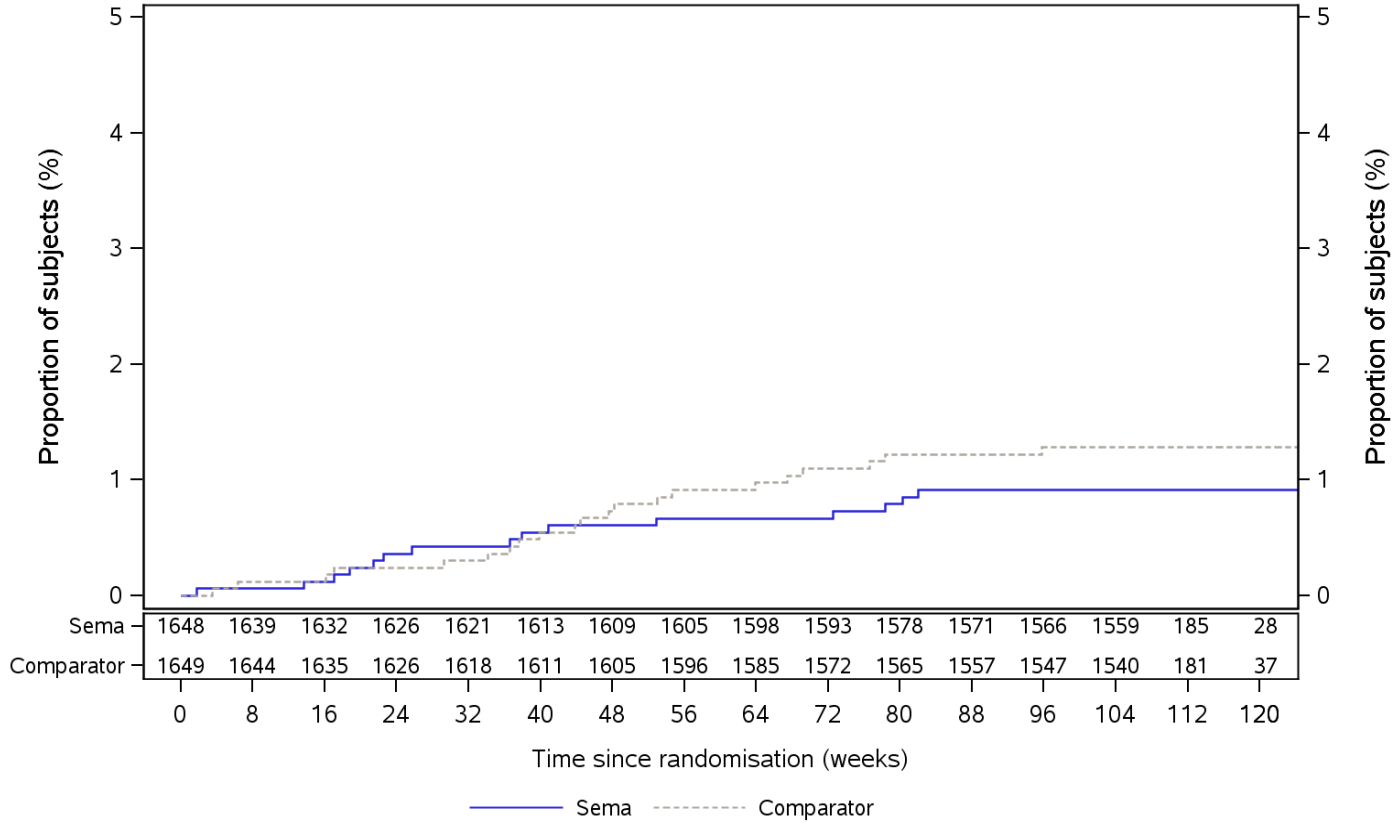
100 Adverse events - preferred term "Insomnia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:13:56 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_insomnia_ae_all_s6.png

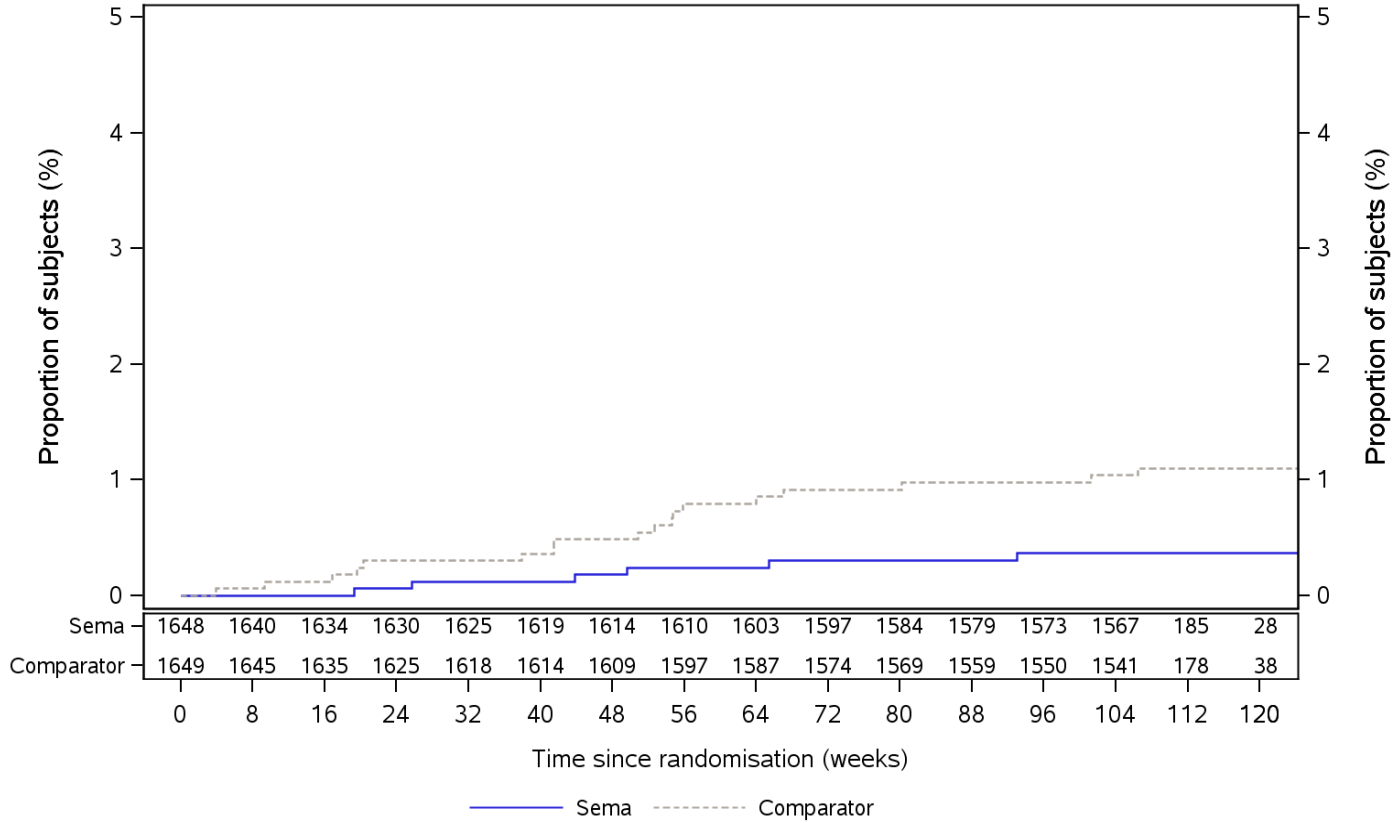
101 Adverse events - preferred term "Ischaemic stroke" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:14:17 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_is_ae_all_s6.png

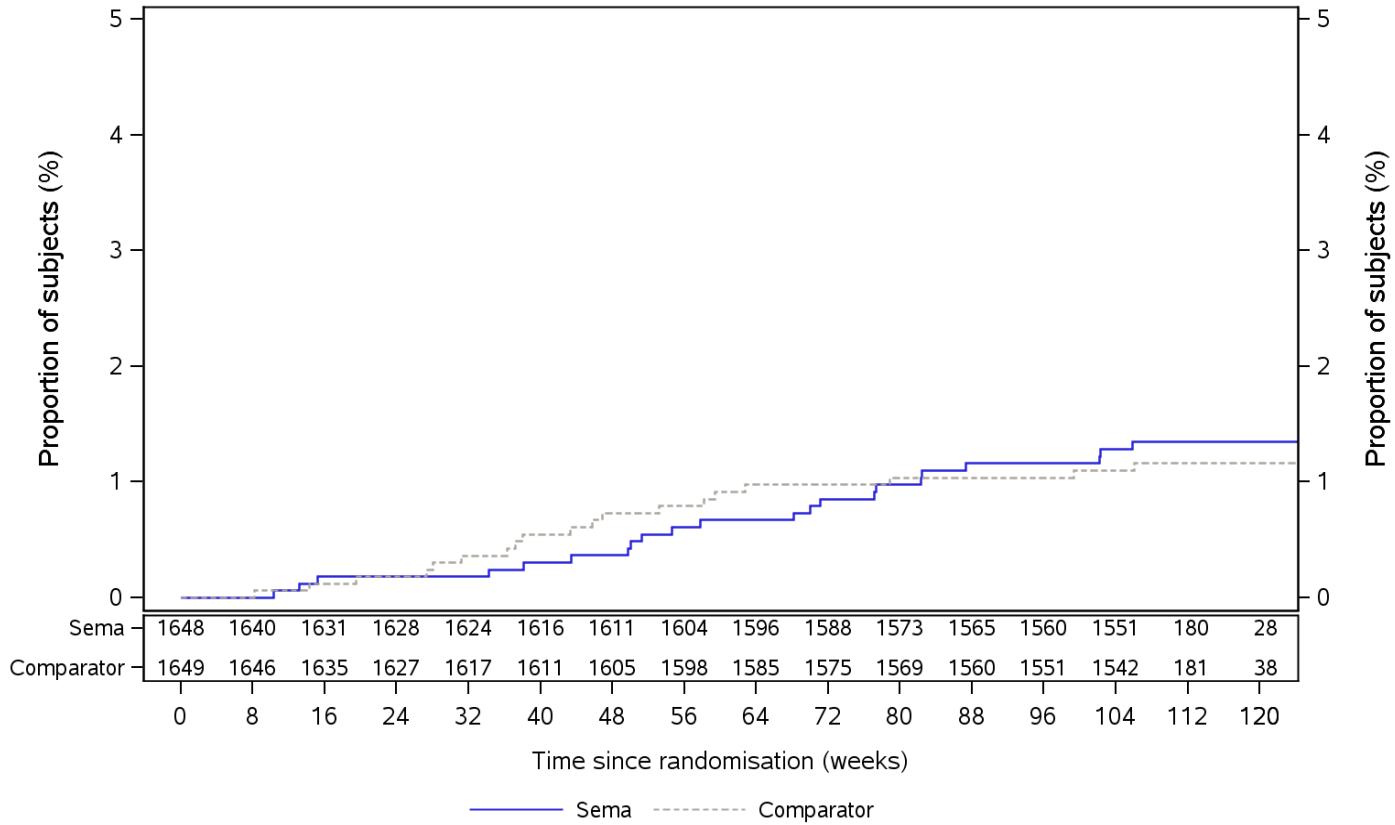
102 Adverse events - preferred term "Joint swelling" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:14:36 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_joinswel_ae_all_s6.png

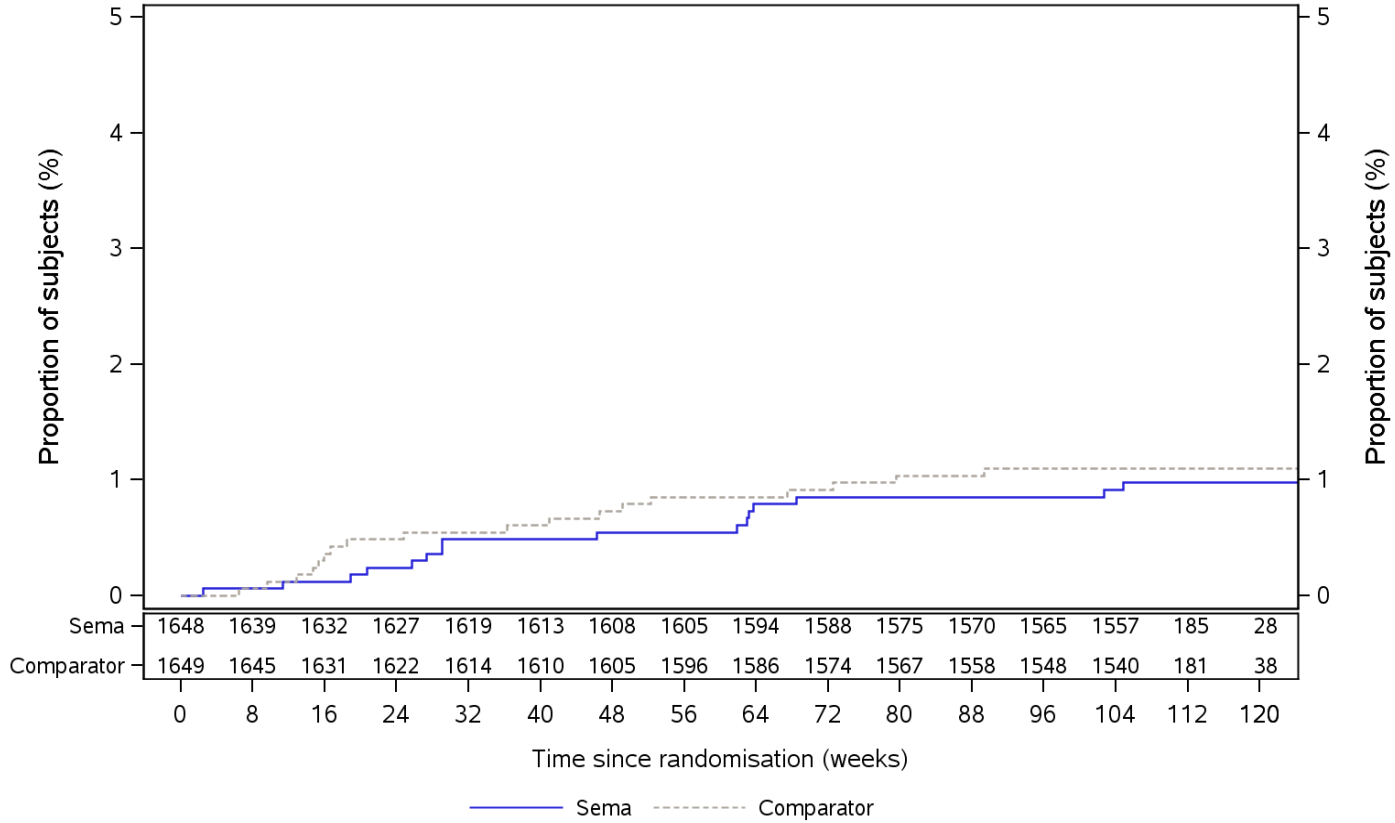
103 Adverse events - preferred term "Large intestine polyp" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:14:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_larintpol_ae_all_s6.png

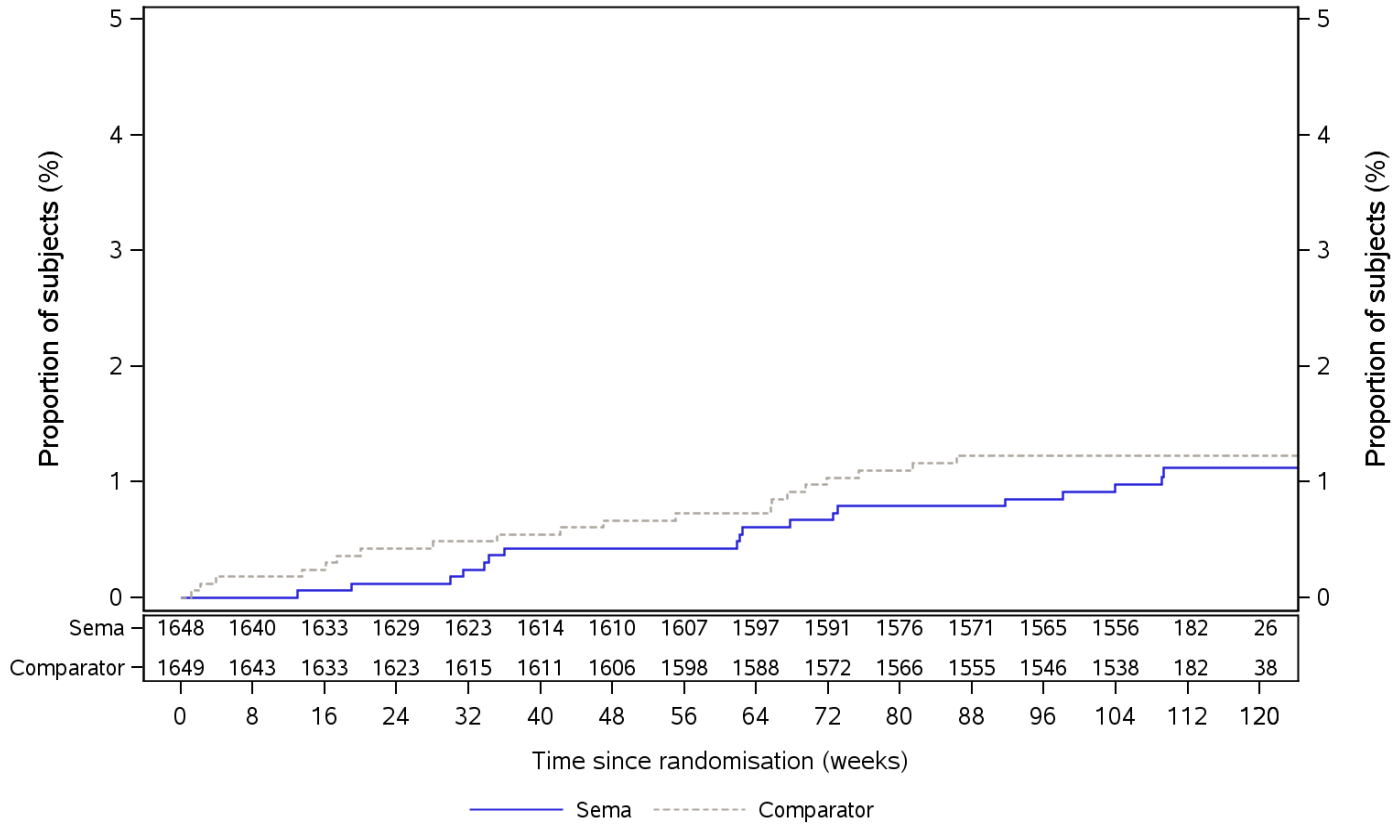
104 Adverse events - preferred term "Ligament sprain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:15:15 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_ligaspra_ae_all_s6.png

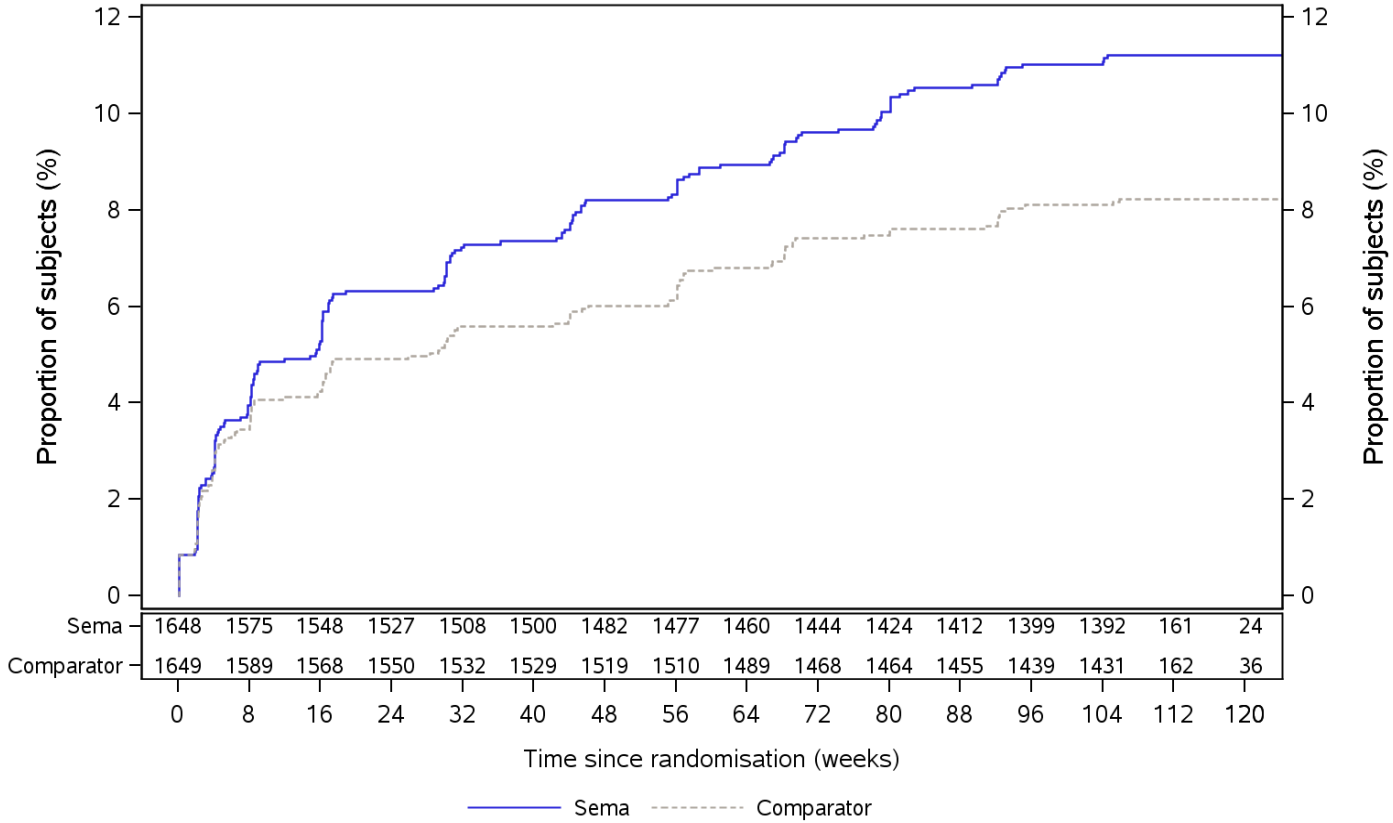
105 Adverse events - preferred term "Limb injury" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:15:36 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_limbinju_ae_all_s6.png

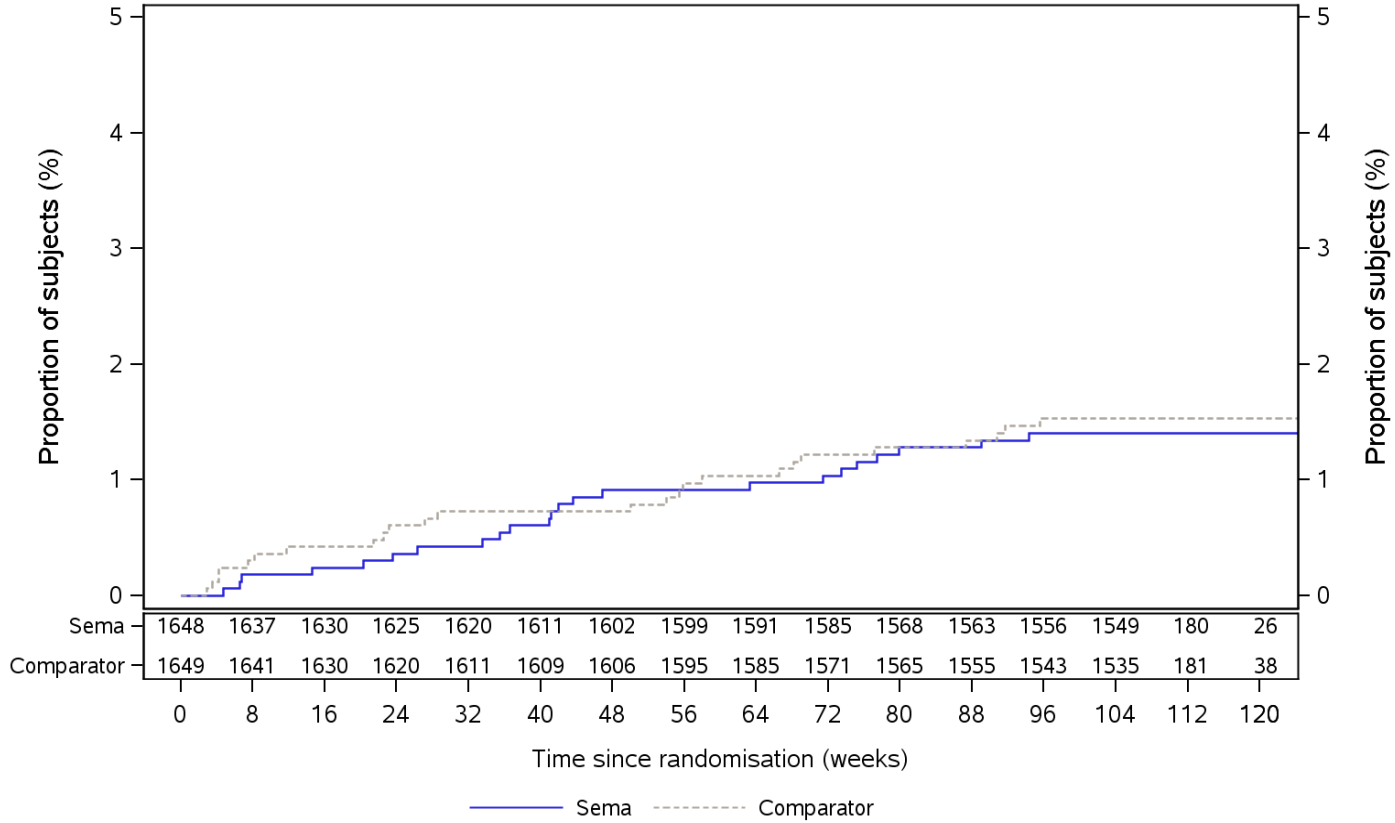
106 Adverse events - preferred term "Lipase increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:15:54 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_lipaincr_ae_all_s6.png

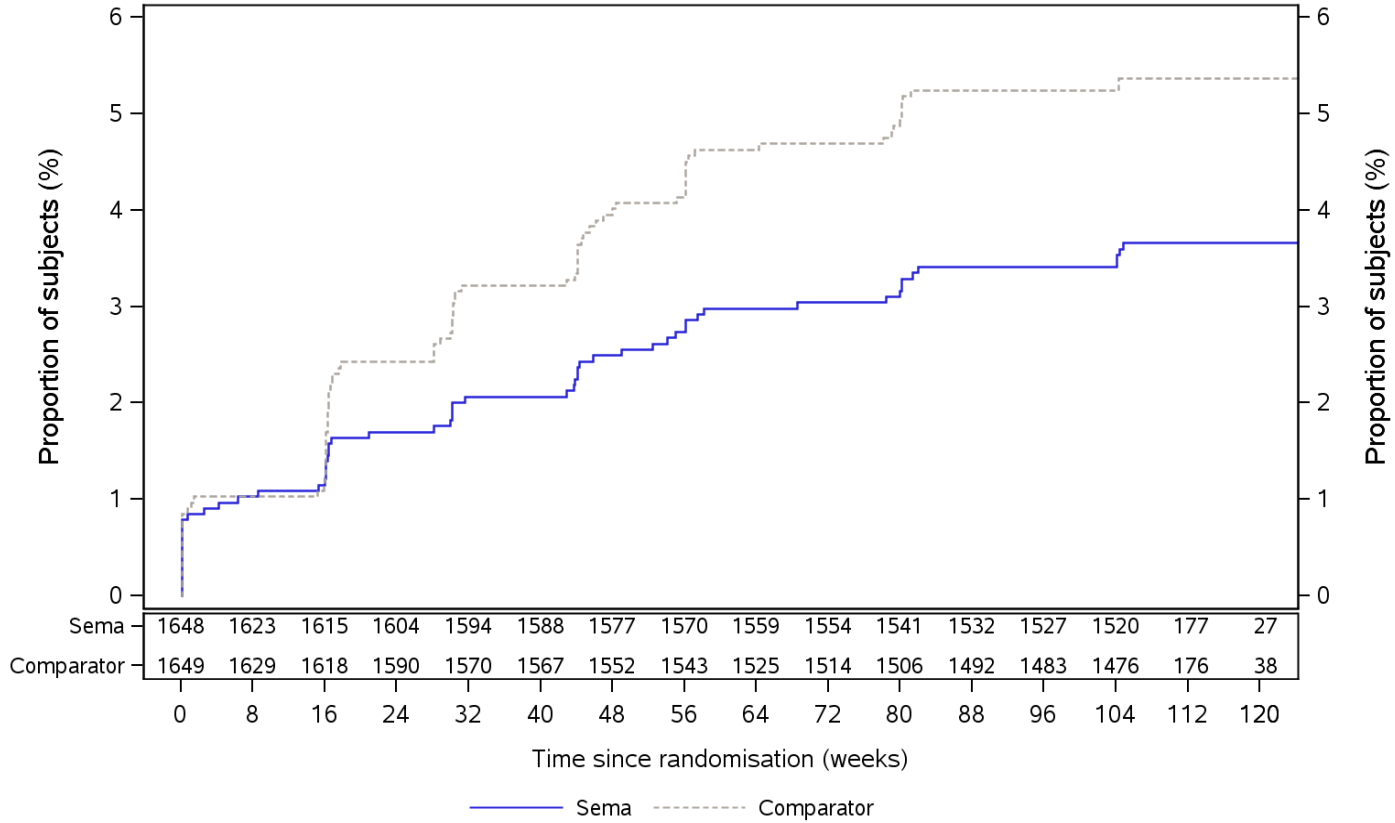
107 Adverse events - preferred term "Localised infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:16:13 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_locainfe_ae_all_s6.png

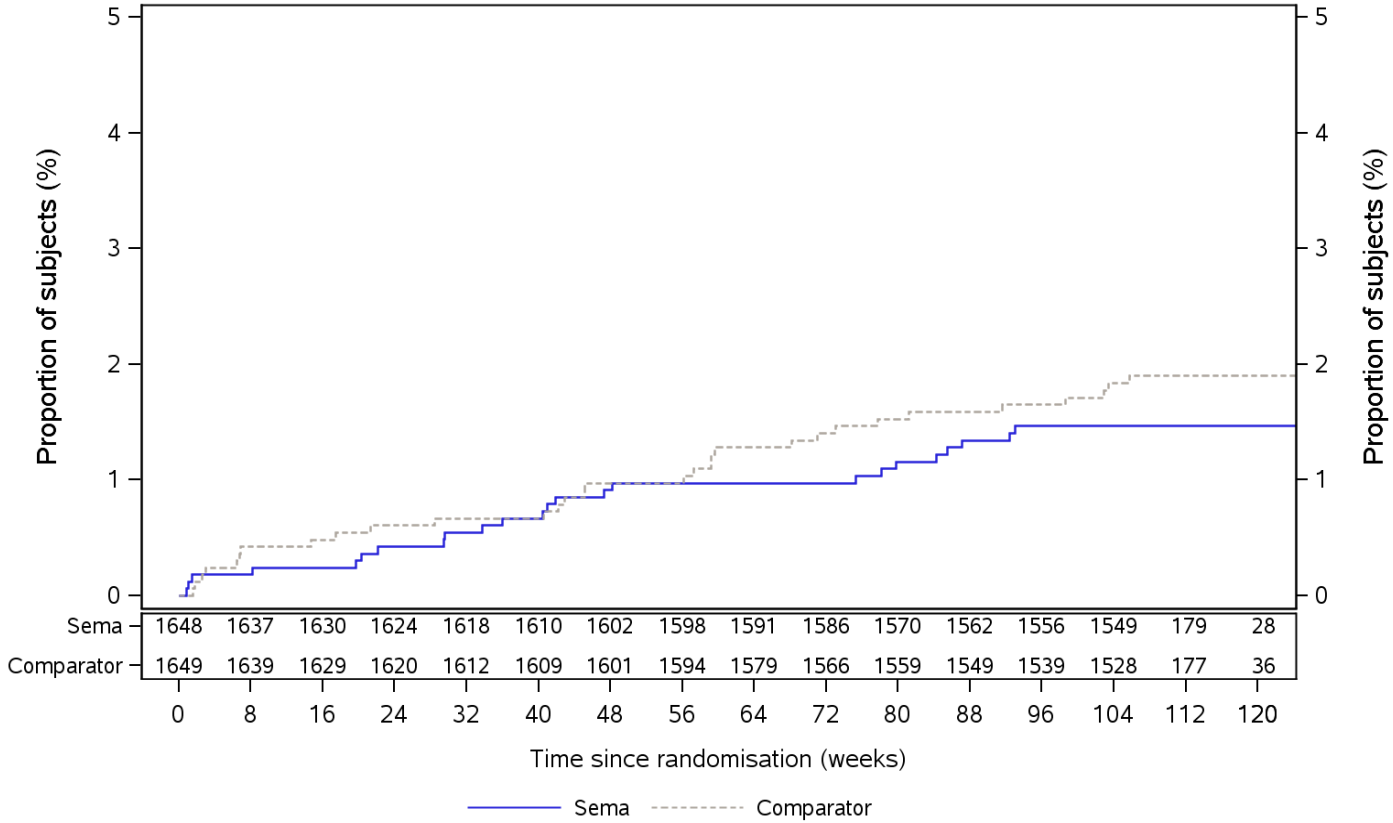
108 Adverse events - preferred term "Microalbuminuria" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:16:33 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_microalb_ae_all_s6.png

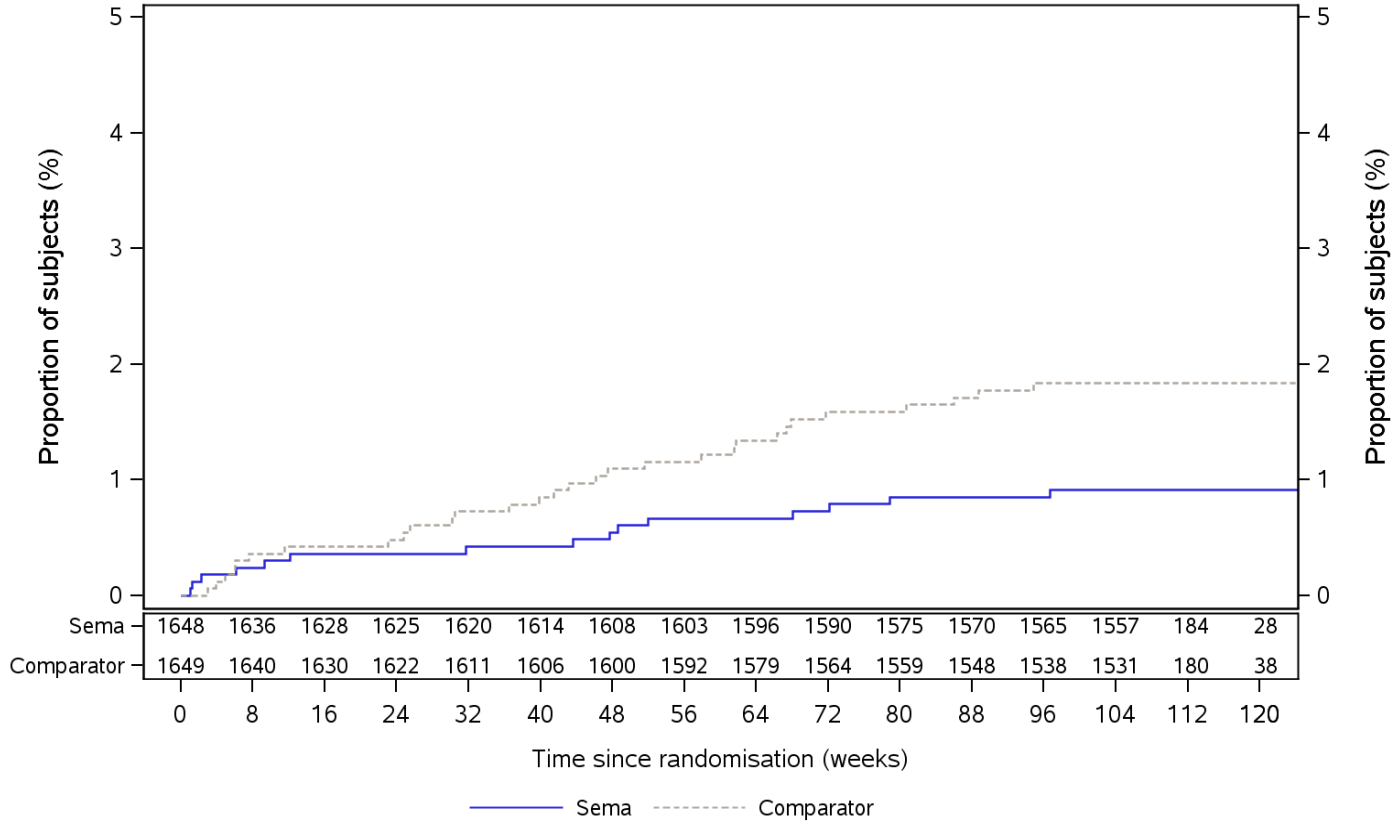
109 Adverse events - preferred term "Muscle spasms" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:16:52 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_muscspas_ae_all_s6.png

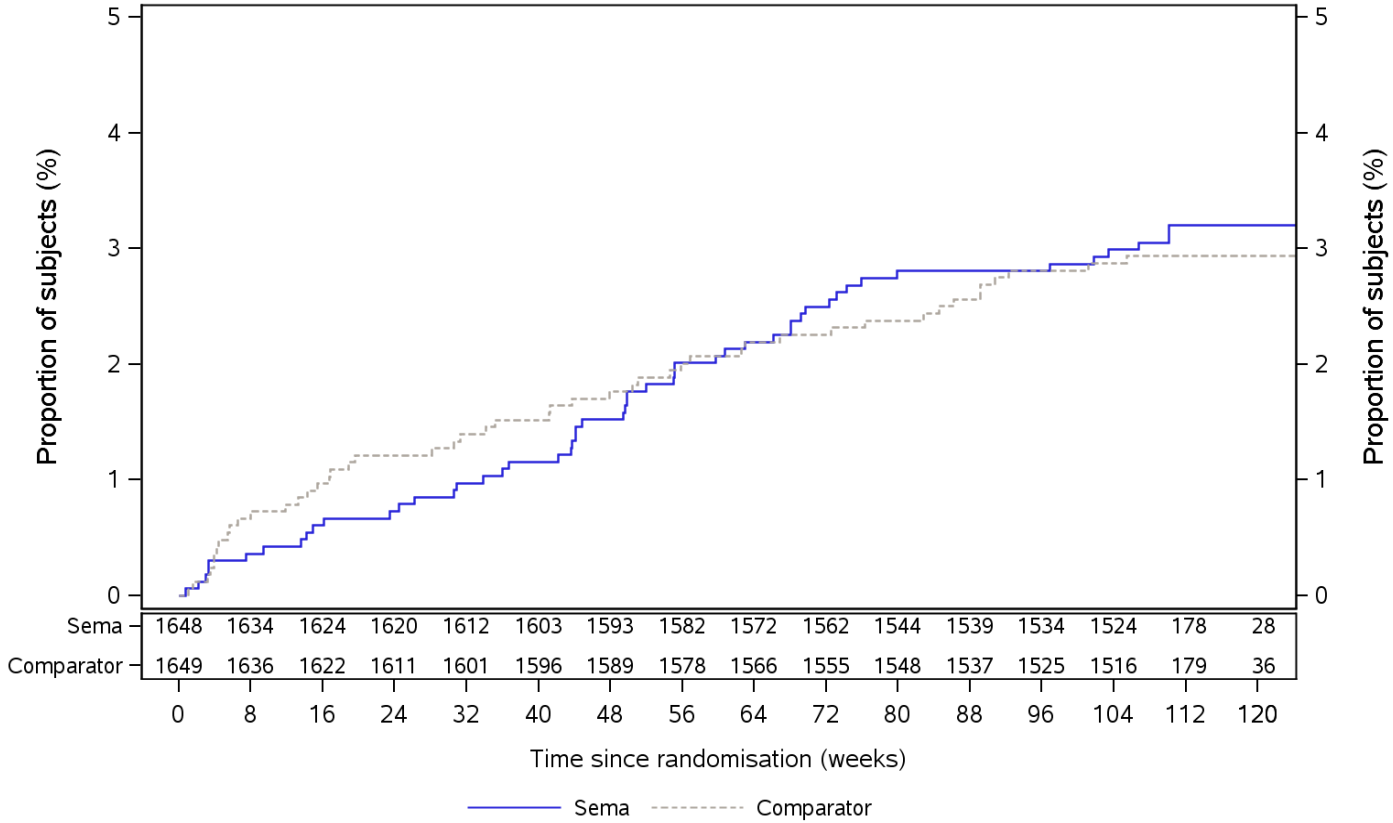
110 Adverse events - preferred term "Musculoskeletal chest pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:17:11 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_muschepai_ae_all_s6.png

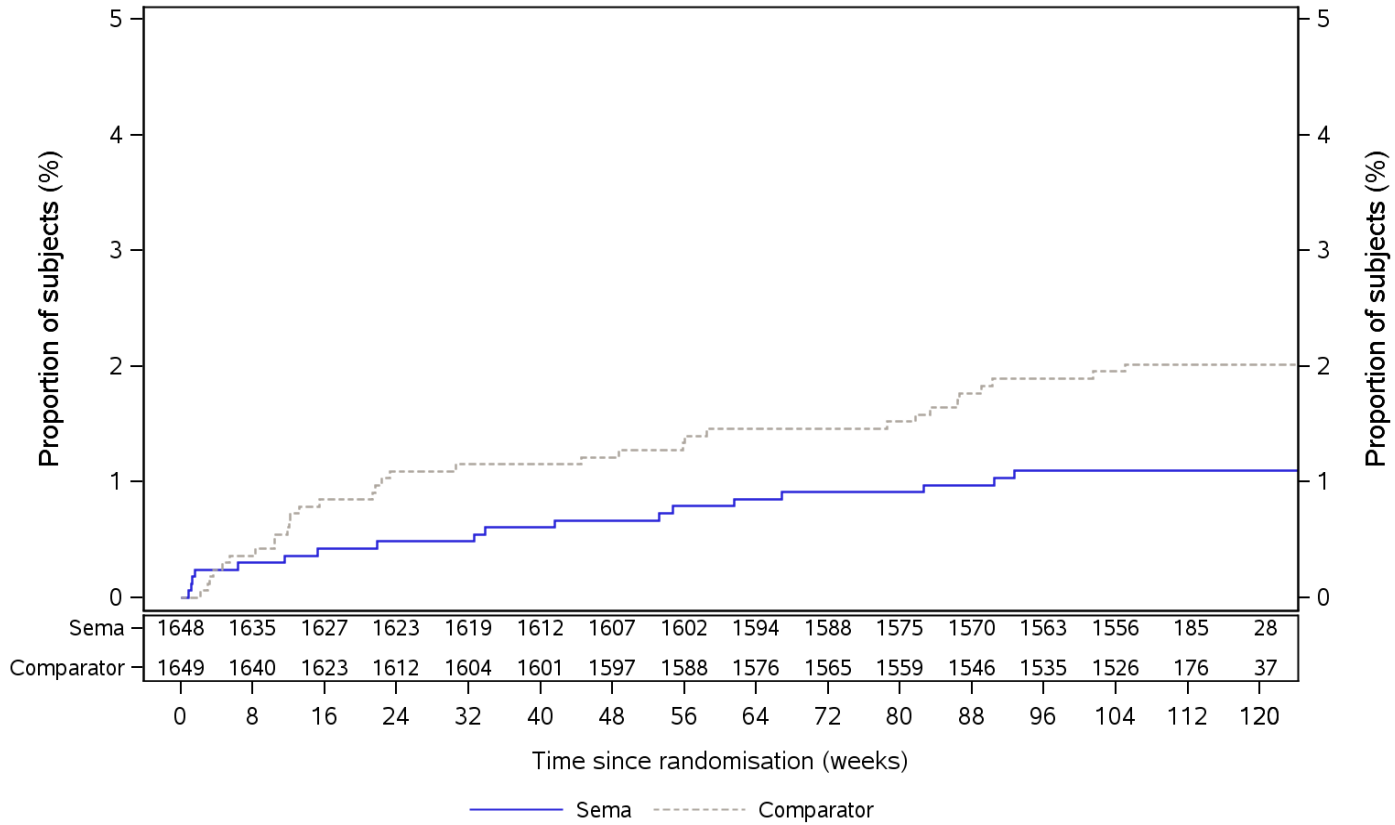
111 Adverse events - preferred term "Musculoskeletal pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:17:30 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_muscpain_ae_all_s6.png

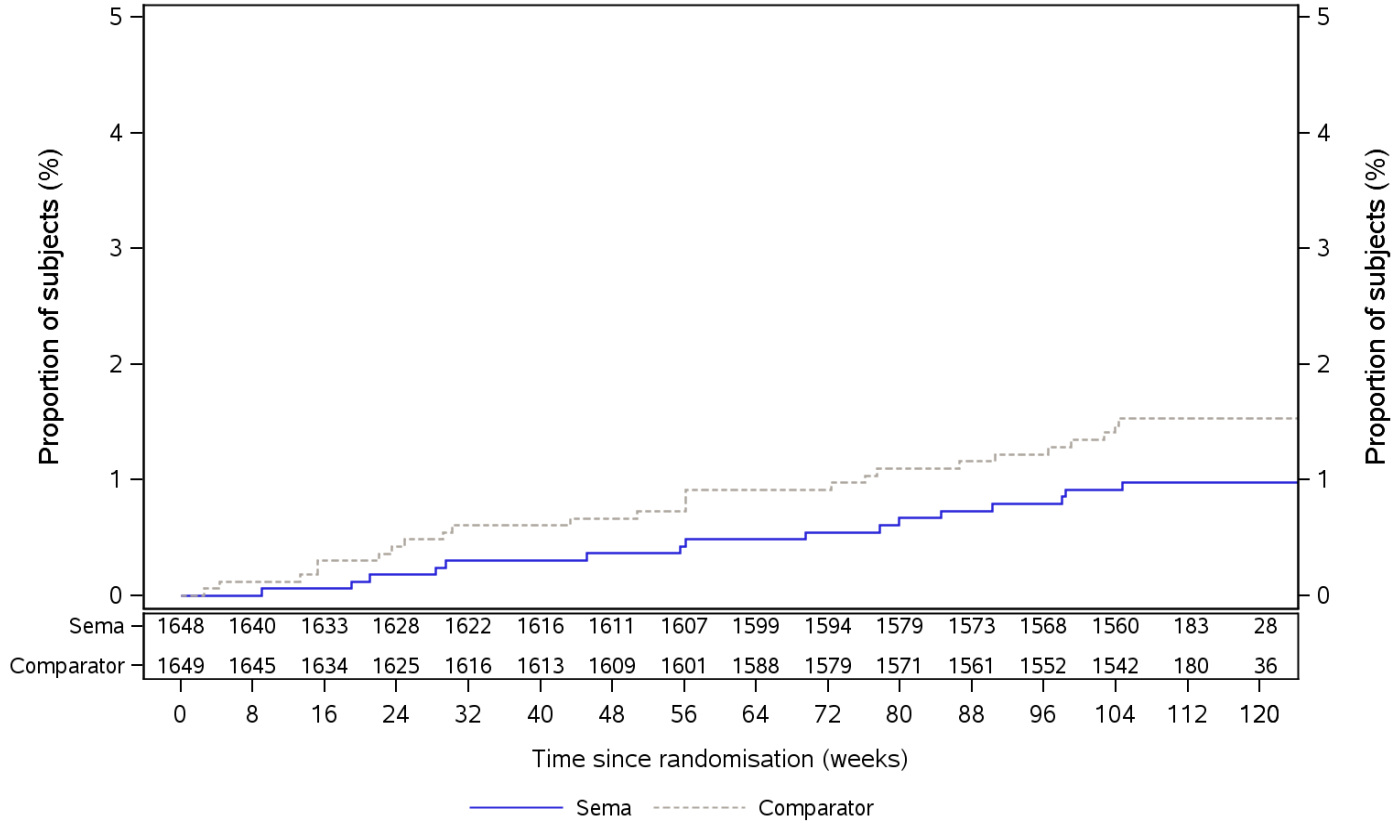
112 Adverse events - preferred term "Myalgia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:17:49 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_myalgia_ae_all_s6.png

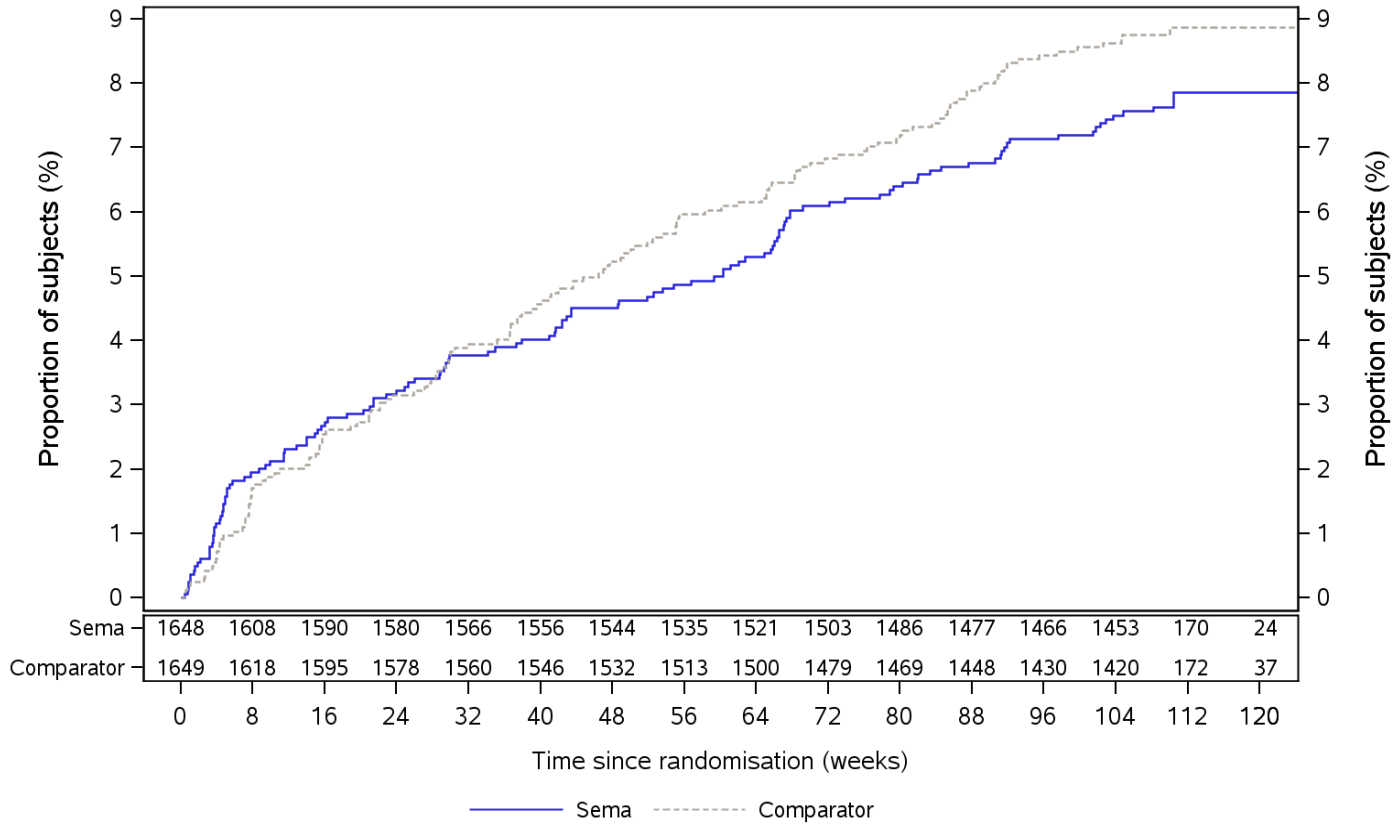
113 Adverse events - preferred term "Myocardial infarction" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:18:09 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_mf_ae_all_s6.png

114 Adverse events - preferred term "Nasopharyngitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
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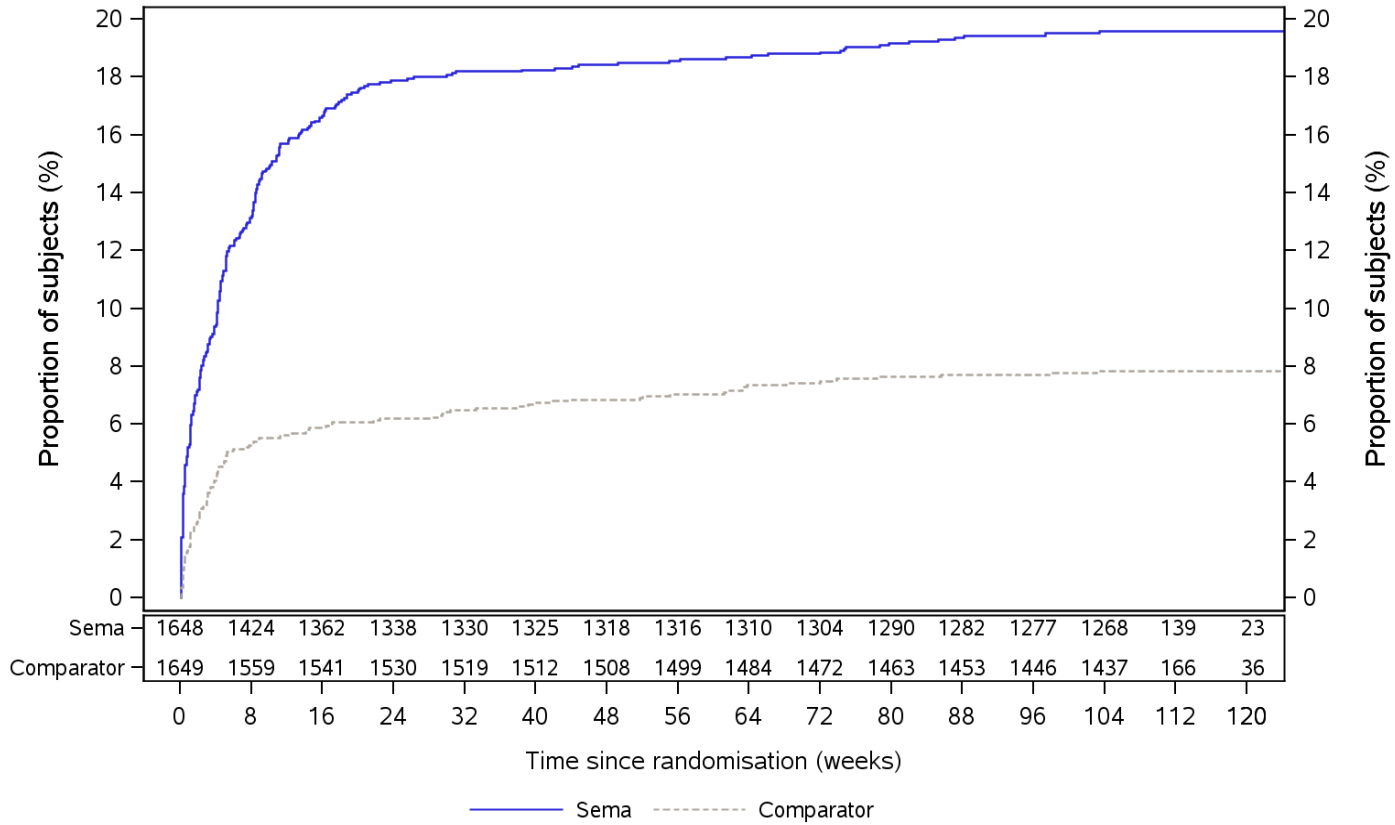
115 Adverse events - preferred term "Nausea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

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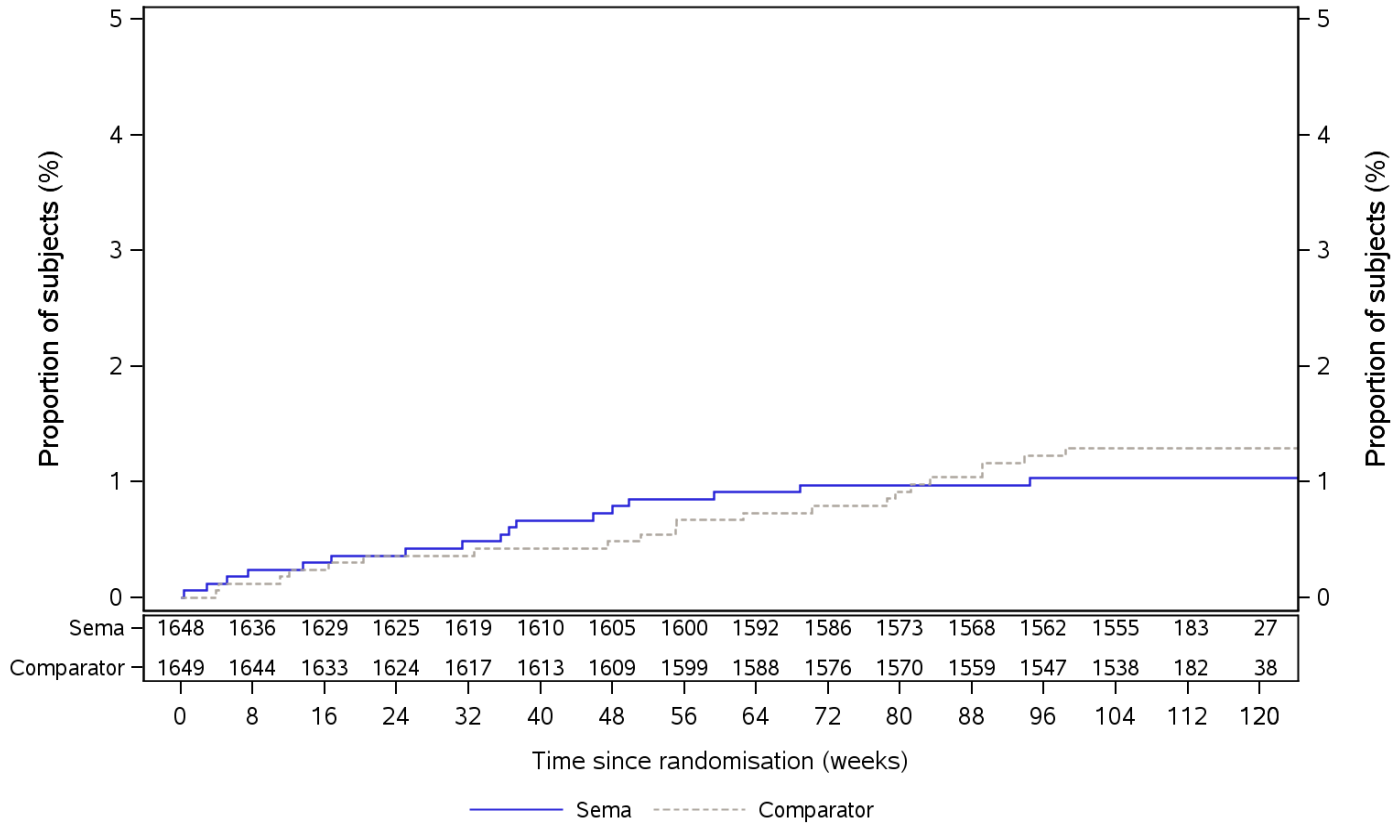
26MAY2020:11:18:46 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nausea_ae_all_s6.png

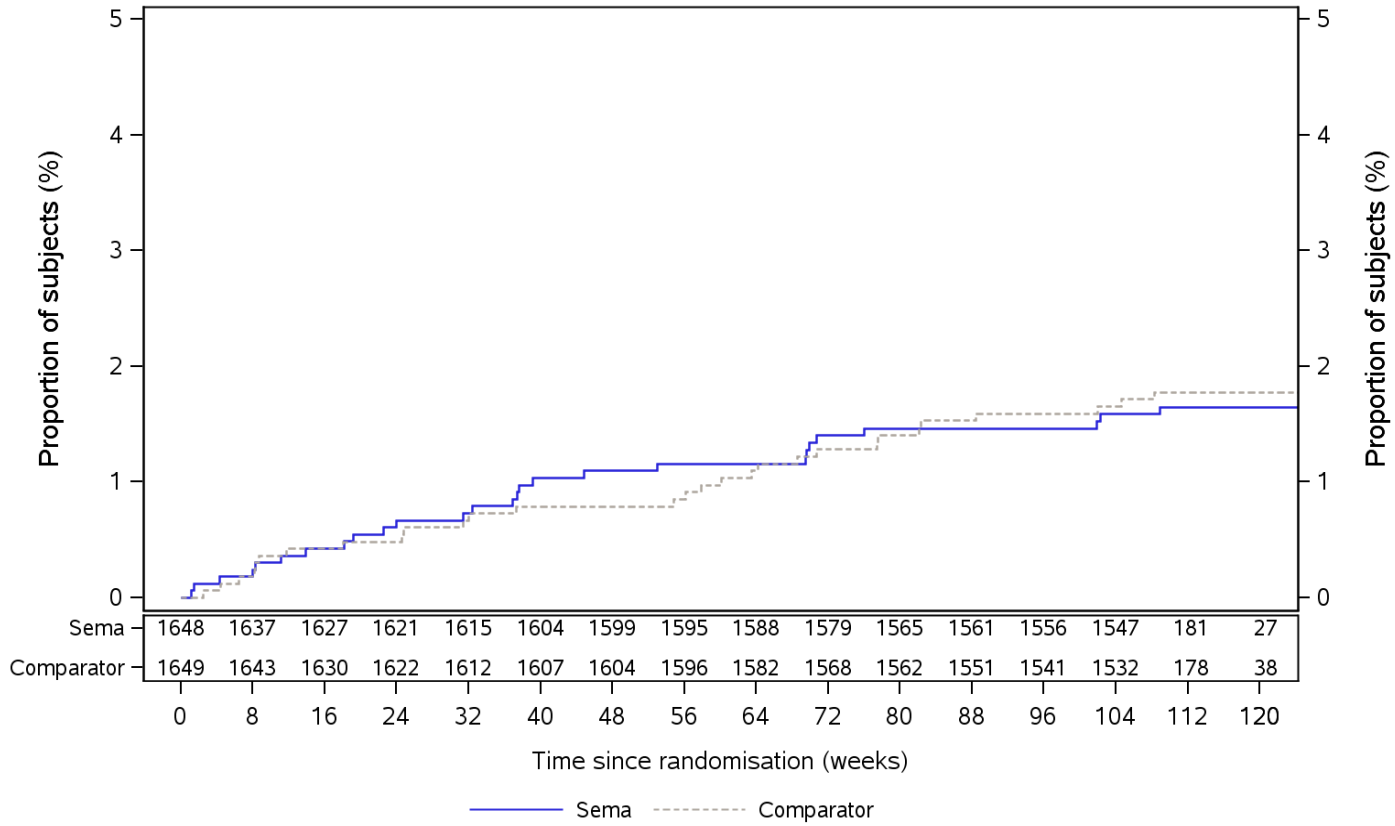
116 Adverse events - preferred term "Neck pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:19:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_neckpain_ae_all_s6.png

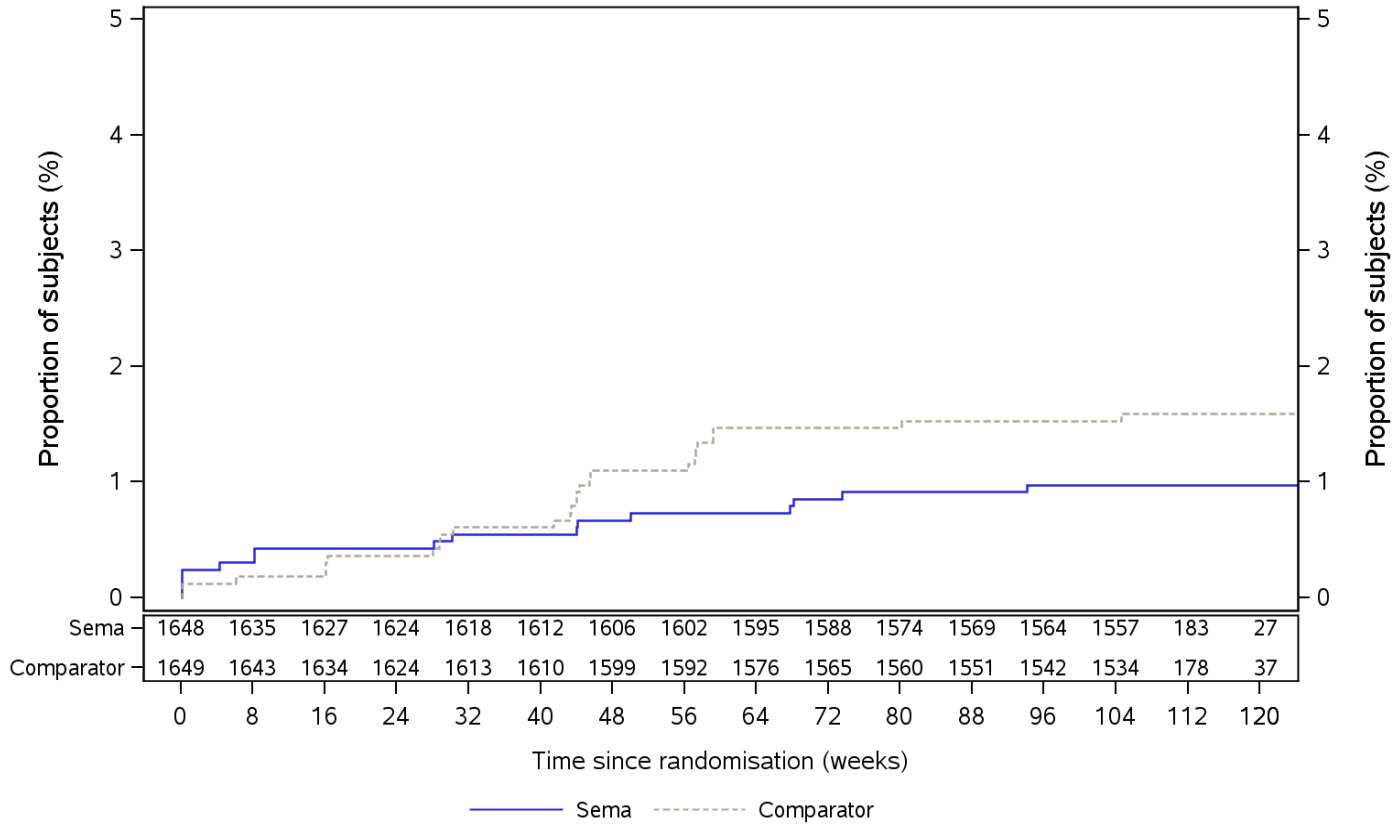
117 Adverse events - preferred term "Nephrolithiasis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:19:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nephroli_ae_all_s6.png

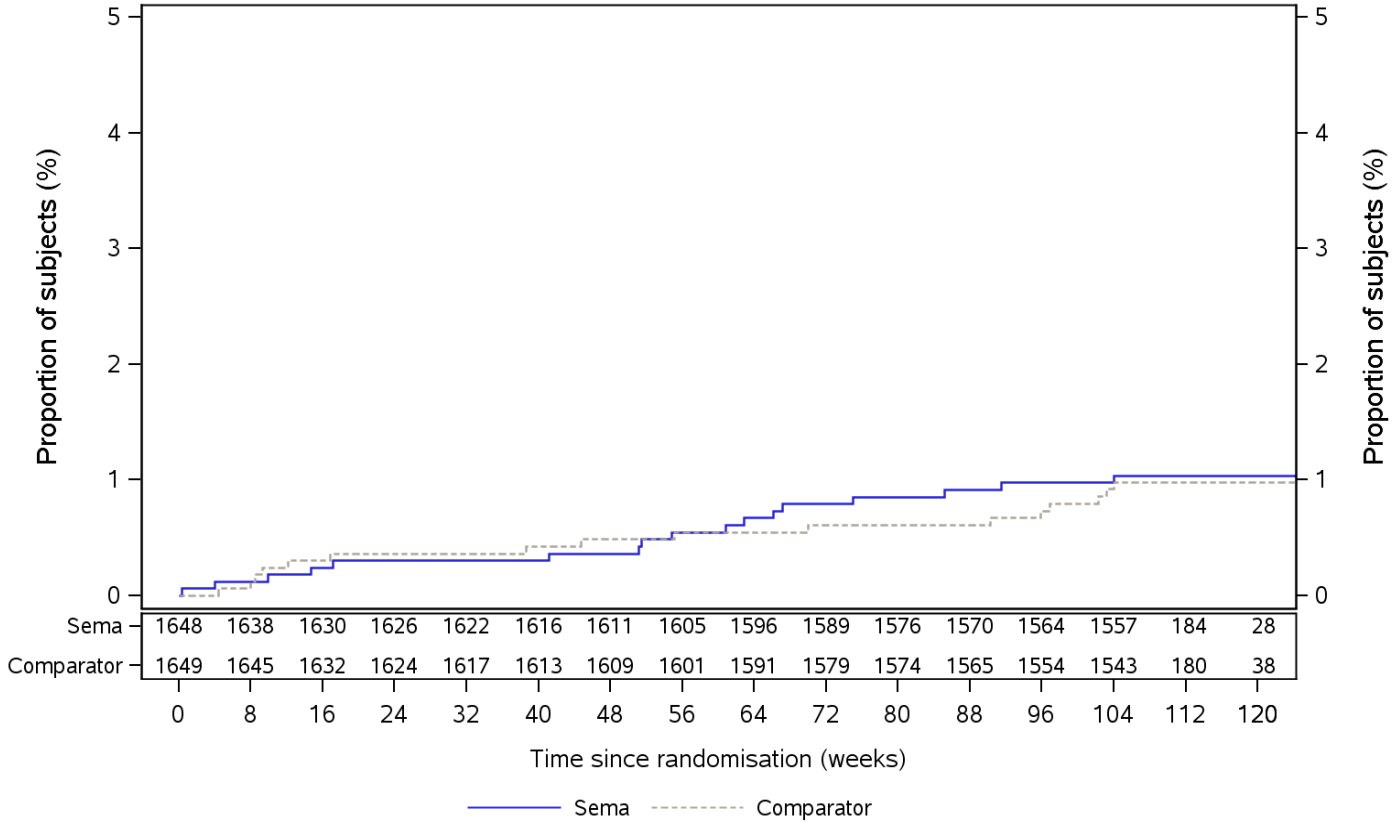
118 Adverse events - preferred term "Nephropathy" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:19:45 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nephropa_ae_all_s6.png

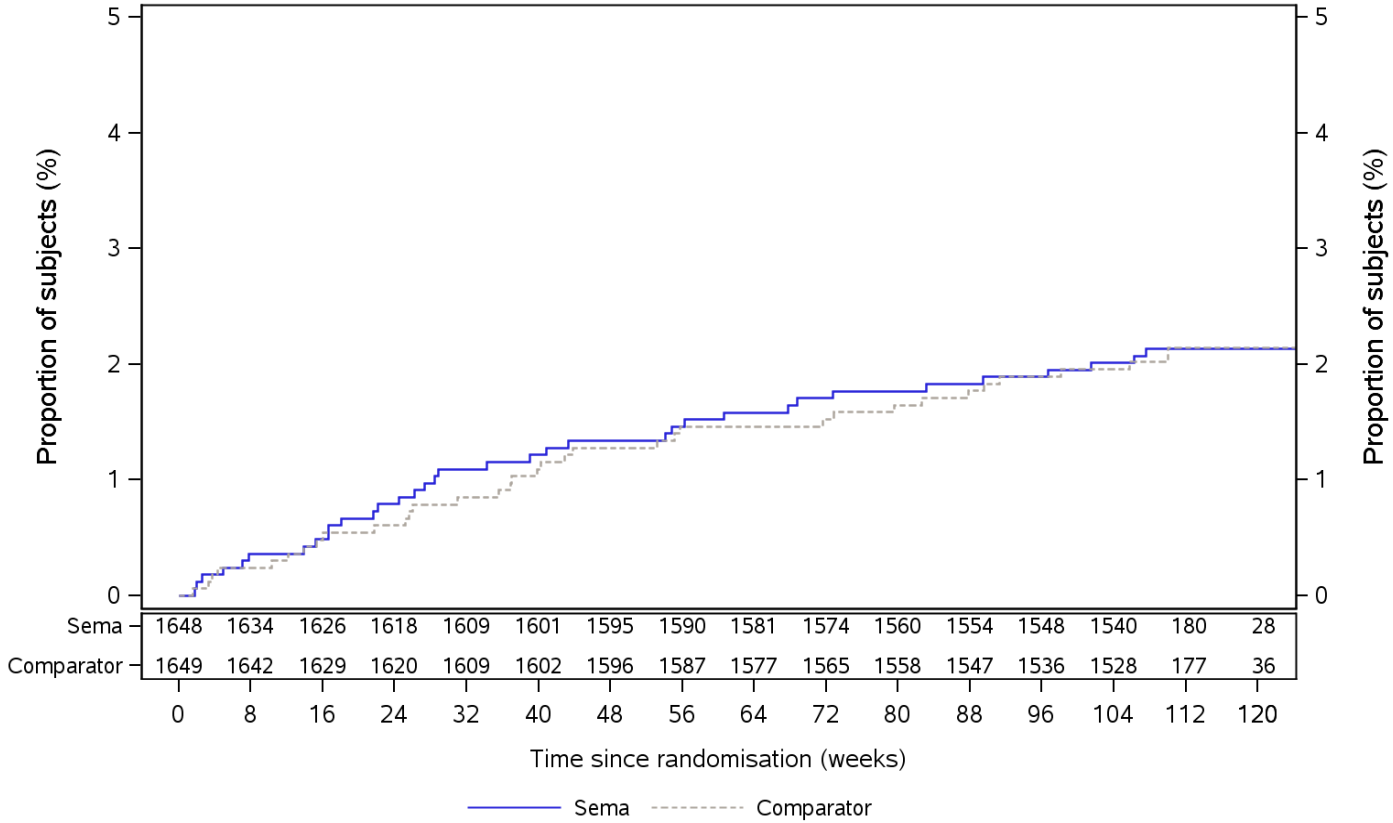
119 Adverse events - preferred term "Neuropathy peripheral" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:20:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_neurperi_ae_all_s6.png

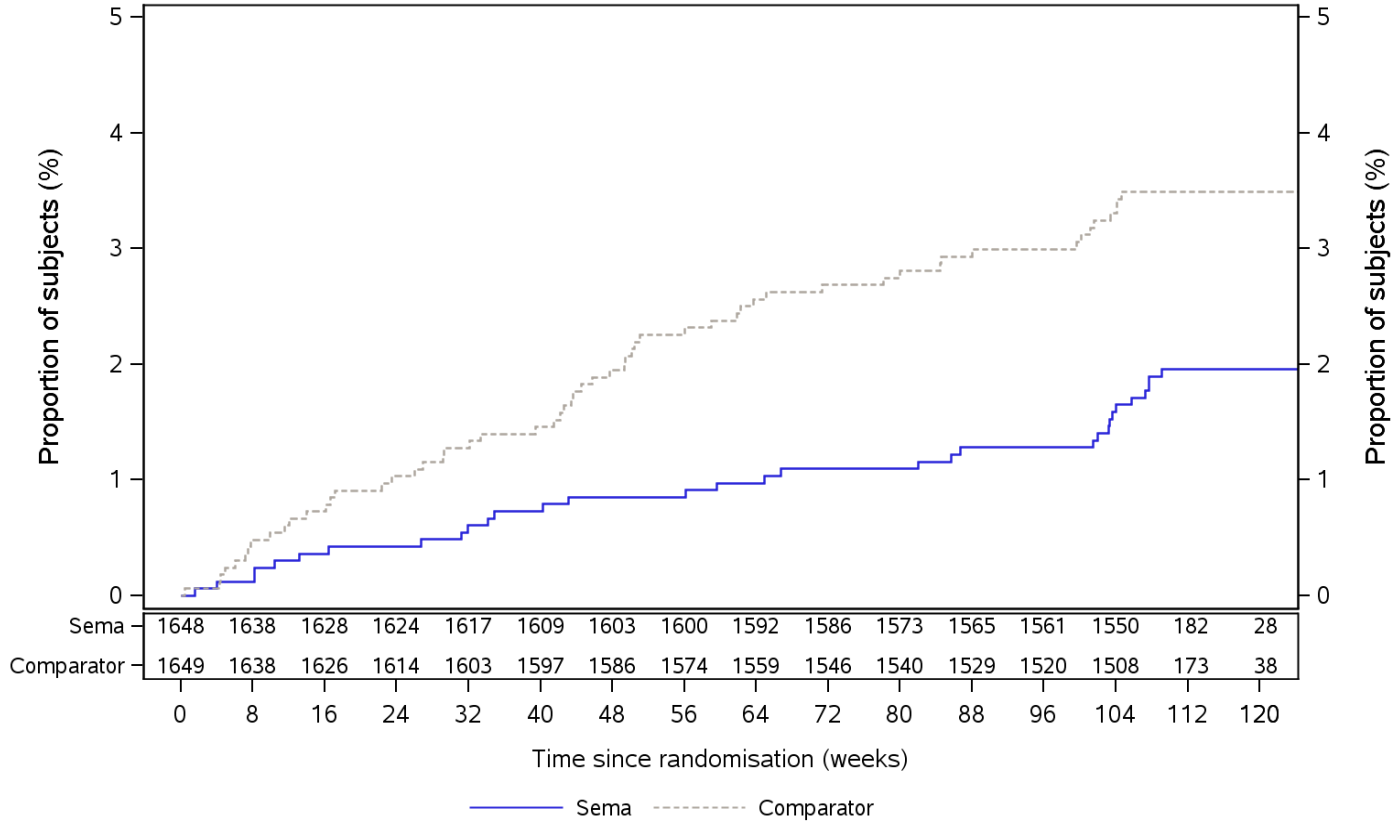
120 Adverse events - preferred term "Non-cardiac chest pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:20:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_noncarche_ae_all_s6.png

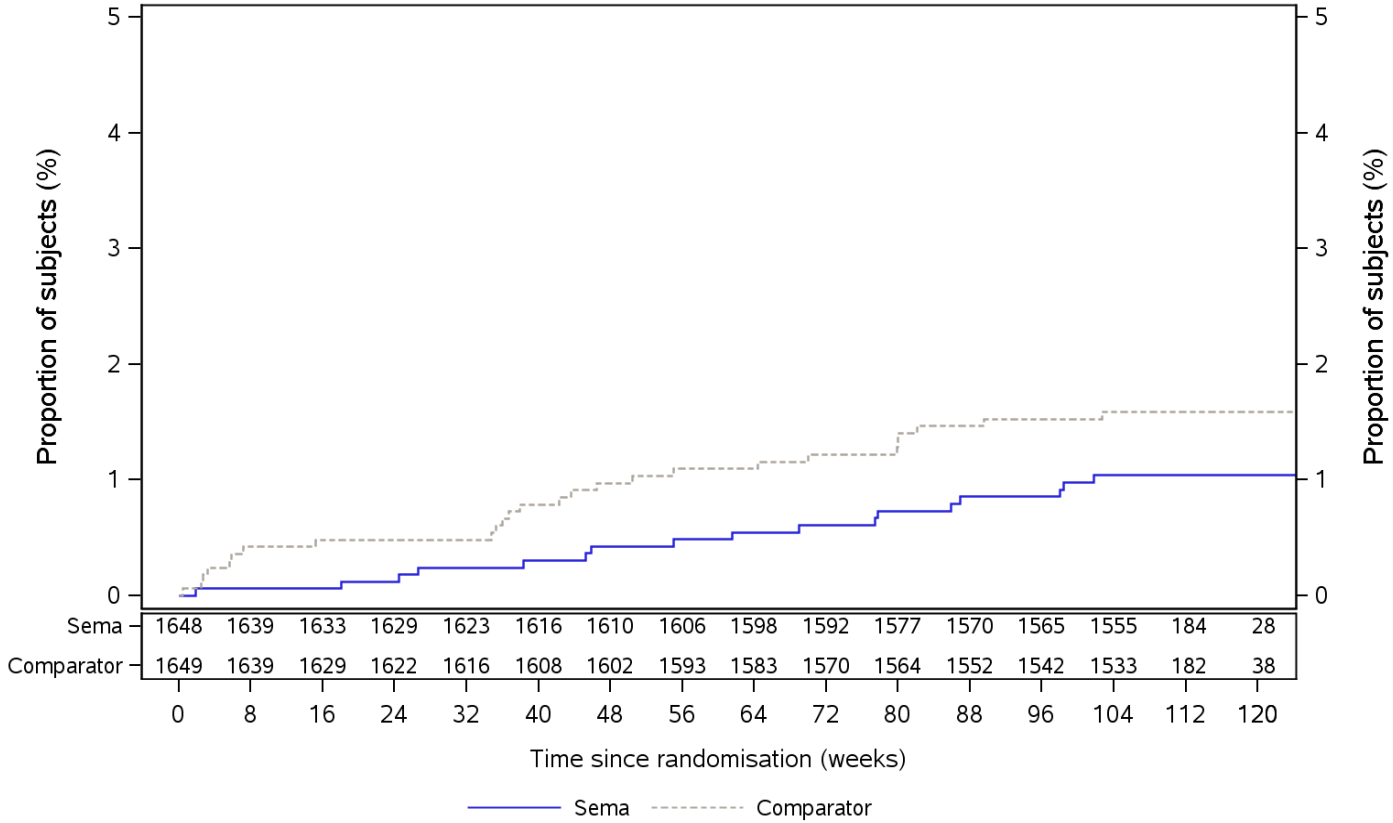
121 Adverse events - preferred term "Oedema peripheral" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:20:46 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_oedeperi_ae_all_s6.png

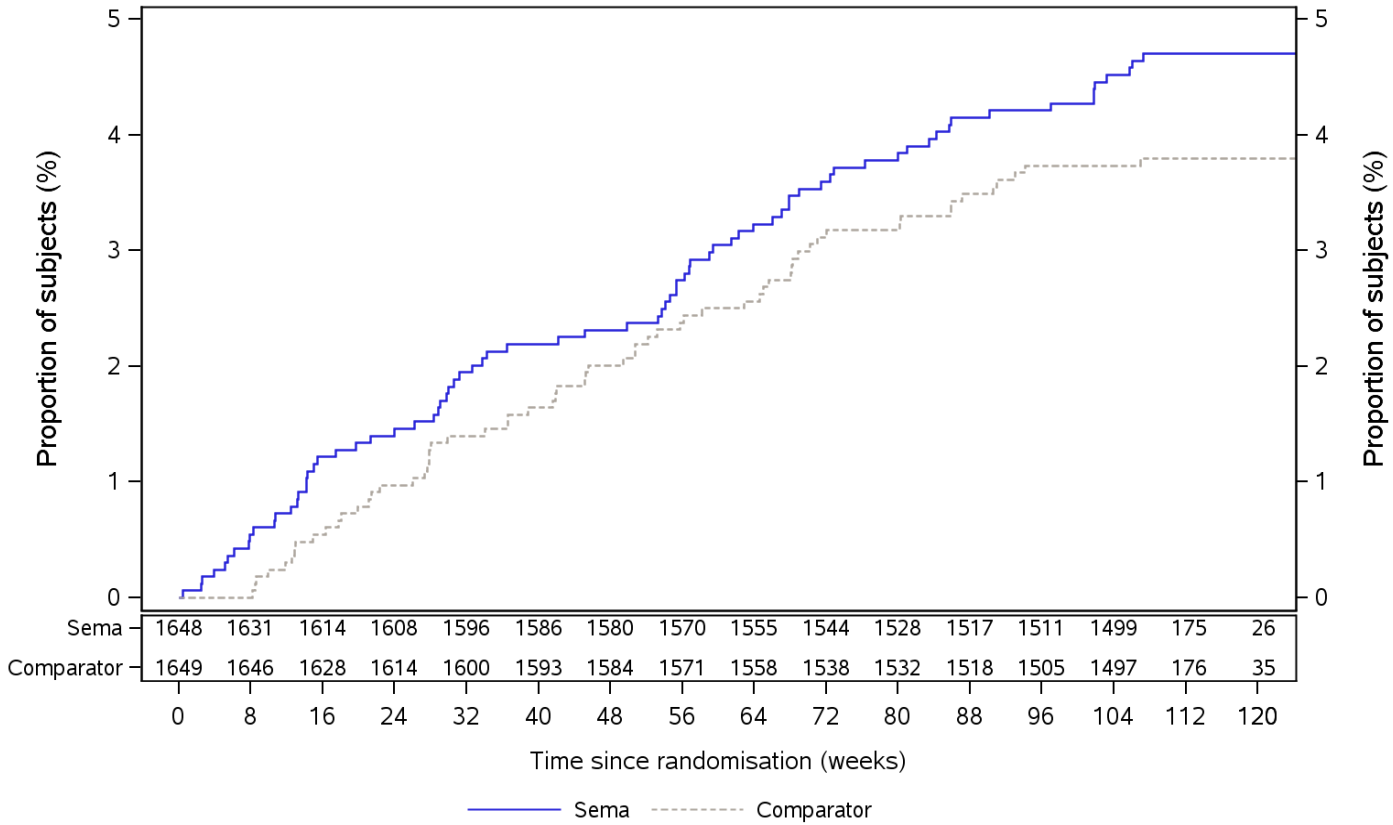
122 Adverse events - preferred term "Oropharyngeal pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:21:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_oroppain_ae_all_s6.png

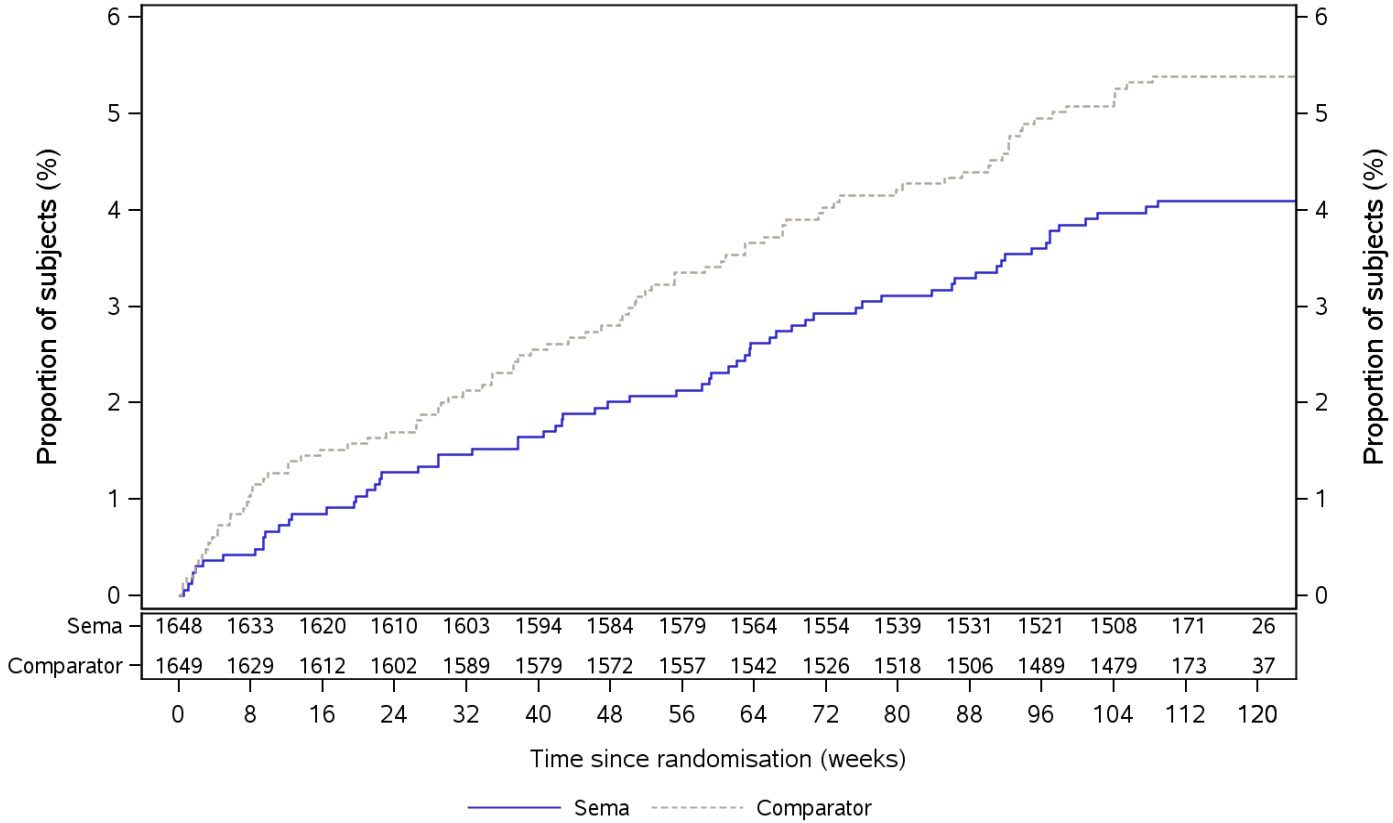
123 Adverse events - preferred term "Osteoarthritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:21:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_ost_ae_all_s6.png

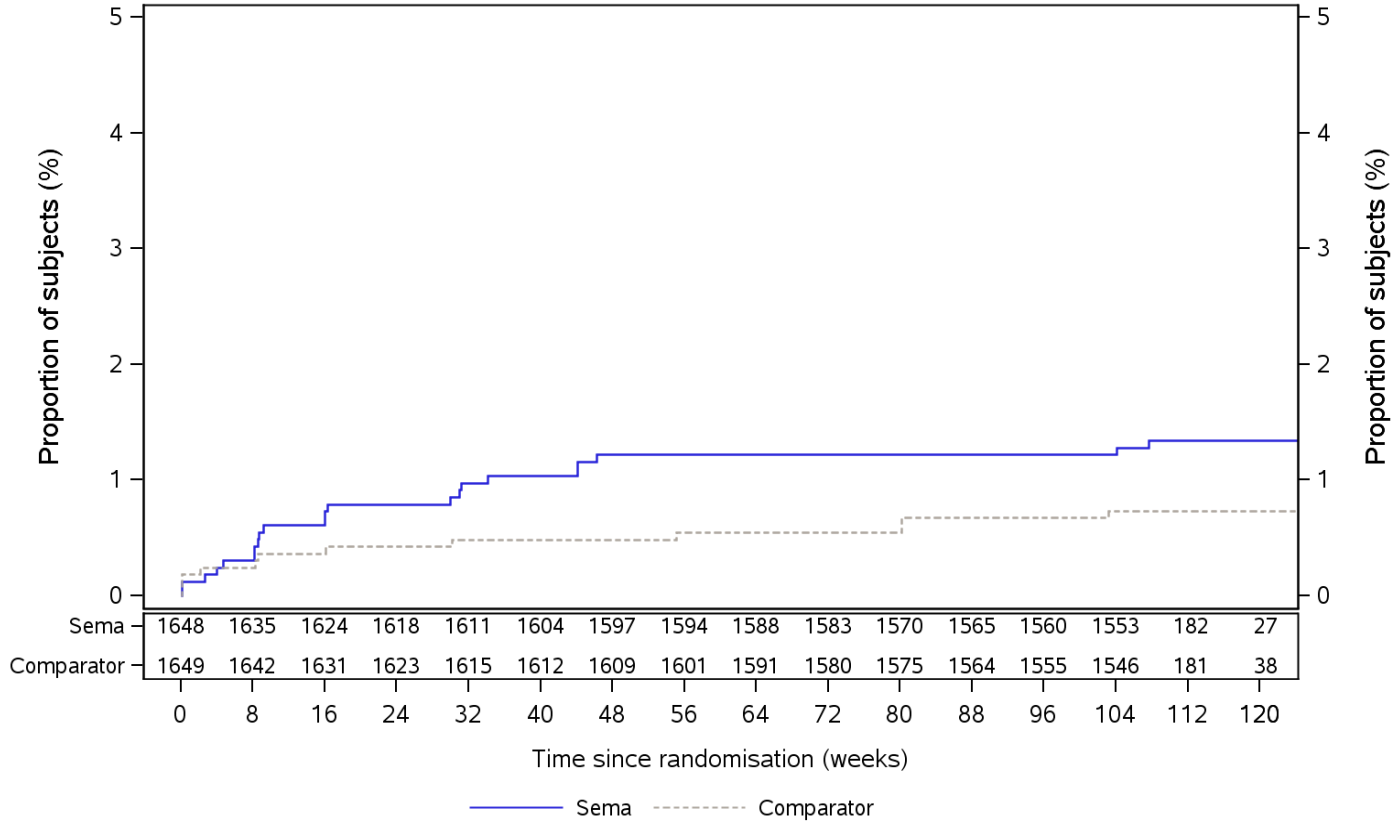
124 Adverse events - preferred term "Pain in extremity" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:21:44 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_paiinext_ae_all_s6.png

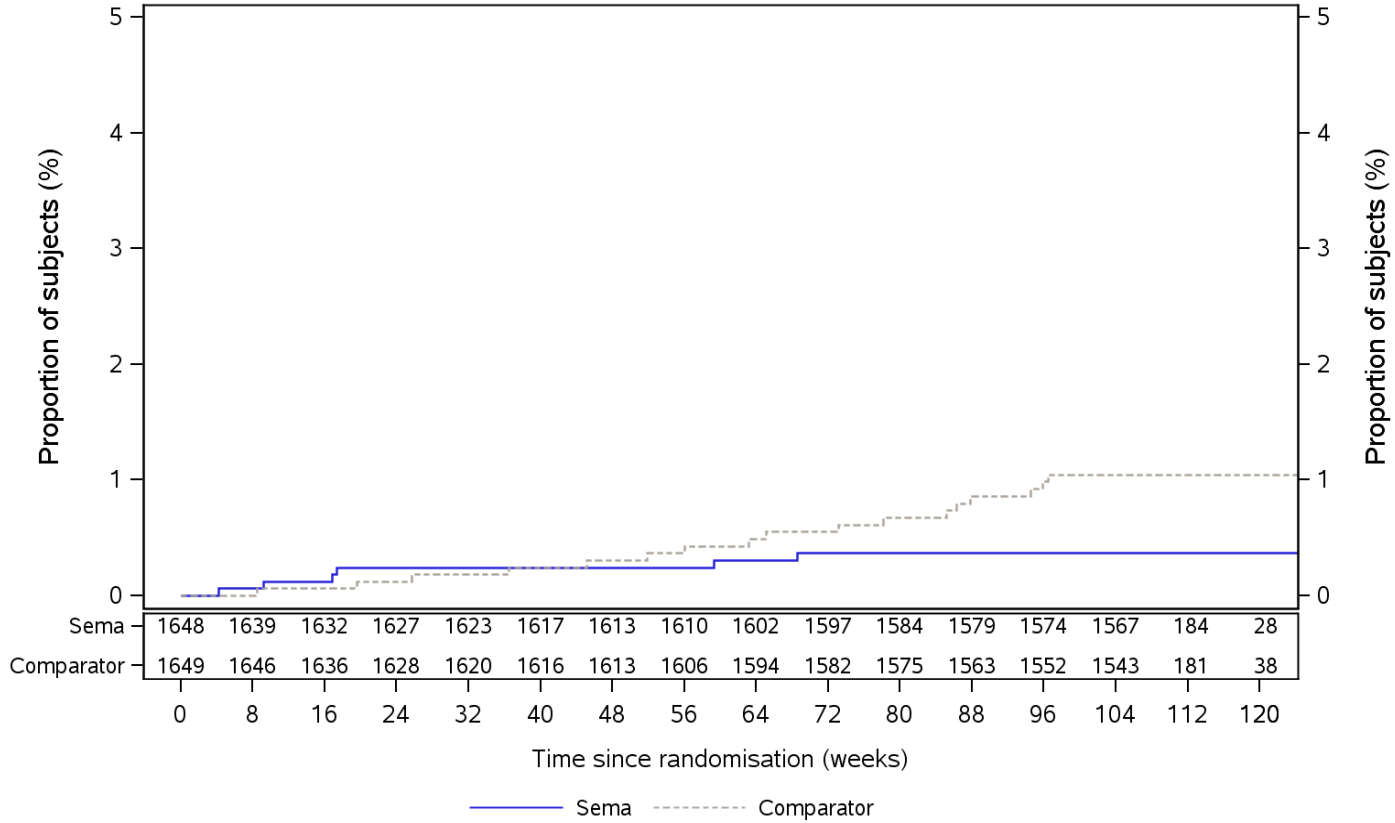
125 Adverse events - preferred term "Pancreatic enzymes increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:22:04 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_panenzinc_ae_all_s6.png

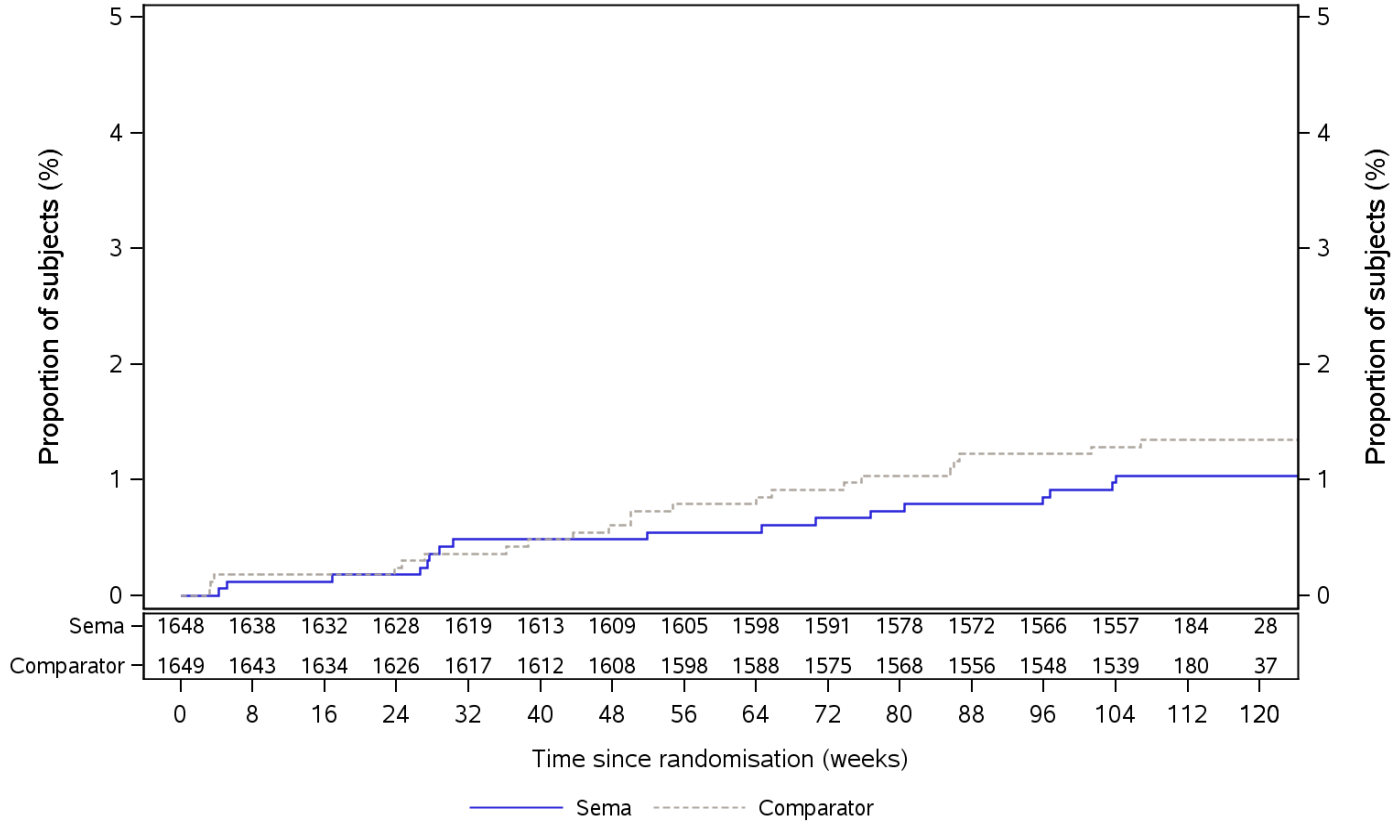
126 Adverse events - preferred term "Peripheral revascularisation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:22:23 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_perireva_ae_all_s6.png

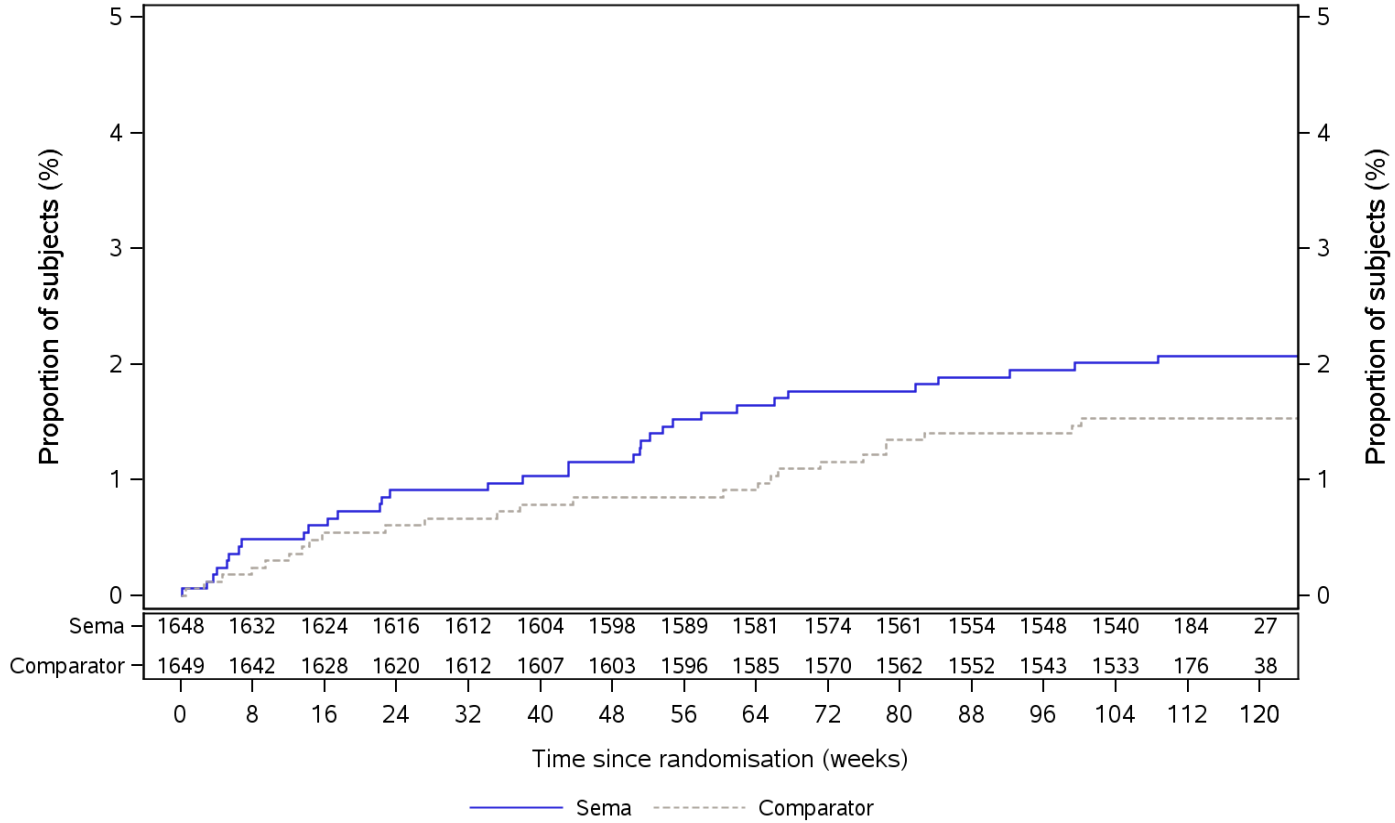
127 Adverse events - preferred term "Peripheral swelling" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:22:42 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_periswel_ae_all_s6.png

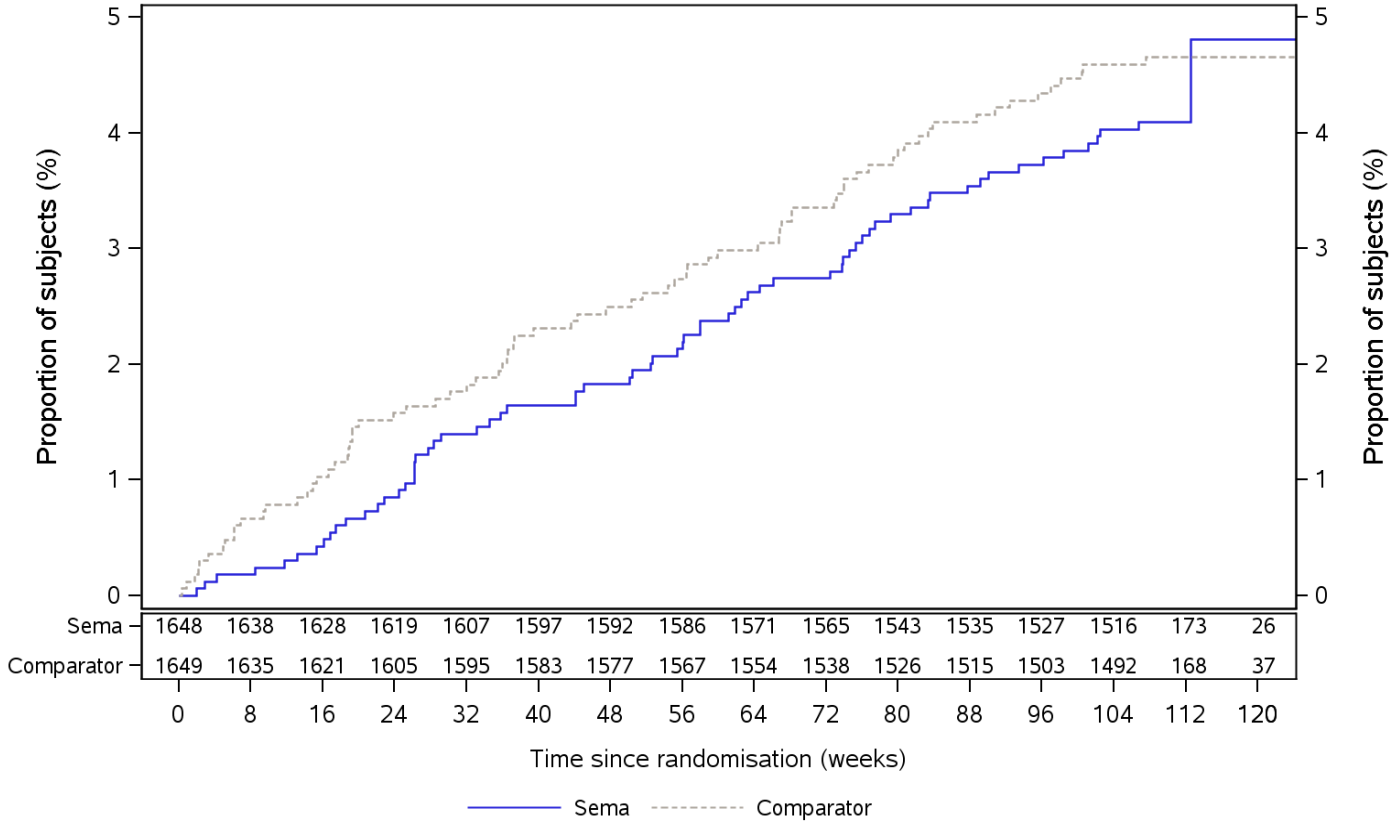
128 Adverse events - preferred term "Pharyngitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:23:01 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pharyngi_ae_all_s6.png

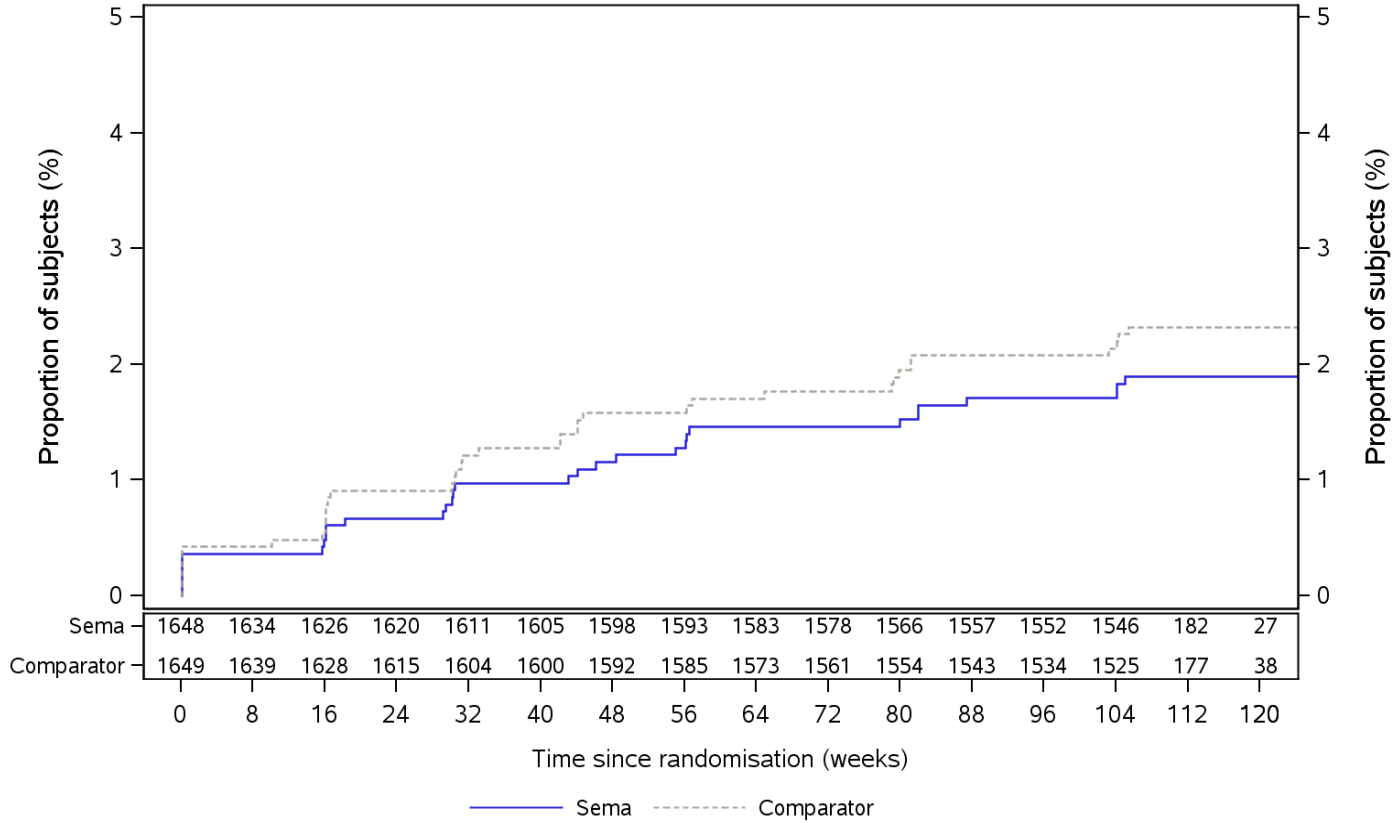
129 Adverse events - preferred term "Pneumonia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:23:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pneu_ae_all_s6.png

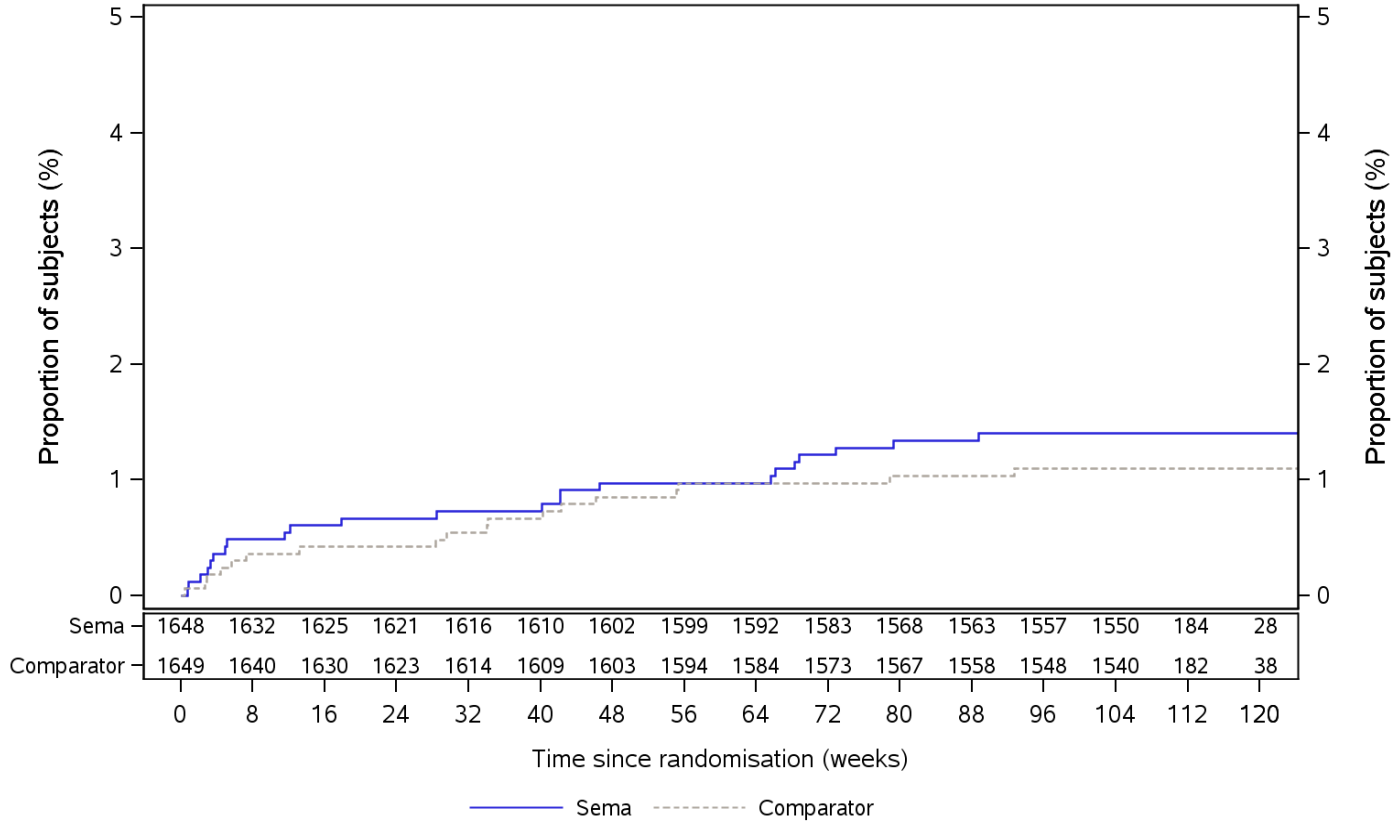
130 Adverse events - preferred term "Proteinuria" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:23:39 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_proteinu_ae_all_s6.png

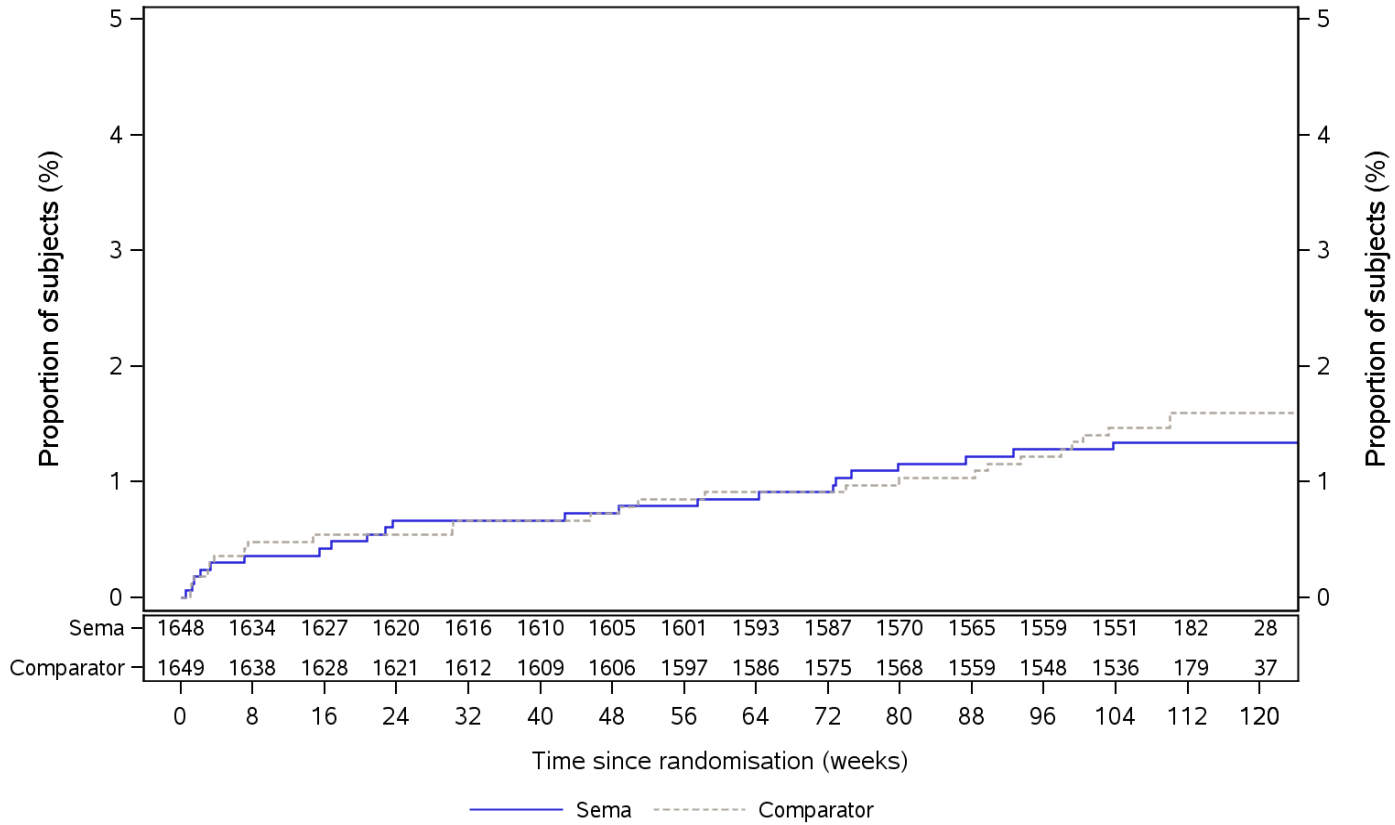
131 Adverse events - preferred term "Pruritus" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:23:59 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pruritus_ae_all_s6.png

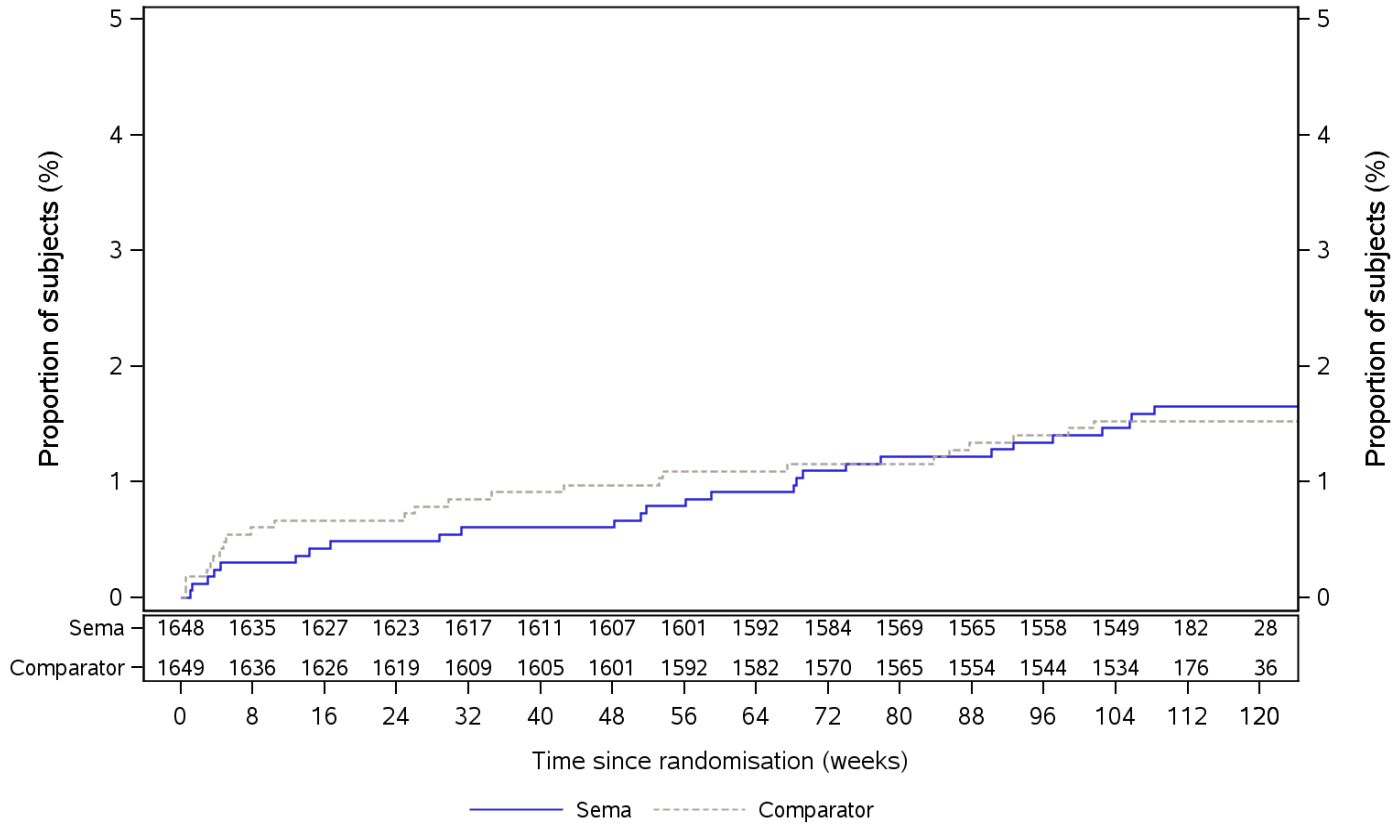
132 Adverse events - preferred term "Pyrexia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:24:19 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pyrexia_ae_all_s6.png

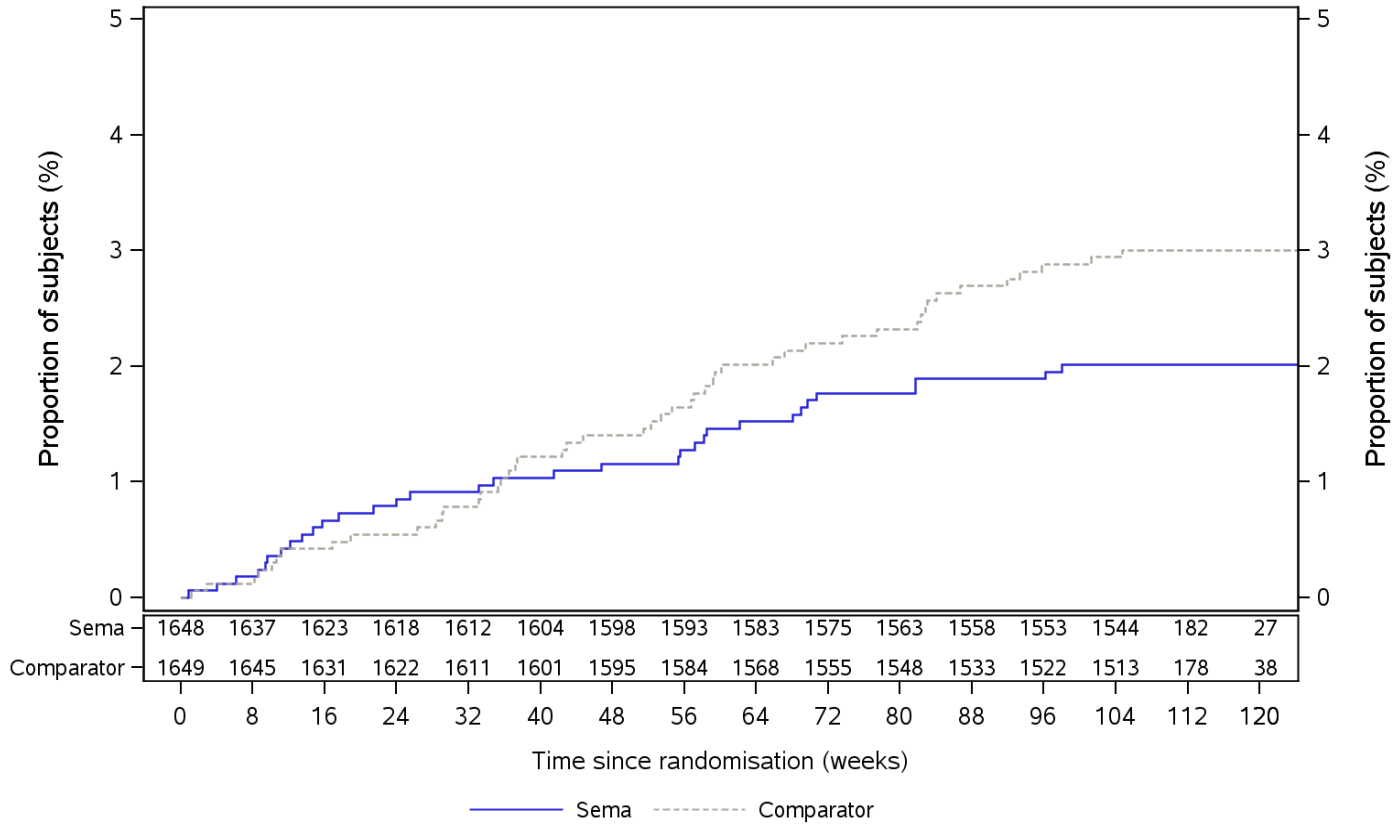
133 Adverse events - preferred term "Rash" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:24:38 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_rash_ae_all_s6.png

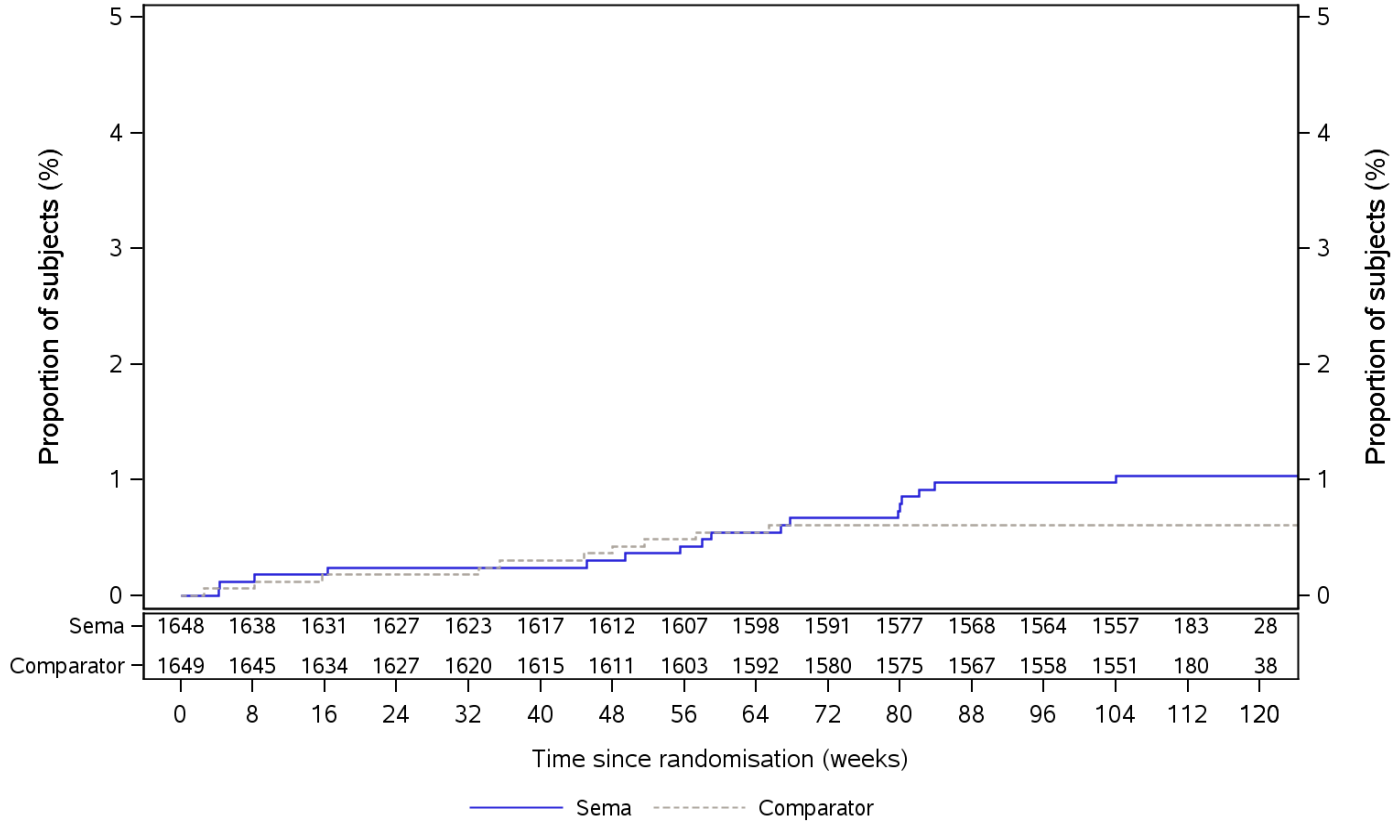
134 Adverse events - preferred term "Renal cyst" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:24:57 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_renacyst_ae_all_s6.png

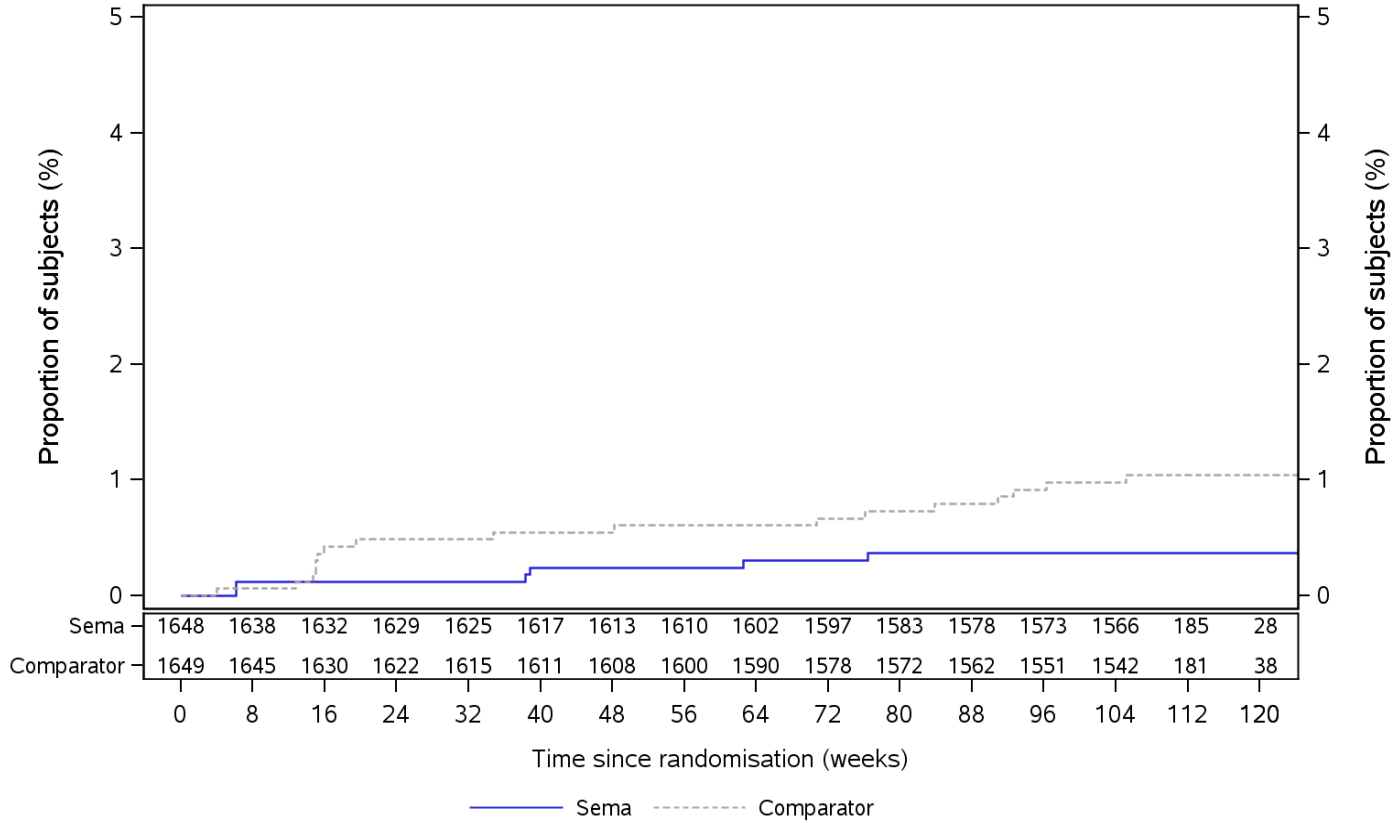
135 Adverse events - preferred term "Renal impairment" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:25:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_renaimpa_ae_all_s6.png

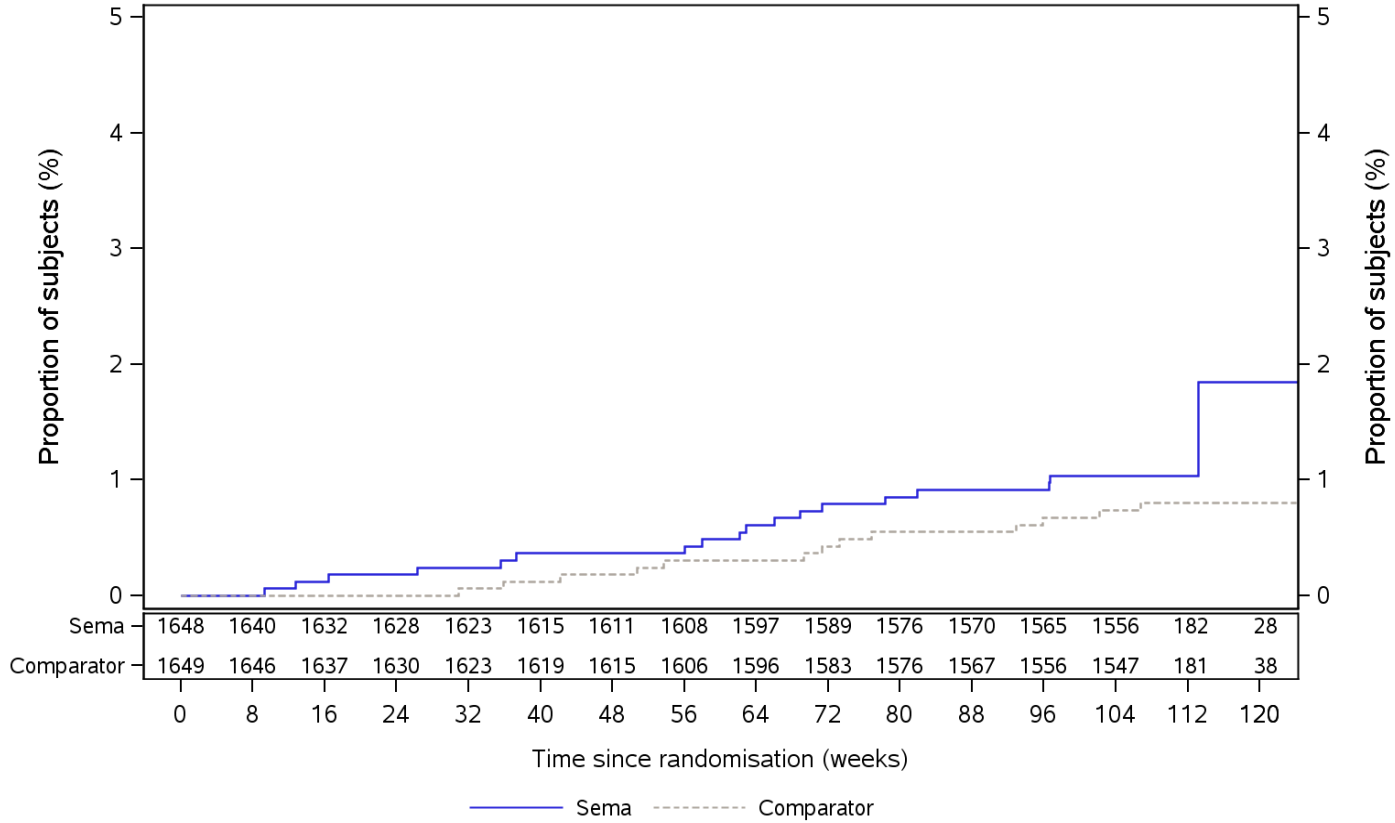
136 Adverse events - preferred term "Rhinitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:25:37 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_rhinitis_ae_all_s6.png

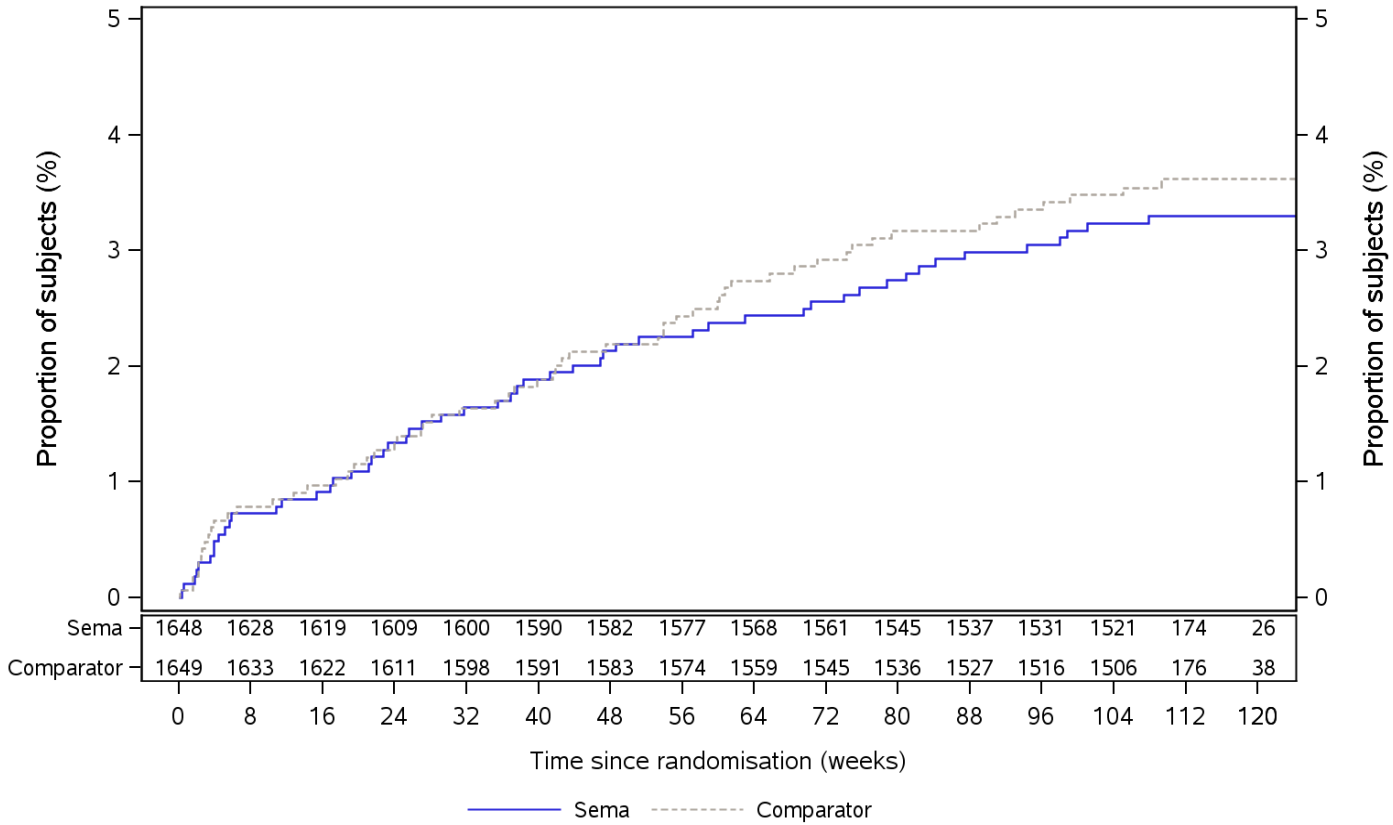
137 Adverse events - preferred term "Road traffic accident" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:25:57 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_roatraacc_ae_all_s6.png

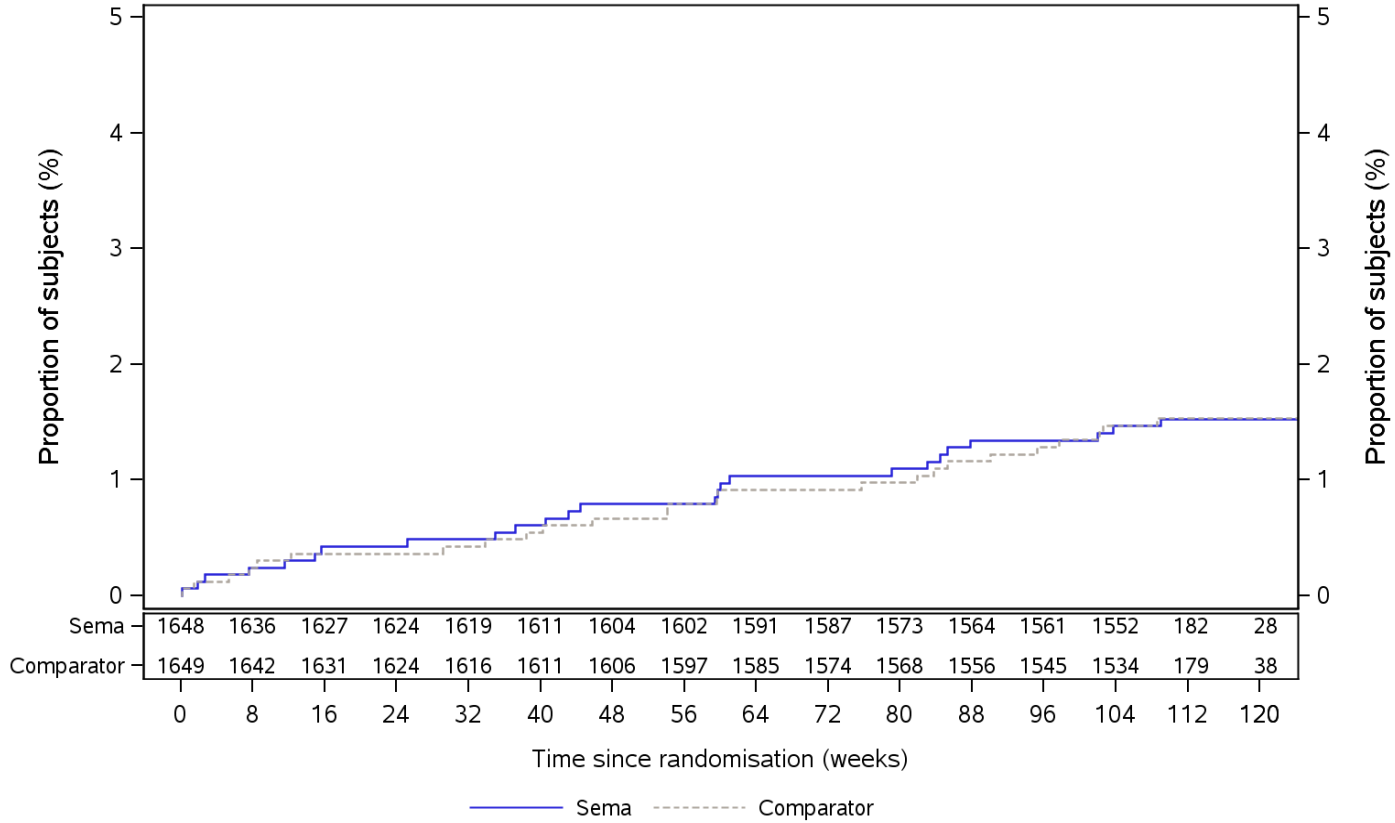
138 Adverse events - preferred term "Sinusitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:26:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_sinusiti_ae_all_s6.png

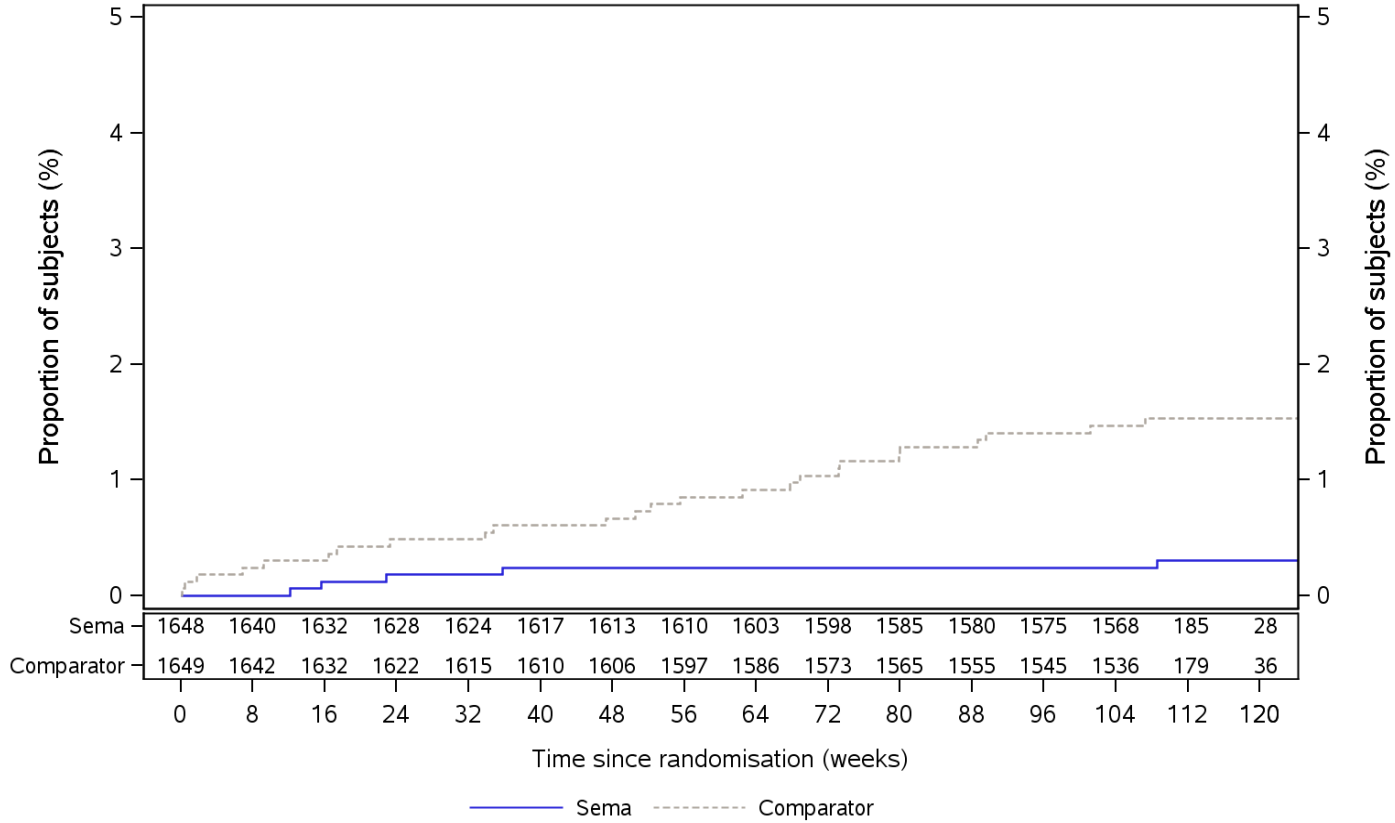
139 Adverse events - preferred term "Skin ulcer" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:26:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_skinulce_ae_all_s6.png

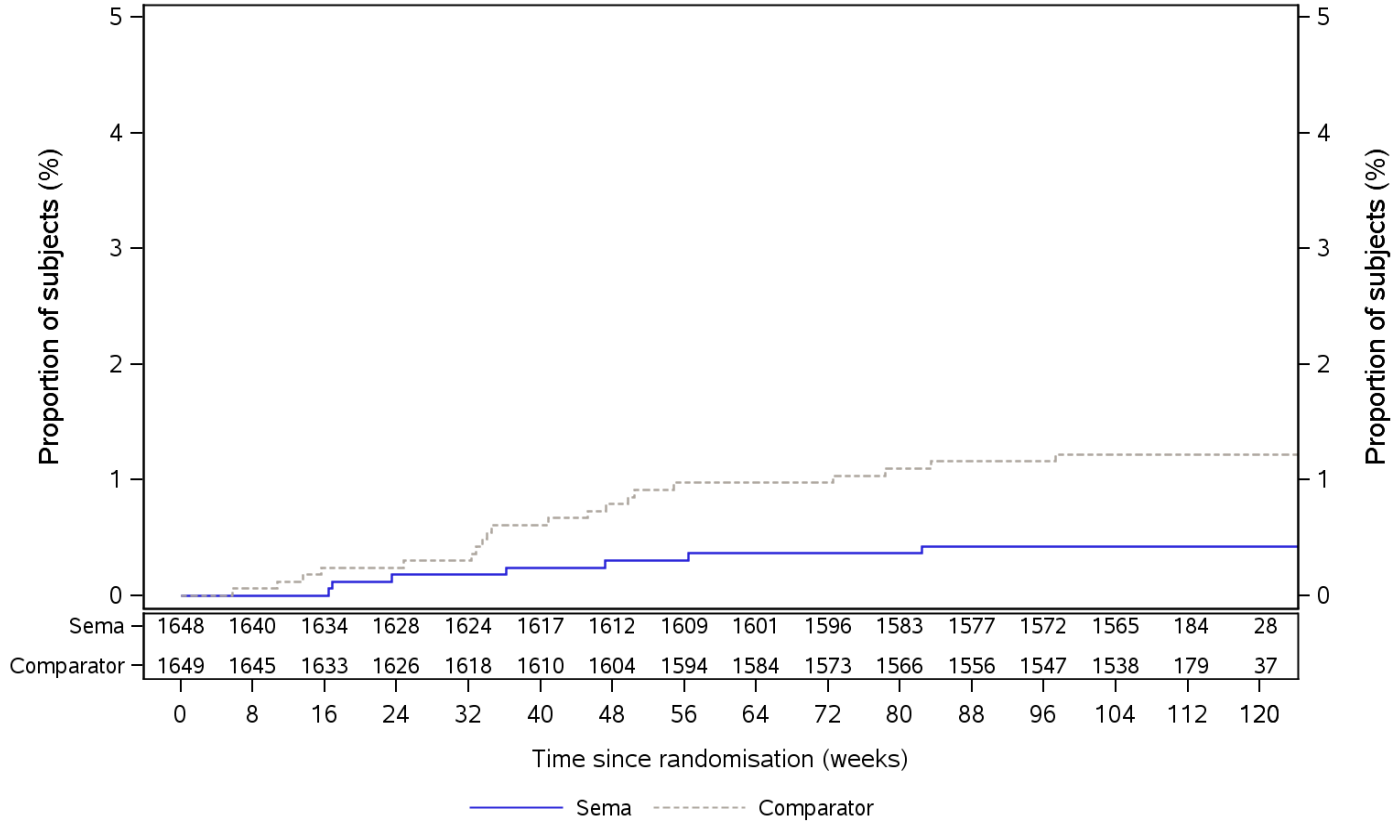
140 Adverse events - preferred term "Sleep apnoea syndrome" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:26:56 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_sleapnsyn_ae_all_s6.png

141 Adverse events - preferred term "Spinal osteoarthritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

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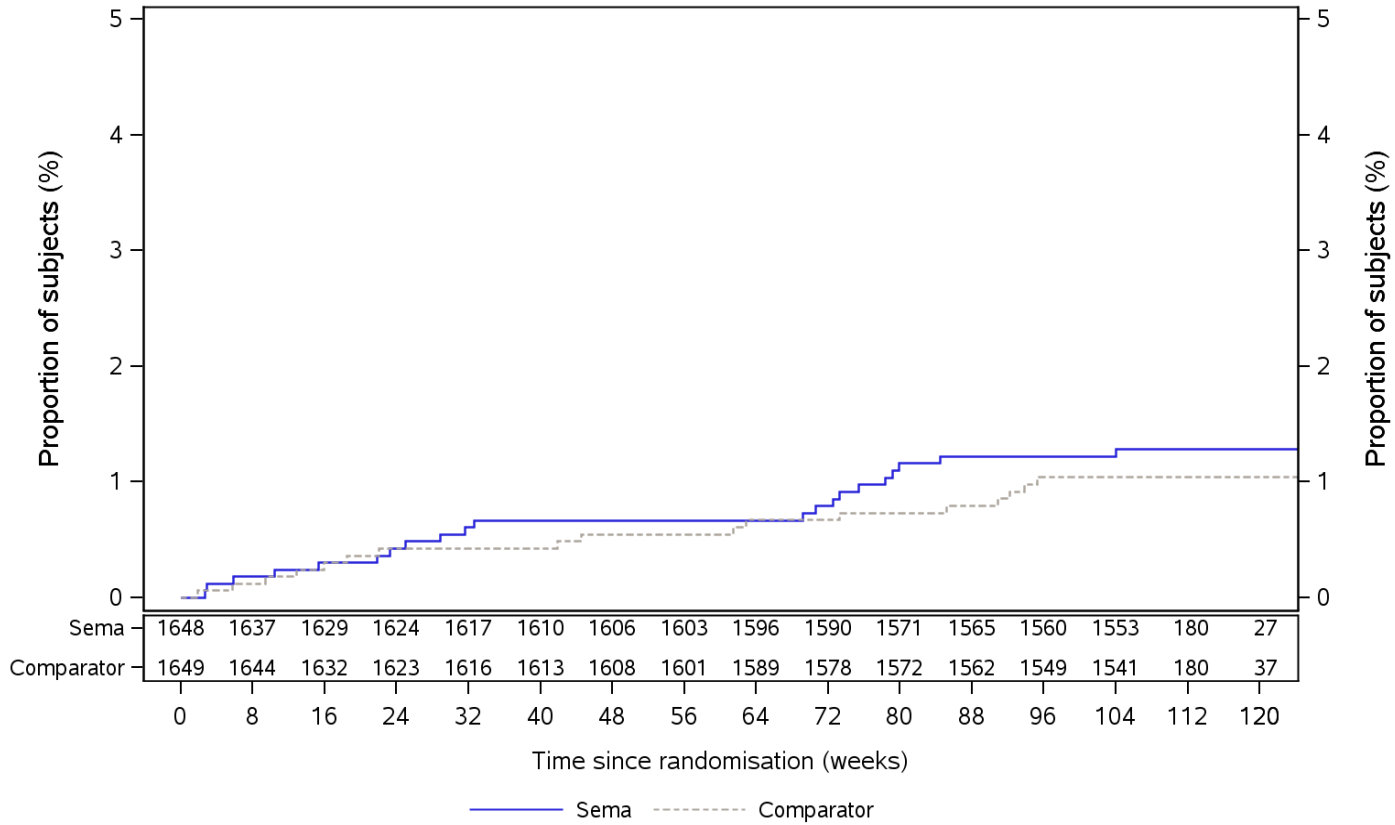
26MAY2020:11:27:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_spinoste_ae_all_s6.png

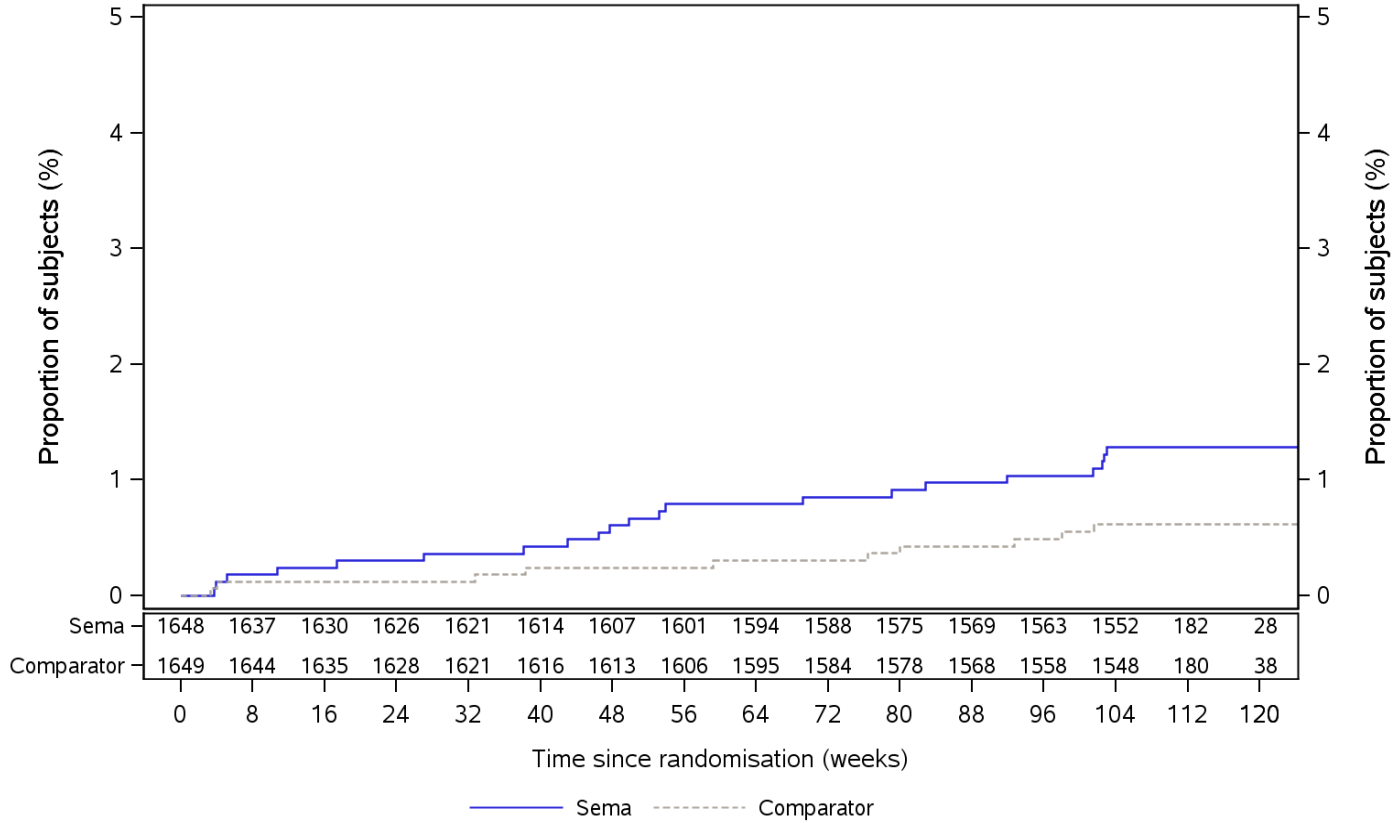
142 Adverse events - preferred term "Syncope" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:27:36 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_syncope_ae_all_s6.png

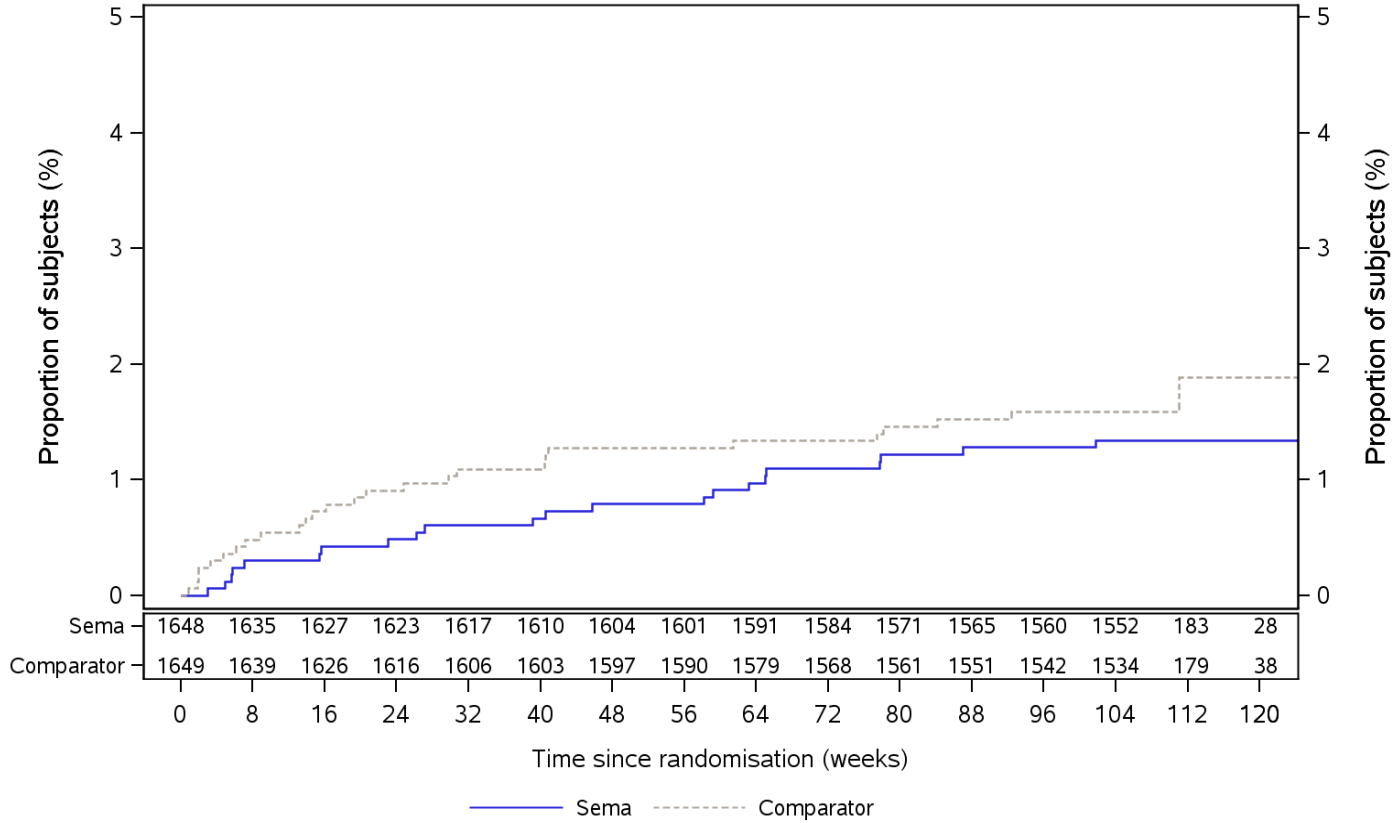
143 Adverse events - preferred term "Tooth infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:27:56 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_tootinfe_ae_all_s6.png

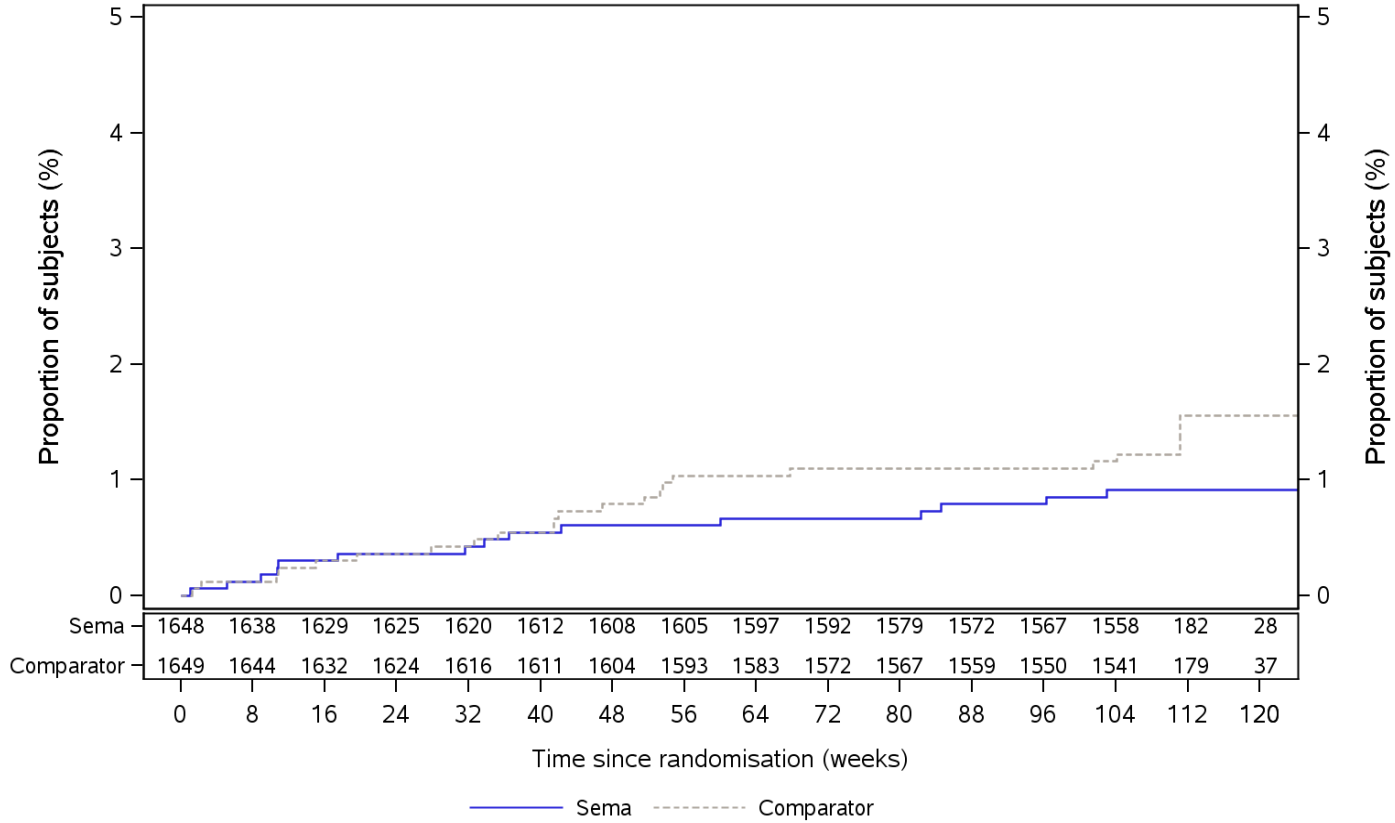
144 Adverse events - preferred term "Toothache" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:28:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_toothach_ae_all_s6.png

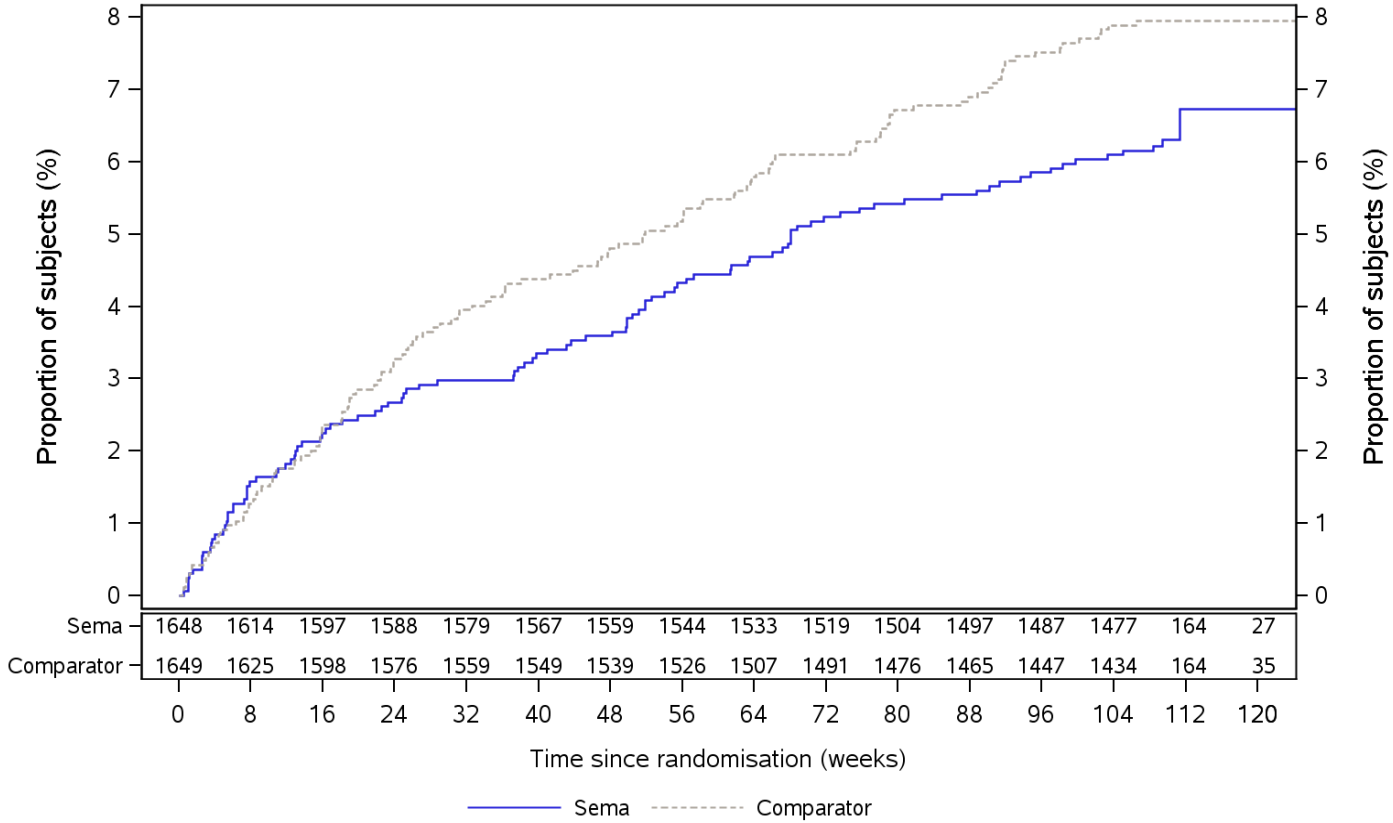
145 Adverse events - preferred term "Transient ischaemic attack" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:28:36 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_tia_ae_all_s6.png

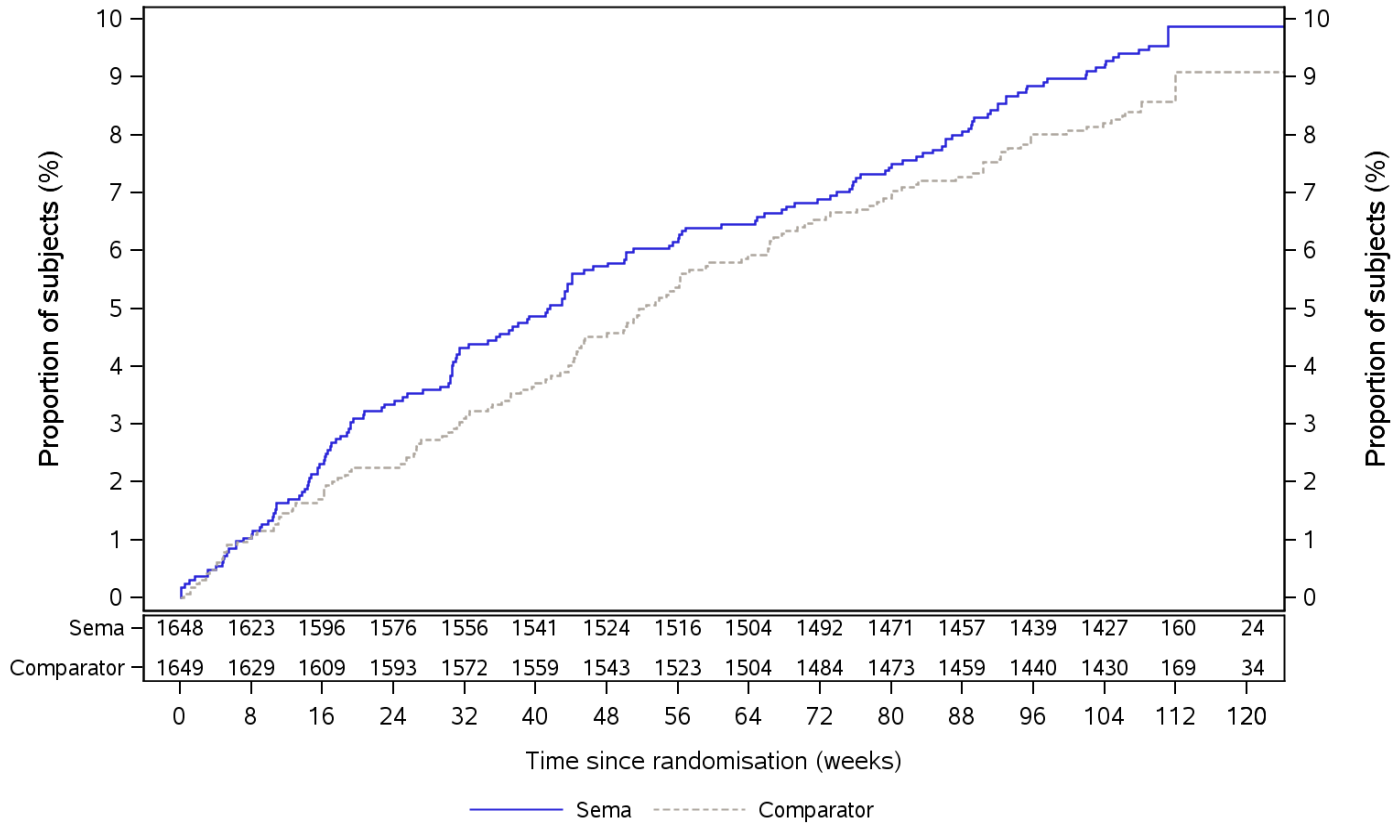
146 Adverse events - preferred term "Upper respiratory tract infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:28:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_upprestra_ae_all_s6.png

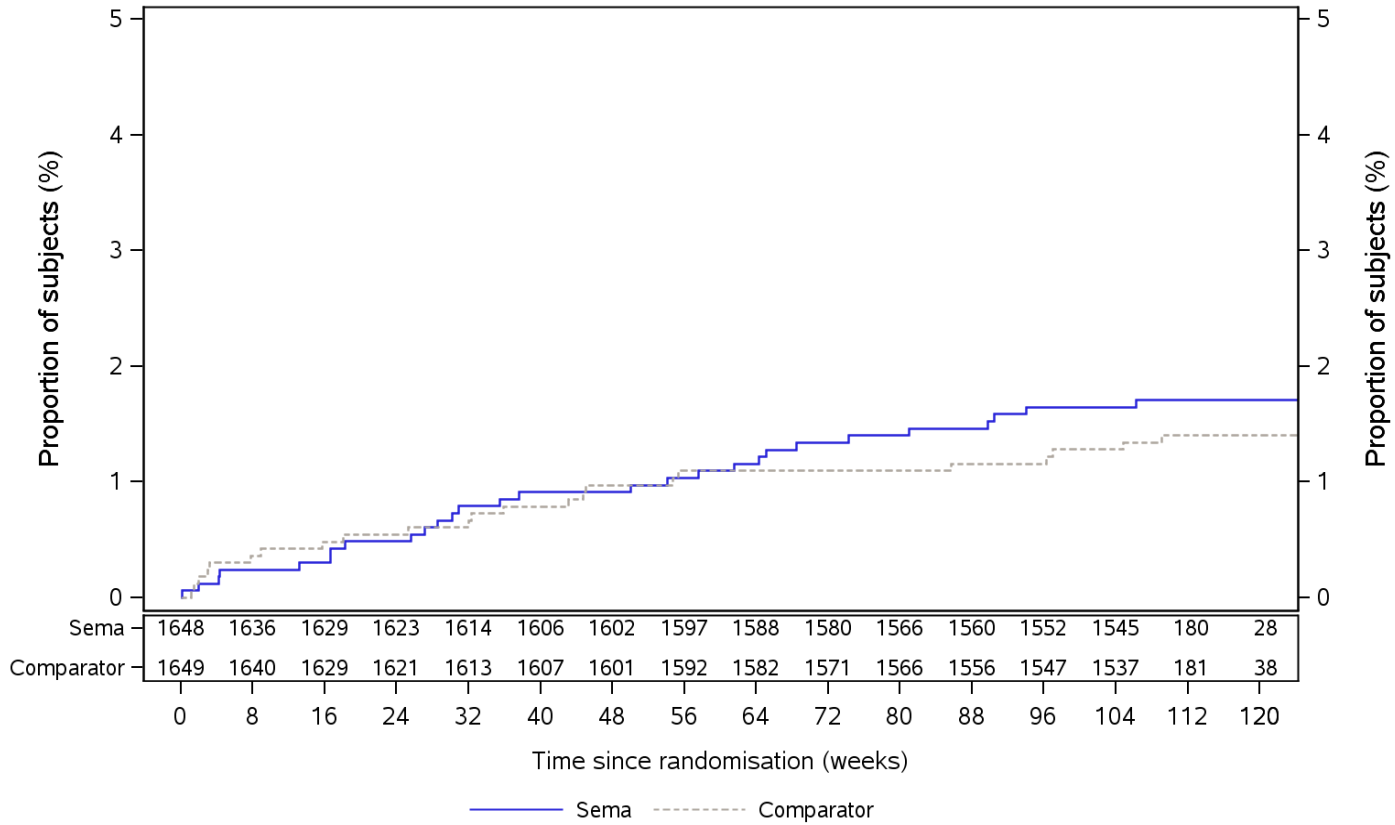
147 Adverse events - preferred term "Urinary tract infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:29:15 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_uritrainf_ae_all_s6.png

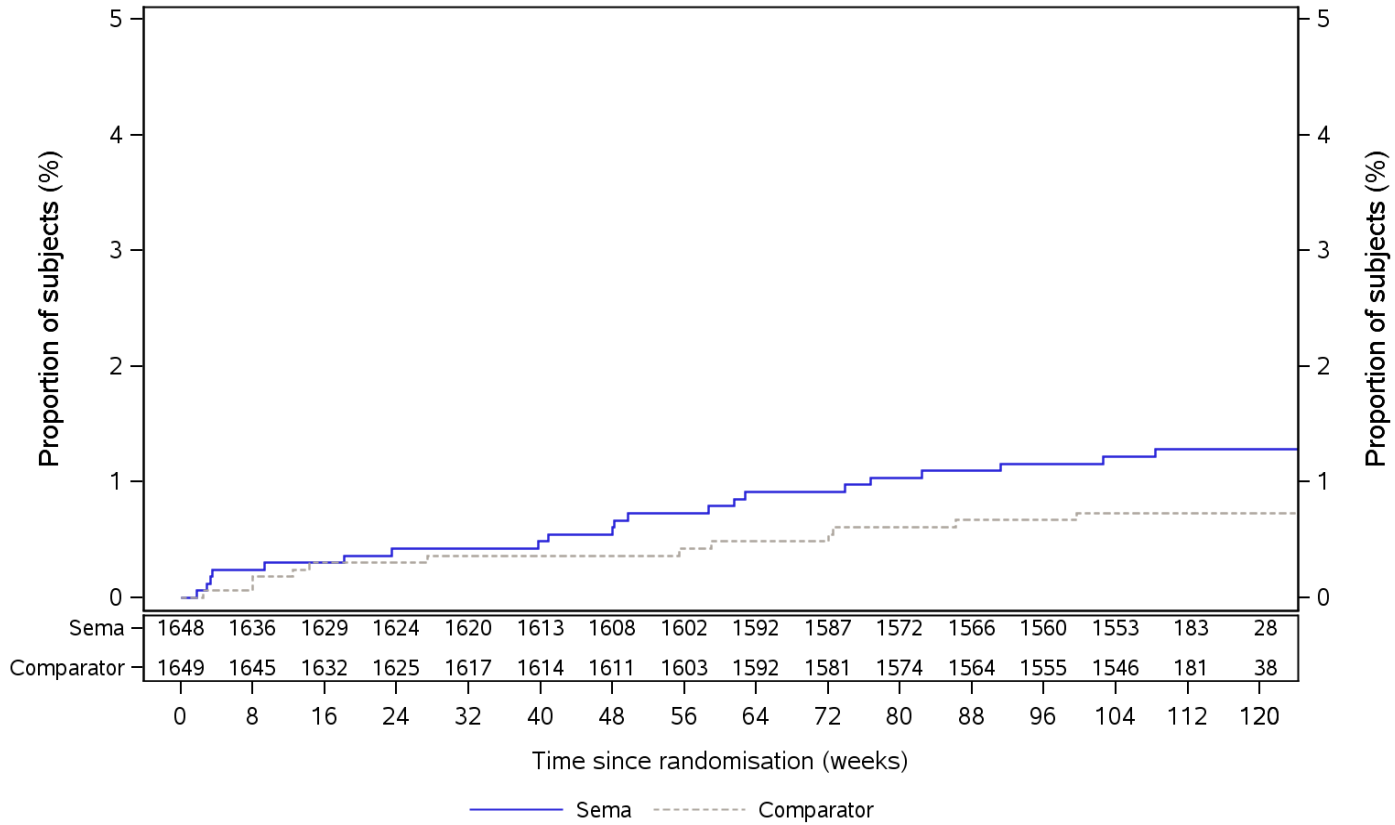
148 Adverse events - preferred term "Vertigo" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:29:34 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_vertigo_ae_all_s6.png

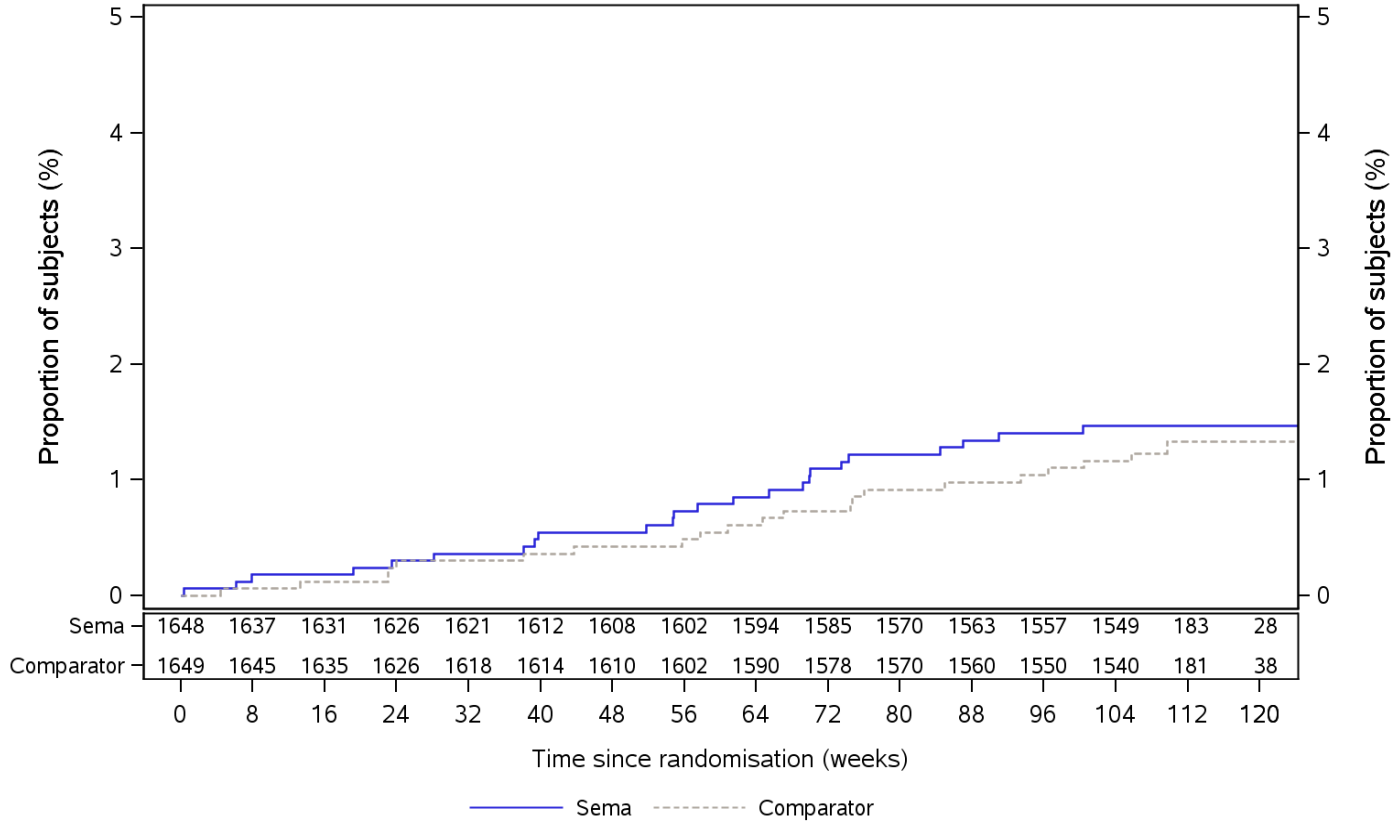
149 Adverse events - preferred term "Viral infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:29:54 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_virainfe_ae_all_s6.png

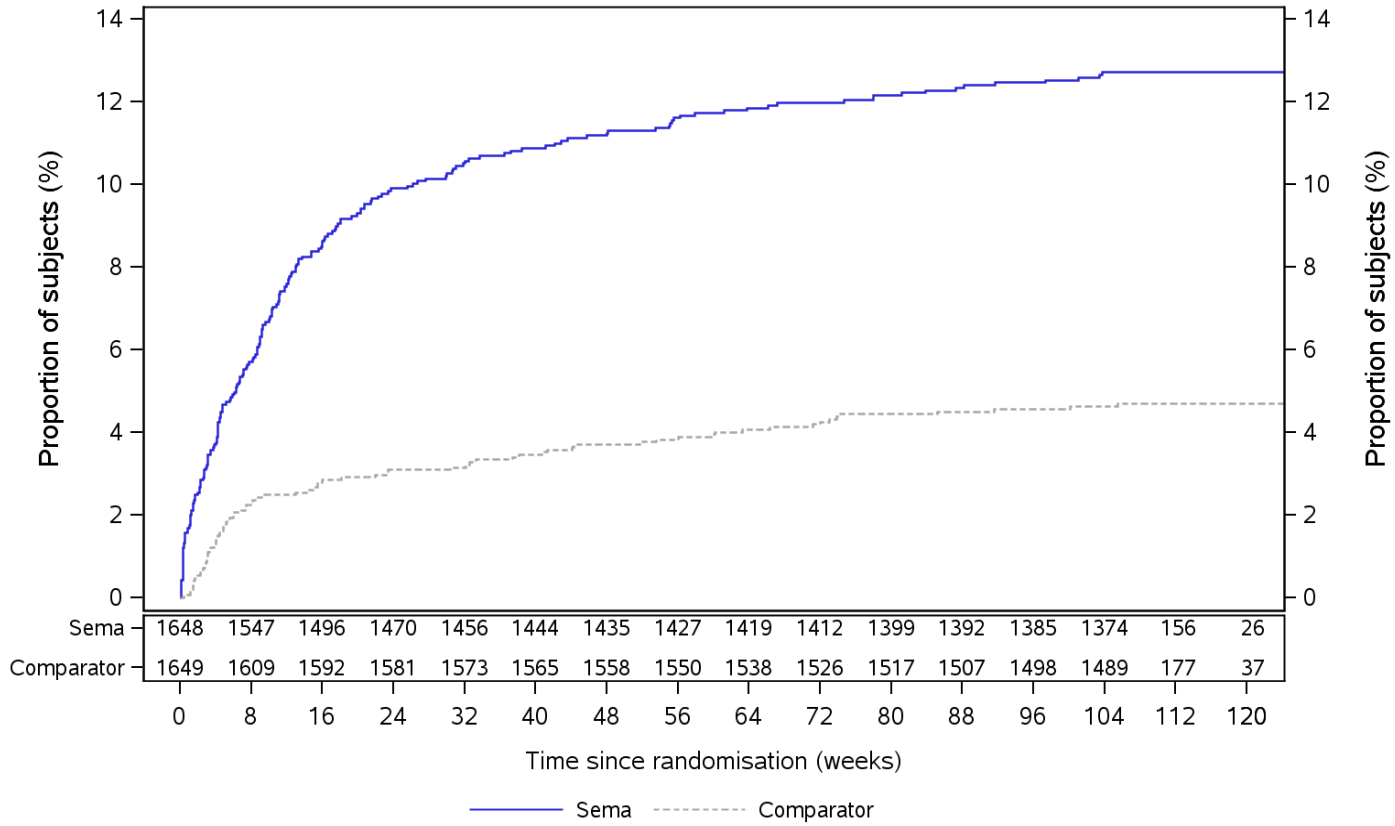
150 Adverse events - preferred term "Vitamin D deficiency" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:30:13 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_vitddef_ae_all_s6.png

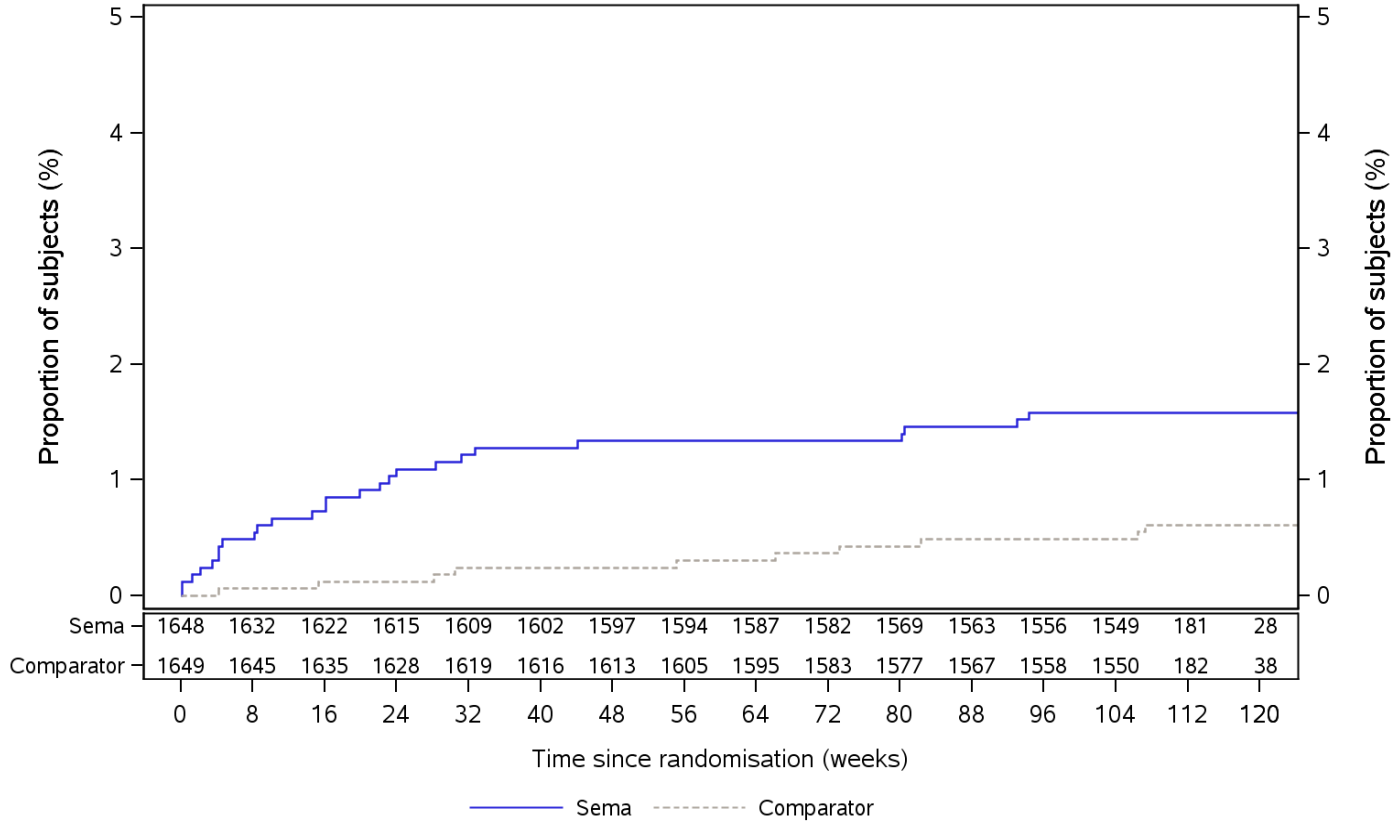
151 Adverse events - preferred term "Vomiting" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:30:31 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_vomiting_ae_all_s6.png

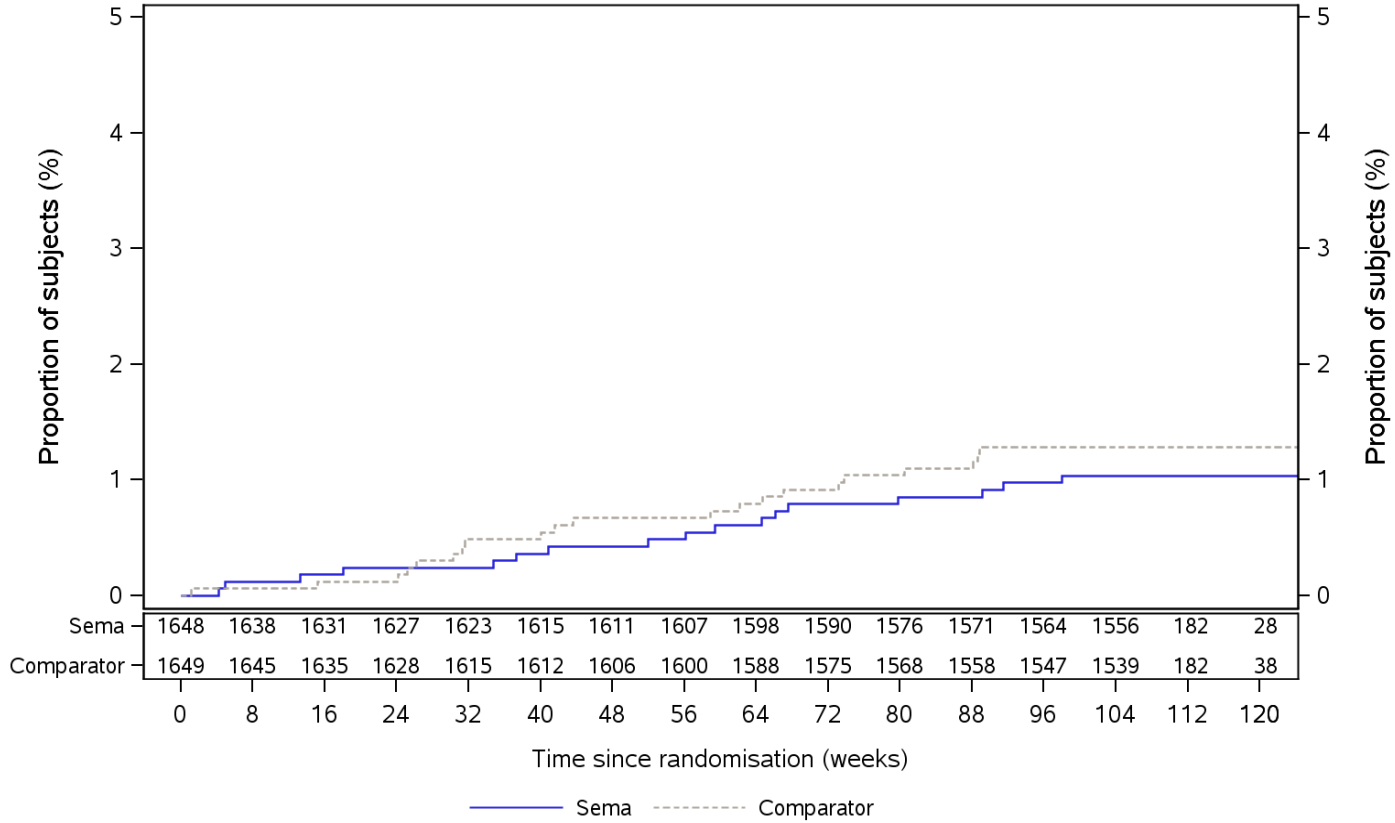
152 Adverse events - preferred term "Weight decreased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:30:51 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_weigdecr_ae_all_s6.png

153 Adverse events - preferred term "Wound" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set

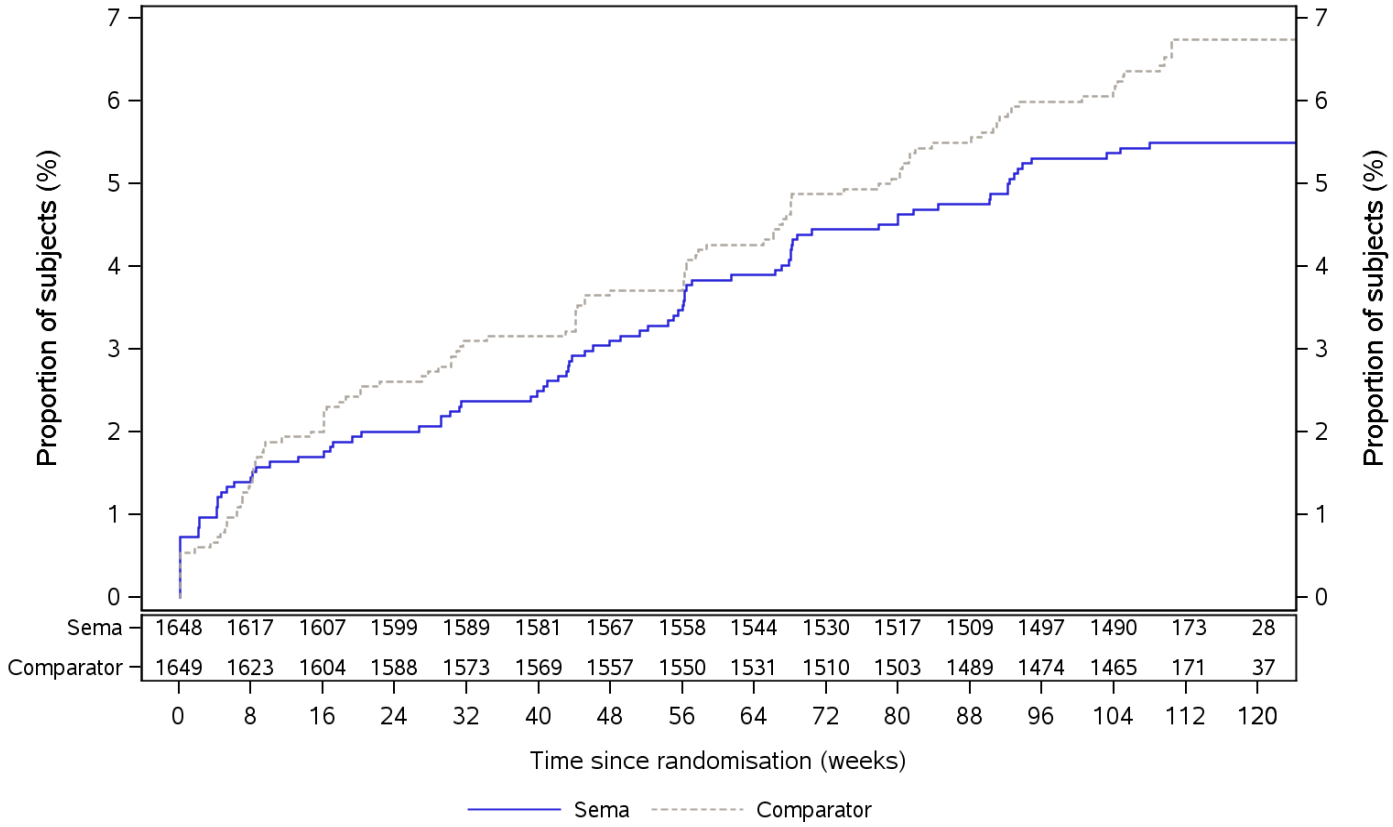


Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:11:31:10 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_wound_ae_all_s6.png

SUSTAIN 6 – Kumulative Inzidenz (UE nach Schweregrad nach SOC und PT)

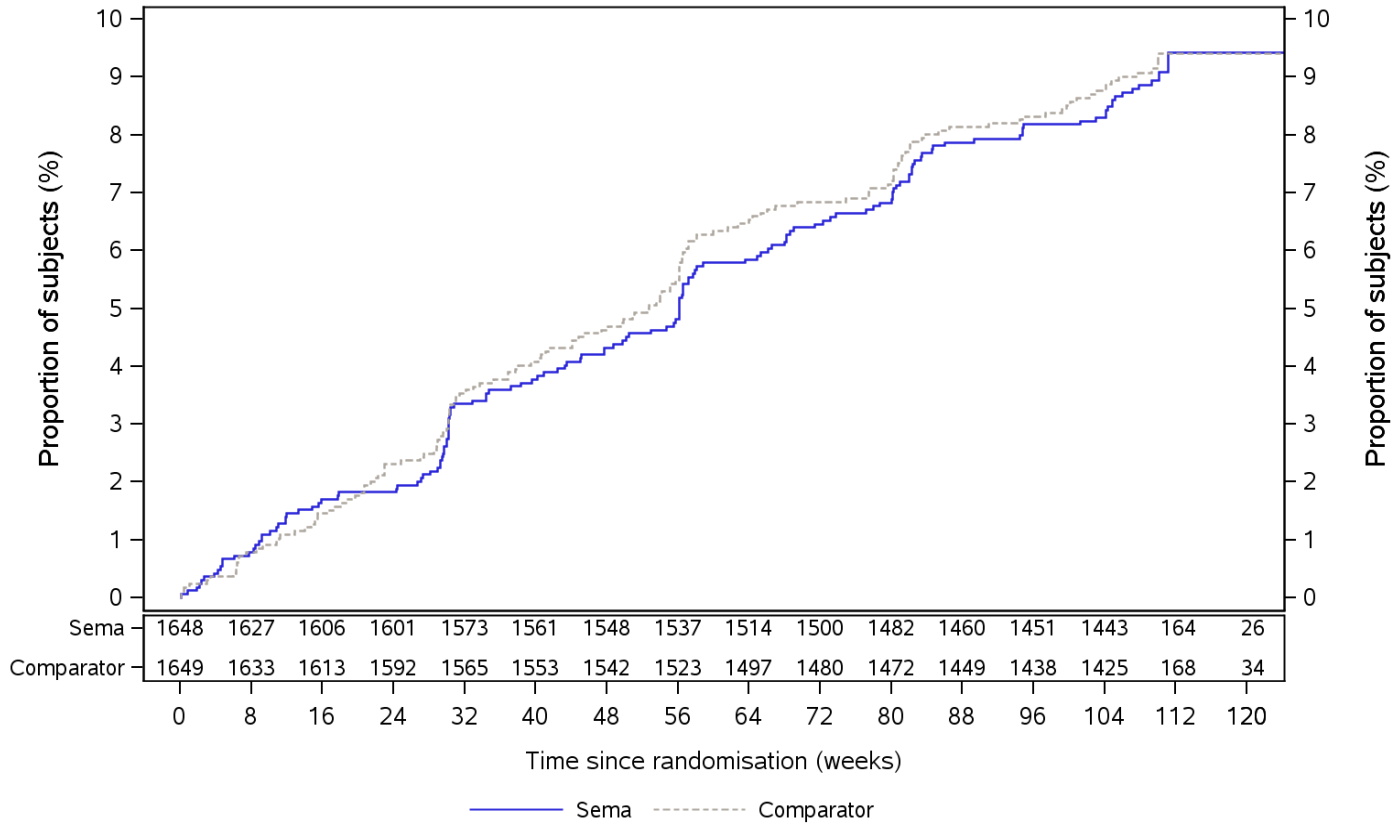
1 Mild adverse events - system organ class "Blood and lymphatic system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:49:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_blsd_ae_mi_s6.png

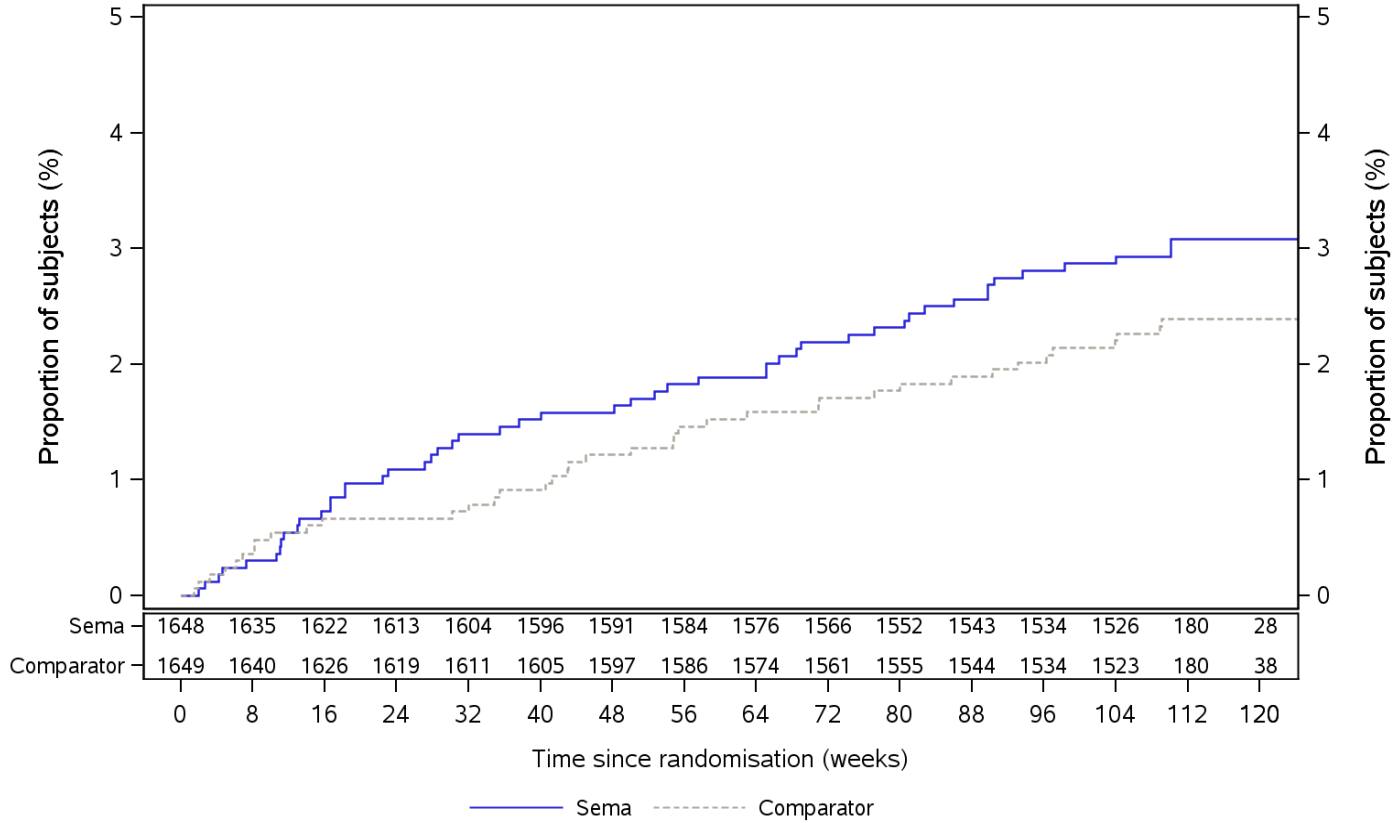
2 Mild adverse events - system organ class "Cardiac disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:49:41 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_cd_ae_mi_s6.png

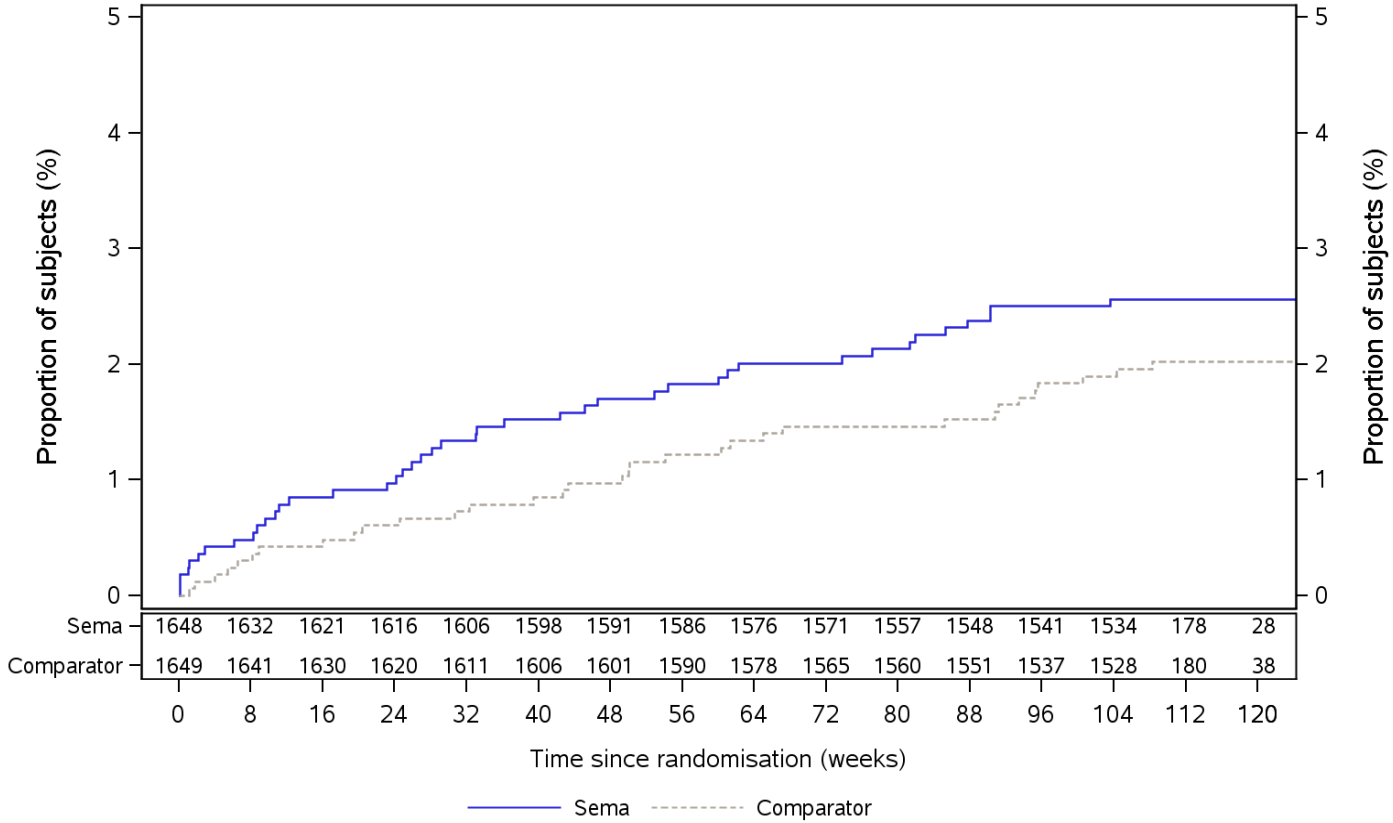
3 Mild adverse events - system organ class "Ear and labyrinth disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:49:59 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_earandlab_ae_mi_s6.png

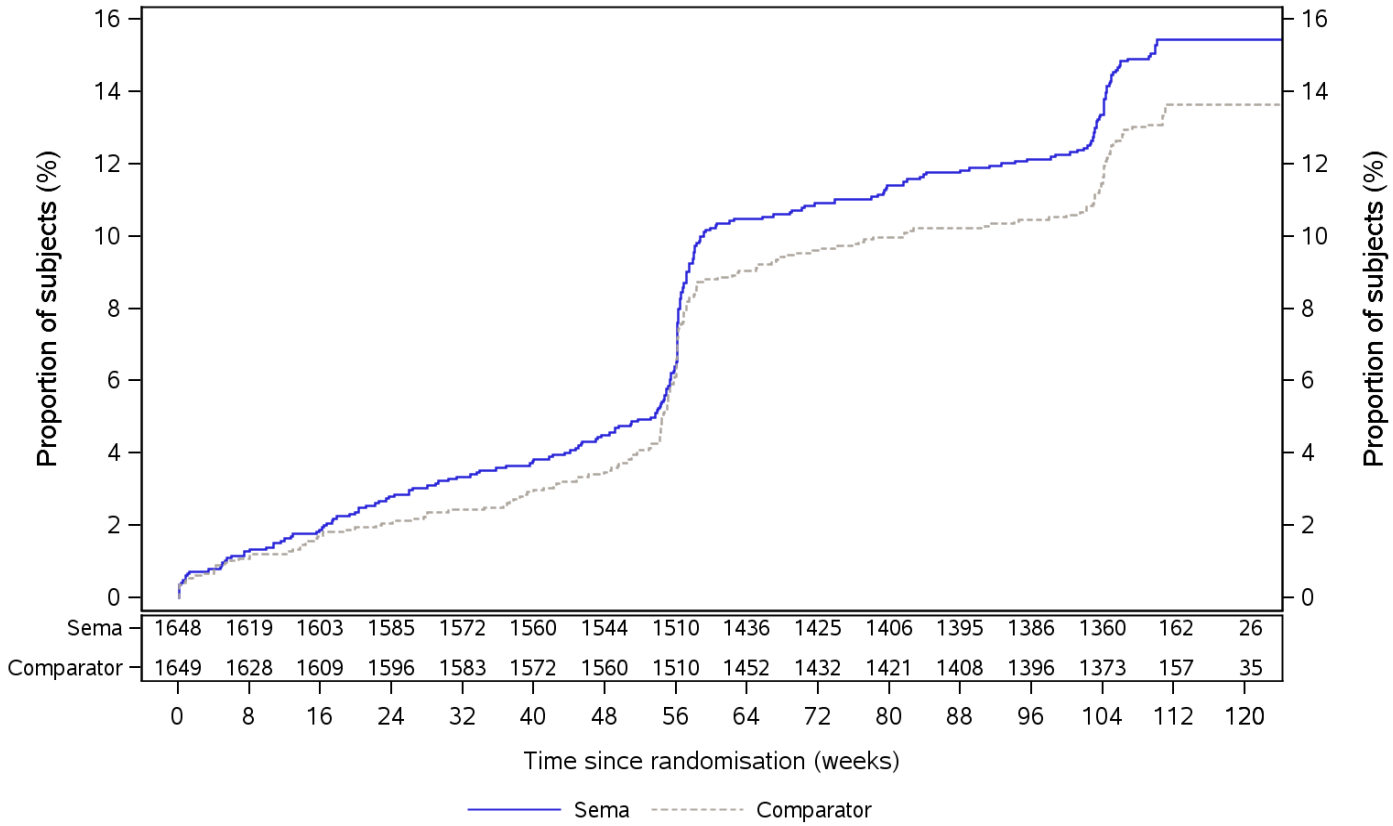
4 Mild adverse events - system organ class "Endocrine disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:50:19 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_endodiso_ae_mi_s6.png

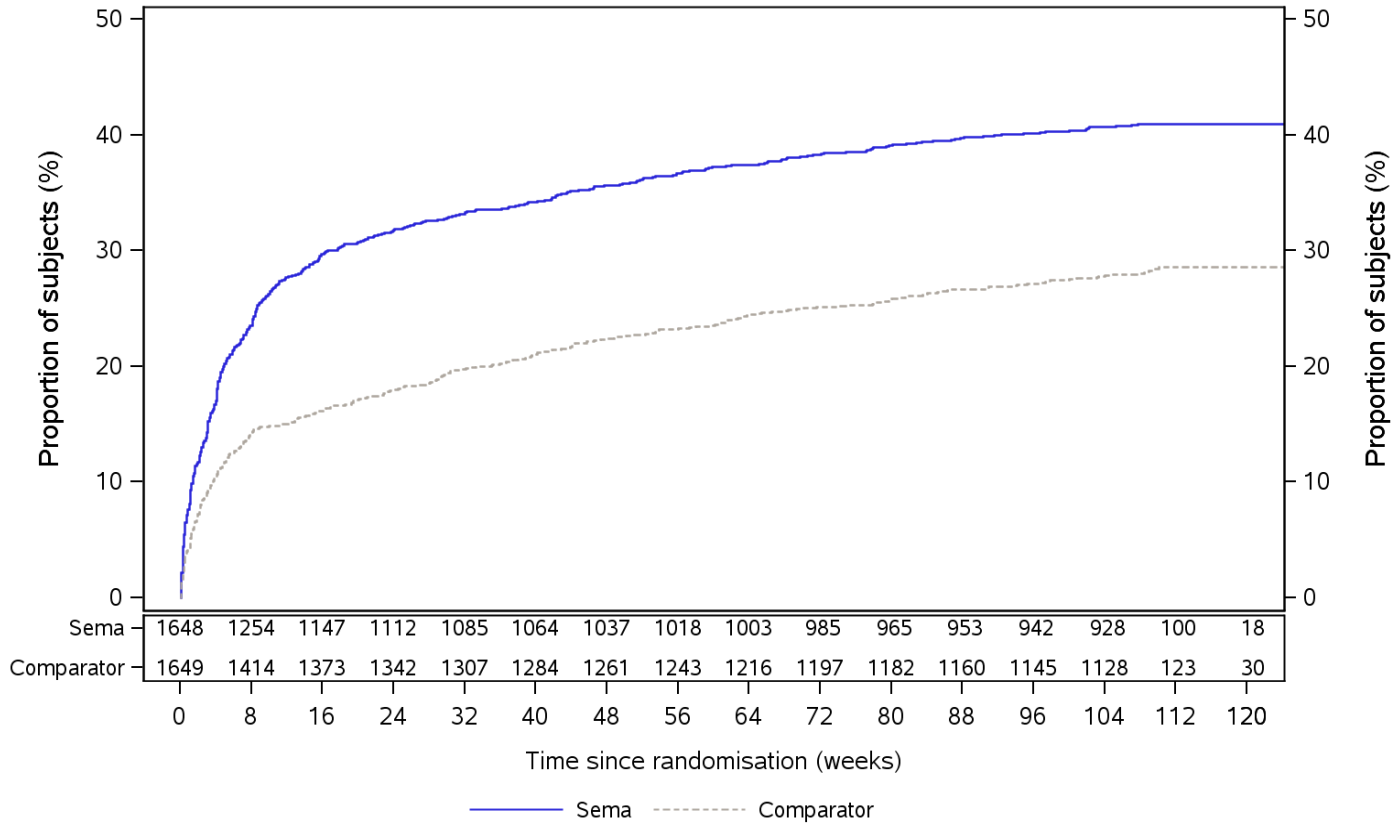
5 Mild adverse events - system organ class "Eye disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:50:37 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ed_ae_mi_s6.png

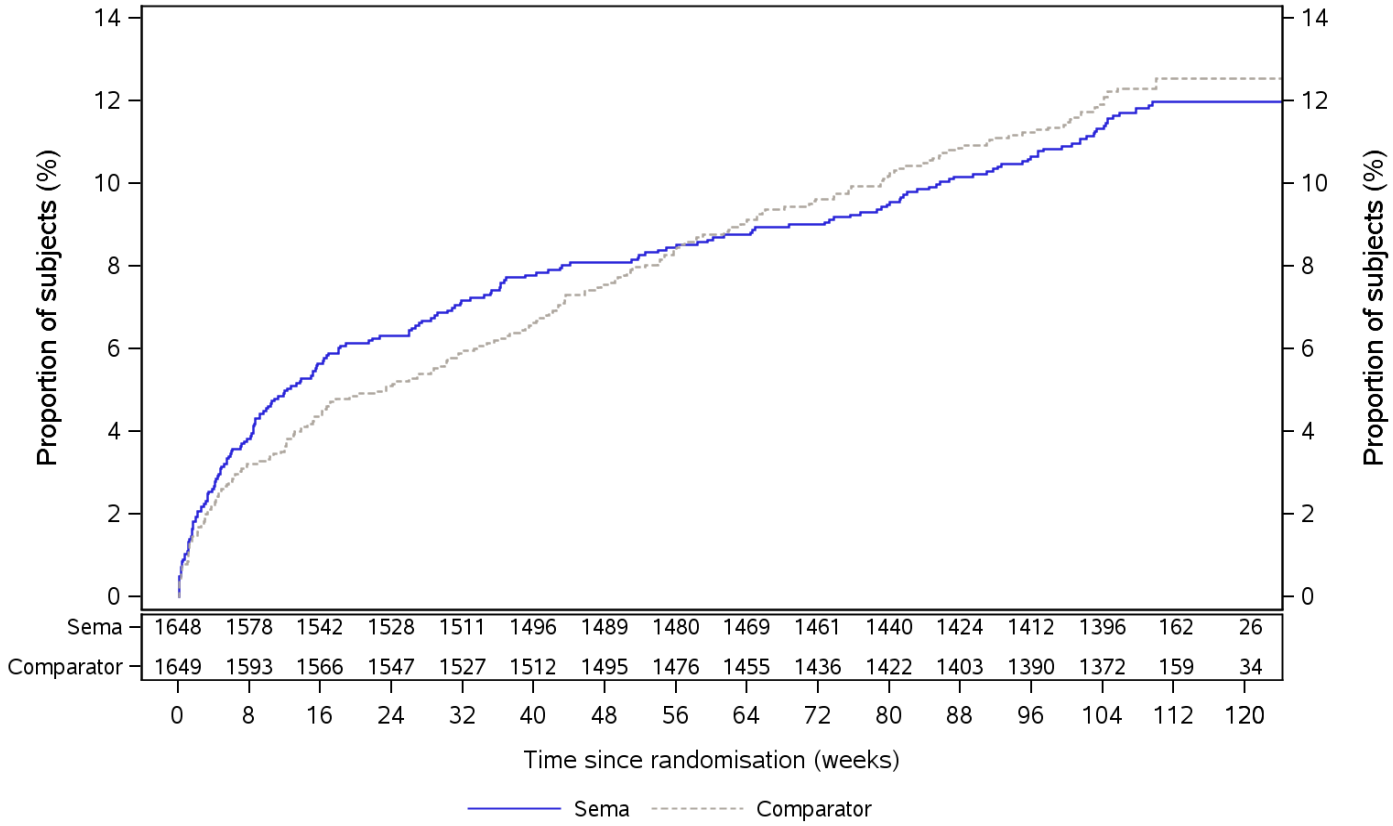
6 Mild adverse events - system organ class "Gastrointestinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:50:52 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_gd_ae_mi_s6.png

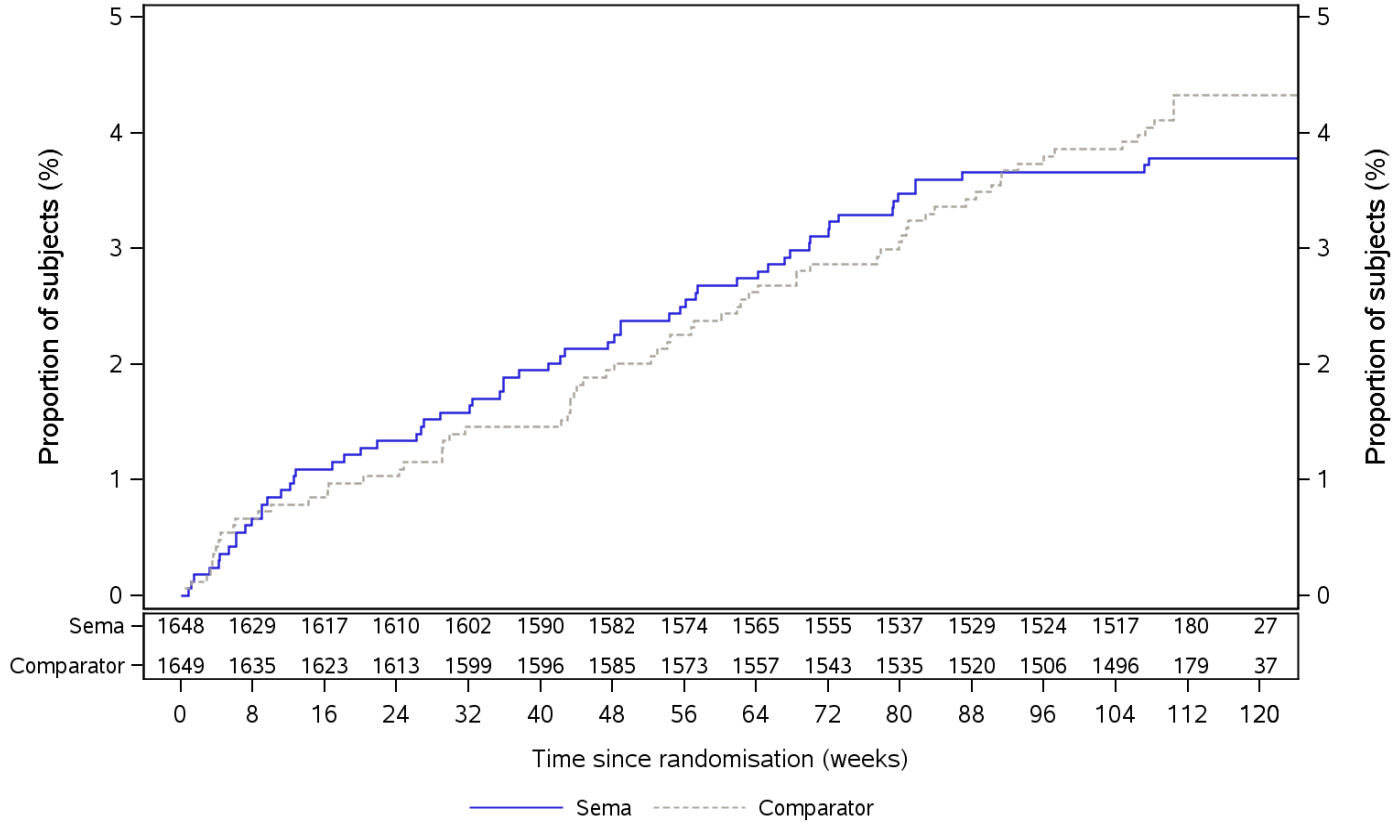
7 Mild adverse events - system organ class "General disorders and administration site conditions" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:51:10 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_gdasc_ae_mi_s6.png

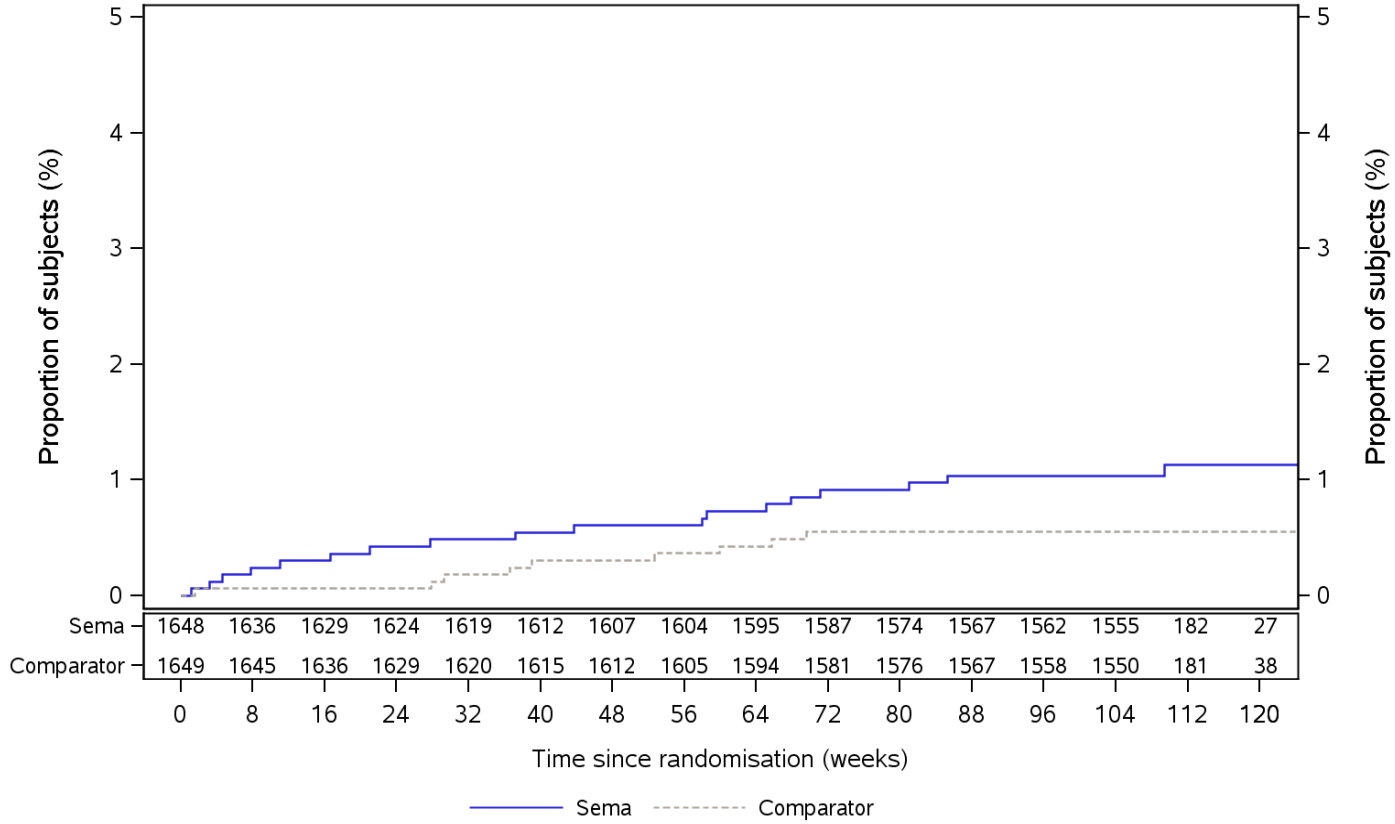
8 Mild adverse events - system organ class "Hepatobiliary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:51:28 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_hd_ae_mi_s6.png

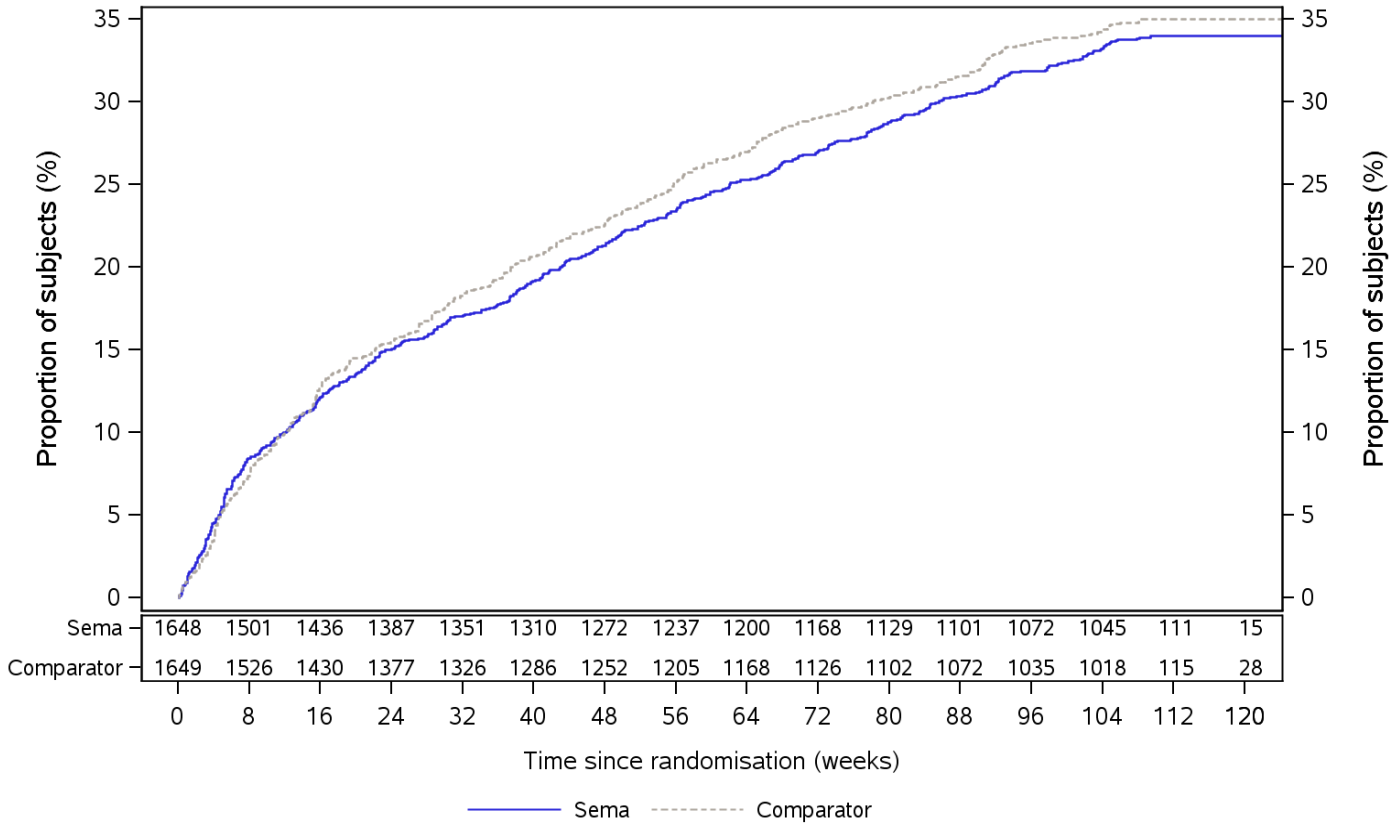
9 Mild adverse events - system organ class "Immune system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:51:48 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_immsysdis_ae_mi_s6.png

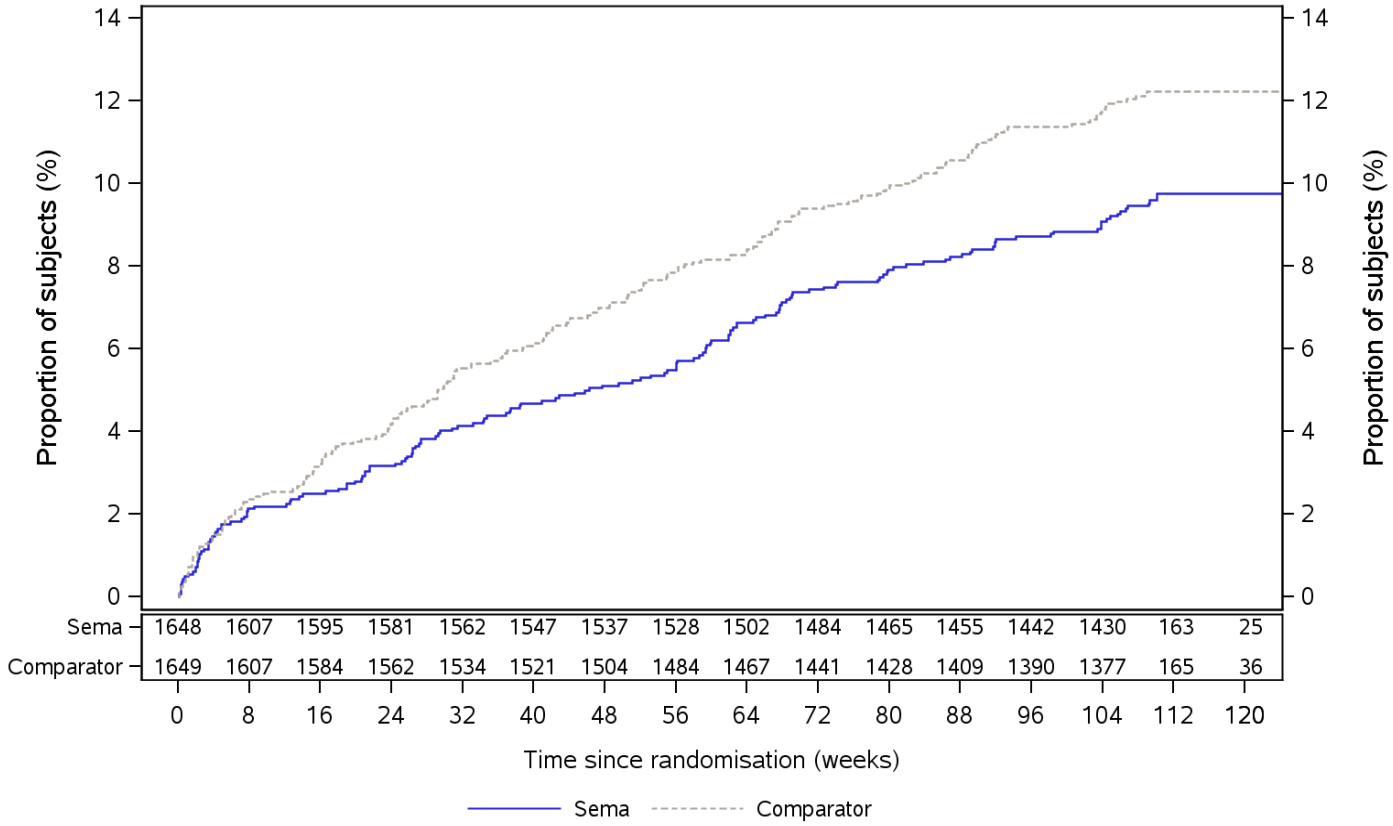
10 Mild adverse events - system organ class "Infections and infestations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:52:04 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ii_ae_mi_s6.png

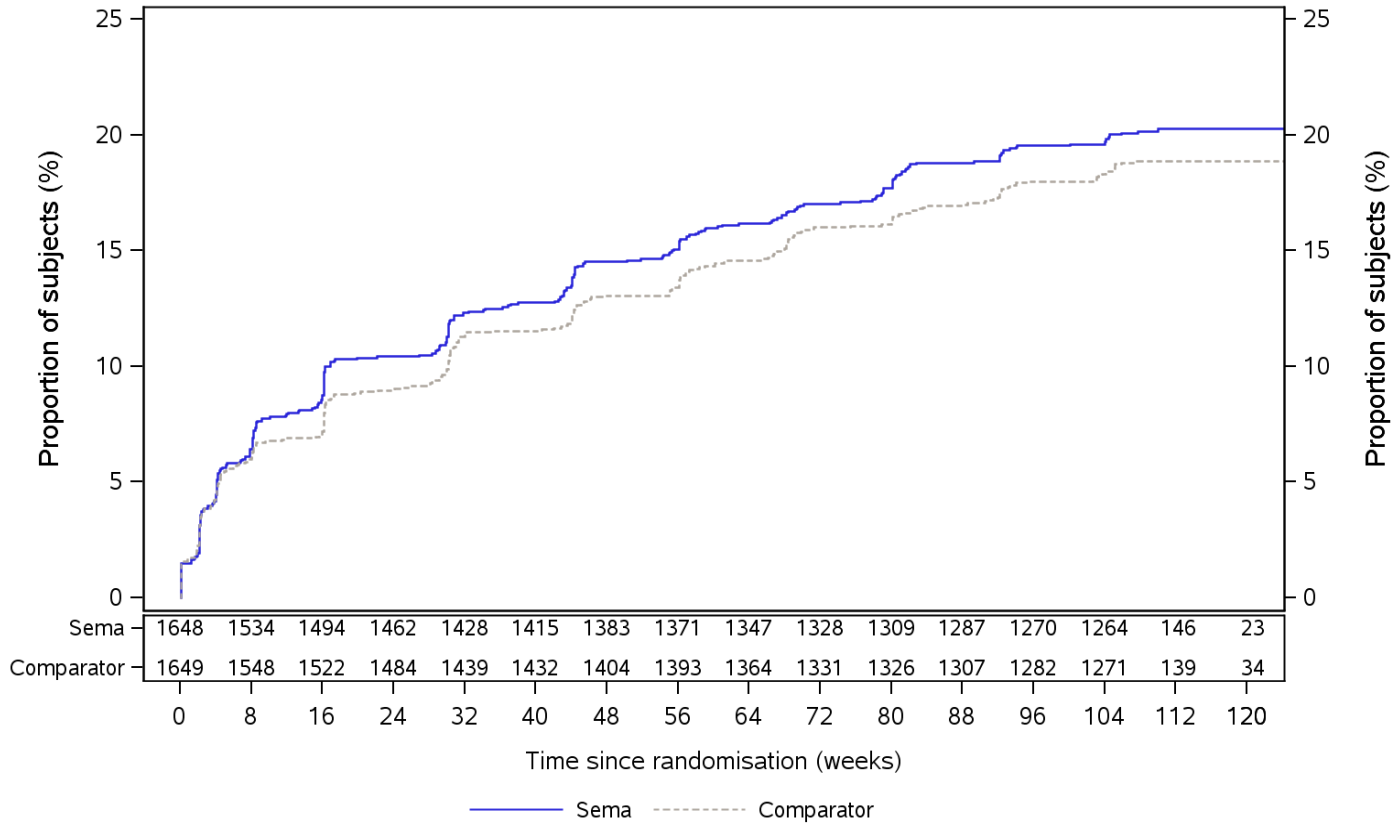
11 Mild adverse events - system organ class "Injury, poisoning and procedural complications" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:52:22 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_lppc_ae_mi_s6.png

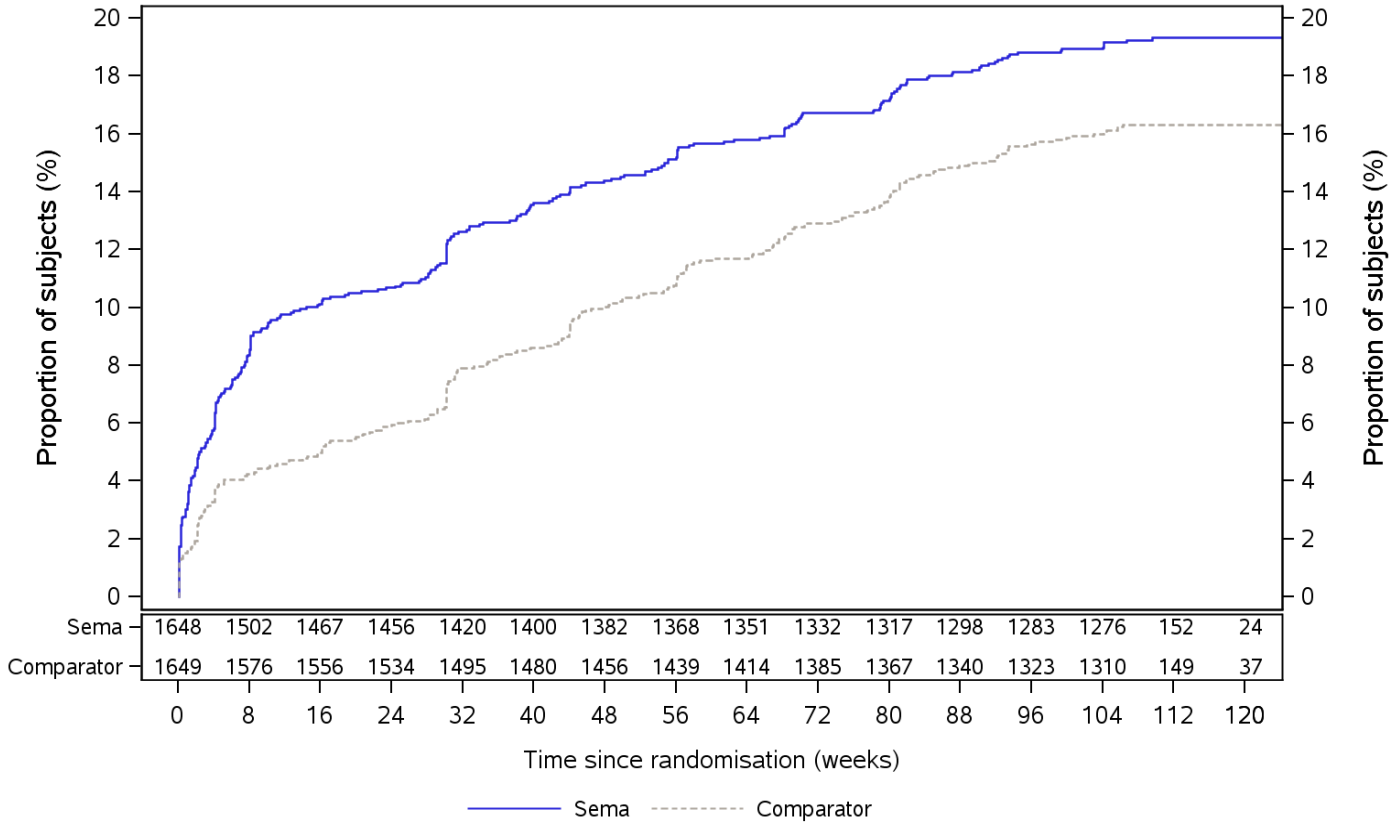
12 Mild adverse events - system organ class "Investigations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:52:41 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_investig_ae_mi_s6.png

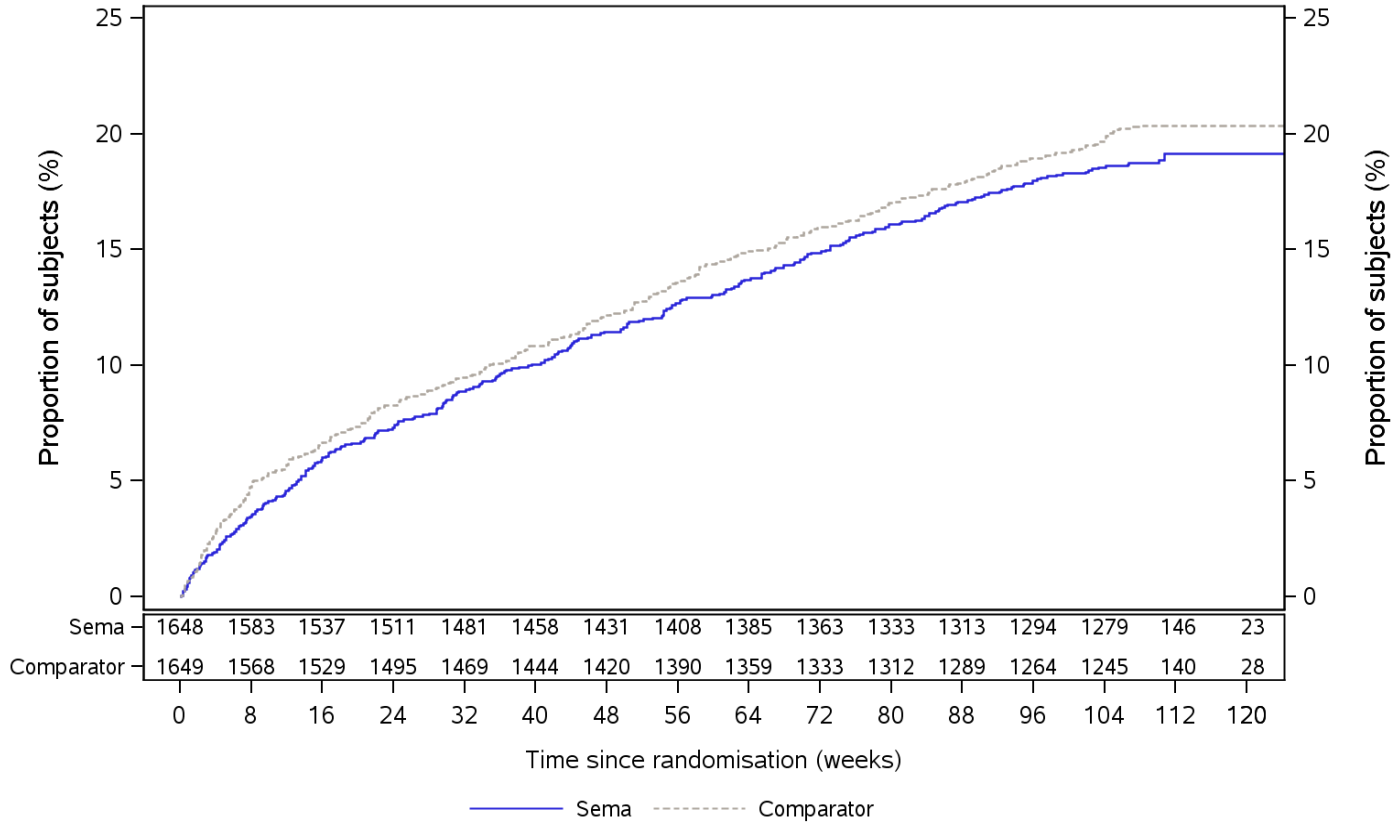
13 Mild adverse events - system organ class "Metabolism and nutrition disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:52:59 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_mnd_ae_mi_s6.png

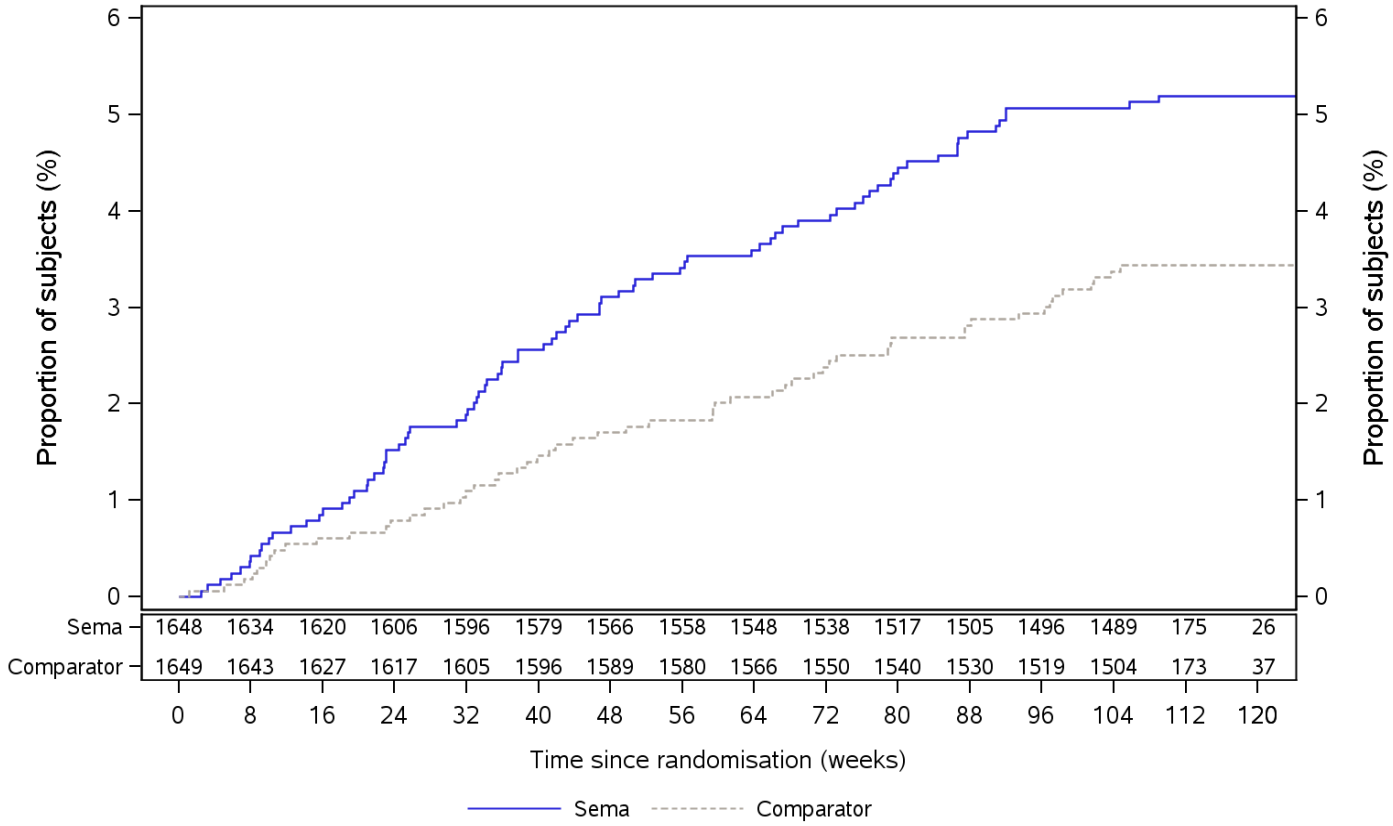
14 Mild adverse events - system organ class "Musculoskeletal and connective tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:53:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_mctd_ae_mi_s6.png

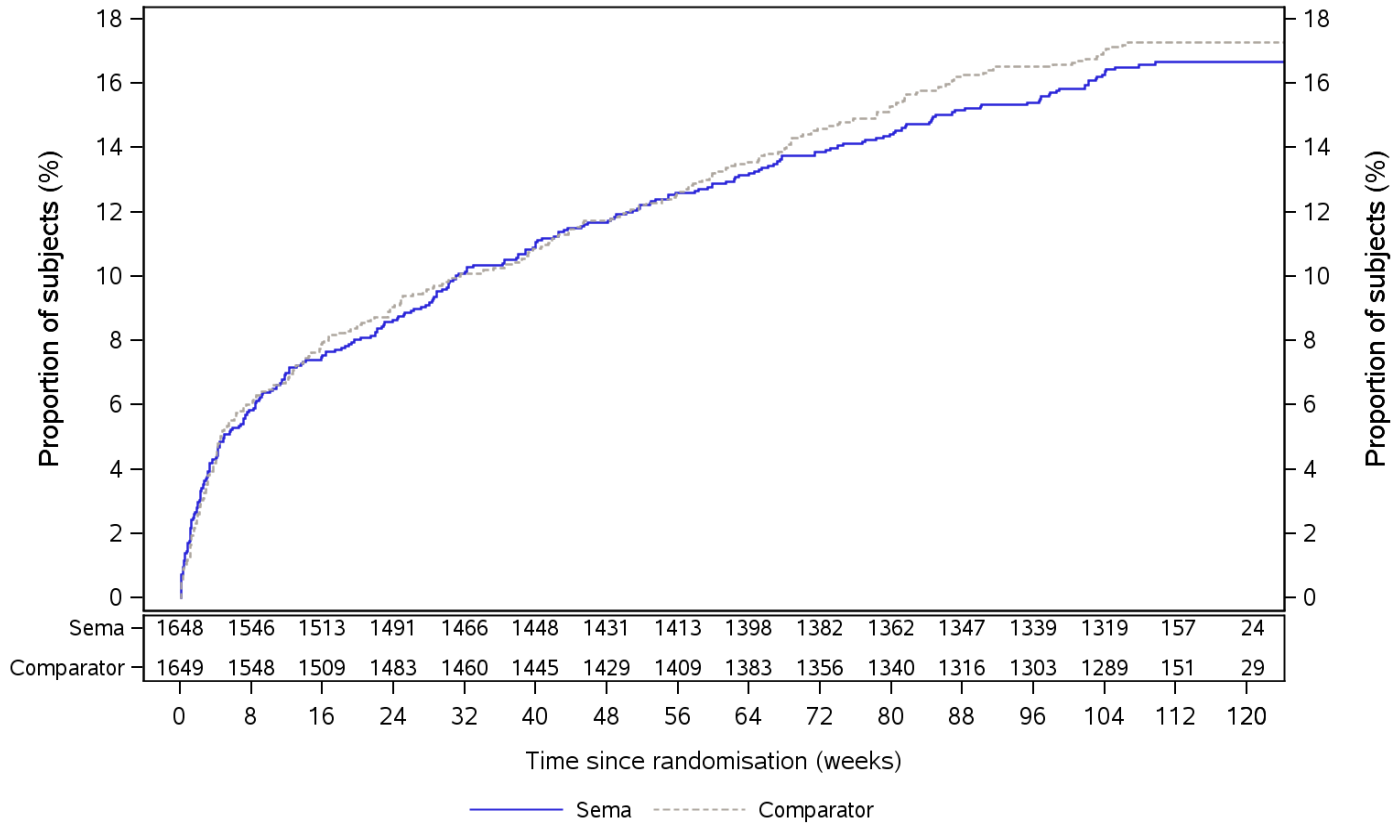
15 Mild adverse events - system organ class "Neoplasms benign, malignant and unspecified (incl cysts and polyps)" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:53:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_nbmu_ae_mi_s6.png

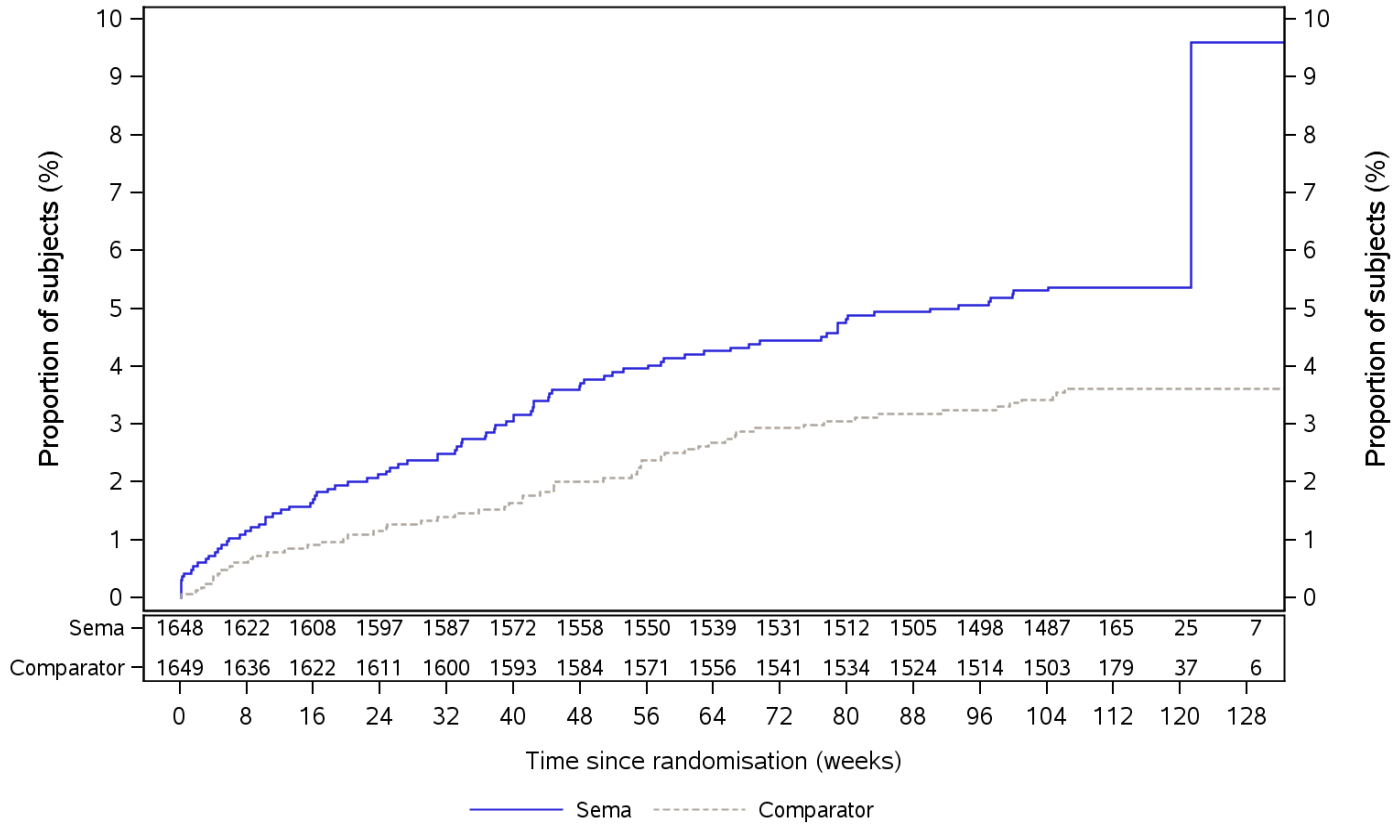
16 Mild adverse events - system organ class "Nervous system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:53:53 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_nsd_ae_mi_s6.png

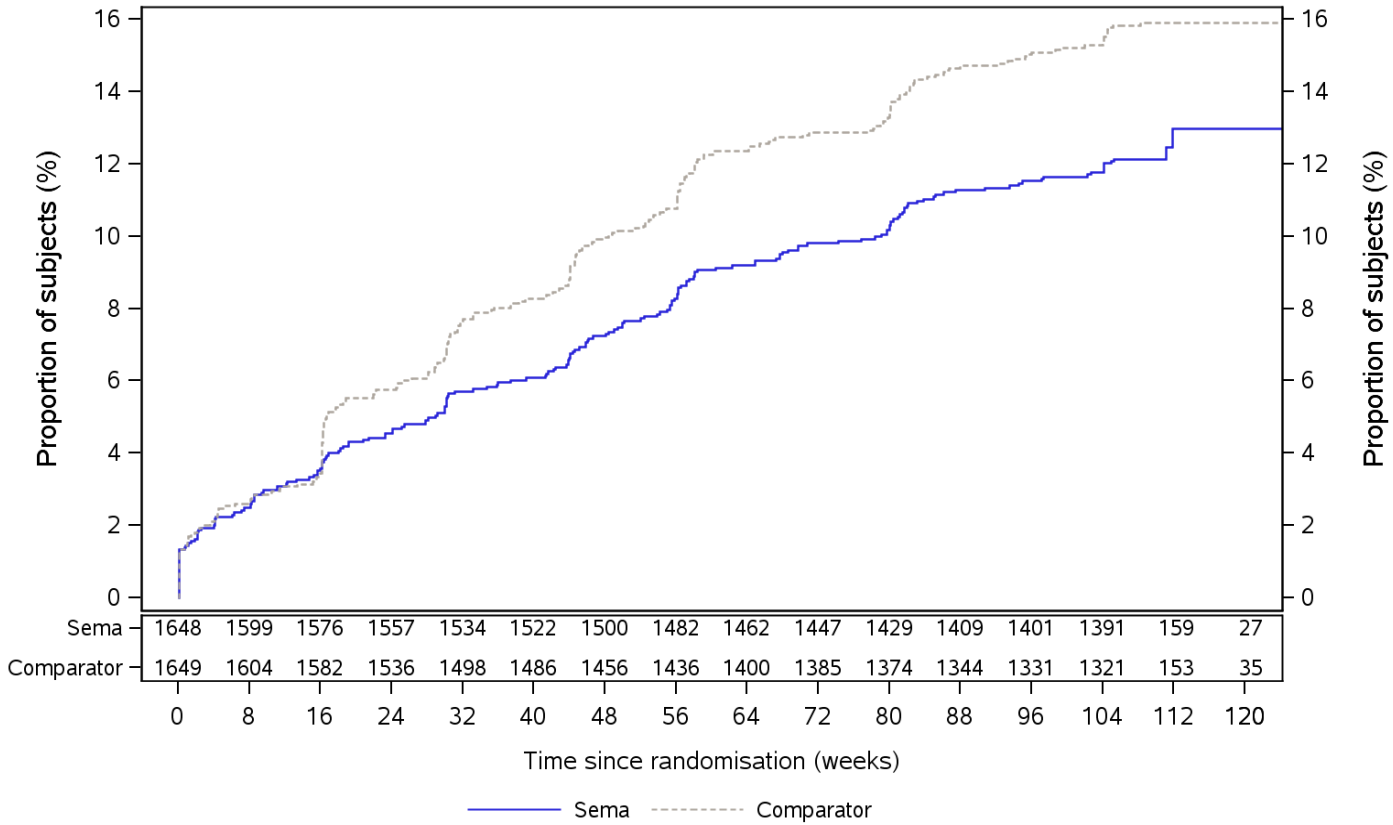
17 Mild adverse events - system organ class "Psychiatric disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:54:12 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_psycdiso_ae_mi_s6.png

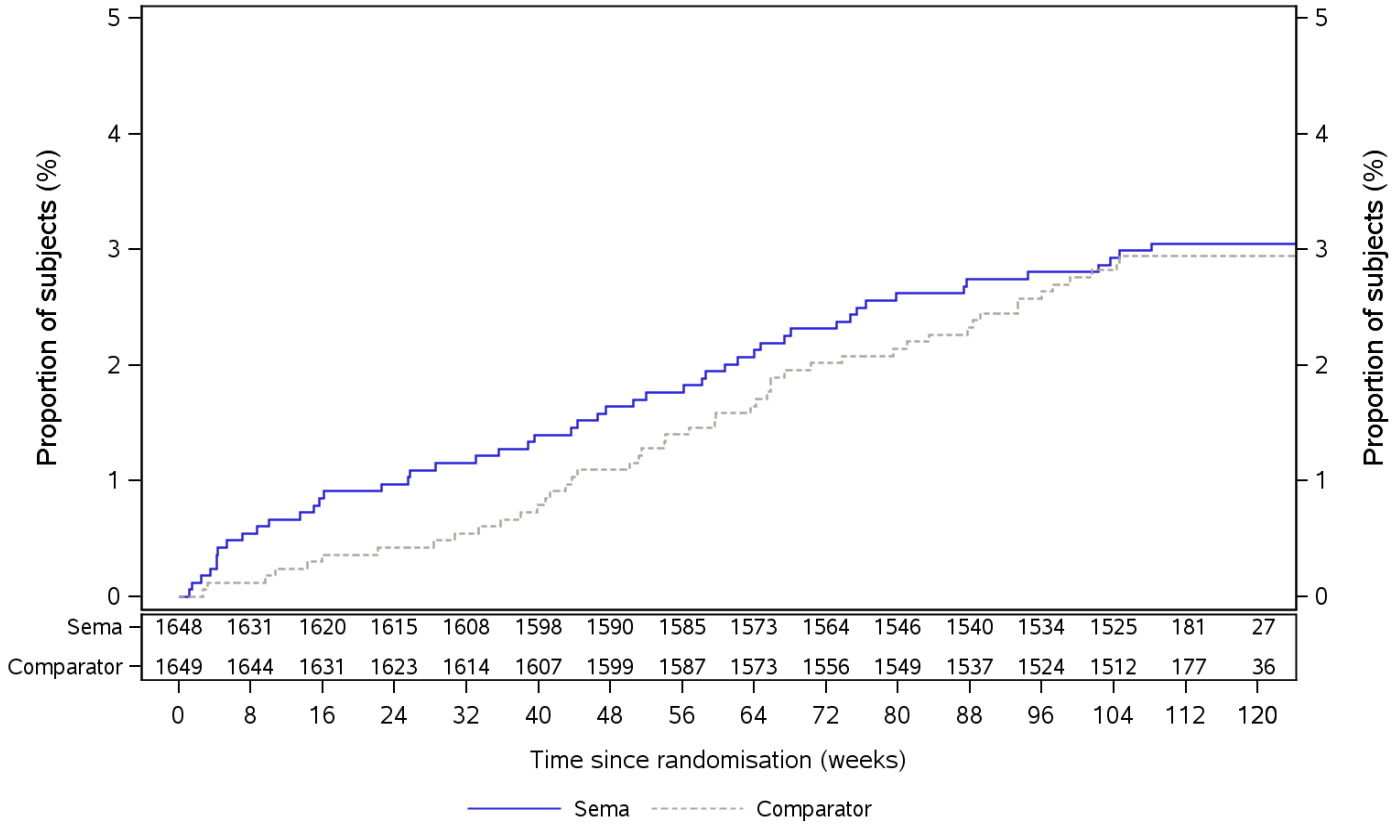
18 Mild adverse events - system organ class "Renal and urinary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:54:29 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_rud_ae_mi_s6.png

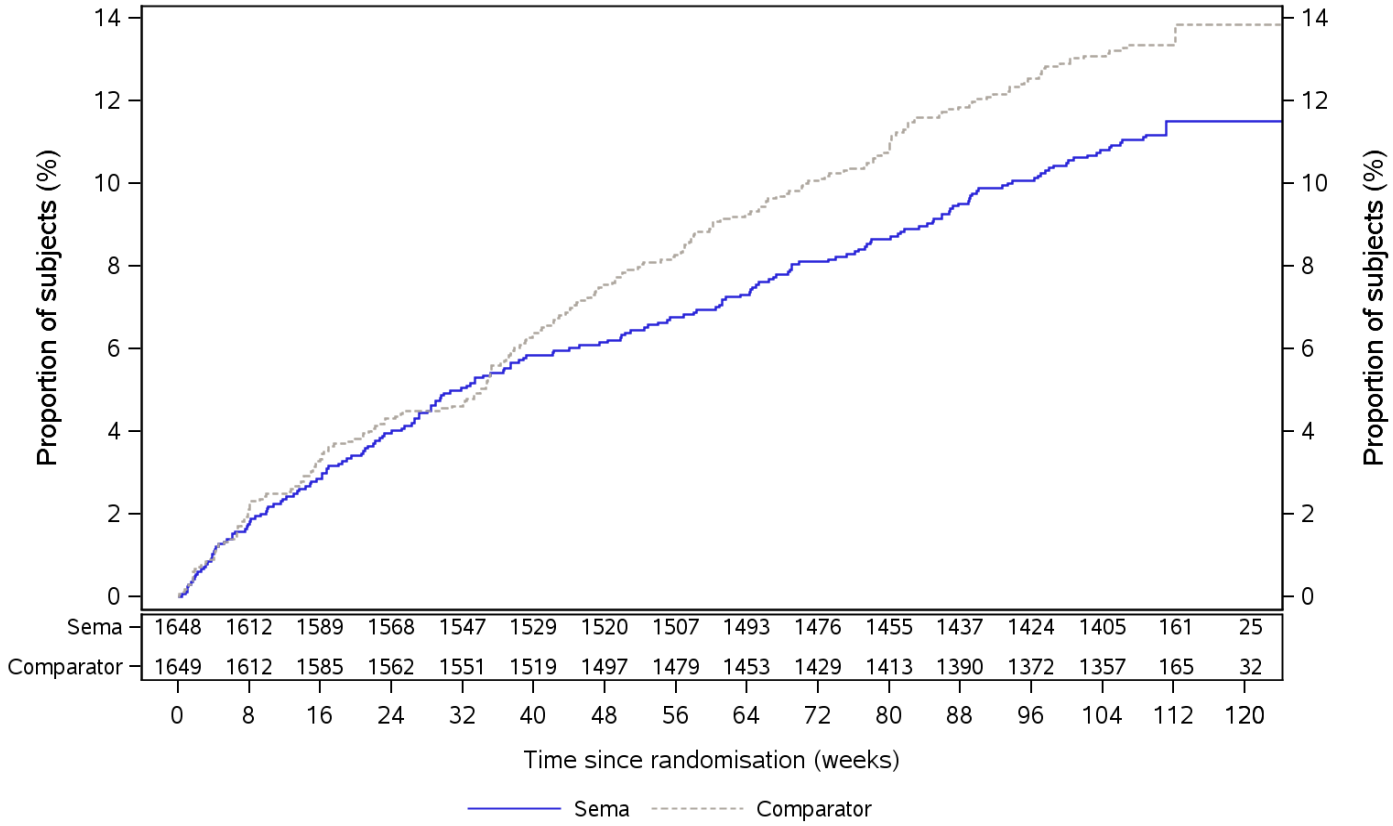
19 Mild adverse events - system organ class "Reproductive system and breast disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:54:49 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_repsysand_ae_mi_s6.png

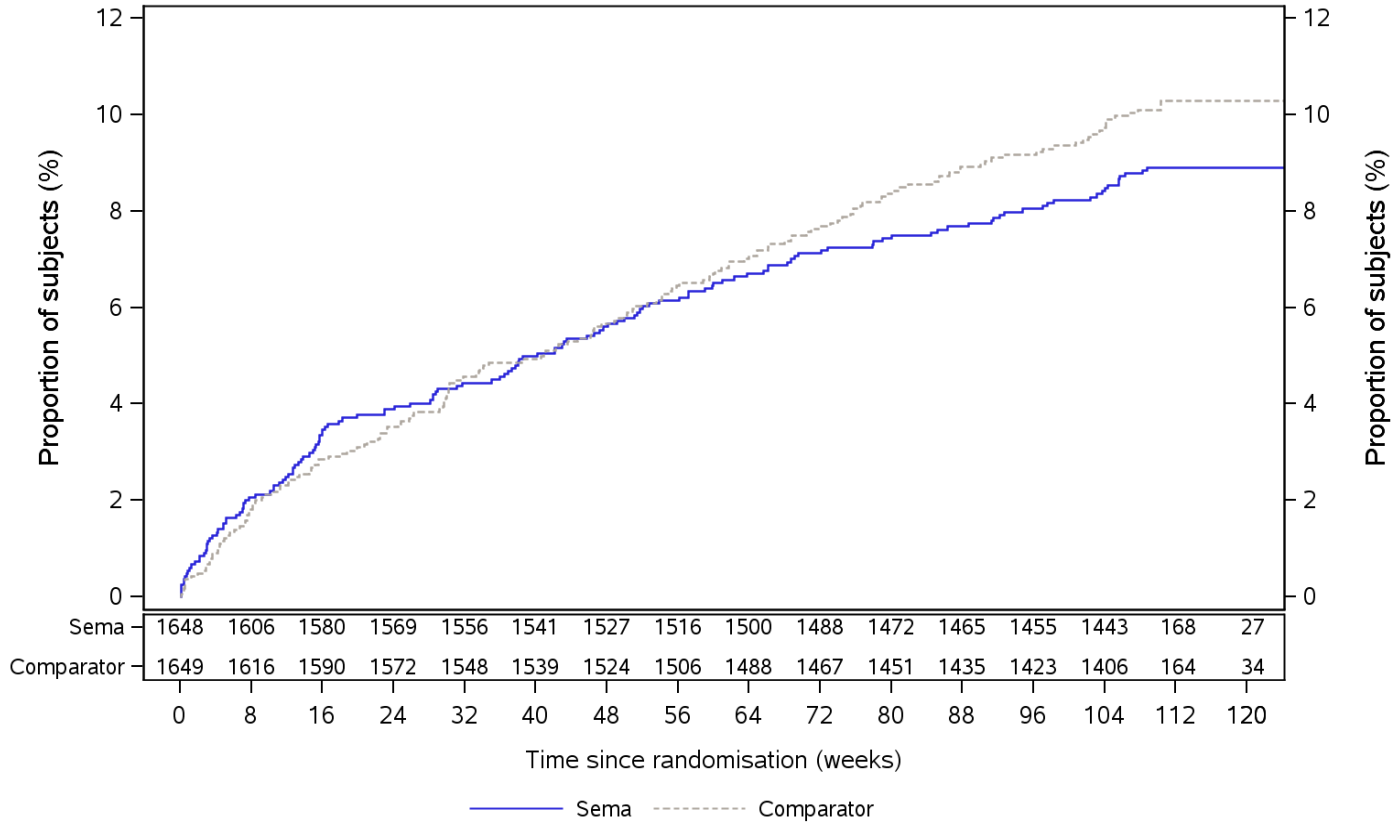
20 Mild adverse events - system organ class "Respiratory, thoracic and mediastinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:55:08 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_rtmd_ae_mi_s6.png

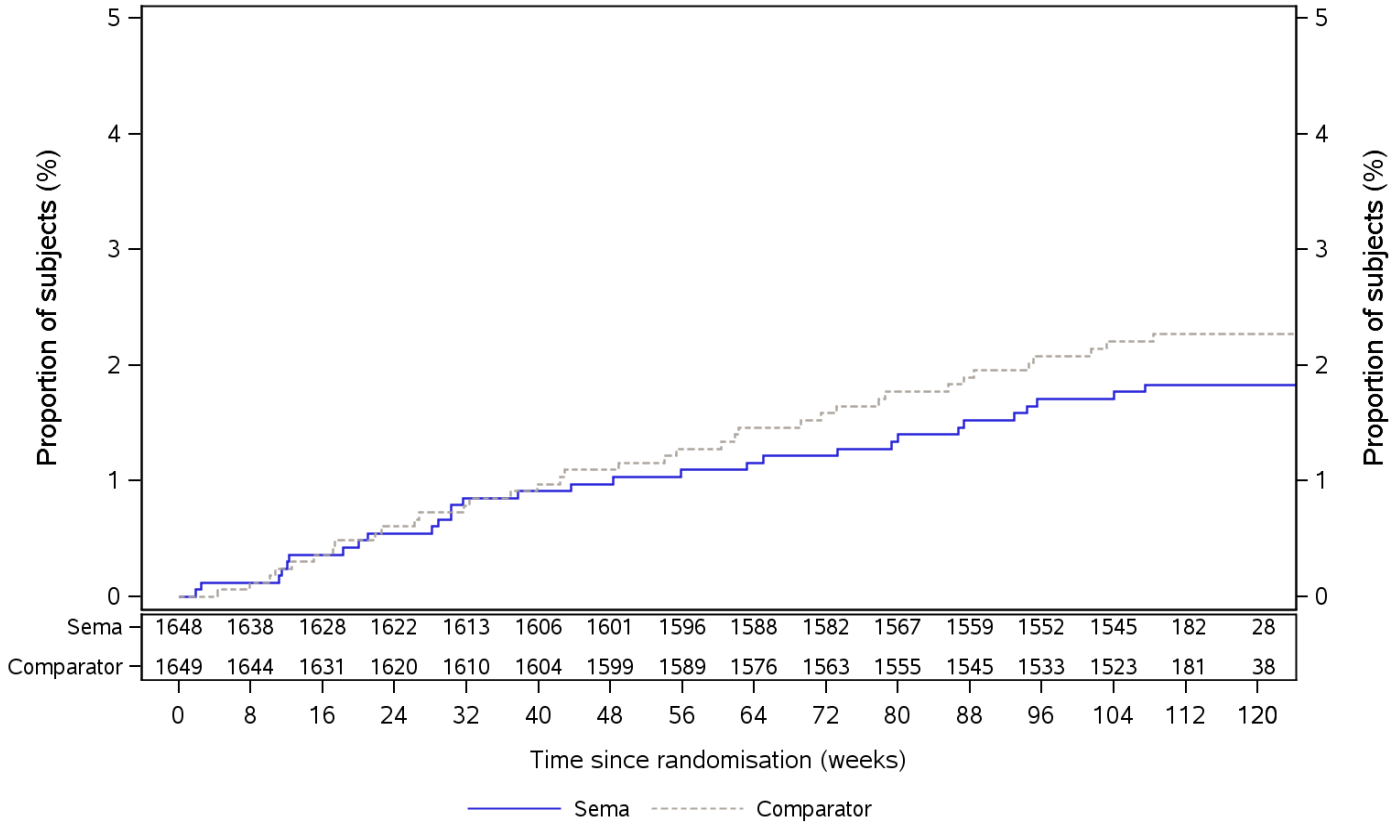
21 Mild adverse events - system organ class "Skin and subcutaneous tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:55:27 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_sstd_ae_mi_s6.png

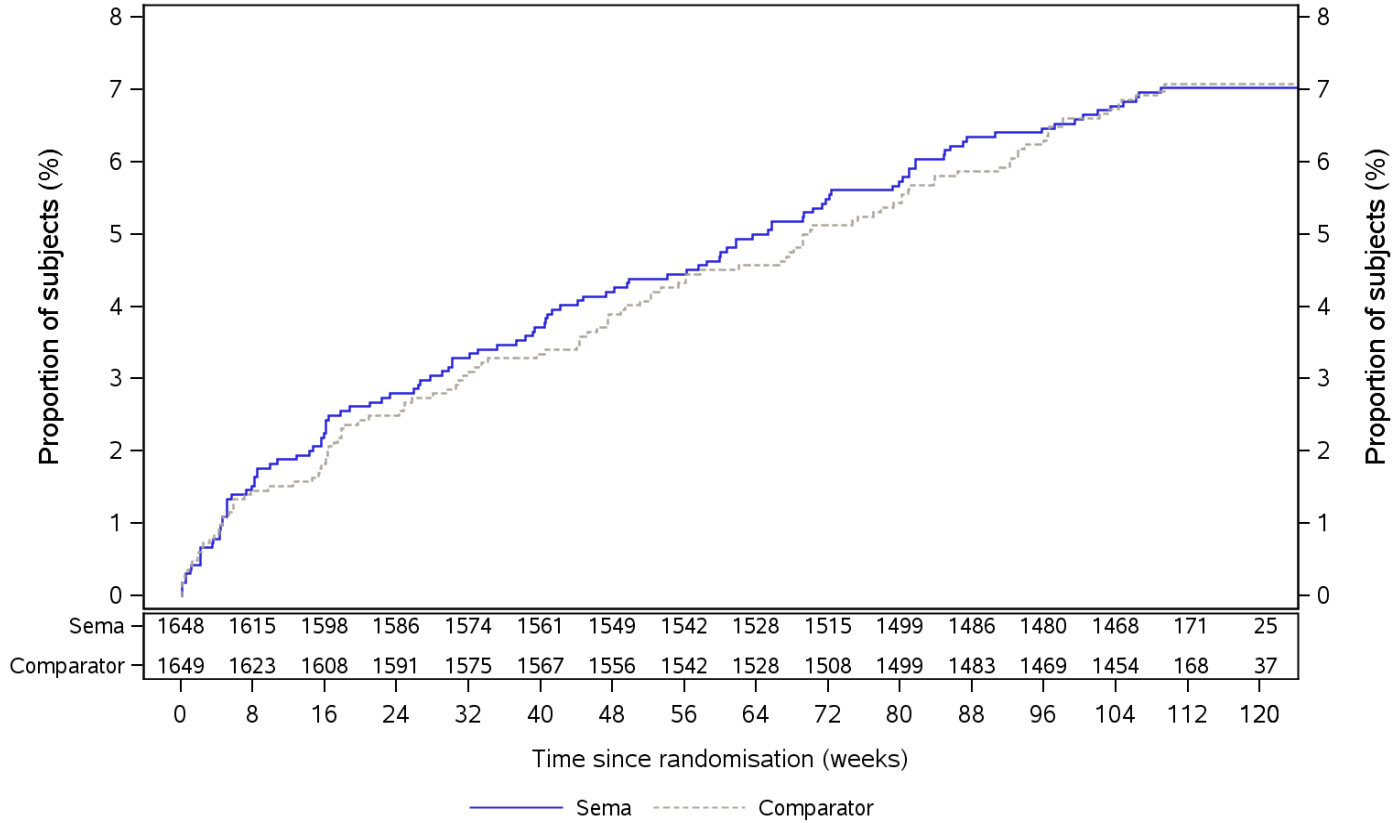
22 Mild adverse events - system organ class "Surgical and medical procedures" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:55:46 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_smp_ae_mi_s6.png

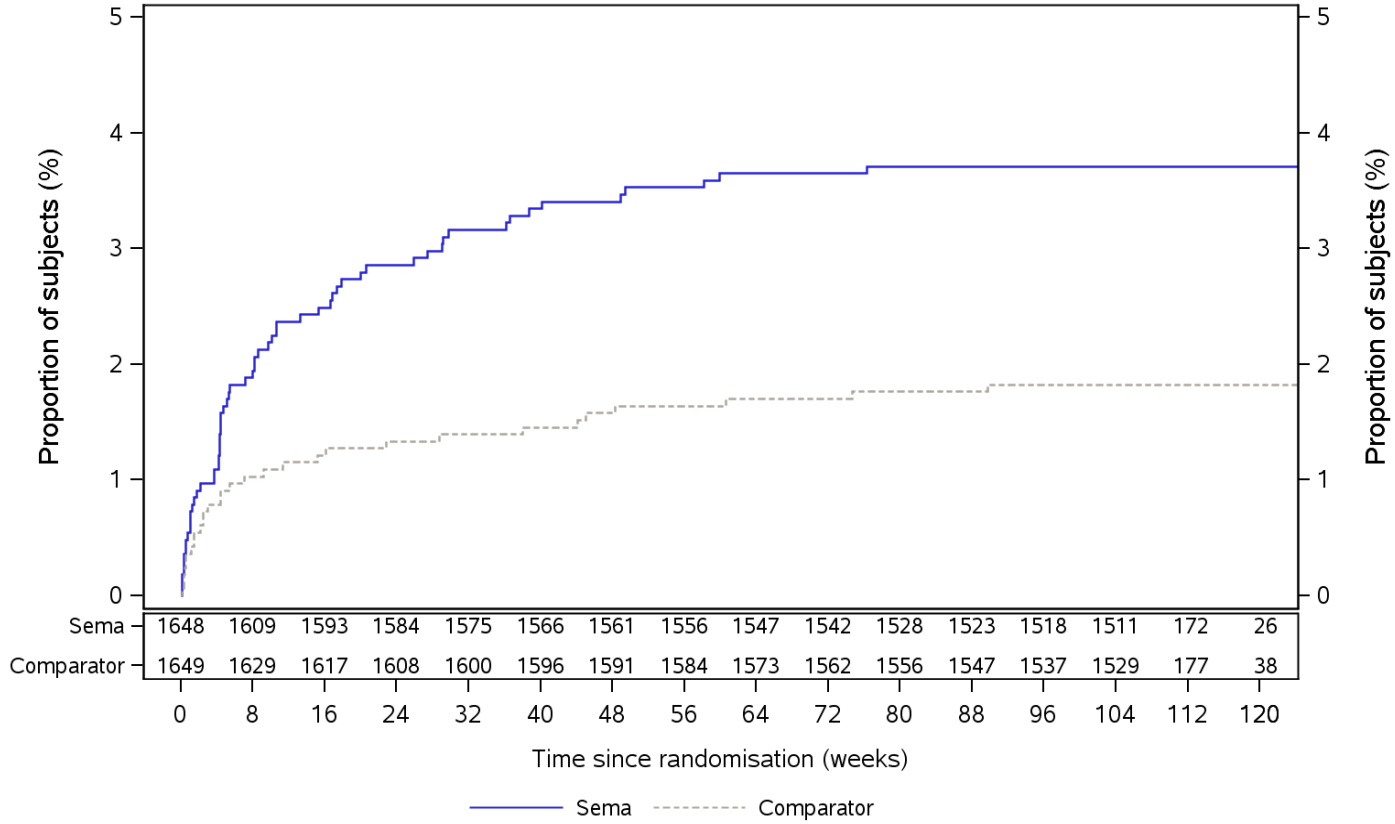
23 Mild adverse events - system organ class "Vascular disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:56:05 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_vd_ae_mi_s6.png

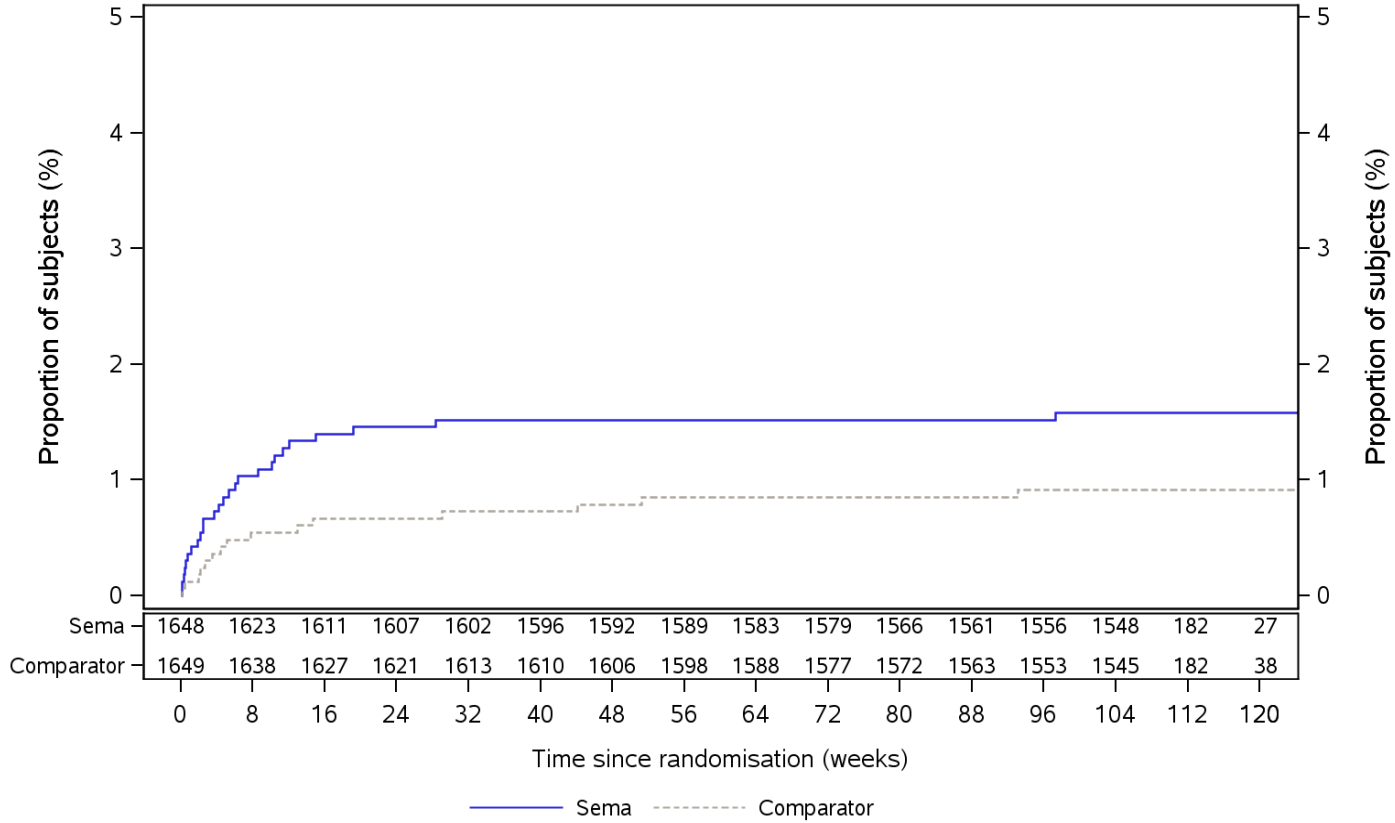
24 Mild adverse events - preferred term "Abdominal discomfort" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:56:26 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdodisc_ae_mi_s6.png

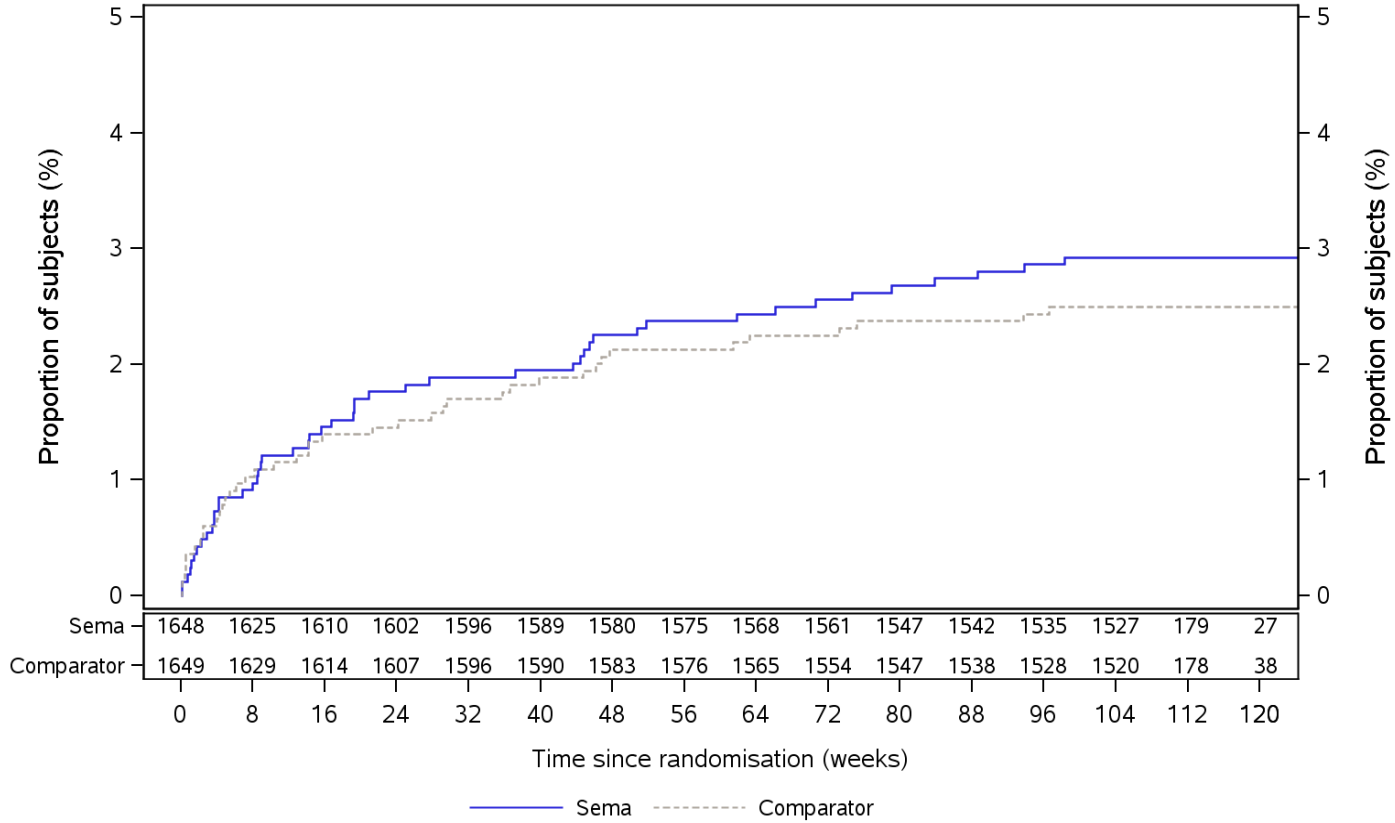
25 Mild adverse events - preferred term "Abdominal distension" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:56:46 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdodist_ae_mi_s6.png

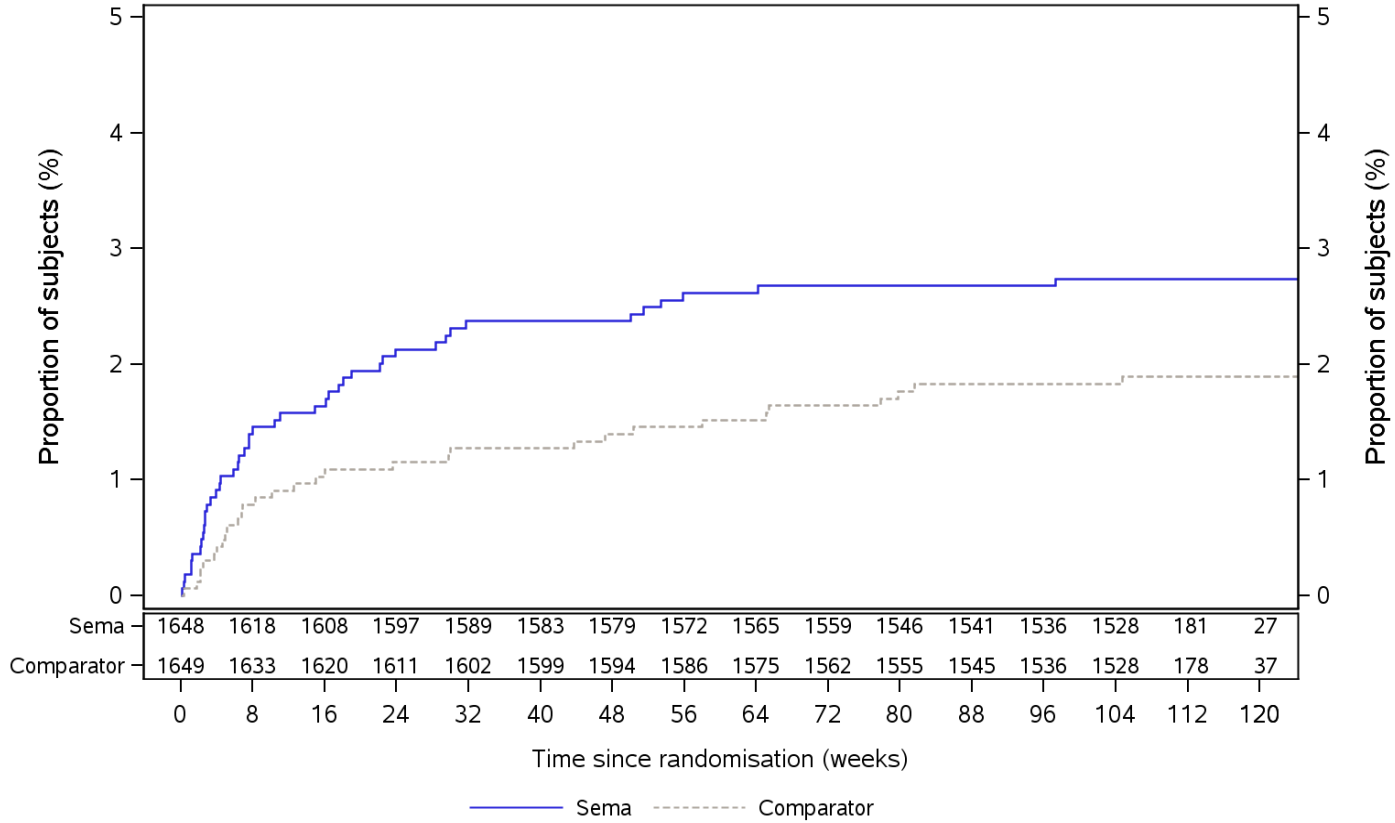
26 Mild adverse events - preferred term "Abdominal pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:57:04 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdopain_ae_mi_s6.png

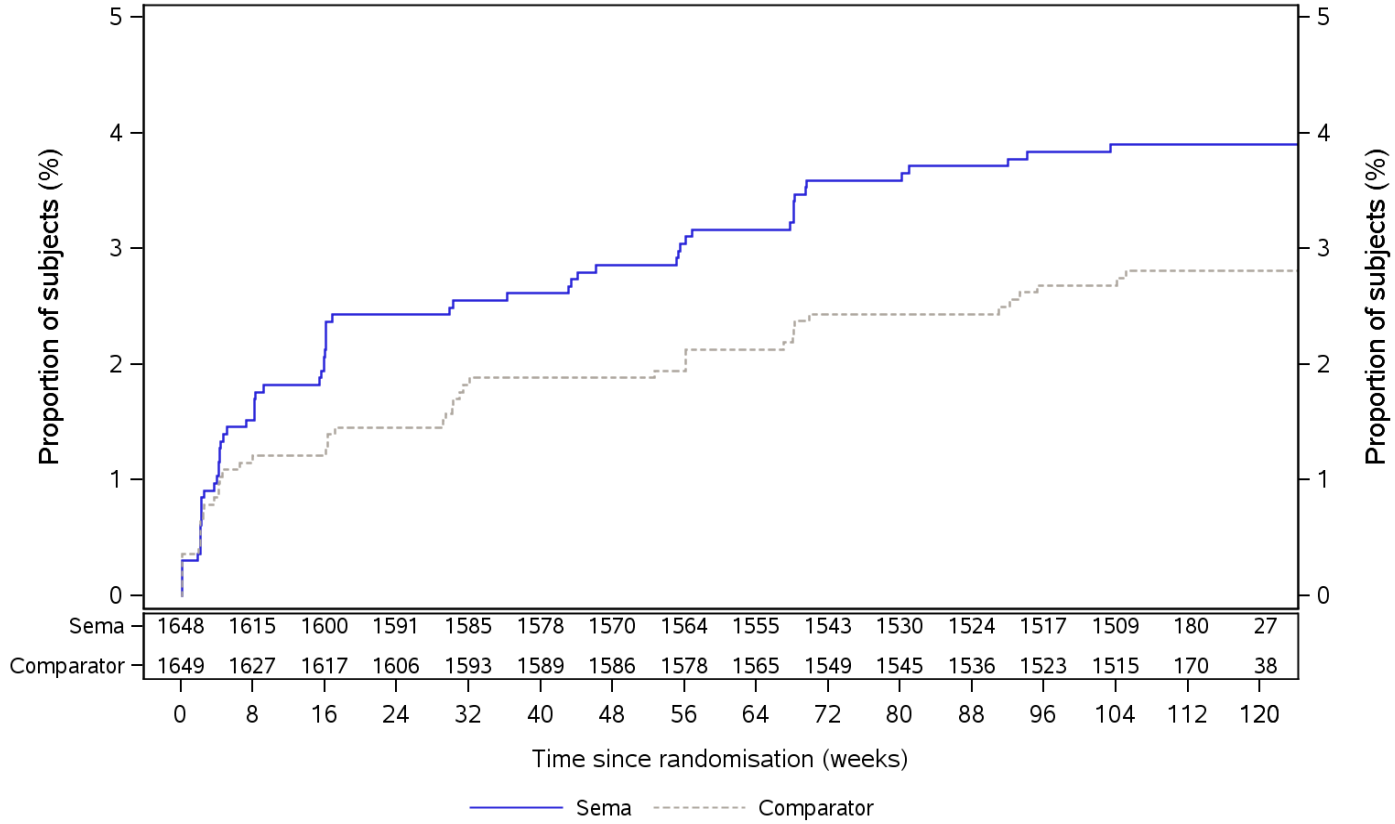
27 Mild adverse events - preferred term "Abdominal pain upper" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:57:24 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdpaiupp_ae_mi_s6.png

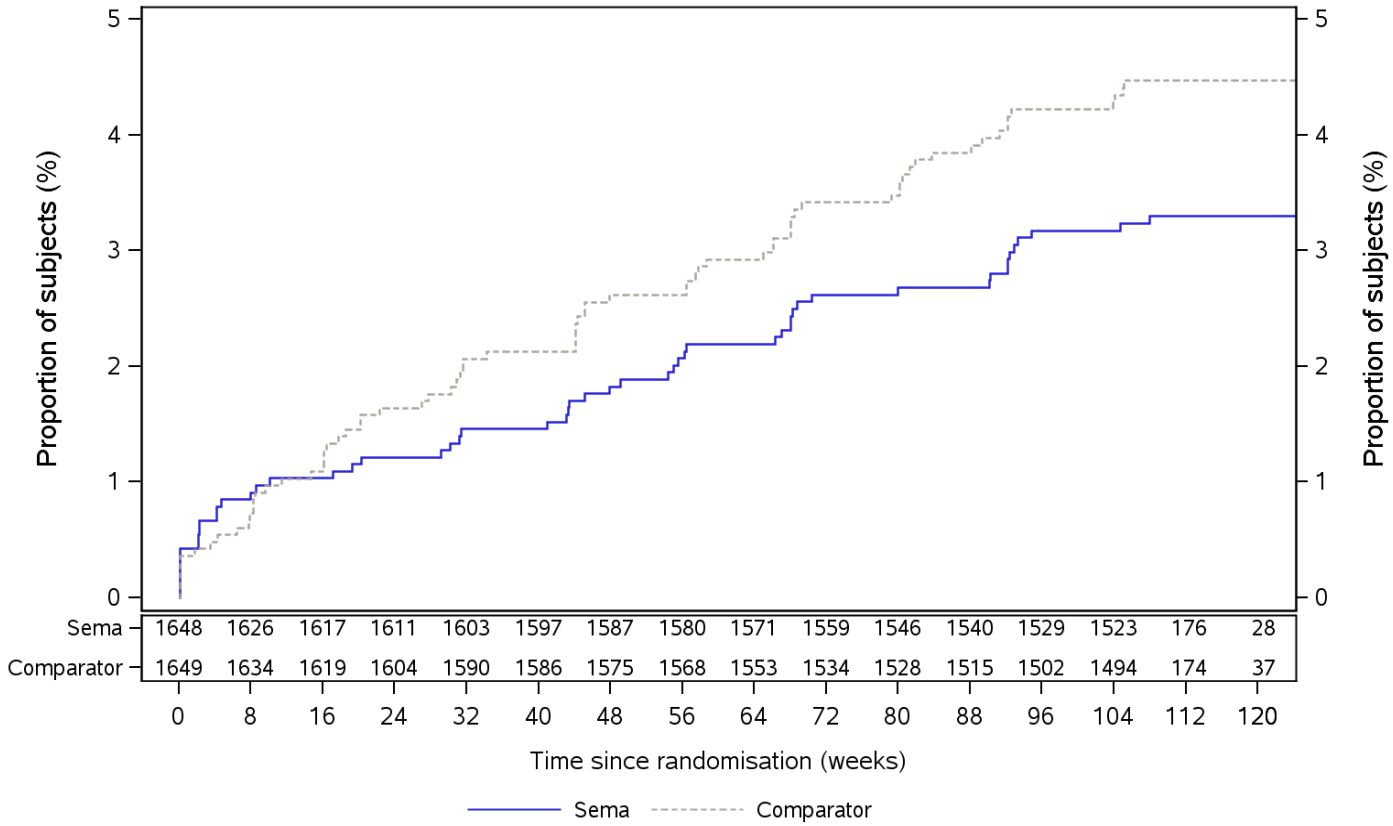
28 Mild adverse events - preferred term "Amylase increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:57:43 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_amylincr_ae_mi_s6.png

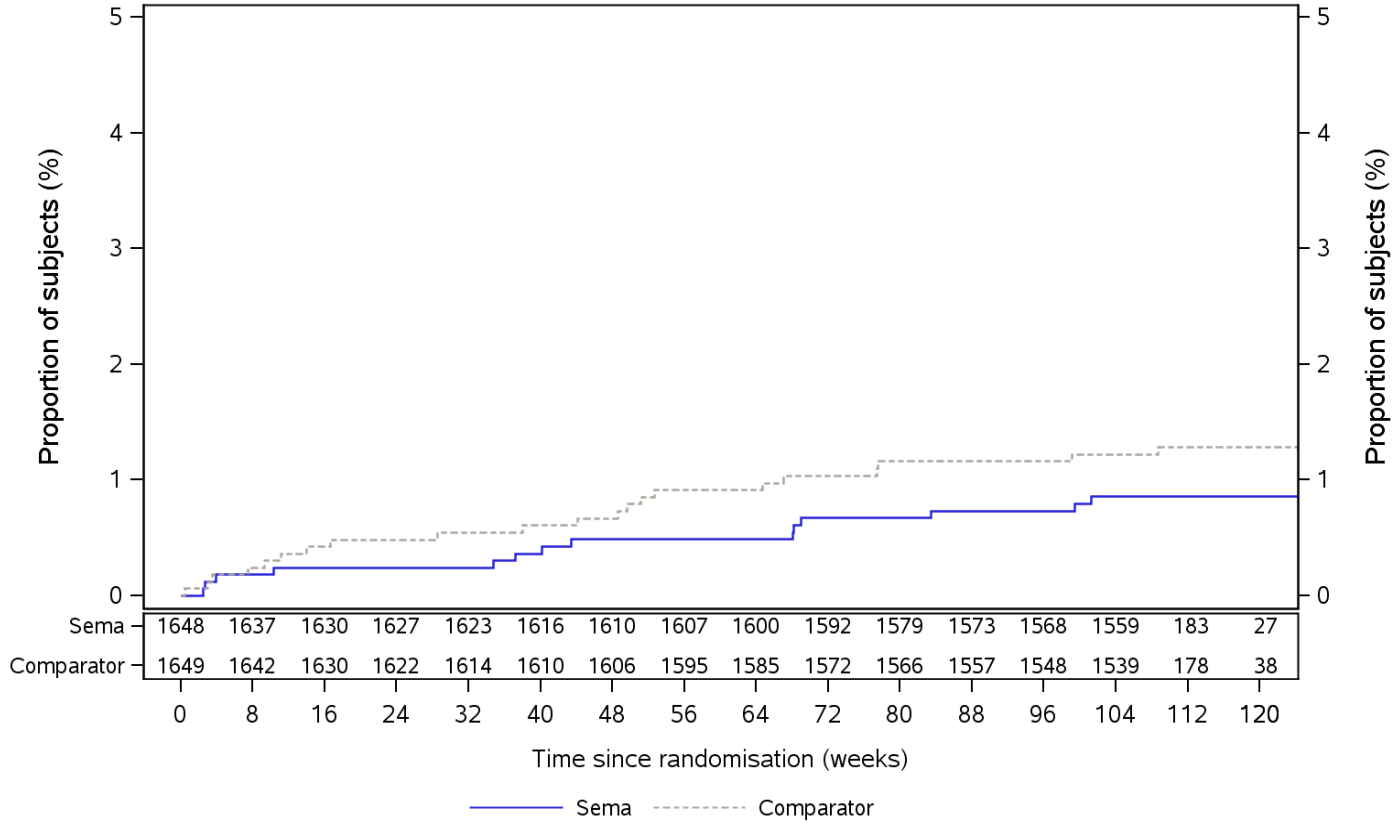
29 Mild adverse events - preferred term "Anaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:58:02 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_anaemia_ae_mi_s6.png

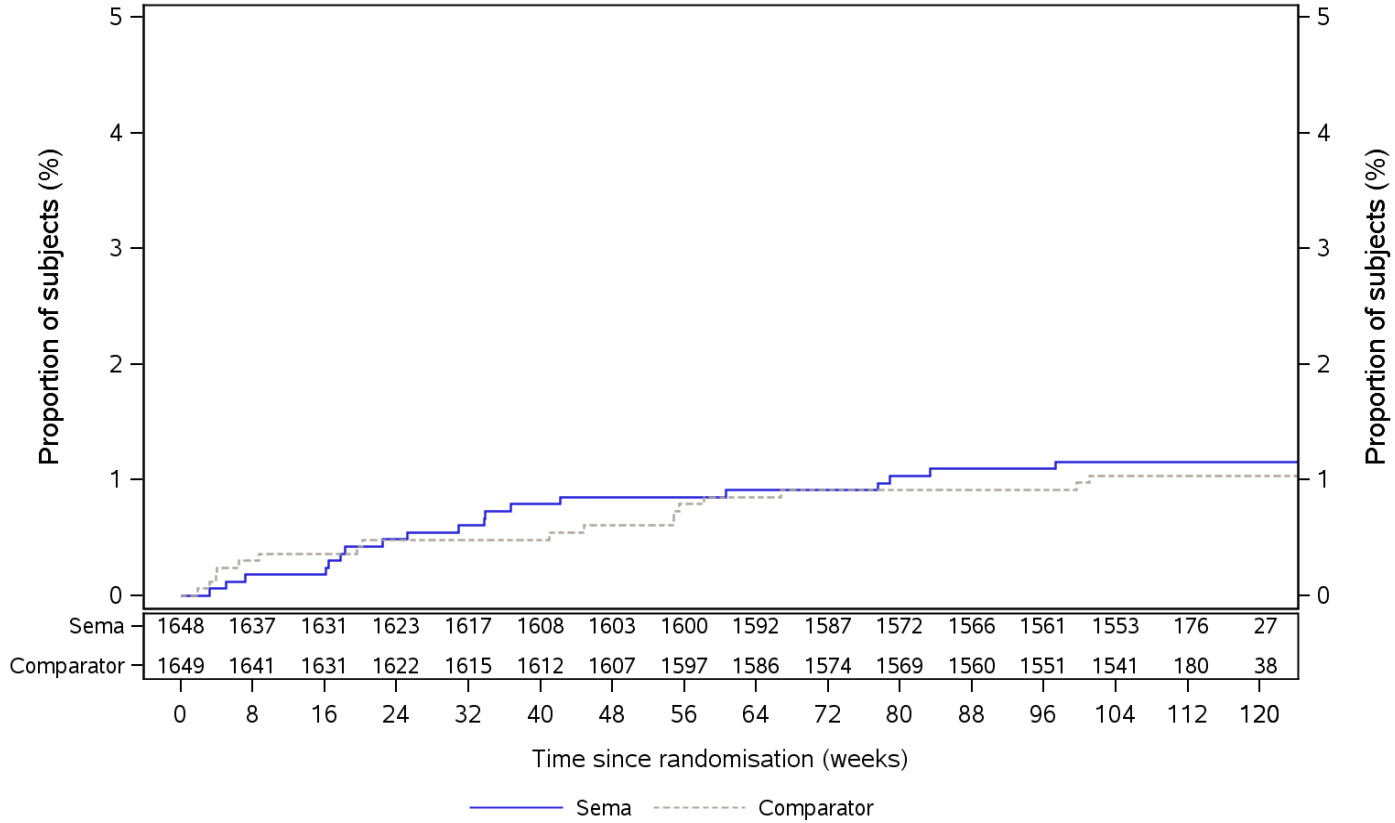
30 Mild adverse events - preferred term "Angina pectoris" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:58:22 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_ap_ae_mi_s6.png

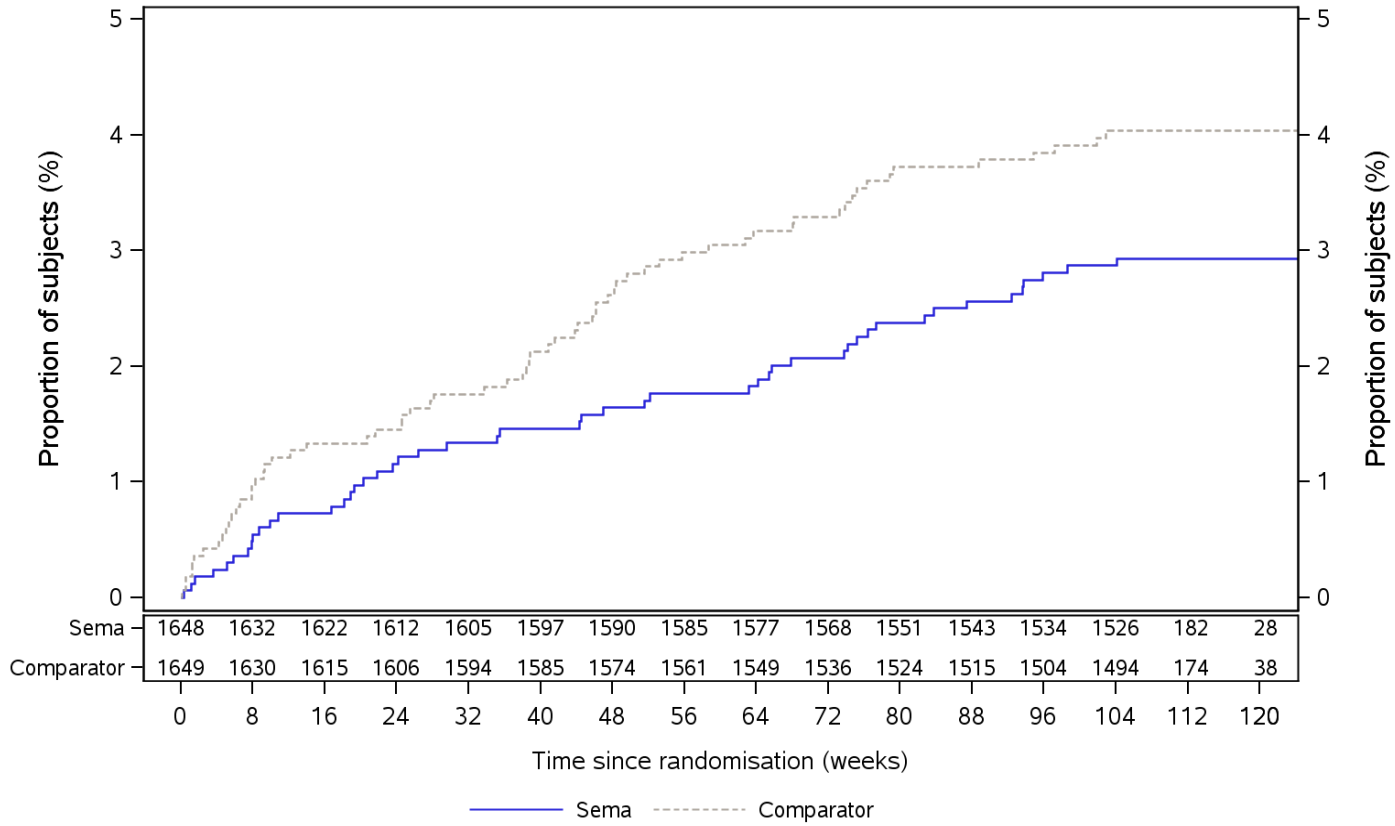
31 Mild adverse events - preferred term "Anxiety" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:58:41 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_anxiety_ae_mi_s6.png

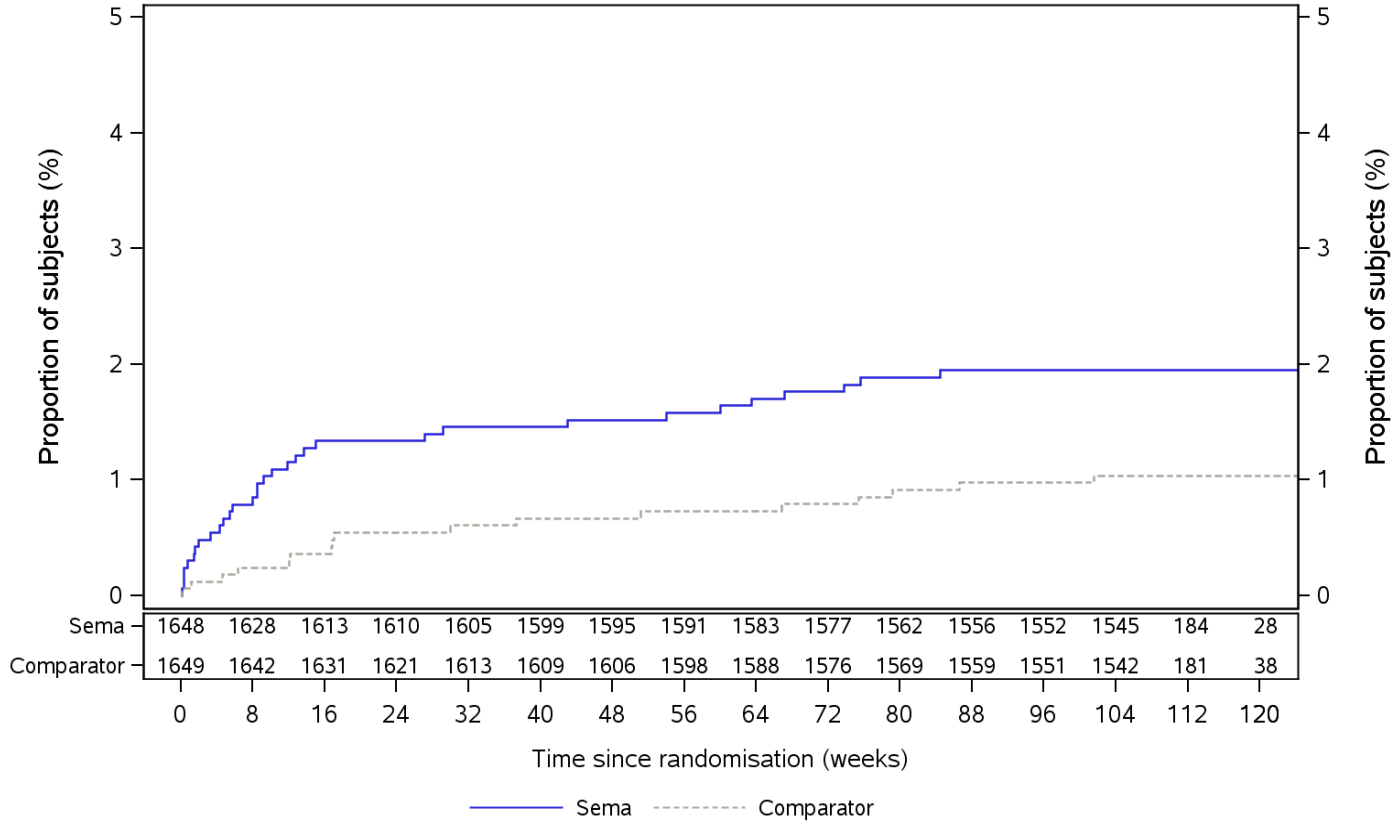
32 Mild adverse events - preferred term "Arthralgia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:59:00 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_arthralg_ae_mi_s6.png

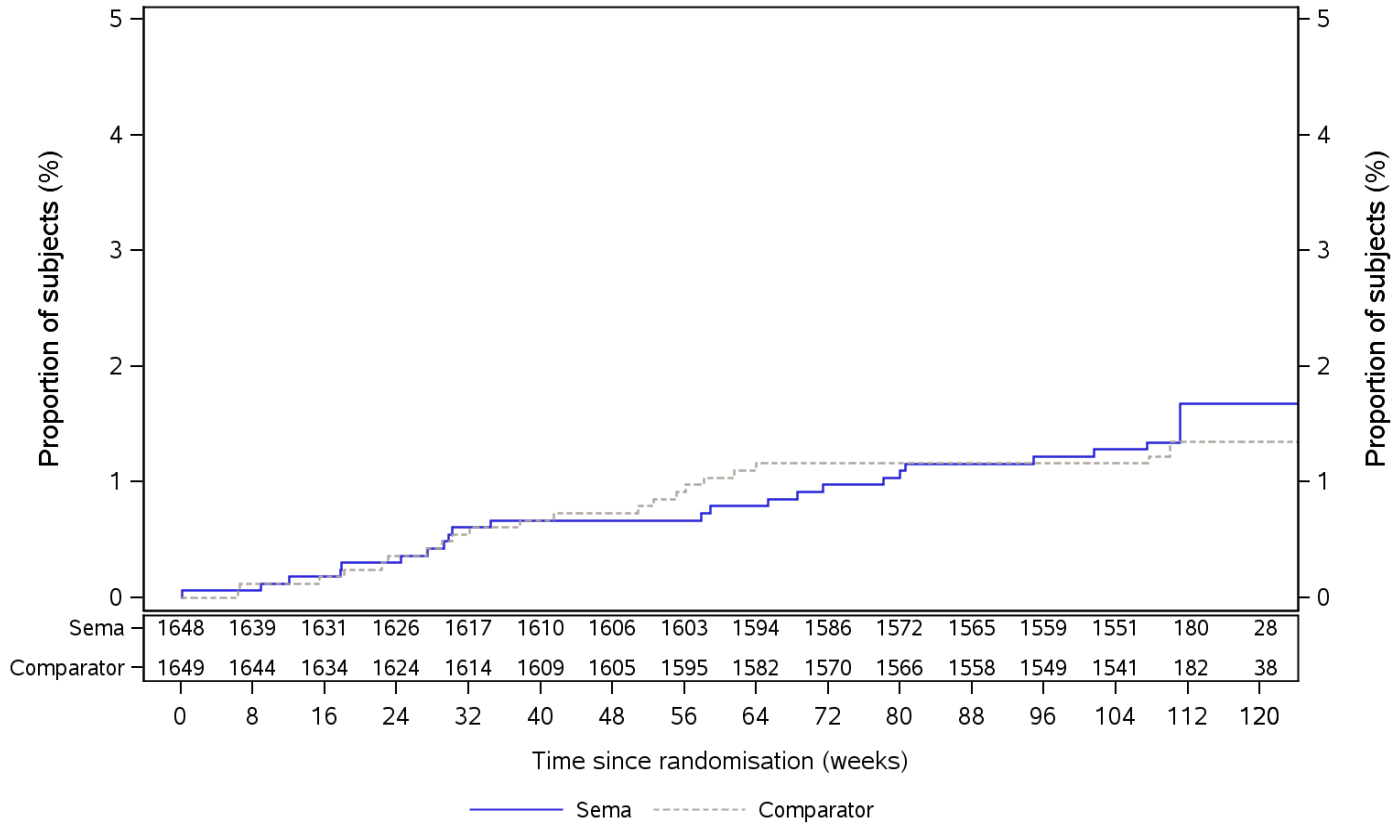
33 Mild adverse events - preferred term "Asthenia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:59:19 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_asthenia_ae_mi_s6.png

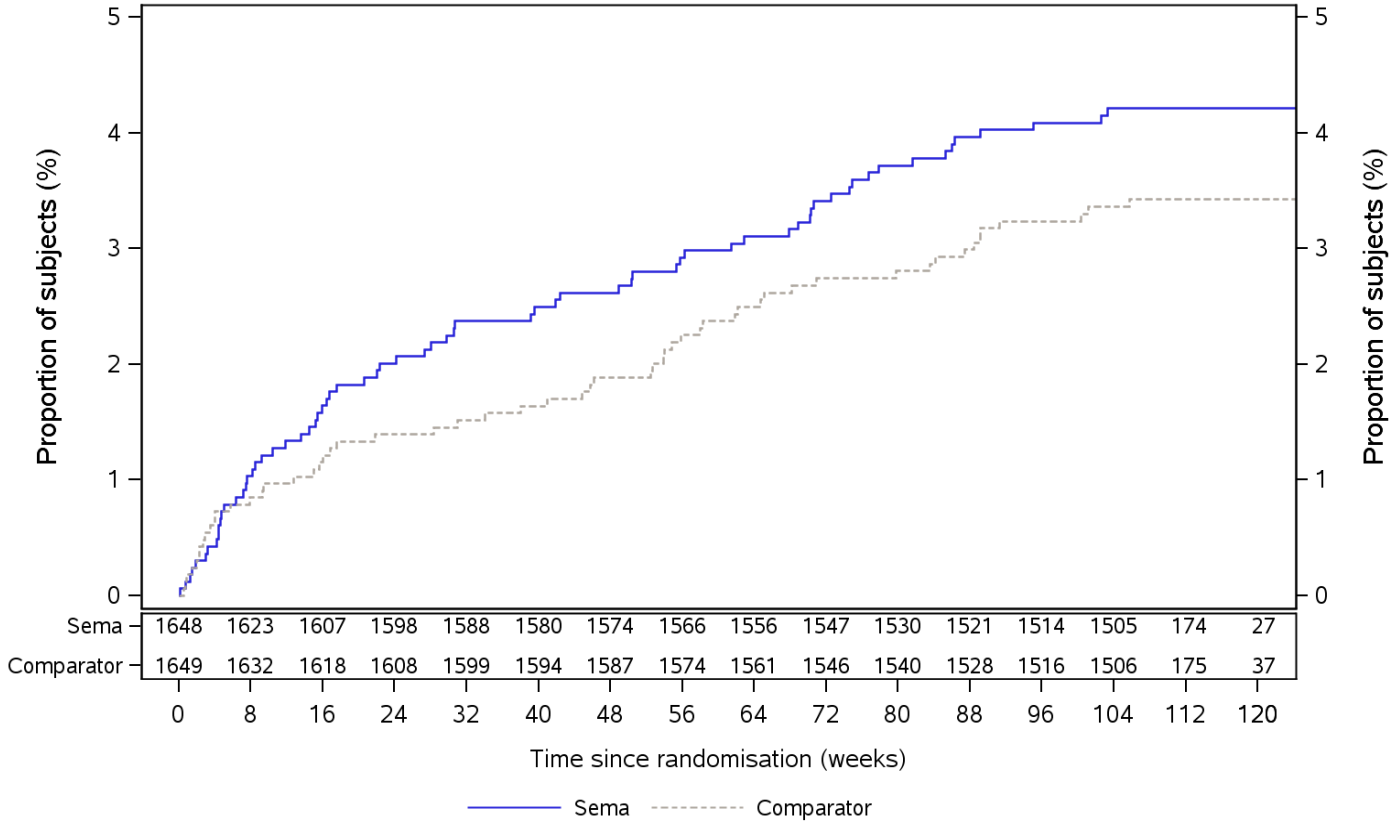
34 Mild adverse events - preferred term "Atrial fibrillation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:59:38 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_af_ae_mi_s6.png

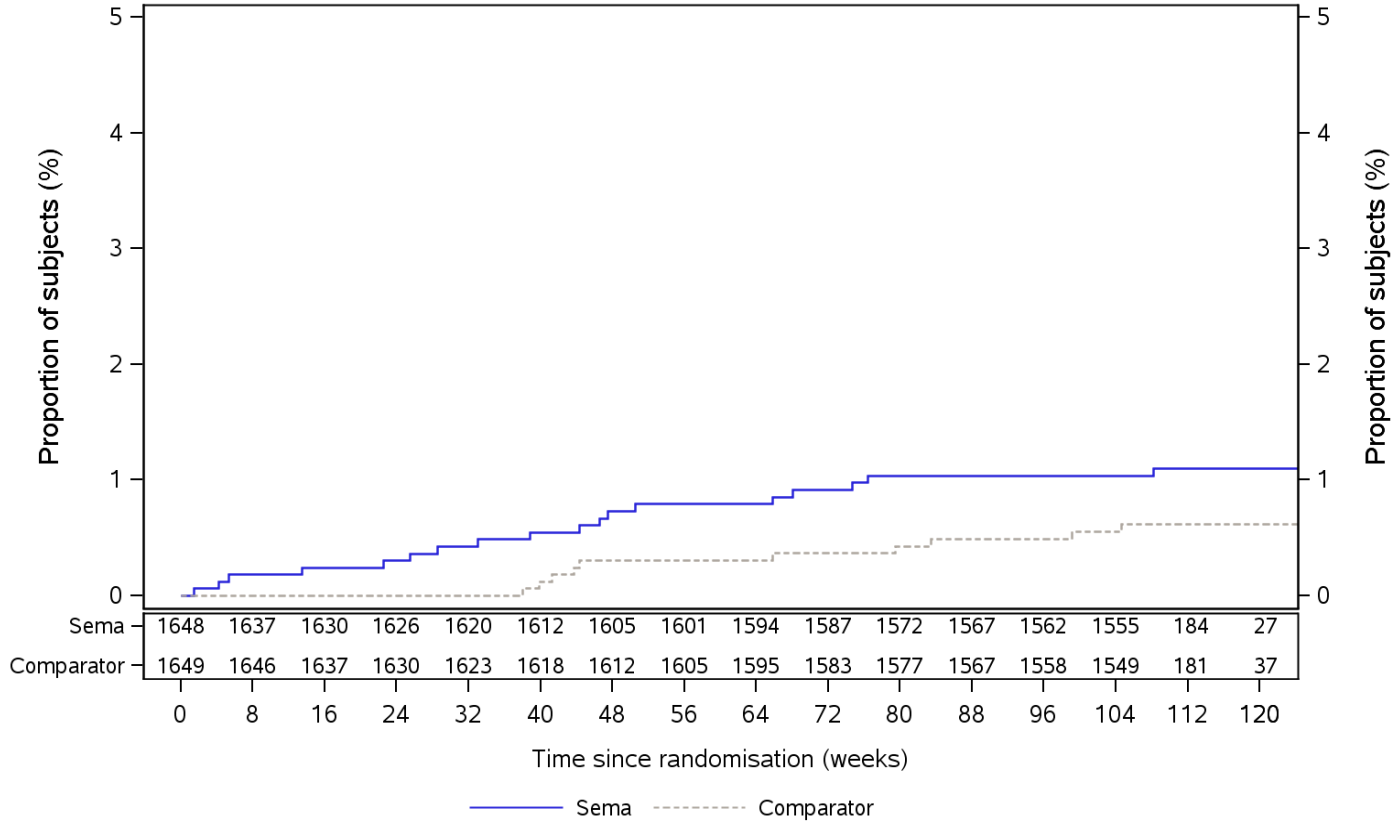
35 Mild adverse events - preferred term "Back pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:10:59:58 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_backpain_ae_mi_s6.png

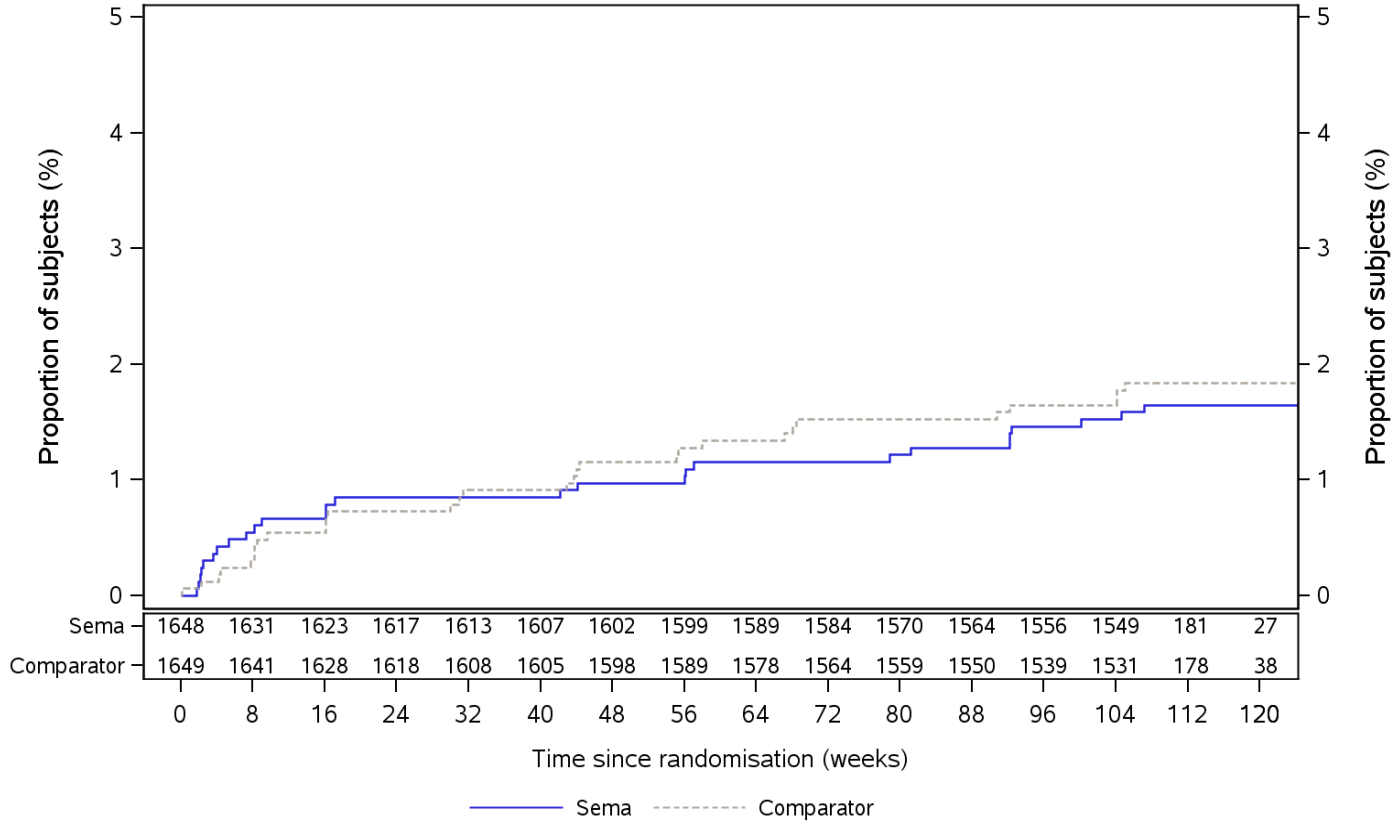
36 Mild adverse events - preferred term "Benign prostatic hyperplasia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:00:18 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_benprohyp_ae_mi_s6.png

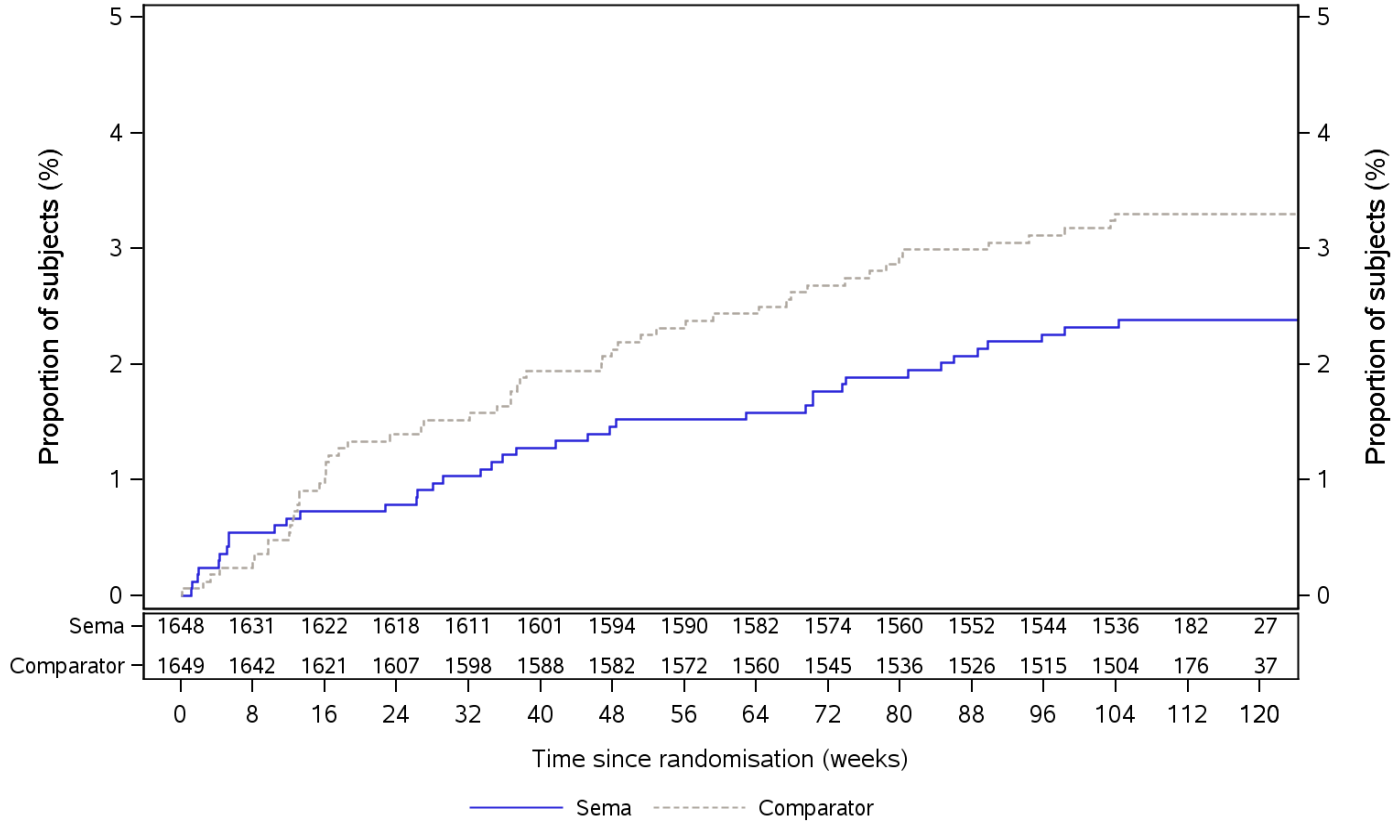
37 Mild adverse events - preferred term "Blood creatinine increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:00:45 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_blocreinc_ae_mi_s6.png

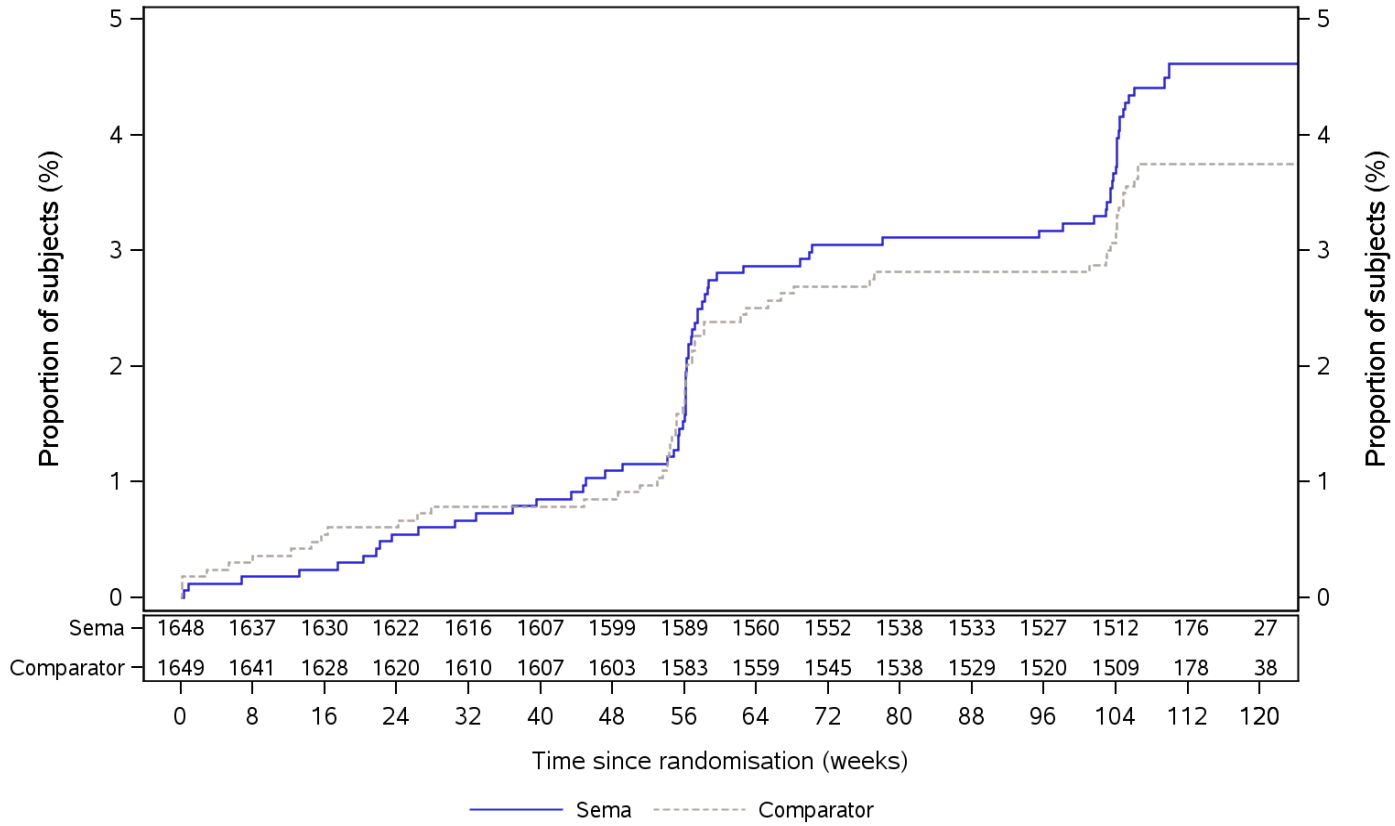
38 Mild adverse events - preferred term "Bronchitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:01:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_bronchit_ae_mi_s6.png

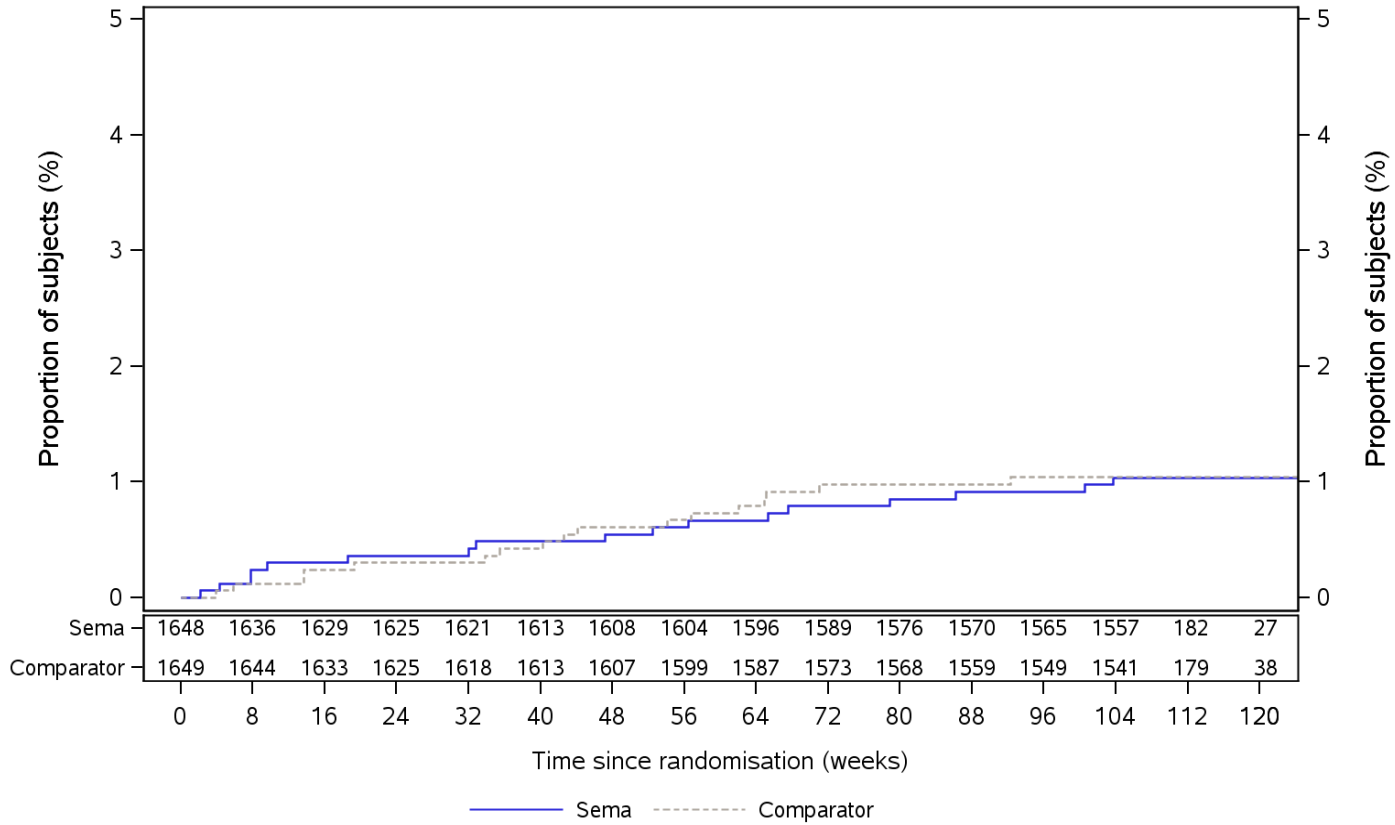
39 Mild adverse events - preferred term "Cataract" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:01:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cataract_ae_mi_s6.png

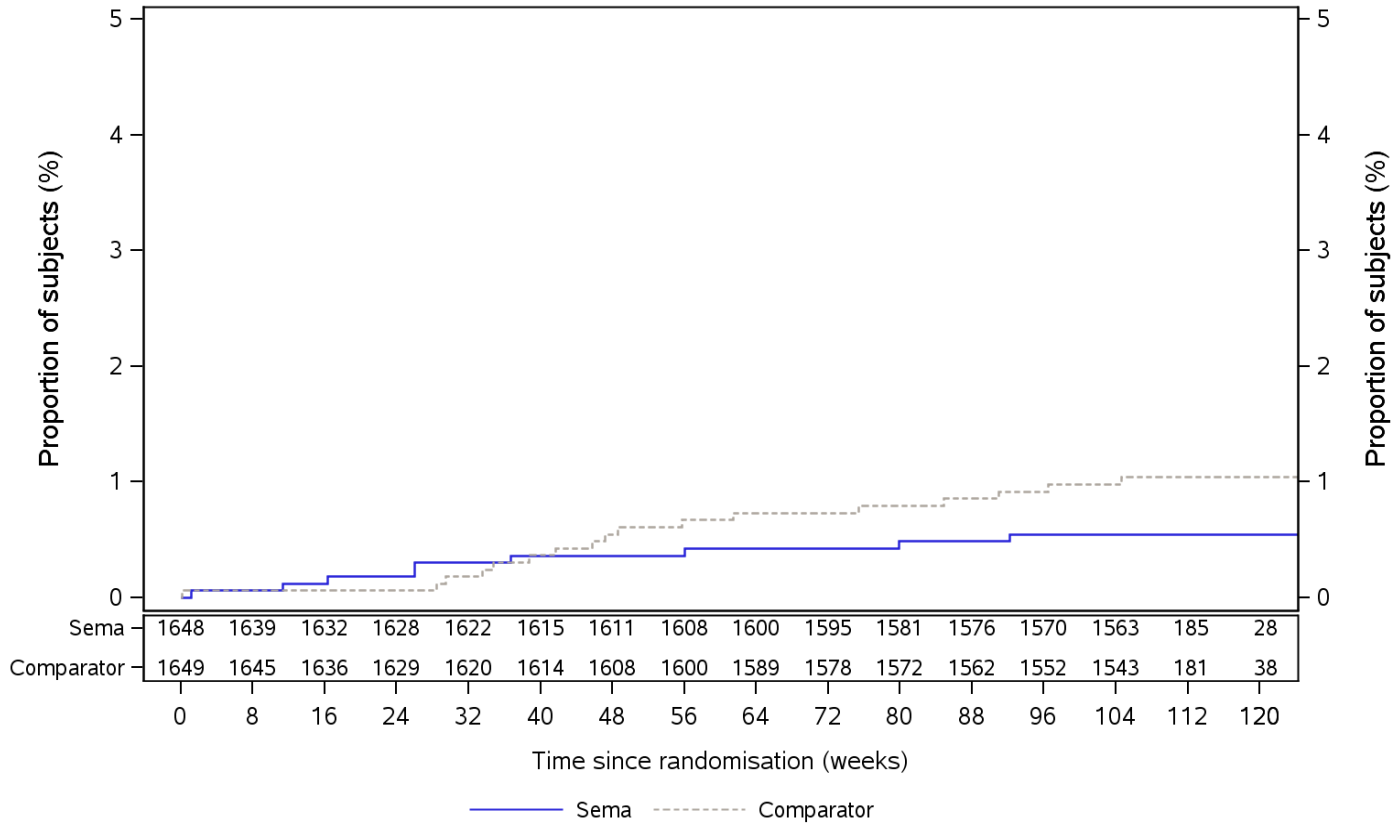
40 Mild adverse events - preferred term "Cellulitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:01:44 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cellulit_ae_mi_s6.png

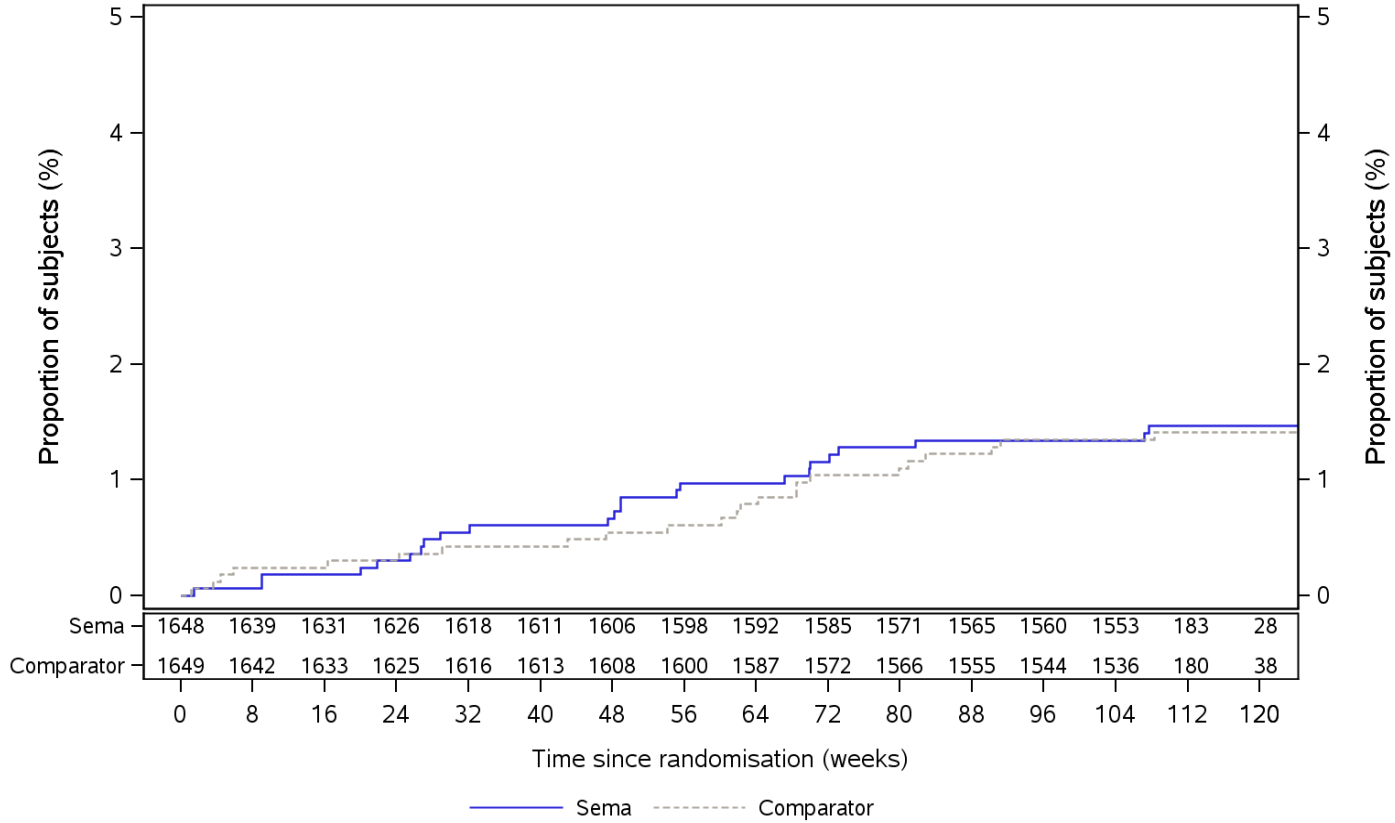
41 Mild adverse events - preferred term "Chest pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:02:03 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_chespain_ae_mi_s6.png

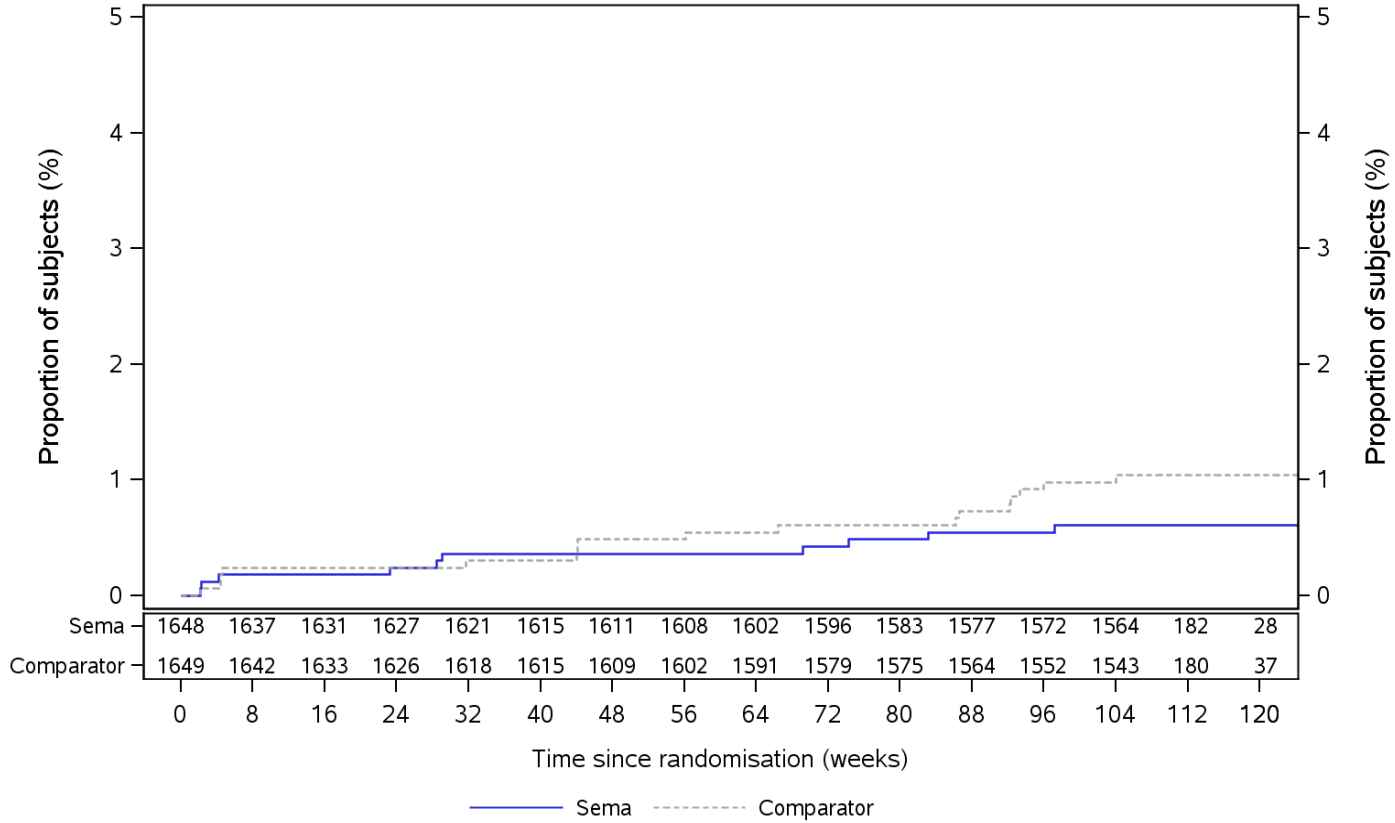
42 Mild adverse events - preferred term "Cholelithiasis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:02:23 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cholelit_ae_mi_s6.png

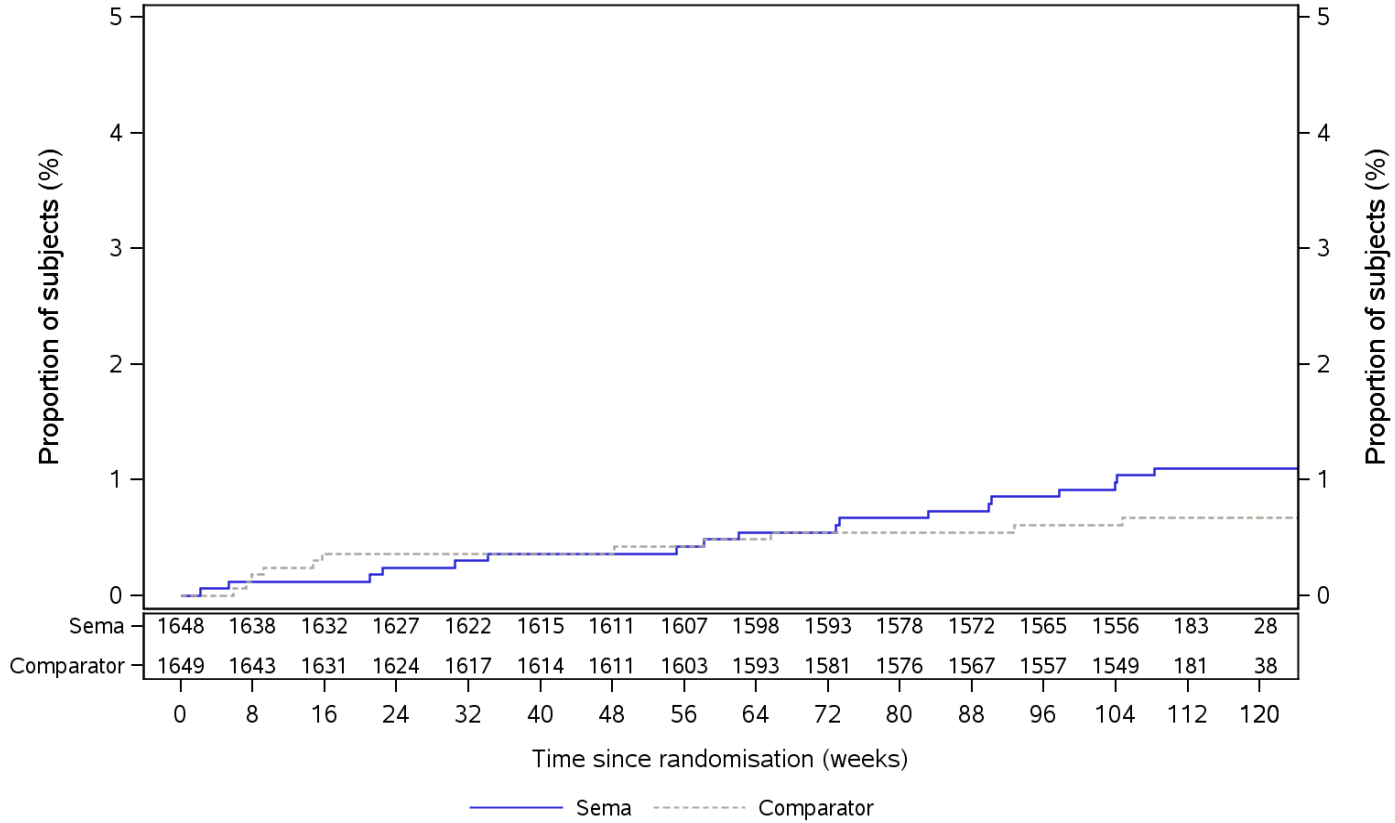
43 Mild adverse events - preferred term "Chronic kidney disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:02:44 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_chrkiddis_ae_mi_s6.png

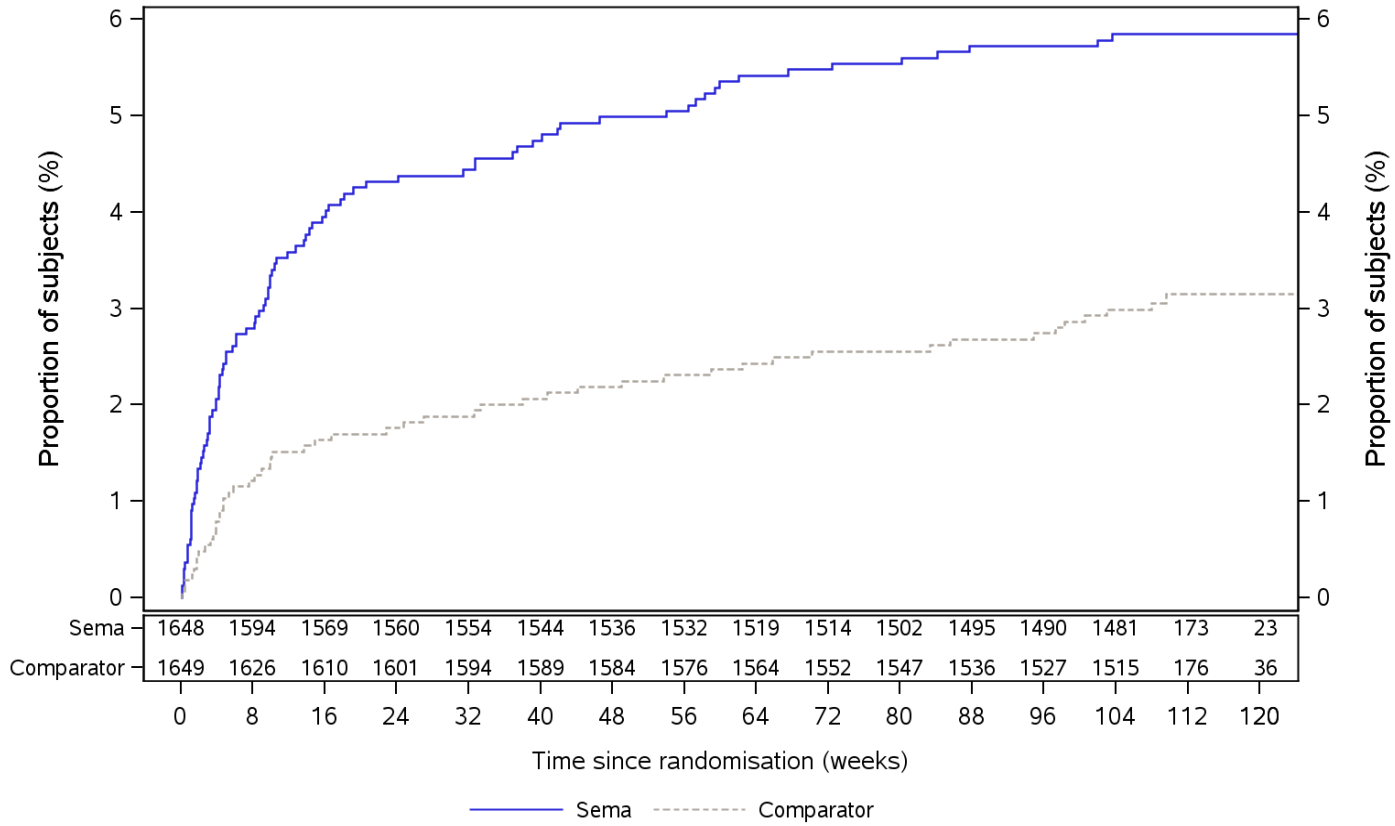
44 Mild adverse events - preferred term "Conjunctivitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:03:05 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_conjunct_ae_mi_s6.png

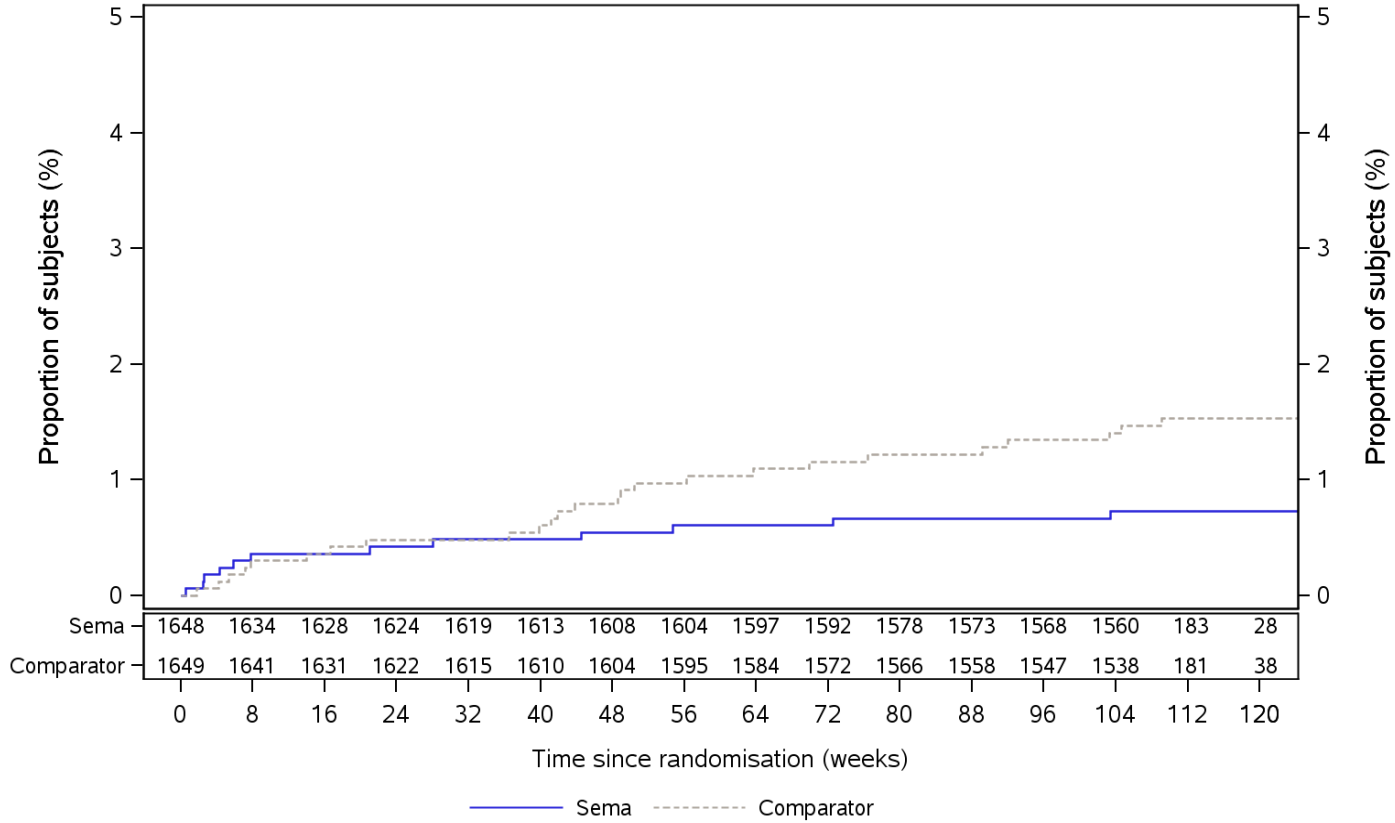
45 Mild adverse events - preferred term "Constipation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:03:30 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_constipa_ae_mi_s6.png

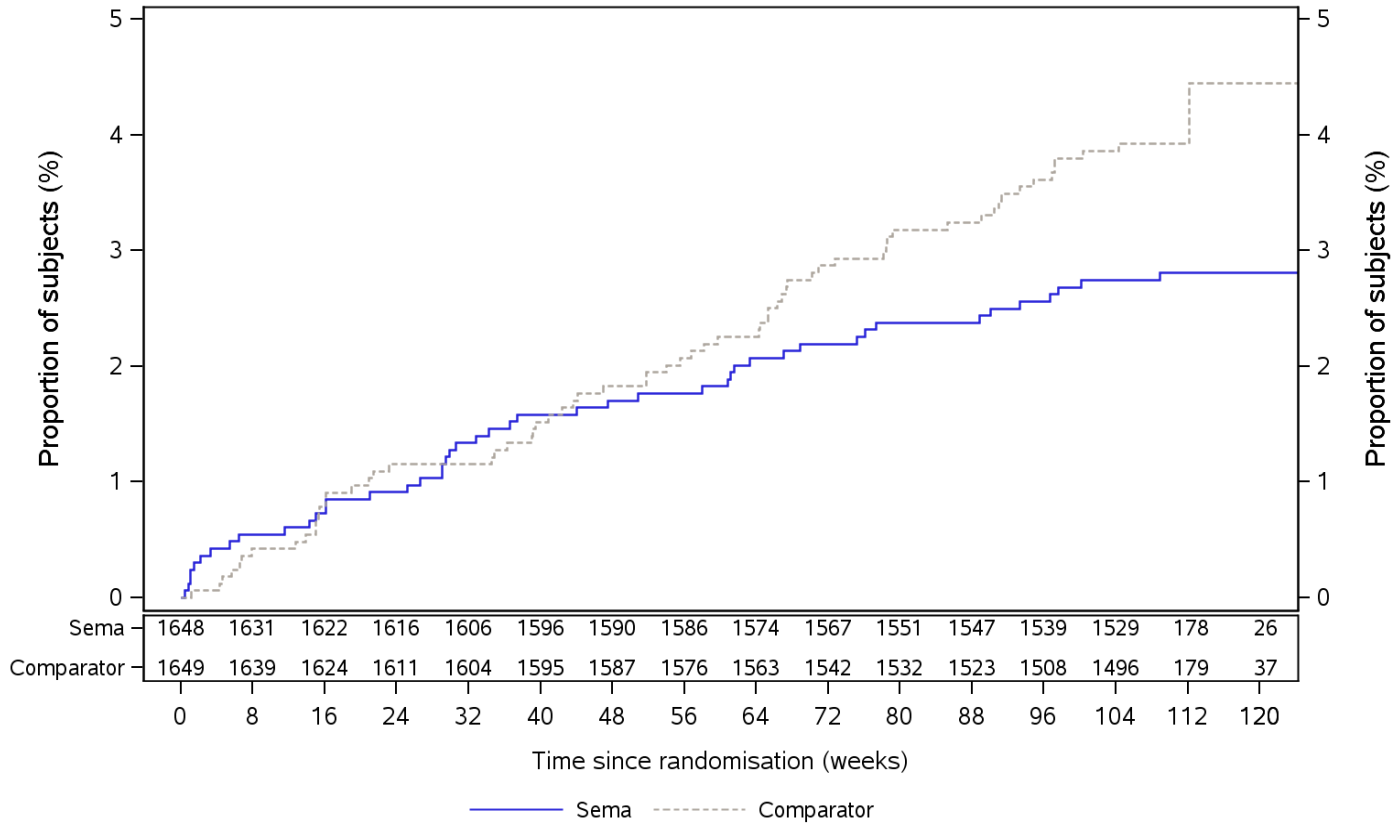
46 Mild adverse events - preferred term "Contusion" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:03:50 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_contusio_ae_mi_s6.png

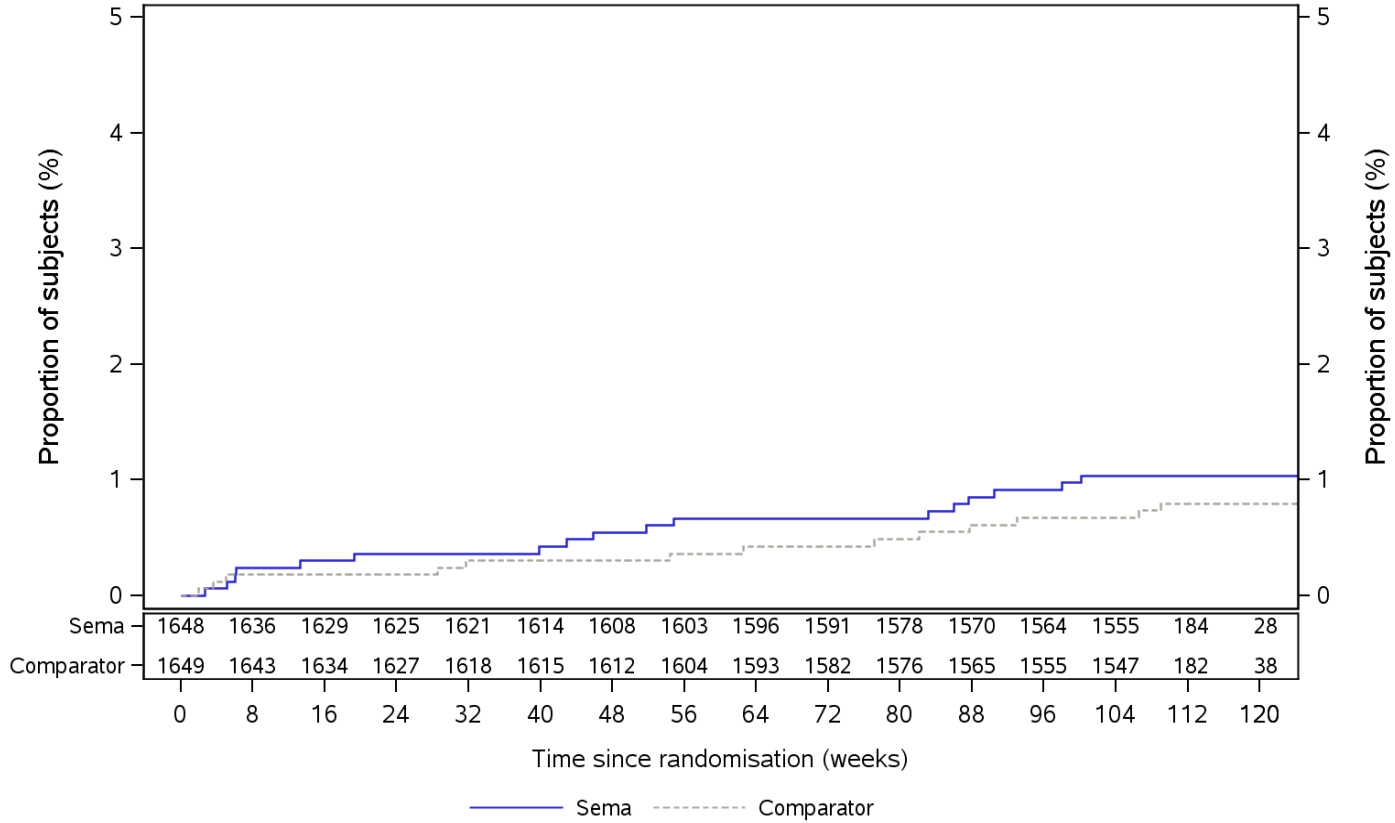
47 Mild adverse events - preferred term "Cough" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:04:09 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cough_ae_mi_s6.png

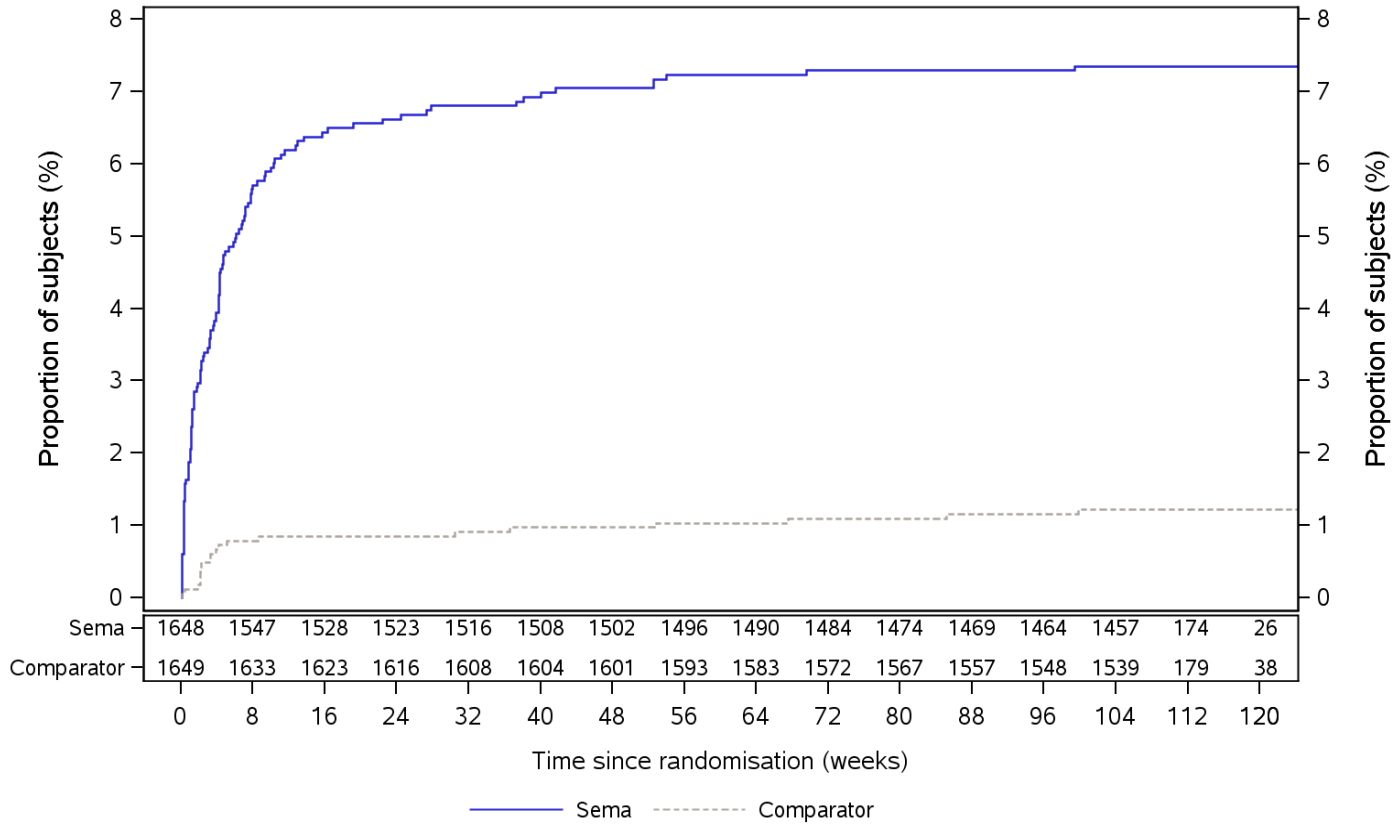
48 Mild adverse events - preferred term "Cystitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:04:29 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cystitis_ae_mi_s6.png

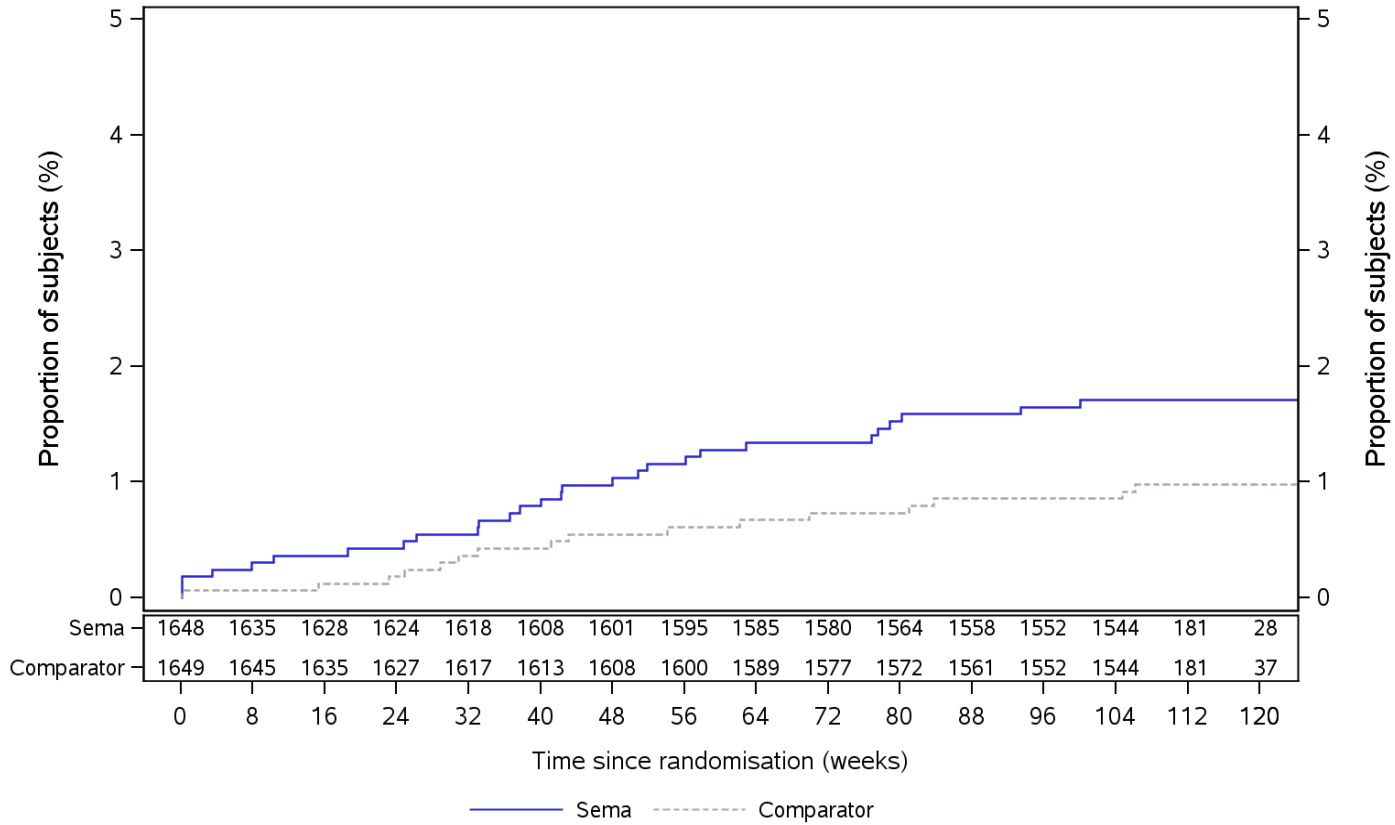
49 Mild adverse events - preferred term "Decreased appetite" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:04:48 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_decrappe_ae_mi_s6.png

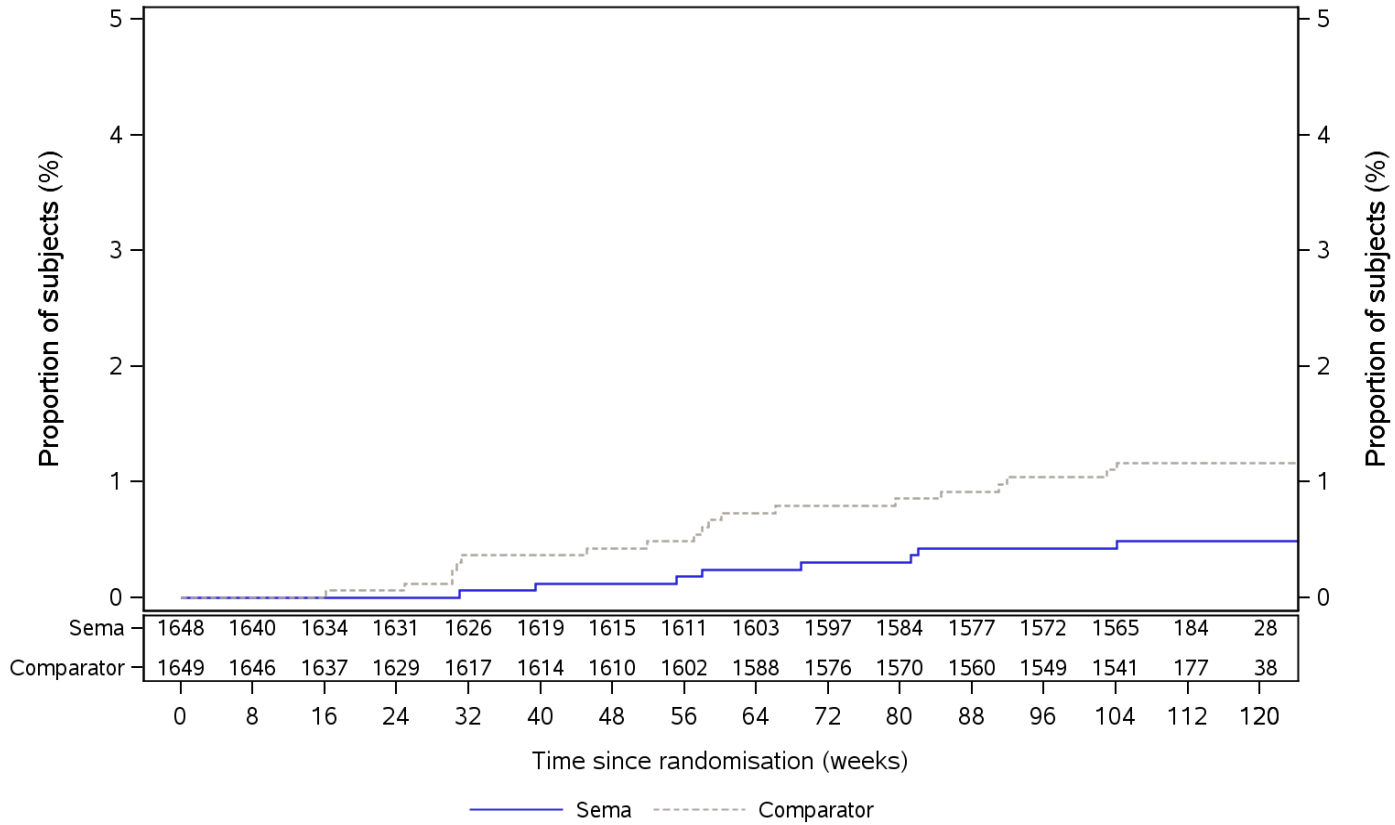
50 Mild adverse events - preferred term "Depression" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:05:08 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_depressi_ae_mi_s6.png

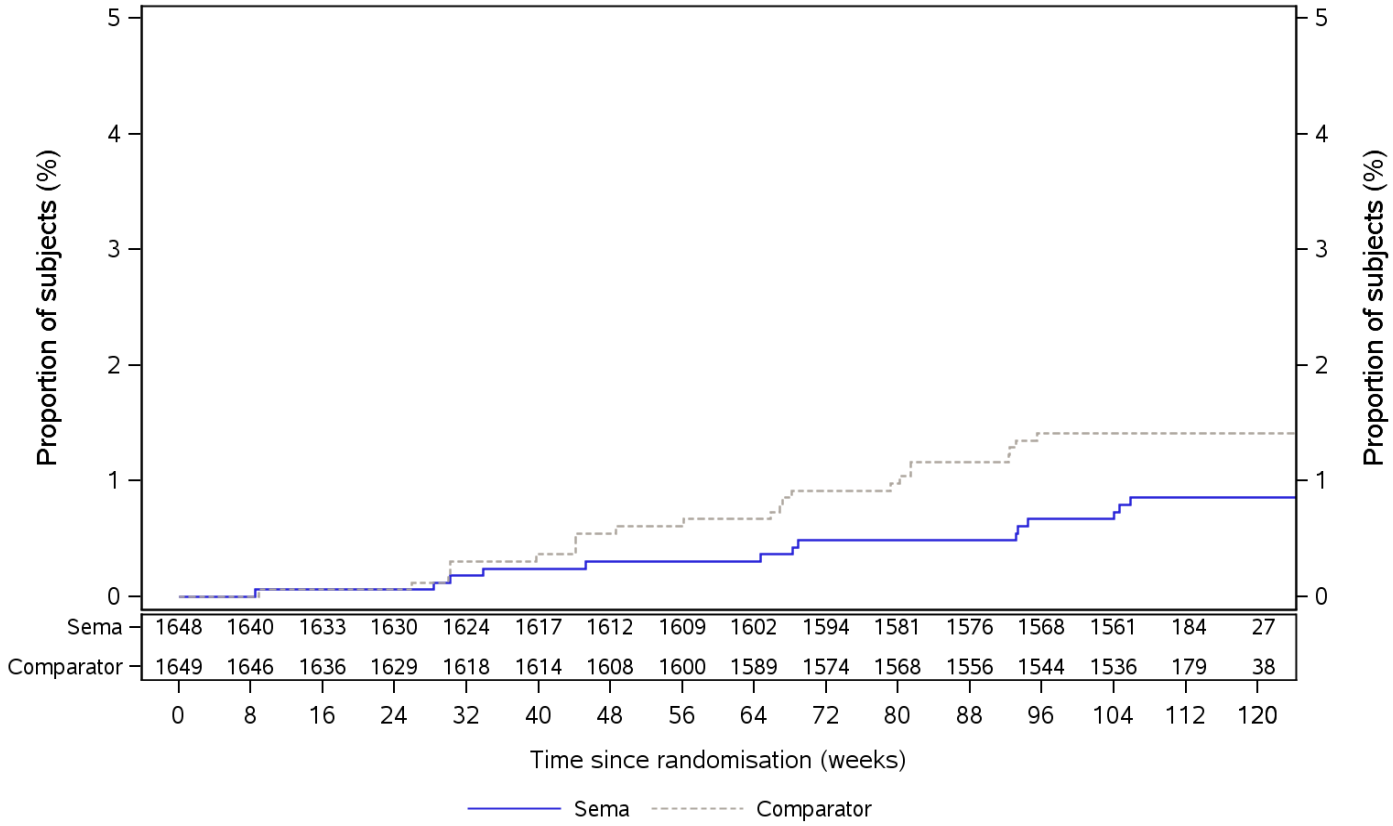
51 Mild adverse events - preferred term "Diabetes mellitus" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:05:32 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabmell_ae_mi_s6.png

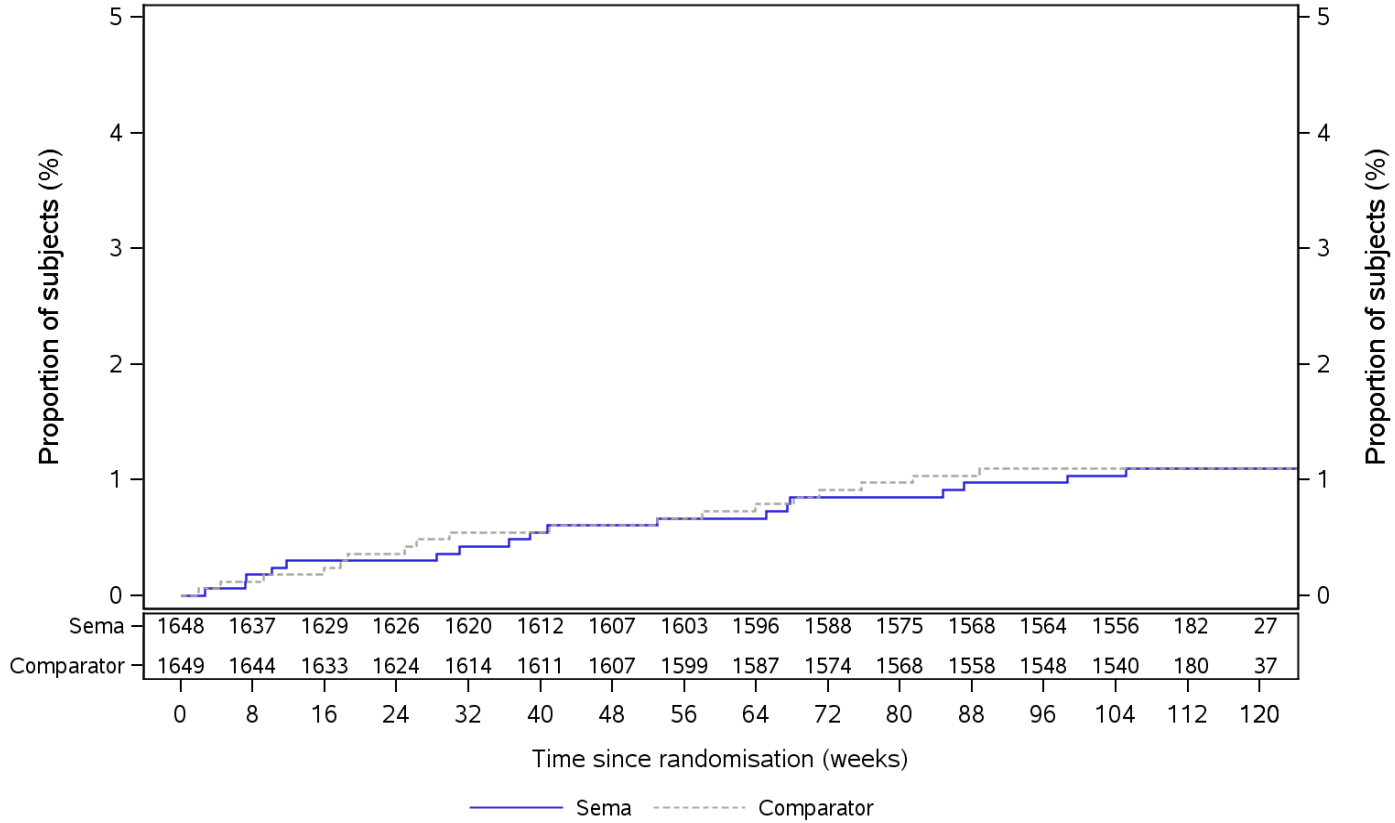
52 Mild adverse events - preferred term "Diabetes mellitus inadequate control" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:05:56 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diamelina_ae_mi_s6.png

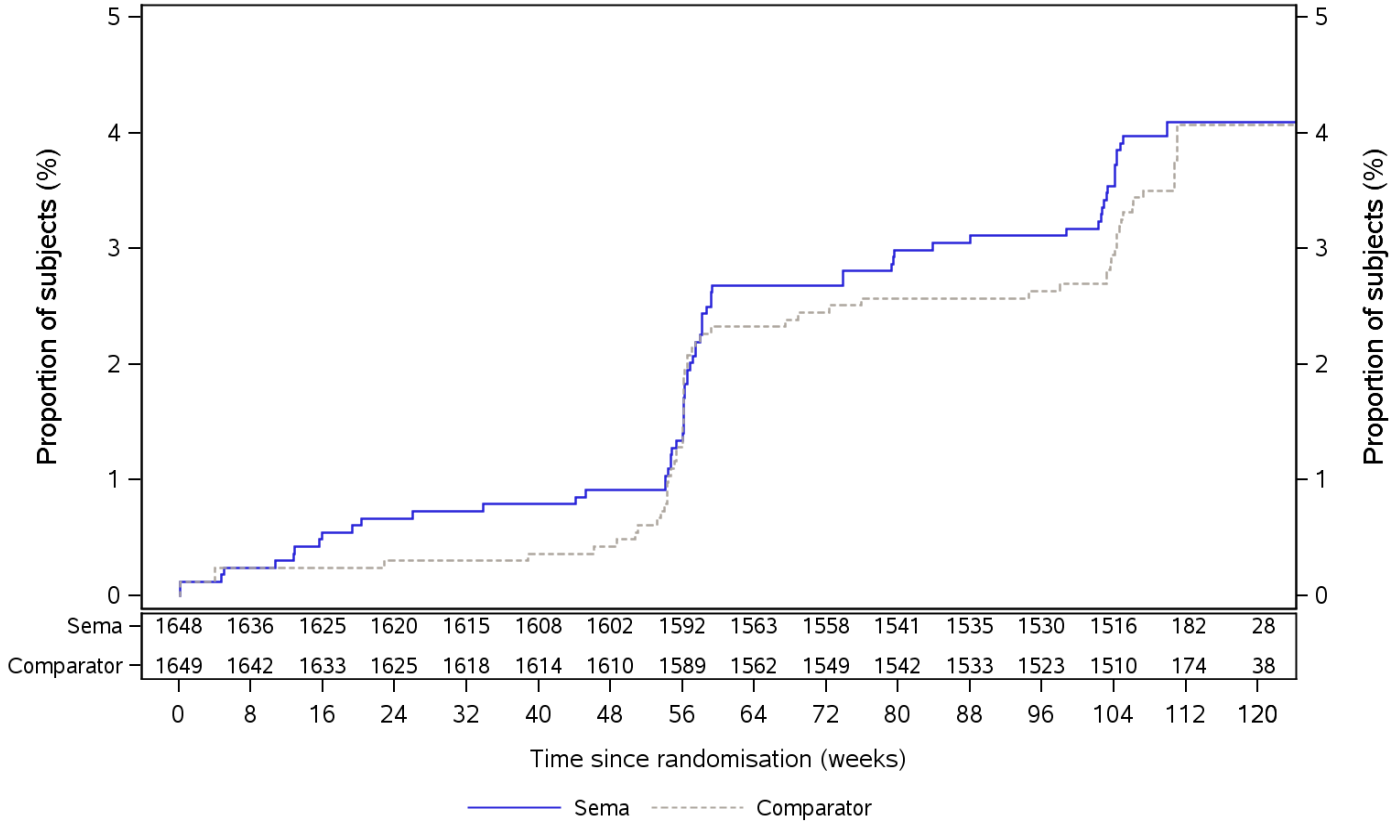
53 Mild adverse events - preferred term "Diabetic neuropathy" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:06:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabneur_ae_mi_s6.png

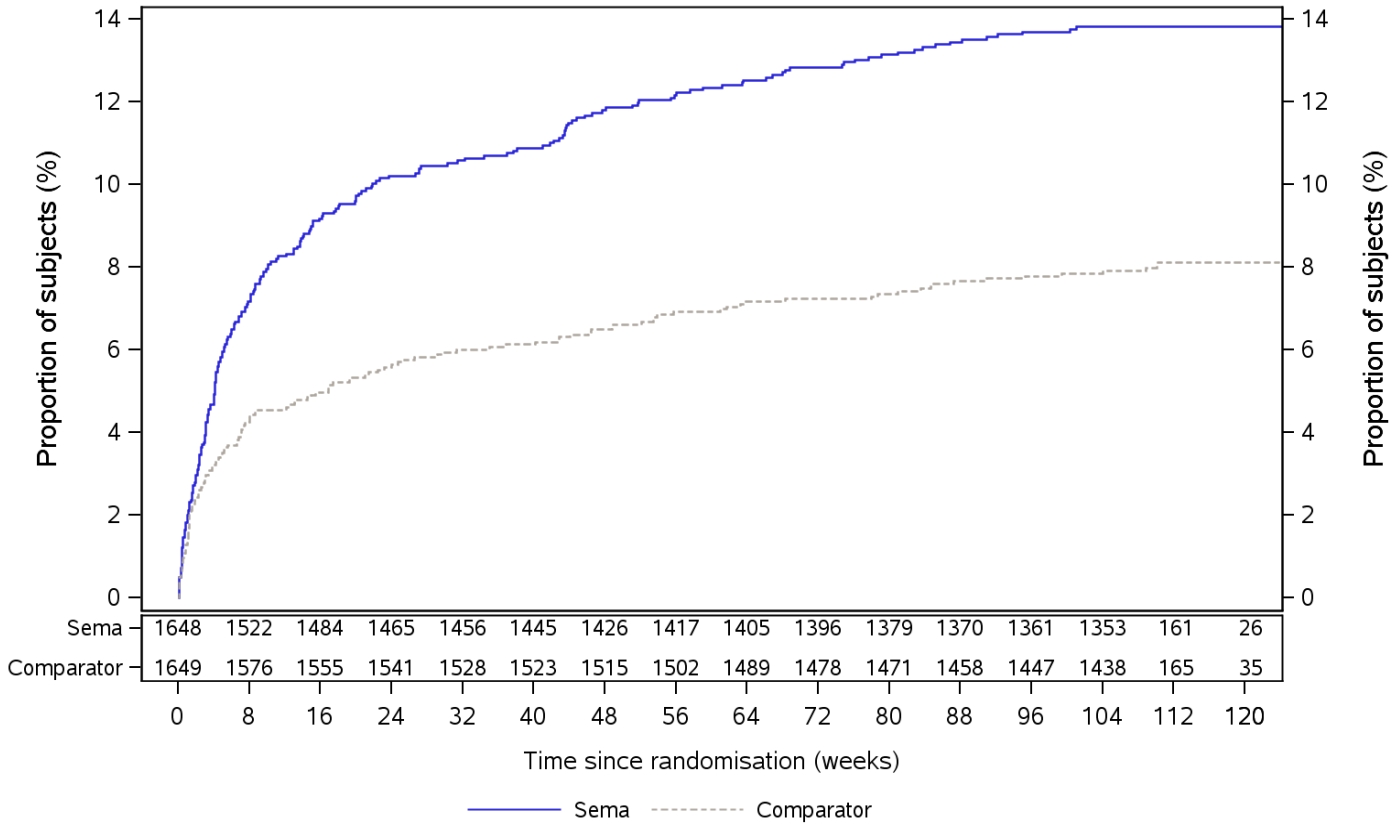
54 Mild adverse events - preferred term "Diabetic retinopathy" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:06:39 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabreti_ae_mi_s6.png

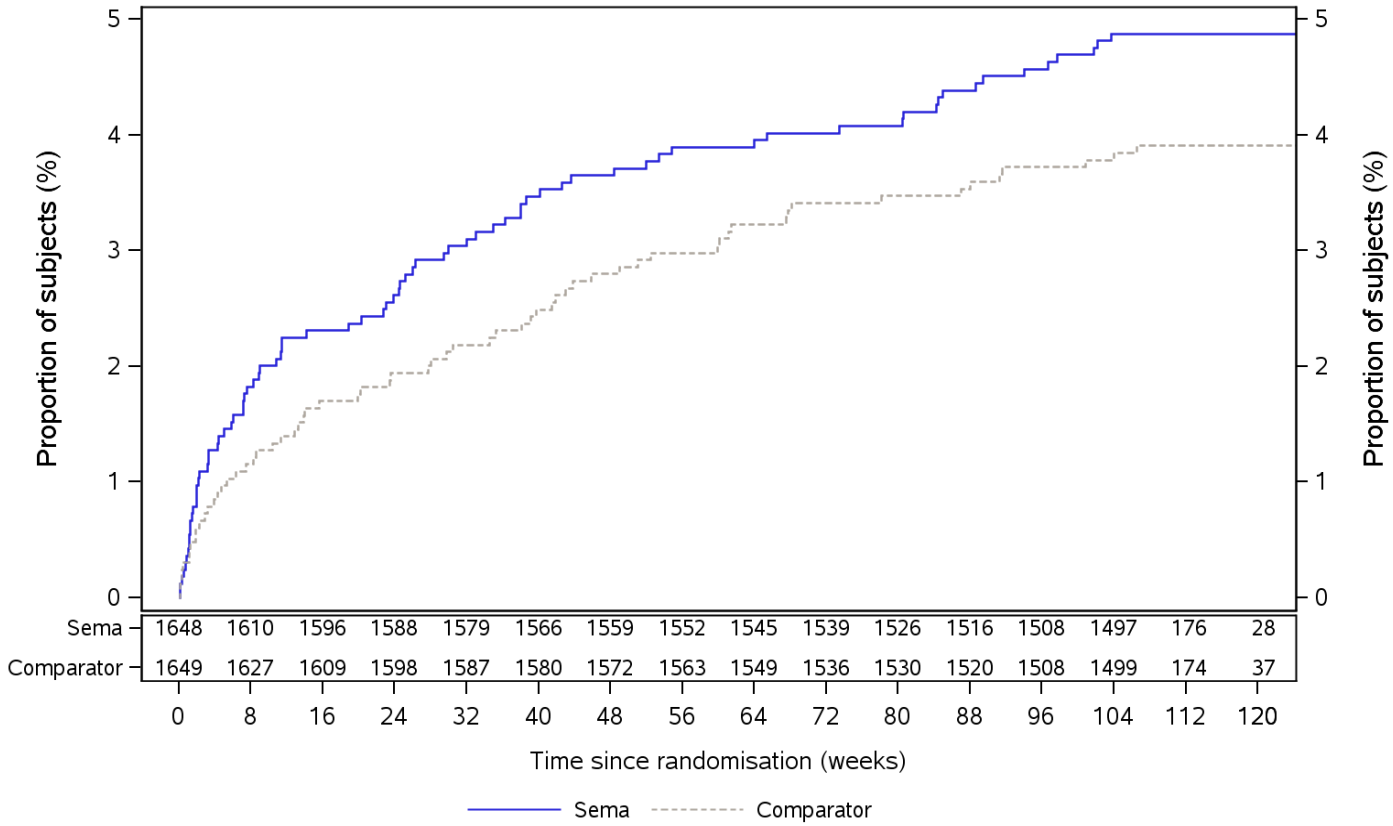
55 Mild adverse events - preferred term "Diarrhoea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:06:57 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diarrhoe_ae_mi_s6.png

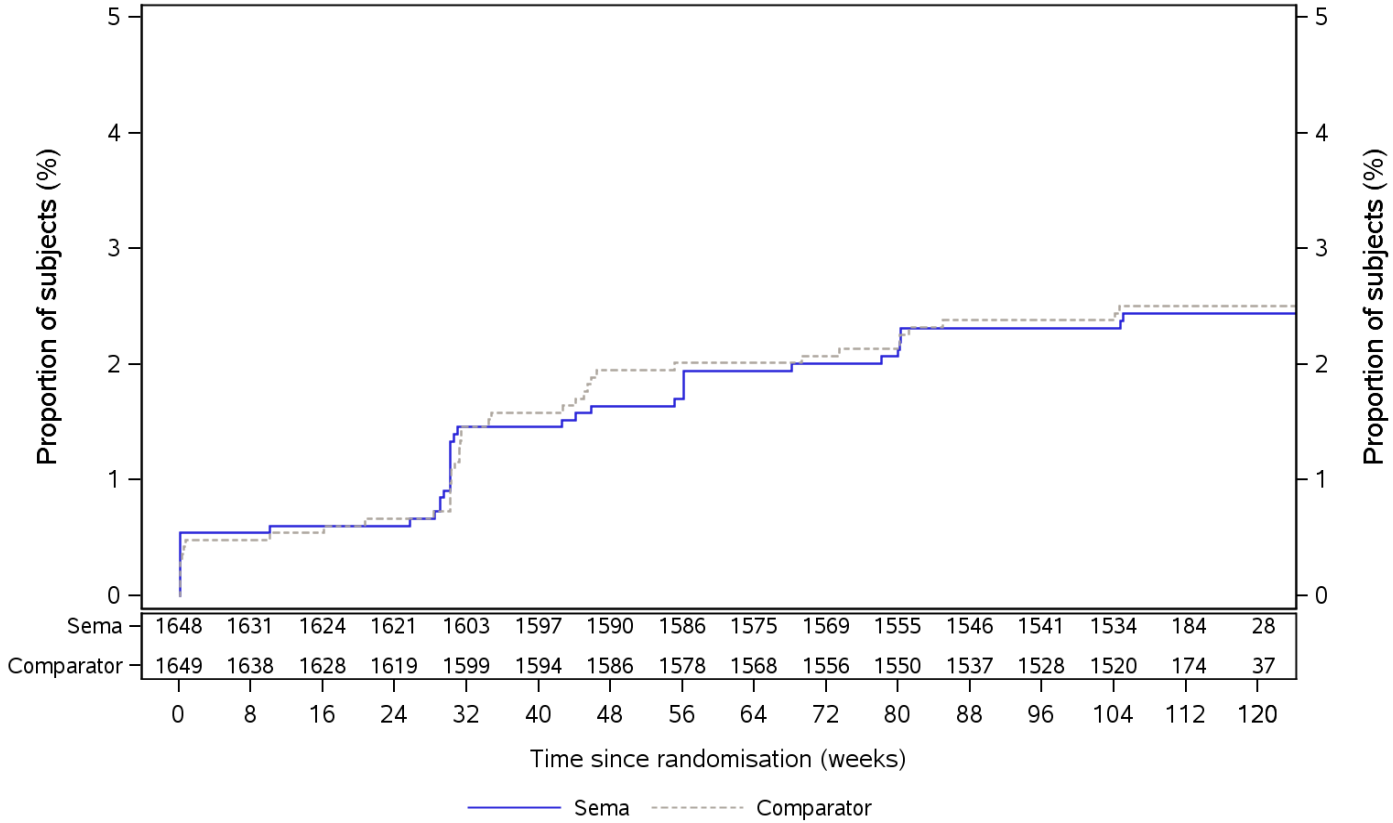
56 Mild adverse events - preferred term "Dizziness" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:07:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dizzines_ae_mi_s6.png

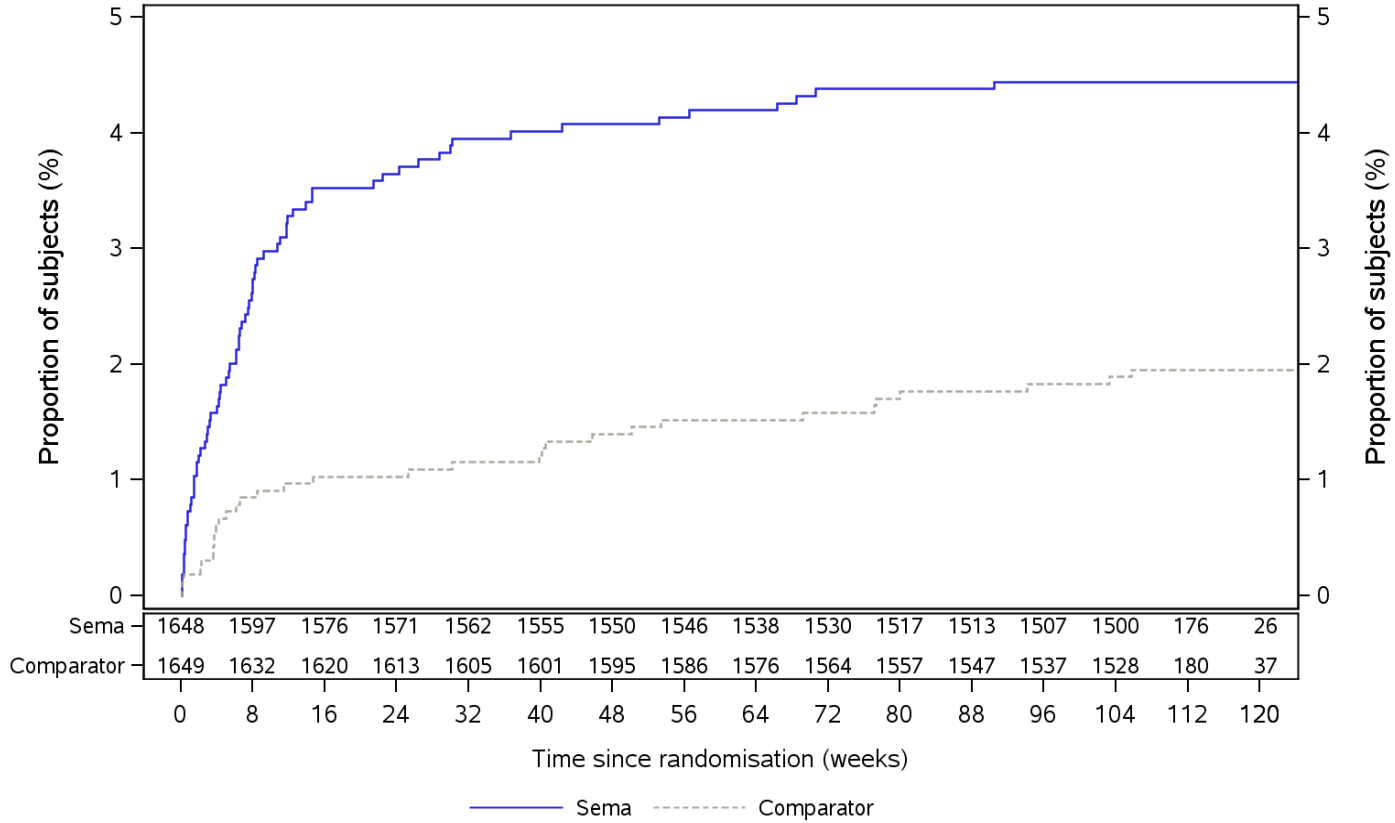
57 Mild adverse events - preferred term "Dyslipidaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:07:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dyslipid_ae_mi_s6.png

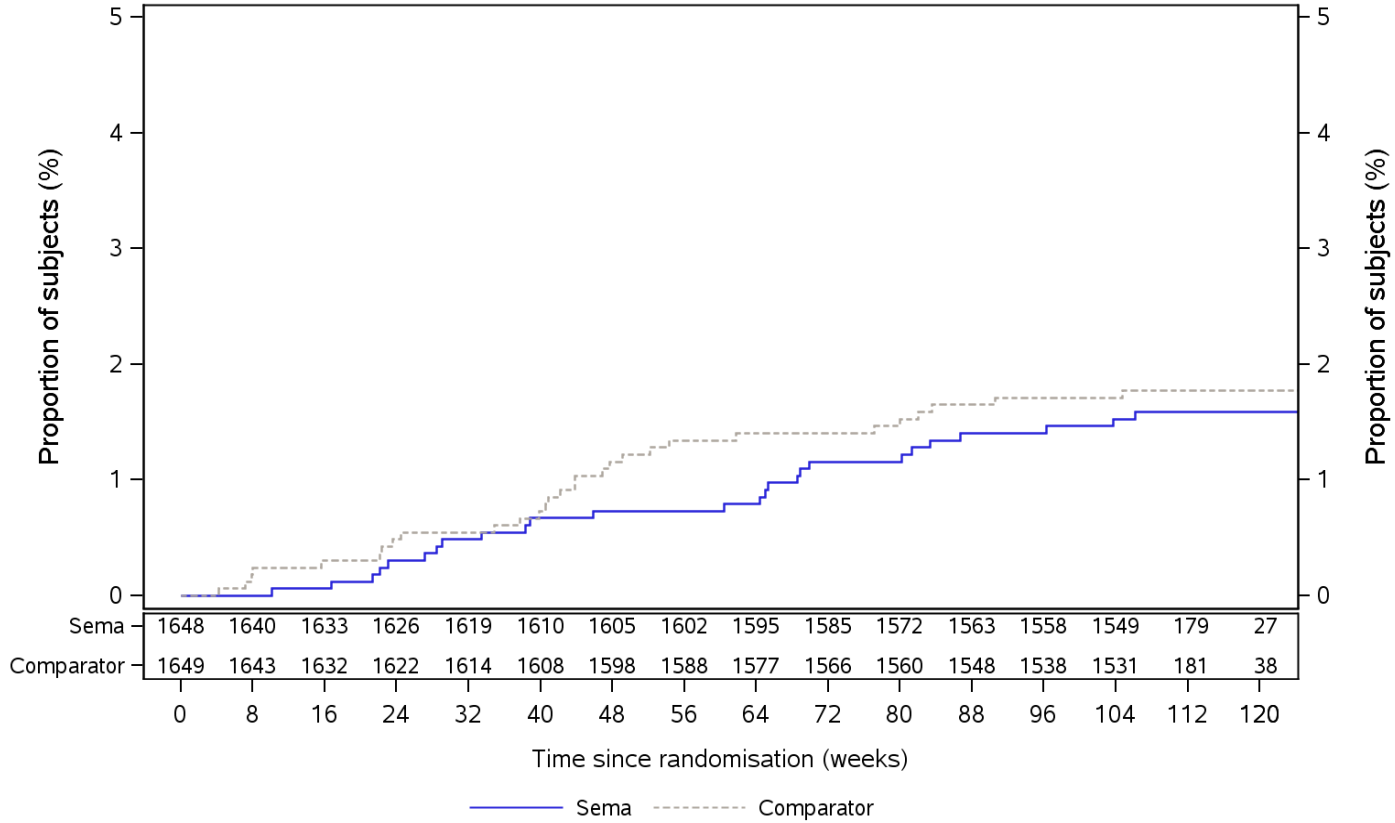
58 Mild adverse events - preferred term "Dyspepsia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:07:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dyspepsi_ae_mi_s6.png

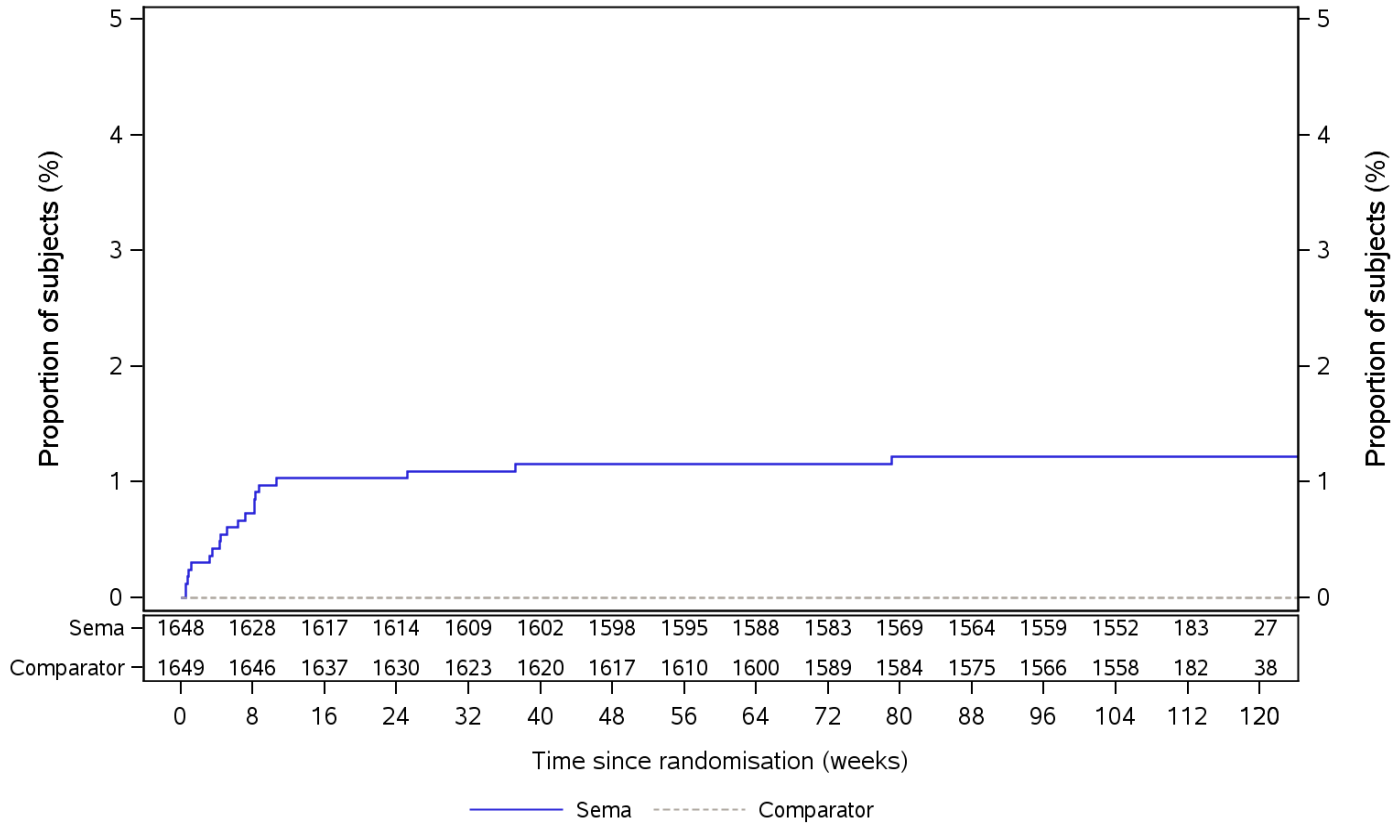
59 Mild adverse events - preferred term "Dyspnoea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:08:15 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dyspnoea_ae_mi_s6.png

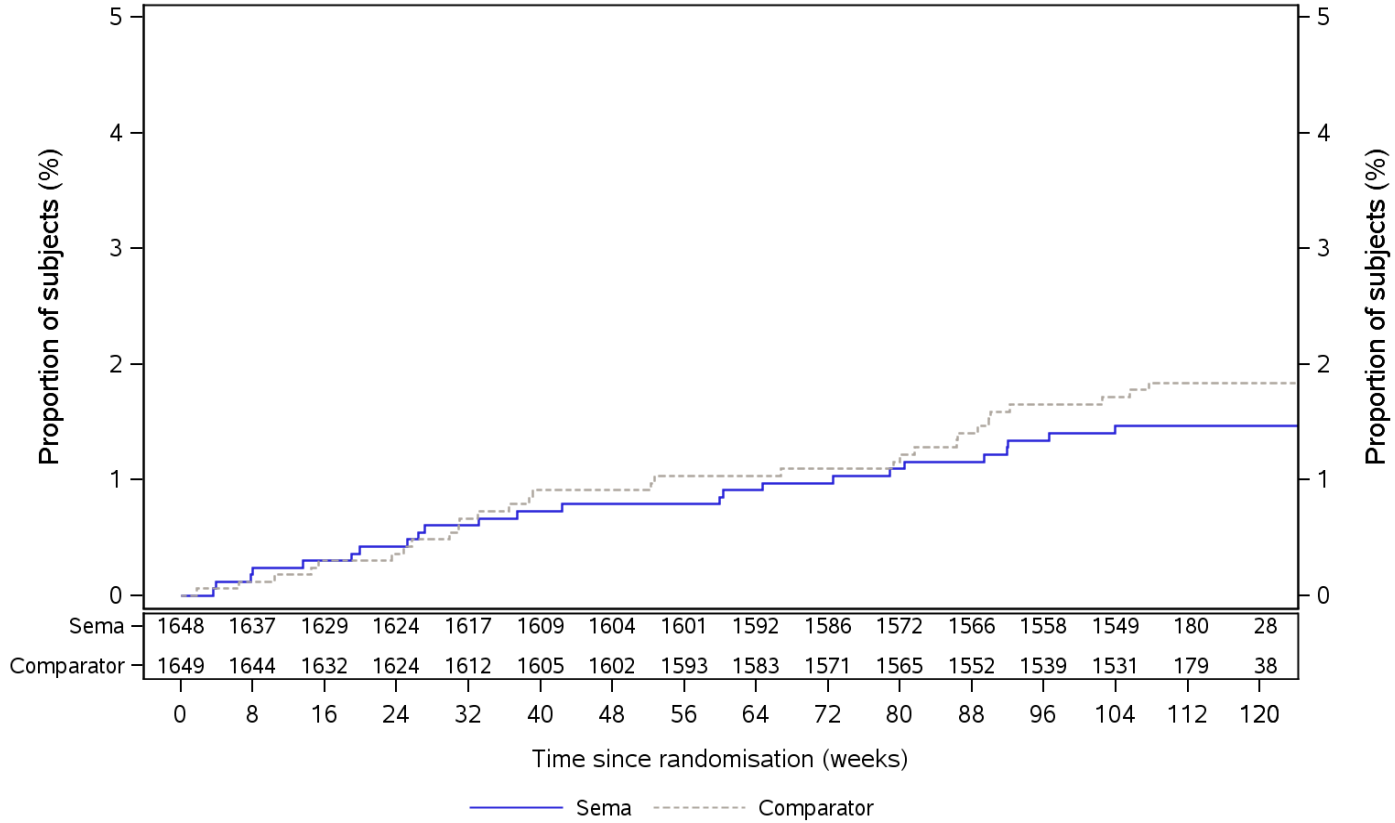
60 Mild adverse events - preferred term "Eructation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:08:34 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_eructati_ae_mi_s6.png

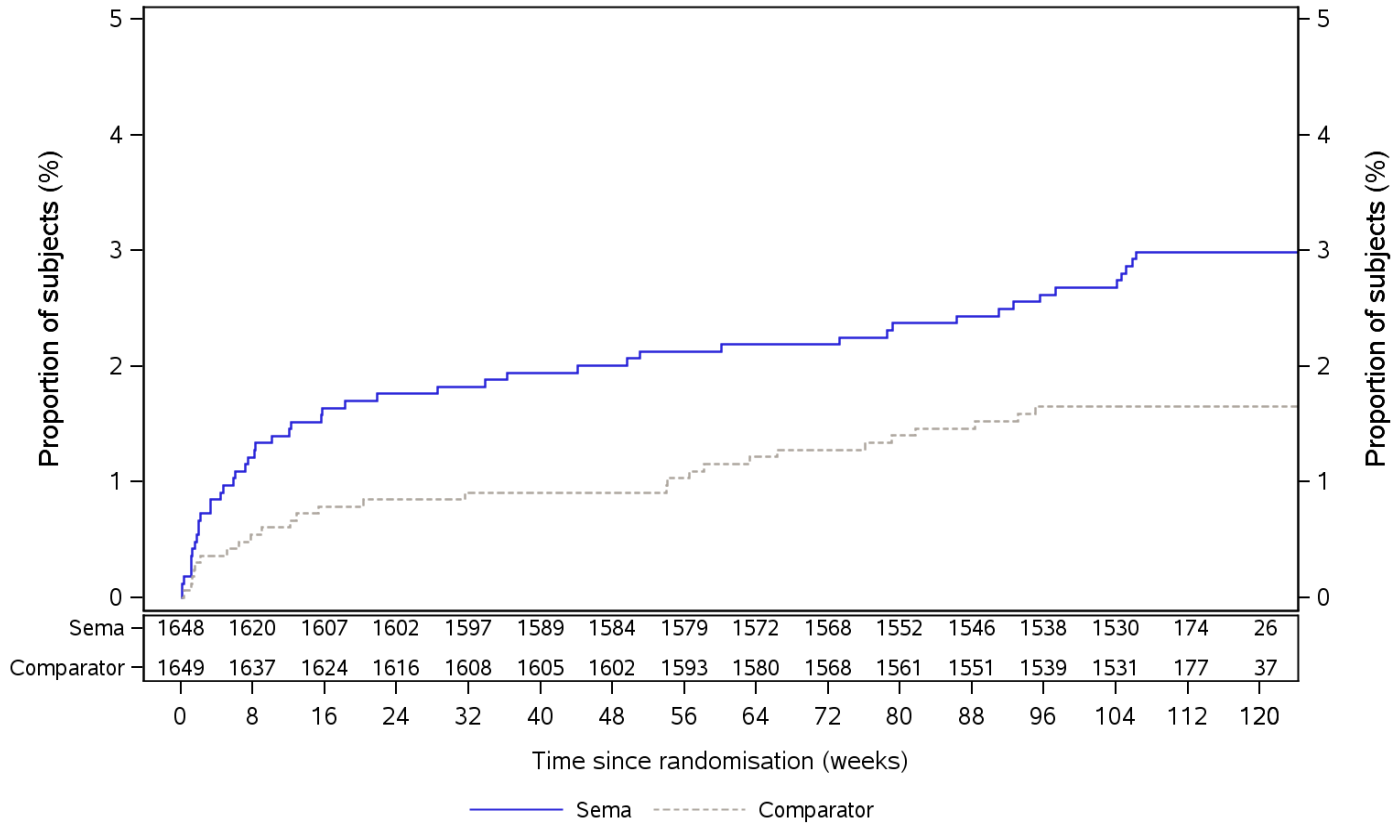
61 Mild adverse events - preferred term "Fall" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:08:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_fall_ae_mi_s6.png

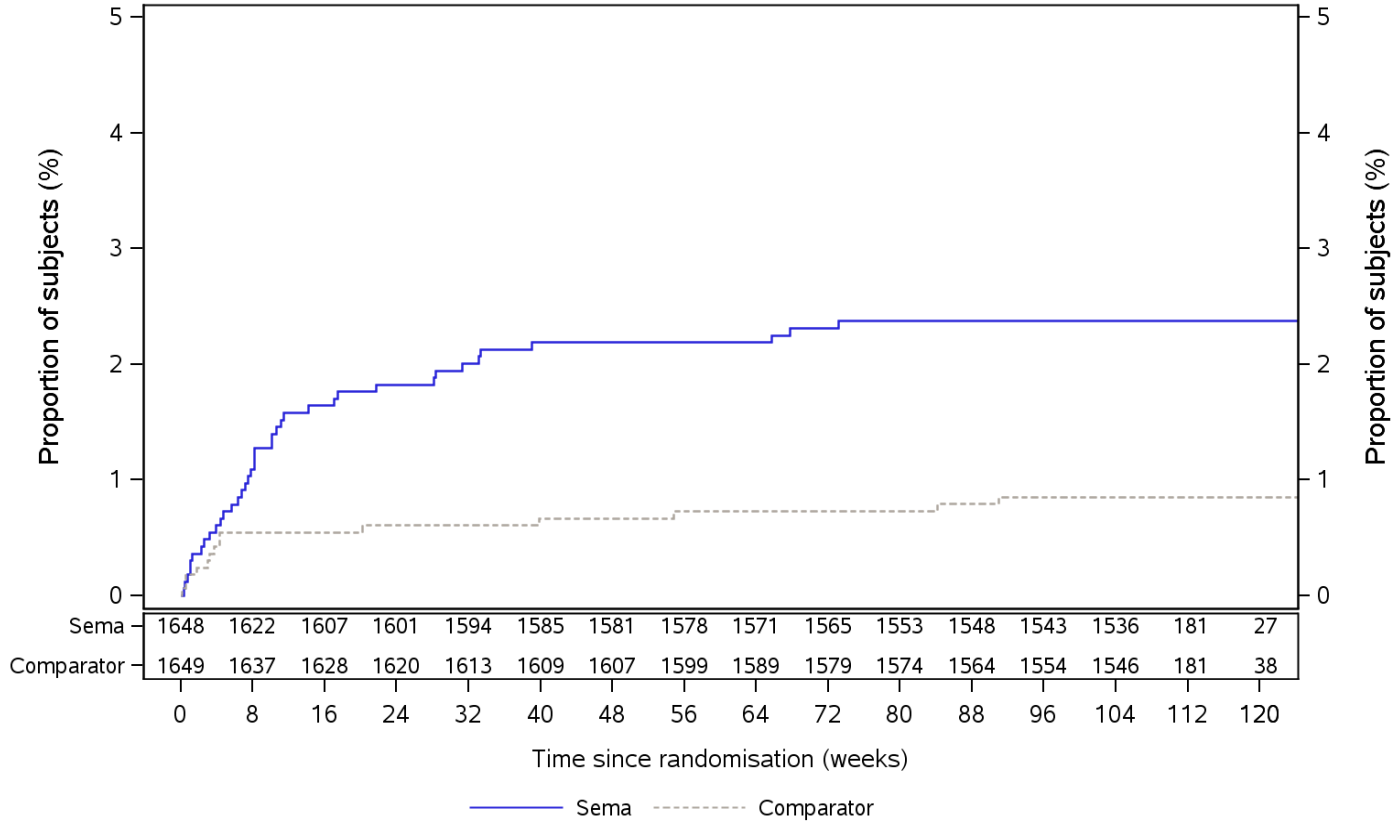
62 Mild adverse events - preferred term "Fatigue" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:09:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_fatigue_ae_mi_s6.png

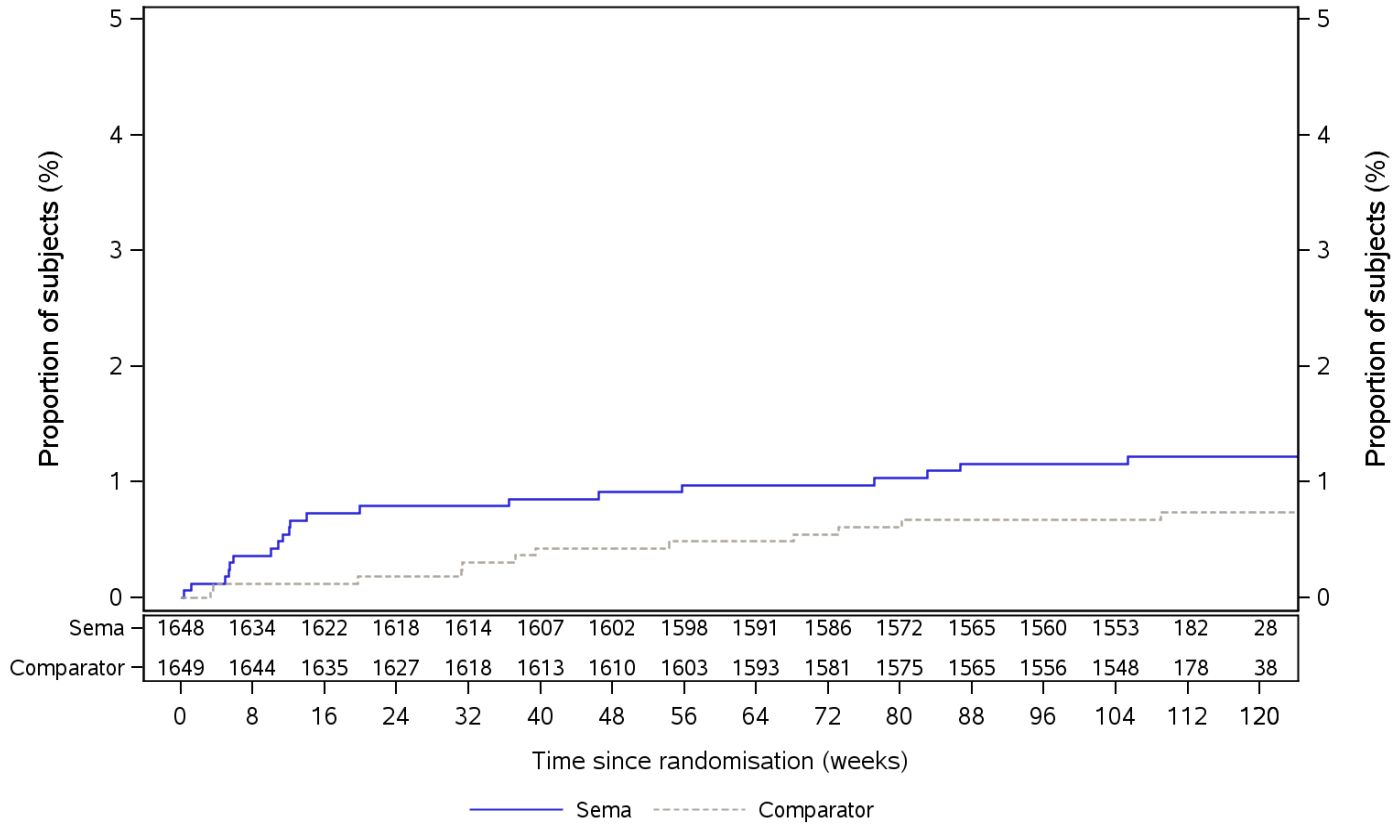
63 Mild adverse events - preferred term "Flatulence" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:09:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_flatulen_ae_mi_s6.png

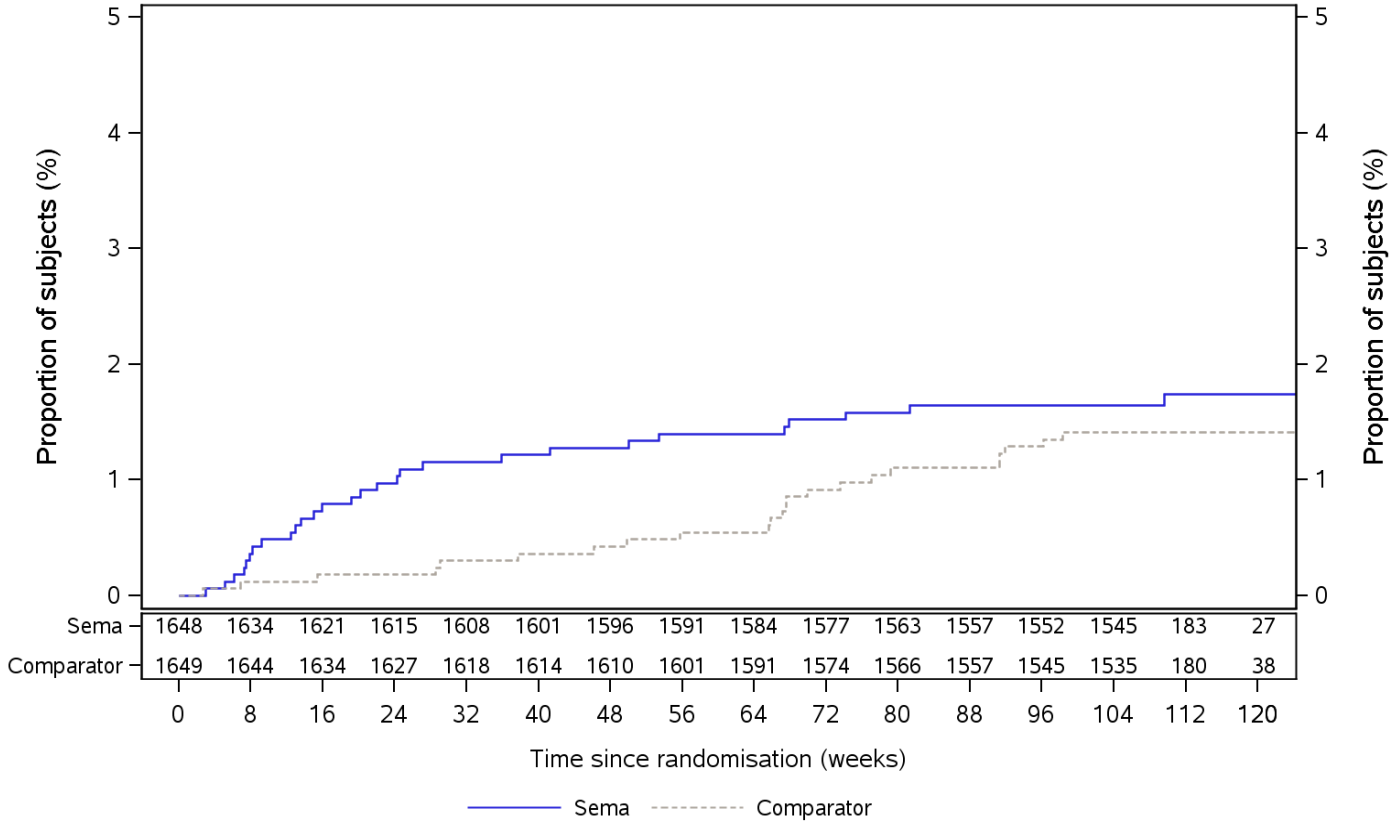
64 Mild adverse events - preferred term "Gastritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:09:54 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gastriti_ae_mi_s6.png

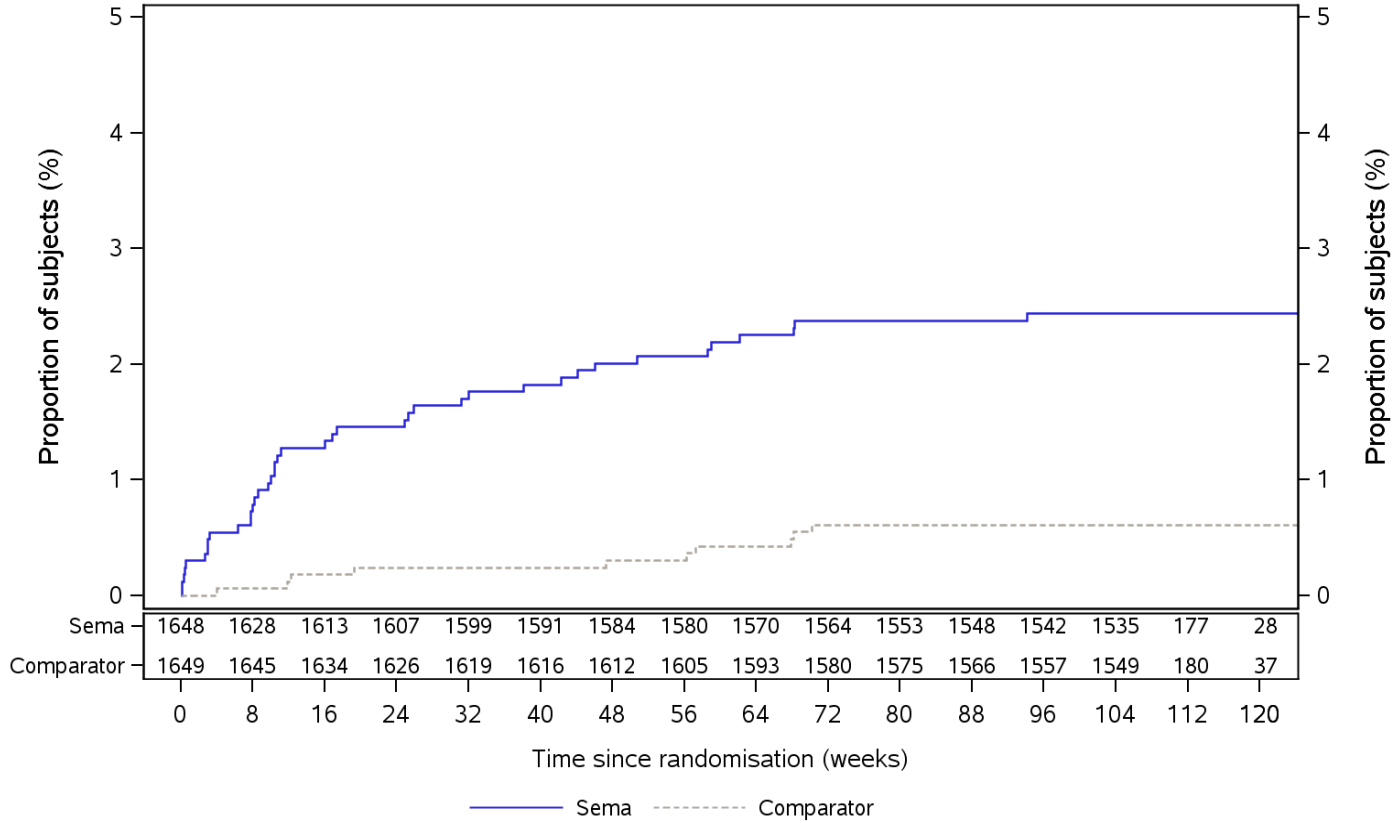
65 Mild adverse events - preferred term "Gastroenteritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:10:14 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gastroen_ae_mi_s6.png

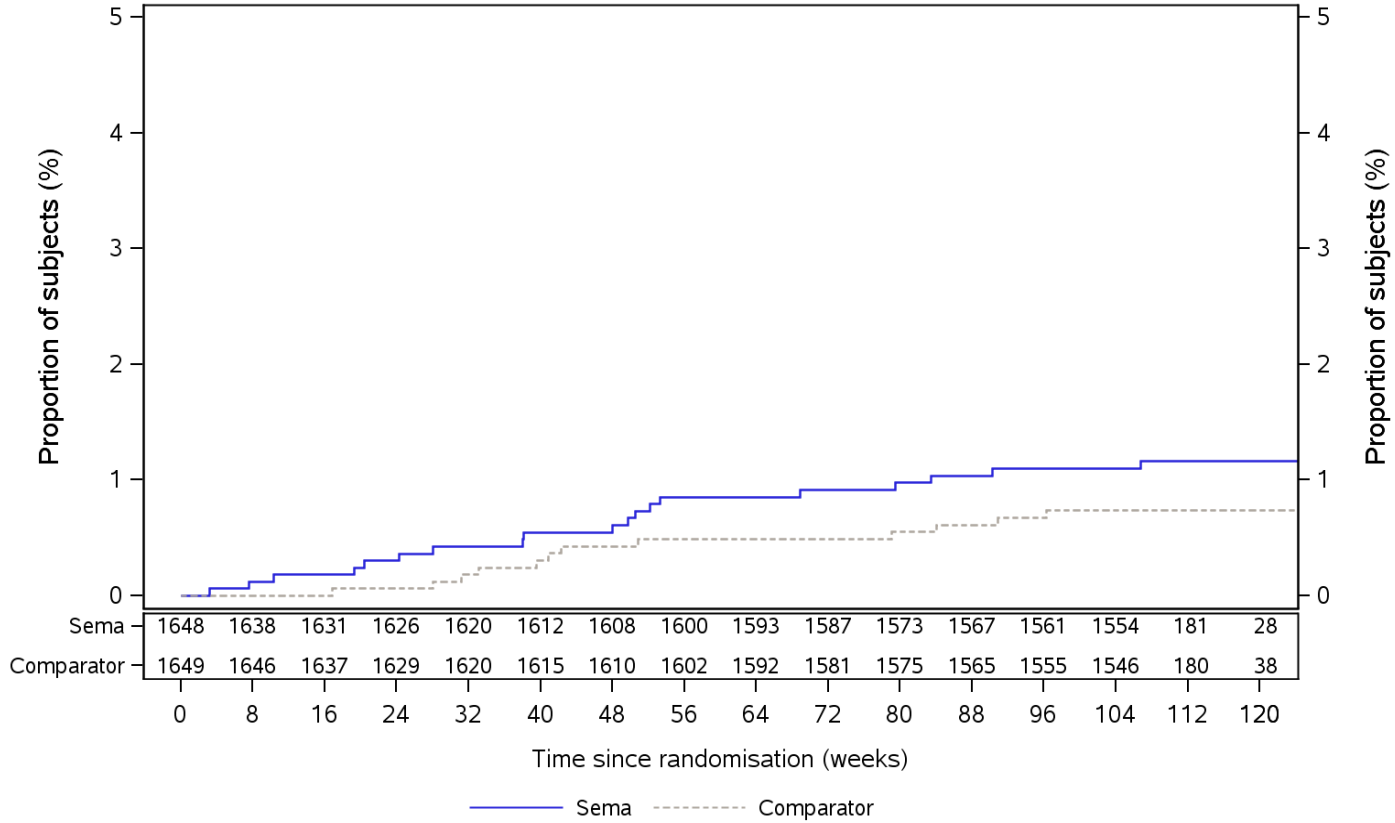
66 Mild adverse events - preferred term "Gastrooesophageal reflux disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:10:34 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gasrefdis_ae_mi_s6.png

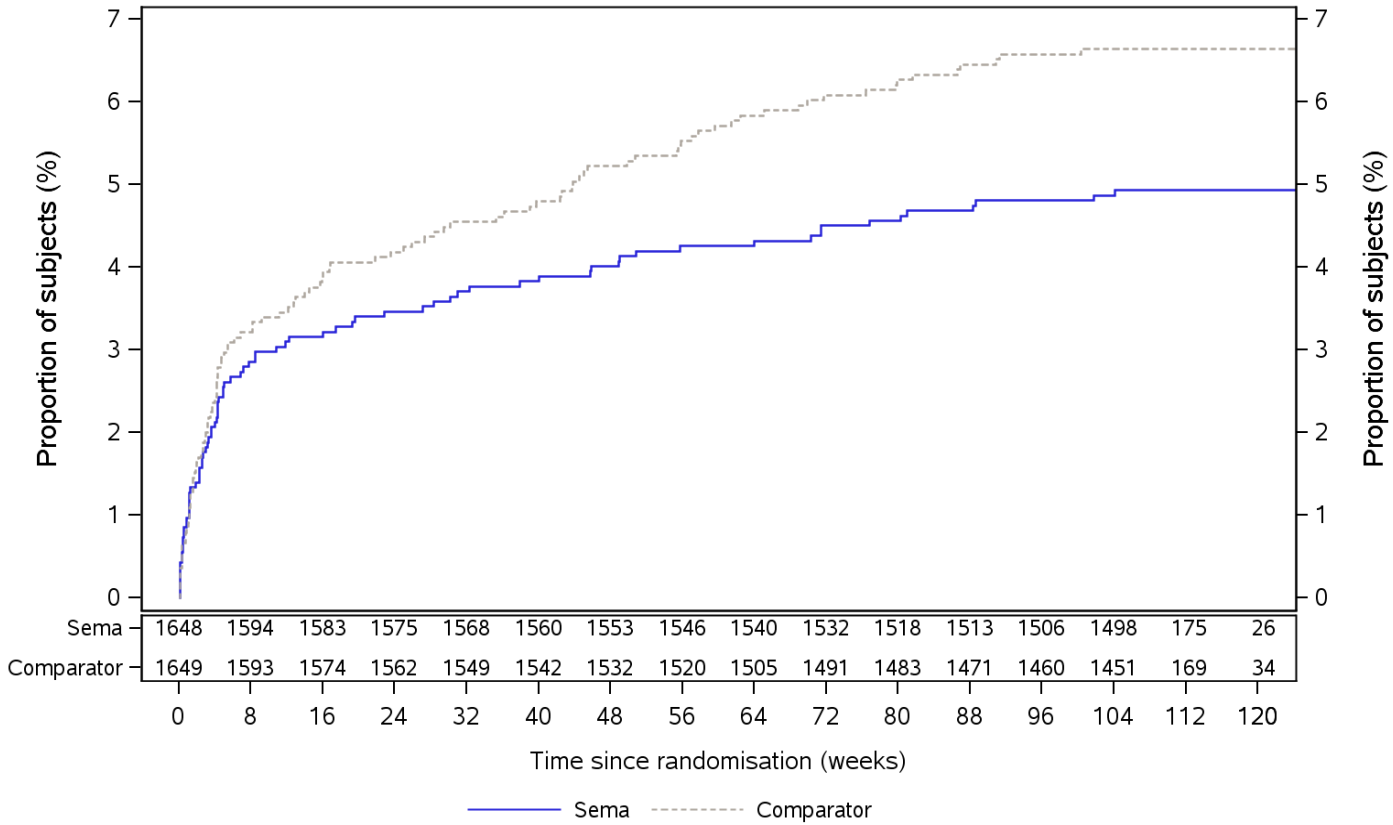
67 Mild adverse events - preferred term "Haemorrhoids" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:10:53 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_haemorrh_ae_mi_s6.png

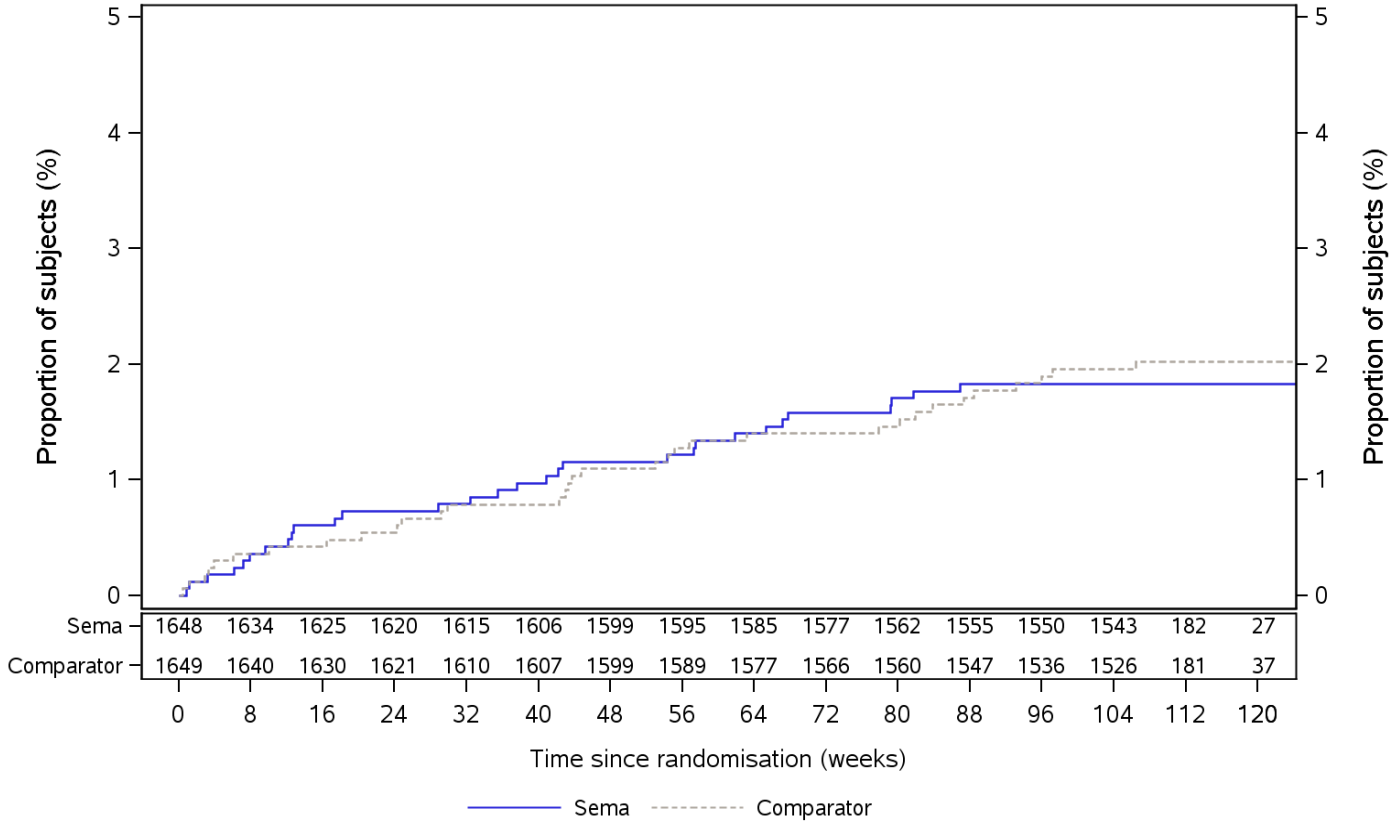
68 Mild adverse events - preferred term "Headache" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:11:13 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_headache_ae_mi_s6.png

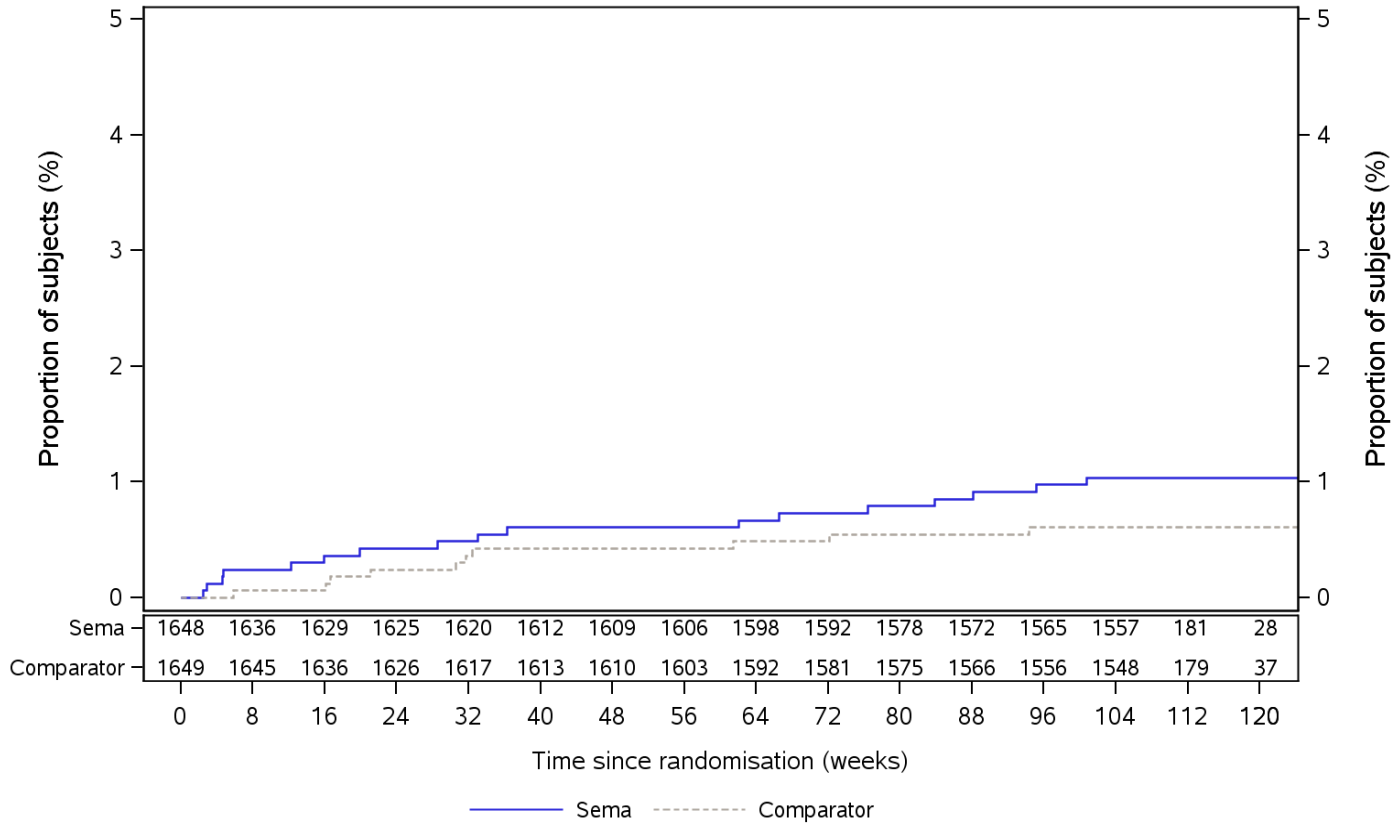
69 Mild adverse events - preferred term "Hepatic steatosis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:11:32 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hepastea_ae_mi_s6.png

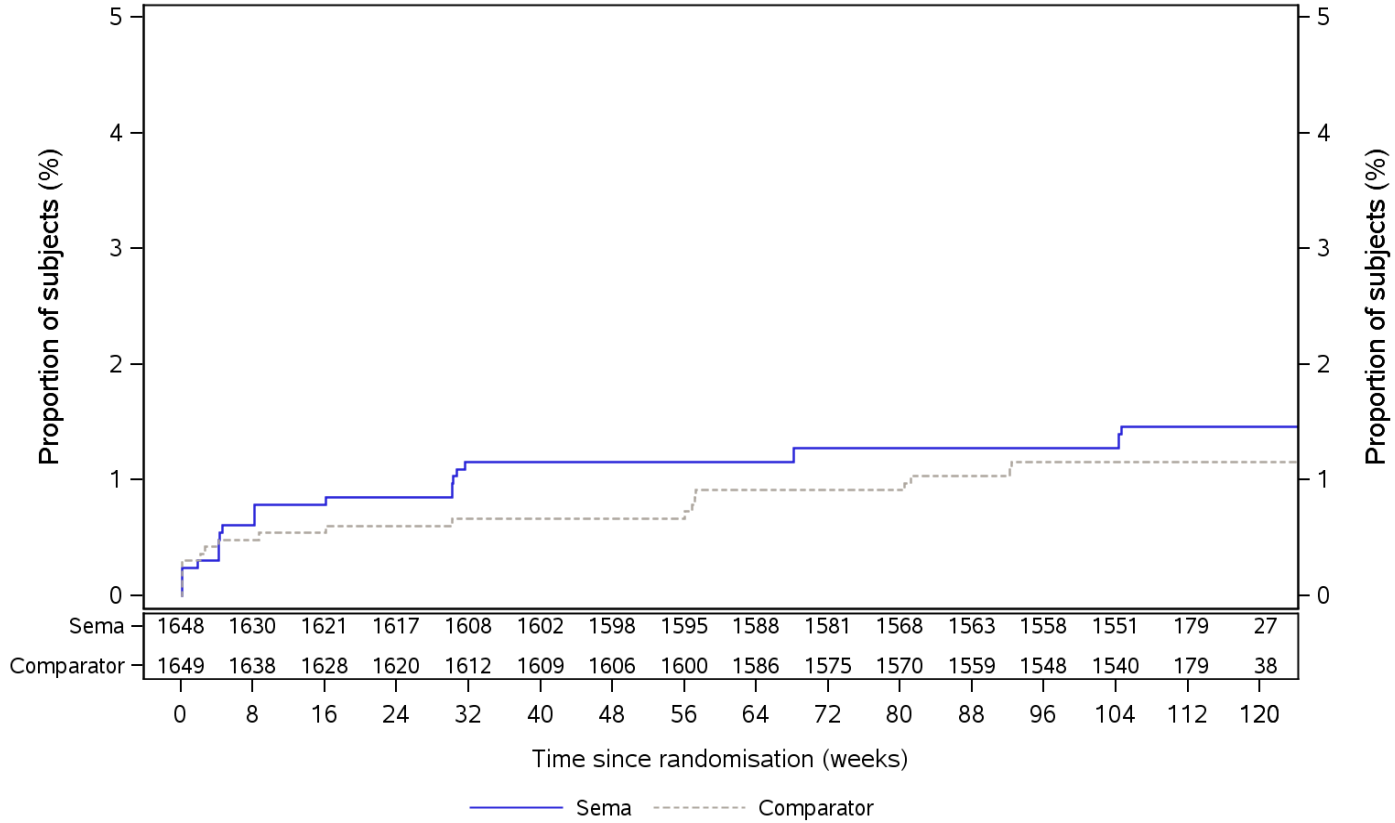
70 Mild adverse events - preferred term "Herpes zoster" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:11:52 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_herpzost_ae_mi_s6.png

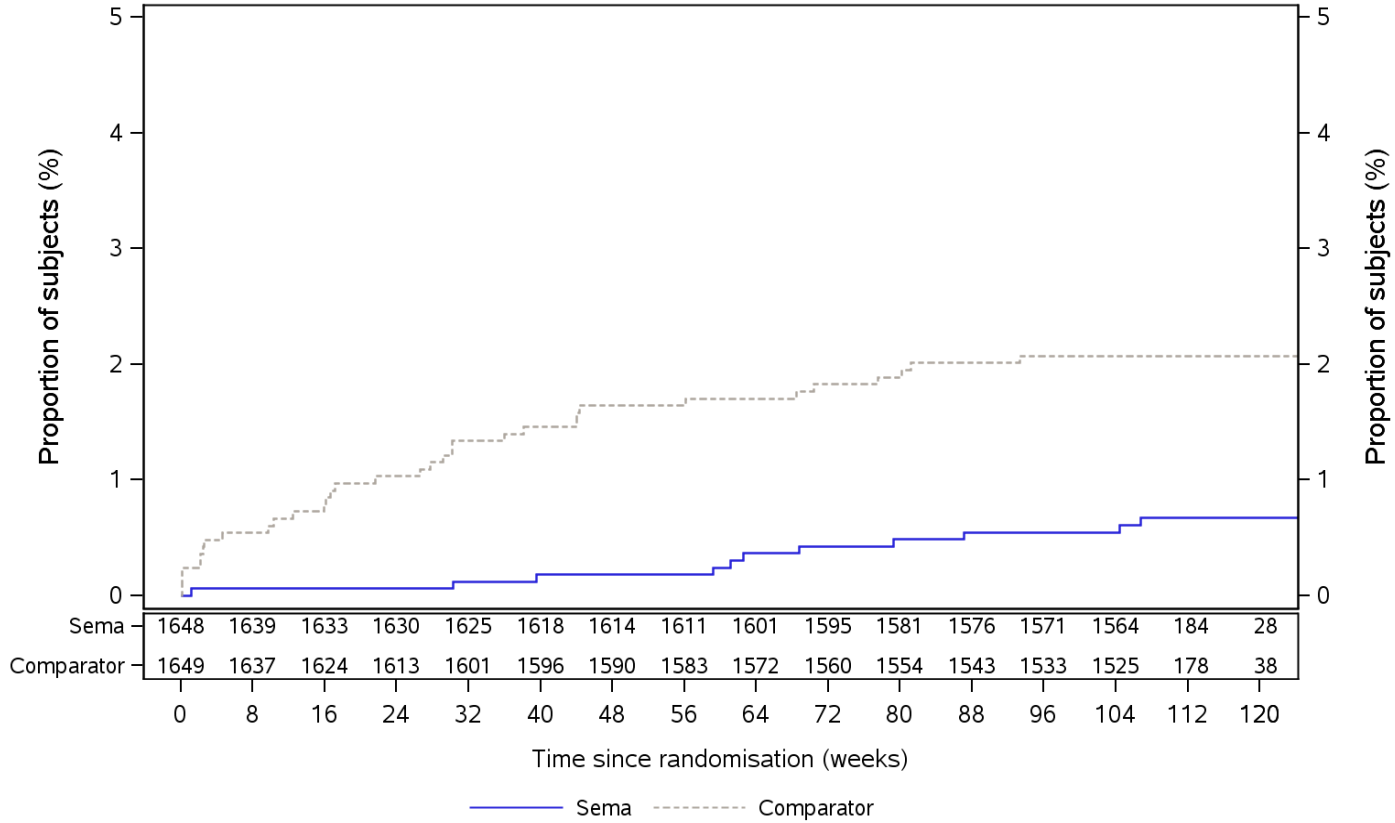
71 Mild adverse events - preferred term "Hypercalcaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:12:11 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypercal_ae_mi_s6.png

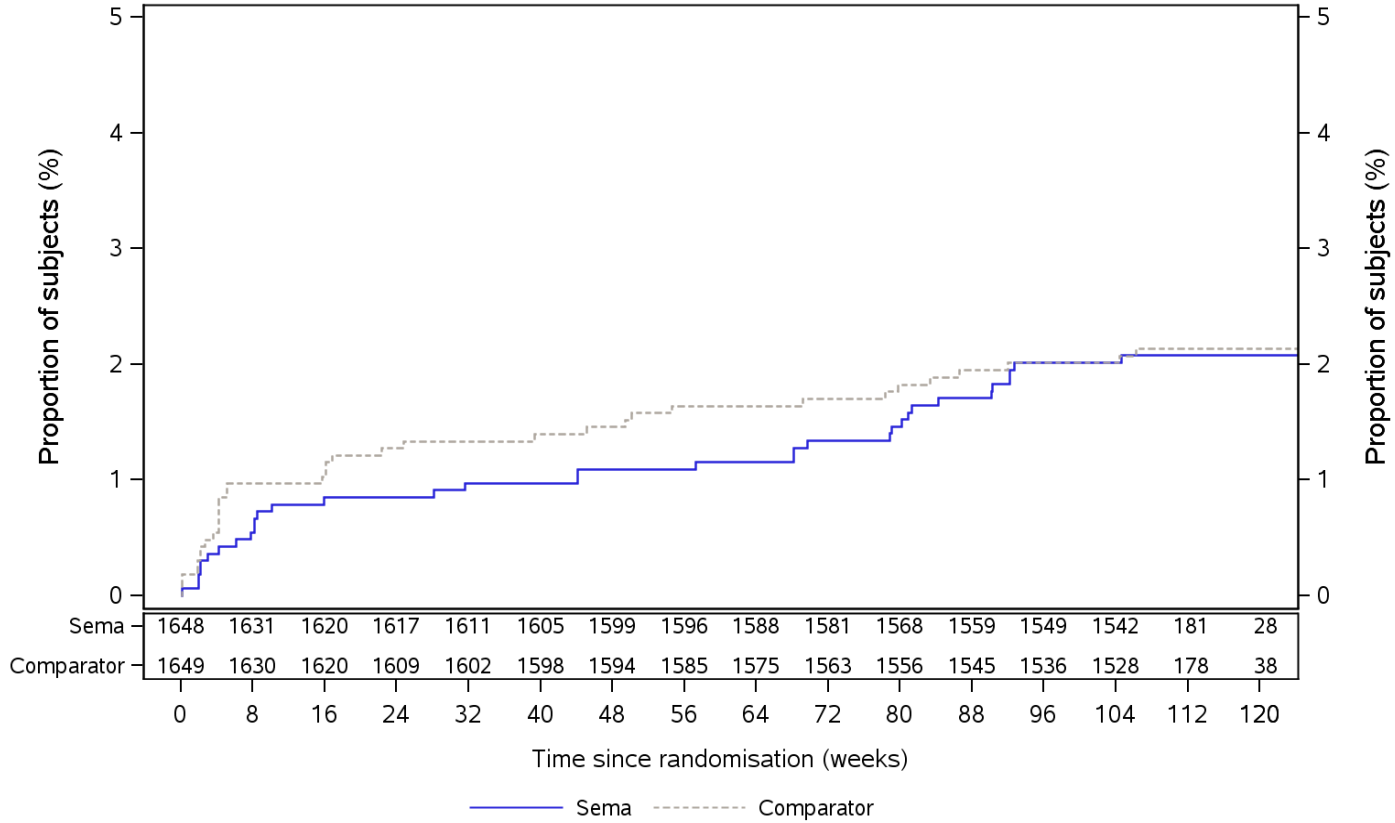
72 Mild adverse events - preferred term "Hyperglycaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:12:31 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypergly_ae_mi_s6.png

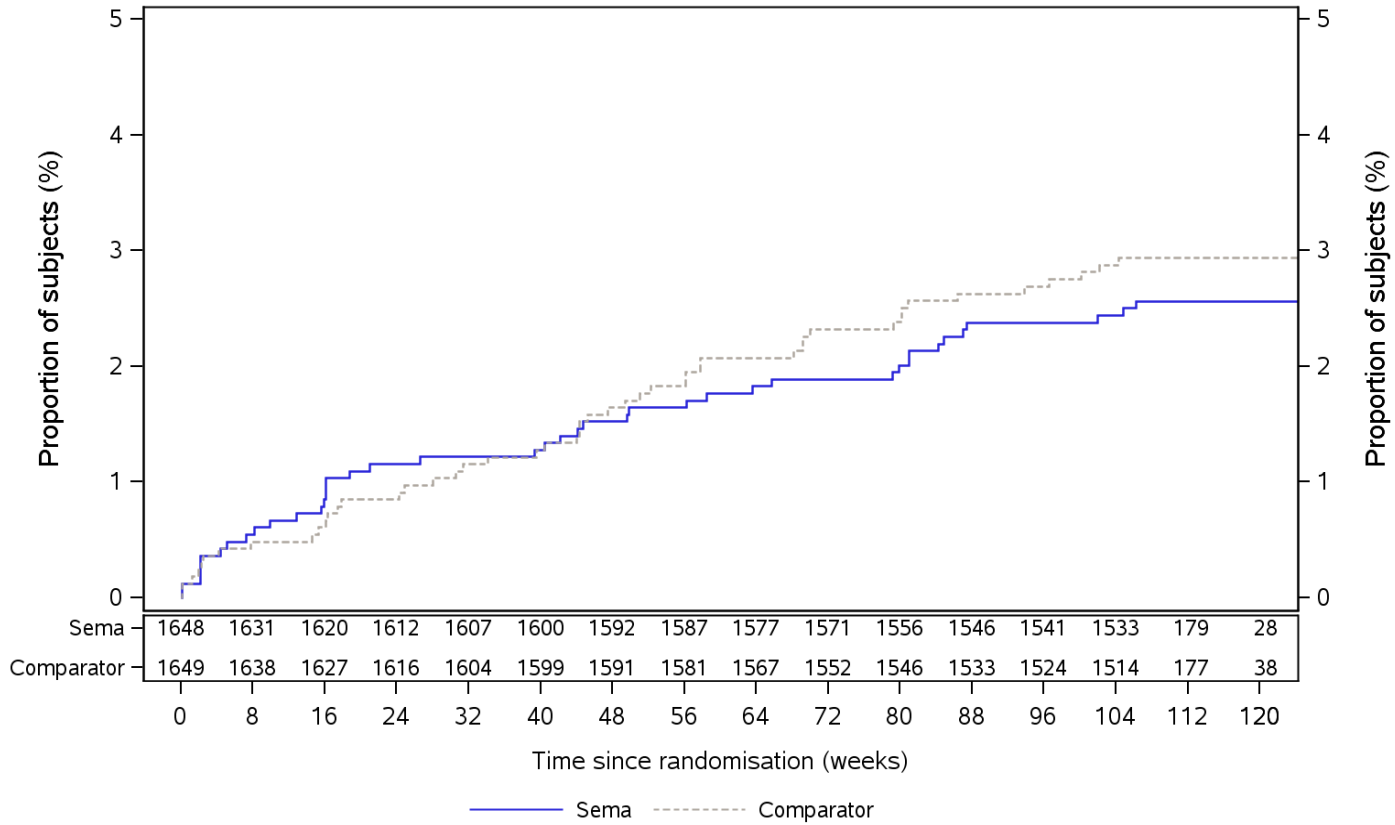
73 Mild adverse events - preferred term "Hyperkalaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:12:50 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hyperkal_ae_mi_s6.png

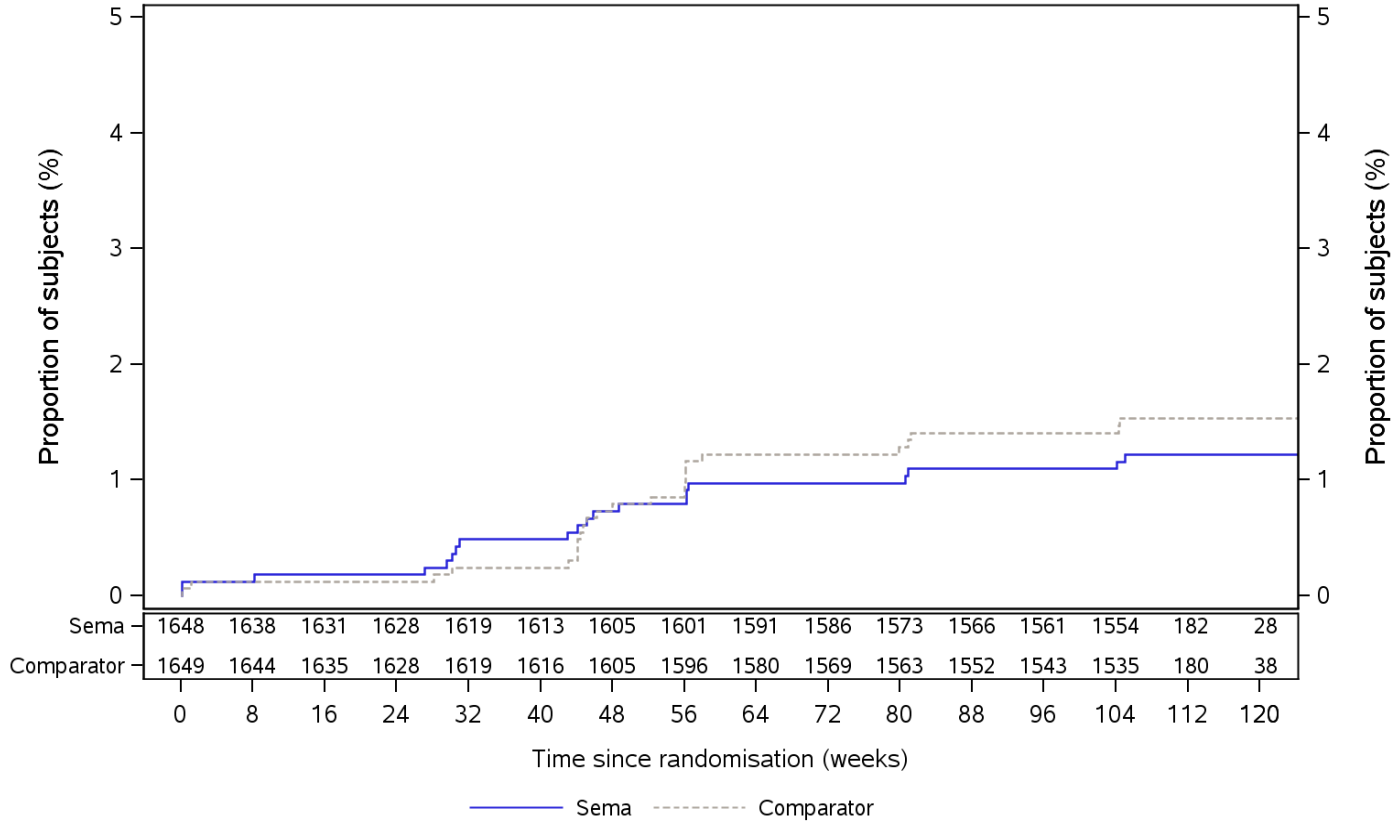
74 Mild adverse events - preferred term "Hypertension" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:13:09 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hyperten_ae_mi_s6.png

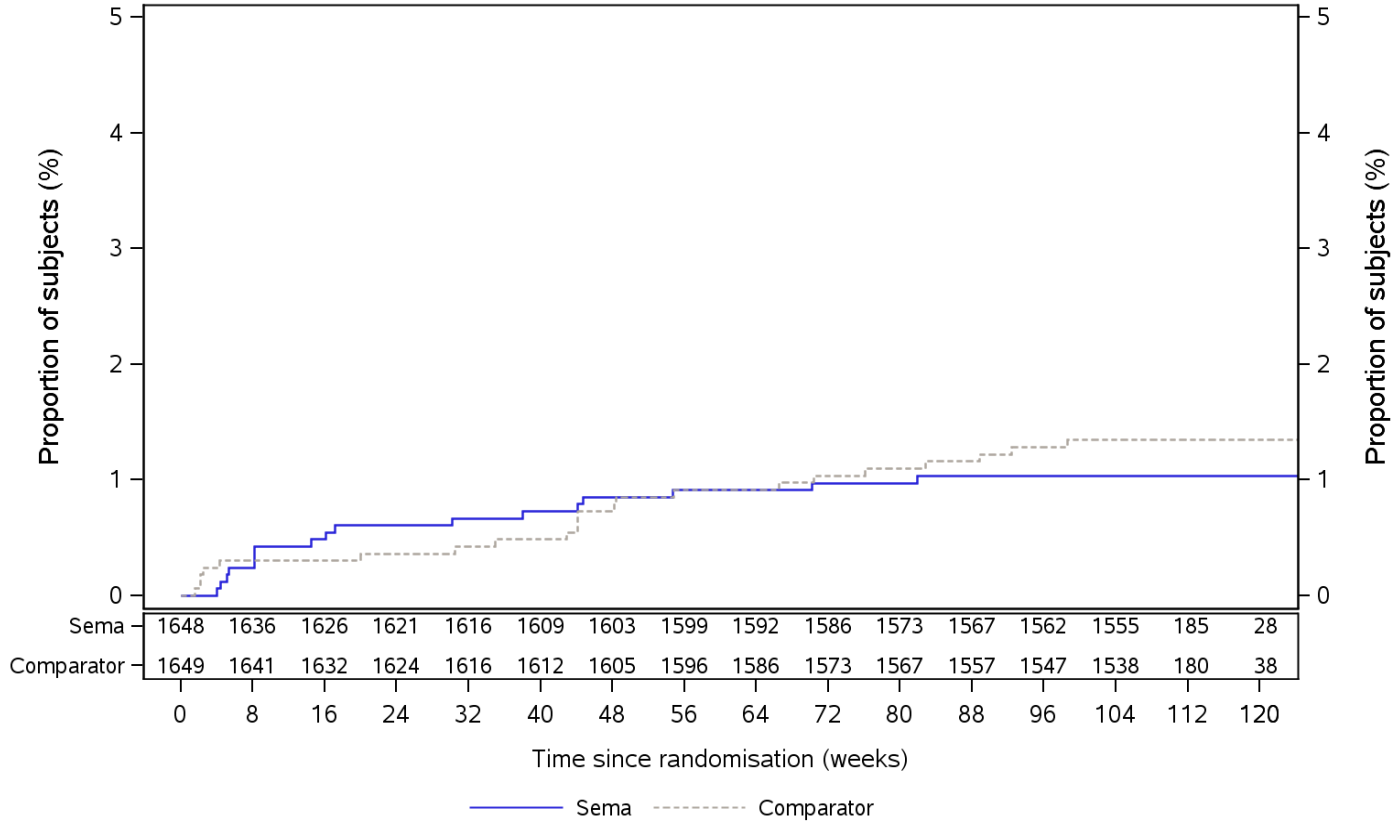
75 Mild adverse events - preferred term "Hypertriglyceridaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:13:29 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypertri_ae_mi_s6.png

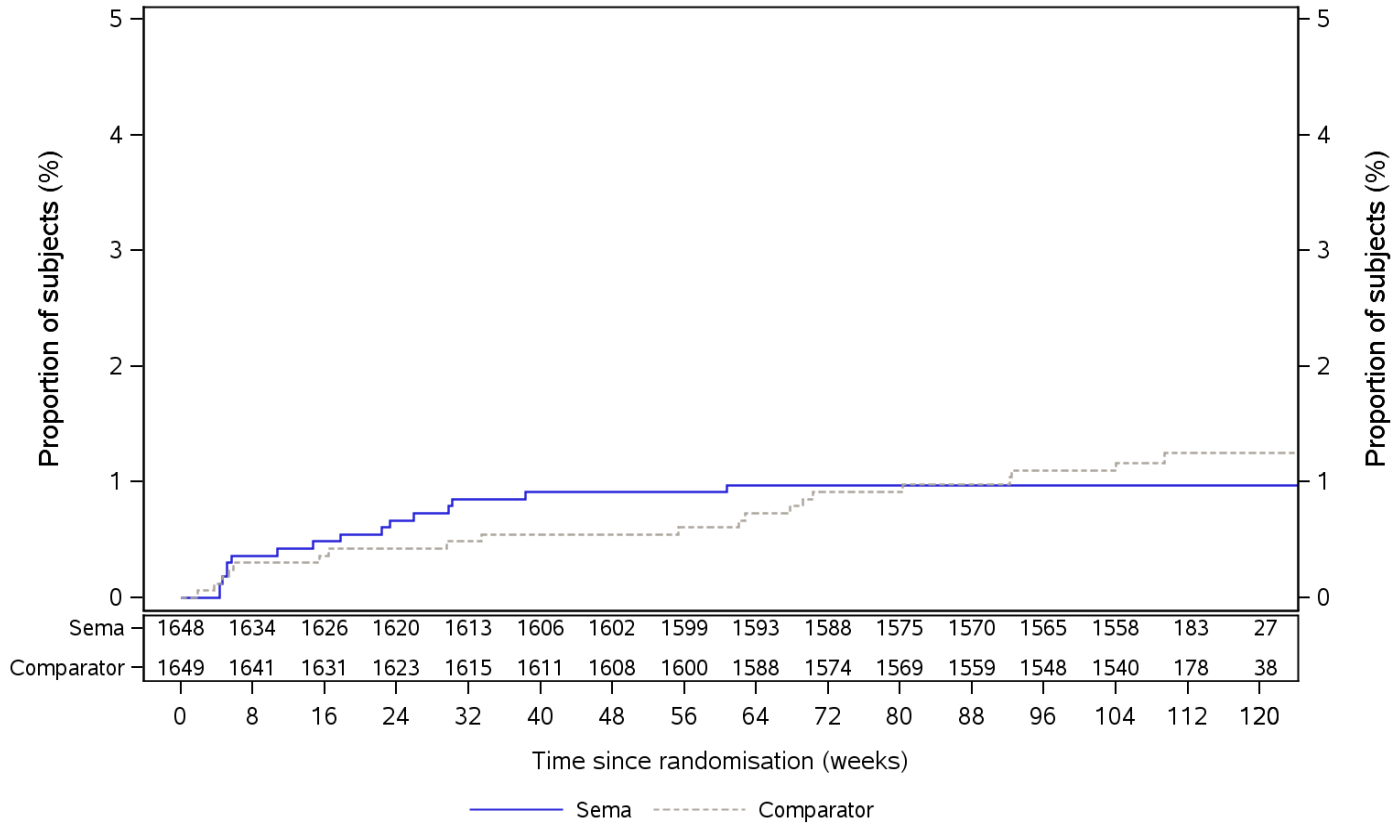
76 Mild adverse events - preferred term "Hypokalaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:13:48 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypokala_ae_mi_s6.png

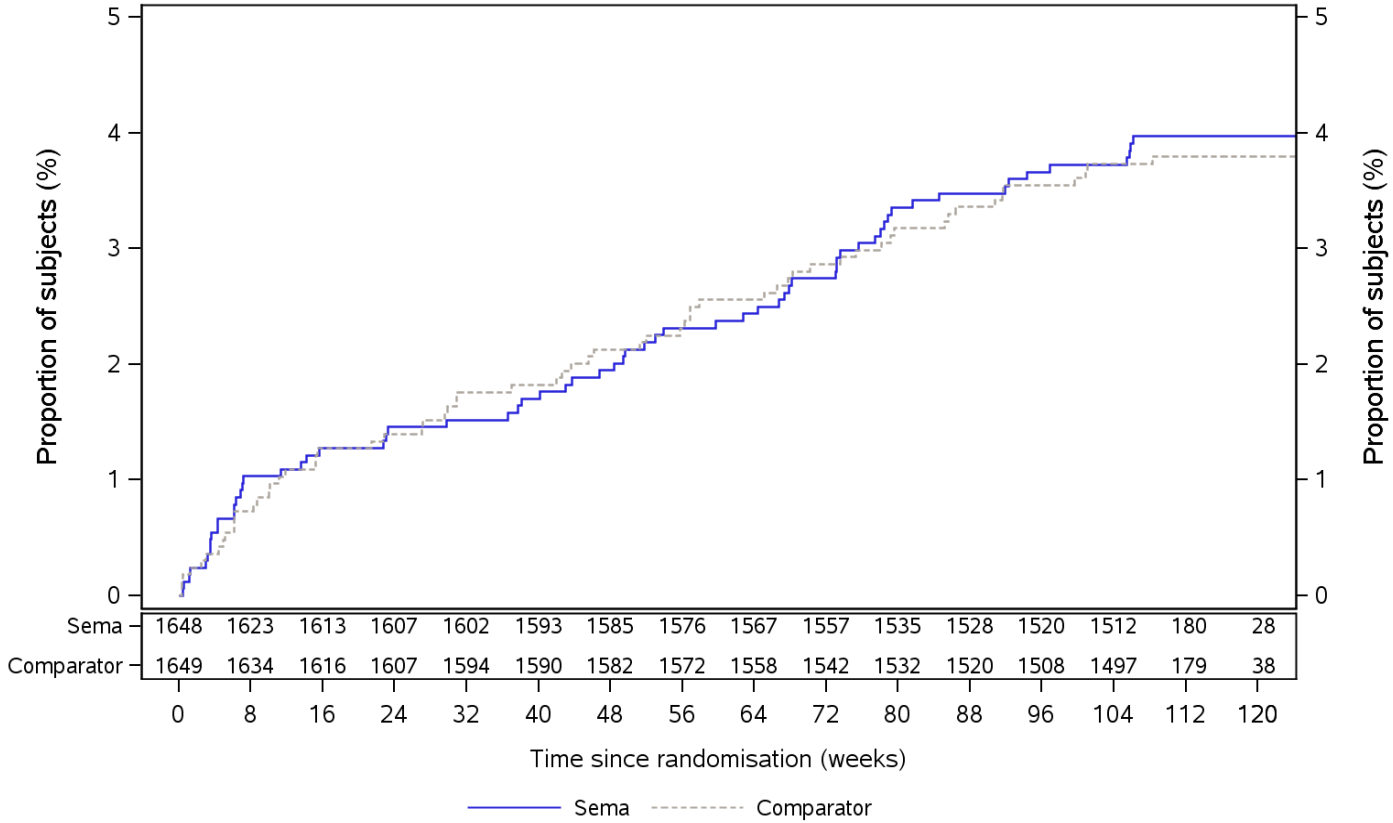
77 Mild adverse events - preferred term "Hypotension" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:14:07 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypotens_ae_mi_s6.png

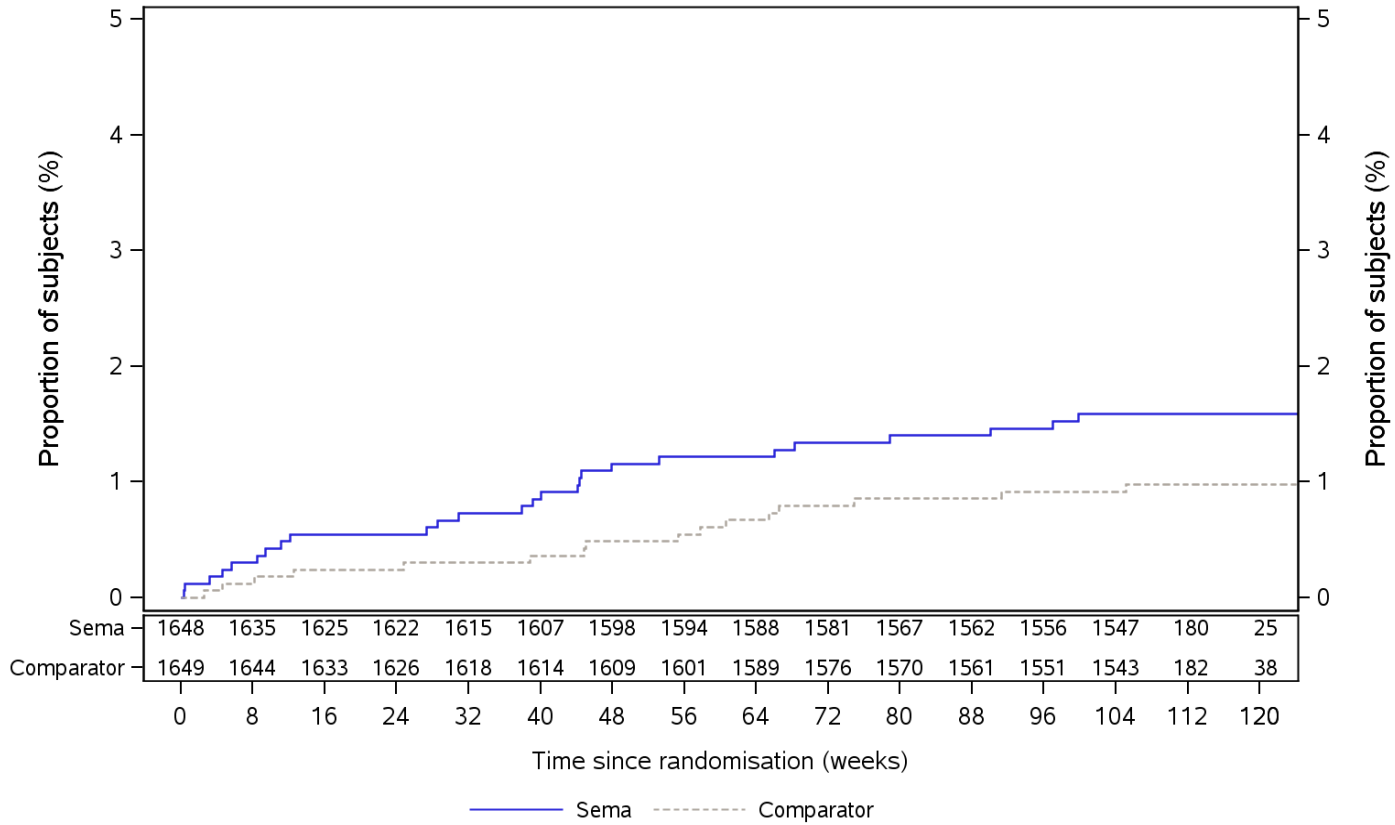
78 Mild adverse events - preferred term "Influenza" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:14:26 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_influenz_ae_mi_s6.png

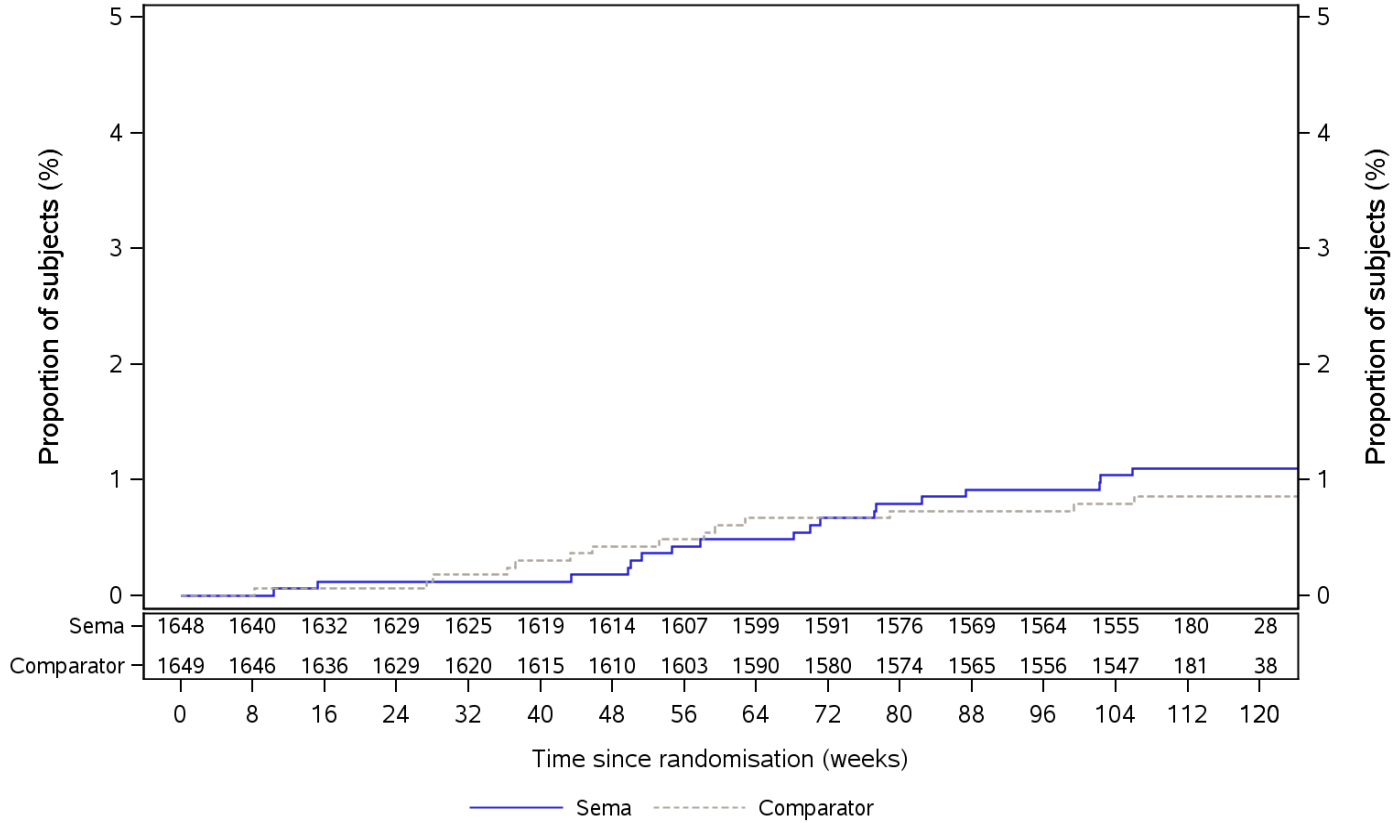
79 Mild adverse events - preferred term "Insomnia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:14:45 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_insomnia_ae_mi_s6.png

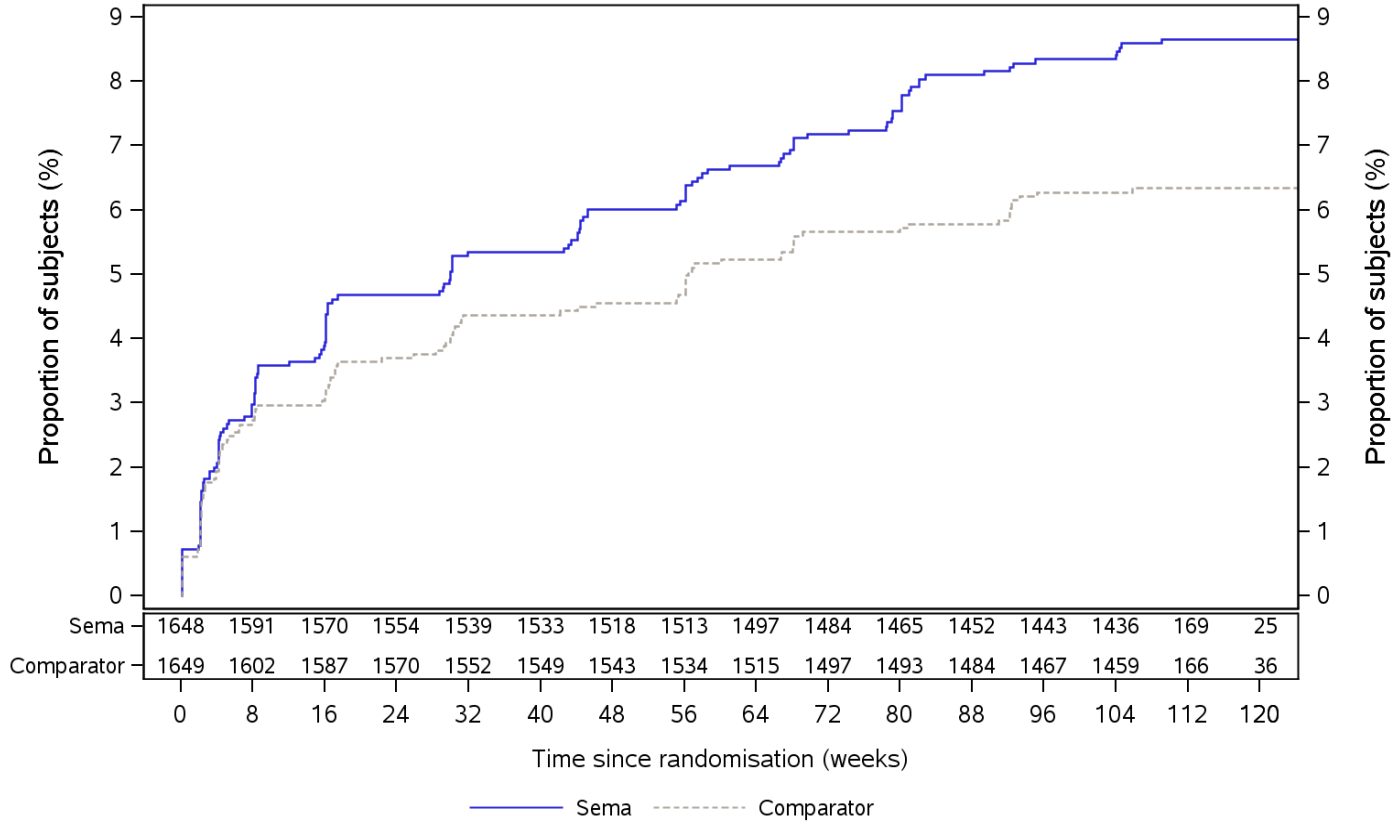
80 Mild adverse events - preferred term "Large intestine polyp" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:15:05 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_larintpol_ae_mi_s6.png

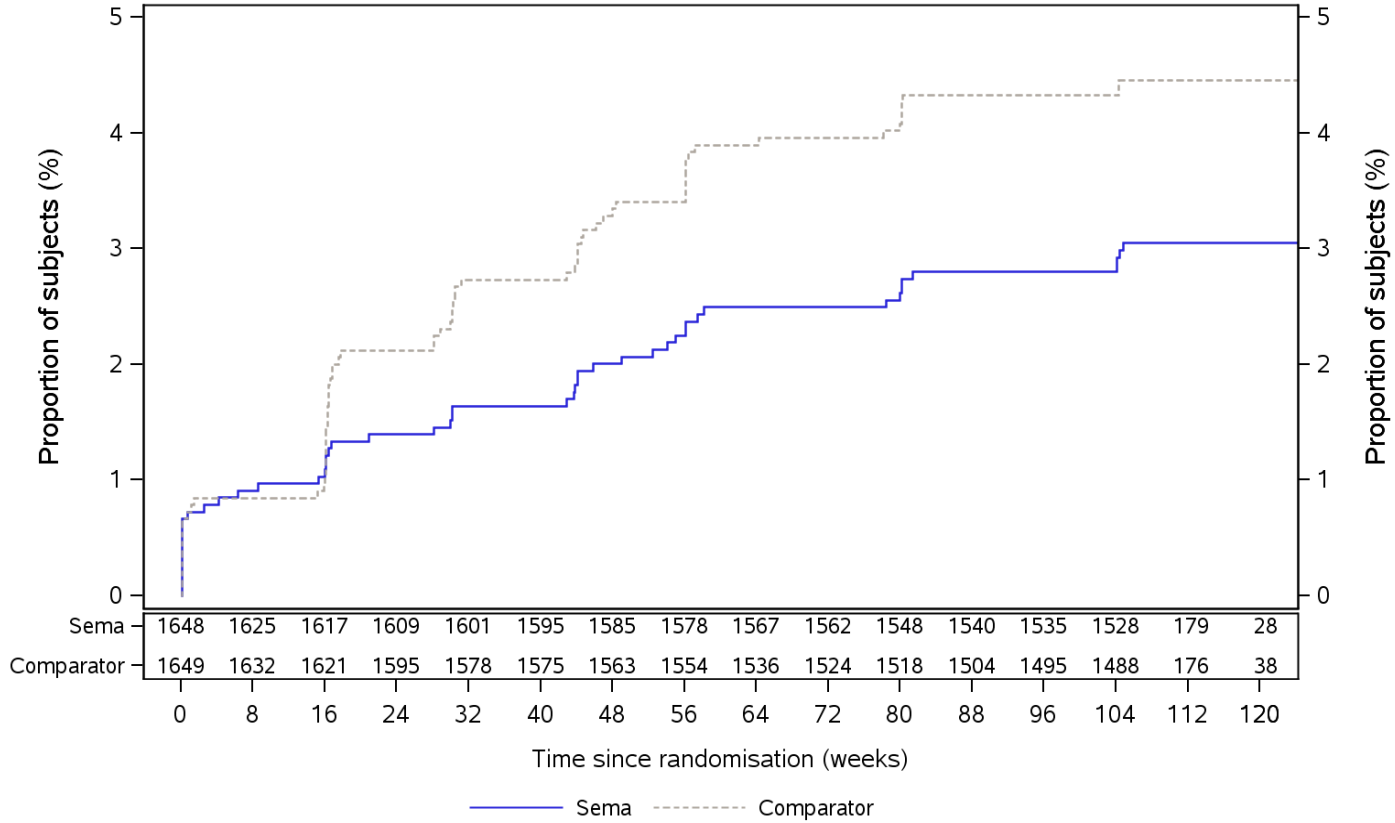
81 Mild adverse events - preferred term "Lipase increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:15:24 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_lipaincr_ae_mi_s6.png

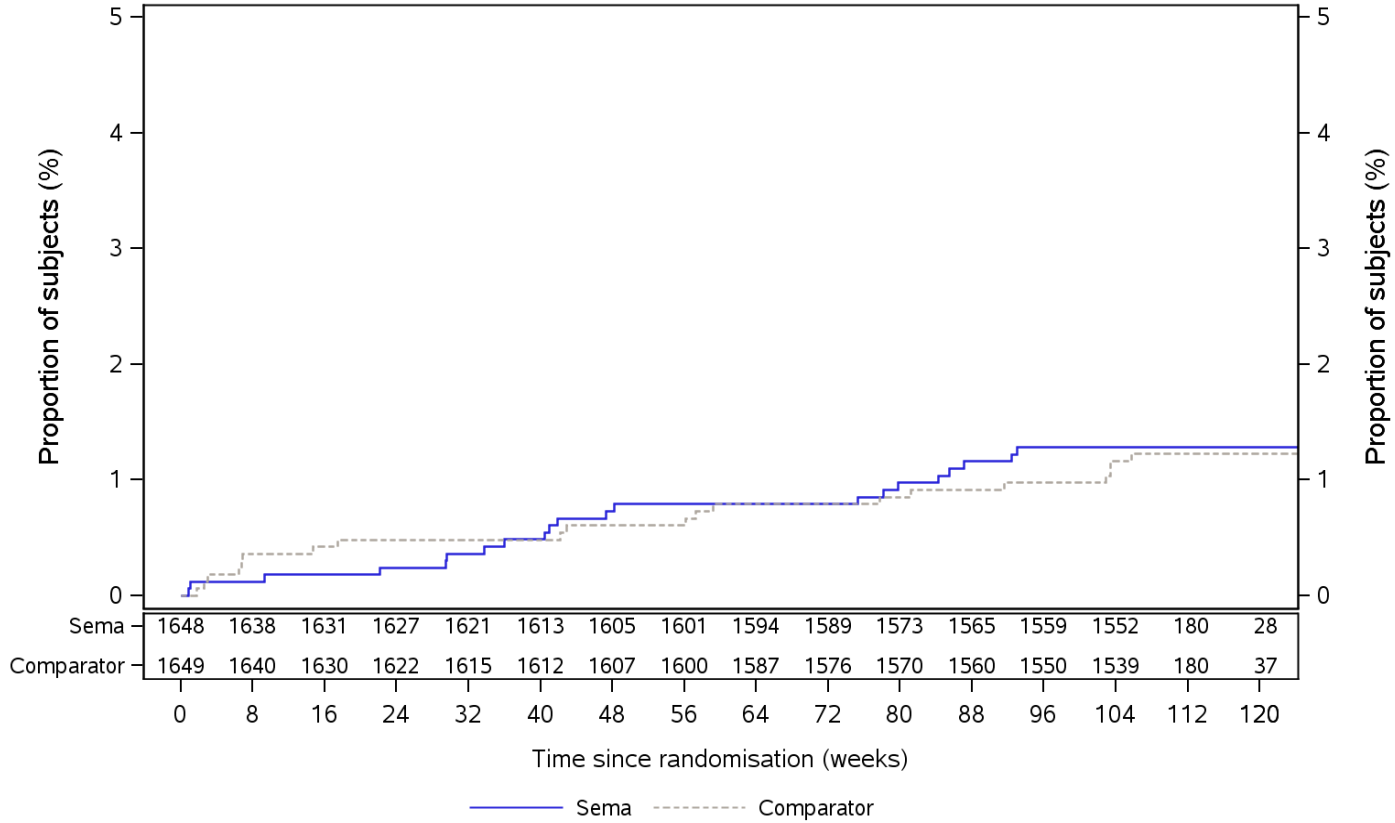
82 Mild adverse events - preferred term "Microalbuminuria" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:15:43 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_microalb_ae_mi_s6.png

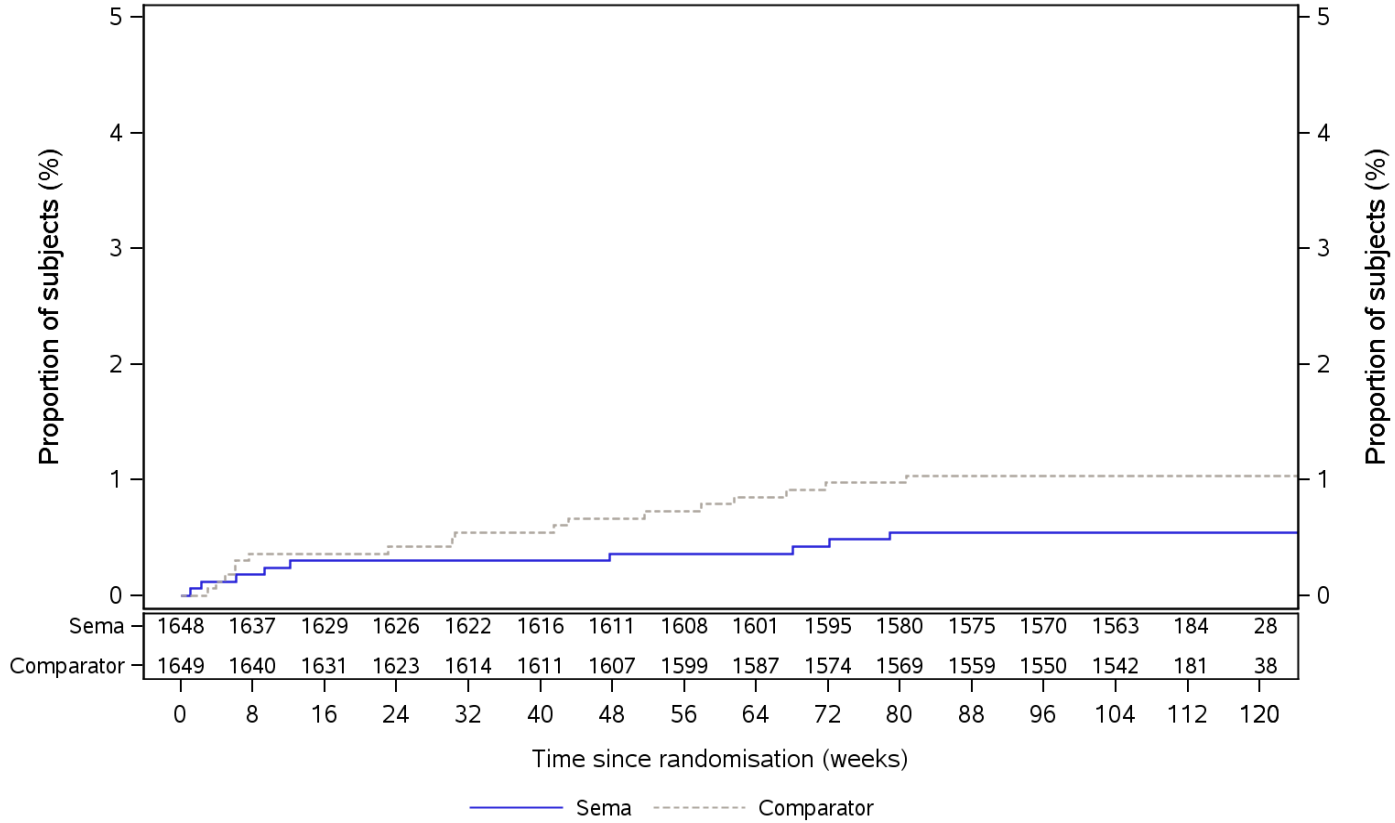
83 Mild adverse events - preferred term "Muscle spasms" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:16:02 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_muscspas_ae_mi_s6.png

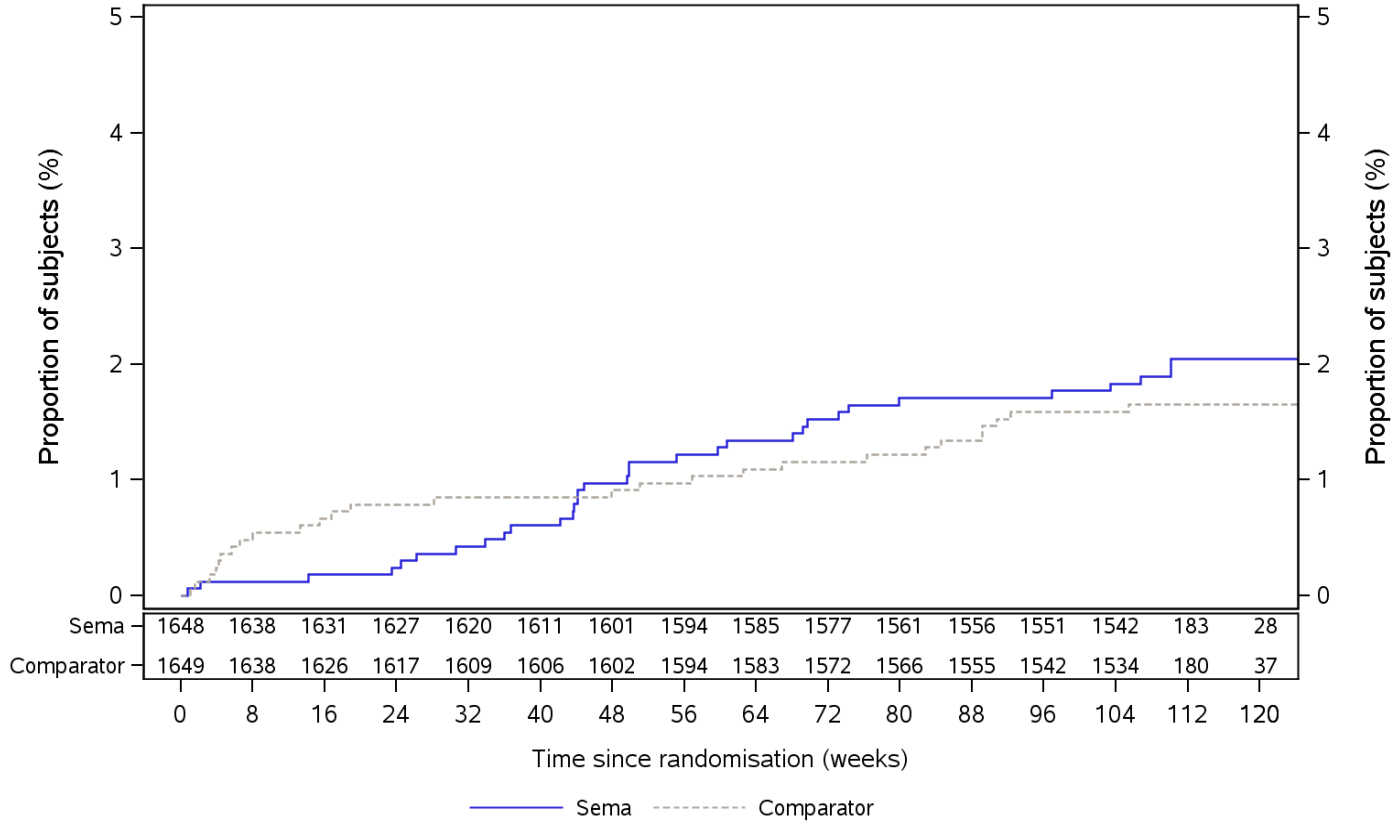
84 Mild adverse events - preferred term "Musculoskeletal chest pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:16:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_muschepai_ae_mi_s6.png

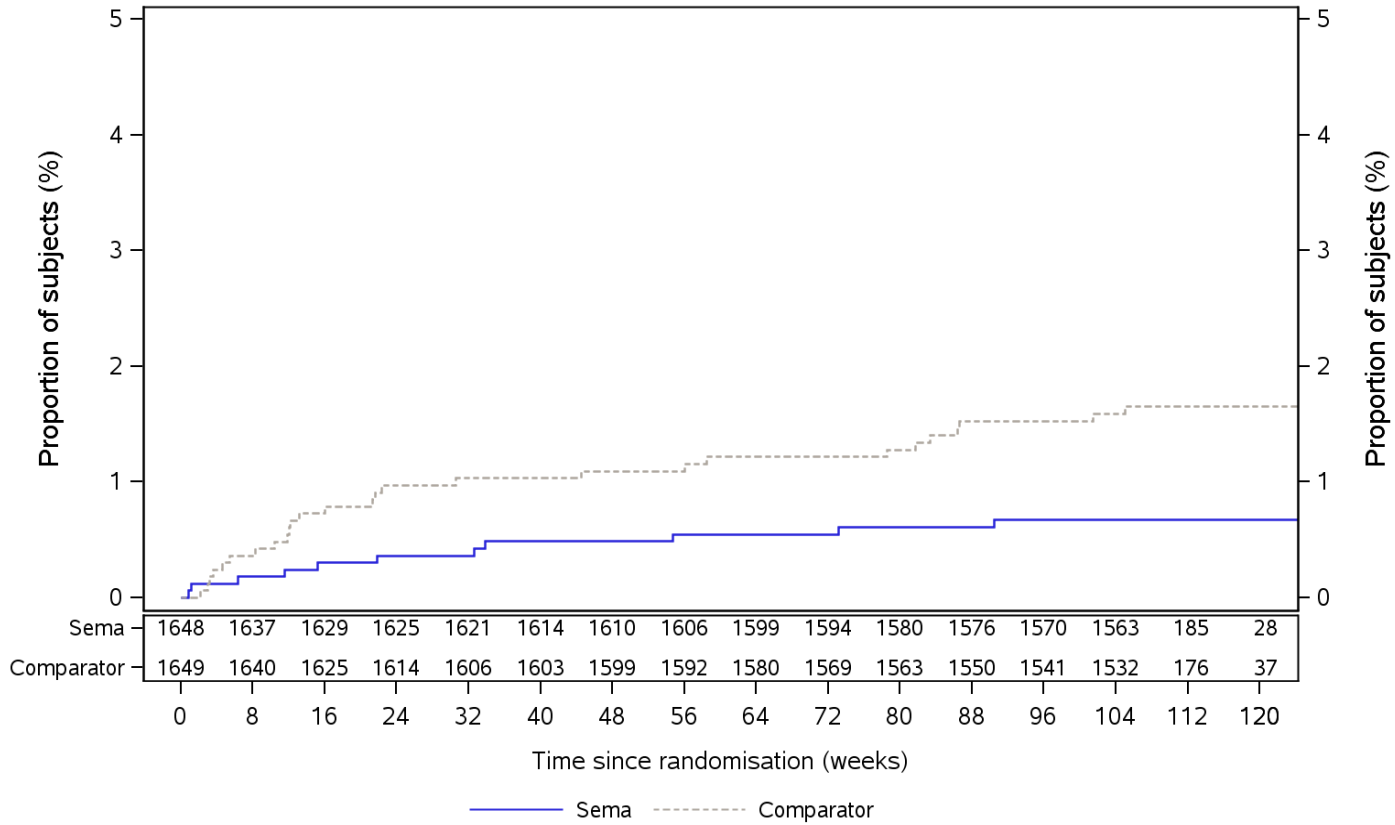
85 Mild adverse events - preferred term "Musculoskeletal pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:16:40 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_muscpain_ae_mi_s6.png

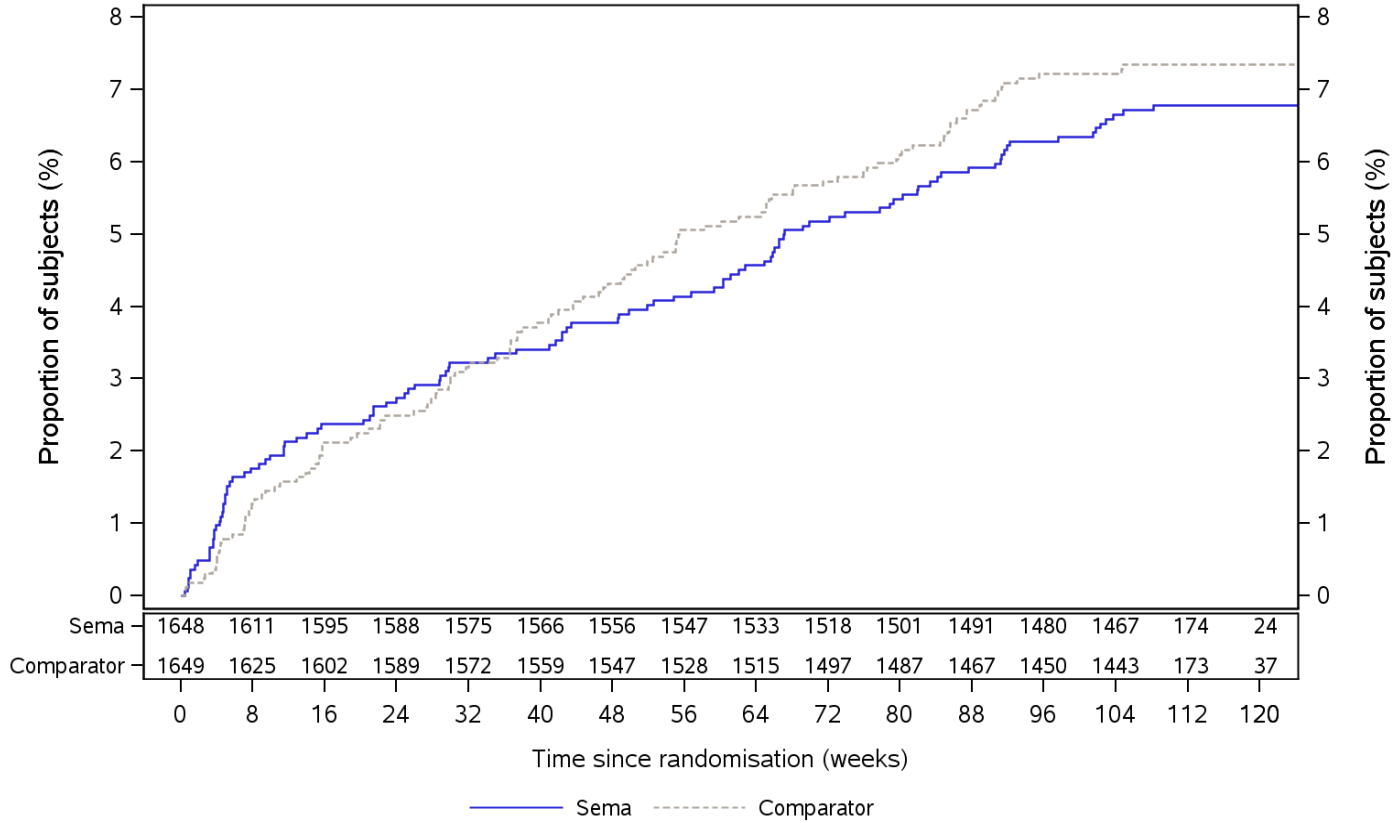
86 Mild adverse events - preferred term "Myalgia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:16:59 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_myalgia_ae_mi_s6.png

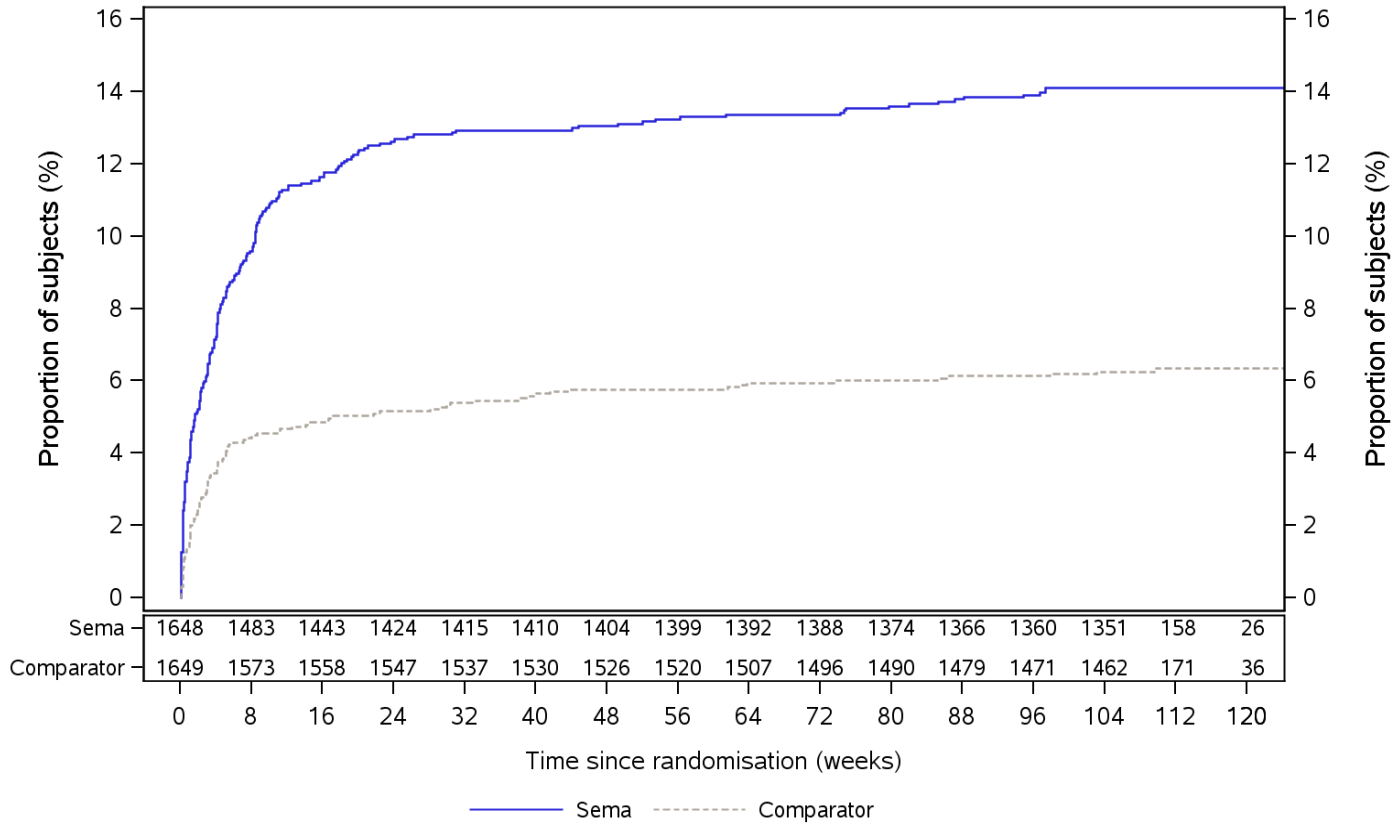
87 Mild adverse events - preferred term "Nasopharyngitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:17:17 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nasophar_ae_mi_s6.png

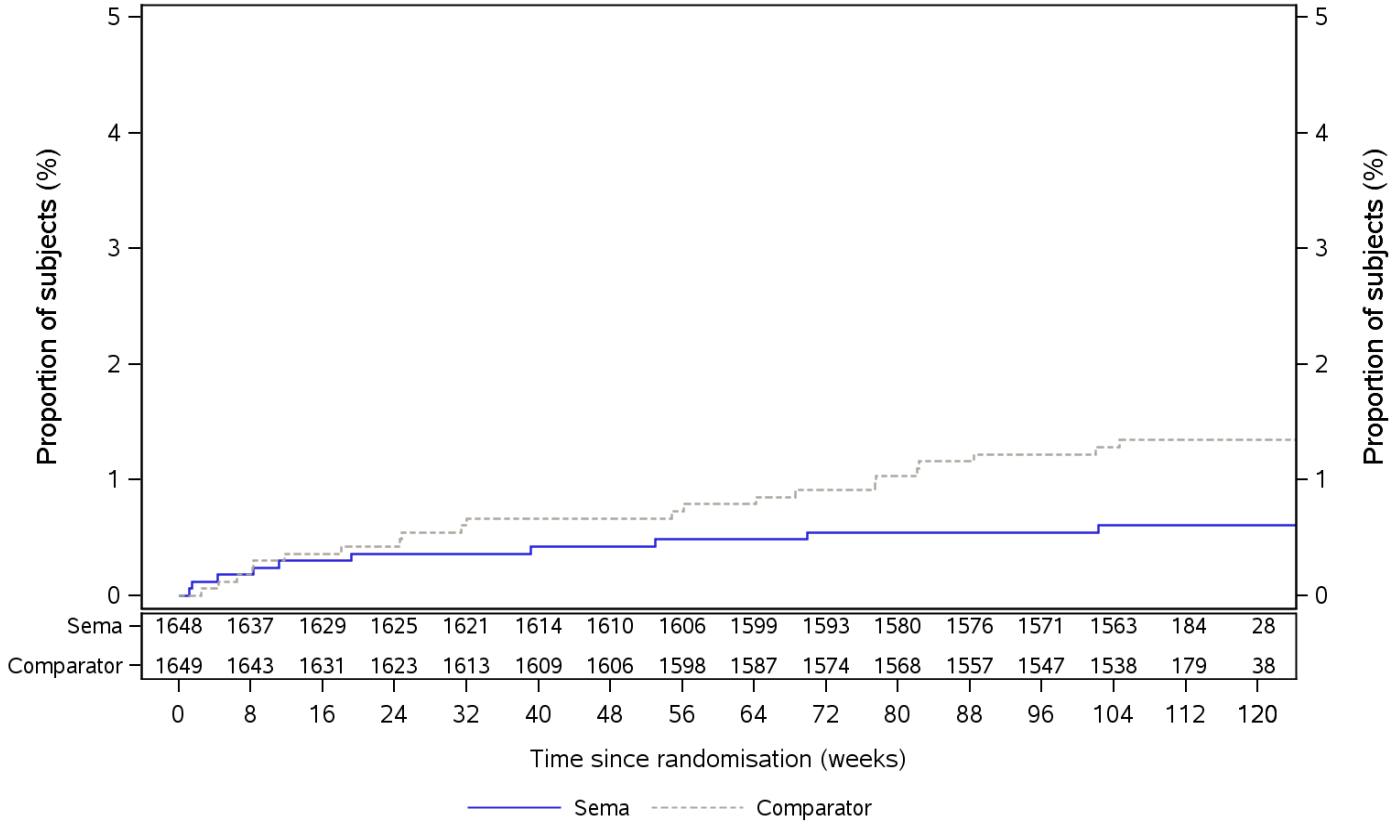
88 Mild adverse events - preferred term "Nausea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:17:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nausea_ae_mi_s6.png

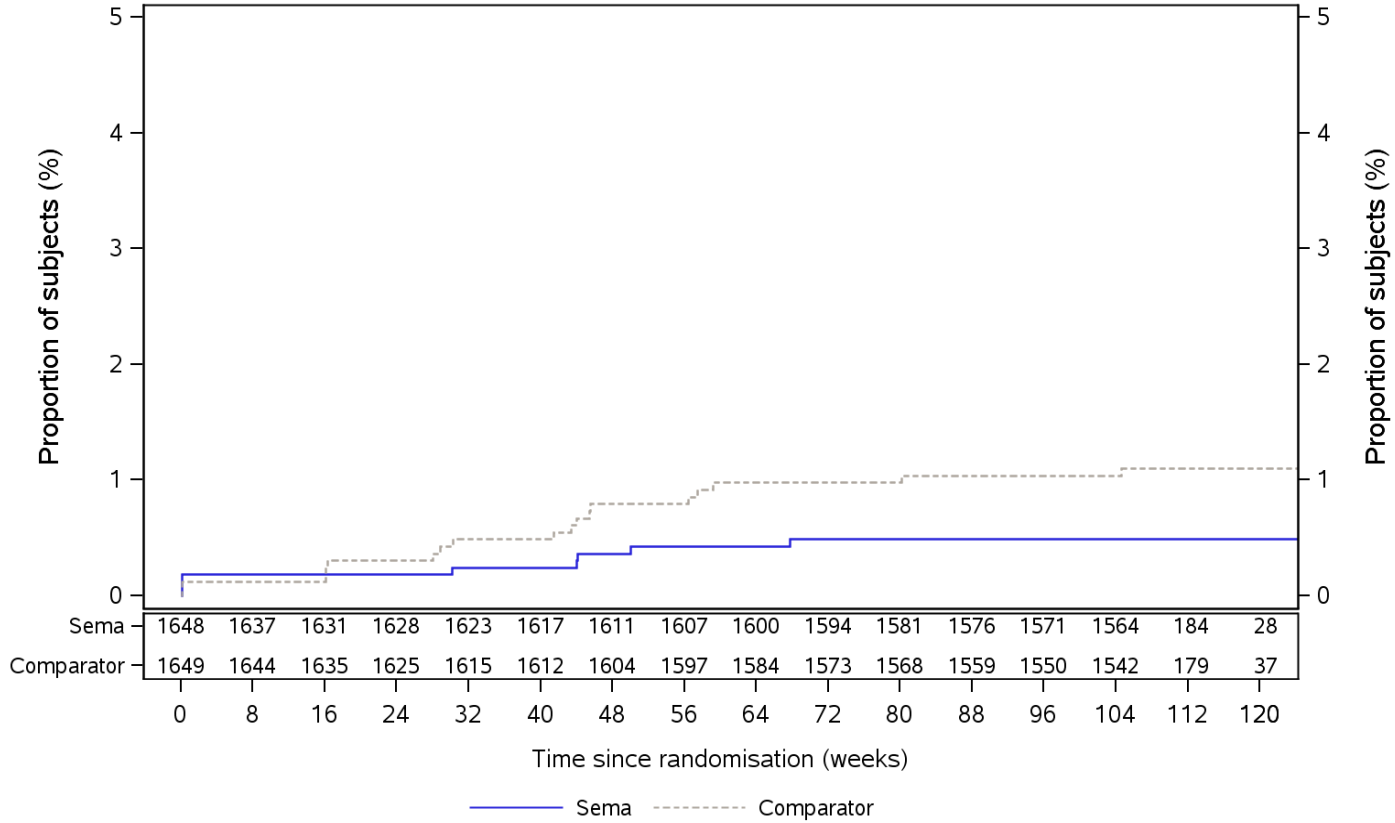
89 Mild adverse events - preferred term "Nephrolithiasis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:17:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nephroli_ae_mi_s6.png

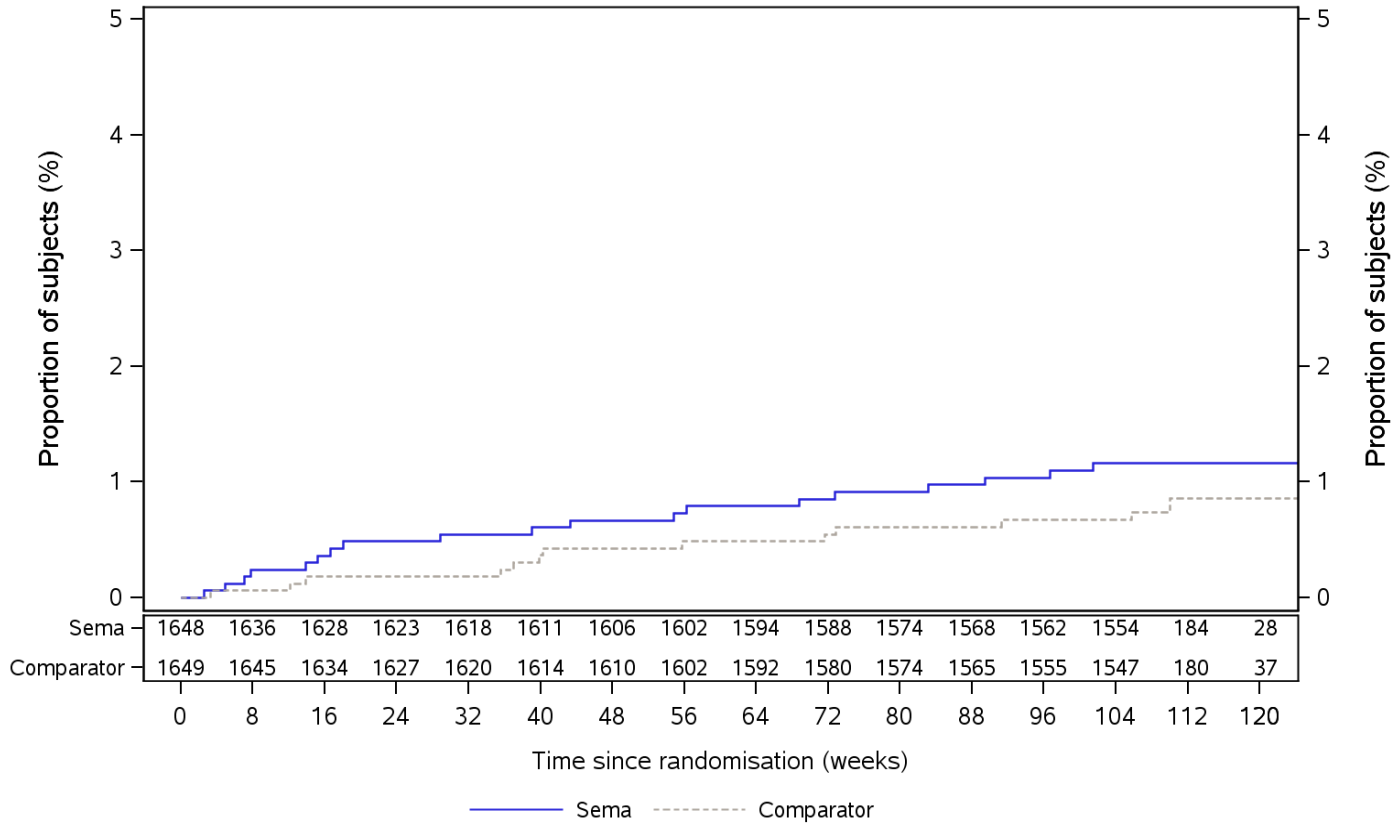
90 Mild adverse events - preferred term "Nephropathy" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:18:14 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nephropa_ae_mi_s6.png

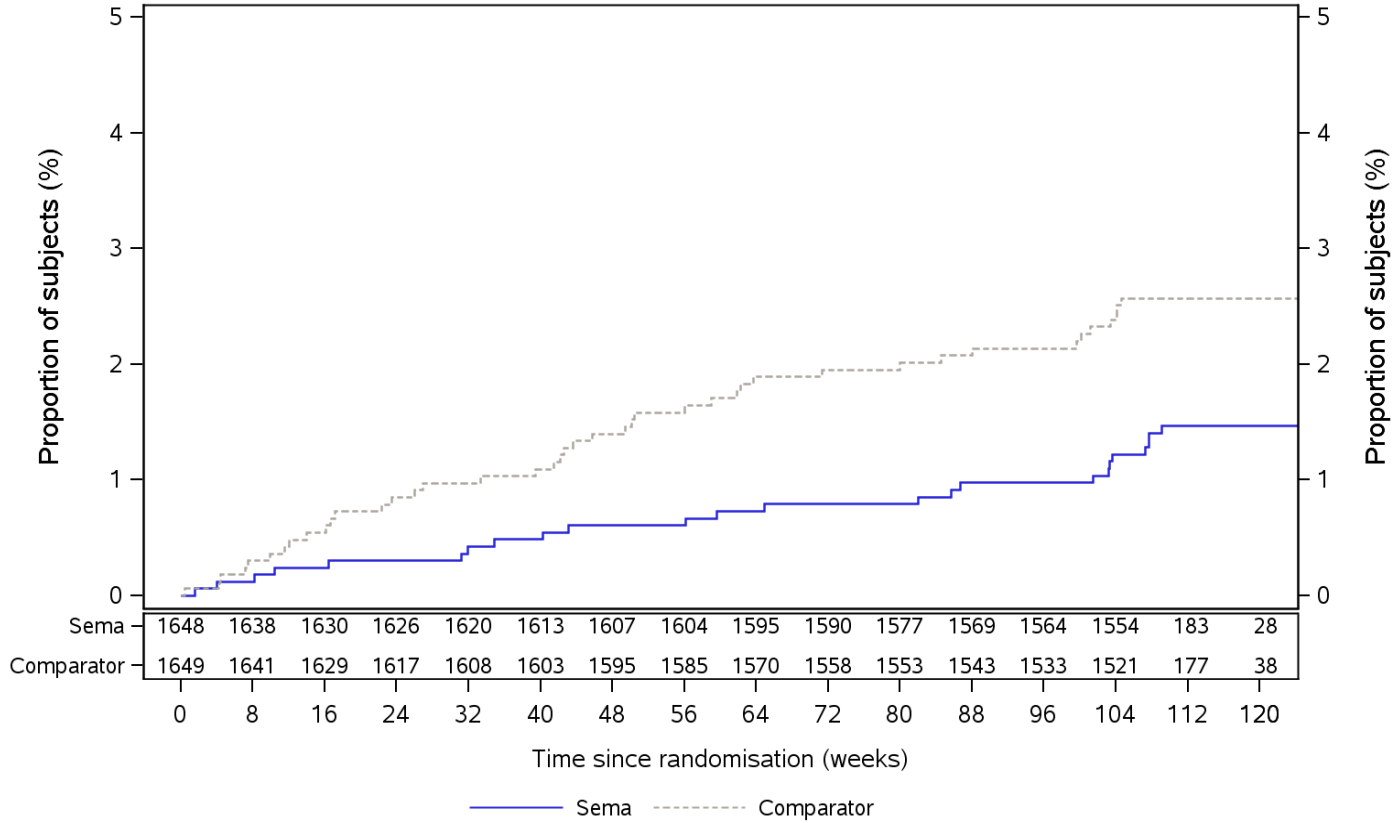
91 Mild adverse events - preferred term "Non-cardiac chest pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:18:32 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_noncarche_ae_mi_s6.png

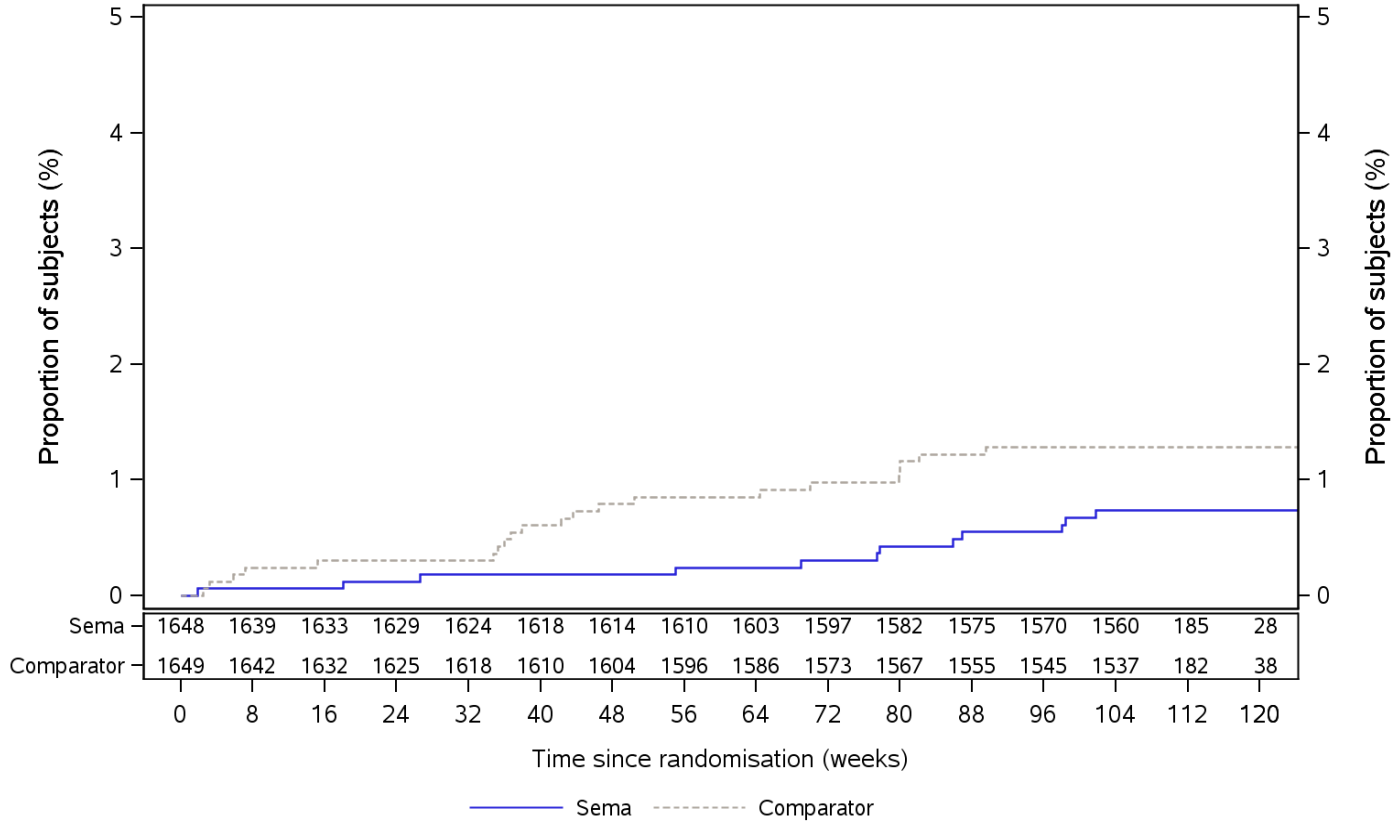
92 Mild adverse events - preferred term "Oedema peripheral" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:18:51 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_oedeperi_ae_mi_s6.png

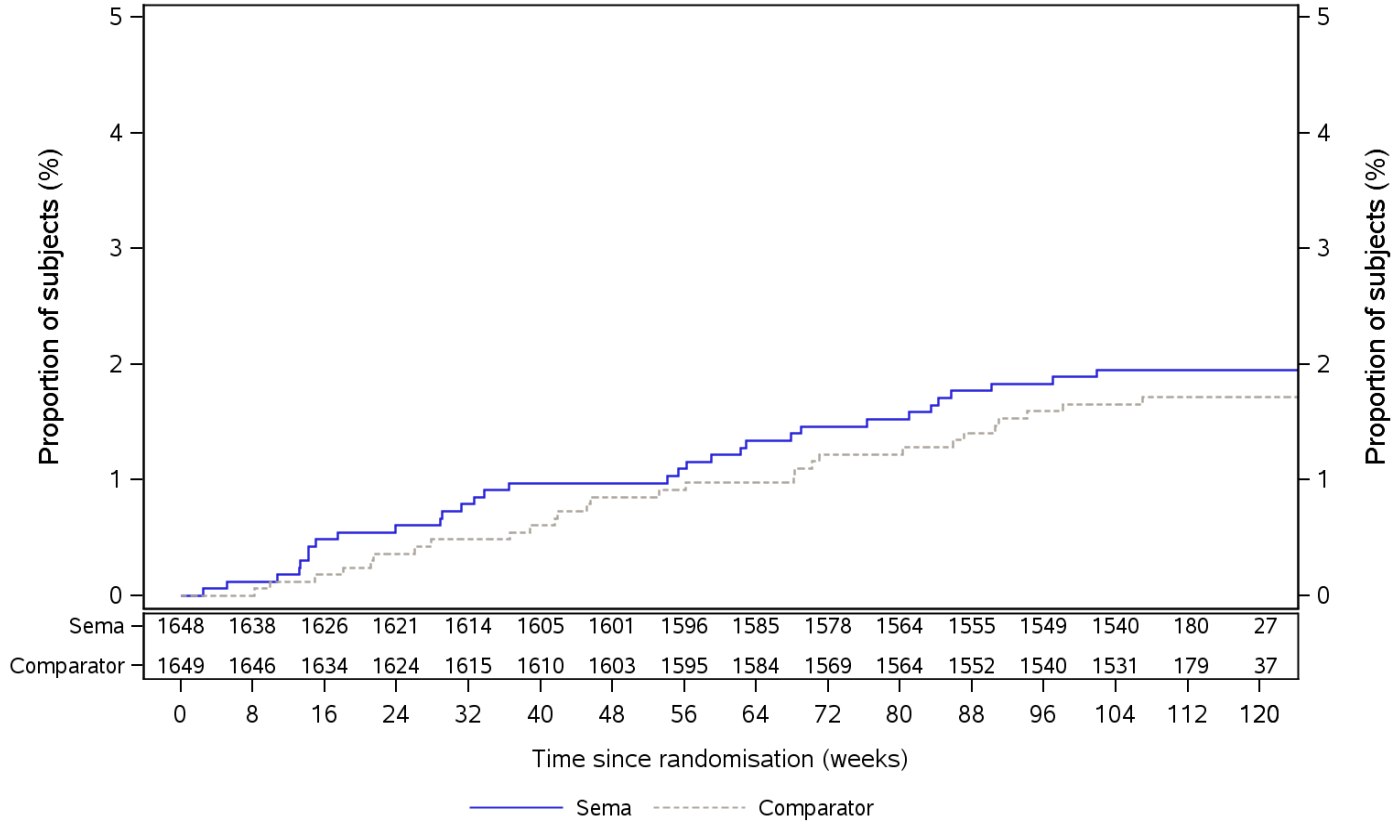
93 Mild adverse events - preferred term "Oropharyngeal pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:19:10 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_oroppain_ae_mi_s6.png

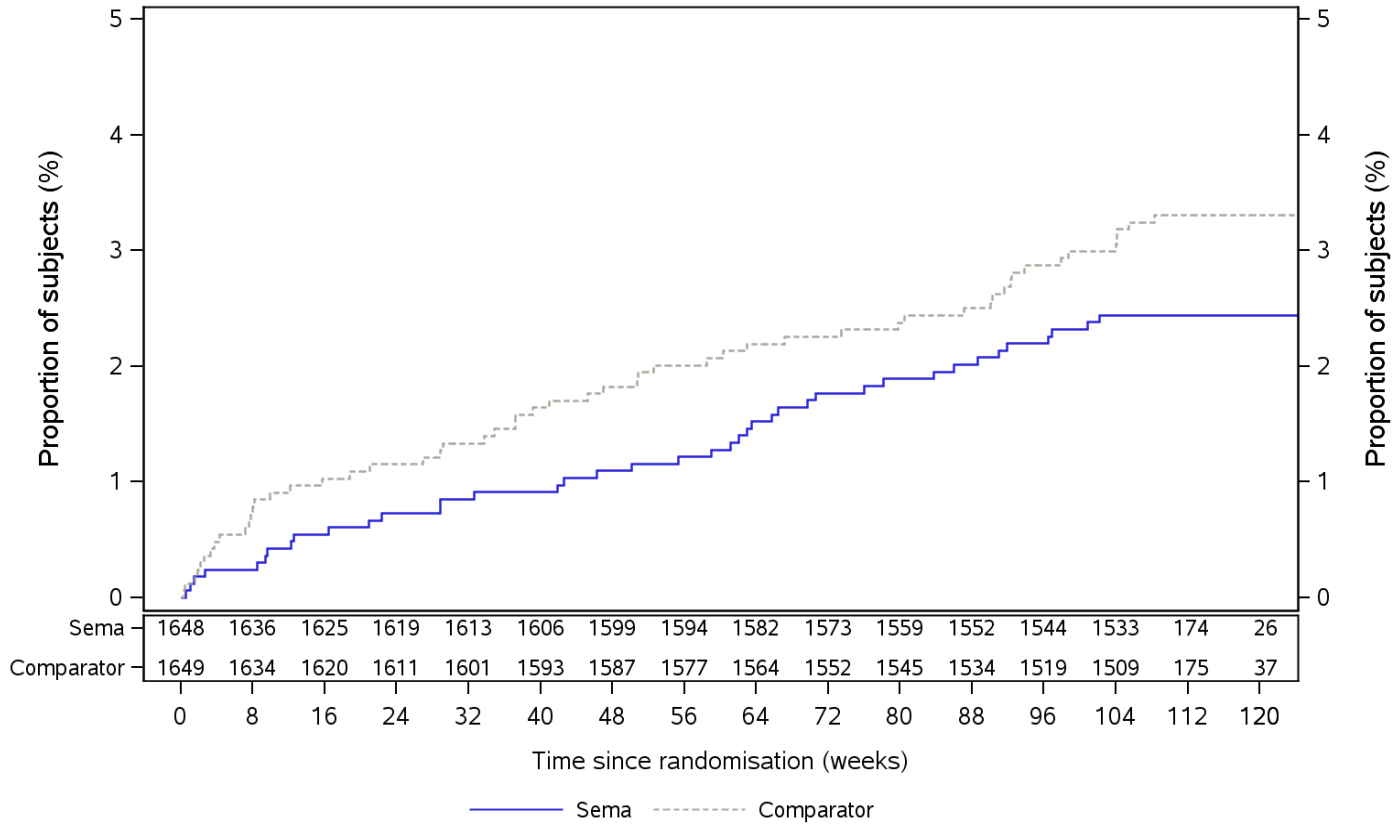
94 Mild adverse events - preferred term "Osteoarthritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:19:29 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_ost_ae_mi_s6.png

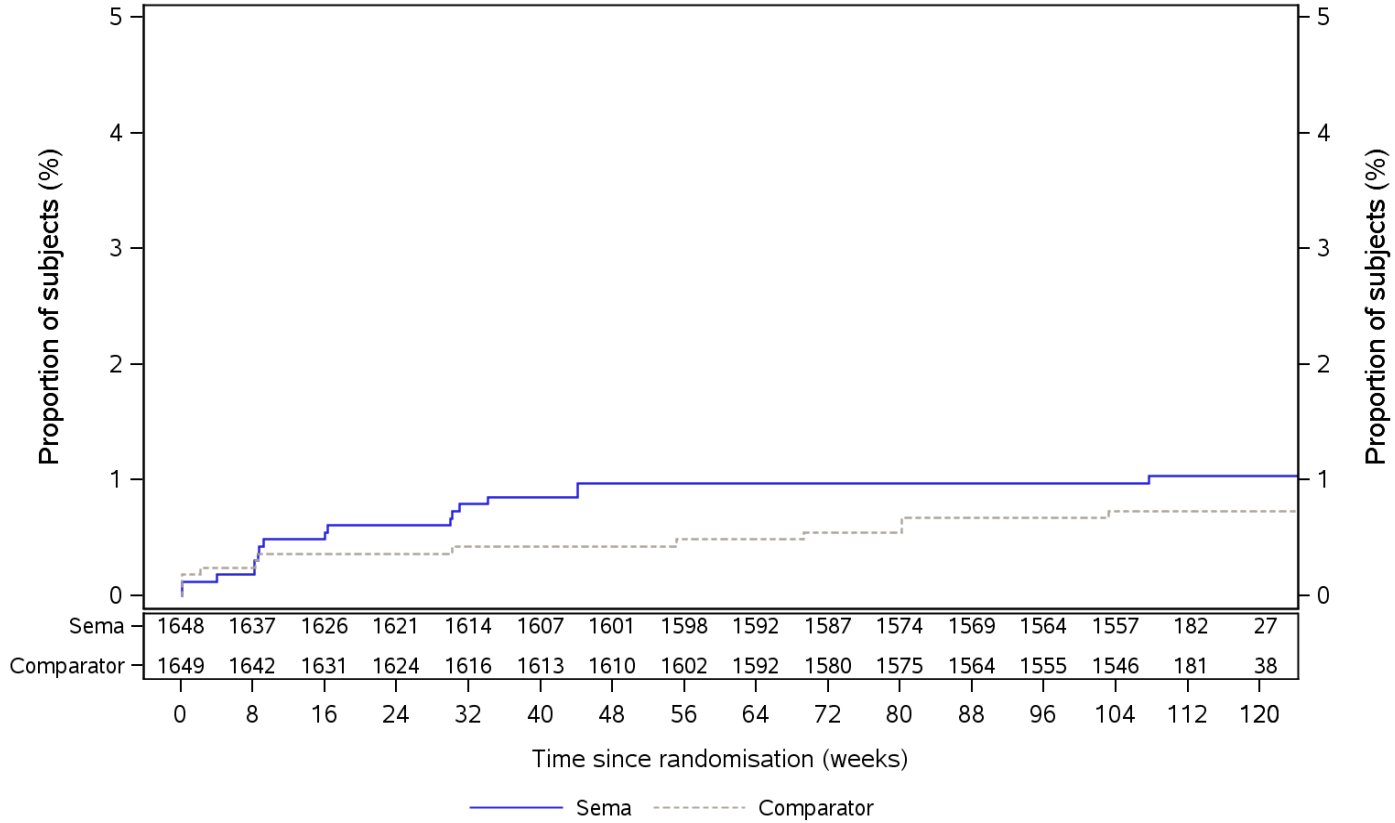
95 Mild adverse events - preferred term "Pain in extremity" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:19:49 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_paiinext_ae_mi_s6.png

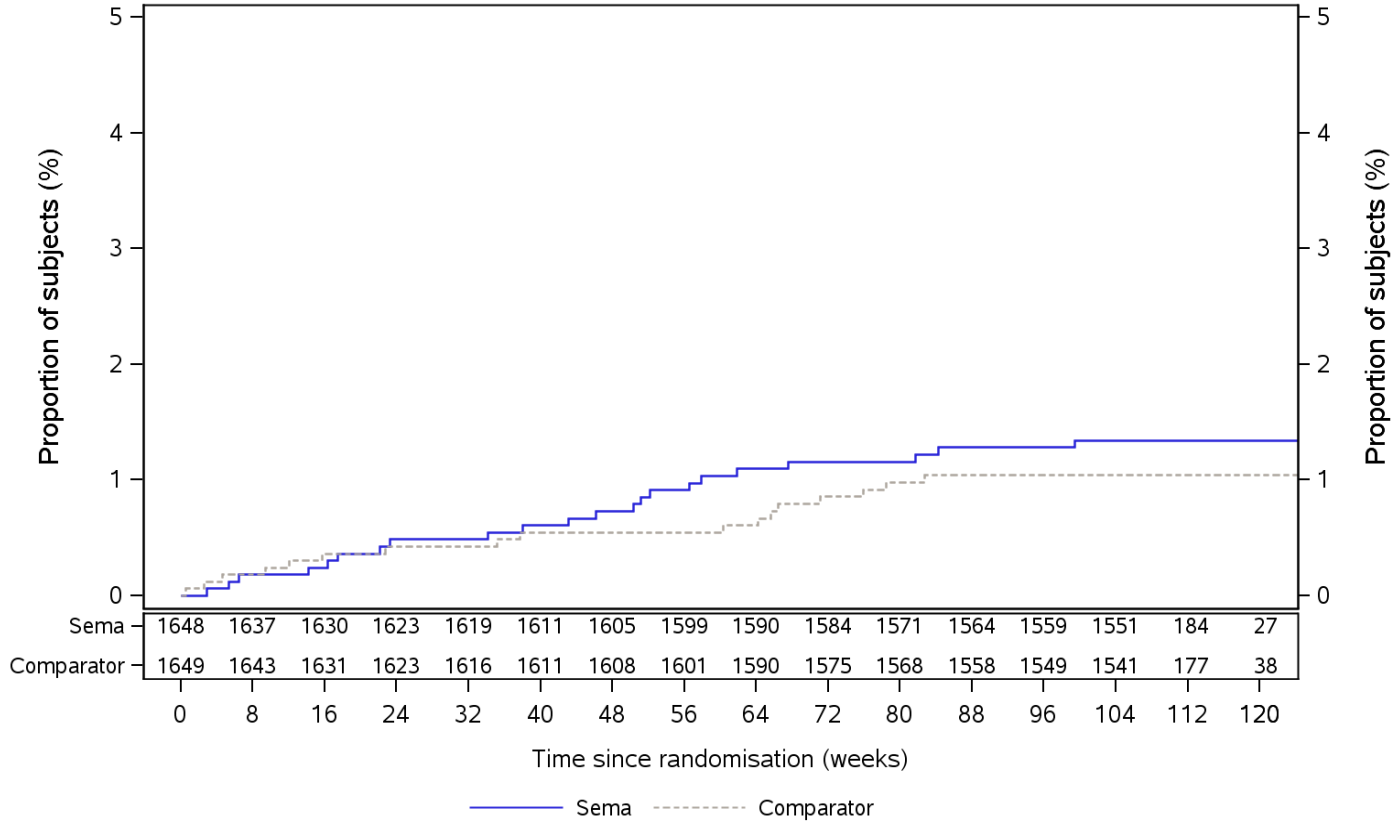
96 Mild adverse events - preferred term "Pancreatic enzymes increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:20:08 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_panenzinc_ae_mi_s6.png

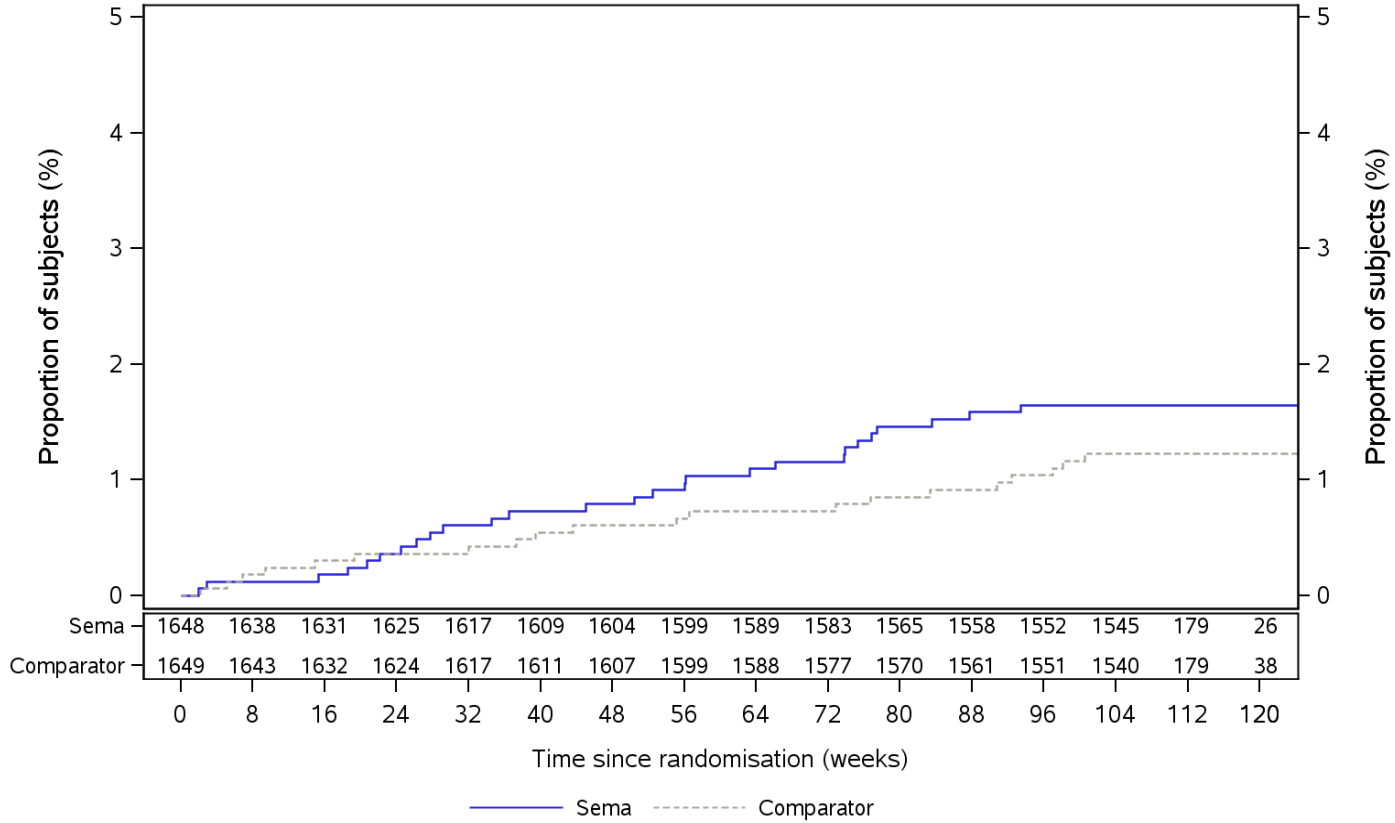
97 Mild adverse events - preferred term "Pharyngitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:20:28 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pharyngi_ae_mi_s6.png

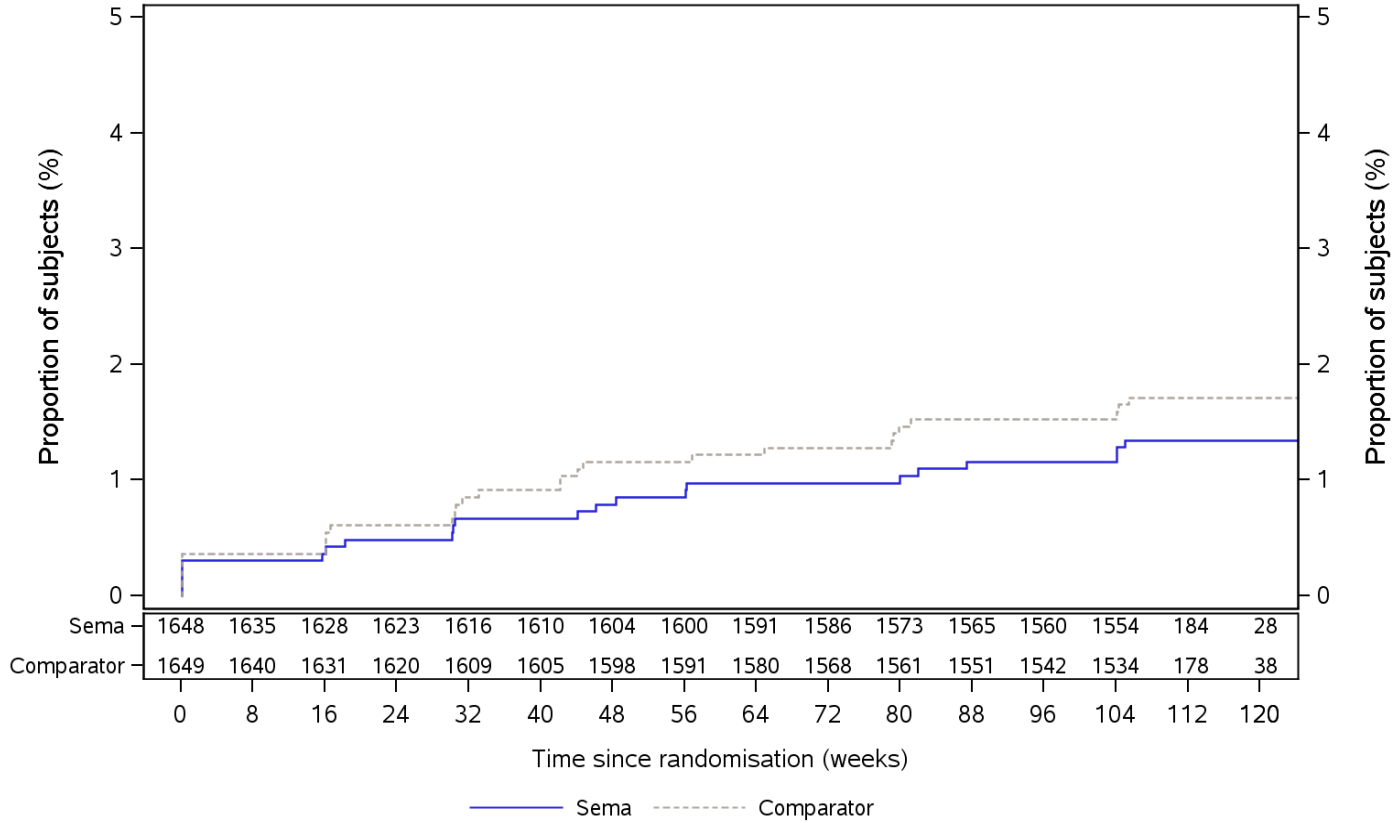
98 Mild adverse events - preferred term "Pneumonia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:20:46 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pneu_ae_mi_s6.png

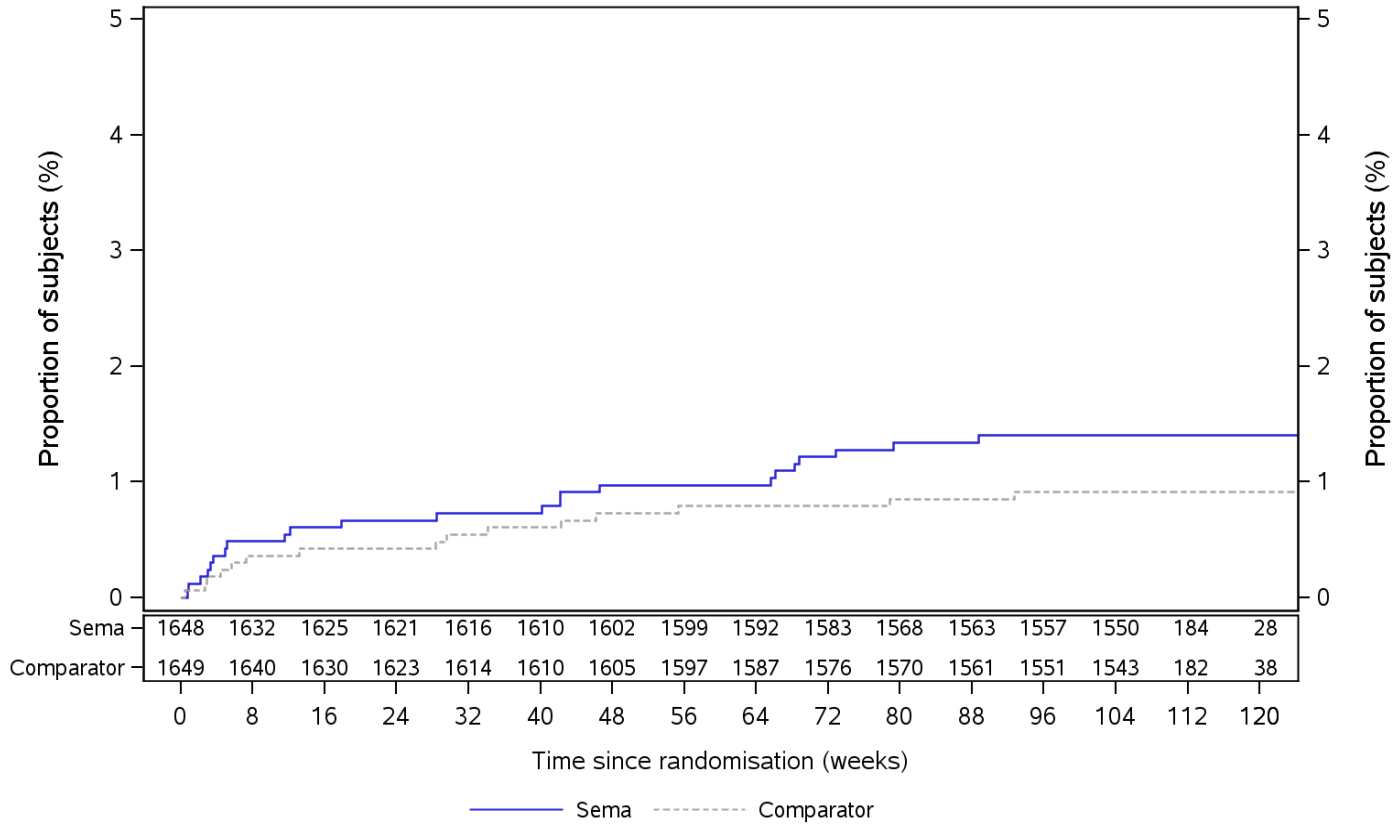
99 Mild adverse events - preferred term "Proteinuria" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:21:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_proteinu_ae_mi_s6.png

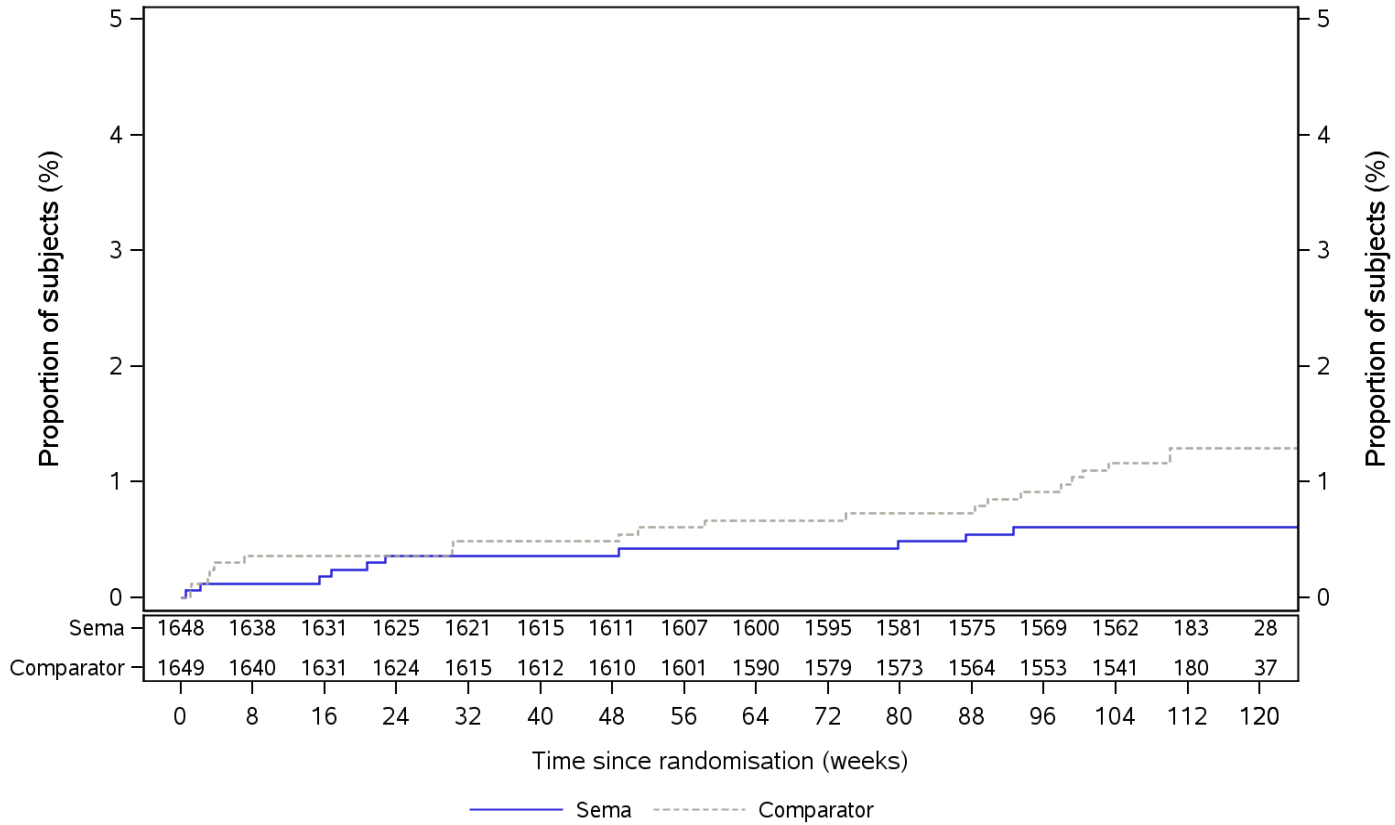
100 Mild adverse events - preferred term "Pruritus" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:21:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pruritus_ae_mi_s6.png

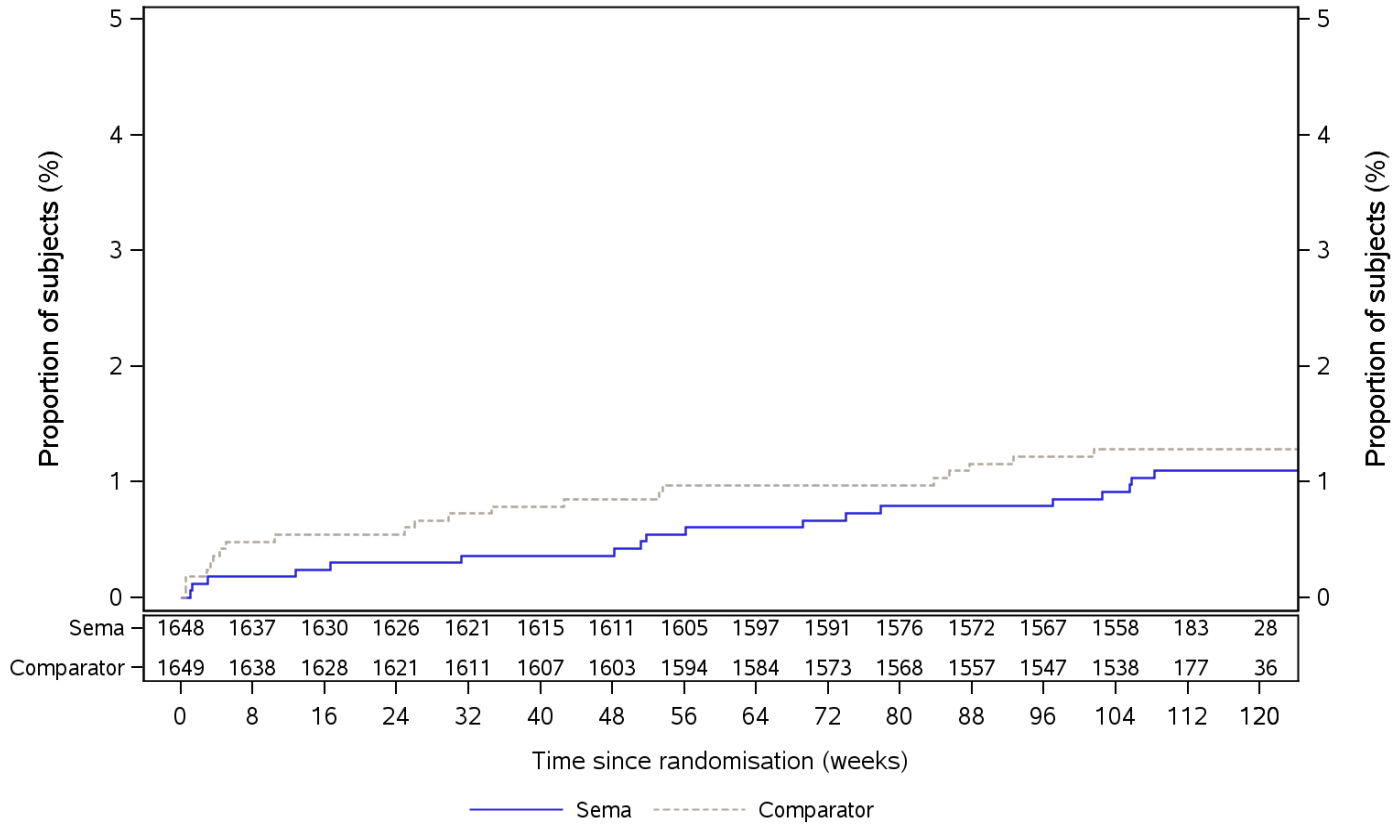
101 Mild adverse events - preferred term "Pyrexia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:21:46 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pyrexia_ae_mi_s6.png

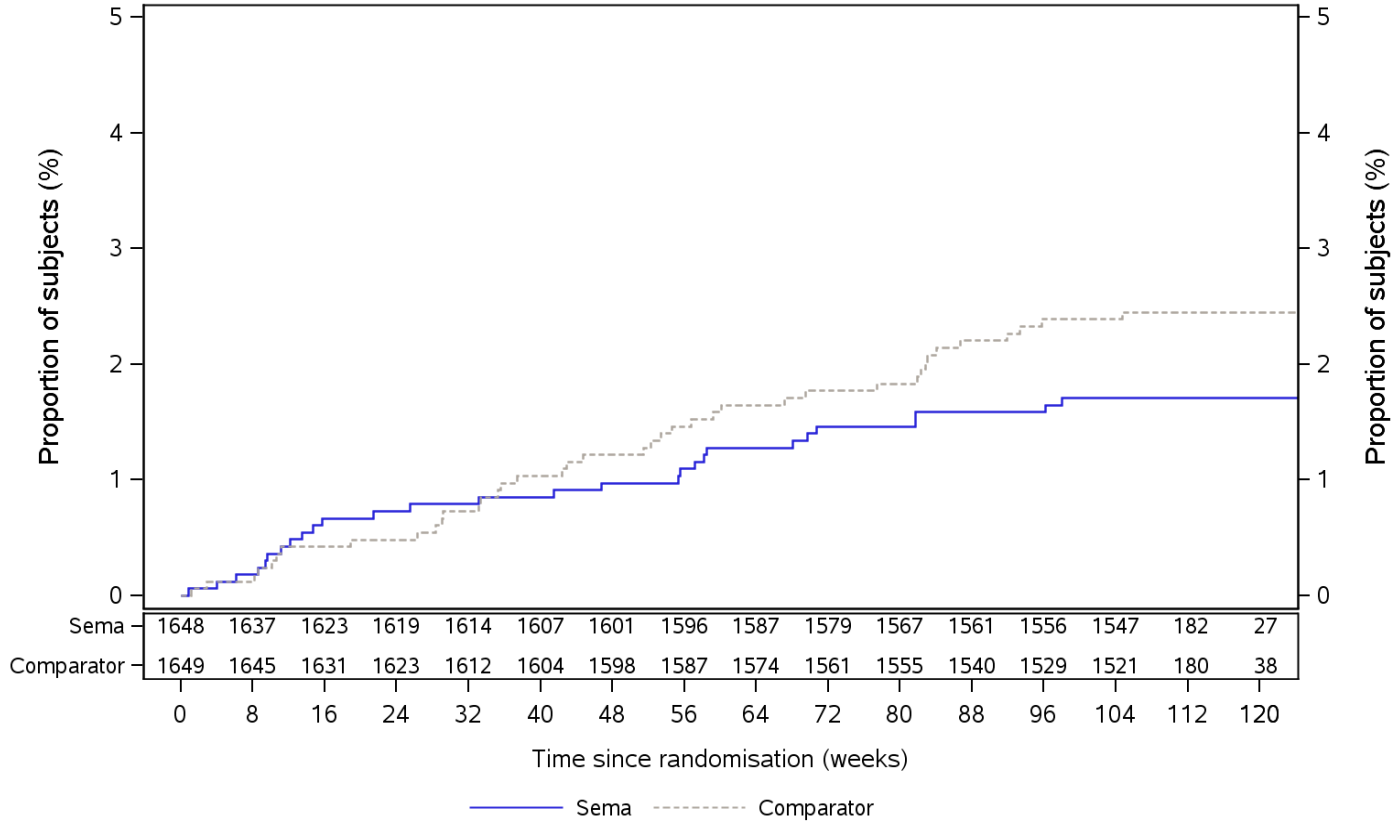
102 Mild adverse events - preferred term "Rash" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:22:05 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_rash_ae_mi_s6.png

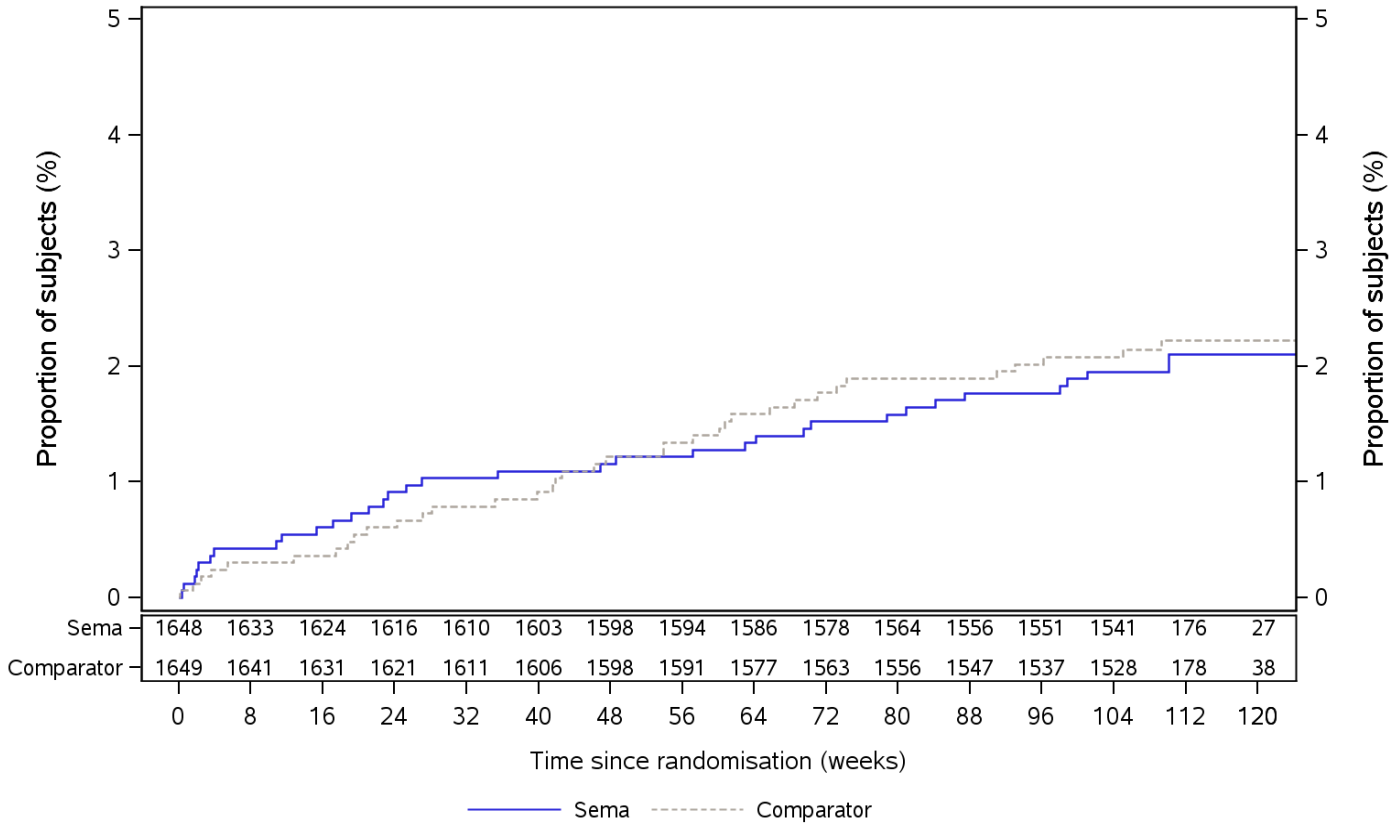
103 Mild adverse events - preferred term "Renal cyst" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:22:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_renacyst_ae_mi_s6.png

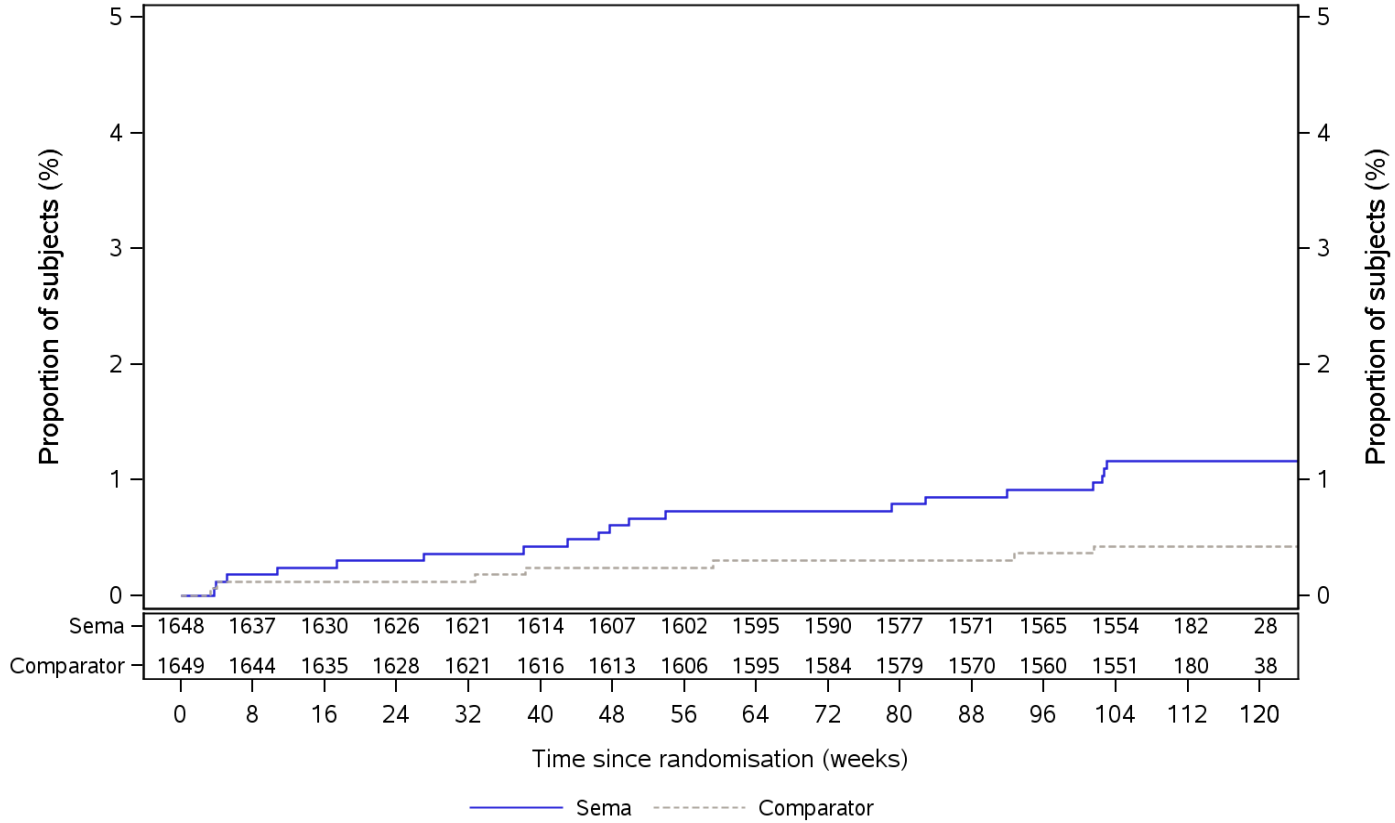
104 Mild adverse events - preferred term "Sinusitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:22:45 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_sinusiti_ae_mi_s6.png

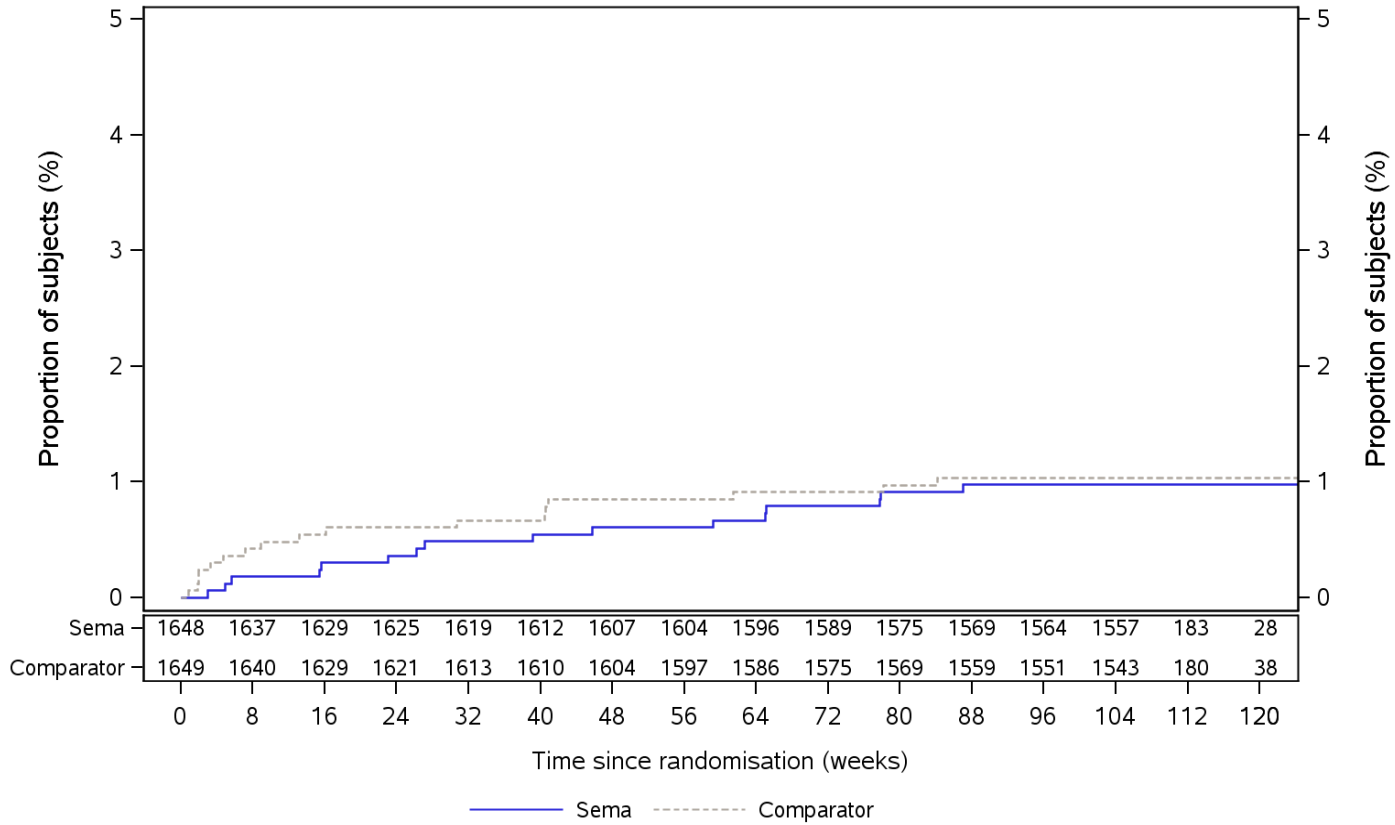
105 Mild adverse events - preferred term "Tooth infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:23:03 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_tootinfe_ae_mi_s6.png

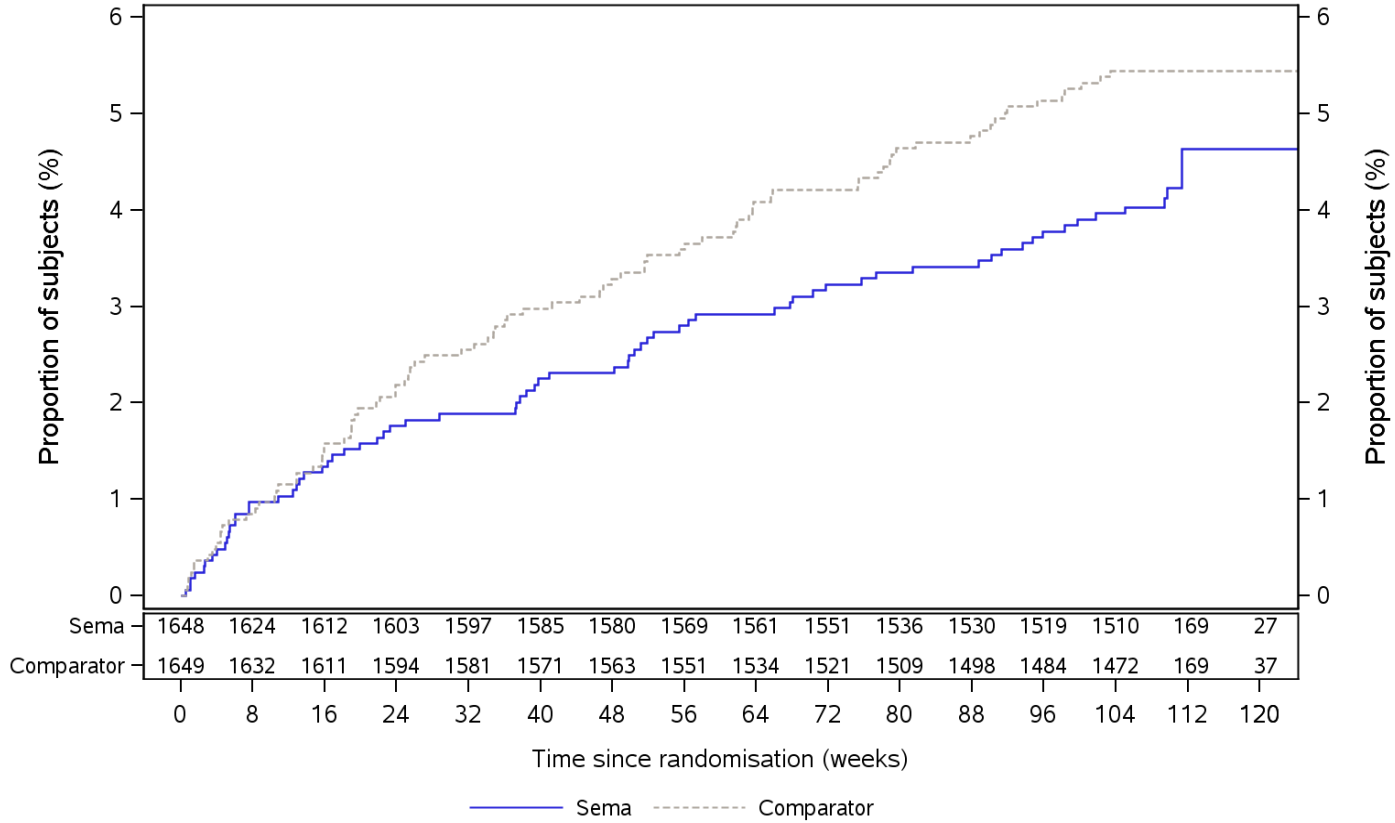
106 Mild adverse events - preferred term "Toothache" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:23:24 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_toothach_ae_mi_s6.png

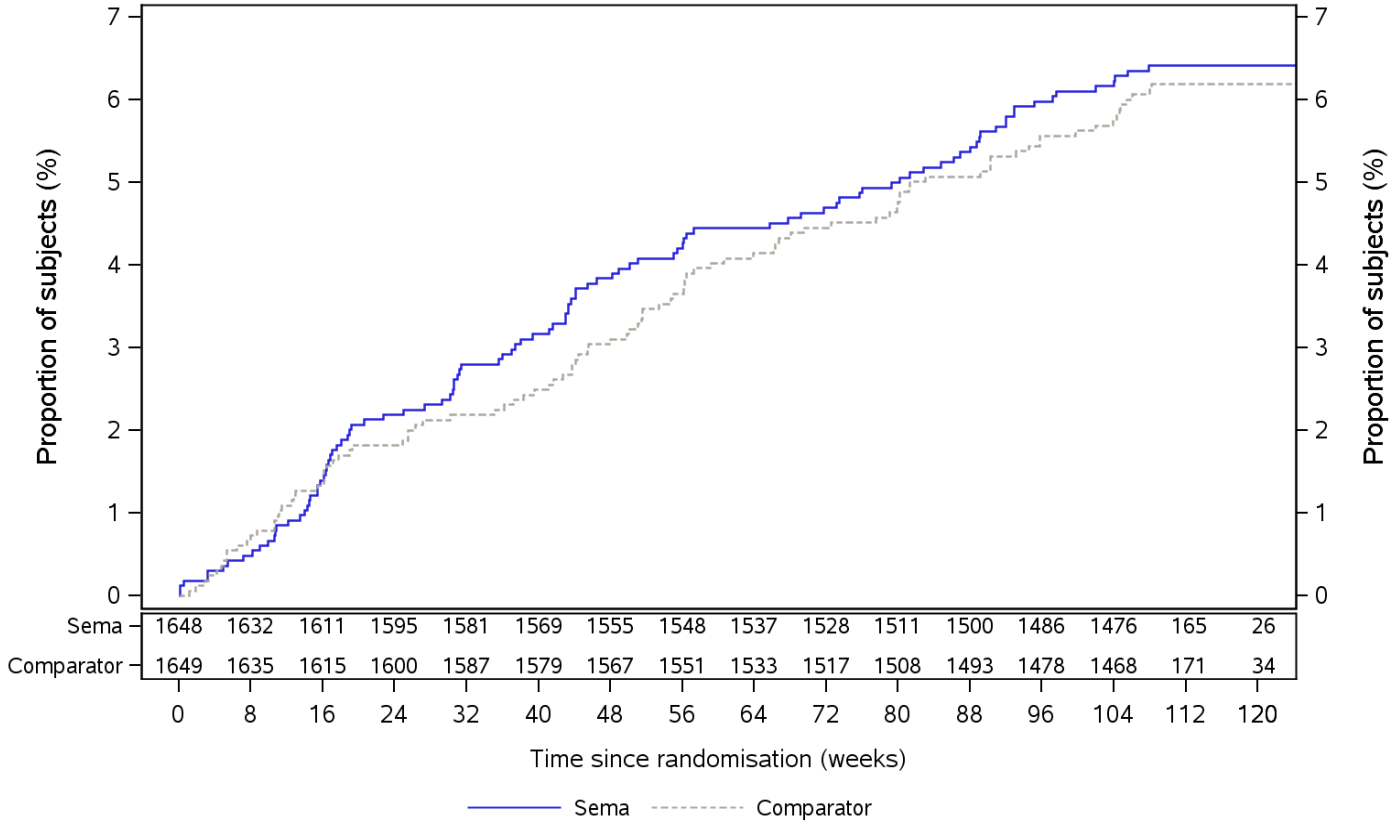
107 Mild adverse events - preferred term "Upper respiratory tract infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:23:44 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_upprestra_ae_mi_s6.png

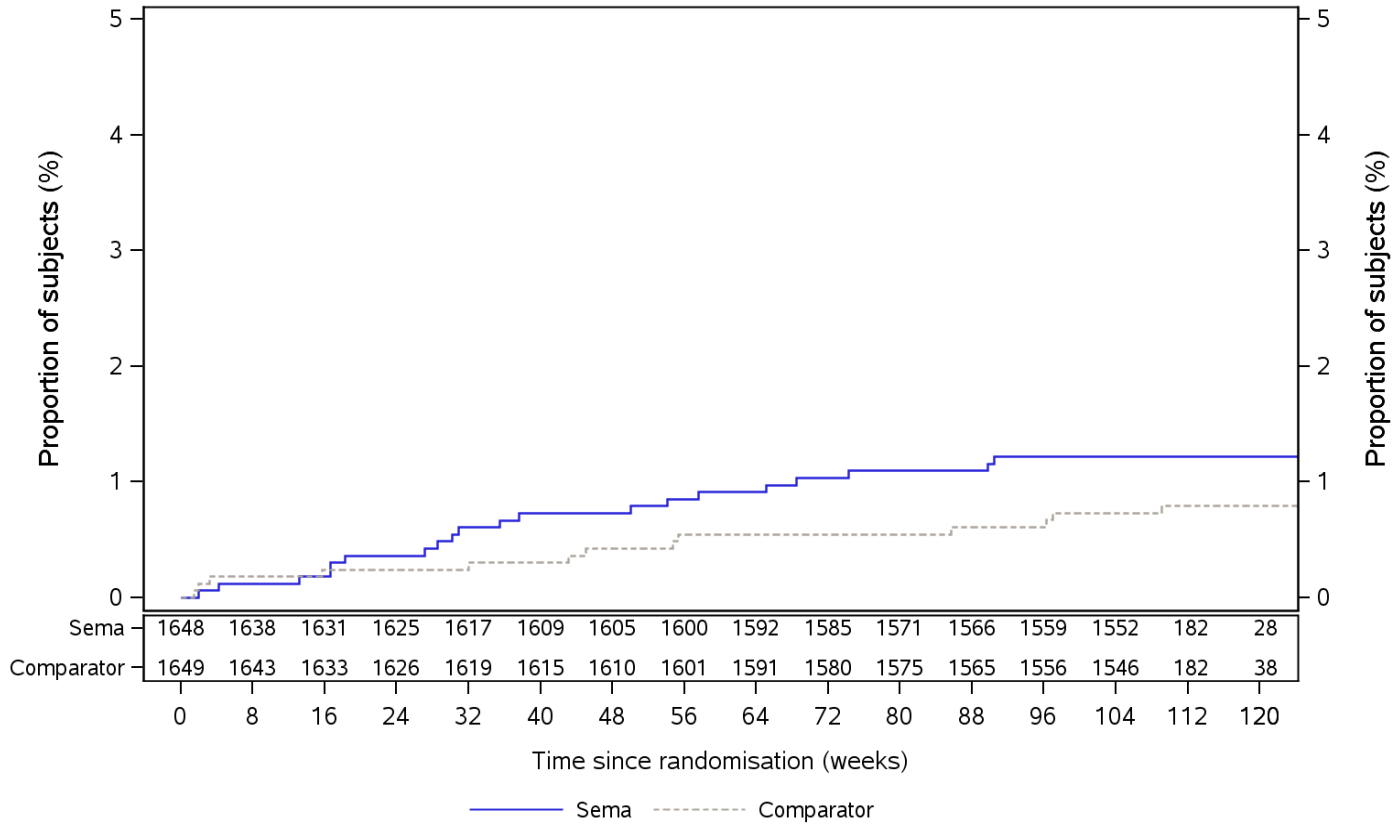
108 Mild adverse events - preferred term "Urinary tract infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:24:03 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_uritrainf_ae_mi_s6.png

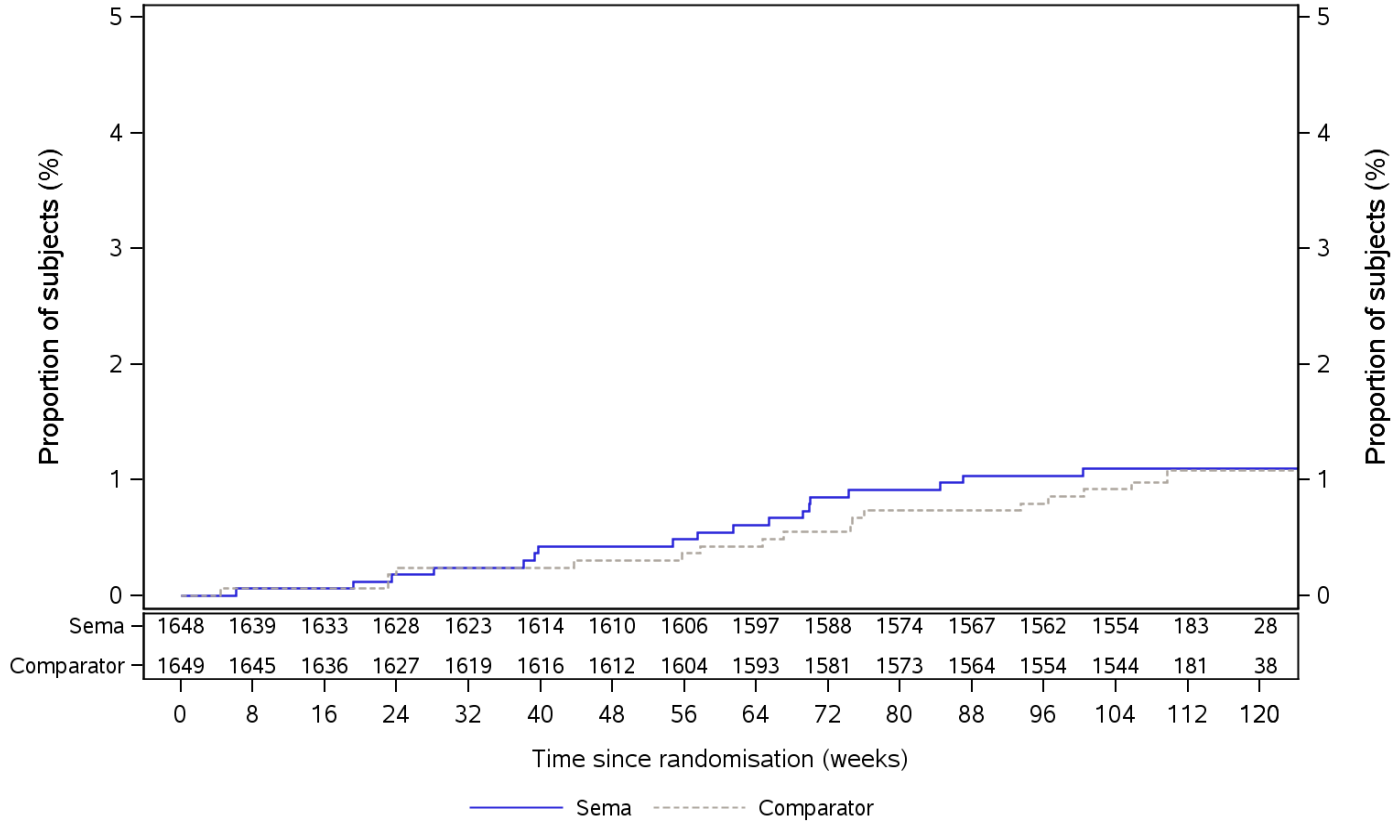
109 Mild adverse events - preferred term "Vertigo" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:24:22 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_vertigo_ae_mi_s6.png

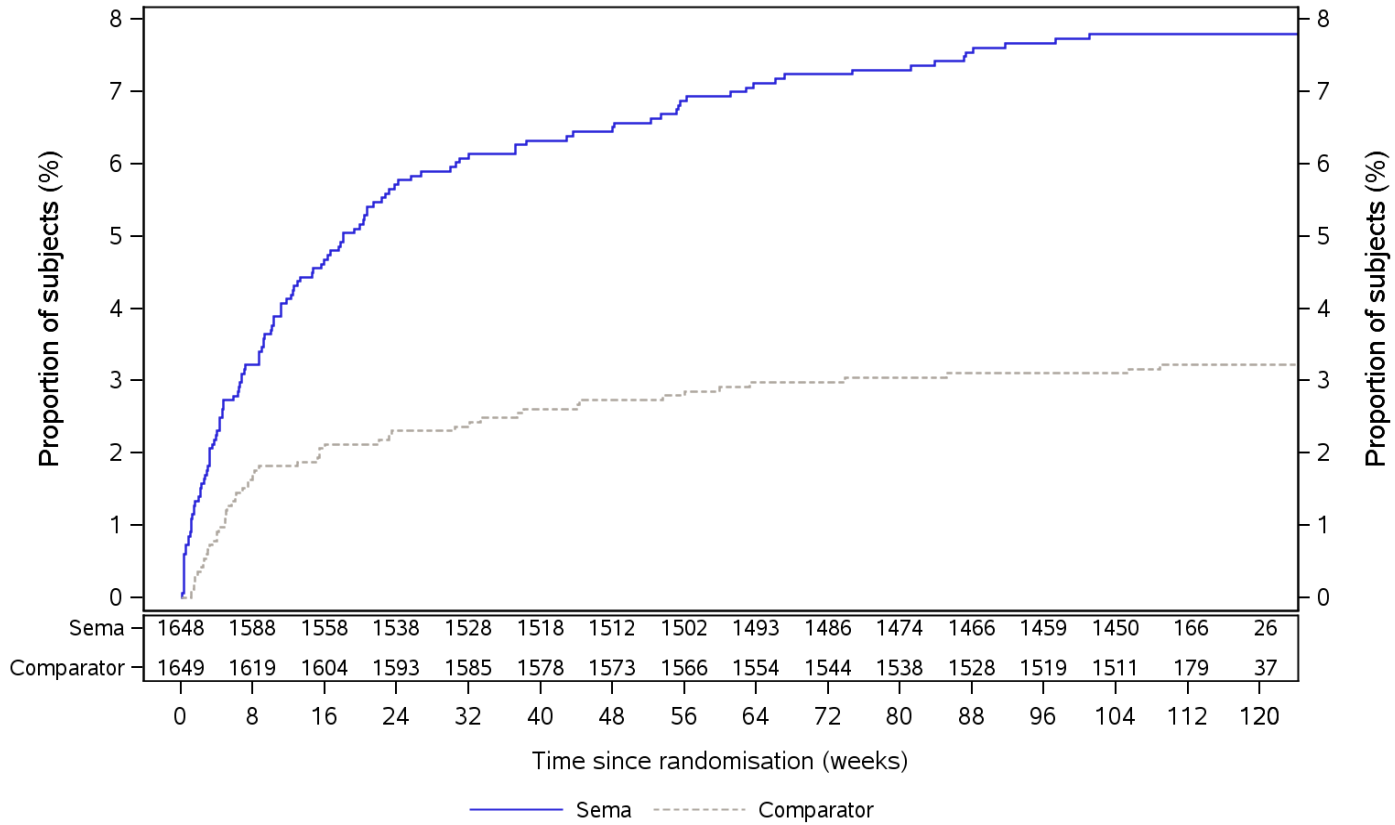
110 Mild adverse events - preferred term "Vitamin D deficiency" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:24:42 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_vitddef_ae_mi_s6.png

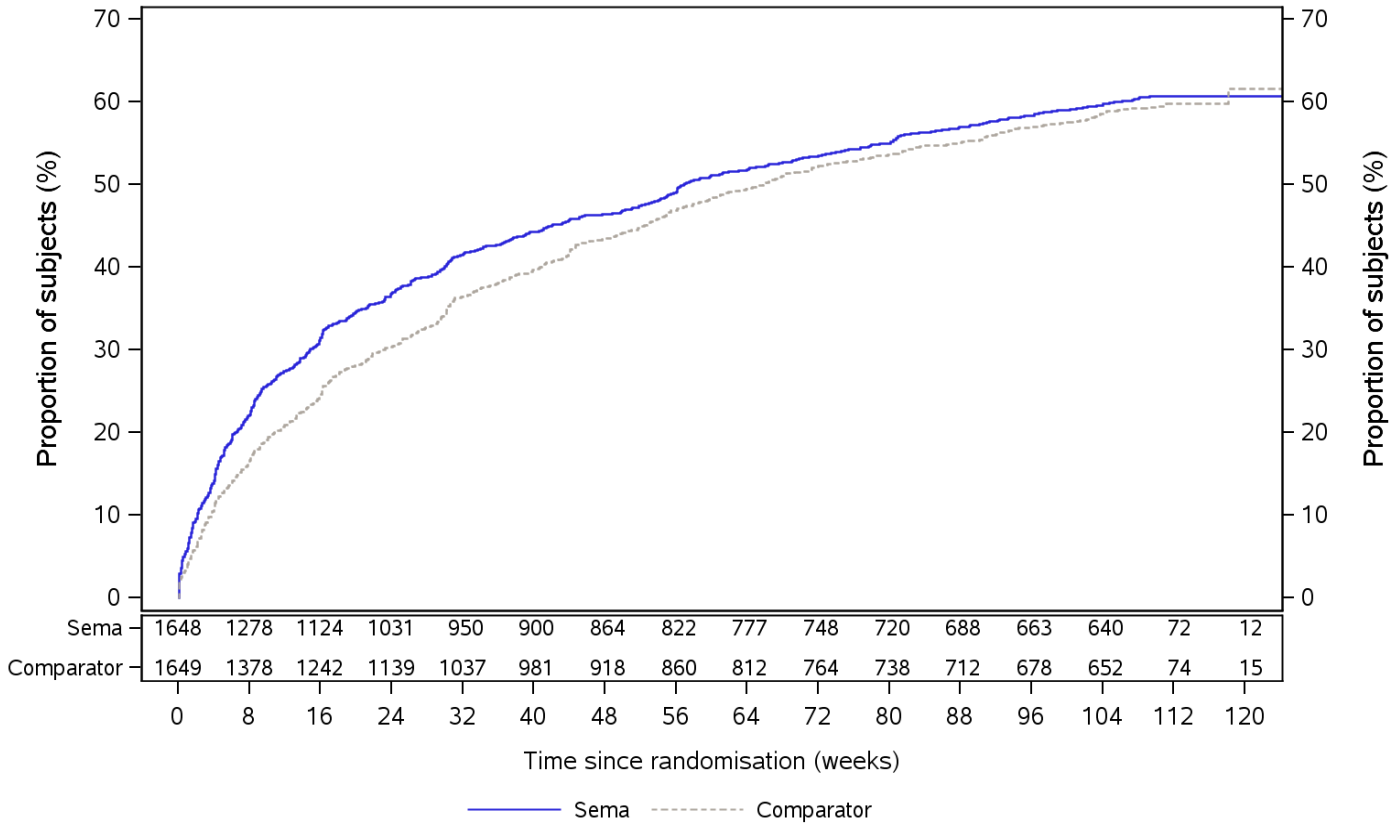
111 Mild adverse events - preferred term "Vomiting" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:25:00 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_vomiting_ae_mi_s6.png

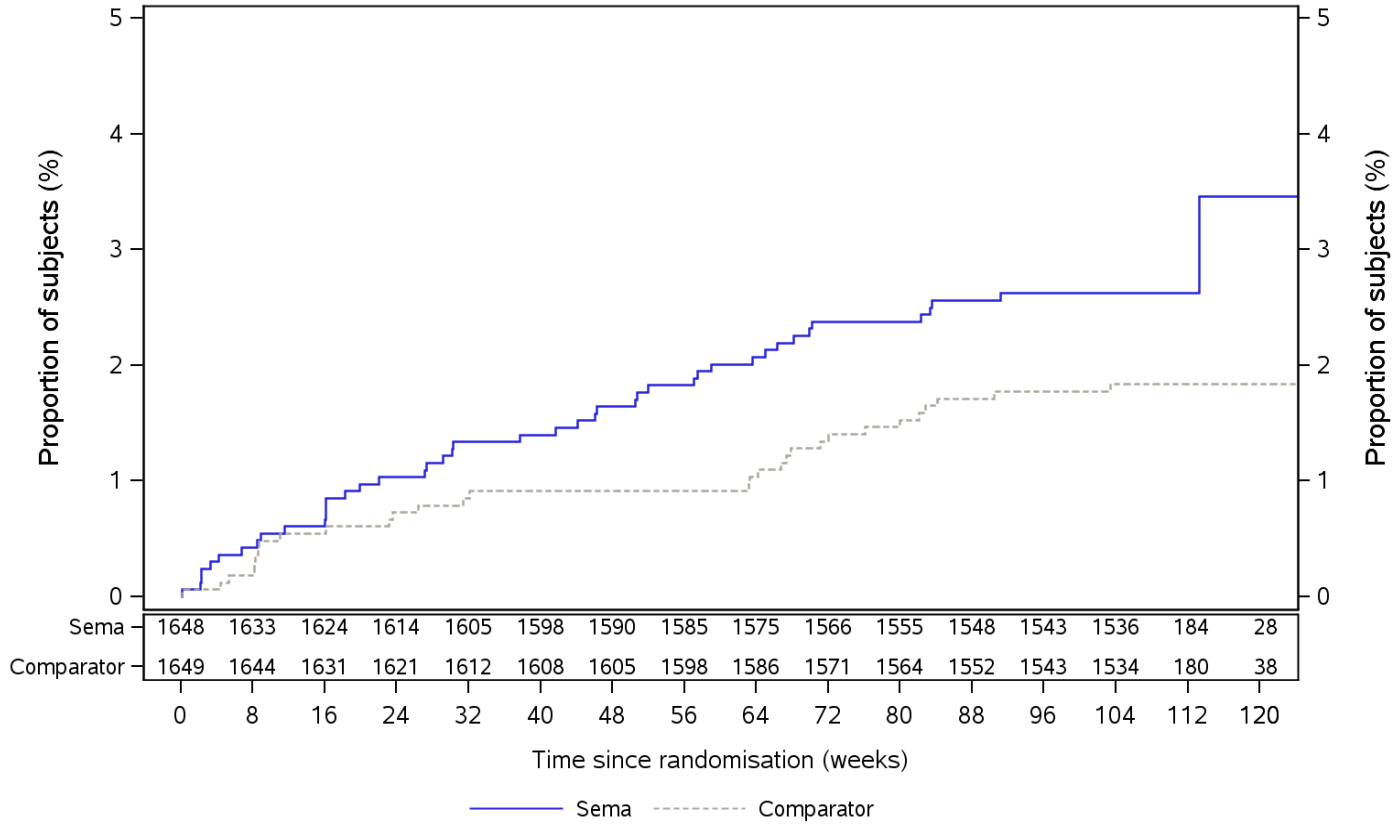
112 Moderate adverse events - cumulative incidence plot -Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
17JUN2020:11:23:36 - f_cif_tte_s6_add.sas/f_cif_saf_ae_mo_s6_add.png

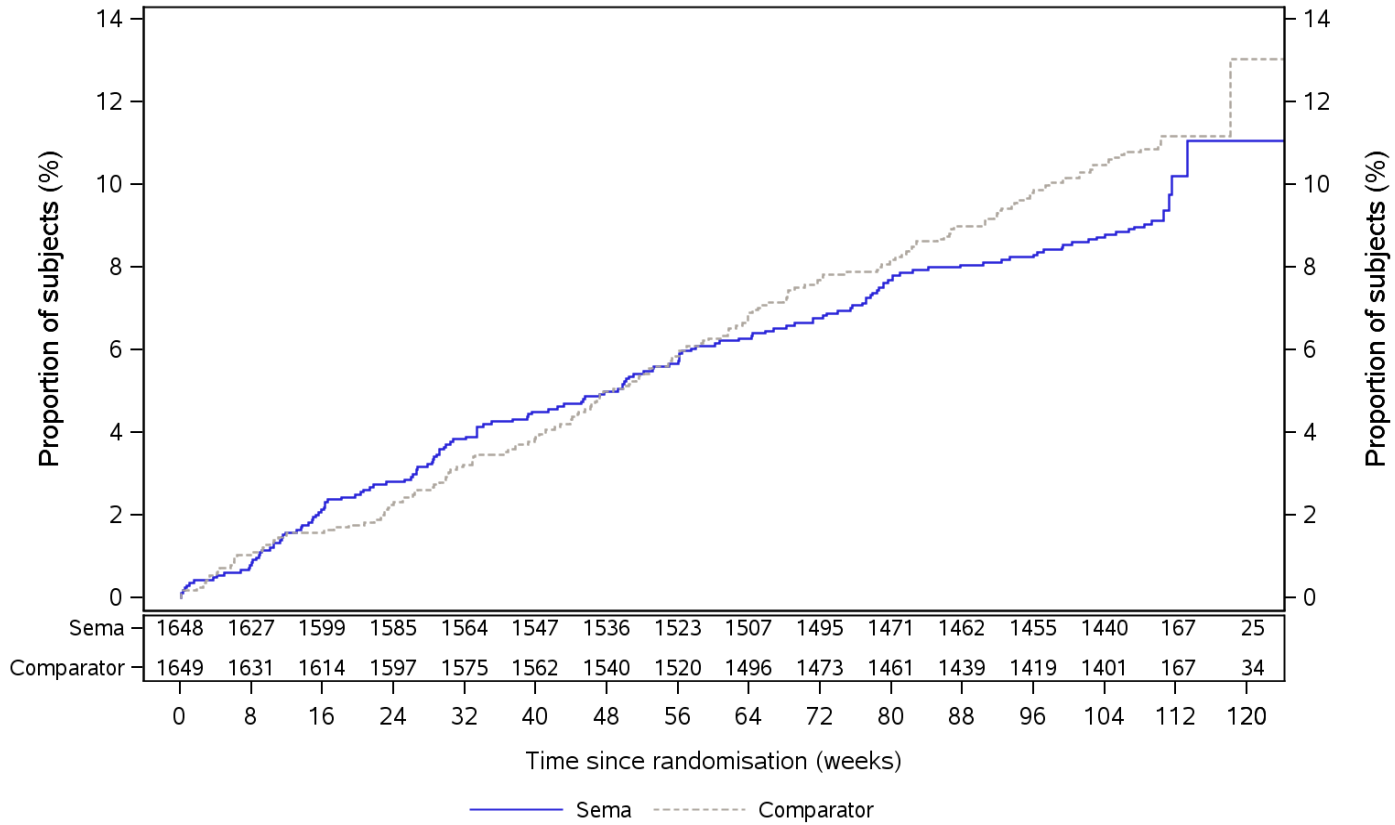
113 Moderate adverse events - system organ class "Blood and lymphatic system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:25:23 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_blsd_ae_mo_s6.png

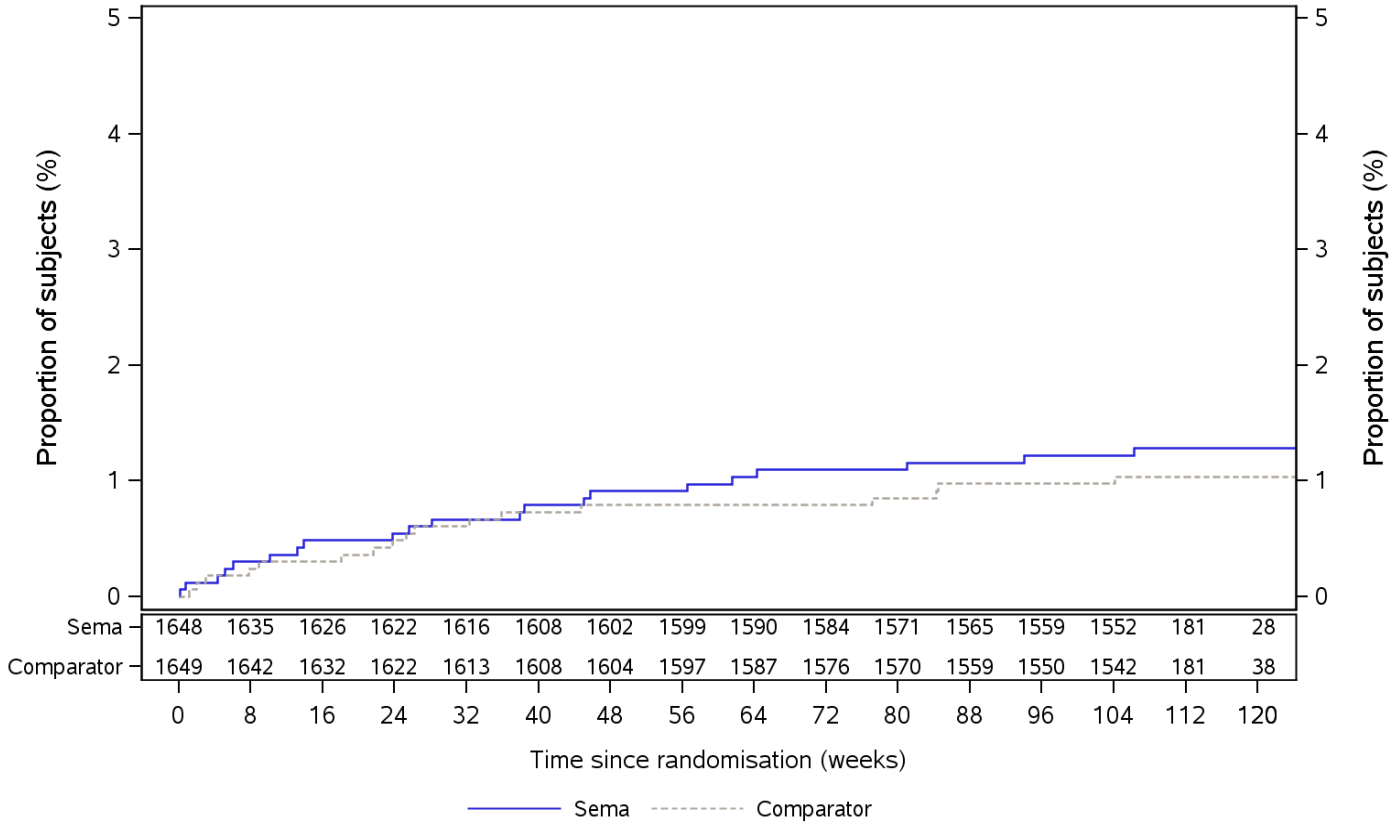
114 Moderate adverse events - system organ class "Cardiac disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:25:42 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_cd_ae_mo_s6.png

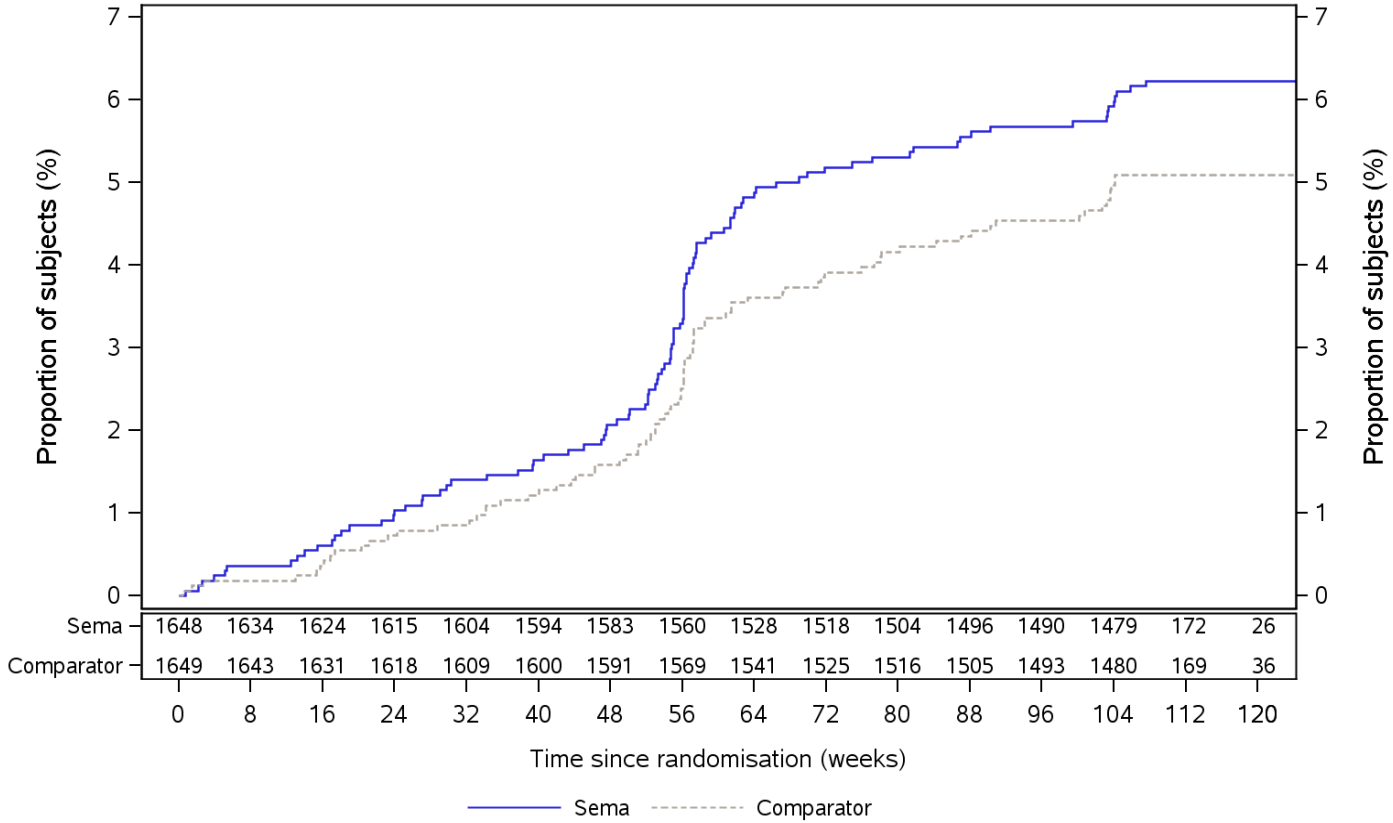
115 Moderate adverse events - system organ class "Ear and labyrinth disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:26:02 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_earandlab_ae_mo_s6.png

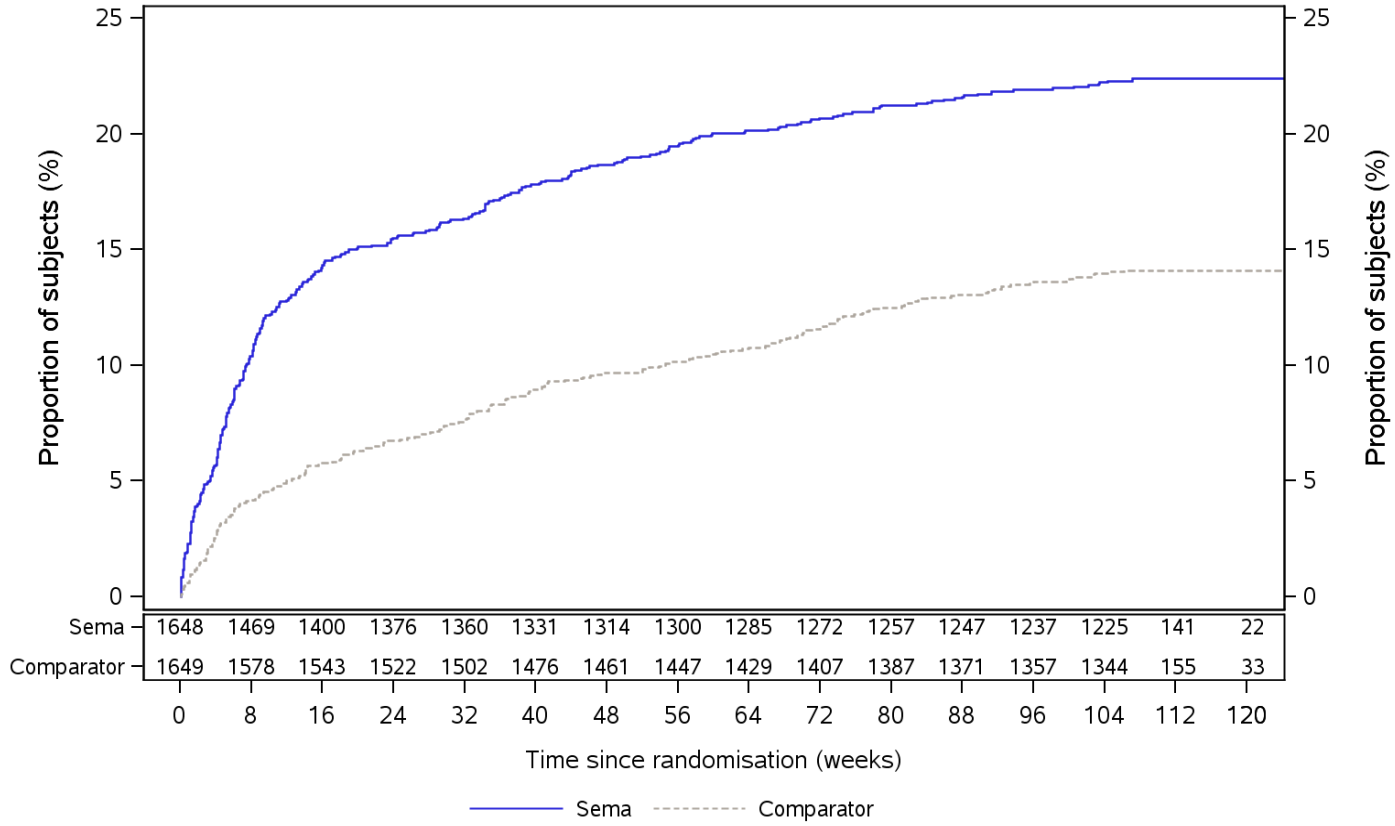
116 Moderate adverse events - system organ class "Eye disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:26:20 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ed_ae_mo_s6.png

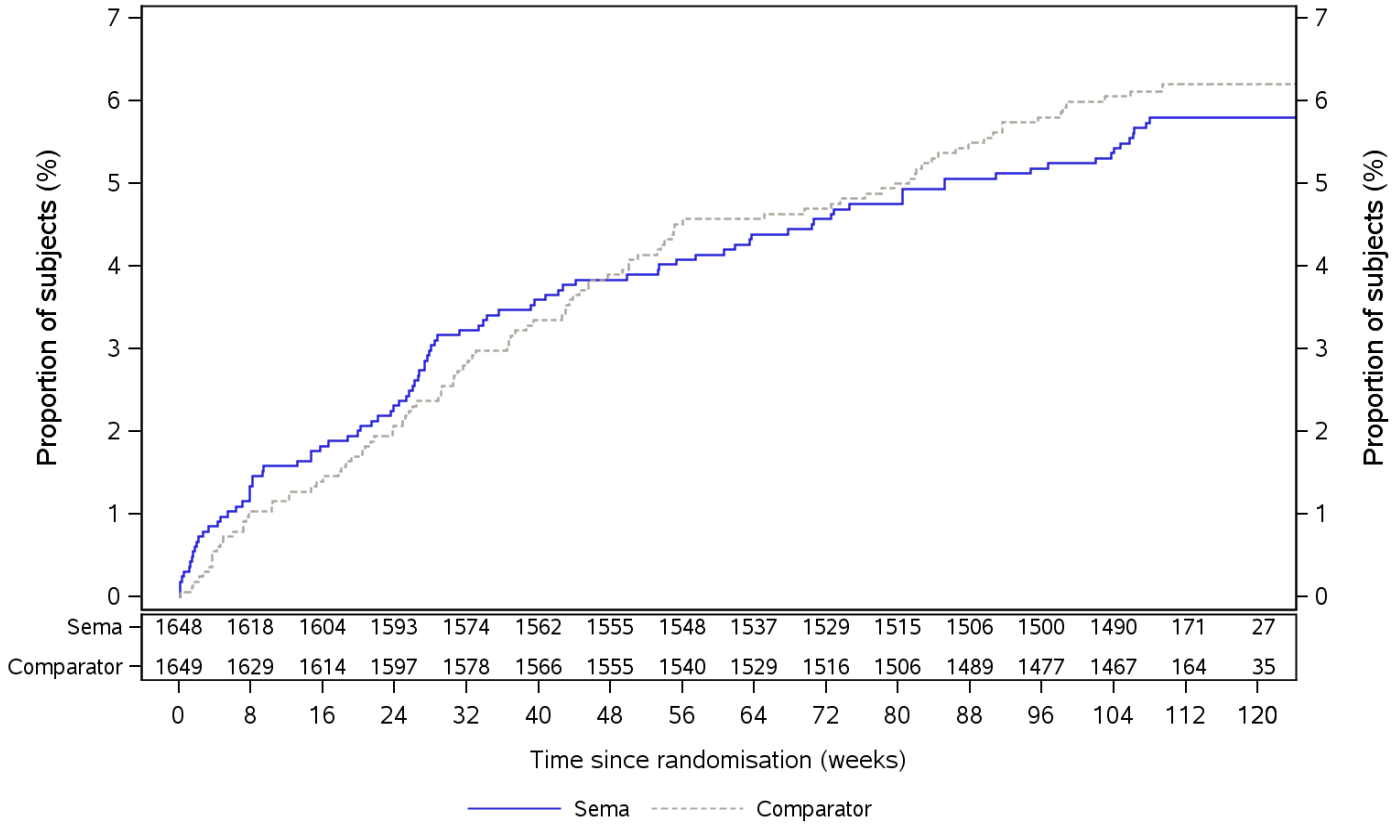
117 Moderate adverse events - system organ class "Gastrointestinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:26:37 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_gd_ae_mo_s6.png

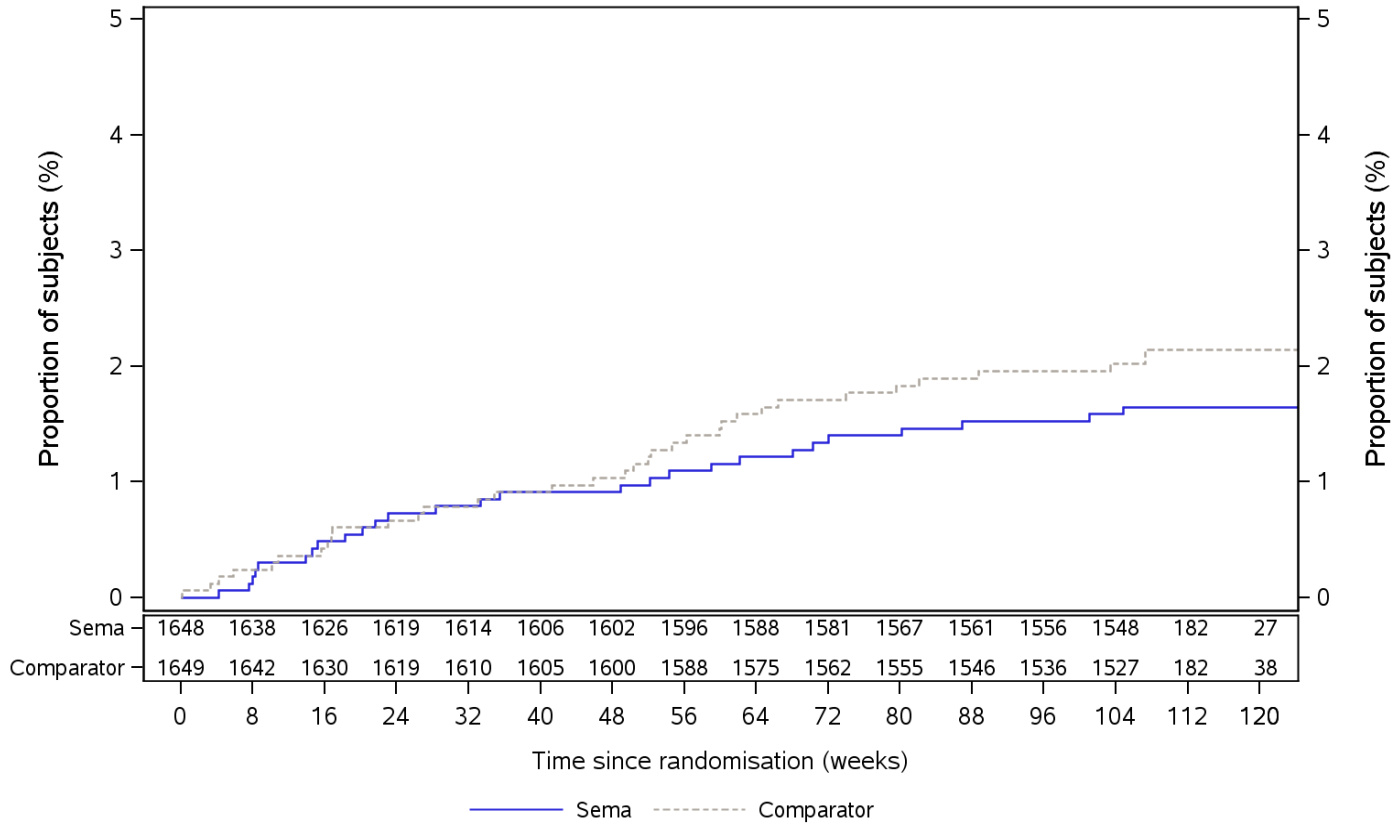
118 Moderate adverse events - system organ class "General disorders and administration site conditions" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:26:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_gdasc_ae_mo_s6.png

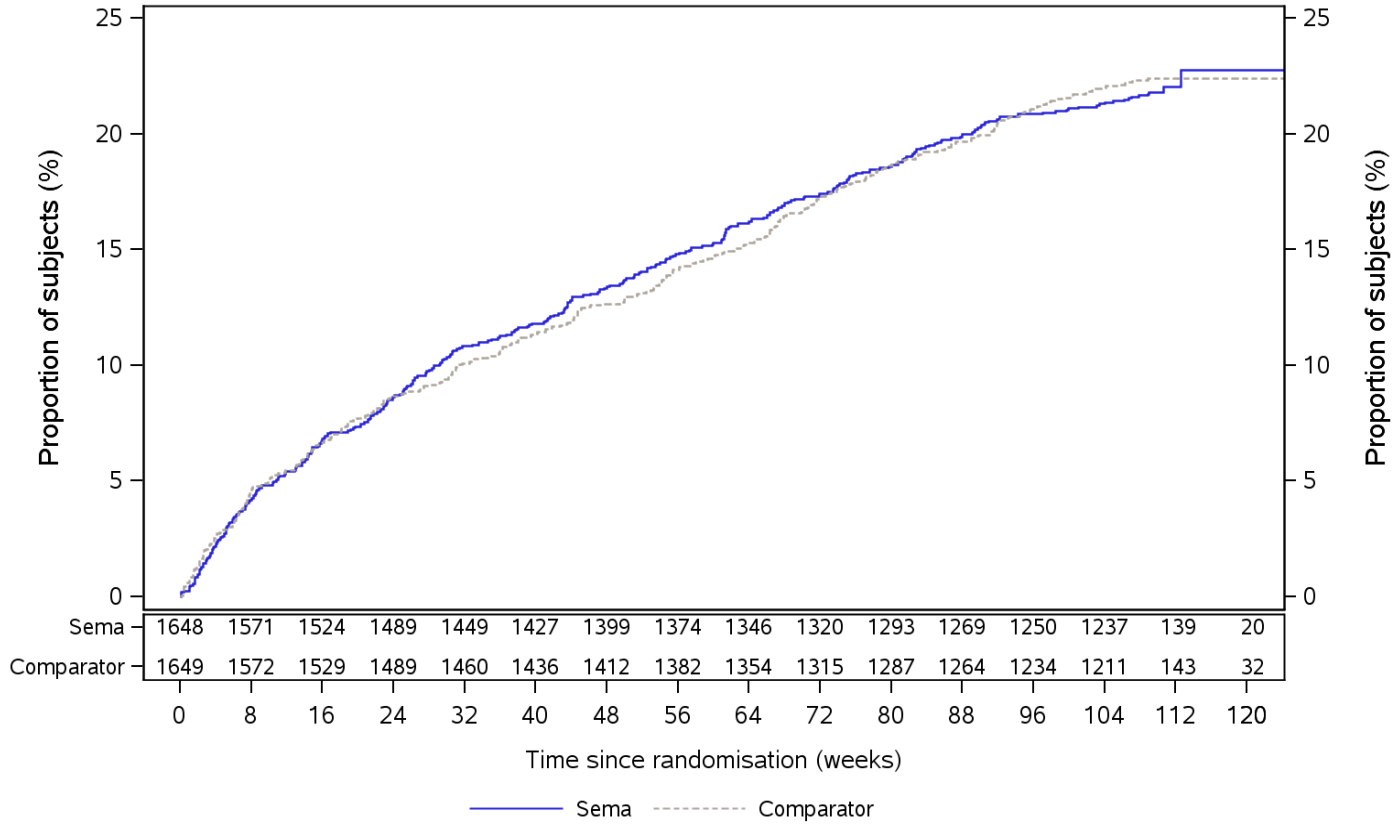
119 Moderate adverse events - system organ class "Hepatobiliary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:27:14 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_hd_ae_mo_s6.png

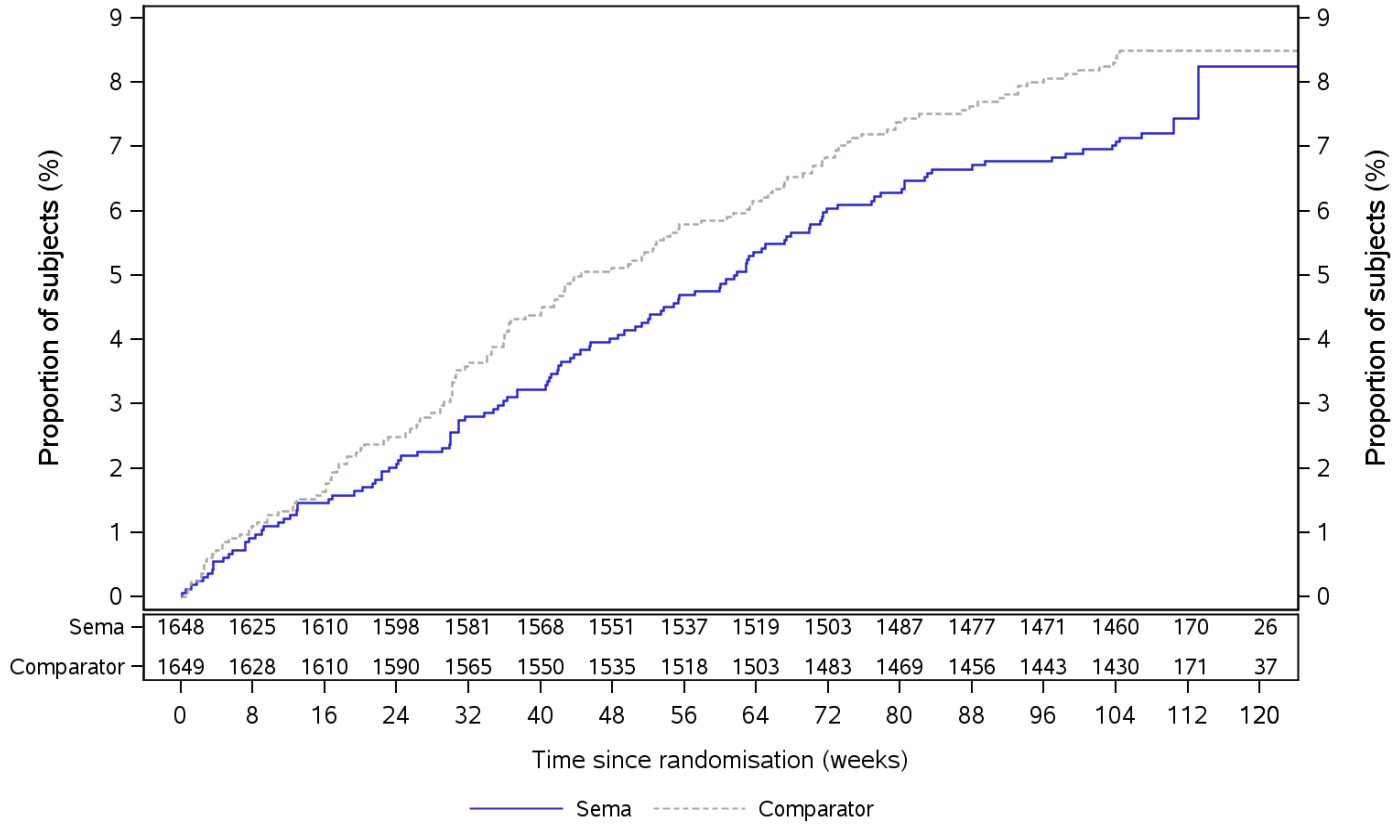
120 Moderate adverse events - system organ class "Infections and infestations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:27:31 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ii_ae_mo_s6.png

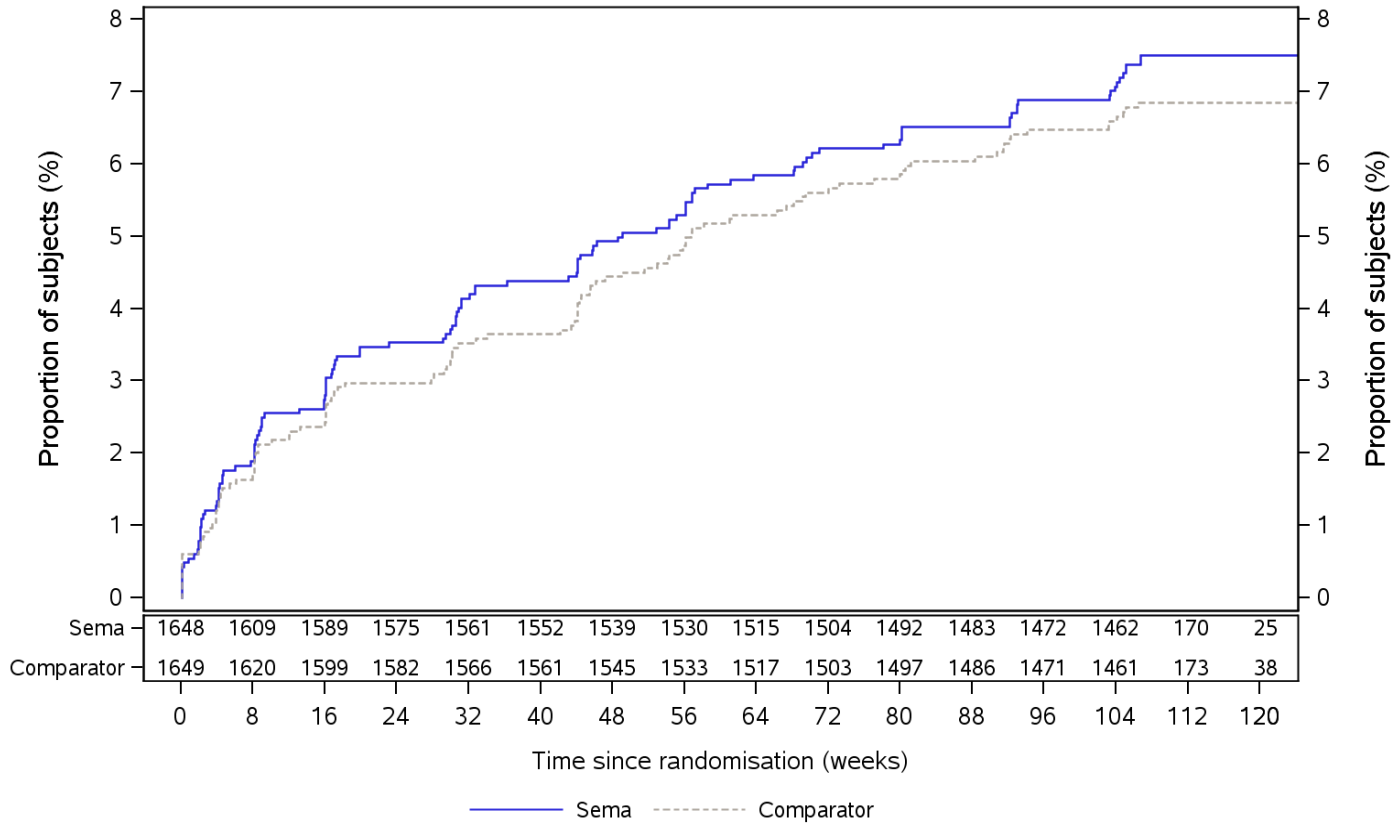
121 Moderate adverse events - system organ class "Injury, poisoning and procedural complications" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:27:49 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ippc_ae_mo_s6.png

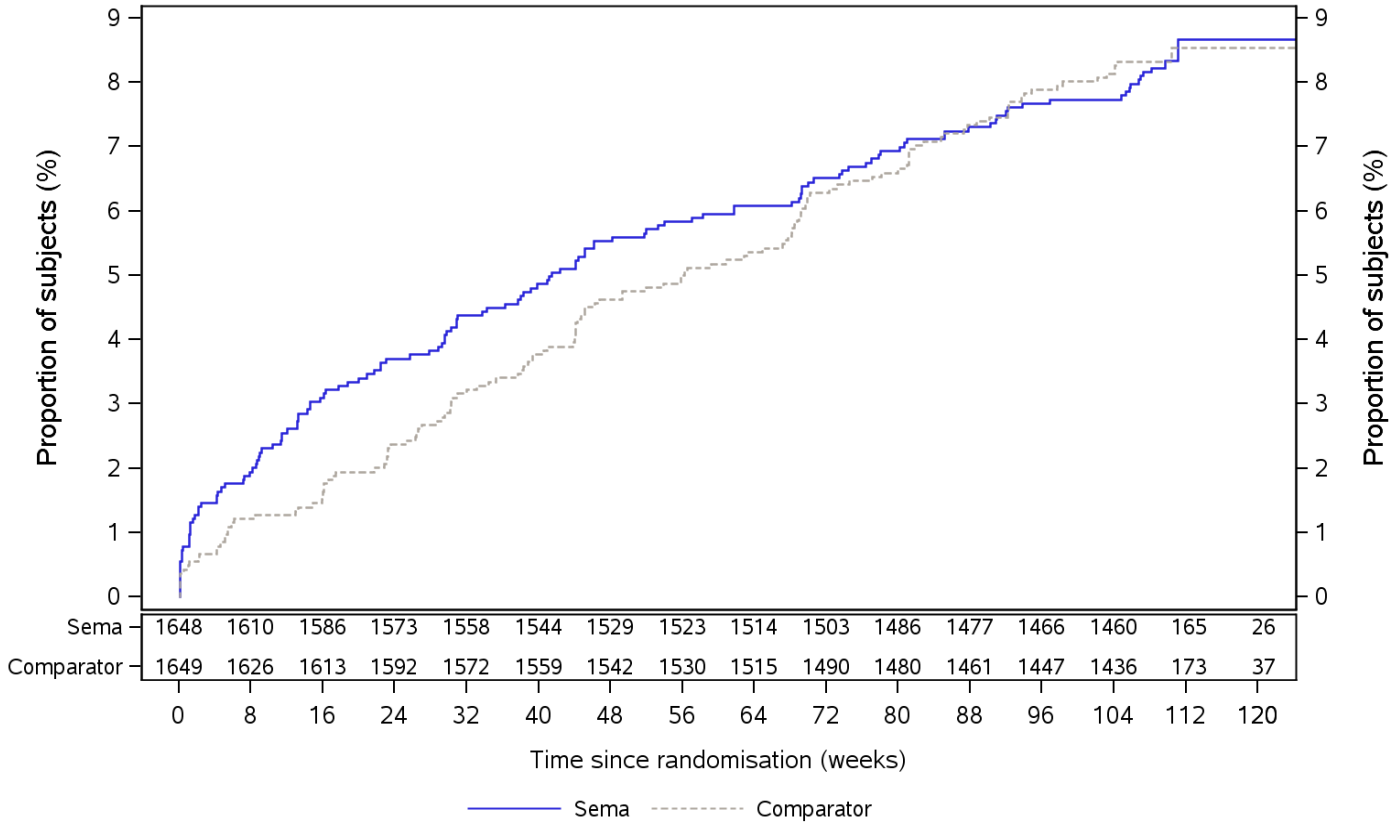
122 Moderate adverse events - system organ class "Investigations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:28:07 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_investig_ae_mo_s6.png

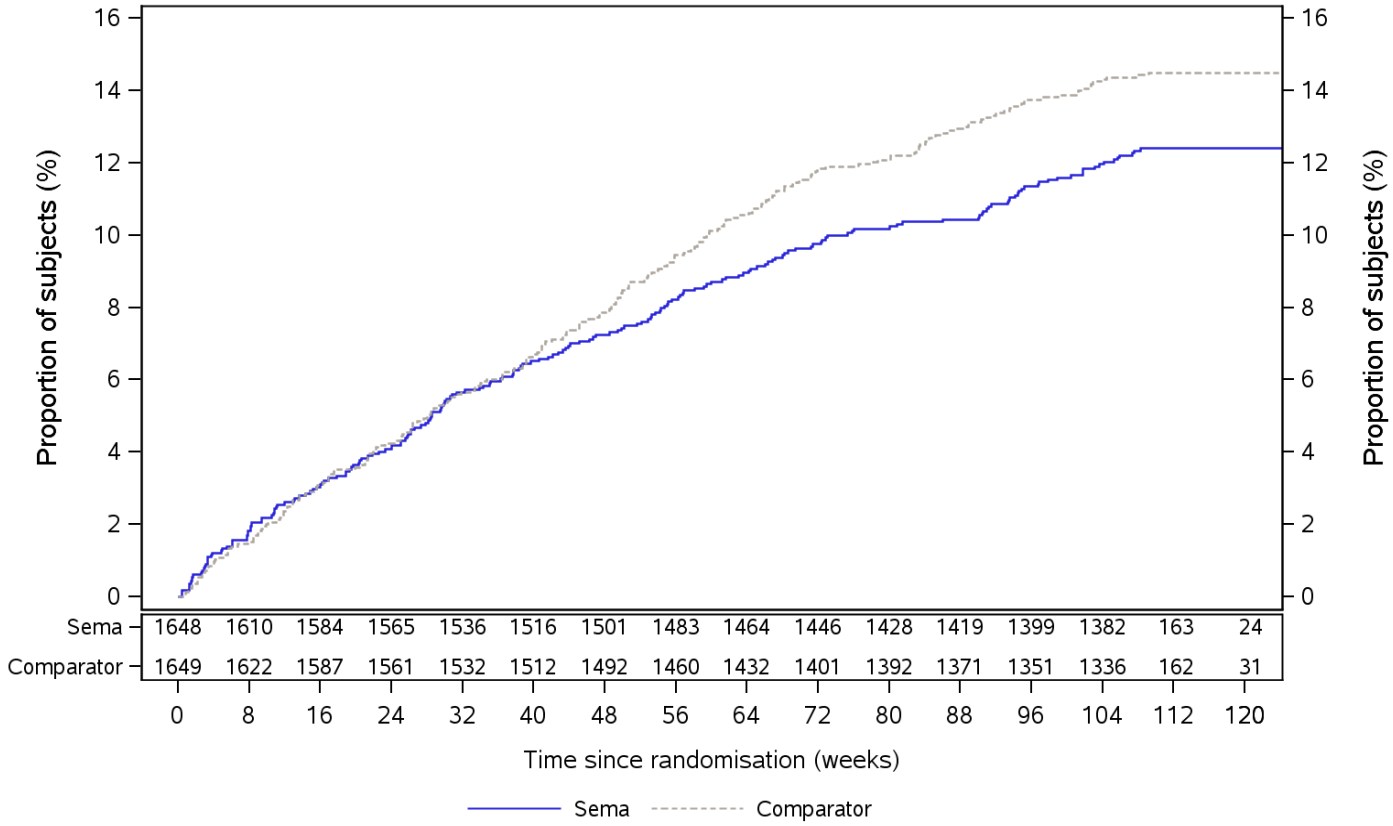
123 Moderate adverse events - system organ class "Metabolism and nutrition disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:28:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_mnd_ae_mo_s6.png

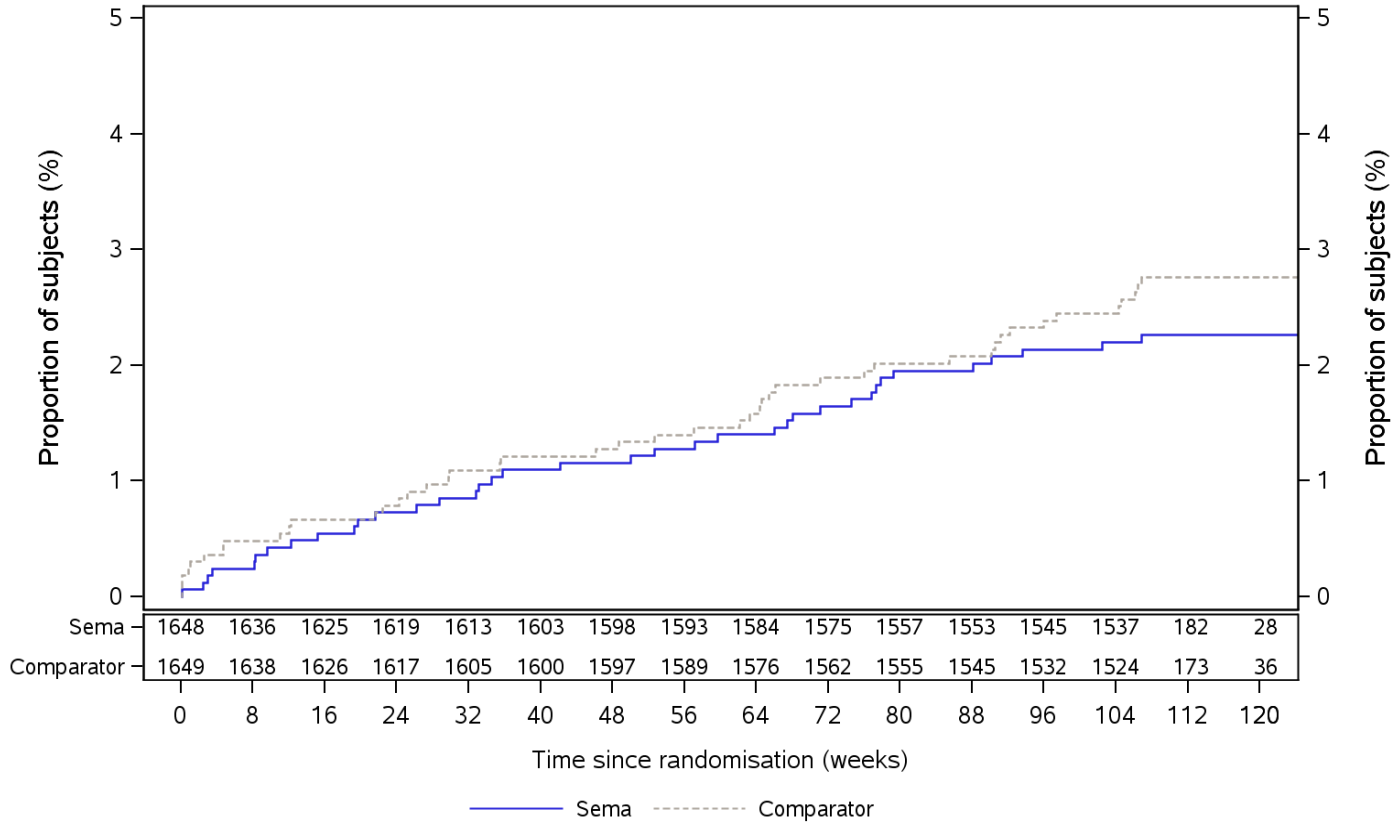
124 Moderate adverse events - system organ class "Musculoskeletal and connective tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:28:44 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_mctd_ae_mo_s6.png

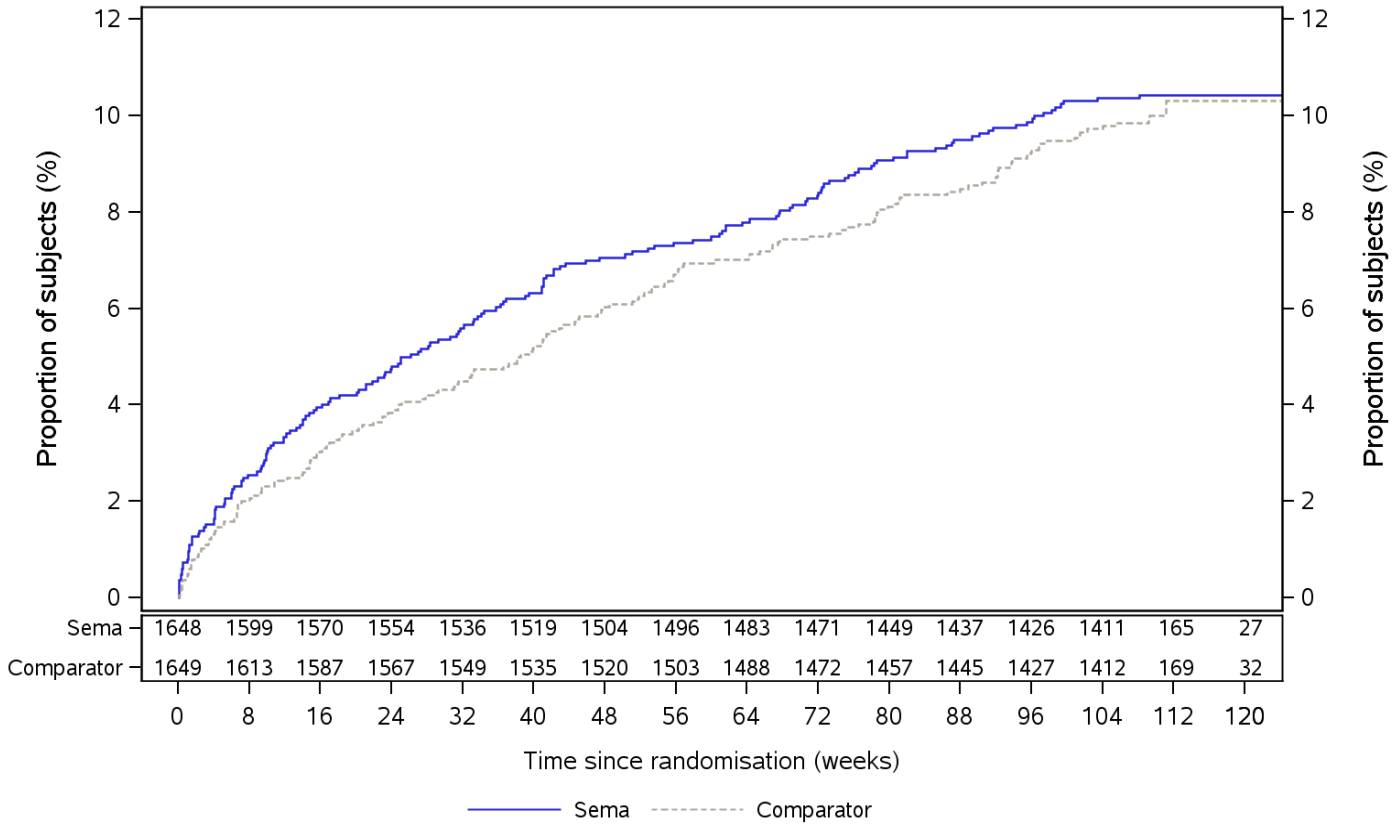
125 Moderate adverse events - system organ class "Neoplasms benign, malignant and unspecified (incl cysts and polyps)" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:29:03 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_nbmu_ae_mo_s6.png

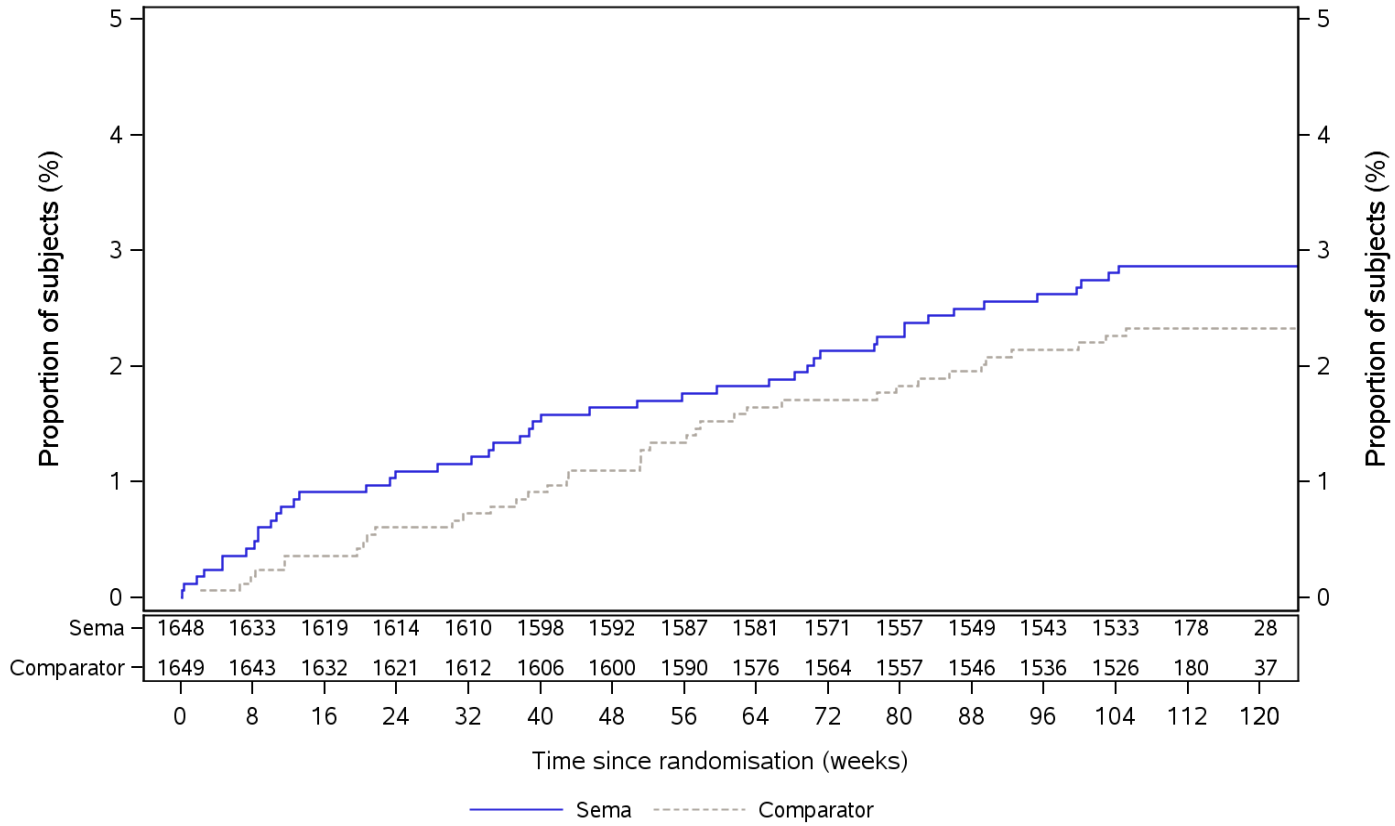
126 Moderate adverse events - system organ class "Nervous system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:29:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_nsd_ae_mo_s6.png

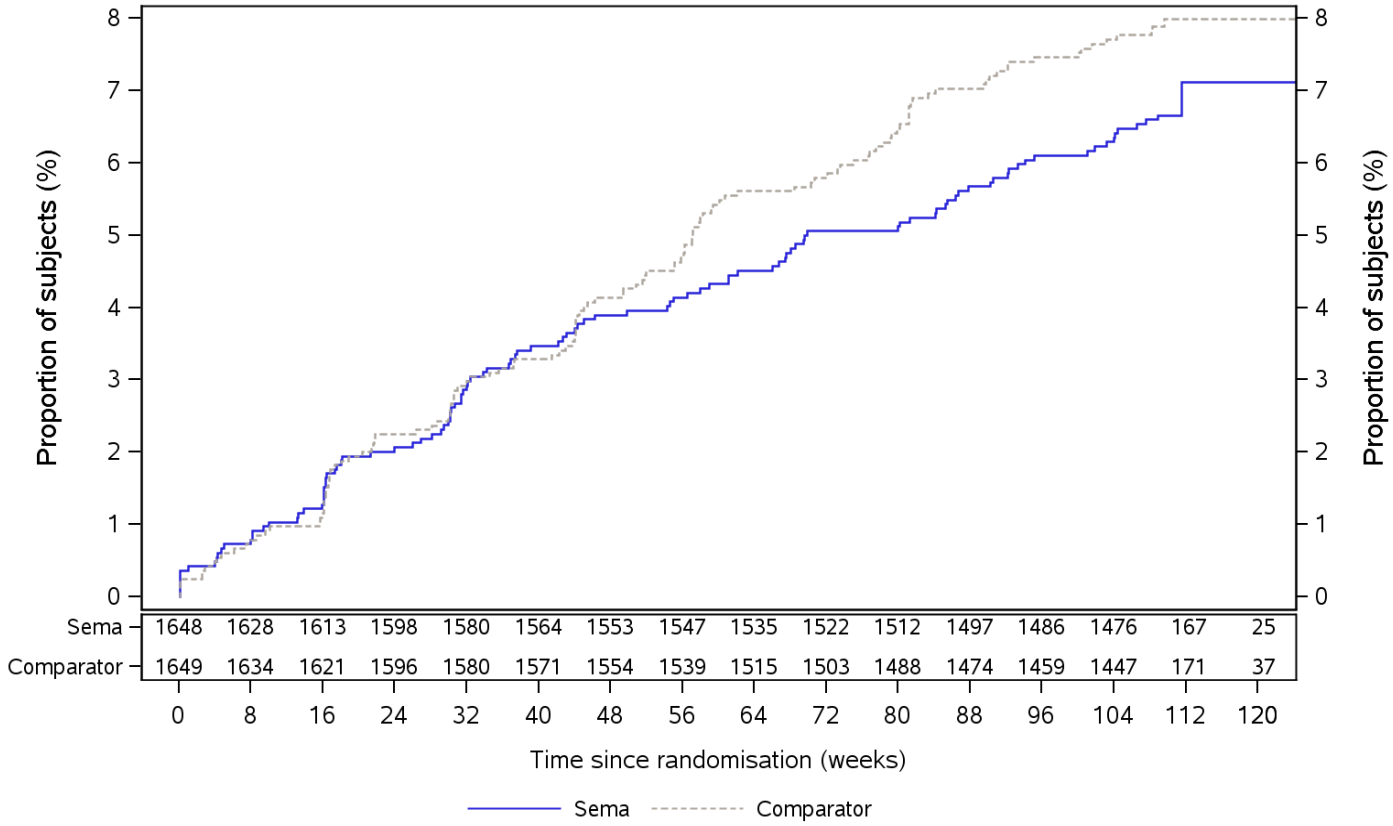
127 Moderate adverse events - system organ class "Psychiatric disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:29:39 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_psycdiso_ae_mo_s6.png

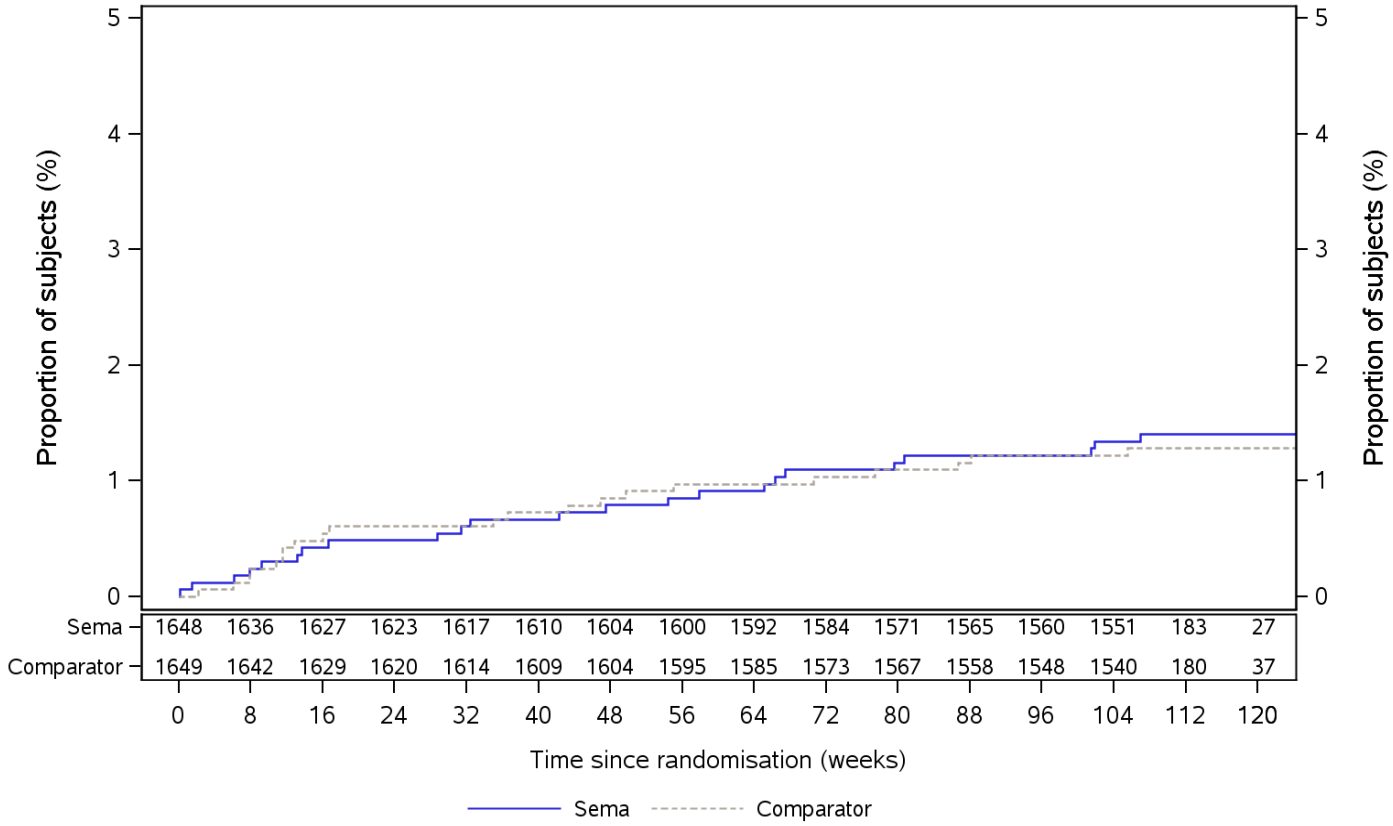
128 Moderate adverse events - system organ class "Renal and urinary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:29:57 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_rud_ae_mo_s6.png

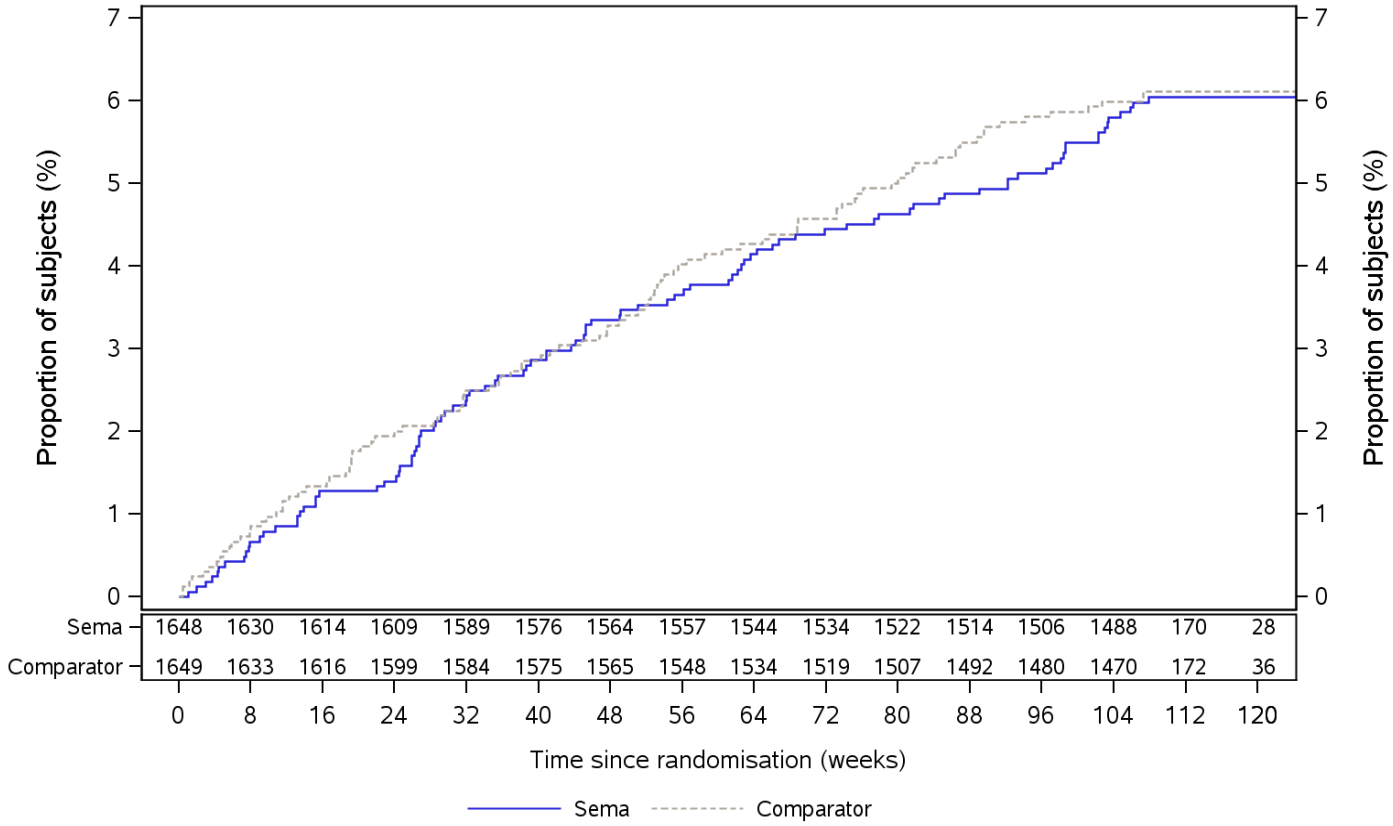
129 Moderate adverse events - system organ class "Reproductive system and breast disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:30:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_repsysand_ae_mo_s6.png

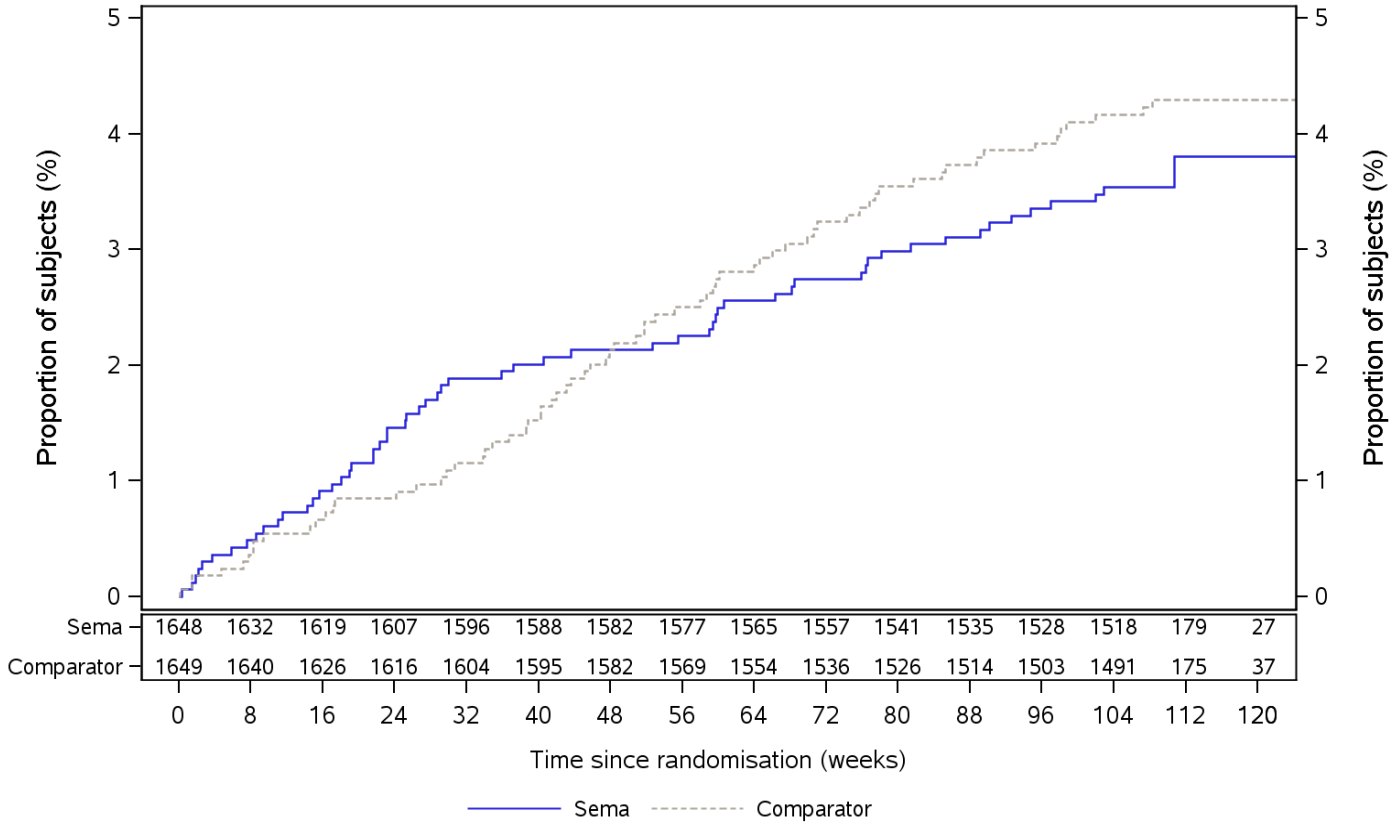
130 Moderate adverse events - system organ class "Respiratory, thoracic and mediastinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:30:34 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_rtmd_ae_mo_s6.png

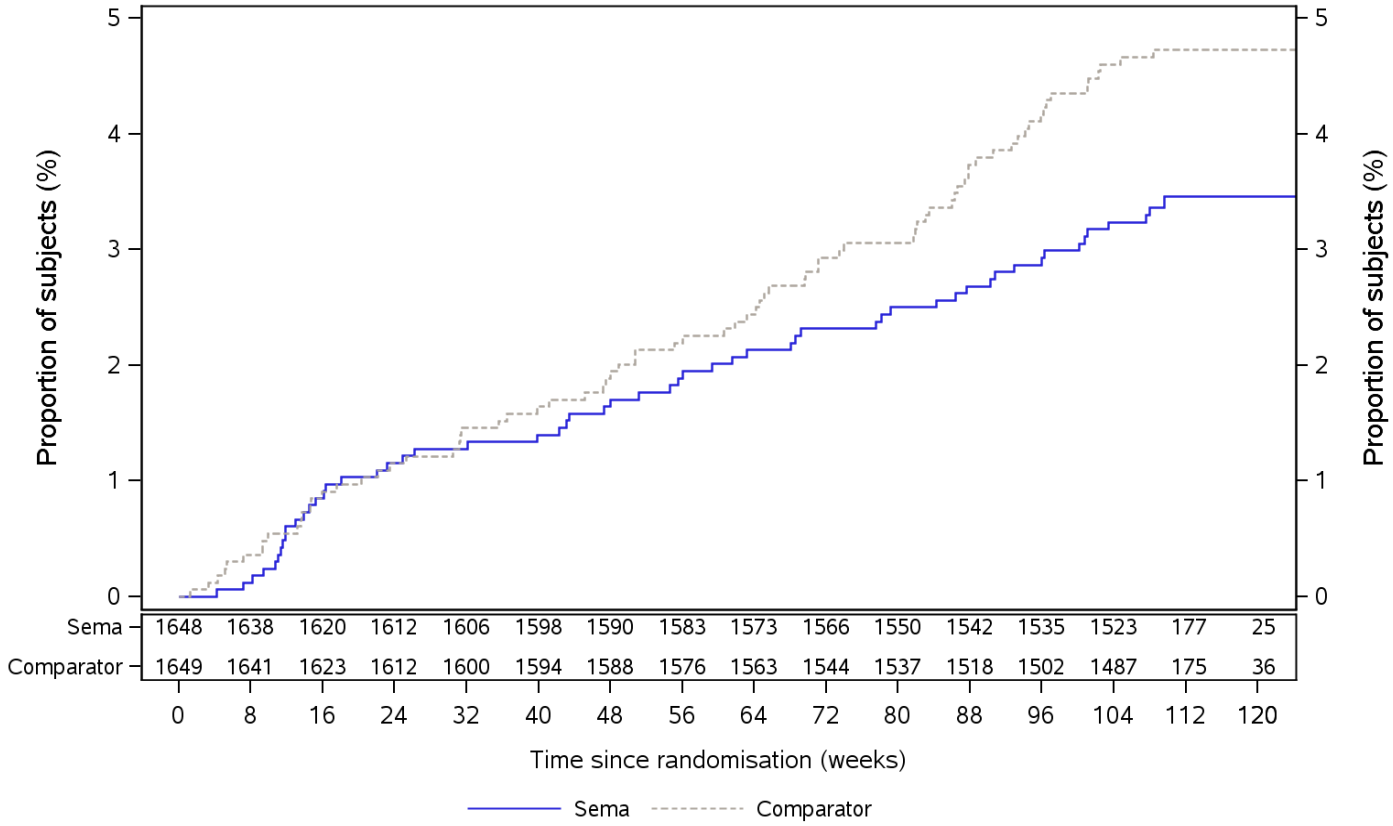
131 Moderate adverse events - system organ class "Skin and subcutaneous tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:30:52 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_sstd_ae_mo_s6.png

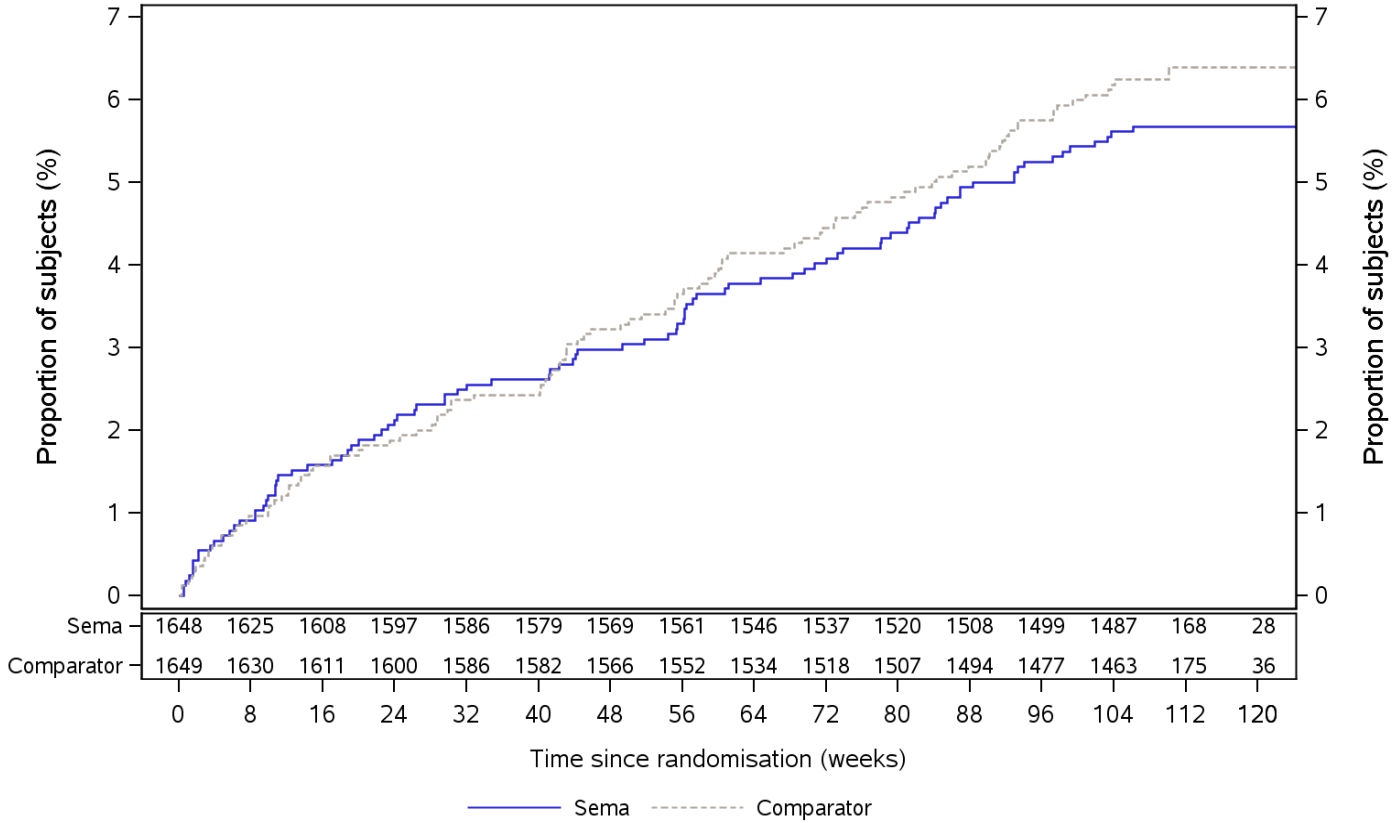
132 Moderate adverse events - system organ class "Surgical and medical procedures" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:31:11 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_smp_ae_mo_s6.png

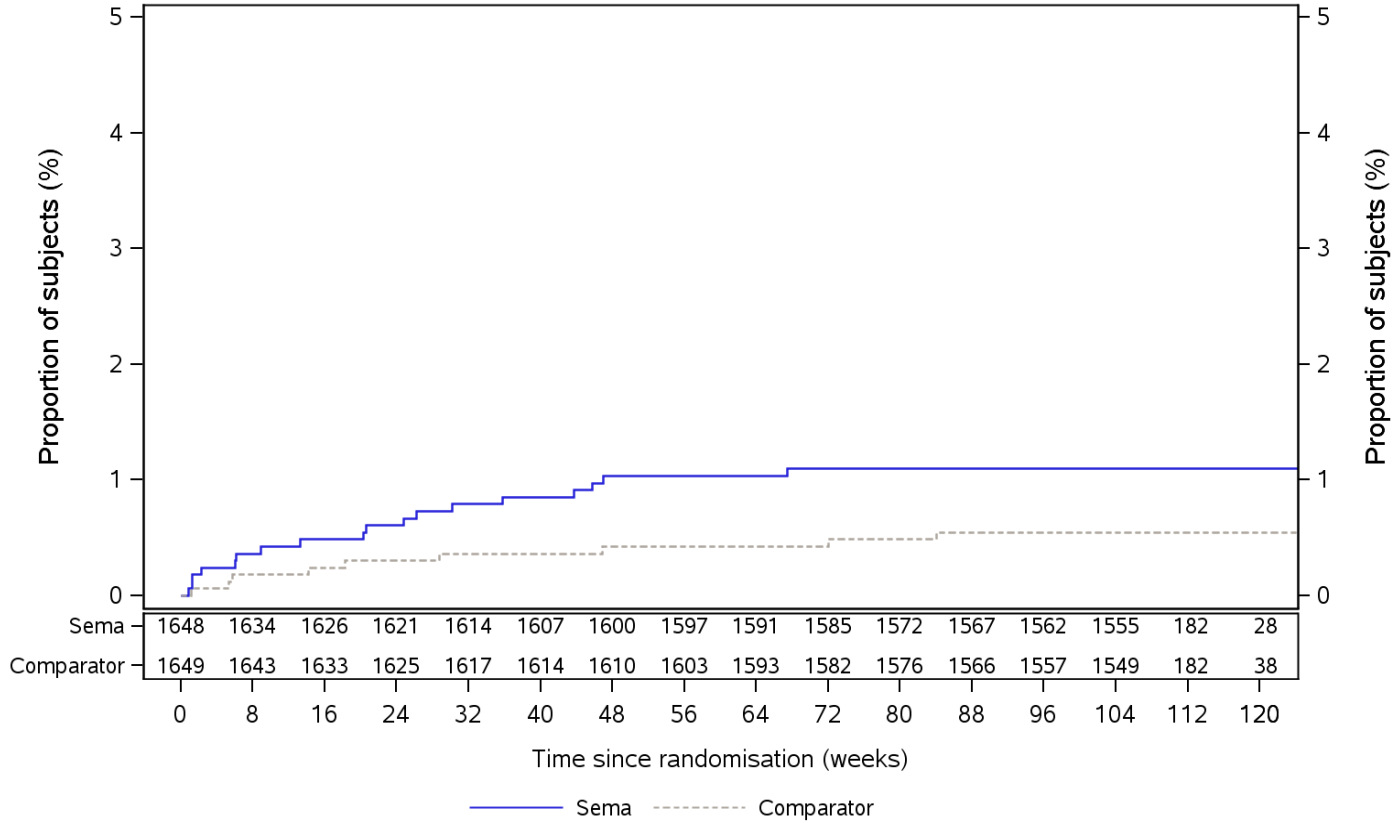
133 Moderate adverse events - system organ class "Vascular disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:31:29 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_vd_ae_mo_s6.png

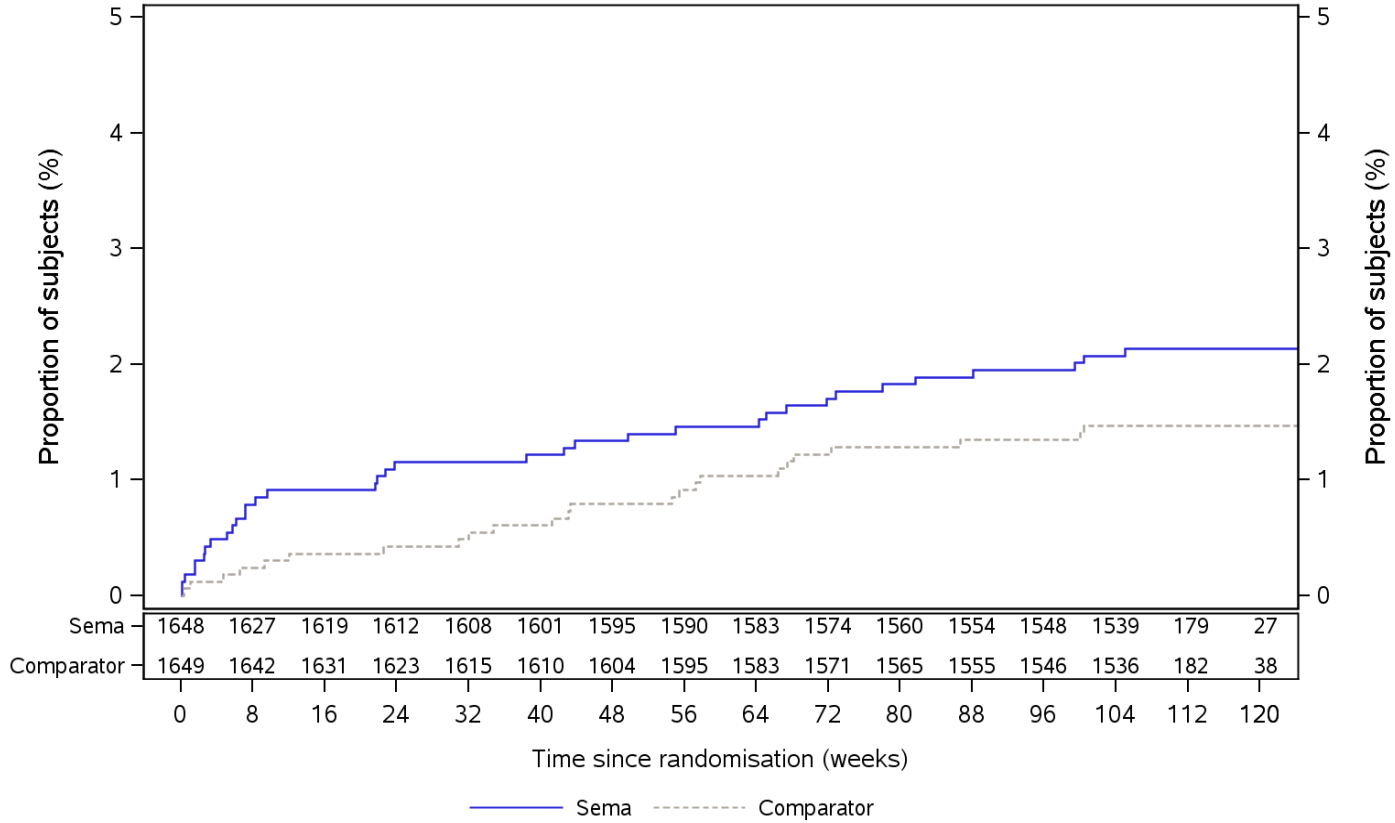
134 Moderate adverse events - preferred term "Abdominal discomfort" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:31:48 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdodisc_ae_mo_s6.png

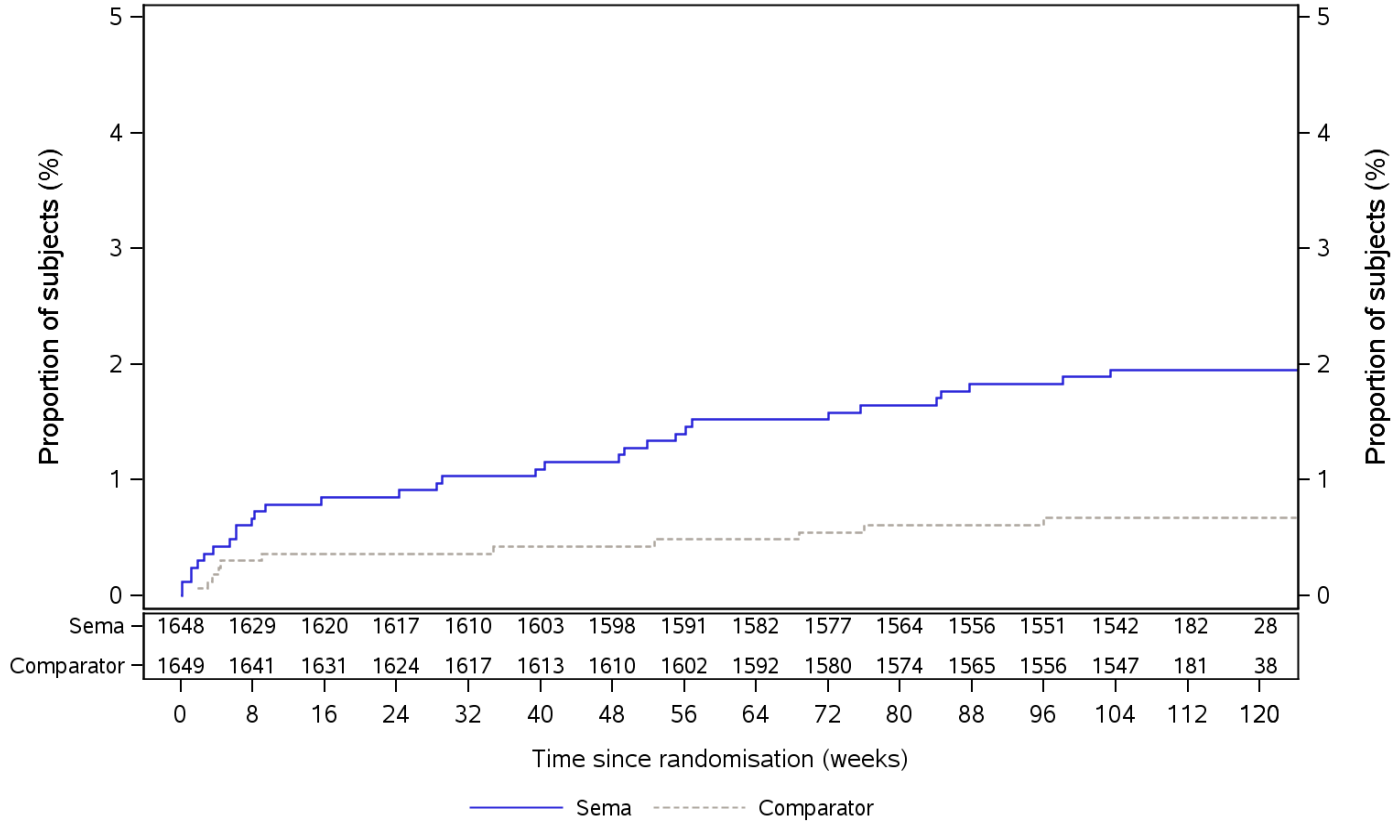
135 Moderate adverse events - preferred term "Abdominal pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:32:07 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdopain_ae_mo_s6.png

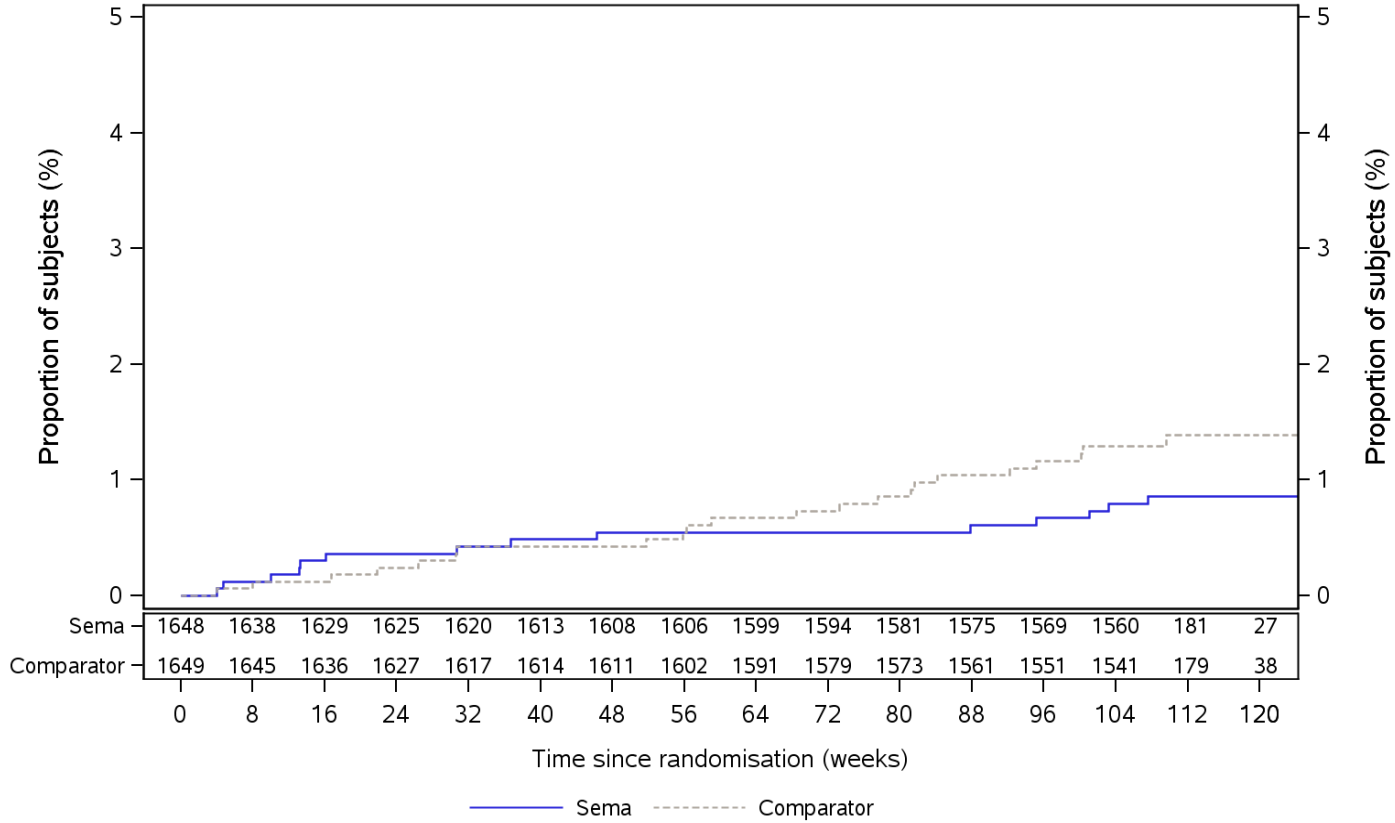
136 Moderate adverse events - preferred term "Abdominal pain upper" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:32:26 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_abdpaiupp_ae_mo_s6.png

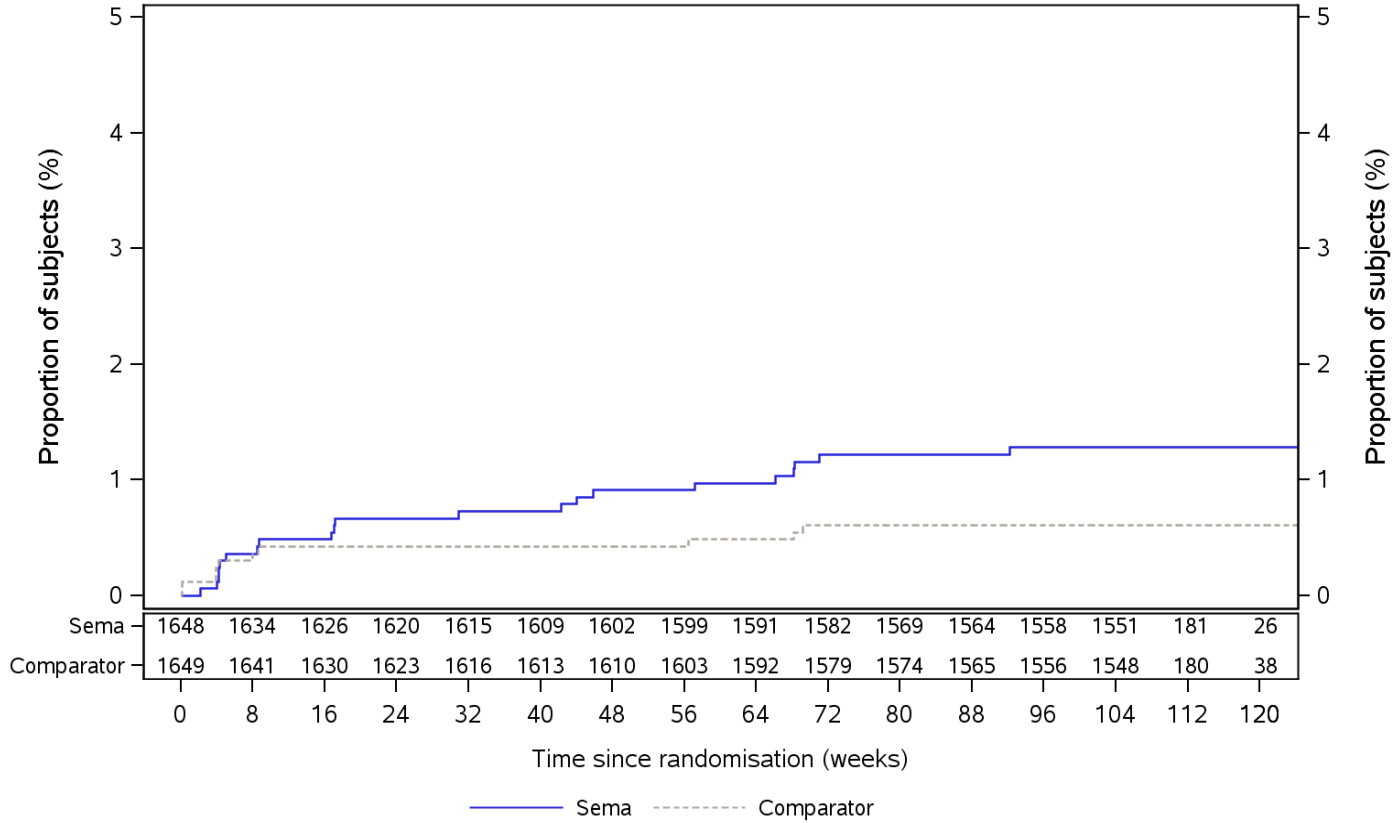
137 Moderate adverse events - preferred term "Acute kidney injury" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:32:44 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_aki_ae_mo_s6.png

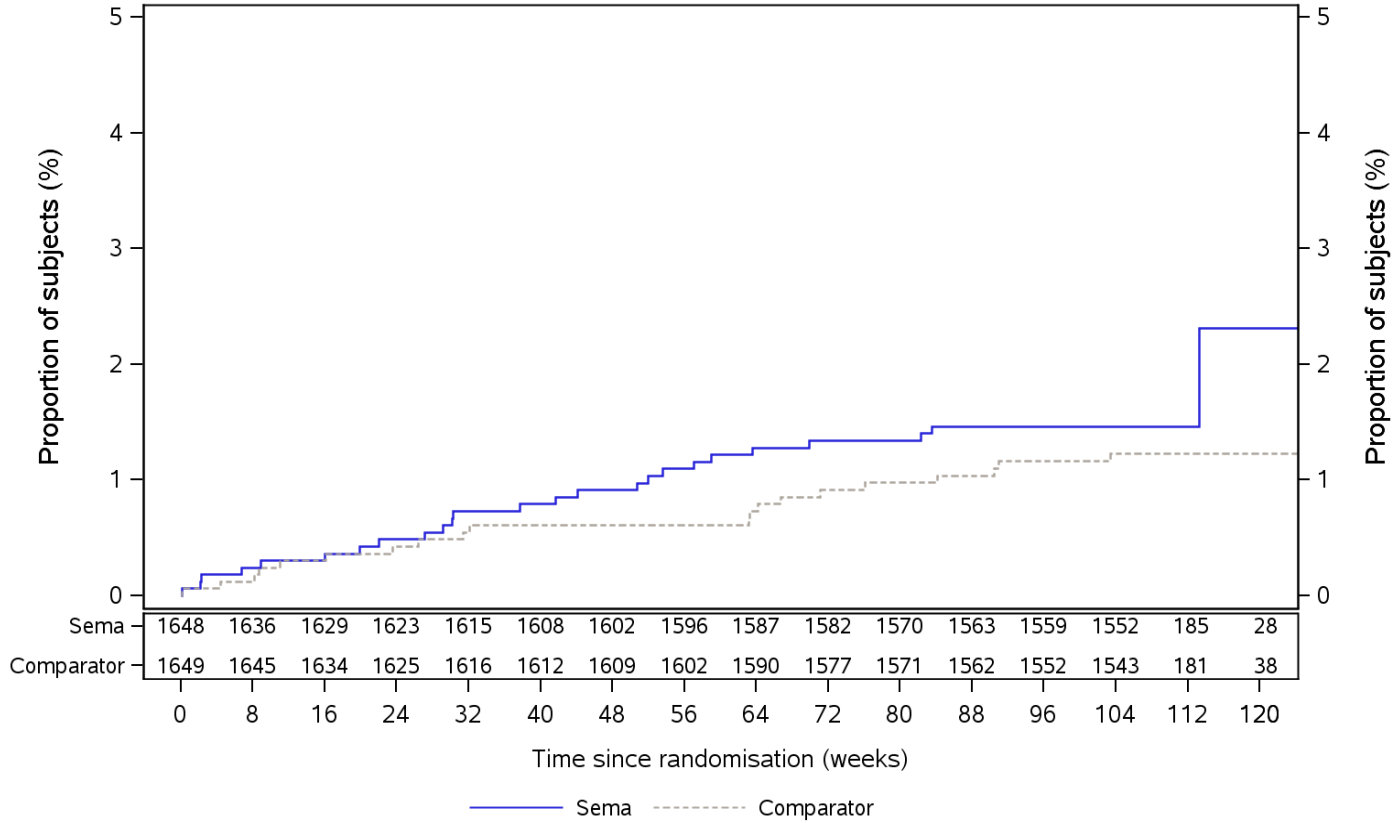
138 Moderate adverse events - preferred term "Amylase increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:33:03 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_amylincr_ae_mo_s6.png

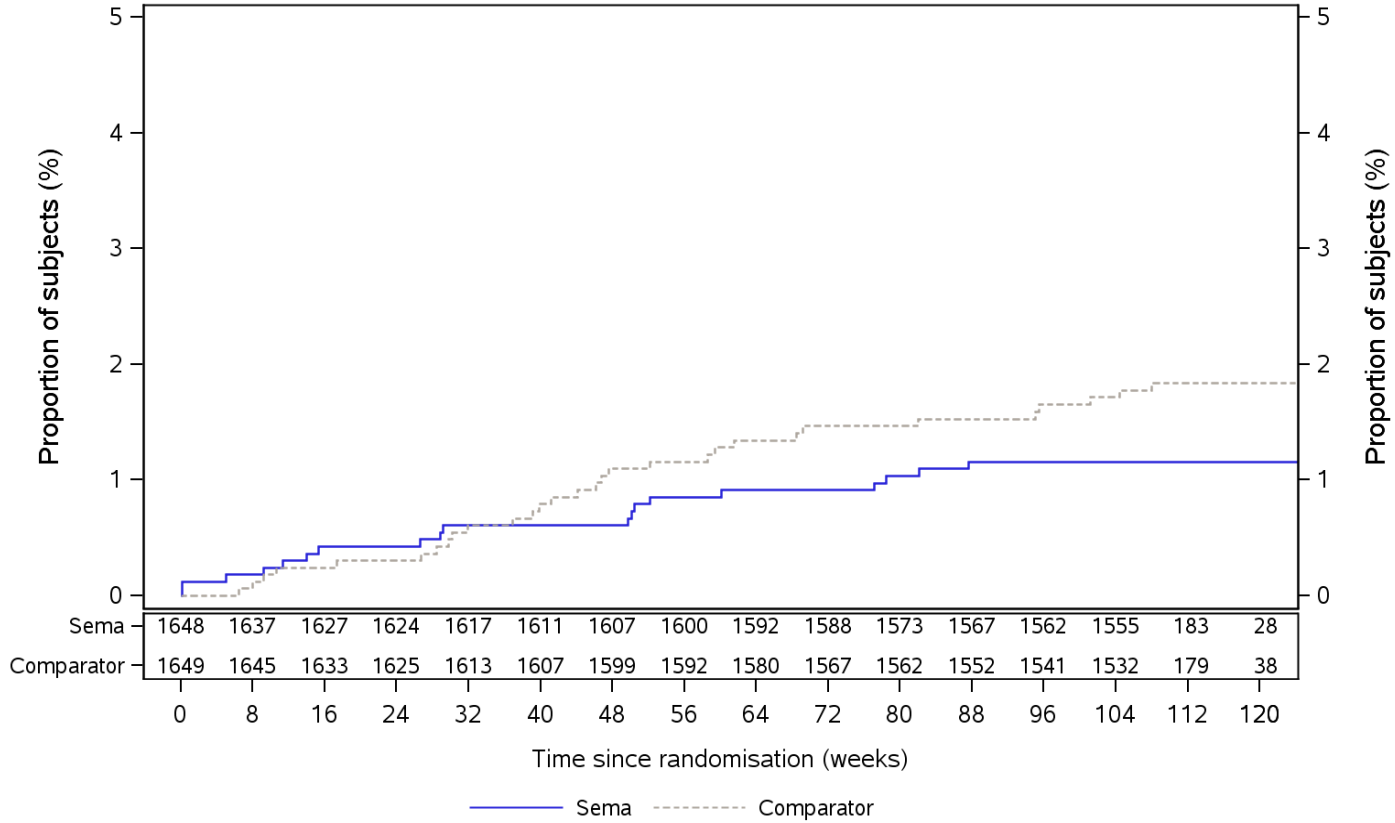
139 Moderate adverse events - preferred term "Anaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:33:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_anaemia_ae_mo_s6.png

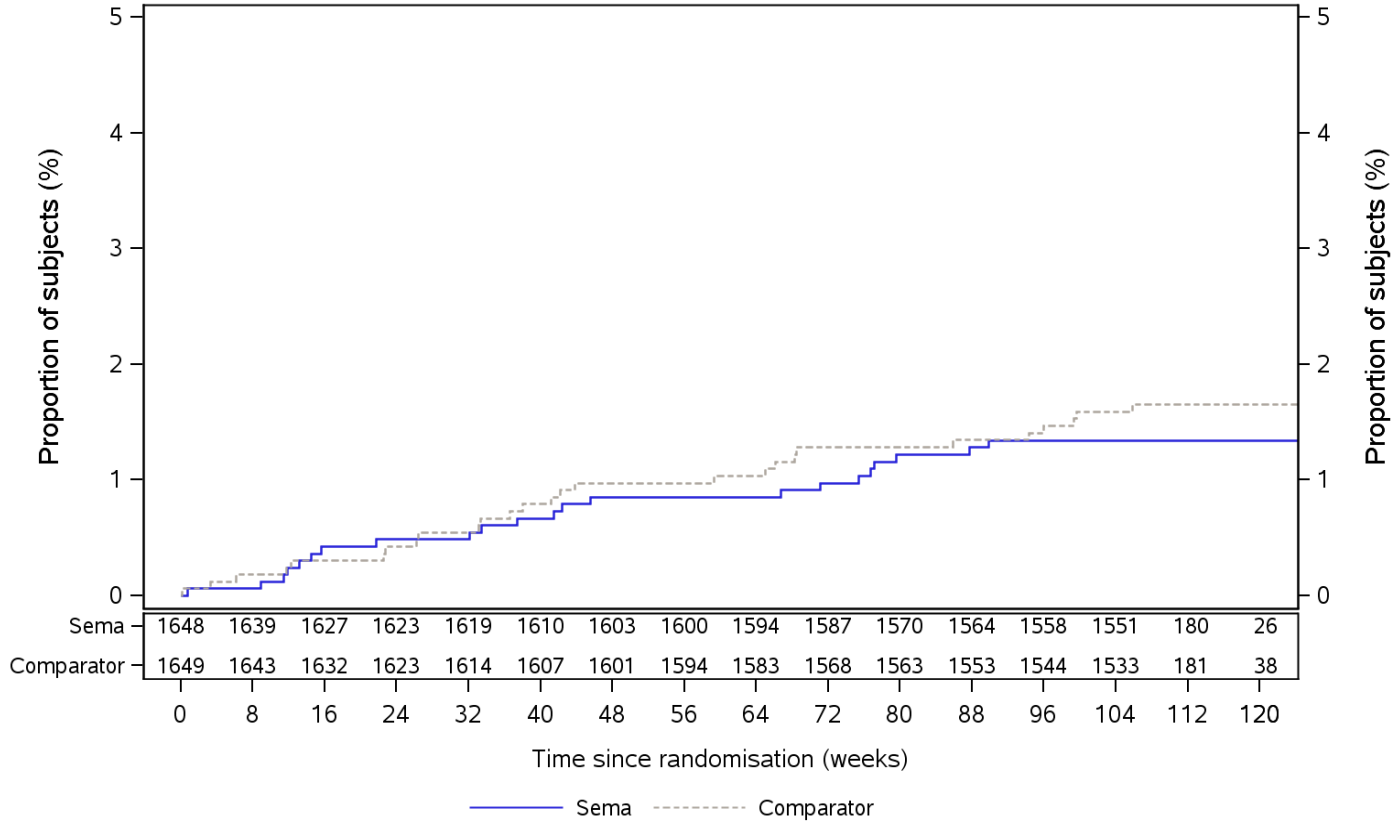
140 Moderate adverse events - preferred term "Angina pectoris" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:33:40 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_ap_ae_mo_s6.png

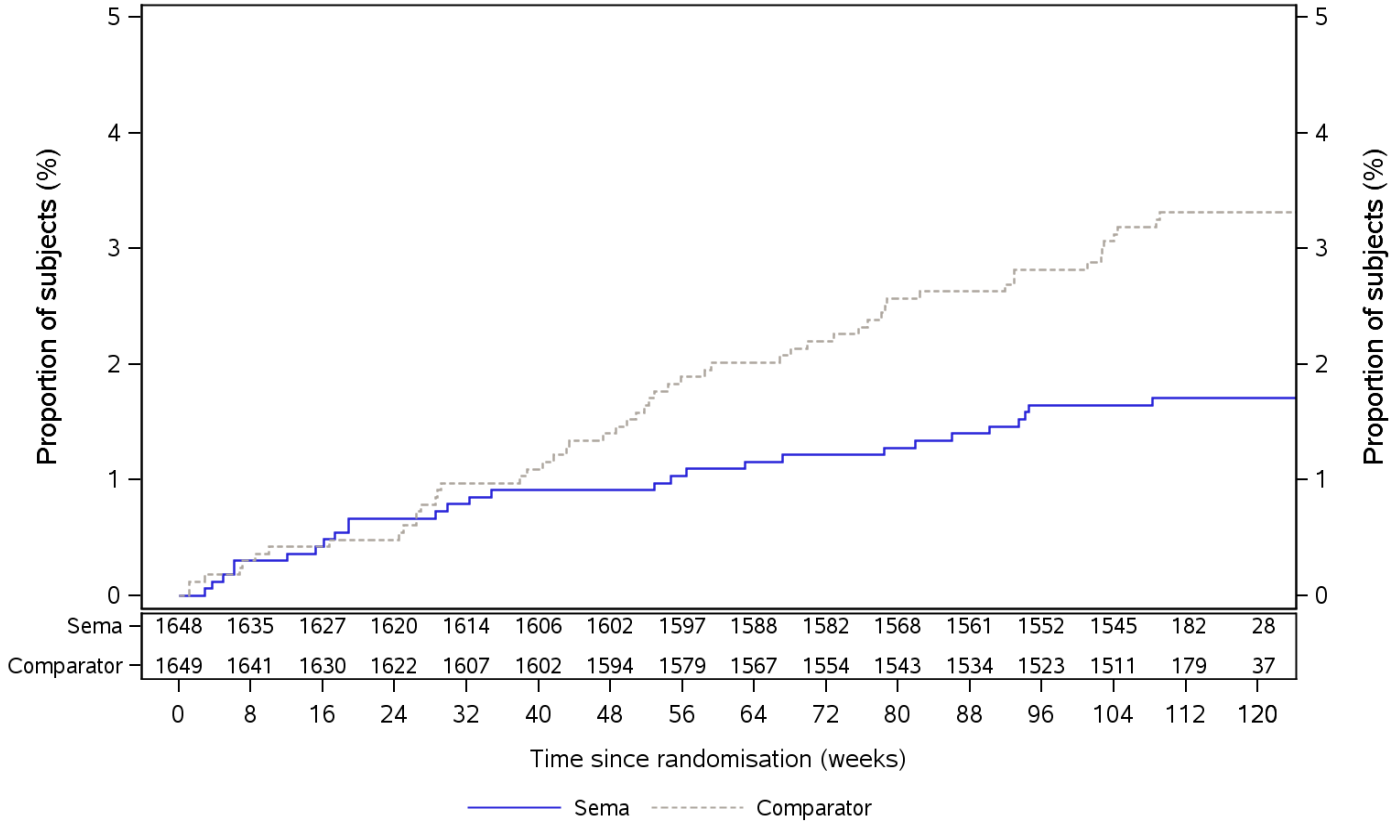
141 Moderate adverse events - preferred term "Angina unstable" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:33:58 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_au_ae_mo_s6.png

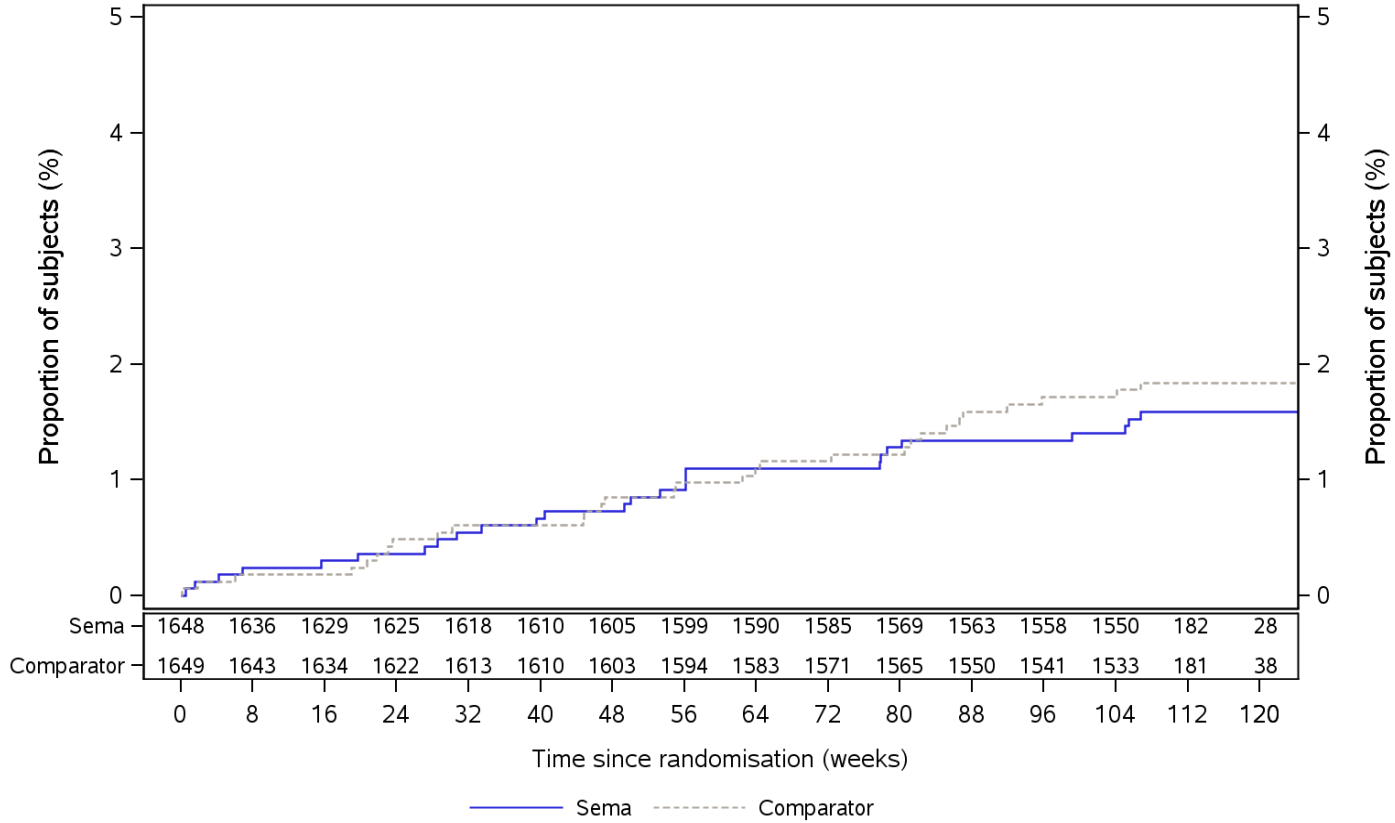
142 Moderate adverse events - preferred term "Arthralgia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:34:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_arthralg_ae_mo_s6.png

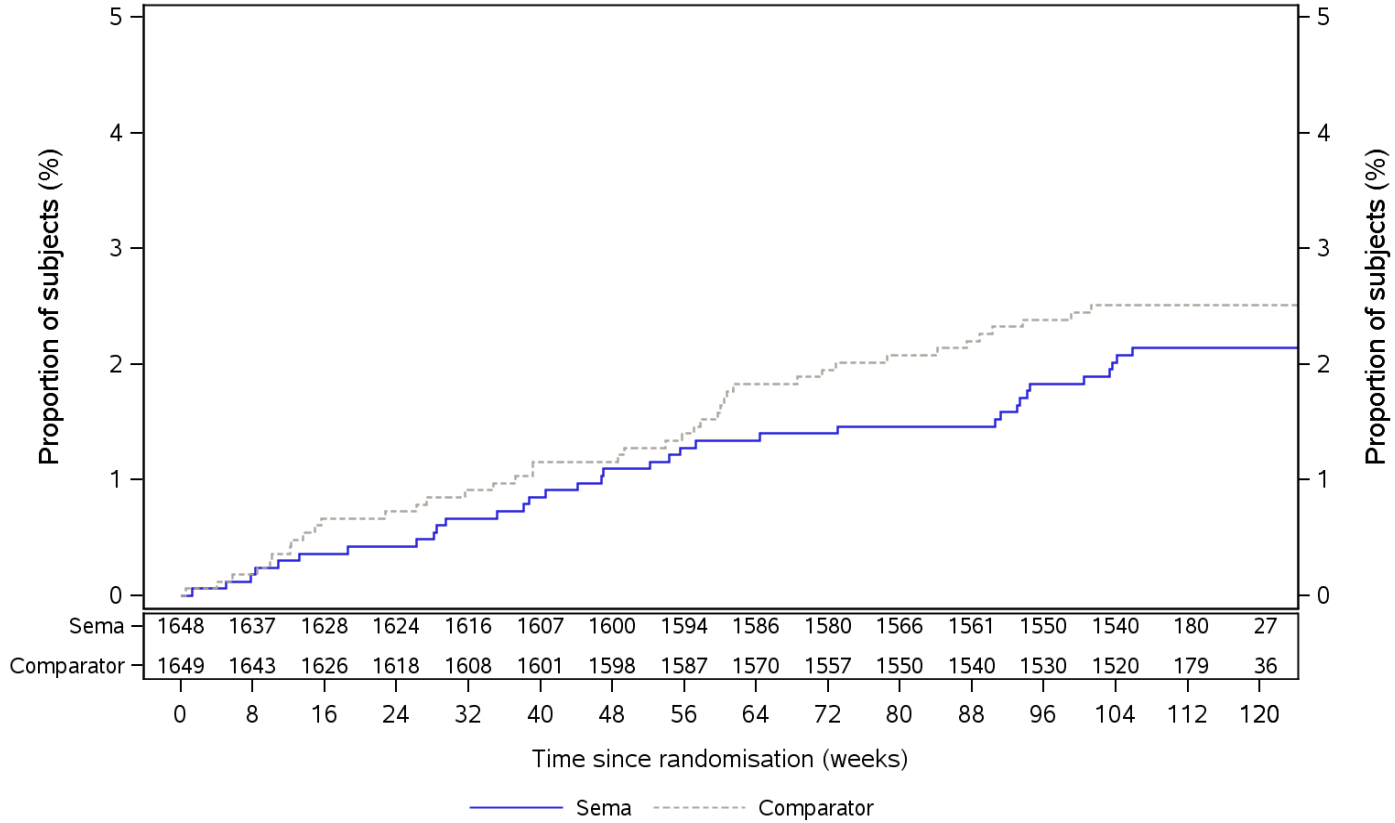
143 Moderate adverse events - preferred term "Atrial fibrillation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:34:35 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_af_ae_mo_s6.png

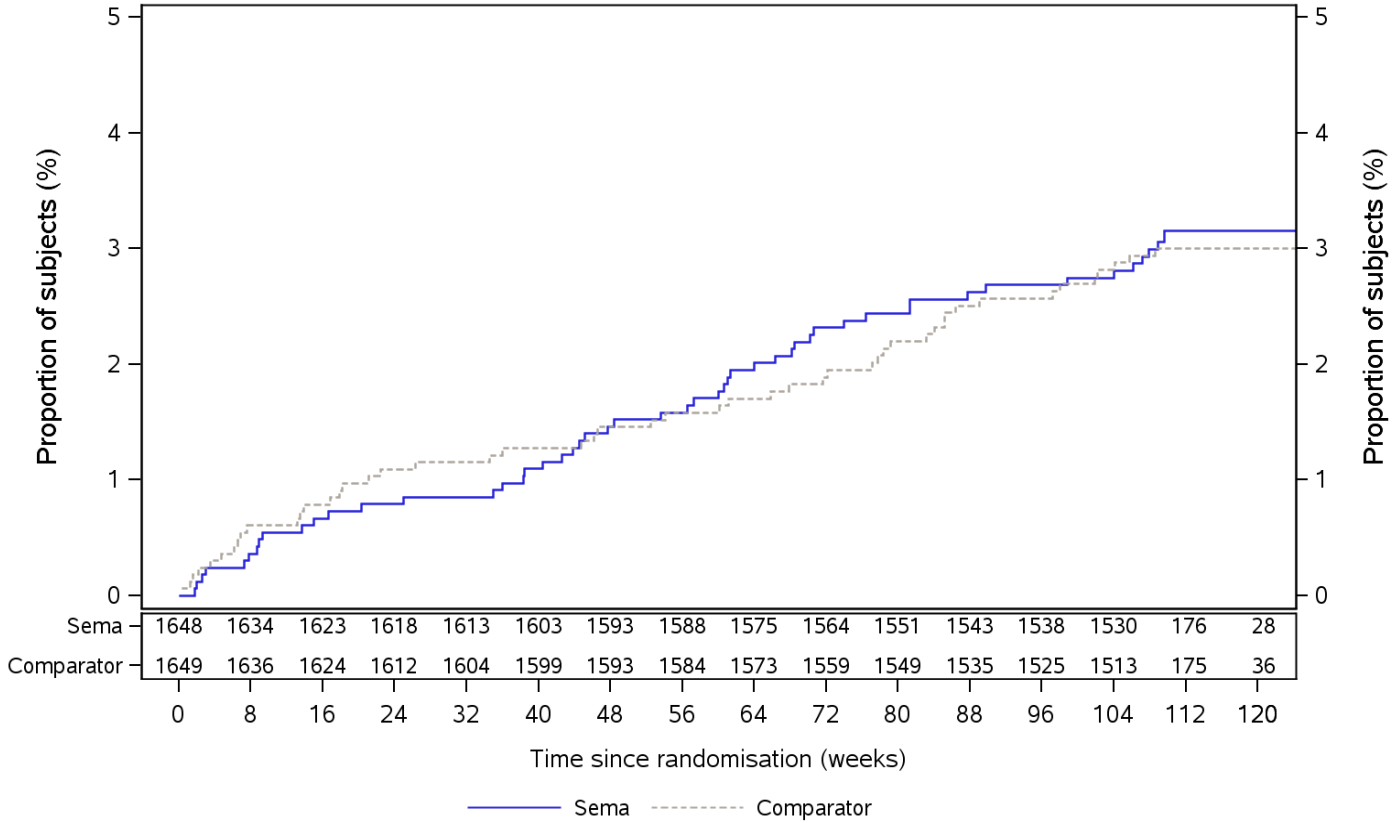
144 Moderate adverse events - preferred term "Back pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:34:54 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_backpain_ae_mo_s6.png

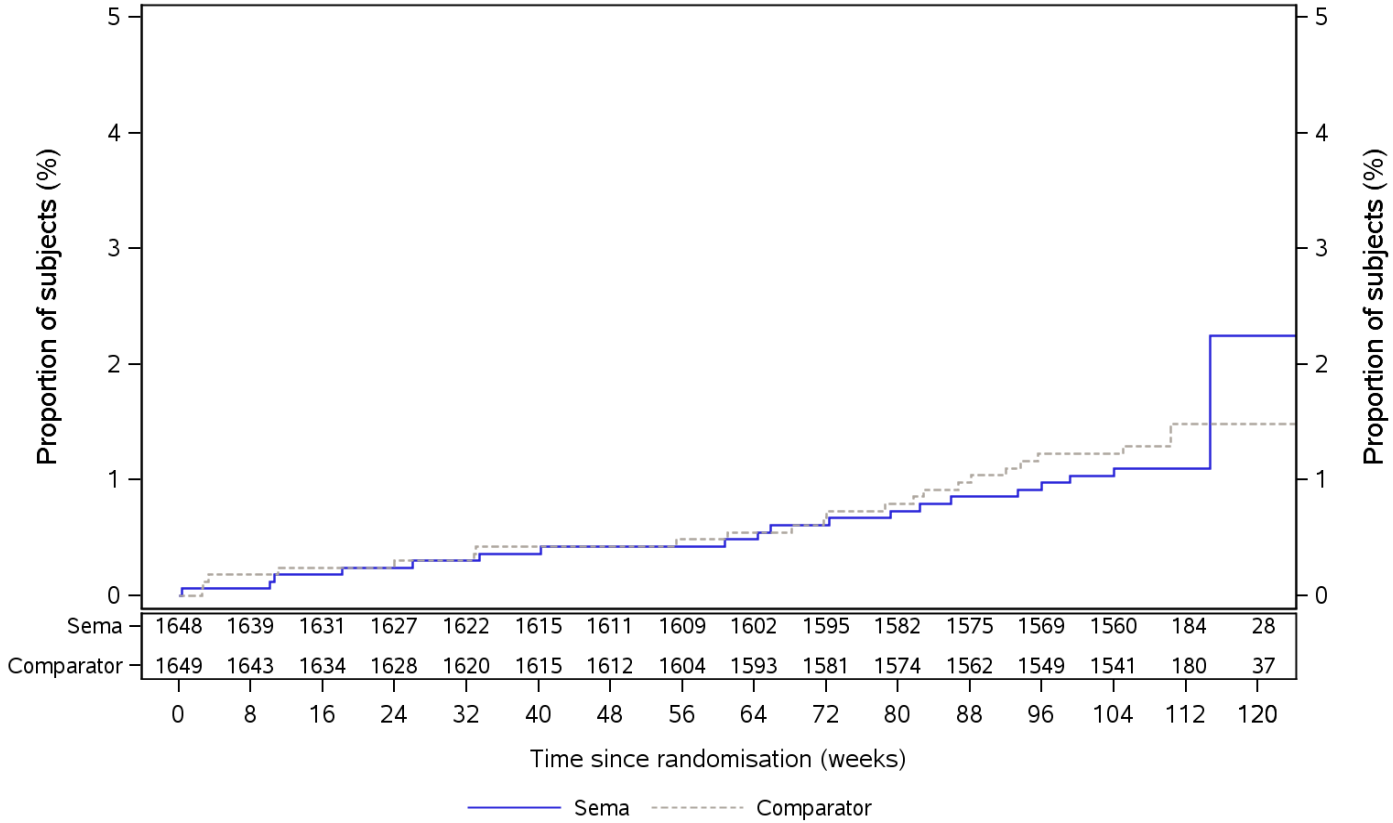
145 Moderate adverse events - preferred term "Bronchitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:35:13 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_bronchit_ae_mo_s6.png

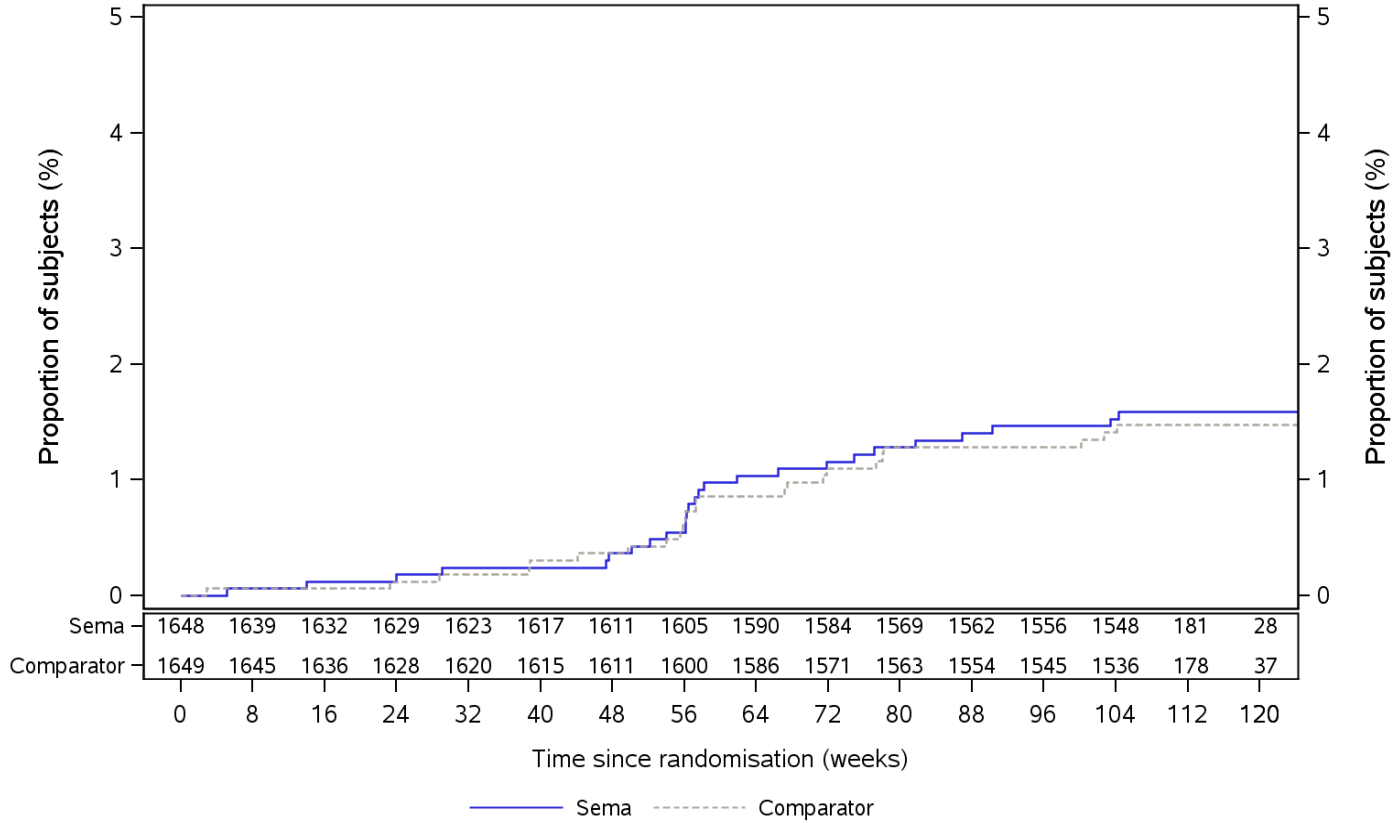
146 Moderate adverse events - preferred term "Cardiac failure congestive" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:35:32 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cfc_ae_mo_s6.png

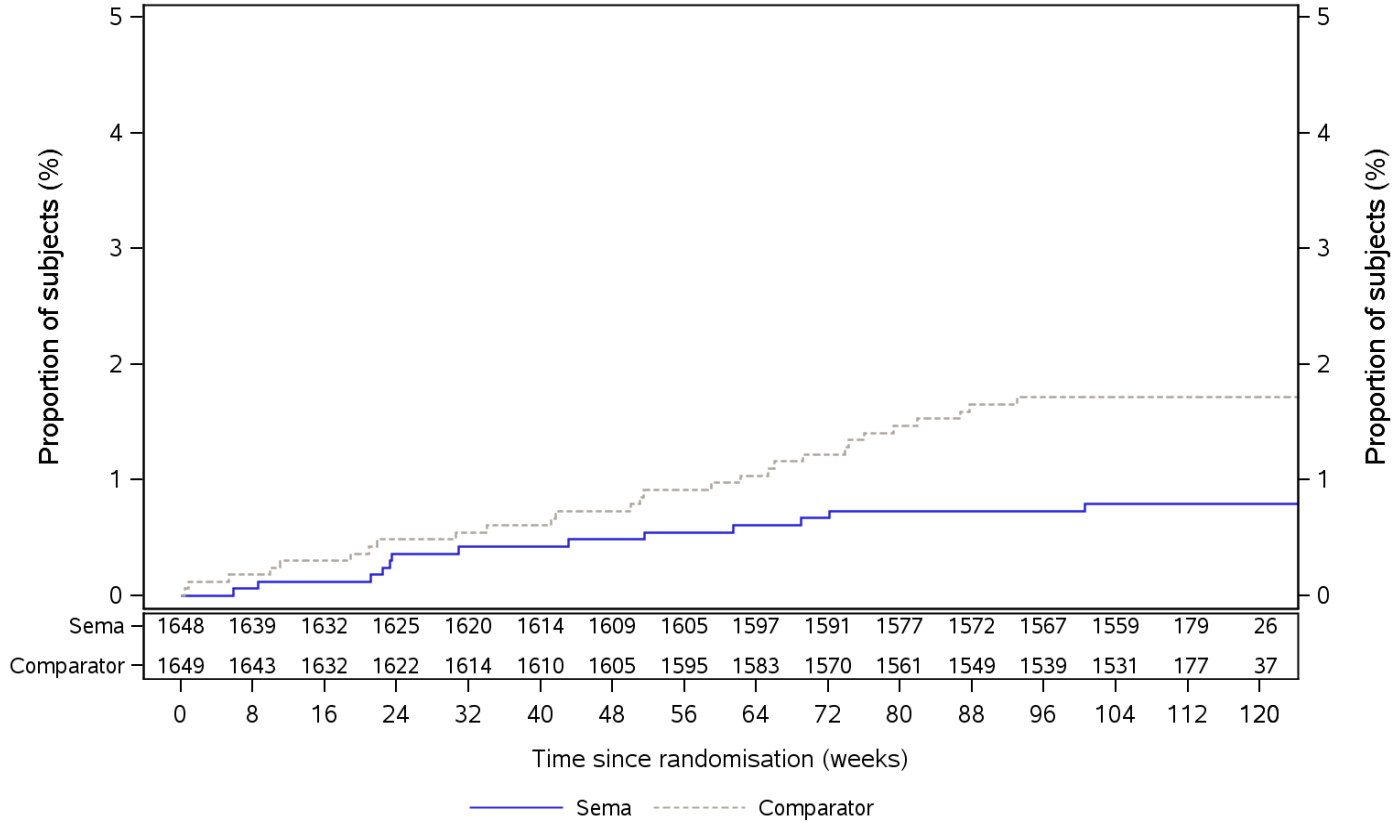
147 Moderate adverse events - preferred term "Cataract" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:35:51 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cataract_ae_mo_s6.png

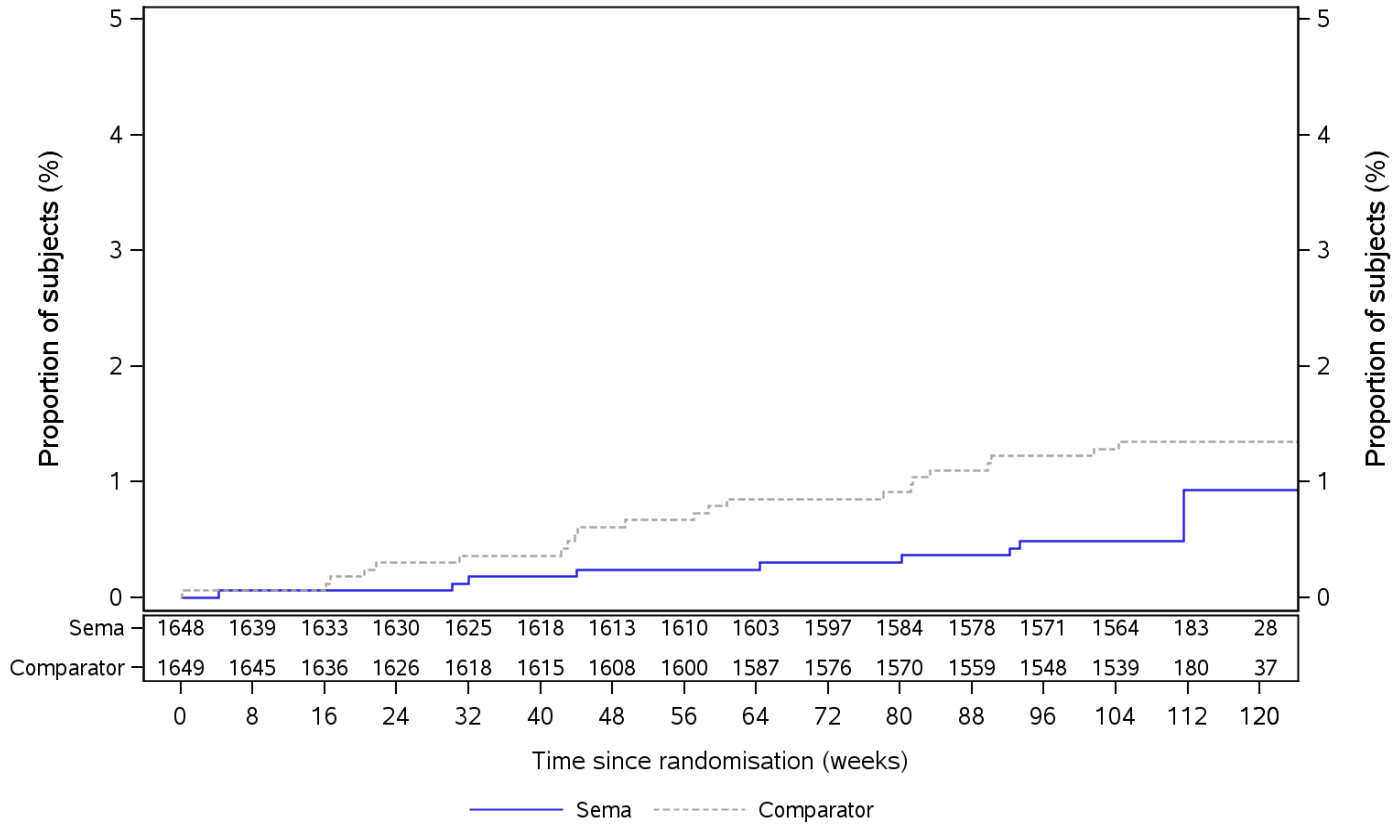
148 Moderate adverse events - preferred term "Cellulitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:36:10 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cellulit_ae_mo_s6.png

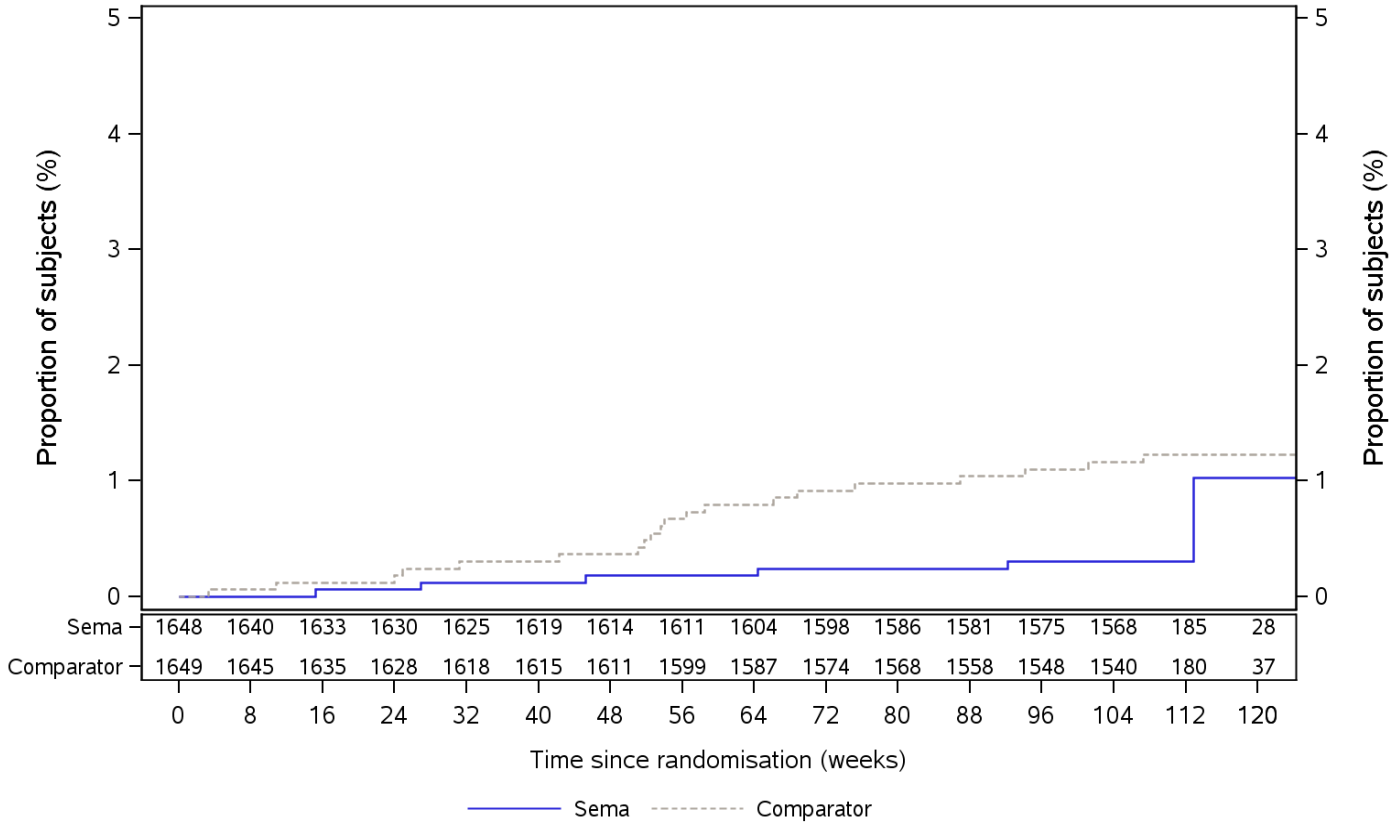
149 Moderate adverse events - preferred term "Chronic kidney disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:36:28 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_chrkiddis_ae_mo_s6.png

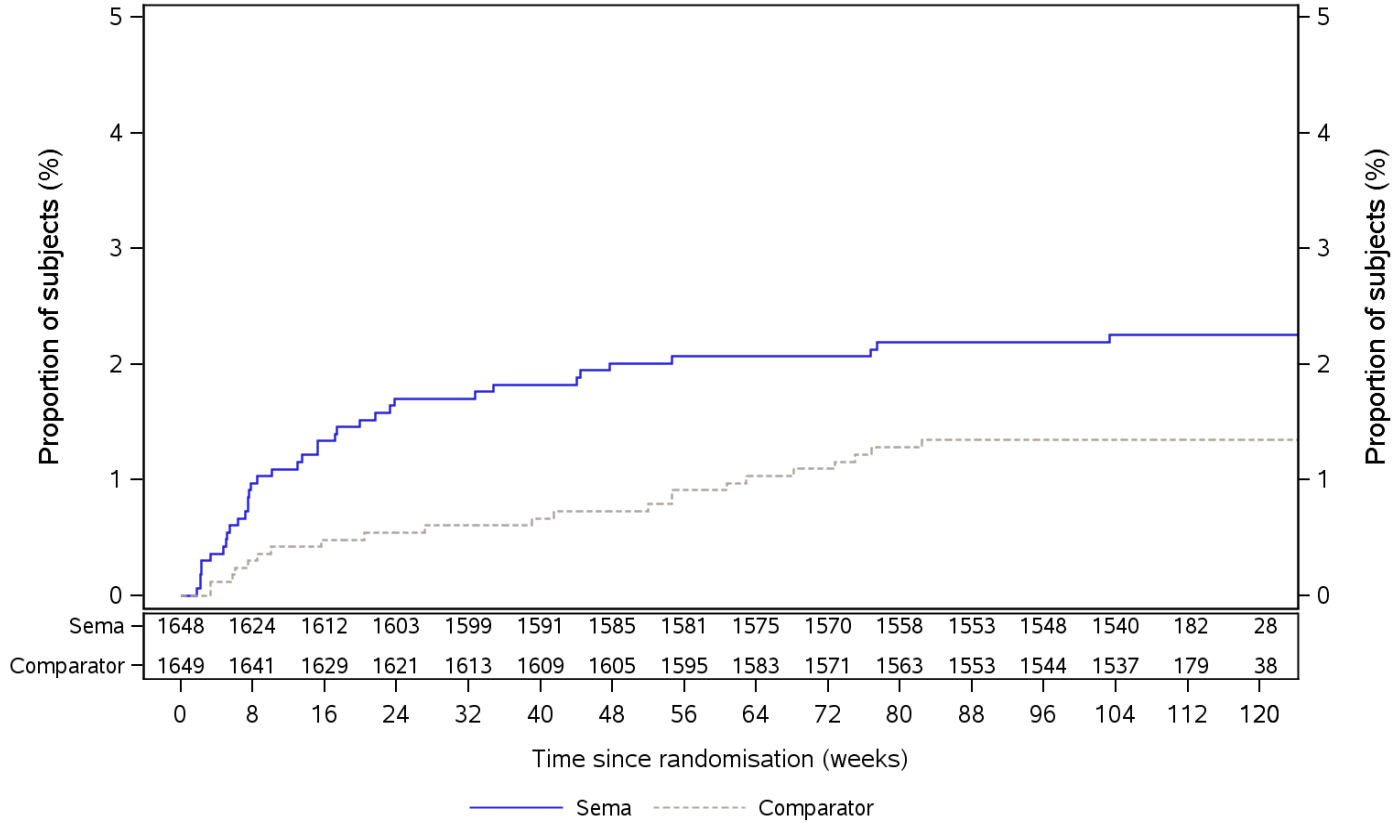
150 Moderate adverse events - preferred term "Chronic obstructive pulmonary disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:36:46 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_chrobspul_ae_mo_s6.png

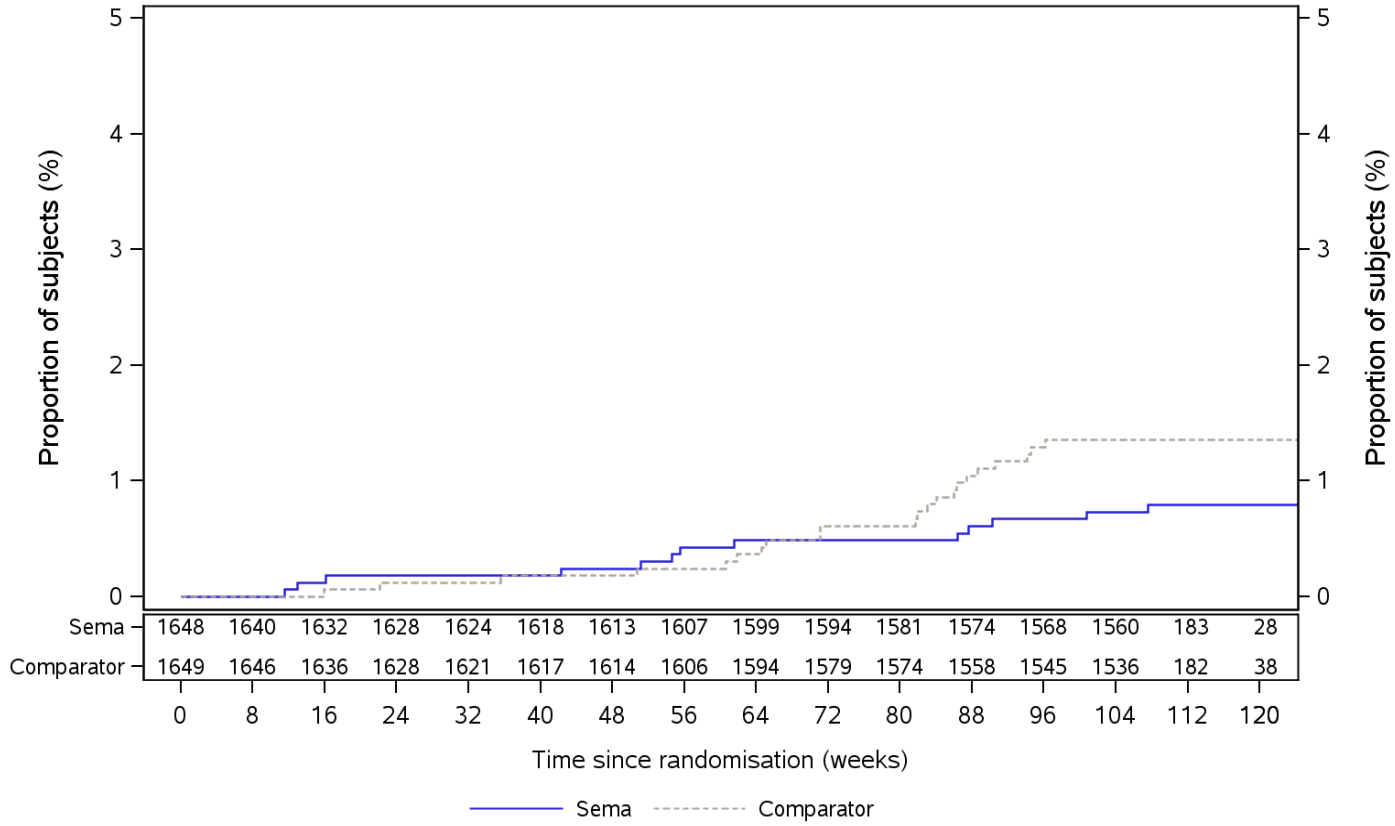
151 Moderate adverse events - preferred term "Constipation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:37:04 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_constipa_ae_mo_s6.png

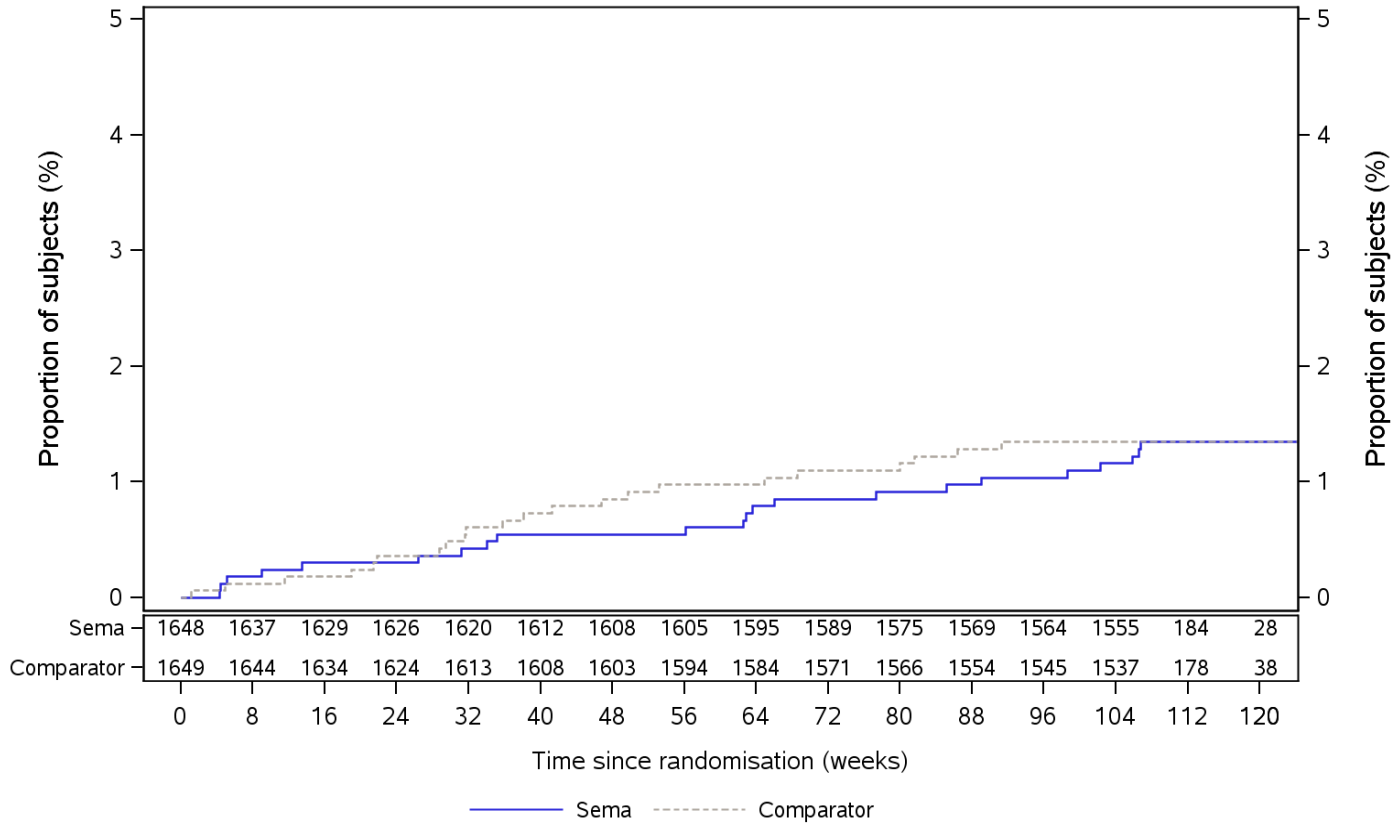
152 Moderate adverse events - preferred term "Coronary arterial stent insertion" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:37:23 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_casi_ae_mo_s6.png

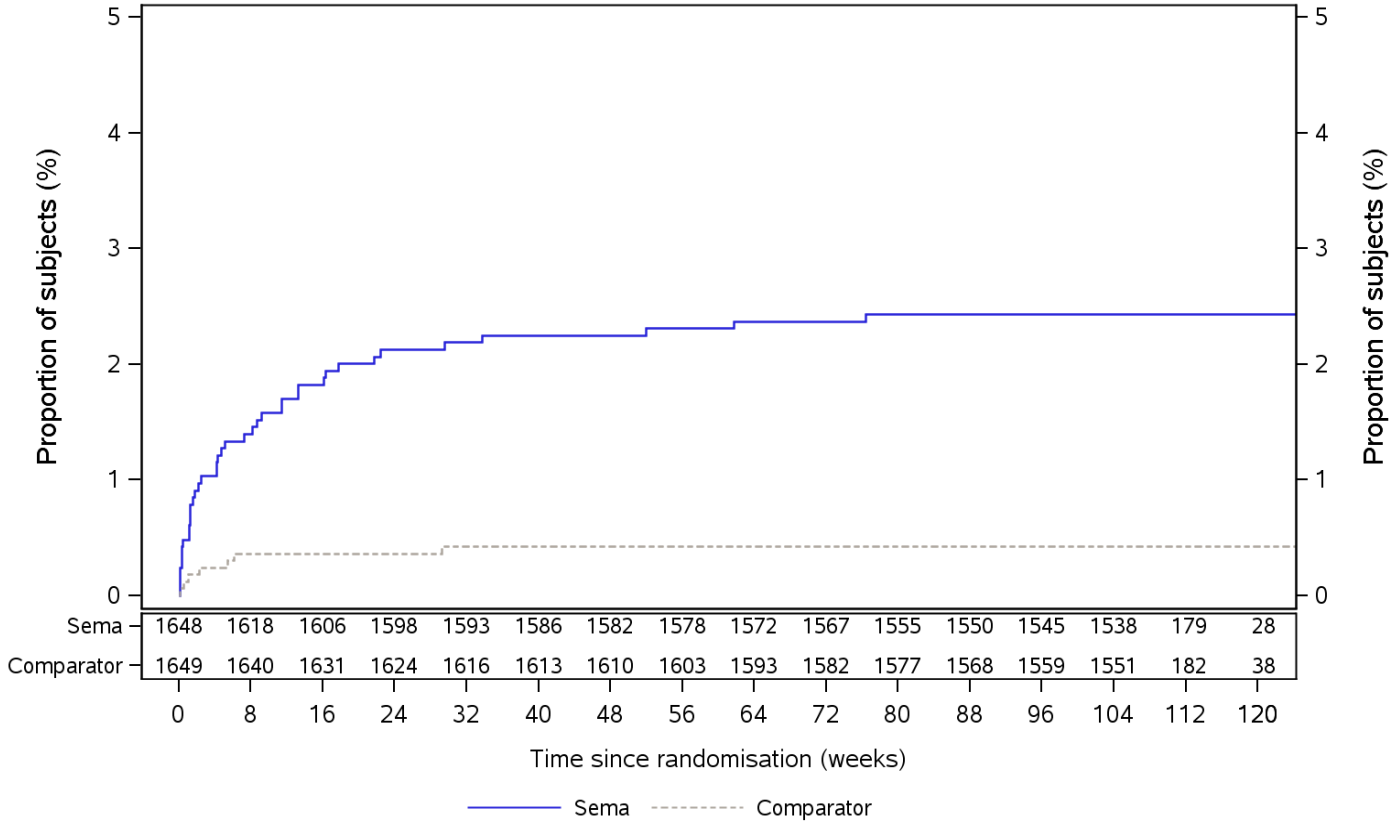
153 Moderate adverse events - preferred term "Cough" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:37:42 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cough_ae_mo_s6.png

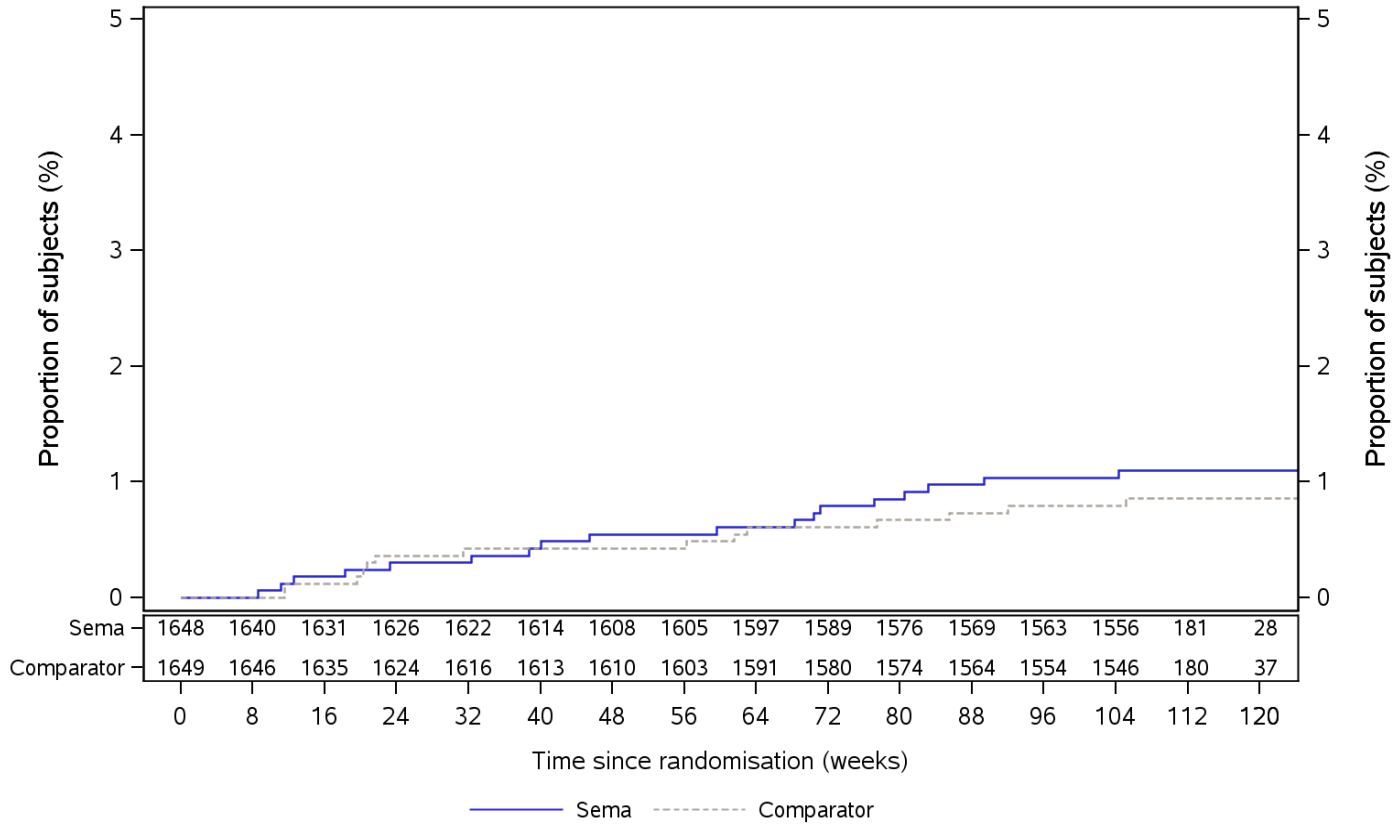
154 Moderate adverse events - preferred term "Decreased appetite" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:38:00 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_decrappe_ae_mo_s6.png

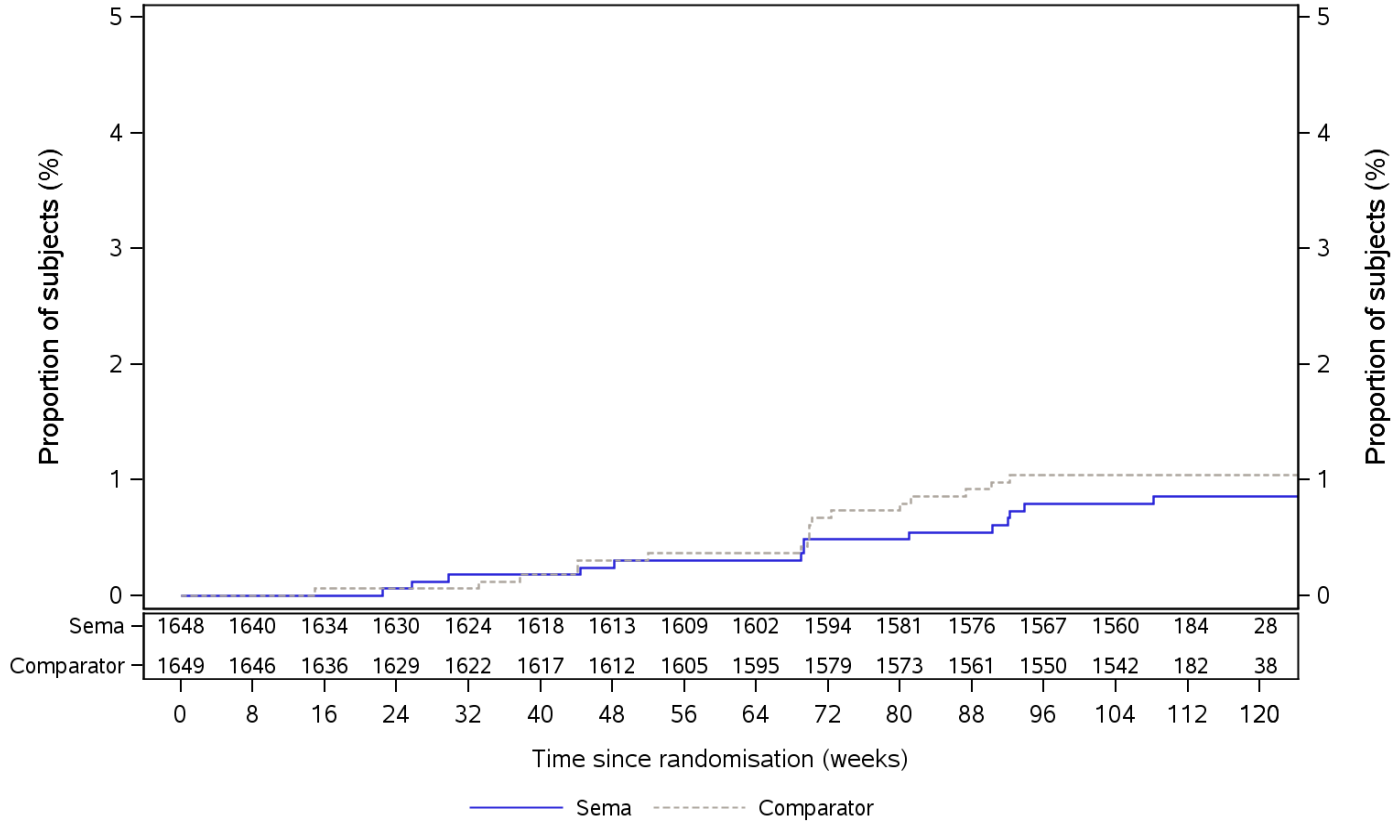
155 Moderate adverse events - preferred term "Depression" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:38:19 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_depressi_ae_mo_s6.png

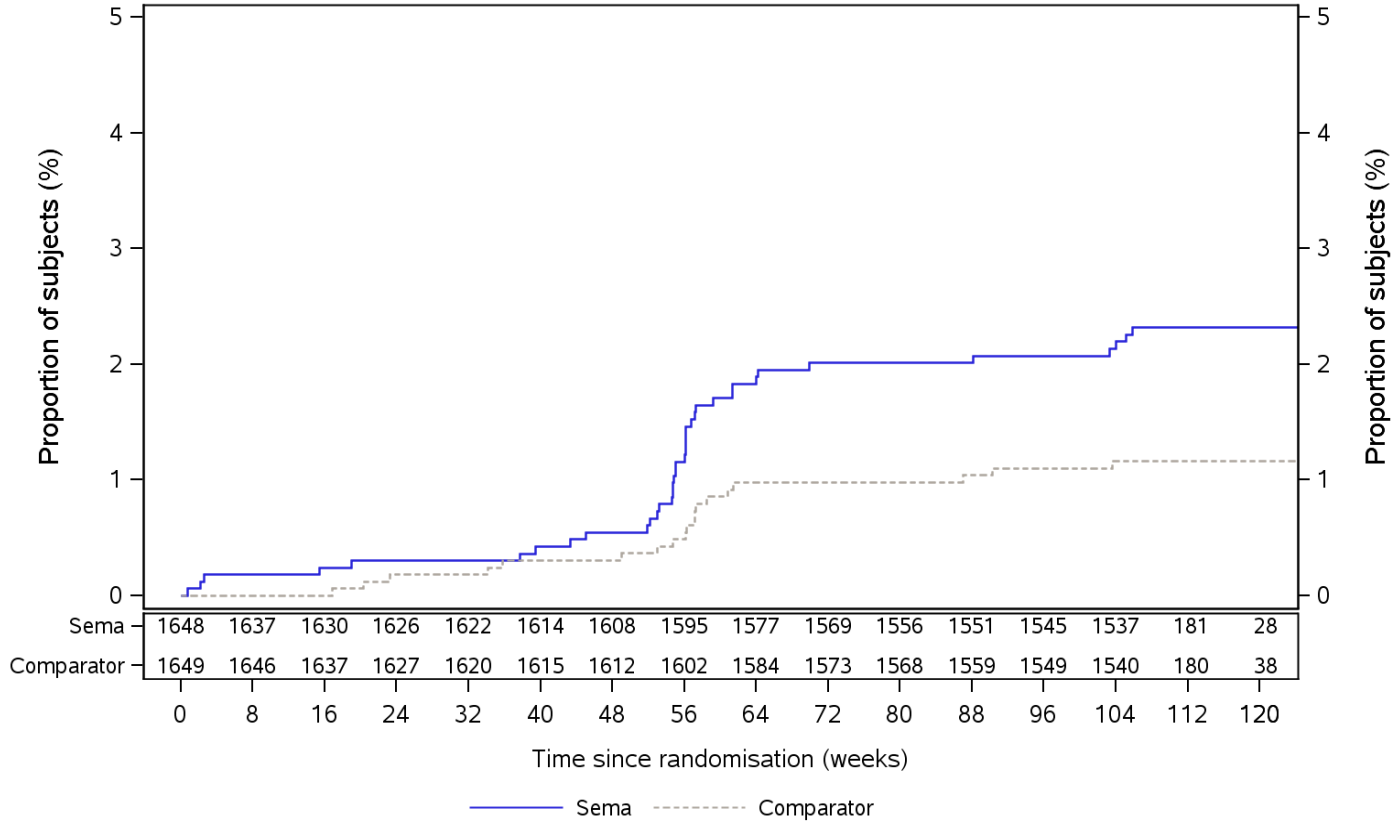
156 Moderate adverse events - preferred term "Diabetes mellitus" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:38:38 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabmell_ae_mo_s6.png

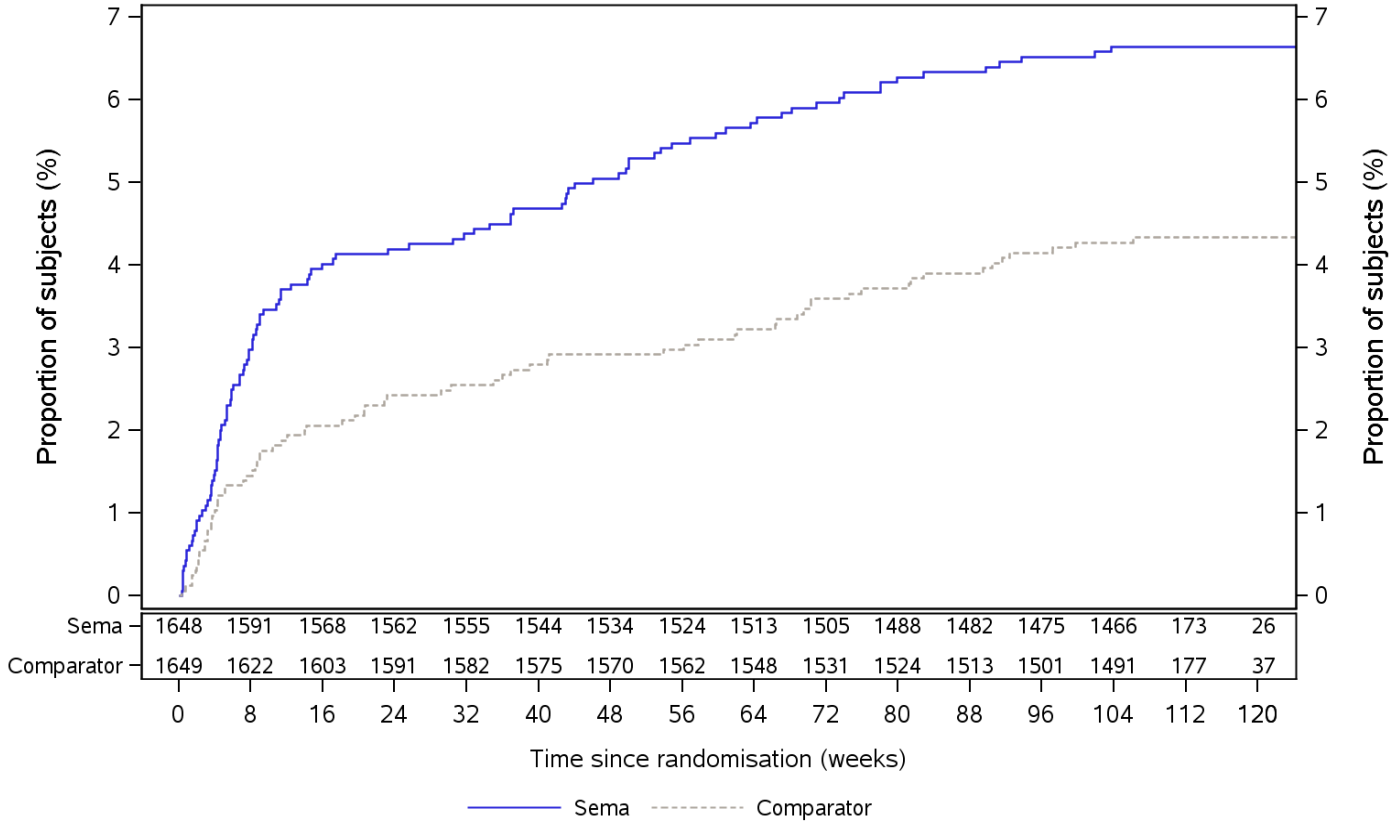
157 Moderate adverse events - preferred term "Diabetic retinopathy" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:38:56 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diabreti_ae_mo_s6.png

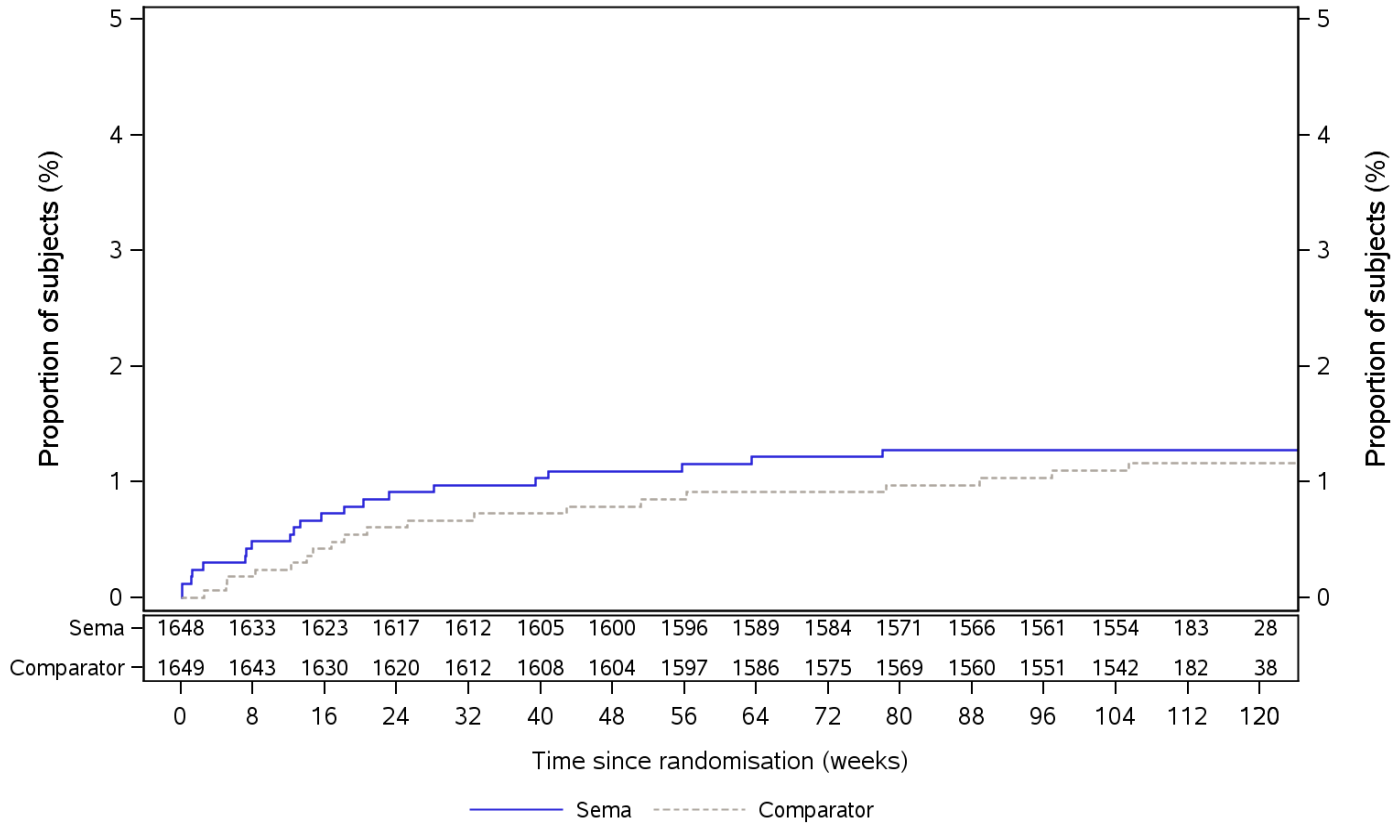
158 Moderate adverse events - preferred term "Diarrhoea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:39:14 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_diarrhoe_ae_mo_s6.png

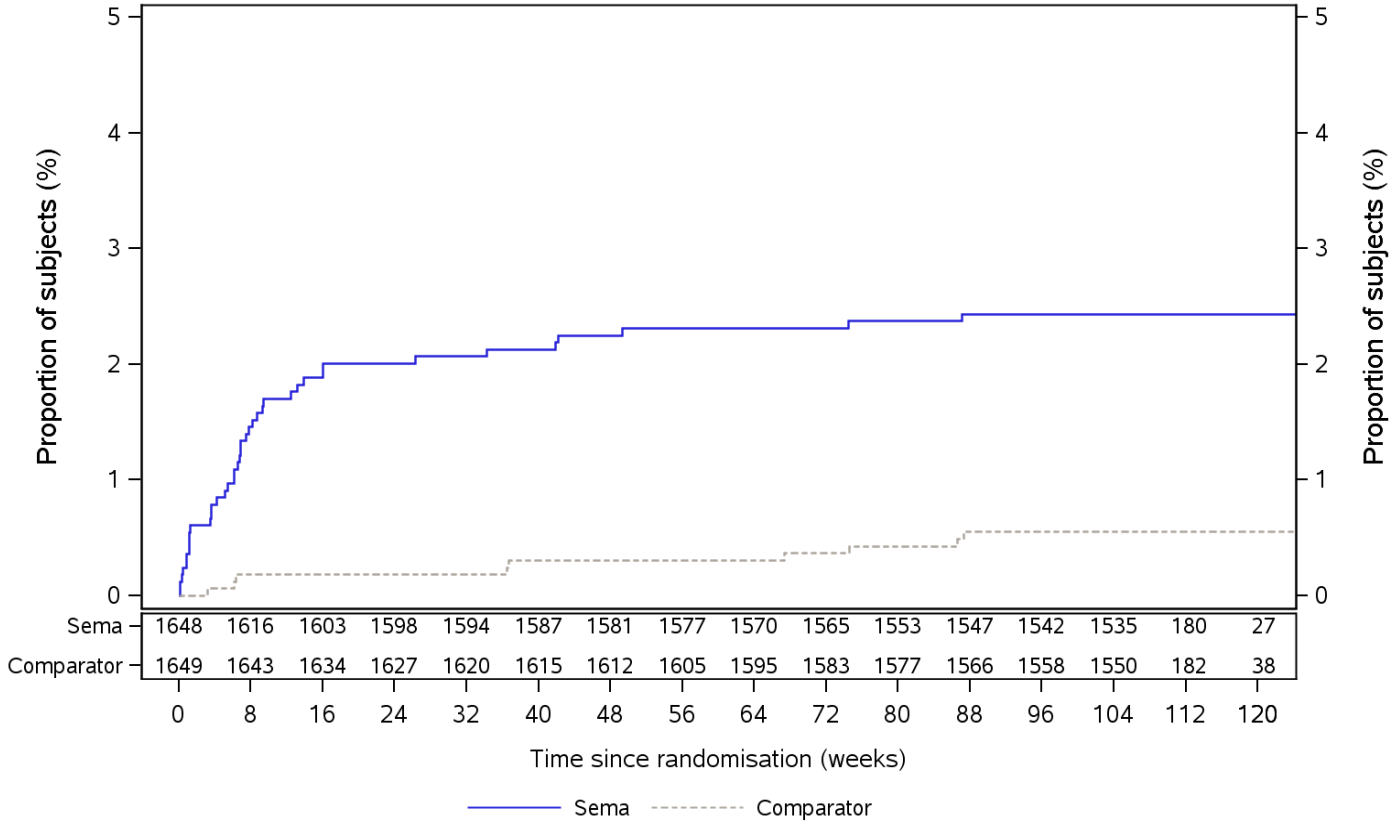
159 Moderate adverse events - preferred term "Dizziness" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:39:32 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dizzines_ae_mo_s6.png

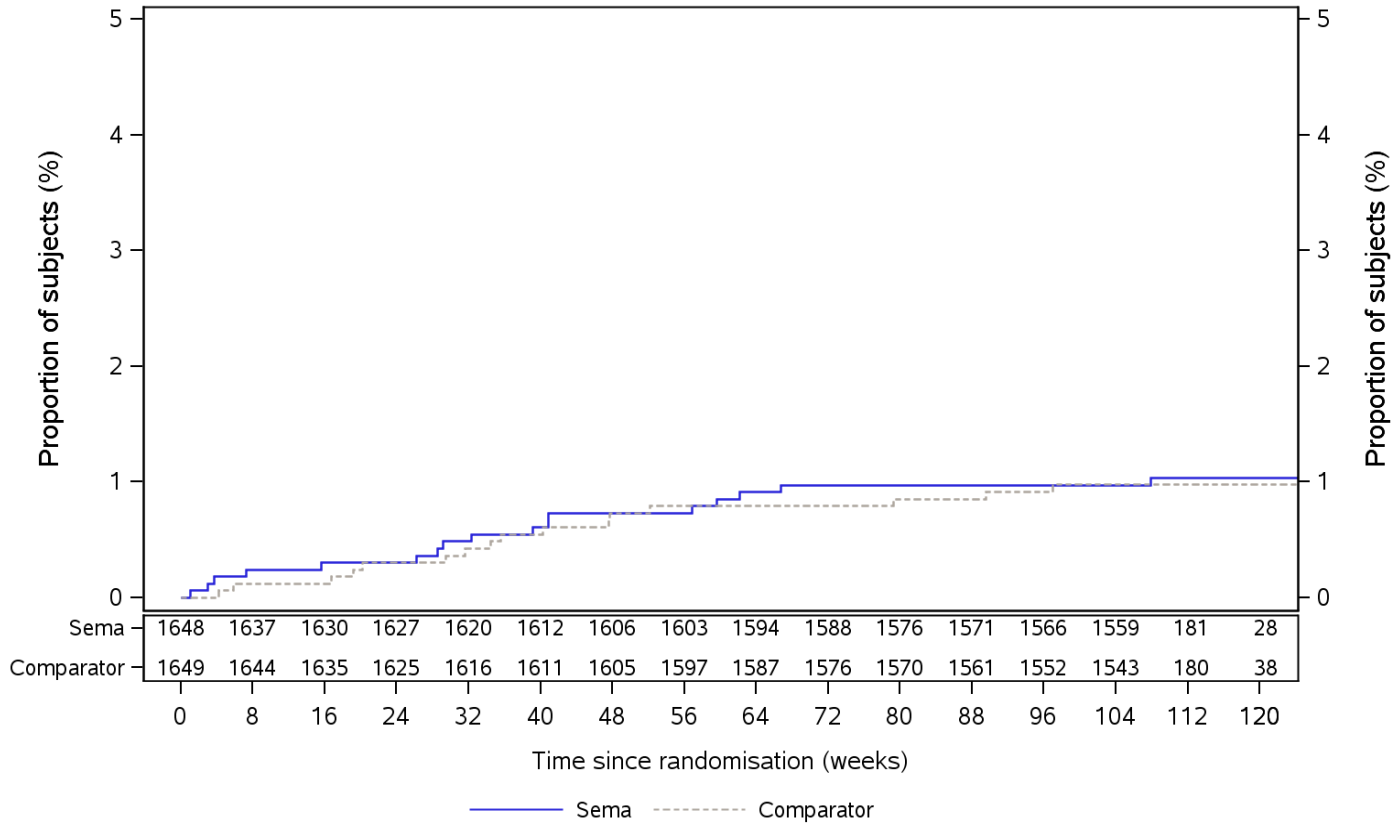
160 Moderate adverse events - preferred term "Dyspepsia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:39:50 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dyspepsi_ae_mo_s6.png

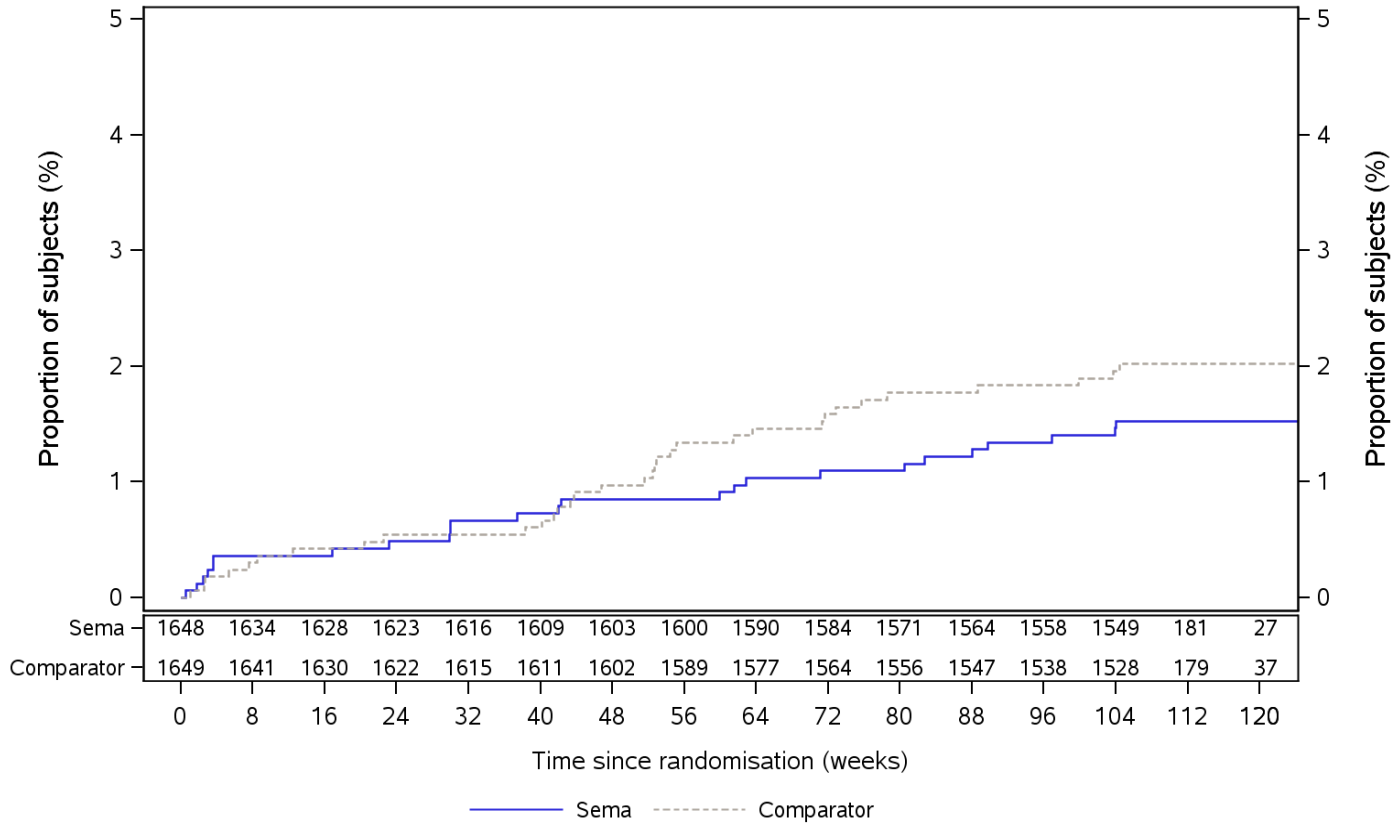
161 Moderate adverse events - preferred term "Dyspnoea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:40:09 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_dyspnoea_ae_mo_s6.png

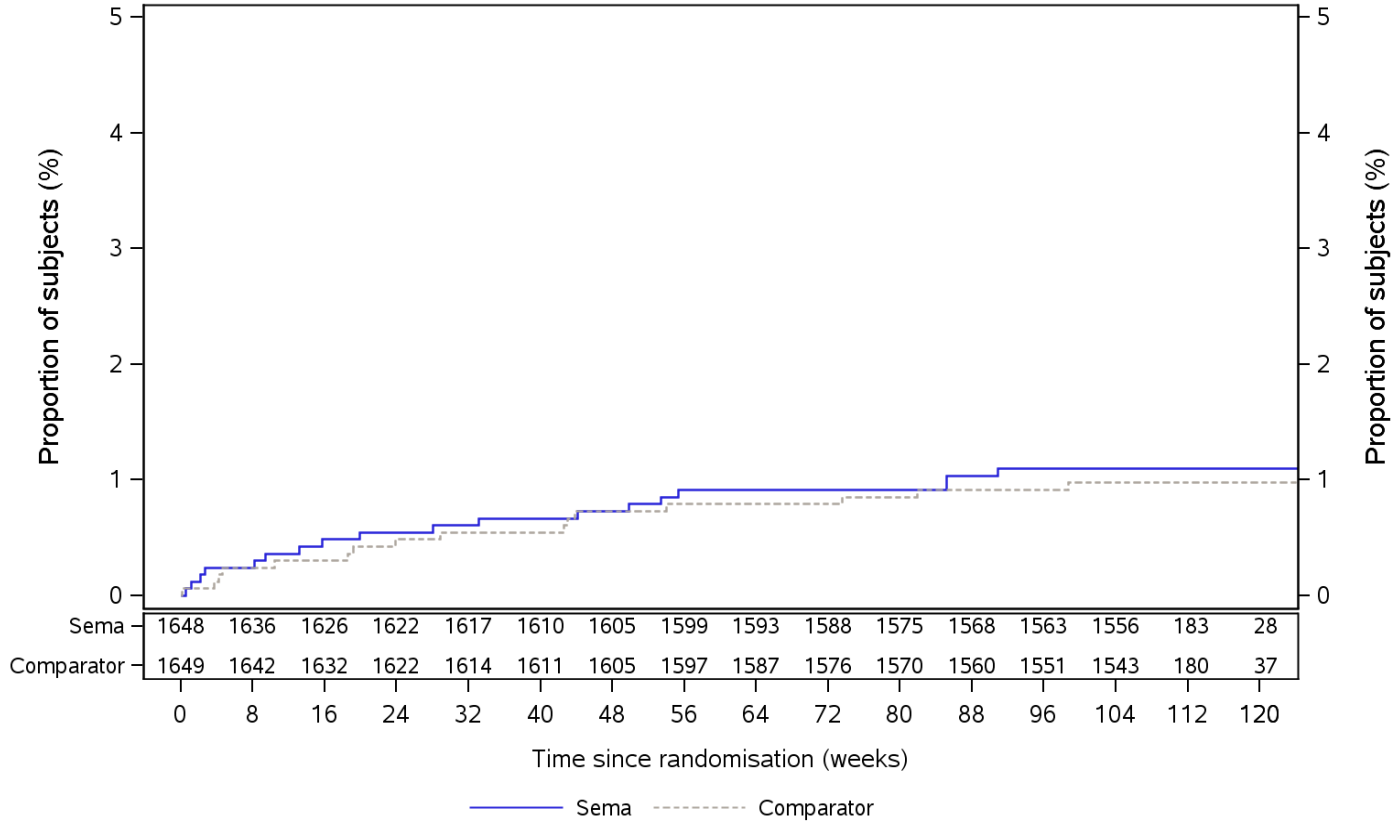
162 Moderate adverse events - preferred term "Fall" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:40:28 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_fall_ae_mo_s6.png

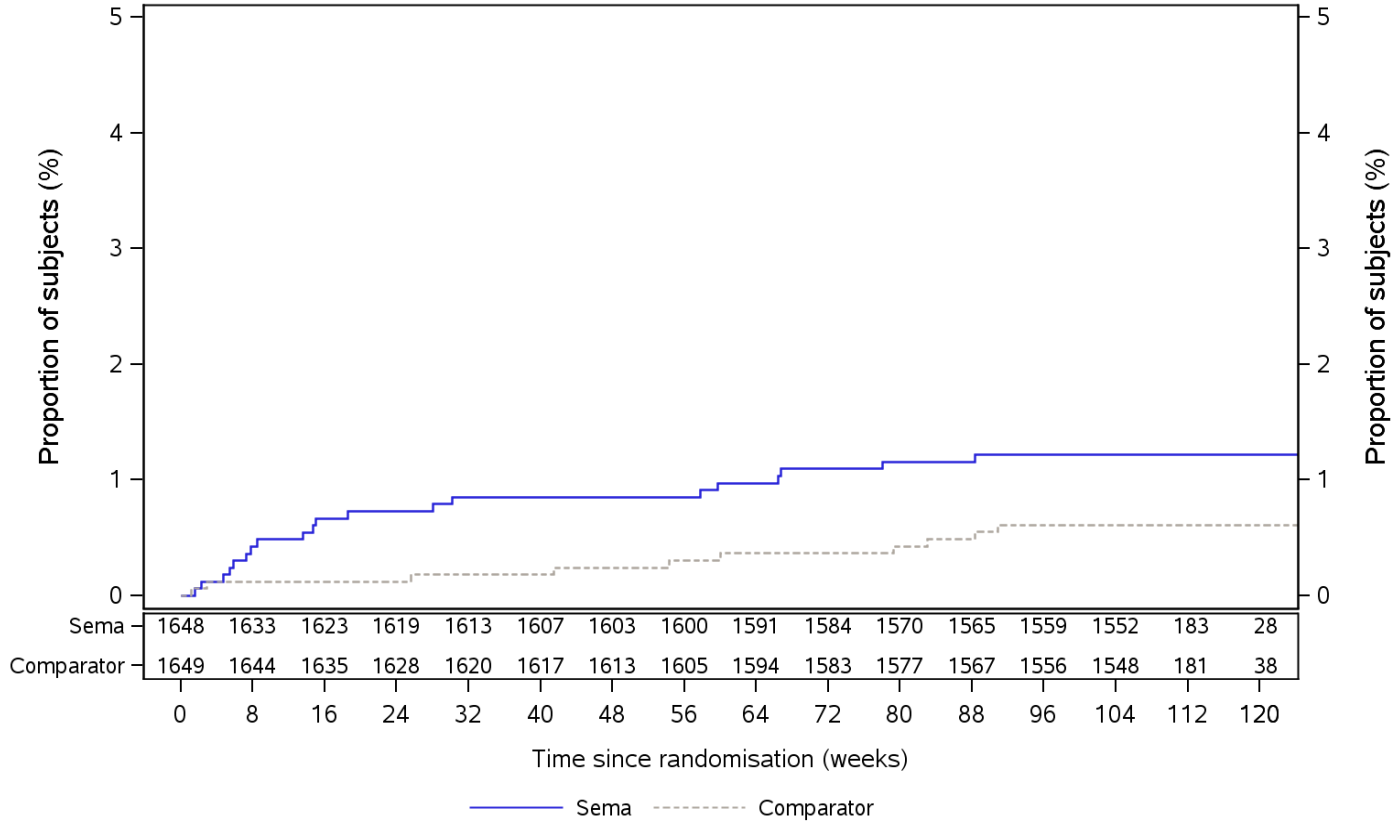
163 Moderate adverse events - preferred term "Fatigue" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:40:46 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_fatigue_ae_mo_s6.png

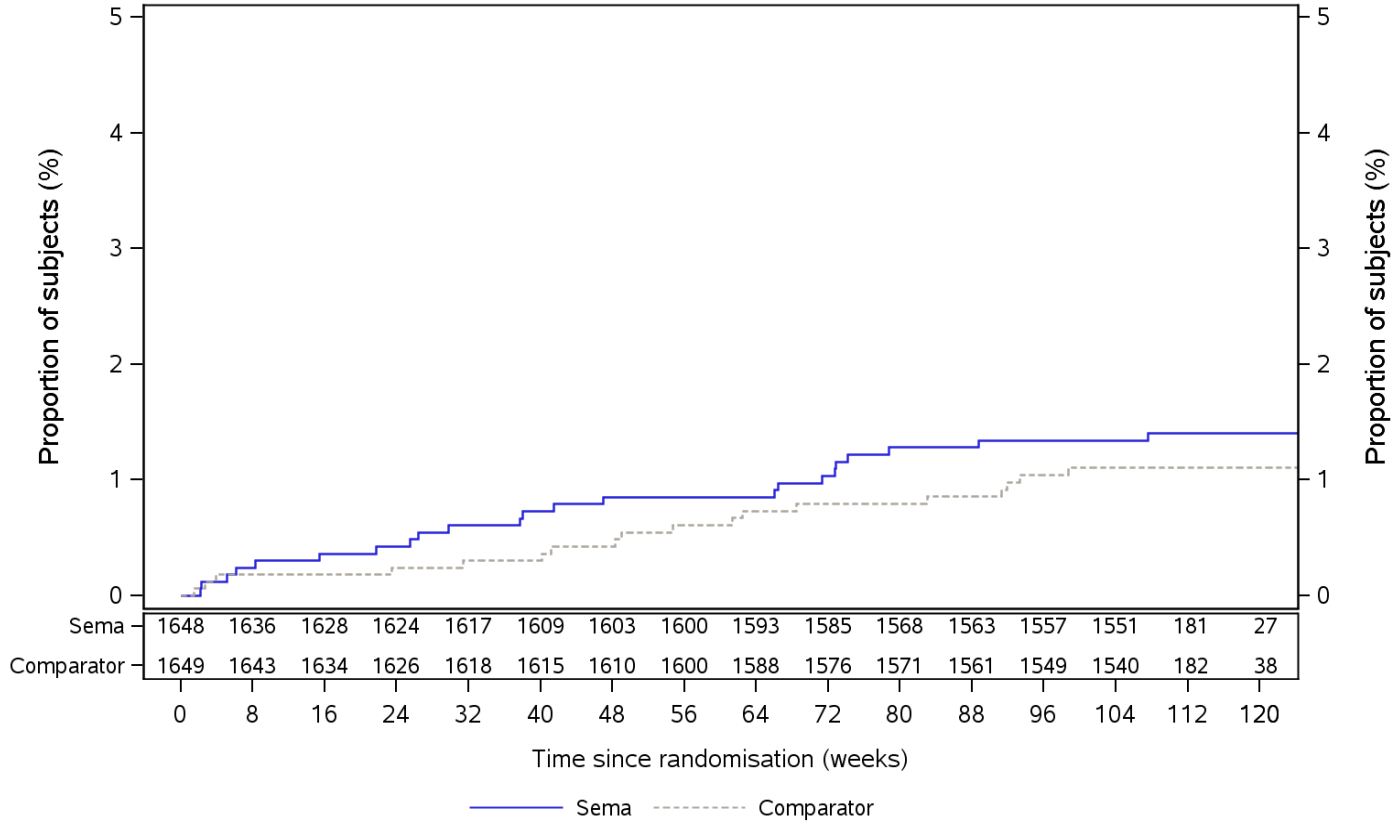
164 Moderate adverse events - preferred term "Gastritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:41:05 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gastriti_ae_mo_s6.png

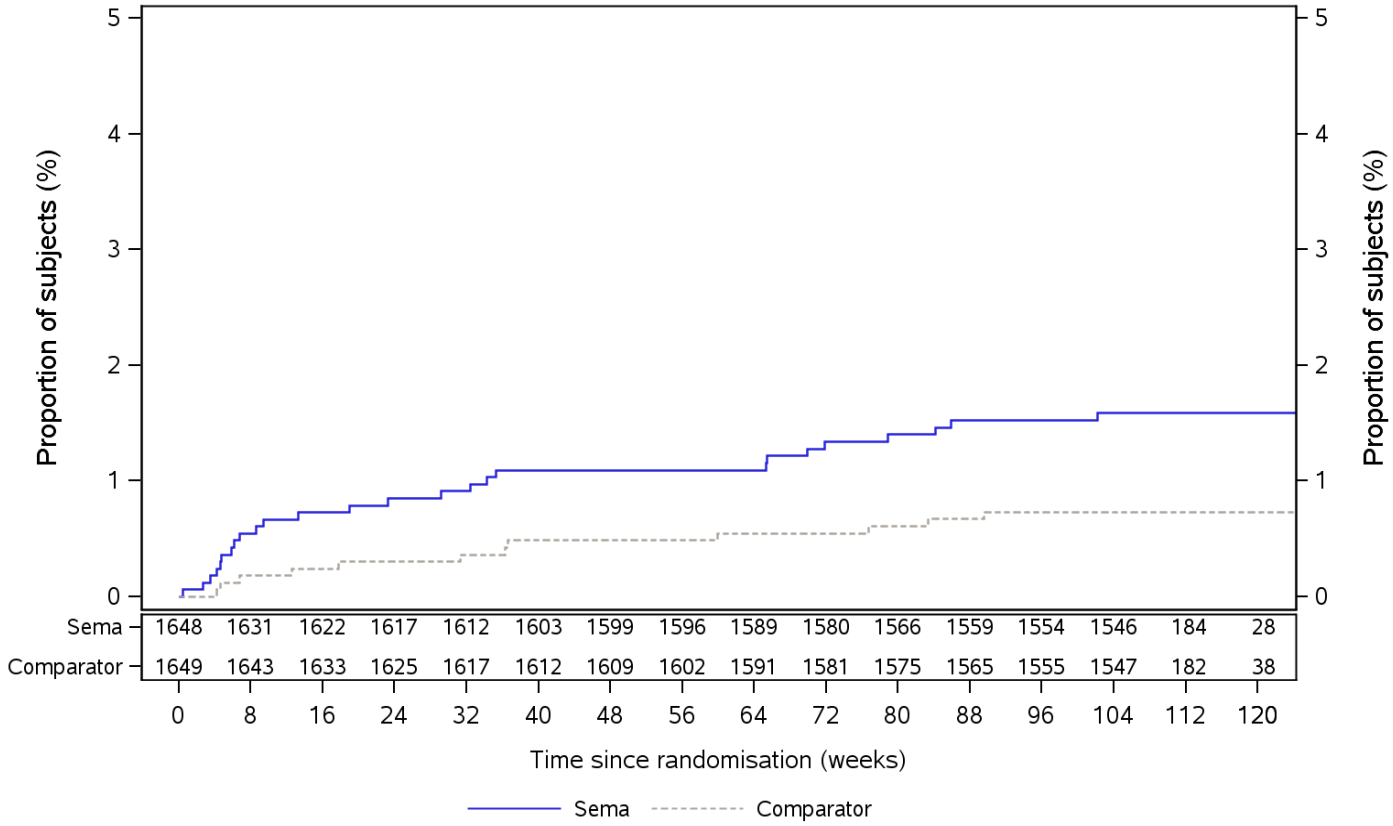
165 Moderate adverse events - preferred term "Gastroenteritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:41:24 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gastroen_ae_mo_s6.png

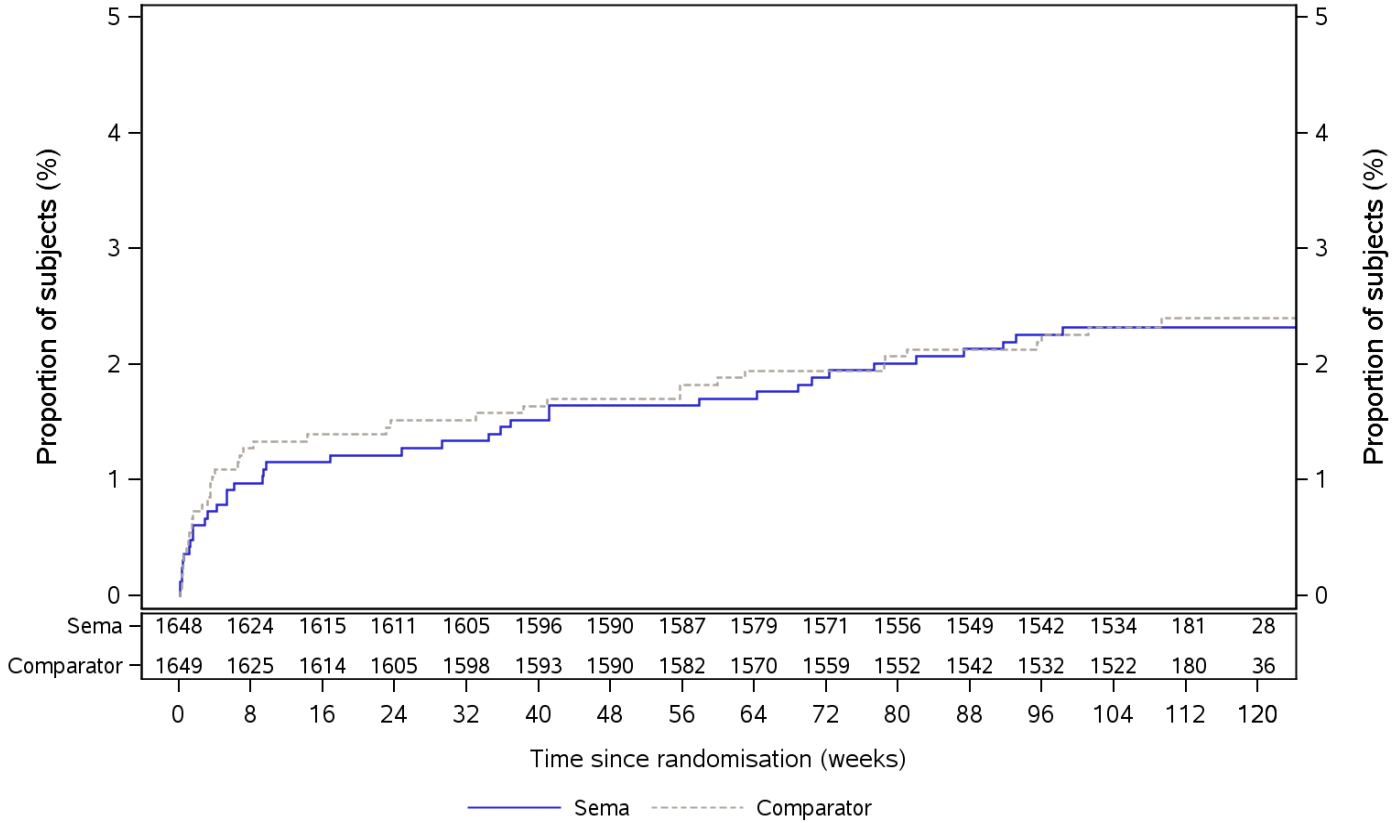
166 Moderate adverse events - preferred term "Gastrooesophageal reflux disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:41:42 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_gasrefdis_ae_mo_s6.png

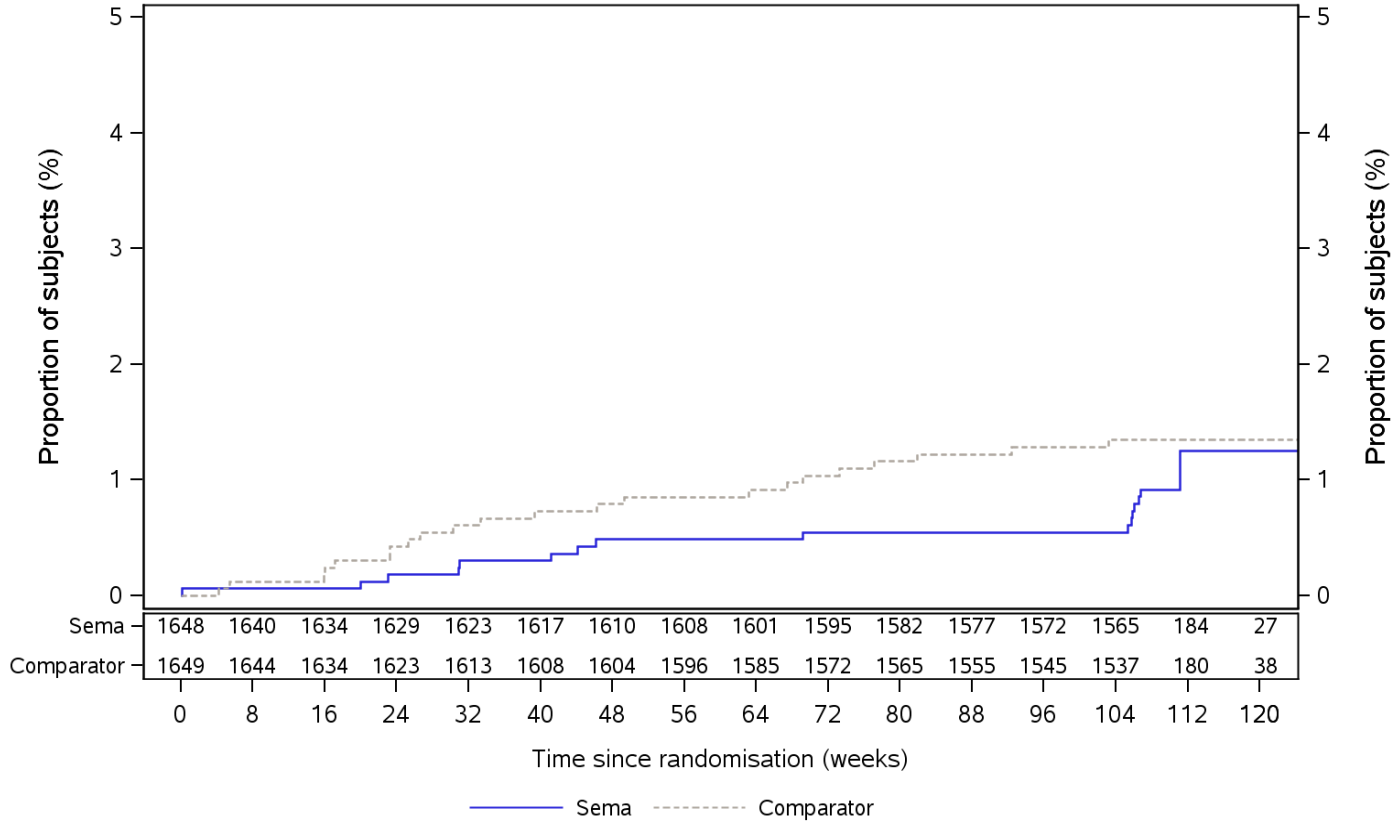
167 Moderate adverse events - preferred term "Headache" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:42:00 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_headache_ae_mo_s6.png

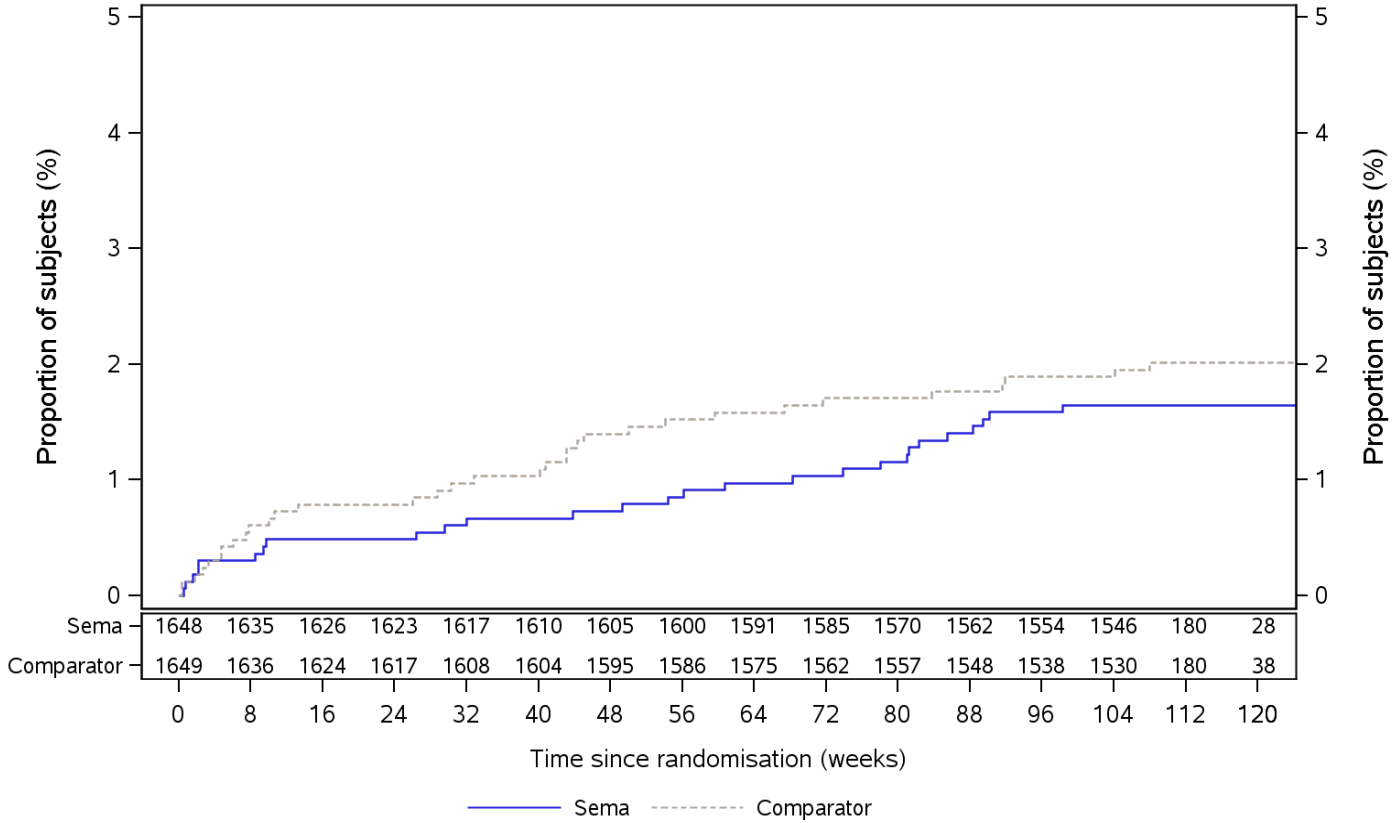
168 Moderate adverse events - preferred term "Hyperglycaemia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:42:18 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hypergly_ae_mo_s6.png

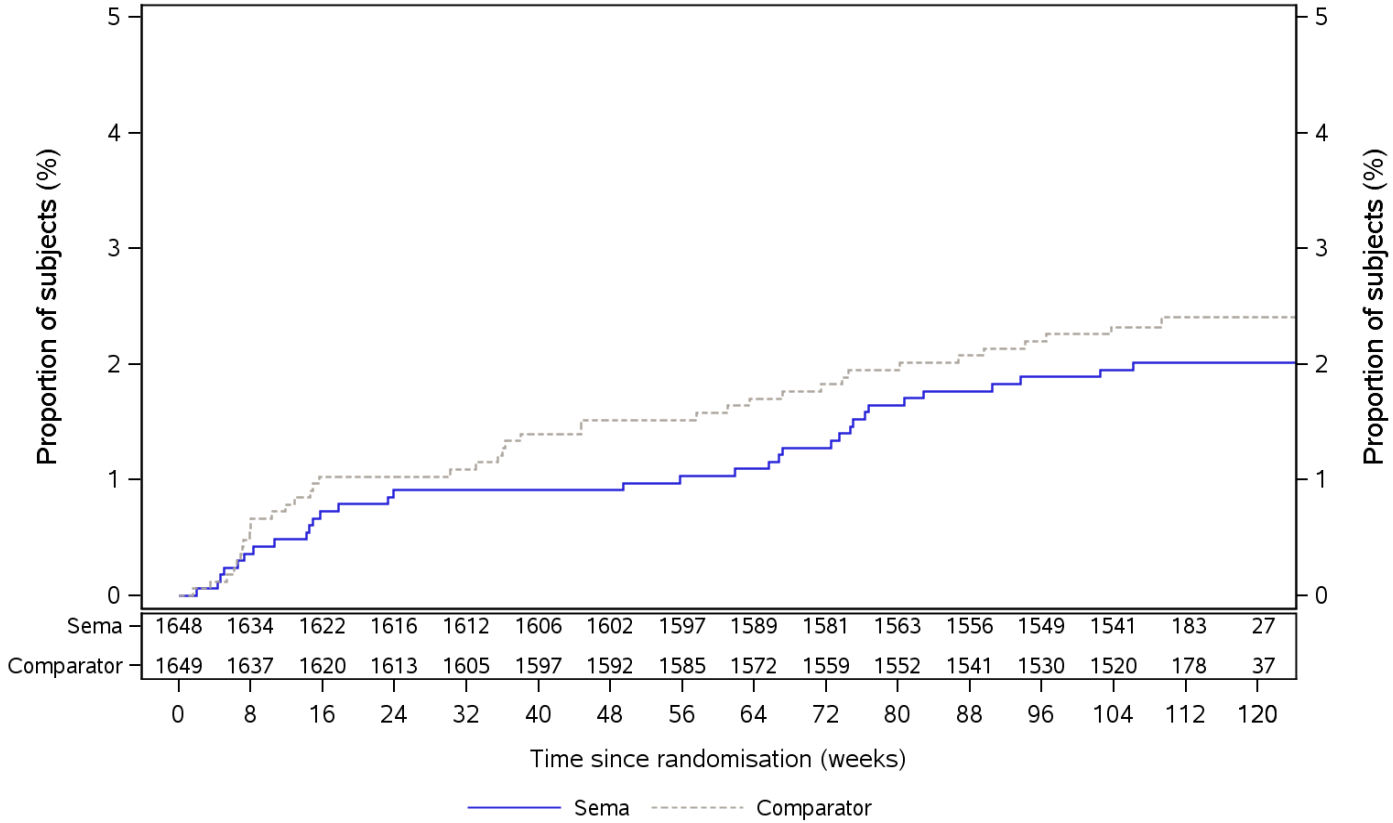
169 Moderate adverse events - preferred term "Hypertension" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:42:36 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_hyperten_ae_mo_s6.png

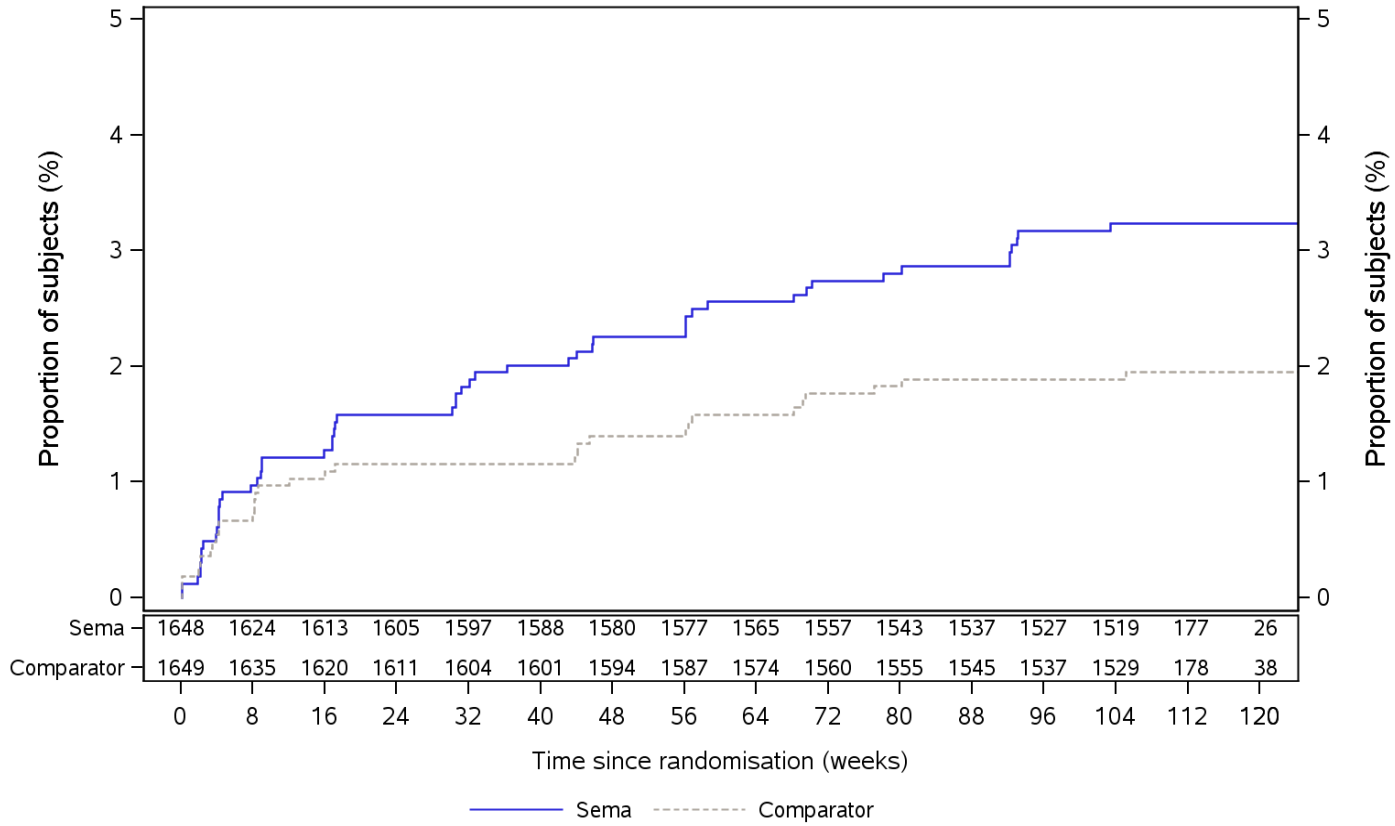
170 Moderate adverse events - preferred term "Influenza" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:42:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_influenz_ae_mo_s6.png

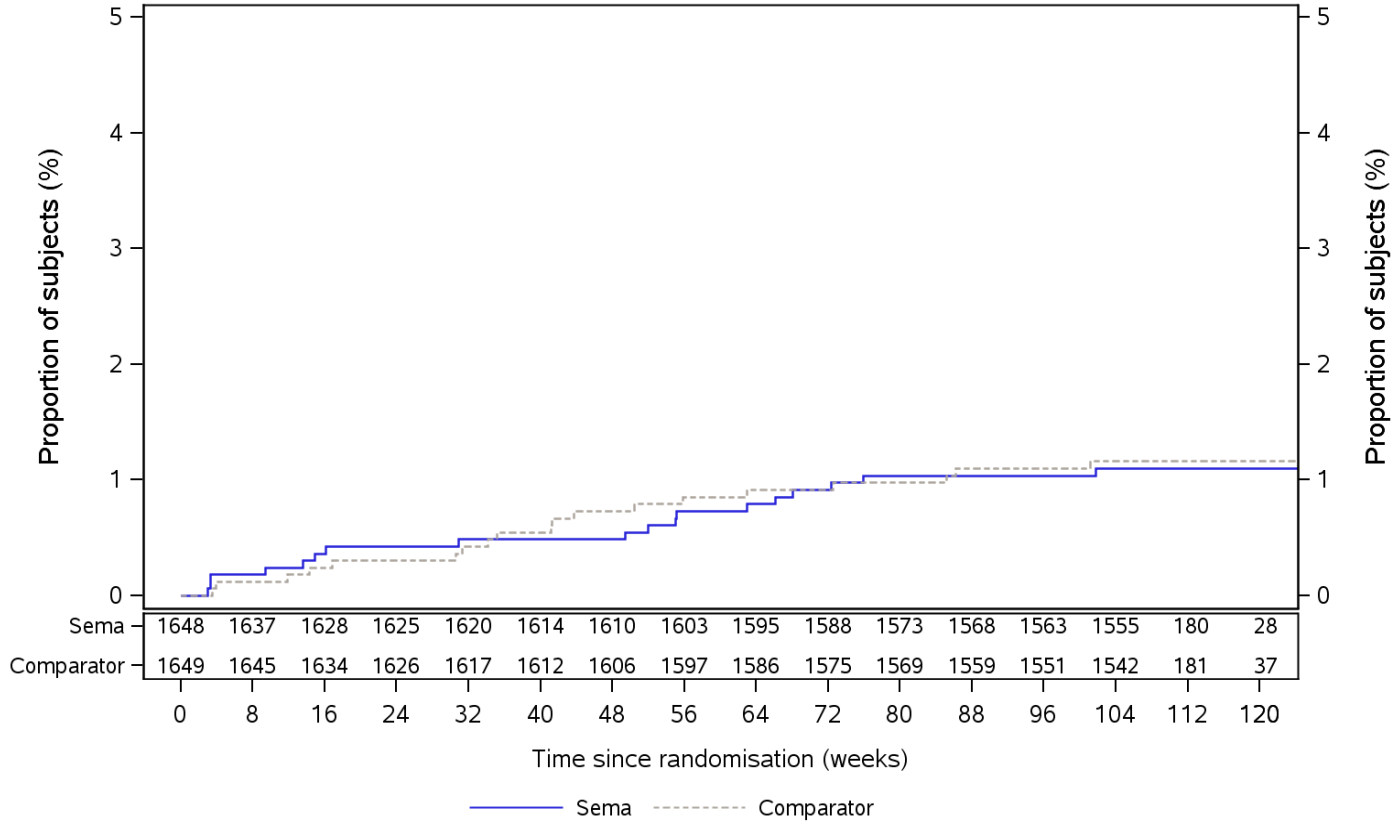
171 Moderate adverse events - preferred term "Lipase increased" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:43:13 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_lipaincr_ae_mo_s6.png

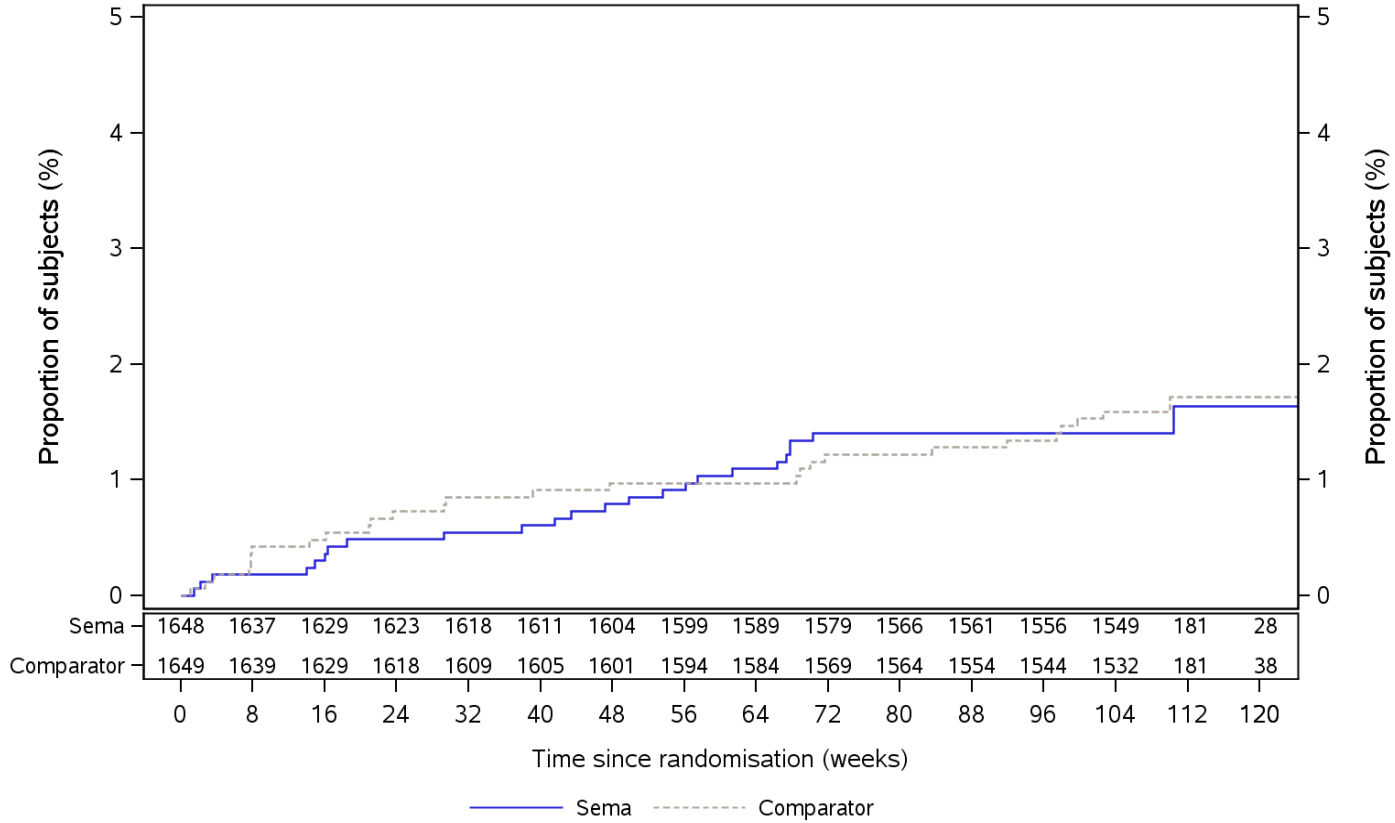
172 Moderate adverse events - preferred term "Musculoskeletal pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:43:31 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_muscpain_ae_mo_s6.png

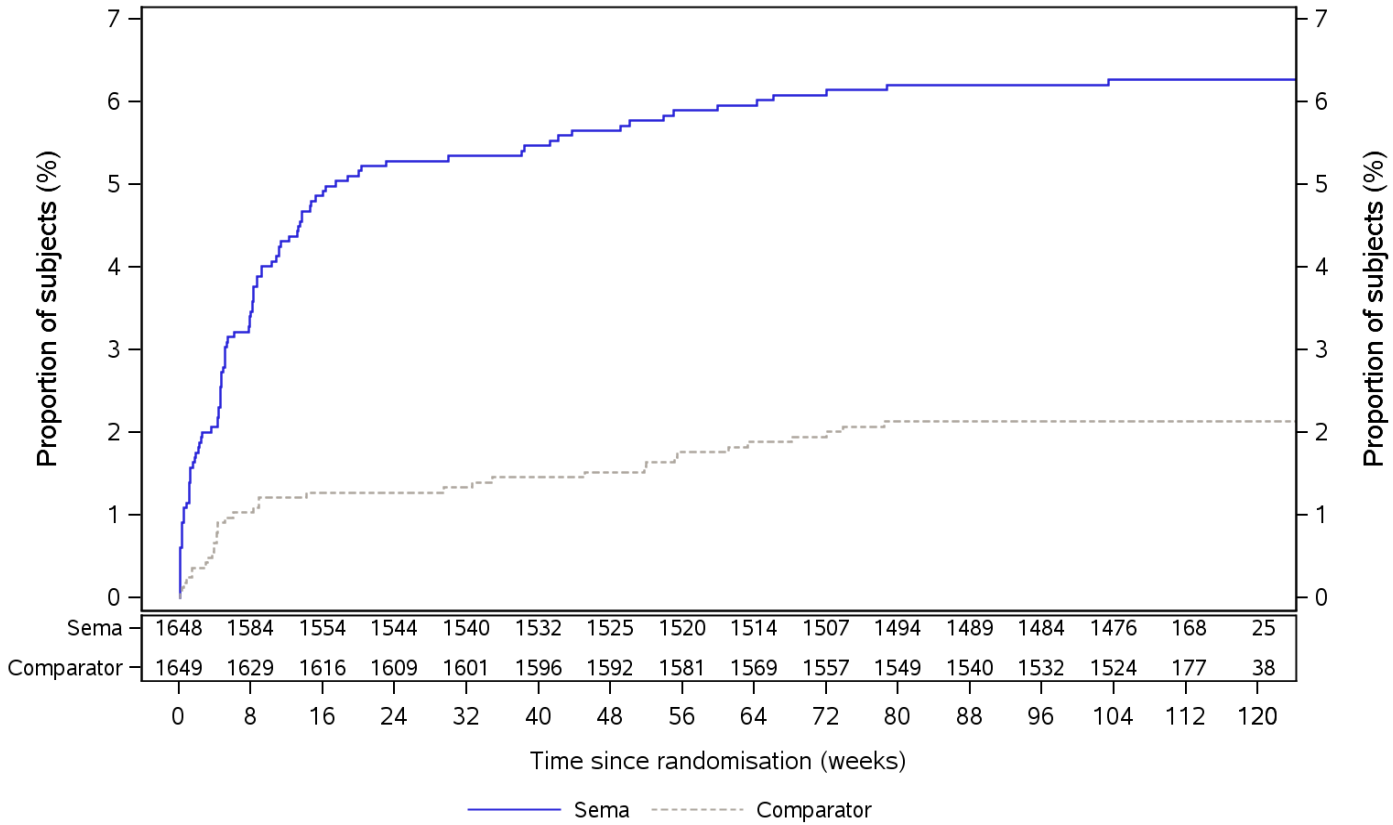
173 Moderate adverse events - preferred term "Nasopharyngitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:43:50 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nasophar_ae_mo_s6.png

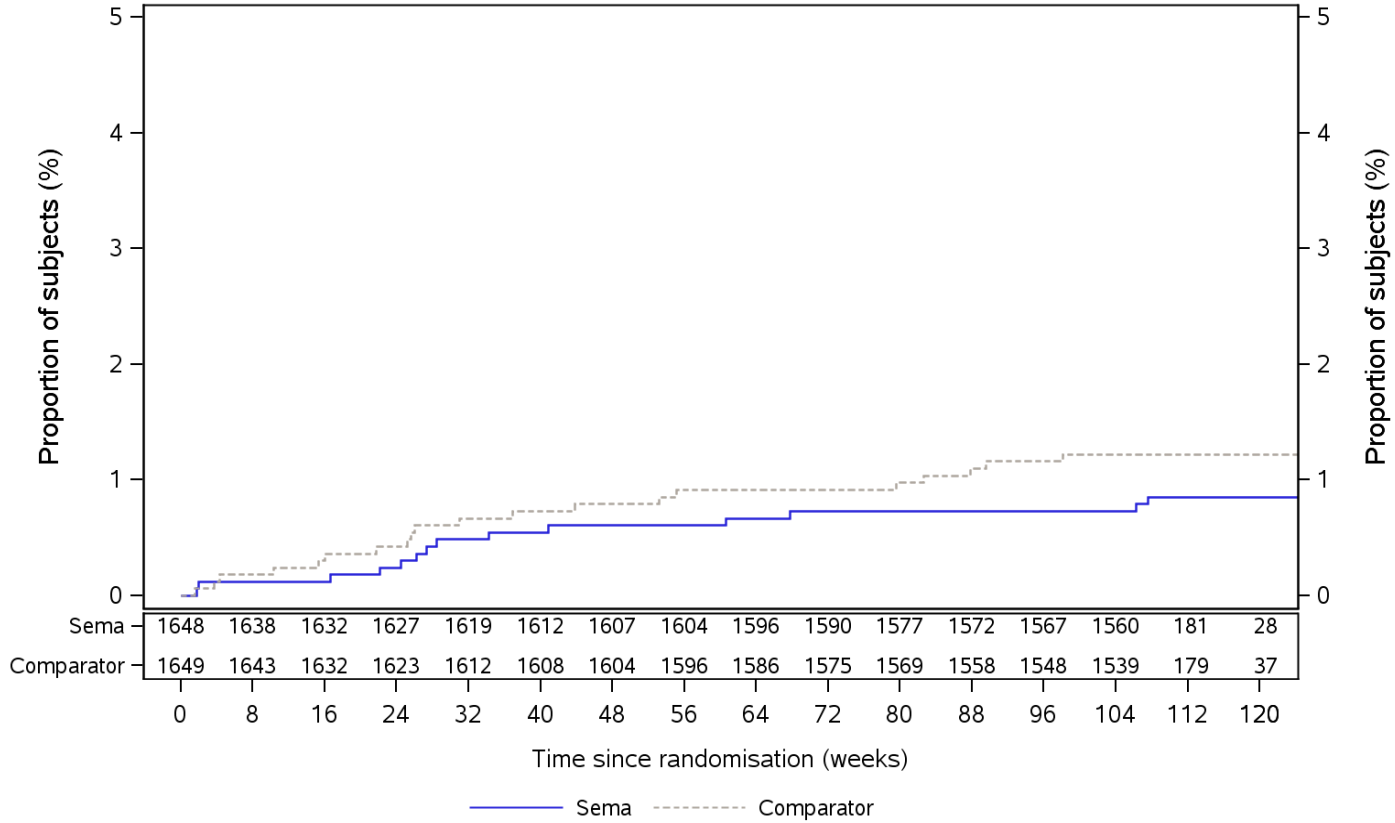
174 Moderate adverse events - preferred term "Nausea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:44:08 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nausea_ae_mo_s6.png

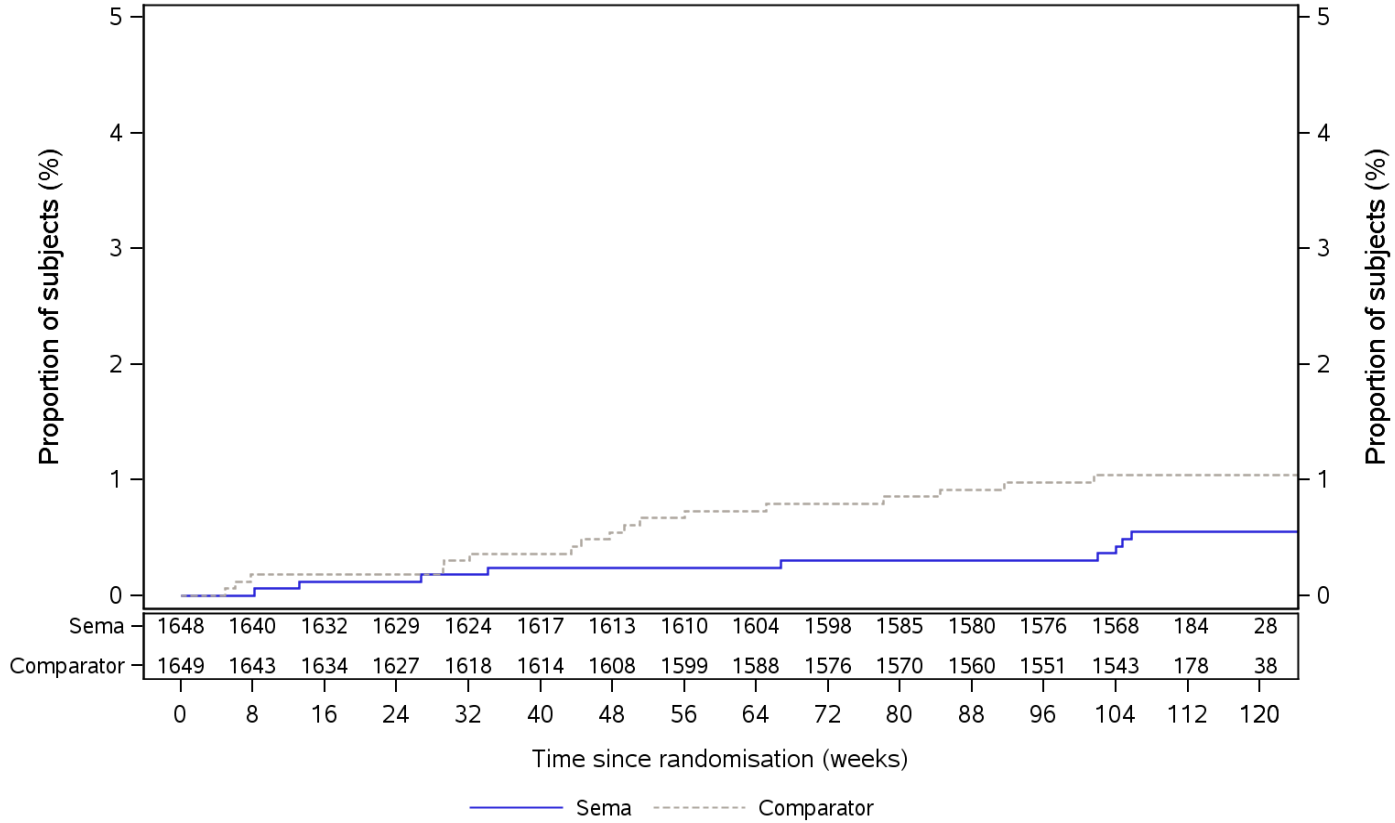
175 Moderate adverse events - preferred term "Non-cardiac chest pain" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:44:26 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_noncarche_ae_mo_s6.png

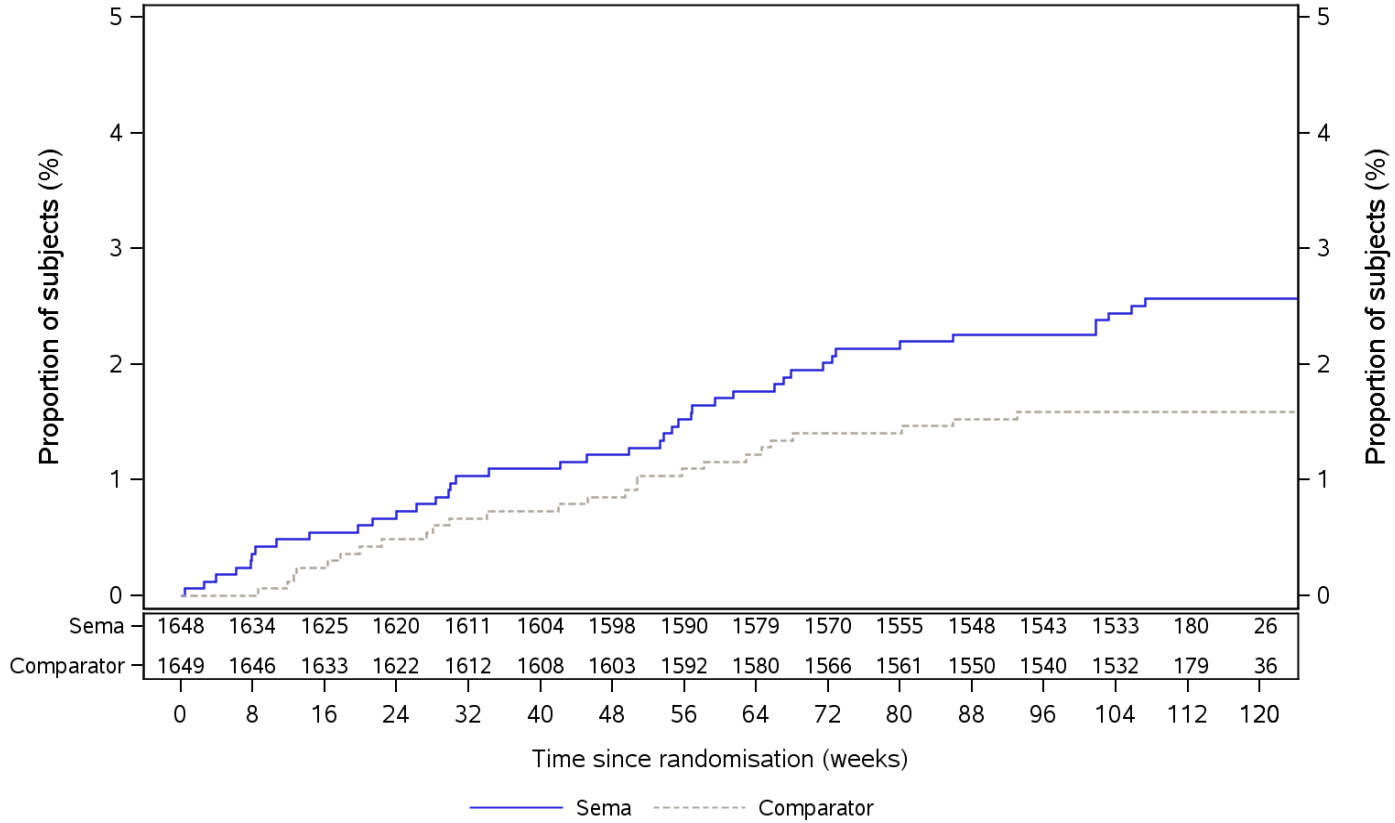
176 Moderate adverse events - preferred term "Oedema peripheral" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:44:45 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_oedeperi_ae_mo_s6.png

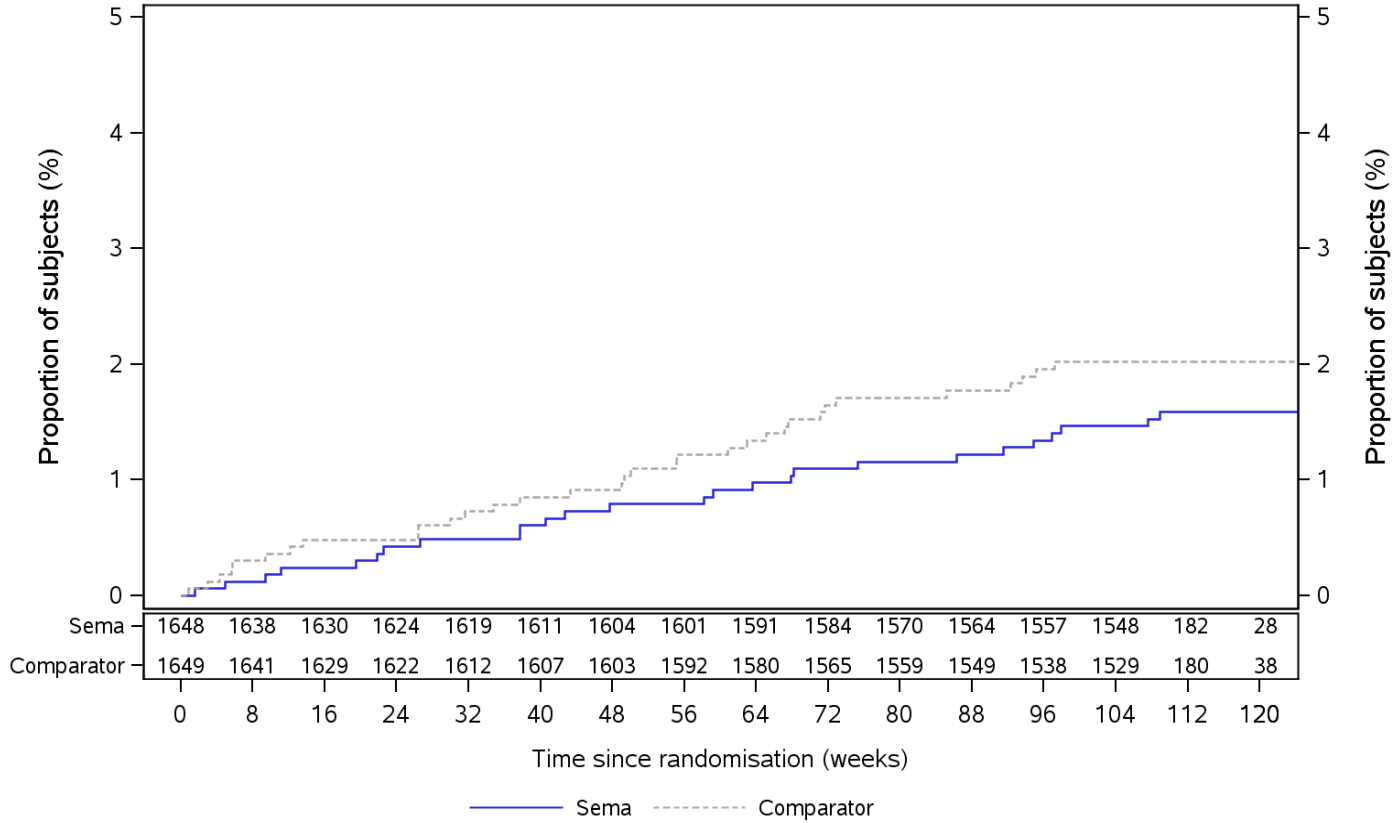
177 Moderate adverse events - preferred term "Osteoarthritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:45:03 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_ost_ae_mo_s6.png

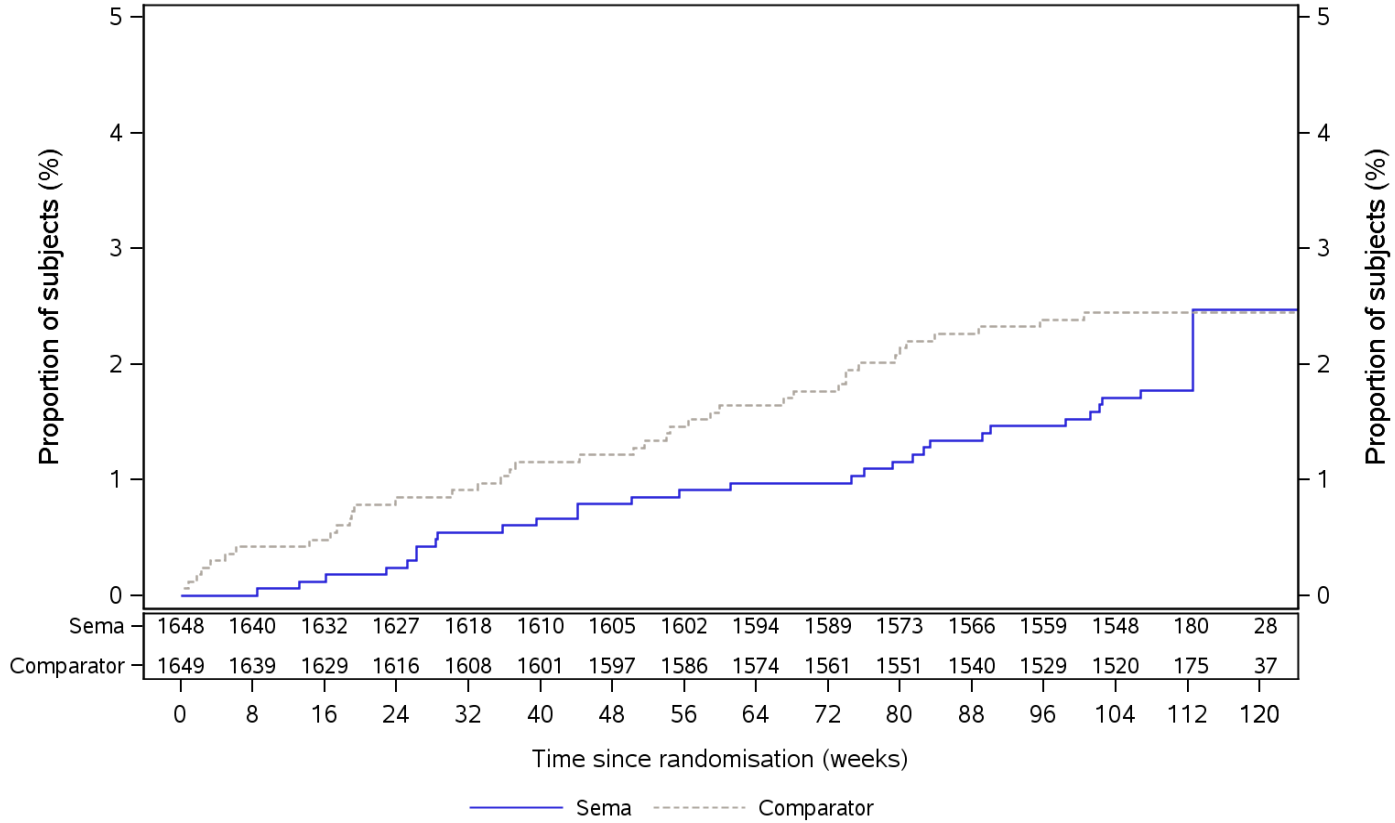
178 Moderate adverse events - preferred term "Pain in extremity" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:45:21 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_paiinext_ae_mo_s6.png

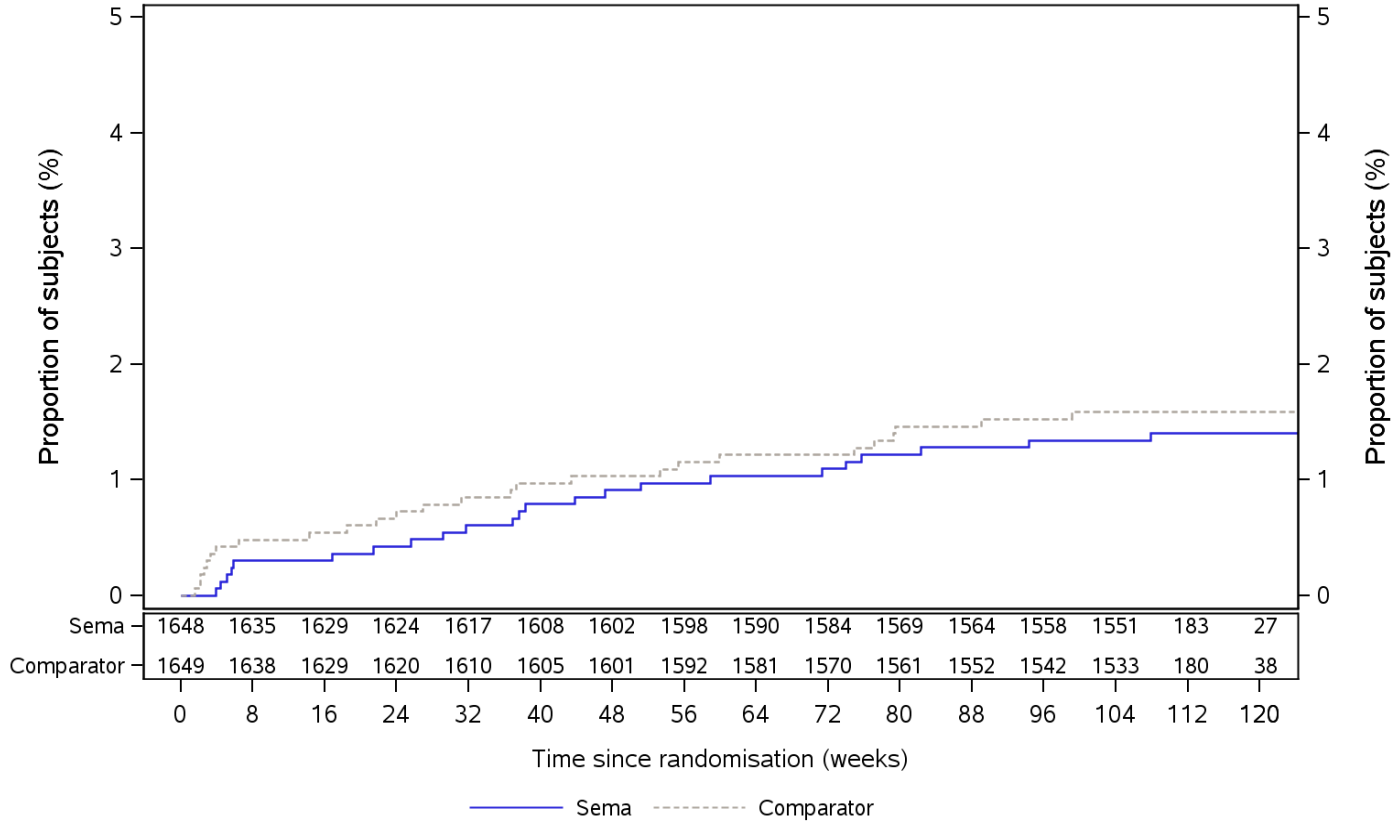
179 Moderate adverse events - preferred term "Pneumonia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:45:41 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pneu_ae_mo_s6.png

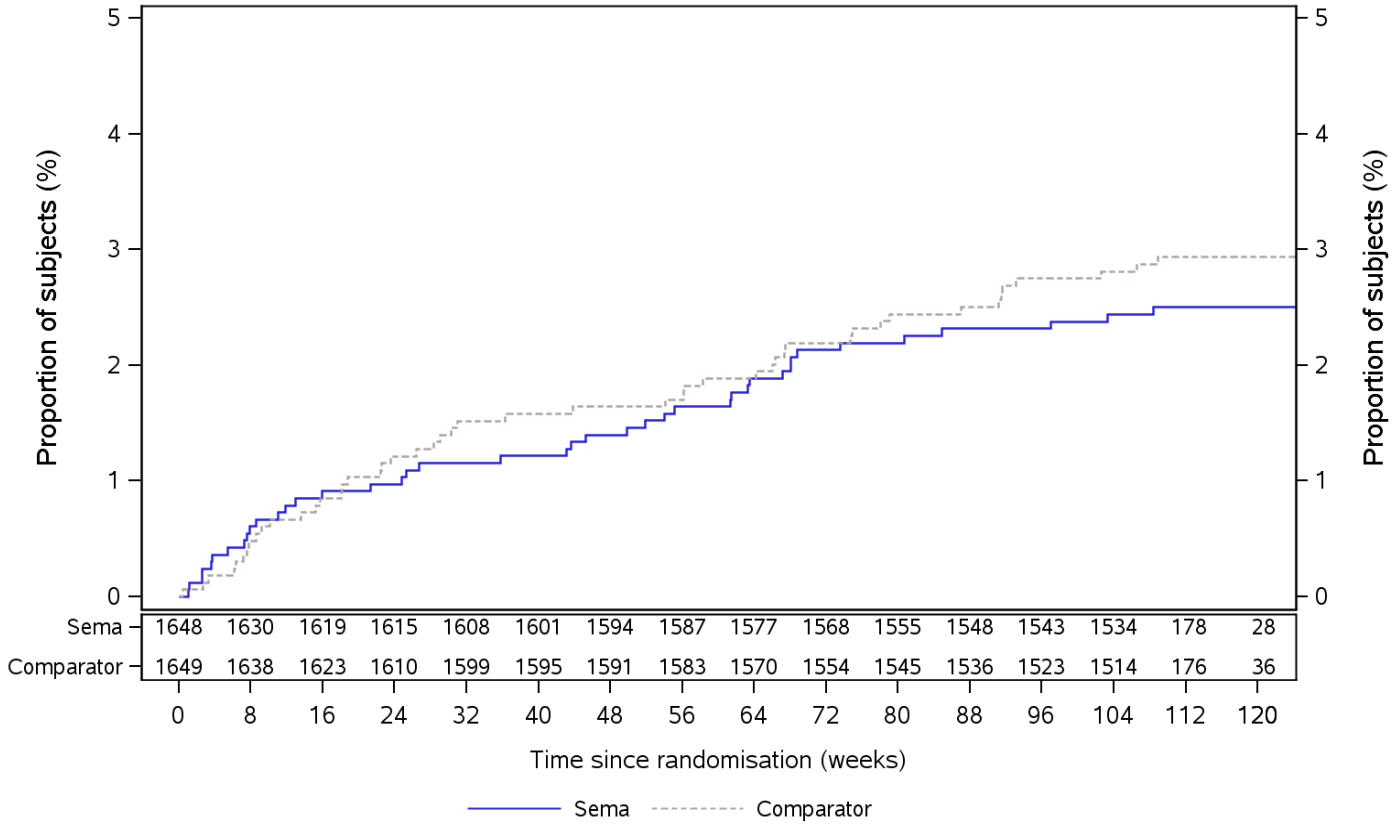
180 Moderate adverse events - preferred term "Sinusitis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:46:00 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_sinusiti_ae_mo_s6.png

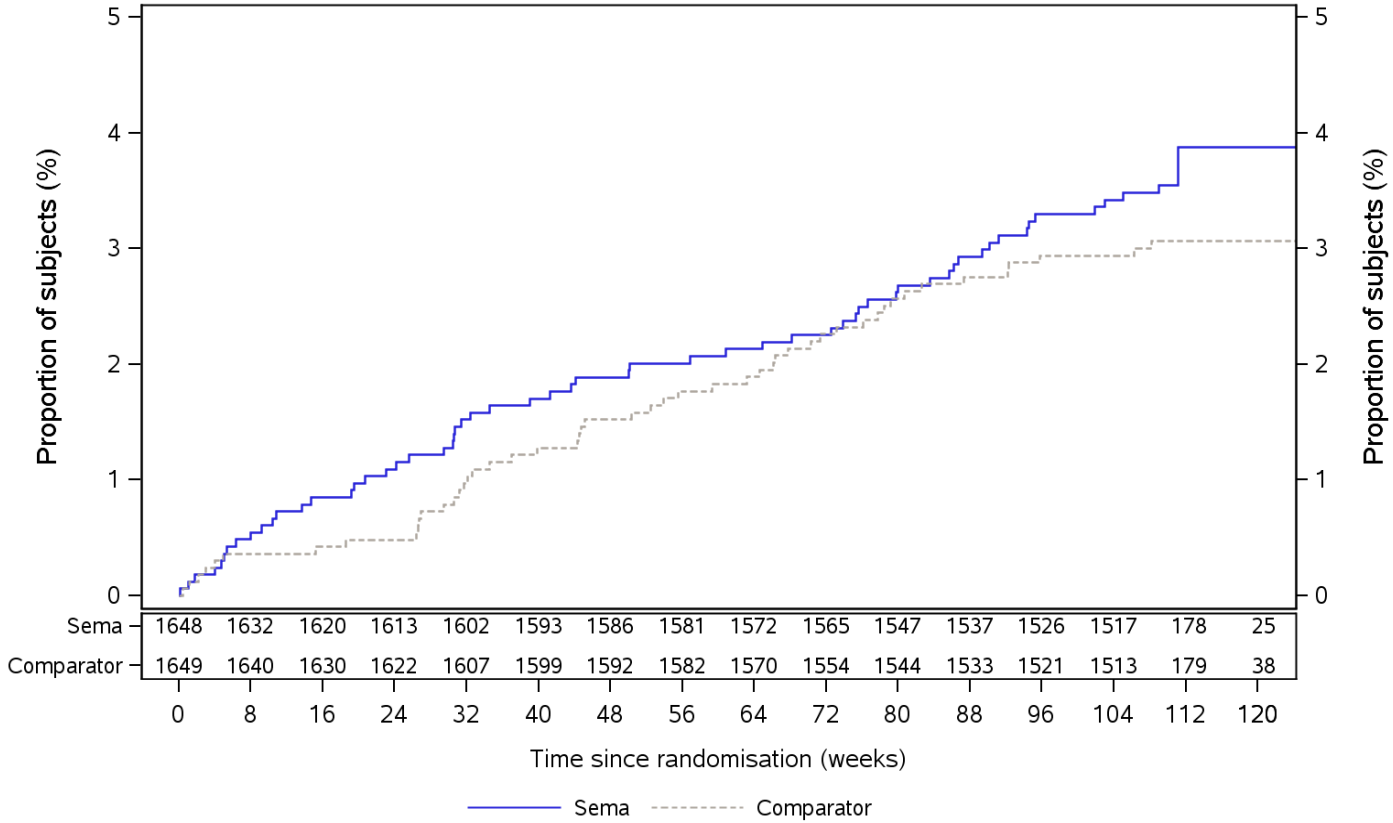
181 Moderate adverse events - preferred term "Upper respiratory tract infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:46:19 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_upprestra_ae_mo_s6.png

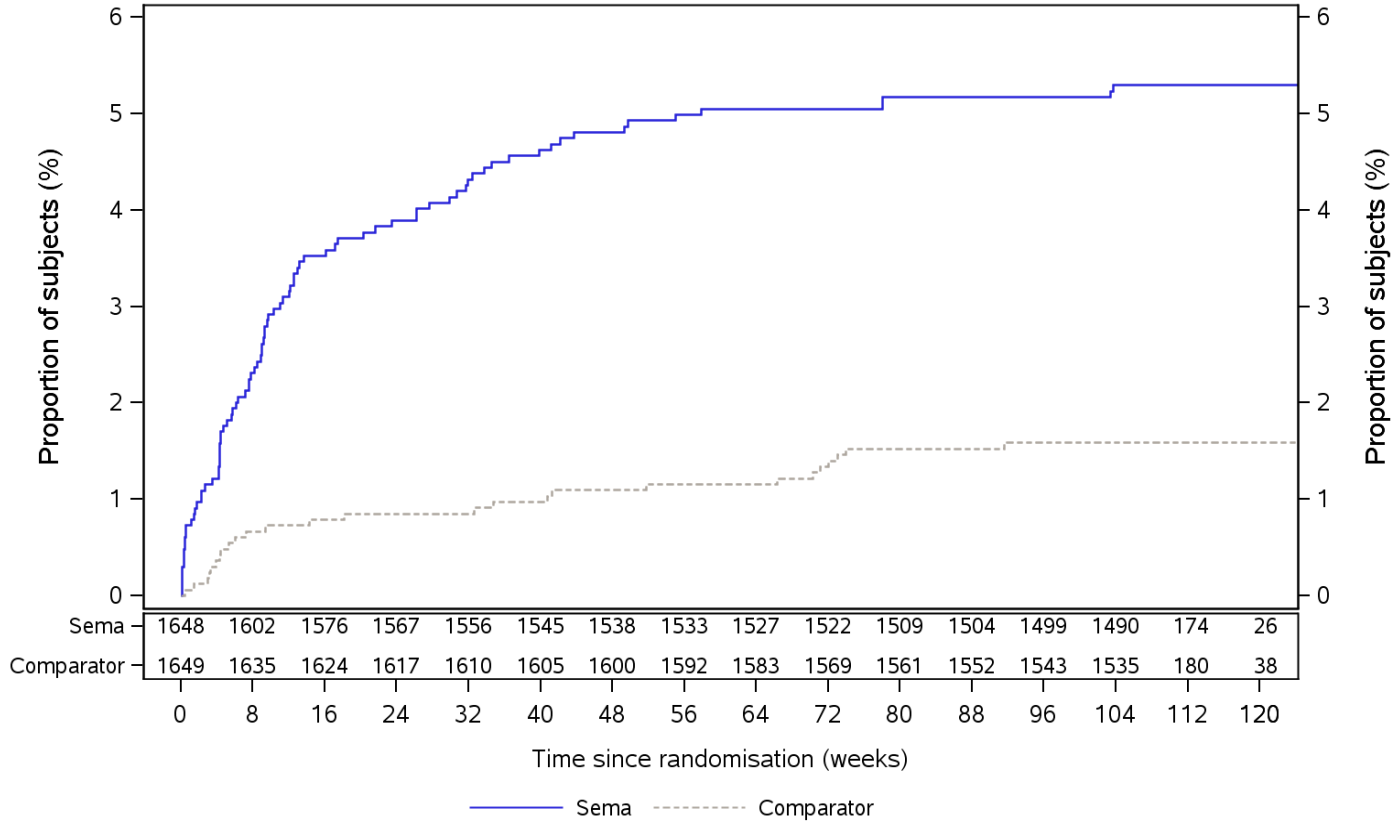
182 Moderate adverse events - preferred term "Urinary tract infection" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:46:37 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_uritrainf_ae_mo_s6.png

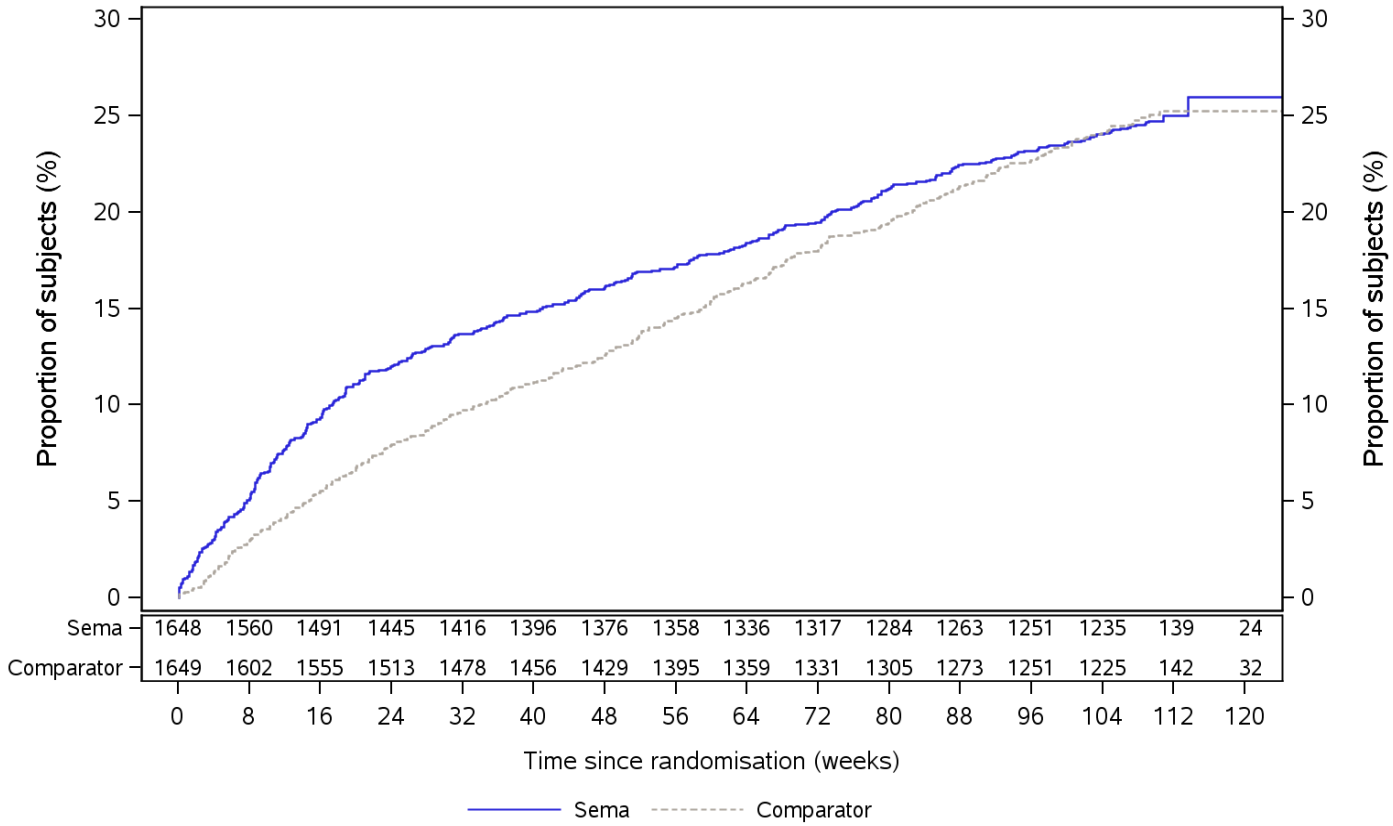
183 Moderate adverse events - preferred term "Vomiting" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:46:56 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_vomiting_ae_mo_s6.png

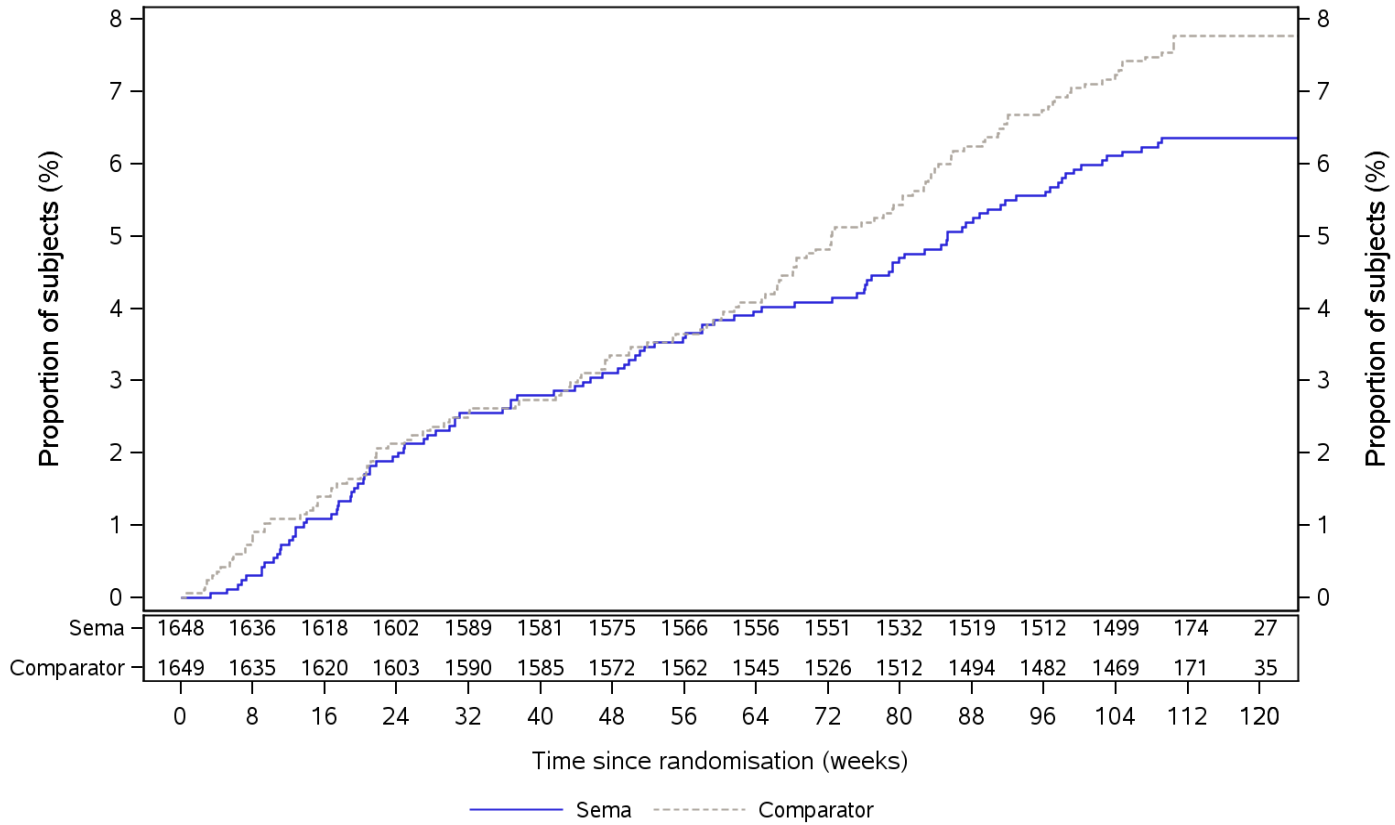
184 Severe adverse events - cumulative incidence plot -Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
17JUN2020:11:23:53 - f_cif_tte_s6_add.sas/f_cif_saf_ae_se_s6_add.png

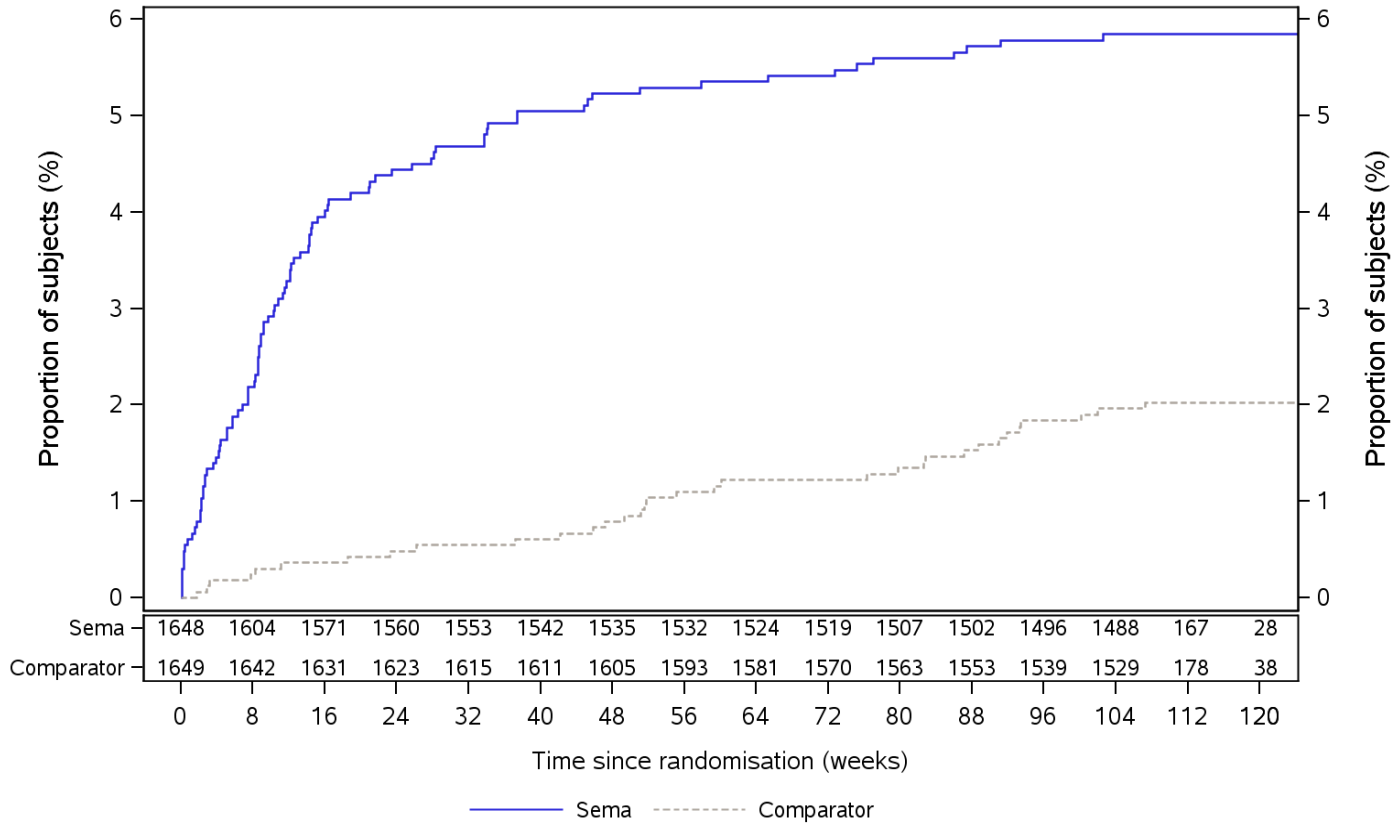
185 Severe adverse events - system organ class "Cardiac disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:47:16 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_cd_ae_se_s6.png

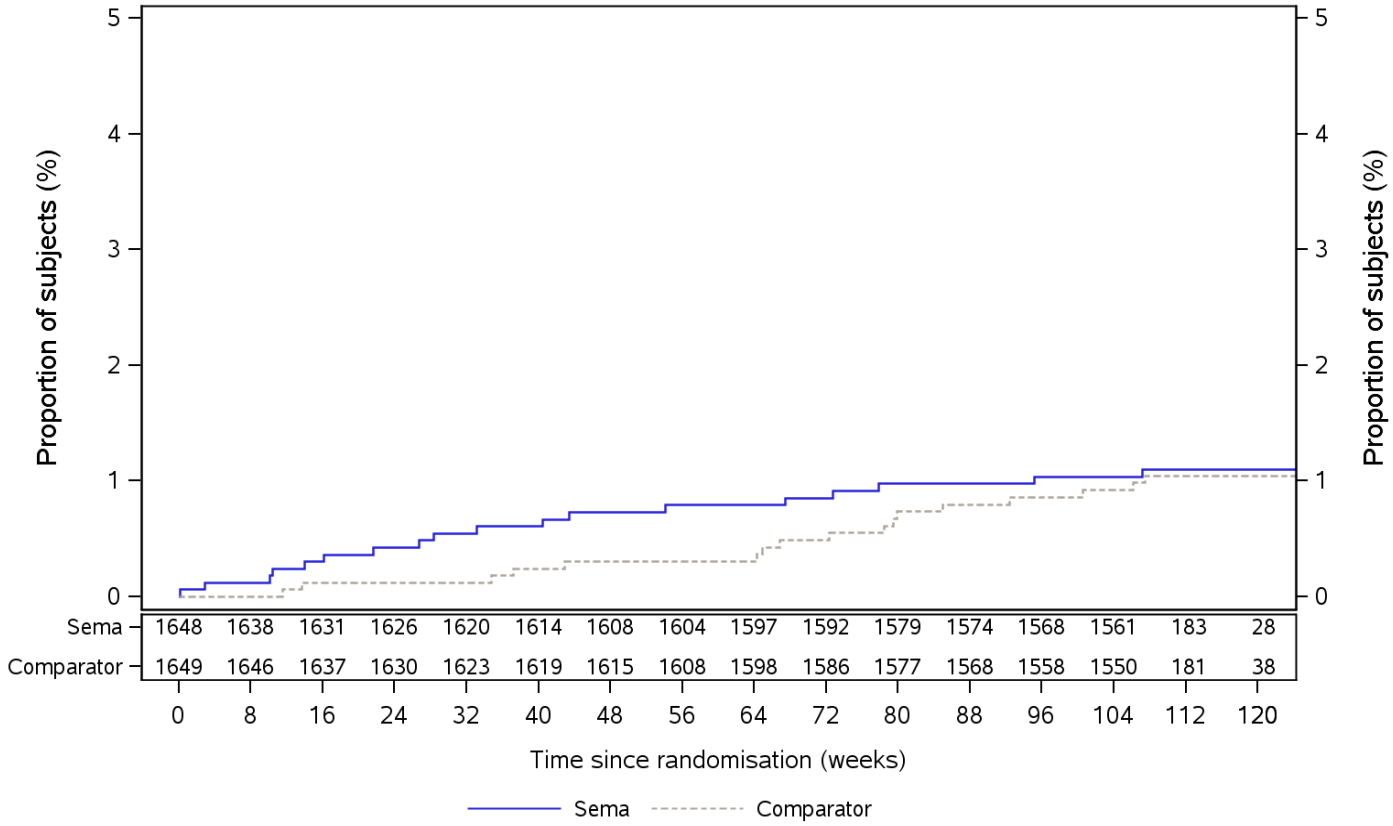
186 Severe adverse events - system organ class "Gastrointestinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:47:34 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_gd_ae_se_s6.png

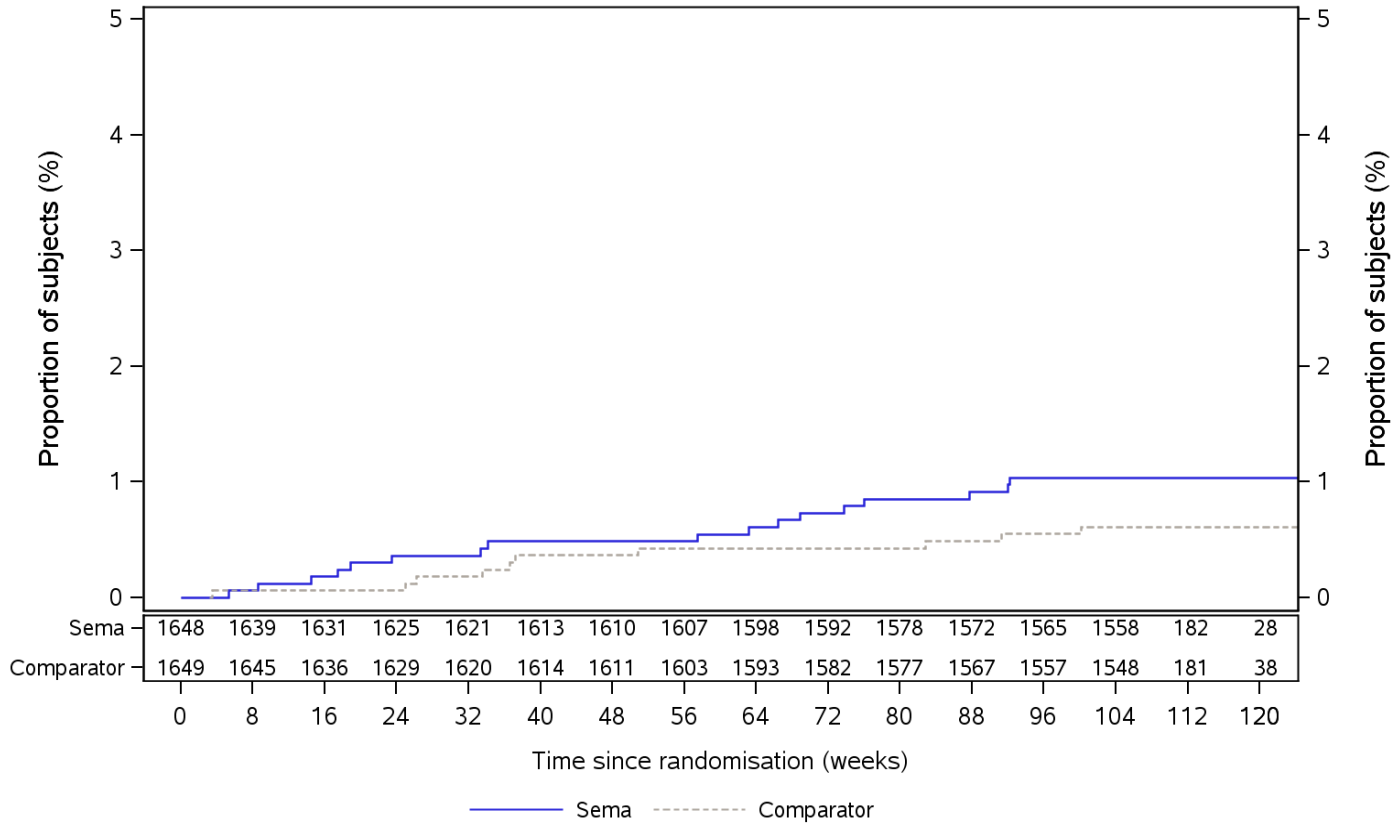
187 Severe adverse events - system organ class "General disorders and administration site conditions" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:47:53 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_gdasc_ae_se_s6.png

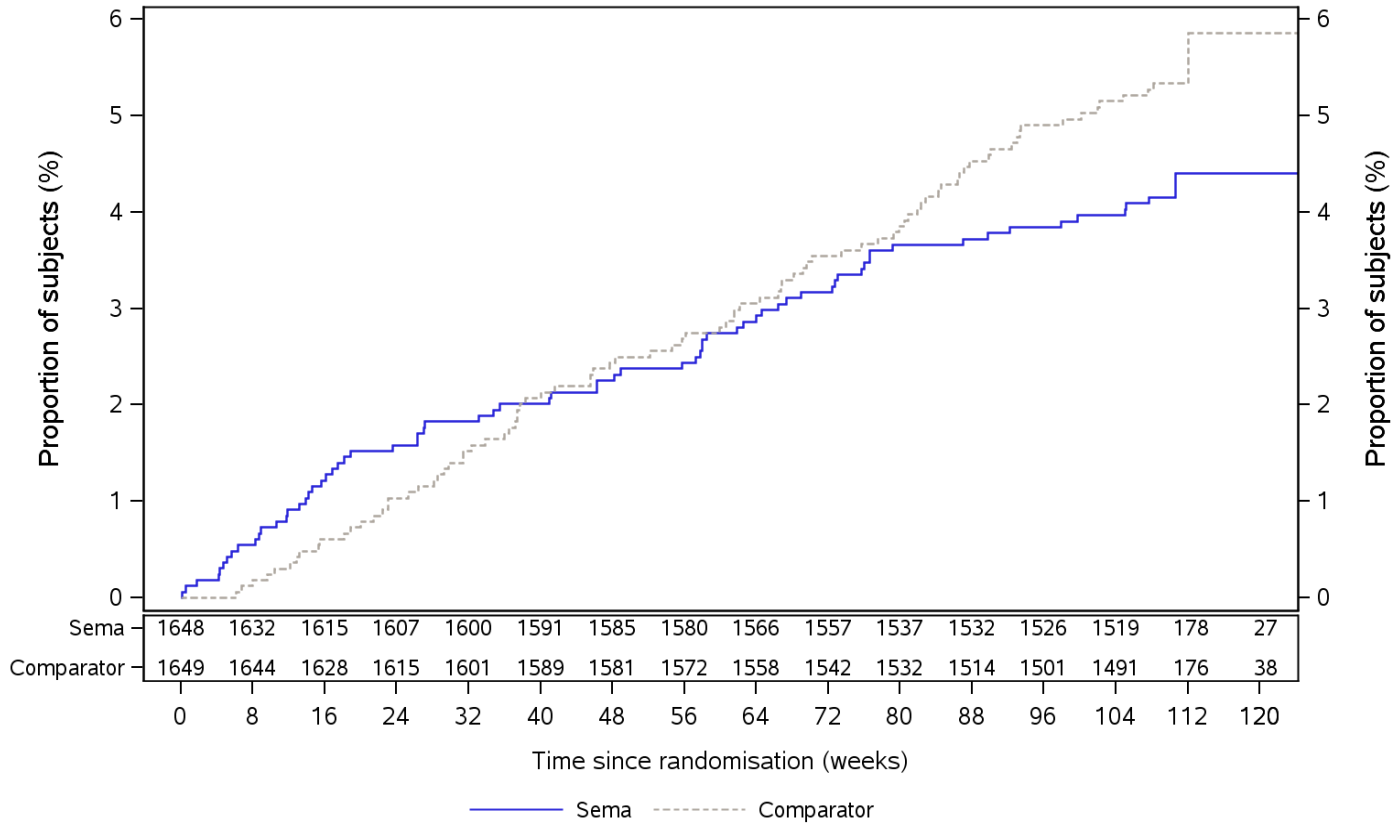
188 Severe adverse events - system organ class "Hepatobiliary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:48:12 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_hd_ae_se_s6.png

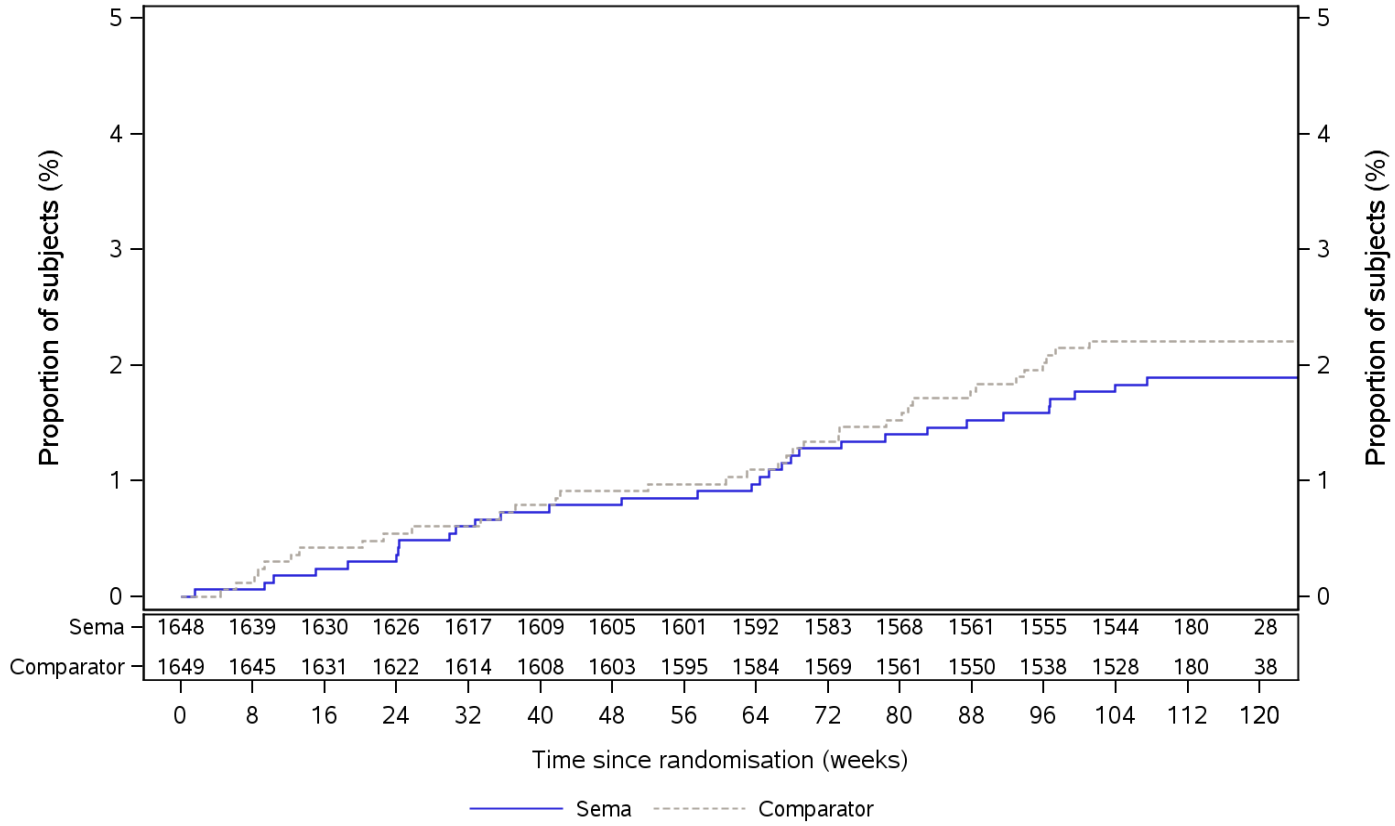
189 Severe adverse events - system organ class "Infections and infestations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:48:29 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ii_ae_se_s6.png

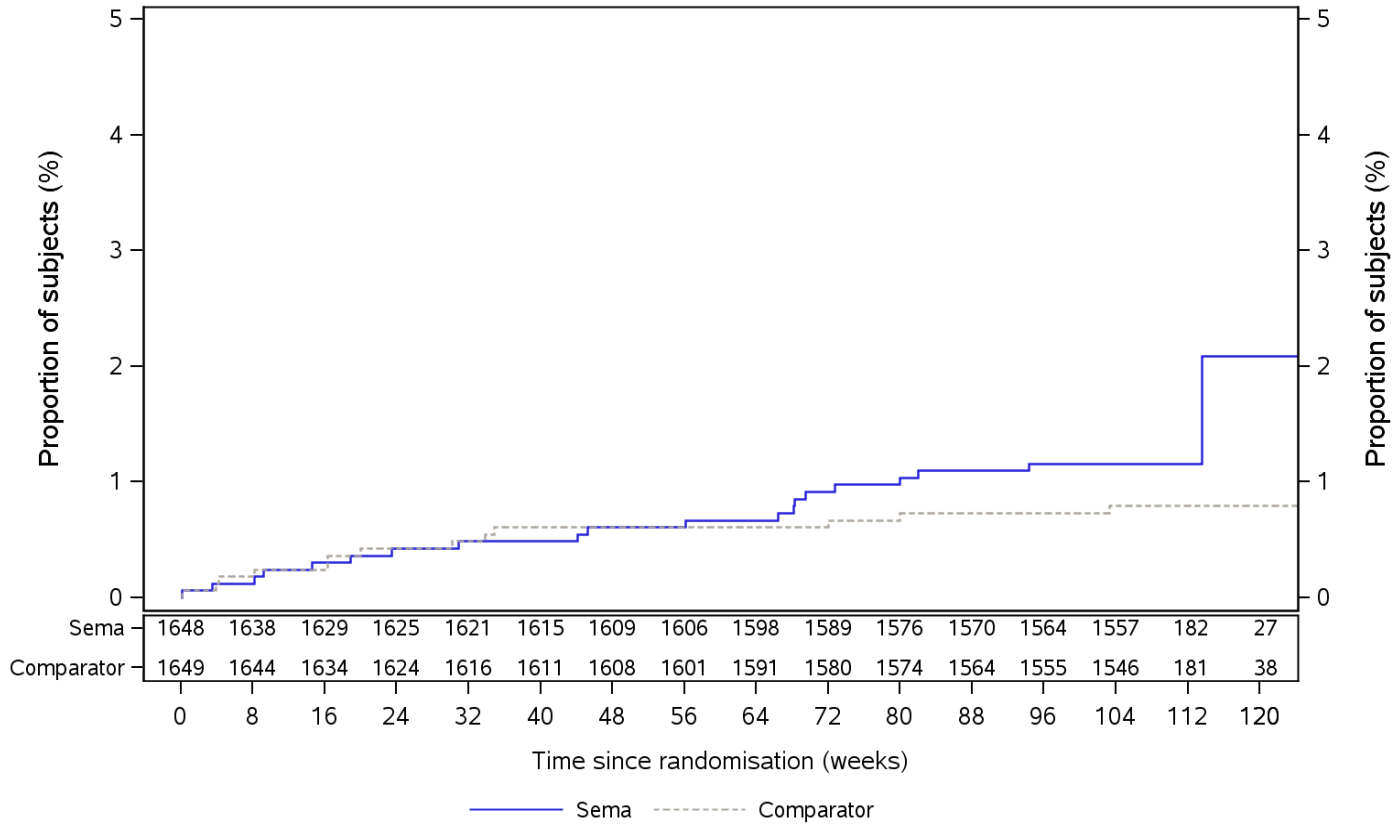
190 Severe adverse events - system organ class "Injury, poisoning and procedural complications" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:48:48 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_ippc_ae_se_s6.png

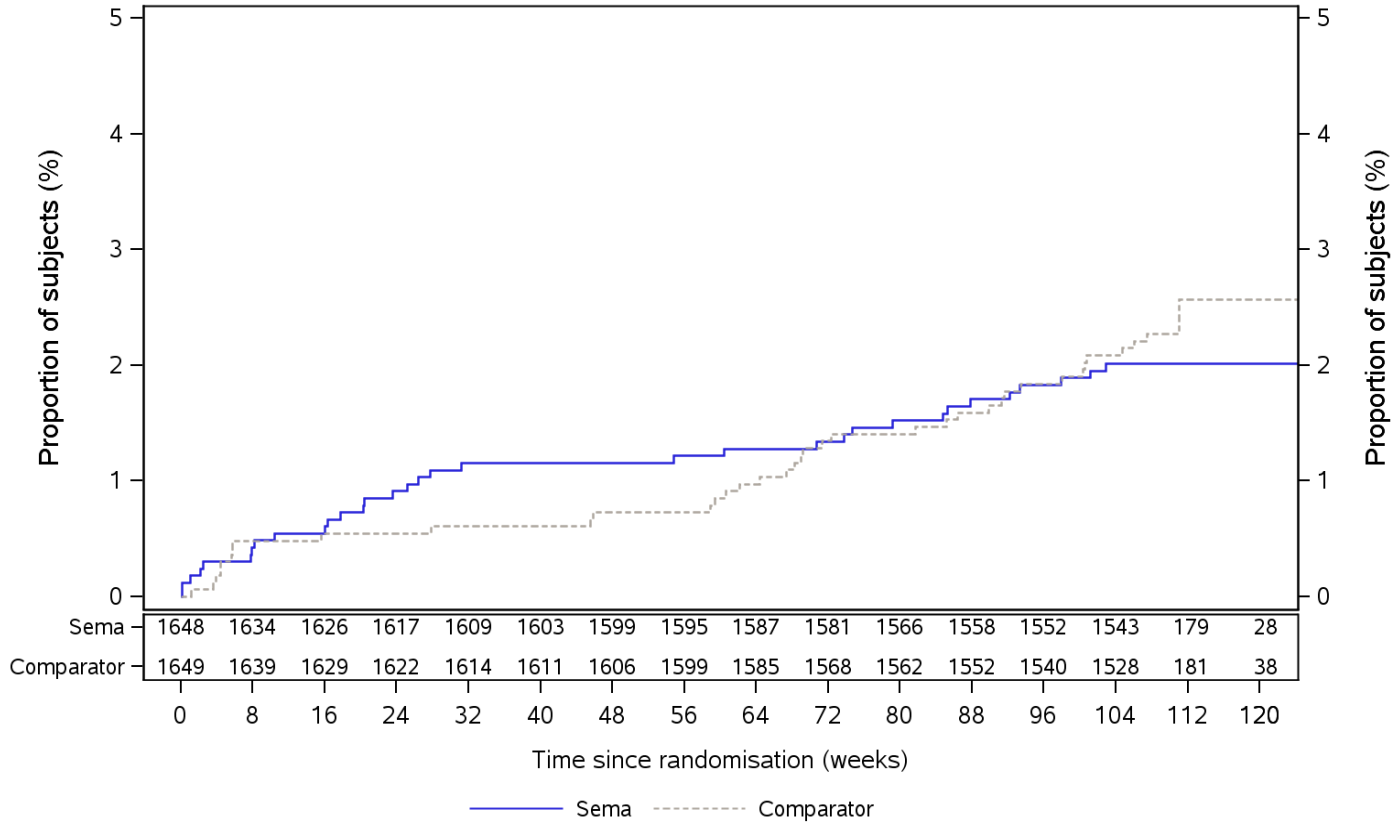
191 Severe adverse events - system organ class "Investigations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:49:06 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_investig_ae_se_s6.png

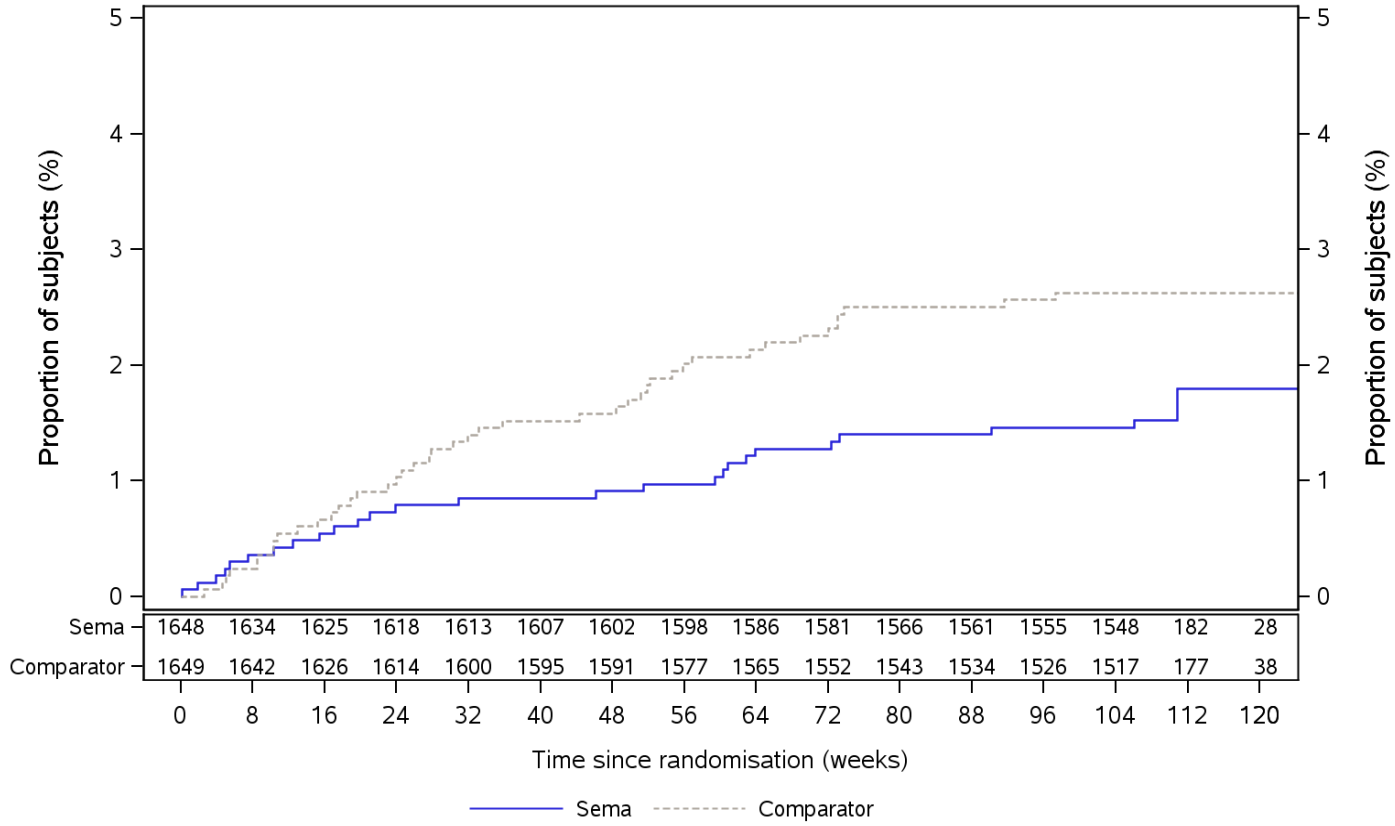
192 Severe adverse events - system organ class "Metabolism and nutrition disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:49:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_mnd_ae_se_s6.png

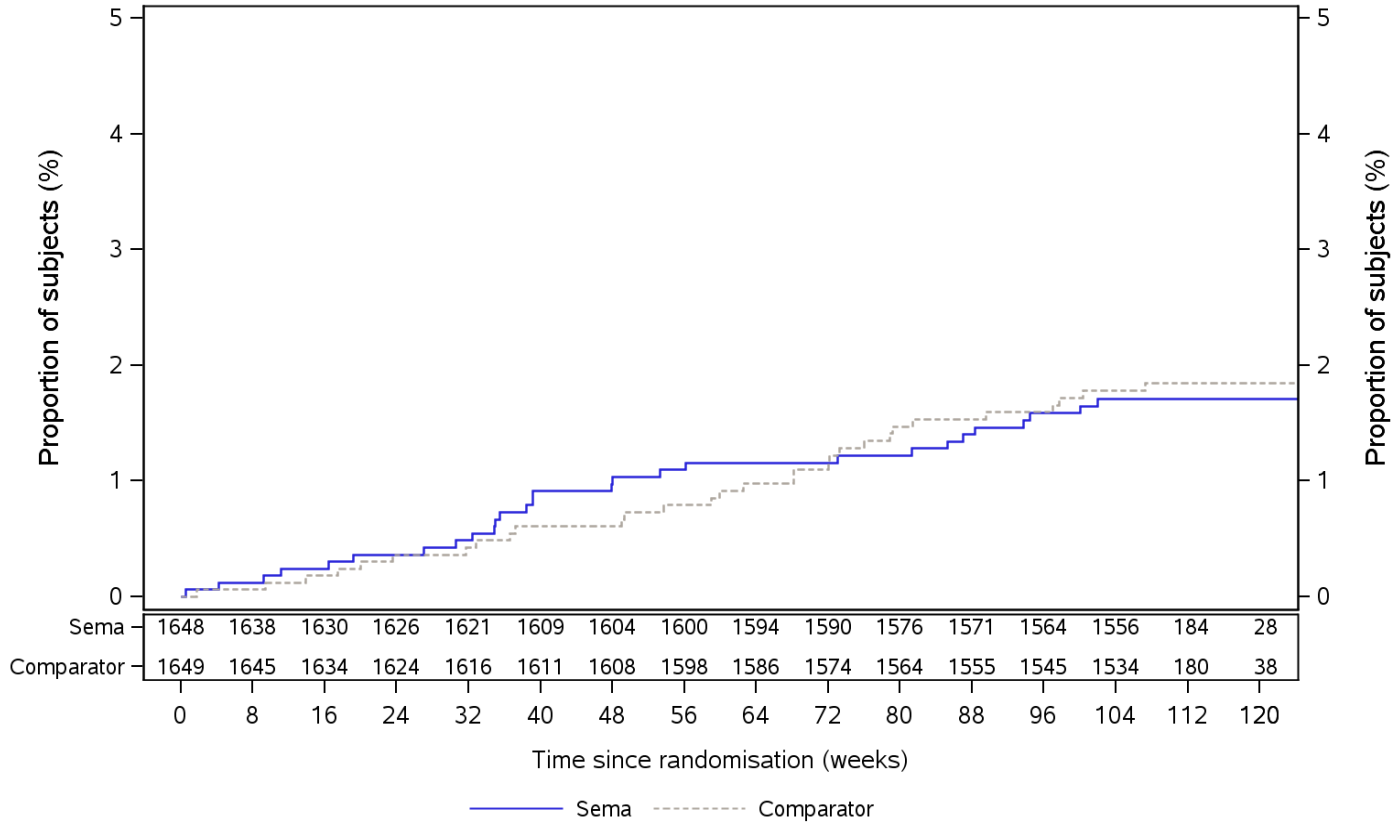
193 Severe adverse events - system organ class "Musculoskeletal and connective tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:49:42 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_mctd_ae_se_s6.png

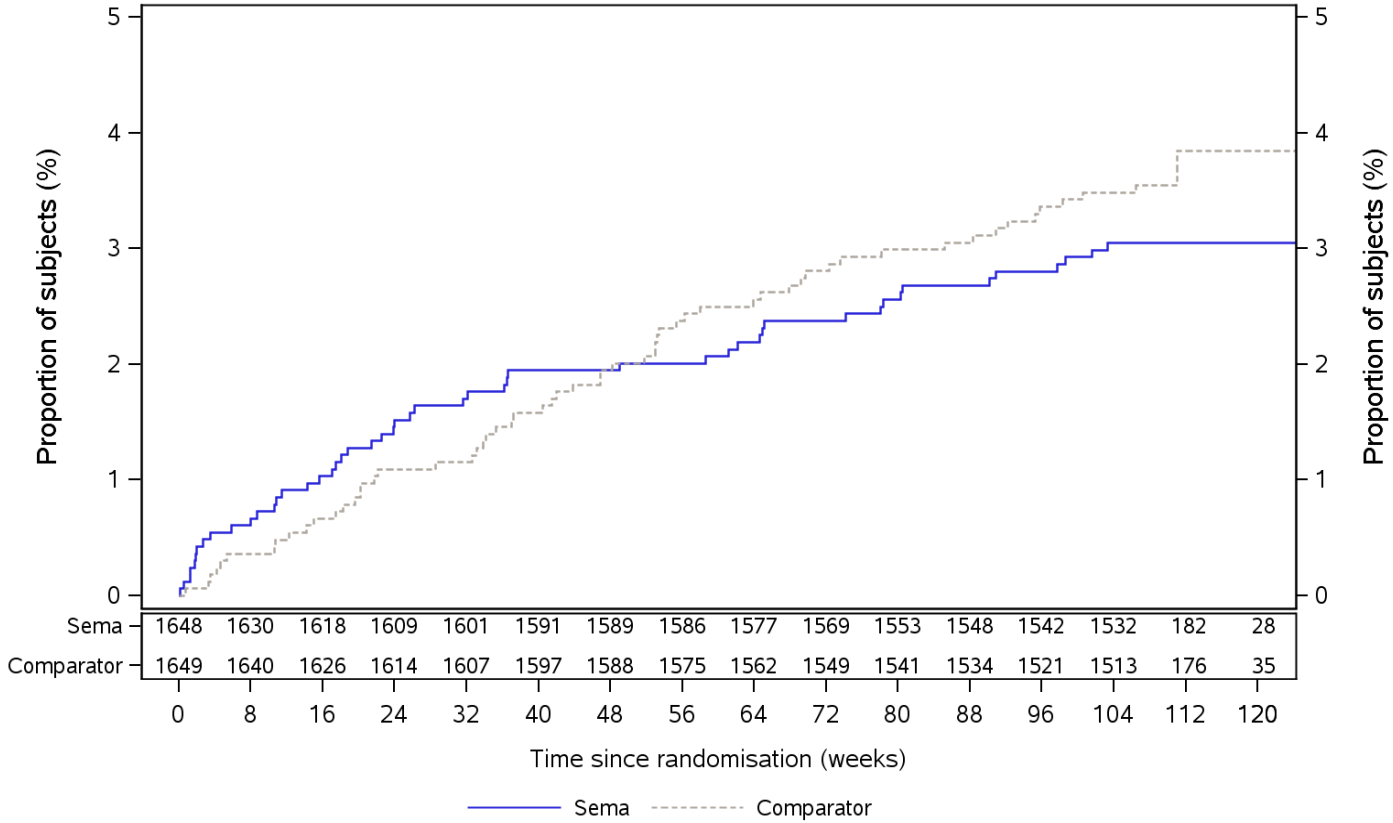
194 Severe adverse events - system organ class "Neoplasms benign, malignant and unspecified (incl cysts and polyps)" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:50:01 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_nbmu_ae_se_s6.png

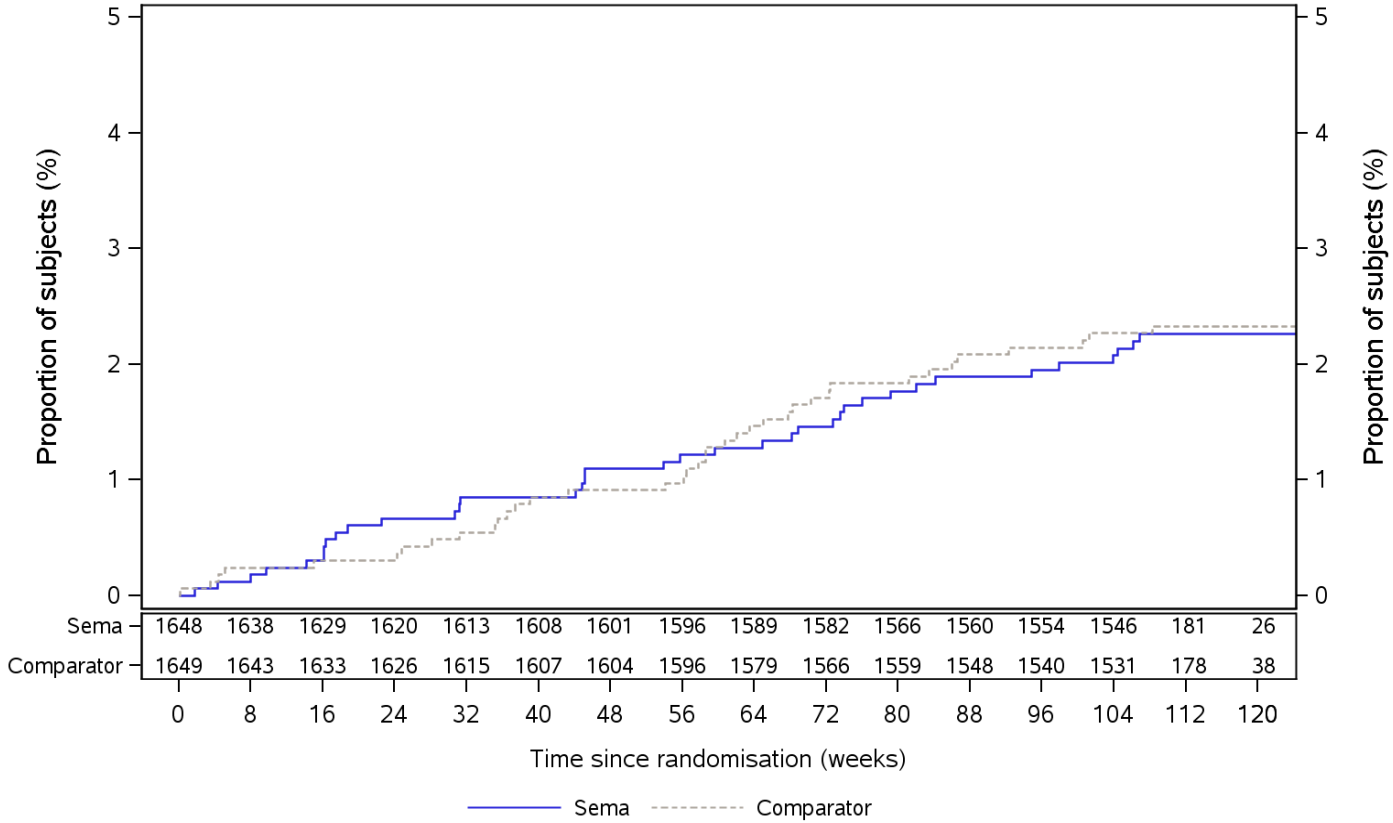
195 Severe adverse events - system organ class "Nervous system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:50:19 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_nsd_ae_se_s6.png

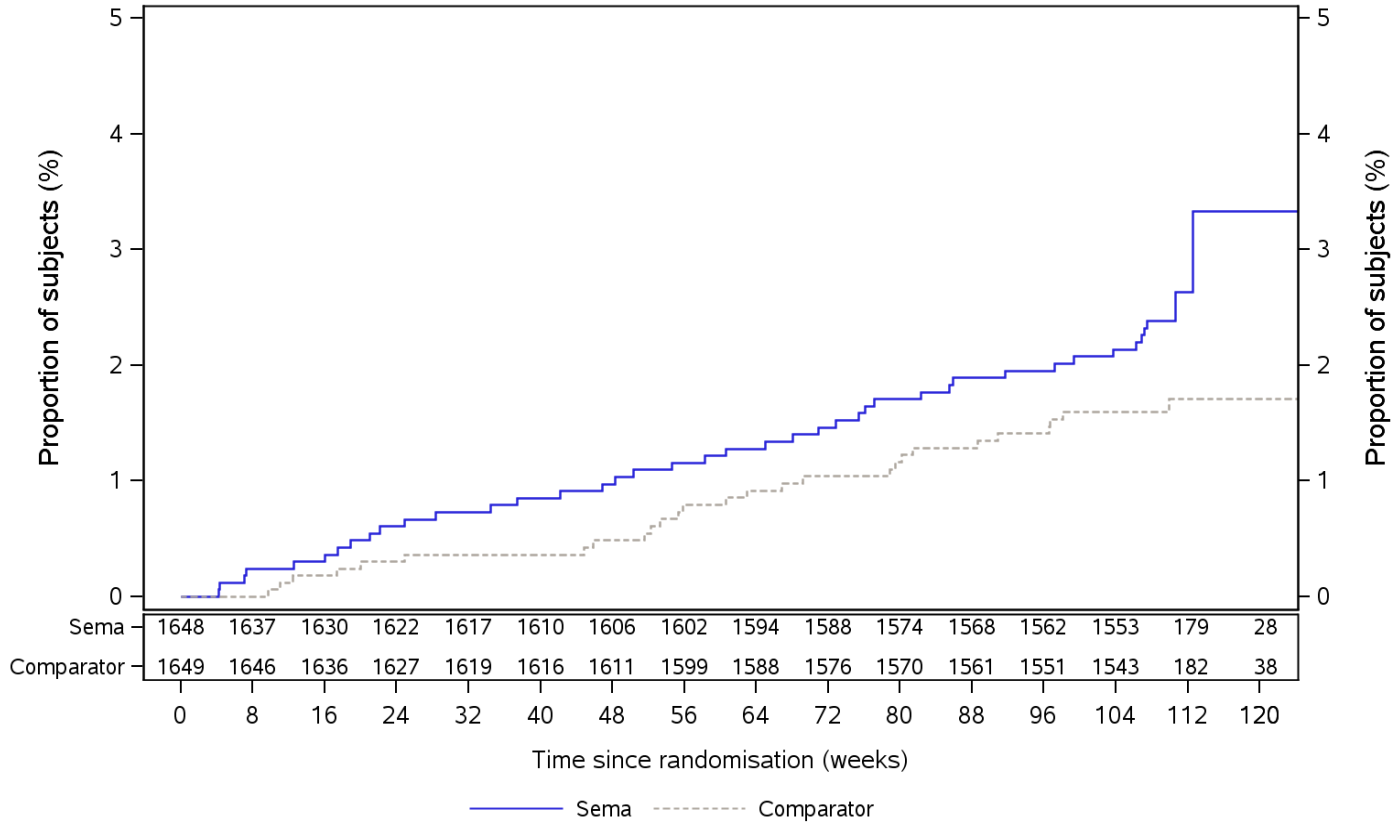
196 Severe adverse events - system organ class "Renal and urinary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:50:37 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_rud_ae_se_s6.png

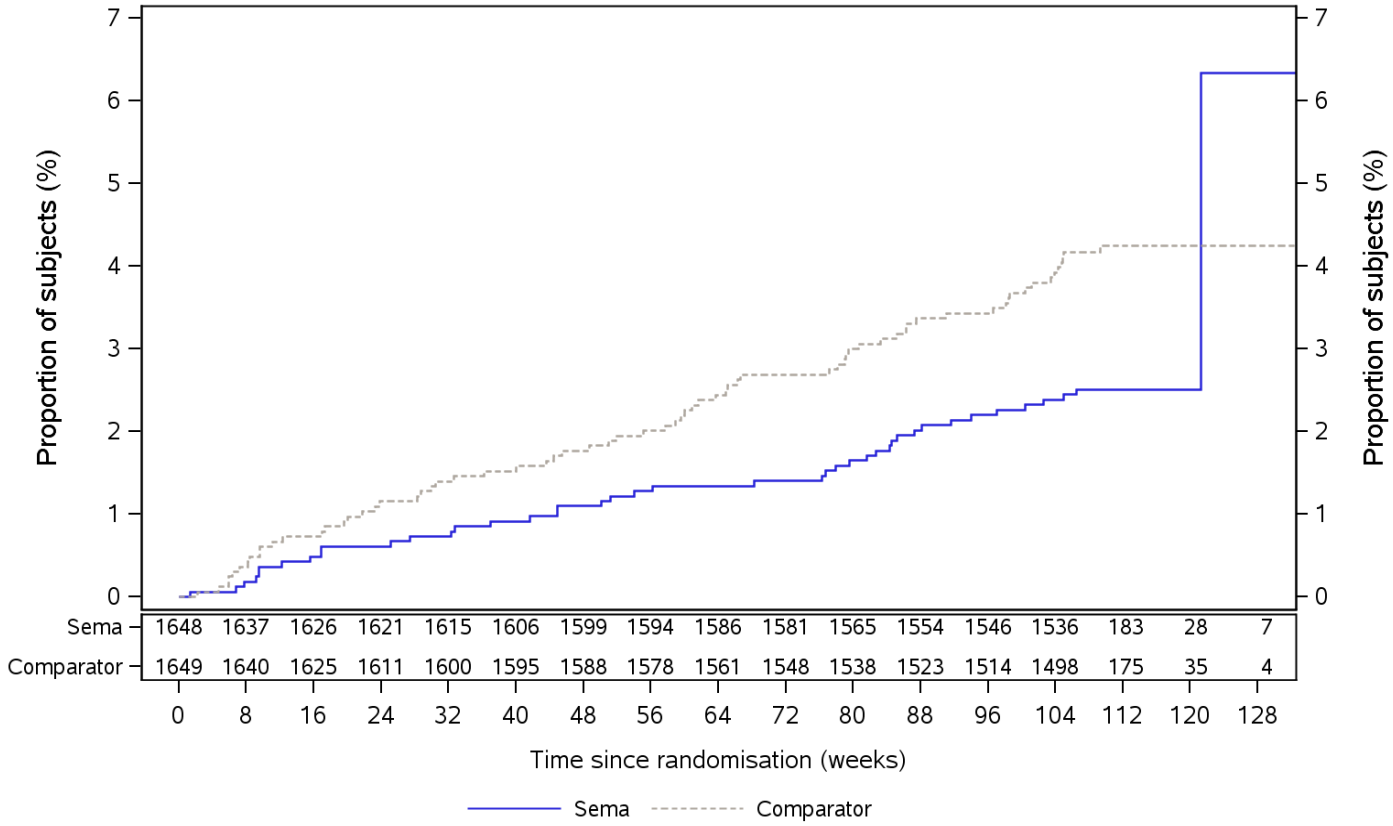
197 Severe adverse events - system organ class "Respiratory, thoracic and mediastinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:50:55 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_rtmd_ae_se_s6.png

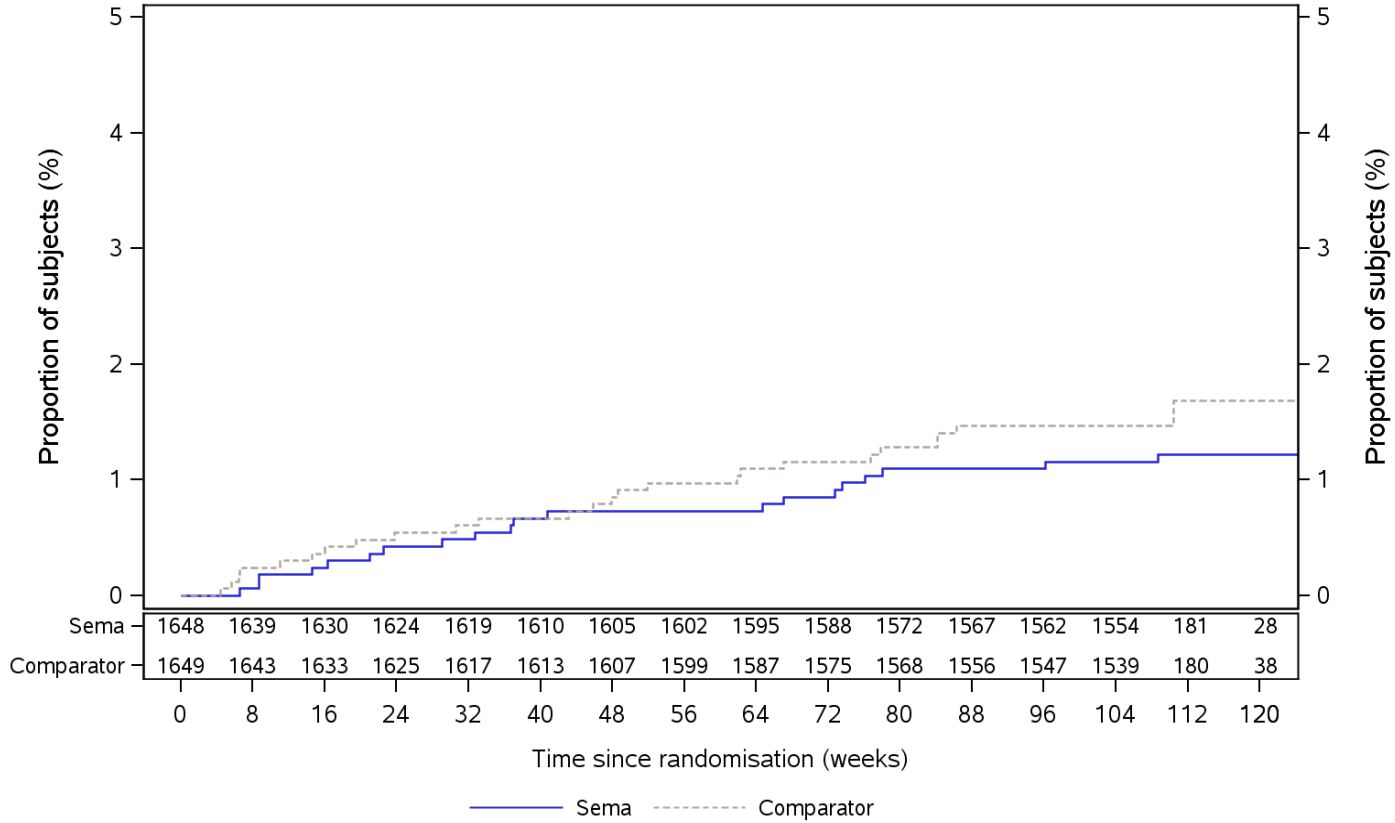
198 Severe adverse events - system organ class "Surgical and medical procedures" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:51:12 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_smp_ae_se_s6.png

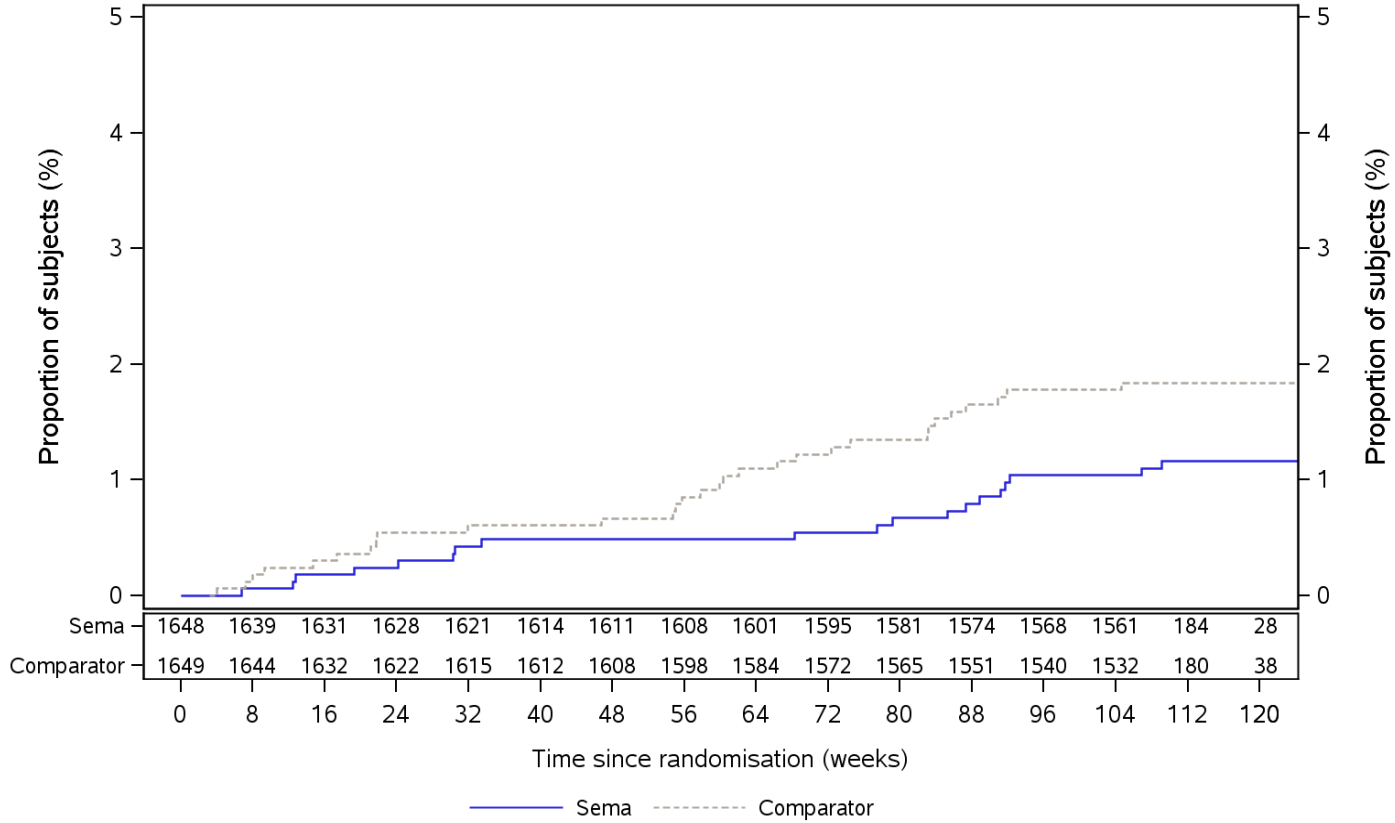
199 Severe adverse events - system organ class "Vascular disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:51:30 - f_cif_tte_soc_pt_s6_add.sas/f_cif_soc_vd_ae_se_s6.png

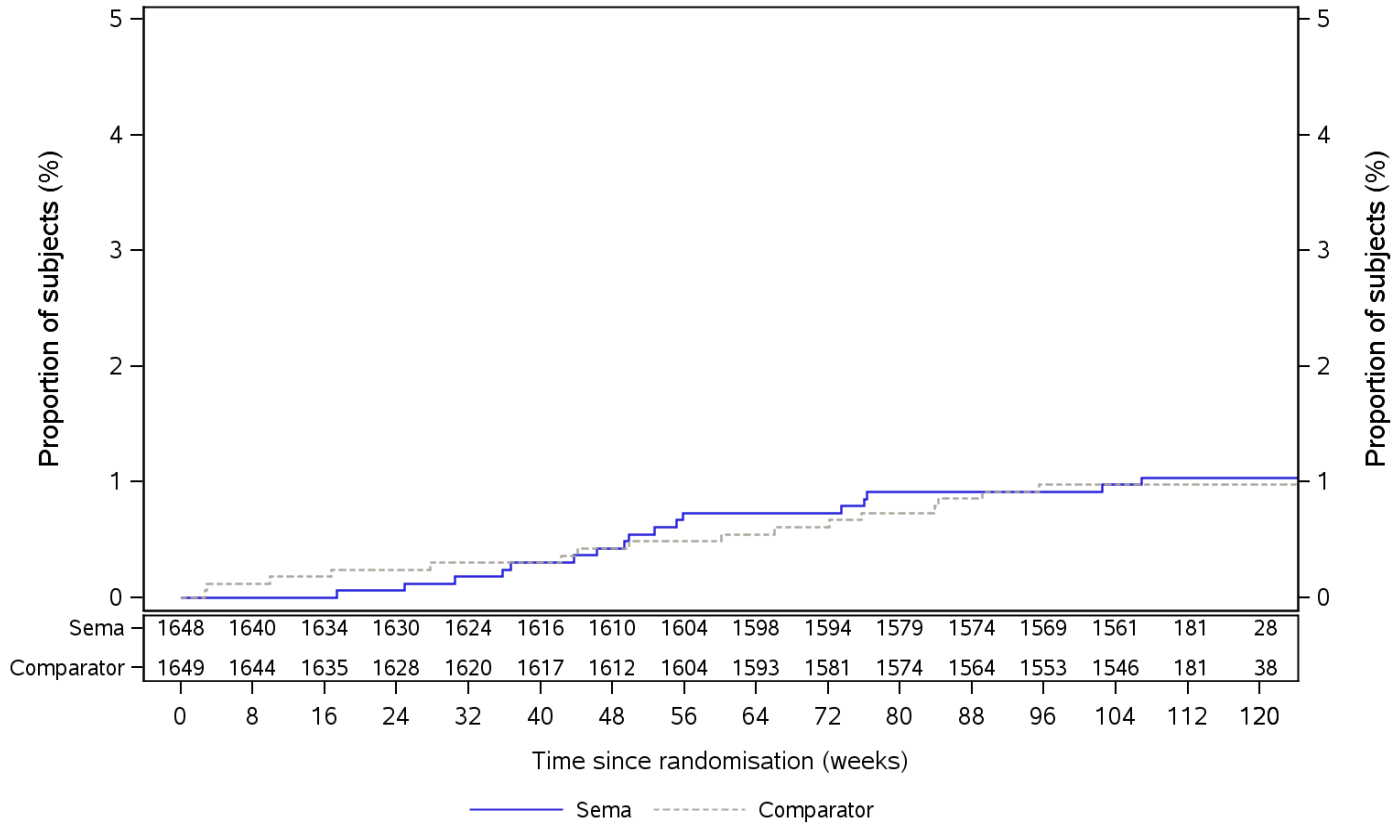
200 Severe adverse events - preferred term "Acute myocardial infarction" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:51:48 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_ami_ae_se_s6.png

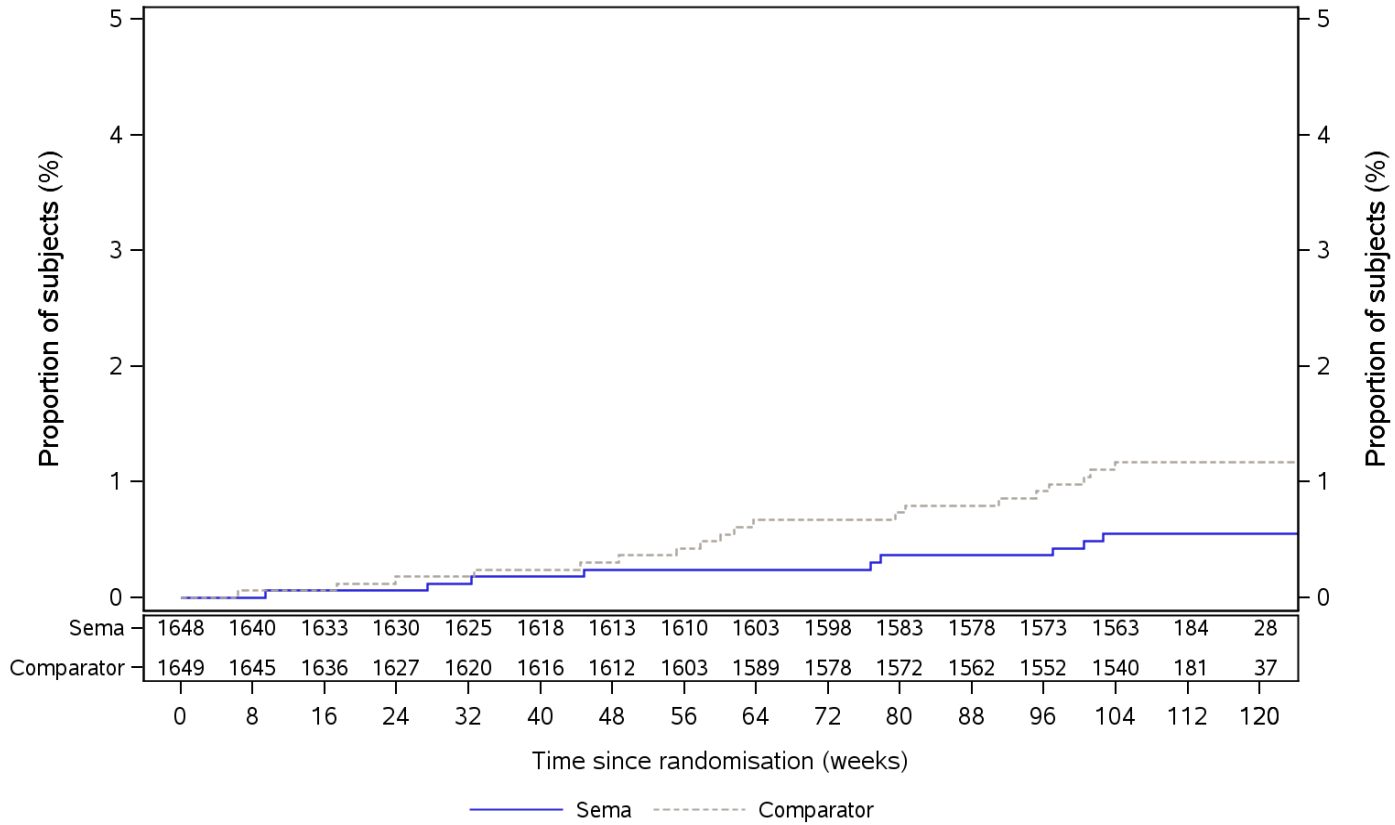
201 Severe adverse events - preferred term "Cardiac failure congestive" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:52:07 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cfc_ae_se_s6.png

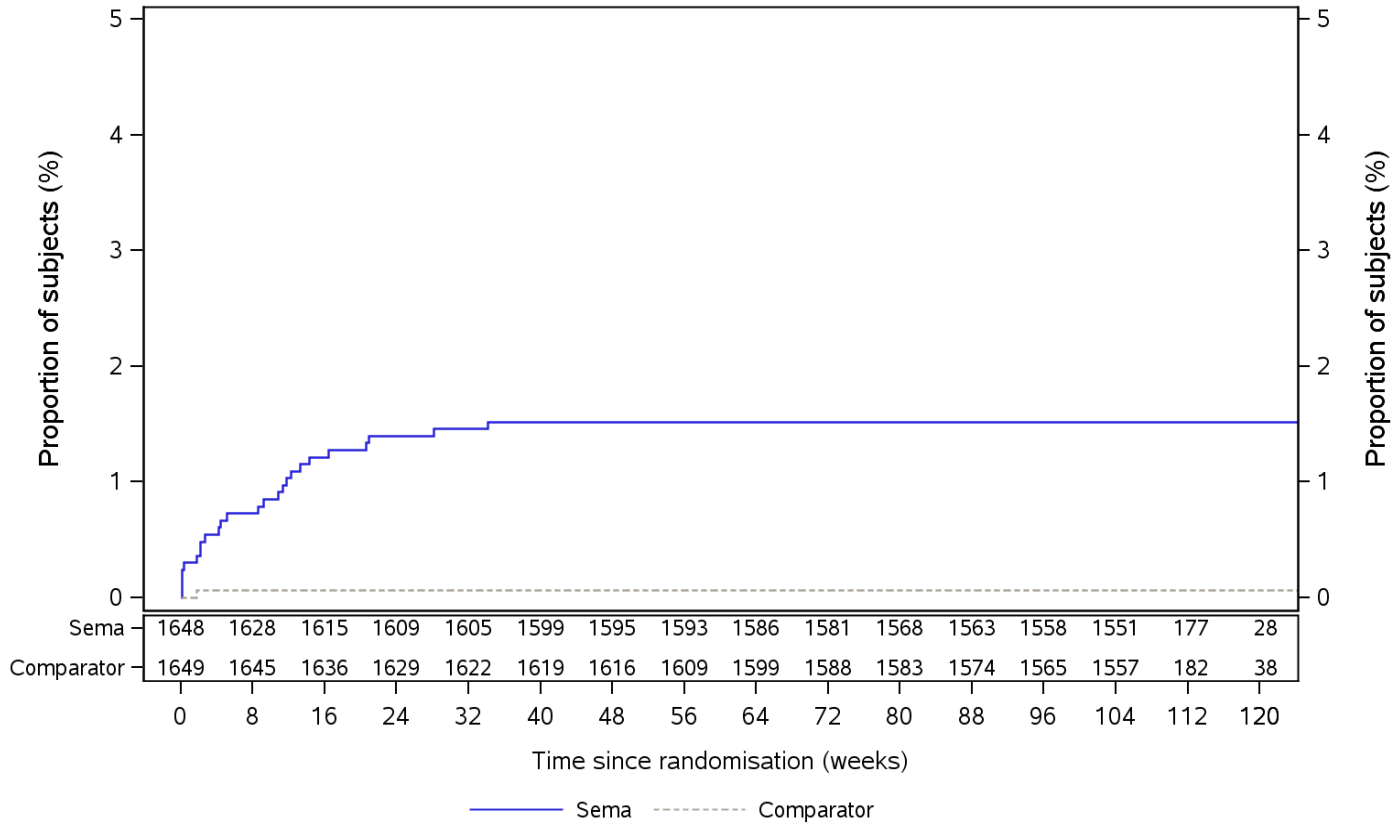
202 Severe adverse events - preferred term "Coronary artery bypass" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:52:25 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_cab_ae_se_s6.png

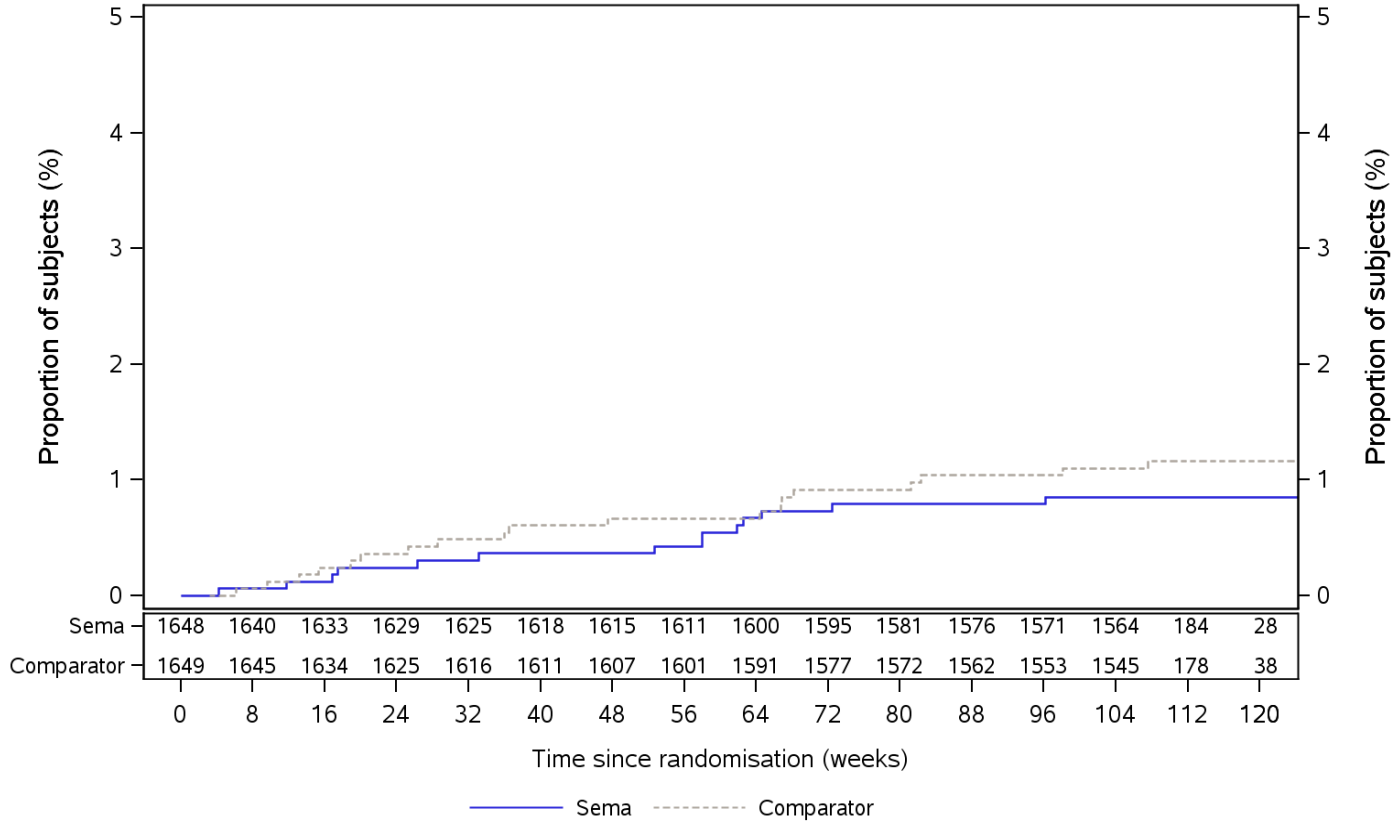
203 Severe adverse events - preferred term "Nausea" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:52:43 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_nausea_ae_se_s6.png

204 Severe adverse events - preferred term "Pneumonia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set

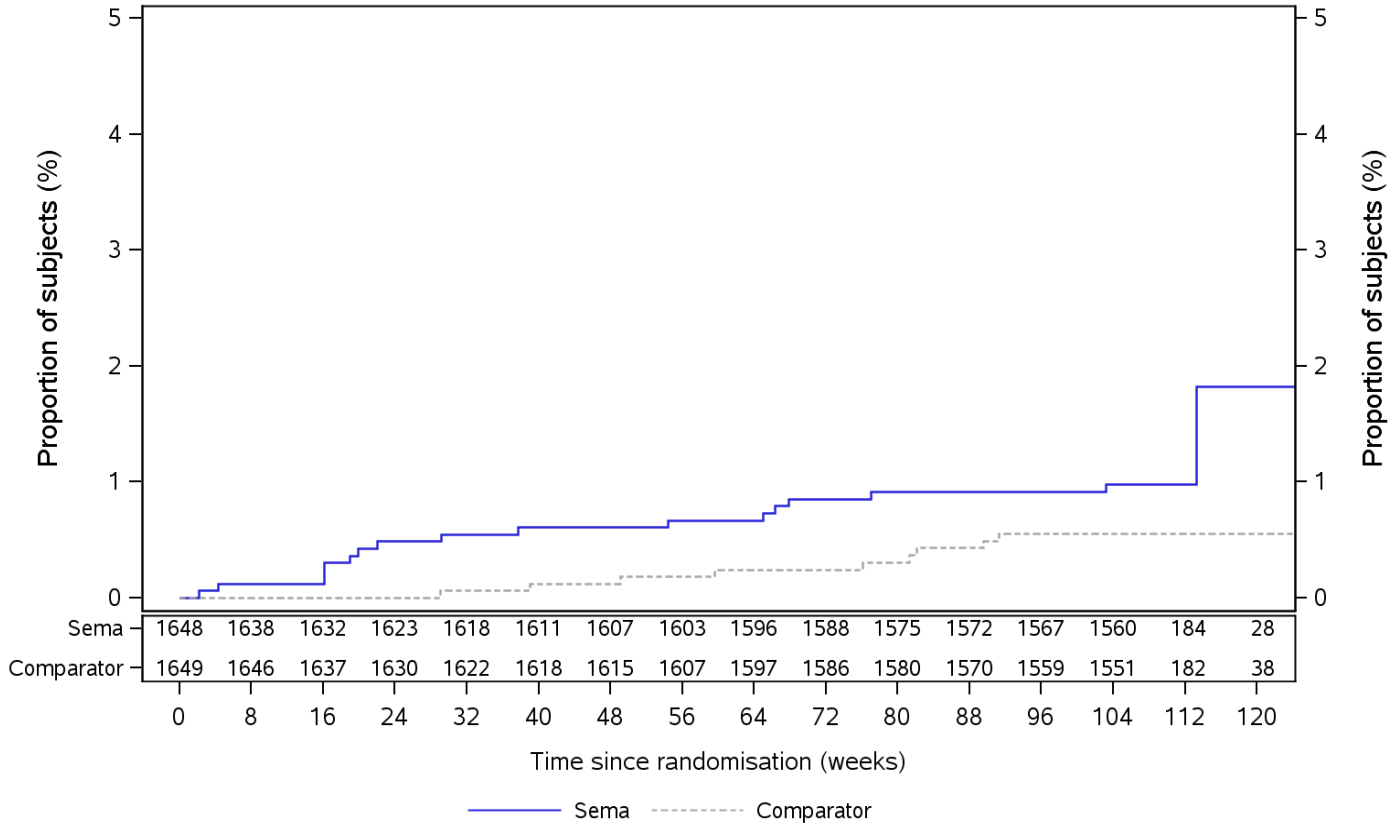


Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
16JUN2020:11:53:02 - f_cif_tte_soc_pt_s6_add.sas/f_cif_pt_pneu_ae_se_s6.png

SUSTAIN 6 – Kumulative Inzidenz (SUE nach SOC und PT)

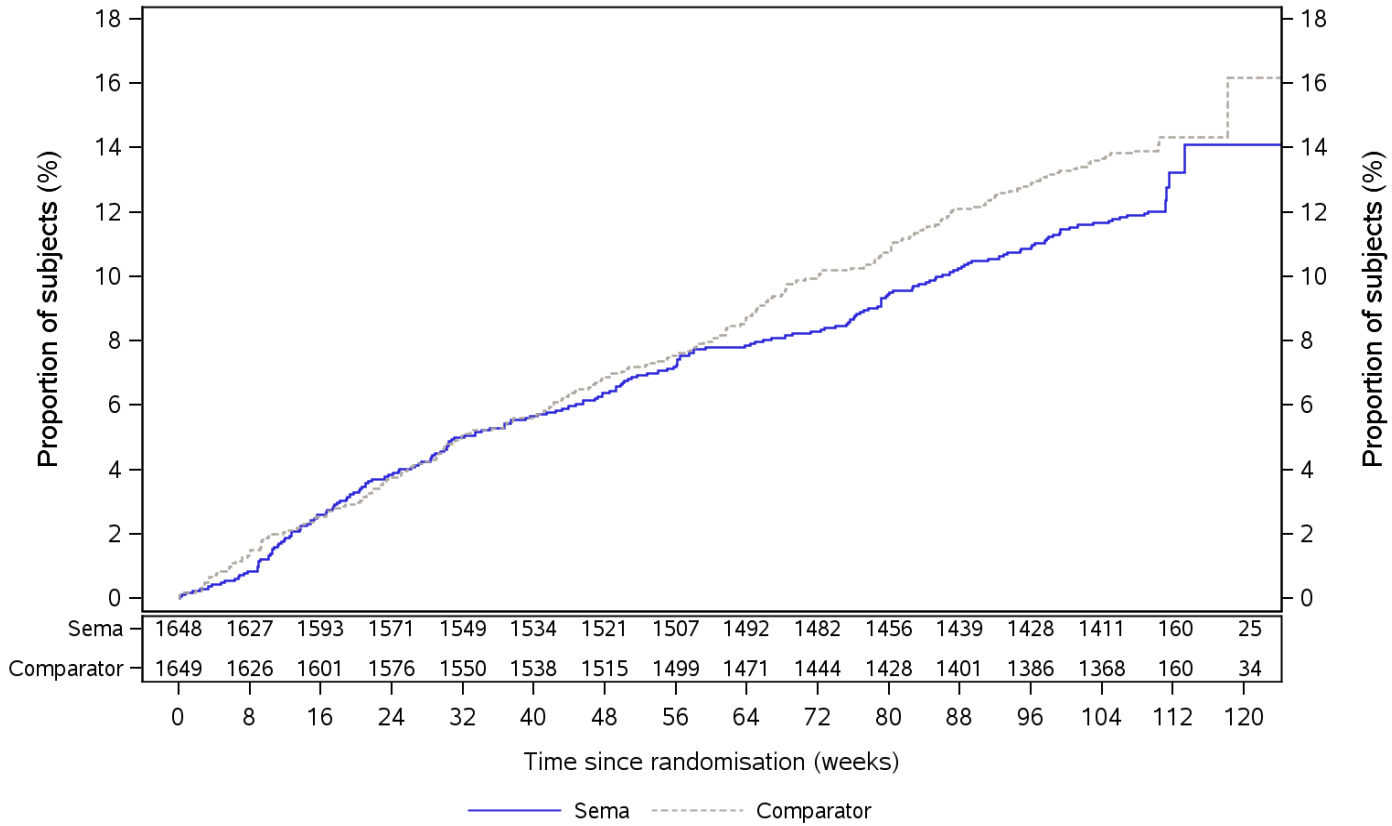
1 Serious adverse events - system organ class "Blood and lymphatic system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:35:39 - f_cif_tte_s6.sas/f_cif_soc_blsd_sae_s6.png

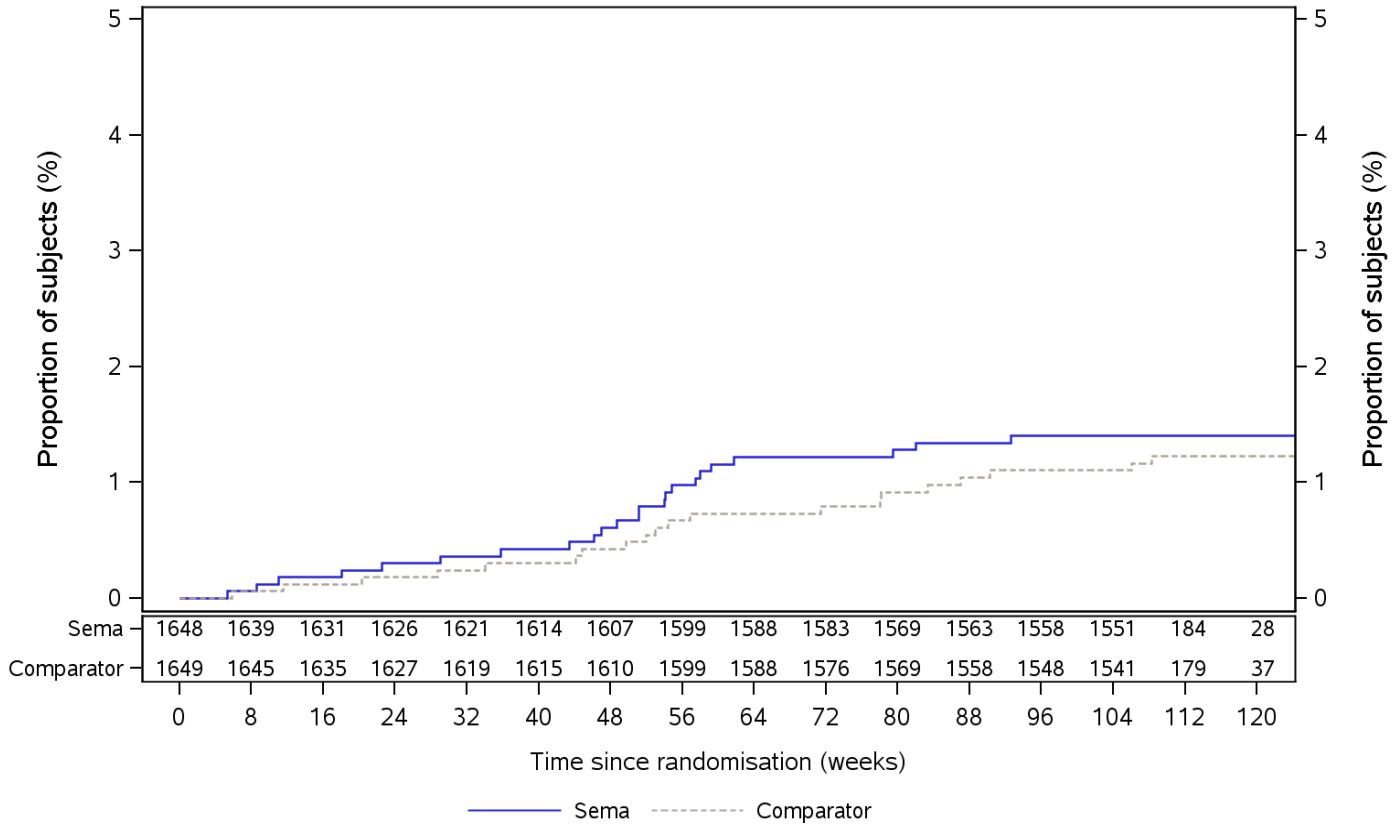
2 Serious adverse events - system organ class "Cardiac disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:35:56 - f_cif_tte_s6.sas/f_cif_soc_cd_sae_s6.png

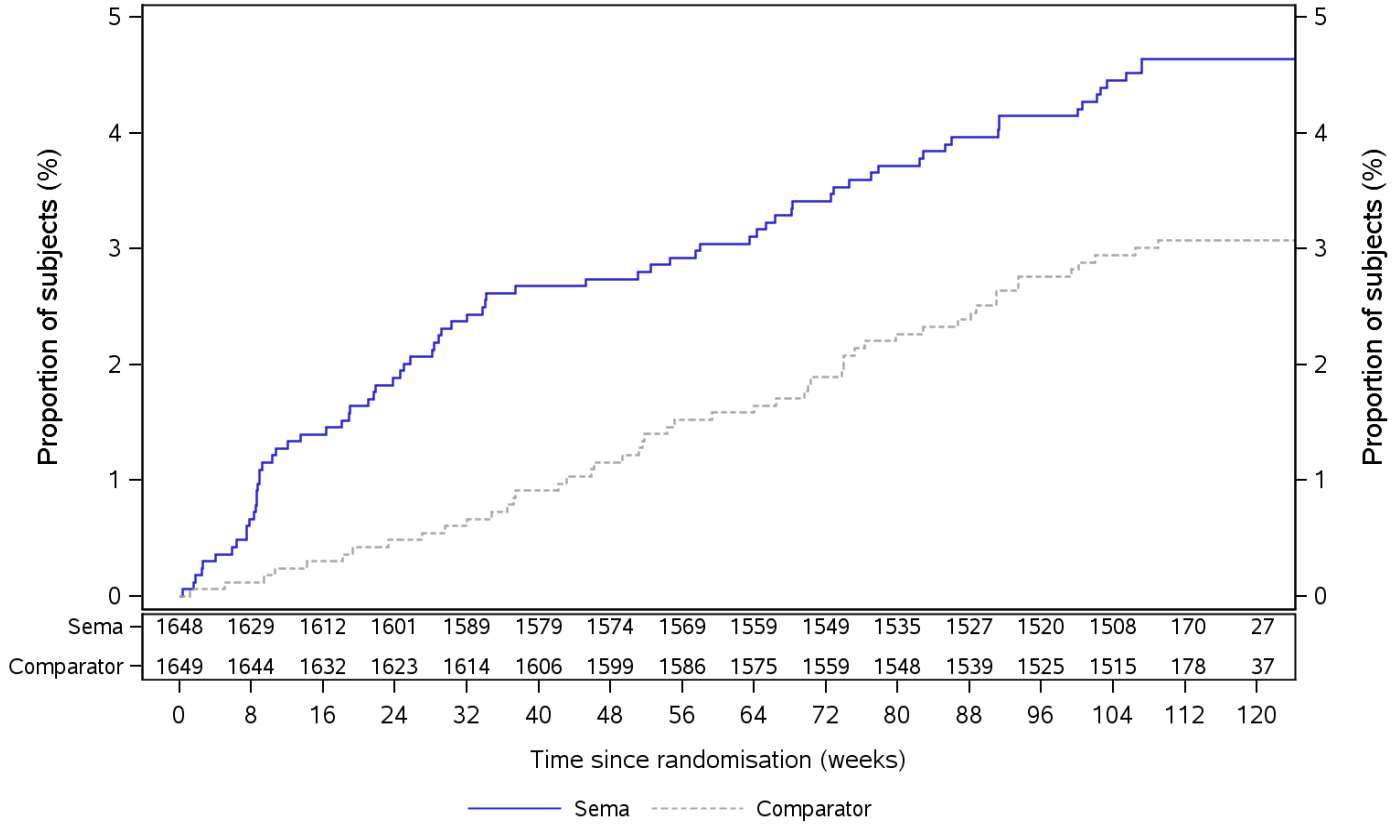
3 Serious adverse events - system organ class "Eye disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:36:15 - f_cif_tte_s6.sas/f_cif_soc_ed_sae_s6.png

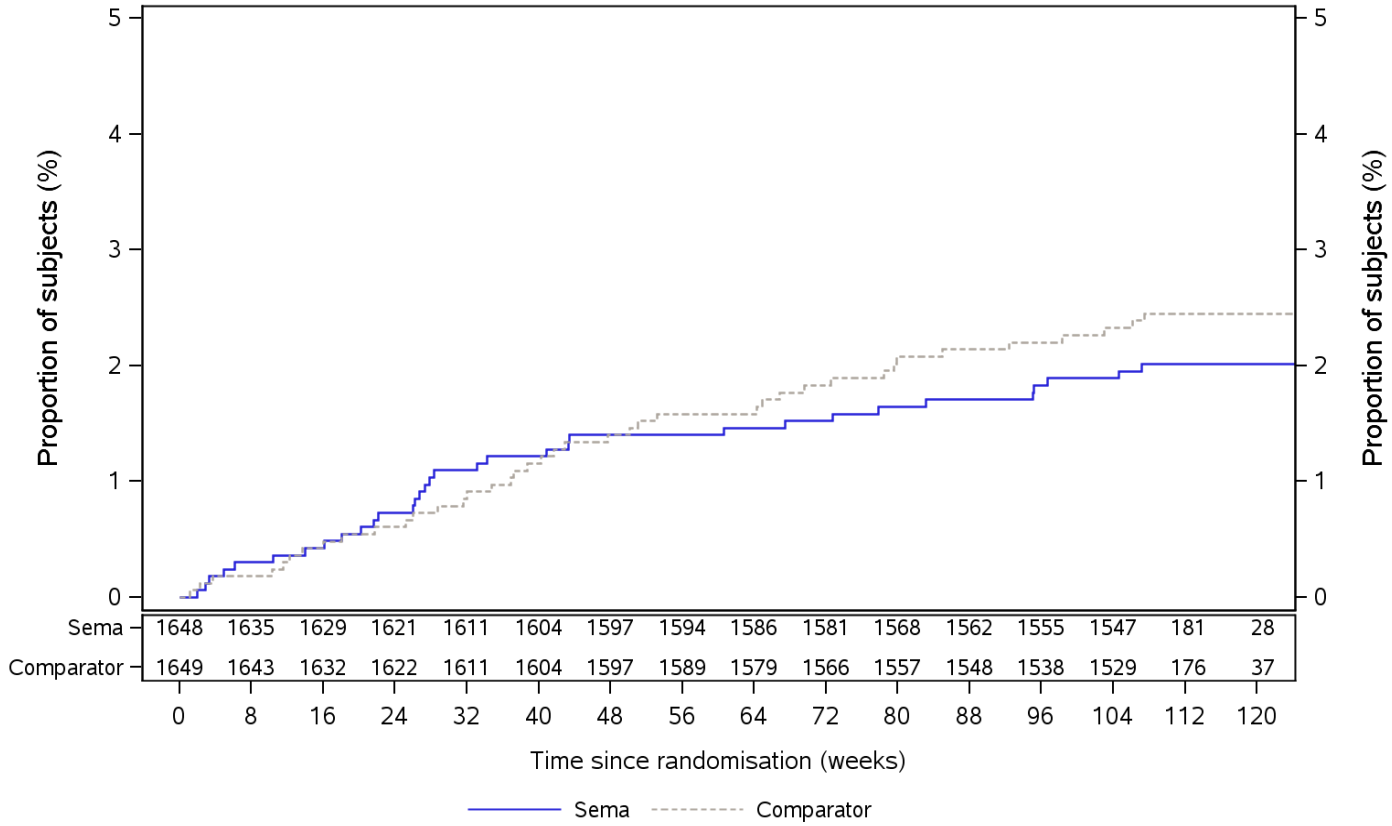
4 Serious adverse events - system organ class "Gastrointestinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:36:32 - f_cif_tte_s6.sas/f_cif_soc_gd_sae_s6.png

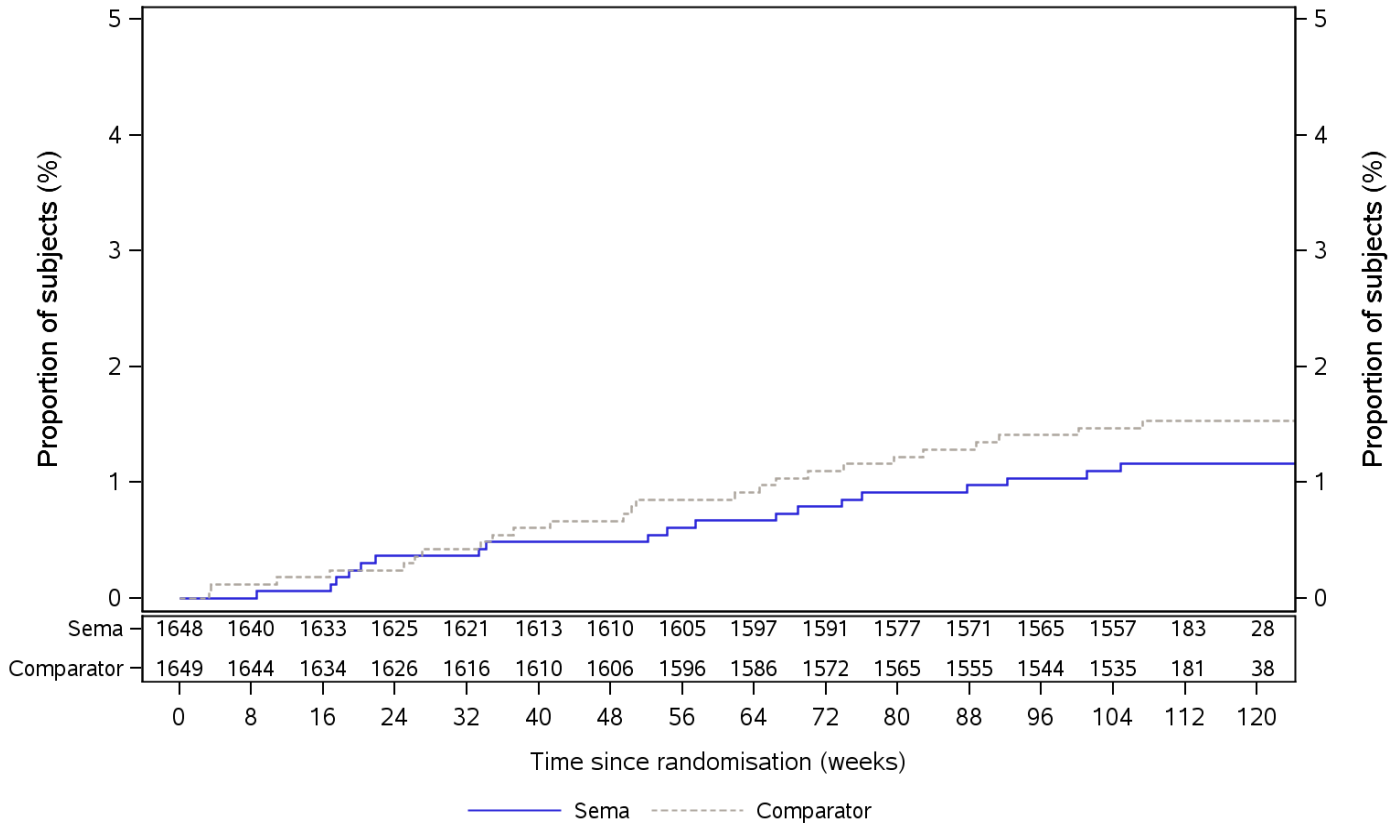
5 Serious adverse events - system organ class "General disorders and administration site conditions" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:36:50 - f_cif_tte_s6.sas/f_cif_soc_gdasc_sae_s6.png

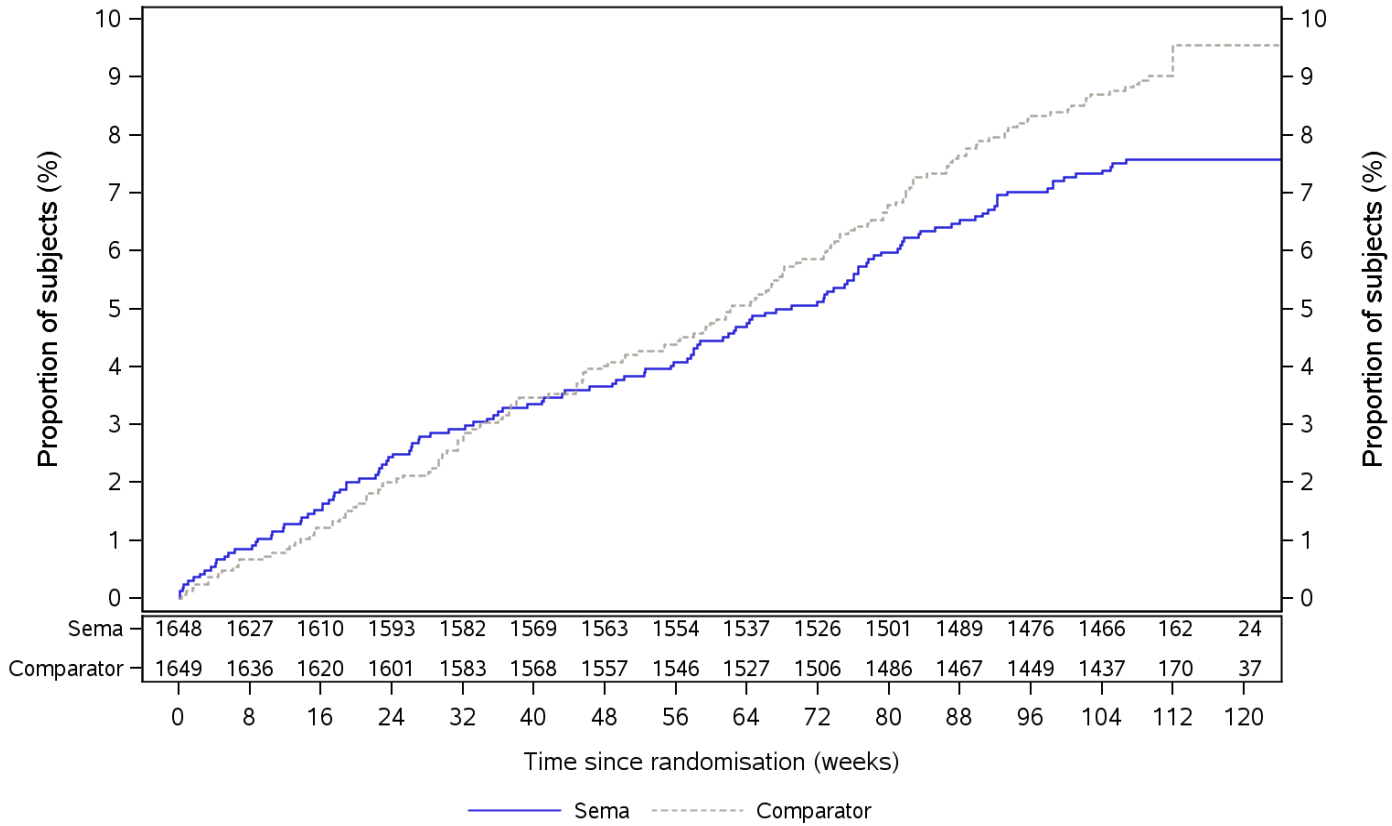
6 Serious adverse events - system organ class "Hepatobiliary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:37:09 - f_cif_tte_s6.sas/f_cif_soc_hd_sae_s6.png

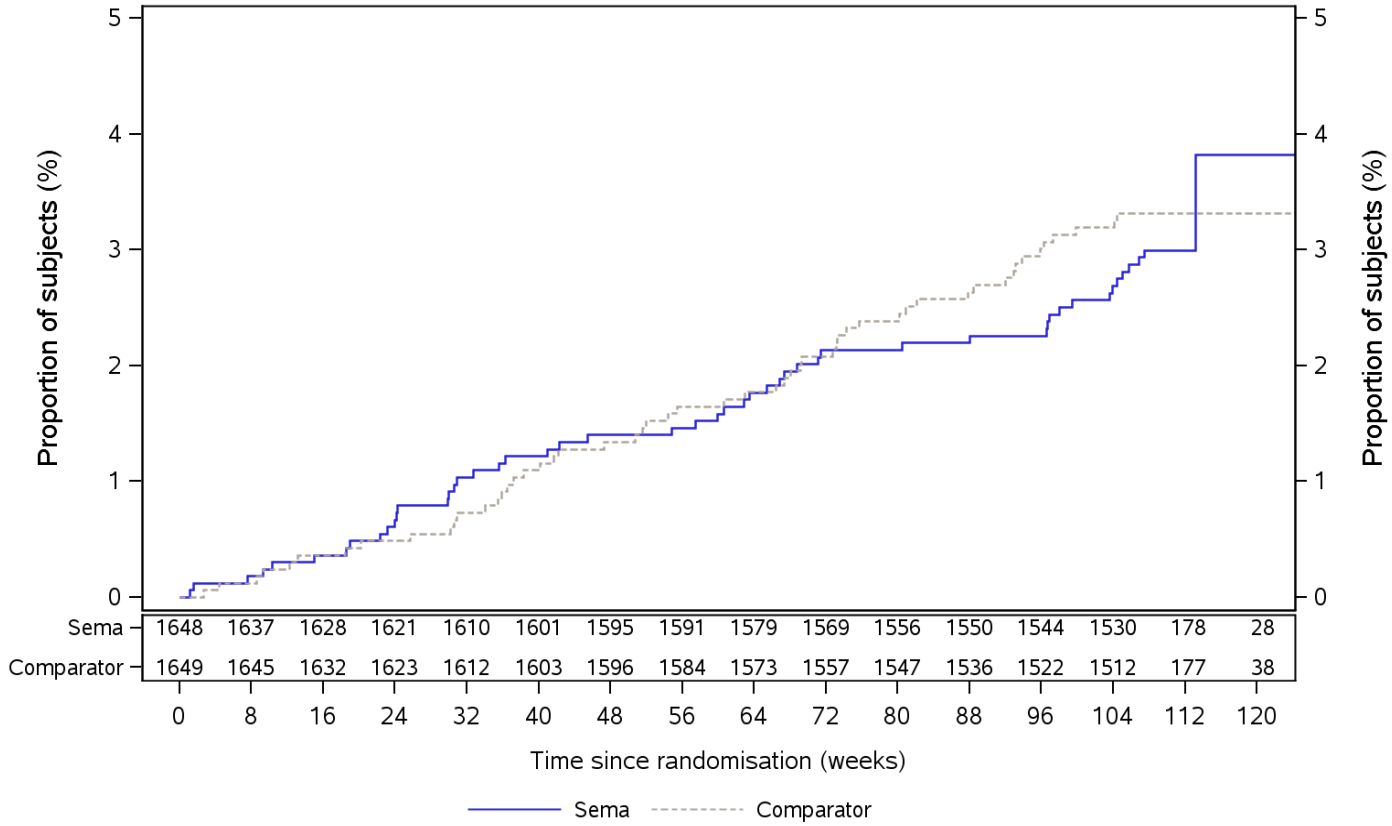
7 Serious adverse events - system organ class "Infections and infestations" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:37:27 - f_cif_tte_s6.sas/f_cif_soc_ii_sae_s6.png

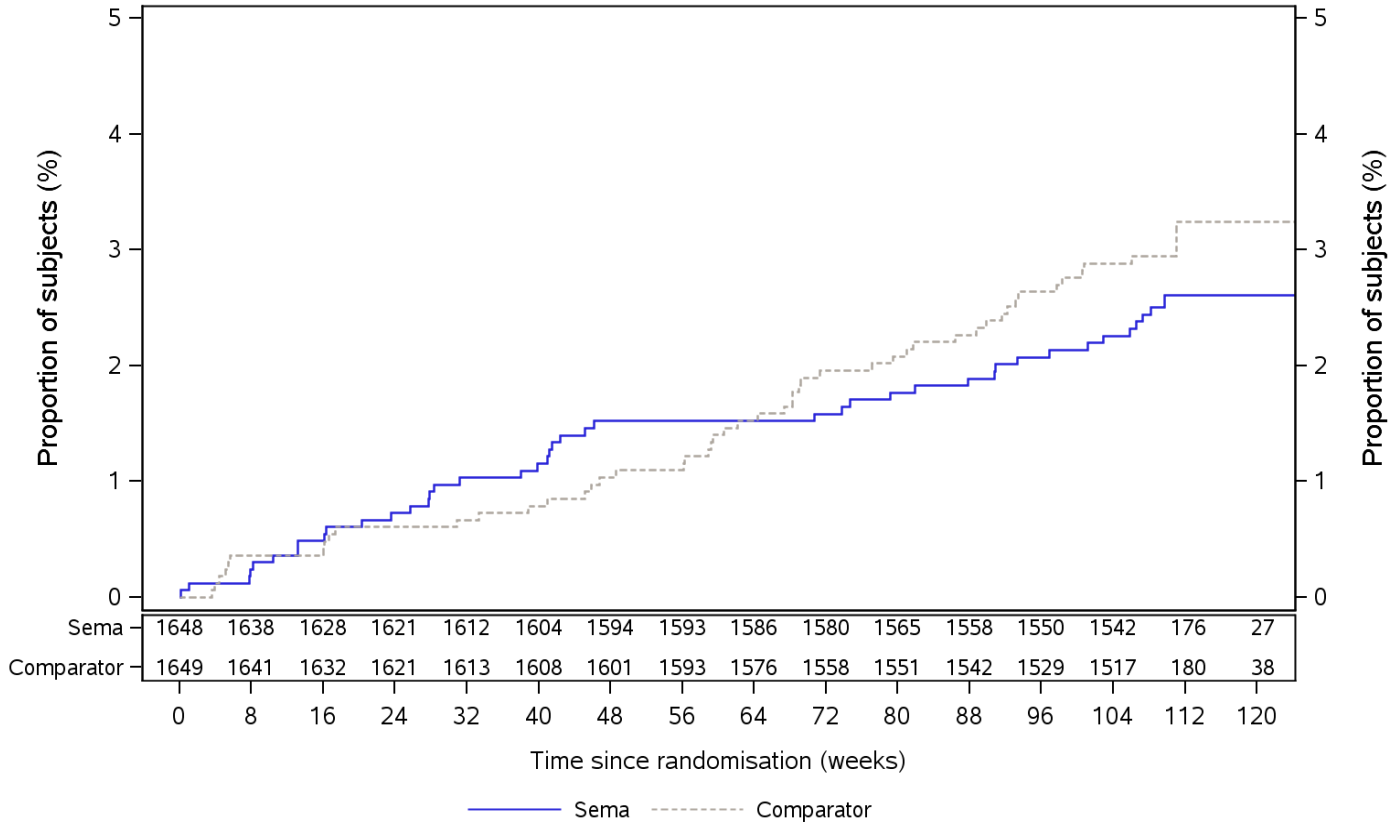
8 Serious adverse events - system organ class "Injury, poisoning and procedural complications" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:37:45 - f_cif_tte_s6.sas/f_cif_soc_ippc_sae_s6.png

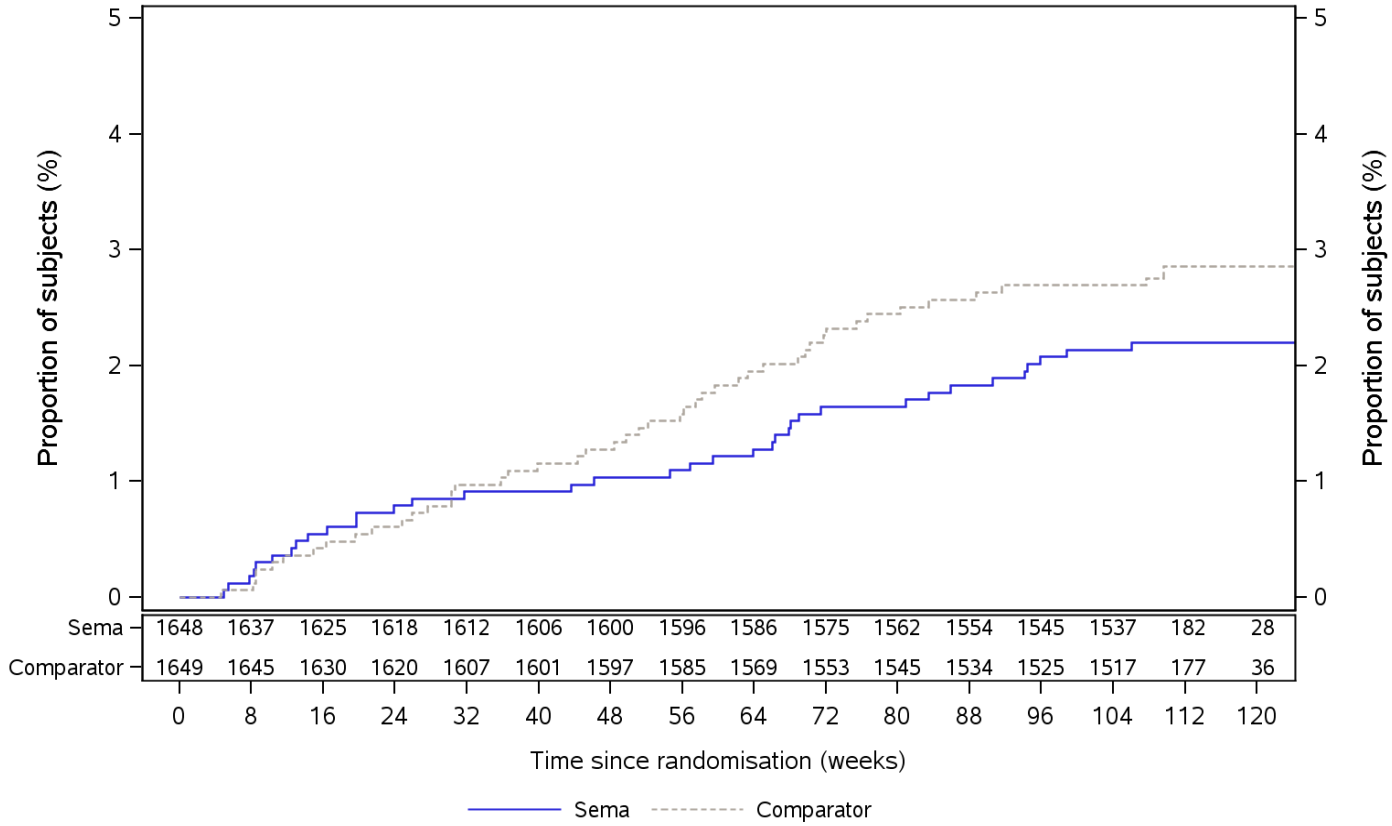
9 Serious adverse events - system organ class "Metabolism and nutrition disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:38:03 - f_cif_tte_s6.sas/f_cif_soc_mnd_sae_s6.png

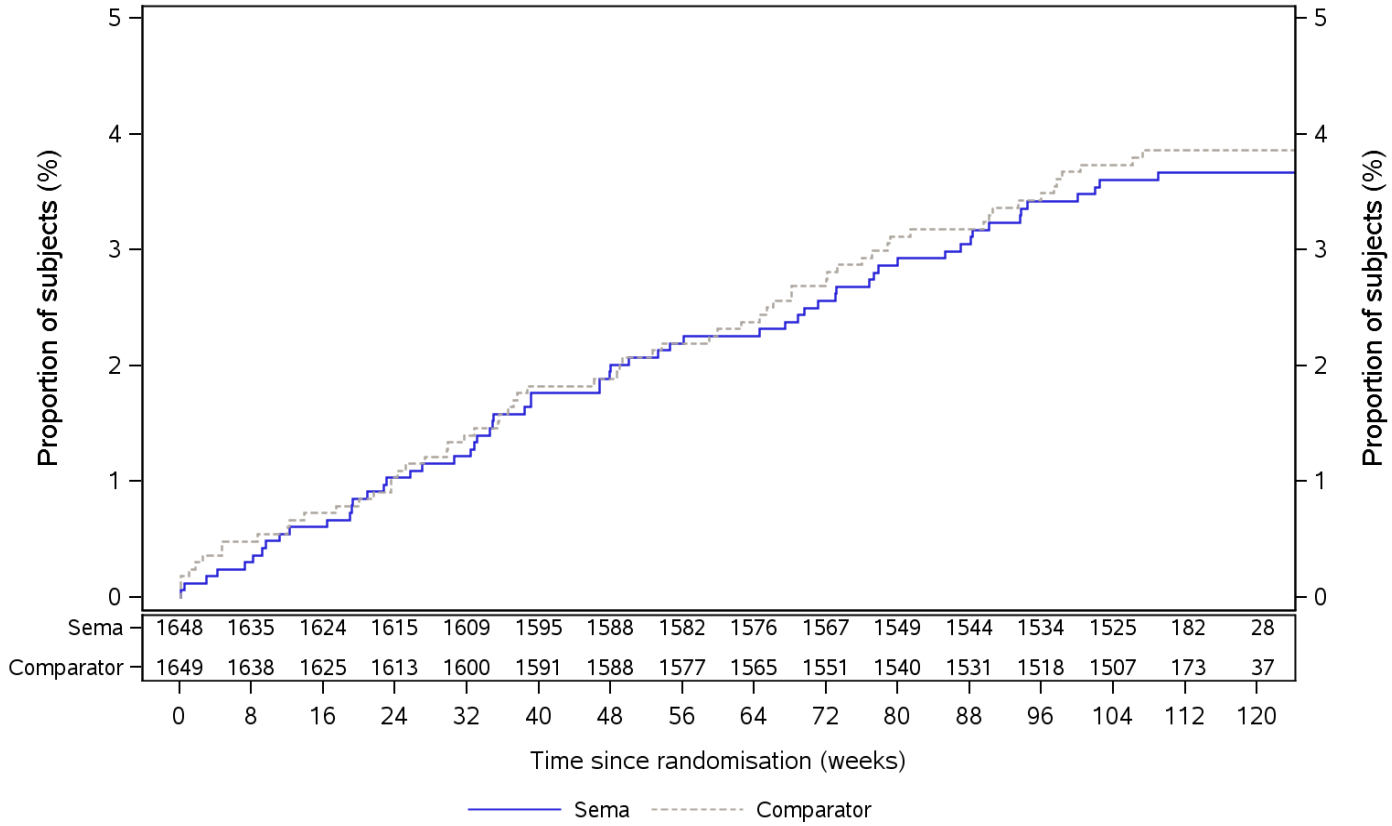
10 Serious adverse events - system organ class "Musculoskeletal and connective tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:38:20 - f_cif_tte_s6.sas/f_cif_soc_mctd_sae_s6.png

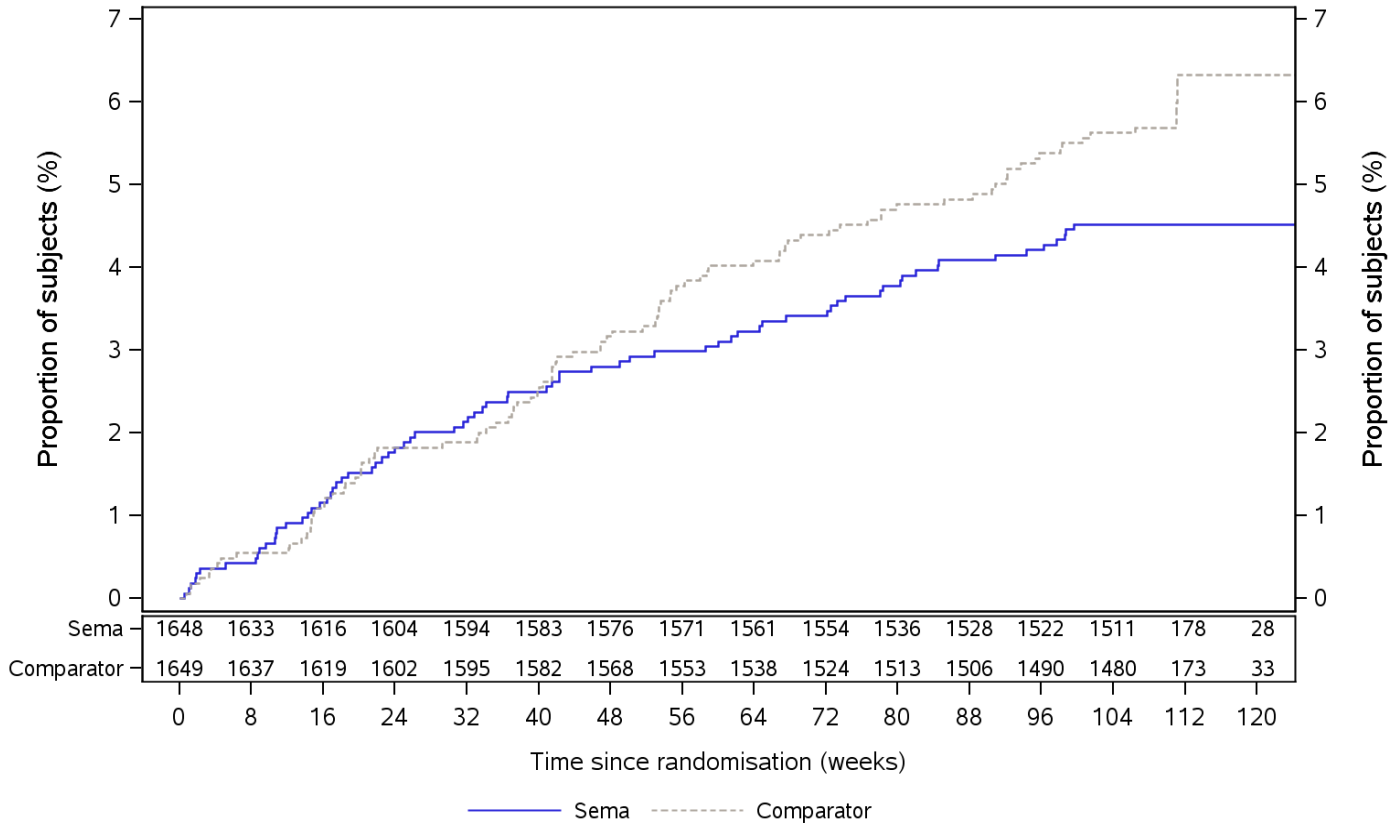
11 Serious adverse events - system organ class "Neoplasms benign, malignant and unspecified (incl cysts and polyps)" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:38:38 - f_cif_tte_s6.sas/f_cif_soc_nbmu_sae_s6.png

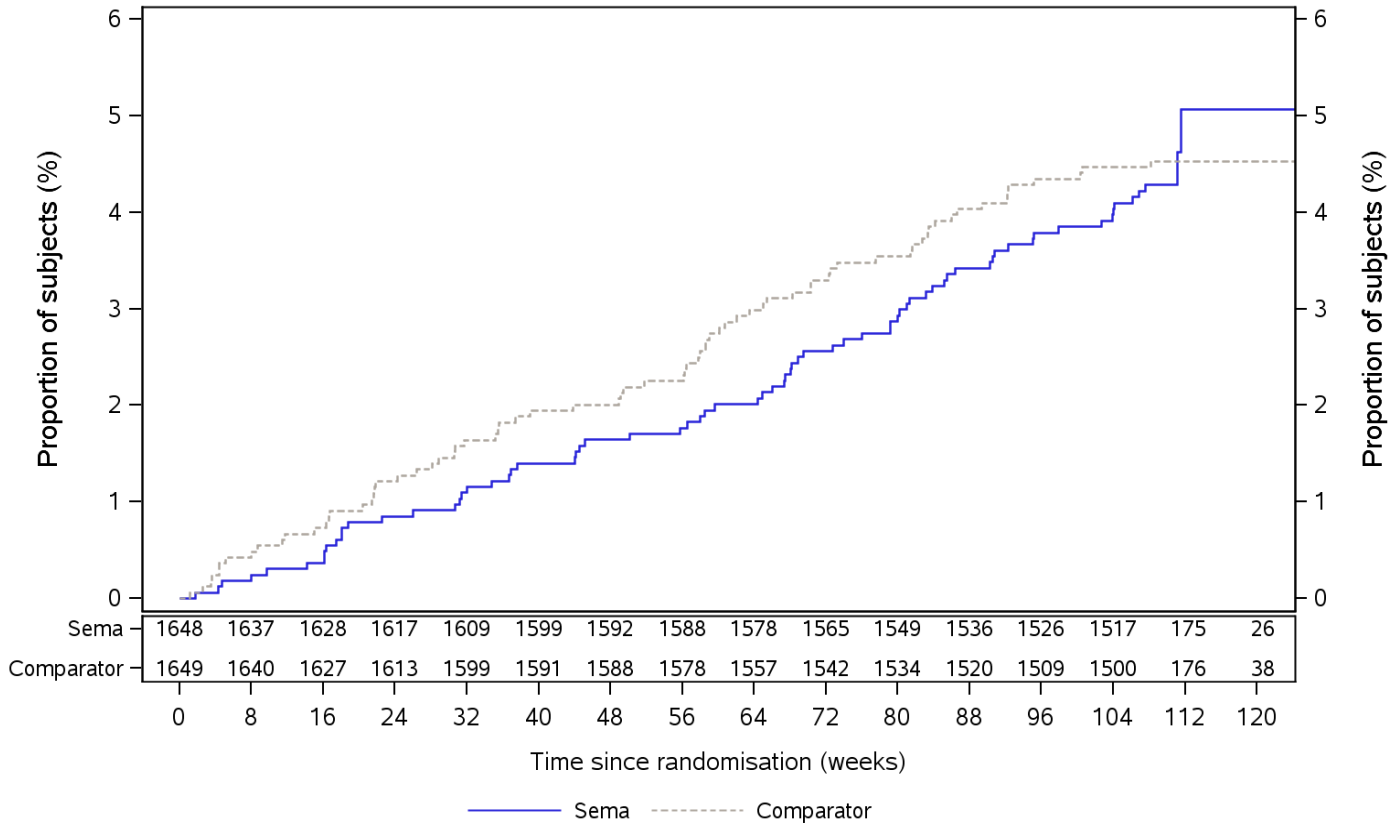
12 Serious adverse events - system organ class "Nervous system disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:38:57 - f_cif_tte_s6.sas/f_cif_soc_nsd_sae_s6.png

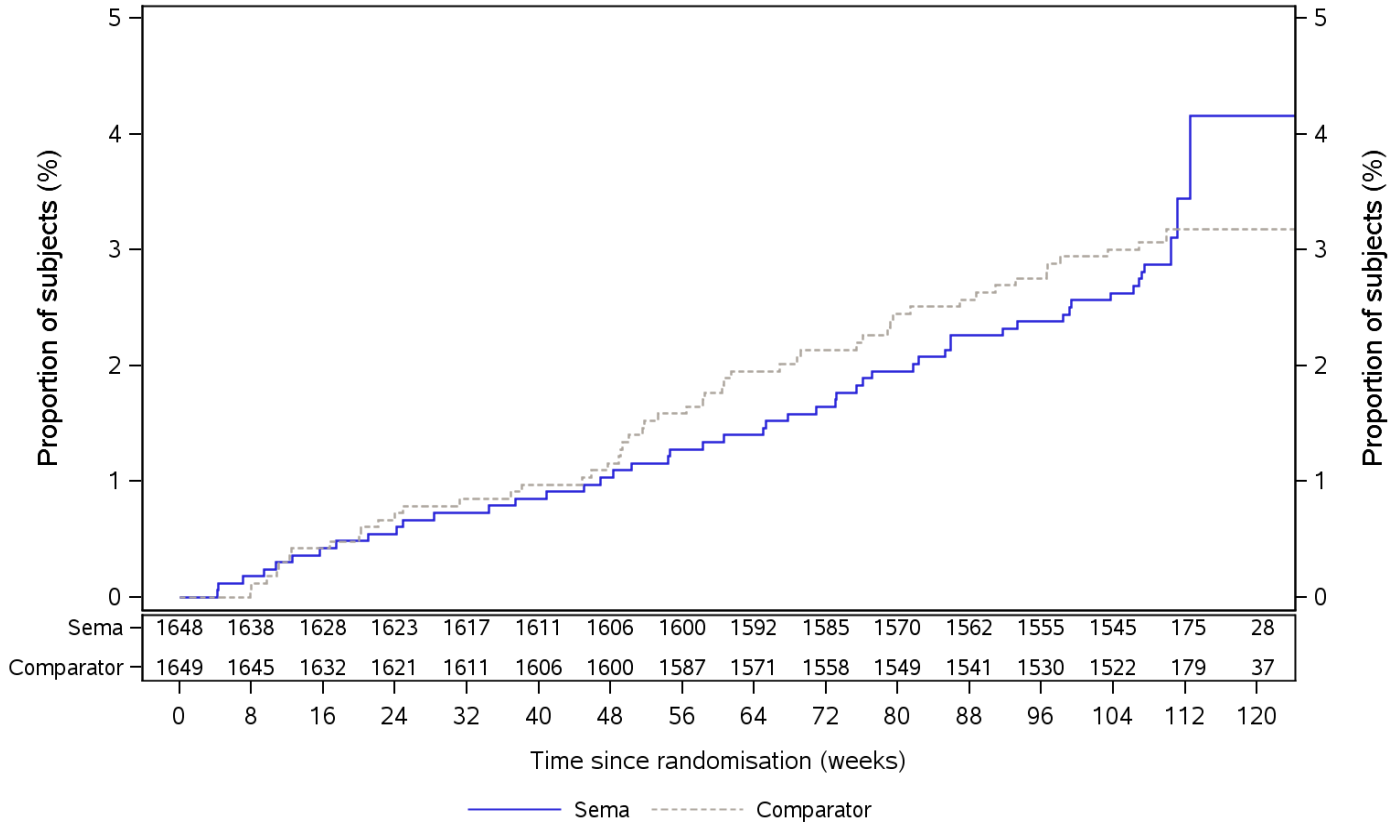
13 Serious adverse events - system organ class "Renal and urinary disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:39:16 - f_cif_tte_s6.sas/f_cif_soc_rud_sae_s6.png

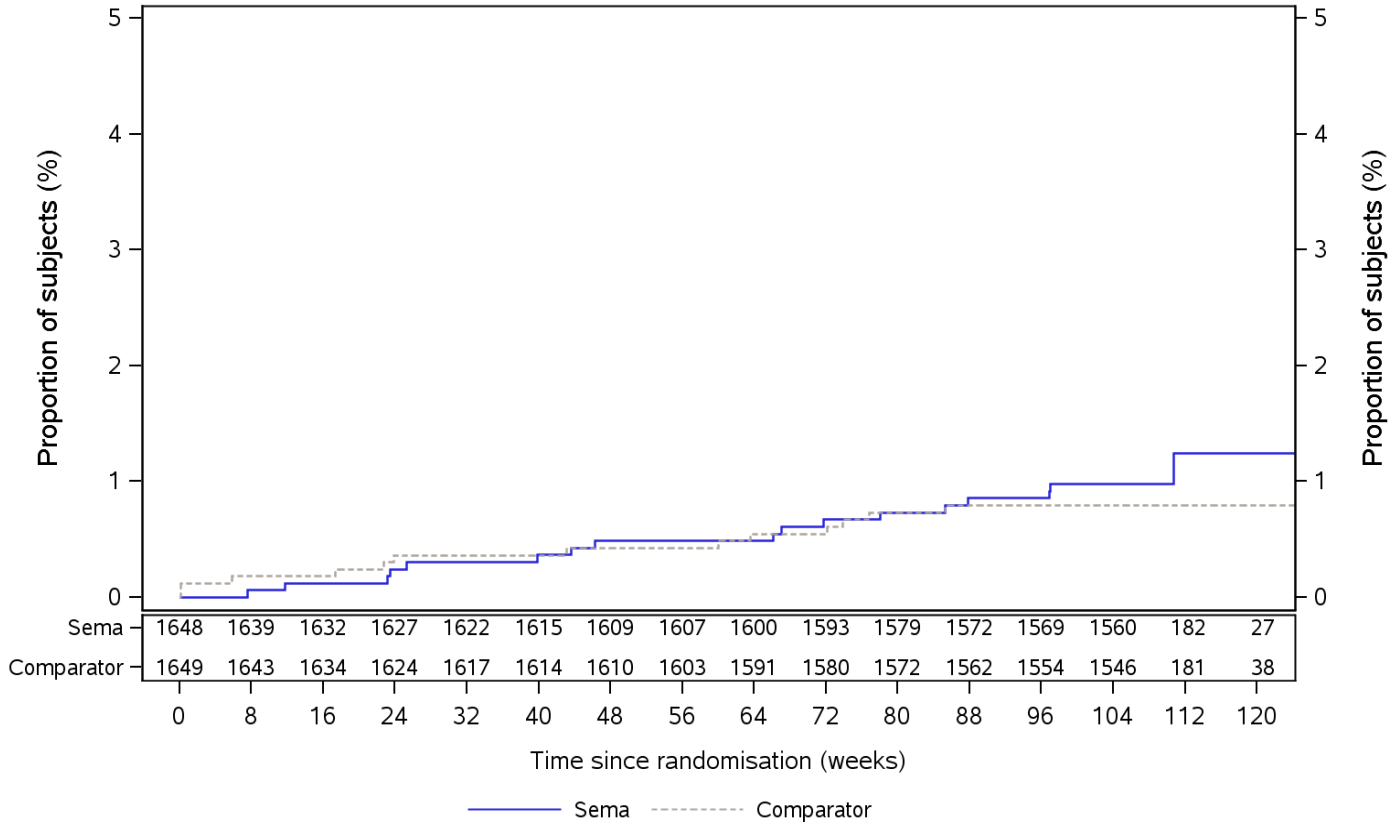
14 Serious adverse events - system organ class "Respiratory, thoracic and mediastinal disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:39:34 - f_cif_tte_s6.sas/f_cif_soc_rtmd_sae_s6.png

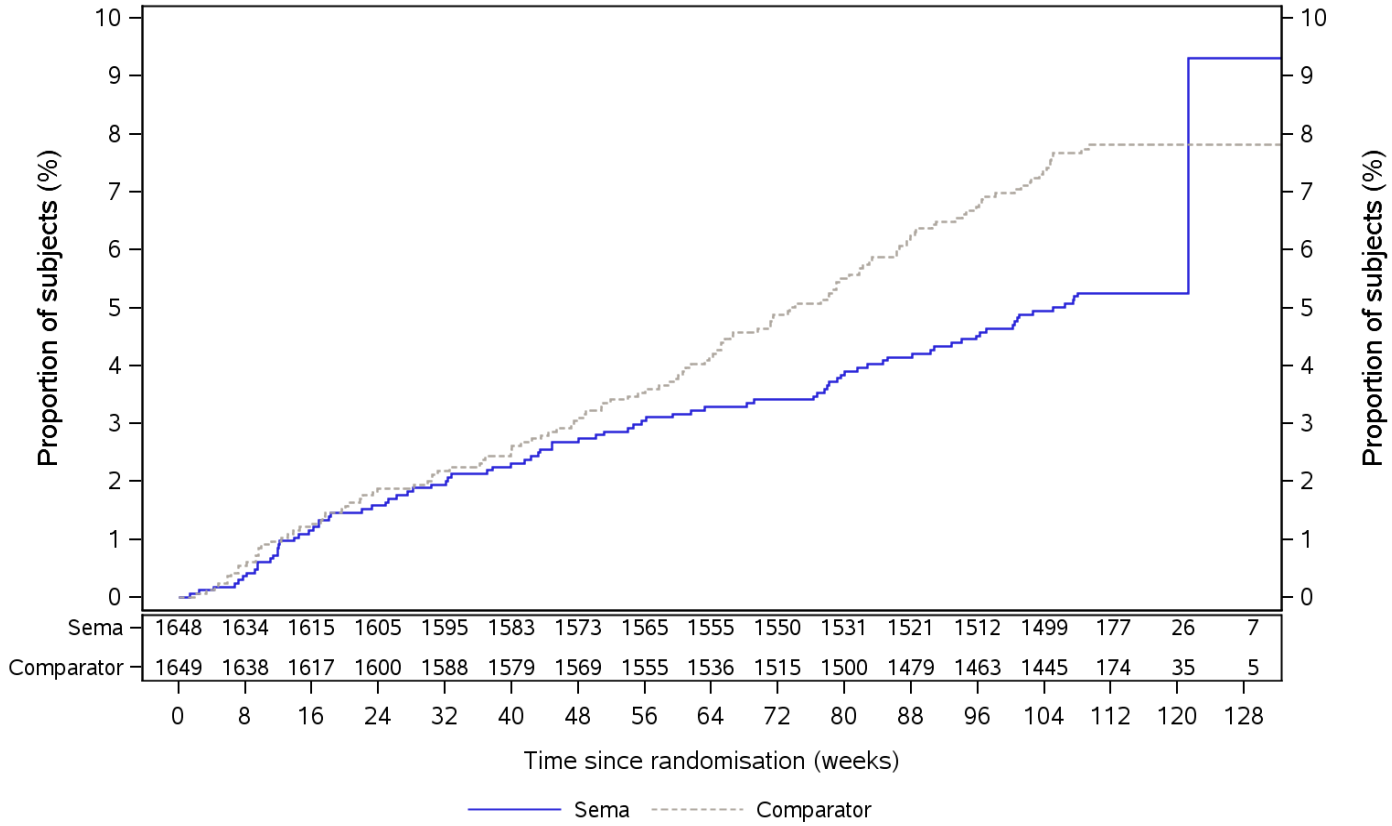
15 Serious adverse events - system organ class "Skin and subcutaneous tissue disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:39:53 - f_cif_tte_s6.sas/f_cif_soc_sstd_sae_s6.png

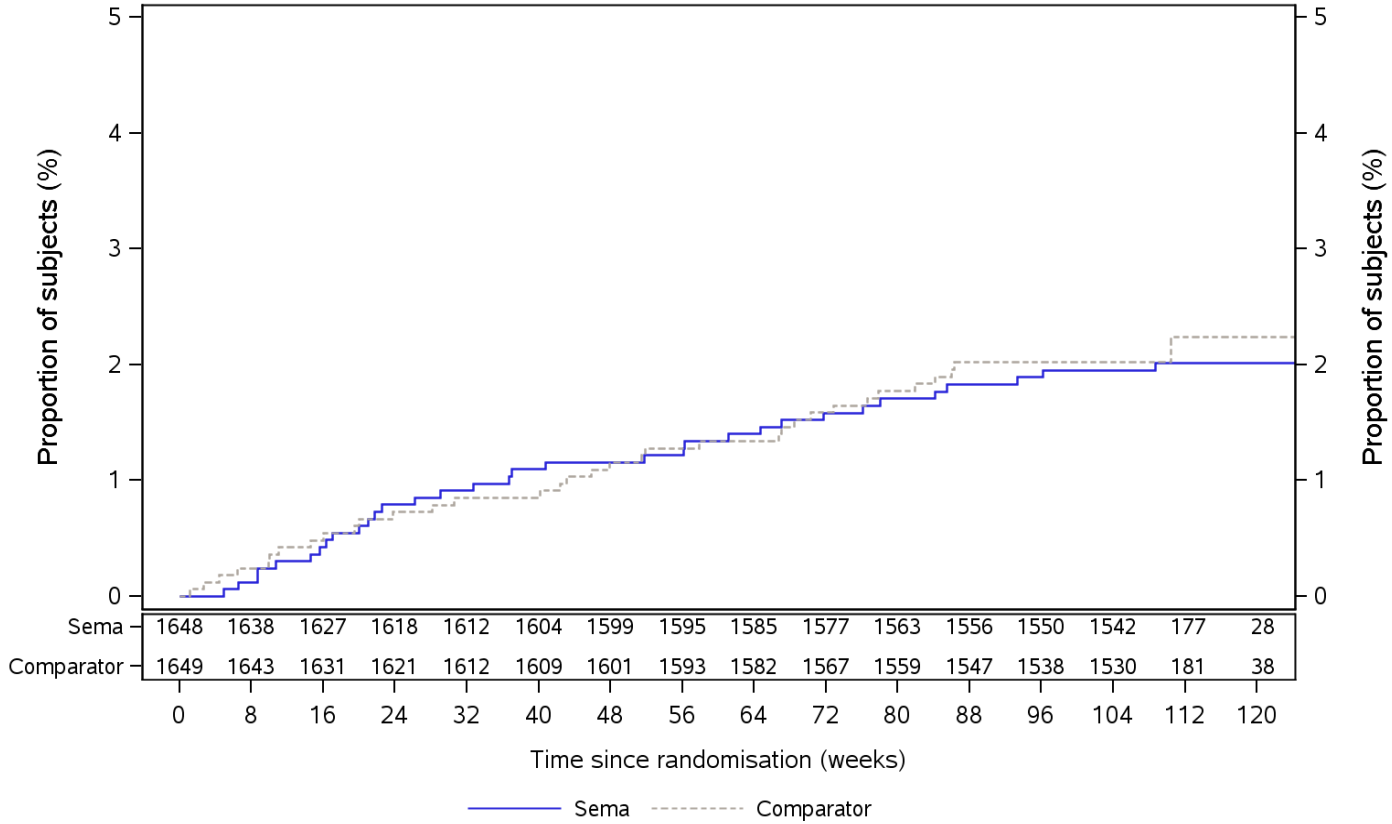
16 Serious adverse events - system organ class "Surgical and medical procedures" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:40:11 - f_cif_tte_s6.sas/f_cif_soc_smp_sae_s6.png

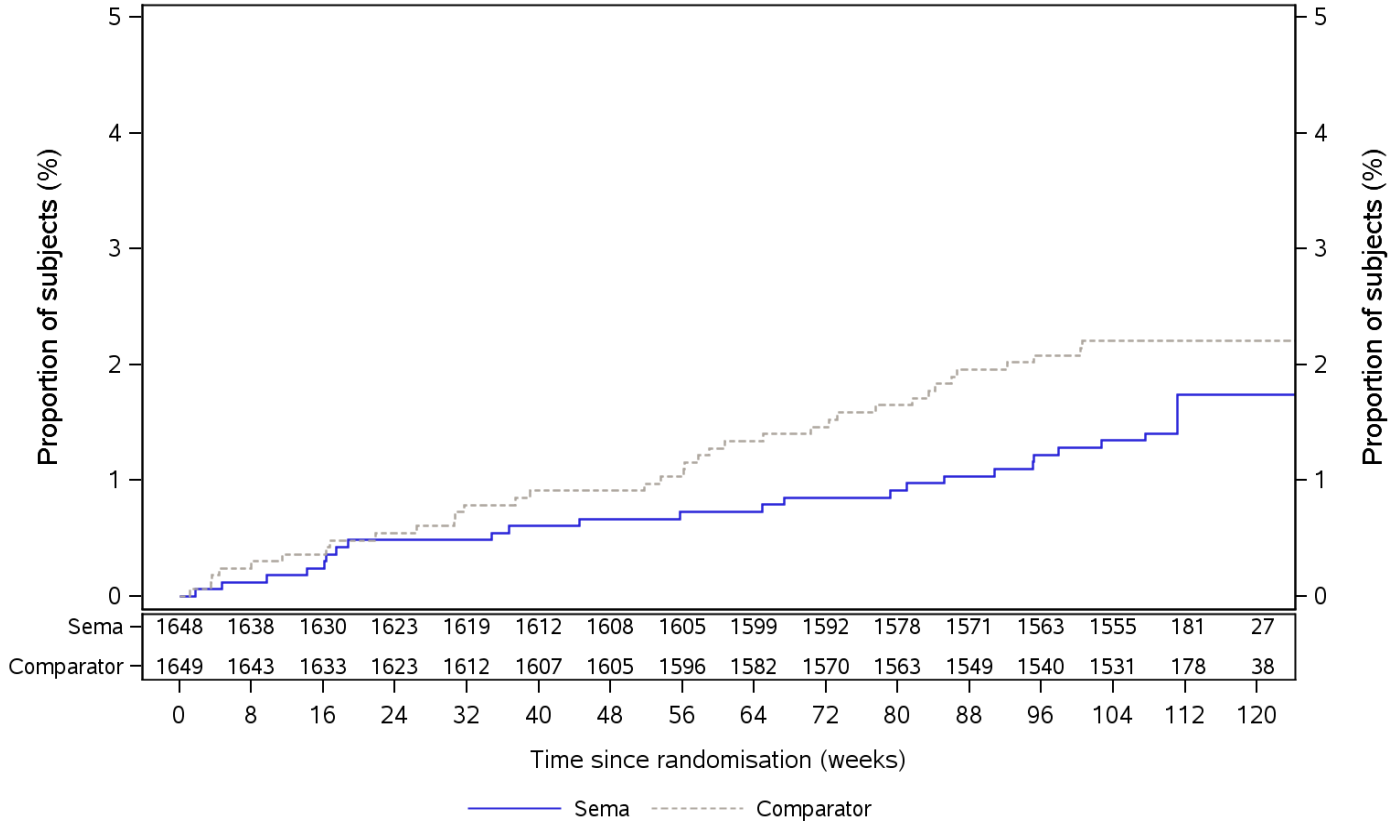
17 Serious adverse events - system organ class "Vascular disorders" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:40:30 - f_cif_tte_s6.sas/f_cif_soc_vd_sae_s6.png

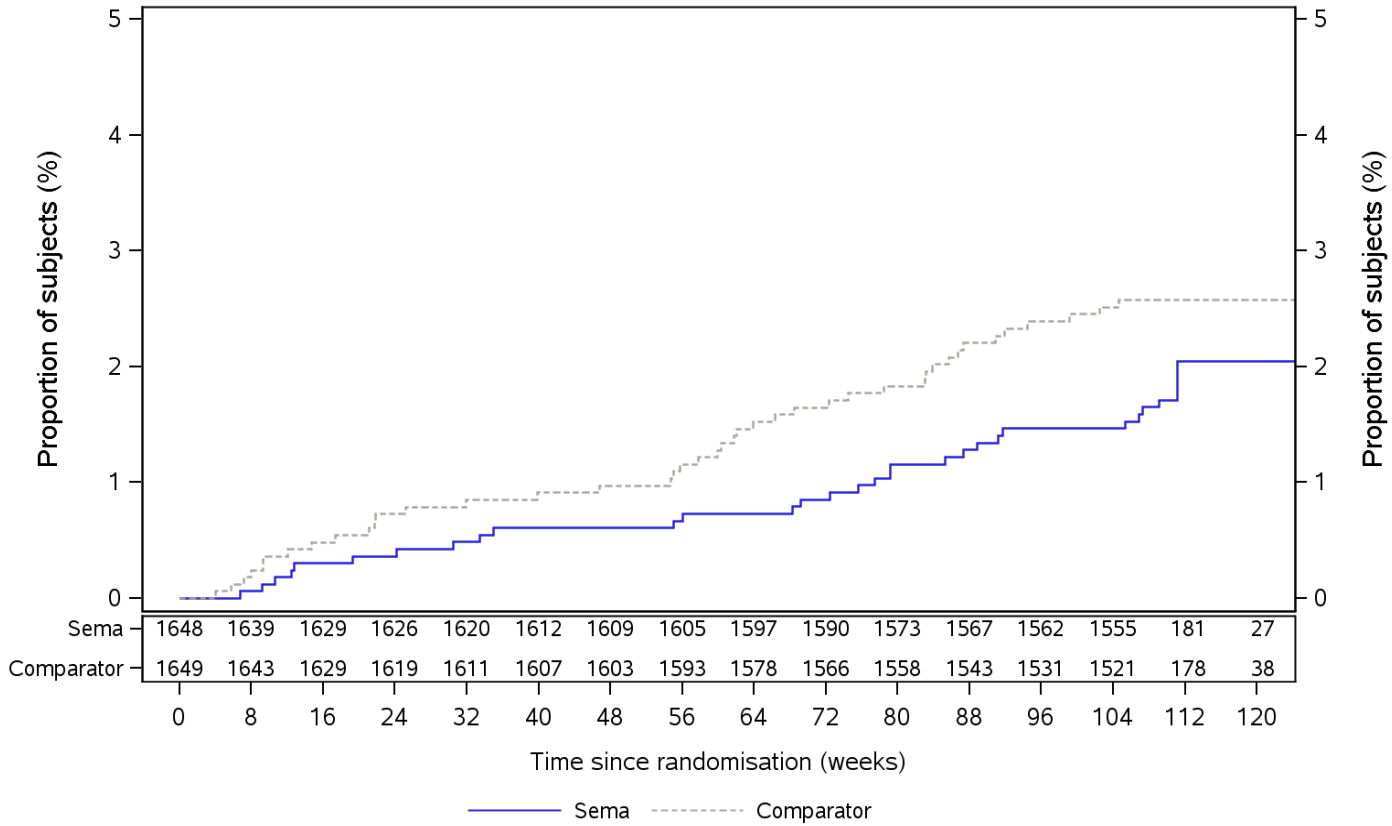
18 Serious adverse events - preferred term "Acute kidney injury" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:40:48 - f_cif_tte_s6.sas/f_cif_pt_aki_sae_s6.png

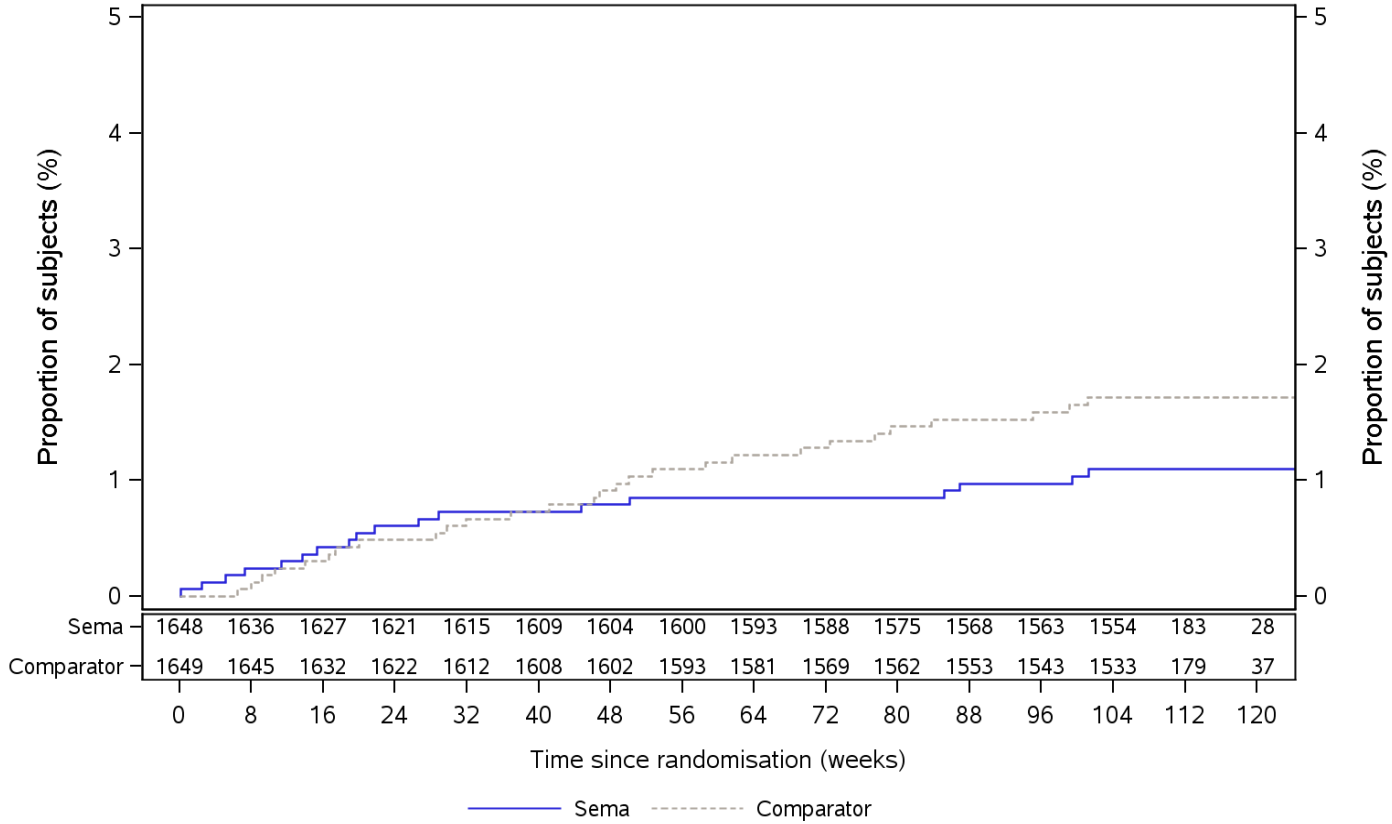
19 Serious adverse events - preferred term "Acute myocardial infarction" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:41:06 - f_cif_tte_s6.sas/f_cif_pt_ami_sae_s6.png

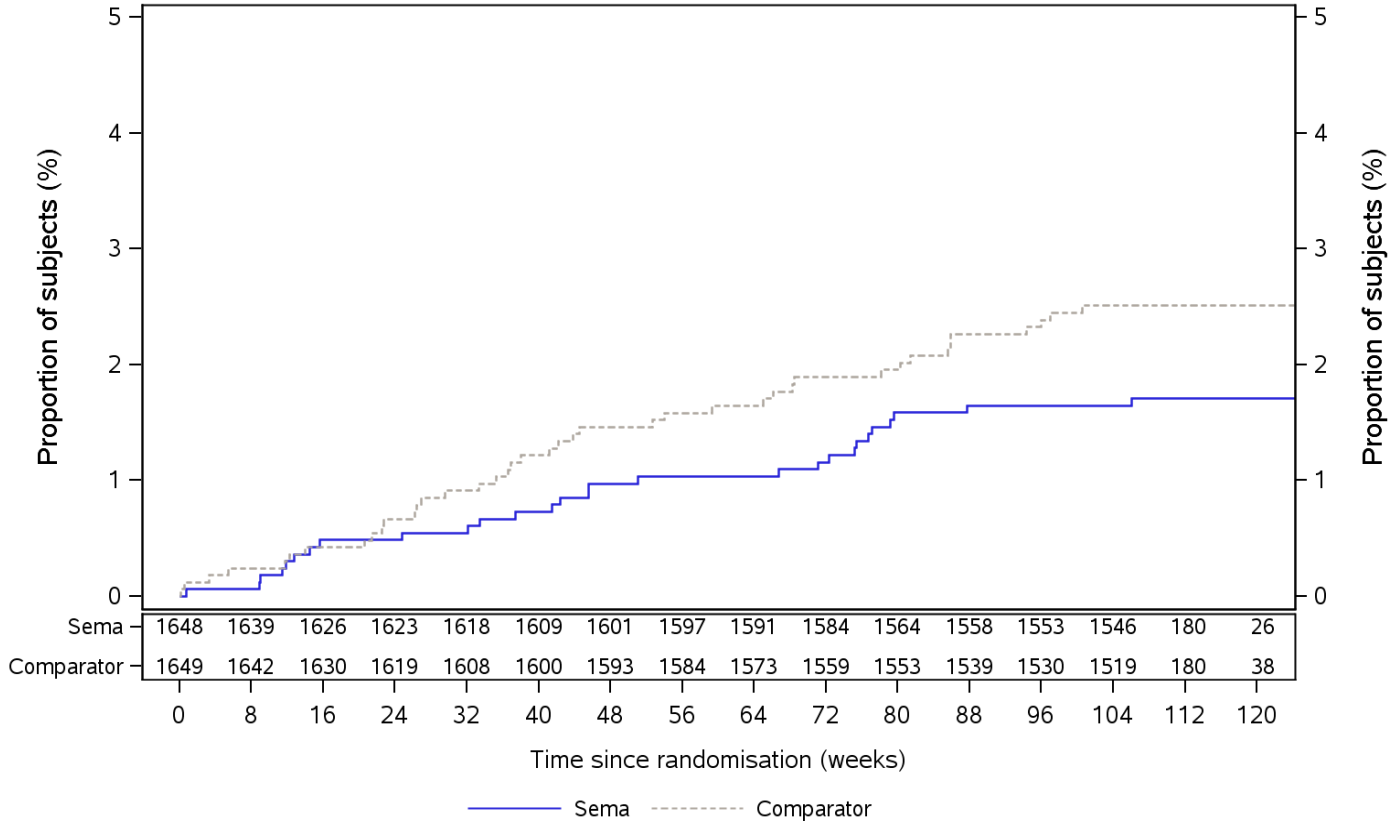
20 Serious adverse events - preferred term "Angina pectoris" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:41:25 - f_cif_tte_s6.sas/f_cif_pt_ap_sae_s6.png

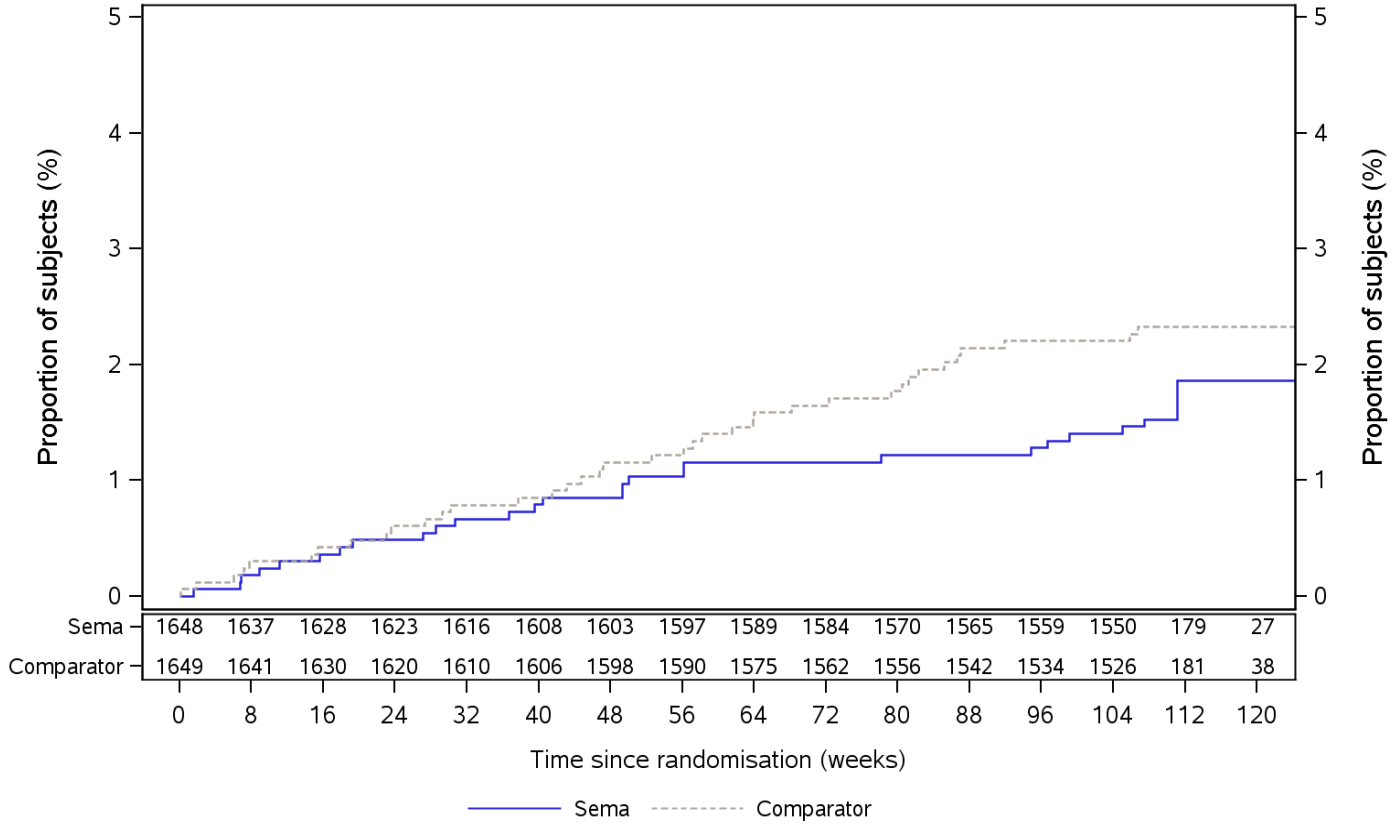
21 Serious adverse events - preferred term "Angina unstable" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:41:43 - f_cif_tte_s6.sas/f_cif_pt_au_sae_s6.png

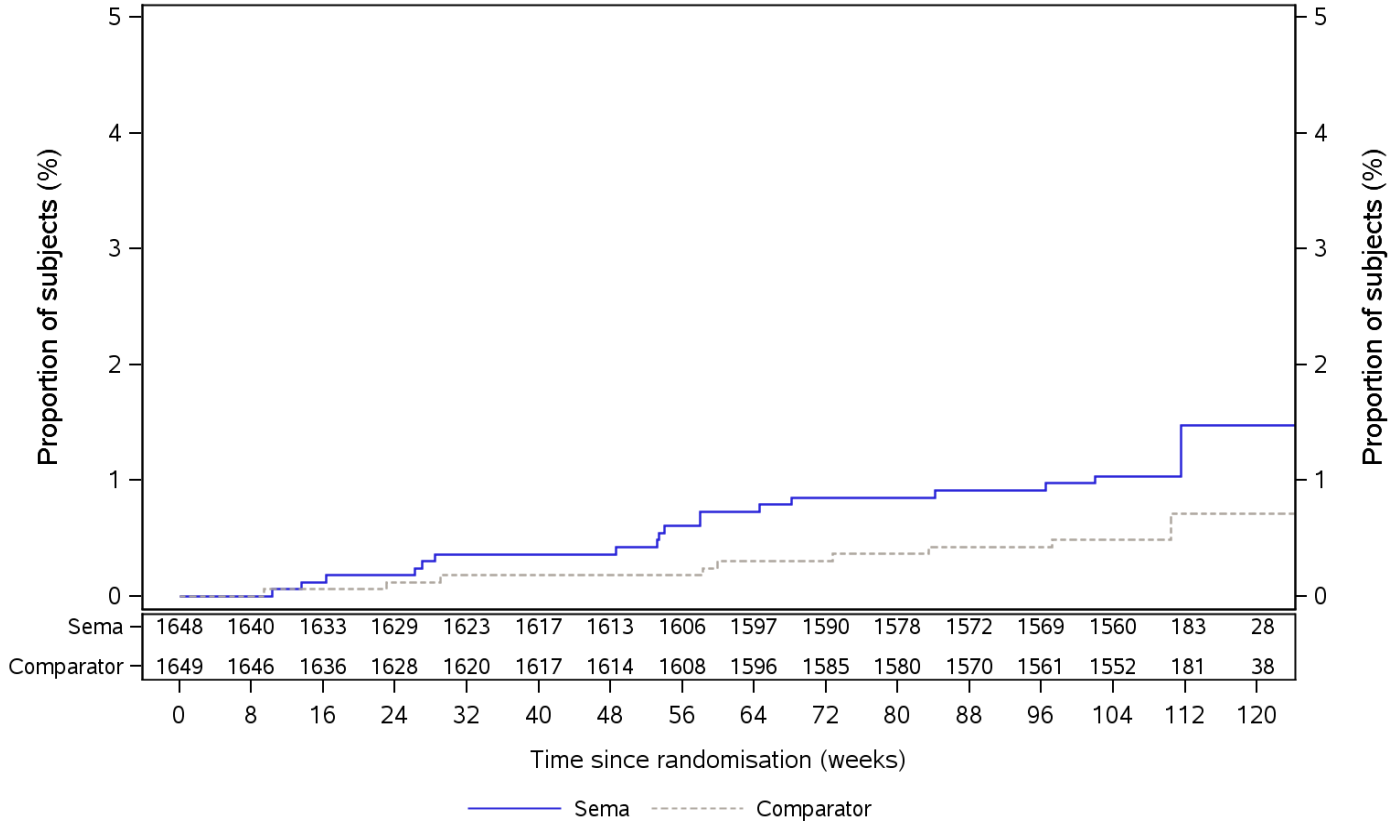
22 Serious adverse events - preferred term "Atrial fibrillation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:42:01 - f_cif_tte_s6.sas/f_cif_pt_af_sae_s6.png

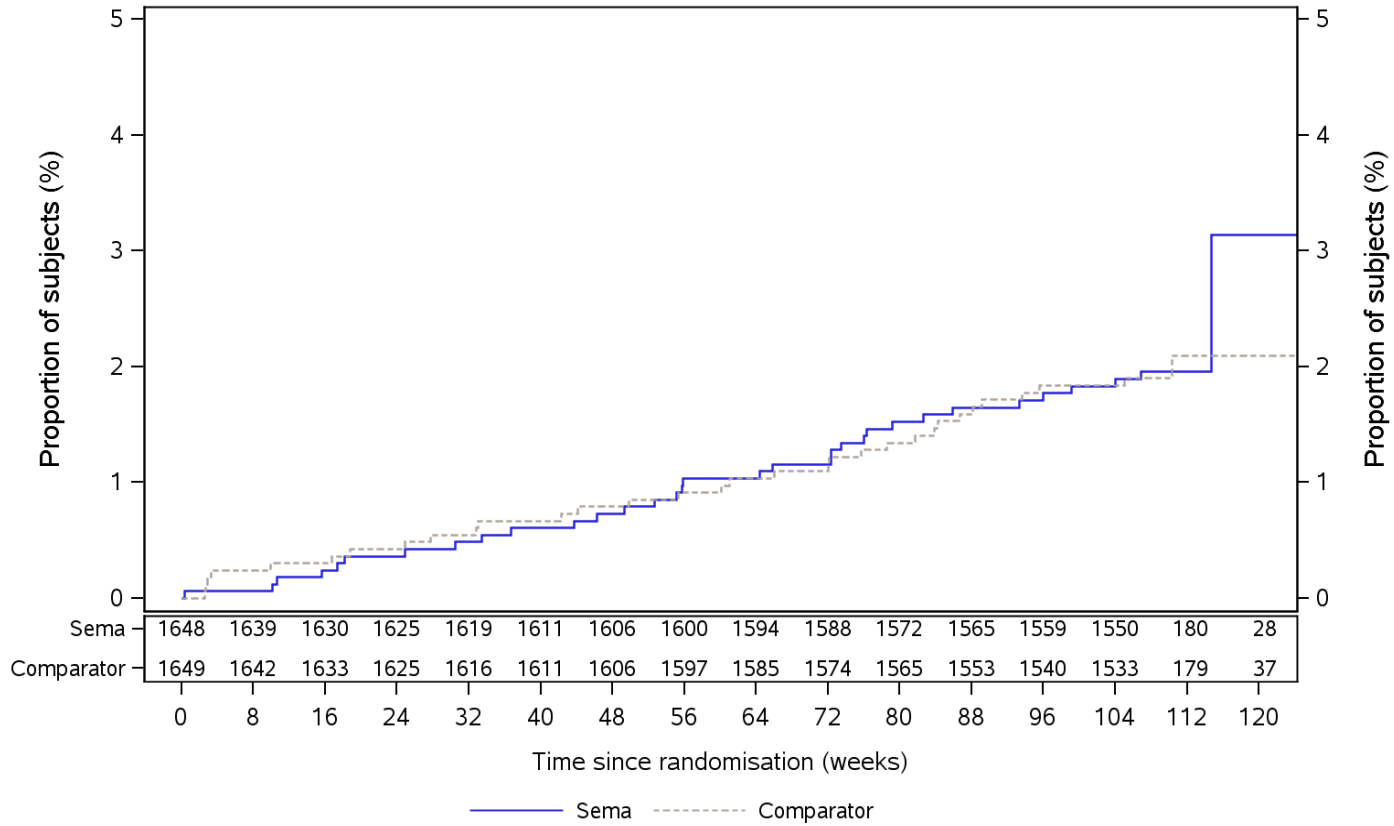
23 Serious adverse events - preferred term "Cardiac failure" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:42:19 - f_cif_tte_s6.sas/f_cif_pt_cf_sae_s6.png

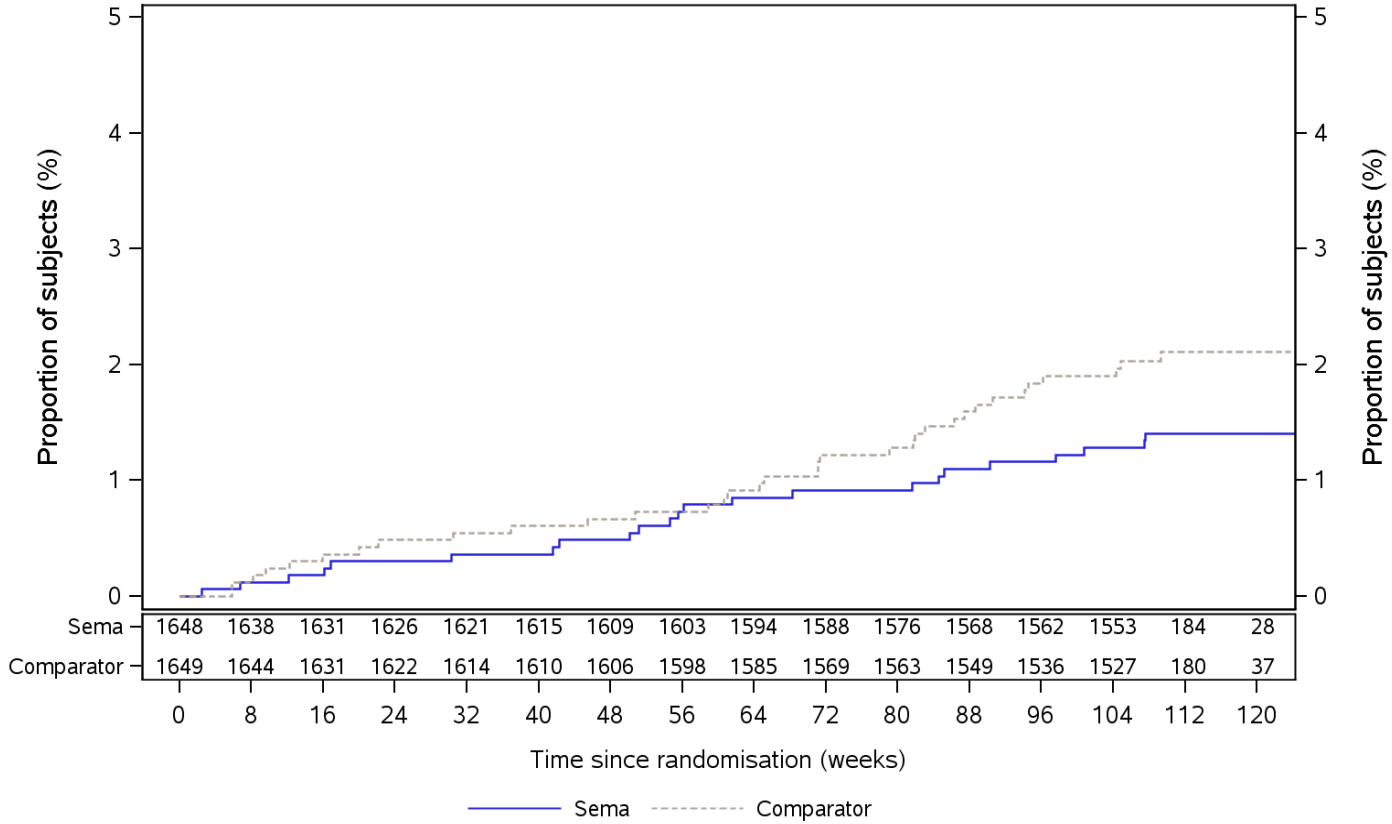
24 Serious adverse events - preferred term "Cardiac failure congestive" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:42:37 - f_cif_tte_s6.sas/f_cif_pt_cfc_sae_s6.png

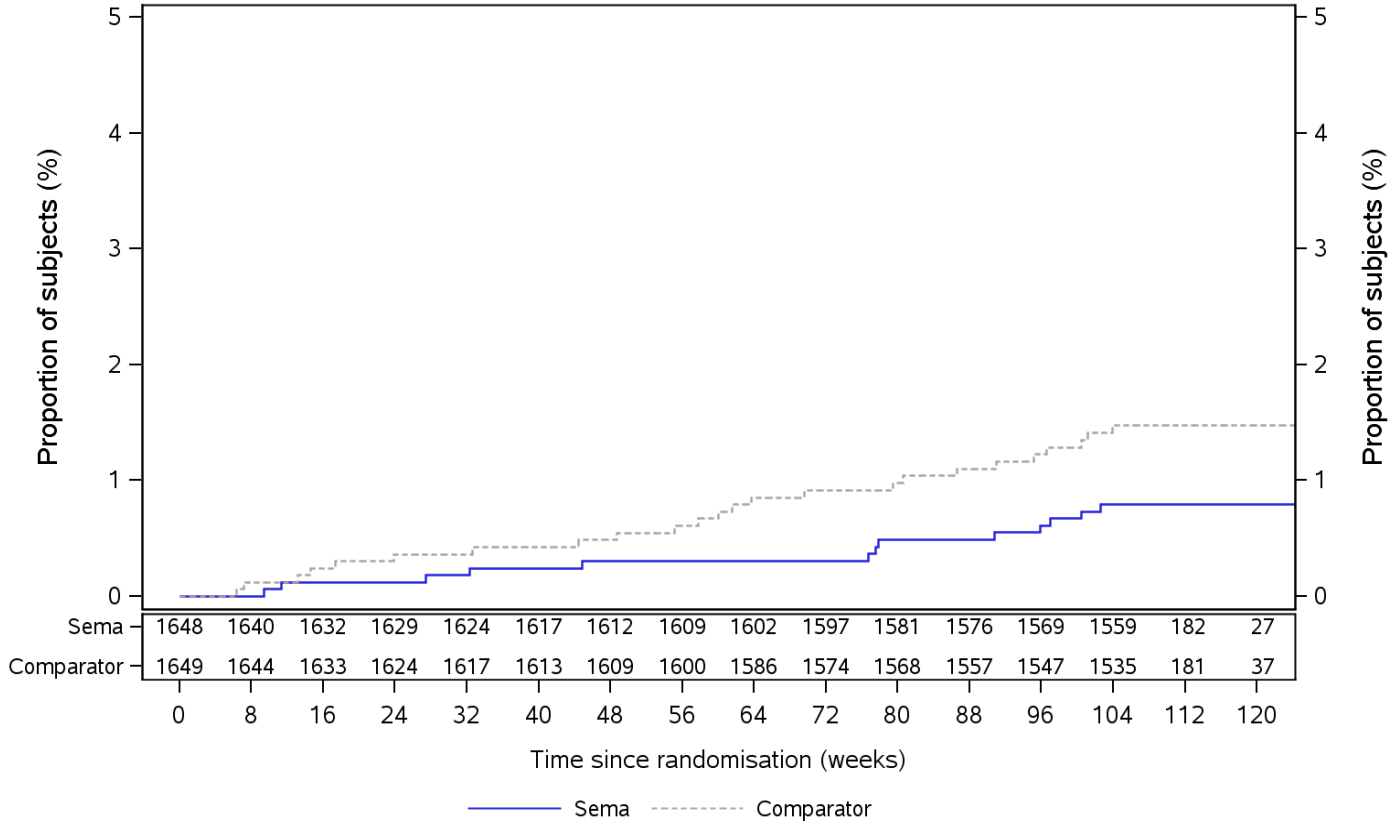
25 Serious adverse events - preferred term "Coronary arterial stent insertion" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:42:55 - f_cif_tte_s6.sas/f_cif_pt_casi_sae_s6.png

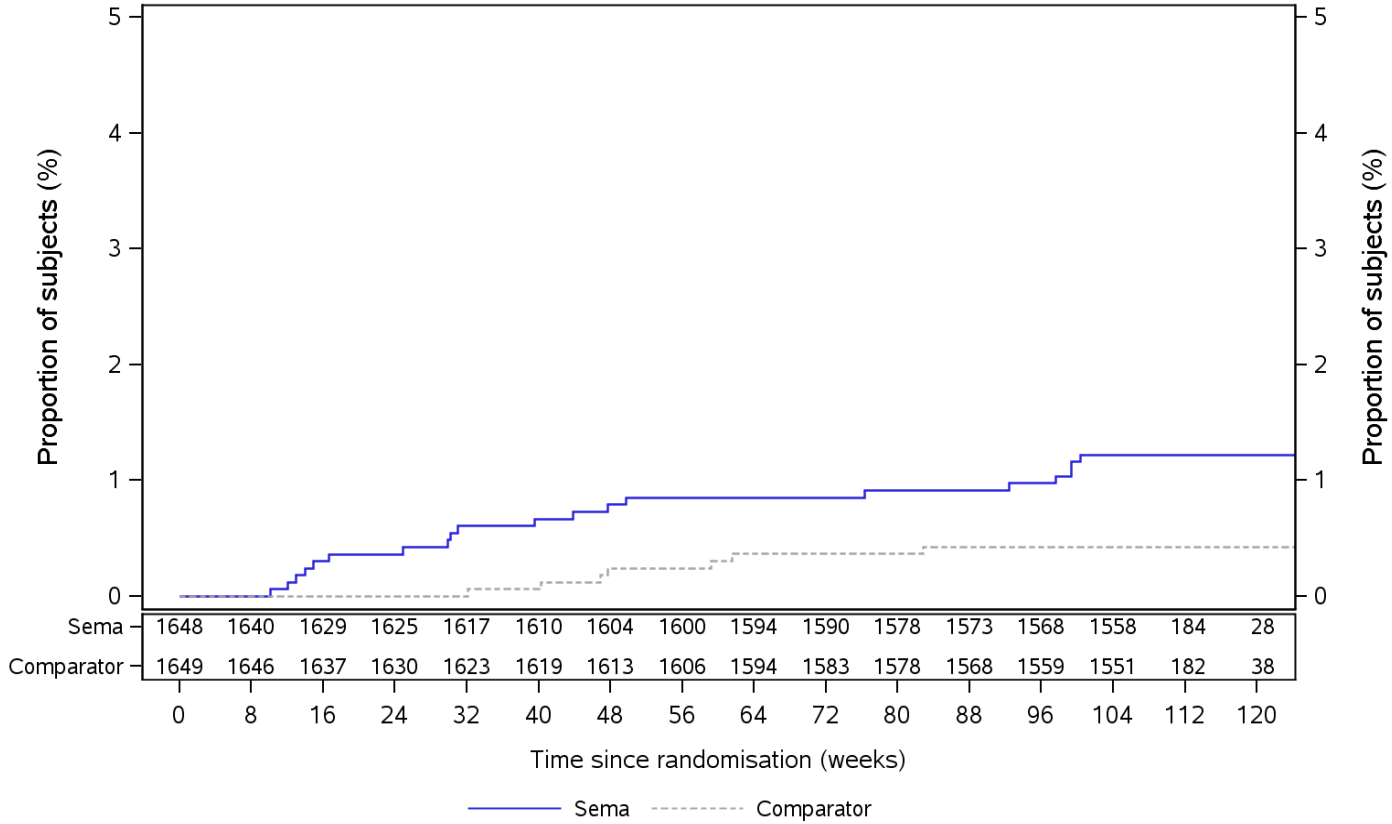
26 Serious adverse events - preferred term "Coronary artery bypass" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:43:13 - f_cif_tte_s6.sas/f_cif_pt_cab_sae_s6.png

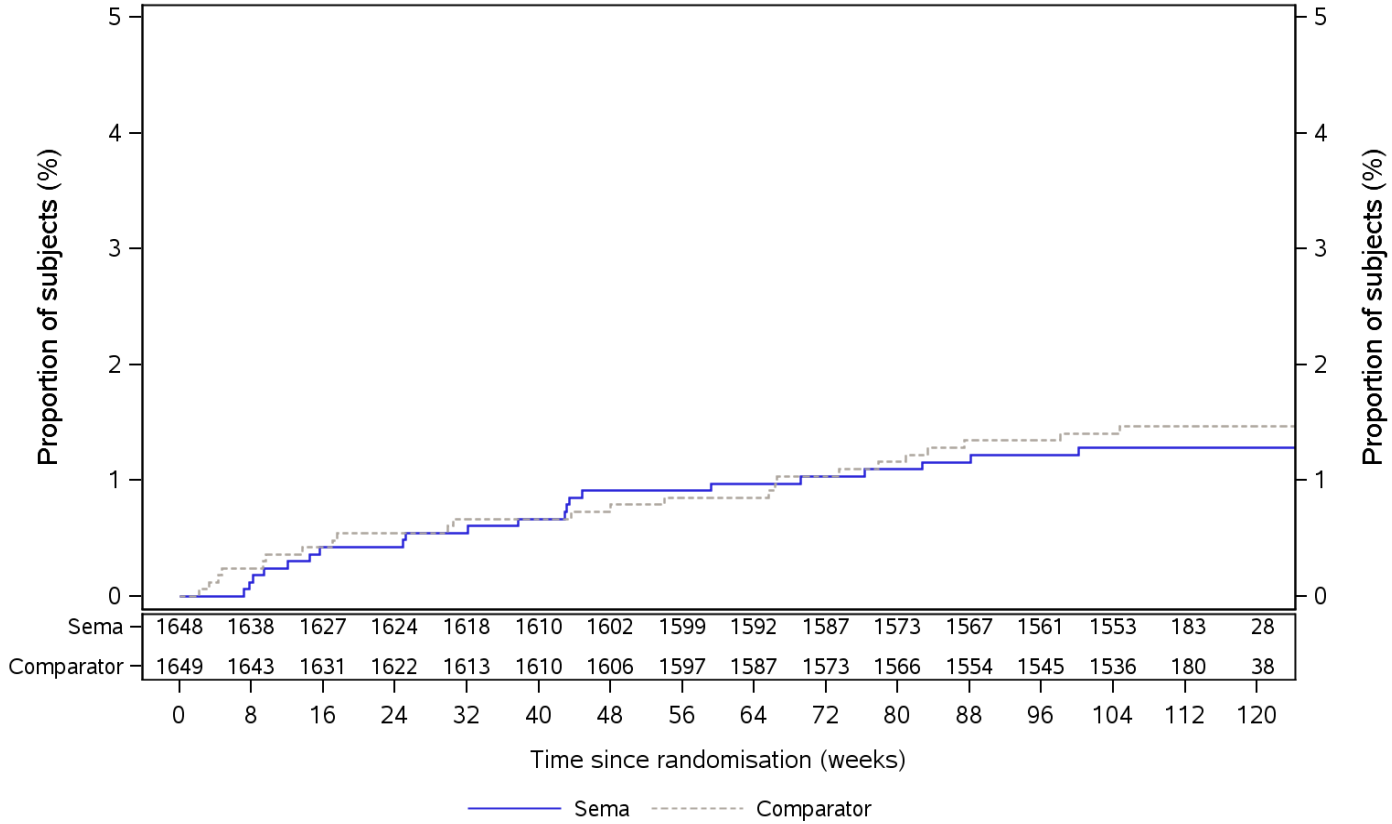
27 Serious adverse events - preferred term "Coronary artery disease" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:43:31 - f_cif_tte_s6.sas/f_cif_pt_cad_sae_s6.png

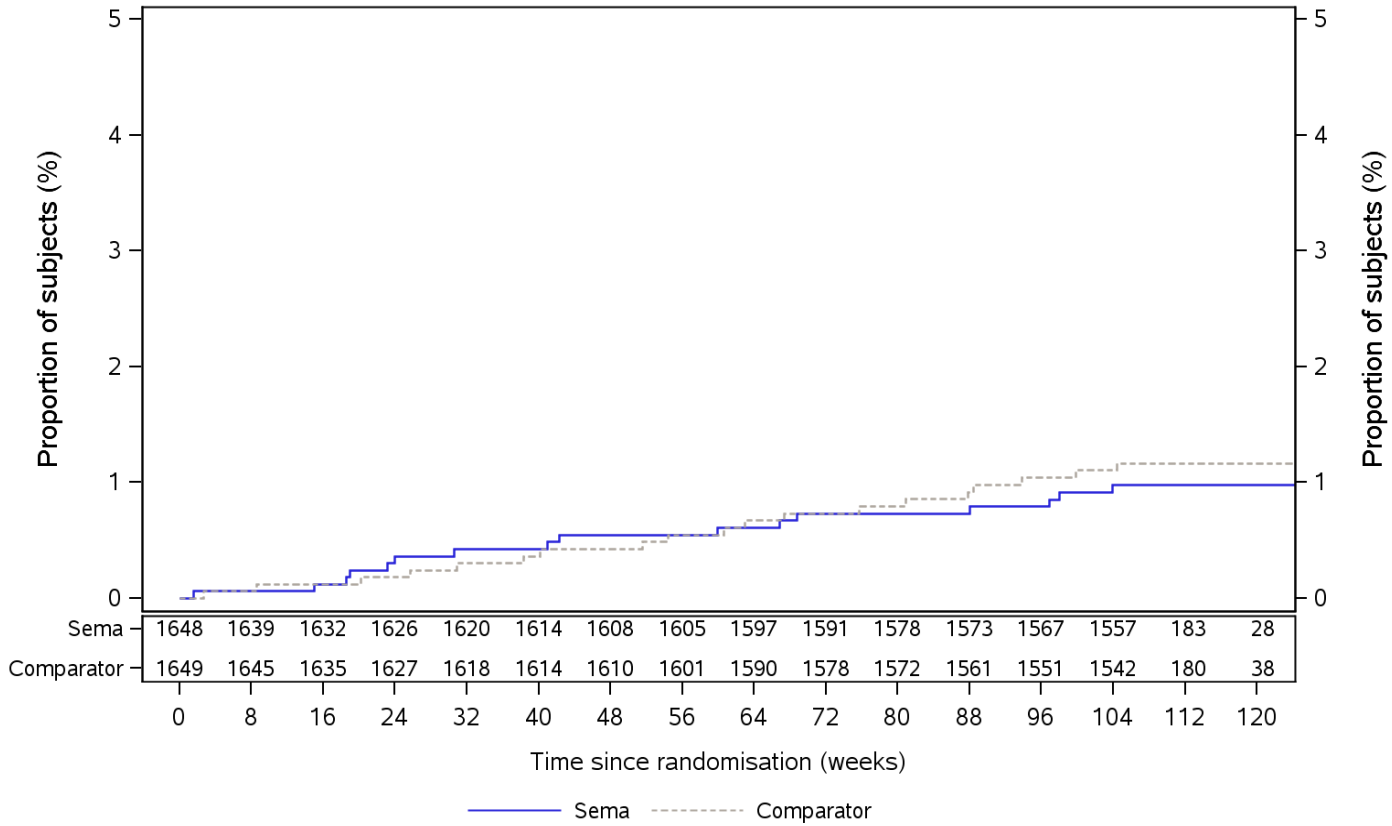
28 Serious adverse events - preferred term "Coronary revascularisation" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:43:49 - f_cif_tte_s6.sas/f_cif_pt_cr_sae_s6.png

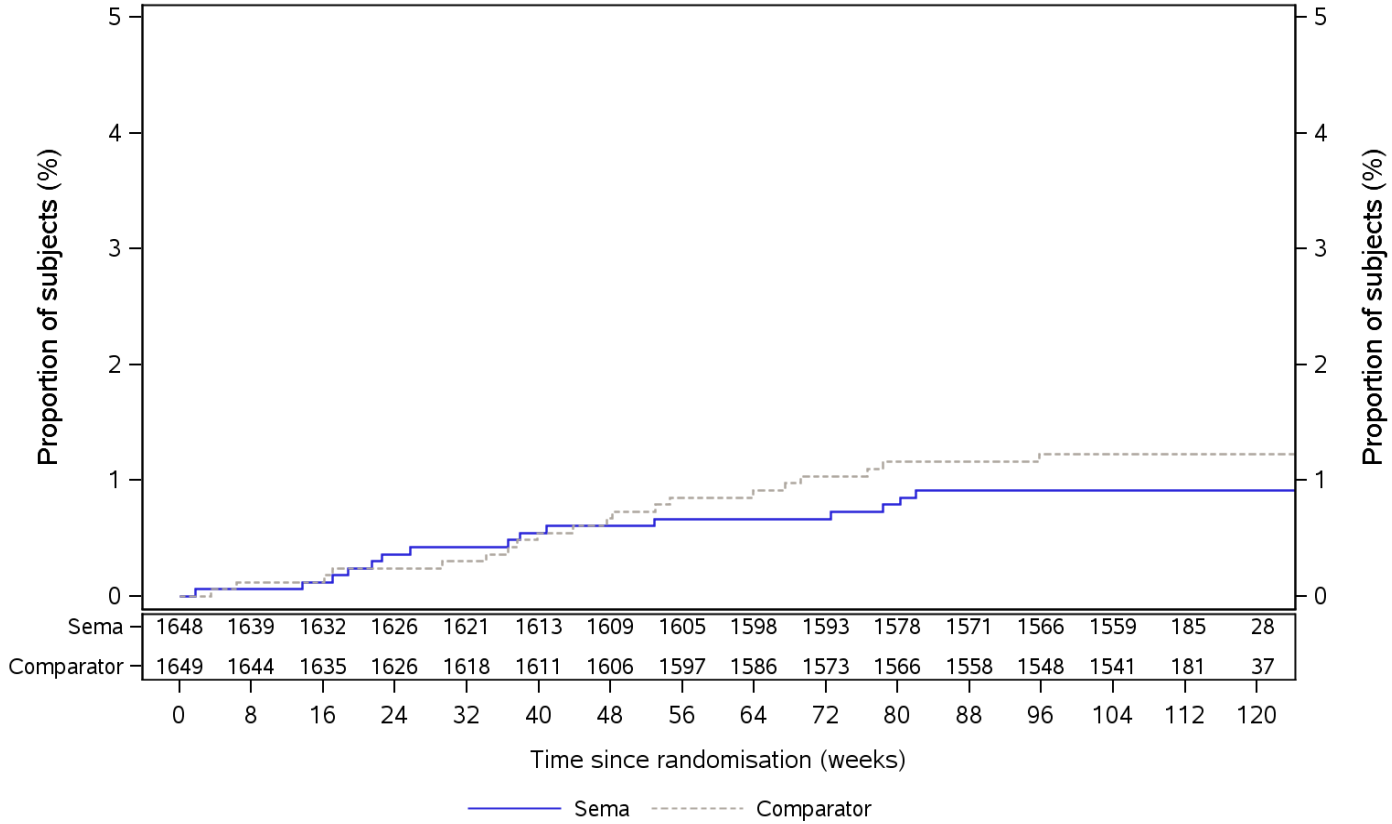
29 Serious adverse events - preferred term "Fall" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:44:06 - f_cif_tte_s6.sas/f_cif_pt_fall_sae_s6.png

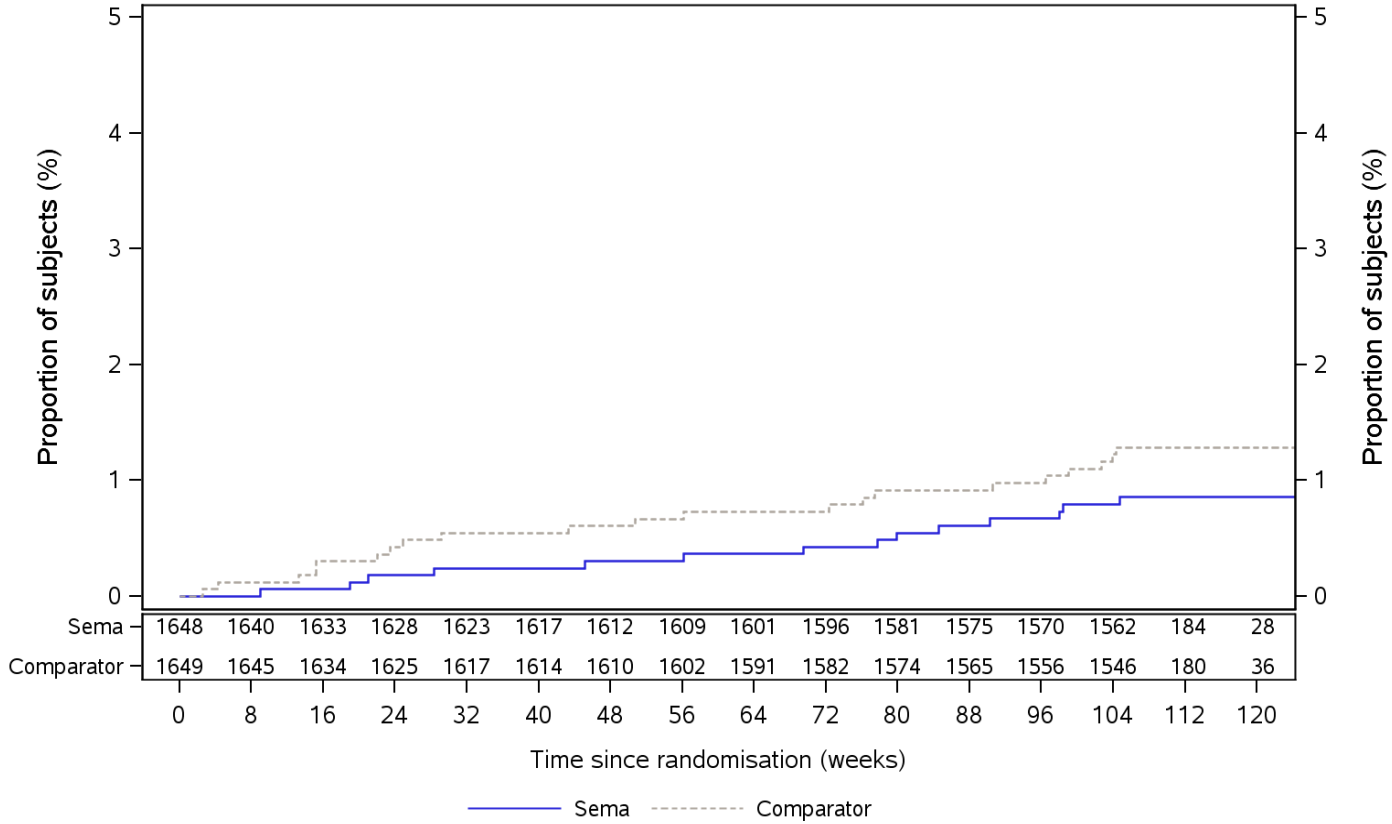
30 Serious adverse events - preferred term "Ischaemic stroke" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:44:24 - f_cif_tte_s6.sas/f_cif_pt_is_sae_s6.png

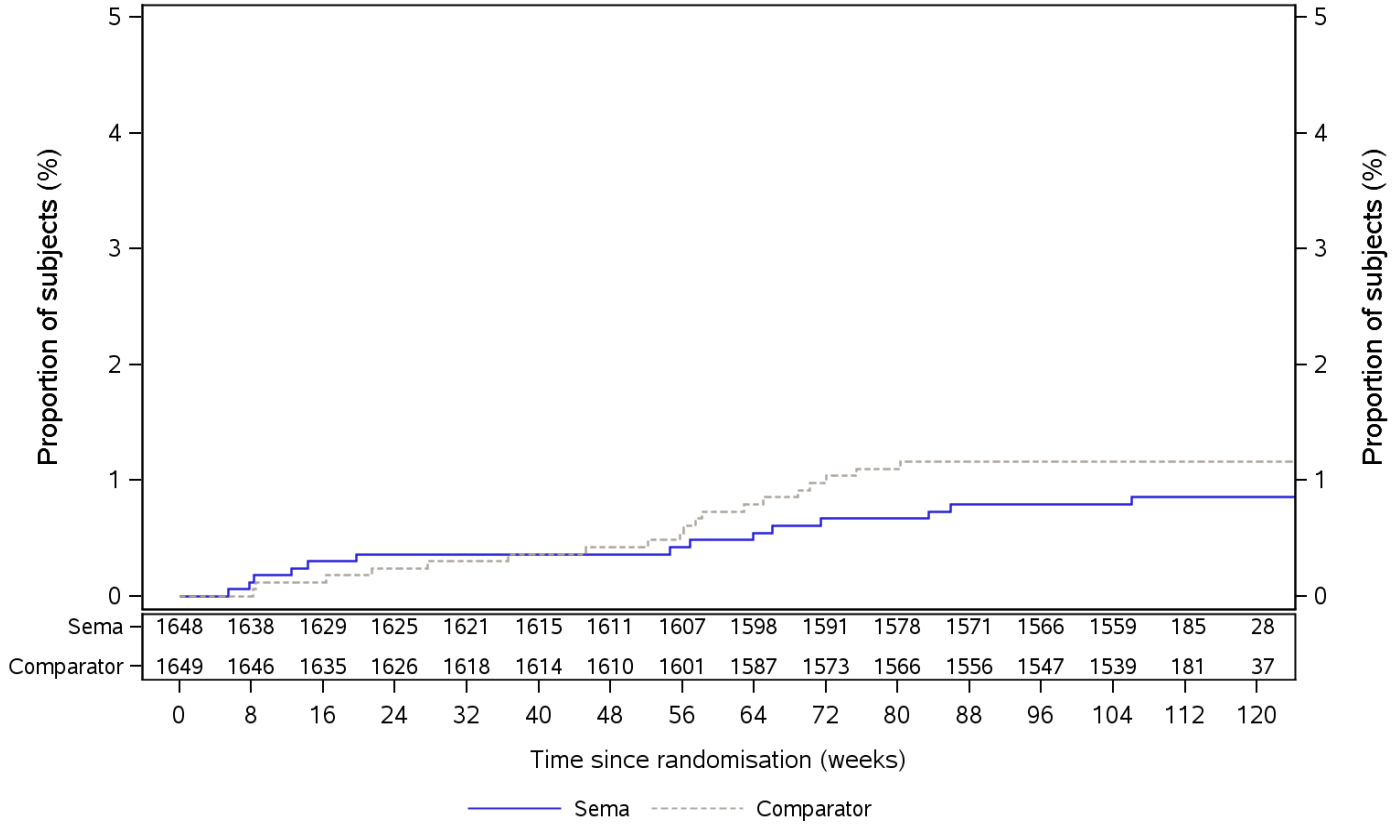
31 Serious adverse events - preferred term "Myocardial infarction" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:44:41 - f_cif_tte_s6.sas/f_cif_pt_mf_sae_s6.png

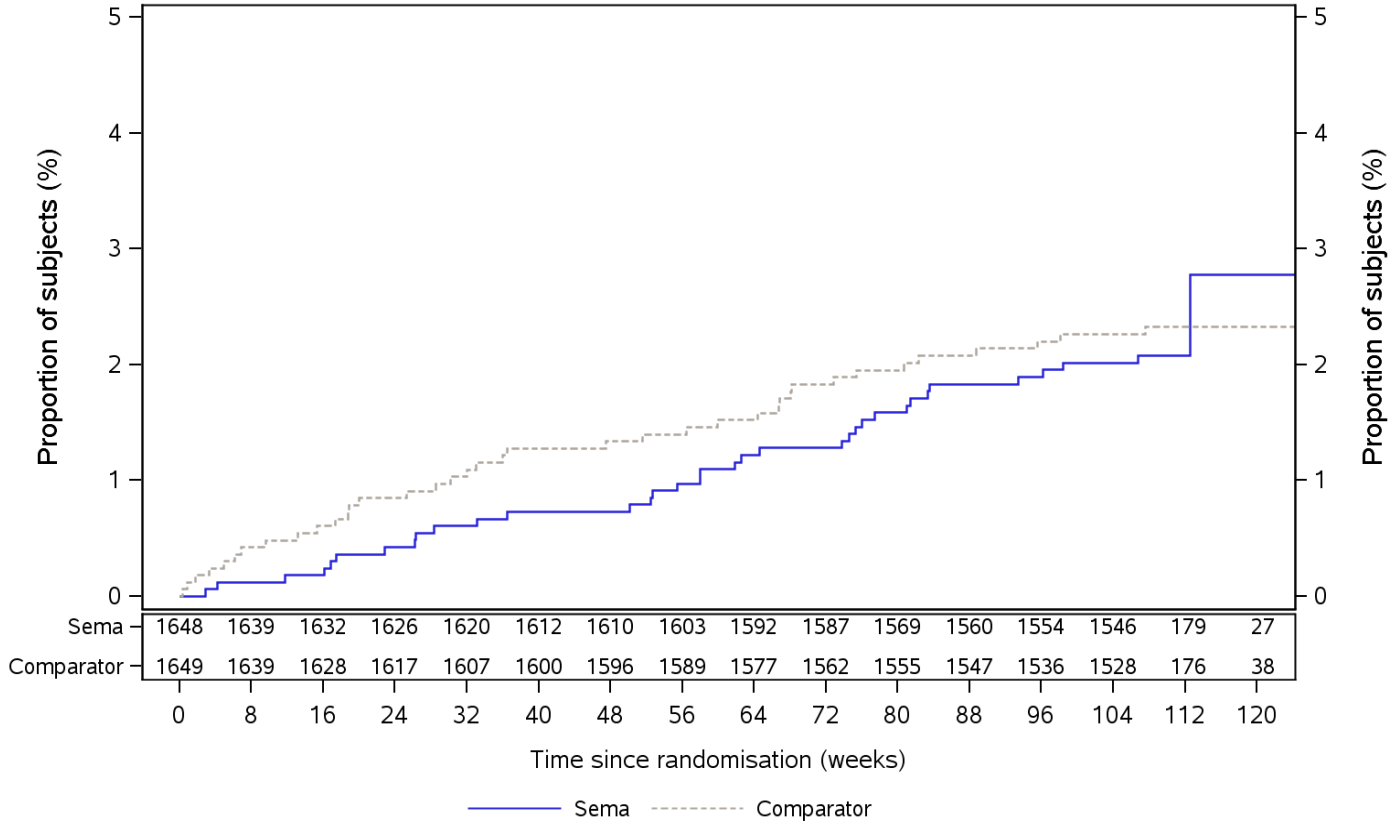
32 Serious adverse events - preferred term "Osteoarthritis" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:44:59 - f_cif_tte_s6.sas/f_cif_pt_ost_sae_s6.png

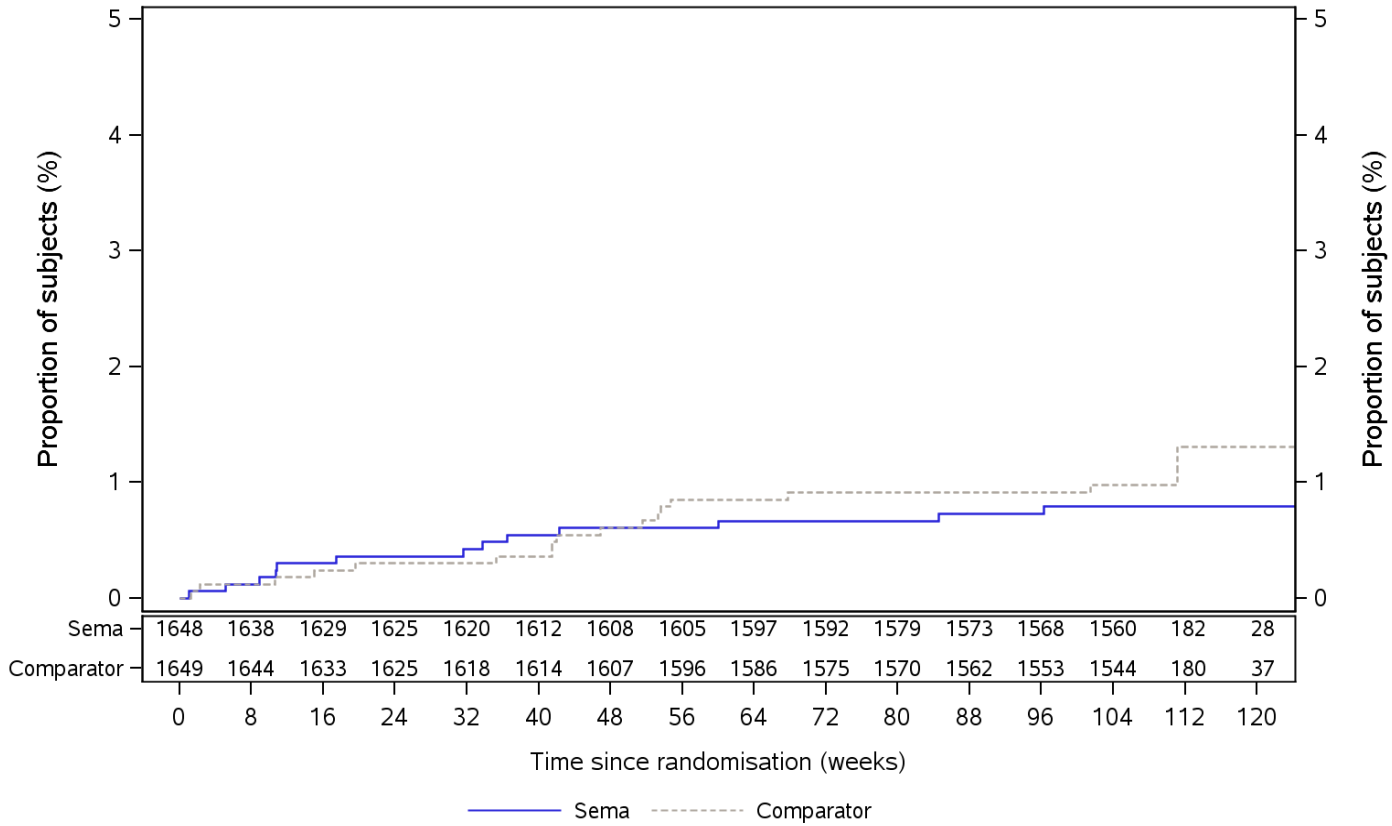
33 Serious adverse events - preferred term "Pneumonia" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:45:17 - f_cif_tte_s6.sas/f_cif_pt_pneu_sae_s6.png

34 Serious adverse events - preferred term "Transient ischaemic attack" - cumulative incidence plot - Sustain 6 - in-trial - full analysis set



Cumulative incidence estimates are based on time from randomisation to first event (with competing cause of death modelled as competing risk). Subjects were censored at the end of their in-trial observation period. Survival probabilities in percent corrected for competing risks can be derived as 100 - cumulative incidence estimates (in percent).
MedDRA version 20.1

nn9924/nn9924-submission-package/germany
26MAY2020:10:45:35 - f_cif_tte_s6.sas/f_cif_pt_tia_sae_s6.png

SUSTAIN 6 – Subgruppen – Mortalität / Morbidität / Gesundheitsbezogene Lebensqualität

1 Time-to-event analysis of overall mortality - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	62 (3.76%)	62	1649	60 (3.64%)	60	1.031 [0.723;1.470]	0.8666	
Age groups --- < 65y vs. >=65y									0.1144*
<65y	855	32 (3.74%)	32	844	22 (2.61%)	22	1.431 [0.832;2.463]	0.1954*	
>=65y	793	30 (3.78%)	30	805	38 (4.72%)	38	0.799 [0.495;1.290]	0.3583	
Gender --- male vs. female									0.2348
Male	1013	39 (3.85%)	39	989	43 (4.35%)	43	0.883 [0.573;1.362]	0.5740	
Female	635	23 (3.62%)	23	660	17 (2.58%)	17	1.402 [0.749;2.624]	0.2911	
Race --- white vs. non-white									0.9068
White	1384	56 (4.05%)	56	1352	53 (3.92%)	53	1.029 [0.707;1.499]	0.8801	
Non-white	264	6 (2.27%)	6	297	7 (2.36%)	7	0.961 [0.323;2.859]	0.9427	
Region --- Europe vs. rest of world									0.6260
Europe	326	12 (3.68%)	12	306	9 (2.94%)	9	1.255 [0.529;2.979]	0.6063	
Rest of World	1322	50 (3.78%)	50	1343	51 (3.80%)	51	0.992 [0.671;1.465]	0.9659	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.9149
Baseline HbA1c <8%	595	17 (2.86%)	17	628	18 (2.87%)	18	0.993 [0.512;1.926]	0.9828	
Baseline HbA1c >= 8%	1053	45 (4.27%)	45	1021	42 (4.11%)	42	1.036 [0.680;1.578]	0.8685	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.2572
Retinopathy present at baseline	510	22 (4.31%)	22	459	25 (5.45%)	25	0.783 [0.442;1.389]	0.4039	
Unknown or no baseline retinopathy	1138	40 (3.51%)	40	1190	35 (2.94%)	35	1.195 [0.759;1.882]	0.4407	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.5616
0.5 mg/week	826	30 (3.63%)	30	824	32 (3.88%)	32	0.929 [0.565;1.530]	0.7735	
1.0 mg/week	822	32 (3.89%)	32	825	28 (3.39%)	28	1.147 [0.691;1.905]	0.5955	
Baseline CV disease --- clinical vs. sub-clinical									0.8299
Clinical	1353	58 (4.29%)	58	1382	56 (4.05%)	56	1.055 [0.731;1.524]	0.7732	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of overall mortality - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	4 (1.36%)	4	267	4 (1.50%)	4	0.902 [0.226;3.605]	0.8841	
Baseline insulin use --- yes vs. no									0.2867
Yes	956	41 (4.29%)	41	957	34 (3.55%)	34	1.202 [0.763;1.894]	0.4279	
No	692	21 (3.03%)	21	692	26 (3.76%)	26	0.807 [0.454;1.434]	0.4645	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.4328
GFR >= 30	46	5 (10.87%)	5	61	4 (6.56%)	4	1.735 [0.466;6.462]	0.4112	
GFR < 30	1602	57 (3.56%)	57	1588	56 (3.53%)	56	1.005 [0.695;1.453]	0.9800	
OECD country --- yes vs. no									0.8221
Yes	1174	45 (3.83%)	45	1136	41 (3.61%)	41	1.058 [0.693;1.616]	0.7930	
No	474	17 (3.59%)	17	513	19 (3.70%)	19	0.968 [0.503;1.862]	0.9219	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

2 Time-to-event analysis of CV death (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	44 (2.67%)	44	1649	46 (2.79%)	46	0.955 [0.631;1.443]	0.8258	
Age groups --- < 65y vs. >=65y									0.1642*
<65y	855	24 (2.81%)	24	844	18 (2.13%)	18	1.312 [0.712;2.417]	0.3838	
>=65y	793	20 (2.52%)	20	805	28 (3.48%)	28	0.724 [0.408;1.285]	0.2694	
Gender --- male vs. female									0.4644
Male	1013	30 (2.96%)	30	989	34 (3.44%)	34	0.860 [0.526;1.404]	0.5456	
Female	635	14 (2.20%)	14	660	12 (1.82%)	12	1.209 [0.559;2.614]	0.6294	
Race --- white vs. non-white									0.6259
White	1384	41 (2.96%)	41	1352	41 (3.03%)	41	0.975 [0.632;1.503]	0.9084	
Non-white	264	3 (1.14%)	3	297	5 (1.68%)	5	0.672 [0.161;2.812]	0.5864	
Region --- Europe vs. rest of world									0.2389
Europe	326	5 (1.53%)	5	306	9 (2.94%)	9	0.524 [0.176;1.563]	0.2465	
Rest of World	1322	39 (2.95%)	39	1343	37 (2.76%)	37	1.066 [0.680;1.672]	0.7802	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.7570
Baseline HbA1c <8%	595	13 (2.18%)	13	628	13 (2.07%)	13	1.050 [0.487;2.266]	0.9004	
Baseline HbA1c >= 8%	1053	31 (2.94%)	31	1021	33 (3.23%)	33	0.909 [0.557;1.485]	0.7045	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.0880*
Retinopathy present at baseline	510	14 (2.75%)	14	459	21 (4.58%)	21	0.594 [0.302;1.168]	0.1312*	
Unknown or no baseline retinopathy	1138	30 (2.64%)	30	1190	25 (2.10%)	25	1.255 [0.738;2.135]	0.4009	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.8678
0.5 mg/week	826	21 (2.54%)	21	824	21 (2.55%)	21	0.992 [0.542;1.816]	0.9781	
1.0 mg/week	822	23 (2.80%)	23	825	25 (3.03%)	25	0.924 [0.525;1.628]	0.7849	
Baseline CV disease --- clinical vs. sub-clinical									0.6082
Clinical	1353	42 (3.10%)	42	1382	45 (3.26%)	45	0.952 [0.625;1.449]	0.8168	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of CV death (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	2 (0.68%)	2	267	1 (0.37%)	1	1.799 [0.163;19.80]	0.6313	
Baseline insulin use --- yes vs. no									0.1749*
Yes	956	31 (3.24%)	31	957	26 (2.72%)	26	1.188 [0.706;2.001]	0.5168	
No	692	13 (1.88%)	13	692	20 (2.89%)	20	0.650 [0.323;1.307]	0.2267	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.9201
GFR >= 30	46	3 (6.52%)	3	61	4 (6.56%)	4	1.044 [0.234;4.665]	0.9551	
GFR < 30	1602	41 (2.56%)	41	1588	42 (2.64%)	42	0.964 [0.627;1.482]	0.8670	
OECD country --- yes vs. no									0.8035
Yes	1174	30 (2.56%)	30	1136	29 (2.55%)	29	0.997 [0.598;1.661]	0.9900	
No	474	14 (2.95%)	14	513	17 (3.31%)	17	0.892 [0.440;1.810]	0.7522	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

3 Time-to-event analysis of cardiovascular morbidity (MACE) overall (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	108 (6.55%)	129	1649	146 (8.85%)	165	0.729 [0.569;0.935]	0.0129**	
Age groups --- < 65y vs. >=65y									0.9489
<65y	855	53 (6.20%)	60	844	70 (8.29%)	77	0.736 [0.515;1.052]	0.0924*	
>=65y	793	55 (6.94%)	69	805	76 (9.44%)	88	0.724 [0.512;1.025]	0.0684*	
Gender --- male vs. female									0.4516
Male	1013	73 (7.21%)	87	989	103 (10.41%)	120	0.680 [0.504;0.918]	0.0119**	
Female	635	35 (5.51%)	42	660	43 (6.52%)	45	0.836 [0.535;1.307]	0.4329	
Race --- white vs. non-white									0.4628
White	1384	93 (6.72%)	112	1352	118 (8.73%)	134	0.760 [0.579;0.998]	0.0479**	
Non-white	264	15 (5.68%)	17	297	28 (9.43%)	31	0.588 [0.314;1.102]	0.0974*	
Region --- Europe vs. rest of world									0.5575
Europe	326	18 (5.52%)	23	306	27 (8.82%)	29	0.621 [0.342;1.128]	0.1175*	
Rest of World	1322	90 (6.81%)	106	1343	119 (8.86%)	136	0.756 [0.575;0.994]	0.0451**	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.8014
Baseline HbA1c <8%	595	32 (5.38%)	37	628	48 (7.64%)	53	0.692 [0.443;1.082]	0.1068*	
Baseline HbA1c >= 8%	1053	76 (7.22%)	92	1021	98 (9.60%)	112	0.742 [0.550;1.001]	0.0505*	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.0670*
Retinopathy present at baseline	510	34 (6.67%)	40	459	56 (12.20%)	60	0.524 [0.342;0.802]	0.0030**	
Unknown or no baseline retinopathy	1138	74 (6.50%)	89	1190	90 (7.56%)	105	0.856 [0.630;1.165]	0.3230	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.8028
0.5 mg/week	826	59 (7.14%)	69	824	77 (9.34%)	79	0.751 [0.535;1.054]	0.0976*	
1.0 mg/week	822	49 (5.96%)	60	825	69 (8.36%)	86	0.705 [0.489;1.016]	0.0609*	
Baseline CV disease --- clinical vs. sub-clinical									0.4927
Clinical	1353	98 (7.24%)	118	1382	137 (9.91%)	155	0.719 [0.555;0.932]	0.0127**	

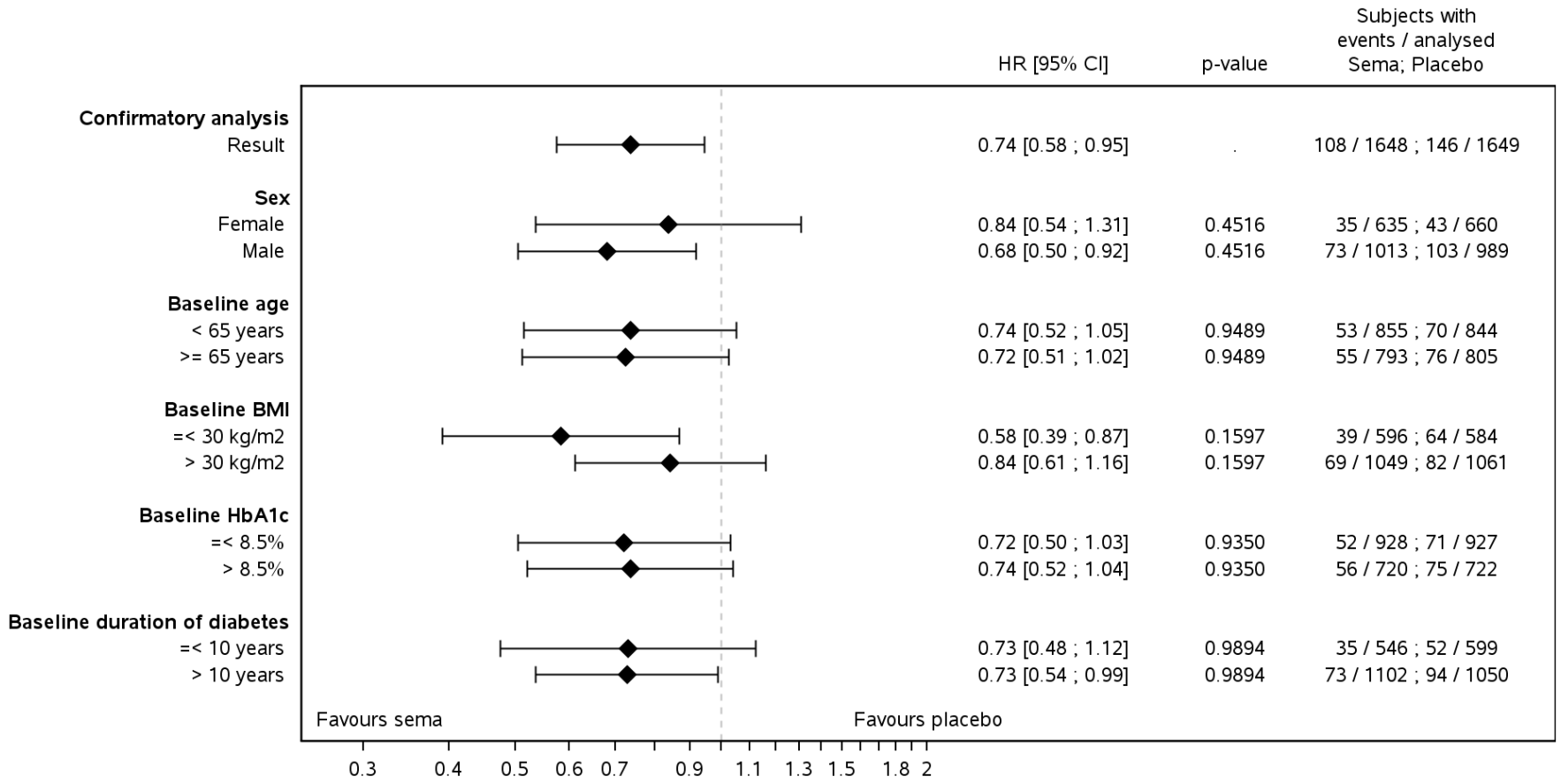
Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of cardiovascular morbidity (MACE) overall (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	10 (3.39%)	11	267	9 (3.37%)	10	0.998 [0.406;2.457]	0.9972	
Baseline insulin use --- yes vs. no									0.0630*
Yes	956	78 (8.16%)	90	957	89 (9.30%)	103	0.864 [0.637;1.171]	0.3447	
No	692	30 (4.34%)	39	692	57 (8.24%)	62	0.519 [0.334;0.808]	0.0037**	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.9769
GFR >= 30	46	6 (13.04%)	7	61	11 (18.03%)	16	0.727 [0.269;1.965]	0.5295	
GFR < 30	1602	102 (6.37%)	122	1588	135 (8.50%)	149	0.738 [0.571;0.954]	0.0205**	
OECD country --- yes vs. no									0.8103
Yes	1174	78 (6.64%)	93	1136	100 (8.80%)	113	0.743 [0.553;1.000]	0.0498**	
No	474	30 (6.33%)	36	513	46 (8.97%)	52	0.695 [0.439;1.101]	0.1215*	

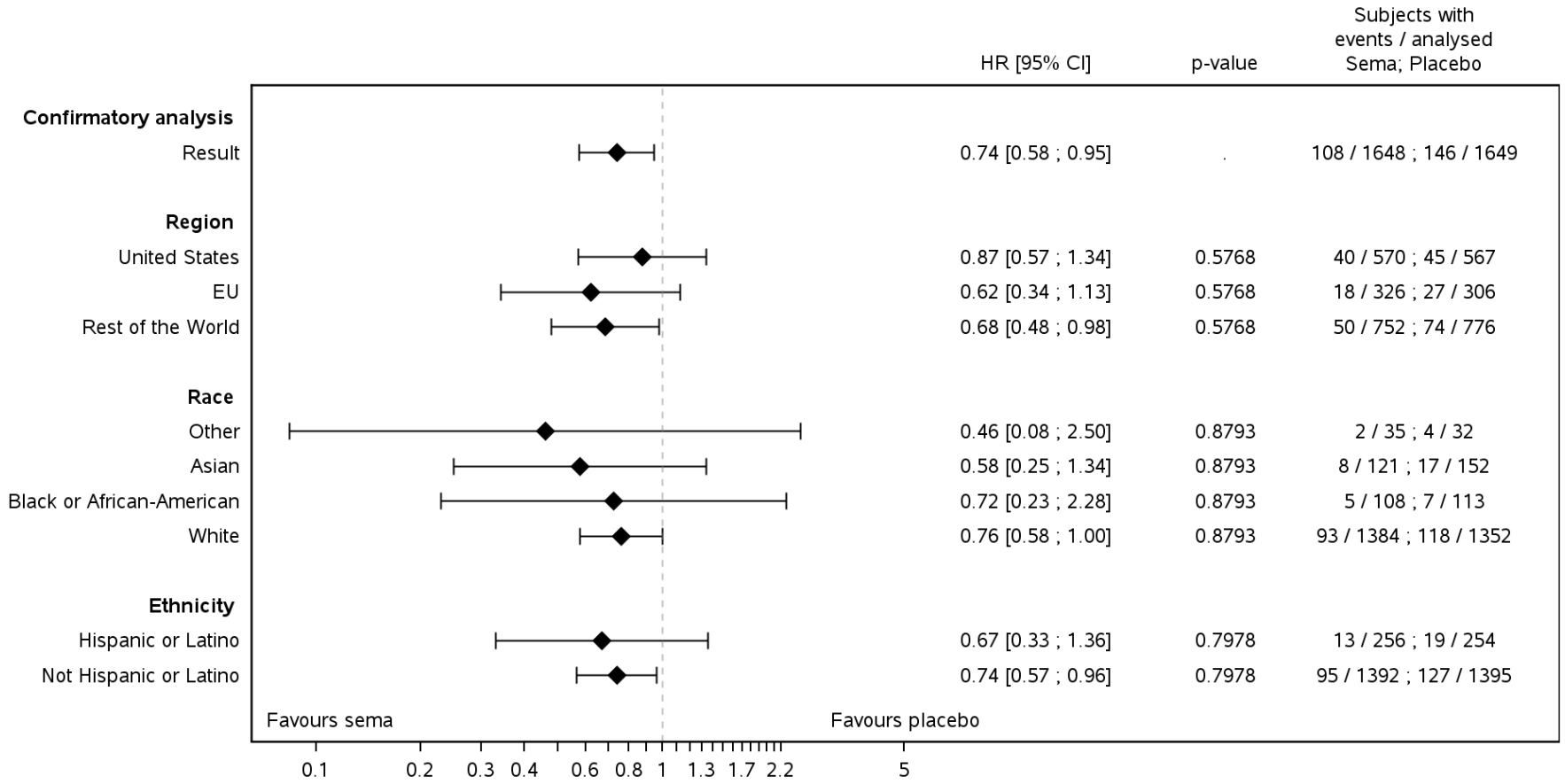
Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

4 Time-to-event analysis of MACE (only adjudicated events) - in trial - full analysis set



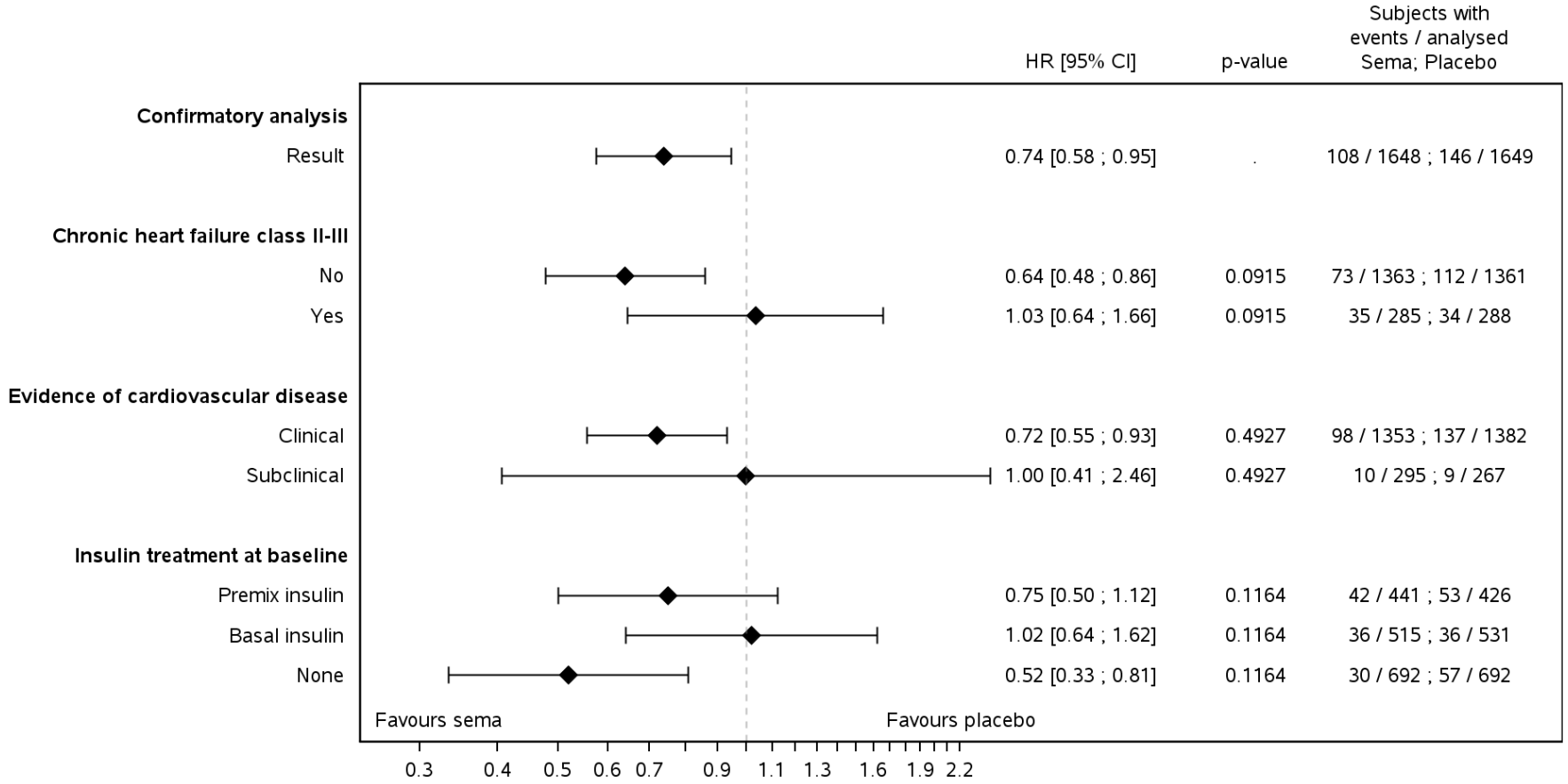
HR: Estimated hazard ratio CI: confidence interval Summary of results from sub-group analyses of time to first EAC confirmed MACE. Estimated hazard ratios and associated confidence intervals are from a Cox proportional hazards model with an interaction between treatment (semaglutide, placebo) and the relevant sub-group as fixed factor.
The p-value is from the Wald test of the interaction effect.

nn9535/nn9535-3744/freeze_20161007_ctr_er
09OCT2016:15:08:24 - zt_time2mace_subgrp.sas/f_stat_forest_mace_subgrp1.png



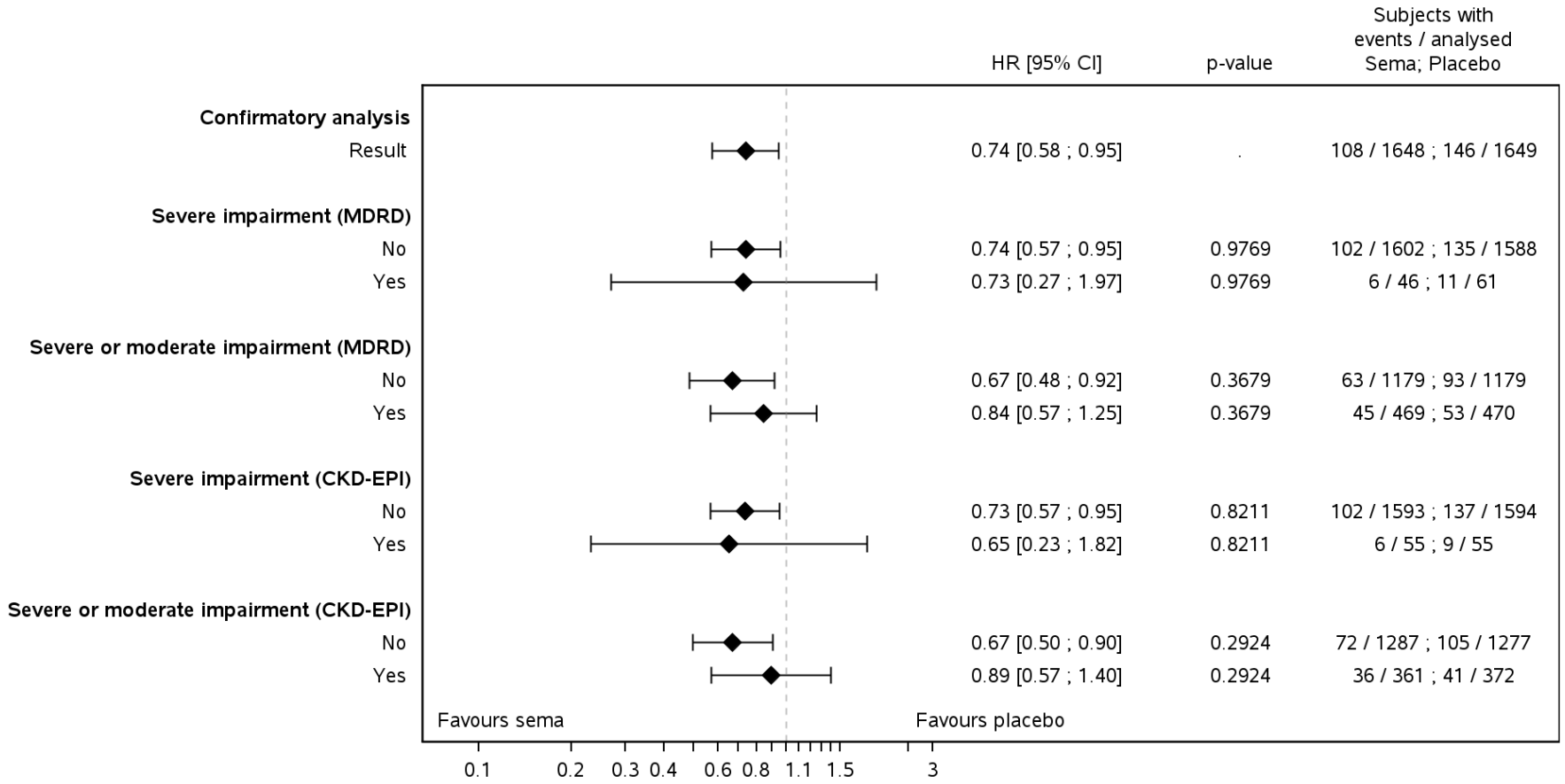
HR: Estimated hazard ratio CI: confidence interval Summary of results from sub-group analyses of time to first EAC confirmed MACE. Estimated hazard ratios and associated confidence intervals are from a Cox proportional hazards model with an interaction between treatment (semaglutide, placebo) and the relevant sub-group as fixed factor.
The p-value is from the Wald test of the interaction effect.

nn9535/nn9535-3744/freeze_20161007_ctr_er
09OCT2016:15:08:25 - zt_time2mace_subgrp.sas/f_stat_forest_mace_subgrp2.png



HR: Estimated hazard ratio CI: confidence interval Summary of results from sub-group analyses of time to first EAC confirmed MACE. Estimated hazard ratios and associated confidence intervals are from a Cox proportional hazards model with an interaction between treatment (semaglutide, placebo) and the relevant sub-group as fixed factor.
The p-value is from the Wald test of the interaction effect.

nn9535/nn9535-3744/freeze_20161007_ctr_er
09OCT2016:15:08:26 - zt_time2mace_subgrp.sas/f_stat_forest_mace_subgrp3.png



HR: Estimated hazard ratio CI: confidence interval Summary of results from sub-group analyses of time to first EAC confirmed MACE. Estimated hazard ratios and associated confidence intervals are from a Cox proportional hazards model with an interaction between treatment (semaglutide, placebo) and the relevant sub-group as fixed factor.
The p-value is from the Wald test of the interaction effect.

nn9535/nn9535-3744/freeze_20161007_ctr_er
09OCT2016:15:08:28 - zt_time2mace_subgrp.sas/f_stat_forest_mace_subgrp4.png

5 Time-to-event analysis of non-fatal stroke (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	27 (1.64%)	27	1649	44 (2.67%)	44	0.608 [0.377;0.982]	0.0421**	
Age groups --- < 65y vs. >=65y									0.2664
<65y	855	10 (1.17%)	10	844	22 (2.61%)	22	0.445 [0.211;0.940]	0.0339**	
>=65y	793	17 (2.14%)	17	805	22 (2.73%)	22	0.776 [0.412;1.461]	0.4322	
Gender --- male vs. female									0.7431
Male	1013	18 (1.78%)	18	989	27 (2.73%)	27	0.645 [0.355;1.171]	0.1495*	
Female	635	9 (1.42%)	9	660	17 (2.58%)	17	0.545 [0.243;1.223]	0.1412*	
Race --- white vs. non-white									0.1379*
White	1384	26 (1.88%)	26	1352	36 (2.66%)	36	0.700 [0.423;1.159]	0.1654*	
Non-white	264	1 (0.38%)	1	297	8 (2.69%)	8	0.139 [0.017;1.108]	0.0624*	
Region --- Europe vs. rest of world									0.9645
Europe	326	6 (1.84%)	6	306	9 (2.94%)	9	0.620 [0.221;1.742]	0.3645	
Rest of World	1322	21 (1.59%)	21	1343	35 (2.61%)	35	0.604 [0.352;1.037]	0.0677*	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.3446
Baseline HbA1c <8%	595	7 (1.18%)	7	628	17 (2.71%)	17	0.429 [0.178;1.035]	0.0595*	
Baseline HbA1c >= 8%	1053	20 (1.90%)	20	1021	27 (2.64%)	27	0.713 [0.400;1.271]	0.2515	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.8917
Retinopathy present at baseline	510	12 (2.35%)	12	459	17 (3.70%)	17	0.620 [0.296;1.297]	0.2041	
Unknown or no baseline retinopathy	1138	15 (1.32%)	15	1190	27 (2.27%)	27	0.579 [0.308;1.089]	0.0898*	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.6837
0.5 mg/week	826	16 (1.94%)	16	824	28 (3.40%)	28	0.561 [0.304;1.037]	0.0651*	
1.0 mg/week	822	11 (1.34%)	11	825	16 (1.94%)	16	0.688 [0.319;1.483]	0.3401	
Baseline CV disease --- clinical vs. sub-clinical									0.3479
Clinical	1353	25 (1.85%)	25	1382	38 (2.75%)	38	0.666 [0.402;1.104]	0.1150*	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of non-fatal stroke (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	2 (0.68%)	2	267	6 (2.25%)	6	0.298 [0.060;1.478]	0.1385*	
Baseline insulin use --- yes vs. no									0.8758
Yes	956	18 (1.88%)	18	957	30 (3.13%)	30	0.592 [0.330;1.061]	0.0784*	
No	692	9 (1.30%)	9	692	14 (2.02%)	14	0.642 [0.278;1.483]	0.2995	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.7788
GFR >= 30	46	1 (2.17%)	1	61	3 (4.92%)	3	0.447 [0.046;4.295]	0.4853	
GFR < 30	1602	26 (1.62%)	26	1588	41 (2.58%)	41	0.623 [0.381;1.018]	0.0587*	
OECD country --- yes vs. no									0.9397
Yes	1174	20 (1.70%)	20	1136	32 (2.82%)	32	0.599 [0.343;1.048]	0.0725*	
No	474	7 (1.48%)	7	513	12 (2.34%)	12	0.625 [0.246;1.587]	0.3230	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

6 Time-to-event analysis of non-fatal myocardial infarction (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	47 (2.85%)	58	1649	64 (3.88%)	75	0.729 [0.501;1.063]	0.1004*	
Age groups --- < 65y vs. >=65y									0.3128
<65y	855	20 (2.34%)	26	844	33 (3.91%)	37	0.594 [0.341;1.035]	0.0660*	
>=65y	793	27 (3.40%)	32	805	31 (3.85%)	38	0.877 [0.524;1.470]	0.6196	
Gender --- male vs. female									0.3353
Male	1013	32 (3.16%)	39	989	48 (4.85%)	59	0.644 [0.412;1.008]	0.0541*	
Female	635	15 (2.36%)	19	660	16 (2.42%)	16	0.971 [0.480;1.964]	0.9350	
Race --- white vs. non-white									0.5710
White	1384	35 (2.53%)	45	1352	49 (3.62%)	57	0.693 [0.449;1.069]	0.0973*	
Non-white	264	12 (4.55%)	13	297	15 (5.05%)	18	0.892 [0.418;1.906]	0.7681	
Region --- Europe vs. rest of world									0.7270
Europe	326	9 (2.76%)	12	306	10 (3.27%)	11	0.845 [0.343;2.080]	0.7141	
Rest of World	1322	38 (2.87%)	46	1343	54 (4.02%)	64	0.708 [0.468;1.073]	0.1033*	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.9648
Baseline HbA1c <8%	595	14 (2.35%)	17	628	20 (3.18%)	23	0.734 [0.371;1.454]	0.3758	
Baseline HbA1c >= 8%	1053	33 (3.13%)	41	1021	44 (4.31%)	52	0.721 [0.459;1.132]	0.1556*	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.2147
Retinopathy present at baseline	510	12 (2.35%)	14	459	21 (4.58%)	22	0.501 [0.247;1.018]	0.0561*	
Unknown or no baseline retinopathy	1138	35 (3.08%)	44	1190	43 (3.61%)	53	0.851 [0.545;1.330]	0.4800	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.3844
0.5 mg/week	826	26 (3.15%)	32	824	30 (3.64%)	30	0.859 [0.508;1.453]	0.5720	
1.0 mg/week	822	21 (2.55%)	26	825	34 (4.12%)	45	0.614 [0.357;1.059]	0.0793*	
Baseline CV disease --- clinical vs. sub-clinical									0.1824*
Clinical	1353	41 (3.03%)	51	1382	61 (4.41%)	72	0.680 [0.458;1.011]	0.0566*	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of non-fatal myocardial infarction (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	6 (2.03%)	7	267	3 (1.12%)	3	1.814 [0.454;7.253]	0.3997	
Baseline insulin use --- yes vs. no									0.0393**
Yes	956	36 (3.77%)	41	957	37 (3.87%)	47	0.971 [0.613;1.536]	0.8986	
No	692	11 (1.59%)	17	692	27 (3.90%)	28	0.402 [0.200;0.811]	0.0109**	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.8885
GFR >= 30	46	3 (6.52%)	3	61	5 (8.20%)	9	0.815 [0.195;3.412]	0.7800	
GFR < 30	1602	44 (2.75%)	55	1588	59 (3.72%)	66	0.733 [0.496;1.084]	0.1195*	
OECD country --- yes vs. no									0.9809
Yes	1174	34 (2.90%)	43	1136	45 (3.96%)	52	0.726 [0.465;1.133]	0.1589*	
No	474	13 (2.74%)	15	513	19 (3.70%)	23	0.733 [0.362;1.485]	0.3892	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

7 Time-to-event analysis of transient ischemic attack - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	15 (0.91%)	17	1649	21 (1.27%)	23	0.713 [0.367;1.383]	0.3166	
Age groups --- < 65y vs. >=65y									0.3722
<65y	855	5 (0.58%)	5	844	10 (1.18%)	11	0.492 [0.168;1.441]	0.1959*	
>=65y	793	10 (1.26%)	12	805	11 (1.37%)	12	0.920 [0.391;2.167]	0.8489	
Gender --- male vs. female									0.1973*
Male	1013	7 (0.69%)	8	989	14 (1.42%)	16	0.486 [0.196;1.203]	0.1188*	
Female	635	8 (1.26%)	9	660	7 (1.06%)	7	1.189 [0.431;3.279]	0.7379	
Race --- white vs. non-white									0.3204
White	1384	13 (0.94%)	14	1352	20 (1.48%)	22	0.633 [0.315;1.273]	0.1993*	
Non-white	264	2 (0.76%)	3	297	1 (0.34%)	1	2.248 [0.204;24.79]	0.5084	
Region --- Europe vs. rest of world									0.5843
Europe	326	4 (1.23%)	4	306	7 (2.29%)	8	0.530 [0.155;1.812]	0.3118	
Rest of World	1322	11 (0.83%)	13	1343	14 (1.04%)	15	0.797 [0.362;1.757]	0.5743	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.9538
Baseline HbA1c <8%	595	7 (1.18%)	8	628	10 (1.59%)	12	0.733 [0.279;1.926]	0.5287	
Baseline HbA1c >= 8%	1053	8 (0.76%)	9	1021	11 (1.08%)	11	0.705 [0.283;1.753]	0.4517	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.9874
Retinopathy present at baseline	510	4 (0.78%)	5	459	5 (1.09%)	5	0.711 [0.191;2.648]	0.6113	
Unknown or no baseline retinopathy	1138	11 (0.97%)	12	1190	16 (1.34%)	18	0.720 [0.334;1.551]	0.4015	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.8095
0.5 mg/week	826	8 (0.97%)	9	824	12 (1.46%)	14	0.662 [0.271;1.619]	0.3660	
1.0 mg/week	822	7 (0.85%)	8	825	9 (1.09%)	9	0.780 [0.290;2.094]	0.6217	
Baseline CV disease --- clinical vs. sub-clinical									0.9829
Clinical	1353	15 (1.11%)	17	1382	19 (1.37%)	21	0.805 [0.409;1.585]	0.5307	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of transient ischemic attack - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	0 (0.00%)	0	267	2 (0.75%)	2	<0.001 [<0.001;no est.]	0.9826	
Baseline insulin use --- yes vs. no									0.7296
Yes	956	7 (0.73%)	8	957	11 (1.15%)	12	0.634 [0.246;1.635]	0.3453	
No	692	8 (1.16%)	9	692	10 (1.45%)	11	0.801 [0.316;2.029]	0.6396	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.9891
GFR >= 30	46	0 (0.00%)	0	61	1 (1.64%)	1	<0.001 [<0.001;no est.]	0.9889	
GFR < 30	1602	15 (0.94%)	17	1588	20 (1.26%)	22	0.741 [0.379;1.448]	0.3805	
OECD country --- yes vs. no									0.9716
Yes	1174	13 (1.11%)	14	1136	18 (1.58%)	20	0.696 [0.341;1.421]	0.3200	
No	474	2 (0.42%)	3	513	3 (0.58%)	3	0.721 [0.121;4.315]	0.7202	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

8 Time-to-event analysis of unstable angina requiring hospitalisation (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	22 (1.33%)	24	1649	27 (1.64%)	28	0.813 [0.463;1.427]	0.4699	
Age groups --- < 65y vs. >=65y									0.3253
<65y	855	13 (1.52%)	14	844	12 (1.42%)	12	1.070 [0.488;2.346]	0.8649	
>=65y	793	9 (1.13%)	10	805	15 (1.86%)	16	0.604 [0.264;1.381]	0.2322	
Gender --- male vs. female									0.3488
Male	1013	13 (1.28%)	14	989	19 (1.92%)	20	0.664 [0.328;1.345]	0.2553	
Female	635	9 (1.42%)	10	660	8 (1.21%)	8	1.170 [0.451;3.033]	0.7465	
Race --- white vs. non-white									0.6151
White	1384	18 (1.30%)	19	1352	23 (1.70%)	24	0.762 [0.411;1.411]	0.3867	
Non-white	264	4 (1.52%)	5	297	4 (1.35%)	4	1.124 [0.281;4.493]	0.8689	
Region --- Europe vs. rest of world									0.8358
Europe	326	3 (0.92%)	3	306	4 (1.31%)	4	0.704 [0.158;3.147]	0.6464	
Rest of World	1322	19 (1.44%)	21	1343	23 (1.71%)	24	0.836 [0.455;1.534]	0.5625	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.9751
Baseline HbA1c <8%	595	7 (1.18%)	7	628	9 (1.43%)	9	0.820 [0.305;2.201]	0.6931	
Baseline HbA1c >= 8%	1053	15 (1.42%)	17	1021	18 (1.76%)	19	0.804 [0.405;1.596]	0.5329	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.8927
Retinopathy present at baseline	510	5 (0.98%)	5	459	5 (1.09%)	5	0.889 [0.257;3.072]	0.8530	
Unknown or no baseline retinopathy	1138	17 (1.49%)	19	1190	22 (1.85%)	23	0.808 [0.429;1.522]	0.5096	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.7237
0.5 mg/week	826	12 (1.45%)	13	824	16 (1.94%)	17	0.743 [0.352;1.571]	0.4368	
1.0 mg/week	822	10 (1.22%)	11	825	11 (1.33%)	11	0.912 [0.387;2.148]	0.8336	
Baseline CV disease --- clinical vs. sub-clinical									0.6110
Clinical	1353	21 (1.55%)	23	1382	25 (1.81%)	26	0.856 [0.479;1.528]	0.5984	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of unstable angina requiring hospitalisation (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	1 (0.34%)	1	267	2 (0.75%)	2	0.451 [0.041;4.971]	0.5153	
Baseline insulin use --- yes vs. no									0.9819
Yes	956	13 (1.36%)	15	957	16 (1.67%)	17	0.808 [0.389;1.680]	0.5683	
No	692	9 (1.30%)	9	692	11 (1.59%)	11	0.819 [0.339;1.976]	0.6566	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.9875
GFR >= 30	46	0 (0.00%)	0	61	1 (1.64%)	1	<0.001 [<0.001;no est.]	0.9873	
GFR < 30	1602	22 (1.37%)	24	1588	26 (1.64%)	27	0.835 [0.473;1.474]	0.5346	
OECD country --- yes vs. no									0.2169
Yes	1174	15 (1.28%)	16	1136	22 (1.94%)	23	0.657 [0.341;1.266]	0.2097	
No	474	7 (1.48%)	8	513	5 (0.97%)	5	1.511 [0.480;4.761]	0.4808	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

9 Time-to-event analysis of heart failure requiring hospital admission (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	59 (3.58%)	81	1649	54 (3.27%)	71	1.094 [0.756;1.583]	0.6329	
Age groups --- < 65y vs. >=65y									0.0951*
<65y	855	28 (3.27%)	42	844	17 (2.01%)	27	1.633 [0.894;2.983]	0.1109*	
>=65y	793	31 (3.91%)	39	805	37 (4.60%)	44	0.848 [0.526;1.367]	0.4992	
Gender --- male vs. female									0.5501
Male	1013	41 (4.05%)	58	989	34 (3.44%)	47	1.182 [0.750;1.863]	0.4703	
Female	635	18 (2.83%)	23	660	20 (3.03%)	24	0.931 [0.493;1.761]	0.8268	
Race --- white vs. non-white									0.0607*
White	1384	47 (3.40%)	66	1352	49 (3.62%)	66	0.936 [0.627;1.397]	0.7460	
Non-white	264	12 (4.55%)	15	297	5 (1.68%)	5	2.727 [0.961;7.740]	0.0595*	
Region --- Europe vs. rest of world									0.3905
Europe	326	9 (2.76%)	12	306	11 (3.59%)	13	0.772 [0.320;1.863]	0.5646	
Rest of World	1322	50 (3.78%)	69	1343	43 (3.20%)	58	1.181 [0.786;1.775]	0.4238	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.8842
Baseline HbA1c <8%	595	20 (3.36%)	30	628	20 (3.18%)	26	1.053 [0.567;1.957]	0.8705	
Baseline HbA1c >= 8%	1053	39 (3.70%)	51	1021	34 (3.33%)	45	1.115 [0.704;1.766]	0.6426	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.7015
Retinopathy present at baseline	510	25 (4.90%)	40	459	19 (4.14%)	22	1.181 [0.650;2.145]	0.5844	
Unknown or no baseline retinopathy	1138	34 (2.99%)	41	1190	35 (2.94%)	49	1.018 [0.635;1.632]	0.9413	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.3394
0.5 mg/week	826	37 (4.48%)	51	824	29 (3.52%)	36	1.274 [0.784;2.072]	0.3283	
1.0 mg/week	822	22 (2.68%)	30	825	25 (3.03%)	35	0.884 [0.498;1.567]	0.6719	
Baseline CV disease --- clinical vs. sub-clinical									0.8469
Clinical	1353	51 (3.77%)	73	1382	48 (3.47%)	64	1.086 [0.732;1.610]	0.6830	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of heart failure requiring hospital admission (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	8 (2.71%)	8	267	6 (2.25%)	7	1.213 [0.421;3.497]	0.7202	
Baseline insulin use --- yes vs. no									0.7768
Yes	956	43 (4.50%)	57	957	38 (3.97%)	51	1.130 [0.731;1.749]	0.5819	
No	692	16 (2.31%)	24	692	16 (2.31%)	20	1.004 [0.502;2.008]	0.9906	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.9311
GFR >= 30	46	5 (10.87%)	8	61	6 (9.84%)	7	1.178 [0.360;3.860]	0.7867	
GFR < 30	1602	54 (3.37%)	73	1588	48 (3.02%)	64	1.115 [0.756;1.645]	0.5835	
OECD country --- yes vs. no									0.0833*
Yes	1174	41 (3.49%)	60	1136	44 (3.87%)	60	0.900 [0.588;1.377]	0.6265	
No	474	18 (3.80%)	21	513	10 (1.95%)	11	1.962 [0.906;4.251]	0.0874*	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

10 Time-to-event analysis of coronary revascularisation (only adjudicated events) - in trial - full analysis set

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Novo Nordisk

3: Time to first event - cox model - in trial - FAS

Comparison	Events/Subjects	Hazard ratio	Lower 95% CI	Upper 95% CI	p-value	Interaction p-value
Time to first occurrence of EAC confirmed coronary revascularisation						
Entire FAS						
No subgroup(s)						
Sema / Placebo	70 (1648) / 103 (1649)	0.678	0.500	0.919	0.0122	
Subgroup: Age						
<65y						
Sema / Placebo	42 (855) / 55 (844)	0.749	0.501	1.119	0.1581	0.4171
>=65y						
Sema / Placebo	28 (793) / 48 (805)	0.580	0.364	0.925	0.0222	
Subgroup: Gender						
Male						
Sema / Placebo	45 (1013) / 71 (989)	0.608	0.419	0.883	0.0090	0.3895
Female						
Sema / Placebo	25 (635) / 32 (660)	0.806	0.478	1.361	0.4199	
Subgroup: Region						
Europe						
Sema / Placebo	13 (326) / 18 (306)	0.677	0.332	1.382	0.2841	0.9804
Rest of World						
Sema / Placebo	57 (1322) / 85 (1343)	0.671	0.479	0.938	0.0196	
Subgroup: OECD country						
Yes						
Sema / Placebo	54 (1174) / 87 (1136)	0.590	0.420	0.828	0.0023	0.1250
No						
Sema / Placebo	16 (474) / 16 (513)	1.079	0.540	2.157	0.8301	
Subgroup: Race						
White						
Sema / Placebo	61 (1384) / 83 (1352)	0.710	0.510	0.989	0.0426	0.4019
Non-white						
Sema / Placebo	9 (264) / 20 (297)	0.493	0.225	1.083	0.0782	

The 'entire FAS' are stratified Cox models. The subgroup analsyes are not stratified
Data is 'in-trial' and FAS (as randomised)

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Time to first event - cox model - in trial - FAS

Comparison	Events/Subjects	Hazard ratio	Lower 95% CI	Upper 95% CI	p-value	Interaction p-value
Subgroup: Severity of Disease						
Baseline HbA1c <8%						
Sema / Placebo	26 (595) / 37 (628)	0.735	0.445	1.213	0.2279	0.6554
Baseline HbA1c >= 8%						
Sema / Placebo	44 (1053) / 66 (1021)	0.636	0.435	0.932	0.0202	
Subgroup: Retinopathy at Baseline						
Retinopathy present at baseline						
Sema / Placebo	10 (510) / 29 (459)	0.299	0.146	0.614	0.0010	0.0068
No baseline retinopathy						
Sema / Placebo	52 (1023) / 72 (1089)	0.762	0.533	1.089	0.1352	
Unknown retinopathy at baseline						
Sema / Placebo	8 (115) / 2 (101)	3.701	0.786	17.421	0.0978	
Subgroup: Retinopathy at Baseline						
Retinopathy present at baseline						
Sema / Placebo	10 (510) / 29 (459)	0.299	0.146	0.614	0.0010	0.0105
Unknown or no baseline retinopathy						
Sema / Placebo	60 (1138) / 74 (1190)	0.845	0.601	1.188	0.3334	
Subgroup: Baseline CV disease						
Clinical						
Sema / Placebo	65 (1353) / 99 (1382)	0.661	0.483	0.904	0.0095	0.4380
Sub-clinical						
Sema / Placebo	5 (295) / 4 (267)	1.128	0.303	4.202	0.8572	
Subgroup: Baseline Insulin Use						
Yes						
Sema / Placebo	38 (956) / 66 (957)	0.564	0.378	0.841	0.0049	0.1775
No						
Sema / Placebo	32 (692) / 37 (692)	0.863	0.538	1.386	0.5431	
Subgroup: Baseline renal Impairment						
GFR >= 30						
Sema / Placebo	(46) / 6 (61)	0.000	0.000		0.9751	0.9757
GFR < 30						

The 'entire FAS' are stratified Cox models. The subgroup analsyes are not stratified
Data is 'in-trial' and FAS (as randomised)

nn9535/nn9535-exploratory/heeot008
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11 Time-to-event analysis of nephropathy (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	62 (3.76%)	68	1649	100 (6.06%)	106	0.609 [0.444;0.837]	0.0022**	
Age groups --- < 65y vs. >=65y									0.6727
<65y	855	36 (4.21%)	41	844	54 (6.40%)	59	0.647 [0.424;0.986]	0.0428**	
>=65y	793	26 (3.28%)	27	805	46 (5.71%)	47	0.563 [0.348;0.911]	0.0194**	
Gender --- male vs. female									0.4182
Male	1013	42 (4.15%)	47	989	60 (6.07%)	62	0.672 [0.453;0.996]	0.0479**	
Female	635	20 (3.15%)	21	660	40 (6.06%)	44	0.510 [0.298;0.873]	0.0140**	
Race --- white vs. non-white									0.3672
White	1384	50 (3.61%)	54	1352	72 (5.33%)	75	0.668 [0.466;0.958]	0.0283**	
Non-white	264	12 (4.55%)	14	297	28 (9.43%)	31	0.469 [0.239;0.923]	0.0284**	
Region --- Europe vs. rest of world									0.9909
Europe	326	10 (3.07%)	10	306	15 (4.90%)	16	0.614 [0.276;1.366]	0.2320	
Rest of World	1322	52 (3.93%)	58	1343	85 (6.33%)	90	0.611 [0.433;0.862]	0.0051**	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.2200
Baseline HbA1c <8%	595	21 (3.53%)	21	628	27 (4.30%)	29	0.816 [0.461;1.443]	0.4845	
Baseline HbA1c >= 8%	1053	41 (3.89%)	47	1021	73 (7.15%)	77	0.531 [0.362;0.778]	0.0012**	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.1866*
Retinopathy present at baseline	510	21 (4.12%)	23	459	40 (8.71%)	44	0.454 [0.268;0.769]	0.0034**	
Unknown or no baseline retinopathy	1138	41 (3.60%)	45	1190	60 (5.04%)	62	0.708 [0.476;1.053]	0.0885*	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.5788
0.5 mg/week	826	37 (4.48%)	40	824	55 (6.67%)	58	0.658 [0.434;0.998]	0.0491**	
1.0 mg/week	822	25 (3.04%)	28	825	45 (5.45%)	48	0.549 [0.336;0.895]	0.0161**	
Baseline CV disease --- clinical vs. sub-clinical									0.7163
Clinical	1353	53 (3.92%)	58	1382	85 (6.15%)	91	0.627 [0.445;0.883]	0.0076**	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of nephropathy (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	9 (3.05%)	10	267	15 (5.62%)	15	0.531 [0.232;1.213]	0.1330*	
Baseline insulin use --- yes vs. no									0.1553*
Yes	956	41 (4.29%)	47	957	76 (7.94%)	82	0.525 [0.359;0.768]	0.0009**	
No	692	21 (3.03%)	21	692	24 (3.47%)	24	0.871 [0.485;1.565]	0.6447	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.2375
GFR >= 30	46	11 (23.91%)	12	61	15 (24.59%)	17	0.976 [0.449;2.125]	0.9520	
GFR < 30	1602	51 (3.18%)	56	1588	85 (5.35%)	89	0.584 [0.413;0.827]	0.0024**	
OECD country --- yes vs. no									0.0400**
Yes	1174	47 (4.00%)	50	1136	58 (5.11%)	61	0.777 [0.529;1.142]	0.1991*	
No	474	15 (3.16%)	18	513	42 (8.19%)	45	0.372 [0.206;0.670]	0.0010**	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

12 Time-to-event analysis of diabetic retinopathy (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
All subjects (total)	1648	50 (3.03%)	62	1649	29 (1.76%)	36	1.733 [1.097;2.739]	0.0184**	
Age groups --- < 65y vs. >=65y									0.9553
<65y	855	35 (4.09%)	43	844	20 (2.37%)	27	1.742 [1.006;3.018]	0.0477**	
>=65y	793	15 (1.89%)	19	805	9 (1.12%)	9	1.693 [0.741;3.869]	0.2116	
Gender --- male vs. female									0.4616
Male	1013	34 (3.36%)	45	989	17 (1.72%)	24	1.972 [1.102;3.530]	0.0222**	
Female	635	16 (2.52%)	17	660	12 (1.82%)	12	1.381 [0.653;2.920]	0.3977	
Race --- white vs. non-white									0.8118
White	1384	43 (3.11%)	53	1352	25 (1.85%)	32	1.687 [1.031;2.763]	0.0375**	
Non-white	264	7 (2.65%)	9	297	4 (1.35%)	4	1.982 [0.580;6.770]	0.2751	
Region --- Europe vs. rest of world									0.2528
Europe	326	9 (2.76%)	11	306	8 (2.61%)	9	1.057 [0.408;2.740]	0.9087	
Rest of World	1322	41 (3.10%)	51	1343	21 (1.56%)	27	1.995 [1.179;3.375]	0.0101**	
Severity of disease --- baseline HbA1c <8% vs. >=8%									0.0829*
Baseline HbA1c <8%	595	15 (2.52%)	20	628	4 (0.64%)	5	3.991 [1.325;12.02]	0.0139**	
Baseline HbA1c >= 8%	1053	35 (3.32%)	42	1021	25 (2.45%)	31	1.360 [0.814;2.273]	0.2398	
Retinopathy at baseline --- retinopathy present at baseline vs. unknown or no baseline retinopathy									0.9280
Retinopathy present at baseline	510	42 (8.24%)	54	459	24 (5.23%)	31	1.585 [0.960;2.618]	0.0717*	
Unknown or no baseline retinopathy	1138	8 (0.70%)	8	1190	5 (0.42%)	5	1.677 [0.549;5.127]	0.3642	
Treatment dose volume --- 0.5 mg vs 1.0 mg per week									0.9099
0.5 mg/week	826	25 (3.03%)	28	824	14 (1.70%)	20	1.781 [0.926;3.426]	0.0838*	
1.0 mg/week	822	25 (3.04%)	34	825	15 (1.82%)	16	1.689 [0.891;3.204]	0.1085*	
Baseline CV disease --- clinical vs. sub-clinical									0.0950*
Clinical	1353	38 (2.81%)	47	1382	27 (1.95%)	33	1.441 [0.880;2.361]	0.1463*	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

Time-to-event analysis of diabetic retinopathy (only adjudicated events) - in trial - full analysis set

	Sema			Comparator			Sema vs. Comparator		
Subgroup	N	n (%)	E	N	n (%)	E	Hazard-Ratio [95%-CI]	p-value	p-value Interaction
Sub-clinical	295	12 (4.07%)	15	267	2 (0.75%)	3	5.519 [1.235;24.66]	0.0253**	
Baseline insulin use --- yes vs. no									0.9778
Yes	956	38 (3.97%)	50	957	22 (2.30%)	29	1.742 [1.031;2.945]	0.0382**	
No	692	12 (1.73%)	12	692	7 (1.01%)	7	1.716 [0.676;4.358]	0.2562	
Baseline renal impairment --- GFR < 30 vs. GFR >= 30									0.5534
GFR >= 30	46	4 (8.70%)	7	61	2 (3.28%)	2	2.885 [0.529;15.75]	0.2211	
GFR < 30	1602	46 (2.87%)	55	1588	27 (1.70%)	34	1.693 [1.053;2.724]	0.0298**	
OECD country --- yes vs. no									0.1251*
Yes	1174	27 (2.30%)	36	1136	20 (1.76%)	27	1.311 [0.735;2.337]	0.3587	
No	474	23 (4.85%)	26	513	9 (1.75%)	9	2.786 [1.289;6.022]	0.0092**	

Entire trial population over all indications: pooled Semaglutide arms (0,5 mg + 1,0 mg) vs. pooled placebo arms (0,5 mg + 1,0 mg)
N: Number of subjects, n: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events,
CI: Confidence interval, not est.: not estimated, *: 0,05 <= p-value < 0,20, **: p-value < 0,05
The hazard ratio estimate and confidence limits are derived based on a time-to-event analysis by using a Cox proportional hazards model. The model includes treatment arm as fixed factor. If minimum of the two or four N is zero then the regressions was not attempted because data is too sparse.

13 HbA1c (%) - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1648	1472	8.70 (1.5)	7.40 (1.5)	-1.26 (0.0)	1649	1649	1448	8.70 (1.5)	8.27 (1.5)	-0.39 (0.0)	-0.87 [-0.97;-0.77] <0.0001	-0.54 [-0.61;-0.47]	
Gender															0.3797
Female	635	635	563	8.81 (1.6)	7.42 (1.6)	-1.32 (0.1)	660	660	569	8.85 (1.6)	8.38 (1.6)	-0.40 (0.1)	-0.93 [-1.09;-0.77] <0.0001	-0.55 [-0.66;-0.43]	
Male	1013	1013	909	8.64 (1.4)	7.39 (1.4)	-1.22 (0.0)	989	989	879	8.60 (1.4)	8.20 (1.5)	-0.38 (0.0)	-0.84 [-0.96;-0.71] <0.0001	-0.54 [-0.63;-0.44]	
Age															0.1143
< 65	855	855	764	8.94 (1.6)	7.52 (1.6)	-1.37 (0.0)	844	844	744	8.92 (1.5)	8.45 (1.7)	-0.42 (0.0)	-0.95 [-1.09;-0.81] <0.0001	-0.54 [-0.64;-0.44]	
65 <=	793	793	708	8.44 (1.2)	7.28 (1.4)	-1.14 (0.1)	805	805	704	8.47 (1.4)	8.09 (1.4)	-0.35 (0.1)	-0.79 [-0.93;-0.65] <0.0001	-0.55 [-0.66;-0.45]	
HbA1c at baseline (disease severity)															0.0199*
< 8.0	595	595	537	7.43 (0.3)	6.86 (1.0)	-0.55 (0.1)	628	628	562	7.40 (0.3)	7.58 (1.1)	0.17 (0.1)	-0.73 [-0.89;-0.57] <0.0001	-0.71 [-0.83;-0.58]	
8.0 <=	1053	1053	935	9.42 (1.3)	7.72 (1.6)	-1.69 (0.0)	1021	1021	886	9.50 (1.3)	8.71 (1.6)	-0.72 (0.0)	-0.97 [-1.09;-0.84] <0.0001	-0.52 [-0.61;-0.42]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

HbA1c (%) - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.0446*
West Europe	228	228	204	8.29 (1.1)	7.31 (1.4)	-0.96 (0.1)	205	205	193	8.24 (1.1)	7.90 (1.3)	-0.34 (0.1)	-0.62 [-0.88;-0.35] <0.0001	-0.43 [-0.63;-0.23]	
Rest of World	1420	1420	1268	8.77 (1.5)	7.42 (1.5)	-1.31 (0.0)	1444	1444	1255	8.76 (1.5)	8.33 (1.5)	-0.39 (0.0)	-0.91 [-1.02;-0.81] <0.0001	-0.56 [-0.64;-0.48]	
Region B															0.0053*
OECD	1174	1174	1024	8.63 (1.4)	7.40 (1.5)	-1.15 (0.0)	1136	1136	964	8.56 (1.4)	8.14 (1.5)	-0.37 (0.0)	-0.77 [-0.89;-0.65] <0.0001	-0.51 [-0.60;-0.42]	
Non-OECD	474	474	448	8.89 (1.5)	7.40 (1.3)	-1.51 (0.1)	513	513	484	9.02 (1.5)	8.53 (1.6)	-0.43 (0.1)	-1.08 [-1.25;-0.90] <0.0001	-0.62 [-0.75;-0.49]	
Treatment dose volume															<0.0001*
0.5 mg/week	826	826	741	8.67 (1.4)	7.55 (1.5)	-1.08 (0.0)	824	824	724	8.70 (1.5)	8.23 (1.5)	-0.40 (0.1)	-0.68 [-0.81;-0.54] <0.0001	-0.43 [-0.53;-0.32]	
1.0 mg/week	822	822	731	8.73 (1.5)	7.25 (1.4)	-1.44 (0.1)	825	825	724	8.70 (1.5)	8.31 (1.6)	-0.37 (0.1)	-1.07 [-1.21;-0.93] <0.0001	-0.65 [-0.76;-0.55]	
Baseline insulin use															0.3252
No	692	692	618	8.47 (1.4)	7.07 (1.3)	-1.34 (0.1)	692	692	615	8.43 (1.4)	7.99 (1.5)	-0.41 (0.1)	-0.93 [-1.08;-0.78] <0.0001	-0.59 [-0.70;-0.47]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

HbA1c (%) - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs. Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	956	854	8.87 (1.4)	7.64 (1.5)	-1.20 (0.0)	957	957	833	8.89 (1.5)	8.48 (1.5)	-0.37 (0.0)	-0.83 [-0.96;-0.70] <0.0001	-0.51 [-0.60;-0.41]	
Baseline Renal impairment															0.9651
GFR < 30	46	46	38	8.95 (1.6)	7.34 (1.6)	-1.36 (0.2)	61	61	48	8.56 (1.6)	8.09 (2.0)	-0.50 (0.2)	-0.86 [-1.44;-0.28] 0.0038	-0.54 [-0.97;-0.10]	
30 <= GFR	1602	1602	1434	8.70 (1.4)	7.41 (1.5)	-1.26 (0.0)	1588	1588	1400	8.70 (1.5)	8.28 (1.5)	-0.38 (0.0)	-0.87 [-0.97;-0.77] <0.0001	-0.54 [-0.62;-0.47]	
Evidence of CV disease at screening															0.3084
CV DISEASE	1353	1353	1196	8.71 (1.5)	7.42 (1.5)	-1.24 (0.0)	1382	1382	1200	8.69 (1.5)	8.26 (1.5)	-0.39 (0.0)	-0.85 [-0.96;-0.74] <0.0001	-0.53 [-0.61;-0.45]	
CV RISK FACTORS ONLY	295	295	276	8.65 (1.4)	7.33 (1.3)	-1.36 (0.1)	267	267	248	8.76 (1.4)	8.31 (1.4)	-0.38 (0.1)	-0.98 [-1.22;-0.75] <0.0001	-0.59 [-0.76;-0.41]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

14 Body weight (kg) - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1646	1479	92.33 (20.7)	87.90 (20.7)	-4.23 (0.2)	1649	1645	1450	91.86 (20.5)	91.13 (20.6)	-0.57 (0.2)	-3.66 [-4.09;-3.23] <0.0001	-0.61 [-0.69;-0.54]	
Gender															0.1697
Female	635	635	568	85.44 (19.0)	80.49 (18.0)	-4.76 (0.2)	660	660	573	85.98 (18.4)	84.86 (17.9)	-0.71 (0.2)	-4.04 [-4.73;-3.36] <0.0001	-0.65 [-0.77;-0.53]	
Male	1013	1011	911	96.66 (20.5)	92.52 (20.9)	-3.90 (0.2)	989	985	877	95.80 (21.0)	95.23 (21.3)	-0.47 (0.2)	-3.43 [-3.98;-2.88] <0.0001	-0.59 [-0.68;-0.49]	
Age															0.3542
< 65	855	854	768	93.99 (21.3)	89.98 (20.9)	-3.83 (0.2)	844	841	742	93.32 (21.7)	92.94 (21.8)	-0.36 (0.2)	-3.47 [-4.07;-2.87] <0.0001	-0.58 [-0.68;-0.48]	
65 <=	793	792	711	90.54 (19.8)	85.65 (20.2)	-4.66 (0.2)	805	804	708	90.33 (19.2)	89.25 (19.2)	-0.79 (0.2)	-3.87 [-4.49;-3.26] <0.0001	-0.65 [-0.75;-0.54]	
HbA1c at baseline (disease severity)															0.1320
< 8.0	595	595	541	91.66 (19.4)	86.40 (19.2)	-5.17 (0.3)	628	626	564	92.76 (20.3)	91.66 (20.4)	-1.06 (0.2)	-4.11 [-4.80;-3.41] <0.0001	-0.67 [-0.79;-0.55]	
8.0 <=	1053	1051	938	92.70 (21.3)	88.77 (21.4)	-3.69 (0.2)	1021	1019	886	91.31 (20.7)	90.80 (20.8)	-0.26 (0.2)	-3.43 [-3.97;-2.89] <0.0001	-0.59 [-0.68;-0.49]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

Body weight (kg) - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.6804
West Europe	228	228	206	91.66 (16.8)	87.45 (17.0)	-4.28 (0.4)	205	205	192	92.72 (18.6)	92.50 (18.4)	-0.40 (0.4)	-3.89 [-5.05;-2.72] <0.0001	-0.71 [-0.91;-0.50]	
Rest of World	1420	1418	1273	92.43 (21.2)	87.97 (21.2)	-4.22 (0.2)	1444	1440	1258	91.74 (20.8)	90.92 (21.0)	-0.60 (0.2)	-3.62 [-4.09;-3.16] <0.0001	-0.60 [-0.68;-0.52]	
Region B															0.5353
OECD	1174	1172	1030	94.52 (20.9)	89.82 (21.1)	-4.63 (0.2)	1136	1134	966	94.71 (21.1)	93.89 (21.2)	-0.90 (0.2)	-3.73 [-4.25;-3.21] <0.0001	-0.58 [-0.67;-0.49]	
Non-OECD	474	474	449	86.92 (19.1)	83.49 (19.1)	-3.34 (0.3)	513	511	484	85.54 (17.7)	85.63 (18.2)	0.10 (0.3)	-3.44 [-4.20;-2.68] <0.0001	-0.68 [-0.82;-0.55]	
Treatment dose volume															0.0004*
0.5 mg/week	826	825	742	91.80 (20.3)	87.95 (20.5)	-3.58 (0.2)	824	822	726	91.83 (20.3)	90.91 (20.1)	-0.68 (0.2)	-2.89 [-3.50;-2.29] <0.0001	-0.51 [-0.61;-0.40]	
1.0 mg/week	822	821	737	92.86 (21.1)	87.85 (20.9)	-4.89 (0.2)	825	823	724	91.90 (20.8)	91.36 (21.1)	-0.46 (0.2)	-4.43 [-5.04;-3.83] <0.0001	-0.71 [-0.82;-0.61]	
Baseline insulin use															0.0383*
No	692	692	625	90.98 (19.2)	86.55 (19.1)	-4.27 (0.2)	692	689	614	91.71 (20.5)	90.50 (20.2)	-1.14 (0.2)	-3.13 [-3.79;-2.47] <0.0001	-0.54 [-0.66;-0.43]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

Body weight (kg) - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	854	93.31 (21.6)	88.88 (21.7)	-4.20 (0.2)	957	956	836	91.97 (20.6)	91.60 (21.0)	-0.15 (0.2)	-4.05 [-4.61;-3.48] <0.0001	-0.66 [-0.76;-0.56]	
Baseline Renal impairment															0.2084
GFR < 30	46	46	38	86.39 (18.4)	79.67 (17.0)	-6.71 (1.0)	61	61	48	84.77 (21.5)	83.19 (21.8)	-1.46 (0.9)	-5.26 [-7.78;-2.73] <0.0001	-0.70 [-1.14;-0.27]	
30 <= GFR	1602	1600	1441	92.50 (20.7)	88.12 (20.7)	-4.16 (0.2)	1588	1584	1402	92.13 (20.5)	91.41 (20.6)	-0.55 (0.2)	-3.61 [-4.05;-3.18] <0.0001	-0.61 [-0.69;-0.54]	
Evidence of CV disease at screening															0.9196
CV DISEASE	1353	1352	1201	93.10 (20.5)	88.62 (20.7)	-4.26 (0.2)	1382	1378	1199	92.78 (20.5)	92.16 (20.7)	-0.59 (0.2)	-3.67 [-4.14;-3.20] <0.0001	-0.60 [-0.68;-0.52]	
CV RISK FACTORS ONLY	295	294	278	88.76 (20.9)	84.78 (20.5)	-4.09 (0.4)	267	267	251	87.13 (20.0)	86.24 (19.4)	-0.48 (0.4)	-3.61 [-4.62;-2.60] <0.0001	-0.69 [-0.87;-0.52]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

15 SF-36 - Physical Functioning - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1467	41.38 (10.7)	42.35 (10.9)	0.62 (0.2)	1649	1647	1443	40.31 (11.4)	40.48 (11.7)	-0.55 (0.2)	1.17 [0.54;1.81] 0.0003	0.09 [0.01;0.16]	
Gender															0.8343
Female	635	634	561	38.85 (10.6)	40.35 (10.7)	1.18 (0.4)	660	659	575	37.40 (11.0)	38.30 (11.4)	0.10 (0.4)	1.08 [0.06;2.10] 0.0372	0.06 [-0.05;0.18]	
Male	1013	1010	906	42.97 (10.4)	43.59 (10.8)	0.25 (0.3)	989	988	868	42.24 (11.2)	41.93 (11.7)	-0.97 (0.3)	1.22 [0.41;2.04] 0.0033	0.10 [0.01;0.20]	
Age															0.7845
< 65	855	854	765	42.32 (10.8)	44.00 (10.6)	1.41 (0.3)	844	842	741	40.93 (11.5)	42.06 (11.4)	0.33 (0.3)	1.08 [0.20;1.96] 0.0164	0.06 [-0.04;0.16]	
65 <=	793	790	702	40.38 (10.4)	40.56 (10.9)	-0.24 (0.3)	805	805	702	39.65 (11.2)	38.82 (11.9)	-1.49 (0.3)	1.25 [0.34;2.16] 0.0069	0.11 [0.01;0.22]	
HbA1c at baseline (disease severity)															0.6281
< 8.0	595	594	536	42.16 (10.4)	43.19 (10.4)	0.79 (0.4)	628	627	559	40.76 (11.1)	40.80 (11.8)	-0.60 (0.4)	1.38 [0.34;2.42] 0.0092	0.09 [-0.02;0.21]	
8.0 <=	1053	1050	931	40.95 (10.8)	41.87 (11.2)	0.53 (0.3)	1021	1020	884	40.02 (11.5)	40.28 (11.7)	-0.53 (0.3)	1.06 [0.25;1.86] 0.0102	0.08 [-0.01;0.17]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Physical Functioning - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.1801
West Europe	228	226	205	42.05 (10.9)	42.25 (11.0)	-0.17 (0.6)	205	205	191	41.09 (12.7)	39.27 (12.6)	-2.45 (0.6)	2.28 [0.55;4.00] 0.0098	0.21 [0.02;0.41]	
Rest of World	1420	1418	1262	41.28 (10.6)	42.37 (10.9)	0.75 (0.2)	1444	1442	1252	40.19 (11.2)	40.66 (11.6)	-0.26 (0.2)	1.01 [0.32;1.69] 0.0040	0.07 [-0.01;0.15]	
Region B															0.4230
OECD	1174	1170	1020	40.86 (11.0)	41.84 (11.2)	0.59 (0.3)	1136	1134	958	39.57 (11.8)	39.64 (12.2)	-0.80 (0.3)	1.39 [0.62;2.16] 0.0004	0.10 [0.01;0.19]	
Non-OECD	474	474	447	42.68 (9.6)	43.52 (10.2)	0.72 (0.4)	513	513	485	41.93 (10.2)	42.14 (10.7)	-0.11 (0.4)	0.83 [-0.29;1.96] 0.1476	0.06 [-0.07;0.19]	
Treatment dose volume															0.1848
0.5 mg/week	826	825	734	41.51 (10.6)	42.10 (10.7)	0.23 (0.3)	824	823	727	40.11 (11.4)	40.35 (11.8)	-0.51 (0.3)	0.74 [-0.16;1.64] 0.1052	0.02 [-0.08;0.13]	
1.0 mg/week	822	819	733	41.26 (10.7)	42.60 (11.1)	1.01 (0.3)	825	824	716	40.50 (11.3)	40.62 (11.6)	-0.60 (0.3)	1.60 [0.70;2.51] 0.0005	0.15 [0.05;0.25]	
Baseline insulin use															0.3088
No	692	690	616	42.25 (10.4)	43.15 (10.7)	0.60 (0.4)	692	691	612	41.68 (11.3)	42.14 (11.4)	-0.19 (0.4)	0.79 [-0.19;1.77] 0.1157	0.08 [-0.04;0.19]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Physical Functioning - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	851	40.76 (10.8)	41.77 (11.0)	0.63 (0.3)	957	956	831	39.31 (11.3)	39.25 (11.8)	-0.82 (0.3)	1.46 [0.62;2.29] 0.0007	0.09 [-0.00;0.19]	
Baseline Renal impairment															0.5320
GFR < 30	46	46	38	37.54 (10.6)	40.64 (11.1)	1.63 (1.4)	61	61	48	37.26 (8.8)	37.70 (11.3)	-0.72 (1.3)	2.34 [-1.39;6.07] 0.2179	0.22 [-0.20;0.65]	
30 <= GFR	1602	1598	1429	41.49 (10.7)	42.40 (10.9)	0.59 (0.2)	1588	1586	1395	40.42 (11.4)	40.58 (11.7)	-0.55 (0.2)	1.14 [0.49;1.78] 0.0006	0.08 [0.01;0.16]	
Evidence of CV disease at screening															0.1601
CV DISEASE	1353	1350	1191	40.95 (10.7)	41.88 (11.1)	0.55 (0.3)	1382	1380	1194	39.93 (11.4)	40.20 (11.7)	-0.40 (0.3)	0.96 [0.26;1.66] 0.0075	0.07 [-0.02;0.15]	
CV RISK FACTORS ONLY	295	294	276	43.39 (10.2)	44.40 (9.9)	0.89 (0.5)	267	267	249	42.26 (10.7)	41.82 (11.6)	-1.26 (0.6)	2.15 [0.65;3.65] 0.0051	0.18 [0.01;0.35]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

16 SF-36 - Role-Physical - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1467	42.19 (11.0)	43.09 (11.0)	0.61 (0.2)	1649	1648	1443	41.52 (11.5)	41.77 (11.2)	-0.33 (0.2)	0.95 [0.27;1.63] 0.0064	0.05 [-0.02;0.13]	
Gender															0.6812
Female	635	634	561	40.33 (10.8)	41.53 (11.0)	1.07 (0.4)	660	659	575	39.50 (11.3)	39.93 (10.7)	-0.05 (0.4)	1.12 [0.03;2.21] 0.0450	0.06 [-0.06;0.17]	
Male	1013	1010	906	43.36 (11.1)	44.06 (11.0)	0.32 (0.3)	989	989	868	42.86 (11.4)	42.99 (11.4)	-0.51 (0.3)	0.82 [-0.05;1.70] 0.0645	0.06 [-0.04;0.15]	
Age															0.1694
< 65	855	854	765	42.51 (11.2)	43.95 (11.1)	1.30 (0.3)	844	843	741	41.51 (11.7)	43.00 (10.9)	0.82 (0.3)	0.47 [-0.47;1.42] 0.3246	-0.00 [-0.11;0.10]	
65 <=	793	790	702	41.84 (10.9)	42.16 (10.9)	-0.13 (0.4)	805	805	702	41.52 (11.2)	40.48 (11.4)	-1.55 (0.4)	1.43 [0.45;2.40] 0.0042	0.12 [0.01;0.22]	
HbA1c at baseline (disease severity)															0.9895
< 8.0	595	594	536	42.99 (10.8)	43.51 (10.5)	0.40 (0.4)	628	628	559	41.86 (11.3)	41.92 (11.4)	-0.54 (0.4)	0.94 [-0.17;2.05] 0.0978	0.04 [-0.08;0.16]	
8.0 <=	1053	1050	931	41.74 (11.2)	42.85 (11.3)	0.74 (0.3)	1021	1020	884	41.30 (11.6)	41.68 (11.1)	-0.21 (0.3)	0.95 [0.09;1.81] 0.0311	0.06 [-0.03;0.16]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Role-Physical - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.7082
West Europe	228	226	205	43.29 (11.5)	42.10 (11.2)	-1.58 (0.7)	205	205	191	42.39 (12.5)	40.20 (12.6)	-2.87 (0.7)	1.29 [-0.56;3.14] 0.1724	0.05 [-0.14;0.25]	
Rest of World	1420	1418	1262	42.02 (11.0)	43.25 (11.0)	0.97 (0.3)	1444	1443	1252	41.39 (11.3)	42.01 (10.9)	0.06 (0.3)	0.91 [0.18;1.64] 0.0151	0.06 [-0.02;0.14]	
Region B															0.9813
OECD	1174	1170	1020	42.28 (11.3)	42.81 (11.4)	0.10 (0.3)	1136	1135	958	41.55 (11.7)	41.36 (11.7)	-0.90 (0.3)	0.99 [0.17;1.82] 0.0185	0.05 [-0.04;0.14]	
Non-OECD	474	474	447	41.98 (10.5)	43.73 (10.2)	1.79 (0.4)	513	513	485	41.43 (10.9)	42.58 (10.1)	0.78 (0.4)	1.01 [-0.19;2.22] 0.0997	0.08 [-0.05;0.20]	
Treatment dose volume															0.5421
0.5 mg/week	826	825	734	42.08 (11.2)	42.63 (10.9)	0.23 (0.3)	824	823	727	41.59 (11.6)	41.63 (11.2)	-0.51 (0.3)	0.74 [-0.23;1.70] 0.1334	0.04 [-0.06;0.15]	
1.0 mg/week	822	819	733	42.30 (10.9)	43.55 (11.1)	1.01 (0.3)	825	825	716	41.44 (11.4)	41.91 (11.2)	-0.16 (0.4)	1.16 [0.19;2.13] 0.0187	0.07 [-0.04;0.17]	
Baseline insulin use															0.0386*
No	692	690	616	42.97 (10.8)	43.77 (10.7)	0.35 (0.4)	692	692	612	42.83 (11.2)	43.63 (10.6)	0.24 (0.4)	0.11 [-0.94;1.16] 0.8397	0.01 [-0.10;0.12]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Role-Physical - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	851	41.63 (11.2)	42.60 (11.2)	0.80 (0.3)	957	956	831	40.57 (11.6)	40.41 (11.4)	-0.76 (0.3)	1.57 [0.67;2.46] 0.0006	0.09 [-0.01;0.18]	
Baseline Renal impairment															0.2369
GFR < 30	46	46	38	38.96 (10.9)	42.42 (11.1)	2.48 (1.5)	61	61	48	39.99 (9.8)	38.89 (12.0)	-0.84 (1.4)	3.32 [-0.67;7.32] 0.1029	0.26 [-0.17;0.68]	
30 <= GFR	1602	1598	1429	42.28 (11.0)	43.11 (11.0)	0.56 (0.2)	1588	1587	1395	41.57 (11.5)	41.87 (11.2)	-0.31 (0.3)	0.88 [0.19;1.57] 0.0130	0.05 [-0.03;0.12]	
Evidence of CV disease at screening															0.0761
CV DISEASE	1353	1350	1191	41.69 (11.1)	42.63 (11.2)	0.62 (0.3)	1382	1381	1194	41.14 (11.5)	41.64 (11.2)	-0.04 (0.3)	0.66 [-0.09;1.41] 0.0854	0.04 [-0.04;0.12]	
CV RISK FACTORS ONLY	295	294	276	44.49 (10.5)	45.10 (10.1)	0.54 (0.6)	267	267	249	43.48 (11.1)	42.40 (11.1)	-1.72 (0.6)	2.27 [0.66;3.88] 0.0057	0.14 [-0.03;0.31]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

17 SF-36 - Bodily Pain - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs. Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1467	45.87 (11.0)	47.20 (11.3)	1.16 (0.2)	1649	1648	1443	45.61 (11.2)	46.09 (11.4)	0.18 (0.3)	0.98 [0.29;1.67] 0.0056	0.08 [0.01;0.15]	
Gender															0.0757
Female	635	634	561	42.95 (10.7)	44.76 (11.6)	1.60 (0.4)	660	659	575	42.94 (11.0)	44.45 (11.3)	1.42 (0.4)	0.18 [-0.92;1.29] 0.7456	0.00 [-0.11;0.12]	
Male	1013	1010	906	47.71 (10.7)	48.70 (10.8)	0.86 (0.3)	989	989	868	47.39 (11.0)	47.18 (11.4)	-0.61 (0.3)	1.47 [0.58;2.35] 0.0012	0.14 [0.04;0.23]	
Age															0.3766
< 65	855	854	765	46.00 (11.1)	47.73 (11.3)	1.60 (0.3)	844	843	741	45.13 (11.3)	46.66 (11.2)	0.93 (0.3)	0.67 [-0.29;1.63] 0.1741	0.03 [-0.07;0.13]	
65 <=	793	790	702	45.74 (10.9)	46.62 (11.2)	0.68 (0.4)	805	805	702	46.12 (11.1)	45.50 (11.6)	-0.61 (0.4)	1.29 [0.30;2.29] 0.0111	0.13 [0.03;0.24]	
HbA1c at baseline (disease severity)															0.4907
< 8.0	595	594	536	46.52 (10.7)	47.24 (10.9)	0.56 (0.4)	628	628	559	46.20 (11.0)	45.69 (11.5)	-0.71 (0.4)	1.27 [0.14;2.40] 0.0271	0.10 [-0.02;0.22]	
8.0 <=	1053	1050	931	45.51 (11.1)	47.17 (11.5)	1.51 (0.3)	1021	1020	884	45.25 (11.3)	46.35 (11.4)	0.74 (0.3)	0.77 [-0.11;1.65] 0.0846	0.06 [-0.03;0.16]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Bodily Pain - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.2501
West Europe	228	226	205	47.08 (11.6)	46.28 (12.4)	-0.96 (0.7)	205	205	191	47.12 (12.3)	46.28 (12.7)	-0.92 (0.7)	-0.04 [-1.92;1.84] 0.9657	-0.01 [-0.21;0.19]	
Rest of World	1420	1418	1262	45.68 (10.9)	47.34 (11.1)	1.50 (0.3)	1444	1443	1252	45.40 (11.0)	46.06 (11.2)	0.35 (0.3)	1.14 [0.40;1.89] 0.0026	0.10 [0.02;0.18]	
Region B															0.2557
OECD	1174	1170	1020	45.74 (11.1)	46.39 (11.4)	0.45 (0.3)	1136	1135	958	45.22 (11.3)	45.30 (11.5)	-0.33 (0.3)	0.78 [-0.06;1.62] 0.0677	0.05 [-0.04;0.13]	
Non-OECD	474	474	447	46.21 (10.6)	49.03 (10.6)	2.79 (0.4)	513	513	485	46.49 (10.9)	47.67 (11.1)	1.15 (0.4)	1.64 [0.42;2.86] 0.0084	0.17 [0.04;0.30]	
Treatment dose volume															0.1411
0.5 mg/week	826	825	734	46.14 (11.1)	46.81 (11.3)	0.54 (0.4)	824	823	727	45.35 (11.0)	45.81 (11.2)	0.08 (0.4)	0.46 [-0.52;1.43] 0.3571	0.00 [-0.10;0.11]	
1.0 mg/week	822	819	733	45.61 (10.8)	47.59 (11.2)	1.78 (0.4)	825	825	716	45.87 (11.4)	46.38 (11.6)	0.28 (0.4)	1.50 [0.52;2.48] 0.0028	0.16 [0.05;0.26]	
Baseline insulin use															0.1912
No	692	690	616	45.98 (10.9)	47.23 (11.0)	0.82 (0.4)	692	692	612	46.81 (11.1)	47.26 (11.3)	0.39 (0.4)	0.44 [-0.63;1.50] 0.4202	0.07 [-0.04;0.18]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Bodily Pain - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	851	45.80 (11.1)	47.17 (11.5)	1.40 (0.3)	957	956	831	44.74 (11.2)	45.23 (11.4)	0.03 (0.3)	1.37 [0.46;2.28] 0.0032	0.09 [-0.01;0.18]	
Baseline Renal impairment															0.6637
GFR < 30	46	46	38	43.99 (10.5)	45.69 (12.1)	0.85 (1.5)	61	61	48	45.81 (10.6)	46.43 (11.9)	0.76 (1.4)	0.09 [-3.96;4.15] 0.9648	0.06 [-0.37;0.49]	
30 <= GFR	1602	1598	1429	45.93 (11.0)	47.24 (11.2)	1.16 (0.3)	1588	1587	1395	45.60 (11.2)	46.08 (11.4)	0.16 (0.3)	1.00 [0.30;1.71] 0.0051	0.08 [0.01;0.15]	
Evidence of CV disease at screening															0.4514
CV DISEASE	1353	1350	1191	45.63 (11.0)	46.88 (11.3)	1.08 (0.3)	1382	1381	1194	45.37 (11.2)	45.91 (11.4)	0.23 (0.3)	0.85 [0.09;1.62] 0.0286	0.07 [-0.01;0.15]	
CV RISK FACTORS ONLY	295	294	276	46.98 (10.7)	48.55 (11.1)	1.48 (0.6)	267	267	249	46.85 (11.2)	46.99 (11.5)	-0.06 (0.6)	1.55 [-0.09;3.18] 0.0635	0.12 [-0.05;0.29]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

18 SF-36 - General Health - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1467	42.46 (9.4)	44.61 (9.5)	2.10 (0.2)	1649	1648	1443	42.04 (9.9)	43.35 (9.9)	0.94 (0.2)	1.16 [0.58;1.74] <0.0001	0.12 [0.04;0.19]	
Gender															0.9332
Female	635	634	561	41.22 (9.2)	44.05 (9.4)	2.73 (0.3)	660	659	575	40.75 (9.7)	42.65 (9.6)	1.54 (0.3)	1.19 [0.26;2.12] 0.0122	0.12 [0.00;0.23]	
Male	1013	1010	906	43.24 (9.3)	44.95 (9.5)	1.70 (0.3)	989	989	868	42.90 (10.0)	43.81 (10.1)	0.56 (0.3)	1.14 [0.39;1.88] 0.0027	0.12 [0.03;0.21]	
Age															0.0938
< 65	855	854	765	41.62 (9.4)	44.14 (9.5)	2.46 (0.3)	844	843	741	40.86 (10.0)	43.18 (9.9)	1.78 (0.3)	0.67 [-0.13;1.48] 0.1016	0.04 [-0.06;0.14]	
65 <=	793	790	702	43.37 (9.2)	45.12 (9.5)	1.72 (0.3)	805	805	702	43.28 (9.6)	43.53 (9.8)	0.05 (0.3)	1.67 [0.83;2.50] <0.0001	0.20 [0.09;0.30]	
HbA1c at baseline (disease severity)															0.6378
< 8.0	595	594	536	43.60 (9.3)	45.35 (9.5)	1.71 (0.3)	628	628	559	43.09 (9.8)	44.24 (9.8)	0.73 (0.3)	0.98 [0.03;1.93] 0.0424	0.10 [-0.02;0.22]	
8.0 <=	1053	1050	931	41.82 (9.3)	44.18 (9.5)	2.33 (0.3)	1021	1020	884	41.39 (9.9)	42.78 (9.9)	1.07 (0.3)	1.27 [0.53;2.00] 0.0007	0.13 [0.03;0.22]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - General Health - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.6214
West Europe	228	226	205	42.78 (9.4)	43.29 (9.5)	0.45 (0.6)	205	205	191	42.41 (10.4)	41.83 (10.8)	-1.08 (0.6)	1.53 [-0.04;3.11] 0.0556	0.15 [-0.04;0.35]	
Rest of World	1420	1418	1262	42.41 (9.3)	44.82 (9.5)	2.36 (0.2)	1444	1443	1252	41.99 (9.8)	43.58 (9.7)	1.25 (0.2)	1.11 [0.49;1.73] 0.0005	0.11 [0.04;0.19]	
Region B															0.9031
OECD	1174	1170	1020	42.94 (9.5)	44.75 (9.7)	1.73 (0.2)	1136	1135	958	42.18 (9.9)	43.28 (10.1)	0.52 (0.3)	1.20 [0.50;1.91] 0.0008	0.10 [0.01;0.19]	
Non-OECD	474	474	447	41.29 (8.8)	44.28 (8.9)	2.92 (0.4)	513	513	485	41.73 (9.9)	43.49 (9.3)	1.79 (0.4)	1.13 [0.10;2.15] 0.0315	0.17 [0.04;0.29]	
Treatment dose volume															0.3971
0.5 mg/week	826	825	734	42.59 (9.5)	44.29 (9.3)	1.63 (0.3)	824	823	727	41.96 (9.7)	43.09 (9.7)	0.72 (0.3)	0.91 [0.09;1.72] 0.0300	0.08 [-0.02;0.18]	
1.0 mg/week	822	819	733	42.33 (9.2)	44.93 (9.6)	2.57 (0.3)	825	825	716	42.12 (10.0)	43.61 (10.0)	1.17 (0.3)	1.41 [0.58;2.23] 0.0008	0.15 [0.05;0.26]	
Baseline insulin use															0.0038*
No	692	690	616	42.95 (9.1)	45.28 (9.3)	1.92 (0.3)	692	692	612	43.68 (9.7)	45.55 (9.5)	1.76 (0.3)	0.16 [-0.74;1.05] 0.7330	0.05 [-0.06;0.16]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - General Health - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	851	42.11 (9.5)	44.12 (9.6)	2.23 (0.3)	957	956	831	40.85 (9.8)	41.72 (9.8)	0.34 (0.3)	1.89 [1.13;2.65] <0.0001	0.16 [0.07;0.26]	
Baseline Renal impairment															0.4355
GFR < 30	46	46	38	40.08 (9.1)	43.41 (9.7)	4.19 (1.3)	61	61	48	38.77 (9.2)	40.48 (11.1)	1.70 (1.2)	2.49 [-0.91;5.89] 0.1512	0.18 [-0.25;0.61]	
30 <= GFR	1602	1598	1429	42.53 (9.4)	44.64 (9.5)	2.04 (0.2)	1588	1587	1395	42.17 (9.9)	43.45 (9.8)	0.92 (0.2)	1.12 [0.53;1.70] 0.0002	0.12 [0.04;0.19]	
Evidence of CV disease at screening															0.3329
CV DISEASE	1353	1350	1191	42.35 (9.4)	44.35 (9.6)	2.02 (0.2)	1382	1381	1194	41.66 (9.9)	43.07 (9.9)	1.00 (0.2)	1.02 [0.38;1.66] 0.0018	0.09 [0.01;0.17]	
CV RISK FACTORS ONLY	295	294	276	42.98 (9.1)	45.73 (8.7)	2.42 (0.5)	267	267	249	44.02 (9.6)	44.68 (9.7)	0.65 (0.5)	1.77 [0.40;3.14] 0.0113	0.22 [0.05;0.40]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

19 SF-36 - Vitality - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1467	48.79 (10.0)	49.88 (10.2)	0.86 (0.2)	1649	1648	1443	48.63 (10.6)	49.13 (10.2)	0.08 (0.2)	0.78 [0.17;1.39] 0.0125	0.08 [0.01;0.16]	
Gender															0.5888
Female	635	634	561	46.67 (9.8)	48.10 (10.5)	1.11 (0.4)	660	659	575	47.00 (10.5)	47.86 (10.3)	0.55 (0.4)	0.55 [-0.42;1.53] 0.2665	0.08 [-0.03;0.20]	
Male	1013	1010	906	50.12 (9.8)	50.98 (9.8)	0.69 (0.3)	989	989	868	49.72 (10.5)	49.97 (10.1)	-0.21 (0.3)	0.90 [0.12;1.68] 0.0242	0.08 [-0.01;0.18]	
Age															0.8664
< 65	855	854	765	48.63 (10.0)	50.24 (10.4)	1.40 (0.3)	844	843	741	48.08 (10.8)	49.44 (10.3)	0.68 (0.3)	0.72 [-0.13;1.57] 0.0962	0.06 [-0.04;0.16]	
65 <=	793	790	702	48.96 (10.0)	49.49 (9.9)	0.27 (0.3)	805	805	702	49.21 (10.3)	48.80 (10.2)	-0.55 (0.3)	0.83 [-0.05;1.71] 0.0658	0.11 [0.00;0.21]	
HbA1c at baseline (disease severity)															0.5082
< 8.0	595	594	536	49.67 (9.7)	50.28 (9.7)	0.64 (0.4)	628	628	559	49.16 (10.2)	49.08 (10.3)	-0.40 (0.4)	1.04 [0.04;2.04] 0.0413	0.09 [-0.02;0.21]	
8.0 <=	1053	1050	931	48.29 (10.1)	49.65 (10.4)	1.00 (0.3)	1021	1020	884	48.31 (10.8)	49.16 (10.2)	0.38 (0.3)	0.61 [-0.16;1.39] 0.1209	0.07 [-0.02;0.17]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Vitality - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.2613
West Europe	228	226	205	48.33 (10.8)	48.53 (10.7)	-0.14 (0.6)	205	205	191	49.49 (11.4)	47.77 (11.1)	-1.82 (0.6)	1.67 [0.01;3.33] 0.0482	0.22 [0.02;0.42]	
Rest of World	1420	1418	1262	48.86 (9.8)	50.10 (10.0)	1.02 (0.2)	1444	1443	1252	48.51 (10.5)	49.34 (10.1)	0.37 (0.2)	0.65 [-0.01;1.31] 0.0523	0.06 [-0.02;0.14]	
Region B															0.3131
OECD	1174	1170	1020	48.63 (10.1)	49.49 (10.4)	0.68 (0.3)	1136	1135	958	48.03 (10.8)	48.24 (10.5)	-0.36 (0.3)	1.05 [0.30;1.79] 0.0057	0.08 [-0.01;0.17]	
Non-OECD	474	474	447	49.19 (9.6)	50.76 (9.6)	1.30 (0.4)	513	513	485	49.97 (9.9)	50.88 (9.5)	0.93 (0.4)	0.37 [-0.71;1.45] 0.5018	0.10 [-0.03;0.22]	
Treatment dose volume															0.1424
0.5 mg/week	826	825	734	48.95 (10.3)	49.44 (10.1)	0.18 (0.3)	824	823	727	48.50 (10.7)	48.88 (10.0)	-0.15 (0.3)	0.32 [-0.54;1.18] 0.4636	0.02 [-0.09;0.12]	
1.0 mg/week	822	819	733	48.63 (9.6)	50.32 (10.2)	1.55 (0.3)	825	825	716	48.76 (10.5)	49.38 (10.4)	0.31 (0.3)	1.24 [0.37;2.10] 0.0052	0.15 [0.05;0.26]	
Baseline insulin use															0.1106
No	692	690	616	48.97 (10.0)	50.43 (10.0)	0.92 (0.3)	692	692	612	49.90 (10.5)	50.81 (10.0)	0.72 (0.3)	0.20 [-0.74;1.14] 0.6814	0.06 [-0.05;0.18]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Vitality - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	851	48.66 (10.0)	49.48 (10.2)	0.82 (0.3)	957	956	831	47.71 (10.6)	47.89 (10.3)	-0.39 (0.3)	1.21 [0.40;2.01] 0.0033	0.10 [0.00;0.19]	
Baseline Renal impairment															0.4735
GFR < 30	46	46	38	46.93 (9.7)	48.07 (9.9)	1.56 (1.4)	61	61	48	46.67 (10.5)	46.43 (12.4)	-0.52 (1.2)	2.07 [-1.51;5.66] 0.2573	0.20 [-0.23;0.63]	
30 <= GFR	1602	1598	1429	48.84 (10.0)	49.93 (10.2)	0.84 (0.2)	1588	1587	1395	48.71 (10.6)	49.22 (10.1)	0.10 (0.2)	0.74 [0.12;1.36] 0.0193	0.08 [0.00;0.15]	
Evidence of CV disease at screening															0.6685
CV DISEASE	1353	1350	1191	48.47 (9.9)	49.56 (10.3)	0.86 (0.2)	1382	1381	1194	48.29 (10.7)	48.75 (10.3)	0.02 (0.2)	0.84 [0.17;1.52] 0.0145	0.09 [0.01;0.17]	
CV RISK FACTORS ONLY	295	294	276	50.23 (10.1)	51.28 (9.2)	0.86 (0.5)	267	267	249	50.43 (10.0)	50.93 (9.9)	0.36 (0.5)	0.49 [-0.95;1.94] 0.5021	0.03 [-0.14;0.21]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

20 SF-36 - Social Functioning - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1467	46.07 (10.7)	46.61 (10.7)	0.26 (0.3)	1649	1648	1443	46.05 (10.8)	46.09 (10.9)	-0.28 (0.3)	0.53 [-0.17;1.23] 0.1347	0.05 [-0.02;0.13]	
Gender															0.3074
Female	635	634	561	44.25 (11.1)	45.09 (11.5)	0.63 (0.4)	660	659	575	43.96 (11.1)	44.92 (11.2)	0.56 (0.4)	0.06 [-1.05;1.18] 0.9096	-0.00 [-0.12;0.11]	
Male	1013	1010	906	47.22 (10.3)	47.55 (10.2)	0.00 (0.3)	989	989	868	47.45 (10.4)	46.87 (10.7)	-0.81 (0.3)	0.81 [-0.08;1.71] 0.0758	0.10 [0.00;0.19]	
Age															0.3807
< 65	855	854	765	45.55 (10.8)	46.55 (10.7)	0.83 (0.3)	844	843	741	44.98 (11.0)	46.18 (10.9)	0.60 (0.4)	0.23 [-0.75;1.20] 0.6489	-0.00 [-0.11;0.10]	
65 <=	793	790	702	46.65 (10.6)	46.67 (10.8)	-0.36 (0.4)	805	805	702	47.18 (10.5)	46.00 (10.9)	-1.21 (0.4)	0.85 [-0.16;1.86] 0.0972	0.11 [0.00;0.21]	
HbA1c at baseline (disease severity)															0.2205
< 8.0	595	594	536	46.83 (10.6)	46.96 (10.6)	-0.20 (0.4)	628	628	559	46.77 (10.6)	45.82 (11.1)	-1.28 (0.4)	1.08 [-0.06;2.22] 0.0627	0.10 [-0.02;0.22]	
8.0 <=	1053	1050	931	45.65 (10.7)	46.41 (10.8)	0.53 (0.3)	1021	1020	884	45.62 (10.9)	46.26 (10.8)	0.35 (0.3)	0.18 [-0.70;1.07] 0.6883	0.02 [-0.07;0.11]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Social Functioning - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.0321*
West Europe	228	226	205	47.56 (10.8)	47.14 (10.7)	-0.92 (0.7)	205	205	191	47.91 (11.3)	44.80 (13.0)	-3.39 (0.7)	2.47 [0.57;4.37] 0.0107	0.23 [0.03;0.43]	
Rest of World	1420	1418	1262	45.84 (10.7)	46.52 (10.8)	0.44 (0.3)	1444	1443	1252	45.79 (10.7)	46.29 (10.6)	0.20 (0.3)	0.24 [-0.51;0.99] 0.5316	0.03 [-0.05;0.10]	
Region B															0.1610
OECD	1174	1170	1020	46.40 (11.0)	46.45 (11.3)	-0.33 (0.3)	1136	1135	958	46.18 (11.3)	45.49 (11.6)	-1.27 (0.3)	0.94 [0.09;1.79] 0.0298	0.08 [-0.01;0.16]	
Non-OECD	474	474	447	45.26 (9.9)	46.98 (9.4)	1.57 (0.5)	513	513	485	45.78 (9.7)	47.28 (9.4)	1.70 (0.4)	-0.13 [-1.37;1.10] 0.8335	0.02 [-0.11;0.15]	
Treatment dose volume															0.1169
0.5 mg/week	826	825	734	46.17 (10.6)	46.09 (10.9)	-0.43 (0.4)	824	823	727	46.17 (10.5)	46.11 (10.6)	-0.41 (0.4)	-0.02 [-1.01;0.96] 0.9610	-0.00 [-0.11;0.10]	
1.0 mg/week	822	819	733	45.97 (10.8)	47.13 (10.6)	0.95 (0.4)	825	825	716	45.94 (11.1)	46.08 (11.2)	-0.15 (0.4)	1.09 [0.10;2.08] 0.0306	0.11 [0.01;0.21]	
Baseline insulin use															0.2305
No	692	690	616	46.19 (10.7)	47.21 (10.5)	0.39 (0.4)	692	692	612	47.14 (10.4)	47.61 (10.1)	0.36 (0.4)	0.03 [-1.04;1.11] 0.9521	0.05 [-0.06;0.17]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Social Functioning - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	851	45.99 (10.7)	46.18 (10.9)	0.16 (0.3)	957	956	831	45.27 (11.0)	44.98 (11.4)	-0.74 (0.3)	0.90 [-0.02;1.82] 0.0554	0.05 [-0.04;0.15]	
Baseline Renal impairment															0.7817
GFR < 30	46	46	38	44.16 (11.0)	44.36 (11.6)	-1.23 (1.6)	61	61	48	45.23 (10.9)	44.35 (12.7)	-1.19 (1.4)	-0.04 [-4.14;4.06] 0.9858	0.01 [-0.42;0.43]	
30 <= GFR	1602	1598	1429	46.13 (10.7)	46.67 (10.7)	0.30 (0.3)	1588	1587	1395	46.09 (10.8)	46.15 (10.8)	-0.25 (0.3)	0.55 [-0.16;1.26] 0.1283	0.05 [-0.02;0.13]	
Evidence of CV disease at screening															0.6109
CV DISEASE	1353	1350	1191	45.97 (10.8)	46.27 (11.0)	0.09 (0.3)	1382	1381	1194	45.69 (11.0)	45.74 (11.0)	-0.35 (0.3)	0.45 [-0.32;1.22] 0.2547	0.04 [-0.04;0.12]	
CV RISK FACTORS ONLY	295	294	276	46.55 (10.4)	48.10 (9.5)	0.99 (0.6)	267	267	249	47.92 (9.6)	47.76 (10.3)	0.07 (0.6)	0.92 [-0.73;2.57] 0.2737	0.12 [-0.05;0.29]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

21 SF-36 - Role-Emotional - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1466	43.21 (12.6)	43.70 (12.5)	0.43 (0.3)	1649	1648	1443	42.40 (13.1)	42.68 (12.8)	-0.32 (0.3)	0.75 [-0.07;1.57] 0.0740	0.03 [-0.04;0.10]	
Gender															0.9207
Female	635	634	561	40.75 (12.7)	41.61 (12.7)	1.00 (0.5)	660	659	575	39.62 (13.5)	40.54 (13.0)	0.32 (0.5)	0.68 [-0.63;1.99] 0.3104	0.01 [-0.11;0.12]	
Male	1013	1010	905	44.75 (12.3)	44.99 (12.2)	0.05 (0.4)	989	989	868	44.26 (12.5)	44.10 (12.5)	-0.71 (0.4)	0.76 [-0.29;1.82] 0.1536	0.05 [-0.05;0.14]	
Age															0.4512
< 65	855	854	765	43.05 (12.4)	43.77 (12.4)	0.74 (0.4)	844	843	741	41.75 (13.2)	42.90 (12.7)	0.30 (0.4)	0.44 [-0.70;1.58] 0.4524	-0.01 [-0.11;0.09]	
65 <=	793	790	701	43.38 (12.7)	43.62 (12.6)	0.09 (0.4)	805	805	702	43.08 (13.0)	42.46 (13.0)	-0.98 (0.4)	1.07 [-0.11;2.25] 0.0763	0.07 [-0.03;0.18]	
HbA1c at baseline (disease severity)															0.7058
< 8.0	595	594	535	44.08 (12.4)	44.24 (12.4)	0.09 (0.5)	628	628	559	43.29 (12.7)	42.92 (12.6)	-0.86 (0.5)	0.95 [-0.39;2.29] 0.1652	0.04 [-0.07;0.16]	
8.0 <=	1053	1050	931	42.71 (12.7)	43.39 (12.6)	0.63 (0.4)	1021	1020	884	41.86 (13.3)	42.53 (13.0)	0.01 (0.4)	0.62 [-0.42;1.66] 0.2404	0.02 [-0.07;0.11]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Role-Emotional - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.3440
West Europe	228	226	205	44.87 (12.4)	44.03 (13.0)	-1.00 (0.8)	205	205	191	43.72 (14.1)	41.75 (14.4)	-2.76 (0.8)	1.76 [-0.48;3.99] 0.1230	0.08 [-0.12;0.27]	
Rest of World	1420	1418	1261	42.94 (12.6)	43.64 (12.4)	0.66 (0.3)	1444	1443	1252	42.22 (12.9)	42.82 (12.5)	0.06 (0.3)	0.60 [-0.29;1.48] 0.1848	0.02 [-0.06;0.10]	
Region B															0.7293
OECD	1174	1170	1019	44.16 (12.5)	44.05 (13.1)	-0.28 (0.4)	1136	1135	958	43.03 (13.2)	42.74 (13.4)	-1.16 (0.4)	0.88 [-0.12;1.87] 0.0858	0.02 [-0.07;0.11]	
Non-OECD	474	474	447	40.85 (12.4)	42.90 (11.1)	1.97 (0.5)	513	513	485	41.02 (12.7)	42.57 (11.7)	1.41 (0.5)	0.56 [-0.89;2.02] 0.4472	0.06 [-0.07;0.19]	
Treatment dose volume															0.6250
0.5 mg/week	826	825	734	42.66 (13.0)	43.25 (12.6)	0.19 (0.4)	824	823	727	42.20 (13.1)	42.40 (12.6)	-0.35 (0.4)	0.54 [-0.61;1.70] 0.3572	0.01 [-0.09;0.12]	
1.0 mg/week	822	819	732	43.76 (12.1)	44.15 (12.4)	0.67 (0.4)	825	825	716	42.61 (13.1)	42.96 (13.0)	-0.29 (0.4)	0.95 [-0.21;2.12] 0.1085	0.04 [-0.06;0.15]	
Baseline insulin use															0.2305
No	692	690	616	43.17 (12.5)	44.22 (12.5)	0.56 (0.5)	692	692	612	43.67 (12.8)	44.40 (11.8)	0.39 (0.5)	0.16 [-1.10;1.43] 0.8021	0.04 [-0.07;0.15]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Role-Emotional - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	850	43.23 (12.7)	43.32 (12.5)	0.34 (0.4)	957	956	831	41.48 (13.3)	41.42 (13.4)	-0.84 (0.4)	1.18 [0.10;2.26] 0.0326	0.02 [-0.07;0.12]	
Baseline Renal impairment															0.1648
GFR < 30	46	46	38	38.30 (14.7)	42.99 (13.3)	3.02 (1.8)	61	61	48	40.84 (12.8)	39.84 (13.2)	-1.09 (1.6)	4.11 [-0.70;8.92] 0.0942	0.28 [-0.15;0.71]	
30 <= GFR	1602	1598	1428	43.35 (12.5)	43.72 (12.5)	0.36 (0.3)	1588	1587	1395	42.46 (13.1)	42.78 (12.8)	-0.29 (0.3)	0.65 [-0.19;1.48] 0.1277	0.02 [-0.05;0.09]	
Evidence of CV disease at screening															0.7774
CV DISEASE	1353	1350	1190	43.06 (12.7)	43.53 (12.8)	0.39 (0.3)	1382	1381	1194	42.24 (13.3)	42.46 (12.9)	-0.41 (0.3)	0.80 [-0.10;1.71] 0.0822	0.03 [-0.05;0.12]	
CV RISK FACTORS ONLY	295	294	276	43.87 (11.9)	44.43 (11.4)	0.61 (0.7)	267	267	249	43.26 (12.1)	43.76 (12.2)	0.11 (0.7)	0.50 [-1.44;2.43] 0.6159	-0.00 [-0.17;0.17]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

22 SF-36 - Mental Health - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1467	47.40 (11.1)	48.37 (10.9)	0.76 (0.2)	1649	1648	1443	48.09 (11.1)	47.96 (11.0)	-0.24 (0.2)	1.00 [0.35;1.65] 0.0026	0.14 [0.06;0.21]	
Gender															0.2437
Female	635	634	561	44.74 (11.6)	46.14 (11.6)	1.16 (0.4)	660	659	575	45.67 (11.6)	46.24 (11.0)	0.67 (0.4)	0.50 [-0.54;1.53] 0.3479	0.09 [-0.02;0.21]	
Male	1013	1010	906	49.06 (10.4)	49.74 (10.2)	0.48 (0.3)	989	989	868	49.70 (10.6)	49.11 (10.8)	-0.80 (0.3)	1.29 [0.46;2.12] 0.0024	0.17 [0.08;0.26]	
Age															0.6434
< 65	855	854	765	46.04 (11.4)	47.65 (11.2)	1.26 (0.3)	844	843	741	46.72 (11.4)	47.38 (11.2)	0.42 (0.3)	0.85 [-0.05;1.75] 0.0649	0.12 [0.02;0.22]	
65 <=	793	790	702	48.86 (10.6)	49.14 (10.6)	0.22 (0.3)	805	805	702	49.52 (10.7)	48.58 (10.7)	-0.93 (0.3)	1.16 [0.22;2.09] 0.0153	0.16 [0.05;0.26]	
HbA1c at baseline (disease severity)															0.5107
< 8.0	595	594	536	48.22 (10.9)	49.22 (10.8)	0.70 (0.4)	628	628	559	48.94 (10.6)	48.49 (10.4)	-0.58 (0.4)	1.28 [0.22;2.34] 0.0177	0.16 [0.04;0.28]	
8.0 <=	1053	1050	931	46.93 (11.2)	47.87 (11.0)	0.80 (0.3)	1021	1020	884	47.56 (11.4)	47.63 (11.3)	-0.03 (0.3)	0.83 [0.01;1.65] 0.0473	0.12 [0.03;0.21]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Mental Health - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.2716
West Europe	228	226	205	47.95 (11.0)	48.65 (11.1)	0.30 (0.6)	205	205	191	49.36 (11.2)	47.70 (11.3)	-1.62 (0.6)	1.92 [0.16;3.68] 0.0327	0.24 [0.04;0.44]	
Rest of World	1420	1418	1262	47.31 (11.1)	48.32 (10.9)	0.83 (0.3)	1444	1443	1252	47.91 (11.1)	48.01 (10.9)	-0.02 (0.3)	0.86 [0.16;1.55] 0.0160	0.12 [0.04;0.20]	
Region B															0.1505
OECD	1174	1170	1020	48.44 (10.9)	49.25 (10.7)	0.55 (0.3)	1136	1135	958	48.96 (11.0)	48.55 (10.9)	-0.77 (0.3)	1.31 [0.53;2.10] 0.0011	0.16 [0.07;0.25]	
Non-OECD	474	474	447	44.82 (11.2)	46.35 (11.1)	1.17 (0.4)	513	513	485	46.16 (11.2)	46.81 (11.0)	0.88 (0.4)	0.29 [-0.86;1.44] 0.6174	0.11 [-0.02;0.23]	
Treatment dose volume															0.1951
0.5 mg/week	826	825	734	47.06 (11.2)	47.98 (11.1)	0.52 (0.3)	824	823	727	48.02 (11.3)	48.00 (10.8)	-0.05 (0.3)	0.57 [-0.34;1.48] 0.2211	0.10 [-0.00;0.20]	
1.0 mg/week	822	819	733	47.73 (10.9)	48.76 (10.7)	1.00 (0.3)	825	825	716	48.15 (11.0)	47.93 (11.1)	-0.43 (0.3)	1.43 [0.51;2.35] 0.0024	0.18 [0.07;0.28]	
Baseline insulin use															0.6085
No	692	690	616	47.13 (11.1)	49.03 (10.4)	1.23 (0.4)	692	692	612	49.33 (10.8)	49.55 (10.6)	0.43 (0.4)	0.80 [-0.20;1.80] 0.1172	0.17 [0.06;0.29]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Mental Health - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	851	47.59 (11.1)	47.89 (11.3)	0.42 (0.3)	957	956	831	47.19 (11.3)	46.80 (11.1)	-0.72 (0.3)	1.14 [0.29;1.99] 0.0087	0.11 [0.02;0.21]	
Baseline Renal impairment															0.7578
GFR < 30	46	46	38	45.49 (11.0)	48.01 (10.6)	2.48 (1.4)	61	61	48	48.66 (10.1)	48.89 (11.0)	0.90 (1.3)	1.59 [-2.21;5.38] 0.4130	0.23 [-0.20;0.65]	
30 <= GFR	1602	1598	1429	47.45 (11.1)	48.38 (10.9)	0.71 (0.2)	1588	1587	1395	48.07 (11.2)	47.93 (11.0)	-0.27 (0.2)	0.98 [0.32;1.64] 0.0035	0.14 [0.06;0.21]	
Evidence of CV disease at screening															0.4185
CV DISEASE	1353	1350	1191	47.48 (11.0)	48.34 (11.0)	0.69 (0.3)	1382	1381	1194	48.03 (11.1)	48.02 (11.0)	-0.19 (0.3)	0.87 [0.16;1.59] 0.0170	0.13 [0.05;0.21]	
CV RISK FACTORS ONLY	295	294	276	47.04 (11.4)	48.47 (10.8)	1.09 (0.5)	267	267	249	48.40 (11.4)	47.72 (11.0)	-0.48 (0.6)	1.57 [0.04;3.10] 0.0443	0.17 [0.00;0.35]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

23 SF-36 - Physical component summary - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1466	42.29 (9.6)	43.69 (9.7)	1.13 (0.2)	1649	1647	1443	41.40 (9.9)	42.03 (10.2)	0.08 (0.2)	1.05 [0.50;1.60] 0.0002	0.09 [0.02;0.16]	
Gender															0.7414
Female	635	634	561	40.33 (9.2)	42.23 (9.7)	1.62 (0.3)	660	659	575	39.33 (9.6)	40.53 (10.1)	0.69 (0.3)	0.93 [0.05;1.81] 0.0374	0.06 [-0.05;0.18]	
Male	1013	1010	905	43.51 (9.6)	44.60 (9.6)	0.82 (0.3)	989	988	868	42.78 (9.9)	43.03 (10.1)	-0.31 (0.3)	1.12 [0.42;1.83] 0.0018	0.11 [0.02;0.20]	
Age															0.1860
< 65	855	854	765	42.95 (9.6)	44.89 (9.6)	1.76 (0.3)	844	842	741	41.63 (10.0)	43.36 (9.9)	1.07 (0.3)	0.68 [-0.07;1.44] 0.0769	0.02 [-0.08;0.12]	
65 <=	793	790	701	41.57 (9.4)	42.39 (9.7)	0.45 (0.3)	805	805	702	41.16 (9.8)	40.63 (10.3)	-0.96 (0.3)	1.42 [0.64;2.20] 0.0004	0.16 [0.05;0.26]	
HbA1c at baseline (disease severity)															0.9242
< 8.0	595	594	535	43.05 (9.5)	44.12 (9.4)	0.92 (0.3)	628	627	559	41.80 (9.8)	42.15 (10.6)	-0.16 (0.3)	1.08 [0.18;1.98] 0.0181	0.08 [-0.04;0.20]	
8.0 <=	1053	1050	931	41.85 (9.6)	43.45 (9.9)	1.26 (0.2)	1021	1020	884	41.15 (10.0)	41.96 (9.9)	0.23 (0.3)	1.03 [0.33;1.72] 0.0038	0.10 [0.00;0.19]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Physical component summary - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.9512
West Europe	228	226	205	42.95 (9.9)	42.51 (10.1)	-0.71 (0.5)	205	205	191	42.09 (11.7)	40.86 (11.6)	-1.73 (0.5)	1.02 [-0.47;2.50] 0.1800	0.07 [-0.13;0.27]	
Rest of World	1420	1418	1261	42.18 (9.5)	43.89 (9.6)	1.43 (0.2)	1444	1442	1252	41.30 (9.6)	42.21 (9.9)	0.36 (0.2)	1.07 [0.48;1.66] 0.0004	0.10 [0.02;0.17]	
Region B															0.6046
OECD	1174	1170	1019	41.75 (10.0)	42.89 (10.0)	0.81 (0.2)	1136	1134	958	40.67 (10.4)	41.10 (10.6)	-0.21 (0.2)	1.01 [0.35;1.68] 0.0029	0.07 [-0.02;0.16]	
Non-OECD	474	474	447	43.62 (8.3)	45.53 (8.7)	1.92 (0.4)	513	513	485	42.99 (8.5)	43.87 (9.0)	0.60 (0.3)	1.32 [0.36;2.29] 0.0074	0.14 [0.01;0.27]	
Treatment dose volume															0.1602
0.5 mg/week	826	825	734	42.60 (9.4)	43.38 (9.3)	0.58 (0.3)	824	823	727	41.29 (9.7)	41.81 (10.2)	-0.08 (0.3)	0.66 [-0.12;1.43] 0.0957	0.02 [-0.08;0.13]	
1.0 mg/week	822	819	732	41.97 (9.7)	44.01 (10.1)	1.69 (0.3)	825	824	716	41.50 (10.1)	42.26 (10.1)	0.24 (0.3)	1.44 [0.67;2.22] 0.0003	0.15 [0.05;0.26]	
Baseline insulin use															0.0242*
No	692	690	616	43.15 (9.5)	44.21 (9.6)	0.75 (0.3)	692	691	612	42.74 (9.6)	43.67 (9.8)	0.43 (0.3)	0.31 [-0.53;1.16] 0.4653	0.03 [-0.09;0.14]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Physical component summary - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs. Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	850	41.66 (9.6)	43.32 (9.8)	1.41 (0.3)	957	956	831	40.43 (10.0)	40.83 (10.3)	-0.18 (0.3)	1.59 [0.87;2.31] <0.0001	0.13 [0.04;0.23]	
Baseline Renal impairment															0.7463
GFR < 30	46	46	38	39.66 (9.7)	42.13 (10.3)	1.71 (1.2)	61	61	48	38.95 (8.4)	39.51 (10.9)	0.14 (1.1)	1.57 [-1.64;4.79] 0.3372	0.14 [-0.28;0.57]	
30 <= GFR	1602	1598	1428	42.36 (9.5)	43.74 (9.7)	1.12 (0.2)	1588	1586	1395	41.49 (10.0)	42.12 (10.1)	0.08 (0.2)	1.04 [0.48;1.59] 0.0003	0.09 [0.01;0.16]	
Evidence of CV disease at screening															0.0623
CV DISEASE	1353	1350	1190	41.82 (9.7)	43.20 (9.9)	1.09 (0.2)	1382	1380	1194	40.97 (9.9)	41.76 (10.2)	0.29 (0.2)	0.81 [0.20;1.41] 0.0091	0.06 [-0.02;0.14]	
CV RISK FACTORS ONLY	295	294	276	44.42 (8.8)	45.84 (8.6)	1.29 (0.5)	267	267	249	43.61 (9.7)	43.32 (10.1)	-0.88 (0.5)	2.17 [0.87;3.46] 0.0010	0.22 [0.05;0.39]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

24 SF-36 - Mental component summary - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
All subjects (total)	1648	1644	1466	47.91 (11.5)	48.50 (11.1)	0.43 (0.2)	1649	1647	1443	48.21 (11.4)	48.27 (11.2)	-0.14 (0.2)	0.57 [-0.11;1.25] 0.1023	0.08 [0.00;0.15]	
Gender															0.3496
Female	635	634	561	45.68 (11.8)	46.58 (12.0)	0.77 (0.4)	660	659	575	46.08 (11.9)	46.78 (11.4)	0.62 (0.4)	0.15 [-0.95;1.24] 0.7949	0.04 [-0.08;0.16]	
Male	1013	1010	905	49.31 (11.0)	49.69 (10.4)	0.20 (0.3)	989	988	868	49.63 (10.9)	49.25 (10.9)	-0.61 (0.3)	0.81 [-0.06;1.69] 0.0686	0.10 [0.01;0.20]	
Age															0.5190
< 65	855	854	765	46.75 (11.5)	47.73 (11.2)	0.76 (0.3)	844	842	741	46.76 (11.5)	47.61 (11.4)	0.41 (0.3)	0.35 [-0.60;1.31] 0.4653	0.04 [-0.06;0.15]	
65 <=	793	790	701	49.16 (11.3)	49.35 (11.0)	0.09 (0.4)	805	805	702	49.73 (11.2)	48.97 (10.9)	-0.72 (0.4)	0.81 [-0.18;1.79] 0.1094	0.11 [0.01;0.22]	
HbA1c at baseline (disease severity)															0.4080
< 8.0	595	594	535	48.74 (11.2)	49.08 (11.0)	0.14 (0.4)	628	627	559	49.10 (11.2)	48.48 (11.0)	-0.80 (0.4)	0.94 [-0.18;2.06] 0.1000	0.11 [-0.00;0.23]	
8.0 <=	1053	1050	931	47.44 (11.6)	48.17 (11.2)	0.61 (0.3)	1021	1020	884	47.67 (11.6)	48.13 (11.3)	0.27 (0.3)	0.34 [-0.53;1.21] 0.4400	0.05 [-0.04;0.14]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Mental component summary - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Region A															0.1206
West Europe	228	226	205	48.78 (11.3)	48.86 (11.4)	-0.30 (0.7)	205	205	191	49.67 (11.7)	47.55 (11.7)	-2.24 (0.7)	1.94 [0.09;3.80] 0.0403	0.21 [0.01;0.41]	
Rest of World	1420	1418	1261	47.77 (11.5)	48.44 (11.1)	0.55 (0.3)	1444	1442	1252	48.00 (11.4)	48.38 (11.1)	0.19 (0.3)	0.36 [-0.37;1.10] 0.3346	0.06 [-0.02;0.13]	
Region B															0.1837
OECD	1174	1170	1019	49.00 (11.2)	49.18 (11.3)	-0.04 (0.3)	1136	1134	958	49.00 (11.5)	48.53 (11.5)	-0.94 (0.3)	0.91 [0.07;1.74] 0.0327	0.09 [0.00;0.18]	
Non-OECD	474	474	447	45.22 (11.6)	46.96 (10.6)	1.43 (0.4)	513	513	485	46.48 (11.1)	47.76 (10.5)	1.52 (0.4)	-0.09 [-1.30;1.12] 0.8823	0.07 [-0.06;0.19]	
Treatment dose volume															0.2507
0.5 mg/week	826	825	734	47.53 (11.6)	48.03 (11.2)	0.06 (0.3)	824	823	727	48.16 (11.5)	48.19 (10.9)	-0.11 (0.3)	0.17 [-0.79;1.14] 0.7289	0.04 [-0.06;0.14]	
1.0 mg/week	822	819	732	48.29 (11.3)	48.97 (11.1)	0.81 (0.3)	825	824	716	48.27 (11.4)	48.35 (11.4)	-0.16 (0.4)	0.97 [0.00;1.94] 0.0496	0.11 [0.01;0.21]	
Baseline insulin use															0.4529
No	692	690	616	47.52 (11.4)	49.06 (11.1)	0.86 (0.4)	692	691	612	49.33 (11.0)	49.83 (10.6)	0.60 (0.4)	0.26 [-0.79;1.32] 0.6244	0.11 [-0.01;0.22]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SF-36 - Mental component summary - ANCOVA - Sustain 6 - in-trial - full analysis set

	Sema						Comparator						Sema vs.Comparator		
Subgroup	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	N	Nbase	N EOT visit	Mean base (SD)	Mean EOT visit (SD)	Est. CFB (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI]	p-value int.
Yes	956	954	850	48.19 (11.5)	48.10 (11.2)	0.12 (0.3)	957	956	831	47.40 (11.7)	47.12 (11.4)	-0.67 (0.3)	0.79 [-0.11;1.69] 0.0837	0.06 [-0.04;0.15]	
Baseline Renal impairment															0.4833
GFR < 30	46	46	38	45.41 (12.0)	47.63 (11.8)	1.69 (1.5)	61	61	48	48.05 (11.3)	47.39 (10.9)	-0.29 (1.4)	1.98 [-2.03;5.99] 0.3322	0.22 [-0.21;0.64]	
30 <= GFR	1602	1598	1428	47.98 (11.4)	48.52 (11.1)	0.40 (0.2)	1588	1586	1395	48.22 (11.5)	48.30 (11.2)	-0.13 (0.3)	0.53 [-0.17;1.22] 0.1361	0.07 [-0.00;0.15]	
Evidence of CV disease at screening															0.7441
CV DISEASE	1353	1350	1190	47.97 (11.5)	48.45 (11.3)	0.36 (0.3)	1382	1380	1194	48.09 (11.6)	48.12 (11.2)	-0.26 (0.3)	0.62 [-0.13;1.38] 0.1057	0.08 [0.00;0.16]	
CV RISK FACTORS ONLY	295	294	276	47.63 (11.4)	48.73 (10.4)	0.78 (0.6)	267	267	249	48.82 (10.9)	49.00 (10.9)	0.45 (0.6)	0.33 [-1.29;1.94] 0.6912	0.05 [-0.12;0.23]	

N: number of subjects in the analysis set, Nbase: number of subjects with an observation at baseline, N EOT visit: number of subjects with an observation at EOT visit, base: baseline, CI: confidence interval, EOT: end of treatment, Est. CFB: estimated change from baseline, ETD: estimated treatment difference, Mean: observed arithmetic mean, SD: standard deviation, SE: standard error, 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), *: p-value int. < 0,05
Change from baseline was analysed using an ANCOVA model with treatment (or interaction between treatment and subgroup, if applicable) and stratification factor as fixed factors and the corresponding baseline value as a covariate. Missing post-baseline values were not imputed.

SUSTAIN 6 – Subgruppen – Sicherheit – Gesamtraten UE / SUE / Abbruch / UESI

1 Adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1648	1472 (89.3%)	176 (10.7%)	4 (0.2%)	0 (0.0%)	1649	1484 (90.0%)	165 (10.0%)	6 (0.4%)	0 (0.0%)	1.10 [1.03;1.19]	0.0075	
Gender													0.1277
Female	635	571 (89.9%)	64 (10.1%)	2 (0.3%)	0 (0.0%)	660	585 (88.6%)	75 (11.4%)	5 (0.8%)	0 (0.0%)	1.18 [1.06;1.33]	0.0040	
Male	1013	901 (88.9%)	112 (11.1%)	2 (0.2%)	0 (0.0%)	989	899 (90.9%)	90 (9.1%)	1 (0.1%)	0 (0.0%)	1.06 [0.96;1.16]	0.2460	
Age													0.8905
< 65	855	753 (88.1%)	102 (11.9%)	3 (0.4%)	0 (0.0%)	844	752 (89.1%)	92 (10.9%)	1 (0.1%)	0 (0.0%)	1.10 [0.99;1.22]	0.0683	
65 <=	793	719 (90.7%)	74 (9.3%)	1 (0.1%)	0 (0.0%)	805	732 (90.9%)	73 (9.1%)	5 (0.6%)	0 (0.0%)	1.11 [1.00;1.23]	0.0475	
HbA1c at baseline (disease severity)													0.8830
< 8.0	595	535 (89.9%)	60 (10.1%)	0 (0.0%)	0 (0.0%)	628	568 (90.4%)	60 (9.6%)	0 (0.0%)	0 (0.0%)	1.11 [0.99;1.25]	0.0766	
8.0 <=	1053	937 (89.0%)	116 (11.0%)	4 (0.4%)	0 (0.0%)	1021	916 (89.7%)	105 (10.3%)	6 (0.6%)	0 (0.0%)	1.10 [1.00;1.21]	0.0399	
Region A													0.3461
West Europe	228	204 (89.5%)	24 (10.5%)	0 (0.0%)	0 (0.0%)	205	186 (90.7%)	19 (9.3%)	0 (0.0%)	0 (0.0%)	1.21 [0.99;1.47]	0.0649	
Rest of World	1420	1268 (89.3%)	152 (10.7%)	4 (0.3%)	0 (0.0%)	1444	1298 (89.9%)	146 (10.1%)	6 (0.4%)	0 (0.0%)	1.09 [1.01;1.18]	0.0322	
Region B													0.2642

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	1077 (91.7%)	97 (8.3%)	4 (0.3%)	0 (0.0%)	1136	1043 (91.8%)	93 (8.2%)	6 (0.5%)	0 (0.0%)	1.13 [1.04;1.23]	0.0056	
Non-OECD	474	395 (83.3%)	79 (16.7%)	0 (0.0%)	0 (0.0%)	513	441 (86.0%)	72 (14.0%)	0 (0.0%)	0 (0.0%)	1.03 [0.90;1.18]	0.6739	
Treatment dose volume													0.0977
0.5 mg/week	826	740 (89.6%)	86 (10.4%)	3 (0.4%)	0 (0.0%)	824	748 (90.8%)	76 (9.2%)	3 (0.4%)	0 (0.0%)	1.04 [0.94;1.15]	0.4893	
1.0 mg/week	822	732 (89.1%)	90 (10.9%)	1 (0.1%)	0 (0.0%)	825	736 (89.2%)	89 (10.8%)	3 (0.4%)	0 (0.0%)	1.17 [1.06;1.30]	0.0025	
Baseline insulin use													0.9950
No	692	605 (87.4%)	87 (12.6%)	3 (0.4%)	0 (0.0%)	692	616 (89.0%)	76 (11.0%)	1 (0.1%)	0 (0.0%)	1.10 [0.99;1.23]	0.0884	
Yes	956	867 (90.7%)	89 (9.3%)	1 (0.1%)	0 (0.0%)	957	868 (90.7%)	89 (9.3%)	5 (0.5%)	0 (0.0%)	1.10 [1.00;1.21]	0.0413	
Baseline Renal impairment													0.9607
GFR < 30	46	42 (91.3%)	4 (8.7%)	0 (0.0%)	0 (0.0%)	61	58 (95.1%)	3 (4.9%)	0 (0.0%)	0 (0.0%)	1.12 [0.75;1.66]	0.5894	
30 <= GFR	1602	1430 (89.3%)	172 (10.7%)	4 (0.2%)	0 (0.0%)	1588	1426 (89.8%)	162 (10.2%)	6 (0.4%)	0 (0.0%)	1.10 [1.03;1.19]	0.0081	
Evidence of CV disease at screening													0.5179
CV DISEASE	1353	1212 (89.6%)	141 (10.4%)	3 (0.2%)	0 (0.0%)	1382	1246 (90.2%)	136 (9.8%)	5 (0.4%)	0 (0.0%)	1.09 [1.01;1.18]	0.0287	
CV RISK FACTORS ONLY	295	260 (88.1%)	35 (11.9%)	1 (0.3%)	0 (0.0%)	267	238 (89.1%)	29 (10.9%)	1 (0.4%)	0 (0.0%)	1.16 [0.98;1.39]	0.0905	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

2 Mild adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	1321 (80.2%)	327 (19.8%)	17 (1.0%)	10 (0.6%)	1649	1320 (80.0%)	329 (20.0%)	30 (1.8%)	15 (0.9%)	1.09 [1.01;1.17]	0.0322	
Gender													0.5159
Female	635	511 (80.5%)	124 (19.5%)	9 (1.4%)	4 (0.6%)	660	524 (79.4%)	136 (20.6%)	11 (1.7%)	3 (0.5%)	1.12 [0.99;1.27]	0.0638	
Male	1013	810 (80.0%)	203 (20.0%)	8 (0.8%)	6 (0.6%)	989	796 (80.5%)	193 (19.5%)	19 (1.9%)	12 (1.2%)	1.07 [0.97;1.18]	0.2035	
Age													0.5610
< 65	855	674 (78.8%)	181 (21.2%)	9 (1.1%)	4 (0.5%)	844	670 (79.4%)	174 (20.6%)	15 (1.8%)	6 (0.7%)	1.06 [0.96;1.18]	0.2565	
65 <=	793	647 (81.6%)	146 (18.4%)	8 (1.0%)	6 (0.8%)	805	650 (80.7%)	155 (19.3%)	15 (1.9%)	9 (1.1%)	1.11 [1.00;1.24]	0.0537	
HbA1c at baseline (disease severity)													0.7652
< 8.0	595	481 (80.8%)	114 (19.2%)	2 (0.3%)	2 (0.3%)	628	504 (80.3%)	124 (19.7%)	6 (1.0%)	3 (0.5%)	1.10 [0.97;1.25]	0.1193	
8.0 <=	1053	840 (79.8%)	213 (20.2%)	15 (1.4%)	8 (0.8%)	1021	816 (79.9%)	205 (20.1%)	24 (2.4%)	12 (1.2%)	1.08 [0.98;1.19]	0.1257	
Region A													0.1420
West Europe	228	193 (84.6%)	35 (15.4%)	1 (0.4%)	1 (0.4%)	205	169 (82.4%)	36 (17.6%)	2 (1.0%)	0 (0.0%)	1.26 [1.02;1.54]	0.0309	
Rest of World	1420	1128 (79.4%)	292 (20.6%)	16 (1.1%)	9 (0.6%)	1444	1151 (79.7%)	293 (20.3%)	28 (1.9%)	15 (1.0%)	1.06 [0.98;1.15]	0.1461	
Region B													0.0314*

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Mild adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	983 (83.7%)	191 (16.3%)	13 (1.1%)	6 (0.5%)	1136	929 (81.8%)	207 (18.2%)	24 (2.1%)	9 (0.8%)	1.14 [1.05;1.25]	0.0034	
Non-OECD	474	338 (71.3%)	136 (28.7%)	4 (0.8%)	4 (0.8%)	513	391 (76.2%)	122 (23.8%)	6 (1.2%)	6 (1.2%)	0.95 [0.82;1.10]	0.4711	
Treatment dose volume													0.1975
0.5 mg/week	826	661 (80.0%)	165 (20.0%)	8 (1.0%)	5 (0.6%)	824	664 (80.6%)	160 (19.4%)	15 (1.8%)	8 (1.0%)	1.03 [0.93;1.15]	0.5574	
1.0 mg/week	822	660 (80.3%)	162 (19.7%)	9 (1.1%)	5 (0.6%)	825	656 (79.5%)	169 (20.5%)	15 (1.8%)	7 (0.8%)	1.14 [1.02;1.27]	0.0162	
Baseline insulin use													0.3771
No	692	537 (77.6%)	155 (22.4%)	8 (1.2%)	3 (0.4%)	692	552 (79.8%)	140 (20.2%)	9 (1.3%)	6 (0.9%)	1.04 [0.93;1.18]	0.4818	
Yes	956	784 (82.0%)	172 (18.0%)	9 (0.9%)	7 (0.7%)	957	768 (80.3%)	189 (19.7%)	21 (2.2%)	9 (0.9%)	1.12 [1.01;1.24]	0.0267	
Baseline Renal impairment													0.4794
GFR < 30	46	36 (78.3%)	10 (21.7%)	2 (4.3%)	2 (4.3%)	61	51 (83.6%)	10 (16.4%)	0 (0.0%)	0 (0.0%)	0.93 [0.61;1.43]	0.7548	
30 <= GFR	1602	1285 (80.2%)	317 (19.8%)	15 (0.9%)	8 (0.5%)	1588	1269 (79.9%)	319 (20.1%)	30 (1.9%)	15 (0.9%)	1.09 [1.01;1.18]	0.0254	
Evidence of CV disease at screening													0.7332
CV DISEASE	1353	1091 (80.6%)	262 (19.4%)	14 (1.0%)	9 (0.7%)	1382	1105 (80.0%)	277 (20.0%)	29 (2.1%)	15 (1.1%)	1.09 [1.01;1.19]	0.0340	
CV RISK FACTORS ONLY	295	230 (78.0%)	65 (22.0%)	3 (1.0%)	1 (0.3%)	267	215 (80.5%)	52 (19.5%)	1 (0.4%)	0 (0.0%)	1.06 [0.88;1.27]	0.5618	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

3 Moderate adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	997 (60.5%)	651 (39.5%)	29 (1.8%)	19 (1.2%)	1649	978 (59.3%)	671 (40.7%)	35 (2.1%)	23 (1.4%)	1.08 [0.99;1.18]	0.0748	
Gender													0.8435
Female	635	389 (61.3%)	246 (38.7%)	11 (1.7%)	7 (1.1%)	660	391 (59.2%)	269 (40.8%)	10 (1.5%)	5 (0.8%)	1.10 [0.95;1.26]	0.1991	
Male	1013	608 (60.0%)	405 (40.0%)	18 (1.8%)	12 (1.2%)	989	587 (59.4%)	402 (40.6%)	25 (2.5%)	18 (1.8%)	1.08 [0.96;1.21]	0.2023	
Age													0.5645
< 65	855	496 (58.0%)	359 (42.0%)	20 (2.3%)	14 (1.6%)	844	464 (55.0%)	380 (45.0%)	17 (2.0%)	11 (1.3%)	1.11 [0.98;1.27]	0.0924	
65 <=	793	501 (63.2%)	292 (36.8%)	9 (1.1%)	5 (0.6%)	805	514 (63.9%)	291 (36.1%)	18 (2.2%)	12 (1.5%)	1.06 [0.94;1.20]	0.3657	
HbA1c at baseline (disease severity)													0.1634
< 8.0	595	361 (60.7%)	234 (39.3%)	8 (1.3%)	5 (0.8%)	628	392 (62.4%)	236 (37.6%)	10 (1.6%)	7 (1.1%)	1.00 [0.87;1.15]	0.9911	
8.0 <=	1053	636 (60.4%)	417 (39.6%)	21 (2.0%)	14 (1.3%)	1021	586 (57.4%)	435 (42.6%)	25 (2.4%)	16 (1.6%)	1.14 [1.02;1.27]	0.0231	
Region A													0.6654
West Europe	228	139 (61.0%)	89 (39.0%)	1 (0.4%)	1 (0.4%)	205	121 (59.0%)	84 (41.0%)	2 (1.0%)	1 (0.5%)	1.14 [0.89;1.45]	0.2943	
Rest of World	1420	858 (60.4%)	562 (39.6%)	28 (2.0%)	18 (1.3%)	1444	857 (59.3%)	587 (40.7%)	33 (2.3%)	22 (1.5%)	1.08 [0.98;1.18]	0.1322	
Region B													0.1681

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Moderate adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema				Comparator				Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	754 (64.2%)	420 (35.8%)	22 (1.9%)	12 (1.0%)	1136	738 (65.0%)	398 (35.0%)	27 (2.4%)	15 (1.3%)	1.03 [0.93;1.14]	0.5447	
Non-OECD	474	243 (51.3%)	231 (48.7%)	7 (1.5%)	7 (1.5%)	513	240 (46.8%)	273 (53.2%)	8 (1.6%)	8 (1.6%)	1.19 [1.00;1.42]	0.0535	
Treatment dose volume													0.7670
0.5 mg/week	826	497 (60.2%)	329 (39.8%)	18 (2.2%)	11 (1.3%)	824	485 (58.9%)	339 (41.1%)	17 (2.1%)	12 (1.5%)	1.07 [0.94;1.21]	0.2936	
1.0 mg/week	822	500 (60.8%)	322 (39.2%)	11 (1.3%)	8 (1.0%)	825	493 (59.8%)	332 (40.2%)	18 (2.2%)	11 (1.3%)	1.10 [0.97;1.24]	0.1399	
Baseline insulin use													0.0376*
No	692	417 (60.3%)	275 (39.7%)	12 (1.7%)	5 (0.7%)	692	387 (55.9%)	305 (44.1%)	13 (1.9%)	9 (1.3%)	1.21 [1.05;1.39]	0.0067	
Yes	956	580 (60.7%)	376 (39.3%)	17 (1.8%)	14 (1.5%)	957	591 (61.8%)	366 (38.2%)	22 (2.3%)	14 (1.5%)	1.00 [0.89;1.12]	0.9883	
Baseline Renal impairment													0.3701
GFR < 30	46	28 (60.9%)	18 (39.1%)	3 (6.5%)	3 (6.5%)	61	45 (73.8%)	16 (26.2%)	2 (3.3%)	2 (3.3%)	0.88 [0.55;1.41]	0.5906	
30 <= GFR	1602	969 (60.5%)	633 (39.5%)	26 (1.6%)	16 (1.0%)	1588	933 (58.8%)	655 (41.2%)	33 (2.1%)	21 (1.3%)	1.09 [1.00;1.20]	0.0495	
Evidence of CV disease at screening													0.4571
CV DISEASE	1353	840 (62.1%)	513 (37.9%)	26 (1.9%)	18 (1.3%)	1382	845 (61.1%)	537 (38.9%)	32 (2.3%)	21 (1.5%)	1.07 [0.97;1.18]	0.1573	
CV RISK FACTORS ONLY	295	157 (53.2%)	138 (46.8%)	3 (1.0%)	1 (0.3%)	267	133 (49.8%)	134 (50.2%)	3 (1.1%)	2 (0.7%)	1.18 [0.93;1.48]	0.1647	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

4 Severe adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	407 (24.7%)	1241 (75.3%)	22 (1.3%)	1 (0.1%)	1649	410 (24.9%)	1239 (75.1%)	31 (1.9%)	2 (0.1%)	1.02 [0.89;1.17]	0.7921	
Gender													0.1269
Female	635	156 (24.6%)	479 (75.4%)	8 (1.3%)	0 (0.0%)	660	145 (22.0%)	515 (78.0%)	18 (2.7%)	1 (0.2%)	1.17 [0.93;1.47]	0.1762	
Male	1013	251 (24.8%)	762 (75.2%)	14 (1.4%)	1 (0.1%)	989	265 (26.8%)	724 (73.2%)	13 (1.3%)	1 (0.1%)	0.94 [0.79;1.11]	0.4568	
Age													0.2232
< 65	855	202 (23.6%)	653 (76.4%)	11 (1.3%)	1 (0.1%)	844	185 (21.9%)	659 (78.1%)	17 (2.0%)	0 (0.0%)	1.12 [0.91;1.36]	0.2847	
65 <=	793	205 (25.9%)	588 (74.1%)	11 (1.4%)	0 (0.0%)	805	225 (28.0%)	580 (72.0%)	14 (1.7%)	2 (0.2%)	0.94 [0.78;1.14]	0.5208	
HbA1c at baseline (disease severity)													0.4133
< 8.0	595	147 (24.7%)	448 (75.3%)	6 (1.0%)	1 (0.2%)	628	146 (23.2%)	482 (76.8%)	10 (1.6%)	1 (0.2%)	1.10 [0.87;1.38]	0.4226	
8.0 <=	1053	260 (24.7%)	793 (75.3%)	16 (1.5%)	0 (0.0%)	1021	264 (25.9%)	757 (74.1%)	21 (2.1%)	1 (0.1%)	0.97 [0.82;1.16]	0.7690	
Region A													0.3846
West Europe	228	66 (28.9%)	162 (71.1%)	3 (1.3%)	0 (0.0%)	205	54 (26.3%)	151 (73.7%)	3 (1.5%)	0 (0.0%)	1.18 [0.82;1.69]	0.3702	
Rest of World	1420	341 (24.0%)	1079 (76.0%)	19 (1.3%)	1 (0.1%)	1444	356 (24.7%)	1088 (75.3%)	28 (1.9%)	2 (0.1%)	0.99 [0.85;1.15]	0.9143	
Region B													0.1312

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	315 (26.8%)	859 (73.2%)	21 (1.8%)	1 (0.1%)	1136	327 (28.8%)	809 (71.2%)	29 (2.6%)	1 (0.1%)	0.95 [0.82;1.11]	0.5365	
Non-OECD	474	92 (19.4%)	382 (80.6%)	1 (0.2%)	0 (0.0%)	513	83 (16.2%)	430 (83.8%)	2 (0.4%)	1 (0.2%)	1.23 [0.92;1.66]	0.1676	
Treatment dose volume													0.2408
0.5 mg/week	826	200 (24.2%)	626 (75.8%)	11 (1.3%)	0 (0.0%)	824	216 (26.2%)	608 (73.8%)	17 (2.1%)	1 (0.1%)	0.94 [0.78;1.14]	0.5251	
1.0 mg/week	822	207 (25.2%)	615 (74.8%)	11 (1.3%)	1 (0.1%)	825	194 (23.5%)	631 (76.5%)	14 (1.7%)	1 (0.1%)	1.11 [0.91;1.35]	0.3078	
Baseline insulin use													0.0316*
No	692	169 (24.4%)	523 (75.6%)	11 (1.6%)	0 (0.0%)	692	144 (20.8%)	548 (79.2%)	13 (1.9%)	2 (0.3%)	1.23 [0.99;1.54]	0.0664	
Yes	956	238 (24.9%)	718 (75.1%)	11 (1.2%)	1 (0.1%)	957	266 (27.8%)	691 (72.2%)	18 (1.9%)	0 (0.0%)	0.90 [0.76;1.08]	0.2528	
Baseline Renal impairment													0.5012
GFR < 30	46	18 (39.1%)	28 (60.9%)	0 (0.0%)	0 (0.0%)	61	28 (45.9%)	33 (54.1%)	0 (0.0%)	0 (0.0%)	0.84 [0.47;1.52]	0.5684	
30 <= GFR	1602	389 (24.3%)	1213 (75.7%)	22 (1.4%)	1 (0.1%)	1588	382 (24.1%)	1206 (75.9%)	31 (2.0%)	2 (0.1%)	1.04 [0.90;1.19]	0.6116	
Evidence of CV disease at screening													0.9550
CV DISEASE	1353	361 (26.7%)	992 (73.3%)	20 (1.5%)	1 (0.1%)	1382	368 (26.6%)	1014 (73.4%)	29 (2.1%)	2 (0.1%)	1.03 [0.89;1.19]	0.7001	
CV RISK FACTORS ONLY	295	46 (15.6%)	249 (84.4%)	2 (0.7%)	0 (0.0%)	267	42 (15.7%)	225 (84.3%)	2 (0.7%)	0 (0.0%)	1.02 [0.67;1.54]	0.9411	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

5 Serious adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	565 (34.3%)	1083 (65.7%)	21 (1.3%)	1 (0.1%)	1649	627 (38.0%)	1022 (62.0%)	25 (1.5%)	0 (0.0%)	0.90 [0.80;1.01]	0.0610	
Gender													0.9536
Female	635	203 (32.0%)	432 (68.0%)	7 (1.1%)	0 (0.0%)	660	236 (35.8%)	424 (64.2%)	15 (2.3%)	0 (0.0%)	0.89 [0.74;1.08]	0.2301	
Male	1013	362 (35.7%)	651 (64.3%)	14 (1.4%)	1 (0.1%)	989	391 (39.5%)	598 (60.5%)	10 (1.0%)	0 (0.0%)	0.90 [0.78;1.04]	0.1391	
Age													0.3509
< 65	855	261 (30.5%)	594 (69.5%)	11 (1.3%)	1 (0.1%)	844	301 (35.7%)	543 (64.3%)	13 (1.5%)	0 (0.0%)	0.85 [0.72;1.00]	0.0524	
65 <=	793	304 (38.3%)	489 (61.7%)	10 (1.3%)	0 (0.0%)	805	326 (40.5%)	479 (59.5%)	12 (1.5%)	0 (0.0%)	0.95 [0.81;1.11]	0.4850	
HbA1c at baseline (disease severity)													0.9276
< 8.0	595	209 (35.1%)	386 (64.9%)	6 (1.0%)	1 (0.2%)	628	243 (38.7%)	385 (61.3%)	9 (1.4%)	0 (0.0%)	0.89 [0.74;1.07]	0.2236	
8.0 <=	1053	356 (33.8%)	697 (66.2%)	15 (1.4%)	0 (0.0%)	1021	384 (37.6%)	637 (62.4%)	16 (1.6%)	0 (0.0%)	0.90 [0.78;1.04]	0.1578	
Region A													0.4420
West Europe	228	86 (37.7%)	142 (62.3%)	3 (1.3%)	0 (0.0%)	205	80 (39.0%)	125 (61.0%)	2 (1.0%)	0 (0.0%)	1.00 [0.74;1.36]	0.9938	
Rest of World	1420	479 (33.7%)	941 (66.3%)	18 (1.3%)	1 (0.1%)	1444	547 (37.9%)	897 (62.1%)	23 (1.6%)	0 (0.0%)	0.88 [0.78;1.00]	0.0416	
Region B													0.6139

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	423 (36.0%)	751 (64.0%)	20 (1.7%)	1 (0.1%)	1136	462 (40.7%)	674 (59.3%)	24 (2.1%)	0 (0.0%)	0.88 [0.77;1.00]	0.0480	
Non-OECD	474	142 (30.0%)	332 (70.0%)	1 (0.2%)	0 (0.0%)	513	165 (32.2%)	348 (67.8%)	1 (0.2%)	0 (0.0%)	0.94 [0.75;1.17]	0.5636	
Treatment dose volume													0.4664
0.5 mg/week	826	289 (35.0%)	537 (65.0%)	11 (1.3%)	0 (0.0%)	824	329 (39.9%)	495 (60.1%)	15 (1.8%)	0 (0.0%)	0.86 [0.73;1.01]	0.0624	
1.0 mg/week	822	276 (33.6%)	546 (66.4%)	10 (1.2%)	1 (0.1%)	825	298 (36.1%)	527 (63.9%)	10 (1.2%)	0 (0.0%)	0.94 [0.80;1.10]	0.4320	
Baseline insulin use													0.8450
No	692	218 (31.5%)	474 (68.5%)	11 (1.6%)	0 (0.0%)	692	242 (35.0%)	450 (65.0%)	10 (1.4%)	0 (0.0%)	0.91 [0.76;1.09]	0.3065	
Yes	956	347 (36.3%)	609 (63.7%)	10 (1.0%)	1 (0.1%)	957	385 (40.2%)	572 (59.8%)	15 (1.6%)	0 (0.0%)	0.89 [0.77;1.03]	0.1085	
Baseline Renal impairment													0.6797
GFR < 30	46	21 (45.7%)	25 (54.3%)	0 (0.0%)	0 (0.0%)	61	33 (54.1%)	28 (45.9%)	0 (0.0%)	0 (0.0%)	0.80 [0.47;1.39]	0.4355	
30 <= GFR	1602	544 (34.0%)	1058 (66.0%)	21 (1.3%)	1 (0.1%)	1588	594 (37.4%)	994 (62.6%)	25 (1.6%)	0 (0.0%)	0.90 [0.81;1.02]	0.0924	
Evidence of CV disease at screening													0.6912
CV DISEASE	1353	496 (36.7%)	857 (63.3%)	18 (1.3%)	1 (0.1%)	1382	561 (40.6%)	821 (59.4%)	23 (1.7%)	0 (0.0%)	0.90 [0.79;1.01]	0.0733	
CV RISK FACTORS ONLY	295	69 (23.4%)	226 (76.6%)	3 (1.0%)	0 (0.0%)	267	66 (24.7%)	201 (75.3%)	2 (0.7%)	0 (0.0%)	0.96 [0.69;1.35]	0.8264	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

6 Serious adverse events excluding morbidity endpoints - comprehensive approach with PTs only - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	492 (29.9%)	1156 (70.1%)	30 (1.8%)	10 (0.6%)	1649	544 (33.0%)	1105 (67.0%)	39 (2.4%)	11 (0.7%)	0.90 [0.80;1.02]	0.1025	
Gender													0.8406
Female	635	184 (29.0%)	451 (71.0%)	11 (1.7%)	4 (0.6%)	660	209 (31.7%)	451 (68.3%)	20 (3.0%)	4 (0.6%)	0.92 [0.75;1.12]	0.3919	
Male	1013	308 (30.4%)	705 (69.6%)	19 (1.9%)	6 (0.6%)	989	335 (33.9%)	654 (66.1%)	19 (1.9%)	7 (0.7%)	0.89 [0.77;1.04]	0.1547	
Age													0.2124
< 65	855	217 (25.4%)	638 (74.6%)	17 (2.0%)	7 (0.8%)	844	255 (30.2%)	589 (69.8%)	24 (2.8%)	9 (1.1%)	0.83 [0.69;1.00]	0.0471	
65 <=	793	275 (34.7%)	518 (65.3%)	13 (1.6%)	3 (0.4%)	805	289 (35.9%)	516 (64.1%)	15 (1.9%)	2 (0.2%)	0.97 [0.82;1.15]	0.7440	
HbA1c at baseline (disease severity)													0.9341
< 8.0	595	188 (31.6%)	407 (68.4%)	8 (1.3%)	3 (0.5%)	628	219 (34.9%)	409 (65.1%)	10 (1.6%)	1 (0.2%)	0.90 [0.74;1.09]	0.2857	
8.0 <=	1053	304 (28.9%)	749 (71.1%)	22 (2.1%)	7 (0.7%)	1021	325 (31.8%)	696 (68.2%)	29 (2.8%)	10 (1.0%)	0.91 [0.78;1.06]	0.2309	
Region A													0.4023
West Europe	228	77 (33.8%)	151 (66.2%)	3 (1.3%)	0 (0.0%)	205	70 (34.1%)	135 (65.9%)	3 (1.5%)	0 (0.0%)	1.03 [0.74;1.42]	0.8780	
Rest of World	1420	415 (29.2%)	1005 (70.8%)	27 (1.9%)	10 (0.7%)	1444	474 (32.8%)	970 (67.2%)	36 (2.5%)	11 (0.8%)	0.88 [0.77;1.01]	0.0652	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events excluding morbidity endpoints - comprehensive approach with PTs only - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
Region B													0.7396
OECD	1174	378 (32.2%)	796 (67.8%)	24 (2.0%)	5 (0.4%)	1136	411 (36.2%)	725 (63.8%)	32 (2.8%)	5 (0.4%)	0.89 [0.77;1.02]	0.0867	
Non-OECD	474	114 (24.1%)	360 (75.9%)	6 (1.3%)	5 (1.1%)	513	133 (25.9%)	380 (74.1%)	7 (1.4%)	6 (1.2%)	0.93 [0.72;1.19]	0.5647	
Treatment dose volume													0.3798
0.5 mg/week	826	246 (29.8%)	580 (70.2%)	17 (2.1%)	6 (0.7%)	824	282 (34.2%)	542 (65.8%)	22 (2.7%)	6 (0.7%)	0.86 [0.72;1.02]	0.0744	
1.0 mg/week	822	246 (29.9%)	576 (70.1%)	13 (1.6%)	4 (0.5%)	825	262 (31.8%)	563 (68.2%)	17 (2.1%)	5 (0.6%)	0.95 [0.80;1.14]	0.6016	
Baseline insulin use													0.6728
No	692	196 (28.3%)	496 (71.7%)	14 (2.0%)	3 (0.4%)	692	213 (30.8%)	479 (69.2%)	16 (2.3%)	6 (0.9%)	0.93 [0.77;1.13]	0.4797	
Yes	956	296 (31.0%)	660 (69.0%)	16 (1.7%)	7 (0.7%)	957	331 (34.6%)	626 (65.4%)	23 (2.4%)	5 (0.5%)	0.88 [0.76;1.03]	0.1221	
Baseline Renal impairment													0.7277
GFR < 30	46	17 (37.0%)	29 (63.0%)	2 (4.3%)	2 (4.3%)	61	27 (44.3%)	34 (55.7%)	2 (3.3%)	1 (1.6%)	0.82 [0.44;1.50]	0.5098	
30 <= GFR	1602	475 (29.7%)	1127 (70.3%)	28 (1.7%)	8 (0.5%)	1588	517 (32.6%)	1071 (67.4%)	37 (2.3%)	10 (0.6%)	0.91 [0.80;1.03]	0.1392	
Evidence of CV disease at screening													0.9465
CV DISEASE	1353	434 (32.1%)	919 (67.9%)	26 (1.9%)	9 (0.7%)	1382	486 (35.2%)	896 (64.8%)	37 (2.7%)	11 (0.8%)	0.91 [0.80;1.03]	0.1454	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events excluding morbidity endpoints - comprehensive approach with PTs only - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator	
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value
CV RISK FACTORS ONLY	295	58 (19.7%)	237 (80.3%)	4 (1.4%)	1 (0.3%)	267	58 (21.7%)	209 (78.3%)	2 (0.7%)	0 (0.0%)	0.92 [0.64;1.32]	0.6551

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

7 Adverse events leading to trial product discontinuation - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	215 (13.0%)	1433 (87.0%)	65 (3.9%)	46 (2.8%)	1649	110 (6.7%)	1539 (93.3%)	79 (4.8%)	50 (3.0%)	2.05 [1.63;2.58]	<0.0001	
Gender													0.2462
Female	635	89 (14.0%)	546 (86.0%)	24 (3.8%)	17 (2.7%)	660	40 (6.1%)	620 (93.9%)	30 (4.5%)	14 (2.1%)	2.43 [1.67;3.53]	<0.0001	
Male	1013	126 (12.4%)	887 (87.6%)	41 (4.0%)	29 (2.9%)	989	70 (7.1%)	919 (92.9%)	49 (5.0%)	36 (3.6%)	1.84 [1.37;2.46]	<0.0001	
Age													0.1216
< 65	855	82 (9.6%)	773 (90.4%)	33 (3.9%)	24 (2.8%)	844	50 (5.9%)	794 (94.1%)	38 (4.5%)	20 (2.4%)	1.66 [1.17;2.37]	0.0045	
65 <=	793	133 (16.8%)	660 (83.2%)	32 (4.0%)	22 (2.8%)	805	60 (7.5%)	745 (92.5%)	41 (5.1%)	30 (3.7%)	2.40 [1.77;3.26]	<0.0001	
HbA1c at baseline (disease severity)													0.5463
< 8.0	595	90 (15.1%)	505 (84.9%)	16 (2.7%)	11 (1.8%)	628	45 (7.2%)	583 (92.8%)	23 (3.7%)	14 (2.2%)	2.24 [1.56;3.20]	<0.0001	
8.0 <=	1053	125 (11.9%)	928 (88.1%)	49 (4.7%)	35 (3.3%)	1021	65 (6.4%)	956 (93.6%)	56 (5.5%)	36 (3.5%)	1.94 [1.44;2.62]	<0.0001	
Region A													0.6468
West Europe	228	52 (22.8%)	176 (77.2%)	7 (3.1%)	5 (2.2%)	205	23 (11.2%)	182 (88.8%)	1 (0.5%)	0 (0.0%)	2.25 [1.38;3.68]	0.0012	
Rest of World	1420	163 (11.5%)	1257 (88.5%)	58 (4.1%)	41 (2.9%)	1444	87 (6.0%)	1357 (94.0%)	78 (5.4%)	50 (3.5%)	1.98 [1.52;2.56]	<0.0001	
Region B													0.6655

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events leading to trial product discontinuation - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	189 (16.1%)	985 (83.9%)	49 (4.2%)	31 (2.6%)	1136	94 (8.3%)	1042 (91.7%)	61 (5.4%)	33 (2.9%)	2.06 [1.61;2.64]	<0.0001	
Non-OECD	474	26 (5.5%)	448 (94.5%)	16 (3.4%)	15 (3.2%)	513	16 (3.1%)	497 (96.9%)	18 (3.5%)	17 (3.3%)	1.78 [0.96;3.32]	0.0694	
Treatment dose volume													0.8871
0.5 mg/week	826	97 (11.7%)	729 (88.3%)	34 (4.1%)	23 (2.8%)	824	48 (5.8%)	776 (94.2%)	44 (5.3%)	27 (3.3%)	2.09 [1.48;2.95]	<0.0001	
1.0 mg/week	822	118 (14.4%)	704 (85.6%)	31 (3.8%)	23 (2.8%)	825	62 (7.5%)	763 (92.5%)	35 (4.2%)	23 (2.8%)	2.02 [1.49;2.75]	<0.0001	
Baseline insulin use													0.7550
No	692	90 (13.0%)	602 (87.0%)	26 (3.8%)	16 (2.3%)	692	48 (6.9%)	644 (93.1%)	30 (4.3%)	20 (2.9%)	1.96 [1.38;2.79]	0.0002	
Yes	956	125 (13.1%)	831 (86.9%)	39 (4.1%)	30 (3.1%)	957	62 (6.5%)	895 (93.5%)	49 (5.1%)	30 (3.1%)	2.11 [1.56;2.86]	<0.0001	
Baseline Renal impairment													0.8274
GFR < 30	46	9 (19.6%)	37 (80.4%)	4 (8.7%)	4 (8.7%)	61	7 (11.5%)	54 (88.5%)	5 (8.2%)	4 (6.6%)	1.85 [0.69;4.97]	0.2212	
30 <= GFR	1602	206 (12.9%)	1396 (87.1%)	61 (3.8%)	42 (2.6%)	1588	103 (6.5%)	1485 (93.5%)	74 (4.7%)	46 (2.9%)	2.07 [1.64;2.63]	<0.0001	
Evidence of CV disease at screening													0.5025
CV DISEASE	1353	185 (13.7%)	1168 (86.3%)	60 (4.4%)	43 (3.2%)	1382	99 (7.2%)	1283 (92.8%)	75 (5.4%)	48 (3.5%)	2.00 [1.57;2.55]	<0.0001	
CV RISK FACTORS ONLY	295	30 (10.2%)	265 (89.8%)	5 (1.7%)	3 (1.0%)	267	11 (4.1%)	256 (95.9%)	4 (1.5%)	2 (0.7%)	2.57 [1.29;5.13]	0.0074	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

8 Hypoglycaemic episodes – serious adverse events - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	17 (1.0%)	1631 (99.0%)	84 (5.1%)	60 (3.6%)	1649	15 (0.9%)	1634 (99.1%)	100 (6.1%)	60 (3.6%)	1.13 [0.57;2.27]	0.7267	
Gender													0.5853
Female	635	7 (1.1%)	628 (98.9%)	31 (4.9%)	21 (3.3%)	660	5 (0.8%)	655 (99.2%)	37 (5.6%)	17 (2.6%)	1.46 [0.46;4.58]	0.5218	
Male	1013	10 (1.0%)	1003 (99.0%)	53 (5.2%)	39 (3.8%)	989	10 (1.0%)	979 (99.0%)	63 (6.4%)	43 (4.3%)	0.97 [0.41;2.34]	0.9519	
Age													0.0772
< 65	855	10 (1.2%)	845 (98.8%)	43 (5.0%)	30 (3.5%)	844	4 (0.5%)	840 (99.5%)	48 (5.7%)	22 (2.6%)	2.48 [0.78;7.89]	0.1255	
65 <=	793	7 (0.9%)	786 (99.1%)	41 (5.2%)	30 (3.8%)	805	11 (1.4%)	794 (98.6%)	52 (6.5%)	38 (4.7%)	0.64 [0.25;1.65]	0.3586	
HbA1c at baseline (disease severity)													0.7749
< 8.0	595	5 (0.8%)	590 (99.2%)	23 (3.9%)	17 (2.9%)	628	4 (0.6%)	624 (99.4%)	30 (4.8%)	18 (2.9%)	1.32 [0.35;4.92]	0.6783	
8.0 <=	1053	12 (1.1%)	1041 (98.9%)	61 (5.8%)	43 (4.1%)	1021	11 (1.1%)	1010 (98.9%)	70 (6.9%)	42 (4.1%)	1.05 [0.46;2.39]	0.9003	
Region A													0.9843
West Europe	228	0 (0.0%)	228 (100%)	12 (5.3%)	9 (3.9%)	205	4 (2.0%)	201 (98.0%)	7 (3.4%)	2 (1.0%)	Not est	Not est	
Rest of World	1420	17 (1.2%)	1403 (98.8%)	72 (5.1%)	51 (3.6%)	1444	11 (0.8%)	1433 (99.2%)	93 (6.4%)	58 (4.0%)	1.57 [0.73;3.35]	0.2444	
Region B													0.7158

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Hypoglycaemic episodes - serious adverse events - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	13 (1.1%)	1161 (98.9%)	67 (5.7%)	44 (3.7%)	1136	12 (1.1%)	1124 (98.9%)	80 (7.0%)	41 (3.6%)	1.05 [0.48;2.30]	0.9071	
Non-OECD	474	4 (0.8%)	470 (99.2%)	17 (3.6%)	16 (3.4%)	513	3 (0.6%)	510 (99.4%)	20 (3.9%)	19 (3.7%)	1.43 [0.32;6.41]	0.6368	
Treatment dose volume													0.0879
0.5 mg/week	826	12 (1.5%)	814 (98.5%)	41 (5.0%)	28 (3.4%)	824	6 (0.7%)	818 (99.3%)	52 (6.3%)	32 (3.9%)	2.00 [0.75;5.32]	0.1672	
1.0 mg/week	822	5 (0.6%)	817 (99.4%)	43 (5.2%)	32 (3.9%)	825	9 (1.1%)	816 (98.9%)	48 (5.8%)	28 (3.4%)	0.56 [0.19;1.66]	0.2920	
Baseline insulin use													0.8075
No	692	4 (0.6%)	688 (99.4%)	34 (4.9%)	20 (2.9%)	692	3 (0.4%)	689 (99.6%)	37 (5.3%)	26 (3.8%)	1.33 [0.30;5.96]	0.7062	
Yes	956	13 (1.4%)	943 (98.6%)	50 (5.2%)	40 (4.2%)	957	12 (1.3%)	945 (98.7%)	63 (6.6%)	34 (3.6%)	1.08 [0.49;2.37]	0.8460	
Baseline Renal impairment													0.9999
GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
30 <= GFR	1602	17 (1.1%)	1585 (98.9%)	79 (4.9%)	55 (3.4%)	1588	15 (0.9%)	1573 (99.1%)	94 (5.9%)	56 (3.5%)	1.12 [0.56;2.24]	0.7480	
Evidence of CV disease at screening													0.4200
CV DISEASE	1353	14 (1.0%)	1339 (99.0%)	77 (5.7%)	56 (4.1%)	1382	14 (1.0%)	1368 (99.0%)	93 (6.7%)	56 (4.1%)	1.02 [0.49;2.14]	0.9594	
CV RISK FACTORS ONLY	295	3 (1.0%)	292 (99.0%)	7 (2.4%)	4 (1.4%)	267	1 (0.4%)	266 (99.6%)	7 (2.6%)	4 (1.5%)	2.71 [0.28;26.07]	0.3870	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

9 Pancreatitis – serious adverse events - pre-defined MedDRA search - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	4 (0.2%)	1644 (99.8%)	87 (5.3%)	62 (3.8%)	1649	8 (0.5%)	1641 (99.5%)	99 (6.0%)	60 (3.6%)	0.50 [0.15;1.66]	0.2560	
Gender													0.9914
Female	635	1 (0.2%)	634 (99.8%)	33 (5.2%)	23 (3.6%)	660	0 (0.0%)	660 (100%)	37 (5.6%)	17 (2.6%)	Not est	Not est	
Male	1013	3 (0.3%)	1010 (99.7%)	54 (5.3%)	39 (3.8%)	989	8 (0.8%)	981 (99.2%)	62 (6.3%)	43 (4.3%)	0.36 [0.10;1.38]	0.1364	
Age													0.2451
< 65	855	3 (0.4%)	852 (99.6%)	45 (5.3%)	32 (3.7%)	844	3 (0.4%)	841 (99.6%)	47 (5.6%)	22 (2.6%)	0.99 [0.20;4.89]	0.9877	
65 <=	793	1 (0.1%)	792 (99.9%)	42 (5.3%)	30 (3.8%)	805	5 (0.6%)	800 (99.4%)	52 (6.5%)	38 (4.7%)	0.20 [0.02;1.73]	0.1439	
HbA1c at baseline (disease severity)													0.9921
< 8.0	595	0 (0.0%)	595 (100%)	24 (4.0%)	17 (2.9%)	628	1 (0.2%)	627 (99.8%)	30 (4.8%)	18 (2.9%)	Not est	Not est	
8.0 <=	1053	4 (0.4%)	1049 (99.6%)	63 (6.0%)	45 (4.3%)	1021	7 (0.7%)	1014 (99.3%)	69 (6.8%)	42 (4.1%)	0.55 [0.16;1.89]	0.3430	
Region A													0.9912
West Europe	228	0 (0.0%)	228 (100%)	12 (5.3%)	9 (3.9%)	205	2 (1.0%)	203 (99.0%)	7 (3.4%)	2 (1.0%)	Not est	Not est	
Rest of World	1420	4 (0.3%)	1416 (99.7%)	75 (5.3%)	53 (3.7%)	1444	6 (0.4%)	1438 (99.6%)	92 (6.4%)	58 (4.0%)	0.68 [0.19;2.39]	0.5431	
Region B													0.9997

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Pancreatitis - serious adverse events - pre-defined MedDRA search - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	4 (0.3%)	1170 (99.7%)	69 (5.9%)	45 (3.8%)	1136	8 (0.7%)	1128 (99.3%)	79 (7.0%)	41 (3.6%)	0.48 [0.15;1.60]	0.2344	
Non-OECD	474	0 (0.0%)	474 (100%)	18 (3.8%)	17 (3.6%)	513	0 (0.0%)	513 (100%)	20 (3.9%)	19 (3.7%)	Not est	Not est	
Treatment dose volume													0.1213
0.5 mg/week	826	3 (0.4%)	823 (99.6%)	44 (5.3%)	30 (3.6%)	824	2 (0.2%)	822 (99.8%)	52 (6.3%)	32 (3.9%)	1.49 [0.25;8.93]	0.6613	
1.0 mg/week	822	1 (0.1%)	821 (99.9%)	43 (5.2%)	32 (3.9%)	825	6 (0.7%)	819 (99.3%)	47 (5.7%)	28 (3.4%)	0.17 [0.02;1.39]	0.0973	
Baseline insulin use													0.5899
No	692	1 (0.1%)	691 (99.9%)	35 (5.1%)	21 (3.0%)	692	1 (0.1%)	691 (99.9%)	37 (5.3%)	26 (3.8%)	1.00 [0.06;15.96]	0.9989	
Yes	956	3 (0.3%)	953 (99.7%)	52 (5.4%)	41 (4.3%)	957	7 (0.7%)	950 (99.3%)	62 (6.5%)	34 (3.6%)	0.43 [0.11;1.65]	0.2180	
Baseline Renal impairment													0.9933
GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	1 (1.6%)	60 (98.4%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
30 <= GFR	1602	4 (0.2%)	1598 (99.8%)	82 (5.1%)	57 (3.6%)	1588	7 (0.4%)	1581 (99.6%)	93 (5.9%)	56 (3.5%)	0.56 [0.17;1.93]	0.3616	
Evidence of CV disease at screening													0.9900
CV DISEASE	1353	3 (0.2%)	1350 (99.8%)	80 (5.9%)	58 (4.3%)	1382	8 (0.6%)	1374 (99.4%)	92 (6.7%)	56 (4.1%)	0.38 [0.10;1.44]	0.1548	
CV RISK FACTORS ONLY	295	1 (0.3%)	294 (99.7%)	7 (2.4%)	4 (1.4%)	267	0 (0.0%)	267 (100%)	7 (2.6%)	4 (1.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

10 Symptomatic hypoglycaemia with blood glucose < 56 mg/dL - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	382 (23.2%)	1266 (76.8%)	74 (4.5%)	53 (3.2%)	1649	355 (21.5%)	1294 (78.5%)	84 (5.1%)	51 (3.1%)	1.11 [0.96;1.28]	0.1692	
Gender													0.0107*
Female	635	173 (27.2%)	462 (72.8%)	29 (4.6%)	20 (3.1%)	660	139 (21.1%)	521 (78.9%)	34 (5.2%)	16 (2.4%)	1.39 [1.11;1.73]	0.0041	
Male	1013	209 (20.6%)	804 (79.4%)	45 (4.4%)	33 (3.3%)	989	216 (21.8%)	773 (78.2%)	50 (5.1%)	35 (3.5%)	0.95 [0.78;1.14]	0.5697	
Age													0.1824
< 65	855	192 (22.5%)	663 (77.5%)	40 (4.7%)	29 (3.4%)	844	192 (22.7%)	652 (77.3%)	38 (4.5%)	17 (2.0%)	1.01 [0.82;1.23]	0.9460	
65 <=	793	190 (24.0%)	603 (76.0%)	34 (4.3%)	24 (3.0%)	805	163 (20.2%)	642 (79.8%)	46 (5.7%)	34 (4.2%)	1.23 [0.99;1.51]	0.0562	
HbA1c at baseline (disease severity)													0.3078
< 8.0	595	129 (21.7%)	466 (78.3%)	21 (3.5%)	16 (2.7%)	628	138 (22.0%)	490 (78.0%)	25 (4.0%)	16 (2.5%)	1.00 [0.79;1.27]	0.9930	
8.0 <=	1053	253 (24.0%)	800 (76.0%)	53 (5.0%)	37 (3.5%)	1021	217 (21.3%)	804 (78.7%)	59 (5.8%)	35 (3.4%)	1.17 [0.98;1.40]	0.0885	
Region A													0.8637
West Europe	228	50 (21.9%)	178 (78.1%)	11 (4.8%)	8 (3.5%)	205	44 (21.5%)	161 (78.5%)	4 (2.0%)	1 (0.5%)	1.07 [0.71;1.61]	0.7398	
Rest of World	1420	332 (23.4%)	1088 (76.6%)	63 (4.4%)	45 (3.2%)	1444	311 (21.5%)	1133 (78.5%)	80 (5.5%)	50 (3.5%)	1.11 [0.95;1.30]	0.1766	
Region B													0.6069

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.

Symptomatic hypoglycaemia with blood glucose < 56 mg/dL - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	274 (23.3%)	900 (76.7%)	62 (5.3%)	41 (3.5%)	1136	253 (22.3%)	883 (77.7%)	67 (5.9%)	35 (3.1%)	1.08 [0.91;1.28]	0.3873	
Non-OECD	474	108 (22.8%)	366 (77.2%)	12 (2.5%)	12 (2.5%)	513	102 (19.9%)	411 (80.1%)	17 (3.3%)	16 (3.1%)	1.17 [0.89;1.54]	0.2483	
Treatment dose volume													0.8448
0.5 mg/week	826	196 (23.7%)	630 (76.3%)	39 (4.7%)	28 (3.4%)	824	179 (21.7%)	645 (78.3%)	42 (5.1%)	28 (3.4%)	1.12 [0.92;1.37]	0.2639	
1.0 mg/week	822	186 (22.6%)	636 (77.4%)	35 (4.3%)	25 (3.0%)	825	176 (21.3%)	649 (78.7%)	42 (5.1%)	23 (2.8%)	1.09 [0.89;1.34]	0.4100	
Baseline insulin use													0.4531
No	692	79 (11.4%)	613 (88.6%)	33 (4.8%)	20 (2.9%)	692	65 (9.4%)	627 (90.6%)	36 (5.2%)	25 (3.6%)	1.24 [0.89;1.72]	0.1950	
Yes	956	303 (31.7%)	653 (68.3%)	41 (4.3%)	33 (3.5%)	957	290 (30.3%)	667 (69.7%)	48 (5.0%)	26 (2.7%)	1.08 [0.92;1.27]	0.3482	
Baseline Renal impairment													0.1618
GFR < 30	46	13 (28.3%)	33 (71.7%)	4 (8.7%)	4 (8.7%)	61	23 (37.7%)	38 (62.3%)	3 (4.9%)	2 (3.3%)	0.69 [0.35;1.37]	0.2882	
30 <= GFR	1602	369 (23.0%)	1233 (77.0%)	70 (4.4%)	49 (3.1%)	1588	332 (20.9%)	1256 (79.1%)	81 (5.1%)	49 (3.1%)	1.14 [0.98;1.32]	0.0899	
Evidence of CV disease at screening													0.0214*
CV DISEASE	1353	304 (22.5%)	1049 (77.5%)	69 (5.1%)	50 (3.7%)	1382	309 (22.4%)	1073 (77.6%)	78 (5.6%)	48 (3.5%)	1.03 [0.88;1.20]	0.7564	
CV RISK FACTORS ONLY	295	78 (26.4%)	217 (73.6%)	5 (1.7%)	3 (1.0%)	267	46 (17.2%)	221 (82.8%)	6 (2.2%)	3 (1.1%)	1.63 [1.14;2.35]	0.0082	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.

11 Neoplasm – serious adverse events - (pre-defined MedDRA-search) - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value interaction
All subjects (total)	1648	64 (3.9%)	1584 (96.1%)	73 (4.4%)	49 (3.0%)	1649	73 (4.4%)	1576 (95.6%)	90 (5.5%)	52 (3.2%)	0.87 [0.62;1.22]	0.4199	
Gender													0.3528
Female	635	24 (3.8%)	611 (96.2%)	27 (4.3%)	18 (2.8%)	660	23 (3.5%)	637 (96.5%)	34 (5.2%)	14 (2.1%)	1.08 [0.61;1.92]	0.7892	
Male	1013	40 (3.9%)	973 (96.1%)	46 (4.5%)	31 (3.1%)	989	50 (5.1%)	939 (94.9%)	56 (5.7%)	38 (3.8%)	0.77 [0.51;1.17]	0.2254	
Age													0.0369*
< 65	855	20 (2.3%)	835 (97.7%)	39 (4.6%)	27 (3.2%)	844	35 (4.1%)	809 (95.9%)	45 (5.3%)	21 (2.5%)	0.56 [0.32;0.96]	0.0368	
65 <=	793	44 (5.5%)	749 (94.5%)	34 (4.3%)	22 (2.8%)	805	38 (4.7%)	767 (95.3%)	45 (5.6%)	31 (3.9%)	1.17 [0.76;1.81]	0.4693	
HbA1c at baseline (disease severity)													0.8838
< 8.0	595	32 (5.4%)	563 (94.6%)	22 (3.7%)	15 (2.5%)	628	39 (6.2%)	589 (93.8%)	23 (3.7%)	12 (1.9%)	0.86 [0.54;1.37]	0.5304	
8.0 <=	1053	32 (3.0%)	1021 (97.0%)	51 (4.8%)	34 (3.2%)	1021	34 (3.3%)	987 (96.7%)	67 (6.6%)	40 (3.9%)	0.91 [0.56;1.47]	0.6861	
Region A													0.0080*
West Europe	228	21 (9.2%)	207 (90.8%)	8 (3.5%)	5 (2.2%)	205	9 (4.4%)	196 (95.6%)	6 (2.9%)	2 (1.0%)	2.19 [1.00;4.78]	0.0494	
Rest of World	1420	43 (3.0%)	1377 (97.0%)	65 (4.6%)	44 (3.1%)	1444	64 (4.4%)	1380 (95.6%)	84 (5.8%)	50 (3.5%)	0.67 [0.46;0.99]	0.0447	
Region B													0.2786

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Neoplasms – serious adverse events - pre-defined MedDRA search - time-to-event analysis - Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	54 (4.6%)	1120 (95.4%)	57 (4.9%)	34 (2.9%)	1136	55 (4.8%)	1081 (95.2%)	71 (6.3%)	34 (3.0%)	0.95 [0.65;1.38]	0.7796	
Non-OECD	474	10 (2.1%)	464 (97.9%)	16 (3.4%)	15 (3.2%)	513	18 (3.5%)	495 (96.5%)	19 (3.7%)	18 (3.5%)	0.59 [0.27;1.28]	0.1801	
Treatment dose volume													0.0565
0.5 mg/week	826	24 (2.9%)	802 (97.1%)	38 (4.6%)	25 (3.0%)	824	39 (4.7%)	785 (95.3%)	46 (5.6%)	27 (3.3%)	0.61 [0.36;1.01]	0.0535	
1.0 mg/week	822	40 (4.9%)	782 (95.1%)	35 (4.3%)	24 (2.9%)	825	34 (4.1%)	791 (95.9%)	44 (5.3%)	25 (3.0%)	1.18 [0.75;1.86]	0.4807	
Baseline insulin use													0.6593
No	692	31 (4.5%)	661 (95.5%)	27 (3.9%)	14 (2.0%)	692	38 (5.5%)	654 (94.5%)	30 (4.3%)	19 (2.7%)	0.81 [0.50;1.30]	0.3762	
Yes	956	33 (3.5%)	923 (96.5%)	46 (4.8%)	35 (3.7%)	957	35 (3.7%)	922 (96.3%)	60 (6.3%)	33 (3.4%)	0.94 [0.58;1.51]	0.7950	
Baseline Renal impairment													0.9998
GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
30 <= GFR	1602	64 (4.0%)	1538 (96.0%)	68 (4.2%)	44 (2.7%)	1588	73 (4.6%)	1515 (95.4%)	84 (5.3%)	48 (3.0%)	0.86 [0.62;1.21]	0.3848	
Evidence of CV disease at screening													0.5818
CV DISEASE	1353	51 (3.8%)	1302 (96.2%)	68 (5.0%)	47 (3.5%)	1382	62 (4.5%)	1320 (95.5%)	86 (6.2%)	51 (3.7%)	0.83 [0.58;1.21]	0.3346	
CV RISK FACTORS ONLY	295	13 (4.4%)	282 (95.6%)	5 (1.7%)	2 (0.7%)	267	11 (4.1%)	256 (95.9%)	4 (1.5%)	1 (0.4%)	1.07 [0.48;2.38]	0.8718	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

12 Injection site reactions – adverse events - pre-defined MedDRA search - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
All subjects (total)	1648	17 (1.0%)	1631 (99.0%)	87 (5.3%)	62 (3.8%)	1649	21 (1.3%)	1628 (98.7%)	99 (6.0%)	59 (3.6%)	0.81 [0.43;1.53]	0.5155	
Gender													0.1169
Female	635	8 (1.3%)	627 (98.7%)	33 (5.2%)	23 (3.6%)	660	5 (0.8%)	655 (99.2%)	37 (5.6%)	17 (2.6%)	1.66 [0.54;5.07]	0.3741	
Male	1013	9 (0.9%)	1004 (99.1%)	54 (5.3%)	39 (3.8%)	989	16 (1.6%)	973 (98.4%)	62 (6.3%)	42 (4.2%)	0.55 [0.24;1.24]	0.1495	
Age													0.6645
< 65	855	7 (0.8%)	848 (99.2%)	45 (5.3%)	32 (3.7%)	844	10 (1.2%)	834 (98.8%)	47 (5.6%)	21 (2.5%)	0.69 [0.26;1.82]	0.4540	
65 <=	793	10 (1.3%)	783 (98.7%)	42 (5.3%)	30 (3.8%)	805	11 (1.4%)	794 (98.6%)	52 (6.5%)	38 (4.7%)	0.92 [0.39;2.17]	0.8488	
HbA1c at baseline (disease severity)													0.2377
< 8.0	595	11 (1.8%)	584 (98.2%)	24 (4.0%)	17 (2.9%)	628	10 (1.6%)	618 (98.4%)	30 (4.8%)	18 (2.9%)	1.16 [0.49;2.74]	0.7303	
8.0 <=	1053	6 (0.6%)	1047 (99.4%)	63 (6.0%)	45 (4.3%)	1021	11 (1.1%)	1010 (98.9%)	69 (6.8%)	41 (4.0%)	0.53 [0.19;1.43]	0.2072	
Region A													0.1555
West Europe	228	4 (1.8%)	224 (98.2%)	12 (5.3%)	9 (3.9%)	205	9 (4.4%)	196 (95.6%)	7 (3.4%)	2 (1.0%)	0.39 [0.12;1.28]	0.1222	
Rest of World	1420	13 (0.9%)	1407 (99.1%)	75 (5.3%)	53 (3.7%)	1444	12 (0.8%)	1432 (99.2%)	92 (6.4%)	57 (3.9%)	1.10 [0.50;2.41]	0.8091	
Region B													0.7443

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 18.0

Injection site reactions - adverse events - pre-defined MedDRA search - time-to-event analysis -Sustain 6 - in-trial - full analysis set

	Sema					Comparator					Sema vs.Comparator		
Subgroup interaction	N	n(%)	nc(%)	nc'(%)	nccr(%)	N	n(%)	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value
OECD	1174	16 (1.4%)	1158 (98.6%)	69 (5.9%)	45 (3.8%)	1136	19 (1.7%)	1117 (98.3%)	79 (7.0%)	40 (3.5%)	0.81 [0.42;1.58]	0.5460	
Non-OECD	474	1 (0.2%)	473 (99.8%)	18 (3.8%)	17 (3.6%)	513	2 (0.4%)	511 (99.6%)	20 (3.9%)	19 (3.7%)	0.54 [0.05;5.94]	0.6130	
Treatment dose volume													0.8051
0.5 mg/week	826	8 (1.0%)	818 (99.0%)	44 (5.3%)	30 (3.6%)	824	9 (1.1%)	815 (98.9%)	52 (6.3%)	32 (3.9%)	0.88 [0.34;2.29]	0.8006	
1.0 mg/week	822	9 (1.1%)	813 (98.9%)	43 (5.2%)	32 (3.9%)	825	12 (1.5%)	813 (98.5%)	47 (5.7%)	27 (3.3%)	0.75 [0.32;1.79]	0.5186	
Baseline insulin use													0.9168
No	692	10 (1.4%)	682 (98.6%)	35 (5.1%)	21 (3.0%)	692	12 (1.7%)	680 (98.3%)	37 (5.3%)	26 (3.8%)	0.83 [0.36;1.93]	0.6684	
Yes	956	7 (0.7%)	949 (99.3%)	52 (5.4%)	41 (4.3%)	957	9 (0.9%)	948 (99.1%)	62 (6.5%)	33 (3.4%)	0.78 [0.29;2.09]	0.6163	
Baseline Renal impairment													0.9838
GFR < 30	46	2 (4.3%)	44 (95.7%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
30 <= GFR	1602	15 (0.9%)	1587 (99.1%)	82 (5.1%)	57 (3.6%)	1588	21 (1.3%)	1567 (98.7%)	93 (5.9%)	55 (3.5%)	0.71 [0.36;1.37]	0.3042	
Evidence of CV disease at screening													0.9834
CV DISEASE	1353	17 (1.3%)	1336 (98.7%)	80 (5.9%)	58 (4.3%)	1382	20 (1.4%)	1362 (98.6%)	92 (6.7%)	55 (4.0%)	0.87 [0.45;1.66]	0.6666	
CV RISK FACTORS ONLY	295	0 (0.0%)	295 (100%)	7 (2.4%)	4 (1.4%)	267	1 (0.4%)	266 (99.6%)	7 (2.6%)	4 (1.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 18.0

SUSTAIN 6 – Subgruppen – Sicherheit – UE nach SOC und PT

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Gastrointestinal disorders	All subjects (total)	1648	849 (51.5%)	799 (48.5%)	42 (2.5%)	29 (1.8%)	1649	584 (35.4%)	1065 (64.6%)	62 (3.8%)	38 (2.3%)	1.73 [1.55;1.92]	<0.0001	
	Gender													0.8576
	Female	635	354 (55.7%)	281 (44.3%)	16 (2.5%)	10 (1.6%)	660	256 (38.8%)	404 (61.2%)	22 (3.3%)	9 (1.4%)	1.71 [1.46;2.01]	<0.0001	
	Male	1013	495 (48.9%)	518 (51.1%)	26 (2.6%)	19 (1.9%)	989	328 (33.2%)	661 (66.8%)	40 (4.0%)	29 (2.9%)	1.75 [1.52;2.01]	<0.0001	
	Age													0.3859
	< 65	855	413 (48.3%)	442 (51.7%)	22 (2.6%)	17 (2.0%)	844	284 (33.6%)	560 (66.4%)	33 (3.9%)	18 (2.1%)	1.65 [1.42;1.92]	<0.0001	
	65 <=	793	436 (55.0%)	357 (45.0%)	20 (2.5%)	12 (1.5%)	805	300 (37.3%)	505 (62.7%)	29 (3.6%)	20 (2.5%)	1.81 [1.56;2.10]	<0.0001	
	HbA1c at baseline (disease severity)													0.8567
	< 8.0	595	331 (55.6%)	264 (44.4%)	10 (1.7%)	8 (1.3%)	628	245 (39.0%)	383 (61.0%)	19 (3.0%)	12 (1.9%)	1.71 [1.45;2.02]	<0.0001	
	8.0 <=	1053	518 (49.2%)	535 (50.8%)	32 (3.0%)	21 (2.0%)	1021	339 (33.2%)	682 (66.8%)	43 (4.2%)	26 (2.5%)	1.75 [1.52;2.00]	<0.0001	
	Region A													0.8374
	West Europe	228	131 (57.5%)	97 (42.5%)	7 (3.1%)	5 (2.2%)	205	84 (41.0%)	121 (59.0%)	2 (1.0%)	1 (0.5%)	1.77 [1.35;2.33]	<0.0001	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Gastrointestinal disorders	Rest of World	1420	718 (50.6%)	702 (49.4%)	35 (2.5%)	24 (1.7%)	1444	500 (34.6%)	944 (65.4%)	60 (4.2%)	37 (2.6%)	1.72 [1.53;1.92]	<0.0001	
	Region B													0.4487
	OECD	1174	657 (56.0%)	517 (44.0%)	31 (2.6%)	18 (1.5%)	1136	456 (40.1%)	680 (59.9%)	48 (4.2%)	25 (2.2%)	1.68 [1.49;1.89]	<0.0001	
	Non-OECD	474	192 (40.5%)	282 (59.5%)	11 (2.3%)	11 (2.3%)	513	128 (25.0%)	385 (75.0%)	14 (2.7%)	13 (2.5%)	1.85 [1.48;2.32]	<0.0001	
	Treatment dose volume													0.3458
	0.5 mg/week	826	419 (50.7%)	407 (49.3%)	20 (2.4%)	14 (1.7%)	824	294 (35.7%)	530 (64.3%)	31 (3.8%)	19 (2.3%)	1.64 [1.41;1.90]	<0.0001	
	1.0 mg/week	822	430 (52.3%)	392 (47.7%)	22 (2.7%)	15 (1.8%)	825	290 (35.2%)	535 (64.8%)	31 (3.8%)	19 (2.3%)	1.82 [1.56;2.11]	<0.0001	
	Baseline insulin use													0.9286
	No	692	339 (49.0%)	353 (51.0%)	17 (2.5%)	9 (1.3%)	692	234 (33.8%)	458 (66.2%)	23 (3.3%)	17 (2.5%)	1.72 [1.45;2.03]	<0.0001	
	Yes	956	510 (53.3%)	446 (46.7%)	25 (2.6%)	20 (2.1%)	957	350 (36.6%)	607 (63.4%)	39 (4.1%)	21 (2.2%)	1.73 [1.51;1.99]	<0.0001	
	Baseline Renal impairment													0.9983
	GFR < 30	46	27 (58.7%)	19 (41.3%)	3 (6.5%)	3 (6.5%)	61	25 (41.0%)	36 (59.0%)	5 (8.2%)	3 (4.9%)	1.73 [1.00;2.98]	0.0486	
	30 <= GFR	1602	822 (51.3%)	780 (48.7%)	39 (2.4%)	26 (1.6%)	1588	559 (35.2%)	1029 (64.8%)	57 (3.6%)	35 (2.2%)	1.73 [1.55;1.93]	<0.0001	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Gastrointestinal disorders	Evidence of CV disease at screening													0.7353
	CV DISEASE	1353	708 (52.3%)	645 (47.7%)	38 (2.8%)	26 (1.9%)	1382	495 (35.8%)	887 (64.2%)	60 (4.3%)	37 (2.7%)	1.74 [1.55;1.96]	<0.0001	
	CV RISK FACTORS ONLY	295	141 (47.8%)	154 (52.2%)	4 (1.4%)	3 (1.0%)	267	89 (33.3%)	178 (66.7%)	2 (0.7%)	1 (0.4%)	1.66 [1.27;2.16]	0.0002	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Injury, poisoning and procedural complications	All subjects (total)	1648	270 (16.4%)	1378 (83.6%)	74 (4.5%)	53 (3.2%)	1649	327 (19.8%)	1322 (80.2%)	74 (4.5%)	42 (2.5%)	0.81 [0.69;0.95]	0.0087	
	Gender													0.0677
	Female	635	126 (19.8%)	509 (80.2%)	28 (4.4%)	19 (3.0%)	660	135 (20.5%)	525 (79.5%)	28 (4.2%)	13 (2.0%)	0.96 [0.75;1.22]	0.7347	
	Male	1013	144 (14.2%)	869 (85.8%)	46 (4.5%)	34 (3.4%)	989	192 (19.4%)	797 (80.6%)	46 (4.7%)	29 (2.9%)	0.71 [0.57;0.88]	0.0018	
	Age													0.5478
	< 65	855	128 (15.0%)	727 (85.0%)	39 (4.6%)	27 (3.2%)	844	161 (19.1%)	683 (80.9%)	38 (4.5%)	17 (2.0%)	0.77 [0.61;0.97]	0.0245	
	65 <=	793	142 (17.9%)	651 (82.1%)	35 (4.4%)	26 (3.3%)	805	166 (20.6%)	639 (79.4%)	36 (4.5%)	25 (3.1%)	0.85 [0.68;1.06]	0.1430	
	HbA1c at baseline (disease severity)													0.1473
	< 8.0	595	90 (15.1%)	505 (84.9%)	19 (3.2%)	14 (2.4%)	628	132 (21.0%)	496 (79.0%)	24 (3.8%)	15 (2.4%)	0.69 [0.53;0.90]	0.0063	
	8.0 <=	1053	180 (17.1%)	873 (82.9%)	55 (5.2%)	39 (3.7%)	1021	195 (19.1%)	826 (80.9%)	50 (4.9%)	27 (2.6%)	0.88 [0.72;1.08]	0.2264	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Injury, poisoning and procedural complications	Region A													0.4777
	West Europe	228	49 (21.5%)	179 (78.5%)	11 (4.8%)	8 (3.5%)	205	47 (22.9%)	158 (77.1%)	5 (2.4%)	1 (0.5%)	0.92 [0.61;1.37]	0.6684	
	Rest of World	1420	221 (15.6%)	1199 (84.4%)	63 (4.4%)	45 (3.2%)	1444	280 (19.4%)	1164 (80.6%)	69 (4.8%)	41 (2.8%)	0.78 [0.66;0.93]	0.0063	
	Region B													0.2916
	OECD	1174	221 (18.8%)	953 (81.2%)	58 (4.9%)	38 (3.2%)	1136	251 (22.1%)	885 (77.9%)	57 (5.0%)	25 (2.2%)	0.83 [0.70;1.00]	0.0491	
	Non-OECD	474	49 (10.3%)	425 (89.7%)	16 (3.4%)	15 (3.2%)	513	76 (14.8%)	437 (85.2%)	17 (3.3%)	17 (3.3%)	0.67 [0.47;0.96]	0.0299	
	Treatment dose volume													0.3481
	0.5 mg/week	826	132 (16.0%)	694 (84.0%)	37 (4.5%)	26 (3.1%)	824	171 (20.8%)	653 (79.2%)	36 (4.4%)	22 (2.7%)	0.75 [0.59;0.94]	0.0116	
	1.0 mg/week	822	138 (16.8%)	684 (83.2%)	37 (4.5%)	27 (3.3%)	825	156 (18.9%)	669 (81.1%)	38 (4.6%)	20 (2.4%)	0.87 [0.69;1.10]	0.2371	
	Baseline insulin use													0.7146
	No	692	100 (14.5%)	592 (85.5%)	31 (4.5%)	17 (2.5%)	692	126 (18.2%)	566 (81.8%)	30 (4.3%)	21 (3.0%)	0.78 [0.60;1.01]	0.0571	
	Yes	956	170 (17.8%)	786 (82.2%)	43 (4.5%)	36 (3.8%)	957	201 (21.0%)	756 (79.0%)	44 (4.6%)	21 (2.2%)	0.82 [0.67;1.01]	0.0644	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Injury, poisoning and procedural complications	Baseline Renal impairment													0.0148*
	GFR < 30	46	1 (2.2%)	45 (97.8%)	5 (10.9%)	5 (10.9%)	61	17 (27.9%)	44 (72.1%)	3 (4.9%)	2 (3.3%)	0.07 [0.01;0.51]	0.0090	
	30 <= GFR	1602	269 (16.8%)	1333 (83.2%)	69 (4.3%)	48 (3.0%)	1588	310 (19.5%)	1278 (80.5%)	71 (4.5%)	40 (2.5%)	0.84 [0.72;0.99]	0.0391	
	Evidence of CV disease at screening													0.2009
	CV DISEASE	1353	235 (17.4%)	1118 (82.6%)	68 (5.0%)	50 (3.7%)	1382	278 (20.1%)	1104 (79.9%)	68 (4.9%)	38 (2.7%)	0.84 [0.71;1.00]	0.0567	
	CV RISK FACTORS ONLY	295	35 (11.9%)	260 (88.1%)	6 (2.0%)	3 (1.0%)	267	49 (18.4%)	218 (81.6%)	6 (2.2%)	4 (1.5%)	0.62 [0.40;0.96]	0.0323	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Metabolism and nutrition disorders	All subjects (total)	1648	446 (27.1%)	1202 (72.9%)	57 (3.5%)	42 (2.5%)	1649	395 (24.0%)	1254 (76.0%)	70 (4.2%)	40 (2.4%)	1.18 [1.03;1.35]	0.0149	
	Gender													0.1306
	Female	635	188 (29.6%)	447 (70.4%)	20 (3.1%)	13 (2.0%)	660	155 (23.5%)	505 (76.5%)	26 (3.9%)	12 (1.8%)	1.34 [1.09;1.66]	0.0063	
	Male	1013	258 (25.5%)	755 (74.5%)	37 (3.7%)	29 (2.9%)	989	240 (24.3%)	749 (75.7%)	44 (4.4%)	28 (2.8%)	1.09 [0.91;1.30]	0.3524	
	Age													0.8963
	< 65	855	219 (25.6%)	636 (74.4%)	31 (3.6%)	22 (2.6%)	844	189 (22.4%)	655 (77.6%)	36 (4.3%)	15 (1.8%)	1.20 [0.98;1.45]	0.0718	
	65 <=	793	227 (28.6%)	566 (71.4%)	26 (3.3%)	20 (2.5%)	805	206 (25.6%)	599 (74.4%)	34 (4.2%)	25 (3.1%)	1.17 [0.97;1.42]	0.0949	
	HbA1c at baseline (disease severity)													0.0356*
	< 8.0	595	155 (26.1%)	440 (73.9%)	14 (2.4%)	11 (1.8%)	628	121 (19.3%)	507 (80.7%)	22 (3.5%)	13 (2.1%)	1.45 [1.14;1.84]	0.0022	
	8.0 <=	1053	291 (27.6%)	762 (72.4%)	43 (4.1%)	31 (2.9%)	1021	274 (26.8%)	747 (73.2%)	48 (4.7%)	27 (2.6%)	1.06 [0.90;1.25]	0.4723	
	Region A													0.0134*

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Metabolism and nutrition disorders	West Europe	228	71 (31.1%)	157 (68.9%)	8 (3.5%)	7 (3.1%)	205	39 (19.0%)	166 (81.0%)	5 (2.4%)	1 (0.5%)	1.87 [1.27;2.77]	0.0016	
	Rest of World	1420	375 (26.4%)	1045 (73.6%)	49 (3.5%)	35 (2.5%)	1444	356 (24.7%)	1088 (75.3%)	65 (4.5%)	39 (2.7%)	1.11 [0.96;1.28]	0.1700	
	Region B													0.4042
	OECD	1174	342 (29.1%)	832 (70.9%)	45 (3.8%)	30 (2.6%)	1136	287 (25.3%)	849 (74.7%)	53 (4.7%)	24 (2.1%)	1.22 [1.04;1.42]	0.0138	
	Non-OECD	474	104 (21.9%)	370 (78.1%)	12 (2.5%)	12 (2.5%)	513	108 (21.1%)	405 (78.9%)	17 (3.3%)	16 (3.1%)	1.07 [0.81;1.40]	0.6389	
	Treatment dose volume													0.4829
	0.5 mg/week	826	246 (29.8%)	580 (70.2%)	26 (3.1%)	18 (2.2%)	824	210 (25.5%)	614 (74.5%)	37 (4.5%)	21 (2.5%)	1.24 [1.03;1.49]	0.0229	
	1.0 mg/week	822	200 (24.3%)	622 (75.7%)	31 (3.8%)	24 (2.9%)	825	185 (22.4%)	640 (77.6%)	33 (4.0%)	19 (2.3%)	1.12 [0.92;1.37]	0.2540	
	Baseline insulin use													0.4416
	No	692	178 (25.7%)	514 (74.3%)	20 (2.9%)	11 (1.6%)	692	166 (24.0%)	526 (76.0%)	32 (4.6%)	22 (3.2%)	1.11 [0.90;1.37]	0.3321	
	Yes	956	268 (28.0%)	688 (72.0%)	37 (3.9%)	31 (3.2%)	957	229 (23.9%)	728 (76.1%)	38 (4.0%)	18 (1.9%)	1.24 [1.04;1.48]	0.0181	
	Baseline Renal impairment													0.6186

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Metabolism and nutrition disorders	GFR < 30	46	13 (28.3%)	33 (71.7%)	4 (8.7%)	4 (8.7%)	61	19 (31.1%)	42 (68.9%)	3 (4.9%)	2 (3.3%)	1.00 [0.49;2.02]	0.9894	
	30 <= GFR	1602	433 (27.0%)	1169 (73.0%)	53 (3.3%)	38 (2.4%)	1588	376 (23.7%)	1212 (76.3%)	67 (4.2%)	38 (2.4%)	1.19 [1.04;1.37]	0.0117	
	Evidence of CV disease at screening													0.9483
	CV DISEASE	1353	370 (27.3%)	983 (72.7%)	52 (3.8%)	39 (2.9%)	1382	335 (24.2%)	1047 (75.8%)	63 (4.6%)	36 (2.6%)	1.18 [1.02;1.37]	0.0261	
	CV RISK FACTORS ONLY	295	76 (25.8%)	219 (74.2%)	5 (1.7%)	3 (1.0%)	267	60 (22.5%)	207 (77.5%)	7 (2.6%)	4 (1.5%)	1.20 [0.85;1.68]	0.2973	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Psychiatric disorders	All subjects (total)	1648	134 (8.1%)	1514 (91.9%)	77 (4.7%)	54 (3.3%)	1649	102 (6.2%)	1547 (93.8%)	90 (5.5%)	54 (3.3%)	1.33 [1.03;1.72]	0.0288	
	Gender													0.7477
	Female	635	58 (9.1%)	577 (90.9%)	30 (4.7%)	21 (3.3%)	660	48 (7.3%)	612 (92.7%)	34 (5.2%)	16 (2.4%)	1.28 [0.87;1.87]	0.2094	
	Male	1013	76 (7.5%)	937 (92.5%)	47 (4.6%)	33 (3.3%)	989	54 (5.5%)	935 (94.5%)	56 (5.7%)	38 (3.8%)	1.39 [0.98;1.97]	0.0638	
	Age													0.2153
	< 65	855	71 (8.3%)	784 (91.7%)	41 (4.8%)	29 (3.4%)	844	45 (5.3%)	799 (94.7%)	43 (5.1%)	21 (2.5%)	1.58 [1.09;2.29]	0.0166	
	65 <=	793	63 (7.9%)	730 (92.1%)	36 (4.5%)	25 (3.2%)	805	57 (7.1%)	748 (92.9%)	47 (5.8%)	33 (4.1%)	1.14 [0.80;1.63]	0.4804	
	HbA1c at baseline (disease severity)													0.4393
	< 8.0	595	45 (7.6%)	550 (92.4%)	22 (3.7%)	16 (2.7%)	628	41 (6.5%)	587 (93.5%)	26 (4.1%)	15 (2.4%)	1.17 [0.76;1.78]	0.4762	
	8.0 <=	1053	89 (8.5%)	964 (91.5%)	55 (5.2%)	38 (3.6%)	1021	61 (6.0%)	960 (94.0%)	64 (6.3%)	39 (3.8%)	1.44 [1.04;1.99]	0.0283	
	Region A													0.8867
	West Europe	228	25 (11.0%)	203 (89.0%)	9 (3.9%)	6 (2.6%)	205	18 (8.8%)	187 (91.2%)	6 (2.9%)	2 (1.0%)	1.27 [0.69;2.33]	0.4350	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	Sema vs.Comparator p-value int.
Psychiatric disorders	Rest of World	1420	109 (7.7%)	1311 (92.3%)	68 (4.8%)	48 (3.4%)	1444	84 (5.8%)	1360 (94.2%)	84 (5.8%)	52 (3.6%)	1.34 [1.01;1.78]	0.0458	
	Region B													0.7798
	OECD	1174	118 (10.1%)	1056 (89.9%)	59 (5.0%)	37 (3.2%)	1136	90 (7.9%)	1046 (92.1%)	70 (6.2%)	35 (3.1%)	1.29 [0.98;1.70]	0.0680	
	Non-OECD	474	16 (3.4%)	458 (96.6%)	18 (3.8%)	17 (3.6%)	513	12 (2.3%)	501 (97.7%)	20 (3.9%)	19 (3.7%)	1.45 [0.68;3.06]	0.3338	
	Treatment dose volume													0.2665
	0.5 mg/week	826	63 (7.6%)	763 (92.4%)	38 (4.6%)	25 (3.0%)	824	55 (6.7%)	769 (93.3%)	46 (5.6%)	30 (3.6%)	1.15 [0.80;1.66]	0.4411	
	1.0 mg/week	822	71 (8.6%)	751 (91.4%)	39 (4.7%)	29 (3.5%)	825	47 (5.7%)	778 (94.3%)	44 (5.3%)	24 (2.9%)	1.54 [1.07;2.23]	0.0207	
	Baseline insulin use													0.4737
	No	692	52 (7.5%)	640 (92.5%)	31 (4.5%)	18 (2.6%)	692	35 (5.1%)	657 (94.9%)	34 (4.9%)	24 (3.5%)	1.51 [0.98;2.32]	0.0598	
	Yes	956	82 (8.6%)	874 (91.4%)	46 (4.8%)	36 (3.8%)	957	67 (7.0%)	890 (93.0%)	56 (5.9%)	30 (3.1%)	1.24 [0.90;1.71]	0.1908	
	Baseline Renal impairment													0.7735
	GFR < 30	46	5 (10.9%)	41 (89.1%)	4 (8.7%)	4 (8.7%)	61	6 (9.8%)	55 (90.2%)	5 (8.2%)	3 (4.9%)	1.13 [0.34;3.70]	0.8401	
	30 <= GFR	1602	129 (8.1%)	1473 (91.9%)	73 (4.6%)	50 (3.1%)	1588	96 (6.0%)	1492 (94.0%)	85 (5.4%)	51 (3.2%)	1.35 [1.04;1.76]	0.0257	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Psychiatric disorders	Evidence of CV disease at screening													0.3540
	CV DISEASE	1353	119 (8.8%)	1234 (91.2%)	71 (5.2%)	51 (3.8%)	1382	88 (6.4%)	1294 (93.6%)	84 (6.1%)	50 (3.6%)	1.40 [1.07;1.85]	0.0157	
	CV RISK FACTORS ONLY	295	15 (5.1%)	280 (94.9%)	6 (2.0%)	3 (1.0%)	267	14 (5.2%)	253 (94.8%)	6 (2.2%)	4 (1.5%)	0.97 [0.47;2.01]	0.9389	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Renal and urinary disorders	All subjects (total)	1648	314 (19.1%)	1334 (80.9%)	60 (3.6%)	37 (2.2%)	1649	376 (22.8%)	1273 (77.2%)	64 (3.9%)	32 (1.9%)	0.82 [0.70;0.95]	0.0084	
	Gender													0.1072
	Female	635	122 (19.2%)	513 (80.8%)	21 (3.3%)	11 (1.7%)	660	130 (19.7%)	530 (80.3%)	26 (3.9%)	10 (1.5%)	0.96 [0.75;1.23]	0.7384	
	Male	1013	192 (19.0%)	821 (81.0%)	39 (3.8%)	26 (2.6%)	989	246 (24.9%)	743 (75.1%)	38 (3.8%)	22 (2.2%)	0.74 [0.61;0.90]	0.0020	
	Age													0.5018
	< 65	855	152 (17.8%)	703 (82.2%)	30 (3.5%)	17 (2.0%)	844	188 (22.3%)	656 (77.7%)	32 (3.8%)	11 (1.3%)	0.78 [0.63;0.96]	0.0204	
	65 <=	793	162 (20.4%)	631 (79.6%)	30 (3.8%)	20 (2.5%)	805	188 (23.4%)	617 (76.6%)	32 (4.0%)	21 (2.6%)	0.86 [0.70;1.06]	0.1611	
	HbA1c at baseline (disease severity)													0.2291
	< 8.0	595	116 (19.5%)	479 (80.5%)	16 (2.7%)	10 (1.7%)	628	132 (21.0%)	496 (79.0%)	18 (2.9%)	10 (1.6%)	0.92 [0.72;1.18]	0.5237	
	8.0 <=	1053	198 (18.8%)	855 (81.2%)	44 (4.2%)	27 (2.6%)	1021	244 (23.9%)	777 (76.1%)	46 (4.5%)	22 (2.2%)	0.76 [0.63;0.92]	0.0044	
	Region A													0.2830
	West Europe	228	42 (18.4%)	186 (81.6%)	9 (3.9%)	6 (2.6%)	205	37 (18.0%)	168 (82.0%)	6 (2.9%)	1 (0.5%)	1.03 [0.66;1.60]	0.9027	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
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MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Renal and urinary disorders	Rest of World	1420	272 (19.2%)	1148 (80.8%)	51 (3.6%)	31 (2.2%)	1444	339 (23.5%)	1105 (76.5%)	58 (4.0%)	31 (2.1%)	0.79 [0.68;0.93]	0.0048	
	Region B													0.0632
	OECD	1174	235 (20.0%)	939 (80.0%)	48 (4.1%)	26 (2.2%)	1136	251 (22.1%)	885 (77.9%)	52 (4.6%)	21 (1.8%)	0.90 [0.75;1.07]	0.2238	
	Non-OECD	474	79 (16.7%)	395 (83.3%)	12 (2.5%)	11 (2.3%)	513	125 (24.4%)	388 (75.6%)	12 (2.3%)	11 (2.1%)	0.65 [0.49;0.87]	0.0030	
	Treatment dose volume													0.5477
	0.5 mg/week	826	160 (19.4%)	666 (80.6%)	30 (3.6%)	17 (2.1%)	824	197 (23.9%)	627 (76.1%)	34 (4.1%)	18 (2.2%)	0.78 [0.63;0.96]	0.0203	
	1.0 mg/week	822	154 (18.7%)	668 (81.3%)	30 (3.6%)	20 (2.4%)	825	179 (21.7%)	646 (78.3%)	30 (3.6%)	14 (1.7%)	0.86 [0.69;1.06]	0.1586	
	Baseline insulin use													0.5196
	No	692	122 (17.6%)	570 (82.4%)	24 (3.5%)	10 (1.4%)	692	154 (22.3%)	538 (77.7%)	24 (3.5%)	15 (2.2%)	0.77 [0.61;0.98]	0.0307	
	Yes	956	192 (20.1%)	764 (79.9%)	36 (3.8%)	27 (2.8%)	957	222 (23.2%)	735 (76.8%)	40 (4.2%)	17 (1.8%)	0.85 [0.70;1.03]	0.1015	
	Baseline Renal impairment													0.6358
	GFR < 30	46	20 (43.5%)	26 (56.5%)	4 (8.7%)	4 (8.7%)	61	28 (45.9%)	33 (54.1%)	1 (1.6%)	1 (1.6%)	0.95 [0.53;1.68]	0.8494	
	30 <= GFR	1602	294 (18.4%)	1308 (81.6%)	56 (3.5%)	33 (2.1%)	1588	348 (21.9%)	1240 (78.1%)	63 (4.0%)	31 (2.0%)	0.82 [0.70;0.96]	0.0119	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Renal and urinary disorders	Evidence of CV disease at screening													0.0792
	CV DISEASE	1353	259 (19.1%)	1094 (80.9%)	53 (3.9%)	33 (2.4%)	1382	332 (24.0%)	1050 (76.0%)	57 (4.1%)	28 (2.0%)	0.78 [0.66;0.91]	0.0021	
	CV RISK FACTORS ONLY	295	55 (18.6%)	240 (81.4%)	7 (2.4%)	4 (1.4%)	267	44 (16.5%)	223 (83.5%)	7 (2.6%)	4 (1.5%)	1.14 [0.77;1.69]	0.5240	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	All subjects (total)	1648	122 (7.4%)	1526 (92.6%)	76 (4.6%)	52 (3.2%)	1649	170 (10.3%)	1479 (89.7%)	88 (5.3%)	51 (3.1%)	0.71 [0.56;0.89]	0.0034	
	Gender													0.9449
	Female	635	41 (6.5%)	594 (93.5%)	28 (4.4%)	19 (3.0%)	660	59 (8.9%)	601 (91.1%)	36 (5.5%)	16 (2.4%)	0.71 [0.48;1.06]	0.0945	
	Male	1013	81 (8.0%)	932 (92.0%)	48 (4.7%)	33 (3.3%)	989	111 (11.2%)	878 (88.8%)	52 (5.3%)	35 (3.5%)	0.70 [0.53;0.93]	0.0145	
	Age													0.9798
	< 65	855	62 (7.3%)	793 (92.7%)	38 (4.4%)	26 (3.0%)	844	86 (10.2%)	758 (89.8%)	42 (5.0%)	19 (2.3%)	0.70 [0.51;0.98]	0.0352	
	65 <=	793	60 (7.6%)	733 (92.4%)	38 (4.8%)	26 (3.3%)	805	84 (10.4%)	721 (89.6%)	46 (5.7%)	32 (4.0%)	0.71 [0.51;0.99]	0.0414	
	HbA1c at baseline (disease severity)													0.0755
	< 8.0	595	54 (9.1%)	541 (90.9%)	19 (3.2%)	12 (2.0%)	628	62 (9.9%)	566 (90.1%)	24 (3.8%)	15 (2.4%)	0.92 [0.64;1.32]	0.6374	
	8.0 <=	1053	68 (6.5%)	985 (93.5%)	57 (5.4%)	40 (3.8%)	1021	108 (10.6%)	913 (89.4%)	64 (6.3%)	36 (3.5%)	0.60 [0.44;0.81]	0.0008	
	Region A													0.5506

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	West Europe	228	13 (5.7%)	215 (94.3%)	12 (5.3%)	9 (3.9%)	205	20 (9.8%)	185 (90.2%)	7 (3.4%)	2 (1.0%)	0.58 [0.29;1.16]	0.1255	
	Rest of World	1420	109 (7.7%)	1311 (92.3%)	64 (4.5%)	43 (3.0%)	1444	150 (10.4%)	1294 (89.6%)	81 (5.6%)	49 (3.4%)	0.73 [0.57;0.93]	0.0109	
	Region B													0.7124
	OECD	1174	98 (8.3%)	1076 (91.7%)	58 (4.9%)	35 (3.0%)	1136	136 (12.0%)	1000 (88.0%)	71 (6.3%)	35 (3.1%)	0.68 [0.53;0.88]	0.0038	
	Non-OECD	474	24 (5.1%)	450 (94.9%)	18 (3.8%)	17 (3.6%)	513	34 (6.6%)	479 (93.4%)	17 (3.3%)	16 (3.1%)	0.76 [0.45;1.28]	0.3040	
	Treatment dose volume													0.6823
	0.5 mg/week	826	60 (7.3%)	766 (92.7%)	37 (4.5%)	24 (2.9%)	824	87 (10.6%)	737 (89.4%)	46 (5.6%)	27 (3.3%)	0.67 [0.48;0.93]	0.0181	
	1.0 mg/week	822	62 (7.5%)	760 (92.5%)	39 (4.7%)	28 (3.4%)	825	83 (10.1%)	742 (89.9%)	42 (5.1%)	24 (2.9%)	0.74 [0.53;1.03]	0.0746	
	Baseline insulin use													0.2227
	No	692	51 (7.4%)	641 (92.6%)	29 (4.2%)	16 (2.3%)	692	60 (8.7%)	632 (91.3%)	33 (4.8%)	22 (3.2%)	0.85 [0.58;1.23]	0.3828	
	Yes	956	71 (7.4%)	885 (92.6%)	47 (4.9%)	36 (3.8%)	957	110 (11.5%)	847 (88.5%)	55 (5.7%)	29 (3.0%)	0.63 [0.47;0.85]	0.0023	
	Baseline Renal impairment													0.2433

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	GFR < 30	46	2 (4.3%)	44 (95.7%)	5 (10.9%)	5 (10.9%)	61	9 (14.8%)	52 (85.2%)	4 (6.6%)	3 (4.9%)	0.29 [0.06;1.34]	0.1121	
	30 <= GFR	1602	120 (7.5%)	1482 (92.5%)	71 (4.4%)	47 (2.9%)	1588	161 (10.1%)	1427 (89.9%)	84 (5.3%)	48 (3.0%)	0.73 [0.57;0.92]	0.0082	
	Evidence of CV disease at screening													0.3055
	CV DISEASE	1353	110 (8.1%)	1243 (91.9%)	69 (5.1%)	48 (3.5%)	1382	160 (11.6%)	1222 (88.4%)	81 (5.9%)	47 (3.4%)	0.69 [0.54;0.88]	0.0026	
	CV RISK FACTORS ONLY	295	12 (4.1%)	283 (95.9%)	7 (2.4%)	4 (1.4%)	267	10 (3.7%)	257 (96.3%)	7 (2.6%)	4 (1.5%)	1.09 [0.47;2.52]	0.8454	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Abdominal discomfort	All subjects (total)	1648	74 (4.5%)	1574 (95.5%)	86 (5.2%)	61 (3.7%)	1649	37 (2.2%)	1612 (97.8%)	99 (6.0%)	60 (3.6%)	2.03 [1.37;3.01]	0.0005	
	Gender													0.0328*
	Female	635	31 (4.9%)	604 (95.1%)	33 (5.2%)	23 (3.6%)	660	24 (3.6%)	636 (96.4%)	36 (5.5%)	17 (2.6%)	1.35 [0.79;2.30]	0.2711	
	Male	1013	43 (4.2%)	970 (95.8%)	53 (5.2%)	38 (3.8%)	989	13 (1.3%)	976 (98.7%)	63 (6.4%)	43 (4.3%)	3.29 [1.77;6.11]	0.0002	
	Age													0.5273
	< 65	855	32 (3.7%)	823 (96.3%)	45 (5.3%)	32 (3.7%)	844	18 (2.1%)	826 (97.9%)	48 (5.7%)	22 (2.6%)	1.77 [0.99;3.15]	0.0529	
	65 <=	793	42 (5.3%)	751 (94.7%)	41 (5.2%)	29 (3.7%)	805	19 (2.4%)	786 (97.6%)	51 (6.3%)	38 (4.7%)	2.28 [1.33;3.93]	0.0028	
	HbA1c at baseline (disease severity)													0.9294
	< 8.0	595	24 (4.0%)	571 (96.0%)	24 (4.0%)	17 (2.9%)	628	13 (2.1%)	615 (97.9%)	30 (4.8%)	18 (2.9%)	1.97 [1.00;3.87]	0.0488	
	8.0 <=	1053	50 (4.7%)	1003 (95.3%)	62 (5.9%)	44 (4.2%)	1021	24 (2.4%)	997 (97.6%)	69 (6.8%)	42 (4.1%)	2.05 [1.26;3.33]	0.0039	
	Region A													0.5035
	West Europe	228	15 (6.6%)	213 (93.4%)	12 (5.3%)	9 (3.9%)	205	5 (2.4%)	200 (97.6%)	7 (3.4%)	2 (1.0%)	2.76 [1.00;7.59]	0.0494	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Abdominal discomfort	Rest of World	1420	59 (4.2%)	1361 (95.8%)	74 (5.2%)	52 (3.7%)	1444	32 (2.2%)	1412 (97.8%)	92 (6.4%)	58 (4.0%)	1.90 [1.23;2.92]	0.0036	
	Region B													0.0277*
	OECD	1174	72 (6.1%)	1102 (93.9%)	68 (5.8%)	44 (3.7%)	1136	31 (2.7%)	1105 (97.3%)	79 (7.0%)	41 (3.6%)	2.30 [1.51;3.50]	0.0001	
	Non-OECD	474	2 (0.4%)	472 (99.6%)	18 (3.8%)	17 (3.6%)	513	6 (1.2%)	507 (98.8%)	20 (3.9%)	19 (3.7%)	0.36 [0.07;1.77]	0.2082	
	Treatment dose volume													0.1308
	0.5 mg/week	826	35 (4.2%)	791 (95.8%)	43 (5.2%)	29 (3.5%)	824	23 (2.8%)	801 (97.2%)	51 (6.2%)	32 (3.9%)	1.53 [0.90;2.59]	0.1137	
	1.0 mg/week	822	39 (4.7%)	783 (95.3%)	43 (5.2%)	32 (3.9%)	825	14 (1.7%)	811 (98.3%)	48 (5.8%)	28 (3.4%)	2.85 [1.55;5.24]	0.0008	
	Baseline insulin use													0.0546
	No	692	36 (5.2%)	656 (94.8%)	34 (4.9%)	20 (2.9%)	692	11 (1.6%)	681 (98.4%)	37 (5.3%)	26 (3.8%)	3.35 [1.70;6.58]	0.0005	
	Yes	956	38 (4.0%)	918 (96.0%)	52 (5.4%)	41 (4.3%)	957	26 (2.7%)	931 (97.3%)	62 (6.5%)	34 (3.6%)	1.47 [0.89;2.42]	0.1300	
	Baseline Renal impairment													0.9788
	GFR < 30	46	2 (4.3%)	44 (95.7%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	72 (4.5%)	1530 (95.5%)	81 (5.1%)	56 (3.5%)	1588	37 (2.3%)	1551 (97.7%)	93 (5.9%)	56 (3.5%)	1.95 [1.31;2.90]	0.0009	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Abdominal discomfort	Evidence of CV disease at screening													0.0479*
	CV DISEASE	1353	67 (5.0%)	1286 (95.0%)	79 (5.8%)	57 (4.2%)	1382	29 (2.1%)	1353 (97.9%)	92 (6.7%)	56 (4.1%)	2.40 [1.55;3.71]	<0.0001	
	CV RISK FACTORS ONLY	295	7 (2.4%)	288 (97.6%)	7 (2.4%)	4 (1.4%)	267	8 (3.0%)	259 (97.0%)	7 (2.6%)	4 (1.5%)	0.79 [0.29;2.17]	0.6439	

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N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Chest pain	All subjects (total)	1648	16 (1.0%)	1632 (99.0%)	87 (5.3%)	62 (3.8%)	1649	32 (1.9%)	1617 (98.1%)	99 (6.0%)	59 (3.6%)	0.50 [0.27;0.91]	0.0226	
	Gender													0.3505
	Female	635	8 (1.3%)	627 (98.7%)	33 (5.2%)	23 (3.6%)	660	12 (1.8%)	648 (98.2%)	37 (5.6%)	17 (2.6%)	0.69 [0.28;1.69]	0.4180	
	Male	1013	8 (0.8%)	1005 (99.2%)	54 (5.3%)	39 (3.8%)	989	20 (2.0%)	969 (98.0%)	62 (6.3%)	42 (4.2%)	0.39 [0.17;0.88]	0.0235	
	Age													0.8050
	< 65	855	9 (1.1%)	846 (98.9%)	45 (5.3%)	32 (3.7%)	844	19 (2.3%)	825 (97.7%)	48 (5.7%)	22 (2.6%)	0.47 [0.21;1.03]	0.0589	
	65 <=	793	7 (0.9%)	786 (99.1%)	42 (5.3%)	30 (3.8%)	805	13 (1.6%)	792 (98.4%)	51 (6.3%)	37 (4.6%)	0.54 [0.22;1.36]	0.1922	
	HbA1c at baseline (disease severity)													0.7806
	< 8.0	595	8 (1.3%)	587 (98.7%)	24 (4.0%)	17 (2.9%)	628	18 (2.9%)	610 (97.1%)	29 (4.6%)	17 (2.7%)	0.47 [0.20;1.07]	0.0716	
	8.0 <=	1053	8 (0.8%)	1045 (99.2%)	63 (6.0%)	45 (4.3%)	1021	14 (1.4%)	1007 (98.6%)	70 (6.9%)	42 (4.1%)	0.55 [0.23;1.32]	0.1798	
	Region A													0.2432
	West Europe	228	3 (1.3%)	225 (98.7%)	12 (5.3%)	9 (3.9%)	205	2 (1.0%)	203 (99.0%)	7 (3.4%)	2 (1.0%)	1.36 [0.23;8.13]	0.7369	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Chest pain	Rest of World	1420	13 (0.9%)	1407 (99.1%)	75 (5.3%)	53 (3.7%)	1444	30 (2.1%)	1414 (97.9%)	92 (6.4%)	57 (3.9%)	0.44 [0.23;0.84]	0.0127	
	Region B													0.0248*
	OECD	1174	11 (0.9%)	1163 (99.1%)	69 (5.9%)	45 (3.8%)	1136	30 (2.6%)	1106 (97.4%)	79 (7.0%)	40 (3.5%)	0.35 [0.18;0.70]	0.0030	
	Non-OECD	474	5 (1.1%)	469 (98.9%)	18 (3.8%)	17 (3.6%)	513	2 (0.4%)	511 (99.6%)	20 (3.9%)	19 (3.7%)	2.70 [0.52;13.93]	0.2348	
	Treatment dose volume													0.1452
	0.5 mg/week	826	4 (0.5%)	822 (99.5%)	44 (5.3%)	30 (3.6%)	824	15 (1.8%)	809 (98.2%)	51 (6.2%)	31 (3.8%)	0.26 [0.09;0.79]	0.0178	
	1.0 mg/week	822	12 (1.5%)	810 (98.5%)	43 (5.2%)	32 (3.9%)	825	17 (2.1%)	808 (97.9%)	48 (5.8%)	28 (3.4%)	0.71 [0.34;1.48]	0.3578	
	Baseline insulin use													0.8340
	No	692	7 (1.0%)	685 (99.0%)	35 (5.1%)	21 (3.0%)	692	13 (1.9%)	679 (98.1%)	36 (5.2%)	25 (3.6%)	0.54 [0.21;1.34]	0.1839	
	Yes	956	9 (0.9%)	947 (99.1%)	52 (5.4%)	41 (4.3%)	957	19 (2.0%)	938 (98.0%)	63 (6.6%)	34 (3.6%)	0.47 [0.21;1.04]	0.0628	
	Baseline Renal impairment													0.9822
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	1 (1.6%)	60 (98.4%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	16 (1.0%)	1586 (99.0%)	82 (5.1%)	57 (3.6%)	1588	31 (2.0%)	1557 (98.0%)	93 (5.9%)	55 (3.5%)	0.51 [0.28;0.93]	0.0280	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Chest pain	Evidence of CV disease at screening													0.2783
	CV DISEASE	1353	14 (1.0%)	1339 (99.0%)	80 (5.9%)	58 (4.3%)	1382	31 (2.2%)	1351 (97.8%)	92 (6.7%)	55 (4.0%)	0.46 [0.24;0.86]	0.0154	
	CV RISK FACTORS ONLY	295	2 (0.7%)	293 (99.3%)	7 (2.4%)	4 (1.4%)	267	1 (0.4%)	266 (99.6%)	7 (2.6%)	4 (1.5%)	1.81 [0.16;19.95]	0.6283	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Constipation	All subjects (total)	1648	127 (7.7%)	1521 (92.3%)	76 (4.6%)	53 (3.2%)	1649	74 (4.5%)	1575 (95.5%)	90 (5.5%)	54 (3.3%)	1.76 [1.32;2.34]	0.0001	
	Gender													0.7206
	Female	635	48 (7.6%)	587 (92.4%)	30 (4.7%)	21 (3.3%)	660	31 (4.7%)	629 (95.3%)	35 (5.3%)	17 (2.6%)	1.65 [1.05;2.59]	0.0295	
	Male	1013	79 (7.8%)	934 (92.2%)	46 (4.5%)	32 (3.2%)	989	43 (4.3%)	946 (95.7%)	55 (5.6%)	37 (3.7%)	1.84 [1.27;2.66]	0.0013	
	Age													0.4075
	< 65	855	55 (6.4%)	800 (93.6%)	38 (4.4%)	27 (3.2%)	844	27 (3.2%)	817 (96.8%)	45 (5.3%)	21 (2.5%)	2.05 [1.30;3.25]	0.0022	
	65 <=	793	72 (9.1%)	721 (90.9%)	38 (4.8%)	26 (3.3%)	805	47 (5.8%)	758 (94.2%)	45 (5.6%)	33 (4.1%)	1.60 [1.11;2.31]	0.0121	
	HbA1c at baseline (disease severity)													0.1963
	< 8.0	595	52 (8.7%)	543 (91.3%)	22 (3.7%)	16 (2.7%)	628	39 (6.2%)	589 (93.8%)	25 (4.0%)	15 (2.4%)	1.45 [0.96;2.20]	0.0791	
	8.0 <=	1053	75 (7.1%)	978 (92.9%)	54 (5.1%)	37 (3.5%)	1021	35 (3.4%)	986 (96.6%)	65 (6.4%)	39 (3.8%)	2.12 [1.42;3.17]	0.0002	
	Region A													0.9757
	West Europe	228	24 (10.5%)	204 (89.5%)	11 (4.8%)	8 (3.5%)	205	13 (6.3%)	192 (93.7%)	6 (2.9%)	2 (1.0%)	1.73 [0.88;3.41]	0.1098	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Constipation	Rest of World	1420	103 (7.3%)	1317 (92.7%)	65 (4.6%)	45 (3.2%)	1444	61 (4.2%)	1383 (95.8%)	84 (5.8%)	52 (3.6%)	1.75 [1.28;2.41]	0.0005	
	Region B													0.2878
	OECD	1174	106 (9.0%)	1068 (91.0%)	59 (5.0%)	37 (3.2%)	1136	65 (5.7%)	1071 (94.3%)	70 (6.2%)	35 (3.1%)	1.62 [1.19;2.21]	0.0021	
	Non-OECD	474	21 (4.4%)	453 (95.6%)	17 (3.6%)	16 (3.4%)	513	9 (1.8%)	504 (98.2%)	20 (3.9%)	19 (3.7%)	2.56 [1.17;5.59]	0.0183	
	Treatment dose volume													0.0377*
	0.5 mg/week	826	47 (5.7%)	779 (94.3%)	38 (4.6%)	26 (3.1%)	824	38 (4.6%)	786 (95.4%)	46 (5.6%)	28 (3.4%)	1.25 [0.81;1.92]	0.3072	
	1.0 mg/week	822	80 (9.7%)	742 (90.3%)	38 (4.6%)	27 (3.3%)	825	36 (4.4%)	789 (95.6%)	44 (5.3%)	26 (3.2%)	2.31 [1.56;3.43]	<0.0001	
	Baseline insulin use													0.3907
	No	692	44 (6.4%)	648 (93.6%)	29 (4.2%)	17 (2.5%)	692	30 (4.3%)	662 (95.7%)	30 (4.3%)	22 (3.2%)	1.50 [0.94;2.38]	0.0879	
	Yes	956	83 (8.7%)	873 (91.3%)	47 (4.9%)	36 (3.8%)	957	44 (4.6%)	913 (95.4%)	60 (6.3%)	32 (3.3%)	1.94 [1.35;2.80]	0.0004	
	Baseline Renal impairment													0.8607
	GFR < 30	46	7 (15.2%)	39 (84.8%)	5 (10.9%)	5 (10.9%)	61	5 (8.2%)	56 (91.8%)	6 (9.8%)	4 (6.6%)	1.96 [0.62;6.19]	0.2493	
	30 <= GFR	1602	120 (7.5%)	1482 (92.5%)	71 (4.4%)	48 (3.0%)	1588	69 (4.3%)	1519 (95.7%)	84 (5.3%)	50 (3.1%)	1.77 [1.31;2.37]	0.0002	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Constipation	Evidence of CV disease at screening													0.9070
	CV DISEASE	1353	111 (8.2%)	1242 (91.8%)	69 (5.1%)	49 (3.6%)	1382	66 (4.8%)	1316 (95.2%)	84 (6.1%)	51 (3.7%)	1.76 [1.30;2.39]	0.0003	
	CV RISK FACTORS ONLY	295	16 (5.4%)	279 (94.6%)	7 (2.4%)	4 (1.4%)	267	8 (3.0%)	259 (97.0%)	6 (2.2%)	3 (1.1%)	1.86 [0.80;4.34]	0.1526	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Depression	All subjects (total)	1648	51 (3.1%)	1597 (96.9%)	85 (5.2%)	60 (3.6%)	1649	33 (2.0%)	1616 (98.0%)	97 (5.9%)	59 (3.6%)	1.55 [1.00;2.41]	0.0487	
	Gender													0.7348
	Female	635	22 (3.5%)	613 (96.5%)	32 (5.0%)	22 (3.5%)	660	16 (2.4%)	644 (97.6%)	35 (5.3%)	16 (2.4%)	1.44 [0.75;2.73]	0.2706	
	Male	1013	29 (2.9%)	984 (97.1%)	53 (5.2%)	38 (3.8%)	989	17 (1.7%)	972 (98.3%)	62 (6.3%)	43 (4.3%)	1.67 [0.92;3.04]	0.0924	
	Age													0.2484
	< 65	855	30 (3.5%)	825 (96.5%)	44 (5.1%)	31 (3.6%)	844	15 (1.8%)	829 (98.2%)	45 (5.3%)	21 (2.5%)	1.99 [1.07;3.70]	0.0293	
	65 <=	793	21 (2.6%)	772 (97.4%)	41 (5.2%)	29 (3.7%)	805	18 (2.2%)	787 (97.8%)	52 (6.5%)	38 (4.7%)	1.18 [0.63;2.22]	0.5988	
	HbA1c at baseline (disease severity)													0.0452*
	< 8.0	595	20 (3.4%)	575 (96.6%)	24 (4.0%)	17 (2.9%)	628	21 (3.3%)	607 (96.7%)	29 (4.6%)	18 (2.9%)	1.00 [0.54;1.85]	0.9944	
	8.0 <=	1053	31 (2.9%)	1022 (97.1%)	61 (5.8%)	43 (4.1%)	1021	12 (1.2%)	1009 (98.8%)	68 (6.7%)	41 (4.0%)	2.53 [1.30;4.92]	0.0064	
	Region A													0.2069
	West Europe	228	9 (3.9%)	219 (96.1%)	11 (4.8%)	8 (3.5%)	205	9 (4.4%)	196 (95.6%)	6 (2.9%)	2 (1.0%)	0.91 [0.36;2.29]	0.8372	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Depression	Rest of World	1420	42 (3.0%)	1378 (97.0%)	74 (5.2%)	52 (3.7%)	1444	24 (1.7%)	1420 (98.3%)	91 (6.3%)	57 (3.9%)	1.79 [1.08;2.95]	0.0234	
	Region B													0.5982
	OECD	1174	45 (3.8%)	1129 (96.2%)	67 (5.7%)	43 (3.7%)	1136	30 (2.6%)	1106 (97.4%)	77 (6.8%)	40 (3.5%)	1.46 [0.92;2.32]	0.1082	
	Non-OECD	474	6 (1.3%)	468 (98.7%)	18 (3.8%)	17 (3.6%)	513	3 (0.6%)	510 (99.4%)	20 (3.9%)	19 (3.7%)	2.16 [0.54;8.65]	0.2753	
	Treatment dose volume													0.8738
	0.5 mg/week	826	27 (3.3%)	799 (96.7%)	42 (5.1%)	28 (3.4%)	824	18 (2.2%)	806 (97.8%)	50 (6.1%)	32 (3.9%)	1.50 [0.83;2.73]	0.1810	
	1.0 mg/week	822	24 (2.9%)	798 (97.1%)	43 (5.2%)	32 (3.9%)	825	15 (1.8%)	810 (98.2%)	47 (5.7%)	27 (3.3%)	1.61 [0.85;3.08]	0.1462	
	Baseline insulin use													0.5665
	No	692	17 (2.5%)	675 (97.5%)	35 (5.1%)	21 (3.0%)	692	13 (1.9%)	679 (98.1%)	36 (5.2%)	26 (3.8%)	1.31 [0.64;2.70]	0.4609	
	Yes	956	34 (3.6%)	922 (96.4%)	50 (5.2%)	39 (4.1%)	957	20 (2.1%)	937 (97.9%)	61 (6.4%)	33 (3.4%)	1.71 [0.99;2.97]	0.0564	
	Baseline Renal impairment													0.5273
	GFR < 30	46	2 (4.3%)	44 (95.7%)	5 (10.9%)	5 (10.9%)	61	3 (4.9%)	58 (95.1%)	5 (8.2%)	3 (4.9%)	0.90 [0.15;5.37]	0.9051	
	30 <= GFR	1602	49 (3.1%)	1553 (96.9%)	80 (5.0%)	55 (3.4%)	1588	30 (1.9%)	1558 (98.1%)	92 (5.8%)	56 (3.5%)	1.63 [1.03;2.56]	0.0359	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Depression	Evidence of CV disease at screening													0.4116
	CV DISEASE	1353	47 (3.5%)	1306 (96.5%)	78 (5.8%)	56 (4.1%)	1382	29 (2.1%)	1353 (97.9%)	90 (6.5%)	55 (4.0%)	1.67 [1.05;2.65]	0.0307	
	CV RISK FACTORS ONLY	295	4 (1.4%)	291 (98.6%)	7 (2.4%)	4 (1.4%)	267	4 (1.5%)	263 (98.5%)	7 (2.6%)	4 (1.5%)	0.90 [0.23;3.61]	0.8856	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema					Comparator					Sema vs.Comparator		
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Flatulence	All subjects (total)	1648	48 (2.9%)	1600 (97.1%)	84 (5.1%)	60 (3.6%)	1649	17 (1.0%)	1632 (99.0%)	98 (5.9%)	59 (3.6%)	2.85 [1.64;4.96]	0.0002	
	Gender													0.9152
	Female	635	13 (2.0%)	622 (98.0%)	32 (5.0%)	22 (3.5%)	660	5 (0.8%)	655 (99.2%)	37 (5.6%)	17 (2.6%)	2.71 [0.97;7.59]	0.0584	
	Male	1013	35 (3.5%)	978 (96.5%)	52 (5.1%)	38 (3.8%)	989	12 (1.2%)	977 (98.8%)	61 (6.2%)	42 (4.2%)	2.89 [1.50;5.57]	0.0015	
	Age													0.1692
	< 65	855	22 (2.6%)	833 (97.4%)	44 (5.1%)	31 (3.6%)	844	11 (1.3%)	833 (98.7%)	47 (5.6%)	22 (2.6%)	1.99 [0.97;4.11]	0.0620	
	65 <=	793	26 (3.3%)	767 (96.7%)	40 (5.0%)	29 (3.7%)	805	6 (0.7%)	799 (99.3%)	51 (6.3%)	37 (4.6%)	4.45 [1.83;10.81]	0.0010	
	HbA1c at baseline (disease severity)													0.3844
	< 8.0	595	11 (1.8%)	584 (98.2%)	24 (4.0%)	17 (2.9%)	628	6 (1.0%)	622 (99.0%)	30 (4.8%)	18 (2.9%)	1.94 [0.72;5.25]	0.1911	
	8.0 <=	1053	37 (3.5%)	1016 (96.5%)	60 (5.7%)	43 (4.1%)	1021	11 (1.1%)	1010 (98.9%)	68 (6.7%)	41 (4.0%)	3.31 [1.69;6.49]	0.0005	
	Region A													0.1499
	West Europe	228	12 (5.3%)	216 (94.7%)	12 (5.3%)	9 (3.9%)	205	7 (3.4%)	198 (96.6%)	6 (2.9%)	2 (1.0%)	1.57 [0.62;3.98]	0.3439	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Flatulence	Rest of World	1420	36 (2.5%)	1384 (97.5%)	72 (5.1%)	51 (3.6%)	1444	10 (0.7%)	1434 (99.3%)	92 (6.4%)	57 (3.9%)	3.69 [1.83;7.44]	0.0003	
	Region B													0.1460
	OECD	1174	44 (3.7%)	1130 (96.3%)	66 (5.6%)	43 (3.7%)	1136	13 (1.1%)	1123 (98.9%)	78 (6.9%)	40 (3.5%)	3.33 [1.79;6.18]	0.0001	
	Non-OECD	474	4 (0.8%)	470 (99.2%)	18 (3.8%)	17 (3.6%)	513	4 (0.8%)	509 (99.2%)	20 (3.9%)	19 (3.7%)	1.08 [0.27;4.31]	0.9143	
	Treatment dose volume													0.0377*
	0.5 mg/week	826	17 (2.1%)	809 (97.9%)	42 (5.1%)	28 (3.4%)	824	11 (1.3%)	813 (98.7%)	50 (6.1%)	31 (3.8%)	1.55 [0.72;3.30]	0.2596	
	1.0 mg/week	822	31 (3.8%)	791 (96.2%)	42 (5.1%)	32 (3.9%)	825	6 (0.7%)	819 (99.3%)	48 (5.8%)	28 (3.4%)	5.28 [2.20;12.65]	0.0002	
	Baseline insulin use													0.9640
	No	692	20 (2.9%)	672 (97.1%)	34 (4.9%)	20 (2.9%)	692	7 (1.0%)	685 (99.0%)	37 (5.3%)	26 (3.8%)	2.90 [1.23;6.85]	0.0154	
	Yes	956	28 (2.9%)	928 (97.1%)	50 (5.2%)	40 (4.2%)	957	10 (1.0%)	947 (99.0%)	61 (6.4%)	33 (3.4%)	2.82 [1.37;5.81]	0.0048	
	Baseline Renal impairment													0.9848
	GFR < 30	46	1 (2.2%)	45 (97.8%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	47 (2.9%)	1555 (97.1%)	79 (4.9%)	55 (3.4%)	1588	17 (1.1%)	1571 (98.9%)	92 (5.8%)	55 (3.5%)	2.77 [1.59;4.82]	0.0003	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Flatulence	Evidence of CV disease at screening													0.5469
	CV DISEASE	1353	39 (2.9%)	1314 (97.1%)	77 (5.7%)	56 (4.1%)	1382	13 (0.9%)	1369 (99.1%)	91 (6.6%)	55 (4.0%)	3.10 [1.65;5.80]	0.0004	
	CV RISK FACTORS ONLY	295	9 (3.1%)	286 (96.9%)	7 (2.4%)	4 (1.4%)	267	4 (1.5%)	263 (98.5%)	7 (2.6%)	4 (1.5%)	2.05 [0.63;6.67]	0.2307	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Insomnia	All subjects (total)	1648	41 (2.5%)	1607 (97.5%)	82 (5.0%)	57 (3.5%)	1649	24 (1.5%)	1625 (98.5%)	97 (5.9%)	58 (3.5%)	1.72 [1.04;2.84]	0.0351	
	Gender													0.5790
	Female	635	21 (3.3%)	614 (96.7%)	31 (4.9%)	21 (3.3%)	660	11 (1.7%)	649 (98.3%)	37 (5.6%)	17 (2.6%)	2.00 [0.97;4.16]	0.0617	
	Male	1013	20 (2.0%)	993 (98.0%)	51 (5.0%)	36 (3.6%)	989	13 (1.3%)	976 (98.7%)	60 (6.1%)	41 (4.1%)	1.51 [0.75;3.03]	0.2502	
	Age													0.1753
	< 65	855	21 (2.5%)	834 (97.5%)	43 (5.0%)	30 (3.5%)	844	8 (0.9%)	836 (99.1%)	47 (5.6%)	22 (2.6%)	2.62 [1.16;5.91]	0.0205	
	65 <=	793	20 (2.5%)	773 (97.5%)	39 (4.9%)	27 (3.4%)	805	16 (2.0%)	789 (98.0%)	50 (6.2%)	36 (4.5%)	1.27 [0.66;2.45]	0.4765	
	HbA1c at baseline (disease severity)													0.4546
	< 8.0	595	11 (1.8%)	584 (98.2%)	23 (3.9%)	16 (2.7%)	628	9 (1.4%)	619 (98.6%)	28 (4.5%)	17 (2.7%)	1.29 [0.54;3.12]	0.5659	
	8.0 <=	1053	30 (2.8%)	1023 (97.2%)	59 (5.6%)	41 (3.9%)	1021	15 (1.5%)	1006 (98.5%)	69 (6.8%)	41 (4.0%)	1.95 [1.05;3.63]	0.0344	
	Region A													0.4306
	West Europe	228	9 (3.9%)	219 (96.1%)	9 (3.9%)	6 (2.6%)	205	3 (1.5%)	202 (98.5%)	6 (2.9%)	2 (1.0%)	2.75 [0.74;10.16]	0.1291	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Insomnia	Rest of World	1420	32 (2.3%)	1388 (97.7%)	73 (5.1%)	51 (3.6%)	1444	21 (1.5%)	1423 (98.5%)	91 (6.3%)	56 (3.9%)	1.56 [0.90;2.70]	0.1159	
	Region B													0.2762
	OECD	1174	37 (3.2%)	1137 (96.8%)	64 (5.5%)	40 (3.4%)	1136	19 (1.7%)	1117 (98.3%)	77 (6.8%)	39 (3.4%)	1.90 [1.09;3.31]	0.0226	
	Non-OECD	474	4 (0.8%)	470 (99.2%)	18 (3.8%)	17 (3.6%)	513	5 (1.0%)	508 (99.0%)	20 (3.9%)	19 (3.7%)	0.86 [0.23;3.21]	0.8241	
	Treatment dose volume													0.0035*
	0.5 mg/week	826	15 (1.8%)	811 (98.2%)	42 (5.1%)	28 (3.4%)	824	18 (2.2%)	806 (97.8%)	50 (6.1%)	31 (3.8%)	0.83 [0.42;1.64]	0.5916	
	1.0 mg/week	822	26 (3.2%)	796 (96.8%)	40 (4.9%)	29 (3.5%)	825	6 (0.7%)	819 (99.3%)	47 (5.7%)	27 (3.3%)	4.41 [1.82;10.71]	0.0011	
	Baseline insulin use													0.0411*
	No	692	21 (3.0%)	671 (97.0%)	33 (4.8%)	19 (2.7%)	692	6 (0.9%)	686 (99.1%)	37 (5.3%)	26 (3.8%)	3.54 [1.43;8.77]	0.0063	
	Yes	956	20 (2.1%)	936 (97.9%)	49 (5.1%)	38 (4.0%)	957	18 (1.9%)	939 (98.1%)	60 (6.3%)	32 (3.3%)	1.11 [0.59;2.11]	0.7391	
	Baseline Renal impairment													0.8674
	GFR < 30	46	1 (2.2%)	45 (97.8%)	4 (8.7%)	4 (8.7%)	61	1 (1.6%)	60 (98.4%)	6 (9.8%)	4 (6.6%)	1.36 [0.09;21.78]	0.8267	
	30 <= GFR	1602	40 (2.5%)	1562 (97.5%)	78 (4.9%)	53 (3.3%)	1588	23 (1.4%)	1565 (98.6%)	91 (5.7%)	54 (3.4%)	1.73 [1.04;2.89]	0.0357	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Insomnia	Evidence of CV disease at screening													0.0871
	CV DISEASE	1353	38 (2.8%)	1315 (97.2%)	75 (5.5%)	53 (3.9%)	1382	19 (1.4%)	1363 (98.6%)	90 (6.5%)	54 (3.9%)	2.06 [1.19;3.57]	0.0101	
	CV RISK FACTORS ONLY	295	3 (1.0%)	292 (99.0%)	7 (2.4%)	4 (1.4%)	267	5 (1.9%)	262 (98.1%)	7 (2.6%)	4 (1.5%)	0.54 [0.13;2.26]	0.3989	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Nausea	All subjects (total)	1648	323 (19.6%)	1325 (80.4%)	65 (3.9%)	48 (2.9%)	1649	129 (7.8%)	1520 (92.2%)	90 (5.5%)	56 (3.4%)	2.69 [2.19;3.30]	<0.0001	
	Gender													0.7618
	Female	635	167 (26.3%)	468 (73.7%)	25 (3.9%)	18 (2.8%)	660	72 (10.9%)	588 (89.1%)	32 (4.8%)	16 (2.4%)	2.65 [2.01;3.50]	<0.0001	
	Male	1013	156 (15.4%)	857 (84.6%)	40 (3.9%)	30 (3.0%)	989	57 (5.8%)	932 (94.2%)	58 (5.9%)	40 (4.0%)	2.83 [2.09;3.83]	<0.0001	
	Age													0.0456*
	< 65	855	156 (18.2%)	699 (81.8%)	33 (3.9%)	27 (3.2%)	844	74 (8.8%)	770 (91.2%)	42 (5.0%)	20 (2.4%)	2.20 [1.67;2.90]	<0.0001	
	65 <=	793	167 (21.1%)	626 (78.9%)	32 (4.0%)	21 (2.6%)	805	55 (6.8%)	750 (93.2%)	48 (6.0%)	36 (4.5%)	3.35 [2.47;4.55]	<0.0001	
	HbA1c at baseline (disease severity)													0.9950
	< 8.0	595	125 (21.0%)	470 (79.0%)	17 (2.9%)	14 (2.4%)	628	53 (8.4%)	575 (91.6%)	28 (4.5%)	18 (2.9%)	2.70 [1.96;3.72]	<0.0001	
	8.0 <=	1053	198 (18.8%)	855 (81.2%)	48 (4.6%)	34 (3.2%)	1021	76 (7.4%)	945 (92.6%)	62 (6.1%)	38 (3.7%)	2.69 [2.07;3.51]	<0.0001	
	Region A													0.6950
	West Europe	228	58 (25.4%)	170 (74.6%)	11 (4.8%)	9 (3.9%)	205	20 (9.8%)	185 (90.2%)	5 (2.4%)	2 (1.0%)	2.94 [1.77;4.89]	<0.0001	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Nausea	Rest of World	1420	265 (18.7%)	1155 (81.3%)	54 (3.8%)	39 (2.7%)	1444	109 (7.5%)	1335 (92.5%)	85 (5.9%)	54 (3.7%)	2.63 [2.10;3.29]	<0.0001	
	Region B													0.9399
	OECD	1174	276 (23.5%)	898 (76.5%)	48 (4.1%)	32 (2.7%)	1136	109 (9.6%)	1027 (90.4%)	70 (6.2%)	37 (3.3%)	2.67 [2.14;3.34]	<0.0001	
	Non-OECD	474	47 (9.9%)	427 (90.1%)	17 (3.6%)	16 (3.4%)	513	20 (3.9%)	493 (96.1%)	20 (3.9%)	19 (3.7%)	2.62 [1.55;4.41]	0.0003	
	Treatment dose volume													0.4000
	0.5 mg/week	826	143 (17.3%)	683 (82.7%)	30 (3.6%)	22 (2.7%)	824	62 (7.5%)	762 (92.5%)	46 (5.6%)	30 (3.6%)	2.45 [1.82;3.30]	<0.0001	
	1.0 mg/week	822	180 (21.9%)	642 (78.1%)	35 (4.3%)	26 (3.2%)	825	67 (8.1%)	758 (91.9%)	44 (5.3%)	26 (3.2%)	2.92 [2.20;3.86]	<0.0001	
	Baseline insulin use													0.7738
	No	692	134 (19.4%)	558 (80.6%)	25 (3.6%)	16 (2.3%)	692	52 (7.5%)	640 (92.5%)	35 (5.1%)	25 (3.6%)	2.78 [2.02;3.84]	<0.0001	
	Yes	956	189 (19.8%)	767 (80.2%)	40 (4.2%)	32 (3.3%)	957	77 (8.0%)	880 (92.0%)	55 (5.7%)	31 (3.2%)	2.62 [2.01;3.42]	<0.0001	
	Baseline Renal impairment													0.0668
	GFR < 30	46	10 (21.7%)	36 (78.3%)	5 (10.9%)	5 (10.9%)	61	11 (18.0%)	50 (82.0%)	5 (8.2%)	3 (4.9%)	1.24 [0.53;2.91]	0.6254	
	30 <= GFR	1602	313 (19.5%)	1289 (80.5%)	60 (3.7%)	43 (2.7%)	1588	118 (7.4%)	1470 (92.6%)	85 (5.4%)	53 (3.3%)	2.82 [2.29;3.49]	<0.0001	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Nausea	Evidence of CV disease at screening													0.9466
	CV DISEASE	1353	277 (20.5%)	1076 (79.5%)	59 (4.4%)	44 (3.3%)	1382	113 (8.2%)	1269 (91.8%)	84 (6.1%)	52 (3.8%)	2.69 [2.16;3.35]	<0.0001	
	CV RISK FACTORS ONLY	295	46 (15.6%)	249 (84.4%)	6 (2.0%)	4 (1.4%)	267	16 (6.0%)	251 (94.0%)	6 (2.2%)	4 (1.5%)	2.75 [1.56;4.86]	0.0005	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Rhinitis	All subjects (total)	1648	6 (0.4%)	1642 (99.6%)	87 (5.3%)	62 (3.8%)	1649	17 (1.0%)	1632 (99.0%)	100 (6.1%)	60 (3.6%)	0.35 [0.14;0.89]	0.0277	
	Gender													0.2639
	Female	635	4 (0.6%)	631 (99.4%)	33 (5.2%)	23 (3.6%)	660	7 (1.1%)	653 (98.9%)	37 (5.6%)	17 (2.6%)	0.59 [0.17;2.02]	0.4022	
	Male	1013	2 (0.2%)	1011 (99.8%)	54 (5.3%)	39 (3.8%)	989	10 (1.0%)	979 (99.0%)	63 (6.4%)	43 (4.3%)	0.19 [0.04;0.89]	0.0344	
	Age													0.5786
	< 65	855	4 (0.5%)	851 (99.5%)	45 (5.3%)	32 (3.7%)	844	9 (1.1%)	835 (98.9%)	48 (5.7%)	22 (2.6%)	0.44 [0.13;1.42]	0.1691	
	65 <=	793	2 (0.3%)	791 (99.7%)	42 (5.3%)	30 (3.8%)	805	8 (1.0%)	797 (99.0%)	52 (6.5%)	38 (4.7%)	0.25 [0.05;1.19]	0.0813	
	HbA1c at baseline (disease severity)													0.0768
	< 8.0	595	1 (0.2%)	594 (99.8%)	24 (4.0%)	17 (2.9%)	628	11 (1.8%)	617 (98.2%)	30 (4.8%)	18 (2.9%)	0.10 [0.01;0.74]	0.0243	
	8.0 <=	1053	5 (0.5%)	1048 (99.5%)	63 (6.0%)	45 (4.3%)	1021	6 (0.6%)	1015 (99.4%)	70 (6.9%)	42 (4.1%)	0.81 [0.25;2.64]	0.7212	
	Region A													0.9880
	West Europe	228	0 (0.0%)	228 (100%)	12 (5.3%)	9 (3.9%)	205	3 (1.5%)	202 (98.5%)	7 (3.4%)	2 (1.0%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Rhinitis	Rest of World	1420	6 (0.4%)	1414 (99.6%)	75 (5.3%)	53 (3.7%)	1444	14 (1.0%)	1430 (99.0%)	93 (6.4%)	58 (4.0%)	0.43 [0.17;1.13]	0.0867	
	Region B													0.3736
	OECD	1174	4 (0.3%)	1170 (99.7%)	69 (5.9%)	45 (3.8%)	1136	14 (1.2%)	1122 (98.8%)	80 (7.0%)	41 (3.6%)	0.28 [0.09;0.84]	0.0229	
	Non-OECD	474	2 (0.4%)	472 (99.6%)	18 (3.8%)	17 (3.6%)	513	3 (0.6%)	510 (99.4%)	20 (3.9%)	19 (3.7%)	0.72 [0.12;4.29]	0.7148	
	Treatment dose volume													0.0061*
	0.5 mg/week	826	1 (0.1%)	825 (99.9%)	44 (5.3%)	30 (3.6%)	824	15 (1.8%)	809 (98.2%)	52 (6.3%)	32 (3.9%)	0.07 [0.01;0.50]	0.0084	
	1.0 mg/week	822	5 (0.6%)	817 (99.4%)	43 (5.2%)	32 (3.9%)	825	2 (0.2%)	823 (99.8%)	48 (5.8%)	28 (3.4%)	2.52 [0.49;12.97]	0.2699	
	Baseline insulin use													0.9052
	No	692	3 (0.4%)	689 (99.6%)	35 (5.1%)	21 (3.0%)	692	9 (1.3%)	683 (98.7%)	37 (5.3%)	26 (3.8%)	0.33 [0.09;1.23]	0.0990	
	Yes	956	3 (0.3%)	953 (99.7%)	52 (5.4%)	41 (4.3%)	957	8 (0.8%)	949 (99.2%)	63 (6.6%)	34 (3.6%)	0.37 [0.10;1.41]	0.1449	
	Baseline Renal impairment													0.9995
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	6 (0.4%)	1596 (99.6%)	82 (5.1%)	57 (3.6%)	1588	17 (1.1%)	1571 (98.9%)	94 (5.9%)	56 (3.5%)	0.35 [0.14;0.88]	0.0262	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Rhinitis	Evidence of CV disease at screening													0.4873
	CV DISEASE	1353	5 (0.4%)	1348 (99.6%)	80 (5.9%)	58 (4.3%)	1382	16 (1.2%)	1366 (98.8%)	93 (6.7%)	56 (4.1%)	0.32 [0.12;0.87]	0.0252	
	CV RISK FACTORS ONLY	295	1 (0.3%)	294 (99.7%)	7 (2.4%)	4 (1.4%)	267	1 (0.4%)	266 (99.6%)	7 (2.6%)	4 (1.5%)	0.90 [0.06;14.44]	0.9425	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Vomiting	All subjects (total)	1648	209 (12.7%)	1439 (87.3%)	73 (4.4%)	51 (3.1%)	1649	77 (4.7%)	1572 (95.3%)	93 (5.6%)	56 (3.4%)	2.85 [2.19;3.70]	<0.0001	
	Gender													0.7123
	Female	635	106 (16.7%)	529 (83.3%)	27 (4.3%)	19 (3.0%)	660	39 (5.9%)	621 (94.1%)	32 (4.8%)	14 (2.1%)	3.02 [2.09;4.36]	<0.0001	
	Male	1013	103 (10.2%)	910 (89.8%)	46 (4.5%)	32 (3.2%)	989	38 (3.8%)	951 (96.2%)	61 (6.2%)	42 (4.2%)	2.74 [1.89;3.98]	<0.0001	
	Age													0.8067
	< 65	855	108 (12.6%)	747 (87.4%)	37 (4.3%)	26 (3.0%)	844	38 (4.5%)	806 (95.5%)	45 (5.3%)	21 (2.5%)	2.94 [2.03;4.26]	<0.0001	
	65 <=	793	101 (12.7%)	692 (87.3%)	36 (4.5%)	25 (3.2%)	805	39 (4.8%)	766 (95.2%)	48 (6.0%)	35 (4.3%)	2.76 [1.90;3.99]	<0.0001	
	HbA1c at baseline (disease severity)													0.6913
	< 8.0	595	80 (13.4%)	515 (86.6%)	19 (3.2%)	13 (2.2%)	628	29 (4.6%)	599 (95.4%)	29 (4.6%)	18 (2.9%)	3.05 [1.99;4.66]	<0.0001	
	8.0 <=	1053	129 (12.3%)	924 (87.7%)	54 (5.1%)	38 (3.6%)	1021	48 (4.7%)	973 (95.3%)	64 (6.3%)	38 (3.7%)	2.73 [1.96;3.81]	<0.0001	
	Region A													0.4967
	West Europe	228	29 (12.7%)	199 (87.3%)	11 (4.8%)	9 (3.9%)	205	12 (5.9%)	193 (94.1%)	7 (3.4%)	2 (1.0%)	2.29 [1.17;4.49]	0.0158	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

Preferred Term	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Vomiting	Rest of World	1420	180 (12.7%)	1240 (87.3%)	62 (4.4%)	42 (3.0%)	1444	65 (4.5%)	1379 (95.5%)	86 (6.0%)	54 (3.7%)	2.95 [2.22;3.92]	<0.0001	
	Region B													0.2159
	OECD	1174	166 (14.1%)	1008 (85.9%)	56 (4.8%)	35 (3.0%)	1136	65 (5.7%)	1071 (94.3%)	75 (6.6%)	39 (3.4%)	2.60 [1.95;3.46]	<0.0001	
	Non-OECD	474	43 (9.1%)	431 (90.9%)	17 (3.6%)	16 (3.4%)	513	12 (2.3%)	501 (97.7%)	18 (3.5%)	17 (3.3%)	4.04 [2.13;7.66]	<0.0001	
	Treatment dose volume													0.0231*
	0.5 mg/week	826	87 (10.5%)	739 (89.5%)	36 (4.4%)	23 (2.8%)	824	43 (5.2%)	781 (94.8%)	48 (5.8%)	29 (3.5%)	2.08 [1.45;3.00]	<0.0001	
	1.0 mg/week	822	122 (14.8%)	700 (85.2%)	37 (4.5%)	28 (3.4%)	825	34 (4.1%)	791 (95.9%)	45 (5.5%)	27 (3.3%)	3.84 [2.62;5.61]	<0.0001	
	Baseline insulin use													0.1498
	No	692	82 (11.8%)	610 (88.2%)	28 (4.0%)	16 (2.3%)	692	23 (3.3%)	669 (96.7%)	36 (5.2%)	25 (3.6%)	3.73 [2.35;5.93]	<0.0001	
	Yes	956	127 (13.3%)	829 (86.7%)	45 (4.7%)	35 (3.7%)	957	54 (5.6%)	903 (94.4%)	57 (6.0%)	31 (3.2%)	2.47 [1.80;3.40]	<0.0001	
	Baseline Renal impairment													0.5461
	GFR < 30	46	12 (26.1%)	34 (73.9%)	4 (8.7%)	4 (8.7%)	61	8 (13.1%)	53 (86.9%)	6 (9.8%)	4 (6.6%)	2.22 [0.91;5.43]	0.0803	
	30 <= GFR	1602	197 (12.3%)	1405 (87.7%)	69 (4.3%)	47 (2.9%)	1588	69 (4.3%)	1519 (95.7%)	87 (5.5%)	52 (3.3%)	2.96 [2.25;3.90]	<0.0001	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Vomiting	Evidence of CV disease at screening													0.5745
	CV DISEASE	1353	179 (13.2%)	1174 (86.8%)	67 (5.0%)	47 (3.5%)	1382	69 (5.0%)	1313 (95.0%)	89 (6.4%)	53 (3.8%)	2.78 [2.11;3.67]	<0.0001	
	CV RISK FACTORS ONLY	295	30 (10.2%)	265 (89.8%)	6 (2.0%)	4 (1.4%)	267	8 (3.0%)	259 (97.0%)	4 (1.5%)	3 (1.1%)	3.53 [1.62;7.69]	0.0015	

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N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.

MedDRA version 20.1

SUSTAIN 6 – Subgruppen – Sicherheit – SUE nach SOC und PT

Serious adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial - full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Gastrointestinal disorders	All subjects (total)	1648	76 (4.6%)	1572 (95.4%)	77 (4.7%)	52 (3.2%)	1649	50 (3.0%)	1599 (97.0%)	95 (5.8%)	56 (3.4%)	1.54 [1.07;2.19]	0.0185	
	Gender													0.5266
	Female	635	32 (5.0%)	603 (95.0%)	27 (4.3%)	17 (2.7%)	660	19 (2.9%)	641 (97.1%)	36 (5.5%)	16 (2.4%)	1.77 [1.00;3.12]	0.0486	
	Male	1013	44 (4.3%)	969 (95.7%)	50 (4.9%)	35 (3.5%)	989	31 (3.1%)	958 (96.9%)	59 (6.0%)	40 (4.0%)	1.40 [0.88;2.21]	0.1529	
	Age													0.1265
	< 65	855	24 (2.8%)	831 (97.2%)	39 (4.6%)	26 (3.0%)	844	22 (2.6%)	822 (97.4%)	46 (5.5%)	21 (2.5%)	1.08 [0.61;1.92]	0.7966	
	65 <=	793	52 (6.6%)	741 (93.4%)	38 (4.8%)	26 (3.3%)	805	28 (3.5%)	777 (96.5%)	49 (6.1%)	35 (4.3%)	1.92 [1.21;3.04]	0.0054	
	HbA1c at baseline (disease severity)													0.3728
	< 8.0	595	33 (5.5%)	562 (94.5%)	21 (3.5%)	14 (2.4%)	628	19 (3.0%)	609 (97.0%)	28 (4.5%)	16 (2.5%)	1.88 [1.07;3.30]	0.0289	
	8.0 <=	1053	43 (4.1%)	1010 (95.9%)	56 (5.3%)	38 (3.6%)	1021	31 (3.0%)	990 (97.0%)	67 (6.6%)	40 (3.9%)	1.35 [0.85;2.14]	0.2064	
	Region A													0.9005
	West Europe	228	11 (4.8%)	217 (95.2%)	11 (4.8%)	8 (3.5%)	205	7 (3.4%)	198 (96.6%)	6 (2.9%)	1 (0.5%)	1.45 [0.56;3.74]	0.4419	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Gastrointestinal disorders	Rest of World	1420	65 (4.6%)	1355 (95.4%)	66 (4.6%)	44 (3.1%)	1444	43 (3.0%)	1401 (97.0%)	89 (6.2%)	55 (3.8%)	1.55 [1.05;2.28]	0.0262	
	Region B													0.7743
	OECD	1174	62 (5.3%)	1112 (94.7%)	60 (5.1%)	36 (3.1%)	1136	41 (3.6%)	1095 (96.4%)	76 (6.7%)	38 (3.3%)	1.48 [1.00;2.19]	0.0519	
	Non-OECD	474	14 (3.0%)	460 (97.0%)	17 (3.6%)	16 (3.4%)	513	9 (1.8%)	504 (98.2%)	19 (3.7%)	18 (3.5%)	1.69 [0.73;3.91]	0.2176	
	Treatment dose volume													0.2893
	0.5 mg/week	826	41 (5.0%)	785 (95.0%)	39 (4.7%)	25 (3.0%)	824	22 (2.7%)	802 (97.3%)	51 (6.2%)	31 (3.8%)	1.87 [1.12;3.14]	0.0177	
	1.0 mg/week	822	35 (4.3%)	787 (95.7%)	38 (4.6%)	27 (3.3%)	825	28 (3.4%)	797 (96.6%)	44 (5.3%)	25 (3.0%)	1.27 [0.77;2.09]	0.3462	
	Baseline insulin use													0.6366
	No	692	35 (5.1%)	657 (94.9%)	30 (4.3%)	16 (2.3%)	692	21 (3.0%)	671 (97.0%)	36 (5.2%)	25 (3.6%)	1.69 [0.99;2.91]	0.0565	
	Yes	956	41 (4.3%)	915 (95.7%)	47 (4.9%)	36 (3.8%)	957	29 (3.0%)	928 (97.0%)	59 (6.2%)	31 (3.2%)	1.42 [0.88;2.29]	0.1459	
	Baseline Renal impairment													0.5889
	GFR < 30	46	3 (6.5%)	43 (93.5%)	5 (10.9%)	5 (10.9%)	61	4 (6.6%)	57 (93.4%)	5 (8.2%)	3 (4.9%)	1.04 [0.23;4.64]	0.9615	
	30 <= GFR	1602	73 (4.6%)	1529 (95.4%)	72 (4.5%)	47 (2.9%)	1588	46 (2.9%)	1542 (97.1%)	90 (5.7%)	53 (3.3%)	1.59 [1.10;2.30]	0.0141	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vsComparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Gastrointestinal disorders	Evidence of CV disease at screening													0.3628
	CV DISEASE	1353	67 (5.0%)	1286 (95.0%)	70 (5.2%)	48 (3.5%)	1382	47 (3.4%)	1335 (96.6%)	89 (6.4%)	53 (3.8%)	1.47 [1.01;2.13]	0.0433	
	CV RISK FACTORS ONLY	295	9 (3.1%)	286 (96.9%)	7 (2.4%)	4 (1.4%)	267	3 (1.1%)	264 (98.9%)	6 (2.2%)	3 (1.1%)	2.76 [0.75;10.20]	0.1278	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	All subjects (total)	1648	87 (5.3%)	1561 (94.7%)	77 (4.7%)	53 (3.2%)	1649	127 (7.7%)	1522 (92.3%)	90 (5.5%)	53 (3.2%)	0.68 [0.52;0.89]	0.0051	
	Gender													0.2901
	Female	635	32 (5.0%)	603 (95.0%)	28 (4.4%)	19 (3.0%)	660	40 (6.1%)	620 (93.9%)	36 (5.5%)	16 (2.4%)	0.83 [0.52;1.32]	0.4231	
	Male	1013	55 (5.4%)	958 (94.6%)	49 (4.8%)	34 (3.4%)	989	87 (8.8%)	902 (91.2%)	54 (5.5%)	37 (3.7%)	0.61 [0.43;0.85]	0.0037	
	Age													0.6399
	< 65	855	45 (5.3%)	810 (94.7%)	39 (4.6%)	27 (3.2%)	844	69 (8.2%)	775 (91.8%)	43 (5.1%)	20 (2.4%)	0.64 [0.44;0.93]	0.0184	
	65 <=	793	42 (5.3%)	751 (94.7%)	38 (4.8%)	26 (3.3%)	805	58 (7.2%)	747 (92.8%)	47 (5.8%)	33 (4.1%)	0.73 [0.49;1.08]	0.1127	
	HbA1c at baseline (disease severity)													0.1988
	< 8.0	595	35 (5.9%)	560 (94.1%)	20 (3.4%)	13 (2.2%)	628	43 (6.8%)	585 (93.2%)	25 (4.0%)	16 (2.5%)	0.85 [0.55;1.33]	0.4892	
	8.0 <=	1053	52 (4.9%)	1001 (95.1%)	57 (5.4%)	40 (3.8%)	1021	84 (8.2%)	937 (91.8%)	65 (6.4%)	37 (3.6%)	0.59 [0.42;0.83]	0.0028	
	Region A													0.5489

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	West Europe	228	9 (3.9%)	219 (96.1%)	12 (5.3%)	9 (3.9%)	205	15 (7.3%)	190 (92.7%)	7 (3.4%)	2 (1.0%)	0.53 [0.23;1.22]	0.1379	
	Rest of World	1420	78 (5.5%)	1342 (94.5%)	65 (4.6%)	44 (3.1%)	1444	112 (7.8%)	1332 (92.2%)	83 (5.7%)	51 (3.5%)	0.70 [0.52;0.93]	0.0152	
	Region B													0.7305
	OECD	1174	68 (5.8%)	1106 (94.2%)	59 (5.0%)	36 (3.1%)	1136	99 (8.7%)	1037 (91.3%)	73 (6.4%)	37 (3.3%)	0.65 [0.48;0.89]	0.0068	
	Non-OECD	474	19 (4.0%)	455 (96.0%)	18 (3.8%)	17 (3.6%)	513	28 (5.5%)	485 (94.5%)	17 (3.3%)	16 (3.1%)	0.73 [0.41;1.31]	0.2962	
	Treatment dose volume													0.7065
	0.5 mg/week	826	47 (5.7%)	779 (94.3%)	38 (4.6%)	25 (3.0%)	824	65 (7.9%)	759 (92.1%)	47 (5.7%)	28 (3.4%)	0.71 [0.49;1.04]	0.0754	
	1.0 mg/week	822	40 (4.9%)	782 (95.1%)	39 (4.7%)	28 (3.4%)	825	62 (7.5%)	763 (92.5%)	43 (5.2%)	25 (3.0%)	0.64 [0.43;0.95]	0.0280	
	Baseline insulin use													0.3293
	No	692	37 (5.3%)	655 (94.7%)	30 (4.3%)	17 (2.5%)	692	46 (6.6%)	646 (93.4%)	34 (4.9%)	23 (3.3%)	0.80 [0.52;1.23]	0.3143	
	Yes	956	50 (5.2%)	906 (94.8%)	47 (4.9%)	36 (3.8%)	957	81 (8.5%)	876 (91.5%)	56 (5.9%)	30 (3.1%)	0.61 [0.43;0.86]	0.0054	
	Baseline Renal impairment													0.9733

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	6 (9.8%)	55 (90.2%)	5 (8.2%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	87 (5.4%)	1515 (94.6%)	72 (4.5%)	48 (3.0%)	1588	121 (7.6%)	1467 (92.4%)	85 (5.4%)	49 (3.1%)	0.70 [0.53;0.93]	0.0126	
	Evidence of CV disease at screening													0.1055
	CV DISEASE	1353	78 (5.8%)	1275 (94.2%)	70 (5.2%)	49 (3.6%)	1382	122 (8.8%)	1260 (91.2%)	83 (6.0%)	49 (3.5%)	0.64 [0.48;0.85]	0.0023	
	CV RISK FACTORS ONLY	295	9 (3.1%)	286 (96.9%)	7 (2.4%)	4 (1.4%)	267	5 (1.9%)	262 (98.1%)	7 (2.6%)	4 (1.5%)	1.64 [0.55;4.88]	0.3779	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Coronary artery disease	All subjects (total)	1648	20 (1.2%)	1628 (98.8%)	81 (4.9%)	57 (3.5%)	1649	7 (0.4%)	1642 (99.6%)	100 (6.1%)	60 (3.6%)	2.86 [1.21;6.77]	0.0166	
	Gender													0.7634
	Female	635	7 (1.1%)	628 (98.9%)	31 (4.9%)	22 (3.5%)	660	3 (0.5%)	657 (99.5%)	37 (5.6%)	17 (2.6%)	2.43 [0.63;9.39]	0.1988	
	Male	1013	13 (1.3%)	1000 (98.7%)	50 (4.9%)	35 (3.5%)	989	4 (0.4%)	985 (99.6%)	63 (6.4%)	43 (4.3%)	3.18 [1.04;9.75]	0.0431	
	Age													0.7404
	< 65	855	13 (1.5%)	842 (98.5%)	43 (5.0%)	31 (3.6%)	844	5 (0.6%)	839 (99.4%)	48 (5.7%)	22 (2.6%)	2.58 [0.92;7.23]	0.0718	
	65 <=	793	7 (0.9%)	786 (99.1%)	38 (4.8%)	26 (3.3%)	805	2 (0.2%)	803 (99.8%)	52 (6.5%)	38 (4.7%)	3.54 [0.74;17.05]	0.1145	
	HbA1c at baseline (disease severity)													0.1509
	< 8.0	595	9 (1.5%)	586 (98.5%)	23 (3.9%)	16 (2.7%)	628	1 (0.2%)	627 (99.8%)	30 (4.8%)	18 (2.9%)	9.54 [1.21;75.26]	0.0324	
	8.0 <=	1053	11 (1.0%)	1042 (99.0%)	58 (5.5%)	41 (3.9%)	1021	6 (0.6%)	1015 (99.4%)	70 (6.9%)	42 (4.1%)	1.78 [0.66;4.80]	0.2573	
	Region A													0.9891
	West Europe	228	1 (0.4%)	227 (99.6%)	11 (4.8%)	8 (3.5%)	205	0 (0.0%)	205 (100%)	7 (3.4%)	2 (1.0%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Coronary artery disease	Rest of World	1420	19 (1.3%)	1401 (98.7%)	70 (4.9%)	49 (3.5%)	1444	7 (0.5%)	1437 (99.5%)	93 (6.4%)	58 (4.0%)	2.76 [1.16;6.57]	0.0216	
	Region B													0.8994
	OECD	1174	17 (1.4%)	1157 (98.6%)	63 (5.4%)	40 (3.4%)	1136	6 (0.5%)	1130 (99.5%)	80 (7.0%)	41 (3.6%)	2.75 [1.09;6.98]	0.0329	
	Non-OECD	474	3 (0.6%)	471 (99.4%)	18 (3.8%)	17 (3.6%)	513	1 (0.2%)	512 (99.8%)	20 (3.9%)	19 (3.7%)	3.22 [0.34;31.00]	0.3106	
	Treatment dose volume													0.4433
	0.5 mg/week	826	11 (1.3%)	815 (98.7%)	41 (5.0%)	28 (3.4%)	824	5 (0.6%)	819 (99.4%)	52 (6.3%)	32 (3.9%)	2.19 [0.76;6.30]	0.1460	
	1.0 mg/week	822	9 (1.1%)	813 (98.9%)	40 (4.9%)	29 (3.5%)	825	2 (0.2%)	823 (99.8%)	48 (5.8%)	28 (3.4%)	4.54 [0.98;21.00]	0.0530	
	Baseline insulin use													0.2368
	No	692	11 (1.6%)	681 (98.4%)	33 (4.8%)	20 (2.9%)	692	2 (0.3%)	690 (99.7%)	37 (5.3%)	26 (3.8%)	5.53 [1.23;24.96]	0.0261	
	Yes	956	9 (0.9%)	947 (99.1%)	48 (5.0%)	37 (3.9%)	957	5 (0.5%)	952 (99.5%)	63 (6.6%)	34 (3.6%)	1.80 [0.60;5.37]	0.2926	
	Baseline Renal impairment													0.9844
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	1 (1.6%)	60 (98.4%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	20 (1.2%)	1582 (98.8%)	76 (4.7%)	52 (3.2%)	1588	6 (0.4%)	1582 (99.6%)	94 (5.9%)	56 (3.5%)	3.31 [1.33;8.24]	0.0102	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Serious adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Coronary artery disease	Evidence of CV disease at screening													0.9996
	CV DISEASE	1353	20 (1.5%)	1333 (98.5%)	74 (5.5%)	53 (3.9%)	1382	7 (0.5%)	1375 (99.5%)	93 (6.7%)	56 (4.1%)	2.93 [1.24;6.92]	0.0145	
	CV RISK FACTORS ONLY	295	0 (0.0%)	295 (100%)	7 (2.4%)	4 (1.4%)	267	0 (0.0%)	267 (100%)	7 (2.6%)	4 (1.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

SUSTAIN 6 – Subgruppen – Sicherheit - UE nach Schweregrad (schwer)

1 Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema					Comparator					Sema vs.Comparator		
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Cardiac disorders	All subjects (total)	1648	104 (6.3%)	1544 (93.7%)	54 (3.3%)	30 (1.8%)	1649	124 (7.5%)	1525 (92.5%)	64 (3.9%)	28 (1.7%)	0.83 [0.64;1.08]	0.1711	
	Gender													0.2890
	Female	635	39 (6.1%)	596 (93.9%)	19 (3.0%)	10 (1.6%)	660	40 (6.1%)	620 (93.9%)	28 (4.2%)	9 (1.4%)	1.01 [0.65;1.57]	0.9734	
	Male	1013	65 (6.4%)	948 (93.6%)	35 (3.5%)	20 (2.0%)	989	84 (8.5%)	905 (91.5%)	36 (3.6%)	19 (1.9%)	0.75 [0.54;1.04]	0.0807	
	Age													0.5902
	< 65	855	53 (6.2%)	802 (93.8%)	27 (3.2%)	15 (1.8%)	844	58 (6.9%)	786 (93.1%)	30 (3.6%)	7 (0.8%)	0.90 [0.62;1.30]	0.5681	
	65 <=	793	51 (6.4%)	742 (93.6%)	27 (3.4%)	15 (1.9%)	805	66 (8.2%)	739 (91.8%)	34 (4.2%)	21 (2.6%)	0.78 [0.54;1.12]	0.1768	
	HbA1c at baseline (disease severity)													0.9574
	< 8.0	595	33 (5.5%)	562 (94.5%)	14 (2.4%)	7 (1.2%)	628	42 (6.7%)	586 (93.3%)	18 (2.9%)	9 (1.4%)	0.82 [0.52;1.30]	0.3986	
	8.0 <=	1053	71 (6.7%)	982 (93.3%)	40 (3.8%)	23 (2.2%)	1021	82 (8.0%)	939 (92.0%)	46 (4.5%)	19 (1.9%)	0.83 [0.61;1.15]	0.2636	
	Region A													0.5585
	West Europe	228	13 (5.7%)	215 (94.3%)	8 (3.5%)	5 (2.2%)	205	17 (8.3%)	188 (91.7%)	5 (2.4%)	1 (0.5%)	0.68 [0.33;1.40]	0.2982	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor. MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Cardiac disorders	Rest of World	1420	91 (6.4%)	1329 (93.6%)	46 (3.2%)	25 (1.8%)	1444	107 (7.4%)	1337 (92.6%)	59 (4.1%)	27 (1.9%)	0.86 [0.65;1.14]	0.2861	
	Region B													0.1885
	OECD	1174	75 (6.4%)	1099 (93.6%)	44 (3.7%)	21 (1.8%)	1136	96 (8.5%)	1040 (91.5%)	56 (4.9%)	21 (1.8%)	0.75 [0.55;1.01]	0.0596	
	Non-OECD	474	29 (6.1%)	445 (93.9%)	10 (2.1%)	9 (1.9%)	513	28 (5.5%)	485 (94.5%)	8 (1.6%)	7 (1.4%)	1.12 [0.67;1.88]	0.6705	
	Treatment dose volume													0.9659
	0.5 mg/week	826	51 (6.2%)	775 (93.8%)	26 (3.1%)	13 (1.6%)	824	61 (7.4%)	763 (92.6%)	33 (4.0%)	16 (1.9%)	0.83 [0.57;1.20]	0.3213	
	1.0 mg/week	822	53 (6.4%)	769 (93.6%)	28 (3.4%)	17 (2.1%)	825	63 (7.6%)	762 (92.4%)	31 (3.8%)	12 (1.5%)	0.84 [0.58;1.21]	0.3428	
	Baseline insulin use													0.8954
	No	692	39 (5.6%)	653 (94.4%)	25 (3.6%)	12 (1.7%)	692	48 (6.9%)	644 (93.1%)	21 (3.0%)	10 (1.4%)	0.81 [0.53;1.24]	0.3408	
	Yes	956	65 (6.8%)	891 (93.2%)	29 (3.0%)	18 (1.9%)	957	76 (7.9%)	881 (92.1%)	43 (4.5%)	18 (1.9%)	0.84 [0.61;1.18]	0.3162	
	Baseline Renal impairment													0.8804
	GFR < 30	46	6 (13.0%)	40 (87.0%)	3 (6.5%)	3 (6.5%)	61	10 (16.4%)	51 (83.6%)	2 (3.3%)	2 (3.3%)	0.78 [0.28;2.15]	0.6328	
	30 <= GFR	1602	98 (6.1%)	1504 (93.9%)	51 (3.2%)	27 (1.7%)	1588	114 (7.2%)	1474 (92.8%)	62 (3.9%)	26 (1.6%)	0.85 [0.65;1.11]	0.2274	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Cardiac disorders	Evidence of CV disease at screening													0.8885
	CV DISEASE	1353	97 (7.2%)	1256 (92.8%)	49 (3.6%)	28 (2.1%)	1382	116 (8.4%)	1266 (91.6%)	58 (4.2%)	25 (1.8%)	0.85 [0.65;1.11]	0.2323	
	CV RISK FACTORS ONLY	295	7 (2.4%)	288 (97.6%)	5 (1.7%)	2 (0.7%)	267	8 (3.0%)	259 (97.0%)	6 (2.2%)	3 (1.1%)	0.79 [0.29;2.17]	0.6436	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Gastrointestinal disorders	All subjects (total)	1648	96 (5.8%)	1552 (94.2%)	74 (4.5%)	52 (3.2%)	1649	33 (2.0%)	1616 (98.0%)	97 (5.9%)	57 (3.5%)	2.99 [2.02;4.44]	<0.0001	
	Gender													0.2260
	Female	635	45 (7.1%)	590 (92.9%)	27 (4.3%)	19 (3.0%)	660	12 (1.8%)	648 (98.2%)	37 (5.6%)	17 (2.6%)	4.02 [2.13;7.61]	<0.0001	
	Male	1013	51 (5.0%)	962 (95.0%)	47 (4.6%)	33 (3.3%)	989	21 (2.1%)	968 (97.9%)	60 (6.1%)	40 (4.0%)	2.43 [1.46;4.04]	0.0006	
	Age													0.9413
	< 65	855	38 (4.4%)	817 (95.6%)	37 (4.3%)	27 (3.2%)	844	13 (1.5%)	831 (98.5%)	48 (5.7%)	22 (2.6%)	2.95 [1.57;5.54]	0.0008	
	65 <=	793	58 (7.3%)	735 (92.7%)	37 (4.7%)	25 (3.2%)	805	20 (2.5%)	785 (97.5%)	49 (6.1%)	35 (4.3%)	3.04 [1.83;5.06]	<0.0001	
	HbA1c at baseline (disease severity)													0.3481
	< 8.0	595	41 (6.9%)	554 (93.1%)	21 (3.5%)	15 (2.5%)	628	18 (2.9%)	610 (97.1%)	28 (4.5%)	16 (2.5%)	2.49 [1.43;4.33]	0.0013	
	8.0 <=	1053	55 (5.2%)	998 (94.8%)	53 (5.0%)	37 (3.5%)	1021	15 (1.5%)	1006 (98.5%)	69 (6.8%)	41 (4.0%)	3.64 [2.06;6.44]	<0.0001	
	Region A													0.2871
	West Europe	228	21 (9.2%)	207 (90.8%)	11 (4.8%)	8 (3.5%)	205	4 (2.0%)	201 (98.0%)	6 (2.9%)	1 (0.5%)	5.03 [1.73;14.65]	0.0031	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs. Comparator HR [95%-CI]	Sema vs. Comparator p-value	p-value int.
Gastrointestinal disorders	Rest of World	1420	75 (5.3%)	1345 (94.7%)	63 (4.4%)	44 (3.1%)	1444	29 (2.0%)	1415 (98.0%)	91 (6.3%)	56 (3.9%)	2.69 [1.75;4.13]	<0.0001	
	Region B													0.1552
	OECD	1174	84 (7.2%)	1090 (92.8%)	56 (4.8%)	35 (3.0%)	1136	25 (2.2%)	1111 (97.8%)	78 (6.9%)	39 (3.4%)	3.37 [2.16;5.27]	<0.0001	
	Non-OECD	474	12 (2.5%)	462 (97.5%)	18 (3.8%)	17 (3.6%)	513	8 (1.6%)	505 (98.4%)	19 (3.7%)	18 (3.5%)	1.63 [0.67;4.00]	0.2825	
	Treatment dose volume													0.6781
	0.5 mg/week	826	45 (5.4%)	781 (94.6%)	38 (4.6%)	26 (3.1%)	824	14 (1.7%)	810 (98.3%)	51 (6.2%)	31 (3.8%)	3.29 [1.81;5.99]	0.0001	
	1.0 mg/week	822	51 (6.2%)	771 (93.8%)	36 (4.4%)	26 (3.2%)	825	19 (2.3%)	806 (97.7%)	46 (5.6%)	26 (3.2%)	2.78 [1.64;4.70]	0.0001	
	Baseline insulin use													0.9644
	No	692	46 (6.6%)	646 (93.4%)	27 (3.9%)	16 (2.3%)	692	16 (2.3%)	676 (97.7%)	36 (5.2%)	25 (3.6%)	2.97 [1.68;5.24]	0.0002	
	Yes	956	50 (5.2%)	906 (94.8%)	47 (4.9%)	36 (3.8%)	957	17 (1.8%)	940 (98.2%)	61 (6.4%)	32 (3.3%)	3.02 [1.74;5.24]	<0.0001	
	Baseline Renal impairment													0.3302
	GFR < 30	46	3 (6.5%)	43 (93.5%)	5 (10.9%)	5 (10.9%)	61	3 (4.9%)	58 (95.1%)	6 (9.8%)	4 (6.6%)	1.39 [0.28;6.88]	0.6870	
	30 <= GFR	1602	93 (5.8%)	1509 (94.2%)	69 (4.3%)	47 (2.9%)	1588	30 (1.9%)	1558 (98.1%)	91 (5.7%)	53 (3.3%)	3.16 [2.09;4.77]	<0.0001	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Gastrointestinal disorders	Evidence of CV disease at screening													0.7337
	CV DISEASE	1353	84 (6.2%)	1269 (93.8%)	68 (5.0%)	48 (3.5%)	1382	30 (2.2%)	1352 (97.8%)	91 (6.6%)	54 (3.9%)	2.94 [1.94;4.47]	<0.0001	
	CV RISK FACTORS ONLY	295	12 (4.1%)	283 (95.9%)	6 (2.0%)	4 (1.4%)	267	3 (1.1%)	264 (98.9%)	6 (2.2%)	3 (1.1%)	3.71 [1.05;13.15]	0.0423	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
General disorders and administration site conditions	All subjects (total)	1648	18 (1.1%)	1630 (98.9%)	79 (4.8%)	54 (3.3%)	1649	17 (1.0%)	1632 (99.0%)	91 (5.5%)	51 (3.1%)	1.06 [0.55;2.05]	0.8655	
	Gender													0.4124
	Female	635	3 (0.5%)	632 (99.5%)	31 (4.9%)	21 (3.3%)	660	5 (0.8%)	655 (99.2%)	35 (5.3%)	15 (2.3%)	0.62 [0.15;2.60]	0.5142	
	Male	1013	15 (1.5%)	998 (98.5%)	48 (4.7%)	33 (3.3%)	989	12 (1.2%)	977 (98.8%)	56 (5.7%)	36 (3.6%)	1.22 [0.57;2.61]	0.6035	
	Age													0.2105
	< 65	855	8 (0.9%)	847 (99.1%)	41 (4.8%)	28 (3.3%)	844	4 (0.5%)	840 (99.5%)	46 (5.5%)	20 (2.4%)	1.98 [0.60;6.56]	0.2661	
	65 <=	793	10 (1.3%)	783 (98.7%)	38 (4.8%)	26 (3.3%)	805	13 (1.6%)	792 (98.4%)	45 (5.6%)	31 (3.9%)	0.78 [0.34;1.78]	0.5535	
	HbA1c at baseline (disease severity)													0.2774
	< 8.0	595	7 (1.2%)	588 (98.8%)	21 (3.5%)	14 (2.4%)	628	4 (0.6%)	624 (99.4%)	28 (4.5%)	16 (2.5%)	1.85 [0.54;6.31]	0.3273	
	8.0 <=	1053	11 (1.0%)	1042 (99.0%)	58 (5.5%)	40 (3.8%)	1021	13 (1.3%)	1008 (98.7%)	63 (6.2%)	35 (3.4%)	0.82 [0.37;1.83]	0.6267	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
General disorders and administration site conditions	Region A													0.3805
	West Europe	228	3 (1.3%)	225 (98.7%)	12 (5.3%)	9 (3.9%)	205	1 (0.5%)	204 (99.5%)	7 (3.4%)	2 (1.0%)	2.74 [0.29;26.38]	0.3819	
	Rest of World	1420	15 (1.1%)	1405 (98.9%)	67 (4.7%)	45 (3.2%)	1444	16 (1.1%)	1428 (98.9%)	84 (5.8%)	49 (3.4%)	0.95 [0.47;1.92]	0.8873	
	Region B													0.3574
	OECD	1174	14 (1.2%)	1160 (98.8%)	64 (5.5%)	40 (3.4%)	1136	15 (1.3%)	1121 (98.7%)	73 (6.4%)	34 (3.0%)	0.90 [0.44;1.87]	0.7859	
	Non-OECD	474	4 (0.8%)	470 (99.2%)	15 (3.2%)	14 (3.0%)	513	2 (0.4%)	511 (99.6%)	18 (3.5%)	17 (3.3%)	2.15 [0.39;11.74]	0.3762	
	Treatment dose volume													0.6048
	0.5 mg/week	826	8 (1.0%)	818 (99.0%)	39 (4.7%)	25 (3.0%)	824	9 (1.1%)	815 (98.9%)	47 (5.7%)	27 (3.3%)	0.88 [0.34;2.29]	0.8004	
	1.0 mg/week	822	10 (1.2%)	812 (98.8%)	40 (4.9%)	29 (3.5%)	825	8 (1.0%)	817 (99.0%)	44 (5.3%)	24 (2.9%)	1.26 [0.50;3.18]	0.6300	
	Baseline insulin use													0.1110
	No	692	9 (1.3%)	683 (98.7%)	31 (4.5%)	17 (2.5%)	692	4 (0.6%)	688 (99.4%)	35 (5.1%)	24 (3.5%)	2.25 [0.69;7.32]	0.1764	
	Yes	956	9 (0.9%)	947 (99.1%)	48 (5.0%)	37 (3.9%)	957	13 (1.4%)	944 (98.6%)	56 (5.9%)	27 (2.8%)	0.69 [0.30;1.62]	0.3954	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vsComparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
General disorders and administration site conditions	Baseline Renal impairment													0.9829
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	2 (3.3%)	59 (96.7%)	4 (6.6%)	2 (3.3%)	Not est	Not est	
	30 <= GFR	1602	18 (1.1%)	1584 (98.9%)	74 (4.6%)	49 (3.1%)	1588	15 (0.9%)	1573 (99.1%)	87 (5.5%)	49 (3.1%)	1.19 [0.60;2.36]	0.6215	
	Evidence of CV disease at screening													0.6527
	CV DISEASE	1353	16 (1.2%)	1337 (98.8%)	72 (5.3%)	50 (3.7%)	1382	16 (1.2%)	1366 (98.8%)	84 (6.1%)	47 (3.4%)	1.02 [0.51;2.04]	0.9532	
	CV RISK FACTORS ONLY	295	2 (0.7%)	293 (99.3%)	7 (2.4%)	4 (1.4%)	267	1 (0.4%)	266 (99.6%)	7 (2.6%)	4 (1.5%)	1.81 [0.16;19.98]	0.6274	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Hepatobiliary disorders	All subjects (total)	1648	17 (1.0%)	1631 (99.0%)	84 (5.1%)	59 (3.6%)	1649	10 (0.6%)	1639 (99.4%)	100 (6.1%)	60 (3.6%)	1.70 [0.78;3.71]	0.1835	
	Gender													0.9730
	Female	635	5 (0.8%)	630 (99.2%)	31 (4.9%)	21 (3.3%)	660	3 (0.5%)	657 (99.5%)	37 (5.6%)	17 (2.6%)	1.72 [0.41;7.22]	0.4553	
	Male	1013	12 (1.2%)	1001 (98.8%)	53 (5.2%)	38 (3.8%)	989	7 (0.7%)	982 (99.3%)	63 (6.4%)	43 (4.3%)	1.67 [0.66;4.25]	0.2782	
	Age													0.5326
	< 65	855	9 (1.1%)	846 (98.9%)	43 (5.0%)	30 (3.5%)	844	4 (0.5%)	840 (99.5%)	48 (5.7%)	22 (2.6%)	2.23 [0.69;7.23]	0.1825	
	65 <=	793	8 (1.0%)	785 (99.0%)	41 (5.2%)	29 (3.7%)	805	6 (0.7%)	799 (99.3%)	52 (6.5%)	38 (4.7%)	1.35 [0.47;3.88]	0.5825	
	HbA1c at baseline (disease severity)													0.5192
	< 8.0	595	6 (1.0%)	589 (99.0%)	23 (3.9%)	16 (2.7%)	628	5 (0.8%)	623 (99.2%)	30 (4.8%)	18 (2.9%)	1.26 [0.39;4.14]	0.6991	
	8.0 <=	1053	11 (1.0%)	1042 (99.0%)	61 (5.8%)	43 (4.1%)	1021	5 (0.5%)	1016 (99.5%)	70 (6.9%)	42 (4.1%)	2.13 [0.74;6.13]	0.1606	
	Region A													0.9858
	West Europe	228	0 (0.0%)	228 (100%)	12 (5.3%)	9 (3.9%)	205	2 (1.0%)	203 (99.0%)	7 (3.4%)	2 (1.0%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Hepatobiliary disorders	Rest of World	1420	17 (1.2%)	1403 (98.8%)	72 (5.1%)	50 (3.5%)	1444	8 (0.6%)	1436 (99.4%)	93 (6.4%)	58 (4.0%)	2.16 [0.93;5.00]	0.0729	
	Region B													0.9612
	OECD	1174	14 (1.2%)	1160 (98.8%)	66 (5.6%)	42 (3.6%)	1136	8 (0.7%)	1128 (99.3%)	80 (7.0%)	41 (3.6%)	1.69 [0.71;4.04]	0.2341	
	Non-OECD	474	3 (0.6%)	471 (99.4%)	18 (3.8%)	17 (3.6%)	513	2 (0.4%)	511 (99.6%)	20 (3.9%)	19 (3.7%)	1.61 [0.27;9.65]	0.6006	
	Treatment dose volume													0.2936
	0.5 mg/week	826	12 (1.5%)	814 (98.5%)	42 (5.1%)	28 (3.4%)	824	5 (0.6%)	819 (99.4%)	52 (6.3%)	32 (3.9%)	2.39 [0.84;6.78]	0.1017	
	1.0 mg/week	822	5 (0.6%)	817 (99.4%)	42 (5.1%)	31 (3.8%)	825	5 (0.6%)	820 (99.4%)	48 (5.8%)	28 (3.4%)	1.00 [0.29;3.46]	0.9962	
	Baseline insulin use													0.5633
	No	692	7 (1.0%)	685 (99.0%)	34 (4.9%)	20 (2.9%)	692	3 (0.4%)	689 (99.6%)	37 (5.3%)	26 (3.8%)	2.33 [0.60;9.02]	0.2200	
	Yes	956	10 (1.0%)	946 (99.0%)	50 (5.2%)	39 (4.1%)	957	7 (0.7%)	950 (99.3%)	63 (6.6%)	34 (3.6%)	1.43 [0.54;3.75]	0.4697	
	Baseline Renal impairment													0.9997
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	17 (1.1%)	1585 (98.9%)	79 (4.9%)	54 (3.4%)	1588	10 (0.6%)	1578 (99.4%)	94 (5.9%)	56 (3.5%)	1.68 [0.77;3.67]	0.1920	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Hepatobiliary disorders	Evidence of CV disease at screening													0.9854
	CV DISEASE	1353	14 (1.0%)	1339 (99.0%)	77 (5.7%)	55 (4.1%)	1382	10 (0.7%)	1372 (99.3%)	93 (6.7%)	56 (4.1%)	1.43 [0.63;3.21]	0.3904	
	CV RISK FACTORS ONLY	295	3 (1.0%)	292 (99.0%)	7 (2.4%)	4 (1.4%)	267	0 (0.0%)	267 (100%)	7 (2.6%)	4 (1.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs. Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Infections and infestations	All subjects (total)	1648	69 (4.2%)	1579 (95.8%)	74 (4.5%)	49 (3.0%)	1649	88 (5.3%)	1561 (94.7%)	83 (5.0%)	47 (2.9%)	0.78 [0.57;1.07]	0.1277	
	Gender													0.1265
	Female	635	29 (4.6%)	606 (95.4%)	28 (4.4%)	18 (2.8%)	660	28 (4.2%)	632 (95.8%)	30 (4.5%)	12 (1.8%)	1.08 [0.64;1.81]	0.7736	
	Male	1013	40 (3.9%)	973 (96.1%)	46 (4.5%)	31 (3.1%)	989	60 (6.1%)	929 (93.9%)	53 (5.4%)	35 (3.5%)	0.65 [0.43;0.97]	0.0331	
	Age													0.5942
	< 65	855	28 (3.3%)	827 (96.7%)	40 (4.7%)	27 (3.2%)	844	39 (4.6%)	805 (95.4%)	40 (4.7%)	17 (2.0%)	0.71 [0.44;1.15]	0.1665	
	65 <=	793	41 (5.2%)	752 (94.8%)	34 (4.3%)	22 (2.8%)	805	49 (6.1%)	756 (93.9%)	43 (5.3%)	30 (3.7%)	0.84 [0.56;1.28]	0.4246	
	HbA1c at baseline (disease severity)													0.1485
	< 8.0	595	25 (4.2%)	570 (95.8%)	21 (3.5%)	14 (2.4%)	628	24 (3.8%)	604 (96.2%)	29 (4.6%)	17 (2.7%)	1.10 [0.63;1.92]	0.7463	
	8.0 <=	1053	44 (4.2%)	1009 (95.8%)	53 (5.0%)	35 (3.3%)	1021	64 (6.3%)	957 (93.7%)	54 (5.3%)	30 (2.9%)	0.66 [0.45;0.98]	0.0372	
	Region A													0.1327

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema					Comparator					Sema vs.Comparator		
		N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Infections and infestations	West Europe	228	16 (7.0%)	212 (93.0%)	10 (4.4%)	7 (3.1%)	205	11 (5.4%)	194 (94.6%)	7 (3.4%)	2 (1.0%)	1.33 [0.62;2.87]	0.4667	
	Rest of World	1420	53 (3.7%)	1367 (96.3%)	64 (4.5%)	42 (3.0%)	1444	77 (5.3%)	1367 (94.7%)	76 (5.3%)	45 (3.1%)	0.70 [0.49;0.99]	0.0425	
	Region B													0.6649
	OECD	1174	55 (4.7%)	1119 (95.3%)	59 (5.0%)	35 (3.0%)	1136	71 (6.3%)	1065 (93.8%)	67 (5.9%)	32 (2.8%)	0.75 [0.53;1.06]	0.1047	
	Non-OECD	474	14 (3.0%)	460 (97.0%)	15 (3.2%)	14 (3.0%)	513	17 (3.3%)	496 (96.7%)	16 (3.1%)	15 (2.9%)	0.89 [0.44;1.80]	0.7461	
	Treatment dose volume													0.5961
	0.5 mg/week	826	35 (4.2%)	791 (95.8%)	38 (4.6%)	24 (2.9%)	824	48 (5.8%)	776 (94.2%)	46 (5.6%)	27 (3.3%)	0.72 [0.47;1.12]	0.1420	
	1.0 mg/week	822	34 (4.1%)	788 (95.9%)	36 (4.4%)	25 (3.0%)	825	40 (4.8%)	785 (95.2%)	37 (4.5%)	20 (2.4%)	0.86 [0.54;1.35]	0.5048	
	Baseline insulin use													0.3975
	No	692	28 (4.0%)	664 (96.0%)	33 (4.8%)	19 (2.7%)	692	30 (4.3%)	662 (95.7%)	34 (4.9%)	23 (3.3%)	0.93 [0.56;1.56]	0.7938	
	Yes	956	41 (4.3%)	915 (95.7%)	41 (4.3%)	30 (3.1%)	957	58 (6.1%)	899 (93.9%)	49 (5.1%)	24 (2.5%)	0.70 [0.47;1.05]	0.0861	
	Baseline Renal impairment													0.7191

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Infections and infestations	GFR < 30	46	3 (6.5%)	43 (93.5%)	4 (8.7%)	4 (8.7%)	61	4 (6.6%)	57 (93.4%)	4 (6.6%)	2 (3.3%)	1.03 [0.23;4.59]	0.9709	
	30 <= GFR	1602	66 (4.1%)	1536 (95.9%)	70 (4.4%)	45 (2.8%)	1588	84 (5.3%)	1504 (94.7%)	79 (5.0%)	45 (2.8%)	0.78 [0.56;1.07]	0.1238	
	Evidence of CV disease at screening													0.2729
	CV DISEASE	1353	64 (4.7%)	1289 (95.3%)	68 (5.0%)	46 (3.4%)	1382	78 (5.6%)	1304 (94.4%)	77 (5.6%)	43 (3.1%)	0.84 [0.60;1.17]	0.2955	
	CV RISK FACTORS ONLY	295	5 (1.7%)	290 (98.3%)	6 (2.0%)	3 (1.0%)	267	10 (3.7%)	257 (96.3%)	6 (2.2%)	4 (1.5%)	0.45 [0.15;1.31]	0.1417	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Injury, poisoning and procedural complications	All subjects (total)	1648	31 (1.9%)	1617 (98.1%)	85 (5.2%)	60 (3.6%)	1649	36 (2.2%)	1613 (97.8%)	94 (5.7%)	54 (3.3%)	0.86 [0.53;1.39]	0.5314	
	Gender													0.9046
	Female	635	12 (1.9%)	623 (98.1%)	32 (5.0%)	22 (3.5%)	660	15 (2.3%)	645 (97.7%)	34 (5.2%)	14 (2.1%)	0.83 [0.39;1.77]	0.6258	
	Male	1013	19 (1.9%)	994 (98.1%)	53 (5.2%)	38 (3.8%)	989	21 (2.1%)	968 (97.9%)	60 (6.1%)	40 (4.0%)	0.88 [0.47;1.64]	0.6839	
	Age													0.9801
	< 65	855	13 (1.5%)	842 (98.5%)	44 (5.1%)	31 (3.6%)	844	15 (1.8%)	829 (98.2%)	45 (5.3%)	19 (2.3%)	0.85 [0.41;1.79]	0.6758	
	65 <=	793	18 (2.3%)	775 (97.7%)	41 (5.2%)	29 (3.7%)	805	21 (2.6%)	784 (97.4%)	49 (6.1%)	35 (4.3%)	0.86 [0.46;1.62]	0.6492	
	HbA1c at baseline (disease severity)													0.7833
	< 8.0	595	9 (1.5%)	586 (98.5%)	23 (3.9%)	16 (2.7%)	628	10 (1.6%)	618 (98.4%)	29 (4.6%)	17 (2.7%)	0.95 [0.38;2.33]	0.9058	
	8.0 <=	1053	22 (2.1%)	1031 (97.9%)	62 (5.9%)	44 (4.2%)	1021	26 (2.5%)	995 (97.5%)	65 (6.4%)	37 (3.6%)	0.82 [0.46;1.44]	0.4819	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Injury, poisoning and procedural complications	Region A													0.0574
	West Europe	228	10 (4.4%)	218 (95.6%)	12 (5.3%)	9 (3.9%)	205	4 (2.0%)	201 (98.0%)	7 (3.4%)	2 (1.0%)	2.30 [0.72;7.32]	0.1599	
	Rest of World	1420	21 (1.5%)	1399 (98.5%)	73 (5.1%)	51 (3.6%)	1444	32 (2.2%)	1412 (97.8%)	87 (6.0%)	52 (3.6%)	0.66 [0.38;1.15]	0.1415	
	Region B													0.8573
	OECD	1174	26 (2.2%)	1148 (97.8%)	67 (5.7%)	43 (3.7%)	1136	29 (2.6%)	1107 (97.4%)	75 (6.6%)	36 (3.2%)	0.86 [0.51;1.47]	0.5862	
	Non-OECD	474	5 (1.1%)	469 (98.9%)	18 (3.8%)	17 (3.6%)	513	7 (1.4%)	506 (98.6%)	19 (3.7%)	18 (3.5%)	0.77 [0.24;2.42]	0.6534	
	Treatment dose volume													0.8810
	0.5 mg/week	826	17 (2.1%)	809 (97.9%)	43 (5.2%)	29 (3.5%)	824	19 (2.3%)	805 (97.7%)	49 (5.9%)	29 (3.5%)	0.89 [0.46;1.71]	0.7194	
	1.0 mg/week	822	14 (1.7%)	808 (98.3%)	42 (5.1%)	31 (3.8%)	825	17 (2.1%)	808 (97.9%)	45 (5.5%)	25 (3.0%)	0.82 [0.41;1.67]	0.5917	
	Baseline insulin use													0.2266
	No	692	10 (1.4%)	682 (98.6%)	35 (5.1%)	21 (3.0%)	692	7 (1.0%)	685 (99.0%)	37 (5.3%)	26 (3.8%)	1.43 [0.54;3.76]	0.4672	
	Yes	956	21 (2.2%)	935 (97.8%)	50 (5.2%)	39 (4.1%)	957	29 (3.0%)	928 (97.0%)	57 (6.0%)	28 (2.9%)	0.72 [0.41;1.26]	0.2480	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Injury, poisoning and procedural complications	Baseline Renal impairment													0.9848
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	2 (3.3%)	59 (96.7%)	4 (6.6%)	2 (3.3%)	Not est	Not est	
	30 <= GFR	1602	31 (1.9%)	1571 (98.1%)	80 (5.0%)	55 (3.4%)	1588	34 (2.1%)	1554 (97.9%)	90 (5.7%)	52 (3.3%)	0.90 [0.55;1.46]	0.6681	
	Evidence of CV disease at screening													0.1623
	CV DISEASE	1353	29 (2.1%)	1324 (97.9%)	78 (5.8%)	56 (4.1%)	1382	30 (2.2%)	1352 (97.8%)	87 (6.3%)	50 (3.6%)	0.99 [0.59;1.64]	0.9540	
	CV RISK FACTORS ONLY	295	2 (0.7%)	293 (99.3%)	7 (2.4%)	4 (1.4%)	267	6 (2.2%)	261 (97.8%)	7 (2.6%)	4 (1.5%)	0.30 [0.06;1.47]	0.1375	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Investigations	All subjects (total)	1648	20 (1.2%)	1628 (98.8%)	83 (5.0%)	58 (3.5%)	1649	13 (0.8%)	1636 (99.2%)	99 (6.0%)	59 (3.6%)	1.54 [0.77;3.10]	0.2245	
	Gender													0.9720
	Female	635	6 (0.9%)	629 (99.1%)	31 (4.9%)	21 (3.3%)	660	4 (0.6%)	656 (99.4%)	36 (5.5%)	16 (2.4%)	1.56 [0.44;5.54]	0.4896	
	Male	1013	14 (1.4%)	999 (98.6%)	52 (5.1%)	37 (3.7%)	989	9 (0.9%)	980 (99.1%)	63 (6.4%)	43 (4.3%)	1.52 [0.66;3.51]	0.3269	
	Age													0.5573
	< 65	855	12 (1.4%)	843 (98.6%)	43 (5.0%)	30 (3.5%)	844	9 (1.1%)	835 (98.9%)	48 (5.7%)	22 (2.6%)	1.31 [0.55;3.11]	0.5381	
	65 <=	793	8 (1.0%)	785 (99.0%)	40 (5.0%)	28 (3.5%)	805	4 (0.5%)	801 (99.5%)	51 (6.3%)	37 (4.6%)	2.04 [0.62;6.79]	0.2434	
	HbA1c at baseline (disease severity)													0.7960
	< 8.0	595	5 (0.8%)	590 (99.2%)	24 (4.0%)	17 (2.9%)	628	4 (0.6%)	624 (99.4%)	29 (4.6%)	17 (2.7%)	1.32 [0.35;4.91]	0.6800	
	8.0 <=	1053	15 (1.4%)	1038 (98.6%)	59 (5.6%)	41 (3.9%)	1021	9 (0.9%)	1012 (99.1%)	70 (6.9%)	42 (4.1%)	1.62 [0.71;3.70]	0.2534	
	Region A													0.9862
	West Europe	228	2 (0.9%)	226 (99.1%)	11 (4.8%)	8 (3.5%)	205	0 (0.0%)	205 (100%)	7 (3.4%)	2 (1.0%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Investigations	Rest of World	1420	18 (1.3%)	1402 (98.7%)	72 (5.1%)	50 (3.5%)	1444	13 (0.9%)	1431 (99.1%)	92 (6.4%)	57 (3.9%)	1.41 [0.69;2.87]	0.3487	
	Region B													0.8078
	OECD	1174	19 (1.6%)	1155 (98.4%)	65 (5.5%)	41 (3.5%)	1136	12 (1.1%)	1124 (98.9%)	79 (7.0%)	40 (3.5%)	1.54 [0.75;3.17]	0.2436	
	Non-OECD	474	1 (0.2%)	473 (99.8%)	18 (3.8%)	17 (3.6%)	513	1 (0.2%)	512 (99.8%)	20 (3.9%)	19 (3.7%)	1.08 [0.07;17.22]	0.9579	
	Treatment dose volume													0.3094
	0.5 mg/week	826	12 (1.5%)	814 (98.5%)	43 (5.2%)	29 (3.5%)	824	10 (1.2%)	814 (98.8%)	51 (6.2%)	31 (3.8%)	1.19 [0.52;2.76]	0.6809	
	1.0 mg/week	822	8 (1.0%)	814 (99.0%)	40 (4.9%)	29 (3.5%)	825	3 (0.4%)	822 (99.6%)	48 (5.8%)	28 (3.4%)	2.69 [0.71;10.15]	0.1435	
	Baseline insulin use													0.1291
	No	692	10 (1.4%)	682 (98.6%)	32 (4.6%)	18 (2.6%)	692	3 (0.4%)	689 (99.6%)	37 (5.3%)	26 (3.8%)	3.35 [0.92;12.16]	0.0665	
	Yes	956	10 (1.0%)	946 (99.0%)	51 (5.3%)	40 (4.2%)	957	10 (1.0%)	947 (99.0%)	62 (6.5%)	33 (3.4%)	1.00 [0.42;2.40]	0.9995	
	Baseline Renal impairment													0.9828
	GFR < 30	46	2 (4.3%)	44 (95.7%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	18 (1.1%)	1584 (98.9%)	78 (4.9%)	53 (3.3%)	1588	13 (0.8%)	1575 (99.2%)	93 (5.9%)	55 (3.5%)	1.37 [0.67;2.80]	0.3841	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Investigations	Evidence of CV disease at screening													0.2888
	CV DISEASE	1353	19 (1.4%)	1334 (98.6%)	76 (5.6%)	54 (4.0%)	1382	11 (0.8%)	1371 (99.2%)	92 (6.7%)	55 (4.0%)	1.77 [0.84;3.71]	0.1328	
	CV RISK FACTORS ONLY	295	1 (0.3%)	294 (99.7%)	7 (2.4%)	4 (1.4%)	267	2 (0.7%)	265 (99.3%)	7 (2.6%)	4 (1.5%)	0.45 [0.04;5.00]	0.5188	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Metabolism and nutrition disorders	All subjects (total)	1648	33 (2.0%)	1615 (98.0%)	82 (5.0%)	57 (3.5%)	1649	38 (2.3%)	1611 (97.7%)	92 (5.6%)	54 (3.3%)	0.87 [0.54;1.38]	0.5501	
	Gender													0.3564
	Female	635	17 (2.7%)	618 (97.3%)	30 (4.7%)	20 (3.1%)	660	16 (2.4%)	644 (97.6%)	35 (5.3%)	16 (2.4%)	1.10 [0.56;2.18]	0.7798	
	Male	1013	16 (1.6%)	997 (98.4%)	52 (5.1%)	37 (3.7%)	989	22 (2.2%)	967 (97.8%)	57 (5.8%)	38 (3.8%)	0.71 [0.37;1.35]	0.2948	
	Age													0.6915
	< 65	855	13 (1.5%)	842 (98.5%)	42 (4.9%)	29 (3.4%)	844	13 (1.5%)	831 (98.5%)	45 (5.3%)	20 (2.4%)	0.99 [0.46;2.13]	0.9706	
	65 <=	793	20 (2.5%)	773 (97.5%)	40 (5.0%)	28 (3.5%)	805	25 (3.1%)	780 (96.9%)	47 (5.8%)	34 (4.2%)	0.81 [0.45;1.46]	0.4831	
	HbA1c at baseline (disease severity)													0.7381
	< 8.0	595	11 (1.8%)	584 (98.2%)	23 (3.9%)	16 (2.7%)	628	12 (1.9%)	616 (98.1%)	26 (4.1%)	15 (2.4%)	0.97 [0.43;2.19]	0.9388	
	8.0 <=	1053	22 (2.1%)	1031 (97.9%)	59 (5.6%)	41 (3.9%)	1021	26 (2.5%)	995 (97.5%)	66 (6.5%)	39 (3.8%)	0.82 [0.46;1.44]	0.4857	
	Region A													0.8748

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Metabolism and nutrition disorders	West Europe	228	7 (3.1%)	221 (96.9%)	12 (5.3%)	9 (3.9%)	205	8 (3.9%)	197 (96.1%)	6 (2.9%)	1 (0.5%)	0.80 [0.29;2.21]	0.6665	
	Rest of World	1420	26 (1.8%)	1394 (98.2%)	70 (4.9%)	48 (3.4%)	1444	30 (2.1%)	1414 (97.9%)	86 (6.0%)	53 (3.7%)	0.88 [0.52;1.48]	0.6244	
	Region B													0.4541
	OECD	1174	27 (2.3%)	1147 (97.7%)	67 (5.7%)	43 (3.7%)	1136	33 (2.9%)	1103 (97.1%)	72 (6.3%)	35 (3.1%)	0.79 [0.48;1.31]	0.3643	
	Non-OECD	474	6 (1.3%)	468 (98.7%)	15 (3.2%)	14 (3.0%)	513	5 (1.0%)	508 (99.0%)	20 (3.9%)	19 (3.7%)	1.29 [0.39;4.24]	0.6704	
	Treatment dose volume													0.7199
	0.5 mg/week	826	18 (2.2%)	808 (97.8%)	40 (4.8%)	26 (3.1%)	824	19 (2.3%)	805 (97.7%)	49 (5.9%)	29 (3.5%)	0.94 [0.49;1.79]	0.8528	
	1.0 mg/week	822	15 (1.8%)	807 (98.2%)	42 (5.1%)	31 (3.8%)	825	19 (2.3%)	806 (97.7%)	43 (5.2%)	25 (3.0%)	0.79 [0.40;1.56]	0.5017	
	Baseline insulin use													0.2439
	No	692	11 (1.6%)	681 (98.4%)	34 (4.9%)	20 (2.9%)	692	8 (1.2%)	684 (98.8%)	37 (5.3%)	26 (3.8%)	1.38 [0.55;3.42]	0.4918	
	Yes	956	22 (2.3%)	934 (97.7%)	48 (5.0%)	37 (3.9%)	957	30 (3.1%)	927 (96.9%)	55 (5.7%)	28 (2.9%)	0.73 [0.42;1.27]	0.2645	
	Baseline Renal impairment													0.7440

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Metabolism and nutrition disorders	GFR < 30	46	2 (4.3%)	44 (95.7%)	4 (8.7%)	4 (8.7%)	61	4 (6.6%)	57 (93.4%)	4 (6.6%)	3 (4.9%)	0.67 [0.12;3.67]	0.6463	
	30 <= GFR	1602	31 (1.9%)	1571 (98.1%)	78 (4.9%)	53 (3.3%)	1588	34 (2.1%)	1554 (97.9%)	88 (5.5%)	51 (3.2%)	0.90 [0.55;1.47]	0.6776	
	Evidence of CV disease at screening													0.4279
	CV DISEASE	1353	28 (2.1%)	1325 (97.9%)	76 (5.6%)	54 (4.0%)	1382	35 (2.5%)	1347 (97.5%)	85 (6.2%)	50 (3.6%)	0.82 [0.50;1.34]	0.4222	
	CV RISK FACTORS ONLY	295	5 (1.7%)	290 (98.3%)	6 (2.0%)	3 (1.0%)	267	3 (1.1%)	264 (98.9%)	7 (2.6%)	4 (1.5%)	1.51 [0.36;6.30]	0.5751	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Musculoskeletal and connective tissue disorders	All subjects (total)	1648	26 (1.6%)	1622 (98.4%)	87 (5.3%)	62 (3.8%)	1649	43 (2.6%)	1606 (97.4%)	97 (5.9%)	59 (3.6%)	0.60 [0.37;0.98]	0.0404	
	Gender													0.8766
	Female	635	11 (1.7%)	624 (98.3%)	33 (5.2%)	23 (3.6%)	660	18 (2.7%)	642 (97.3%)	37 (5.6%)	17 (2.6%)	0.63 [0.30;1.33]	0.2274	
	Male	1013	15 (1.5%)	998 (98.5%)	54 (5.3%)	39 (3.8%)	989	25 (2.5%)	964 (97.5%)	60 (6.1%)	42 (4.2%)	0.58 [0.31;1.11]	0.0982	
	Age													0.0566
	< 65	855	16 (1.9%)	839 (98.1%)	45 (5.3%)	32 (3.7%)	844	16 (1.9%)	828 (98.1%)	46 (5.5%)	22 (2.6%)	0.99 [0.49;1.97]	0.9673	
	65 <=	793	10 (1.3%)	783 (98.7%)	42 (5.3%)	30 (3.8%)	805	27 (3.4%)	778 (96.6%)	51 (6.3%)	37 (4.6%)	0.37 [0.18;0.77]	0.0075	
	HbA1c at baseline (disease severity)													0.3856
	< 8.0	595	10 (1.7%)	585 (98.3%)	24 (4.0%)	17 (2.9%)	628	22 (3.5%)	606 (96.5%)	29 (4.6%)	18 (2.9%)	0.47 [0.22;1.00]	0.0506	
	8.0 <=	1053	16 (1.5%)	1037 (98.5%)	63 (6.0%)	45 (4.3%)	1021	21 (2.1%)	1000 (97.9%)	68 (6.7%)	41 (4.0%)	0.74 [0.38;1.41]	0.3552	
	Region A													0.6060

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Musculoskeletal and connective tissue disorders	West Europe	228	4 (1.8%)	224 (98.2%)	12 (5.3%)	9 (3.9%)	205	8 (3.9%)	197 (96.1%)	7 (3.4%)	2 (1.0%)	0.45 [0.14;1.49]	0.1910	
	Rest of World	1420	22 (1.5%)	1398 (98.5%)	75 (5.3%)	53 (3.7%)	1444	35 (2.4%)	1409 (97.6%)	90 (6.2%)	57 (3.9%)	0.63 [0.37;1.08]	0.0944	
	Region B													0.5265
	OECD	1174	24 (2.0%)	1150 (98.0%)	69 (5.9%)	45 (3.8%)	1136	41 (3.6%)	1095 (96.4%)	77 (6.8%)	40 (3.5%)	0.56 [0.34;0.93]	0.0247	
	Non-OECD	474	2 (0.4%)	472 (99.6%)	18 (3.8%)	17 (3.6%)	513	2 (0.4%)	511 (99.6%)	20 (3.9%)	19 (3.7%)	1.08 [0.15;7.66]	0.9390	
	Treatment dose volume													0.9581
	0.5 mg/week	826	12 (1.5%)	814 (98.5%)	44 (5.3%)	30 (3.6%)	824	20 (2.4%)	804 (97.6%)	51 (6.2%)	31 (3.8%)	0.59 [0.29;1.21]	0.1523	
	1.0 mg/week	822	14 (1.7%)	808 (98.3%)	43 (5.2%)	32 (3.9%)	825	23 (2.8%)	802 (97.2%)	46 (5.6%)	28 (3.4%)	0.61 [0.31;1.18]	0.1430	
	Baseline insulin use													0.2095
	No	692	13 (1.9%)	679 (98.1%)	35 (5.1%)	21 (3.0%)	692	15 (2.2%)	677 (97.8%)	36 (5.2%)	25 (3.6%)	0.87 [0.41;1.82]	0.7066	
	Yes	956	13 (1.4%)	943 (98.6%)	52 (5.4%)	41 (4.3%)	957	28 (2.9%)	929 (97.1%)	61 (6.4%)	34 (3.6%)	0.46 [0.24;0.89]	0.0205	
	Baseline Renal impairment													0.9767

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Musculoskeletal and connective tissue disorders	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	3 (4.9%)	58 (95.1%)	5 (8.2%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	26 (1.6%)	1576 (98.4%)	82 (5.1%)	57 (3.6%)	1588	40 (2.5%)	1548 (97.5%)	92 (5.8%)	55 (3.5%)	0.64 [0.39;1.05]	0.0766	
	Evidence of CV disease at screening													0.1199
	CV DISEASE	1353	25 (1.8%)	1328 (98.2%)	80 (5.9%)	58 (4.3%)	1382	36 (2.6%)	1346 (97.4%)	90 (6.5%)	55 (4.0%)	0.71 [0.42;1.18]	0.1810	
	CV RISK FACTORS ONLY	295	1 (0.3%)	294 (99.7%)	7 (2.4%)	4 (1.4%)	267	7 (2.6%)	260 (97.4%)	7 (2.6%)	4 (1.5%)	0.13 [0.02;1.04]	0.0540	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	All subjects (total)	1648	28 (1.7%)	1620 (98.3%)	74 (4.5%)	50 (3.0%)	1649	30 (1.8%)	1619 (98.2%)	95 (5.8%)	55 (3.3%)	0.93 [0.56;1.56]	0.7818	
	Gender													0.3930
	Female	635	10 (1.6%)	625 (98.4%)	28 (4.4%)	19 (3.0%)	660	8 (1.2%)	652 (98.8%)	35 (5.3%)	15 (2.3%)	1.29 [0.51;3.28]	0.5865	
	Male	1013	18 (1.8%)	995 (98.2%)	46 (4.5%)	31 (3.1%)	989	22 (2.2%)	967 (97.8%)	60 (6.1%)	40 (4.0%)	0.79 [0.43;1.48]	0.4698	
	Age													0.5016
	< 65	855	9 (1.1%)	846 (98.9%)	40 (4.7%)	28 (3.3%)	844	12 (1.4%)	832 (98.6%)	47 (5.6%)	21 (2.5%)	0.74 [0.31;1.75]	0.4891	
	65 <=	793	19 (2.4%)	774 (97.6%)	34 (4.3%)	22 (2.8%)	805	18 (2.2%)	787 (97.8%)	48 (6.0%)	34 (4.2%)	1.07 [0.56;2.03]	0.8441	
	HbA1c at baseline (disease severity)													0.8784
	< 8.0	595	13 (2.2%)	582 (97.8%)	22 (3.7%)	15 (2.5%)	628	14 (2.2%)	614 (97.8%)	27 (4.3%)	15 (2.4%)	0.98 [0.46;2.08]	0.9556	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	8.0 <=	1053	15 (1.4%)	1038 (98.6%)	52 (4.9%)	35 (3.3%)	1021	16 (1.6%)	1005 (98.4%)	68 (6.7%)	40 (3.9%)	0.90 [0.45;1.83]	0.7765	
	Region A													0.0829
	West Europe	228	11 (4.8%)	217 (95.2%)	8 (3.5%)	5 (2.2%)	205	5 (2.4%)	200 (97.6%)	7 (3.4%)	2 (1.0%)	2.02 [0.70;5.83]	0.1910	
	Rest of World	1420	17 (1.2%)	1403 (98.8%)	66 (4.6%)	45 (3.2%)	1444	25 (1.7%)	1419 (98.3%)	88 (6.1%)	53 (3.7%)	0.69 [0.37;1.27]	0.2298	
	Region B													0.7197
	OECD	1174	23 (2.0%)	1151 (98.0%)	58 (4.9%)	35 (3.0%)	1136	23 (2.0%)	1113 (98.0%)	76 (6.7%)	37 (3.3%)	0.97 [0.54;1.72]	0.9072	
	Non-OECD	474	5 (1.1%)	469 (98.9%)	16 (3.4%)	15 (3.2%)	513	7 (1.4%)	506 (98.6%)	19 (3.7%)	18 (3.5%)	0.76 [0.24;2.41]	0.6451	
	Treatment dose volume													0.2971
	0.5 mg/week	826	14 (1.7%)	812 (98.3%)	39 (4.7%)	26 (3.1%)	824	19 (2.3%)	805 (97.7%)	48 (5.8%)	28 (3.4%)	0.73 [0.37;1.46]	0.3713	
	1.0 mg/week	822	14 (1.7%)	808 (98.3%)	35 (4.3%)	24 (2.9%)	825	11 (1.3%)	814 (98.7%)	47 (5.7%)	27 (3.3%)	1.28 [0.58;2.81]	0.5463	
	Baseline insulin use													0.1838

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	No	692	17 (2.5%)	675 (97.5%)	27 (3.9%)	14 (2.0%)	692	13 (1.9%)	679 (98.1%)	33 (4.8%)	22 (3.2%)	1.31 [0.64;2.69]	0.4663	
	Yes	956	11 (1.2%)	945 (98.8%)	47 (4.9%)	36 (3.8%)	957	17 (1.8%)	940 (98.2%)	62 (6.5%)	33 (3.4%)	0.64 [0.30;1.37]	0.2536	
	Baseline Renal impairment													0.9999
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	28 (1.7%)	1574 (98.3%)	69 (4.3%)	45 (2.8%)	1588	30 (1.9%)	1558 (98.1%)	89 (5.6%)	51 (3.2%)	0.92 [0.55;1.54]	0.7516	
	Evidence of CV disease at screening													0.6742
	CV DISEASE	1353	24 (1.8%)	1329 (98.2%)	69 (5.1%)	48 (3.5%)	1382	25 (1.8%)	1357 (98.2%)	90 (6.5%)	53 (3.8%)	0.98 [0.56;1.71]	0.9356	
	CV RISK FACTORS ONLY	295	4 (1.4%)	291 (98.6%)	5 (1.7%)	2 (0.7%)	267	5 (1.9%)	262 (98.1%)	5 (1.9%)	2 (0.7%)	0.72 [0.19;2.68]	0.6232	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs. Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Nervous system disorders	All subjects (total)	1648	50 (3.0%)	1598 (97.0%)	75 (4.6%)	51 (3.1%)	1649	59 (3.6%)	1590 (96.4%)	87 (5.3%)	50 (3.0%)	0.85 [0.58;1.23]	0.3873	
	Gender													0.1871
	Female	635	24 (3.8%)	611 (96.2%)	29 (4.6%)	19 (3.0%)	660	22 (3.3%)	638 (96.7%)	34 (5.2%)	14 (2.1%)	1.14 [0.64;2.04]	0.6545	
	Male	1013	26 (2.6%)	987 (97.4%)	46 (4.5%)	32 (3.2%)	989	37 (3.7%)	952 (96.3%)	53 (5.4%)	36 (3.6%)	0.68 [0.41;1.13]	0.1342	
	Age													0.0747
	< 65	855	30 (3.5%)	825 (96.5%)	38 (4.4%)	25 (2.9%)	844	25 (3.0%)	819 (97.0%)	43 (5.1%)	20 (2.4%)	1.19 [0.70;2.02]	0.5221	
	65 <=	793	20 (2.5%)	773 (97.5%)	37 (4.7%)	26 (3.3%)	805	34 (4.2%)	771 (95.8%)	44 (5.5%)	30 (3.7%)	0.59 [0.34;1.03]	0.0634	
	HbA1c at baseline (disease severity)													0.9375
	< 8.0	595	18 (3.0%)	577 (97.0%)	20 (3.4%)	14 (2.4%)	628	22 (3.5%)	606 (96.5%)	26 (4.1%)	15 (2.4%)	0.86 [0.46;1.61]	0.6432	
	8.0 <=	1053	32 (3.0%)	1021 (97.0%)	55 (5.2%)	37 (3.5%)	1021	37 (3.6%)	984 (96.4%)	61 (6.0%)	35 (3.4%)	0.84 [0.52;1.34]	0.4596	
	Region A													0.0758
	West Europe	228	4 (1.8%)	224 (98.2%)	11 (4.8%)	8 (3.5%)	205	11 (5.4%)	194 (94.6%)	5 (2.4%)	1 (0.5%)	0.32 [0.10;1.02]	0.0538	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Nervous system disorders	Rest of World	1420	46 (3.2%)	1374 (96.8%)	64 (4.5%)	43 (3.0%)	1444	48 (3.3%)	1396 (96.7%)	82 (5.7%)	49 (3.4%)	0.97 [0.65;1.46]	0.8983	
	Region B													0.1015
	OECD	1174	36 (3.1%)	1138 (96.9%)	60 (5.1%)	37 (3.2%)	1136	49 (4.3%)	1087 (95.7%)	70 (6.2%)	34 (3.0%)	0.71 [0.46;1.09]	0.1146	
	Non-OECD	474	14 (3.0%)	460 (97.0%)	15 (3.2%)	14 (3.0%)	513	10 (1.9%)	503 (98.1%)	17 (3.3%)	16 (3.1%)	1.52 [0.68;3.43]	0.3091	
	Treatment dose volume													0.9844
	0.5 mg/week	826	29 (3.5%)	797 (96.5%)	38 (4.6%)	25 (3.0%)	824	34 (4.1%)	790 (95.9%)	46 (5.6%)	27 (3.3%)	0.85 [0.52;1.39]	0.5167	
	1.0 mg/week	822	21 (2.6%)	801 (97.4%)	37 (4.5%)	26 (3.2%)	825	25 (3.0%)	800 (97.0%)	41 (5.0%)	23 (2.8%)	0.84 [0.47;1.50]	0.5623	
	Baseline insulin use													0.4088
	No	692	18 (2.6%)	674 (97.4%)	31 (4.5%)	17 (2.5%)	692	17 (2.5%)	675 (97.5%)	34 (4.9%)	23 (3.3%)	1.06 [0.55;2.07]	0.8533	
	Yes	956	32 (3.3%)	924 (96.7%)	44 (4.6%)	34 (3.6%)	957	42 (4.4%)	915 (95.6%)	53 (5.5%)	27 (2.8%)	0.76 [0.48;1.20]	0.2370	
	Baseline Renal impairment													0.3932
	GFR < 30	46	1 (2.2%)	45 (97.8%)	4 (8.7%)	4 (8.7%)	61	4 (6.6%)	57 (93.4%)	5 (8.2%)	3 (4.9%)	0.33 [0.04;2.99]	0.3272	
	30 <= GFR	1602	49 (3.1%)	1553 (96.9%)	71 (4.4%)	47 (2.9%)	1588	55 (3.5%)	1533 (96.5%)	82 (5.2%)	47 (3.0%)	0.88 [0.60;1.30]	0.5207	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Nervous system disorders	Evidence of CV disease at screening													0.4794
	CV DISEASE	1353	42 (3.1%)	1311 (96.9%)	68 (5.0%)	47 (3.5%)	1382	53 (3.8%)	1329 (96.2%)	81 (5.9%)	47 (3.4%)	0.81 [0.54;1.21]	0.2991	
	CV RISK FACTORS ONLY	295	8 (2.7%)	287 (97.3%)	7 (2.4%)	4 (1.4%)	267	6 (2.2%)	261 (97.8%)	6 (2.2%)	3 (1.1%)	1.21 [0.42;3.50]	0.7188	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Renal and urinary disorders	All subjects (total)	1648	37 (2.2%)	1611 (97.8%)	77 (4.7%)	52 (3.2%)	1649	38 (2.3%)	1611 (97.7%)	87 (5.3%)	49 (3.0%)	0.97 [0.62;1.53]	0.8990	
	Gender													0.1590
	Female	635	17 (2.7%)	618 (97.3%)	28 (4.4%)	18 (2.8%)	660	12 (1.8%)	648 (98.2%)	35 (5.3%)	15 (2.3%)	1.47 [0.70;3.08]	0.3064	
	Male	1013	20 (2.0%)	993 (98.0%)	49 (4.8%)	34 (3.4%)	989	26 (2.6%)	963 (97.4%)	52 (5.3%)	34 (3.4%)	0.75 [0.42;1.34]	0.3283	
	Age													0.3788
	< 65	855	19 (2.2%)	836 (97.8%)	39 (4.6%)	26 (3.0%)	844	23 (2.7%)	821 (97.3%)	40 (4.7%)	16 (1.9%)	0.81 [0.44;1.49]	0.4940	
	65 <=	793	18 (2.3%)	775 (97.7%)	38 (4.8%)	26 (3.3%)	805	15 (1.9%)	790 (98.1%)	47 (5.8%)	33 (4.1%)	1.22 [0.62;2.42]	0.5688	
	HbA1c at baseline (disease severity)													0.1078
	< 8.0	595	11 (1.8%)	584 (98.2%)	21 (3.5%)	14 (2.4%)	628	19 (3.0%)	609 (97.0%)	23 (3.7%)	13 (2.1%)	0.61 [0.29;1.28]	0.1884	
	8.0 <=	1053	26 (2.5%)	1027 (97.5%)	56 (5.3%)	38 (3.6%)	1021	19 (1.9%)	1002 (98.1%)	64 (6.3%)	36 (3.5%)	1.32 [0.73;2.39]	0.3523	
	Region A													0.5751
	West Europe	228	6 (2.6%)	222 (97.4%)	11 (4.8%)	8 (3.5%)	205	4 (2.0%)	201 (98.0%)	7 (3.4%)	2 (1.0%)	1.36 [0.38;4.82]	0.6341	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs.Comparator HR [95%-CI]	Sema vs.Comparator p-value	p-value int.
Renal and urinary disorders	Rest of World	1420	31 (2.2%)	1389 (97.8%)	66 (4.6%)	44 (3.1%)	1444	34 (2.4%)	1410 (97.6%)	80 (5.5%)	47 (3.3%)	0.92 [0.57;1.50]	0.7459	
	Region B													0.2527
	OECD	1174	29 (2.5%)	1145 (97.5%)	61 (5.2%)	37 (3.2%)	1136	33 (2.9%)	1103 (97.1%)	70 (6.2%)	33 (2.9%)	0.85 [0.51;1.39]	0.5123	
	Non-OECD	474	8 (1.7%)	466 (98.3%)	16 (3.4%)	15 (3.2%)	513	5 (1.0%)	508 (99.0%)	17 (3.3%)	16 (3.1%)	1.73 [0.57;5.28]	0.3370	
	Treatment dose volume													0.7387
	0.5 mg/week	826	22 (2.7%)	804 (97.3%)	36 (4.4%)	22 (2.7%)	824	21 (2.5%)	803 (97.5%)	47 (5.7%)	28 (3.4%)	1.04 [0.57;1.89]	0.9060	
	1.0 mg/week	822	15 (1.8%)	807 (98.2%)	41 (5.0%)	30 (3.6%)	825	17 (2.1%)	808 (97.9%)	40 (4.8%)	21 (2.5%)	0.89 [0.44;1.78]	0.7349	
	Baseline insulin use													0.0804
	No	692	18 (2.6%)	674 (97.4%)	32 (4.6%)	18 (2.6%)	692	11 (1.6%)	681 (98.4%)	36 (5.2%)	25 (3.6%)	1.64 [0.77;3.47]	0.1976	
	Yes	956	19 (2.0%)	937 (98.0%)	45 (4.7%)	34 (3.6%)	957	27 (2.8%)	930 (97.2%)	51 (5.3%)	24 (2.5%)	0.70 [0.39;1.26]	0.2337	
	Baseline Renal impairment													0.8661
	GFR < 30	46	8 (17.4%)	38 (82.6%)	4 (8.7%)	4 (8.7%)	61	11 (18.0%)	50 (82.0%)	2 (3.3%)	1 (1.6%)	0.97 [0.39;2.41]	0.9480	
	30 <= GFR	1602	29 (1.8%)	1573 (98.2%)	73 (4.6%)	48 (3.0%)	1588	27 (1.7%)	1561 (98.3%)	85 (5.4%)	48 (3.0%)	1.06 [0.63;1.79]	0.8223	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs. Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Renal and urinary disorders	Evidence of CV disease at screening													0.5759
	CV DISEASE	1353	35 (2.6%)	1318 (97.4%)	70 (5.2%)	48 (3.5%)	1382	35 (2.5%)	1347 (97.5%)	80 (5.8%)	45 (3.3%)	1.02 [0.64;1.63]	0.9380	
	CV RISK FACTORS ONLY	295	2 (0.7%)	293 (99.3%)	7 (2.4%)	4 (1.4%)	267	3 (1.1%)	264 (98.9%)	7 (2.6%)	4 (1.5%)	0.60 [0.10;3.60]	0.5769	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs. Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Respiratory, thoracic and mediastinal disorders	All subjects (total)	1648	41 (2.5%)	1607 (97.5%)	69 (4.2%)	45 (2.7%)	1649	27 (1.6%)	1622 (98.4%)	88 (5.3%)	49 (3.0%)	1.52 [0.94;2.47]	0.0904	
	Gender													0.5263
	Female	635	13 (2.0%)	622 (98.0%)	27 (4.3%)	18 (2.8%)	660	11 (1.7%)	649 (98.3%)	31 (4.7%)	11 (1.7%)	1.23 [0.55;2.75]	0.6097	
	Male	1013	28 (2.8%)	985 (97.2%)	42 (4.1%)	27 (2.7%)	989	16 (1.6%)	973 (98.4%)	57 (5.8%)	38 (3.8%)	1.71 [0.92;3.16]	0.0872	
	Age													0.6845
	< 65	855	21 (2.5%)	834 (97.5%)	35 (4.1%)	23 (2.7%)	844	15 (1.8%)	829 (98.2%)	43 (5.1%)	18 (2.1%)	1.38 [0.71;2.68]	0.3368	
	65 <=	793	20 (2.5%)	773 (97.5%)	34 (4.3%)	22 (2.8%)	805	12 (1.5%)	793 (98.5%)	45 (5.6%)	31 (3.9%)	1.69 [0.83;3.46]	0.1490	
	HbA1c at baseline (disease severity)													0.3256
	< 8.0	595	14 (2.4%)	581 (97.6%)	19 (3.2%)	12 (2.0%)	628	13 (2.1%)	615 (97.9%)	24 (3.8%)	13 (2.1%)	1.14 [0.53;2.42]	0.7375	
	8.0 <=	1053	27 (2.6%)	1026 (97.4%)	50 (4.7%)	33 (3.1%)	1021	14 (1.4%)	1007 (98.6%)	64 (6.3%)	36 (3.5%)	1.87 [0.98;3.57]	0.0568	
	Region A													0.2917

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Respiratory, thoracic and mediastinal disorders	West Europe	228	5 (2.2%)	223 (97.8%)	11 (4.8%)	8 (3.5%)	205	1 (0.5%)	204 (99.5%)	7 (3.4%)	2 (1.0%)	4.60 [0.54;39.39]	0.1635	
	Rest of World	1420	36 (2.5%)	1384 (97.5%)	58 (4.1%)	37 (2.6%)	1444	26 (1.8%)	1418 (98.2%)	81 (5.6%)	47 (3.3%)	1.41 [0.85;2.33]	0.1863	
	Region B													0.8751
	OECD	1174	32 (2.7%)	1142 (97.3%)	55 (4.7%)	32 (2.7%)	1136	21 (1.8%)	1115 (98.2%)	70 (6.2%)	32 (2.8%)	1.48 [0.85;2.56]	0.1648	
	Non-OECD	474	9 (1.9%)	465 (98.1%)	14 (3.0%)	13 (2.7%)	513	6 (1.2%)	507 (98.8%)	18 (3.5%)	17 (3.3%)	1.62 [0.58;4.56]	0.3585	
	Treatment dose volume													0.7106
	0.5 mg/week	826	18 (2.2%)	808 (97.8%)	38 (4.6%)	25 (3.0%)	824	13 (1.6%)	811 (98.4%)	45 (5.5%)	26 (3.2%)	1.38 [0.68;2.81]	0.3780	
	1.0 mg/week	822	23 (2.8%)	799 (97.2%)	31 (3.8%)	20 (2.4%)	825	14 (1.7%)	811 (98.3%)	43 (5.2%)	23 (2.8%)	1.66 [0.85;3.22]	0.1360	
	Baseline insulin use													0.9011
	No	692	16 (2.3%)	676 (97.7%)	29 (4.2%)	16 (2.3%)	692	11 (1.6%)	681 (98.4%)	33 (4.8%)	22 (3.2%)	1.46 [0.68;3.16]	0.3298	
	Yes	956	25 (2.6%)	931 (97.4%)	40 (4.2%)	29 (3.0%)	957	16 (1.7%)	941 (98.3%)	55 (5.7%)	27 (2.8%)	1.56 [0.83;2.92]	0.1650	
	Baseline Renal impairment													0.3633

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Respiratory, thoracic and mediastinal disorders	GFR < 30	46	3 (6.5%)	43 (93.5%)	4 (8.7%)	4 (8.7%)	61	1 (1.6%)	60 (98.4%)	6 (9.8%)	4 (6.6%)	4.24 [0.44;40.79]	0.2107	
	30 <= GFR	1602	38 (2.4%)	1564 (97.6%)	65 (4.1%)	41 (2.6%)	1588	26 (1.6%)	1562 (98.4%)	82 (5.2%)	45 (2.8%)	1.45 [0.88;2.38]	0.1457	
	Evidence of CV disease at screening													0.4227
	CV DISEASE	1353	37 (2.7%)	1316 (97.3%)	63 (4.7%)	42 (3.1%)	1382	26 (1.9%)	1356 (98.1%)	82 (5.9%)	46 (3.3%)	1.45 [0.88;2.40]	0.1434	
	CV RISK FACTORS ONLY	295	4 (1.4%)	291 (98.6%)	6 (2.0%)	3 (1.0%)	267	1 (0.4%)	266 (99.6%)	6 (2.2%)	3 (1.1%)	3.65 [0.41;32.61]	0.2471	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	All subjects (total)	1648	42 (2.5%)	1606 (97.5%)	82 (5.0%)	57 (3.5%)	1649	69 (4.2%)	1580 (95.8%)	95 (5.8%)	56 (3.4%)	0.60 [0.41;0.88]	0.0095	
	Gender													0.7432
	Female	635	14 (2.2%)	621 (97.8%)	31 (4.9%)	21 (3.3%)	660	22 (3.3%)	638 (96.7%)	37 (5.6%)	17 (2.6%)	0.66 [0.34;1.28]	0.2188	
	Male	1013	28 (2.8%)	985 (97.2%)	51 (5.0%)	36 (3.6%)	989	47 (4.8%)	942 (95.2%)	58 (5.9%)	39 (3.9%)	0.57 [0.36;0.91]	0.0196	
	Age													0.1049
	< 65	855	27 (3.2%)	828 (96.8%)	41 (4.8%)	28 (3.3%)	844	33 (3.9%)	811 (96.1%)	46 (5.5%)	21 (2.5%)	0.80 [0.48;1.33]	0.3904	
	65 <=	793	15 (1.9%)	778 (98.1%)	41 (5.2%)	29 (3.7%)	805	36 (4.5%)	769 (95.5%)	49 (6.1%)	35 (4.3%)	0.42 [0.23;0.76]	0.0044	
	HbA1c at baseline (disease severity)													0.6336
	< 8.0	595	15 (2.5%)	580 (97.5%)	22 (3.7%)	15 (2.5%)	628	23 (3.7%)	605 (96.3%)	27 (4.3%)	16 (2.5%)	0.68 [0.36;1.31]	0.2492	
	8.0 <=	1053	27 (2.6%)	1026 (97.4%)	60 (5.7%)	42 (4.0%)	1021	46 (4.5%)	975 (95.5%)	68 (6.7%)	40 (3.9%)	0.56 [0.35;0.90]	0.0171	
	Region A													0.3588

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs. Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
–														
Surgical and medical procedures	West Europe	228	3 (1.3%)	225 (98.7%)	12 (5.3%)	9 (3.9%)	205	8 (3.9%)	197 (96.1%)	7 (3.4%)	2 (1.0%)	0.34 [0.09;1.26]	0.1066	
	Rest of World	1420	39 (2.7%)	1381 (97.3%)	70 (4.9%)	48 (3.4%)	1444	61 (4.2%)	1383 (95.8%)	88 (6.1%)	54 (3.7%)	0.64 [0.43;0.96]	0.0306	
	Region B													0.3266
	OECD	1174	33 (2.8%)	1141 (97.2%)	64 (5.5%)	40 (3.4%)	1136	58 (5.1%)	1078 (94.9%)	77 (6.8%)	39 (3.4%)	0.54 [0.35;0.83]	0.0049	
	Non-OECD	474	9 (1.9%)	465 (98.1%)	18 (3.8%)	17 (3.6%)	513	11 (2.1%)	502 (97.9%)	18 (3.5%)	17 (3.3%)	0.88 [0.37;2.13]	0.7833	
	Treatment dose volume													0.7301
	0.5 mg/week	826	20 (2.4%)	806 (97.6%)	41 (5.0%)	27 (3.3%)	824	35 (4.2%)	789 (95.8%)	49 (5.9%)	30 (3.6%)	0.56 [0.32;0.97]	0.0398	
	1.0 mg/week	822	22 (2.7%)	800 (97.3%)	41 (5.0%)	30 (3.6%)	825	34 (4.1%)	791 (95.9%)	46 (5.6%)	26 (3.2%)	0.64 [0.38;1.10]	0.1069	
	Baseline insulin use													0.4195
	No	692	19 (2.7%)	673 (97.3%)	34 (4.9%)	20 (2.9%)	692	26 (3.8%)	666 (96.2%)	34 (4.9%)	23 (3.3%)	0.73 [0.40;1.31]	0.2889	
	Yes	956	23 (2.4%)	933 (97.6%)	48 (5.0%)	37 (3.9%)	957	43 (4.5%)	914 (95.5%)	61 (6.4%)	33 (3.4%)	0.53 [0.32;0.87]	0.0131	
	Baseline Renal impairment													0.9809

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs. Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Surgical and medical procedures	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	4 (6.6%)	57 (93.4%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	42 (2.6%)	1560 (97.4%)	77 (4.8%)	52 (3.2%)	1588	65 (4.1%)	1523 (95.9%)	89 (5.6%)	52 (3.3%)	0.63 [0.43;0.93]	0.0209	
	Evidence of CV disease at screening													0.3677
	CV DISEASE	1353	39 (2.9%)	1314 (97.1%)	75 (5.5%)	53 (3.9%)	1382	67 (4.8%)	1315 (95.2%)	88 (6.4%)	52 (3.8%)	0.59 [0.39;0.87]	0.0080	
	CV RISK FACTORS ONLY	295	3 (1.0%)	292 (99.0%)	7 (2.4%)	4 (1.4%)	267	2 (0.7%)	265 (99.3%)	7 (2.6%)	4 (1.5%)	1.36 [0.23;8.14]	0.7359	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs. Comparator HR [95%-CI]	Sema vs. Comparator p-value	p-value int.
Vascular disorders	All subjects (total)	1648	20 (1.2%)	1628 (98.8%)	86 (5.2%)	61 (3.7%)	1649	25 (1.5%)	1624 (98.5%)	94 (5.7%)	55 (3.3%)	0.80 [0.44;1.44]	0.4575	
	Gender													0.2977
	Female	635	10 (1.6%)	625 (98.4%)	32 (5.0%)	22 (3.5%)	660	9 (1.4%)	651 (98.6%)	36 (5.5%)	16 (2.4%)	1.15 [0.47;2.84]	0.7557	
	Male	1013	10 (1.0%)	1003 (99.0%)	54 (5.3%)	39 (3.8%)	989	16 (1.6%)	973 (98.4%)	58 (5.9%)	39 (3.9%)	0.61 [0.28;1.35]	0.2208	
	Age													0.7688
	< 65	855	9 (1.1%)	846 (98.9%)	44 (5.1%)	31 (3.6%)	844	10 (1.2%)	834 (98.8%)	45 (5.3%)	20 (2.4%)	0.89 [0.36;2.19]	0.7975	
	65 <=	793	11 (1.4%)	782 (98.6%)	42 (5.3%)	30 (3.8%)	805	15 (1.9%)	790 (98.1%)	49 (6.1%)	35 (4.3%)	0.74 [0.34;1.62]	0.4552	
	HbA1c at baseline (disease severity)													0.3233
	< 8.0	595	8 (1.3%)	587 (98.7%)	24 (4.0%)	17 (2.9%)	628	7 (1.1%)	621 (98.9%)	27 (4.3%)	15 (2.4%)	1.21 [0.44;3.34]	0.7123	
	8.0 <=	1053	12 (1.1%)	1041 (98.9%)	62 (5.9%)	44 (4.2%)	1021	18 (1.8%)	1003 (98.2%)	67 (6.6%)	40 (3.9%)	0.64 [0.31;1.34]	0.2388	
	Region A													0.5543
	West Europe	228	4 (1.8%)	224 (98.2%)	12 (5.3%)	9 (3.9%)	205	3 (1.5%)	202 (98.5%)	7 (3.4%)	2 (1.0%)	1.21 [0.27;5.39]	0.8050	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

System Organ Class	Subgroup	Sema N	Sema n	Sema nc(%)	Sema nc'(%)	Sema nccr(%)	Comparator N	Comparator n	Comparator nc(%)	Comparator nc'(%)	Comparator nccr(%)	Sema vs. Comparator HR [95%-CI]	Sema vs. Comparator p-value	p-value int.
Vascular disorders	Rest of World	1420	16 (1.1%)	1404 (98.9%)	74 (5.2%)	52 (3.7%)	1444	22 (1.5%)	1422 (98.5%)	87 (6.0%)	53 (3.7%)	0.74 [0.39;1.41]	0.3563	
	Region B													0.5471
	OECD	1174	17 (1.4%)	1157 (98.6%)	68 (5.8%)	44 (3.7%)	1136	19 (1.7%)	1117 (98.3%)	76 (6.7%)	38 (3.3%)	0.87 [0.45;1.67]	0.6654	
	Non-OECD	474	3 (0.6%)	471 (99.4%)	18 (3.8%)	17 (3.6%)	513	6 (1.2%)	507 (98.8%)	18 (3.5%)	17 (3.3%)	0.54 [0.14;2.16]	0.3842	
	Treatment dose volume													0.0223*
	0.5 mg/week	826	15 (1.8%)	811 (98.2%)	43 (5.2%)	29 (3.5%)	824	10 (1.2%)	814 (98.8%)	48 (5.8%)	28 (3.4%)	1.50 [0.67;3.34]	0.3198	
	1.0 mg/week	822	5 (0.6%)	817 (99.4%)	43 (5.2%)	32 (3.9%)	825	15 (1.8%)	810 (98.2%)	46 (5.6%)	27 (3.3%)	0.33 [0.12;0.92]	0.0334	
	Baseline insulin use													0.5759
	No	692	8 (1.2%)	684 (98.8%)	34 (4.9%)	20 (2.9%)	692	8 (1.2%)	684 (98.8%)	35 (5.1%)	24 (3.5%)	1.00 [0.38;2.67]	0.9978	
	Yes	956	12 (1.3%)	944 (98.7%)	52 (5.4%)	41 (4.3%)	957	17 (1.8%)	940 (98.2%)	59 (6.2%)	31 (3.2%)	0.71 [0.34;1.48]	0.3547	
	Baseline Renal impairment													0.2955
	GFR < 30	46	2 (4.3%)	44 (95.7%)	5 (10.9%)	5 (10.9%)	61	1 (1.6%)	60 (98.4%)	6 (9.8%)	4 (6.6%)	2.78 [0.25;30.70]	0.4031	
	30 <= GFR	1602	18 (1.1%)	1584 (98.9%)	81 (5.1%)	56 (3.5%)	1588	24 (1.5%)	1564 (98.5%)	88 (5.5%)	51 (3.2%)	0.74 [0.40;1.37]	0.3393	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by system organ class - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
System Organ Class	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Vascular disorders	Evidence of CV disease at screening													0.3685
	CV DISEASE	1353	19 (1.4%)	1334 (98.6%)	79 (5.8%)	57 (4.2%)	1382	22 (1.6%)	1360 (98.4%)	88 (6.4%)	52 (3.8%)	0.88 [0.48;1.63]	0.6900	
	CV RISK FACTORS ONLY	295	1 (0.3%)	294 (99.7%)	7 (2.4%)	4 (1.4%)	267	3 (1.1%)	264 (98.9%)	6 (2.2%)	3 (1.1%)	0.30 [0.03;2.89]	0.2983	

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N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

2 Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Acute myocardial infarction	All subjects (total)	1648	19 (1.2%)	1629 (98.8%)	79 (4.8%)	54 (3.3%)	1649	30 (1.8%)	1619 (98.2%)	94 (5.7%)	55 (3.3%)	0.63 [0.35;1.12]	0.1131	
	Gender													0.6385
	Female	635	6 (0.9%)	629 (99.1%)	31 (4.9%)	21 (3.3%)	660	8 (1.2%)	652 (98.8%)	37 (5.6%)	17 (2.6%)	0.77 [0.27;2.23]	0.6346	
	Male	1013	13 (1.3%)	1000 (98.7%)	48 (4.7%)	33 (3.3%)	989	22 (2.2%)	967 (97.8%)	57 (5.8%)	38 (3.8%)	0.57 [0.29;1.14]	0.1101	
	Age													0.7209
	< 65	855	8 (0.9%)	847 (99.1%)	41 (4.8%)	28 (3.3%)	844	14 (1.7%)	830 (98.3%)	44 (5.2%)	19 (2.3%)	0.56 [0.23;1.33]	0.1905	
	65 <=	793	11 (1.4%)	782 (98.6%)	38 (4.8%)	26 (3.3%)	805	16 (2.0%)	789 (98.0%)	50 (6.2%)	36 (4.5%)	0.69 [0.32;1.49]	0.3462	
	HbA1c at baseline (disease severity)													0.2228
	< 8.0	595	2 (0.3%)	593 (99.7%)	22 (3.7%)	15 (2.5%)	628	8 (1.3%)	620 (98.7%)	28 (4.5%)	17 (2.7%)	0.26 [0.06;1.23]	0.0902	
	8.0 <=	1053	17 (1.6%)	1036 (98.4%)	57 (5.4%)	39 (3.7%)	1021	22 (2.2%)	999 (97.8%)	66 (6.5%)	38 (3.7%)	0.74 [0.39;1.40]	0.3555	
	Region A													0.7072
	West Europe	228	2 (0.9%)	226 (99.1%)	10 (4.4%)	7 (3.1%)	205	2 (1.0%)	203 (99.0%)	7 (3.4%)	2 (1.0%)	0.91 [0.13;6.42]	0.9205	

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N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs. Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Acute myocardial infarction	Rest of World	1420	17 (1.2%)	1403 (98.8%)	69 (4.9%)	47 (3.3%)	1444	28 (1.9%)	1416 (98.1%)	87 (6.0%)	53 (3.7%)	0.61 [0.33;1.12]	0.1090	
	Region B													0.1201
	OECD	1174	11 (0.9%)	1163 (99.1%)	61 (5.2%)	37 (3.2%)	1136	23 (2.0%)	1113 (98.0%)	75 (6.6%)	37 (3.3%)	0.46 [0.22;0.94]	0.0333	
	Non-OECD	474	8 (1.7%)	466 (98.3%)	18 (3.8%)	17 (3.6%)	513	7 (1.4%)	506 (98.6%)	19 (3.7%)	18 (3.5%)	1.23 [0.45;3.39]	0.6909	
	Treatment dose volume													0.0581
	0.5 mg/week	826	11 (1.3%)	815 (98.7%)	39 (4.7%)	25 (3.0%)	824	9 (1.1%)	815 (98.9%)	52 (6.3%)	32 (3.9%)	1.21 [0.50;2.92]	0.6726	
	1.0 mg/week	822	8 (1.0%)	814 (99.0%)	40 (4.9%)	29 (3.5%)	825	21 (2.5%)	804 (97.5%)	42 (5.1%)	23 (2.8%)	0.38 [0.17;0.86]	0.0196	
	Baseline insulin use													0.9038
	No	692	6 (0.9%)	686 (99.1%)	32 (4.6%)	18 (2.6%)	692	10 (1.4%)	682 (98.6%)	34 (4.9%)	23 (3.3%)	0.60 [0.22;1.64]	0.3175	
	Yes	956	13 (1.4%)	943 (98.6%)	47 (4.9%)	36 (3.8%)	957	20 (2.1%)	937 (97.9%)	60 (6.3%)	32 (3.3%)	0.64 [0.32;1.29]	0.2164	
	Baseline Renal impairment													0.9817
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	4 (6.6%)	57 (93.4%)	5 (8.2%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	19 (1.2%)	1583 (98.8%)	74 (4.6%)	49 (3.1%)	1588	26 (1.6%)	1562 (98.4%)	89 (5.6%)	51 (3.2%)	0.72 [0.40;1.30]	0.2734	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs. Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Acute myocardial infarction	Evidence of CV disease at screening													0.7144
	CV DISEASE	1353	17 (1.3%)	1336 (98.7%)	72 (5.3%)	50 (3.7%)	1382	28 (2.0%)	1354 (98.0%)	87 (6.3%)	51 (3.7%)	0.61 [0.34;1.12]	0.1134	
	CV RISK FACTORS ONLY	295	2 (0.7%)	293 (99.3%)	7 (2.4%)	4 (1.4%)	267	2 (0.7%)	265 (99.3%)	7 (2.6%)	4 (1.5%)	0.90 [0.13;6.40]	0.9173	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs. Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Cardiac failure congestive	All subjects (total)	1648	17 (1.0%)	1631 (99.0%)	80 (4.9%)	55 (3.3%)	1649	16 (1.0%)	1633 (99.0%)	93 (5.6%)	54 (3.3%)	1.06 [0.54;2.10]	0.8673	
	Gender													0.1402
	Female	635	4 (0.6%)	631 (99.4%)	30 (4.7%)	20 (3.1%)	660	8 (1.2%)	652 (98.8%)	34 (5.2%)	15 (2.3%)	0.52 [0.16;1.72]	0.2811	
	Male	1013	13 (1.3%)	1000 (98.7%)	50 (4.9%)	35 (3.5%)	989	8 (0.8%)	981 (99.2%)	59 (6.0%)	39 (3.9%)	1.58 [0.66;3.82]	0.3058	
	Age													0.6397
	< 65	855	11 (1.3%)	844 (98.7%)	41 (4.8%)	28 (3.3%)	844	9 (1.1%)	835 (98.9%)	44 (5.2%)	18 (2.1%)	1.21 [0.50;2.91]	0.6749	
	65 <=	793	6 (0.8%)	787 (99.2%)	39 (4.9%)	27 (3.4%)	805	7 (0.9%)	798 (99.1%)	49 (6.1%)	36 (4.5%)	0.86 [0.29;2.57]	0.7927	
	HbA1c at baseline (disease severity)													0.0731
	< 8.0	595	8 (1.3%)	587 (98.7%)	20 (3.4%)	13 (2.2%)	628	3 (0.5%)	625 (99.5%)	30 (4.8%)	18 (2.9%)	2.82 [0.75;10.62]	0.1259	
	8.0 <=	1053	9 (0.9%)	1044 (99.1%)	60 (5.7%)	42 (4.0%)	1021	13 (1.3%)	1008 (98.7%)	63 (6.2%)	36 (3.5%)	0.67 [0.29;1.56]	0.3509	
	Region A													0.9847
	West Europe	228	0 (0.0%)	228 (100%)	12 (5.3%)	9 (3.9%)	205	2 (1.0%)	203 (99.0%)	6 (2.9%)	1 (0.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Cardiac failure congestive	Rest of World	1420	17 (1.2%)	1403 (98.8%)	68 (4.8%)	46 (3.2%)	1444	14 (1.0%)	1430 (99.0%)	87 (6.0%)	53 (3.7%)	1.23 [0.61;2.50]	0.5658	
	Region B													0.2929
	OECD	1174	14 (1.2%)	1160 (98.8%)	63 (5.4%)	39 (3.3%)	1136	15 (1.3%)	1121 (98.7%)	74 (6.5%)	36 (3.2%)	0.90 [0.43;1.87]	0.7793	
	Non-OECD	474	3 (0.6%)	471 (99.4%)	17 (3.6%)	16 (3.4%)	513	1 (0.2%)	512 (99.8%)	19 (3.7%)	18 (3.5%)	3.23 [0.34;31.02]	0.3103	
	Treatment dose volume													0.3928
	0.5 mg/week	826	10 (1.2%)	816 (98.8%)	38 (4.6%)	24 (2.9%)	824	7 (0.8%)	817 (99.2%)	48 (5.8%)	29 (3.5%)	1.42 [0.54;3.73]	0.4757	
	1.0 mg/week	822	7 (0.9%)	815 (99.1%)	42 (5.1%)	31 (3.8%)	825	9 (1.1%)	816 (98.9%)	45 (5.5%)	25 (3.0%)	0.78 [0.29;2.09]	0.6186	
	Baseline insulin use													0.8263
	No	692	7 (1.0%)	685 (99.0%)	33 (4.8%)	19 (2.7%)	692	6 (0.9%)	686 (99.1%)	36 (5.2%)	25 (3.6%)	1.17 [0.39;3.47]	0.7831	
	Yes	956	10 (1.0%)	946 (99.0%)	47 (4.9%)	36 (3.8%)	957	10 (1.0%)	947 (99.0%)	57 (6.0%)	29 (3.0%)	1.00 [0.41;2.39]	0.9939	
	Baseline Renal impairment													0.8253
	GFR < 30	46	2 (4.3%)	44 (95.7%)	5 (10.9%)	5 (10.9%)	61	3 (4.9%)	58 (95.1%)	3 (4.9%)	2 (3.3%)	0.92 [0.15;5.48]	0.9234	
	30 <= GFR	1602	15 (0.9%)	1587 (99.1%)	75 (4.7%)	50 (3.1%)	1588	13 (0.8%)	1575 (99.2%)	90 (5.7%)	52 (3.3%)	1.14 [0.54;2.39]	0.7307	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Cardiac failure congestive	Evidence of CV disease at screening													1.0000
	CV DISEASE	1353	17 (1.3%)	1336 (98.7%)	73 (5.4%)	51 (3.8%)	1382	16 (1.2%)	1366 (98.8%)	86 (6.2%)	50 (3.6%)	1.08 [0.55;2.14]	0.8194	
	CV RISK FACTORS ONLY	295	0 (0.0%)	295 (100%)	7 (2.4%)	4 (1.4%)	267	0 (0.0%)	267 (100%)	7 (2.6%)	4 (1.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Coronary artery bypass	All subjects (total)	1648	9 (0.5%)	1639 (99.5%)	87 (5.3%)	62 (3.8%)	1649	19 (1.2%)	1630 (98.8%)	98 (5.9%)	58 (3.5%)	0.47 [0.21;1.04]	0.0626	
	Gender													0.0413*
	Female	635	6 (0.9%)	629 (99.1%)	33 (5.2%)	23 (3.6%)	660	5 (0.8%)	655 (99.2%)	37 (5.6%)	17 (2.6%)	1.24 [0.38;4.08]	0.7186	
	Male	1013	3 (0.3%)	1010 (99.7%)	54 (5.3%)	39 (3.8%)	989	14 (1.4%)	975 (98.6%)	61 (6.2%)	41 (4.1%)	0.21 [0.06;0.72]	0.0134	
	Age													0.0609
	< 65	855	8 (0.9%)	847 (99.1%)	45 (5.3%)	32 (3.7%)	844	9 (1.1%)	835 (98.9%)	48 (5.7%)	22 (2.6%)	0.88 [0.34;2.27]	0.7841	
	65 <=	793	1 (0.1%)	792 (99.9%)	42 (5.3%)	30 (3.8%)	805	10 (1.2%)	795 (98.8%)	50 (6.2%)	36 (4.5%)	0.10 [0.01;0.78]	0.0283	
	HbA1c at baseline (disease severity)													0.8888
	< 8.0	595	2 (0.3%)	593 (99.7%)	24 (4.0%)	17 (2.9%)	628	5 (0.8%)	623 (99.2%)	29 (4.6%)	17 (2.7%)	0.42 [0.08;2.17]	0.3002	
	8.0 <=	1053	7 (0.7%)	1046 (99.3%)	63 (6.0%)	45 (4.3%)	1021	14 (1.4%)	1007 (98.6%)	69 (6.8%)	41 (4.0%)	0.48 [0.19;1.19]	0.1133	
	Region A													0.9871
	West Europe	228	1 (0.4%)	227 (99.6%)	12 (5.3%)	9 (3.9%)	205	0 (0.0%)	205 (100%)	7 (3.4%)	2 (1.0%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Coronary artery bypass	Rest of World	1420	8 (0.6%)	1412 (99.4%)	75 (5.3%)	53 (3.7%)	1444	19 (1.3%)	1425 (98.7%)	91 (6.3%)	56 (3.9%)	0.42 [0.19;0.97]	0.0419	
	Region B													0.6016
	OECD	1174	7 (0.6%)	1167 (99.4%)	69 (5.9%)	45 (3.8%)	1136	16 (1.4%)	1120 (98.6%)	78 (6.9%)	39 (3.4%)	0.42 [0.17;1.02]	0.0558	
	Non-OECD	474	2 (0.4%)	472 (99.6%)	18 (3.8%)	17 (3.6%)	513	3 (0.6%)	510 (99.4%)	20 (3.9%)	19 (3.7%)	0.72 [0.12;4.28]	0.7140	
	Treatment dose volume													0.3443
	0.5 mg/week	826	4 (0.5%)	822 (99.5%)	44 (5.3%)	30 (3.6%)	824	12 (1.5%)	812 (98.5%)	51 (6.2%)	31 (3.8%)	0.33 [0.11;1.02]	0.0539	
	1.0 mg/week	822	5 (0.6%)	817 (99.4%)	43 (5.2%)	32 (3.9%)	825	7 (0.8%)	818 (99.2%)	47 (5.7%)	27 (3.3%)	0.72 [0.23;2.25]	0.5670	
	Baseline insulin use													0.5055
	No	692	4 (0.6%)	688 (99.4%)	35 (5.1%)	21 (3.0%)	692	6 (0.9%)	686 (99.1%)	36 (5.2%)	25 (3.6%)	0.66 [0.19;2.35]	0.5260	
	Yes	956	5 (0.5%)	951 (99.5%)	52 (5.4%)	41 (4.3%)	957	13 (1.4%)	944 (98.6%)	62 (6.5%)	33 (3.4%)	0.38 [0.14;1.07]	0.0670	
	Baseline Renal impairment													0.9860
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	3 (4.9%)	58 (95.1%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	9 (0.6%)	1593 (99.4%)	82 (5.1%)	57 (3.6%)	1588	16 (1.0%)	1572 (99.0%)	92 (5.8%)	54 (3.4%)	0.55 [0.24;1.25]	0.1558	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs. Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Coronary artery bypass	Evidence of CV disease at screening													0.9863
	CV DISEASE	1353	9 (0.7%)	1344 (99.3%)	80 (5.9%)	58 (4.3%)	1382	18 (1.3%)	1364 (98.7%)	91 (6.6%)	54 (3.9%)	0.51 [0.23;1.13]	0.0963	
	CV RISK FACTORS ONLY	295	0 (0.0%)	295 (100%)	7 (2.4%)	4 (1.4%)	267	1 (0.4%)	266 (99.6%)	7 (2.6%)	4 (1.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Nausea	All subjects (total)	1648	25 (1.5%)	1623 (98.5%)	83 (5.0%)	60 (3.6%)	1649	1 (0.1%)	1648 (99.9%)	100 (6.1%)	60 (3.6%)	25.22 [3.42;186.10]	0.0016	
	Gender													0.9871
	Female	635	12 (1.9%)	623 (98.1%)	30 (4.7%)	21 (3.3%)	660	1 (0.2%)	659 (99.8%)	37 (5.6%)	17 (2.6%)	12.56 [1.63;96.57]	0.0151	
	Male	1013	13 (1.3%)	1000 (98.7%)	53 (5.2%)	39 (3.8%)	989	0 (0.0%)	989 (100%)	63 (6.4%)	43 (4.3%)	Not est	Not est	
	Age													0.9891
	< 65	855	9 (1.1%)	846 (98.9%)	42 (4.9%)	31 (3.6%)	844	0 (0.0%)	844 (100%)	48 (5.7%)	22 (2.6%)	Not est	Not est	
	65 <=	793	16 (2.0%)	777 (98.0%)	41 (5.2%)	29 (3.7%)	805	1 (0.1%)	804 (99.9%)	52 (6.5%)	38 (4.7%)	16.37 [2.17;123.42]	0.0067	
	HbA1c at baseline (disease severity)													0.9860
	< 8.0	595	9 (1.5%)	586 (98.5%)	23 (3.9%)	17 (2.9%)	628	1 (0.2%)	627 (99.8%)	30 (4.8%)	18 (2.9%)	9.56 [1.21;75.43]	0.0322	
	8.0 <=	1053	16 (1.5%)	1037 (98.5%)	60 (5.7%)	43 (4.1%)	1021	0 (0.0%)	1021 (100%)	70 (6.9%)	42 (4.1%)	Not est	Not est	
	Region A													0.9863

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Nausea	West Europe	228	8 (3.5%)	220 (96.5%)	12 (5.3%)	9 (3.9%)	205	1 (0.5%)	204 (99.5%)	7 (3.4%)	2 (1.0%)	7.29 [0.91;58.31]	0.0610	
	Rest of World	1420	17 (1.2%)	1403 (98.8%)	71 (5.0%)	51 (3.6%)	1444	0 (0.0%)	1444 (100%)	93 (6.4%)	58 (4.0%)	Not est	Not est	
	Region B													0.9896
	OECD	1174	24 (2.0%)	1150 (98.0%)	65 (5.5%)	43 (3.7%)	1136	1 (0.1%)	1135 (99.9%)	80 (7.0%)	41 (3.6%)	23.49 [3.18;173.67]	0.0020	
	Non-OECD	474	1 (0.2%)	473 (99.8%)	18 (3.8%)	17 (3.6%)	513	0 (0.0%)	513 (100%)	20 (3.9%)	19 (3.7%)	Not est	Not est	
	Treatment dose volume													0.9877
	0.5 mg/week	826	10 (1.2%)	816 (98.8%)	43 (5.2%)	30 (3.6%)	824	1 (0.1%)	823 (99.9%)	52 (6.3%)	32 (3.9%)	10.06 [1.29;78.57]	0.0277	
	1.0 mg/week	822	15 (1.8%)	807 (98.2%)	40 (4.9%)	30 (3.6%)	825	0 (0.0%)	825 (100%)	48 (5.8%)	28 (3.4%)	Not est	Not est	
	Baseline insulin use													0.9867
	No	692	11 (1.6%)	681 (98.4%)	32 (4.6%)	20 (2.9%)	692	1 (0.1%)	691 (99.9%)	37 (5.3%)	26 (3.8%)	11.11 [1.43;86.05]	0.0212	
	Yes	956	14 (1.5%)	942 (98.5%)	51 (5.3%)	40 (4.2%)	957	0 (0.0%)	957 (100%)	63 (6.6%)	34 (3.6%)	Not est	Not est	
	Baseline Renal impairment													0.9986
	GFR < 30	46	0 (0.0%)	46 (100%)	5 (10.9%)	5 (10.9%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Nausea	30 <= GFR	1602	25 (1.6%)	1577 (98.4%)	78 (4.9%)	55 (3.4%)	1588	1 (0.1%)	1587 (99.9%)	94 (5.9%)	56 (3.5%)	24.99 [3.39;184.44]	0.0016	
	Evidence of CV disease at screening													0.9896
	CV DISEASE	1353	20 (1.5%)	1333 (98.5%)	77 (5.7%)	56 (4.1%)	1382	1 (0.1%)	1381 (99.9%)	93 (6.7%)	56 (4.1%)	20.59 [2.76;153.39]	0.0032	
	CV RISK FACTORS ONLY	295	5 (1.7%)	290 (98.3%)	6 (2.0%)	4 (1.4%)	267	0 (0.0%)	267 (100%)	7 (2.6%)	4 (1.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Pneumonia	All subjects (total)	1648	14 (0.8%)	1634 (99.2%)	81 (4.9%)	56 (3.4%)	1649	19 (1.2%)	1630 (98.8%)	95 (5.8%)	57 (3.5%)	0.73 [0.37;1.46]	0.3793	
	Gender													0.5090
	Female	635	5 (0.8%)	630 (99.2%)	32 (5.0%)	22 (3.5%)	660	5 (0.8%)	655 (99.2%)	35 (5.3%)	16 (2.4%)	1.03 [0.30;3.57]	0.9575	
	Male	1013	9 (0.9%)	1004 (99.1%)	49 (4.8%)	34 (3.4%)	989	14 (1.4%)	975 (98.6%)	60 (6.1%)	41 (4.1%)	0.62 [0.27;1.44]	0.2708	
	Age													0.7256
	< 65	855	3 (0.4%)	852 (99.6%)	44 (5.1%)	31 (3.6%)	844	5 (0.6%)	839 (99.4%)	47 (5.6%)	22 (2.6%)	0.59 [0.14;2.47]	0.4712	
	65 <=	793	11 (1.4%)	782 (98.6%)	37 (4.7%)	25 (3.2%)	805	14 (1.7%)	791 (98.3%)	48 (6.0%)	35 (4.3%)	0.79 [0.36;1.74]	0.5623	
	HbA1c at baseline (disease severity)													0.9625
	< 8.0	595	5 (0.8%)	590 (99.2%)	23 (3.9%)	16 (2.7%)	628	7 (1.1%)	621 (98.9%)	30 (4.8%)	18 (2.9%)	0.75 [0.24;2.36]	0.6222	
	8.0 <=	1053	9 (0.9%)	1044 (99.1%)	58 (5.5%)	40 (3.8%)	1021	12 (1.2%)	1009 (98.8%)	65 (6.4%)	39 (3.8%)	0.72 [0.31;1.72]	0.4639	
	Region A													0.2429
	West Europe	228	4 (1.8%)	224 (98.2%)	10 (4.4%)	7 (3.1%)	205	2 (1.0%)	203 (99.0%)	7 (3.4%)	2 (1.0%)	1.81 [0.33;9.88]	0.4936	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
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MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial – full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Pneumonia	Rest of World	1420	10 (0.7%)	1410 (99.3%)	71 (5.0%)	49 (3.5%)	1444	17 (1.2%)	1427 (98.8%)	88 (6.1%)	55 (3.8%)	0.59 [0.27;1.30]	0.1917	
	Region B													0.8463
	OECD	1174	11 (0.9%)	1163 (99.1%)	63 (5.4%)	39 (3.3%)	1136	14 (1.2%)	1122 (98.8%)	76 (6.7%)	39 (3.4%)	0.76 [0.34;1.67]	0.4901	
	Non-OECD	474	3 (0.6%)	471 (99.4%)	18 (3.8%)	17 (3.6%)	513	5 (1.0%)	508 (99.0%)	19 (3.7%)	18 (3.5%)	0.64 [0.15;2.70]	0.5471	
	Treatment dose volume													0.2427
	0.5 mg/week	826	6 (0.7%)	820 (99.3%)	42 (5.1%)	28 (3.4%)	824	12 (1.5%)	812 (98.5%)	49 (5.9%)	30 (3.6%)	0.49 [0.19;1.32]	0.1588	
	1.0 mg/week	822	8 (1.0%)	814 (99.0%)	39 (4.7%)	28 (3.4%)	825	7 (0.8%)	818 (99.2%)	46 (5.6%)	27 (3.3%)	1.15 [0.42;3.16]	0.7923	
	Baseline insulin use													0.8503
	No	692	4 (0.6%)	688 (99.4%)	35 (5.1%)	21 (3.0%)	692	6 (0.9%)	686 (99.1%)	37 (5.3%)	26 (3.8%)	0.66 [0.19;2.35]	0.5242	
	Yes	956	10 (1.0%)	946 (99.0%)	46 (4.8%)	35 (3.7%)	957	13 (1.4%)	944 (98.6%)	58 (6.1%)	31 (3.2%)	0.77 [0.34;1.75]	0.5276	
	Baseline Renal impairment													0.9870
	GFR < 30	46	1 (2.2%)	45 (97.8%)	4 (8.7%)	4 (8.7%)	61	0 (0.0%)	61 (100%)	6 (9.8%)	4 (6.6%)	Not est	Not est	
	30 <= GFR	1602	13 (0.8%)	1589 (99.2%)	77 (4.8%)	52 (3.2%)	1588	19 (1.2%)	1569 (98.8%)	89 (5.6%)	53 (3.3%)	0.67 [0.33;1.37]	0.2738	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Severe adverse events by preferred term - time-to-event analysis - Sustain 6 - in-trial - full analysis set

		Sema					Comparator					Sema vs.Comparator		
Preferred Term	Subgroup	N	n	nc(%)	nc'(%)	nccr(%)	N	n	nc(%)	nc'(%)	nccr(%)	HR [95%-CI]	p-value	p-value int.
Pneumonia	Evidence of CV disease at screening													0.9845
	CV DISEASE	1353	14 (1.0%)	1339 (99.0%)	74 (5.5%)	52 (3.8%)	1382	18 (1.3%)	1364 (98.7%)	89 (6.4%)	53 (3.8%)	0.79 [0.39;1.59]	0.5098	
	CV RISK FACTORS ONLY	295	0 (0.0%)	295 (100%)	7 (2.4%)	4 (1.4%)	267	1 (0.4%)	266 (99.6%)	6 (2.2%)	4 (1.5%)	Not est	Not est	

N: number of subjects in the analysis set, n: number of subjects with at least one event, nc: number of censored subjects, nc': number of subjects censored due to non-administrative reasons, nccr: number of patients censored due to competing risks, %: proportion of subjects, HR:
Hazard ratio, CI: Confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 1 (Wald test), p-value interaction: unadjusted two-sided p-value for test of no treatment by subgroup interaction (Wald test), *: p-value interaction < 0.05, CV: cardiovascular, Not est: Not estimated
Time-to-event endpoints (time from randomisation to first event) were analysed using a Cox proportional hazards model with treatment (subgroup, and interaction between treatment and subgroup, if applicable) as fixed factor.
MedDRA version 20.1

Allgemein – Preferred Terms Liste zur Herausrechnung von diabetes-assoziierten Folgekomplikationen aus der Gesamtrate schwerwiegender unerwünschter Ereignisse (SUE) für PIONEER 6 und der Metaanalyse von PIONEER 6 + SUSTAIN 6

No.	SOC cardiac disorders	SOC eye disorders	SOC nervous system disorders	SOC renal and urinary disorders	SOC vascular disorders
1	Acute coronary syndrome	Amaurosis fugax	Brain stem infarction	Azotaemia	Aortic stenosis
2	Acute left ventricular failure	Blindness	Carotid artery occlusion	Chronic kidney disease	Arterial insufficiency
3	Acute myocardial infarction	Cystoid macular oedema	Carotid artery stenosis	Diabetic end stage renal disease	Arteriosclerosis
4	Angina pectoris	Diabetic retinopathy	Cerebellar infarction	Diabetic nephropathy	Extremity necrosis
5	Angina unstable	Macular fibrosis	Cerebral haemorrhage	Renal artery arteriosclerosis	Femoral artery occlusion (LLT)1
6	Arteriosclerosis coronary artery	Macular oedema	Cerebral infarction	Renal artery stenosis	Leriche syndrome
7	Cardiac arrest	Retinal artery occlusion	Cerebral ischaemia	Renal failure	Peripheral arterial occlusive disease
8	Cardiac failure	Retinal degeneration	Cerebellar haemorrhage	Renal impairment	Peripheral artery occlusion
9	Cardiac failure acute	Retinal detachment	Cerebrovascular accident		Peripheral artery stenosis
10	Cardiac failure chronic	Retinal tear	Cerebrovascular disorder		Peripheral ischaemia

[1] Femoral artery occlusion wurde als Lowest Level Term (LLT) berücksichtigt, da femoral artery occlusion in SUSTAIN 6 noch als PT erhoben wurde (MedDRA version 18.0). In PIONEER 6 wurde hingegen bereit MedDRA version 20.1 angewendet. In dieser Version ist femoral artery occlusion als LLT gelistet. Um für die Auswertung von PIONEER 6 und die Metaanalyse ein einheitliches Vorgehen zu gewährleisten wurde jeweils MedDRA version 20.1 herangezogen.

11	Cardiac failure congestive	Retinopathy haemorrhagic	Diabetic neuropathy		Peripheral vascular disorder
12	Cardiogenic shock	Retinopathy proliferative	Embolic stroke		
13	Cardiomyopathy	Vitreous haemorrhage	Haemorrhagic stroke		
14	Cardiopulmonary failure		Hemiparesis		
15	Cardiorenal syndrome		Hypoglycaemic seizure		
16	Cardio-respiratory arrest		Intraventricular haemorrhage		
17	Cardiovascular insufficiency		Ischaemic cerebral infarction		
18	Congestive cardiomyopathy		Ischaemic stroke		
19	Coronary artery disease		Lacunar infarction		
20	Coronary artery occlusion		Lacunar stroke		
21	Coronary artery stenosis		Thalamic infarction		
22	Coronary artery thrombosis		Transient ischaemic attack		
23	Coronary artery insufficiency				
24	Hypertensive heart disease				
25	Hypertensive cardiomyopathy				
26	Ischaemic cardiomyopathy				
27	Left ventricular failure				

28	Myocardial infarction				
29	Myocardial ischaemia				
30	Silent myocardial infarction				

No.	SOC injury, poisoning and procedural complications	SOC general disorders and administration site conditions	SOC infections and infestations	SOC skin and subcutaneous tissue disorders
1	Arterial bypass occlusion	Vascular stent restenosis	Diabetic foot infection	Diabetic foot
2	Coronary artery restenosis		Diabetic gangrene	